Aviva Romm

Botanical Medicine *for* Women's Health

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FOREWORD

Botanical Medicine for Women's Health is being published at an interesting time and speaks simultaneously to a number of converging constituencies. It is a time of growing stress on both the medical system and the patient. Medical care is in crisis with large numbers of under-insured or uninsured patients needing care. Costs are rising from the practice of increasingly technical medicine while patients complain of the decreasing time and attention they are receiving from their medical providers. Further, the burden of chronic disease is growing in an aging population. In one response to these stressors, patient interest is forcing inclusion of alternative medicines and philosophies into mainstream practice. However, in the case of herbal medicine, incorporation into conventional medicine would represent the return to (pardon the pun) the deepest roots of our own medical tradition.

The lineage of herbal medicine is long, distinguished, and of great importance to Western medical tradition. Herbal medicine has been a significant component of a wide array of healing systems beginning early with those of Egypt, Mesopotamia, Greece, and Islam while continuing through the development of medical practice in Medieval and modern Europe. Traditional medical practices from Asia and India as well as Aboriginal traditions on every continent have also used extensive herbal pharmacopeias. Many of our modern pharmaceutical drugs owe their origins to herbal medicine with more than one hundred of the most commonly used drugs derived directly or indirectly from plants.

It is particularly appropriate that this book focuses on the herbal treatment of women's conditions. Historically, women, when given the opportunity to train in medical professions or to operate as lay practitioners, often focused their care on women and their children—either by choice or necessity. Often, the transmission of this tradition was suppressed or marginalized and women had to use the products of the natural world around them rather than the often more toxic products favored by their conventional counterparts. Thus, women's medicine, overseen by female goddesses like Isis or practiced by female practitioners such as Hildegard of Bingen, was largely based on herbal therapies. In fact, rarely were the contributions of these female herbalists recognized by conventional medical history. So, for example, the ''discovery'' of foxglove as a treatment for cardiac conditions is attributed to Sir William Withering and his source, the old lady of Shropshire, is largely forgotten. Thus, I am particularly satisfied that this important herbal textbook is giving serious and scholarly consideration to this traditional practice.

But herbal medicine is not a dead or esoteric art. The World Health Organization estimates that 80% of people in developing countries depend on herbal medicine and traditional practitioners for their primary care. As people migrate from their countries of origin to more industrialized areas, they often bring their traditional practices with them. In modern industrial countries, at least 20% to 30% of people regularly use herbal medicines. For certain conditions, such as HIV, cancer, or other chronic diseases, the numbers have reportedly been much higher. Under-insured patients often substitute herbs or dietary supplements for drugs because of poor access to care or cost of therapy.

These statistics and examples reflect the trend of incorporating traditional healing systems into modern life, moving from self-treatment of self-limiting illness to the care of chronic and more serious medical conditions. Despite the fact that these users are also active consumers of conventional medical services, they often do not disclose their use of herbal medications to their medical practitioners. This withholding arises from a number of causes. Often cited by patients is the belief that most physicians will react negatively to the use of natural products, or worse, that physicians are not knowledgeable about the natural products patients are interested in.

Ironically, despite the fact that herbalists have been advising patients on the use of phytomedicines for millennia and patients are increasing their use of herbal products, herbal practitioners in North America have not generally been incorporated into conventional medical practice. These practitioners and their practices have been largely invisible to the conventional system for a variety of reasons. Patients may self-prescribe from an exploding array of natural health products without the benefit of consultation with an herbalist. In traditional medical systems, other components may be more recognized than the herbal therapy. For example, for Traditional Chinese Medicine as practiced in the West, acupuncture is better known and more broadly used than Chinese herbal medicine. Most importantly, in the United States, the practice of herbal medicine is variable, eclectic, and without standardization or licensure. Whether or not the development of standard herbal practice would represent a desirable outcome, it is a fact that much of the public and most conventional medical practitioners are largely uninformed about what constitutes appropriate training for herbalists and what their appropriate scope of practice should be.

Thus, the clash of cultures and lack of understanding inherent in the crisis of our current medical system offer our greatest opportunity. We will need our traditional knowledge to care for our aging population. Our traditional practitioners will have the opportunity to become more closely integrated into the conventional medical model, and thus reach a broader array of patients. Better communication between paradigms and practitioners is crucial if we are going to meet the needs of our patients and address the growing problems in our medical system. This book, and hopefully others like it,

will aid this process by contributing to our mutual understanding. The careful explication of the practice of traditional herbal medicine will be valuable to conventional practitioners attempting to fill their knowledge gaps and advise their patients appropriately. On the other hand, the inclusion of information from the Western conventional paradigm, especially involving physiology or conventional treatment, will help orient the traditional practitioner to more conventional medical concerns.

It is my hope that in the crisis of modern medicine, we all take the opportunity this book offers to learn from other systems and perhaps reclaim some of the values that have always been at the heart of the practice of the art of medicine.

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June 2008

Foreword

There is a significant gap in modern health care and *Botanical Medicine for Women's Health* goes a long way to fill it. There are many illnesses that women may suffer from, which are inadequately addressed by modern medical advances. These deficiencies are both specific to the types of health problems involved and also to a wider shift in the direction of health care since the Industrial Revolution.

For most of history, medicine was overwhelmingly women's work. People in traditional hunter-gatherer and pastoral societies, the background to the vast majority of human experience, consistently associated child-rearing, food preparation, and health care as a continuum of services most ably performed by women. Women shared their experiences of menstruation, pregnancy, and child care almost exclusively; men very rarely understood how to handle cases when problems arose. Women understood the plants in their environment and appreciated their role as foods and remedies. Whereas men were visible as shamans or priests, anecdotal accounts often suggested that the ''wise woman'' often performed a popular service.

Medicine in those far off times may now seem primitive and ineffective. There is much in *Botanical Medicine for Women's Health* that should cause us to rethink this impression. On the other hand, there are many women who could say that modern medicine is primitive and ineffective. If you have painful or erratic periods, disabling premenstrual symptoms, endometriosis, chronic pelvic inflammation, or cystic ovaries and are only offered the dictative regime of hormones, the sad prescription of antidepressants or tranquillizers, or the erratic and intrusive prospects of surgery, you may think those options need modernizing. If in pregnancy you are one of many for whom a rich life change is encroached upon by the demands of hospitalized obstetrics rather than nurtured in a relationship with an autonomous midwife, you may really feel the loss of something fundamental in health care. If in the upheavals immediately after birth you find yourself alone to cope, you could be forgiven for wondering how sophisticated modern medicine really is. The days when male doctors routinely diagnosed hysteria for any woman's problem they could not understand may now happily be past, but there are still occasional gynecologists who recommend precautionary hysterectomies on the basis that ''you will not miss it.'' Fortunately, there is a refreshing feminizing of medicine today. There are many more women's wellness centers. In some countries, most medical students are now women. However, the techniques available for women doctors to use in women's health care are still blunt.

Perhaps there is still value in reviewing approaches to women's ill health that were developed by women and among women. We can be sure that, over the centuries, many of these approaches emerged because they appeared to work and were reinforced by other women's experiences. Lack of fertility, for example was such a dire prospect for women that it is not surprising that genuinely interesting remedies emerged: To discover that it is possible with some plants to facilitate long-term regulation of the menstrual cycle is truly exciting. The relief of pain and suffering in pelvic conditions that stubbornly resist other medical treatments is immensely rewarding. To find alternatives for emotional and mental anguish can bring transformation. Women's empirical discoveries included plants that we now know contain potentially modulatory steroidal molecules and other prehormonal activity. Some appear to reduce pain and spasm in the womb and other organs. Most old remedies worked softly, apparently in rhythm with the woman's body, mind, and spirit rather than imposing change. Early women's medicine emphasized remedies that were interactive with functions that we now understand are wonderfully complex and interactive. Most importantly, the techniques were embedded in a world where women themselves created the language of care.

In a modern Western context, it is only recently that those who understand the old remedies have found the voice they deserve. This book has effectively marshalled some of the leading practitioners and teachers on the use of plants in women's medicine. With over 30 years of my experience of these matters, the authors in this book have emerged as strong and exciting contributors to a new vision of women's health. Many of these authors, female and male, have worked for years with women in real need. They have learned the hard way what does and does not work. Yes, there are midwife herbalists here, too. That they can bring their years of experience into engagement with modern standards is wonderful. That women at last have an opportunity to rediscover their legacies and well-trodden paths to improved wellness is a cause for celebration.

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PREFACE

Judgments about which phenomena are worth studying, which kinds of data are significant, as well as which descriptions (or theories) of those phenomena are most adequate, satisfying, useful, even reliable, depend critically upon the social, linguistic, and scientific practices of those making the judgment in question.

-Evelyn Fox Keller, PhD

Intuition without knowledge is only so valuable. Knowledge without intuition is just a bunch of facts. Knowledge with intuition starts us on our way to wisdom.

-Tieraona Low Dog, MD, RH (AHG)

Women today are drawn to using herbal medicines for a variety of reasons, among these are the desire for more natural therapies and greater personal empowerment than afforded by conventional medical care; the desire to avoid invasive medical therapies; the perception that herbs are effective and have fewer negative side-effects than many conventional drugs; and for a sense of connection to the natural world and an eco-friendly health choice. Statistics demonstrate that women are the greatest consumers of complementary and alternative (CAM) therapies, including herbal medicines, and that they are willing to pay out of pocket for both practitioners and products that they believe will provide what they are seeking. Herb sales in the US alone are estimated at approximately $4 billion per year.

THE NEED FOR THIS BOOK

It is my belief that one goal of health care providers should be to serve as a resource for their patients, easing the onus that so typically falls to the patient to not only be sick, but to become an expert in their own care regarding any number of conditions and treatments available to them on the vast menu of medical or alternative choices. While medical curricula and practices are rapidly expanding to accommodate consumer demand for CAM therapies, it is challenging for the primary care provider to sort through the surfeit of books, magazines, and medical journal articles available on botanical medicines to determine what is safe and efficacious for patients. Yet the responsibility of learning about these therapies is accepted by the committed practitioner, in order to help patients (many of whom are already using botanical products) make the best choices for effectiveness, safety, product quality, and affordability. A practitioner who is a constant, active learner and critical thinker is able to relieve a tremendous pressure from their patients, allowing them to instead focus on the work of being ill and healing, to whatever capacity possible.

Botanical Medicine for Women's Health strives to offer a realistic appraisal of the therapeutic possibilities of botanical medicines for women in a comprehensive and easily accessible format. Herbal medicines are not universally effective nor are they always the appropriate primary treatment, but they can be an important part of an integrative approach to patient care. Every patient has the right to accurate information about his or her options. There is a tremendous amount that remains unknown about botanical medicines, as well as women's reproductive conditions. We know very little, for example, about the interactions between plants and the endocrine system. We also know very little about common gynecologic conditions, for example, what causes endometriosis, chronic pelvic pain, or uterine fibroids. We do know that many conventional treatments currently being utilized are not supported by evidence of long term efficacy or safety, for example, the treatment of chronic pelvic pain with hysterectomy, and that the search for safe and effective alternatives to many gynecologic treatments is necessary and justified. This book compiles information on traditional and contemporary herbal practices associated with many of the most common gynecologic and obstetric problems women face, perhaps as treatments, perhaps as possibilities for further research.

As an author, I faced innumerable challenges in presenting topics that often have very little scientific substantiation, yet are widely used by herbalists, and conversely, making meaning of data for which there is *in vitro* evidence or evidence in animal models, but which lacks human clinical evidence or the precedence of historical use. It is my hope that readers provide comments on the usability, value, and omissions that need to be addressed to make subsequent editions increasingly helpful and clinically relevant. The importance of elucidating, to the greatest possible extent, herbal practices that are currently being prescribed by practitioners or taken by patients via self-medication, is significant for practitioners and patients, as is the value of admitting there are unanswered questions. It is only by asking the right questions that we can begin to expect meaningful answers. This book seeks to suspend judgment and posits that separate biomedical care and botanical care find the common denominator that patients seek from their practitioner, which is simply–care. It seeks to conceptually combine the rigor of biomedical thinking, reductionism, and skepticism with the holistic, nature-trusting, biophilic orientation of the modern herbalist.

THE STRUCTURE OF *BOTANICAL MEDICINE FOR WOMEN'S HEALTH*

Botanical Medicine for Women's Health begins with Part 1: Foundations of Botanical Medicine, which presents introductory chapters on the role of CAM and botanical medicines in clinical practice, the history of botanical medicines for women, and the principles of botanical medicine practice including botanical medicine safety, formulation and dosing strategies, identifying quality

products, and forms of preparation and administration. Understanding the principles and philosophies underlying herbal medicine practice and product quality optimizes clinical success and safety with herbs therefore it is suggested that readers review Part 1 before using this book for quick reference text.

Following Part 1 the book is divided into Parts 2-4, reflecting the chronology of women's reproductive life cycles: general gynecology and menstruation, childbearing, and perimenopause/menopause. Each part addresses the conditions common to that stage of the life cycle, presenting both relevant medical background and botanical treatments. Chapters follow a standard format, facilitating the book's use as a clinical reference or classroom text. While it was tempting to rank each herb for its ''level of evidence,'' or to present them in some hierarchical scheme, the current ranking schemes, while quite useful for those seeking to practice within a narrow range of what is considered ''acceptable evidence,'' lend a bias against the use of herbs at all for some conditions, and limit the use of herbs severely for other conditions, simply due to lack of certain forms of evidence, when in many cases, the research has simply not been done. Therefore, it was ultimately decided to present the herbs alphabetically, and allow the reader to make her/his determination of what to use based on their own values in ranking of evidence. One will therefore hopefully be amused when reading the chapter on Pain in Labor to find *Cannabis* spp. as the herb listed first. This is not prescriptive, just an alphabetical coincidence and a bit of cosmic humor! Readers will be informed when use of an herb is predicated on traditional or historical use alone and when there is scientific evidence.

Part 5 is a collection of plant profiles on several of the most commonly used botanicals for women, and especially those for which there may be some controversy over use. The appendix, a quick reference dosing and safety chart, concludes the book.

CONTRIBUTING AUTHORS

This book was, in part, made possible by the generous help of the authors whose names appear with the chapters to which they contributed. Each is a well-respected member of the herbal, naturopathic, midwifery, and/or integrative medicine community. The authors whose chapters comprise this book freely donated their time to research and write as part of their overarching commitment that there be a greater understanding not only of botanical medicines, but of integrative healing for women. The authors of this textbook faced unique challenges in finding buried evidence to support what they know so well from the clinic. Creating language to describe an emerging paradigm is no small feat, nor is taking one paradigm and translating into a language which others will understand and to which they can relate.

While chapters were substantially rewritten by the primary author of this text for the purpose of consistency, style, format, and at times to include a more comprehensive or current literature search than individual authors were able to accomplish, every attempt was made to reflect the original intention and tone of the contributors. It is with tremendous gratitude to each of the contributing authors that this book was written.

IN CONCLUSION

It is my hope this text provides readers with the confidence to begin safely integrating botanical therapies for women's health into their practices, playing a small part in turning an already changing tide of medicine in a direction that includes a patient-centered, integrative approach and that respects the healing power of nature and most importantly, patient choice. The possibility that this book may bring intelligent botanical medicine guidelines into the consulting room, and a small alleviation of suffering for those women who use botanical therapies as part of their medicine, is my fondest expectation.

Aviva Romm, CPM, AHG

PREFACE REFERENCES

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Aviva Romm is a Certified Professional Midwife and clinical herbalist in practice for twenty years. She is the President of the American Herbalists Guild, an adjunct faculty for the Massachusetts College of Pharmacy, and guest faculty for the Arizona Center for Integrative Medicine Fellowship, and is on numerous scientific advisory boards, including the American Herbal Pharmacopoeia and Botanical Safety Handbook Committee. Aviva is receiving her MD from the Yale School of Medicine in May 2009 and will be specializing in Internal Medicine and Women's Health.

PART I

Foundations of Botanical Medicine

1 CHAPTER

Botanical Medicines, CAM, and Integrative Medicine: Definitions and Use Prevalence

Aviva Romm

The U.S. medical care system is self-validating. Biomedicine is rarely viewed as a historical and cultural byproduct, but rather is considered to be entirely factual, scientific, and universal. Furthermore, many powerful groups have an interest in the maintenance of existing approaches. Nonetheless, several problems have been identified with this medical care delivery system, including issues of access, quality of care, quality of life, technology use, and costs. The conservative, self-validating nature of biomedicine places severe limits on our ability to rethink our approach to medicine and deepen innovative and viable solutions to these problems. Alternative health care systems exist as a rich readily accessible resource for testable ideas about the practice and organization of medical and health care. By virtue of their popular nature, they seem generally to be well-received, low technology, and low-cost approaches to health problems. The potential contribution of these systems to solutions for the medical care problems we face would seem to be great.

—Carol Sakala[1]

WHAT IS COMPLEMENTARY AND ALTERNATIVE MEDICINE?

The National Institutes of Health (NIH) National Center for Complementary and Alternative Medicine (NCCAM) defines complementary and alternative medicine (CAM) as ''a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine.''[2] Complementary medicine is considered to be those therapies used in conjunction with conventional medicines, whereas alternative medicine is considered to be those therapies used in lieu of conventional medicine, for example, the use of a specific herb to reduce perimenopausal symptoms in lieu of hormone replacement therapy (HRT).[2]

CAM therapy includes traditional Chinese medicine (TCM), Ayurvedic medicine, botanical medicine, nutritional supplements, physical therapies (i.e., massage, acupressure), homeopathy, and mind–body therapies. Spiritual practices, especially prayer, are also commonly listed among CAM therapies. ''CAM therapies. . .share common principles. Unifying themes among CAM practices include individualized treatment plans; belief in the healing power of nature; union of mind, body, and spirit; and often, more time spent with patients.''[3] The term *alternative medicine* creates a sharp distinction between the worlds of nonconventional therapies and conventional medicine in an either/or dichotomy, whereas the term complementary medicine may be ''closer to describing what many people in reality really do; they combine the two worlds. . . .''[3] Indeed, over 80% of the US public uses nonconventional practices and complementary medicines adjunctive to conventional medical care.[4] As CAM therapies are proved safe, they may be integrated into conventional health care approaches, and thus the list of what is considered to be a CAM therapy changes constantly.

WHERE DO BOTANICAL MEDICINES FIT INTO CAM?

NCCAM divides CAM therapies into five distinct categories. Herbal remedies fall under the classification ''biologically based therapies,'' which refers to substances found in nature, including herbs, foods, and vitamins. These substances are broadly classified as dietary supplements. The term *dietary supplement* is specifically defined by the Dietary Supplement Health and Education Act

(DSHEA), enacted in 1994, as a product, other than tobacco, taken by mouth, and intended to supplement the diet, including vitamins, minerals, herbs, and a number of other nutritional supplement products. Forms in which dietary supplements may be sold include extracts and concentrates, tablets, capsules, gel caps, liquids, and powders. Herbal medicines are amongst the most frequently used CAM therapies.[5–7]

HOW WIDESPREAD *IS* CAM USE?

Globally, it is estimated that 70% of all health care is provided by traditional, nonconventional medicine.[8] The World Health Organization (WHO) Traditional Medicine Fact Sheet states ''countries in Africa, Asia and Latin America use traditional medicine to help meet some of their primary health care needs. In Africa, up to 80% of the population still relies on traditional medicine for primary health care.''[9] One of the most commonly used forms of traditional medicine worldwide is botanical medicine.

Surveys indicate that as many as 50% (or more) of all Americans acknowledge using CAM therapies.[10–13] The actual rate of use is likely higher than reported in the United States, suggested by the fact that as many as 50% of patients do not report CAM use to their conventional doctors.[8,14] Surveys typically exclude non–English-speaking respondents, thereby eliminating from the statistical pool those demographic pockets of Americans whose use may be even higher that in the average population; for example, large numbers of Hispanic Americans in certain locales regularly use herbs and spiritual healing practices.[7]

David Eisenberg's seminal surveys on CAM use by Americans, conducted between 1990 and 1997, revealed a 45% increase in the use of CAM therapies during that period with estimated out-of-pocket expenses of up to $27 billion in 1997—up from $14 billion in 1990.[7] American patients' visits to CAM practitioners have been estimated at $600 million per year, exceeding the sum of all visits to primary care physicians.[3,5–8,14,15] Because these visits are mostly out of pocket, fewer individuals might currently use CAM therapies than if they were fully reimbursed by insurance or deductibles were lower. It is likely that there will be a significant increase in CAM use as more coverage is available from insurance companies, and as greater numbers of conventional practitioners integrate their practices to include a broader range of therapies or increase their number of referrals to a wider range of complementary therapists, such as acupuncturists, naturopathic physicians, and herbalists.

WHO USES COMPLEMENTARY AND ALTERNATIVE MEDICINE?

The average US CAM user is a well-educated health consumer, generally with at least a college education and an annual income of $50,000 or greater. Most are women between 30 and 59 years of age.[6,8,14] Individuals whose personal values include a holistic approach to health, environmentalism, feminism, or a desire for personal spiritual growth are more than twice as likely to use CAM therapies.[6,7,14] Additionally, members of numerous ethnic communities, such as Hispanics, African Americans, Asian Americans, and Native Americans, incorporate traditional cultural practices, including the use of herbal medicines, into their healing practices. Having a chronic disease is also an independent predictor of CAM use.[14–16]

WHY ARE PATIENTS TURNING TO CAM?

According to Wayne Jonas, MD, former director of NCCAM, ''Complementary and alternative medicine (CAM) is a health phenomenon that is largely driven by the public, and this is rather unique in medicine.''[5] What is it, in this age of life-saving antibiotics, surgeries, and other seemingly miraculous medical therapies that causes so many individuals to seek therapies outside of conventional medicine? Ostensibly, there are many answers to this question.

CAM therapies are generally seen by Americans as desirable for the prevention of common chronic illnesses, including heart disease, obesity, cancer, and numerous other widespread conditions. In the past 10 years, there has been a dramatic rise in awareness of the benefits of preventative health measures, both by health practitioners and the general public. This awareness is summarized in the following statement: ''Preventive health measures, including education, good nutrition, and appropriate use of safe nutritional supplements will limit the incidence of chronic diseases, and reduce long-term health care expenditures...healthful diets may even mitigate the need for expensive medical procedures.''[17] This message has been reinforced by cancer and heart disease prevention societies, and the multibillion-dollar-a-year nutritional supplements industry. In response, Americans have turned to the health food store as their pharmacy, self-medicating with dietary supplements—which categorically include herbal products. Too often, individuals are getting health information from the Internet, friends and family, magazines and other popular media, and product manufacturers, rather than from well-trained CAM professionals.

A desire for safer products also leads patients to turn to CAM. Consumers place a strong belief in the high margin of safety of dietary supplements, with 53% of 1027 US adults in a survey commissioned by the Dietary Supplement Education Alliance (DSEA) stating they feel that some dietary supplements offer benefits that are not matched by conventional drugs. Fifty-six percent of respondents stated that some dietary supplements offered benefits comparable with those of drugs but with fewer side effects.[13] According to Jonas, concern about the adverse effects of convention medicines is the third most commonly stated reason for turning to CAM.[5] Many individuals maintain the sometimes erroneous belief that ''natural'' means safer and gentler.

Numerous patients hold a simple pragmatic reason for using CAM therapies—they've seen many doctors and tried many medications, and they are still sick. Jonas states, ''In such circumstances, it is logical that patients search for something else that works. So they seek out other alternatives without necessarily abandoning

conventional care.''[5] Conventional medicine may be at its best when treating acute crises, but for the treatment of chronic problems it may fall short of offering either cure or healing, leading patients to seek out systems of treatment that they perceive as addressing the causes of their problem, not just the symptoms. Many prefer palliative solutions that seem safer and less invasive than the medical options with which they may be presented.

High costs of conventional medical care are also a factor. ''Studies indicate that consumers are placing increased reliance on the use of non-traditional health care providers to avoid excessive costs of traditional medical services and to obtain more holistic consideration of their needs.''[17] Although high-quality professional herbal products are not inexpensive, there may be hidden costs to conventional therapies, including more side effects than many herbal medicines. In one study comparing St. John's wort with a typical tricyclic antidepressant drug, both proved close to equally effective in treating depression, although the St. John's wort cost one-fourth the price of the drug and caused one-tenth the side effects of the conventional medication.[5] Cost-effectiveness studies comparing medical interventions with CAM interventions are scarce, and should be conducted more widely.

The desire for a holistic approach, as well as for increased participation in their care may be one of the most significant forces driving the desire for complementary medicine. ''Patients increasingly do not want to be treated simply as a body with a kidney, blood pressure, or blood sugar problem. Rather they want the accompanying social and psychological aspects of their ailments addressed as well.''[5] Many patients simply feel that using alternative and complementary therapies more accurately reflects their personal belief systems.[8,18,19]

Interestingly, dissatisfaction with conventional medicine is not an independent predictor of CAM use, with greater than 95% of Americans still regularly relying on conventional medical doctors.[14,20] It appears that most Americans seek to supplement rather than supplant traditional medical care.[8] According to Brokaw et al., ''Clearly, CAM is offering something that many patients want but are not getting from conventional medical services.''[19]

Some see the use of CAM therapies as an act of self-empowerment and an opportunity to take their health more into their own hands, perhaps a response to the days when ''doctors made the decisions; patients did what they were told.''[6,21] Dr. Atul Gawande, in his compelling and best-selling book, *Complications: A Surgeon's Notes on an Imperfect Science,* states that ''little more than a decade ago. . .doctors did not consult their patients about their desires and priorities, and routinely withheld information—sometimes crucial information, such as what drugs they were on, treatments they were being given, and what their diagnosis was. Patients were even forbidden to look at their own medical records: it wasn't their property. They were regarded as children, too fragile and simpleminded to handle the truth, let alone make decisions. . .and they suffered for it. And they missed out on treatments they might have preferred.''[22]

Chambliss observes, ''Poor physician–patient communication may increase the chance that a patient will turn to alternative medicine. Conventional physicians sometimes alienate patients by minimizing the connection between the mind and the body.''[8] Snyderman and Weil, in *Integrative Medicine: Bringing Medicine Back to Its Roots,* observe that the marked improvements in medical understanding that have been the hallmark of the scientific model have been accompanied by ''an unexpected and unintended erosion of the patient–physician relationship.. . . Burgeoning medical knowledge has created specialties and subspecialties, all of which are necessary; however it has created a dizzying array of practitioners, who generally focus their attention on small pieces of the patient's problem.. . . Managed care, capitation, increased need for documentation and productivity, and major constraints in health care funding have further eroded the patient–physician relationship and, at times, have forces physicians into positions of conflict with patients' needs.. . . Physicians simply do not have the time to be what patients want them to be: open-minded, knowledgeable teachers and caregivers who can hear and understand their needs.''[10] Table 1-1 compares a conventional medical consultation and a CAM consultation.

Linda Hughes, MD, of the University of California, San Francisco, suggests that ''Complementary and alternative medicine is attractive to many people because of its emphasis on treating the whole person, its promotion of good health and well-being, the value it places on

TABLE **1-1**

CAM Consultations vs. Conventional Medicine Consultations

	CAM	CONVENTIONAL MEDICINE
Time	More	Less
Touch	More	Less
History taking	Holistic	Specific
Language used	Healing	Cure
	Holistic	Dualistic
	Subjective	Objective
	Wellness	Illness
Patient's role	Consumer	Sick role
Decision making	Shared	Doctor in paternalistic role
Bedside manner	Empathetic	Professional
Consulting room	Counseling	Clinical

Adrian Furnham, PhD, of the Department of Psychology at University College, London, researches the difference between CAM consultations and conventional consultations. His observations suggested these differences.

Presented in the report, Can Alternative Medicine Be Integrated into Mainstream Care? From the NCCAM-Royal College of Physicians Symposium, January 23–24, 2001, London.

prevention, and its often more personalized approach to patient concerns.''[14] Many CAM practitioners and researchers corroborate this view.* David Spiegel, MD, professor of medicine and biochemistry at Stanford University School of Medicine, described the current state of health care delivery in the United States as having turned doctors into ''biomechanics'' and ''providers.'' ''They are drowning in paperwork,'' he said, ''especially when it comes to reimbursement for CAM modalities.... They haven't been good in helping people reconstitute a relationship with their body and deal with the emotional effects of their disease.''[24]

In summary, complementary and alternative medicine use is increasing because in many aspects, it ''fills patients' needs.''[23]

HOW OFTEN DO WOMEN SEEK CAM THERAPIES AND WHY?

Women seek medical care overall more frequently than men, and also follow more preventative health measures.[25] Therefore, it is no surprise that one of the largest subgroups of CAM users is women. Specifically, they are college-educated, employed women of reproductive age, between 30 and 59 years old.[6,8,11] Women are up to 40% more likely to use CAM therapies than are others.[6]

Although not all women who use CAM define themselves as feminist, in a study by Astin, feminism was cited as one of the three most common personal values contributing to CAM use, with twice as much CAM use likely by women who identified themselves as feminist.[6] This may be a reflection of CAM use as a tool of self-empowerment. The Consumer Healthcare Products/Roper 2001 survey reported that 60% of women, versus 46% of men, were regular dietary supplement users.[25] This pattern of increased use by women is likely to continue. In 1998, the US Surgeon General predicted that gender would be the greatest contributing factor to people's health over the next century, with women predicted to experience significant increases in health-related problems, particularly as baby boomers move into their menopausal years.[25]

The need for personal connection and relationship with health care providers may be a motivating factor for women seeking care from integrative or alternative practitioners. According to feminist theory on gender, communication, and models of learning, women thrive better in environments emphasizing connection.[26] The rampant perception of the depersonalization of medicine and disregard for subjective experience leaves many women feeling alienated. Noted childbirth educator and author, Sheila Kitzinger states: ''There remains a deep-seated suspicion of women's own accounts, which are often dismissed as mere anecdote...female experience, [particularly in relation to childbearing] is often ignored or trivialized because it does not match with 'observable facts' or because it does not match with ['expert'] perceptions of the same event or process.''[27] This phenomenon is recognizable in the cases of PMS and postnatal depression, now acknowledged medical syndromes, but for which women were historically dismissed or pathologized. Models of objectivity and distrust of the experiential in favor of evidence-based may be contrary and counterintuitive to women, who may place more value on intuition and personal experience as valid means of ''knowing.''[26] CAM therapies, typically patient-centered in their philosophies, are inherently more inclusive of the subjective voice—of the ''intuitive and personalized.''[26]

Doctor–patient interactions are frequently hurried, with little time for the patient to ask questions and have concerns addressed. Women often feel uncomfortable questioning or disagreeing with their physician, particularly if the physician is male, and especially if they already feel vulnerable as a result of a challenging health condition. Many women, by social convention, do not exercise their assertive voice (''speak up''), and thus do not experience satisfaction at their medical appointments. Seeing themselves as the passive recipients of health care services rather than consumers with the right to expect certain services for the fees they've paid, women often leave medical appointments feeling vaguely dissatisfied and marginalized.

Because personal interaction with the patient is typically lengthier, and establishment of a partnership rather than hierarchical relationship between client and provider an important aspect of most CAM therapies, women are more likely to feel that their questions and concerns have been acknowledged and addressed in the course of a CAM appointment, and are less likely to feel marginalized by their health care experience. CAM therapies, inherently personalized and individualized, incorporate the client's subjective experience into the development of the protocol. Thus, CAM therapies may be more compatible with women's emotional and psychological needs in the health care relationship.

The absence of the feminine voice in our health institutions may also be a primary contributing factor to women seeking health care outside of these institutions and returning to traditional healing methods, such as the use of herbal therapies. There is a need for inclusion of the emerging feminist perspective, known in academic circles as 'women's ways of knowing,' into the discussion of potential new paradigms for women's medicine. Jeanne Achterberg, in *Woman as Healer: A Panoramic Survey of the Healing Activities of Women from Prehistoric Times to the Present,* states insightfully that

> *The dissonance between women's talents and women's fate bears close attention as it reflects the evolution of institutions that lack the feminine voice. The absence of balance in these institutions has perpetuated a crisis that now extends alarmingly through all levels of health—from the health of tissues, mind, and relationships, to the health of the environment upon which life itself is dependent.*[28]

Women also have significant concerns over the safety of some of the therapies specifically prescribed for women's health. For example, recent back-pedaling by the medical and pharmaceutical establishments on the actual safety and efficacy of HRT has led many women to lose

*References 3, 6, 8, 10, 19, 23.

confidence in a range of pharmaceutical interventions. Turning to herbs and nutritional supplements for the symptomatic relief of menopausal complaints, and even the prevention of cardiovascular disease, seems to many a practical and relatively safe response to the HRT confusion. Erosion of confidence in conventional care makes women increasingly vulnerable to ''natural product'' marketing schemes by pharmaceutical and nutraceutical companies.

With the number of women in the 40 and above age range increasing by 10 million women in the next decade, it is expected that women are likely to be targets for massive dietary supplement, functional food, and OTC (over-the-counter) product advertising campaigns, as this represents multimillions of dollars of profit to the dietary supplements industry. It is essential that health professionals give direct attention to the safety and efficacy of dietary supplements and CAM therapies aimed toward women, sorting the reality from the hype, lest marketing at the expense of their health and pocketbooks victimize women.

WHAT PATIENTS DON'T TELL THEIR DOCTORS

''Most patients who are using CAM are, unfortunately, not talking with their practitioners about it,'' states Ellen Hughes, MD, in *Integrating Complementary and Alterative Medicine into Clinical Practice*.[20] Statistics vary, but research indicates that 20% to 72% of all patients do not inform their physicians of their use of herbs, nutritional supplements, and other CAM therapies.[6–8,20,23,29] In one significant example, almost 50% of patients undergoing surgery at a University of Colorado hospital never informed their doctors about using an alternative therapy within the 2 weeks prior to the surgery.[8]

Wendy Kohatsu, MD, in *Complementary and Alternative Medicine Secrets,* emphasized that it is ''of great concern that two-thirds of patients do not tell their doctors about the use of CAM. Because of growing data about interactions between conventional and CAM therapies, open communication is imperative for all concerned.''[3]

There are several probable reasons for such nondisclosure. Two commonly cited reasons are ''Doctors don't ask because they don't want to know and/or don't feel they have the time; and patients feel reluctant to volunteer such information because they are afraid doctors will think less of them and/or don't feel it's relevant.''[6] According to Hughes, among others, 61% of patients in one survey simply felt it wasn't important to reveal to their doctors, 60% stated that their practitioner ''didn't ask,'' and 31% asserted that it was none of their care provider's business! Twenty percent felt their provider was not knowledgeable enough about CAM to make it worth mentioning, and 13% felt their physician would disapprove and discourage their use of CAM.[14] In an article in *U.S. Pharmacist,* Michael Montagne, PhD, a professor at Massachusetts College of Pharmacy, confirms the possibility that care providers might make derogatory remarks: ''words used by conventional health professionals to describe…why people choose alternative therapies tend to be pejorative, paternalistic, sarcastic, ethnocentric, or negatively biased in some way.''[30] The perception that derogatory attitudes toward CAM users exist, or that physicians are just not interested in taking time to serve as advocates and educators for patients may play a dramatic role in keeping patients from talking to their doctors about CAM use.

Patients may pay the price. Recent surveys indicate that 18% (15 million) of US adults take prescription drugs concurrently with herbs or vitamins, and most are unaware of the potential risks and contraindications of the herbal remedies they use.[30,31] Nondisclosure of CAM use to physicians could result in unfavorable consequences for the patient.[8] For example:

- A patient might be using a less effective CAM treatment in place of a more effective standard therapy.
- A patient might be using an ineffective CAM therapy, wasting the patient's time and money.
- Combining dietary supplements (herbs, vitamins, minerals) with pharmaceutical drugs can lead to unknown or known adverse reactions.
- A patient could be using a potentially dangerous CAM therapy.

Fortunately, and as a general testament to the overall safety of botanical medicines, ''despite this widespread concurrent use of conventional and alternative medicines, documented drug–herb interactions are sparse.''[30]

Approximately 25% of Americans end up substituting herbs for prescription drugs.[14] Lack of knowledge of the use of a complementary therapy may lead the practitioner to misinterpret the effects, including the benefits, of a conventional therapy.[4,29] If health care providers are going to provide safe and effective therapies to their patients, they must be open-minded and knowledgeable enough about CAM therapies to have honest, meaningful, and respectful discussions with their patients, and be able to at least advise their patients about the safety and efficacy of the most common therapies, or be able to provide appropriate resources for information and referrals for competent care.

CAM EDUCATION FOR HEALTH PROFESSIONALS

Health professionals are aware of the growing need for a minimum understanding of CAM, and many physicians and medical students express a direct interest in learning to incorporate CAM practices. As many as 60% of doctors have recommended an alternative therapy to their patients at least once, and half have used them themselves.[3] Yet presently, few medical professionals are fully comfortable with or knowledgeable enough about CAM therapies to actually integrate them as a part of the clinical repertoire, or to be able to thoroughly or accurately educate their patients about the benefits and risks of CAM therapies.[11,14] This lack of comfort with and knowledge about CAM therapies extends to pharmacists and dieticians.[32] They may be particularly concerned about the safety of herbs because they contain pharmacologically active constituents, as opposed to other therapies that may not contain measurable active constituents (i.e., homeopathy) or that are not ingested (i.e., massage

therapy, aromatherapy, Reiki).[11] Then again, the known potential for pharmacologic activity is exactly what makes botanical medicines of special interest.

Many medical students, aware of the growing trend for patients to use nonconventional therapies, admit that they would like to receive training in CAM therapies—particularly botanical medicine.[10,11] Currently, most receive little training, if any, in the use of phytotherapy during the course of their medical education.[10] There is little consensus in the conventional medical world as to what extent, or how to integrate such therapies into medical training and practice. An increasing number of conferences on CAM are a regular feature of the continuing education options available for physicians, pharmacists, nurses, and other health professionals.

As of a 1997–1998 survey of 125 medical schools in the United States, 64% of the 117 schools that responded were offering courses in CAM either as required courses or electives, with only one-third of schools requiring CAM study as part of the formal curriculum.[14,19] This number doubled from 34% in 1995. Botanical medicine is a dominant topic in such courses. However, most of the courses are brief, with fewer than 20 contact hours, and in a lecture series on multiple modalities, students typically receive no more than 2 hours of lecture on any single modality; thus, they are more likely to be introductory survey courses than in depth presentations of clinically applicable information and techniques.[19,29] Additionally the majority of physicians currently practicing received no training in CAM modalities.[20] David Eisenberg states, ''Unless medical students or physicians in practice or in training are exposed to these therapies...unless they actually see a demonstration on a patient, a volunteer, a medical colleague, or themselves, they are simply unable to prescribe it. And they are unable to appreciate the conversation that they may need to have with a patient who wants a referral.''[33] Presently only one-fourth of CAM courses surveyed by Wetzel and Kaptchuk use a case-based teaching approach. Further, it is not realistic to expect physicians to be fully fluent in a wide range of alternative medicines and treatments, while under pressure to remain current on all the developments in their own fields.[23] Although Hughes suggests that the number of physicians who become bilingual will be in great demand, he points to the need for a cooperative environment between physicians and alternative practitioners—in this case, skilled herbalists and naturopathic doctors—for the purpose of referrals and mutual support of the patient.[20,23]

There is an unmistakable demand for increasing the number of CAM courses in medical schools, botanical medicine conferences for health professionals, and even postgraduate courses in botanical medicine for doctors and pharmacists. However, if these courses provide only superficial information, most of which is based on the limited number of herbs for which there is comprehensive scientific evidence, and taught in a way that merely presents herbs as substitutes for pharmaceutical drugs, then patients are not necessarily going to get what they are asking for—an increased sense of individuality, personal care, and attention to their holistic needs in the course of seeking to improve or restore health. Although such care is the cornerstone of traditionally practiced botanical medicine and naturopathic care, herbalists and naturopathic doctors are only rarely featured teachers in such venues. In the integration of medicine, there needs to be increased cooperation between various types of qualified professionals, so that herbs are not treated as softer pharmaceuticals or as discrete entities from herbal medicine. For this to happen, modern, professional herbal practitioners must be consulted for direction in shaping educational programs for health professionals.

TOWARD AN INTEGRATED FUTURE OF HEALTH CARE

There is a crisis in our current health care system. As health professionals, we have the opportunity to remake the health care system into a model that includes compassion, mutual patient and practitioner satisfaction, intelligent scientific rationale, the best technology, and the best natural therapies. In fact, these qualities together may be considered characteristic of what is being referred to as *integrative medicine*. Integrative medicine embodies characteristics that are inherent in the foundational principles of botanical medicine and naturopathic medical care, and is emerging as a discrete model and speciality training in the halls of conventional medicine.

Ben Kligler, MD, and Roberta Lee, MD, leaders in this field, define integrative medicine as

> *a practice that is oriented toward prevention of illness and toward the active pursuit of an optimum state of health. It is the marriage of conventional biomedicine, other healing modalities, and traditional medical systems (Chinese medicine, Ayurveda, homeopathy, and Western herbalism, among others).[34] This involves an understanding of the influences of mind, spirit, and community, as well as the body. It entails developing insight into the patient's culture, beliefs, and lifestyle that will help the provider understand how best to trigger the necessary changes in behavior that will result in improved health. This cannot be done without a sound commitment to the doctor–patient relationship.[35]*

Medical residencies and post-doctoral fellowships in integrative medicine have arisen to meet the educational needs of physicians interested in such training, and a national organization, the Consortium of Academic Health Centers for Integrative Medicine has evolved to support the development of undergraduate integrative medical education for emerging physicians. Harvard Medical School, Yale School of Medicine, Stanford University and Johns Hopkins University are among the many schools now a part of this group. The Consortium defines integrative medicine as follows:

> *Integrative Medicine is the practice of medicine that reaffirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic approaches, healthcare professionals and disciplines to achieve optimal health and healing.*
>
> **Developed and Adopted by The Consortium, May 2004, Edited May 2005**

Integrative practitioners embrace both conventional and alternative practices critically, prioritizing therapeutic options according to the level of benefit, risk, potential toxicity, and cost to the patient. Although integrative practitioners have a wide range of modalities at their disposal, they often are not specialists in any specific modality, having gained only brief exposure to a variety of modalities in their medical training. Some integrative physicians have specialized in a specific modality outside of medical school, for example, obtaining a license in acupuncture or specific training in botanical medicine. Many work in integrative clinics that employ a variety of types of practitioners, or work in conjunction with CAM practitioners in their communities. Integrative medicine practitioners can serve as a bridge for patients seeking both conventional and alternative modalities, with the integrative physician serving as a central figure assisting the patient in orchestrating her health care options.

Natural therapies incorporating herbs tend to acknowledge the multifaceted nature of a client. Finally, there is a growing trust in herbal medicine and a belief in its ability to heal. These factors combine to form a foundation for transforming illness into wellness. How this renewal is achieved by herbal medicine is not through mimicking a medical model of pathology or substituting ''natural'' drugs. One alternative objective in herbal medicine is to assess and address functional disturbances rather than pathology. We look for simple causes that affect our normal function rather than suspecting disease first.

—Amanda McQuade Crawford, MNIMH, RH (AHG)

History of Herbal Medicines for Women

Aviva Romm and David Winston

2 CHAPTER

WOMEN, HERBS, AND HEALTH REFORM: A HISTORICAL SUMMARY

Aviva Romm

> Such ''fathers of herbal medicine'' as Dioscorides did not simply pull their therapeutic theories out of the air. His herbal was the human, largely female heritage finally recorded by a man interested enough in the subject and literate enough to be able to write it down. Ironically, the early records of women's knowledge could be read by very few women.[2]
>
> **—Jennifer Bennett, *Lilies of the Hearth: The Historical Relationship between Women and Plants***

Women's history has always been woven with plants and the healing arts, particularly botanical medicine and midwifery.[1–4] In virtually every culture, without exception, women maintained knowledge of herbal healing for the prevention and treatment of common maladies that afflicted their communities, including herbal treatments for women's complaints. A textbook on botanical medicine for women would not be complete without recognition of the historical role of women healers.

Few records exist to tell us the stories of ancient women healers: their training, their successes, the clinical challenges they faced, or their experiences as women with medical careers.[1] The limited historical records that do exist, however, give us a glimpse of some of the remarkable women healers in ancient times. Given the pharmacy of their day, it is clear that many of these women were highly skilled herbalists.[3,5] Modern history leaves no doubt as to the important role women have played in the resurgence of herbal medicine and traditional healing practices in present-day medicine.

WOMEN HEALERS THROUGHOUT HISTORY

There is a remarkable absence of women healers in the archives of medicine. Information on the practices of women healers must be ''carefully teased out of a few surviving works written by women healers, from relics and artifacts, from myth and song, and from what was written about women.''[1] Although women have long handed herbal knowledge down to their daughters, both orally and in the form of ''stillroom'' books—the herbal equivalent of family recipe books—only a minority of women from the most privileged, educated backgrounds managed to keep comprehensive records or documentation of herbal ''recipes.'' Negligibly few women published serious medical works. On the rare occasion one did, it was frequently under a male pseudonym. Jeanne Achterberg states:

> *The experience of women healers, like the experience of women in general, is a shadow throughout the record of the world that must be sought at the interface of many disciplines: history, anthropology, botany, archaeology, and the behavioral sciences. . . . The available information on woman as healer in the western tradition spans several thousand years, stretching far back into prehistory when conditions were likely to support women as independent and honored healers. During and following those very early years, the role of women healers has been inexorably married to shifts in the ecology, the economy, and the politics in the area in which they lived.*[1]

Women Healers of Ancient Egypt and Ancient Greece

The oldest report of a woman physician dates to circa 3000 BCE. Records from this time indicate that a well-known practicing female physician lived in the city of Sais, where later there was a medical school. One of the earliest known medical documents, the Kahun papyrus (circa 1900 BCE) from Egypt, addresses the diseases of women and children. It has been suggested that this papyrus was written for women practitioners, as in ancient Egypt only women treated women's diseases.[3] Egyptian queens, including Queen Hatshepsut (who reigned from 1503–1482 BCE), encouraged women to become physicians. Hatshepsut herself set up three medical schools as well as botanical gardens. Women healers

were responsible for planting medicinal herb gardens and maintaining pharmacies.

Egyptian belief in the afterlife led to the practice of burying with the dead those things that were important to them in life and that would be needed in their next existence. At least one Egyptian Queen, Mentuhetep, is purported to have been found buried with alabaster ointment jars, vessels for tinctured herbs, dried herbs, and spoons for measurement. Polydamna, also a queen and physician of Egypt, was reputed to have given knowledge of the healing properties of the opium poppy, one of the possible ingredients in the famous sedative nepenthe. She was also alleged to have trained Helen of Troy (circa 2000 BCE), who is thought to have brought herbal knowledge from ancient Egypt to ancient Greece.[3]

The role of women healers was well established in ancient Greece, whereas in Egypt priestesses were often physicians and keepers of healing traditions. Their practices represented a synthesis of the physical and spiritual aspects of healing. One of the most revered deities of healing in ancient Egypt was the goddess Isis, to whom supplicants directed their prayers for healing. The medical practices of ancient Greece led to the development of later Western medical healing practices, including surgery. It has been suggested by scholars that women may have been largely responsible for the initial development of surgical techniques and therapeutics. Leto was the goddess of surgery.

Hygiea, an important goddess in the Greek pantheon and daughter of Asclepias, the legendary father of medicine (circa 900 BCE), is still a part of medicine today. Her statue is found on the fronts of hospitals and her name is invoked daily in our word hygiene, as is her sister's—Panacea—often mentioned in medicine. Both sisters were invoked for the restoration of good health—the practice of hygiene now considered central to preventive medicine. Hundreds of shrines dedicated to this family were erected in ancient Greece. Each woman in the family of Asclepias had her own staff, much like Asclepias', with a snake winding around it—a symbol that has persisted for thousands of years as emblematic of healers—and that is still used today as the symbol of Western medicine.

By the time of Hippocrates (400 BCE), women's role in society had been minimized to that of servants; their role in the healing arts was likewise marginalized. Nonetheless, the contributions of several women healers were recorded. Aristotle's wife Pythias was known to ''assist'' Aristotle in his work; together they wrote a text of their observations of the flora and fauna of one of the Greek islands. She was also involved in the study of anatomy and left detailed illustrations of chick and human embryologic studies. Queen Artemisia of Caria (350 BCE) has been praised by Pliny the Elder and Theophrastus for her healing abilities, and is credited by them for introducing wormwood (*Artemisia* spp.) as a cure for numerous ailments, although there is some debate over the attribution of the botanical name for the Artemisia species to Queen Artemisia as opposed to the goddess Artemis. Pliny (c. 50 CE) wrote of several women who authored medical books, including Elephantis and Lais.[3]

A famed ancient Athenian woman healer, Agnodice, left an extraordinary legacy. At the time of her birth in Greece, women were forbidden to study medicine; the penalty for doing so was death. Women throughout the entire Greek empire recognized her as having started a female medical revolution in Athens, which eventually influenced the practice of medicine. It is said that Agnodice felt so called to practice medicine as a response to the number of women dying as a result of refusal by medical doctors to treat them that she dressed as a man and enrolled at the medical school in Alexandria. Upon graduating, she established her practice, still disguised as a man, but upon being discovered to be a woman, local women flooded to her practice. When authorities discovered her proper identity, she was arrested and put on trial. It is purported that when her patients discovered her plight they threatened to rebuke their husbands by withholding ''marital favors'' if they did not support Agnodice's liberation. Congregating at the courthouse, they threatened to commit suicide en masse if she was not released. Successful in their efforts, Agnodice was freed and permitted to practice—in any manner of clothing she pleased. More significantly, women, with the exception of slaves, were permitted to openly study and practice medicine, treating only the diseases of women and children. This led to a new avenue of social and economic freedom for women in Greece. Numerous famed female physicians followed in Agnodice's footsteps: Theano, Aspsasia, Antiochis, and Cleopatra, a physician practicing at the time of Galen (second century CE). These women specialized in gynecologic and obstetric complaints, wrote extensively, and were renowned for their work.

At the University of Athens there is a fresco of the famed woman physician Aspasia in the company of such leaders as Socrates, Plato, and Sophocles. Her writings remained the standard textbook of gynecology until the time of Trotula. Aspasia employed treatments for problems as diverse as difficult labor, retained placenta, uterine tumors, and peritonitis, for which she performed successful surgeries. Cleopatra also wrote an extensive gynecology text that was distributed throughout Greece and Rome, and used as a standard treatise by doctors and midwives well into the sixteenth century. However, her work had been falsely attributed to a male writer of the sixth century CE. Soranus is later thought to have plagiarized her work extensively in his famed text, *Gynaecology*. This was not uncommon: What is believed to be the oldest medical treatise, written by a woman named Metrodora, was attributed to a man named Metrodorus. The original manuscript written by Metrodora still survives in Italy.

Women Healers in Ancient Rome

Prior to Greek influence in Rome, physicians were disparaged. Families were expected to tend to their own health needs. The spiritual attributions of health and disease received more recognition than the physical, with goddesses such as Diana, Minerva, and Mater Matuta presiding over women's reproductive concerns. Women had better social status in ancient Rome than in ancient

Greece, and Roman women met the arrival of female physicians from Greece with great receptivity. It may be that Roman male rulers were less pleased. Pliny the Elder is quoted as having said that women healers should practice inconspicuously ''so that after they were dead, no one would know that they have lived.''[1] Nonetheless, women healers, mostly from aristocratic families, were busily practicing by the first century CE, being greatly sought after and handsomely paid for their work.

Two successful practitioners were Leoporda and Victoria, both of whom are mentioned in medical writings of the day, with Victoria receiving the dedication to a medical book. In the preface of the book, *Rerum Medicarum*, she is recognized as being a knowledgeable and experienced physician. Inscriptions of tombstones of women physicians from Rome include such accolades as ''mistress of medical sciences'' and ''excellent physician.''[3] Several celebrated women physicians include Olympias, Octavia, Origenia, Margareta (an army surgeon), and Fabiola. The former two wrote books of prescriptions, and the latter was considered to possess remarkable intellectual ability as well as unusual charity. Fabiola opened a hospital for the poor in Rome—the first civil hospital ever founded and thought to be one of the best in Europe at the time. It is said that when she died thousands attended her funeral procession.

Western Europe: The Middle Ages

The Middle Ages were an ambivalent time for women healers. Emerging from the early Middle Ages, during which women healers were considered to be diabolic, little respect was left for ancient traditions deifying women, their bodies, and their connection to nature. St. Jerome, ironically a dear friend and supporter of the healer Fabiola, is quoted as having said that ''woman is the gate of the devil, the path of wickedness, the sting of the serpent, in a word, a perilous object.''[1]

By the Middle Ages, women healers appeared to take two divergent paths: Although midwives were well respected as skilled practitioners within their communities, many so-called cunning women, who were often poor and illiterate, were accused of and tried for witchcraft. Cunning women were thought to be dabbling in sorcery and bewitchment; midwives were often called as witnesses to testify against them at witchcraft trials.[6] Midwives were seen as protectors of the expectant mother; a midwife was ''the key figure in preventing harm…who guaranteed and subtended the order threatened by the witch.''[7]

Midwives were not impervious to accusations of witchcraft. There are notable cases, such as Walpurga Haussman of Dillenge, who was tried as a witch and executed.[6] However, they are mainly notable because they are anomalous cases; some prosecutions were a result of political positioning, whereas others were of previously respectable midwives who slipped into ''irregular healing methods.''[6]

Overall, midwives tended to be well respected in their communities; however, their skills and expertise varied tremendously. Because there were neither formal education programs for midwives, nor standards of practice, the quality of care and skill a midwife possessed was largely individual. Nonetheless, there are impressive, if few, records of women from both the Middle Ages who dedicated themselves to healing and medicine. Empress Eudoxia (420 CE) is attributed with the founding of two medical schools and a hospital in Syria, Jerusalem, and the land that eventually became Mesopotamia. Princess Radegonde of Burgundy studied medicine and opened a hospital for lepers, and Hilda of Whitley was an Anlgo-Saxon princess who became a physician and in 657 CE built an abbey where she practiced medicine and taught many classical academic subjects.

Jacoba Felicie is an example of one tried for the practicing medicine without a license. Brought to trial in 1322 by the Faculty of Medicine at the University of Paris, she was a literate woman from an affluent family. Jacoba, with unspecified medical training, had successfully treated numerous patients who testified at her trial. Yet, the testimonies were used against her as proof that she had committed the cardinal crime, not of healing, but of attempting to cure. In fourteenth-century England, educated women practitioners were likewise the target of campaigns by English physicians seeking to rid themselves of ''worthless and presumptuous women who usurped the profession'' seeking fines and long imprisonment for women who attempted the ''practyse of Fisyk.''[4] Women practitioners who spared their lives had enough fear instilled in them to practice their crafts extremely covertly, if at all.

Although volumes of women's herbal healing traditions were lost during this time, Europeans still depended on plants for medicine, so common household cures persisted. Numerous lay books on herbal medicinal cures were sold for the ''gentlewoman'' to use for keeping her family well, and ironically these books offered much of the same materia medica in use by physicians during that time. However, the revered place of women healers in their communities had been dramatically altered. Attitudes about nature, women, and their bodies also changed considerably, with the Baconian belief that all three were conquerable by medicine and technology.[8]

When the Moors conquered Spain, Spanish women trained in the healing arts of midwifery and alchemy alongside men, with an emphasis on the treatment of gynecologic and obstetric conditions. The renowned Arabic physician Rhazes is said to have learned many new remedies from women, and to have admitted jealousy of women healers, whom he said were often able to find cures where he had failed to successfully treat a patient.

Trotula of Salerno is a legendary female healer of the Middle Ages. It is alleged that Trotula was considered the most distinguished teacher at the medical college in Salerno, Italy, a gathering place for men and women of Greek, Arab, Latin, and Jewish backgrounds studying medicine. She is said to have been the first female professional of medicine at Salerno, in the eleventh or twelfth century, and was called to medicine because she saw women suffering from obstetric and gynecologic complaints that they were too embarrassed to discuss with male doctors. Trotula was an early advocate of healthy diet, regular exercise, hygiene, and reduced stress.

Although her history is not known with certainty, one of the most significant historical discourses on obstetrics and gynecology, referred to as *The Trotula*, actually a compendium of three texts, was either written in part by her, named after her, or is based on her teachings.[9] *The Trotula* remained an authoritative text for several centuries. It is predicated on religious and philosophical notions of the period (i.e., the curse of Eve and women's fall from grace), but the author(s) do not pathologize the normal processes of a woman's body and assert that women have particular needs that should only be evaluated and treated by other women. The clinical portions of the book refer to the menses as ''flowers,'' describing menstruation as a process necessary for fertility, much as trees need flowers to produce fruits. Diagnoses are based on keen observation and include assessment of physical findings from pulse and urine, as well as the patient's features and speech patterns. The text advanced theories and procedures, and was the first to define the diagnosis of syphilis based on its dermatologic manifestations. Trotula appears to have treated all manner of conditions with a variety of practices ranging from medicated oils to cesarean section, if necessary, with awareness of the need for antisepsis in surgery, prescribing topical and internal herbal treatments that may have been efficacious, based on what is known today about their actions. Sensitivity to the intimate needs of women is expressed, for example, by publishing the prescription of a procedure that will allow a woman who has previously lost her virginity to appear a virgin upon first intercourse after marriage, lest she face difficult political, legal, and social consequences. Jeanne Achterberg in *Woman as Healer* describes Trotula of Salerno:

> *She personified the balance that is so critical to the advancement of woman as a health care professional; a knowledge of science, attention to the magic that is embedded in the mind, a mission of service, awareness of suffering and the gift of compassion. She also had the courage to speak, write, and teach with conviction.*[1]

The place of women healers continued to decline dramatically, but another woman healer of the Middle Ages, Hildegard of Bingen, achieved such significant fame that her story bears telling. Hildegard, like many of the other famed women healers, was born of a noble family. She lived between 1098 and 1179 CE in Germany. At 3 years of age, she began receiving visions* and she began religious education at age 8. Her gift of prophecy gave her the uncanny ability to understand religious scriptures immediately, and from an early age she drew the attention of nobles and religious leaders. She also received visions of how life at her abbey was to be lived, ranging from ornate clothing to the development of a language used in the convent—of which nearly a thousand words survive today. Hildegard was known as a gifted intellectual, skilled in both academia and the arts—the latter as a musician and composer. One of her many books, *Cause et Curae*, a collection of five tomes, is a comprehensive medical work in which she describes diagnosis based on four humoral types (sanguine, phlegmatic, melancholic, and choleric), reminiscent of ancient Greek medical descriptions; appropriate behaviors for lifestyle, including recommendations for diet, stress reduction, and moral behaviors; and astrological predictions, for example, for conception. She provides an extensive discourse on gynecology, with recipes for external and internal preparations, as well as applications for over 200 medicinal plants. Her recommendations also included the use of gemstones, incantations, as well as hydrotherapy.[3]

Another of her collections, *Physica*, is comprised of nine books containing treatises on plants and trees, minerals and metals, and animals, including their medicinal and ''energetic'' qualities, and again drawing upon Greek medical descriptions. As is the case with most healers, Hildegard of Bingen's medical protocol reflected the cultural and religious context in which she lived; thus, Christian mysticism pervades her writing. Yet, her role as a woman healer also ran contrary to the common trends of the society in which she lived. Unlike some of the healers already mentioned who made deliberate political choices to develop their arts contrary to popular opinion on the role of women in medicine, Hildegard's calling came to her unbidden, as did her dedication to monastic life. Nonetheless, she represents a high level of intellectual achievement, forwardness in her discussion of women's gynecologic and sexual concerns, and an exemplary level of dedication to social service.

Women Herbalists in the Eighteenth and Nineteenth Centuries

''In the year 1775 my opinion was asked concerning a family recipe for the cure of dropsy. I was told that it had long been kept a secret by an old woman in Shropshire who had sometimes made cures after the more regular practitioners had failed.''[10] This statement was made by the illustrious Dr. William Withering, discussing his discovery of the use of foxglove. He is purported to have paid the woman, a Mrs. Hutton, an undisclosed sum of gold coins for sharing the family ''recipe,'' consisting of 20 herbs for the treatment of what was then considered a virtually incurable condition. Little mention of Mrs. Hutton or her herbal practice, if indeed that is what it was, is otherwise made, but the story of the development of the still-used drug digitalis for the treatment of congestive heart failure is medical legend.

Samuel Thomson, the founder of Thomsonian Herbalism, which for a time was rival to the ''regular'' doctors, wrote in 1834, ''We cannot deny that women possess superior capacities for the science of medicine.''[4] Thomson, like Withering, learned herbal medicine from a countrywoman well versed in the subject, although Thomson studied botanical medicines extensively, whereas Withering learned the secret of only one formula. Yet, in the Victorian era, women interested in the healing arts and plants were relegated to the study of

*The description of the physical symptoms by which Hidlegarde's visions were accompanied is remarkably consistent with the characteristics of migraine headaches, including the prodromal or ''aural'' phase, through to the blinding lights and pain, and finally with the euphoric postmigraine phase. Thus, she may have been a lifelong sufferer of migraine headaches.

botany, which was considered to provide good gentle exercise for the mind and body. Women were discouraged and prevented from the practice of medicine, and eventually even midwifery, the latter of which was taken over, initially by an untrained class of physicians referred to as barber surgeons, which was an accurate name as they were literally both barbers and surgeons.

Women, considered the weaker gender, were seen to be in need of protection from the rigors of intellectual exercise, which might ''damage their delicate constitutions.'' In the Victorian era, a sharp distinction was made between science and superstition. A line was drawn between the intuitive, folkloric, and nonacademic approaches of traditional healers and the linear, academic approaches of medical doctors and scientists. It is ironic, however, that the cures of early doctors were largely unsuccessful, and with the use of heroic treatments such as purges, bleedings, and mercury-based drugs, often led to more harm than good. In direct contrast, although herbal cures were not always successful, they often were, and they rarely caused anything near the magnitude of adverse physical problems caused by the cures of the regular doctors.

By necessity, women resumed their roles as active community healers during the settlement of the United States, delivering babies and tending to the health care needs of families from the east to the west coasts during westward expansion. Some women brought healing remedies with them from Europe, eventually planting gardens with herbs that have now become naturalized throughout much of the United States. Many learned to replace their traditional remedies with indigenous plant species, not infrequently learned about from their native neighbors.

As in Europe, the politics of medicine, which in the United States ultimately gave rise to the American Medical Association, once again eventually usurped the role of the community-wise woman. From witchcraft accusations of seventeenth-century New England to the systematic discrediting of midwives and women doctors through the early 1900s, the history of medicine in the United States tells a story of competing political interests, smear campaigns against ''irregular'' doctors and women, and the development of a medical monopoly by regular physicians.

Until the early 1900s, medical schools for women, blacks, and Native Americans coexisted with medical schools that allowed only males. In 1912, the Flexner report commissioned by the Carnegie Foundation, effectively led to the closure of the former schools, and only those schools sanctioned by the report remained operational.* Although many of the criticisms made in the Flexner report may have accurately portrayed the dismal state of numerous medical programs, there appears to have been no effort made after the report to ensure access to medical education for those whom these schools served.

*Many of the medical programs, for example, Johns Hopkins University and Harvard Medical College, are among those medical colleges that continue to thrive today.

WOMEN'S HEALTH MOVEMENTS

In spite of numerous imposed limitations—or perhaps because of them—women in the United States have been active in health care reform for the better part of the last two centuries. Waves of activism have tended to occur periodically and coincidentally with other social reform movements, such as abolition, suffrage, and the women's rights movement. Women's involvement in health care has transformed medicine in this country, from changing medical practices to humanizing health care institutions, consequently enhancing the status of women socially, economically, and politically.

The Popular Health Movement

The Popular Health Movement is one of the underacknowledged examples of a major women's health reform movement in the United States.[11] Taking place between the 1830s and 1840s, it was a broad-based social movement focused on educating individuals about their bodies, their health, and disease prevention. It was a strategic reaction against the status of the elitist, formally trained physicians who promoted heroic, dangerous treatments that were frequently as incapacitating or deadly as they might have been life saving.[11] Popular health movement educators instead emphasized healthy lifestyles, proper diet, exercise, eliminating corsets, and advocated the use of birth control as well as abstinence in marriage to limit family size.

An emphasis was placed on lay practitioners, including midwives, as it was perceived that gentler treatments were to be found in the hands of women and domestic healers.[11] Alternative health establishments, such as water cure centers, were popularly frequented and physiologic societies were founded that provided women opportunities to learn about and discuss their health concerns. Women were strongly encouraged to go to medical school and liberate information for others. It was firmly believed that medical information should be accessible to all and that the specialized language of doctors, medical journals, and textbooks prevented nonmedical practitioners from understanding what should rightfully be common knowledge.[11]

Although this movement eventually ceded to the times, the post–Civil War period marked the beginning of widening opportunities for women to access greater education. There was a significant increase in the number of women attending medical schools, with women comprising up to 6% of all physicians in the United States. This is a remarkable statistic, since as recently as 1973 in the United States, only 9% of all physicians were female.*

The Women's Medical Movement

Women physicians, continuing the philosophic tradition of the popular health movement, established the

*Currently, the number of female and male medical students is approximately equal, with there often being slightly more women students than male in entering medical school classes; however, specialties such as surgery are more common to men than women.

women's medical movement as a way to publicly challenge the popular medical philosophies regarding women's health championed by conventional physicians. These theories included the belief that women were fragile and that education damaged the female reproductive organs. Limited by constraints that prevented them from working in male-run hospitals, they founded exemplary and successful women's hospitals, employing doctors and nurses of both genders. Boston Women's Medical College became the first contemporary medical school established for the training of female physicians. Eventually merging with Boston University because of financial troubles, the school still exists as the prestigious Boston University College of Medicine.

The Progressive Era

In the early 1900s, referred to as the progressive era, the women's health movement largely wrestled with the issues of legalization of contraception, led by activist Margaret Sanger, which eventually led to the legalization of birth control and the maternal and child health movement, which was trying to increase the safety of motherhood through the establishment of prenatal care and maternal health clinics.[12] New York City was the center of activity for both efforts.

The Women's Health/Self-Help Movement

The 1960s and 1970s saw the rebirth of the women's health movement, once again arising to challenge a male-dominated medical system. The women's self-help movement has continued to tackle such difficult issues as abortion rights, rape, women's cancers, childbirth reform, and the excessive use of surgeries such as hysterectomies, mastectomies, and cesarean sections.

The return to natural medicines and ''lay'' healers that occurred in the post–Civil War era resurfaced in the mid-1960s along with the women's self-help movement. Herbalists—both women and men—began to reclaim the use of herbal medicines again in response to perceptions of over control by the medical system, as well as overuse of medications and invasive treatments. Back-to-nature philosophies consistent with using gentler and more natural remedies, and the desire to be independent of conventional institutions (i.e., the medical establishment), created the modern-day role of herbalists whom, trained by studying the plants themselves, apprenticing themselves to indigenous healers, and studying old texts such as the eclectic medical books, began to quietly practice their art. Similarly, women found themselves training as midwives to meet the needs of increasing numbers of women seeking home births in order to birth without intervention and outside the confines of medical establishments and protocol. Some women learned the arts of midwifery and herbal medicine simultaneously, serving their communities much as the wise women of more ancient times. Many of the most well-known and respected herbalists and midwives of today's herbal movement are those who began in the 1960s and 1970s.

Rebirth of Alternative and Traditional Healing in the Contemporary United States

In recent decades, increasing numbers of women have become disenchanted with the interventionist and impersonal nature of obstetrics and gynecology, as well as other specialties, such as oncology, and have turned to alternative healers for care. Articles on the large number of iatrogenic diseases caused by mis-medication and unnecessary use of procedures in hospitals and doctors' offices has fueled the desire of many to seek more natural medical approaches. This strong public interest in herbal medicine has fed a large economic boon in the natural products industry. Scientific evaluation of herbal medicines has begun, frequently looking to the traditional use of the herbs to direct researchers toward possible medical applications.

Both midwifery and herbal medicine are experiencing resurgence, largely as a result of demand by women patients. Women are making connections between their health and their environments—whether their personal lives, work lives, or physical, ecologic environment. Stress, past abuses, and environmental health risks are increasingly recognized as important factors influencing health. It is fascinating to appreciate that the transformations currently taking place in health care are not sudden or new, but the result of centuries of effort for health care reform by women healers and those unique men practicing alongside these remarkable women, who together continue to shape the history of health care.

ANCIENT TO MODERN HERBAL PRESCRIBING

Aviva Romm

Detailed records of the herbs used as medicines for women's complaints have survived the centuries primarily through ancient treatises and the works of leading herbalists and physicians of their day, Soranus, Galen, Dioscorides, Rhazes, Avicenna, Trotula, Hildegard, and Gerard, among many others who published on gynecologic and obstetric herbal medicine. By the seventeenth century in England, primary health care was most commonly provided by lay people including family members, ''housewyfs,'' local wise women, midwives, and clergy. This led to a flood of publication of ''self-help'' medical books, which included information on diagnosis and treatment, the latter often largely based on herbal prescriptions, and the practice of what has been called ''empirical medicine.''[13] The herbal prescriptions in these books drew from the works of earlier authorities, for example, Gerard and Dioscorides, and were consistent with the standard conventional medical practices of the day, in contrast with today's self-help or alternative health movement, whose practices often differ vastly from conventional therapies.[13]

Although Western herbal medicine has not enjoyed the unbroken lineage of other traditional medicine systems, for example, traditional Chinese medicine or Ayurveda, it is remarkable to observe that many of the herbs used today for gynecologic and obstetric complaints are the same as those used hundreds or thousands

BOX 2-1

Topics Commonly Addressed in Ancient Herbals for Women

Afterbirth retention
Ano-vaginal fistula
Coagulation problems, excessive bleeding
Excessive heat
Breast lesions
Breast pain
Childbirth difficulties
Conception
Constipation
Contraceptives
Diarrhea
Depilatories
Diuresis
Excessive menstruation
Fetal death/expulsion
Hair care
Heart conditions
Hemorrhoids
Infertility
Lochial flow
Menopause
Miscarriage
Nausea
Prolapsed uterus
Pudendal itching
Tumors
Uterine problems
Vaginal hygiene
Vaginal problems

of years ago. There are also many obscure, even bizarre, treatments that fortunately are no longer implemented. The materia medica of Western herbal medicine has been augmented and improved by the addition of herbs that were used by the indigenous inhabitants of North America, and that have been learned by European immigrants in the 400 years since their arrival in North America.

COMMON WOMEN'S COMPLAINTS DISCUSSED IN ANCIENT TEXTS, TREATISES, AND TABLETS

The problems that have arisen in gynecologic and obstetric care historically are not entirely different from those women face today, and some conditions, such as ano-vaginal fistula, which were devastating for women 5000 years ago, remain so today for women in developing nations who lack access to proper preventative and reparative care. Box 2-1 gives a partial list representative of the types of topics that were discussed in herbals for women, although the names of conditions may have differed (e.g., amenorrhea was typically referred to as retention of menses).

COMMON HERBAL PRESCRIPTIONS FOR SELECTED WOMEN'S COMPLAINTS

This chapter is not meant to be an exhaustive accounting of all of the herbal remedies used for women's health since time immemorial. It is meant to illustrate some of the more important remedies that were used historically, occasionally highlighting the unique or strange, and to provide a demonstration of the long historical use of herbs for women's health. The ways in which these herbs may have been used medicinally is highly variable, and included oral administration, topical applications usually to the affected area, fumigation, douching, or as amulets and charms, or with incantations or prayers, in ancient times to one of the many goddesses or gods who presided over the health of women. Although the information presented in the following is strictly botanical, the materia medica of ancient peoples included a variety of nonherbal medicaments, for example, castoreum (musk from the perianal sacs of beavers), which was used by ancient Egyptian midwives to expedite labor, or stones such as malachite and copper salts. The primary resource for this information is *The History of Medications for Women* by Michael J. O'Dowd, a gem of a book for those interested in the history of medicines for women from ancient to modern times.[5]

The information is presented by highlighting selected common gynecologic or obstetric conditions or herbal actions (e.g., lactation, aphrodisiacs), further subdivided by time or culture, and the medicines used. Botanical names are provided when these were identified in the source materials.

Aphrodisiacs

The use of aphrodisiacs to increase libido is documented in most cultures throughout history, even as far back as ancient Assyria (Table 2-1).[5] Herbal sexual stimulants remain popular products and are commonly available over the counter. Women today are most likely to seek aphrodisiac herbs for the treatment of sexual debility, such as in the perimenopausal years, rather than simply to increase an otherwise healthy sex drive.

Breast Abscesses/Breast Disease

Breast disease is commonly mentioned in ancient texts and treatises (Table 2-2). Although the type of breast disease is often not differentiated, it is believed that breast abscesses and breast cancer are usually the subjects. Many herbs, often in the form of poultices and washes, were used topically to treat breast disease.

Labor

A safe, expedient, and minimally painful labor was no less a goal of women living in ancient times than it is today. Herbs were used for all manner of problems that might have arisen during the childbearing process, from the need for pain relief to the need to augment a delayed or stopped labor. Categorically, herbs for childbearing can neatly be split into analgesics and oxytocics (Table 2-3).

TABLE **2-1**

Herbs Used as Aphrodisiacs

LOCATION	HERBS
Ancient Assyria	Five aphrodisiacs were described in *The Assyrian Herbal*, a monograph published in 1942 on Assyrian herbal medications based on fragments of cuneiform script on approximately 660 medical tablets: • Asafetida (*Ferula foetida*) • Stinging nettle (*Urtica dioica*) seed (Fig. 2-1) • Red poppy (*Papaver rhoeas*)
Arabian	• Berberis (unspecified) • Camphor (*Cinnamomum camphora*) • Cubeb (*Piper cubeba*) • Galanga

TABLE **2-2**

Herbs Used for Breast Disease

LOCATION	HERBS
Ancient Assyria	• Chaste berry (*Vitex agnus castus*) extract was applied, either alone or in rose water, as a poultice for breast disorders. • Fenugreek (*Trigonella foenum-graecum*) was applied as a paste, mixed with flour. It was still listed in the 1983 *British Herbal Pharmacopoeia* (BHP) as a treatment for suppurating wounds. • Pine (similar to oil of turpentine)
Ancient Greece and Rome	• Cabbage • Celery (*Apium graveolens*) • Cumin (*Cuminum cymium*) • Fenugreek • Linseed • Mallow • Olive oil
Europe: Late Middle Ages	• Celandine juice (*Chelidonium majus*) • Linseed

Figure 2-1 Stinging nettle (*Urtica dioica*). (Photo by Martin Wall.)

Lactation

Concerns about insufficient breast milk have long plagued lactating mothers, and a number of herbs have been described for improving the quantity and quality of milk (Table 2-4). Wild lettuce *(Lactuca virosa)*, for example, known to have grown wild in ancient Egypt, was given to women after childbirth to promote the increased flow of breast milk. It was described in 1652 by Culpepper in his herbal and in 1735 by John K'Eogh in *Botanologia Universalis Hibernica* as such.[5] It is not used today for this purpose; it is used instead mostly as an anodyne and sedative, for which it also has been used traditionally.

Menstruation

Common menstrual problems included failure to menstruate (possibly due to pregnancy, but also primary or secondary amenorrhea), dysmenorrhea, or excessive menstruation. Remedies for these conditions were widely discussed in ancient and historical texts.

Amenorrhea

The treatment for amenorrhea (Box 2-2), for which there were many different attributed causes, was generally in the form of emmenagogues administered orally and

TABLE 2-3

Herbs Used for Childbearing

LOCATION	HERBS
Analgesics	
Ancient Assyria	Many of the ancient Assyrian pain relieving herbs contained hyoscine (scopolamine) and are herbs that are not considered gentle or safe for use today, with gentler choices preferred by midwives, and controlled pharmaceutical drugs being preferred when there is the need for strong action. • Fox-grape (*Solanum* spp.) • Henbane (*Hyoscyamus niger*) • Mandrake (*Mandragora officinalis*) (Figure 2-2)
Ancient Greece and Rome	• Apples, bread, ground grain, liquid barley, melon, olive oil
Oxytocics	
	Many oxytocic herbs were strong purgatives, and did not exert a direct action on the uterus, whereas others may have had a true oxytocic effect. These are mostly out of use in favor of gentler herbs or controlled pharmaceuticals.
Ancient Assyria	• Galbanum (*Ferula galbaniflua*): used as a fumigant to facilitate childbirth • Castor oil (*Ricinus communis*) was mixed with beer and applied topically to the abdomen overlying the uterus to stimulate contractions, a practice still used today, though without the beer. • Juniper (*Juniperus communis*): taken alone or with plantain (*Plantago psyllium*) to speed delivery (Fig. 2-3)
Ancient Egypt	• Birthwort (*Aristolochia clematis*) to induce labor • Also, basil, fir, frankincense
Ancient Greece and Rome	• Anise seed (*Pimpinella anisum*) • Cedar resin • Dittany • Southernwood (*Artemisia abrotanum*) • Sweet bay
Europe: Late Middle Ages	• Hyssop (*Hyssopus officinalis*) • Madder roots in honey as a suppository (Rubiatinctoria) • Roses in wine

Figure 2-2 Mandrake (*Mandragora officinalis*). (Photo by Martin Wall.)

Figure 2-3 Juniper (*Juniperus communis*). (Photo by Martin Wall.)

topically (Table 2-5). Many emmenagogues are also abortifacients, and may have been used as such. A number of these herbs may have also been used to induce uterine contractions in order to dispel a dead fetus (i.e., from miscarriage or intrauterine fetal death).

Dysmenorrhea

Painful menstruation commonly mentioned in ancient texts remains a common problem addressed in modern herbals for women today (Table 2-6).

Excessive Menstrual Bleeding

Box 2-3 includes an excerpted, translated section from an extensive protocol on uterine prolapse taken from *The Trotula*. Table 2-7 lists some herbs used for excessive menstrual bleeding.

History of American Botanical Medicine: From Thomson to the Eclectics

David Winston*

In the early part of the nineteenth century, medical practice in the United States was in a dismal state. General lack of medical knowledge, poor hygiene, and allopathic medicine's adherence to dangerous treatments made going to a physician both a frightening and hazardous experience. The overuse of bleeding, mercury, arsenic, opium, emetics, and purgatives weakened patients almost as much as did the diseases.[16] In response to the common practice of excessive bleeding and purging, physician William Cobbet said, ''It was one of those great discoveries which are made from time to time for the depopulation of the earth.''[17]

*For historical purposes only.

TABLE **2-4**

Herbs Used for Lactation

LOCATION	HERBS
Europe: Late Middle Ages	• Vervain (*Verbera* spp.) in lukewarm white wine
Ancient Egypt	• Wild lettuce (*Lactuca virosa*)

BOX **2-2**

On Paucity of the Menses

From *The Trotula*[9]

If women have scant menses and emit them with pain, take some betony or some of its powder. Some pennyroyal, sea wormwood, mugwort, of each one handful. Let them be cooked in water or wine until two parts have been consumed. Then strain through a cloth and let her drink it with the juice of fumitory.

Due to the ''regular'' doctors' grim results with his own family and their costly fees, Samuel Thomson (1769–1843), a poorly educated New Hampshire farmer, was driven to create an herbal alternative—Thomsonian Medicine. This system borrowed heavily from Native-American herbal traditions, native sweat baths, and New England folk remedies. It was quite heroic, but substantially less toxic than the orthodox medicines commonly used.[18] Thomson was a product of his times; he was strongly influenced by the individualism associated with Jacksonian Democracy.[19] Upon purchasing a patent, any man or woman could become a botanic physician and practice his simple system. No further training or knowledge was needed. This simplicity is evidenced by Thomson's primary theory ''heat is life, cold is death.'' Anything that increased vital heat was beneficial and anything that impeded circulation and vital force was dangerous (e.g., opium, arsenic, mercury, bleeding). The

TABLE **2-5**

Herbs Used for Amenorrhea

LOCATION	HERBS
Ancient Assyria	• Leaves of the bay tree (*Laurus nobilis*) • Caper (*Capparis spinosa*) • Cypress (*Cupressus* spp.) • Calendula (*Calendula officinalis*) (Fig. 2-4) • Papyrus (*Cyperus papyrum*) • Saffron (*Crocus sativus*)
Ancient Egypt	• Caper Capparis Spinosa • Cumin • Dates • Juniper • Pine oil • Rue • Sesame
Ancient Greece and Rome	• Cucumber (*Cucumis sativus*) • Hellebore
Europe: Late Middle Ages	• Anise seed • Clove (*Syzygium aromaticum*) • Fennel (*Foeniculum vulgare*) • Fern roots • Feverfew (*Tanacetum parthenium*) • Horehound (*Marrubium vulgare*) • Hyssop • Lilies • Mugwort (*Artemisia vulgaris*) • Rue (*Ruta graveolens*) • Shepherd's purse (*Capsella bursa-pastoris*) • Southernwood • White pepper • Wormwood (*Artemisia absinthium*) (Fig. 2-5) • Yarrow (*Achillea millefolium*)

Figure 2-4 Calendula (*Calendula officinalis*). (Photo by Martin Wall.)

Figure 2-5 Wormwood (*Artemisia absinthium*). (Photo by Martin Wall.)

TABLE **2-6**

Herbs Used for Dysmenorrhea

LOCATION	HERBS
Ancient Assyria	• Asafetida • Calendula (*Calendula officinalis*) • Hemp seeds (*Cannabis sativa*): taken in beer as an analgesic and for heavy menstruation • Dried rose (*Rosa* spp.) cooked in wine • Poppy (*Papaver somniferum*) • Mandrake (*Mandragora officinarum*)
Ancient Egypt	• Frankincense • Marijuana
Ancient Greece and Rome	• Absinthium • Bayberry • Cumin • Dill • Linseed

BOX **2-3**

On Descent of the Womb

From *The Trotula*[9]

If it happens that after birth the womb descends to far down from its places, let oats, have first been moistened and put into a sack, be heating and applied. Sometimes the womb is moved from its place, and sometimes it descends, and sometimes it goes all the way out through the vagina. And this happens on account of a weakening of the ligaments and an abundance of cold humors inside.

Treatment

If it descends and does not come all the way out, aromatic substances ought to be applied to the nose, such as balsam, musk, ambergris, spikenard, storax, and similar things. Let her be fumigated from below. . .
But if the woman has come out, let aromatic substances be mixed with juice of wormwood, and from these things let the belly be anointed with a feather. Then take rue, castoreum, and mugwort, and let them be cooked in wine until two parts have been consumed, then give it in a potion.

TABLE **2-7**

Herbs Used for Excessive Menstrual Bleeding

LOCATION	HERBS
Ancient Assyria	• Cassia (a form of cinnamon); cinnamon is still used by herbalists and midwives for heavy uterine bleeding • Calendula (*Calendula officinalis*) • Stinging nettles leaf • Windflower (*Anemone pulsatilla*); pulsatilla is still used by herbalists and midwives today, mostly as an analgesic and antispasmodic for the treatment of dysmenorrhea
Ancient Egypt	• Ale • Date juice • Flax tampons
Ancient Greece and Rome	• Grape seed • Lotus • Myrtle • Pine • Pomegranate peel • Quinces • Tart wine
Arabian	• Raspberry (*Rubus* spp.)
Europe: Late Middle Ages	• Betony (*Pedicularis bracteosa*)

materia medica of these botanic practitioners utilized a limited number of medicines, including stimulant diaphoretics (*Capsicum*, *Achillea millefolium*, *Hedeoma*, *Zanthoxylum americana*, *Zingiber officinalis*), astringents (*Myrica cerifera*, *Quercus* spp., *Commiphora molmol*), emetics (*Lobelia inflata*, *Eupatorium perfoliatum*), sedatives (*Scutellaria lateriflora*, *Cypripedium pubescens*, *Symplocarpus*), and bitters (*Chelone glabra*, *Populus tremuloides*, *Berberis vulgaris*). Thomson's system usually included several ''courses'' of steaming, purging, and sweating followed by tonification of the stomach, lungs, and bowels. Although unpleasant in its pronounced activity, this protocol was actually very successful in treating many common scourges of that time.

One of the many failings in this system was Thomson's total aversion to further medical education; he had a profound anti-intellectual bias against a ''professional class'' of medical physicians. In response to Thomson's rigidity and dictatorial nature, one of his agents and the editor of his journal, Alva Curtis (1797–1881), created his own botanic sect, which became known as the Physio-Medicalists. They founded their own sectarian medical schools and focused on the use of a large materia medica of nontoxic herbs. In addition, they developed a very complex (some would say obtuse) theoretic basis for their practice.[20] Part of the Physio-Medicalist theory included an energetic diagnostic system somewhat similar to the Chinese concept of yin and yang. Patients' constitutions and organ systems were seen as either Asthenic (hypoactive, deficient) or Sthenic (hyperactive, excess). Herbs were prescribed according to information ascertained by pulse, tongue, and other physical diagnostic procedures.

This system never developed strong support in the United States; at their height of popularity in the 1880s, they only numbered 1000 practitioners.[21] Interestingly enough, this system was transplanted to England, where it flourished and was taught at the British School of Phytotherapy until the 1980s.[22]

The most successful sect of botanic physicians—the Eclectic physicians—was founded in the 1820s by Wooster Beach, MD (1794–1868). Eventually, Beach's presence faded and the movement chose a new name, Eclectic Medicine. The Eclectic movement was responsible for popularizing many now well-known herbs. Among these are echinacea (*E. angustifolia*), goldenseal (*Hydrastis canadensis*), black cohosh root/macrotys (*Actaea racemosa* syn. *Actaea racemosa*), cactus (*Selenicereus grandiflorus*), wild indigo (*Baptisia*), blue cohosh root (*Caulophyllum thalictroides*), cascara sagrada (*Rhamus purshiana*), and kava (*Piper methysticum*). The Eclectic philosophy allowed physicians to select therapies from other medical sects such as allopathy, homeopathy, and hydrotherapy that would benefit individual patients.

By the late 1850s, the Eclectics were flourishing; Eclecticism and Homeopathy were the two primary alternatives to medical orthodoxy. This initial success of Eclectic practice was marred by constant internecine fighting, ''the Eclectic resinoid craze,'' and declining enrollment in the Eclectic Medical schools during the Civil War. These problems left the Eclectic Movement in serious decline by 1865.[23] Resinoids—which consisted of the use of constituent resins discovered by John King, MD (1813–1893), and which included Podophyllin, Irisin, Macrotin, and Leptandrin—were stable and active resins precipitated out of liquid extracts. Unfortunately, the drug companies at that time used the same idea to produce ''resinoids'' from the entire materia medica only to belatedly discover these products were mostly inert. The podophyllin

discovered by King is the same resin still used today in dermatology practice for the treatment of human papillomavirus (HPV).

From the depths of economic and organizational collapse, John Milton Scudder, MD (1829–1894) almost single-handedly resurrected Eclectic Medicine. In his books, *Specific Medication & Specific Medicines* and *Specific Diagnosis*, Scudder proposed a new model for practice. In this system, small doses of high-quality medicines (mostly herbal) replaced large quantities of often nauseating polyherbal or chemical preparations. Each medicine was carefully studied to find its ''specific indications'' in clinical practice.[24] No longer were practitioners treating a disease; they now treated individual people. Each remedy was specific to the unique symptom picture the patient displayed. To further clarify the appropriate treatment, a system of differential diagnosis was developed to give the practitioner clear insights to effective prescribing. Pulse, tongue, urine, and other forms of physical diagnosis became essential tools for selecting the appropriate medicines. The major tenents of Specific Medication are:[25]

1. Disease is to be regarded as an impairment of the life of the creature. It may be of the structure in and by which he or she lives or of the forces that give life; but it is the life that is to be regarded in medicine.
2. Disease has distinct expressions, as has health; and they may be recognized by those who train themselves to undertake accurate observation. The expression ''language of disease'' is not a poetic allusion but a statement of fact.
3. There are certain forces in nature, locked up in substances called medicines, that act directly upon the living body, enabling it to resist disease and aiding in a restoration of normal functions and structures.
4. The action of such substances has been determined by observation in the past and is being further known by experiments and observations of the present. Even now our knowledge of the power of drugs is sufficient to enable us to apply them with certainty in a very large number of diseased conditions.
5. We have proved that special drugs meet special conditions of disease. As these conditions of disease have distinct expressions and may be recognized by the physician, we say that these disease expressions become drug indications.
6. Lastly, if these drug indications are followed, the action of remedies will be certain and curative, and the practice of medicine will have a scientific basis, which will ensure continued improvement year by year.

Scudder took the best of Eclectic Medicine, Homeopathy, Rademacher's Organ Remedies, and years of clinical experience to create a unique system of medicine that was based on the use of herbal as well as mineral remedies. Initially, many Eclectics balked at the new system (called Scudderism or Neo-Homeopathy by critics), but experience proved its value and effectiveness. The Golden Era of Eclectic Medical Practice 1875–1895 found over 8000 Eclectic physicians practicing throughout the United States. There were eight legitimate Eclectic Medical Schools, and this ''American System of Herbal Medicine'' seemed secure in its place.

Several prominent Eclectic physicians worked along with Scudder to help spread the word of his new system. John King, MD (1813–1893), whose texts were considered the most authoritative in their day and continued to be studied until the last decade of the nineteenth century was among the most prominent. King, along with J.M. Scudder and J.U. Lloyd, worked to create the medicines and the milieu that allowed Eclectic specific medication to become accepted and then flourish.

The change in centuries brought new ideas that the Eclectics were reluctant to embrace, such as bacteriology, vaccination, and pharmacology. The onslaught of the American Medical Association and the Carnegie Foundation monies, which fueled the AMA's growth and increasing dominance, changes in medical education, and the Flexner report, which damned most sectarian medical schools, all led to a steady decline in status of and enrollment Eclectic schools.

The deaths of the Eclectic leaders left a hole that was difficult to fill. The Eclectics, who were always most popular in rural America, were increasingly seen as a relic of older days. They were considered unscientific, clinging to plant medicines rather than the new miracle drugs created in laboratories (aspirin, sulfa drugs). No longer was orthodox medicine bleeding or poisoning patients and improved hygiene had reduced the dangers of many terrible diseases that were once common. In this changing social, political, and cultural climate, the Eclectics could only be seen to belong to the past, not the bright industrial future of the twentieth century. The Eclectic Medical College, the last school of Eclectic Medicine, closed its doors in 1939. Although few herbalists, MDs, and NDs are fluent in this system of practice, today the rich Eclectic literature with their authors' accumulated knowledge remains available as a valuable resource of accumulated botanical medicine experience.

Specific Indications for Botanicals for Women: Eclectic Medical Tradition
*David Winston**

Tables 2-8 and 2-9 contain a summary and comparison of remedies acting on the reproductive organs of women that were popular among the selected medical physicians.

A note concerning eclectic medicines and doses
Although many Eclectic physicians made their own tinctures, the most popular medicines were Specific Medicines made by Lloyd Brothers of Cincinnati and ''normals'' made by W.S. Merrill, also of Cincinnati. These products were highly concentrated extracts, thus the dosage levels were quite low, especially compared with tinctures. Most dosage levels have been adjusted to reflect currently available preparations.

*For historical purposes only.

TABLE **2-8**

Eclectic Remedies Acting on the Reproductive Organs of Women

Botanical	Black haw (*Viburnum prunifolium*)	Pulsatilla (*Anemone* spp.)	Blue cohosh (*Caulophyllum thalictroides*)	Black cohosh (*Macrotys; Actaea racemosa*)	Chaste tree (*Vitex agnus-castus*)
Action	Acts mildly as a nervine and antispasmodic. Produces muscular relaxation and reduction of reflex irritation during pregnancy. Has a tonic and soothing influence on the entire uterine structures.	Strong-acting nervine, anxiolytic, especially for menstrual, premenstrual, or menopausal problems with intense emotional symptomology.	Has a wide influence on the reproductive organs increasing activity and reducing pain; widely used for uterine and ovarian pain with fullness, ovarian neuralgia, endometritis, endometriosis pain, and mittelschmerz.	Exercises a wide influence on the nerve centers, and their blood supply. Is a mild motor depressant and nerve sedative. Positively relieves muscular soreness or aching, induced or idiopathic, from whatever cause. Relieves erratic nervous conditions; acts directly upon the reproductive functions.	Corpus luteum insufficiency with elevated estrogen and/or deficient progesterone. Highly effective remedy for premenstrual and menopausal anxiety, hot flashes, and uterine fibroids.
General influence on the Menstrual Function	Indicated in dysmenorrhea, with cramp-like or spasmodic pains. Corrects nervous irritation and sympathetic disturbances.	Usually for delayed or scanty menses caused by anxiety, fear, shock, or in weak, depleted anemic girls.	A direct emmenagogue and antispasmodic, it is indicated in amenorrhea, dysmenorrhea, irregular menstruation, and premenstrual syndrome (PMS) anxiety.	In menstrual disorders, accompanied with aching or muscular soreness, and cool skin. Relieves amenorrhea with these symptoms; will control congestive dysmenorrhea. Its influence here is enhanced by aconite or belladonna. Is beneficial in menorrhagia and metrorrhagia; is given in menstrual irregularities of young girls.	Hyper or polymenorrhea, amenorrhea due to hormonal imbalance. Helps to re-establish normal cycle *after* use of birth control pills. Useful for treating a wide range of PMS symptoms.
Prevent miscarriage or abortion	The best of remedies for this purpose, reliable in emergencies if given in full doses, frequently repeated. Reliable in habitual abortion; will prevent induced abortion if membranes are not ruptured. Should be given in advance in habitual cases, and continued past the time.	In atonic conditions during pregnancy, it will restore tonus to the uterus and promote a normal labor.	In small quantities mixed with viburnum it has a reputation for preventing premature labor. NOT RECOMMENDED FOR SELF-MEDICATION DURING PREGNANCY. PROFESSIONAL USE ONLY.	Can not be depended upon. Acts more like ergot; is given only in small doses, for its specific indications.	May be used up to third month of pregnancy to prevent miscarriage and to remedy morning sickness.

(Continued)

TABLE **2-8**

Eclectic Remedies Acting on the Reproductive Organs of Women—cont'd

As a partus-preparator	Abates nerve irritation, restlessness, and hysterical symptoms and erratic pains, contributes to a normal condition; prevents morning sickness, premature contractions; induces cheerfulness and hopefulness and prevents accidents.	In atonic conditions during pregnancy, it will restore tonus to the uterus and promote a normal labor.	Frequently used in combination (mother's cordial), it prevents false labor pains, anxiety and promotes a healthy, easy labor. May cause fetal congestive heart failure. Best to avoid during pregnancy.	The most frequently used remedy for this purpose, less reliable than mitchella; removes erratic pains, and irregular conditions; overcomes hysteria, soothes general muscular irritation; and conduces to a normal, easy, short labor.	Has no direct influence
In labor	Promotes normal conditions, with regular normal contractions, soothes undue muscular irritation. Prevents hemorrhage.	It is beneficial in labors with sluggish, ineffectual, and weak contractions.	Stimulates strong, productive contractions. Useful in pokey labor (rigid os 4–5 cm)	A most reliable oxytocic; produces normal regular intermittent pain; does away with erratic and irregular pains, especially if of rheumatic or neuralgic origin. Prevents postpartum hemorrhage; relieves nervous irritation.	Has no direct influence
After labor	Restores normal tone, and normal capillary circulation, prevents subinvolution, prolapse, and malposition	Can be of benefit with Cimicifuga for postpartum depression.	Helps to expel placenta; reduces postpartum pain; prevents uterine subinvolution	Relieves severe aching and muscular soreness, controls postpartum hemorrhage, promotes normal involution; prevents the recurrence of uterine misplacement; cures persistent leukorrhea, especially if accompanied with relaxation and hypertrophy.	As a galactagogue to stimulate and maintain milk production (most effective first 10 days after birth).
For other conditions including menopause	Valuable during protracted or eruptive fevers, where there is irregular menstruation, with impending uterine inflammation and sepsis. May reduce cyclical outbreaks of herpes.	Excellent remedy for PMS and menopausal anxiety or depression and nervous headaches. Avoid use in acute inflammatory conditions	Effective for menopausal pain; low back pain with pain radiating down the legs; arthritic pain in small joints; spasmodic coughing.	It is of value in fevers with its specific symptomology and in inflammation of the kidneys and bladder. Aching and muscular soreness are its specific indications; menopausal symptoms including depression and hot flashes.	Teenage acne—boys and girls; premenstrual oral and genital herpes; carminative. Hormonally related constipation. Menopausal symptoms including hot flashes, excessive sweating, formication, and anxiety.

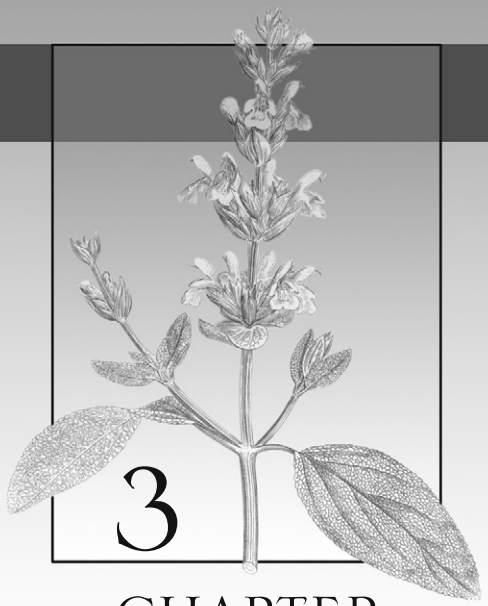
Adapted from Ellingwood F: *New American Materia Medica*.

TABLE **2-9**

Additional Female Reproductive Remedies Used by the Eclectics

American mistletoe herb (*Phoradendron serotinum*)	Uterine hemorrhage, including postpartum bleeding. Used as an oxytocic to stimulate labor; considered more effective than ergot.
Canada fleabane herb (*Conyza canadiense*)	Profuse vaginal discharge or menorrhagia.
Cottonroot bark (*Gossypium herbacium*)	Clotty, scanty menses with lower backache, a feeling of fullness and weight in the pelvis and bladder.
Cramp bark (*Viburnum opulus*)	Spasmodic uterine pain–dysmenorrhea, perineal pain.
Helonias (*Chamaelirium luteum*)	Female reproductive system amphoteric, increases fertility, regulates hormonal levels. Useful for pelvic congestion.
Licorice (*Glycyrrhiza glabra*)	Contains isoflavones (phytoestrogens)—use with white peony and saw palmetto for PCOS.
Motherwort (*Leonurus cardiaca*)	Anxiolytic, antispasmodic, PMS, and menopausal anxiety.
Partridge berry (*Mitchella repens*)	Uterine astringent, menorrhagia, uterine prolapse, feeling of heaviness in abdomen, tender with pressure.
Peach tree bark (*Prunus persica*)	Irritation of the stomach and upper gastrointestinal tract—severe morning sickness.
Raspberry leaf (*Rubus spp*.)	Uterine tonic—useful throughout pregnancy and postpartum, uterine prolapse, menorrhagia.
Saw palmetto (*Serenoa repens*)	Uterine tonic—useful for PCOS, infertility, and pelvic fullness syndrome.
Shepherd's purse—herb (*Capsella bursa-pastoris*)	Heavy bleeding caused by fibroids.
Thuja (*Thuja occidentalis*)	Used topically and orally for venereal warts resulting from human papillomavirus. Also indicated for leukorrhea and urinary dribbling.
Tiger lily (*Lilium lancifolium*)	Used for pelvic congestion and stagnation, ovarian neuralgia.
True unicorn rt. (*Aletris farinosa*)	Polymenorrhagia with labor-like pain and a sense of debility in the pelvis.
Water eryngo (*Eryngium aquafolium*)	Urinary irritation experienced as a constant sexual urge.
White ash bark (*Fraxinus americana*)	Fibroids, especially with heavy bleeding. Uterine hypertrophy with profuse leukorrhea and menstrual bleeding.
White baneberry root (*Actea alba*)	Ovarian cysts with pronounced tenderness upon palpation.
Yarrow herb and flower (*Achillea millefolium*)	Atonic menorrhagia, vaginal leukorrhea, postpartum bleeding, and heavy bleeding from fibroids.

Fundamental Principles of Herbal Medicine



3 CHAPTER

Aviva Romm, Lisa Ganora, David Hoffmann, Eric Yarnell, Kathy Abascal and Mitch Coven

Not everything that can be counted counts, and not everything that counts can be counted.
—Albert Einstein

THE EVIDENCE BASE FOR BOTANICAL MEDICINE

Aviva Romm

Herbal medicine is undergoing rapid evolution as divergent streams of thought meet to redefine it in a modern clinical context. Many Western herbalists and naturopathic physicians share the concern that the mainstreaming of herbal medicine threatens to uproot it from its classical foundation; yet, practitioners are also concerned with having solid scientific validation that the products they recommend, or which their patients might already be using, meet basic standards of safety and efficacy.[1–4] Interestingly, patients are often more interested in anecdotal evidence of safety and risk in contrast to practitioners who are more likely to want detailed and objective evidence of benefit, safety, and risk.[5] There is a tremendous need for a comprehensive way to evaluate herbal medicine efficacy and safety while integrating the concerns and experiences of all of the partners in health care: medical doctors and scientists, traditional practitioners, and those taking herbal medicines both for self-care and as patients.

This chapter proposes an integrative model of evidence-based herbal medicine that allows an intelligent synthesis of the various possible forms of data in the evaluation of botanical medicines, in order to include traditional evidence, scientific findings, and expert consensus based on clinical observation. This chapter also discusses the evidence upon which this text is based. In its broadest and most liberal interpretation, evidence-based medicine (EBM) can embody an ideal fusion of ''clinical and laboratory research data with human experience,'' as suggested by herbalist Simon Mills, rather than the reductionist, prepackaged mind-set that it has been accused of engendering.[6] An integrative model of presenting evidence can be seen in the monograph collections of the European Scientific Cooperative on Phytotherapy (ESCOP), the World Health Organization (WHO), and the *American Herbal Pharmacopoeia* (AHP), all of which acknowledge multiple levels of evidence including traditional use, clinical applications, and relevant science.

WHAT IS EVIDENCE-BASED MEDICINE?

The concept of EBM was first articulated in mid-nineteenth century Paris, and perhaps earlier.[7] Described more recently as ''the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients,''[7] EBM has been widely adopted in conventional medical circles as a hierarchic methodologic model of evaluating and ranking evidence for the determination of what is considered the best and most objective clinical practice. EBM as a packagable product-concept has become big business in medicine—a profitable host of commodities that include national conferences, hand-held computers that can be taken into patient consultations and programmed to generate EBM protocol for patients on the spot, books and journals, undergraduate and postgraduate training programs, and Web-based courses.[7] Centers for the study of EBM have been established, as have extensive databases.[7]

Yet, responses to EBM as a medical paradigm based solely on external, objective evidence to the exclusion of the practitioner's clinical judgment and experience have been highly equivocal, with widely varying criticisms ranging from ''evidence-based medicine being old hat'' to it being a ''dangerous innovation, perpetrated by the arrogant to serve cost-cutters and suppress clinical freedom.'' EBM has been ''criticized for the inappropriateness of much evidence and its application to clinical practice, for logical inconsistencies, for potentially reducing the role of clinical judgment, for difficulties integrating into everyday professional practice, and for cultural bias.''[8] EBM has been critically called ''cookie-cutter'' medicine, systematizing patient treatments according to specified protocol.[9] Ironically, this appears to be a backward step in light of patients' increasing demands for

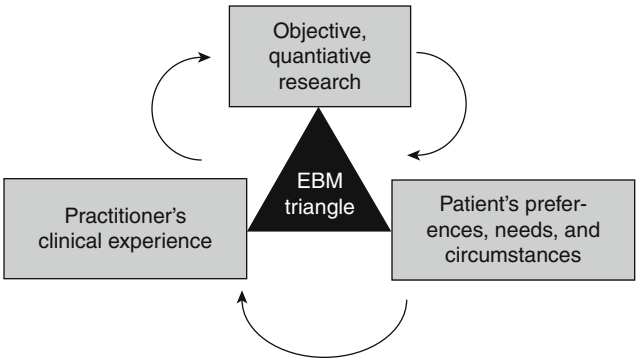


Figure 3-1 The evidence-based medicine triangle.

greater individual attention in medical care. Accusations of EBM being a cost-cutting measure are based upon the belief that streamlining diagnoses and treatments will represent cost savings to managed care organizations.[7–9]

Practitioners naturally want to provide their patients with the best options. Many believe that relying solely on external, quantified evidence will relieve them of the burden of responsibility (or culpability) inherent in exercising individual clinical judgment. However, removing subjective observation and judgment entirely from clinical decision making requires objectifying and homogenizing patients. John Astin, PhD, writing in *Academic Medicine*, states

> *Decisions in medicine, irrespective of how much objective evidence we gather, always involves the weighing of probabilities.... To suggest that randomized controlled trials, meta-analyses and clinical practice guidelines will eliminate the need for clinical judgment is to misrepresent the realities of clinical medicine (both CAM and conventional). If medicine* could *be purely evidence-based (which is highly debatable both practically and financially), then in theory medical care...could essentially be administered by computers and computer algorithms.*[2]

EBM proponents such as David Sackett suggest that the concept of EBM has been misinterpreted to be a one-dimensional orthodoxy based solely on objective, quantitative research methodologies, and that it is actually a much broader model than has been typically conveyed, with external evidence being only one of three important aspects of EBM.[7] The other arms of EBM are the patient's preferences, needs, and circumstances, and the practitioner's clinical experience (Fig. 3-1).

Sackett's description of EBM demonstrates its potential to serve as an integrative model:

> *The practice of evidence-based medicine means integrating individual clinical expertise with the* best available *external clinical evidence from systematic research. By individual clinical expertise we mean the proficiency and judgment that individual clinicians acquire through clinical experience and clinical practice. Increased expertise is reflected in many ways, but especially in more effective and efficient diagnosis and in the more thoughtful identification and compassionate use of individual patients' predicaments, rights, and preferences in making clinical decisions about their care. By* best available *clinical evidence we mean clinically relevant research, often from the basic sciences of medicine, but especially from patient centered clinical research.... Without clinical expertise, practice risks becoming tyrannized by evidence, for even excellent external evidence may be inapplicable to or inappropriate for an individual patient. Without current best evidence, practice risks becoming rapidly out of date, to the detriment of patients.... External clinical evidence can inform, but can never replace, individual clinical expertise, and it is this expertise that decides whether the external evidence applies to the individual patient at all and, if so, how it should be integrated into a clinical decision.*[7]

According to this, evidence-based medicine need not be restricted to reductionist forms such as RCTs and meta-analyses as some suggest (Box 3-1, Fig. 3-1). At its best, it is a ''triangulation of knowledge from education, clinical practice, and the best research available for a given condition or therapy.''[9]

SUPPORTING EVIDENCE FOR BOTANICALS DISCUSSED IN THIS TEXT

The World Health Organization (WHO), and numerous individual nations, in recognition of the widespread use and significance value of traditional medicines and the value of varying levels of evidence, have adopted standards for evaluating and approving the efficacy and safety of traditional herbal medicines. Acceptable forms of evidence include the following:

- Scientific evidence
- Expert opinion; contemporary clinical use by practitioners
- Historical and traditional data
- Ethnobotanical information

It is upon these forms of evidence that this book relies for its supporting data. Readers can determine for themselves whether the supporting evidence accompanying each herb, along with the safety data, adequately substantiates the use of that herb in the context of the practitioner's own practice and expectations of evidence.

Scientific Evidence

Scientific data included in this book may fall into any of the following categories:

- Meta-analyses of randomized controlled trials (RCT)
- Systematic reviews
- Individual RCTs
- At least one well-designed controlled study with expert recommendations
- Other types of well-designed experimental studies
- Other studies: open studies, comparative, correlation, case control, etc.; expert opinion of a committee
- Toxicology studies, in vivo and in vitro studies
- Animal studies*

*The author recognizes that many herbalists are philosophically opposed to the mistreatment of animals for the benefit of science, strongly favoring instead the development of harmless animal studies and ethical human study models. However, given the value of certain information derived from animal studies, for example, teratogenicity and mutagenicity studies, animal studies are regrettably included.

BOX **3-1**

Research Methods for Beginners

For those unfamiliar with research jargon, here is a brief overview of research methodologies and terminology. Research methods are categorized hierarchically in order of highest to lowest value of objectivity and reliability of the varying levels of evidence. The ''evidence pyramid'' is one such scheme for classifying research methods (Fig. 3-2).

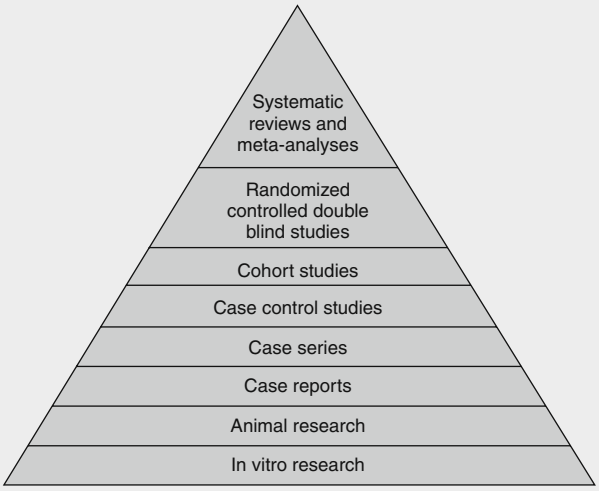


Figure 3-2 The evidence pyramid. (Courtesy of Suny Downstate Medical Center.)

Definitions

A *systematic review* is a method of reviewing multiple clinical trials using a system that minimizes study biases. It consists of a comprehensive survey of all of the primary studies of the highest level of evidence on a topic that have been systematically identified, ranked, and summarized according to explicit methodologies.

A *meta-analysis* is a survey in which the results of the studies included in the review are statistically similar and are combined and analyzed as if they were one study. Meta-analyses have several limitations: Studies rarely agree precisely and often sample sizes of single studies limit the conclusions that can be drawn; biases may be built in if authors selectively include studies that support their own conclusion; studies that demonstrate positive outcomes tend to be selectively published over those that do not; if several weak studies are combined, they may cumulatively give the impression of a strong study.

A *randomized controlled trial* (RCT) is comprised of two groups, a treatment group and a control group. The former receives the treatment being evaluated; the latter receives either no treatment or a default treatment. Participants are then randomly assigned to all groups.

A *double-blind study*, is one in which neither participant nor practitioner knows whether the participant is receiving the treatment being studied or the control treatment. This type of study is thought to be the most effective at eliminating confounding variables such as a placebo effect and bias.

In a *cohort study* participants with a specific condition or those receiving a particular treatment are followed over time and are compared with another group not affected by the condition or following the treatment. Cohort studies have a number of limitations, including possible variability between the two groups, and length of time for the studies, the latter that could lead to changes in participant condition as well as participants dropping out of the study.

Case control studies are those in which patients with a certain condition are compared with those who do not have the condition. Advantages are that they can be done quickly and do not require researchers to have special methods; rather, they depend more upon questionnaires. Case control studies are considered less reliable than RCTs and cohort studies.

Case series and *case reports* are either collections of reports on a series of patients, or a report on the treatment of a single patient. Case reports are considered to lack statistical validity because there are no control groups with which to compare study outcomes.

Problems with Conventional Research Methodologies for Botanical Therapies

Not all CAM therapies (i.e., prayer, homeopathy) are expected to stand up to classic methods of safety and efficacy testing. However, because herbs contain pharmacologically active substances, there is an implicit expectation that if herbs ''really work'' they should be able to measure up to the standards set for conventional drugs. Although this is theoretically sound, it is not reasonable in practice: Whole herbs are not the same as isolated drugs, nor are they applied as such by botanical medicine practitioners. A distinction can be made for single isolated active ingredients derived from botanicals, which are much more like pharmaceutical drugs than they are herbal products. RCTs for herbal products, in which all study group participants receive the same treatment are by definition given in a model antithetical to the way herbs are actually applied clinically by herbalists, wherein choice of herbs, formulation, and dosage are tailored specifically to the patient's unique needs.[6,9] There is also frequently a difference in the form of products used in clinical trials compared with those used by professional botanical medicine practitioners. Typically, botanical medicines are prescribed as multi-ingredient formulas, or as single herbs, in whole plant or whole plant extract forms that are most appropriate to the individual herb

and specific patient. For most herbs, the biological activities of the constituents have not yet even been well characterized.[10]

According to the WHO:

> *Experience has shown that there are real benefits in the long-term use of whole medicinal plants and their extracts, since the constituents in them work in conjunction with each other. However, there is very little research on whole plants because the drug approval process does not accommodate undifferentiated mixtures of natural chemicals, the collective function of which is uncertain. To isolate each active ingredient from each herb would be immensely time-consuming at unsupportable cost, and is almost impossible in the case of preparations.*[11]

Although RCTs may show positive effect, lack of positive RCTs does not mean inefficacy; it may simply indicate a lack of studies, or an inappropriately or ineffectively applied protocol. RCTs can only answer specific questions about general populations: Does this herb given in this group, at this time, in this form, and at this dose treat this condition? They do not answer specific questions about individual patients, and individual patient care is the crux of botanical medicine practice.

Limits of Research and Research Biases

Implicit in relying upon the results of RCTs and other classic trials is the belief that they represent unbiased analyses. This may be a mistaken assumption. Even the RCT, the gold standard of research methodologies and one of the most reliable methodologies for limiting study biases, is not impervious to bias and is not without limitations.[12] Methodologic features of RCTs, including trial quality, have been shown to influence effect sizes; and some researchers believe that eliminating the psychological component of clinical care from trials and minimizing placebo effect may cause studies to bear little resemblance to clinical practice.[13,14]

Politics also influences the choice of which studies get funded; what questions are asked; and whether, where, and how outcomes are published.[15] Limited financial incentive on the part of pharmaceutical companies and researchers to investigate herbal products, particularly whole herbs, is due in part to the limited patentability of botanicals, and leads to fewer funding opportunities.[16,17] Publication bias on the part of medical journals also has recently been raised as a significant concern. Additionally, there may be negative biases in the publication of case reports, with emphasis placed on the negative side effects of botanicals.[3] John Astin, MD writing on CAM, states that the ''approach of selectively citing one negative article while failing to cite any of the positive systematic reviews or meta-analyses is the antithesis of evidence-based medicine. It is, in short, opinion based medicine.''[2] He states further that ''The failure to cite such evidence contributes to a very misleading picture of the state of the scientific evidence base underlying CAM.''[2]

Frequently, herbal medicine as a whole is indicted on the basis of a small number of published negative case reports that are typically followed by a cascade of negative popular media. Although adverse effects and potential harm are rightfully brought to the attention of professionals and the public, there appear to be double standards in the reporting of the potential harmfulness of herbs compared with the volume and severity of reports on the risks of pharmaceutical medications.

Nonetheless, in spite of the billions of dollars of herbal products sold in the United States alone, there are negligible reports of adverse herbal events compared with the volume of reported adverse drug events. In Europe, where millions of units of herbal products are sold and market surveillance and adverse events reporting systems are well established, there too are an amazingly small number of adverse reports.[8] A major concern expressed about herbal medicine is the questionable safety of botanical medicines in pregnancy. Although indeed many are not to be used in pregnancy because of uncertainty about their safety, more than 90% of medications approved since 1980 have not been properly tested for mutagenicity or teratogenicity.[18] Further, a growing body of evidence suggests that only 20% to 37% of conventional medical practices that are commonly accepted and used across a broad range of medical specialties are predicated on evidence from RCTs. Coronary bypass surgery was used for over 20 years before it was subjected to clinical trials.[16,19,20] Although these statistics do not justify lack of evidence for nonconventional therapies, and do not negate the necessity for reliable clinical evidence, it does illustrate that there are sometimes double standards influencing attitudes about nonconventional therapies, and that there may at times be a suspension of common sense in pursuit of the holy grail of evidence (Box 3-2).

Expert Consensus

Well into the early twentieth century, observational studies were considered an important source of medical evidence, declining in perceived value only over the past 20 years.[12] Clinical decision making in medicine was based on observation, personal experience, and intuition.[12] Even the randomized controlled clinical trial (RCT) is only 50 years old and has been established as the definitive method of testing new drugs only since the 1980s.[21]

Although herbal medicine is frequently ''dismissed by the orthodoxy as a fringe activity,''[6] there are actually thousands of well-trained, highly knowledgeable and experienced clinical Western herbalists in numerous countries—England, Scotland, Germany, Australia, New Zealand, Canada, and the United States, to name a few. In Europe, particularly in Germany, phytotherapy is an accepted part of medical practice. Botanical experts are trained as either part of medical education if they are physicians, or in recognized botanical medicine educational programs with consistent curricula. In the United States, 13 states currently recognize naturopathic physicians who have graduated from accredited 4-year naturopathic colleges and passed their medical boards as legitimate physicians whose scope of practice includes botanical medicine. Over the past decade, a number of physicians have also gained significant experience in the clinical use of herbs. Although anecdotal evidence has largely been dismissed as invalid, the consensus of a large body of experts is entirely valid.

BOX **3-2**

A Satirical View of EBM

Parachute Use to Prevent Death and Major Trauma Related to Gravitational Challenge: Systematic Review of Randomized Controlled Trials

Gordon CS Smith, Jill P Pell

Abstract objectives: To determine whether parachutes are effective in preventing major trauma related to gravitational challenge.

Design: Systematic review of randomized controlled trials.

Data sources: Medline, Web of Science, Embase, and the Cochrane Library databases; appropriate internet sites and citation lists.

Study selection: Studies showing the effects of using a parachute during free fall.

Main outcome measure: Death or major trauma, defined as an injury severity score >15.

Results: We were unable to identify any randomized controlled trials of parachute intervention.

Conclusions: As with many interventions intended to prevent ill health, the effectiveness of parachutes has not been subjected to rigorous evaluation by using randomized controlled trials. Advocates of evidence-based medicine have criticized the adoption of interventions evaluated by using only observational data. We think that everyone might benefit if the most radical protagonists of evidence-based medicine organized and participated in a double-blind, randomized, placebo-controlled, crossover trial of the parachute.

BMJ 327: 1459-1461, 2003, http://www.bmj.com.

A large collective body of knowledge from contemporary clinical practitioners provides compelling evidence for the use of herbal medicines. Case studies (n = 1 studies), case series, uncontrolled trials, observational reports, and outcome-based studies all contribute important information to the dialogue on botanicals, ranging from establishing clinical effects that merit further study to providing clinical insights that corroborate traditional uses with modern pharmacologic effects.[22,23] ''Case study research provides a useful tool for investigation of unusual cases or therapies for which effectiveness data are lacking and for preliminary investigation of any factor that may influence patient outcome.'' Qualitative research methods need to be developed further to fully evaluate the efficacy and safety of nonconventional therapies.[21] Collaboration between conventionally trained researchers and traditional and medical herbalists to systematically document herbalists' clinical use of botanical medicines is a rich and yet untapped area for botanical medicine research.

This textbook draws extensively upon the valuable resource of ''contemporary clinical consensus'' (expert opinion), derived from communication with practitioners, surveys, published and unpublished reports, texts, training materials, and symposia.

Traditional Evidence

Historical information referred to in this text is largely derived from classical botanical medicine texts, treatises and herbals, pharmacopoeias, monographs, and academic books on the history of botanical medicines. These appear in the references corresponding to individual chapters. Herbalist Kerry Bone best explains traditional use:

> *Traditional use occurs in the context of a traditional medicine system. This healing system may have evolved over thousands of years and be part of a great culture, or it may be part of a smaller or more primitive system. The important point is that traditional use is the refined knowledge of many generations, carefully evaluated and re-evaluated by many practitioners of the craft. It is not just the anecdotal accounts of a few practitioners.*[24]

Bone defines folk use ''as small-scale use; often in an isolated context.. . . Folk use should therefore not be confused with traditional use. That is not to say that folk use is without value. More that it should be placed in the context of the hypothetical rather than the definite.''[24]

Traditional sources for this text include pharmacopoeias, classic texts on traditional Western herbal practices, and classic texts and materia medica from recognized traditional systems, for example Traditional chinese medicine (TCM) and Ayurveda. Additionally, herbs that are regulated as traditional medicines in nations with established traditional medicines categories are included as traditional medicines.

Ethnobotanical Evidence

Ethnobotanical evidence can be a useful source of information on the historic and cultural uses herbs—especially when illustrating the length of time for which an herb has been used or the diversity of cultures in disparate locations that have independently arrived at a similar use for a specific plant. However, unless how the herb was prepared for use is stated in the ethnobotanical reference, it is often difficult to extrapolate a practical, clinical application. Indigenous peoples commonly use plant medicines externally, ceremonially, and symbolically without the patient ingesting or medicinally applying the herb. Blowing the smoke of an herb over a patient or having the patient wear a piece of a root in a pouch as an amulet is drastically different than having the patient take a concentrated decoction of many grams of the roots. Ethnobotanical uses cited in this book imply ingestion or topical medicinal application of the book unless otherwise specified.

REFERENCES USED IN THE DEVELOPMENT OF THIS TEXT

The following were considered acceptable forms of references for inclusion in this text:

- Academic articles from peer-reviewed medical and CAM journals
- Classic botanical medicine texts and recognized pharmacopoeia

BOX 3-3

Integrative Medicine Texts, Herbal Texts, and Herbal Monographs Referenced in the Book

Barrett M: Handbook of Clinically Tested Remedies, vols 1 and 2, New York, 2004, Haworth Press.

Barton S: Clinical Evidence, London, 2001, BMJ Publishing Group.

Bruneton J: Pharmacognosy, Paris, 1999, Technique and Documentation.

Bruneton J: Toxic Plants Dangerous to Humans and Animals, Paris, 1999, Technique and Documentation.

Blumenthal M: The ABC Clinical Guide to Herbs, Austin, 2003, American Botanical Council.

Blumenthal M, Busse W, Goldberg A, et al.: The Complete German Commission E Monographs Therapeutic Guide to Herbal Medicines, Austin, 1998, American Botanical Council.

Blumenthal M, Goldberg A, Brinckmann J: Herbal Medicine: Expanded Commission E Monographs, Newton, MA, 2000, Integrative Medicine Communications.

Bone K: A Clinical Guide to Blending Liquid Herbs, St. Louis, 2003, Churchill Livingstone.

Bone K: Clinical Applications of Ayurvedic and Chinese Herbs, Queensland, AU, 2000, Phytotherapy Press.

European Scientific Cooperative on Phytotherapy (ESCOP): ESCOP Monographs: The Scientific Foundation for Herbal Medicinal Products, ed 2, New York, 2003, Thieme.

Evans WC: Trease and Evans' Pharmacognosy, London, 1998, Saunders.

Felter HW, JU Lloyd: King's American Dispensatory, vols 1 and 2, 1898, ed 18, Sandy Oregon, 1983, Eclectic Medical Publications.

Hoffmann D: Medical Herbalism: The Science and Practice of Herbal Medicine, Rochester, VT, 2003, Healing Arts Press.

Kligler B, Lee R: Integrative Medicine: Principles for Practice, New York, 2004, McGraw-Hill.

Kohatsu W: Complementary and Alternative Medicine Secrets, Philadelphia, 2002, Hanley & Belfus.

Kraft K, Hobbs C: Pocket Guide to Herbal Medicine, New York, 2004, Thieme.

LowDog T, Micozzi M: Women's Health in Complementary and Integrative Medicine: A Clinical Guide, St. Louis, 2004, Elsevier.

McGuffin M, Hobbs C, Upton R, et al.: American Herbal Products Association Botanical Safety Handbook, Boca Raton, 1997, CRC Press.

McKenna DJ, Jones K, Hughes K, et al.: Botanical Medicines: The Desk Reference for Major Herbal Supplements, New York, 2002, Haworth Press.

Mills S, Bone K: Principles and Practice of Phytotherapy, Edinburgh, 2000, Churchill Livingstone.

Moerman D: Native American Ethnobotany, Portland, 2000, Timber Press.

O'Dowd MJ: The History of Medications for Women: Materia medica woman, New York, 2001, Parthenon Publishing Group.

Rakel D: Integrative Medicine, Philadelphia, 2003, Saunders.

Rotblatt M, Ziment I: Evidence-Based Herbal Medicine, Philadelphia, 2002, Hanley & Belfus.

Upton R: American Herbal Pharmacopoeis and Therapeutic Compendium Series, Santa Cruz, CA, 2004, American Herbal Pharmacopoeia.

Weiss R, Fintelmann V: Herbal Medicine, ed 2, New York, 2000, Thieme.

Wichtl M: Herbal Drugs and Phytopharmaceuticals: A Handbook for Practice on a Scientific Basis, Stuttgart, 2004, Medpharm.

WHO: The World Health Organization Monographs, Geneva, WHO.

- Definitive evidence-based botanical medicine texts and reference books
- Recognized monographs (e.g., those published by AHP, ESCOP, and WHO)
- Ethnobotanical and historic references

Boxes 3-3 and 3-4 give a complete list of botanical medicine texts, monographs, and databases consulted for this book.

IS THERE ADEQUATE EVIDENCE FOR BOTANICAL MEDICINES?

Although it is frequently stated that botanical medicines are poorly studied, a quick examination of a comprehensive database (e.g. Ovid) should dispel that myth. In addition to clinical studies, there are numerous in vitro and in vivo human tissue, cell, and animal studies on herbal products and isolated constituents.[8] In Europe, clinical research into herbal medicine has been established for decades.[17] With the establishment of NCCAM, the priority for herbal research has continued to grow in the United States. Although there are a limited number of RCTs for most herbs, those that have been conducted should establish a compelling argument for the efficacy of herbal medicines. Efficacy studies and meta-analyses are growing in number and include positive reports in the Cochrane Collaboration on ginkgo for cognitive impairment and dementia, echinacea for cold treatment, St. John's wort for treatment of mild to moderate depression, and feverfew for the treatment of migraines, and RCTs for St. John's wort for treatment of mild to moderate depression, kava for anxiety, chaste tree berry for PMS, and horse chestnut for venous insufficiency, among others.[8,24]

It is also important to remember that few botanical approaches have been disproved or proved dangerous.[2] As conventional medicine moves toward a more

BOX **3-4**

Internet Databases Consulted in This Text

CAB Abstracts
http://www.cabi.org/

CINAHL
http://www.cinahl.com/

HerbMed
http://www.herbmed.org
Longwood Herbal Taskforce
http://www.mcphs.edu/

MD Consult
http://www.mdconsult.com/

Medline
http://www.ncbi.nlm.nih.gov/

Natural Standard
http://www.naturalstandard.com/

Ovid
http://www.ovid.com/

STATRef
http://www.statref.com/

integrated model of health care that incorporates herbal medicines, and as botanical medicine practitioners increasingly work with medical professionals, there will be an inherent need to blend languages and approaches to create a useful and mutually respectful paradigm. Change will have to be reflected not only in clinical and educational settings but also in research models. An inclusive, holistic interpretation of EBM allows the possibility of it being used as an ideal model incorporating the best available objective evidence (scientific, traditional, ethnobotanical, etc.) with practitioner experience and patient preferences and circumstances.

CONSTITUENTS OF MEDICINAL PLANTS

Lisa Ganora

An understanding of herbal constituents can help practitioners develop greater discernment in preparing and using botanical medicines. Phytochemistry focuses on the physical aspect of a plant's healing powers—the molecules and compounds behind observable qualities, actions, and clinical effects. These structures are readily identifiable on a sensory level, permitting organoleptic analysis of many herbs, imparting, for example, scent resulting from the small, volatile compounds in essential oils; bitter taste from certain lactones or alkaloids; colorful hues of light reflected by the antioxidant flavonoid pigments; and the slippery texture of the heteropolysaccharides known as mucilages. When approaching the study of phytochemistry in a holistic way, we transcend the world of dry abstraction and experience the tangible realm of what plants really do: We integrate sensory experience, beauty, and practical application with knowledge of the unseen architecture of life.

Naming an herbal constituent gives only a bare hint of its character, classification, relationships, and properties. No molecule exists naturally in isolation, and so must always be considered within the broader context of its biosynthetic origin, its companion molecules, and the plant matrix from which it arises. At the same time, the science of chemistry enables us to make fine distinctions on a very small scale. A sense of balance between details and context is important for incorporating phytochemical information into our knowledge base as practitioners. We must consider not only the structure of an individual compound, but also how this compound behaves in relationship to other molecules in the plant, the extract, the herbal formula, and the individual consuming the product.

Molecules are, profoundly and literally, patterns of energy in relationship. These patterns of energy interact with other patterns of energy—biological molecules—in the human body to effect changes in health. When reading the following material, try to keep this in mind. The molecular world is far more mystical, fluid, and dynamic than college chemistry classes might have suggested.

SYNERGY AND VARIABILITY

A living plant contains myriad compounds that work synergistically to protect the plant from harm and carry out all the processes of its metabolism. Interestingly, many of these molecules have similar functions in plants and humans. For instance, the berberine in *Mahonia aquifolium* (Oregon grape; Fig. 3-3) is an example of an antimicrobial compound that protects against fungal and bacterial infection in both plants and humans. Another example is the class of molecules known as flavonoids, which occur in all green plants. In the chloroplasts, flavonoids act as primary antioxidants to protect the delicate light-harvesting compounds from ultraviolet and free radical damage. In the human body, these same compounds act as antioxidants, anticarcinogens, and anti-inflammatories by virtue of their radical quenching activities.

From a practitioner's perspective, an herb is chosen for therapeutic effects based on its particular ''personality.'' Physically, this characteristic is encoded within the unique blend of constituents inside the plant. Rather than investing in the concept of active ingredients, we can more usefully entertain the idea of synergistic activity complexes: sets of constituents that may potentiate, stabilize, or attenuate each other to produce a characteristic set of herbal actions. As we discuss phytochemicals on an individual basis, we must always remember that the reductionist perspective provides only a small and relatively static snapshot of a dynamic and complex process. The scientific information concerning the properties of isolated phytochemicals must always be interpreted within a larger context.

Phytochemical variability is an important concern for the herbal practitioner. We must keep in mind that the chemical profile of a living plant is a system that constantly adapts to conditions in the environment. For example, seasonal variability is demonstrated in

Figure 3-3 Oregon grape (*Mahonia aquifolium*). (Photo by Martin Wall.)

Taraxacum officinalis (dandelion) by levels of the therapeutic oligosaccharide inulin (a soluble fiber) known to range from 2% to 40% in spring and fall roots, respectively. In this same herb, the levels of sesquiterpene lactones (digestive bitters) vary tremendously among the seasons, accounting for the sweetness of early spring leaves as opposed to their pronounced bitterness later in the summer. Along with seasonal variation, the herbalist must consider phytochemical variations owing to time of day, rainfall, soil composition, growing location, companion plants, fungi, and insects, developmental stage of the herb, and traditionalists might argue, phases of the moon, vitality of the plant, and energetic or spiritual relationships between the plant and the people who harvest and use its medicine. In addition, many species have chemotypes, or significantly differing chemical races, which may be difficult to distinguish visually. Therefore, proper growing conditions and harvesting time and techniques largely determine the efficacy of individual herb products, and any assessment of product quality must consider these variables.

It is interesting and important to consider that traditional rituals and prescriptions for botanical harvest and preparation have often taken such factors into account based on intuitive knowledge or empirical observations. Today, these abilities are supplemented by data from precise analytic evaluation. The three perspectives of tradition, organoleptics, and science can be combined to develop a holistic understanding of constituents and their significance in herbal medicine.

CONSTITUENT CLASSIFICATION

Constituents may be classified according to structural similarities, biosynthetic relationships, or therapeutic actions. For example, hamamelitannin, a compound from witch hazel (*Hamamelis virginiana*) could be classified as a hydrolyzable tannin (structural), a polyphenol (biosynthetic), or an astringent (action). In this scheme, the compounds are classified mainly from a biosynthetic perspective, which overarches and includes structural considerations; therapeutic actions often, but not always, fall in line with this approach. This classification helps us to understand the place of an individual compound within the entire panoply of medicinal metabolites.

A Word about Glycosides

There is often confusion about the meaning of the term *glycoside*. There is not a distinct phytochemical category for glycosides; rather, any type or class or molecule may occur in the form of a glycoside. Simply put, a glycoside is any molecule with one or more sugar groups attached. The molecule without its additional sugar group(s) is called an aglycone. For example, the purple anthocyanin compound called cyanidin can occur as a free aglycone, or in the form of numerous glycosides with various different sugar groups attached. Well-known groups of compounds such as the cyanogenic glycosides and the cardiac glycosides are best classified according to the structure of their aglycons: The former are amino acid derivatives, whereas the latter are steroidal compounds.

Herbal Constituent Categories

The main categories of herbal constituents are:
- Carbohydrates and derivatives
- Lipids
- Amino acids and derivatives
- Phenolic compounds
- Terpenes
- Steroidal compounds
- Alkaloids

Although there is considerable variation within each of these categories, the compounds are related by biosynthetic origin and basic structural organization. Within each major category are a number of distinct subcategories (because of space limitations, only the most prominent are listed here). Although they are related chemically, we cannot necessarily assume that all of the compounds within a subcategory have similar physiologic actions. For example, the beneficial anticancer lignans in flax (*Linum ussitissimum)* have a completely different character than the powerful cytotoxic lignan podophyllotoxin from mayapple (*Podophyllum peltatum*) or the suspected adaptogenic lignans in schisandra (*Schisandra chinensis*).

1. Carbohydrates and derivatives
   a. Monosaccharides: simple sugars, for example, glucose (first product of photosynthesis; human blood sugar) and fructose (fruit sugar)
   b. Disaccharides: composed of two simple sugars bonded together, for example, sucrose in *Saccharum* (sugar cane)
   c. Oligosaccharides: short chains of simple sugars, for example, inulin in dandelion (*Taraxacum officinale*) (Fig. 3-4, *A*) and chicory (*Cichorium intybus*) (Fig. 3-4, *B*)
   d. Polysaccharides: long chains of simple sugars, for example, mucilage in marshmallow (*Althea officinalis*), immunomodulating polysaccharides in echinacea (*Echinacea* spp.) (Fig. 3-5) or medicinal mushrooms; starch and cellulose
   e. Organic acids: derived from monosaccharides, for example, oxalic acid in sheep sorrel (*Rumex*); formic acid in nettles (*Urtica dioica*) stingers

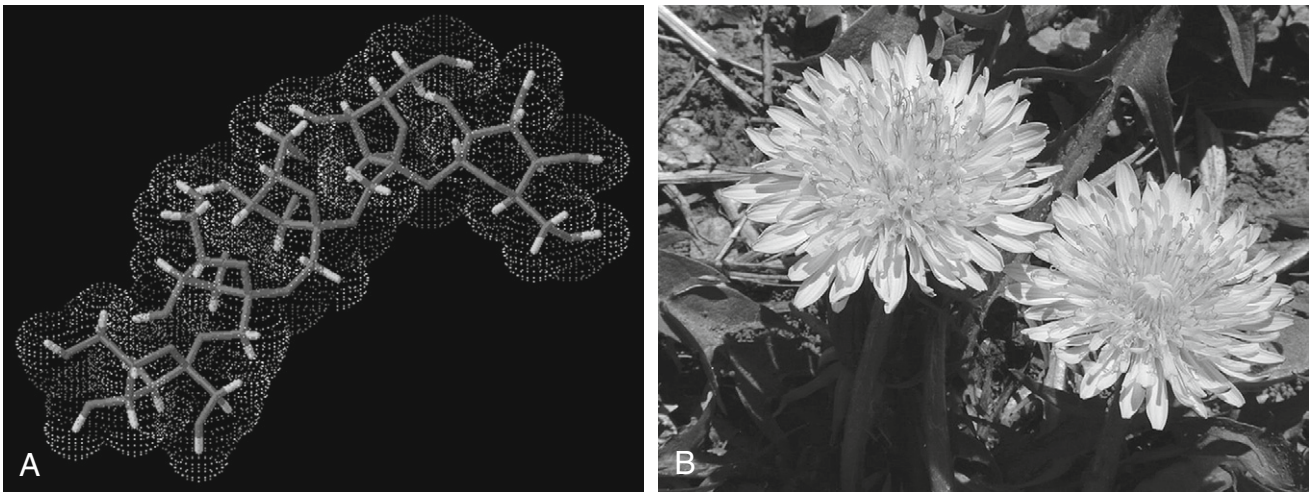


Figure 3-4 A, Inulin. (Courtesy Lisa Ganora.) **B, Dandelion (*Taraxacum officinale*).** (Photo by Martin Wall.)

Figure 3-5 Echinacea (*Echinacea pallida*). (Photo by Martin Wall.)

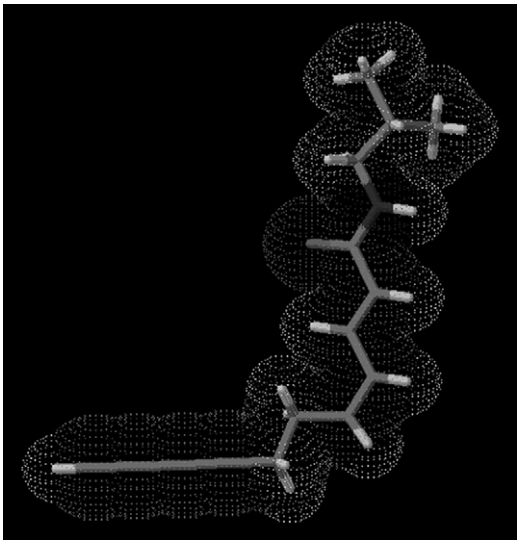


Figure 3-6 Isobutylamide molecule. (Courtesy Lisa Ganora.)

2. Lipids (sometimes called polyketides)
   a. Fatty acids: simple lipids, for example, ALA, GLA, DHA, EPA
   b. Triglycerides (triacylglycerols or neutral fats): main component of dietary oils such as olive oil
   c. Phospholipids: main component of cell membranes in plants and animals; for example, phosphatidylcholine (PC), phosphatidylserine (PS)
   d. Alkylamides: nitrogenous lipids with actions on the immune system, for example, isobutylamides in echinacea (*Echinacea angustifolia*; *E. purpurea*) (Fig. 3-6)
   e. Polyacetylenes: antimicrobial or toxic molecules with carbon-carbon triple bonds, for example, arctinal in burdock (*Arctium lappa*) seed
3. Amino acids and derivatives
   a. Amino acids: building blocks of proteins; precursors of many types of molecules; for example, phenylalanine, cysteine, lysine
   b. Sulfated amino acid derivatives: sulfur compounds in garlic and onions (*Allium* spp.) (Figure (Fig. 3-7), for example, allicin; glucosinolates and derivatives in cabbages, broccoli, mustards (*Brassica* spp.) species, for example, sulforaphane
   c. Cyanogenic glycosides: cyanide-generating compounds, for example, prunasin in wild cherry (*Prunus serotina*) (Fig. 3-8)
   d. Amines
      i. Aromatic amines: neuroactive compounds, for example, ephedrine in ephedra (*Ephedra sinensis*); histamine in nettles stingers
      ii. Methylxanthines: central nervous system stimulants, for example, caffeine in cofee (coffea theobroma); theophylline in tea (*Camellia sinensis*)
4. Phenolic compounds (sometimes called polyphenols)
   a. Phenolic acids and phenylpropanoids: variety of actions, for example, antioxidant chlorogenic

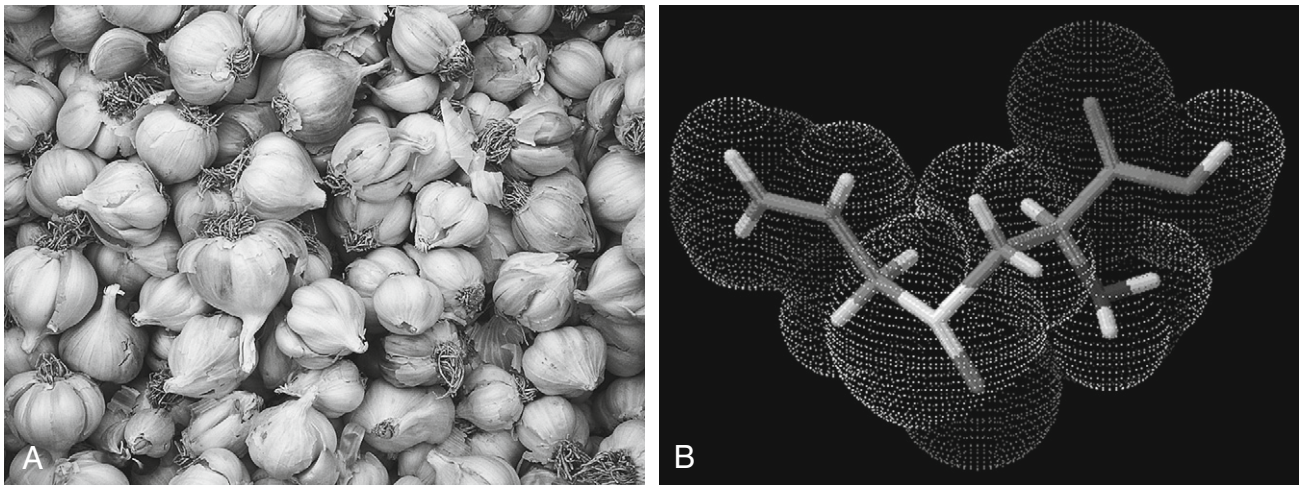


Figure 3-7 A, Garlic (*Allium sativum*). (Photo by Martin Wall.) **B, Alliin molecule.** (Courtesy Lisa Ganora.)

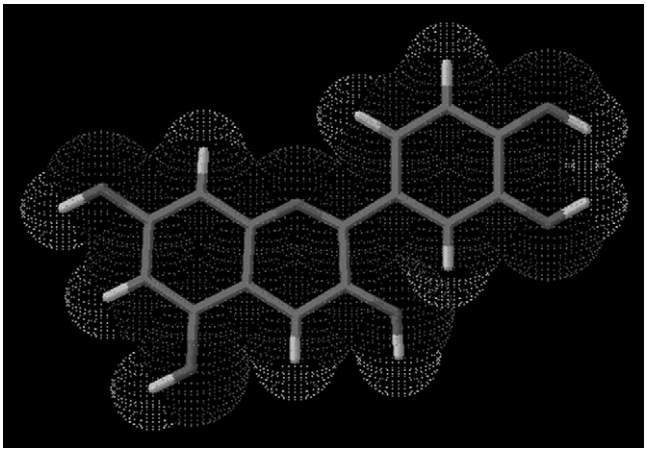


Figure 3-8 Cyanidin molecule. (Courtesy Lisa Ganora.)

acid in for example, blueberry, cranberry (*Vaccinium* spp.) carminative anethole in fennel (*Foeniculum vulgare*) seeds

b. Phenylpropanoid derivatives: for example, vasoactive capsaicin in cayenne (*Capsicum annum*); anti-inflammatory curcumin in tumeric (*Curcuma longa*)
c. Coumarins: venotonics such as aesculin in horse chestnut (*Aesculus hippocastanum)*; melilotoside in sweet clover (*Melilotus*). Note: coumarins per se are not blood thinners; dicoumarol, formed from them by fungal action in moldy dried plant material, is a potent anticoagulant and the molecular basis for the drug Coumadin.
d. Lignans: anticarcinogenic phytoestrogens, for example, secoisolariciresinol in Flaxseed; antioxidants, for example, NDGA in chaparral (*Larrea* spp.); wide variety of activities; some are toxic
e. Stilbenoids: antioxidant, anti-inflammatory, anti-mutagenic compounds, for example, resveratrol in grape skins and seed
f. Xanthones: yellow pigments, for example, the anti-depressant synergist norathyriol in St. John's wort (*Hypericum perforatum*); the hepatoprotective gentisin from gentian (*Gentiana lutea*)
g. Styrylpyrones: for example, the antispasmodic kavalactones in kava kava (*Piper methysticum*)
h. Flavonoids: thousands of compounds, generally antioxidant, anti-inflammatory, cardioprotective or hepatoprotective, and anticarcinogenic/carcinostatic; some are antispasmodic and antiallergenic as well
    i. Anthocyanins: for example, cyanidin in blue/purple/red fruits and berries such as elder berries *(Sambucus* spp.)
    ii. Chalcones and aurones: for example, the licochalcones from licorice (*Glycyrrhiza glabra)* root
    iii. Flavanols: for example, catechin from green tea
    iv. Flavanones: for example, hesperidin from *Citrus* species; flavanones are sometimes called citrus bioflavonoids or Vitamin P
    v. Flavonols: for example, quercetin from onion (*Allium sepa*)
    vi. Flavones: for example, apigenin from parsley (*Petroselinum* spp.)
    vii. Hydrolyzable tannins: for example, ellagitannins in strawberry (*Fragaria* spp.); gallotannins in oak bark (*Quercus* spp.)
    viii. Condensed tannins (including proanthocyanidins): for example, OPCs in grape skins and seeds; the flavins in black tea
i. Isoflavonoids: phytoestrogenic compounds, for example, genistein in soybean (*Glycine*), biochanin A in red clover (*Trifolium pratense*)
j. Benzofurans: rare; for example, the antibacterial usnic acid from usnea (*Usnea barbata*)
k. Chromones: also rare; for example, the cardiotonic and bronchodilatory khellin from khella (*Ammi visnaga*)
l. Quinones:
    i. Benzoquinones, for example, the cardioprotective coenzyme Q10
    ii. Naphthoquinones, for example, antifungal juglone from black walnut (*Juglans nigra*)

iii. Anthraquinones, for example, aperient emodin in yellow dock (*Rumex crispus*), cascarosides in cascara sagrada (*Frangulas purshiana*)

m. Phloroglucinol derivatives, rare; for example, the antidepressant synergist hyperforin in St. John's wort; the psychoactive THC in *Cannabis* spp.

5. Terpenes (sometimes called isoprenoids)
   a. Monoterpenes, small volatile molecules in the essential oils of many plants; for example, the anticarcinogenic limonene in *Citrus* peel; the antiemetic menthol in peppermint (*Mentha x piperita*)
      i. Iridoids (monoterpene lactones): for example, the mosquito-repellant nepetalactone from catnip (*Nepeta cataria*)
      ii. Secoiridoids: bitter compounds, for example, gentiopicrin from yellow gentian (*Gentiana luteum*)
   b. Sesquiterpenes: heavier volatile compounds in many essential oils; for example, the anti-inflammatory alpha-bisoprolol in chamomile (*Matricaria recutita*)
      i. Sesquiterpene lactones: digestive bitters such as lactucin from chicory; anti-inflammatory parthenolide from feverfew (*Tanacetum parthenium*)
   c. Diterpenes: resinous compounds, for example, the antitussive, antimicrobial grindelic acid in gumweed (*Grindelia* spp.)
   d. Triterpenes (including triterpene saponins): for example, triterpene glycosides in black cohosh (*Actaea racemosa*); saponins such as the anti-inflammatory, hepatoprotective, immunomodulant glycyrrhizin in licorice
   e. Tetraterpenes (carotenoids): oil-soluble antioxidant and anticarcinogenic compounds
   f. Lycopene, from tomatoes
      i. Carotenes: alpha-, beta-, delta-, and gamma-carotenes in orange/yellow vegetables and flowers and in green leaves
      ii. Xanthophylls (oxygenated carotenoids) including lutein and capsanthin (from red peppers, sweet or hot)
6. Steroidal compounds
   a. Phytosterols: cell-membembrane plant steroids analogous to cholesterol; for example, beta-sitosterol in saw palmetto (*Serenoa repens*) (Fig. 3-9)
   b. Steroidal saponins: for example, the adaptogenic ginsenosides from *Panax* species; the venotonic ruscogenin in butcher's broom (*Ruscus aculeatus*)
   c. Cardiac glycosides (cardenolides): potent cardioactive compounds including convallatoxin from lily-of-the-valley (*Convallaria majalis*) and digitoxin from foxglove (*Digitalis purpurea*)
7. Alkaloids (there are many subcategories; these are the most commonly encountered in herbalism)
   a. Betalain alkaloids: potent antioxidants/anticarcinogens including red/purple betalains from beets, poke week (*Phytolacca americana*) berries, and yellow betaxanthins from yellow beets and prickly pear cactus (*Opuntia ficus-indica*)
   b. Indole alkaloids: a large and varied class which includes potent compounds such as yohimbine from yohimbe (*Pausinystalia yohimbe*); the ergoline alkaloids from morning glory (*Ipomoea* spp.) and ergot fungus (*Claviceps*) fungi; quinine from *Cinchona* species; and reserpine from Indian snakeroot (*Rauwolfia serpentina*)
   c. Isoquinoline alkaloids: a large class which includes the familiar protoberberines—for example, berberine and hydrastine from goldenseal (*Hydrastis canadensis*); also includes sanguinarine from bloodroot (*Sanguinaria canadensis*) and eschscholzidine from California poppy (*Eschscholzia californica*) (Fig. 3-10); the morphinan alkaloids from opium poppy (*Papaver somniferum*) are isoquinoline derivatives
   d. Piperidine alkaloids: varied compounds including the bronchodilatory, antispasmodic lobeline from lobelia (*Lobelia inflata*); the highly toxic coniine from poison hemlock (*Conium*); and the pungent, absorption-enhancing piperine from black pepper (*Piper nigrum*)
   e. Pyrrolizidine alkaloids: toxicity varies considerably; the most toxic (for example, macrocyclic esters: senkirkine, retrorsine) are found in *Senecio*, *Heliotropium*, and *Crotalaria* spp.; others (for example, symphytine, intermedin) occur in comfrey (*Symphytum officinale*), borage (*Borago officinalis*), and other Boraginaceae; non-toxic PAs (for example, tussilagine) occur in *Echinacea* spp.
   f. Steroidal alkaloids: structurally related to steroidal saponins, these include the narcotic or toxic Solanaceous (Nightshade family) alkaloids such as solanine, solasodine, and tomatine
   g. Tropane alkaloids: potent neuroactive or psychoactive compounds such as hyoscyamine and scopolamine in deadly nightshade (*Atropa belladonna*), sacred jimsonweed (*Datura inoxia*), and henbane (*Hyoscyamus niger*)

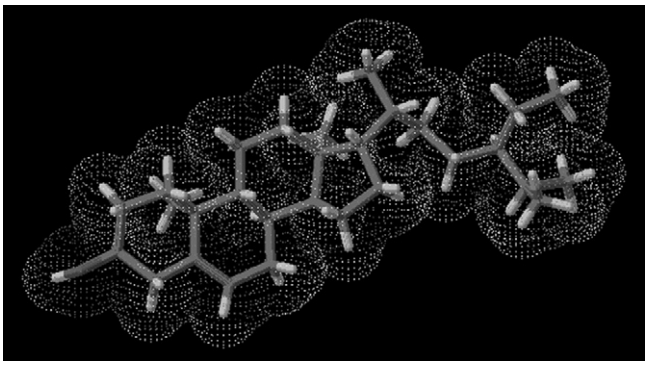


Figure 3-9 Beta-sitosterol molecule. (Courtesy Lisa Ganora.)

SOLUBILITY

The question often arises concerning whether the herbalist should use a water extraction (infusion, decoction, tea, or soup) versus an alcohol extraction (tincture, extract, or fluid extract) or some other type of material. There is a definite difference between these preparations; one brings a different range and concentration of constituents out of a plant than does another. Much of this difference is based on the solubility of the constituents within the

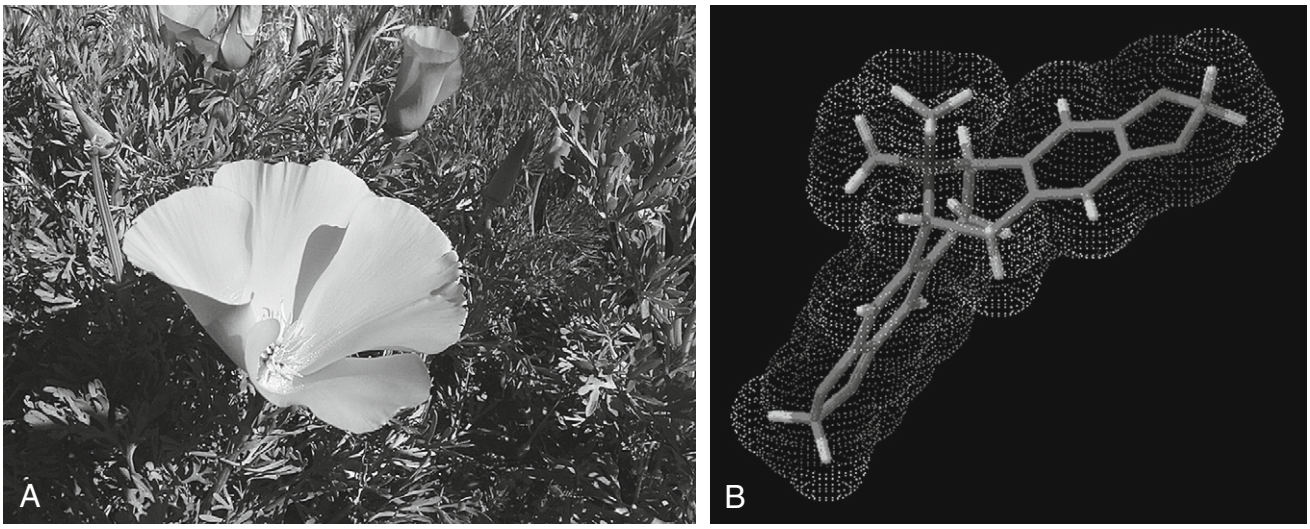


Figure 3-10 A, California poppy (*Eschscholzia californica*). (Photo by Martin Wall.) **B, Californidine molecule.** (Courtesy Lisa Ganora.)

herb. The solubilities of isolated constituents can be found in tables, but those values are subject to change within the matrices of different plants. In fact, they can vary considerably. Solubility is influenced by many factors, including pH, heat, concentration, and the presence of salts, tannins, and various other constituents. It can be difficult to predict, and practical experience, organoleptic evaluation, and analytical analysis must be used to determine which extraction methods are most efficacious for which compounds (see Forms of Administration).

Sometimes when different extracts are combined (or an extract is mixed with water), a precipitate forms; this cloudy or granular matter contains constituents that have suddenly become insoluble owing to changes in the overall properties of the solution. For example, polysaccharides often precipitate out of solution as the ethanol content is increased. Conversely, a high-alcohol resinous extract produces a milky precipitate in water as the resins fall out of solution. Another example is when alkaloids precipitate out of an acidic water solution as it becomes more basic.

The list given in Table 3-1 is oversimplified; there are numerous exceptions. It should be kept in mind that most compounds have at least some degree of solubility in water, alcohol, and oil menstrua. It is often more helpful to think of solubility on a continuum, rather than in absolute terms such as soluble or insoluble. For example, we may think of certain compounds as being only alcohol soluble or only oil soluble; but a small concentration of these molecules can dissolve in water as well.

THE ACTIONS OF HERBS

David Hoffmann

The therapeutic information throughout this textbook is presented in terms of both the actions of traditional herbal medicine and contemporary science. A table describing therapeutic goals and the corresponding therapeutic actions of herbs introduces the botanical protocol for each clinical condition, followed by more detailed traditional, pharmacologic, and clinical descriptions. This chapter presents a discussion of herbal actions from a traditional perspective, familiarizing the reader with this vocabulary. Herbal actions reflect observations of outcomes of herbal use, and the terms presented in the following, with a few exceptions, for example, adaptogen and phytoestrogen, have been used sometimes for centuries. Although the terms or concepts may seem archaic at times, for example, ''alterative,'' scientific research commonly bears out many of these traditional actions. Some of the actions are identical to those used in conventional medicine, for example, diaphoretic or antimicrobial, although the mechanisms of action of herbs may be similar or different to those of conventional medications. Clinically, the medical herbalist will find the actions to be relevant and useful descriptions that assist in the specific selection of herbs to match patients' conditions. Further, an understanding of these terms is essential to understanding numerous botanical texts, both old and modern, which employ them.

This section is not an exhaustive presentation of herbal actions nor the all of the herbs associated with each action; rather, it is an overview, focusing on terms and herbs that are relevant to the conditions presented in this book. It is divided into ''General Actions'' and ''Gynecologic and Obstetric Actions.'' General botanical textbooks such as *Principles and Practice of Herbal Medicine* and *Medical Herbalism* offer in-depth discussions of herbal actions and their relationship to botanical science.

GENERAL ACTIONS

Adaptogen

Soviet scientists coined the term *adaptogen* in 1964 to describe herbs that increase the body's nonspecific resistance and vitality, helping the body adapt to and defend against the effects of various stressors and increase work capacity and efficiency and ability to concentrate. (See Chapter 7 for a comprehensive discussion of adaptogens.)

TABLE 3-1

Solubility

LIQUID	SOLUBLE CONSTITUENTS
Water	Most carbohydrates (monosaccharides, oligosaccharides, polysaccharides); mucilages and gums in cold water; starch in hot water
	Organic acids (especially in basic solutions)
	Many polyphenols (especially glycosides) and flavonoids (generally more soluble in alkaline solutions); tannins (hydrolyzable and condensed) in hot water
	B complex vitamins and vitamin C
	Some alkaloids, including betalains and berberine (alkaloids in general are more soluble in acidic solutions)
	Aromatic amines (i.e., ephedrine), more so in acidic solutions
	Amino acids and proteins (including enzymes)
	Saponins (often foam when shaken in water)
	Salts of fatty acids in a basic solution (soaps)
	Monoterpenes and sesquiterpenes are soluble in steam (i.e., steam-distilled essential oils)
Ethanol or ethanol/water	Many alkaloids (generally around 50% ethanol/water ratio)
	Some polyphenols (especially aglycons) including stilbenoids, lignins
	Terpenes (including mono-, sesqui-, di-, and triterpenes), generally above 50% ethanol/water ratio
	Resins (need high ethanol/water ratio, approximately 90%)
Oil	Lipids including fatty acids
	Terpenes (including carotenoids and xanthophylls)
	Some polyphenols (especially aglycons), including some phenylpropanoids and derivatives
	Steroidal compounds (including phytosterols)
	Vitamins D, E (tocopherols, tocotrienols), A, K

For an herb to be classified as an adaptogen it must:
- Show nonspecific activity
- Have a normalizing influence independent of the nature of the pathological state
- Be innocuous and not influence normal body functions more than required

Adaptogens appear to moderate the stress response in the following ways:
- *More rapid but less exaggerated response:* Blood glucose rises more rapidly after the onset of stress, but does not rise as high.
- *More sustained peak:* Blood glucose is elevated (and thus available for cell function) for a longer period of time.
- *More gradual decline:* There is a less precipitous drop in blood glucose.

Adaptogens are used to minimize stress reactions and provide protection against the long-term effects of stress. These effects may be related to adaptogens' effects on glucose metabolism:
1. Increase blood glucose level by stimulating the liver to convert glycogen to glucose
2. Enhance the entry of glucose into cells
3. Enhance the utilization of glucose within cells

The specific mechanisms of adaptogenic activity have not yet been entirely elucidated, but some generalizations can be made. Pretreatment with adaptogens appears to alter endocrine functions of the pituitary adrenal gland axis. Regular pretreatment with adaptogens causes a normalization of stress hormone levels and a generally decreased predisposition to stress. Other body systems also respond to the direct or indirect regulatory influences of adaptogens. For example, adaptogens have been shown to influence the hypothalamic-pituitary-adrenal axis (HPA axis), to confer immunostimulatory actions, and to activate cognitive functions. A number of herbs can be described as adaptogens (Box 3-5 and Fig. 3-11), based upon both clinical and in vitro research.

Alterative

Alteratives "alter" the body's metabolic processes, improving a range of functions from nutrition to elimination (Box 3-6 and Fig. 3-12). Folk healing traditions sometimes invoke the concept of "blood cleansing," which, although hinting at much, is technically inaccurate, as blood does not require "cleansing." Traditionally, these herbs may have been used, along with bitters (see the following) for spring cleansing, or when there was infection or skin disease. Many of the herbs with this action help the body eliminate waste through the kidneys, liver, lungs, or skin. Some work by stimulating digestive function, some are immunomodulators, whereas others work through unknown mechanisms of action. Immunologic research on certain secondary plant products, especially saponins, has led to some interesting suggestions for the basis of alterative action; however, the specifics of plant activity are the result of the way the whole plant works upon the human body, not simply specific active ingredients. Alteratives can be used as supportive therapy in many diverse conditions, and should be considered first for cases of chronic inflammatory or degenerative diseases. These include skin diseases,

BOX 3-5

Adaptogenic Herbs

Eleuthero (*Eleutherococcus senticosus*)
Reishi (*Ganoderma lucidum*)
Licorice (*Glycyrrhiza glabra*) (Fig. 3-11)
Holy basil (*Ocimum sanctum*)
Korean ginseng (*Panax ginseng*)
American ginseng (*Panax quinquefolius*)
Rhaponticum (*Rhaponticum carthimoides*)
Rose stonecrop (*Rhodiola rosea*)
Schisandra (*Schisandra chinensis*)
Nettle (*Urtica dioica*)
Ashwagandha (*Withania somnifera*)

Figure 3-11 Licorice (*Glycyrrhiza glabra*). (Photo by Martin Wall.)

BOX 3-6

Alterative Herbs

Garlic (*Allium sativum*)
Burdock (*Arctium lappa*)
Wild indigo (*Baptisia tinctoria*)
Calendula (*Calendula officinalis*)
Echinacea (*Echinacea* spp.)
Cleavers (*Galium aparine*)
Golden seal (*Hydrastis canadensis*)
Blue flag (*Iris versicolor*) (Fig. 3-12)

Figure 3-12 Blue flag (*Iris versicolor*). (Photo by Martin Wall.)

Oregon grape (*Mahonia aquifolium*)
Yellow dock (*Rumex crispus*)
Blood root (*Sanguinaria canadensis*)
Figwort (*Scrophularia nodosa*)
Sarsaparilla (*Smilax* spp.)
Dandelion (*Taraxacum officinale*)
Red clover (*Trifolium pretense*)

various types of arthritis, and a wide range of autoimmune problems.

Analgesic

Analgesics (Box 3-7 and Fig. 3-13) relieve pain. Mild analgesic herbs are referred to as anodynes. Analgesic activity may be owing to anti-inflammatory action (*Dioscorea villosa*) or central effects (e.g., *Piscidea piscipula, Piper methysticum*) and can range from mild to strong effects. Most of the strongest herbal analgesics are no longer legally available for herbal prescription, such as opium poppy extracts and cannabis products. The action of analgesics is considered cooling.

Antiemetic/Antinauseant

These are herbs that alleviate nausea and prevent or reduce vomiting (Box 3-8 and Fig. 3-14). This property is generally the result of the presence of volatile oils in the plant, many of which have antispasmodic effect. They are relaxing to the digestive system, and in some cases have a direct action on the medulla (vomiting center) of the brain. They are useful in the treatment of morning sickness, hyperemesis gravidarum, motion sickness, chemotherapy-induced nausea, and nausea related to colds and general stomach upset.

Anti-Inflammatory

Anti-inflammatory herbs (Box 3-9 and Fig. 3-15) relieve inflammation, largely without the side effects of steroidal anti-inflammatory drugs. They are beneficial for relieving pain and discomfort, but offer the greatest benefit when used in combination with other remedies to address the underlying problems causing inflammation. Inflammation is a normal physiologic response to infection and other pathologies. Through localized biochemical and tissue changes, the inflammatory reaction facilitates healing. Sometimes however inflammation itself becomes so intense that it becomes part of the problem, and herbal remedies can be used to provide some measure of relief without full suppression. This can help to further facilitate the healing process, allowing the body to respond normally but without undue suffering or damage to the patient.

Anti-inflammatory herbs can be classified in terms of the body system (Table 3-2) or tissue for which they are most appropriate or by their pharmacologic mode of action. There are four primary categories of anti-inflammatory herbs:

- Salicylate-Containing Anti-Inflammatory Herbs
- Plants Containing Steroid Precursors
- Essential Oil-Rich Plants
- Resin-Containing Plants

Salicylate-Containing Anti-Inflammatory Herbs

Numerous herbs contain salicylic acid salts, the molecule from which aspirin was developed. These are most useful for musculoskeletal inflammations, such as arthritis. Herbs containing significant quantities of salicylic acid have a marked anti-inflammatory effect, without posing the dangers to the stomach associated with aspirin. In fact, *Filipendula ulmaria*, rich in salicylates, has been

BOX 3-7

Herbal Analgesics

Pulsatilla (*Anemone pulsatilla*)
Dong quai (*Angelica sinensis*)
Birch (*Betula* spp.)
Marijuana (*Cannabis sativa*)
Black cohosh (*Actaea racemosa*)
Corydalis (*Corydalis* spp.)
Wild yam (*Dioscorea villosa*)
California poppy (*Eschscholtzia californica*)
Rupturewort (*Herniaria glabra*)
Kava kava (*Piper Methysticum*)
Jamaican dogwood (*Piscidea piscipula*)
Willow (*Salix* spp.) (Fig. 3-13)
Black haw (*Viburnum opulus*)
Cramp bark (*Viburnum prunifolium*)
Ashwagandha (*Withania somnifera*)

Figure 3-13 Willow (*Salix* spp). (Photo by Martin Wall.)

BOX **3-8**

Herbal Antiemetics/Antinauseants

Marijuana (*Cannabis sativa*)
Cinnamon (*Cinnamomum zeylanicum*)
Chamomile (*Matricaria recutita*)
Peppermint (*Mentha piperita*) (Fig. 3-14)
Ginger (*Zingiber officinalis*)

Figure 3-14 Peppermint (*Mentha piperita*). (Photo by Martin Wall.)

used to staunch mild stomach bleeding. Other plants rich in these constituents include *Salix* spp., *Gaultheria procumbens*, *Betula* spp., and *Viburnum prunifolium*.

Plants Containing Steroid Precursors
Steroids were first isolated from plant material, and some herbs contain molecules that may be metabolized by the body into inflammation-fighting steroidal molecules. Herbs rich in these steroids are effective anti-inflammatories, and are especially useful in the treatment of inflammation of autoimmune origin. Examples are *Glycyrrhiza glabra* and *Dioscorea villosa*, which contains diosgenin.

Essential Oil-Rich Plants
Many aromatic herbs rich in essential oils have anti-inflammatory actions. One of the best of these remedies is *Matricaria recutita*, which is rich in terpenes such as bisabolol and chamazulene. These herbs are especially useful for digestive system inflammations when taken by mouth, for respiratory problems when inhaled in some form, and for skin inflammations when used topically. *Calendula officinalis* and *Hypericum perforatum* are other well-known plants containing oils that soothe and reduce inflammation.

Resin-Containing Plants
A number of resin-containing plants reduce inflammation in some areas of the body, but may cause gastric inflammation limiting their usefulness. Many, nonetheless, are invaluable in the treatment of arthritic conditions. Examples are *Menyanthes trifoliata*, *Harpagophytum procumbens*, and *Guaiacum officinale*. These herbs are not discussed further in this textbook.

Other Types of Anti-Inflammatory Herbs
As is usual with herbal remedies, no clear-cut chemical basis can be identified to explain the anti-inflammatory actions of some plants. Of the many remedies in this group, we can mention *Actaea racemosa*. Demulcent herbs often have an *apparently* anti-inflammatory effect, but this is related to their ability to soothe inflamed surfaces, not to reductions in the cellular inflammatory response (see demulcents).

Antimicrobial

Antimicrobial herbs (Box 3-10) help the body to destroy or resist pathogenic microorganisms, including bacteria, fungi, and viruses. It would be a mistake to attempt an overarching generalization about mechanisms of action for herbal antimicrobials. The use of the term *antimicrobial* is a description of expected outcome, rather than a description of mechanisms. Antimicrobial effects may be related to direct interactions with pathogens or indirectly mediated via the herb's interaction with the immune system. As examples of the diversity of mechanisms involved (Table 3-3), consider the following: *Melaleuca alternifolia* (tea tree) contains an oil rich in terpinene-4-ol that directly interferes with a pathogen's metabolism, thus killing it. Other herbs rich in volatile oils also work directly to kill microorganisms. Examples include *Allium sativum, Thymus vulgaris*, and *Eucalyptus* spp. *Echinacea* directly stimulates the body's own immune response, and thus is often an effective antimicrobial agent. *Vaccinium macrocarpon* (cranberry juice) blocks the adhesion of uropathogenic *E. coli* to the walls of the bladder, thus offering a useful treatment for cystitis.

Antispasmodic/Spasmolytic

Antispasmodic herbs (Box 3-11 and Fig. 3-16) relieve muscle tension and spasm, both in the musculoskeletal system and the smooth muscle of the hollow organs (i.e., bladder, uterus, stomach, intestine, gallbladder) (Table 3-4). The term *antispasmodic* is synonymous with

BOX **3-9**

Anti-Inflammatory Herbs

Yarrow (*Achillea millefolium*)
Black cohosh (*Actaea racemosa*)
Horse chestnut (*Aesculus hippocastanum*)
Lady's mantle (*Alchemilla arvensis*)
Marshmallow (*Althaea officinalis*)
Angelica (*Angelica archangelica*)
Dong quai (*Angelica sinensis*)
Birch (*Betula* spp.)
Borage (*Borago officinalis*)
Calendula (*Calendula officinalis*)
Green tea (*Camellia chinensis*) (Fig. 3-15)
Wild yam (*Dioscorea villosa*)
Echinacea (*Echinacea* spp.)
Meadowsweet (*Filipendula ulmaria*)
Cleavers (*Galium aparine*)
Licorice (*Glycyrrhiza glabra*)
Witch hazel (*Hamamelis virginiana*)
Devil's claw (*Harpagophytum procumbens*)
St. John's wort (*Hypericum perforatum*)
Lavender (*Lavendula officinalis*)
Chamomile (*Matricaria recutita*)
Peppermint (*Mentha piperata*)
White peony (*Paeonia lactiflora*)
Butterbur (*Petasites hybridus*)
Plantain (*Plantago major*)
Quaking aspen (*Populus tremuloides*)
Rehmannia (*Rehmannia glutinosa*)
Willow (*Salix* spp.)
Sage (*Salvia officinalis*)
Chinese skullcap (*Scutellaria baicalensis*)
Golden rod (*Solidago canadensis*)
Chickweed (*Stellaria media*)
Comfrey (*Symphytum officinale*)
Feverfew (*Tanacetum parthenium*)
Cramp bark (*Viburnum opulus*)
Black haw (*Viburnum prunifolium*)
Corn silk (*Zea mays*)
Ginger (*Zingiber officinale*)

Figure 3-15 Green tea (*Camellia chinensis*). (Photo by Martin Wall.)

spasmolytic. Uterine antispasmodics, which typically work on the bladder as well, are listed separately under gynecologic and obstetric actions. Antispasmodics usually have peripheral action and generally are not sedating.

Astringent

The basic action of astringents (Box 3-12 and Fig. 3-17) is to tonify or tighten tissue. They are sometimes called *styptics* when applied externally to stop bleeding, and *antihemorrhagics* when used for internal bleeding. Astringent action results from a diverse group of complex chemicals called tannins or gallotannins that share chemical and physical properties. All members of this group have phenolic characteristics, are soluble in water, and have molecular weights ranging from 500 to 3,000. There are two groups: derivatives of flavonols called *condensed tannins* and the more important

TABLE **3-2**

Body System Affinities of Anti-Inflammatory Herbs

BODY SYSTEM	EXAMPLES OF HERBS
Circulatory	*Tilia platyphyllos*, *Crataegus* spp., *Aesculus hippocastanum*, and *Achillea millefolium*
Digestive	*Matricaria recutita, Dioscorea villosa, Glycyrrhiza glabra, Hydrastis canadensis, Calendula*, and *Mentha piperita*. Demulcent remedies rich in mucilage, such as *Althaea officinalis*, can have the localized effect of reducing inflammation through contact soothing.
Urinary	*Solidago virgaurea*, *Zea mays*
Reproductive	*Alchemilla arvensis*, *Caulophyllum thalictroides*
Musculoskeletal	*Salix* spp., *Filipendula ulmaria*, *Populus tremuloides*, and *Betula* spp., *Harpagophytum procumbens*, *Actaea racemosa*, *Tanacetum parthenium*, and *Dioscorea villosa*
Nervous	*Hypericum perforatum*
Skin	*Calendula officinalis*, *Hypericum perforatum*, *Commiphora molmol*, *Hydrastis canadensis*, *Arnica montana*, *Stellaria media*, and *Plantago major*

BOX **3-10**

Herbal Antimicrobials

Yarrow (*Achillea millefolium*)
Garlic (*Allium sativum*)
Bearberry (*Arctostaphylos uva-ursi*)
Wormwood (*Artemisia absinthium*)
Wild indigo (*Baptisia tinctoria*)
Calendula (*Calendula officinalis*)
Myrrh (*Commiphora molmol*)
Goldthread (*Coptis chinensis*)
Echinacea (*Echinacea* spp.)
Eucalyptus (*Eucalyptus* spp.)
Reishi (*Ganoderma lucidum*)
Licorice (*Glycyrrhiza glabra*)
Goldenseal (*Hydrastis canadensis*)
St. John's wort (*Hypericum perforatum*)
Lavender (*Lavendula officinalis*)
Oregon grape (*Mahonia aquifolium*)
Tea tree (*Melaleuca alternifolia*)
Lemon balm (*Melissa officinalis*)
Peppermint (*Mentha piperata*)
Olive (*Olea europaea*)
Oregano (*Origanum vulgare*)
Aniseed (*Pimpinella anisum*)
Plantain (*Plantago major*)
Rosemary (*Rosmarinus officinalis*)
Sage (*Salvia officinalis*)
Blood root (*Sanguinaria canadensis*)
Thuja (*Thuja occidentalis*)
Thyme (*Thymus vulgaris*)
Usnea (*Usnea barbata*)
Cranberry (*Vaccinium macrocarpon*)

hydrolyzable tannins. The name *tannin* comes from the use of these constituents in the tanning industry. They have the effect of precipitating, or denaturing, protein molecules. They also precipitate starch, gelatin, alkaloids, and salts of heavy metals. One of the few incompatibilities

TABLE **3-3**

Body System Affinities for Antimicrobials

BODY SYSTEM	EXAMPLES OF HERBS
Urinary	*Arctostaphylos uva-ursi*, *Achillea millefolium*
Reproductive	*Calendula officinalis*, *Echinacea* spp., *Allium sativum*, *Thymus vulgaris*
Nervous	*Hypericum perforatum*, *Melissa officinalis*

found when making herbal medicines is that astringent, tannin-rich remedies create precipitates with herbs high in alkaloids. This alteration of protein is how animal skin is turned into leather. In other words, astringents produce a kind of temporary leather coat on the surface of tissue. Because of this activity, tannins have a number of therapeutic benefits. They:

- Reduce irritation on the surface of tissues through a sort of numbing action
- Reduce surface inflammation
- Create a barrier against infection, which is of great help for wounds and burns

Astringents have a role in a wide range of problems in many parts of the body (Table 3-5) but are of great importance in wound healing and conditions affecting the digestive system. In the gut, they reduce inflammation, improve symptoms of diarrhea, and are widely used in various diseases of digestion. However, long-term use as medicine or too much tea in the diet can be deleterious to health, as this will eventually inhibit proper food absorption across the gut wall.

Bitter

Quite simply, these are remedies that have a bitter taste, although their actions are anything but simple. These herbs (Box 3-13 and Fig. 3-18) can range from mildly bitter-tasting remedies, for example, *Achillea millefolium* and *Taraxacum officinale* leaf, to profoundly distasteful herbs, such as *Ruta graveolens* and *Artemisia absinthium*. The constituents that contribute bitterness to an herb

BOX 3-11

Antispasmodic Herbs

Angelica (*Angelica archangelica*)
Mugwort (*Artemisia vulgaris*)
Black cohosh (*Actaea racemosa*)
Wild yam (*Dioscorea villosa*)
Sundew (*Drosera rotundifolia*)
California poppy (*Eschscholzia californica*)
Fennel (*Foeniculum vulgare*)
Licorice (*Glycyrrhiza glabra*)
Hops (*Humulus lupulus*) (Fig. 3-16)

Figure 3-16 Hops (*Humulus lupulus*). (Photo by Martin Wall.)

St. John's wort (*Hypericum perforatum*)
Wild lettuce (*Lactuca virosa*)
Lavender (*Lavandula* spp.)
Motherwort (*Leonurus cardiaca*)
Lobelia (*Lobelia inflata*)
Chamomile (*Matricaria recutita*)
Peppermint (*Mentha piperita*)
Catnip (*Nepeta cataria*)
Aniseed (*Pimpinella anisum*)
Kava-kava (*Piper methysticum*)
Jamaican dogwood (*Piscidia erythrina*)
Skullcap (*Scutellaria lateriflora*)
Skunk cabbage (*Symplocarpus foetidus*)
Feverfew (*Tanacetum parthenium*)
Thyme (*Thymus vulgaris*)
Linden (*Tilia platyphyllos*)
Damiana (*Turnera diffusa*)
Cramp bark (*Viburnum opulus*)
Black haw (*Viburnum prunifolium*)
Ginger (*Zingiber officinale*)

are described as *bitter principles*. Taste is a phenomenon of chemoreception; a range of molecular structures share the bitter property. Great diversity and complexity are found among these bitter principles, but it appears that they all work in a similar way by triggering a lingual sensory response. Examples of such constituents include

TABLE 3-4

Body System Affinities with Antispasmodics/ Spasmolytic

BODY SYSTEM	EXAMPLES OF HERBS
Cardiovascular	*Leonurus cardiaca*, *Viburnum opulus*, *Actaea racemosa*
Digestive	*Matricaria recutita*, *Viburnum opulus*, *Viburnum prunifolium*, *Valeriana officinalis*, *Humulus lupulus*, *Mentha piperita*, *Salvia officinalis*, *Foeniculum vulgare*, *Dioscorea villosa*
Urinary	*Viburnum opulus*, *Viburnum prunifolium*, *Dioscorea villosa*, *Piper methysticum*
Reproductive	*Viburnum opulus*, *Viburnum prunifolium*, *Dioscorea villosa*, *Actaea racemosa*
Musculoskeletal	*Piper methysticum*, *Viburnum opulus*, *Viburnum prunifolium*, *Lobelia inflate*, *Valeriana officinalis*, *Scutellaria lateriflora*, *Actaea racemosa*

monoterpenes, iridoids, sesquiterpenes, and alkaloids. Absinthin, found in plants of the genus *Artemisia*, such as *Artemisia absinthium*, is so bitter it can be tasted at dilutions of 1:30,000! A reflex is stimulated by bitter taste, directed by the nerves to the central nervous system. From there, a message goes to the gut, giving rise to the release of the digestive hormone gastrin. This in turn leads to a whole range of effects, all of value to the digestive process. Among the many actions of bitters, they:

- Stimulate appetite
- Stimulate release of digestive juices from the pancreas, duodenum, and liver
- Aid the liver in detoxification work and increase the flow of bile
- Help regulate secretion of pancreatic hormones that regulate blood sugar, insulin, and glucagon
- Help the gut wall repair damage

The tonic effects of these remedies go beyond specific digestive hormone activity. As digestion and assimilation of food is basic to health, bitter stimulation can often fundamentally affect health far beyond the simple mechanics of digestion (Table 3-6). In general, these benefits do not occur unless the bitter herb is tasted, so they should not be given in a capsule intended to help the patient avoid the unpleasant taste.

There are a number of contraindications to the use of bitters. Do not use bitters in the following conditions:

- Pregnancy
- Kidney stones
- Gallbladder disease
- Gastroesophageal reflux
- Hiatal hernia
- Gastritis
- Peptic ulcer disease

BOX **3-12**

Herbal Astringents

Yarrow (*Achillea millefolium*)
Horse chestnut (*Aesculus hippocastanum*)
Uva ursi (*Arctostaphylos uva-ursi*)
Green tea (*Camellia sinensis*)
Shepherd's purse (*Capsella bursa-pastoris*)
Horsetail (*Equisetum arvense*)
Cranesbill (*Geranium maculatum*)
Witch hazel (*Hamamelis virginiana*)
Bayberry (*Myrica cerifera*)
Plantain (*Plantago major*)
Oak (*Quercus* spp.) (Fig. 3-17)

Figure 3-17 Oak (*Quercus* spp.). (Photo by Martin Wall.)

Raspberry (*Rubus idaeus*)
Blackberry (*Rubus villosus*)
Sage (*Salvia officinalis*)
Goldenrod (*Solidago virgaurea*)

TABLE **3-5**

Body System Affinities with Astringents

BODY SYSTEM	EXAMPLES OF HERBS
Digestive	*Quercus* spp., *Hamamelis virginiana*, *Geranium maculatum*, *Hydrastis canadensis*, *Salvia officinalis*
Urinary system	*Equisetum arvense*, *Achillea millefolium*
Reproductive	*Alchemilla arvensis*, *Hydrastis canadensis*, *capsella burso-postoris*, *Achillea millifolium*
Skin	*Achillea millefolium*, *Hamamelis virginiana*, *Plantago major*, *Quercus* spp.

Cardiac Herbs

Some of the remedies in this group (Box 3-14 and Fig. 3-19) are powerful cardioactive agents, such as *Digitalis* (foxglove), whereas others are gentle and generally safe cardiotonics, like *Crataegus* (hawthorn) and *Tilia* (linden):

- *Cardiotonic*. These are plants that have an observable beneficial action on the heart and blood vessels but do not contain cardiac glycosides. How they work is either completely obscure or an area of pharmacologic debate, but flavones appear to be major contributors to their beneficial actions. Examples of traditionally used cardiotonic herbs in Western herbalism are *Crataegus, Tilia platyphyllos, Allium sativum*, and *Leonurus cardiaca*.
- *Cardioactive*. These plants owe their effects on the heart to their content of cardiac glycosides, and thus have both the benefits and drawbacks of these constituents. The main danger is that glycosides will accumulate in the body, as their elimination rates tend to be low. Clinically trained phytotherapists prefer to use *Convallaria majalis* over *Digitalis*, as there is less chance of such problems developing. However, without appropriate training as to the safe use of *Convallaria*, phytotherapists should avoid the use of this herb, too.

Care must be taken with these herbs, particularly when patients are on cardiac medications or have cardiac conditions.

Carminative

Carminatives (Box 3-15 and Fig. 3-20) are specifically antispasmodic to the bowel, easing cramping, griping, and the discomfort caused by flatulence. Their mode of action appears related to the complex of volatile oils they contain. These terpene oils have local anti-inflammatory and antispasmodic effects upon the mucous lining and muscle layers of the alimentary canal. An example is farnesene, a constituent of many complex plant volatile oils with carminative actions, such as *Matricaria recutita*. *Origanum compactum* is a species of oregano used as an antispasmodic remedy for the gastrointestinal tract, especially in Morocco. Belgian researchers have found that the infusion of flowers and leaves inhibits contractions triggered in guinea pig ileum by acetylcholine,

BOX 3-13

Herbal Bitters

Yarrow (*Achillea millefolium*)
Wormwood (*Artemisia absinthium*)
Mugwort (*Artemisia vulgaris*)
Berberry (*Berberis vulgaris*)
Centaury (*Centaurium erythraea*)
Boneset (*Eupatorium perfoliatum*)
Gentian (*Gentiana lutea*)
Golden seal (*Hydrastis canadensis*)
Horehound (*Marrubium vulgare*)
Chamomile (*Matricaria recutita*)
Rue (*Ruta graveolens*)
Tansy (*Tanacetum vulgare*) (Fig. 3-18)
Dandelion (*Taraxacum officinale*)

Figure 3-18 Tansy (*Tanacetum vulgare*). (Photo by Martin Wall.)

histamine, serotonin, nicotine, 1,1-dimethyl-4-phenylpiperazine iodide, and even electrical stimulation. The main active components in the essential oil were identified as thymol and carvacrol. This example may help explain the well-known actions of all of the carminative remedies.

TABLE 3-6

Body System Affinities for Bitters

BODY SYSTEM	EXAMPLES OF HERBS
Cardiovascular	*Humulus lupulus*, *Valeriana officinalis*
Digestive	*Artemisia vulgaris*, *Berberis vulgaris*, *Centaurium erythraea*, *Chelidonium majus*, *Gentiana lutea*, *Hydrastis canadensis*, *Humulus lupulus*
Reproductive	*Leonurus cardiaca*, *Artemisia vulgaris*, *Achillea millefolium*
Nervous	*Gentiana lutea*, *Artemisia vulgaris*
Skin	*Taraxacum officinalis*, *Arctium lappa*

Cholagogue

Cholagogues (Box 3-16) have the specific effect of stimulating the flow of bile from the liver. Most bitters and hepatics are also cholagogues. These herbs are of great help to digestion, assimilation, and elimination.

Cholagogues are contraindicated in the presence of the following conditions:

- Painful gallstones
- Acute bilious colic
- Obstructive jaundice
- Acute cholecystitis, unless gallstones have been ruled out
- Acute viral hepatitis
- Liver disorders

Demulcent

Demulcent herbs (Box 3-17 and Fig. 3-21) soothe and protect irritated or inflamed tissue. When used topically, they are called emollients. As with many other herbal actions, pharmacology does not provide an adequate explanation for how demulcents work. They are rich in carbohydrate mucilage made up of complex polysaccharide molecules. Thus, they become slimy and gummy when they come in contact with water. This physical property has a clear and direct action on the lining of the intestines, where it soothes and reduces irritation by direct contact. However, some demulcents have similar actions far from the site of their absorption into the body, for example, the urinary tract or lungs (Table 3-7). Clearly, these remedies do not work through a direct action, because the mucilage breaks down into its constituent parts as it is absorbed, and thus cannot soothe by direct contact with the target tissue. However, there is no doubt that some herbs do act as demulcents to the urinary tract or lungs—it is simply unclear how they do so. In general, all mucilage-containing demulcents have the following general properties:

- Reduce irritation down the whole length of the bowel
- Lessen the sensitivity of the digestive system to gastric acids and to digestive bitters
- Help prevent diarrhea secondary to inflammation/irritation

BOX **3-14**

Cardiovascular Herbs

Yarrow (*Achillea millefolium*)
Horse chestnut (*Aesculus hippocastanum*)
Garlic (*Allium sativum*)
Cayenne (*Capsicum annuum*)
Coleus (*Coleus forskolii*)
Lily of the valley (*Convallaria majalis*) (Fig. 3-19)

Figure 3-19 Lily of the valley (*Convallaria majalis*). (Photo by Martin Wall.)

Hawthorn (*Crataegus* spp.)
Ginkgo (*Ginkgo biloba*)
Motherwort (*Leonurus cardiaca*)
Bugleweed (*Lycopus* spp.)
Lemon balm (*Melissa officinalis*)
Rosemary (*Rosmarinus officinalis*)
Linden (*Tilia platyphyllos*)

BOX **3-15**

Herbal Carminatives

Dill (*Anethum graveolens*)
Angelica (*Angelica archangelica*)
Caraway (*Carum carvi*)
Cinnamon (*Cinnamomum* spp.)
Cardamon (*Elettaria cardamomum*)
Fennel (*Foeniculum vulgare*)
Hops (*Humulus lupulus*)
Chamomile (*Matricaria recutita*)
Lemon balm (*Melissa officinalis*)
Peppermint (*Mentha piperita*)
Aniseed (*Pimpinella anisum*) (Fig. 3-20)

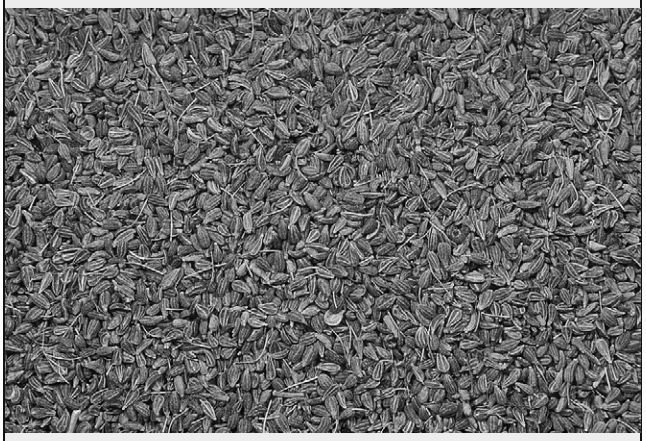


Figure 3-20 Aniseed (*Pimpinella anisum*). (Photo by Martin Wall.)

Sage (*Salvia officinalis*)
Thyme (*Thymus* spp.)
Valerian (*Valeriana officinalis*)
Ginger (*Zingiber officinale*)

- Reduce digestive muscle spasms that cause colic
- Ease coughing by soothing bronchial tension
- Relax painful spasms in the bladder and urinary system, and sometimes even in the uterus

Diuretic

Strictly speaking, a diuretic (Box 3-18) is a remedy that increases urination. In the ancient traditions of herbal medicine, the term *diuretic* tends to be applied more broadly to herbs that have some sort of beneficial action on the urinary system (Table 3-8). Thus, the term may be used to describe not only true diuretics, but also urinary demulcents and anti-inflammatory remedies. Needless to say, this can lead to confusion when selecting remedies for a particular individual. (Table 3-9). Many diaphoretic herbs act as diuretics when taken cold. The term *diuretic* is used in the strict sense throughout this textbook. When urinary antispasmodics, tonics, or demulcents are required, these terms are specified.

BOX 3-16

Herbal Cholagogues

Wild indigo (*Baptisia tinctoria*)
Barberry (*Berberis vulgaris*)
Celandine (*Chelidonium majus*)
Balmony (*Chelone glabra*)
Fringe tree bark (*Chionanthus virginicus*)
Artichoke (*Cynara scolymus*)
Wild yam (*Dioscorea villosa*)
Boneset (*Eupatorium perfoliatum*)
Fumitory (*Fumaria officinalis*)
Gentian (*Gentiana luteaa*)
Golden seal (*Hydrastis canadensis*)
Blue flag (*Iris versicolor*)
Butternut (*Juglans cinerea*)
Black root (*Laplander virginica*)
Oregon mountain grape (*Mahonia aquifolium*)
Lemon balm (*Melissa officinalis*)
Boldo (*Peumus boldus*)
Rosemary (*Rosmarinus officinalis*)
Yellow dock (*Rumex crispus*)
Sage (*Salvia officinalis*)
Dandelion (*Taraxacum officinale*)

There are number of ways to categorize diuretics, but first, an important distinction must be made between two broad groups of plant diuretics:

- Plants that act as diuretics by increasing kidney blood flow
- Plants that reduce water reabsorption in the nephrons of the kidney

The first group of herbs includes not only diuretics but also all cardioactive and circulatory stimulant herbs. These increase blood flow to the kidney through effects on the heart or other parts of the body. Because more blood passes through the kidney, more urine is produced. Caffeine-containing herbs, such as tea and coffee, also have this effect. The second group may work via many different means, but as is often the case with medicinal plants, a dearth of research in this area limits the value of taking an overtly pharmacologic perspective.

Hepatic

Hepatic herbs (Box 3-19) stimulate or support liver function in a range of ways. Traditionally, they were considered to tone, strengthen liver function, and, in some cases, increase the flow of bile (also see Bitter). They are also classically included as primary components of treatments for skin conditions. Little is known about their mechanisms of action; however, they are widely used by herbalists for the treatment of gynecologic conditions in which there is hormonal dysregulation. Although there is no apparent justification for such use, this nearly ubiquitous practice in Western herbal medicine may stem from the belief that improved liver function may lead to improved hormonal conjugation and elimination. Western herbs such as *Leonurus cardiaca* and *Taraxacum officinale* are commonly used this way, as is the TCM herb *Bupleurum falcatum*, in combination with other TCM or Western herbs. The hepatic herbs listed in Box 3-19 are otherwise not largely used this way gynecologically but are used to improve digestion and phase 1 and 2 detoxification (Table 3-10).

BOX 3-17

Herbal Demulcents

Marshmallow (*Althaea officinalis*)
Oat (*Avena sativa*)
Iceland moss (*Cetraria islandica*)
Irish moss (*Chondrus crispus*)
Licorice (*Glycyrrhiza glabra*)
Flax (*Linum usitatissimum*)
Comfrey (*Symphytum officinale*) (Fig. 3-21)

Figure 3-21 Comfrey (*Symphytum officinale*). (Photo by Martin Wall.)

Coltsfoot (*Tussilago farfara*)
Slippery elm (*Ulmus rubra*)
Mullein (*Verbascum thapsus*)
Cornsilk (*Zea mays*)

TABLE **3-7**

Body System Affinities for Demulcents

BODY SYSTEM	EXAMPLES OF HERBS
Digestive	*Symphytum officinale*, *Althaea officinalis*, *Cetraria islandica*, *Chondrus crispus*, *Glycyrrhiza glabra*, *Linum usitatissimum*, *Ulmus rubra*
Urinary	*Althea officinalis*
Skin	*Symphytum officinale*, *Althaea officinalis*, *Plantago major*, *Stellaria media*, *Ulmus rubra*

BOX **3-18**

Herbal Diuretics

Buchu (*Agathosma betulina*)
Celery seed (*Apium graveolens*)
Juniper (*Juniperus communis*)
Pellitory of the wall (*Parietaria judaica*)
Parsley (*Petroselinum crispum*)
Boldo (*Peumus boldus*)
Saw palmetto (*Serenoa repens*)
Dandelion (*Taraxacum officinale leat*)
Linden (*Tilia platyphyllos*)
Corn silk (*Zea mays*)

TABLE **3-8**

Types of Urinary Tract Herbs

ACTION	HERBS
Anti-inflammatory	*Arctostaphylos uva-ursi*, *Galium aparine*, *Zea mays*, *Althea officinalis*
Antilithic	*Collinsonia canadensis*, *Eupatorium purpureum*
Antimicrobial	*Achillea millefolium*, *Arctostaphylos uva-ursi*, *Vaccinium macrocarpon*
Astringent	*Achillea millefolium*, *Arctostaphylos uva-ursi*, *Equisetum arvense*
Demulcent	*Arctostaphylos uva-ursi*, *Zea mays*

Hepatoprotective herbs (Box 3-20), which are given their own separate category, specifically serve as antioxidants, and support phase 1 and phase 2 detoxification, whereas actually protecting the hepatocytes from oxidative and other damage. Vegetables in the *Brassicacae family* (e.g., broccoli, kale, collard greens, cabbage) are also hepatoprotective.

Laxatives

Herbal laxatives (Box 3-21) can act owing to chemical constituents in the herb, usually anthraquinones, that stimulate bowel peristalsis—some quite aggressively (purgatives) or gently (aperients)—or they can work by the simple mechanism of providing lubrication or bulk, which has a mechanical and not chemical action in the bowel. The aperients and bulk laxatives are useful for constipation that may accompany menstrual complaints such as PMS or uterine fibroids or that may occur during pregnancy. They are taken as teas for best results.

TABLE **3-9**

Body System Affinities for Diuretics

BODY SYSTEM	EXAMPLES OF HERBS
Bladder	*Vaccinium macrocarpon*, *Achillea millefolium*, *Zea mays*, *Arctostaphyl uvarursi*
Cardiovascular	*Convallaria majalis*, *Taraxacum officinale*, *Achillea millefolium*
Skin	*Galium aparine*, *Taraxacum officinale*

BOX **3-19**

Hepatic Herbs

Yarrow (*Achillea millefolium*)
Agrimony (*Agrimonia eupatoria*)
Oregon grape (*Berberis aquifolium*)
Barberry (*Berberis vulgaris*)
Centaury (*Centaurium erythraea*)
Balmony (*Chelone glabra*)
Fringe tree (*Chionanthus virginicus*)
Tumeric (*Curcuma longa*)
Artichoke (*Cynara scolymus*)
Gentian (*Gentiana lutea*)
Golden seal (*Hydrastis canadensis*)
Motherwort (*Leonurus cardiaca*)
Yellow dock (*Rumex crispus*)
Milk thistle (*Silybum marianum*)
Dandelion (*Taraxacum officinale*)

TABLE **3-10**

Body System Affinities for Hepatic Herbs

BODY SYSTEM	EXAMPLES OF HERBS
Digestive	*Agrimonia eupatoria*, *Berberis vulgaris*, *Juglans cinerea*, *Taraxacum officinale* root, *Chionanthus virginicus* bark, *Gentiana lutea*
Reproductive	*Hydrastis canadensis*, *Berberis vulgaris*
Skin	*Iris versicolor*, *Taraxacum officinale*, *Hydrastis canadensis*, *Mahonia aquifolium*, and *Rumex crispus*

BOX 3-20

Hepatoprotective Herbs

Calendula (*Calendula officinalis*)
Tumeric (*Curcuma longa*)
Rosemary (*Rosmarinus officinalis*)
Schizandra (*Schisandra chinensis*)
Milk thistle (*Silybum marianum*)

BOX 3-21

Laxatives

Herbal Aperients
Licorice (*Glycyrrhiza glabra*)
Yellow dock (*Rumex crispus*)
Bulk laxatives
Flax seed
Psyllium seed

Demulcent laxatives
Irish moss (*Chondrus crispus*)
Licorice (*Glycyrrhiza glabra*)
Slippery Elm bark (*Ulmus rubra*)

TABLE 3-11

Body System Affinities for Nervines

BODY SYSTEM	EXAMPLES OF HERBS
Cardiovascular	*Melissa officinalis*, *Tilia platyphyllos*, and *Leonurus cardiaca*
Digestive	*Melissa officinalis*, *Matricaria recutita*, and *Lavandula* spp., *Humulus lupulus*, *Valeriana officinalis*
Reproductive	*Actaea racemosa*, *Caulophyllum thalictroides*, *Viburnum* spp., *Leonurus cardiaca*
Musculoskeletal	*Actaea racemosa*, *Viburnum prunifolium*
Skin	All nervines may help the skin in an indirect way, but the following have a good reputation for skin conditions: *Scutellaria lateriflora*, *Hypericum perforatum*, and *Actaea racemose*

Nervines

A nervine is an herb with a beneficial effect upon the nervous system, generally relaxing or restorative in nature. Nervines are commonly included in many formulae for any number of conditions, or given as a separate formula, as many illnesses are accompanied by a stress component, affect sleep, or are stressful (Table 3-11). Nervines are divided into a number of categories based on their effects, some of which are elaborated in Table 3-12 (Fig. 3-22).

TABLE 3-12

Nervine Categories

NERVINE ACTION	HERBAL EXAMPLES
Antispasmodic	*Piper methysticum*, *Valeriana officinalis* (Fig. 3-22), *Viburnum opulus*, *Actaea recemosa*, *passiflora incornata*
Antidepressant	*Hypericum perforatum*, *Melissa officinalis*
Adaptogen	*Withania somnifera*
Analgesic	*Piscicida erythrina*, *Gelsemium sempervirens*
Anxiolytic	*Piper methysticum*, *passiflora incarnata*
Relaxant	*Passiflora incarnata*, *Scutellaria lateriflora*, *Valeriana officinalis*, *Verbena officinalis*
Sedative	*Humulus lupulus*, *Passiflora incarnata*, *Valeriana officinalis*
Stimulant	*Coffea arabica*, *Camelia sinensis*, *Cola vera*, *Paulinia cupana*
Tonic	*Avena sativa*, *Hypericum perforatum*, *Scutellaria lateriflora*, *Adaptogens* (see Adaptogen)

Figure 3-22 Valerian (*Valeriana officinalis*). (Photo by Martin Wall.)

Nervine Tonics

Perhaps the most important contribution herbs can make to the whole field of neurology lies in their ability to strengthen and nourish the nervous system. They are commonly prescribed in cases of emotional or mental stress or nervous debility. This invaluable group of tonic remedies is best exemplified by *Avena sativa*, which has no additional relaxing or stimulating effects. Nervine tonics that also have a relaxing effect include *Scutellaria lateriflora* and *Hypericum perforatum*.

Nervine Relaxants

This group of nervines (Box 3-22) are most important in times of stress, overwhelm, and confusion. They are used in a broad holistic way to promote calm and rest at lower doses and gentle sleep at higher doses. Many nervine relaxants can be selected on the basis of their secondary actions to treat additional problems. This is one of the great benefits of using herbal remedies to help with stress and anxiety. In addition to the herbs that work directly on the nervous system, antispasmodic herbs—those that affect the peripheral nerves and the muscle—may have an indirect relaxing action on the whole system. Putting the physical body at ease promotes ease in the psyche. Many nervine relaxants have this antispasmodic action. Sedating herbs (Box 3-23), or hypnotics, can be used to induce deeper relaxation when there is extreme tension, inability to sleep, or pain.

Anxiolytic Herbs

Herbs in this category (Box 3-24) are used to relieve the mental and physical symptoms of anxiety. They are generally not sedating or consciousness impairing at lower doses, at which they can be used regularly to relieve chronic anxiety. They can be applied at higher doses or higher dose frequencies for relief of acute anxiety.

Antidepressant Herbs

Much media attention and scientific research has gone into the herb St. John's wort, which is the most widely used antidepressant agent in all of Europe, for the treatment of mild to moderate depression. The actions of most herbs used as antidepressants have not been elucidated. St. John's wort contains active ingredients that appear, among other actions, to act as MAO inhibitors. The historical use of this herb as an antidepressant is ancient, long preceding the existence of psychiatry as a medical field. Depression, as with other conditions in the herbal clinic, is treated comprehensively, with attention to the whole patient, not just his or her neurotransmitters. Herbs play a small but important role in the botanical clinical treatment of depression (Box 3-25 and Fig. 3-23).

GYNECOLOGIC AND OBSTETRIC ACTIONS

Aphrodisiacs

Herbal aphrodisiacs (Box 3-26) have a long history of use both as sexual stimulants for pleasure's sake and for the

BOX 3-22

Nervine Relaxants

Pulsatilla (*Anemone pulsatilla*)
Milky oats (*Avena sativa*)
Black cohosh (*Actaea racemosa*)
California poppy (*Eschscholzia californica*)
Hops (*Humulus lupulus*)
St. John's wort (*Hypericum perforatum*)
Lavender (*Lavandula* spp.)
Motherwort (*Leonurus cardiaca*)
Lobelia (*Lobelia inflata*)
Chamomile (*Matricaria recutita*)
Lemon balm (*Melissa officinalis*)
Passion flower (*Passiflora incarnata*)
Kava (*Piper methysticum*)
Jamaican dogwood (*Piscidia erythrina*)
Pulsatilla (*Pulsatilla vulgaris*)
Skullcap (*Scutellaria lateriflora*)
Wood betony (*Stachys betonica*)
Linden (*Tilia platyphyllos*)
Damiana (*Turnera diffusa*)
Valerian (*Valeriana officinalis*)
Vervain (*Verbena officinalis*)
Cramp bark (*Viburnum opulus*)
Black haw (*Viburnum prunifolium*)
Ashwagandha (*Withania somnifera*)
Zizyphus (*Zizyphus spinosa*)

BOX 3-23

Sedatives

Pulsatilla (*Anemone pulsatilla*)
Corydalis (*Corydalis ambigua*)
California poppy (*Eschscholtzia californica*)
Hops (*Humulus lupulus*)
Jamaican dogwood (*Piscidea erythrina*)
Valerian (*Valeriana off.*)
Ashwagandha (*Withania somnifera*)

BOX 3-24

Anxiolytic Herbs

California poppy (*Eschscholtzia californica*)
Lavender (*Lavendula officinalis*)
Motherwort (*Leonurus cardiaca*)
Chamomile (*Matricaria recutita*)
Passion flower (*Passiflora incarnata*)
Kava kava (*Piper methysticum*)
Skullcap (*Scutellaria lateriflora*)
Valerian (*Valeriana officinalis*)
Blue vervain (*Verbena officinalis*)
Ashwagandha (*Withania somnifera*)

BOX **3-25**

Antidepressants

St. John's wort (*Hypericum perforatum*)
Lavender (*Lavendula officinalis*)
Motherwort (*Leonurus cardiaca*)
Lemon balm (*Melissa officinalis*)
Passion flower (*Passiflora incarnata*) (Fig. 3-23)
Kava kava *Piper methysticum*)
Ashwagandha (*Withania somnifera*)

Figure 3-23 Passion flower (*Passiflora incarnata*). (Photo by Martin Wall.)

treatment of sexual debility. Numerous herbs from many cultures are ascribed with the ability to improve sexual function. Few of these have significant research or clinical trials behind them. Their activity is variously attributed to stimulating action, especially the warming, spicy and fragrant herbs; kidney tonic function, improved strength of the reproductive/sexual activities; nervine relaxation activity, improved vaginal tissue tone and lubrication; and increased pelvic circulation.

BOX **3-26**

Herbal Aphrodisiacs

Garlic (*Allium sativum*)
Dong quai (*Angelica sinensis*)
Shatavari (*Asparagus racemosus*)
Milky oats (*Avena sativa*)
Marijuana (*Cannabis* spp.)
Cinnamon (*Cinnamomum* spp.)
Cardamom (*Elettaria cardamomum*)
Epimedium (*Epimedium aceranthus*)
Longan (*Euphoria longan*)
Licorice (*Glycyrrhiza glabra*)
Wolf berry (*Lycium chinense*)
Ginseng (*Panax ginseng*)
Yohimbe (*Pausinystalia yohimbe*)
Ho shou wu (*Polygonum multiflorum*)
Rehmannia (*Rehmannia glutinosa*)
Schisandra (*Schisandra chinensis*)
Saw palmetto (*Serenoa serrulata*)
Tribulus (*Tribulus terrestris*)
Damiana (*Turnera aphrodisiaca, T. diffusa*)

Emmenagogue

Strictly speaking, emmenagogues (Box 3-27 and Fig. 3-24) are herbs that stimulate menstrual flow, and are typically used to treat amenorrhea. Several are abortifacient; thus, emmenagogues are contraindicated in pregnancy. In TCM, the concept of an emmenagogue is applied to those herbs that increase general blood flow, for example, *Salvia miltiorrhiza*, and may be used for gynecologic purposes, but also to improve cardiovascular function. Today, many herbals use the term *emmenagogue* broadly to denote remedies that tone and normalize the function of the female reproductive system; however, this is inaccurate. Of the many plants that stimulate menstruation, some also have a tonic effect. Some appear to work through hormonal activity, and others through local irritation, whereas some may have effects on coagulation or uterine circulation. They should be used with great care.

Galactagogue

Galactagogues (Box 3-28) stimulate the production or flow of breast milk in lactating women. They may act hormonally, or may include herbs that are nutritive, to improve milk quality and quantity. Nervines are commonly combined with galactagogues to encourage relaxation and thereby facilitate the letdown reflex.

Hormonal Regulator

Many claims are be made about plants that affect hormonal balance (Box 3-29), but we will limit our discussion here to those that have an observable influence. Little endocrine research has been undertaken on herbs, so it is impossible to be specific about their actions. Thus, the herbalist usually talks in terms of *hormonal*

BOX 3-27

Herbal Emmenagogues

Dong guai (*Angelica sinensis*)
Mugwort (*Artemisia vulgaris*) (Fig. 3-24)

Figure 3-24 Mugwort (*Artemisia vulgaris*). (Photo by Martin Wall.)

Blue cohosh (*Caulophyllum thalictroides*)
Cotton root (*Gossypium herbaceum*)
Motherwort (*Leonurus cardiaca*)
Pennyroyal (*Mentha pulegium*)
Rue (*Ruta graveolens*)
Sage (*Salvia officinalis*)
Feverfew (*Tanacetum parthenium*)
Tansy (*Tanacetum vulgare*)
Ginger (*Zingiber officinale*)

BOX 3-28

Galactogogue Herbs

Marshmallow (*Althea officinalis*)
Milky oats (*Avena sativa*)
Fennel (*Foeniculum vulgare*)
Chamomile (*Matricaria recutita*)
Anise seed (*Pimpinella anisum*)
Fenugreek (*Trigonella foenum graceum*)
Chaste berry (*Vitex agnes-castus*)

BOX 3-29

Hormone-Regulating Herbs

Dong quai (*Angelica sinensis*)
Blue cohosh (*Caulophyllum thalictroides*)
False unicorn (*Chamaelirium luteum*)
Black cohosh (*Actaea racemosa*)
Wild yam (*Dioscorea villosa*)
Fennel (*Foeniculum vulgare*)
Soy (*Glycine max*)
Licorice (*Glycyrrhiza glabra*)
Motherwort (*Leonurus cardiaca*)
White peony (*Paeonia laterflora*)
Sarsaparilla (*Smilax ornata*)
Tribulus (*Tribulus terrestris*)
Red clover (*Trifolium pratense*)
Blue vervain (*Verbena officinalis*)
Chaste berry (*Vitex agnus castus*)

BOX 3-30

Ovarian Tonic Herbs

Blue cohosh (*Caulophyllum thalictroides*)
White peony (*Paeonia lactiflora*)
False unicorn (*Chamaelirium luteum*)
Chaste berry (*Vitex agnes-castus*)

modulator or *hormonal regulator*. The most important of these herbs in the European tradition is *Vitex agnus-castus*.

Ovarian Tonics

Herbs in this category (Box 3-30) have demonstrated or alleged direct or indirect stimulating effects on the ovaries and are thus used when there is hormonal dysregulation at the level of the ovary, infertility, when there is poor ovarian circulation suspected, and when there are ovarian cysts or endometriosis of the ovary.

Oxytocic or *Partus Preparator*

These are herbs (Box 3-31) that have been used to promote or increase uterine activity, facilitating labor or expulsion of the placenta. (See Chapters 12 and 15 for a complete discussion of this category of herbs.)

BOX 3-31

Oxytocic/spikenard (*Partus Preparator* Herbs

Spikenard (*Aralia racemosa*)
Blue cohosh (*Caullophylum thalictroides*)
Cotton root (*Gossypium herbaceum*)
Partridge berry (*Mitchella repens*)
Schisandra (*Schizandra chinensis*)

Phytoestrogen

This is a relatively new term in the herbal nomenclature, referring to herbs that contain isoflavones with estrogen-like activity. Many herbs in this category are legumes, such as soy and red clover. Several volatile oil-rich herbs may also have estrogen activity, such as anise seed and fennel. A great deal of attention has been directed toward research on the potential health benefits of phytoestrogens for the prevention of a variety of conditions and diseases, especially menopausal complaints, cancer, and osteoporosis, as well as their risks. Other herbs, for example, black cohosh and dong quai, which have been proposed to act as SERMS (Selective Estrogen Receptor Modulators), have not been found to have hormonal activity.

Uterine Astringent/Antihemorrhagic

A number of herbs (Box 3-32 and Fig. 3-25) are used to reduce uterine blood loss whether related to menorrhagia, metrorrhagia, or organic disease, such as fibroids. How these herbs work is an important but unanswered question. No astringent tannin can reach uterine tissue from the gut. It is possible that some, but not all, of these herbs have some kind of hormonal effect. Of the many valuable remedies listed as astringents earlier in this chapter, perhaps the most valued is *Achillea millefolium*.

Uterine Antispasmodic

There are a number of valuable remedies (Box 3-33) that impact the complex autonomic innervation and smooth musculature of the reproductive system. These are used for the treatment of dysmenorrhea, endometriosis, chronic pelvic pain, irritable uterus of pregnancy, painful labor contractions, and other painful or spasmodic conditions of the uterus.

Uterine Circulatory Stimulant

These herbs (Box 3-34) are a subset of uterine tonics, and are used to improve circulation to the uterus when there is ischemic pain, for example, with dysmenorrhea. They are also used to improve circulation in order to reduce uterine/pelvic congestion, such as with uterine fibromyomas. They are mostly contraindicated during pregnancy unless otherwise specified [i.e., *Zingiber officinalis* for nausea and vomiting of pregnancy (NVP)].

Uterine Tonic

The term emmenagogue is sometimes used to describe herbs that are actually uterine tonics (Box 3-35) but that do not necessarily stimulate menstrual flow. These are plants that have a toning, strengthening, nourishing effect upon both the tissue and function of the female reproductive system. We do not have a good understanding of how and why they work, but this should not invalidate their observed therapeutic value. They are commonly applied for conditions such as endometriosis,

BOX 3-32

Uterine Astringent/Antihemorrhagic Herbs

Yarrow (*Achillea millefolium*)
Lady's mantle (*Alchemilla vulgaris*)
Shepherd's purse (*Capsella bursa-pastoris*)
Cinnamomum spp.
Erigeron canadensis
Cranesbill (*Geranium maculatum*)
Hamamelis virginiana
Myrica cerifera
Panax notoginseng
Rubus idaeus
Trillium erectum (Fig. 3-25)

Figure 3-25 *Trillium erectum.* (Photo by Martin Wall.)

BOX 3-33

Uterine Antispasmodic Herbs

Black cohosh (*Actaea racemosa*)
Pulsatilla (*Anemone pulsatilla*)
Dong quai (*Angelica sinensis*)
Corydalis (*Corydalis ambigua*)
Wild yam (*Dioscorea villosa*)
Motherwort (*Leonurus cardiaca*)
Chamomile (*Matricaria recutita*)
White peony (*Paeonia lactiflora*)
Jamaican dogwood (*Piscidea piscipula*)
Cramp bark (*Viburnum opulus*)
Black haw (*Viburnum prunifolium*)

uterine fibromyomas, dysmenorrhea, metrorrhagia, dysfunctional uterine bleeding, and other conditions in which the uterus is ''boggy,'' there is regularly excessive bleeding, or there are pain and spasmodic activity. For the, latter, they are often combined with uterine antispasmodics.

BOX 3-34

Uterine Circulatory Stimulant Herbs

Dong quai (*Angelica sinensis*)
Peony (*Paeonia* spp.)
Ginger (*Zingiber officinalis*)
Cinnamon (*Cinnamomum cassia*)
Motherwort (*Leonurus cardiaca*)

BOX 3-35

Uterine Tonic Herbs

Black cohosh (*Actaea racemosa*)
Yarrow (*Achillea millefolium*)
Lady's mantle (*Alchemilla vulgaris*)
Dong quai (*Angelica sinensis*)
Blue cohosh (*Caulophyllum thalictroides*)
False unicorn (*Chamaelirium luteum**)
Goldenseal (*Hydrastis candensis*)
Motherwort (*Leonurus cardiaca*)
Partridge berry (*Mitchella repens*)
Raspberry leaf (*Rubus idaeus*)
Bethroot (*Trillium erectum*)
Black haw (*Viburnum opulus*)
Cramp bark (*Viburnum prunifolium*)

*False unicorn is an endangered botanical, therefore, use only cultivated herbal products.

SELECTION CRITERIA, FORMULATION, AND PRESCRIBING

Aviva Romm

Herbal medicine encourages the physician to treat the patient as an individual and, hence, to switch from a fixed therapy regimen to a more individualized type of therapy.

—Rudolph Weiss[26]

The herbal products market offers patients and practitioners an overwhelming array of formulae from which to choose for virtually any conceivable condition. Some products based on traditional formulation principles and herbal indications, but many are based primarily on marketing trends and, sometimes, misinformation. Understanding the principles of herbal formulation allows the practitioner to effectively understand and evaluate formulas, both their individual ingredients and how they work as a whole, selecting those that might offer benefit to their patients, as well as rejecting those that are ineffective at best, and potentially harmful at worst.

Building a successful herbal formula—determining the correct herbs, their correct proportions, and the dosing strategy—is a central skill in herbal medicine practice. It is in custom formulation that herbal medicine is most tailored to patients' unique needs, and most greatly departs from conventional medical care with its standardized prescriptions. It is also where much of the science with which we struggle to validate herbal medicine efficacy becomes limited and we are forced to rely on practitioner experience and tradition.[26,27]

There are numerous factors to consider when choosing which herbs to include in a formula, the exact proportions of all of the herbs, and the prescribing schedule. Dosing is discussed separately in this chapter.

SELECTION CRITERIA

Multiple factors influence the selection of herbs for the individual patient, including the patient's condition, the system of herbal medicine used by the practitioner, the actions of specific herbs and the systems they affect, the availability, ecology, cost, and likelihood of compliance with various protocols (Table 3-13).

TABLE 3-13

Summary of Factors Affecting Herb Selection Criteria

FACTOR	DESCRIPTION
Individual patient's condition	Accurate diagnosis, understanding of underlying or concomitant factors, history, etc.
Herbal medicine system	Assessment of patient and understanding and prescribing of herbs is consistent with an herbal medicine system or context (i.e., Western herbal medicine, TCM, Ayurveda)
Herbal actions	Understanding the pharmacologic, biologic, traditional, and synergistic actions of herbal medicines
Availability	Patients' ability to obtain ingredients in herbal formulae
Financial considerations	Patients' ability to afford herbal formulae in adequate amounts and for adequate durations for efficacy
Ecological considerations	Use of herbs that are not endangered or rare; recognizing the intrinsic relationship between planetary health and individual in medical health choices
Compliance and aesthetics	Patients' ability to adhere to protocol, based on ease of obtaining and preparing herbs and palatability

Prescribing for the Individual Patient's Condition

The most important factor determining the selection of herbs is the patient's condition, both currently and constitutionally. This is determined by differential diagnosis and physical assessment, the patient's overall health status (current and past medical history), and an understanding of underlying factors associated with the disease or disorder process, including but not limited to health of the major body systems (i.e., whether there are chronic digestive or circulatory problems) and social, emotional, and psychological stressors and factors affecting the patient.

The Herbal Medicine System

The system of herbal medicine to which the practitioner subscribes determines the language of the diagnosis, which in turn influences the selection of herbs and/or the rationale for their use. For example, a Western biomedical herbal practitioner diagnosing a patient with symptoms of vaginal itching, yellowish-white discharge, and frequent urination might diagnose *vaginal candidiasis*, whereas a TCM practitioner might diagnose the same patient damp heat and blood deficiency. Although there is some crossover in the herbs that are selected by each practitioner (e.g., both may end up with a berberine-containing herb in the final formula, perhaps *Coptis chinensis* [goldthread] or *Hydrastis canadensis* [goldenseal]), the language to describe their inclusion differs. The Western practitioner would include one of these herbs for their antimicrobial, anti-inflammatory constituents; the TCM practitioner would describe these same effects as ''heat clearing'' and ''cooling.'' The TCM practitioner might also include herbs that nourish the blood, such as a combination of *Angelica sinensis* and *Rehmannia glutinosa* as part of a larger formula for treating the perceived underlying blood deficiency. The Western practitioner may also separately provide tonics for the patient with recurrent problems with vaginal candidiasis.

Practitioners must define for themselves the system of herbal medicine they are using, and from this they can define the language that will shape their system of herb selection. This book focuses primarily on a Western system of herbal medicine, using both Western biomedical knowledge of herbs, as well as traditional Western herbal philosophies. Additionally, representing the synthesis of herbal traditions that now comprises Western herbal medicine, herbs from the Chinese and Indian materia medica are included, based on both their traditional uses and actions, and modern pharmacologic understanding of these herbs.

The Herbs and Their Actions

Integral to the ability to create an herbal formula is knowledge of the properties, actions, appropriate indications, and contraindications of each herb. The American Herbalists Guild, the oldest and largest professional organization for herbal practitioners in the United States, requires their professional members to have a working knowledge of at least 150 different herbs. The British medical herbalist regularly uses more than 250 herbs in practice, and a TCM practitioner might select from among 2000 different medicines in the Chinese pharmacopoeia.[28] This breadth of knowledge is something that comes with time and experience, as well as a great deal of study. Practitioners must also have on hand a selection of reliable reference books, including materia medica, monographs, and pharmacopoeias. At first, the practitioner frequently refers to these books but over time gains intimate knowledge of a wide variety of herbs that allow more spontaneity in formula development. However, even experienced practitioners regularly turn to their reference books.

Practitioners learn a great deal about the actions and energetics of herbs from their own clinical observations and those of their colleagues. For example, the herb *Angelica sinensis* (Dong quai), classified as a warming herb in TCM, is traditionally used as a postnatal tonic. Yet, as a midwife, I observed three distinct cases in my practice in which a breastfeeding newborn developed the appearance of a heat rash in conjunction with the mother's consumption of the herb as part of a tea. In each case the rash disappeared with cessation of tea intake, and in one case, with retrial, reappeared. Such observations should not be discounted but gathered and collated to add to the growing body of knowledge of modern herbal medicine. This side effect of *A. sinensis* case is now documented in the *Angelica sinensis* monograph of the *American Herbal Pharmacopoeia* as well as the *A. sinensis* Survey of the American Herbalists Guild.[29,30] Herbal practitioners generally develop a repertory of herbs they most frequently use and that they find most effective. The selection varies with the practitioner's specialty; in other words, a gynecologic specialist draws from a slightly different materia medica than a practitioner who specializes in immune disorders.

Availability of Herbs

Patients must be able to readily obtain the herbs and products in their prescriptions. Many herbal practitioners prefer to fill the prescription themselves in order to retain quality control and guarantee that the patient leaves an appointment with the intended formulas. If the practitioner plans to fill the prescription from his or her own dispensary, the herbs must be in stock, or a similar and adequate substitute must be available.[27] Not all health professionals want to run a complete dispensary through their practice; there are several high-quality and reliable herb companies that provide formulation services, filling prescriptions and shipping products directly to patients; however, this can be a costly option.

Financial Considerations

In the United States, herbal prescriptions, even when made by a licensed practitioner, are not reimbursable by insurance companies.[31] Although Americans have demonstrated that they are willing to pay out of pocket for herbal medicines, cost is a major concern for many. It is important to discuss financial ability with patients in order to provide a protocol that will allow them to take enough of the herbs for a sufficient duration of

time to have the desired effect, and not add high herbal costs to their burden of health care costs.[27] Herbal prescriptions may need to be tailored to meet the needs of the patient's budget, such as prescribing teas as a less expensive option to tinctures, and teaching patients to make their products whenever possible, rather than purchasing them pre-made at health food retailers.[27] Expensive, exotic, ''designer'' herbs and herbal products are not necessarily more effective than simple herbs, and in fact, many trendy products may be less safe and effective than time-tested home remedies.

Herbal formulas often need to be changed or modified as patients start to experience results; also, sometimes the correct formula is not achieved immediately, requiring a new prescription (and thus the patient must purchase a different formula) after trying an initial protocol for only a short time. In TCM, it is not uncommon for the Chinese doctor to alter an herbal prescription every few days. Careful attention to formulating and prescribing the minimum effective dose can reduce product waste and loss of money to the patient; however, it is not possible to entirely eliminate this factor from herbal practice, and this should be clearly explained to patients prior to initiating an herbal protocol.

Herbal practitioners may choose to maintain a dispensary as a way to offer a cost saving to their patients, making herbal products available to their patients nearly at cost, marking the products up only enough to cover the cost of stocking and maintaining the inventory, and filling prescriptions. Keep in mind that in a busy practice, it might require the help of a full- or part-time employee solely for that purpose. This service allows the practitioner to provide high-quality products at a fraction of their cost in retail institutions. Practitioners choosing to do this will want to investigate the good manufacturing practices (GMPs) of their jurisdiction in order to comply with all manufacturing and labeling laws that might pertain to them. Additionally, practitioners might want to consider carrying product liability insurance.

Ecologic Considerations

Widespread use of herbal medicines can lead to overharvesting of frequently used or rare plant populations. This is exacerbated by the vagaries of fashion, whereby a certain herb will be promoted excessively (and often inappropriately). This problem has a historical precedent, for example, in the destruction of large stands of the American ginseng population by Daniel Boone and other pioneers who profited from its harvest and export to China, or in the depopulation of the American Lady's Slipper (*Cypripedium pubescens*) owing to its popularity in the nineteenth and early twentieth centuries as a sedative. Modern examples of this are *Hydrastis canadensis* (goldenseal), and *Chamaelirium luteum* (False unicorn) an American woodland plant endangered in the wild and difficult to cultivate. In a broader philosophical sense, one cannot ultimately separate the health of the environment from the health of the individual; thus, attention to ecological herbalism is part of the responsibility the practitioner assumes in assuring the long-term health of patients. Thus, a responsible herbalist avoids the use of endangered plants and seeks appropriate substitutes wherever possible (Box 3-36).[27,28]

Adherence

Herbal preparations can be time consuming for patients to make and are not always pleasant tasting, factors that can reduce patient adherence to otherwise good herbal protocol. If the herbs are not taken, they will not work! An in-office dispensary reduces the need for the patient to seek out herbs on his or her own, minimizing time and expense, and maximizing the likelihood that the herbs will actually be obtained. Selecting the form of the herb that will most likely encourage its use is also important. For example, a single working mother may be more likely to take a tincture, tablets, or capsules that she does not have to prepare, and which can easily fit into her purse, than a tea that she has to prepare at

BOX 3-36

United Plant Savers (UpS) ''At-Risk'' and ''To Watch'' Lists

United Plant Savers, a nonprofit group dedicated to the preservation of native botanical medicine species, lists the following herbs that may be discussed in this textbook as either ''at-risk'' or ''to watch.'' Herbs listed in this chart should only be obtained from cultivated sources, and not from wild harvest.

At-Risk
American ginseng (*Panax quinquefolius*)
Black cohosh (*Actaea racemosa*)
Blue cohosh (Caulophyllum thalictroides)
Echinacea (*Echinacea* spp.)
Eyebright (*Euphrasia* spp.)
Goldenseal (*Hydrastis canadensis*)
Helonias root (*Chamaelirium luteum*)
Lomatium (*Lomatium dissectum*)
Slippery elm (*Ulmus rubra*)
Trillium, beth root (*Trillium* sp.)
True unicorn (*Aletris farinosa*)
Wild yam (*Dioscorea villosa*, *D.* sp.)

To-Watch
Arnica (*Arnica* spp.)
Cascara sagrada (*Rhamus purshimia*)
Goldthread (*Coptis* spp.)
Kava Kava (*Piper methysticum*) (Hawaii only)
Lobelia (*Lobelia* spp.)
Oregon grape (*Mahonia* spp.)
Partridge berry (*Mitchella repens*)
Pipsissewa (*Chimaphila umbellata*)
Spikenard (*Aralia racemosa, A. californica*)
Wild Indigo (*Baptisia tinctoria*)

home and carry along on her busy day. These considerations can be discussed with patients prior to writing their prescriptions.

Taste is not always possible to fully mask with herbs, particularly with bitters, in which the bitter taste is partly necessary for the effects of the medicine. However, much can be done to improve the taste of many herbs. In teas, infusions, and decoctions a corrigent (a flavoring agent) such as licorice, anise seed, spearmint, or peppermint may be used in tinctures, glycerine, elderberry syrup, the aforementioned herbs, or one or two drops of a pleasant-flavored essential oil, such as anise seed, cinnamon, peppermint, or spearmint may be used. Tinctures may be taken heavily diluted in water, or taken in a small amount of juice to mask the taste. With experience practitioners can learn to combine herbs to maximally enhance their taste; however, it is inevitable that some herbs have a very strong taste. This should be explained to patients in advance, and if necessary a very small amount (e.g., ½ ounce of tincture) of the herbal product mixed and sent home with the patient to see if the product is tolerable prior to assembling a full prescription. For patients who find the taste of liquid and alcohol extracts intolerable, capsules and tablets may be substituted for some herbs.

FORMULATING

An effective formula will lead to the desired health outcome with maximal benefits, patient adherence, and minimal, if any, side effects. It will be cost-effective and ecologically sustainable. Most herbalists have a single technique they prefer for formula development, and create all formulae based on a skeleton model of their preferred method. There is no right or wrong way to design an herbal formula—herbal formulation is as much an art as it is a science. General formulation strategies follow.

Establishing Therapeutic Goals and Priorities

Before developing protocol and formulae for an individual patient, clear therapeutic goals and priorities must be established. These should be based on the patient's needs and personal treatment goals, an understanding of the condition from a Western biomedical perspective, and an understanding of the condition based on the traditional concepts of the system of herbal medicine being practiced.[32]

Therapeutic priorities are based on the immediate needs of the patient and a ranking of the urgency of various presenting symptoms and conditions. Optimally, a therapeutic plan is devised that addresses the most urgent and challenging symptoms for the patient, while beginning to address underlying conditions in a systematic manner. Kerry Bone, in his book *A Clinical Guide to Blending Liquid Herbs*, defines the following as goals for Western herbal prescribing for the individual patient. These key concepts can be considered guiding principles for identifying the overall therapeutic goals for the formula:[32]

- Raise the vitality in order to enhance the patient's ability to resist disease.
- Relieve the underlying causes that either predispose the patient or provoke the disease process.
- Reduce the effect of the sustaining causes of the disease process; for example, inflammation.
- Promote and nourish healthy functioning of tissues, organs, and systems related to the condition being treated.
- Control counterproductive symptoms that interfere with healing.

The Structure of an Herbal Formula

Herbal formulae follow many styles from single-drug ingredients (''monotherapy'') known as ''simples'' to the 15 to 20 ingredient formulas typical of TCM. All herbs in a formula should support the therapeutic goals either directly, or by supporting the actions of the primary herbs in the formula. An herbal formula should not contain so many ingredients that the patient is receiving inadequate amounts of the individual herbs.

Key formula ingredients are as follows:

- The *primary* or *main* ingredient(s)
- The *adjuvant*(s), *supporting*, or *secondary* ingredient(s) that enhance or complement the effects of the primary ingredients in a specific manner
- A *corrigent*, an ingredient to enhance the flavor or tolerance of the preparation

Additionally, herbalists may add one or more of the following to a formula:

- *Warming, carminative* herbs such as ginger or cinnamon to prevent digestive discomfort from an herbal formula and to enhance the metabolism of the formula. This practice is now being validated by research demonstrating that the addition of a spice (for example, black pepper or its constituent piperine) to an herbal, or even a pharmaceutical protocol such as antibiotic therapy, enhances the uptake of the drug, and reduces the amount of drug required for therapeutic efficacy.
- *Trophorestorative* or *tonic herbs* that support specifically stressed body systems.
- *Nervines*, as stress is a common component of health problems, either as an underlying factor, or as a result of the presence of illness.
- *Anti-irritants*—herbs that reduce the irritating effects of other herbs in the formula for example a mucilagenous herb.

Generally, one to three main ingredients are used, one to two adjuvants, one corrigent, and one ''warming'' herb.[26] Commonly a single herb in the formula will serve multiple purposes; an herb such as ginger or cinnamon may act as both a corrigent and a carminative.

The German Commission E specifies guidelines for the inclusion of herbs in herbal combination products.might be included if:

- The use of the various components with identical or different effects leads to additive or synergistic effects; and/or
- The combination leads to a super additive effect of the fixed combination compared with that of the individual components; and/or

- The combination leads to reduction or elimination of undesirable effects of individual components; and/or
- The combination leads to a simplification of therapy or improvement in therapy safety, compliance, or absorption.[26]

Exquisite formulating; that is, using the minimal number of the most exact herbs in a formula should be every practitioner's goal. For some patients a single formula with only a few herbs may be effective for treatment. For many patients, it will be necessary to provide more than one formula at a time, for example, the use of a tincture and a topical application in the case of a skin condition or vaginal infection, or the prescription of a formula for acute use and another for chronic use. For example, a patient with chronic anxiety during the day and insomnia at night may be prescribed a general nervine tonic with adaptogens for regular daily use, with a separate formula consisting of sedative herbs for acute insomnia, to be taken only before bed or as needed.

Traditional Chinese Medicine bases the structure of the formula on the ancient Chinese structure of government. There is an Emperor that determines the overall approach (and may be equated to the primary herb), various Ministers that support and carry out the wishes of the Emperor (adjuvants), Assistants who create the agenda for government and set the political climate and tone, and Servants who carry out the work (warming stimulants). In the context of the herbal formula, this means that the herbs are layered or each considered in juxtaposition to the other parts of the formula as well as for their own merit. The Chinese art of compounding, or making herbal formulas, is impressive and their energetic principles may be successfully applied to Western herbal formulations as well.[27]

Steps to Developing a Formula

Mills and Bone best elucidate key formulation concepts in their textbook, *Principles and Practice of Phytotherapy: Modern Herbal Medicine*. To develop a formula:[6]

1. Determine the treatment goals based on traditional herbal concepts, the conventional medical understanding, and the patient's case.
2. Make sure the goals are individualized to the needs of the specific case.
3. Decide upon the immediate treatment priorities.
4. Determine what actions are required, based on the treatment goals.
5. Choose reliable herbs that have the desired actions, with as much overlap as possible to minimize the number of herbs in the overall formula.
6. If a particular action needs to be emphasized, select more than one herb with this action, or include a single very effective herb with the desired action.
7. Combine the herbs in appropriate proportions and doses.

Selecting the Herbs

Once the therapeutic goals and necessary herbal actions have been determined, the specific herbs must be selected. The simplest method, especially when one is a beginner, is to take a fresh piece of paper and on it create columns of the various therapeutic actions needed for the formula. Under each column, select herbs from your references and knowledge base that fit the category and the specifics of the patient's condition. Because many herbs have multiple actions, you will find that herbs appear more than once on the page, under different columns. Narrow your selection by first choosing those herbs that address more than one need (Fig. 3-26). For example, if there is upper respiratory infection and you are seeking an herb that is antiviral, anti-inflammatory, and expectorant, licorice might be an excellent choice, as it possesses all of these actions. It is also a corrigent, thus minimizing the need for an additional flavoring agent for an infusion or tincture. Next, select herbs that most specifically address any remaining symptoms or conditions that are intended to be addressed by this formula, keeping an eye to the key components of a formula outlined in the preceding. Finally, make sure that there are no contraindications to any of the herbs you have selected for the patient, including potential herb–drug interactions, or herb–herb interactions within the formula, or between formulae if more than one prescription has been given.

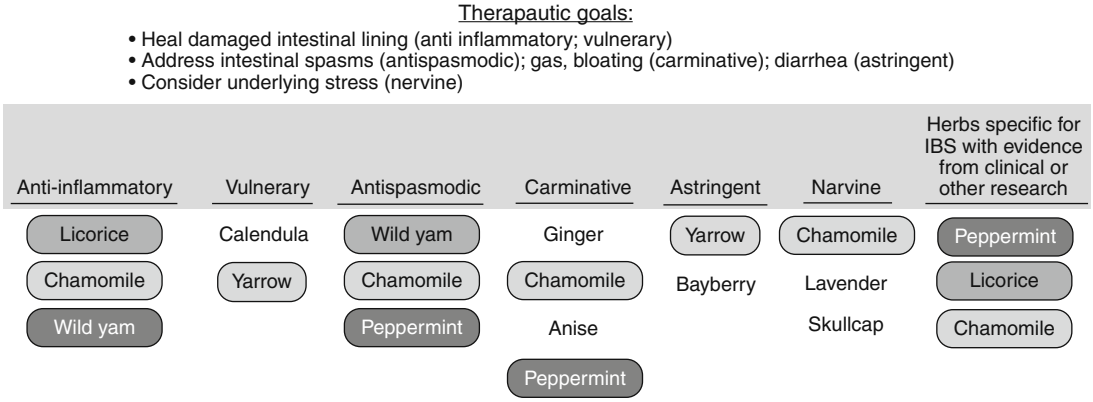


Figure 3-26 Sample formula development for patient with IBD. Note: see page 59 for formula.

Note that the form of preparation you are giving will also affect your selection of herbs; therefore, you must select the preparation form that will allow you to effectively deliver the medication to the patient. For example, if you are prescribing highly bitter or unpleasant tasting herbs, you will want to use a form that is most palatable, probably a tincture or possibly a capsule; if you are prescribing demulcent, mucilaginous herbs, you will want to use a tea or infusion, as many mucilaginous herbs are not highly soluble in alcohol.

Determining the Correct Proportions of Herbs in a Formula

The amount of each herb in a formula depends on the relative importance of the herb in the formula (i.e., whether it is a primary herb, a secondary herb, or a flavoring), the amount of each herb required for therapeutic action, and the strength of, and safe dosing range for each herb. Synergistic activity between herbs should be considered; the presence of more than one herb with a similar action often allows the formulator to reduce the volume of one or other of the herbs. Tincture formulae are built around a final product volume of 100 mL. Infusions can be prepared by the cup, typically 1 to 3 tsp of herb per cup of water, and decoctions are typically based on a 28 g (1 ounce) herbs: 1 L (1 quart) water ratio.

The herbs in infusions and decoctions are measured in ''parts,'' or the proportion of individual herbs compared with the whole. If you consider a formula to be comprised of 100 parts as a total amount, then each herb would be assigned a certain number of parts, similar to the percentage of the herb in the formula. The word parts can then be translated into ounces, grams, teaspoons, etc., based on the measurement you are using and the total volume you need to prepare. In this book, rather than assuming 100 parts for a whole formula, the formulae assume 10 parts to make the numbers more manageable. Here is a sample formula as an example of the ''parts'' system:

Sample Cold Infusion (Macerate)

Bowel Anti-Inflammatory Blend

Marshmallow root	(Althaea officinalis)	4 parts
Chamomile	(Matricaria recutita)	4 parts
Ginger	(Zingiber officinalis)	1 part
Peppermint	(Mentha piperita)	1 part
	Total:	**10 parts**

To prepare: Mix the herbs. Steep 1 tbs herb/250 mL cold water for 1 hour, stirring a couple of times. Strain; bring to a boil for 1 minute, and serve warm or at room temperature.
Dose: 1–3 cups per days as needed.
Indications: Irritable bowel syndrome (IBS); bowel inflammation; stomach upset; dyspepsia (heartburn)

In this example, you can see that there are 10 parts total. The parts are written in descending order of volume. In this case, marshmallow and chamomile happen to also be the primary herbs in the recipe. Ginger and peppermint are important bowel anti-inflammatory herbs, but in this recipe also serve as secondary and adjunct herbs, the ginger warming the digestion and improving the taste, and the peppermint acting as a carminative and also improving the taste.

Selecting Herb Strength (w:v Ratio) When Using Tinctures

Tincture strength based on weight to volume (w:v) ratio is discussed in Botanical Preparations. When preparing a formula, the practitioner must determine what strength of each herb in the formula to use. The relationship between extract strength and clinical efficacy is a matter of debate, and has been poorly evaluated. The preparations available, even to professionals, are highly variable ranging from 1:1 fluid extracts (FE) through 1:5 extracts for commonly used herbs, and 1:10 for highly potent, restricted, or potentially dangerous herbs. Historically, European herbal practitioners have relied primarily on 1:1 FE, and the higher dilutions of 1:5 and 1:10 strengths, with fairly high doses required for the 1:5 extracts. Unfortunately, there is so much variability in the US market, and such a wide variety of factors that determine actual product potency, that it is difficult to determine the resulting clinical difference in the various strengths available, the difference becoming theoretical and somewhat arbitrary.

The potency of the final product is determined by numerous factors, including the quality of the starting material, the plant parts used (e.g., one herb manufacturer may prepare a Hypericum tincture using the entire 2 to 4 feet of the plant, whereas another company may use only the active, medicinal top 4 to 8 inches of the flowering plant, resulting in a potentially very different product), the solubility of the individual herb(s), use of the proper solvent, solvent percentage, and w:v ratio. Because of this variability, it becomes almost impossible to recommend specific w:v ratios and alcohol percentages in the sample formulae in this text. It is assumed that tinctures are being purchased from manufacturers who prepare their products according to proper standards and specifications, and using high-quality starting materials. Practitioners should not be concerned if the suggested strength is not available, requiring the practitioner to rely on a slightly higher or lower w:v ratio, as long as one stays within the 1:2 to 1:4 strength range. Going from a tincture to an FE (1:1) can significantly increase the potency of a product and is not recommended as a substitute in the suggested formulae. When a 1:5 or 1:10 is recommended, this indicates that an herb is potentially toxic in higher amounts and this strength should not be exceeded unless the formula is properly modified to include a reduction in the overall volume of that herb.

Putting It All Together

The following sample formula is based upon the herb selection strategy presented earlier in this section; this formula represents a standard herbal prescription, including common and botanical names for the herbs, herbs

strengths and volumes, and recommended dose. The vegetable glycerin is optional for taste, and may be replaced with 10 mL of *Pimpinella anisum* (anise seed).

Sample Formula for IBD

Mix the following tinctures:

Chamomile	(*Matricaria recutita*)	30 mL
Wild yam	(*Dioscorea villosa*)	25 mL
Licorice	(*Glycyrrhiza glabra*)	15 mL
Yarrow	(*Achillea millefolium*)	10 mL
Peppermint	(*Mentha piperita*)	10 mL
	(*Vegetable glycerin*)	10 mL
	Total:	**100 mL**

Dose: 5 mL of tincture in a small amount of warm water two to three times daily.

The Prescribing Schedule

How often a patient should take the prescribed formula(e) depends on the severity and urgency of the condition, the strength and safety of the herbs, and the likelihood of the patient's adherance. The following is a general summary of the prescribing range for various herbal products:

- Tinctures: 2–7 mL, 1–3 times daily
- Decoctions: ¼–2 cups daily
- Infusions: 1–6 cups daily
- Capsules and Tablets: 1–3 capsules, 1–3 times daily

Occasionally, products are prescribed with special instructions, for example, *Vitex agnus castus* is often prescribed in a single 5 mL dose in the morning, or other herbs may be prescribed for taking prior to bed, with meals, or only during a specific phase of the menstrual cycle.[33]

In acute conditions the prescribing schedule may be more aggressive. For example, a woman experiencing uterine contractions with a threatened miscarriage may take a uterine antispasmodic formula every 15 minutes for a set period of time (e.g., 2 hours) in a reduced dose until relief is achieved.

Where adherance is a concern, the practitioner may ask the patient how often she will realistically take the prescribed formula, and adjust the individual dose to accommodate a daily therapeutic dose in that intake frequency. For example, if a woman tells you she will not take her formula at the office, prescribing a formula to be taken 2.5 mL four times daily will be ineffectual. Better to prescribe a dose of 5 mL twice daily, if the herbs in the compound are safe in that individual dose.

PRESCRIPTION WRITING

In Europe, where herbal medicine is part of the norm in the health care system, herbal prescription writing follows traditional prescription nomenclature (Tables 3-14 and 3-15), allowing herbal formulae written by the practitioner to be easily read and prepared in the pharmacy. Although most practitioners in the United States will not likely be sending their patients to the ''herbal pharmacy'' to have their prescriptions filled, it is worthwhile to understand the formal language of the prescription, especially when using European herbals and pharmacopoeia. Latin binomials should be given for all plants in a prescription to guarantee use of the proper plant genus and species in the product. Practitioners should at all times create an accurate record of exactly what was prescribed in each patient's chart.

TABLE **3-14**

Plant Parts: English and Latin Names, and Abbreviations

PLANT PART	LATIN NAME SINGULAR (PLURAL)	ABBREVIATION
Leaf	folium (folia)	fol.
Flower	flos (flores)	Flor.
Fruit	fructus (fructus)	fruct.
Herb	herba (herbae)	herb.
Root	radix (radices)	rad.
Rhizome	rhizoma (rhizomae)	rhiz.
Bark	cortex (cortices)	cort.

From Kraft K, Hobbs C: Pocket Guide to Herbal Medicine, Stuttgart, 2004, Thieme. (Reprinted with permission)

BOTANICAL PREPARATION FORMS

Eric Yarnell, Kathy Abascal, Mitch Coven*

Herbal products range from simple, crude herbs in raw and tea forms to sophisticated standardized extracts with fixed concentrations of specific constituents. Using the most appropriate forms of administration can maximize efficacy and patient adherence. Patient-determined factors, such as time limitations, financial considerations, taste aversions, and extenuating factors (e.g., history of alcohol abuse leading to current alcohol avoidance), help to narrow preparation choices to the preparation to further the likelihood of patient implementation. This section reviews the various types of commonly used herbal preparations, their advantages and disadvantages, and preparation methods (Table 3-16).

PREPARATION FORMS

Powdered Herbs, Capsules, Tablets, and Pills

Powdered herbs—the finely ground form of the crude herb—are a simple and cost-effective way for patients to take herbal medicines. Generally, the powder is pressed into tablets or pills, or may be encapsulated (Fig. 3-27), but occasionally palatable herbs are taken with hot water or even sprinkled onto foods.

*Special thanks to Ed Smith, RH(AHG), and David Bunting for their editorial assistance with this chapter.

TABLE 3-15

Prescription Writing: Terms and Abbreviations

ENGLISH INSTRUCTION	LATIN EQUIVALENT	PRECRIPTION NOMENCLATURE/ ABBREVIATION
Equal parts of each ingredient	ana partes aequales	Aa. (aa.)
Water	aqua	aqu.
Add	adde	add.
Or similar	aut similia	aut. simil.
With	cum	c.
Cut	consisus	cc., conc.
Crushed	contusus	cont.
Give the patient	da	d.
Give and label as follows	detur signetur	d.s.
Make, prepare	fiat	Ft.
Drops	gutta, guttae	Gtt. (gtt.)
Make an infusion	infunde	Inf
Mix	misce	m.
Mix and make	misce, fiat	M. f.
Mix and make a tea	misce fiat species	M. ft. spec.
Mix and make an ointment	misce fiat unguentum	M. ft. ungt.
Mix, give, label as	misce, da, signe	M.D.S.
After meals	post cibum	p.c.
Pills	Pilliulae	pill.
Powder, pulverize	pulvus, pulveratus	pulv.
Take	recipe	Rx
Label	signa	S.
Tea	species	spec.
Suppository	suppositorium	supp.
Divide into X doses	tales doses	Tal. dosis No. X
Tincture	tinctura	tct., tr.
Ointment	unguentum	ungt.

Advantages

Tablets, pills, and capsules are inexpensive and are a widely recognized form of medicine to patients accustomed to Western medicine, thus are easily accepted by most. Powdered herbs present the whole herb to the patient's digestive system and thus may be a preferred choice when the therapeutic goal requires direct contact between the herb and the GI tract, as is the case with mucilaginous and vulnerary herbs used to treat IBS.

Disadvantages

The grinding of the herb into powder generates heat that may degrade valuable medicinal constituents. Once ground, powdered herbs oxidize more readily than whole herbs, given the vast increase in exposed surface area. The time from harvest to purchase is an unknown factor that may significantly affect the medicinal qualities of the preparation. Thus, the medicinal activity and quality of powders is highly variable and can be unreliable and practitioners must evaluate individual companies and products for quality.

Liquid Extracts

The most common forms of liquid extracts are:

- Aqueous extracts (teas, infusions, decoctions)
- Hydroethanolic extracts (tinctures, fluid extracts)
- Glycerin extracts (glycerites)

Any of these forms may be further manufactured into additional product forms, such as by concentrating liquid extracts and adding binders to form tablets or transforming a decoction into syrup. Plant constituents may be water soluble, soluble only in alcohol, or have extractability somewhere in between. For instance, alkaloids are typically soluble in 45% alcohol, but hydrastine, an alkaloid found in *Hydrastis canadensis* (goldenseal) root (Fig. 3-28), may require a 70+% alcohol menstruum for full extraction. On the other hand, berberine another alkaloid found in goldenseal, is poorly soluble in alcohol. A high percentage alcohol tincture will have a different hydrastine: berberine ratio than a tincture made with a lower percentage alcohol and an aqueous extraction may have berberine but no hydrastine. The situation is complicated by the fact that multiple constituents within the herb interact in solution and affect each other's solubility.

The choice of solvent, or menstruum, changes the chemical profile and thus the medicinal qualities of the product (Table 3-17). This is an area where comparative outcome research is lacking, although a few basic studies do exist. For example, one French study found

TABLE **3-16**

Summary of Internal Botanical Preparations

PREPARATION TYPE	SOLVENT(S)	SHELF-LIFE*	BENEFITS	PROBLEMS	OTHER NOTES
Crude powdered herb	None	12 months for above ground parts and up to 3 years on roots if properly stored	Whole herb (all constituents present), pills readily accepted, relatively inexpensive, easy to dispense and formulate	Damaged by processing, mold contamination, batch-to-batch variability high, may be difficult to swallow and hard to digest	Freeze-dried powders may have longer shelf-life.
Granule	Water, sometimes wine or oil	12–24 months	Decreased dose needed, palatable, easy to dispense and formulate, relatively inexpensive	Little research, short history of use, batch-to-batch variability high	Starch may be added.
Standardized extracts	Variable	Variable (12–24 months presumably)	Well researched (sometimes), dosing objectively determined, easy to dispense, less batch-to-batch variability	Relatively expensive, may have solvent residues, little history of use, can not formulate, potential loss of beneficial constituents not assayed, capsules possibly difficult to swallow	Higher environmental impact if solvents used
Hot infusion or deco ction	Water	Hours to days (if refrigerated)	Inexpensive, easy to formulate, benefits of water**	Time consuming to prepare, complex to dispense, bad taste	Will not extract hydrophobic constituents
Cold infusion	Water	Hours to days (if refrigerated)	Inexpensive, easy to formulate, benefits of water**	Time consuming to prepare, complex to dispense	Will not extract hydrophobic constituents
Tincture	Ethanol, water, sometimes glycerin	Years to decades	Easy to formulate and dispense, relatively broad extract, easy to swallow and absorb, fast acting	Moderately expensive, contain ethanol, flavor often unpalatable	Differing ethanol and ratio concentrations, extracts different ranges of constituents

(Continued)

TABLE 3-16

Summary of Internal Botanical Preparations—cont'd

PREPARATION TYPE	SOLVENT(S)	SHELF-IFE*	BENEFITS	PROBLEMS	OTHER NOTES
Fluid extract	As tincture	As tincture	As tincture but more concentrated, thus lower doses required	As tincture, increased processing may damage some constituents, only works with dry raw material	As tincture
Glycerite	Glycerin, water	2–5 years,	Easy to formulate and dispense, easy to swallow, palatable	Moderately expensive	Only extracts hydrophilic constituents
Syrup	Simple carbohydrate, water	1–2 years	As glycerite	Moderately expensive, relatively poor preservative	As glycerite
Acetract	Vinegar, water, sometimes ethanol and/or glycerin	1 year or more depending upon formula	Easy to formulate and dispense, easy to swallow, effectively extracts alkaloids	Moderately expensive, poor preservative, does not extract other constituents well	Used exclusively with alkaloid-rich herbs
Volatile oil, steam distilled	None	1–3 years	Easy to formulate and dispense, multiple modes of application, very low doses needed (concentrated), some objective doses established	Expensive, narrow therapeutic window (concentrated)	
Volatile oil, supercritical carbon dioxide	Carbon dioxide	Unknown (presumably 1–3 years)	As volatile oil, steam distilled	As volatile oil, steam distilled	New technology with little clinical research or use
Hydrosol	Water	Weeks to months	Inexpensive, dilute tinctures for topical use	Questionable if medicinally useful, extremely dilute, spoils quickly	

*Assuming optimal storage conditions.
**The patient takes in the water simultaneous with the herb, which brings additional benefits, such as increased diuresis.

that a 30% ethanol tincture of *Viburnum opulus* (cramp bark) was five times more potent as a spasmolytic in vitro than a 60% ethanol tincture.[34] Herbalists will commonly report that one form of an herb over another is consistently more effective in the clinic; for example, many find licorice decoction more effective than tincture for controlling inflammation. Herbal manufacturers and practitioners rely largely on pharmacopeial values for determining extraction methods and standards.

Advantages

The advantages of liquid extracts over solid forms vary with the specific form of liquid extract, and the herb. In general, liquid extracts are easy to swallow, absorb, and assimilate. Water-based preparations are typically inexpensive to prepare and often have a wide margin of safety because they are relatively dilute, although this is

Figure 3-27 Herbs in various forms.

Figure 3-28 Goldenseal (*Hydrastis canadensis*). (Photo by Martin Wall.)

TABLE **3-17**

General Solubility of Botanical Compounds

PHYTOCHEMICAL CATEGORY	MOST SOLUBLE IN... (ETHANOL %)	WATER SOLUBILITY
Proteins, lectins	25%	Very high
Tannins	25–30%	High (in hot water)
Saponins	25–30%	High
Carbohydrates	25–30%	High (in cold water)
Glycosides	25–30%	High
Alkaloids	45%	Marginal
Alkaloid salts	25–30%	High
Monoterpenoids, sesquiterpenoids, diterpenoids	60%	Low
Phenylpropanoids	60%	Low
Lignans	80–90%	Very low
Resins	90%	Very low
Lipids	90%	Very low

Note: There are exceptions in every category.
From Yarnell E: Phytochemistry and Pharmacy for Practitioners of Botanical Medicine, Wenatchee, WA, 2003, Healing Mountain Publishing.

not a reliable safety guideline; hydroethanolic extracts are characteristically concentrated and thus easy to store, transport, and take in small but high potency doses.

Disadvantages

Water-based products such as teas, infusions, and decoctions require patient preparation, may be cumbersome to transport, have a short shelf-life, and often present palatability issues. Aqueous extracts make only the water-soluble constituents available to the patient, which may be undesirable or desirable, depending upon the therapeutic goal and required constituents. Hydroethanolic products require alcohol consumption, present a more concentrated product with thus a potentially smaller margin of safety for many herbs, and can be costly. Products prepared with solvents other than ethanol may contain undesirable solvent residues.

Aqueous Extracts (Teas, Infusions, and Decoctions)

Historically, herbs were most commonly prescribed as simple aqueous extracts to be consumed orally, or used in baths, douches, rinses, compresses, and other applications. There are four basic aqueous extracts:

- Teas
- Hot infusions, made by steeping the herbs in hot water for varying length of time
- Cold infusions (macerates) made by steeping the herb in cold water for a prolonged period (4 to 8+ hours)
- Decoctions, made by simmering or boiling the herb in water generally from 20 minutes to 1 hour

Tea is considered a culinary preparation; however, many teas, such as green tea, can provide significant medicinal benefit when consumed in adequate amounts over a prolonged period of time.

Infusions are principally made from the above ground parts of dried herbs, including leaves, stems, flowers, aromatic seeds (e.g., anise and fennel seeds), and fruits. The water is boiled, the heat turned off, the water poured over the herbs in a vessel (cup, tea pot, glass canning jar), and the steeping carried out in the closed vessel. When prepared this way, fragile plant parts are extracted with minimal damage to constituents. To some extent, even volatile oils contained in aromatic plants are preserved, as they condense on the lid and fall back into the water. Dried or fresh plant material can be used. Infusions are a poor choice where hydrophobic constituents are sought for their medicinal effect, including alkaloids, resins, and lipids, although it is a misconception that alkaloids are not extracted well in water as many are. Typically 1 tablespoon of dried herb per cup (250 mL) of boiling is used. Steeping time is generally as follows:

- Aromatic plants/plant parts: 10–15 minutes
- Nonaromatic leaves and flowers: 30 minutes to 1 hour
- Woody plant parts and soft roots: 1–4 hours

Cold infusions, also called *macerates*, are prepared by steeping the dried herb in an appropriate volume of cold water, typically from 2 to 8 hours, depending on the herb and its extractability. Cold infusions are well suited to extracting mucilaginous compounds in a palatable manner and are also often preferred when one wants to minimize tannin extraction from tannin-rich herbs, such as uva ursi (*Arctostaphylos uva ursi*) or red raspberry leaf (*Rubus idaeus*). Because no boiling water or alcohol is used to prepare cold infusions, microorganisms that would otherwise be killed might remain in the final cold infusion product. Caution may be warranted in using cold-infusions with immuno-compromised patients. A solution is to prepare the cold infusion, and then bring it to a quick boil before consuming.

Decoctions are prepared by simmering or boiling aqueous extracts. Decoctions use the seeds, roots, and barks of dried plants, with the exclusion of aromatic seeds. The additional heat provided through simmering or boiling enables water to penetrate into the dense tissue and releases constituents. As with infusions, the quality of the herb is paramount. Root decoctions are often quite bitter and unpalatable to the general public, and as a result, patient willingness to drink decoctions may be poor. This is certainly a disadvantage when compliance is desired. Typically 7 to 28 grams (¼ to 1 ounce) of herb is used per liter of boiling water, and simmered 20 minutes or longer depending upon the desired strength and concentration.

Syrups

Syrups are concentrated, sweet preparations made from a water infusion or decoction base that has been simmered down to a significantly reduced volume, usually one-quarter of the original volume. Sucrose and honey are the most commonly used sweeteners. A sweet alcohol such as brandy, or glycerin or another preservative may be added to extend the shelf-life of syrup from several days to several weeks or even months. Refrigeration is typically required to keep home-made syrups. The concentration of simple sugars needed to prevent microbial growth is fairly high, often between 25% and 50% of the total volume. Syrups are very palatable medicines but expose the patient to the regular consumption of sugar, and thus may not be optimal for regular, long-term use. Syrups can be used for short-term delivery when the unpalatably of the herbs would otherwise prevent compliance.

Hydroethanolic Extracts (Tinctures and Fluid Extracts)

Tinctures are hydroethanolic extracts. The combination of water and alcohol optimizes the solubility of plants constituents when both water- and alcohol-soluble constituents are desired in the final product. Alcohol content ranges from 30% to 95% ethanol depending upon the amount of alcohol required for optimal extraction and preservation of the desired constituents. Tinctures have a long shelf-life (frequently many years), preserving the tincture from bacteria and fermentation, even when left at room temperature; however, they should ideally be kept in a cool location away from direct heat and light.[35] Some research shows substantial degradation of individual constituents at room temperature after 3 to 6 months; thus, studies are needed to determine optimal

storage conditions and shelf-life for various plants. This could play a significant role in cost-savings to patients and industry, as well as play a substantial role in plant preservation by eliminating waste that occurs as a result of unnecessarily short expiration dates. Also, by determining which plants have a short shelf-life, such studies could help to maximize medicinal plant efficacy by ensuring that patients receive fresh product. Indeed, some constituent may degrade over time, making certain medicines less effective for specific conditions requiring the presence of those constituents, but other constituents may remain intact, preserving the usefulness of the plant for other conditions. Table 3-17 illustrates the effectiveness of alcohol at extracting many constituents.

Hydroethanolic extract potency is expressed as a ratio in weight: volume (w:v). A 1:1 extract or a fluid extract (FE) signifies that 1 g of the herb material by weight was extracted with 1 mL of liquid solvent, a 1:2 extract uses 1 g of herb to 2 mL of liquid solvent, etc. The weight of the fresh plant macerations includes the water weight of the raw material. An average fresh herb is 67% water by weight, where three pounds dry down to one pound. The amount of actual plant tissue in 1:2 fresh plant maceration is equivalent to 1:6 dry plant maceration. This can be confusing because the 1:2 fresh plant maceration seems more potent by threefold, yet they use the same amount of plant tissue and can be viewed as equivalent. The significance of w:v ratios in terms of clinical potency and formulation is discussed in Selection Criteria, Formulation, and Prescribing and Dosing.

There are four main types of hydroethanolic extracts:
- Fresh plant tinctures prepared by maceration
- Dried plant tinctures prepared by maceration
- Dried plant tinctures prepared by percolation
- Dried plant fluid extracts prepared by percolation

Fresh Plant Macerations

Fresh plant macerations are prepared by soaking the freshly cut herb in a hydroethanolic menstruum for 14 to 30 days, after which the mixture is pressed under high pressure then filtered to obtain a final extract. Most fresh plant concentrations have a 1:2 or 1:3 w:v ratio; however, sometimes herbs that are potentially toxic are intentionally made more dilute (e.g., 1:10). Fresh plant tinctures capture constituents close to harvest without exposing plants to the drying process, which for many plants can reduce their potency. Thus, certain herbs with temperature-sensitive constituents are prepared only as fresh tinctures. The actions of herbs may be different depending upon whether they are prepared fresh or dried. *Lobelia inflata*, for example, is parasympathomimetic when fresh and primarily emetic when dried, fresh pulsatilla is significantly more toxic than dried, and *Frangula purshiana* (cascara sagrada) bark, must be dried before preparing to eliminate the plant's cathartic qualities.

Dried Plant Macerations

Dried plant macerations are prepared in the same way as fresh, but the starting material is first dried. Owing to the reduced water volume in the dried starting material, these tinctures are generally prepared in 1:5 w:v concentrations. It is difficult to make these more concentrated. Except in very resinous plants such as *Commiphora molmol* (myrrh), the menstruum seldom exceeds 60% to70% ethanol. Tinctures with a lower w:v ratio have often been concentrated by evaporation techniques.

Percolation

Percolation is a distinctly different process than maceration (Fig. 3-29). In percolation, the powder is first macerated in a small amount of alcohol for 24 hours. The moistened herb is next packed into a percolation cone and the menstruum poured over the top of the herb. The menstruum is allowed to ''percolate'' through the herb in a continuous flow, with an extraction rate of one to three drops per second. Menstruum is moved through the herb until the desired amount of tincture has been produced. The weight: volume ratio is predetermined, and historically was done to a 1:5 concentration. Percolations are being produced at much higher concentrations of 1:2 and 1:3 ratios, although these have not been shown to represent more thorough extractions.

It is undetermined whether percolation provides a superior tincture compared with maceration. Maceration allows the use of fresh or dry starting material and requires less equipment, whereas percolations can only

Figure 3-29 Maceration set-up.

be performed with dried, powdered starting material and percolation cones. Percolations can be produced at much higher concentrations and in a shorter period of time, typically 2 to 3 days.

Percolation can yield a *fluid extract* (FE), by definition, a 1:1 w:v extract. FEs are concentrated and thus are particularly suitable for herbs that require high dosing for efficacy. FEs cannot be prepared by maceration without the application of additional heat or vacuum to remove excess liquid, processing steps that may damage important plant compounds. A straight FE is also not a true 1:1 unless re-percolation is used to fully exhaust the plant material. There is no consensus on the potency of fluid extracts compared with other tinctures. Most manufacturers and practitioners agree that fluid extracts are not proportionally more potent than other concentrations; for example, a 1:1 percolate is *not* necessarily five times more potent than a 1:5 percolate or macerate, owing to the fact that phytochemicals remain in the marc after a 1:1 extract. Clinical trials have not compared fluid extracts to tinctures of the same plant so exact differences in potency are not known. Many plants are unsuitable as fluid extracts. At 1:1 concentrations, the solvent can become supersaturated, and with certain herbs, the resulting product may become an unusable, gelatinous mass.

Care must be taken in combining tannin- and resin-containing tinctures in formulas to avoid precipitating out the tannins and possibly the resins, as well. Tannins will also form insoluble complexes with alkaloids and thus tannin- and alkaloid-rich tinctures are generally considered incompatible. It is unknown to what extent mixing other tinctures precipitates out desired compounds. In many cases, mixing will only result in minor precipitates that are invisible to the naked eye and likely remain bioavailable when ingested.

Standardized Extracts

Standardization (Box 3-37) refers to the manufacture of botanical extracts with consistent methods and materials to ensure that products contain the desired ingredients and consistent, reliable quality. Optimal standardization practices begin with the starting materials: guaranteeing correct plant species, quality of the materials to be used, and sometimes the identification of marker compounds to ensure identity, quality, and strength. Marker compounds are then reassessed in the final product to confirm that the contents and quality of the final products

BOX 3-37

The American Herbal Products Association: Standardization of Botanical Products White Paper

In recent years, the US marketplace has seen an increasing appreciation of the health-promoting benefits of herbal preparations. Both consumers and health care practitioners are becoming more receptive to their use. Many people, however, have reservations about the use of herbal products due to the chemical complexity of such products and the perceived difficulty in ensuring batch-to-batch product reproducibility. In order to address this concern, there has been a trend in the marketplace toward the use of ''standardized'' preparations; and in most cases, this word ''standardized'' is associated with a quantitative claim for the content of a particular constituent or constituents. The constituent or constituents that are the subject of such a quantitative claim are commonly known in the United States as ''marker compounds'' or ''markers.''

Based on the attention such a specification focuses on the marker compound(s), the layperson often naturally assumes that the marker content is of paramount importance in guaranteeing the reproducibility or even the efficacy of the extract. Furthermore, it is often assumed that the marker is the only factor of such importance. Neither of these assumptions is correct. Marker compounds often bear little or no relationship to the efficacy of the preparation, and reproducible marker content is indicative of a reproducible product only if used in the context of a complete body of raw material and manufacturing controls. Standardization is a complex process requiring attention to a wide variety of parameters, with the ultimate goal of enhancing the batch-to-batch reproducibility of the entire spectrum of constituents, not just one or a few.

In broad terms, standardization is the complete body of information and controls that serves to optimize the batch-to-batch consistency of a botanical product. Standardization is achieved by reducing the inherent variation of natural product composition through quality assurance practices applied to agricultural and manufacturing processes. Standardization seeks to enhance the reproducibility of a product's safety and efficacy by providing the product with a more consistent composition. In any botanical, there are many compounds and types of compounds that work together once the product is ingested. Some compounds in the plant may enhance or diminish the physiologic effects of others. Other compounds, although having no direct physiologic effect, may nevertheless influence the stability, solubility, and bioavailability of the physiologically relevant compounds. Therefore, by directly or indirectly enhancing the reproducibility of the complete composition of the product, standardization serves to enhance the batch-to-batch consistency of the product's effect.

American Herbal Products Association: Excerpts from Standardization of Botanical Products: White Paper, Silverspring, MD, June 2003, AHPA.

matches that of the starting materials. This is particularly common for hydroethanolic extract. Unfortunately, the concept of standardization has been misconstrued by manufacturers and consumers, and sometimes misrepresented as a marketing tool by the former, to mean ''active constituents.''

There is insufficient research detailing the exact role of chemical markers in clinical efficacy. In some cases, markers play a critical role in plant efficacy, for example, as with the flavonolignan complex known as silymarin from *Silybum marianum* (milk thistle). In other instances, the markers chosen have been clearly shown to be only one among many important compounds, such as hypericin from *Hypericum perforatum*.[36] In still other cases, the markers chosen have not yet been definitively shown to even be associated with quality raw materials, such as echinacoside from *Echinacea* spp.[37]

Advantages

Standardization of manufacturing procedures and material quality provides a measure of control over batch-to-batch variability and adds greater certainty to dosing. When using extracts that were used in clinical trials, it increases the likelihood of similar efficacy.

Disadvantages

There are no fixed requirements for standardization in the United States, there is a near total absence of published research showing that any particular standardization scheme is clinically superior to any other type of product, and there is some evidence that concentrating plants to specific constituents may actually have detrimental effects clinically. For example, recent evidence suggests that the practice of concentrating Hypericum products to higher hyperforin concentrations that found in nature, may lead to the highly publicized effects of the herb interfering with CYP450 and consequently, leading to herb–drug interactions with this plant.

Blending poor quality batches of raw product with higher quality batches to obtain desired standardization to certain constituents, or ''spiking'' batches with the marker compound are known practices among less reputable manufacturers. This practice reduces overall batch quality, and potentially product safety, with aggressively concentrated ''actives.'' It has proved to be relatively easy to fool standardization testing methods, with inferior products with nonetheless, impressive but incorrect labels.

The potential also exists for crowding out yet unmeasured but beneficial constituents with aggressive standardization. Standardization may also leave undesirable solvent residue in the final product. It is not required that solvents be listed on the label, thus such products may mislead the practitioner or consumer expecting a ''natural'' product free of chemical contamination.

Careful label reading is essential to ensure that the patient actually gets a product that contains the desired amount of the standardized constituent. For example, some manufacturers sell 300-mg milk thistle seed capsules containing 80-mg silymarin, whereas others offer 300-mg milk thistle seed capsules standardized to 80% silymarin. The latter contains 240 mg silymarin; significantly more than the former product, although on a quick read the products seem identical.

Concentrated Powdered Extracts (Granules)

Granules originated in traditional Chinese and Ayurvedic herbalism. Crude herbs are first decocted, usually in water, but traditionally may have been decoction in wine or stir-fried in honey. The liquid extract is then concentrated and vacuum dried onto small particles of herb or starch. The final granules usually have a 5:1 w:v concentration (5 g of crude herb concentrated into 1 g of granule extracted). The granules can then be taken as is chased by water or another beverage, or reconstituted into a tea by dissolving in hot water. They can also be pressed into pills or encapsulated. Some companies capture the essential oils during processing and add them back in before vacuum drying.

Advantages

Granules allow practitioners to dispense relatively high doses of plant material in a small volume. They also reduce palatability problems, particularly when taken as a pill. They are easy to dispense and formulate. They are fairly stable and last at least 2 years if stored in a dark, cool place.

Disadvantages

Damage may occur to some constituents during the extraction process, and thus not all herbs may be optimally effective in this dose form. Also, herbs high in low water soluble phytochemicals are not optimally extracted into 5:1 decocted powder extracts either. The appropriate traditional decoction method (water, alcohol, etc.) must be chosen to extract the intended constituents prior to granulation, or efficacy may be decreased. Practitioners should question manufacturers about production processes to ensure that proper preparation procedures are in effect.

Glycerin Extracts (Glycerites)

Glycerin, technically an alcohol, has solubility very similar to water, a sweet taste, and a viscous consistency. It is used to prepare ''alcohol-free'' tinctures, and to preserve and sweeten the taste of liquid extracts. Glycerin has very different biological properties than ethanol. It is suitable for preparing extracts of plants that contain primarily water-soluble compounds, and is not generally able to dissolve alkaloids, resins, lipids, lignins, phenylpropanoids, or terpenoids. Glycerin can be obtained from plants, animals, or petroleum. Most tincture manufacturers use vegetable glycerin, but it is advisable to inquire to make sure that this is the case. Today, there are many glycerites of plants containing constituents that are not soluble in water, such as some of goldenseal's alkaloids. Typically, an alcohol tincture is prepared, the alcohol is then evaporated off and glycerin is added, although this process removes volatile constituents.

Advantages

Glycerin tastes sweet. This makes glycerites relatively palatable to many consumers compared with ethanol

tinctures. Glycerin can be used to make macerations from fresh or dry starting material, using a procedure otherwise identical to tincturing by maceration. However, this is only efficacious if water-soluble compounds are desired.

Disadvantages

Unlike ethanol, which actually slightly increases absorption of many constituents, glycerin slightly interferes. Glycerites have a shorter shelf-life than tinctures. A minimum of 50% glycerin is necessary to prevent microbial growth in glycerites. Glycerin's viscosity and stickiness make it unsuitable for percolation. That said, glycerin is sometimes added in small percentages to hold constituents in solution even in percolations, as in the case with *Cinnamomum verum* (cinnamon). Typically 5% glycerin is added to the menstruum in such instances.

Fluid Acetracts

A fluid acetract is technically an extract of a plant in 100% acetic acid (100% acetic acid is dangerous to handle and ingest). Practically it refers to an extract using 3% to 6% acetic acid (vinegar). At this concentration microbial growth will occur, so ethanol is often included in the menstruum, changing the solvent nature of the menstruum. Acetracts are prepared by maceration in the same way as tinctures, have a shelf-life of not longer than a year, and must be kept refrigerated.

Vinegar extracts are uncommon for medicinal use today, but have a long history of use in botanical medicine. Alkaloids from alkaloidal salts become water soluble in acidic solvents. As a result, vinegar is a good extraction medium for alkaloid-containing plants like goldenseal, lobelia, and *Sanguinaria canadensis* (bloodroot). Vinegar extracts will have a longer shelf life when water is not added in the preparation process. It has been suggested that macerations of dried plants may produce better results than extracts from fresh plants where the water contained in the plant may excessively dilute the vinegar.

Essential Oils

Essential oils are traditionally prepared by steam distillation. The phenylpropanoids and/or terpenoids in the starting material boil and are condensed along with water into a capture vessel. The resulting oil can then easily be decanted from the water, with which it will not mix. Note that the heat involved in this process changes many of the constituents, and thus distilled volatile oils do not exactly match the compounds found in the plant. Research on a volatile oil cannot thus be directly extrapolated back to use of the crude herb. For example, *Matricaria recutita* (chamomile) leaf and flower contains matricin, which is converted to chamazulene by steam distillation. Chamazulene is not found in unheated, crude chamomile. Many medicinal properties of chamazulene have been discovered that do not necessarily apply to crude chamomile.

Volatile oils of all types are highly concentrated, potent extracts. Most plants contain at most 1% to 2% terpenoids and/or phenylpropanoids, which are therefore being concentrated 50 to 100 times to produce a volatile oil. They are always used in extremely low doses and with great care. These complex mixtures are lipophilic and thus have serious potential, in case of overdose, to cause harm to the highly fatty tissues of the nervous system in particular. With oral dosing, there is also concern about potential harm to the liver. A typical oral dose for an average-sized adult is three drops three times daily, although this will vary with the oil. Essential oils are thus generally administered only by inhalation or topically. Note that transcutaneous absorption of significant amounts of essential oil can also lead to toxicity; topical use can also lead to contact dermatitis. They are generally not applied undiluted (neet) to the skin. A sample of the oil should be patch tested prior to extensive application, and a highly diluted product should be used.

Processes other than steam distillation can also produce essential oils. Some plants will yield oil by simple expression, whereas others are extracted using organic solvents. Petroleum ether is one of the most common solvents in current use, having replaced the highly toxic benzene.

Supercritical Carbon Dioxide (CO_2) Extracts

In recent years, supercritical CO_2 technology has been applied to extraction of botanical medicines. When carbon dioxide is placed under enormous pressure, it changes into a state between a liquid and a gas known as the supercritical state. When the pressure is removed from a supercritical system, the carbon dioxide returns to a gaseous state and leaves the final extract free of solvent. Supercritical carbon dioxide is a fairly broad spectrum solvent of many constituents of interest in plants, particularly low molecular weight terpenoids and phenylpropanoids; however, according to Steven Dentali, PhD., a natural products chemist, other solvents are often added to supercritical CO_2 because its solvent range is limited. Fatty acids and their glycerides are slightly soluble. Simple organic acids, carbohydrates, amino acids, proteins, and most inorganic salts are virtually insoluble. Thus, supercritical carbon dioxide extracts are usually most like volatile oils, although they are chemically distinct because there are none of the heat-generated byproducts unique to steam distilled volatile oils. There is no historical data, and little research, to support the use of supercritical extracts as an alternative to a tincture or a tea. Owing to the potential toxicity of essential oils when used internally, caution is advised in evaluating the use of these extracts as medicines although they appear highly useful as a method for concentrating specific constituents.

Freeze-Dried Botanicals

Freeze-drying (lyophilizing) is a dehydration process that removes the water from a substance by exposure to dry, freezing air. It is variously described as a process in which no heat or chemicals are involved and as a process in which chemical solvents are used to extract the plants, after which the extract is flash-evaporated at low temperature in a partial vacuum to remove the solvents. The solid residue is then packed into capsules.

Opinions vary with some claiming that freeze-dried herbs are superior to other types of dried herbs and others arguing that freeze-dried herbs are unstable owing to their hygroscopic nature, which leads to rapid degradation upon exposure to air once a product bottle is opened by the consumer. Studies may support this concern. One study that showed that air-dried oregano had a lower rehydration rate than freeze dried.[38] Another study found that freeze-drying of spearmint resulted in substantial losses in oxygenated terpenes and sesquiterpenes compared with oven or air drying.[39] In a study of basil, freeze-dried leaf had a lower content of volatile oils than oven-dried.[40] Freeze-dried aloe had a lower content of organic and fatty acids compared with oven-dried aloe.[42] On the other hand, freeze-dried seaweed had a higher content of total amino acids, lipids, and vitamin C compared with sun- and oven-dried seaweed, although the oven-dried had the highest mineral content.[42] A pilot clinical trial found 600 mg freeze-dried, powdered *Urtica dioica* (stinging nettle) leaf one or more times a day significantly more effective than placebo at reducing symptoms of allergic rhinitis.[43] In addition, many studies, especially pharmacologic studies, use lyophilized herbs. Whether freeze-drying is beneficial may depend on the plant in question. Research comparing the activity of freeze-dried versus herbs preserved by other means has not been conducted in any systematic fashion.

Injectable Botanicals

Injection of botanical extracts by various routes has been practiced since at least the end of the nineteenth century, when intradermal or intramuscular injection of extracts of *Lobelia inflata* (lobelia), among other herbs, was popular among the Eclectic physicians in North America. Since that time, more sophisticated extracts suitable for intravenous injection have appeared in Europe and Asia where herbal products are largely regulated as pharmaceutical drugs, but are rarely encountered in North America.

Crude herbs and extracts of herbs are generally unsafe for injection, particularly intravenous injection. Saponins are often hemolytic and tannins can damage the liver, kidneys, and nervous system.[6] Many modern injectables, such as silymarin, glycyrrhizin, and schisandra represent single compounds or a limited number of compounds. Others, for example, extracts of *Viscum album* (European mistletoe) or *Echinacea* spp., are complex extracts. All preparations intended for injection must be sterile.

There are a number of older studies of injectables in the European, and particularly German, literature. For example, intramuscular injectable extracts of *Echinacea* spp. known as Echinacin® have been shown to be helpful for treatment of pertussis.[44] One of the best-studied injectable botanicals is an extract of European mistletoe used subcutaneously to induce immune responses for treatment of cancer and AIDS patients.[45] Intravenous glycyrrhizin combined with cysteine and glycine (2:1:20 ratio) has been effective in clinical trials for patients with hepatitis B, hepatitis C, and HIV infection.[46–48] Intravenous silymarin has been used in German and other European hospitals to treat poisoning by *Amanita phylloides* (death cap mushroom).[49] Use of injectable botanical extracts and botanical compounds is common in China. Extracts for intravenous and/or intramuscular injection from *Angelica sinensis* (dong quai) root, *Rabdosia rubescens* (dong ling cao) herb, *Salvia miltiorrhiza* (Chinese sage, dan shen) root, *Allium sativum* (garlic) bulb, *Corydalis yanhusuo* (yan hu suo) root, *Artemisia annua* (sweet Annie, qinghao) herb, and many others have been the subject of numerous Chinese clinical trials showing efficacy.[50]

Few generalizations can be made about injectable botanicals. Each individual agent must meet unique standards specific to that herb. Anyone purchasing injectable botanical extracts should be certain about the safety of the product. Various professional licensing laws do not specifically mention injectable botanicals in almost all cases. Some licensed health professionals use them quietly or under more general provisions of medical licenses with unknown potential for legal problems. Ultimately, it is anticipated that as research evidence supporting efficacy of these agents mounts, injectable botanicals will become more available and officially recognized.

Topical Applications

Numerous dose forms are available to deliver herbs to the skin or for transcutaneous absorption (Table 3-18). Each will be reviewed in turn below.

There is surprisingly little information on the extent to which plant constituents are absorbed cutaneously. Most botanicals used topically have a long history of use and have good safety profiles. However, certain compounds such as toxic pyrrolizidine alkaloids and methyl salicylate reportedly are absorbed to some extent through the skin—enough to potentially warrant concern with significant or long-term use, or use on open skin or inflamed skin and wounds that will absorb compounds more readily and extensively.

Creams

A cream is an oil-in-water emulsion and is essentially the same as a lotion (although lotions tend to be thinner). Creams and water-based extracts, including tinctures, mix together well. Fixed oils such as safflower and sunflower seed oils are typically used as a base.

Creams are thin, easily applied, and are generally well absorbed. Because they tend to be moistening or only mildly drying, they are preferred in cold, dry climates. They are not appropriate for application to open wounds. Both short-term and chronic uses are appropriate. Creams have long shelf-lives, particularly if natural antioxidants and antimicrobials are included to reduce oxidation and microbial growth. Synthetic preservatives are not recommended.

Salves and Ointments

Salves, or ointments, are topical products in which the herbs are extracted into vegetable oils by maceration at either room temperature for a specified length of time, in a low heat infusion or in a higher heat decoction. After filtration, the herbal oil is then combined with

TABLE 3-18

Summary Chart of External Preparations and Bases

PREPARATION TYPE	TYPICAL BASE
Bath, sitz bath, hand-and-foot bath	Aqueous
Compress	Aqueous
Cream	Oil/aqueous to which has been added or in which has been extracted one or a combination of the following: whole herb, powder, tincture, essential oil
Douche	Aqueous
Enema	Aqueous
Gel	Aqueous
Oil	Oil
Pessary	Whole herb/tincture/essential oil
Plaster	Whole herb
Poultice	Whole herb
Powder	Whole herb
Salve/ointment	Oil and wax to which has been added one or a combination of the following: whole herb, powder, tincture, essential oil
Steam inhalation	Aqueous
Suppository/bolus	Oil to which has been added or in which has been extracted one or a combination of the following: whole herb, powder, tincture, essential oil
Wash	Aqueous or dilute hydroethanolic

beeswax so the product is a solid at room temperature. Commonly salves are vulnerary, used to soothe and heal skin conditions. Some salves are antimicrobial; others are for muscle ache, bruising, and ischemia. Salves are sold in wide-top jars, and are applied with the finger, massaging the product directly into affected tissue.

Poultices and Compresses

A poultice is the direct application of the crude, fresh herb to the skin. A compress or fomentation is the application of a cloth that has been soaked is a plant. Usually, the extract (i.e., tea, dilute tincture) is an infusion or decoction, although dilute tinctures are also applied this way. Poultices, compresses, and powders are primarily used short term for wounds, bruises, sprains, or strains. They can be messy and generally require the patient to sit or lie still during use for thirty minutes or longer several times a day for optimal results. Poultices and compresses have extremely short shelf lives, and must be prepared for each application.

Great care is warranted to make sure that contaminated herbal material is not put into or on any wound. In early stages of wound healing, moist herbal compresses will generally work best, provided they are changed many times a day. Ointments applied too early can delay healing, and should never be applied to puncture wounds, as this can create an anaerobic environment.

Powder

Powdered herbs can be applied directly to the skin or mixed with water or other extracts to form a paste. They are typically applied dry to weeping skin conditions to absorb discharge and impart antimicrobial or vulnerary action.

SPECIAL PREPARATIONS

Aviva Romm

Gynecologic conditions sometimes require the use of special botanical preparations for direct application of herbal medicines to affected tissue. The most common of these preparations are vaginal rinses, douches, sitz baths, suppositories, and pessaries. This section provides instructions for preparing the special herbal applications used in this book, and not described fully in Botanical Preparations. Specific herbs for various conditions are presented under their respective conditions and may be incorporated into these general instructions. Most of these preparations are easy to prepare, inexpensive, and require minimal supplies.

WATER-BASED PREPARATIONS

Infusions and decoctions, often with the addition of tinctures or essential oils, are the foundation of water-based preparations, and are used to create vaginal rinses, douches, and baths.

Vaginal Rinses

Perivaginal rinses are commonly recommended for the treatment of vulvovagintiis to reduce pain and inflammation, and when there is dysuria associated with urinary tract infection (UTI), or to reduce perianal microbial contamination that can lead to UTI, such as from *E. coli*. They may also be used postnatally for the repair of episiotomy damage or perineal tears from birth.

To prepare a vaginal rinse: Fill a ''peri'' bottle or a clean, plastic squeeze bottle with a well-strained, strong infusion or decoction. Squeeze the warm or room temperature liquid over the affected area either during or after urination. This significantly reduces inflammation and stinging, and promotes tissue healing. One to two teaspoons of sea salt may be added to each 8-ounce bottle.

Douches

Douches are prepared the same way as vaginal rinses, except that the infusion or decoction is placed in a douche bottle or bag apparatus. Vulnerary, antimicrobial, and astringent herbs are commonly used, and may include *Calendula officinalis, Thymus vulgaris, Usnea barbata, Achillea millefolium, Myrica cerifera*, and many others. The addition of several drops of antimicrobial essential oil is common when douching is intended for the treatment of vaginal infection, however regular douching is not recommended and can be counter productive.

Herbal Baths

Herbal baths can be a rejuvenating ritual, an opportunity for relaxation, or a healing external application. They are useful for a variety of complaints: sore muscles, exhaustion, stress, irritability, insomnia, headache, and respiratory congestion. Sitz baths can be used to facilitate tissue repair (e.g., to heal an episiotomy wound), to reduce inflammation (as with hemorrhoids and postnatal perineal trauma), and genitourinary infection (e.g., vaginal candidiasis). Care must be taken with baths to avoid burns from overly hot water.

A full herbal bath can be made two ways. One is to fill a cotton cloth, clean sack, or large cotton tea sack with at least 1 ounce of aromatic or mucilaginous herbs. Fasten the closed cloth to the faucet and let hot bath water run through the sack while filling the tub. Squeeze the sack now and then to wring out the ''tea.'' This will make a mild but pleasant herb bath. The second method is to prepare 2 quarts of a strong herbal infusion or decoction, strain out the herbs, and pour the liquid into the tub of water. Additionally, a few drops of essential oil may be added to the bath after it is filled to add to the aromatic or antimicrobial effects of the bath.

If using aromatic herbs, keeping the door to the bathroom closed while filling the tub will allow the aroma of the herbs to fill the air. This adds to the relaxing effect of the bath.

A sitz bath is prepared as the second method of the full herbal bath. One quart of strong decoction, or 2 of quarts of strong infusion, are placed in a sitz bath, or alternatively, in a shallow tub with filled with just enough water to reach hip level. Sea salt and antimicrobial essential oils such as lavender, thyme, rosemary, or oregano are commonly added to the water for additional antiseptic effects.

OIL-BASED PREPARATIONS

Oil-based preparations rely on the use of olive oil, almond oil, coconut oil, cocoa butter, or other oils as a base, to which are added medicated herbal oils, essential oils, herbal powders, and tinctures. Note that when herbal tinctures are added to suppositories, the oil–water combination will create slightly separated layers in the finished product.

Suppositories and Pessaries

Suppositories allow for the insertion of herbal preparations into a body orifice. They are commonly used for vaginal and rectal complaints. The word suppository is derived from the Latin *suppositorum*, which means, ''something placed beneath.'' Pessary is an interchangeable term, referring specifically to a vaginal suppository. Suppositories, like many of the other preparations discussed in this section, are made from herbs that are anti-inflammatory to the mucous membranes, astringent to excessive discharges and damaged tissue, and antimicrobial. They are used extensively for vaginal infections and inflammation, cervical dysplasia, rectal fissures, and hemorrhoids.

Suppository molds can easily be prepared at home by patients, using aluminum foil that has been folded several times lengthwise, and then widthwise, to form a trough approximately 8 inches in length and ½ inch in width. Alternatively, suppository molds can be purchased from apothecary supply shops. The base of the suppository is a combination of coconut oil and cocoa butter, to which is added the desired combination of medicated oils, powdered herbs, and tinctures. This is then poured into the mold, refrigerated to harden, cut into pieces the size of the patient's pinky finger, and inserted as needed. It is recommended that women wear a sanitary napkin when the suppository is in place, lest the melting oil stain the undergarments.

To prepare a suppository:

1. Melt ¼ cup each of cocoa butter and coconut oil.
2. Add 2 tablespoons of powdered herbs, for example, a combination of *Hydrastis canadensis, Ulmus rubra, and Althea officinalis* powders.
3. Add 15 drops of essential oil, for example, *Lavandula officinalis* and *Thymus vulgaris* and/or 1 tablespoon of appropriate herbal tincture.
4. Add 1 tablespoon of infused oil of *Calendula officinalis* (Fig. 3-30).
5. Stir well and pour into the suppository mold. Refrigerate until firm. Insert vaginally or rectally as needed.

Suppositories will keep in the refrigerator or freezer for many weeks.

Salves (Ointments)

Salves are used for healing skin trauma and irritated or dry tissue. They are relatively easy to prepare and stored in a cool, dark environment, have a long shelf-life—often up to a year or more. Salve can be made from pre-made infused oil or by simmering herbs in oil to extract their constituents. Additionally, dried powdered herbs, essential oils, and tinctures can be added to a salve. Herbs commonly used in salves include *Calendula officinalis, Plantago lanceolata, Stellaria media, Hamamelis virga urea, Hypericum perforatum, Commiphora mol mol, Hydrastis canadensis*, and *Symphytum officinale* (radix or folia).

(Note: If making salve from pre-made oil, begin with step 3. See the following for directions on making herbal oil.) To prepare herbal salve:

1. Place 1 ounce of dried herbs and ½ of a cup of good-quality olive oil in a small saucepan. Simmer for 1 hour on a very low flame with the pot covered. Add additional oil if necessary to keep the herbs immerse, and watch carefully to avoid scorching.
2. Strain the herbs well through a cotton cloth or cheesecloth, squeezing as much of the oil as possible out of the plant material. You may need to let the oil cool before this can be done.
3. Pour the extracted oil into a clean, dry saucepan, adding ½ ounce of grated beeswax per every 4 ounces of oil. Melt over a low flame, stirring constantly until the beeswax is fully dissolved.
4. Check for readiness by pouring 1 teaspoon of the product into a small clean glass jar and placing in the freezer for 3 to 5 minutes. The salve should

Figure 3-30 Calendula (*Calendula officinalis*). (Photo by Martin Wall.)

be firm and solid without being so hard that it can not be melted into your skin. If the consistency is correct, then pour the salve into small jars, cool to room temperature, cover, label, and store. If your salve is too soft, add more beeswax; if it is too hard, add more oil.

Preparing herbal oil for use in salve: Take the finely cut herb(s) of your choice and place in a clean, dry glass jar with a lid. Cover the herb material with olive oil, extending 1 inch above the top of the herbs. Cover and place the container in the sun or a warm location for 2 weeks. Shake the container daily. Strain the liquid into a clean glass jar, discarding the herb material. Store in a cool, dark place. This oil can be used to prepare salve, or alone as a medicated oil. The herbs used must be extractable in oil.

BOTANICAL MEDICINE DOSING

*Aviva Romm**

The goal of the practitioner is to provide an effective dose of a medication—enough to elicit a therapeutic response, yet not so much as to cause undesirable side effects or toxicity. Finding a *minimum effective dose* is ideal as it maximizes efficacy and safety, and is also the most economical for the patient.

What constitutes an effective dose is a matter of some debate amongst phytotherapists. For solid forms of herbal medicines (e.g., dried bulk herbs to be used in teas and decoctions), dosing amounts are fairly standard. However there are varying schools of although for tincture prescribing, with practices ranging anywhere from giving single drops (''drop dosing'') of a botanical medicine to using large doses (as much as 5 to 10 mL of tincture three times daily), the latter common in European herbal medicine and among medical herbalists. The drop dose strategy is not consistent with traditional prescribing practices, nor do most herbalist feels it bears out clinically, but seems to be based on homeopathic prescribing patterns and interpretations of the apparently low doses used in Eclectic medicine. The homeopathic dose application is not conducive to the use of herbs for their phytochemical constituents, but reflects an *energetic* model of herbal medicine. Although Eclectic medicines may have been used in low doses, they were actually highly concentrated pharmaceutical-like preparations requiring a low dose. Looking to traditional systems of herbal medicine, such as traditional Chinese medicine (TCM) and Ayurvedic medicine, one finds that high doses of

*The author wishes to thank Ed Smith of HerbPharm for his guidance in preparing the discussion on tincture strength and Paul Bergner for his work in elucidating the concepts of physiologic and pharmacologic dosing.

botanical prescriptions are the norm, with patients instructed to take as many as 30 g per day of an herb in tea or decoction form. Tinctures were not typically used other than in the form of medicated wines.

Western herbal practitioners worldwide most commonly subscribe to what is referred to as a ''physiologic'' dosing strategy, that is, giving only enough of the botanical medicine to have a therapeutic effect, whereas others may prefer a ''pharmacologic'' dosing strategy, prescribing larger doses to elicit a marked response.[51] Physiologic dosing is most appropriate for herbal products that are intended for long-term, regular use, as in the treatment of chronic conditions, or for the treatment of mild conditions. Pharmacologic dosing is more commonly used for acute or serious conditions requiring a quick response.

The complexity of dosing with tinctures is due to the fact that tinctures do not come in a single standard strength. They are available in a variety of strengths and concentrations, are made from both fresh and dried material, are made from material harvested at various times leading to natural chemical variation in the product, and are made from starting materials of varying quality. As described in Herbal Preparations, tinctures are prepared in varying strengths, with ratios of herb to extraction menstruum (e.g., 1:2, 1:3, 1:4, etc.) affecting the strength of the final product.

Further, even if two different tinctures of the same herb are 1:5, that does not mean they are the same strength. Take a 1:5 feverfew (*Tanacetum parthenium*) tincture, for example. One may be made from whole feverfew plants (woody stem and all), and another from only leaf and flowers that have been stripped clean of stems, greatly affecting the composition and strength of the final product. Or, whereas some companies use the whole St. John's wort (*Hypericum perfoliatum*) plant (2 to 4 feet tall) stems and all, others use only the medicinal flowering tops and an additional 2 to 6 inches, depending upon the height of the plants. The latter will yield a more potent medicine. One calendula (*Calendula officinalis*) tincture may be made from old, faded, odorless, fumigated calendula flowers, and another from recently and properly dried, organically cultivated calendula that is still rich in color, aroma and flavor, and activity. Two different tinctures could be 1:5 from the same herb material, but can still be different strengths because different menstruum or extraction methods were used, or the same extraction methods may have been used, but with different extraction efficiency.

Fresh herb tinctures can appear stronger than they actually are, but that is because of the math. For example, 1:2 fresh tinctures, when calculated according to equivalent dry herb are often only around 1:8 or 1:10, depending upon the amount of water weight of the fresh herb. Some herbs require ''curing'' in order to extract their full therapeutic potential. For example, it is necessary to activate endogenous enzymes in wild cherry bark (*Prunus serotina*) during extraction in order to enable hydrolysis of the bark's cyanogenic glycosides. Thus two 1:4 wild cherry tinctures—one hydrolyzed, and one not—are by no means equal in potential therapeutic activity (or potential toxicity). Simply put, there is no universal menstruum, herb/menstruum ratio, or extraction technique for all herbs. Each herb needs to be extracted according to its own unique physical and chemical characteristics and the strength and activity of the medication desired.

It is important to note that the ratio of herb to menstruum in a tincture is not always reflective of tincture strength. Although a 1:2 tincture is a stronger tincture than a 1:3, 1:4, or even 1:10 of the same herb, a 1:10 is not always a weak tincture. Many herbs that would be toxic in more concentrated strengths are standardly prepared as 1:10 tinctures according to the Brussels Protocol of the early twentieth century. Arnica (*Arnica montana*), for example, is prepared as such based on pharmacopeial standards, and given its potential toxicity, a 1:10 may still provide quite a strong medicine.

Although it may seem most reasonable to rely on the results of botanical clinical trials, using only those doses that were found to be successful, most herbs have not been subject to clinical trials and therefore there are only a limited number of herbs that have scientifically established doses. The preparations used in clinical trial do not necessarily have phytoequivalence to herbs sold on the common market, often making clinical trial doses irrelevant to the consumer and the practitioner. Further, the success of doses in clinical trials is relevant to those patients in the clinical trial, and does not necessarily apply to others who may not match the characteristics of trial subjects, for example, for weight, age, metabolism, and health status. In fact, age, weight, and clinical status (i.e., pregnancy, immune status, etc.) will all affect what is an appropriate dose for an individual patient. Finally, clinical trials most often do not reflect traditional or modern clinical herbal practice strategies, and thus dosing information derived from clinical trials, may be irrelevant to how the herb is used by the herbalist, which will most likely be in combination with other herbs, for example.

Dosages for the individual patient can be derived from a standard dosage range, as presented in Appendix 2. These were derived from a composite of what are considered some of the most authoritative information sources currently available in botanical medicine, with the traditional dose referring to the doses expected to be used by herbalists in clinical practice, and the clinical trial dose being based on the ranges determined effective in positive clinical trials, when available. Doses are provided for the form in which each herb is typically used.

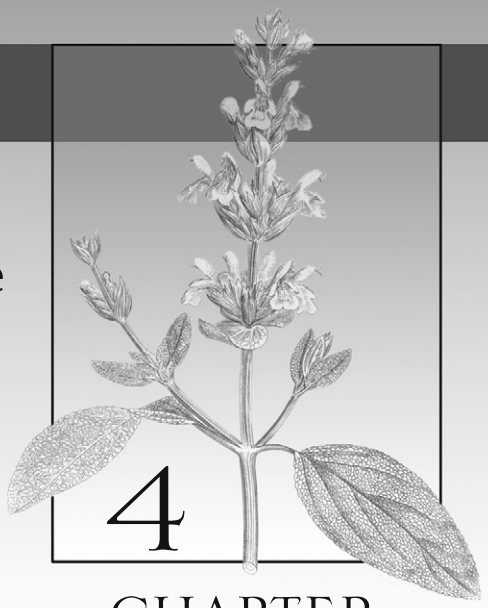
The dosage range for tinctures assumes that a 1:4 tincture is being used unless otherwise indicated. Should practitioners be using more or less concentrated products, such as 1:3 or 1:5 strengths, doses can easily be adjusted mathematically, or the given dose can simply be used at the lower or higher range, respectively. Although extrapolation from a 1:4 to a 1:2 or 1:1 extract cannot be directly made by simply proportional adjustment, one can get a relatively good approximation of a safe and effective dose by dividing the dose of a 1:4 tincture by 4. Doses are based on the assumption that the

patient is a nonpregnant, adult with an average weight or approximately 140 pounds. Adjustments for substantial weight variations, particularly for women who are more slight, can be made by using herbs in the lower range for women significantly (>20 lb) below the average. Lower doses are also generally appropriate for chronic conditions, whereas higher doses may be required in acute conditions; however, lower doses can also be given with greater frequency for acute conditions.

Dosing of herbal medicines, unlike pharmaceutical drugs, is not an exact science. Traditional doses are based on experience, trial and error, and historical use. Individual patients may benefit with lower doses or may require slightly higher doses. A complete list of doses for all herbs included in this text is found in Appendix 1.

Guidelines for Herbal Medicine Use

Roy Upton and Aviva Romm



4 CHAPTER

BOTANICAL MEDICINE SAFETY: GUIDELINES FOR PRACTITIONERS

Roy Upton

Estimates suggest that as many as 50% of Americans use some type of herbal supplements, as many as 18% use them in conjunction with pharmaceutical drugs, and most do not inform their health care providers of herbal medicine use (see Chapter 1).[1–8] Botanical medicine safety has, therefore, become a critical issue for practitioners, whether themselves prescribing herbal medicines in practice, or in caring for patients who are self-medicating with herbs.

One central role of the practitioner must be to maximize patient safety and treatment efficacy, minimizing the likelihood of risk, and helping patients to make the most appropriate decisions regarding both conventional and natural therapies.

Assessing the safety of individual botanical medicines can be challenging due to lack of a rigorous scientific evidence base for many herbs. Practitioners must rely on a composite of information to assemble a clear picture of whether an herb is not only generally safe, but safe for an individual patient. This takes time, requires quick access to information, and can still leave the practitioner with a sense of uncertainty. A number of resources can be used for making safety determinations, including historical literature, adverse events reports, safety reviews, books, herb–drug interaction charts, and botanical monographs.

Numerous and complex factors influence botanical medicine safety and risk, including:

- The safety profile of individual plants
- Potential allergic or idiosyncratic reactions
- Potential or known interactions with other substances (e.g., herb–drug interactions)
- Product adulteration or contamination (e.g., heavy metals, pharmaceuticals, or other contaminants)
- Substitutions (the accidental or deliberate use of the wrong herb)
- Timing of use (e.g., prior to surgery or during pregnancy/lactation)
- Dosage
- Duration of use (e.g., potential for accumulate toxicity)
- Lack of appropriate therapy for a medical condition

Botanical medicine safety is a broad and complex subject, far larger than can be adequately addressed in a single chapter. Nonetheless, a text on botanical medicine would be incomplete without addressing this critical topic. This chapter provides an overview of the most pertinent botanical medicine safety concerns relevant to clinical practice. It is suggested that readers obtain additional references on this topic, recommendations for which appear in Table 4-1.

The American Herbal Products Association has classified herbs according to the following safety scale:

Class 1. Herbs that can be safely consumed when used appropriately.

- No significant adverse events in clinical trials
- No case reports with significant adverse events and high probability of causality
- No identified concerns for use during pregnancy or lactation
- No innately toxic constituents
- History of safe traditional use
- Toxicity associated with excessive use is not a basis for exclusion from this class
- Idiosyncratic, minor, or self-limiting side effects are not bases for exclusion from this class

Class 2. Herbs for which the following use restrictions apply, unless otherwise directed by an expert qualified in the use of the described substance:

2a: For external use only

- Toxicity demonstrated with crude preparation taken at traditional dose
- Adverse event data in humans with probability of causality of toxicity (hepatotoxicity, nephrotoxicity, neurotoxicity)

2b: Not to be used during pregnancy

- Adverse event data in human exists and has probability of causality
- Data in animals suggesting teratogenicity or fetal wastage

TABLE 4-1

Resources for Assessing Botanical Medicine Safety

BOTANICAL	AUTHOR/EDITOR	PUBLISHER
Texts		
Adverse Effects of Herbal Drugs (three volumes)	DeSmet P.	Springer Verlag
Botanical Dietary Supplements: Quality, Safety, and Efficacy	Mahady, G., Fong H., Farnsworth N.	Swets and Zeilinger
Botanical Safety Handbook	McGuffin M., Hobbs C., Upton R., Goldberg A.	CRC Press, Boca Raton, FL
Commission E (translated)	Blumenthal M. (ed.)	American Botanical Council, Austin, TX
Expanded Commission E	Blumenthal M. (ed.)	American Botanical Council, Austin, TX
Herb-Drug Interaction Handbook	Herr SM.	Church St. Books
Herb, Nutrient, and Drug Interactions	Stargrove, M. Treasure, J.	Elsevier Mosby
The Essential Guide to Herbal Safety	Bone K., Mills S.	Churchill Livingstone
Toxicology and Clinical Pharmacology of Herbal Products	Cupp M.	Humana Press
Monographs		
American Herbal Pharmacopoeia (AHP)	Upton R. (ed.)	American Herbal Pharmacopoeia, Scotts Valley, CA
European Scientific Cooperative of Phytotherapy (ESCOP)	ESCOP	ESCOP
World Health Organization (WHO)	World Health Organization	Geneva, Switzerland
Websites		
The Cochrane Library	http://www.cochrane.org/	
Health Canada	http://www.hc-sc.gc.ca	
The National Center for Complementary and Alternative Medicine (NCCAM)	www.nccam.nih.gov	National Institutes of Health
Natural Medicines Comprehensive Database	www.naturaldatabase.com	
Natural Standard	http://www.naturalstandard.com/*	Elsevier Mosby
Natural Standard Herb and Supplemental Handbook: The Clinical Bottom Line	http://naturalstandard.com/*	Elsevier Mosby
Natural Standard Herb and Supplement Reference: Evidence–Based Clinical Reviews	http://naturalstandard.com/*	Elsevier Mosby
Office of Dietary Supplements (ODS)	www.ods.od.nih.gov	National Institutes of Health
TOXNET	http://toxnet.nlm.nih.gov	National Library of Medicine

*Requires subscription.

- Traditional use contraindicates (abortifacient or uterine stimulant)

2c: Not to be used while nursing

- Potential hepatotoxicity or neurotoxicity
- Bioavailability in breast milk has been demonstrated
- Traditional use contraindicates
- Adverse event data in human exists and has probability of causality

2d: Other specific use restrictions as noted

- Information exists for unsafe use by specific populations

Class 3. Herbs for which significant data exist to recommend the following labeling:
''To be used only under the supervision of an expert qualified in the appropriate use of this substance.'' Labeling must include proper use information: dosage, contradictions, potential adverse effects and drug interactions, and any other relevant information related to the safe use of the substance.

- Narrow therapeutic range
- Identified safety concerns in many populations

Class 4. Herbs for which insufficient data are available for classification.

- No significant history of traditional use

ADVERSE DRUG REACTIONS, HERBAL ADVERSE EVENT REPORTS, AND ADVERSE EVENTS REPORTING SYSTEMS

Several operational definitions exist regarding what constitutes adverse drug reactions (ADRs) of varying severity. According to the World Health Organization (WHO), an ADR is defined as ''Any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or

therapy of disease, or for the modification of physiologic function.''[9] For reporting purposes, the FDA categorizes a serious adverse event as one in which ''the patient outcome is death, life-threatening (real risk of dying), hospitalization (initial or prolonged), disability (significant, persistent, or permanent), congenital anomaly, or required intervention to prevent permanent impairment or damage.''[10] The American Society of Health-System Pharmacists (ASHP) defines a significant ADR as any unexpected, unintended, undesired, or excessive response to a drug that:

- Requires discontinuing the drug
- Requires changing the drug therapy
- Requires modifying the dose (except for minor dosage adjustments)
- Necessitates admission to a hospital
- Prolongs stay in a health care facility
- Necessitates supportive treatment
- Significantly complicates diagnosis
- Negatively affects prognosis
- Results in temporary or permanent harm, disability, or death

Consistent with this definition, allergic and idiosyncratic reactions are also considered ADRs.[11] Not technically classified as ADRs are side effects, which are defined by ASHP as ''an expected, well-known reaction resulting in little or no change in patient management (e.g., drowsiness or dry mouth due to administration of certain antihistamines or nausea associated with the use of antineoplastics)'' and that has ''a predictable frequency and an effect whose intensity and occurrence are related to the size of the dose.'' Also not categorized as ADRs are ''drug withdrawal, drug-abuse syndromes, accidental poisoning, and drug-overdose complications.''[11]

Following the thalidomide disaster of the 1950s, WHO established and has maintained an international adverse drug events reporting system. Since 1978, the WHO International Drug Monitoring Program (IDMP) has collected ADR reports from 60 participating nations, and now includes both pharmaceutical and botanical medicine information. Of the more than 2.5 million reports in their International Drug Information System (INTDIS) database, approximately 10,000 relate to herbal medicines, primarily involving multiple ingredients.[12] This demonstrates a remarkably low incidence of serious ADRs resulting from herbal products, especially when compared with that of pharmaceutical drugs and the much larger worldwide consumption of botanicals compared with conventional medications. Many of the reports were associated with negative interactions with conventional medications and most side effects were reported for people 60 to 69 years of age.

A retrospective review of adverse effects reports (AERs) due to herbal medicines made to the National Poisons Unit of the United Kingdom was conducted in 1991. Between 1983 and 1989 a total of 1070 inquiries were made. Twenty-five percent of reports were of subjects with acute symptoms. Most confirmed adverse events were due to herbal sedatives.[13] Ernst conducted a survey of complementary and alternative medicine users in the United Kingdom. Of those who had reported use of herbal medicines, 8% reported having observed adverse effects, none of which were considered serious.[13]

Adverse events associated with dietary supplements are not effectively monitored in the United States.[14] The main AER systems are local and national poison control centers and the FDA's MedWatch program, all of which have serious limitations. Most reporting systems, including these, are passive systems with no criteria for submission, no verification of the authenticity or accuracy of reports, and no effective follow-up or investigation. In order to be meaningful, AERs must be critically reviewed and products analyzed. Yet, neither a systematic review of the patient or event is conducted, nor is the product involved in an event typically analyzed, making it impossible to establish a causal relationship between an event and an herb/herbal product. Further, recording practices are highly variable between systems and between centers within the same reporting system and there is often selection bias.[14]

A relatively recent survey of data from US poison control centers evaluated the incidence of AERs for all dietary supplements.[14] In a 10-month period, 1466 reports of potential events due to ingestion of supplements were made. More than one-third of these (534) were unintentional ingestions; 471 reported no symptoms. Half (741) of the total reports produced symptoms. The reviewers reported that 66% (489) were associated with dietary supplement exposure with varying degrees of confidence and 27% (132) were considered to be either definitely or probably related, whereas 34% (166) were reported as definitely or probably unrelated. The balance of reports (39%; 190) represented a 50% chance for the event to be correlated to supplement use. Ninety of the subjects used supplements in an attempted suicide, whereas the others used supplements for various reasons, ranging from the treatment of specific conditions (35%) to enhanced athletic performance (10%) and dieting (14%), among others. Botanicals most frequently associated with adverse events included ma huang (*Ephedra sinensis*), St. John's wort (*Hypericum perforatum*), guarana (*Paullinia cupana*), and ginseng (species not identified). Of a total of 401 calls specifically related to adverse events of dietary supplements, 286 events were classified as mild, 89 as moderate, and 22 as severe, with a total of four deaths. Subjects experiencing symptoms were taking as many as 44 ingredients concurrently and had more serious adverse events than did those taking fewer supplements long-term. However, 89% of these adverse events were considered mild (57%) or moderate (32%); 11% were reported as severe or resulted in death. Most acute reports (95%) were considered mild (77%) or moderate (18%), and 4% severe or death. Many of these reports suffer from the same limitations of not being subjected to critical review or product characterization. Of all the supplement adverse events reported, only 12 products were retrieved for analysis. In comparison, a total of 61,229 calls regarding adverse events due to other consumed substances, mostly pharmaceuticals, were made in the same time period.

CATEGORIES OF COMMON HERBAL ADVERSE EFFECTS

The Toxicologic Medical Unit of Guy's and St. Thomas Hospital in London conducted a 5-year toxicologic review of adverse events caused by herbal drugs based on reports made to the National Poison Control Center.[15] Drowsiness and dizziness followed by vomiting, diarrhea, abdominal pain, and nausea were the most commonly reported side effects. Other events of note included agitation and irritability, cardiac arrhythmias, psychological disturbances, and facial flushing. Interaction of botanical and conventional anticoagulants has resulted in reports of abnormal bleeding, and effects of interactions with herbs that rely on the cytochrome P450 enzyme system have resulted in elevations or decreases in serum drug concentrations affecting clearance times, efficacy, and toxicity. Reports of liver abnormalities were most commonly associated with Chinese herbal medicines.

Allergic and Idiosyncratic Reactions

An allergic reaction is defined as an immunologic hypersensitivity, occurring as the result of unusual sensitivity to a drug.[11] Allergic reactions occur via immune-mediated mechanisms, for example, the development of drug-specific antibodies, reactions to drug–antibody complexes, or release of inflammatory compounds. They are largely unpredictable and can range from minor complaints such as itchy eyes, runny nose, and minor skin reactions, to fatal anaphylactic shock. Allergic reactions to herbal medicines are uncommon, but may result from a compound inherent to the plant, or from contamination of the plant with molds, fungi, or other agents. Patients with known sensitivity to specific allergens, for example, members of the Asteraceae family, should use herbs in this family with caution or avoid them altogether. Plants in this family are rich in sesquiterpene lactones, a constituent with known allergenicity, and primarily responsible for allergic reactions; however, any plant may cause a reaction in any individual.[16]

An idiosyncratic reaction is defined as an abnormal susceptibility to a drug peculiar to the individual.[11] Idiosyncratic drug reactions (IDRs) are also immune mediated, and may result in severe skin reactions, anaphylaxis, blood dyscrasias, hepatotoxicity, and internal organ involvement. Symptoms such as fever and joint pain may accompany an IDR. The immune involvement appears to be a result of the interaction of cellular proteins with reactive drug metabolites, and thus differs slightly from the etiology of allergic reactions. These types of reactions occur very infrequently, are independent of dose, and are highly unpredictable. Risk factors for idiosyncratic reactions include increasing age, concurrent use of multiple medications (polypharmacy), hepatic disease, renal disease, malnutrition and/or decreased body weight, chronic alcohol consumption, and gender (women are more susceptible to IDRs). Specific enzyme deficiencies may be involved in some IDRs. Hepatotoxicity reactions reported with use of kava kava (Piper methysticum) are most likely a result of idiosyncratic reaction to this herb.[16]

Skin reactions, such as contact dermatitis, irritation, and burns are the most common types of allergic reaction to herbs, and are associated with the topical application of irritating herbs or repeated exposure through handling of herbs, such as among employees in the herbal manufacturing industry. Asthma is also known to occur as a result of repeated exposure in this latter population. Care must therefore be taken when applying external therapies and also with repeated exposure to herbs and dust from herbs. Reports of contact dermatitis, allergic reaction, or other skin irritation are especially common with garlic (*Allium sativum*), mustard powder, cayenne pepper (*Capsicum annum*), and members of the Asteraceae family. Oral administration of the following herbs has also been associated with general skin reaction: echinacea (*Echinacea* spp.), goldenrod (*Solidago virgaurea*), and kava.[16]

Adverse Reactions Caused by Overdose

There are a number of reported incidences of overdose with herbal products, including unintentional overdose, as well as suicide attempts, most of which have failed.[17] There is little information regarding the treatment of overdose of herbal products. As with all pharmacologic agents, treatment should be based on the herb's mechanisms of action and the reaction.

Reactions Due to Specific Herbs and Toxic Compounds in Plants

Ephedra (Ma Huang)

In the United States, herbal dietary supplement adverse events resulting from the ingestion of ephedrine-containing preparations based on the botanical ma huang (Ephedra sinensis) have been the most widely experienced and reported. Claims of several thousand of such ''ephedra-related'' adverse events by the Food and Drug Administration (FDA) have led to both state and federal restrictions against the inclusion of ephedra in dietary supplements. Over-the-counter (OTC) medications containing ephedrine have remained on the market.

Ma huang has been used in Chinese herbal medicine since at least the first century, primarily for acute conditions of the upper respiratory system. TCM practitioners and Western herbalists have used this herb with a high degree of safety. Pharmacologically, it is an adrenomimetic, mimicking the effects of epinephrine, eliciting a central nervous stimulating effect and accompanying thermogenic and appetite suppressant effects; thus, it is used in weight loss and ''energy-enhancing'' products. Both of these categories are subject to overuse and abuse for those seeking quick weight loss solutions and enhanced athletic performance. However, because the mechanism is one of putting the body into an artificial state of induced stress, the use of ephedra for both indications is counter to principles of most natural health care providers. In actuality, a review of the adverse events collected by FDA show that adverse events caused by the botanical itself are rare and even perhaps nonexistent. Rather, ephedra-related adverse effects have

been alleged for products that contain concentrated amounts of ephedrine, usually in combination with high concentrations of caffeine. The most common side effects are nervous irritability, anxiety, heart palpitations, and hypertension. Although in most subjects these are minor and reversible upon discontinuation of the preparation, in some they have been associated with significant adverse effects and reportedly even fatal outcomes. Unfortunately, the ban on all ephedra products has led to a prohibition against the legitimate and appropriate use of the crude herb ma huang by herbal practitioners.

Kava Kava *(Piper methysticum)*

Since 2000, the traditionally used South Pacific anxiolytic herb kava kava has been reported to be associated with approximately 60 reports of hepatotoxicity. About 26 reports were generated between Germany and Switzerland, several in the United Kingdom, and the FDA collected another 26. A large number of the subjects were concomitantly taking potentially hepatotoxic drugs; some had been diagnosed with elevated liver enzymes prior to kava use, and in at least one case, elevated liver enzymes returned to normal when the subject discontinued combined kava use and chemotherapy. In the majority of these cases and based on formal toxicologic reviews of the available data, causal relationship could be established. Of these cases, it appears that in four of the original 26 European reports hepatotoxicity may have been exacerbated by kava, and from the available information, there appears to have been one person whose hepatotoxicity was directly related to kava consumption. The majority of other cases could not be linked directly to kava.

Nevertheless, based on these reports several countries have adopted restrictions on kava sales. For example, in Australia, kava products must be prepared as aqueous (nonalcohol) solutions of whole or peeled rhizome, and must not contain a recommended daily dose of more than 250 mg of kava lactones; tablets or capsules must not exceed 125 mg/tablet; tea bags must not exceed 3 g/tea bag. If a product contains more than 25 mg/dose, then appropriate warning labels must accompany the product. In the United Kingdom, legislation was enacted as of 2002 to prohibit the sale of foods containing kava, and herbal products were limited to 625 mg/dose. In June 2002, Germany banned the therapeutic use of kava completely.[16] A review was conducted by the FDA. Due to the lack of compelling data about a causal relationship, no ban was imposed in the United States. However, fear of potential litigation has caused product liability insurance carriers to deny coverage for kava products, ostensibly eliminating widespread availability of kava. Such events have to be juxtaposed against prevalence of use. In Europe alone, more than 100 million daily doses are used. The Swiss regulatory agency in charge of the control of medicines reported the following: ''It is estimated that 8 cases of hepatotoxicity have occurred in a total of 40 million daily doses or 1 case per 170,000 courses of treatments of 30-days duration.''[18] The normal incidence of hepatotoxicity in the population at large is 10 in 10,000. This suggests that hepatotoxic events of kava are much less than what is normally observed in the population at large. For a thorough review of kava safety, see *The Essential Guide to Herbal Safety*.

Toxic Plants Not Typically Used

Some plants contain known toxins so potent that the plants are not typically used medicinally nor sold on the common market. If they are prescribed, they are generally done so by licensed care providers (e.g., ND, MD, LAc) and under strict controls. Therefore, these herbs pose little threat to the average patient, with the exception of accidental substitutions (e.g., that of digitalis leaf in a plantain product in the late 1990s), use of toxic herbs by medical herbalists, or as a result of prescription by a licensed care provider. Many plants—including commonly consumed foods—contain compounds that might be toxic if consumed in large doses and/or for prolonged periods of time. If used properly, these too pose little risk to the average patient. However, several compounds found in herbs have recently been or continue to be sold on the market that should signal a red flag to practitioners, as they are known or suspected to cause significant damage when taken in medicinal doses or for a sustained time. These are discussed briefly in the following.

Pyrrolizidine Alkaloids

The unsaturated form of pyrrolizidine alkaloids (PAs) found in a number of commonly used medicinal plants, for example, comfrey (*Symphytum officinale*), coltsfoot (*Tussilago farfara*), or plants in the genus Senecio, can directly cause veno-occlusive disease (VOD) and have resulted in fatalities, usually when consumed as a survival food during times of drought or famine or when used medicinally over a prolonged period of time or in susceptible individuals. Because a number of botanicals used medicinally contain toxic PAs, and because some herb references continue to recommend such botanicals, caution is warranted (Box 4-1). Not all forms of PAs, such as the saturated PAs found in Echinacea species, are converted to toxic pyrroles, and therefore plants containing nontoxic PAs (saturated) should be distinguished from those that are toxic.[16]

Aristolochic Acids

Aristolochic acid (AA), even in small amounts, can cause both stomach and kidney cancer.[19] A ban on AA-containing plants (Table 4-2) has been implemented in many countries, and the FDA issued a consumer

BOX 4-1

Botanicals Containing Toxic Pyrrolizidine Alkaloids (PAs)

Borage leaf (*Borago officinalis*)
Butterbur leaf and root (*Petasites hybridus*)
Coltsfoot leaf (*Tussilago farfara*)
Comfrey leaf and root (*Symphytum officinalis, S. asperulum, S. uplandicum*)
Eyebright aerial part (*Euphrasia officinalis*)
Life root (*Senecio aureus*)

advisory in 2001 warning the public about this problem. However, many products that may contain AA remain on the market in Asia. Domestically, plants that may be confused with AA-containing plants have been subjected to systematic analysis at the point of importation before they are allowed in commerce. Herbal practitioners must be vigilant about herbal and supplement products that may be mixed with AA-containing plants and ensure that manufactured products prescribed have the necessary controls to avoid adulterants.

Botanical Quality Standards and Reactions Caused by Contamination and Adulteration of Herbs

The safety of any medicinal product is partly dependent on the manner in which the product is produced. Although individuals, organizations, industry, and government are actively working to establish national quality control (QC) standards, current standards are not a guarantee for herbal products in the United States, or those imported from countries such as China and India. European herbal product standards are generally stricter than most other countries, including the United States; thus, European herbal products have a greater likelihood of safety and quality. The most important aspects of QC include the accurate identification, relative purity, and relative quality of raw material used in herbal products (Tables 4-3 and 4-4).

TABLE 4-2

Botanicals Containing Aristolochic Acids (AAs) or Those That May Be Mixed with AA-Containing Plants

AA-CONTAINING PLANTS	POSSIBLE SUBSTITUTIONS*
Aristolochia (Aristolochia fang ji)	Stephania (*Stephania tetrandra*) Akebia (*Akebia* spp.)
Aristolochia manshuriensis	Clematis (*Clematis* spp.)
Wild ginger (*Asarum* spp.)	Used intentionally

*These botanicals do not contain AA. It is recommended that these botanicals be subjected to AA testing to prevent adulteration. For a more complete listing see: http://www.cfsan.fda.gov/~dms/ds-bot2.html

The safety of plants may also be affected by the presence of contaminants not naturally occurring in the plants, including heavy metals (taken up from the soil naturally, resulting from pollution, or their addition as part of traditional formulation or processing, as may be the case with TCM or Ayurvedic preparations and prescriptions), microbial contamination (owing to animal feces or poor handling under unhygienic conditions), or processes that are applied to the plant (e.g., sterilization with ethylene oxide gas, pesticides, fungicide, or gamma irradiation). By law, herbal products that enter the market must be safe for consumption as a food and be free of toxic microbial contamination. Similarly, certain treatments, such as with pesticides and irradiation, are not permitted on herbal products unless expressly approved. Nonetheless, because herbs are obtained from a variety of sources worldwide, many of which routinely use such treatments, herbal products may contain one or more of these contaminants.

Most herbs and botanical products are not tested before importation into the United States. It is impossible for consumers and health professionals to determine if such contaminations are present without subjecting the product to extensive testing. Again, any presence of a known pathogen (e.g., Escherichia coliform) or prohibited treatment (certain pesticides or gamma irradiation) renders a product adulterated and subject to removal from the market by the FDA. However, regulatory oversight in this area is almost nonexistent. The best way for practitioners to avoid potentially contaminated or adulterated products is to become knowledgeable of the practices of suppliers and manufacturers, and identify those with high quality standards (see Identifying Quality Botanical Medicine Products). Companies that are run by or employ qualified herbalists on their staff and that serve the needs of health professionals are often the most reliable, but this in itself is not a guarantee of quality.[20]

Traditional Chinese Herbal Medicines Mixed with Conventional Pharmaceutical Drugs

It is not uncommon for Chinese herbal products made in Asia, including those sold in the United States, to be adulterated with conventional pharmaceutical drugs.[21] Adulterants have included caffeine, paracetamol, indomethacin, hydrochlorothiazide, prednisolone, barbiturates, and corticosteroids.[22] The purpose for the

TABLE 4-3

Potential Toxic Plant Adulterations Causing Safety Concerns

BOTANICAL NOMENCLATURE	POTENTIAL ADULTERANT	POTENTIAL ADVERSE EVENT
Black cohosh	Other species of cohosh	Some species of cohosh are toxic
Echinacea purpurea and others species	Missouri snakeroot	Allergic reaction in sensitive individuals
Siberian ginseng (eleuthera)	Chinese silk vine	Birth defects if used in pregnancy
Skullcap	Germander	Hepatotoxicity
Chinese star anise	Japanese star anise	Convulsions
Stephania	Aristolochia fang ji	Nephrotoxicity, cancer

TABLE **4-4**

Potential Contaminants of Herbal Products

ADULTERATING AGENT	EXAMPLES
Botanicals	Aristolochic acid-containing plants, belladonna, Chinese silk vine, digitalis, germander, Japanese star anise, non-medicinal plant parts
Filth	Dirt, insect fragments
Microorganisms*	Toxic strains of *E. coli*, *Staphylococcus aureus*, salmonella, shigella, *Pseudomonas aeruginosa*
Microbial toxins	Aflatoxins, bacterial endotoxins
Pesticides**	Chlorinated pesticides (DDT, DDE, aldrin, dieldrin), fungicides, herbicides
Sterilization Agents†	Ethylene oxide, methyl bromide, phosphine, gamma-irradiation
Heavy metals‡	Arsenic, cadmium, lead, mercury
Conventional Drugs§	Analgesics, anticoagulants, anti-inflammatories, benzodiazepines corticosteroids, hormones

*Current law prohibits the presence of toxic microorganisms in herbal products. Contaminated products can be removed from the market. To date, there have been no published reports of herbal products toxicity from such microorganisms.

**Although some of these pesticides have been banned in the United States for decades, they may still be in use in other countries. Conversely, some pesticides may be approved for use in common foods but lack approval for use on herbal products.

†These sterilization processes, although approved for use in certain foods, are not approved for use on herbal products.

‡Heavy metals in food and water is a problem worldwide but have been specifically noted to occur in numerous herbal medicine products manufactured in China.

§It is prohibited to combine conventional drugs in products marketed as dietary supplements.

inclusion of pharmaceutical drugs in botanical products is presumed increased efficacy. However, inclusion of such substances is not consistent with principles of traditional Chinese medicines. In a survey evaluating herbal products used in hospitals in Taiwan, approximately 24% of 2406 herbal drugs tested contained pharmaceuticals.

Significantly, in most cases the pharmaceutical adulterants are not disclosed on the product label or packaging. Herbal products adulterated with conventional medications have been found to be manufactured in Mainland China, Hong Kong, and Taiwan.[21] In the United States, under dietary supplement regulations, such products are considered to be adulterated and are subject to removal from the market. Thus far, there have been no reports of the addition of pharmaceuticals in domestically made Chinese herbal products. Although there are undoubtedly high-quality herbal products manufactured in Asia, it is currently almost impossible for consumers and most health professionals (even trained TCM practitioners) to differentiate between adulterated and nonadulterated products. Thus, patients using some traditional Chinese herbal medicine products in combination with conventional medications may be also be unknowingly subjected to unexpected drug–drug interactions via a pharmaceutical adulterant.

Ayurvedic Herbs and Heavy Metal Contamination

In traditional Ayurvedic medicine, the addition of metals is common in selected herbal preparations. These are considered to contribute specific desired activities and are processed in a manner in which it is believed to reduce their toxicity, although this latter assertion has not been critically documented. Additionally, if indeed processing does reduce the toxicity of heavy metals, there is no guarantee that all manufacturers apply these techniques appropriately. The prevalence of heavy metals in Ayurvedic preparations has been reported.

In a study conducted by Saper et al., it was found that one of five Ayurvedic herbal products produced in South Asia and sold in Boston-area South Asian grocery stores contained potentially harmful levels of lead, mercury, and/or arsenic. If taken as recommended by the manufacturers, 20% of products could result in heavy metal intakes above published regulatory standards.[23] The products selected, however, were not necessarily representative of typical Ayurvedic products, as most included heavy metals as ingredients, whereas the majority of Ayurvedic herbal products do not. The Indian government has recently made testing for heavy metals compulsory and labeling for heavy metals within permissible limits mandatory for Ayurvedic medicine products produced in India and destined for export beginning January 1, 2006, as part of an attempt to address this problem.[24]

HERB–DRUG INTERACTIONS

Herb–drug interactions are the most prevalent source of reported adverse effects worldwide and warrant serious concern. According to a 1998 report by Eisenberg et al., 61.5% of patients who used nonconventional therapies did not disclose this to their physicians.[25] In another survey, conducted among patients at the Mayo Clinic, even though patients were asked about supplement use in a written intake form, approximately half did not disclose this until engaged in a structured interview.[26] The same subjects similarly did not report on their prevalence of OTC medication use. These findings suggest that health professionals must be proactive in garnering information about both supplement and OTC drug use. Herbs and pharmaceutical drugs can interact either predictably or unpredictably with both positive and negative results (Table 4-5). Such modulation may be due to direct pharmacologic activity or may lead to changes in the P450 enzyme system that affects drug absorption or clearance. For orally consumed medications, hydrophilic fibers and demulcents can interfere with absorption of conventional drugs, thereby decreasing their efficacy, whereas certain spices (e.g., black pepper, ginger) may increase drug absorption. Many botanical types of tannin (e.g., white oak bark, witch hazel) are capable of binding to

TABLE 4-5

Potential Interactions of Commonly Used Herbs with Conventional Pharmaceuticals

BOTANICAL	CONVENTIONAL MEDICATION	INTERACTION	EVIDENCE
Aloe (*Aloe vera*)	Glyburide	Potentiates activity	Human studies
Ashwagandha (*Withania somnifera*)	Barbiturates; diazepam, clonazepam	Additive effect; prolongs barbiturate-induced sleeping times; potentiates the effects of diazepam and clonazepam	Case report; animal studies
Astragalus (*Astragalus* spp.)	Acyclovir, interleukin, interferon; immunosuppressive agents	Enhances effectiveness of each; may antagonize the effects of immunosuppressives	Pharmacologic mechanisms
Chaste tree (*Vitex agnus-castus*)	Dopaminergic agents	May potentiate the effects	Animal studies
Dong quai (*Angelica sinensis*)	Anticoagulants	Increased risk of bleeding	Case report
Ephedra (*Ephedra sinensis*)	Stimulants	Potentiates the effects of stimulants	Case reports; Pharmacologic mechanisms
Garlic (*Allium sativum*)	Anticoagulants; ritonavir, saquinavir	Potentiates anticoagulant activity; GI discomfort; 51% decrease in plasma levels of saquinavir	Case reports; pharmacologic mechanisms
Ginkgo (*Ginkgo biloba*)	Anticoagulants	Potentiates anticoagulant activity	Case reports, in vitro assays; clinical studies fail to show a potentiation
Ginseng (*Panax ginseng*)	Phenelzine; warfarin; hypoglycemic medications; corticosteroids; digoxin; Lasix; estrogen replacement therapy (ERT)	Mania; increased cAMP; increased anticoagulant effects; increased hypoglycemic effects; increased side effects of corticosteroids; increased serum digoxin levels; decreased efficacy of Lasix; postmenopausal bleeding or mastalgia when taken with ERT	Case reports
Goldenseal (*Hydrastis canadensis*)	Drugs metabolized by P450 system	Inhibits CYP 3A4	Pharmacologic mechanisms
Gymnema (*Gymnema sylvestris*)	Insulin	May increase insulin-producing islet cells; enhances the effects of glyburide and tolbutamide	Animal studies; human clinical trials
Hawthorn (*Crataegus* spp.)	Digoxin, cardiac glycosides in general; theophylline, caffeine, papaverine, adrenaline, sodium nitrate, adenosine; barbiturates	Additive effect on cardiac glycosides; increases coronary artery dilating effects of a number of drugs; increases barbiturate-induced sleeping times	Clinical experience, Pharmacologic mechanisms
Hydrophilic fibers (flax seed, guar gum, psyllium seeds)	Digoxin, paracetamol, bumetanide, metformin, phenoxymethylpenicillin, glibenclamide	Slows gastric absorption	Case reports
Kava (*Piper methysticium*)	Alprazolam, anesthetics, anxiolytics and barbiturates in general, cimetidine, levodopa, terazosin	Potentiation or additive effects resulting in CNS depression; dopamine antagonism	Case reports; Pharmacologic screening

TABLE **4-5**

Potential Interactions of Commonly Used Herbs with Conventional Pharmaceuticals—cont'd

BOTANICAL	CONVENTIONAL MEDICATION	INTERACTION	EVIDENCE
Licorice (*Glycyrrhiza* spp.)	Corticosteroids; potassium sparing diuretics; monoamine oxidase inhibitors (MAOIs); oral contraceptives	Potassium loss; increased corticosteroids plasma levels; increased salt and water retention; increased side effects of MAOIs; glycyrrhizin decreases plasma clearance, increases AUC, increases plasma concentrations of prednisone; potentiates cutaneous vasoconstrictor response	Case reports of hypokalemia; may cause preterm birth; most reports due to excessive consumption of licorice candy, which is most often made with anise (Pimpinella spp.); case reports
Papaya (*Carica paw paw*)	Warfarin	Increased INR	Case reports
Psyllium (*Psyllium ovata*)	Lithium	Decreased lithium concentrations	Case reports
Pepper (*Piper nigrum*)	Phenytoin	Increased absorption of conventional drugs	Clinical trials; Pharmacologic mechanisms
Reishi mushroom (*Ganoderma lucidum*)	Chlorpromazine, reserpine, barbitals; amphetamines; anticoagulants; statin drugs; immunosuppressive agents	Increases sedative effects of conventional drugs; antagonizes amphetamines; may potentiate the effects of anticoagulants and statin drugs; may antagonize the effect of immunosuppressant agents	Pharmacologic mechanisms
Chinese sage (*Salvia miltiorrhiza*)	Anticoagulants	Potentiates effects	Case report
Schisandra (*Schisandra chinensis*)	Chlorpromazine, reserpine, and pentobarbital; amphetamines, caffeine; Adriamycin, acetaminophen; vasoconstrictors and sympathomimetics	Prolongs barbital-induced sleeping times; enhances CNS-inhibitory effects of chlorpromazine, reserpine, and pentobarbital; antagonizes CNS-stimulatory effects of amphetamines and caffeine; reduces cardiotoxicity of Adriamycin and hepatotoxicity of acetaminophen; may increase risk of hypertension if taken with vasoconstrictors and sympathomimetics	Pharmacologic mechanisms
Eleuthero (*Eleutherococcus senticosus*)	Digoxin	Increased plasma level	Case report validated by rechallenge
Stinging nettles (*Urtica dioica*)	Nonsteroidal anti-inflammatories (NSAIDs)	Increased therapeutic effect	Controlled trial

(Continued)

TABLE 4-5

Potential Interactions of Commonly Used Herbs with Conventional Pharmaceuticals—cont'd

BOTANICAL	CONVENTIONAL MEDICATION	INTERACTION	EVIDENCE
St. John's wort (*Hypericum perforatum*)	5-aminolevulinic acid, amitriptyline, cyclosporine, digoxin, indinavir, midazolam, nefazodone, nevirapine, oral contraceptives, paroxetine, phenprocoumon, saquinavir, sertraline, simvastatin, tacrolimus, trazodone, theophylline, warfarin, photosensitizing agents, oral contraceptives	Increases metabolic capacity of cytochrome P enzymes (reduces plasma levels of medications metabolized via these pathways); increases activity of P-glycoprotein; synergistic serotonin uptake inhibition; may potentiate photosensitization, mild serotonin syndrome, decreased theophylline concentrations, reduces efficacy of oral contraceptives	Case reports/case series
Valerian (*Valeriana officinalis*)	GABAergic agents; barbiturates	Additive effects; prolongs barbiturate-induced sleeping times	Clinical findings
Yohimbe (*Pausinystalia johimbe*)	Centrally acting antihypertensives, tricyclic anti-depressants	May antagonize guanabenz and methyldopa; clinically observed CNS effects and hypertension when given with tricyclic antidepressants	In vitro assay; clinical finding

both alkaloid and mineral drugs resulting in decreased absorption of these. (See Appendix 3 for a comprehensive table of potential herb–drug interactions for common herbs.) *The Botanical Safety Handbook* (CRC Press) provides a list of botanicals known to interact with conventional medications.

Combining any substances (e.g., herbs–drugs, drugs–drugs, herbs–herbs, etc.) can lead to synergistic, or positive (additive, potentiating), or negative (antagonistic) effects. Only synergistic effects truly constitute herb–drug interactions in that a new substance is formed in the interaction. In additive effects, the substances are not actually interacting with each other; they are simply both having simultaneous effects on the body. This is not widely explained in the herbal literature, but is an important distinction.

Reports of Interactions

The literature consists mainly of case reports and pharmacologic data that have not been assessed for clinical relevance.[27] Patients or physicians make most individual case reports, usually after having experienced or observed an unexpected adverse reaction. Case reports, which typically are not subjected to critical review, are among the most unreliable body of information from an evidence-based perspective. There have been a few critical reviews that provide some meaningful guidance regarding herb–drug interactions (Box 4-2). Researchers Izzo and Ernst conducted a systematic review of herb–drug interactions of seven of the most popularly used botanicals: garlic, ginkgo, St. John's wort, saw palmetto, kava kava, Asian ginseng, and echinacea. Clinical data were collected from standard databases, recent articles and books, and interviews with herbal product manufacturers,[10] herbal experts,[8] and organizations related to medical herbalism.[24] In a 21-year period (1979–2000), a total of 41 case reports or case series in 23 publications and 17 clinical trials were obtained. Of these, only 12 interactions could be considered life threatening (mostly associated with a dangerous reduction in blood plasma levels of cyclosporine in organ transplant patients using St. John's wort) owing to a putative effect on cytochrome P450 systems.[28]

The paucity of incidences of herb–drug interactions for these seven botanicals should also be viewed within the context of their total use. Definitive data regarding actual herb use are lacking, but available published marketing reports for ginkgo, kava, and St. John's wort provide some guidance. Ginkgo is by far the most widely used and prescribed medicinal herb in the world. According to a review of DeFeudis, from 1979 to 1998, approximately 110 million daily doses of ginkgo leaf extract were sold in France alone. According to market data of Dr. Willmar Schwabe GmbH, the makers and world's leading marketer of the most clinically tested ginkgo extract (EGb 761), in the period from 1979 to 1997, it was estimated that more than 2 billion daily doses of ginkgo extract were distributed worldwide. A more recent report estimates that from 1997 to 2002, 1.375 billion daily treatments of ginkgo

BOX **4-2**

Herb–Drug Interactions Literature: Case Reports Evaluation

The following 10-point evaluation scheme was established by medical herbalist Jonathan Treasure as a means to determine the validity and reliability of herb–drug interactions as presented in case reports in the medical literature. Many botanical researchers/authors have postulated that without a complete report, including the information described in the following, it is not possible to make an accurate evaluation of the significance of an herb–drug interactions case report.

1–5 Necessary

1. Positive ID of Herb (form, brand, ingredients, dose, duration)
2. Adequate Description of Case (full details of the ADR and patient Hx)
3. Plausible pharmacologic timing
4. Other possible explanations ruled out
5. Concomitant medications noted (+dosage or none stated)

6–10 Substantiating

6. Confirmation by objective measures (e.g., serum levels drug)
7. Plausible or established pharmacologic mechanism
8. ADR ceases on withdrawal herb
9. ADR event reproduced by rechallenge
10. Previous exposure linked to same ADR

single preparations have been administered in Germany alone. Up until 2003, a total of only four case reports of potential interactions between ginkgo and conventional medications had been published.[29] Two of these were associated with bleeding events. This has led to significant concerns raised regarding its potential to increase the effects of anticoagulants. However, such events, if causal, are rare. More than 40 clinical trials with several thousand subjects have been conducted using the EGb 761 ginkgo extract with no reports of increased bleeding. A number of studies have specifically looked at its potential for increasing the anticoagulant effects of aspirin and warfarin with mostly negative results; it has been included in pharmacovigilance reviews throughout Europe for decades. Nonetheless even in cases in which an interaction has not been definitively confirmed, caution should be advised.

As of 2001, St. John's wort was the primary antidepressant used throughout Europe with approximately 66 million daily doses in Germany, outselling most conventional antidepressants. Up until the 2000 review of Izzo and Ernst, a total of 29 potential interactions were reported. Most of those were associated with decreased blood cyclosporine levels due to enhanced hepatic enzyme induction (cytochrome P450). Others were associated with an additive effect of St. John's wort wi selective serotonin reuptake inhibitors (SSRIs). Again, considering the prevalence of St. John's wort use, such incidences of adverse effects are rare. With increased understanding that St. John's wort does affect P450 enzyme systems, such interactions can be more readily predicted and therefore minimized (see Drugs Metabolized via Cytochrome P450 System).[28]

Categories of Herb–Drug Interactions

Anticoagulants

One of the most significant areas of concern regarding herb–drug interactions relates to coagulation. A number of plants have been reported to interact with anticoagulant agents, most specifically with warfarin and aspirin. The most common interaction reported has been enhancement or potentiation of anticoagulant effects. However, inhibition of anticoagulant effects is also possible, through vitamin K pathways. Many foods and herbs contain high amounts of vitamin K and may decrease the efficacy of warfarin, thereby increasing the risk of thrombosis or myocardial infarction. Most available reports are from individual cases and may represent isolated events. Other researchers and reviewers have raised concern over theorized mechanisms of action or the presence of specific compounds that may affect coagulation. Some of these may present real concerns, whereas others have not resulted in adverse events in actual clinical use. Regardless, caution is advised when using any medication with purported anticoagulation activity in conjunction with other anticoagulants, and prior to surgery, or in those with bleeding problems.

According to case reports, ginkgo and garlic are among the botanicals most widely reported as interacting with anticoagulants. For ginkgo, there are at least two case reports of interactions, one each with aspirin and warfarin.[30,31] In neither case could an association be definitively determined. However, upon cessation of ginkgo, bleeding times returned to baseline norms. An anticoagulant effect of ginkgo is partially supported by the presence of ginkgolide B, which exhibits in vitro inhibition of platelet activating factor. However, the amount of ginkgolide B in ginkgo extract is very small and is unlikely to contribute to this activity in a significant clinical way. There have been a number of other case reports suggesting an association between bleeding events and use of ginkgo. Conversely, ginkgo has also been one of the most researched botanicals and subject of numerous meta-analyses and evidence-based reviews. None of the formal trials have noted any bleeding problems. Some of these have specifically investigated the effects of ginkgo in conjunction with anticoagulants with negative findings.[29] Ginkgo extract is one of the most widely prescribed and broadly used of all approved botanical drugs worldwide. The scarcity of reports relative to its widespread supervised and unsupervised use suggests that bleeding is not a common problem, although caution is advised.

Garlic has been reported to thin the blood by at least three different mechanisms; fibrinolytic activity, inhibition of platelet aggregation, and decreased fibrinogen activity. Most of these findings were from human studies with very small patient populations.[32] Consumption of garlic as a food has not been implicated in bleeding

events, suggesting that cooked garlic, which is most commonly consumed, does not contain the compounds responsible for the anticoagulant effects. This is likely as numerous studies suggest that allicin, which is lost in cooking, is associated with its putative anticoagulant activity. Thus, varying preparations may elicit different actions, depending upon the constituents present in the preparation. Primarily, supplemental forms of garlic preparations, especially those delivering allicin, should not be used, or should be used very cautiously in those with bleeding problems, using anticoagulants or prior to surgery.

Herbs that contain salicin, such as willow (*Salix* spp.), meadowsweet (*Filipendula ulmaria*), and birch (*Betula* spp.), have been noted as potential substances that may enhance the effects of anticoagulants. This is based on the fact that salicin was a precursor of acetyl salicylic acid (aspirin). However, with few exceptions, clinical trials with salicin-containing herbs have yet to demonstrate any blood thinning activity of these substances. Salicin does not appear to affect platelet aggregation in the same manner as does aspirin. There have been two case reports regarding anticoagulant activity of the oils of birch and wintergreen, both of which contain methylsalicylates.

Herbs that contain coumarin or closely related compounds have also been suspected of causing bleeding events or enhancing the effects of anticoagulants. Coumarin itself is not active in humans; in order for it to have activity it must undergo a transformation due to different types of molds. Reports of bleeding due to coumarin-containing herbs, most notably sweet melilot (*Melilotus officinalis*) have been made owing to consumption of fermented leaves by cattle. Reports regarding an anticoagulant effect of coumarin-containing herbs in humans have only rarely been made.

Other botanicals that have been reported to potentiate the effects of anticoagulants include those that inhibit platelet aggregation through an inhibition of thromboxane synthetase (e.g., ginger), arachidonic acid (e.g., those rich in essential fatty acids), or epinephrine (e.g., garlic). A number of Chinese herbs have been implicated in bleeding problems. Most notably these include Chinese salvia (*Salvia miltiorrhiza*), dong quai (Angelica sinensis), and corydalis (*Corydalis yanhusuo*). These botanicals are classified as possessing blood thinning properties from a traditional Chinese medical perspective and so such an effect is predictable. In the case of dong quai, which is commonly used in the treatment of gynecological conditions and anemia, a 46-year-old woman experienced a greater than twofold elevation in prothrombin time (from 16.2 to 27 seconds) and International Normalized Ratio (INR) (from 2.3 to 4.9) after consumption of a commercial dong quai product. No other cause for the increase could be determined and coagulation values returned to acceptable levels within 1 month after discontinuing dong quai.[33] Similar increases in INR have been reported for Chinese salvia, one of the most commonly used botanicals in Chinese medicine for increasing blood circulation. Conversely, high doses of green tea (*Camellia* spp.), as well as ginseng, have been reported to decrease the effects of warfarin.[34,35]

A relatively large number of medicinal plants can potentially interact with conventional anticoagulant medications. Therefore, monitoring of bleeding signs and INR is warranted when using botanicals with known effects on bleeding mechanisms or those with a history of use in altering circulation. These same botanicals should also be avoided immediately prior to surgery (Table 4-6).

Anesthetics, Anticonvulsants, Barbiturates, Benzodiazepines, Opioids, Sedatives

Hundreds of plants have been used historically for their sedative, pain killing, and anticonvulsant activity. Used in combination with similarly acting medications enhancement of activity resulting in loss of muscular coordination or a prolongation of anesthesia- or barbiturate-induced sleeping times has been observed. Compounds in valerian root, for example, display an affinity for barbiturate, GABA-A, peripheral benzodiazepine, serotonin, and opioid receptors, whereas California poppy (*Eschscholzia californica*) contains the alkaloid chelerythrine, which is a protein kinase inhibitor (Table 4-7).

Cardiovascular Medications

A number of botanicals directly or indirectly affect the cardiovascular system and may interact with cardiovascular medications. A variety of mechanisms of action may be included in these effects: direct antihypertensive activity through diuresis (juniper berry), vasodilatation (hawthorn leaf with flower), and muscular relaxation (cramp bark). A number of other botanicals can affect blood pressure indirectly through a number of functions, including: cholesterol-lowering effects (garlic-*Allium sativum*; guggul-*Commiphora mukul*), adaptogens (eleuthero), nervines (skullcap-*Scutellaria lateriflora*; zizyphus-*Zizyphus spinosa*), and weight loss aids (guggul). The most widely studied botanical in Western herbal medicine for the treatment of cardiovascular disease is hawthorn (*Crataegus* spp.). It possesses a number of pharmacologic activities that make it ideal for the treatment of Stage I and II cardiac insufficiency. Most importantly it primarily exhibits positive inotropic activity, thereby slowing the heart and making for a stronger, more efficient heartbeat, much like beta-blockers. Because of this it can potentiate the effects of other positively inotropic agents such as digitalis. In the 1980s in Germany, it was a relatively common practice for physicians to prescribe hawthorn alternately with digitalis preparations to reduce the prevalence of accumulated toxicity often associated with digoxin glycosides. However, taken together without modifying the dose of digitalis can result in additive and potentially dangerous effects.

Cholesterolemic drugs, such as the statins, inhibit cholesterol biosynthesis through an inhibition of HMG-coenzyme reductase. Any botanical that has a cholesterol lowering effect through the same pathway may result in potentiation. The primary botanicals used by American consumers for reducing cholesterol levels include red yeast (contains lovastatin, which acts similarly to statin drugs), garlic, and gum guggul resin. Although this potential interaction is not life threatening, it may require modifying the dose of conventional medications. Other classes

TABLE **4-6**

Botanicals Best Avoided Prior to Surgery or with Anticoagulants

BOTANICAL	ACTION
Alfalfa (*Medicago sativa*)	Potential anticoagulant effect if the material was subjected to fermentation; potential coagulant activity due to vitamin K content
Angelica (*Angelica* spp.)	Possible anticoagulant effects
Asafoetida (*Ferula foetida*)	In vivo anticoagulation
Borage seed oil (*Borago officinalis*)	Possible anticoagulant effects of gamma linolenic acid (GLA)
Black currant seed oil (*Ribes nigrum*)	Possible anticoagulant effects of gamma linolenic acid (GLA)
Cayenne pepper (*Capsicum annum*)	Antiplatelet aggregation due to capsaicin
Chamomile flowers (*Matricaria chamomilla*)	Potential anticoagulant effect
Chinese salvia root (*Saliva miltiorrhiza*)	Anticoagulant effect
Chinese skullcap (*Scutellaria baicalensis*)	Inhibits vitamin K reductase
Cornsilk (*Zea mays*)	Contains vitamin K
Devil's claw (*Harpagophytum procumbens*)	Possible anticoagulant effects
Evening primrose seed oil (*Oenothera biennis*)	Possible anticoagulant effects of gamma linolenic acid (GLA)
Fenugreek seed (*Trigonella foenum*)	Anticoagulant effect
Feverfew leaf (*Tanacetum parthenium*)	Inhibits platelet aggregation
Garlic bulb (*Allium sativum*)	Anticoagulant effect; can interact with warfarin
Ginger root (*Zingiberis officinalis*)	Inhibits platelet aggregation
Ginkgo leaf (*Ginkgo biloba*)	Potential anticoagulant effect
Ginseng root (*Panax ginseng*)	May exacerbate hypertension; inhibits platelet aggregation
Horse chestnut seed (*Aesculus hippocastanum*)	Potential anticoagulant effect due to saponin compounds (esculetin, osthole)
Licorice root (*Glycyrrhiza* spp.)	Potential anticoagulant effect
Papain (from papaya)	Potential for increased bleeding
Parsley leaf (*Petroselinum crispum*)	Contains vitamin K
Pau D'Arco (*Tabebuia* spp.)	Potential anticoagulant effect due to lapachol, which works similarly to warfarin
Red clover blossoms (*Trifolium repens*)	Potential anticoagulant effect
Shepherd's purse (*Capsella bursa-pastoris*)	Contains vitamin K
St. John's wort herb (*Hypericum perforatum*)	Prolongs effects of anesthesia
Stinging nettles leaf (*Urtica dioica*)	Contains vitamin K
Turmeric root (*Curcuma longa*)	Potential anticoagulant effect

of botanicals, such as laxatives, may indirectly negatively interact with cardiovascular medications by causing potassium loss (Table 4-8).

Drugs Metabolized via Cytochrome P450 System

In recent years, a number of botanicals have been shown to affect the metabolization of numerous conventional medications through a modulation of the cytochrome P450 enzyme system. Approximately 80% of drugs are metabolized by this system and include calcium channel blockers, cyclosporine, loxapine, oral antihistamines, and oral penicillin, to name just a few. Taking a botanical that affects this system can elicit an inhibitory or stimulatory activity, resulting in either too slow or too rapid drug clearance, with either negative or positive effects. Stimulation of this system can cause substances to be metabolized rapidly, compromising the clinical efficacy of the drug if effective concentrations are not maintained. If this system is inhibited, drugs can accumulate in the blood too fast or for extended periods of time, thus increasing their toxicity. No formal human investigations to date regarding the potentially positive interaction between botanical and conventional medications have been conducted.

Several botanicals have demonstrated a relatively strong in vitro effect on CYP450 3A4 (CYP3A4), including St. John's wort (*Hypericum perforatum*), goldenseal (*Hydrastis canadensis*), cat's claw (*Uncaria tomentosa*), echinacea (*Echinacea angustifolia*), chamomile (*Matricaria chamomilla*), and licorice (*Glycyrrhiza glabra*).[36] However, in vitro data may not accurately reflect what occurs in humans. Most cytochrome P450 effects that are reported are due to negative observations derived from case reports or from in vitro data that may have no clinical relevance. In a few of the most noted cases, St. John's wort, was shown to inhibit CYP3A4 in vitro and stimulate it in vivo. According to case reports, two transplant patients were medicated with cyclosporine to prevent organ rejection. After self-medicating with St. John's wort, cyclosporine plasma levels were found to be 25% to 50% lower than expected resulting in acute organ rejection in one of the subjects. Upon discontinuation of the botanical, drug plasma levels returned to expected levels. Other such case reports have been made

TABLE 4-7

Botanicals That May Interact with Sedatives

BOTANICAL	INTERACTING MEDICATIONS	POSSIBLE EFFECT
Ashwagandha (*Withania somnifera*)	Barbiturates	Potentiation
Black currant seed oil	Anticonvulsants	May decrease seizure threshold
Borage seed oil	Anticonvulsants	May decrease seizure threshold
California poppy (*Eschscholzia californica*)	Analgesics, sedatives	Potentiation
Catnip (*Nepeta cataria*)	Barbiturates	Potentiation
Chamomile (*Anthemis nobilis*)	Barbiturates	Potentiation
Cramp bark (*Viburnum opulus*)	Anticonvulsants	Contains salicylates, may increase effect
Siberian ginseng (*Eleutherococcus senticosus*)	Barbiturates	Potentiation
Evening primrose (*Oenothera biensis*)	Anticonvulsants	May decrease seizure threshold
Hops (*Humulus lupulus*)	Sedatives	Potentiation
Kava kava (*Piper methysticum*)	Anesthetics, barbiturates	Prolonged sedation times
Passion flower (*Passiflora incarnata*)	Barbiturates	Potentiation
Schizandra (*Schisandra chinensis*)	Barbiturates	Potentiation
St. John's wort (*Hypericum perforatum*)	Anesthetics, benzodiazepines	Prolonged anesthesia times; decreased efficacy in some cases, increased effects in others; binds to GABA receptor
Valerian (*Valeriana officinalis*)	Anesthetics, barbiturates, benzodiazepines	Prolonged sedation times; binds to multiple neurologic receptors
Willow (*Salix* spp.)	Anticonvulsants	Contains salicylates, may increase effect
Wintergreen (*Gaultheria procumbens*)	Anticonvulsants	Contains salicylates, may increase effect

TABLE 4-8

Botanicals That May Interact with Cardiovascular Medications

THERAPEUTIC CATEGORY	BOTANICAL	EFFECT
Antiarrhythmics	Digitalis*, lily of the valley, squill	All contain cardiac glycosides
Anticoagulants	See Table 4-5	
Antihypertensives	Digitalis, garlic, hawthorn, lily of the valley, squill	
Calcium channel blockers	Coltsfoot	
Cardiac glycosides	Digitalis, figwort, lily of the valley, squill; eleuthera; hawthorn	Some contain cardiac glycosides; eleuthera can increase plasma digoxin levels; hawthorn is positively inotropic
Cholesterolemic agents	Artichoke, fenugreek, garlic, ginger, guggul, red rice yeast	Increased therapeutic effect; red rice yeast contains lovastatin
Diuretics	Agrimony, arjuna, birch leaves, celery seed, corn silk tassels, couch grass, goldenrod, horsetail, juniper berry, phyllanthus, Rehmannia	Increased potassium loss

*Digitalis is not available as a botanical dietary supplement and is rarely prescribed by medical herbalists.

suggesting strongly that St. John's wort and other botanicals that upregulate the cytochrome P450 system must not be used in conjunction with immunosuppressant drugs in organ transplant patients (see http://medicine.iupui.edu/flockhart/table.htm for a regularly updated resource on substances that interact with the cytochrome system).[37]

Hypoglycemic Agents

There is very little data regarding the effects of botanicals on insulin-dependent diabetes. Some botanicals are reported to have an effect directly on insulin production and islet cells, others modify glucose levels through decreased glucose absorption, and others may have an effect on insulin resistance. There are no definitive data

on the appropriate use of antidiabetic botanicals in the treatment of diabetes. High fiber intake can inhibit glucose absorption as can consumption of mucilaginous herbs. Use of such herbs in conjunction with hypoglycemic therapies can potentially result in decreased glucose absorption that can alter insulin needs. Some antidiabetic medications such as glibenclamide specifically have been reported to be affected by the use of high fiber botanicals such as konjac mannan (*Amorphophallus konjac*), a once popular weight loss supplement (Box 4-3).

Immune Suppressants and Immune-Enhancing Therapies

Many botanicals possess immunomodulatory activity. Some of these, such as echinacea, are used for the prevention or reduction of severity of colds and flu. Others, such as astragalus and Reishi mushrooms, are used for general immune enhancement or specifically in conjunction with conventional cancer therapies. Prudence dictates that such herbs should not be used in conjunction with immunosuppressant therapies such as those used in organ transplant patients or in those with autoimmune disease. There are case reports of Echinacea exacerbating symptoms of lupus and rheumatoid arthritis. There are very little data regarding the use of botanicals with immunosuppressive therapies (Box 4-4). No well-designed trials regarding such combined therapies are available. There are limited data suggesting a positive effect of these when used in conjunction with conventional therapies.[38–40] Many integrated health care professionals use such botanicals to reduce side effects of conventional therapies and minimize the risk of contracting opportunistic infections. Currently, the available evidence regarding the usefulness of natural therapies appears to be stronger for improvement of symptoms than it is for slowing of disease progression.[41] The use of immune modulating botanicals must be weighed against the cytotoxic therapies of Western medicine.

Diuretics

Pharmacologic evidence regarding definite diuretic activity of many botanicals is lacking, yet they are very commonly used. In general, use of diuretics can lead to potassium loss, which can potentially lead to fatal arrhythmias. This does not appear to have been reported with use of herbal diuretics. There are, however, some reports of potassium loss through the excessive use of purging cathartics as part of weight loss programs, some that also contain diuretics. Part of the reason may be that many herbal diuretics, for example dandelion leaf (*Taraxacum officinale*), also contain high amounts of potassium, which may actually result in increased in serum potassium levels (Box 4-5). Nonetheless, care

BOX 4-3

Botanicals That May Interact with Hypoglycemic Agents

Agrimony (*Agrimonia eupatoria*)
Alfalfa (*Medicago sativa*)
Aloe juice (*Aloe* spp.)
American ginseng (*Panax quincefolius*)
Bitter melon (*Momordica charantia*)
Bilberry leaves (*Vaccinium myrtillus*)
Dandelion root (*Taraxacum officinale*)
Devil's club (*Oplopanax horridus*)
Fenugreek (*Trigonella foenum-graecum*)
Garlic (*Allium sativa*)
Ginseng (*Panax ginseng*)
Guar gum (*Cyamopsis tetragonaloba*)
Gymnema (*Gymnema sylvestre*)
Jambul seeds (*Syzygium cumini*)
Madagasgar Periwinkle (*Vinca roseus*)
Maitake mushroom (*Grifola frondosa*)
Marshmallow root (*Althaea officinalis*)
Prickly pear cactus (*Opuntia* spp.)

BOX 4-4

Botanicals Generally Contraindicated with Immunosuppressive Therapies

Astragalus (*Astragalus membranacues*)
Atractylodes (*Atractylodes* spp.)
Echinacea spp.
Eleuthero (*Eleutherococcus senticosus*)
Grifola mushroom (Grifola umbellata)
Licorice root (*Glycyrrhiza glabra*)
Maitake mushroom (*Grifola frondosa*)
Ginseng (*Panax ginseng*)
Poria (*Poria cocos*)
Reishi mushroom (*Ganoderma lucidum*)
Schisandra (*Schisandra chinensis*)

BOX 4-5

Herbal Diuretics

Agrimony (*Agrimonia eupatorium*)
Arjuna (*Terminalia arjuna*)
Birch leaves (*Betula* spp.)
Boldo (*Peumus boldus*)
Celery seed (*Apium graveolens*)
Corn silk tassels (*Zea mays*)
Couch grass (*Agropyron repens*)
Dandelion leaf (*Taraxacum officinalis*)
Elder flowers (*Sambucus* spp.)
Goldenrod (*Solidago spp.*)
Horsetail (*Equisetum arvense*)
Juniper berry (*Juniperus communis*)
Parsley leaf (*Petroselinium crispum*)
Phyllanthus (*Phyllanthus niruri*)
Rehmania (*Rehmania glutinosa*)
Shepherd's purse (*Capsella bursa-pastoris*)
Stinging nettles (*Urtica dioica*)
Yarrow (*Achillea millefolium*)

should be taken when using diuretics with patients on medications that have narrow therapeutic windows, or when potassium depletion may place the patient at risk.

Tannins and Iron Availability

Botanicals rich in tannins, a common constituent of many barks and leaves, can decrease the absorption of certain classes of drugs, most notably alkaloidal and mineral drugs such as colchicine, ephedrine, copper, iron, and zinc; thus, individuals with specific deficiencies (e.g., iron, zinc) may be advised to avoid tannin-rich botanicals for the duration of supplementation (Box 4-6).

LACK OF APPROPRIATE THERAPY OR DISCONTINUATION OF CONVENTIONAL CARE

Many conventional medical practitioners are legitimately concerned that a patient may defer ''proper'' treatment of a condition in hope that a natural therapy can resolve their problem, that a natural therapy may interfere with the safety or efficacy of a conventional treatment being followed, or that a patient may discontinue an effective treatment in hopes of benefit from a potentially ineffective natural treatment. Unfortunately, there are few clear guidelines for determining the relative efficacy of an herbal versus conventional drug therapy. As noted, a number of studies have compared herbal with conventional medications, with some studies either showing equal or greater efficacy. Some have also demonstrated a better safety profile than the conventional (e.g., ginkgo) and conventional nosotropics (St. John's wort and imipramine). However, these are few and far between and more research in this area is needed. Where the literature is clear, one role of the practitioner can be to help the patient choose the therapy that has the greatest level of efficacy and safety. Health professionals must additionally balance the right of patients to choose the therapy they feel is best for them with the best medical opinion that can be offered.

BOX 4-6

Tannin-Rich Botanicals

Agrimony (*Agrimonia eupatorium*)
Bayberry (*Myrica cerifera*)
Behada (*Terminalia belerica*)
Blackberry leaf (*Rubus villosa*)
Black walnut (*Juglans nigra*)
Green tea (*Camellia* spp.)
Guarana (*Paullinia cupana*)
Horse chestnut (*Aesculus hippocastanum*)
Maté (*Ilex paraguayiensis*)
Raspberry leaf (*Rubus idaeus*)
Rhubarb (*Rheum palmatum*)
Sheep sorrel (*Rumex* spp.)
Uva ursi (*Arctostaphylos uva-ursi*)
White oak (*Quercus* spp.)
Willow (*Salix* spp.)
Witch hazel (*Hammamelis virginica*)
Yellow dock (*Rumex crispum*)

TIMING OF HERB USE

Use of Herbs Prior to Surgery

A number of botanicals should be avoided, or used with care, prior to or when undergoing surgery, largely due to theoretical or known risks of interactions with coagulation therapies or anesthesia. Patients must also be queried regarding their use of botanicals at this time. As noted, there are a number of botanicals with blood-thinning potential, such as ginkgo, garlic, dong quai, and red clover, whose use is so common that patients might not report these in a standard medical history intake. There are also botanicals that have been reported to interact with general anesthesia, most notably, St. John's wort, which may intensify or prolong the effects of anesthesia. The American Society of Anesthesiologists (http://www.asahq.org/patientEducation/herbal.htm) recommends that patients stop taking herbal supplements 2 to 3 weeks prior to surgery because they may affect anesthesia and bleeding times, and cause dangerous fluctuations in blood pressure. If there is not enough time prior to surgery to stop, patients are recommended to bring the products to their primary care physician so an assessment of any danger can be made.

Use of Herbs in Pregnancy and Lactation

There are many conditions associated with pregnancy for which expectant mothers seek natural therapies, sometimes in the hopes of avoiding what they perceive to be more toxic conventional medications. Such conditions include morning sickness, threatened miscarriage, vaginal infections, anemia, varicose veins, hemorrhoids, depression, anxiety, and sleeplessness. One survey of emergency room visits reported that 14.5% of women used herbal remedies during pregnancy.[42] In addition to unsupervised herb use by consumers, approximately 50% of midwives and naturopathic physicians routinely prescribe herbal medicines during pregnancy, including a prominent use of botanicals such as black and blue cohosh (*Actaea racemosa, Caulophyllum thalictroides*), castor oil (*Ricinus communis*), and evening primrose oil (*Oenethera biensis*) for inducing labor. Considering whether to use an herbal medicine during pregnancy requires skill and sound judgment on the part of the practitioner, or in the case of self-medication, careful consideration on the part of the consuming woman. Minimally, the relative health of the expectant mother, the indication, and the appropriateness or inappropriateness of other medications or therapies must be considered. Ultimately, with herbal medicines, the choice of medications should be made by the expectant mother with full knowledge of the potential consequences. There are also significant legal liabilities that are incurred when using herbs in pregnancy. A list of botanicals that should not be used in pregnancy except under the care of a qualified health care professional is provided in Chapter 12, where the special considerations of herb safety during pregnancy are extensively addressed in Chapter 12.

THE RELATIVE SAFETY OF CONVENTIONAL DRUGS AND HERBAL MEDICINES: KEEPING IT ALL IN PERSPECTIVE

When assessing the safety of herbal medicines, it is important to remain cognizant of the relative risks associated with approved medications, used singly and in combination with other agents. It is a common misconception that because a medication is FDA approved it is safe when used as indicated. However, in 1990, the United States General Accounting Office (GAO) reviewed 198 FDA-approved drugs and reported that of these, approximately 102 (51.5%) had serious post-approval side effects. These included anaphylaxis, cardiac failure, hepatic and renal failure, birth defects, blindness, and death.[43] At the time of the report, all but two of the medications remained on the market. One study reported that among 1000 older adult patients admitted to the hospital from the emergency room, 538 were exposed to 1087 drug–drug interactions.[44] In a review of hospital surveillance reports of adverse events associated with approved medications, Lazarou et al. reported that 2,216,000 patients experienced serious adverse effects resulting in 60,000 to 140,000 fatalities annually as a result of the correct use of conventional drugs.[45] Not included in this figure were deaths due to misuse of medications (i.e., improper prescribing, dosing, combining), accounting for another 200,000 patients annually. These figures make adverse events due to approved conventional medications one of the leading causes of death in the United States, almost as many deaths as are associated with smoking, and more than those related to alcohol, recreational drugs, and firearms. Additionally, adverse events associated with conventional drugs have been reported to be the number one cause of hospital admissions (at a cost of $116 million annually), and once in the hospital, approximately 35% of patients are likely to experience an additional adverse drug reaction. In total, this represents estimated extra health care costs of $77 billion annually.[46] With this perspective in mind, it may be advantageous for practitioners to wisely counsel patients about the potential benefits of herbal medicines as a means of reducing the high propensity for adverse events due to conventional medications.

Such a belief is reflected in the experience of numerous integrative medical practitioners, conventionally trained physicians who gain further training in various aspects of natural medicine. According to David Rakel, one leading CAM practitioner, ''Although it's important to be aware of drug–herb interactions, we need to be less concerned about them than about interactions between prescribed drugs. Drug–herb interactions are generally much less severe than drug–drug interactions.''[47] Samuel D. Benjamin, Director of the Center for Complementary and Alternative Medicine and Associate Professor of Pediatrics and Family Medicine at the State University of New York, Stony Brook, stated that, ''The overwhelming majority of interactions are not related to the use of herbals. Drug–herb interactions don't compare to drug–drug interactions. Herbals are less toxic than pharmaceuticals.''[47] According to medical researcher Adriane Fugh-Berman, Assistant Clinical Professor of Health Care Sciences at George Washington University School of Medicine and Health Sciences, drug–drug ''interactions kill people every day. What I have been really trying to convey to people. . .is that drug interactions are much more common and severe than drug–herb interactions. As clinicians we should be alert to both types but take pains to keep drug–herb interactions in context.''[47]

GUIDELINES FOR PRACTITIONERS

Emergency Room Personnel

Emergency room attendants should be aware of the conditions they are most likely to encounter in patients who have reported a reaction thought to be correlated with consumption of an herbal product. These include the following:

- *Allergic reactions:* Any therapy can elicit allergic reactions in any individual in an unanticipated manner. Most specifically, anaphylaxis, angioedema, bronchospasm, contact dermatitis, and/or urticaria may occur. Cross-reactivity may occur with substances known to commonly cause allergic reactions such as ragweed pollen. Although rare, such reports have been made in those consuming members of the ragweed family.
- *Skin rash:* There are numerous reasons for skin rashes to be caused by herbal products, including allergic reactions (ragweed family or iodine-containing plants in those sensitive to these agents), photosensitizing agents (St. John's wort, rue, psoralen-containing herbs such as some angelica species and lomatium [*Lomatium dissectum*]), or topical irritants (garlic, mustard, and poke root plasters, and essential oils).
- *Elevated liver enzymes:* This is one of the more common adverse effects due to herbal products. Those most associated with this reaction include: direct hepatotoxins such as PA-containing herbs; botanical preparations with added pharmaceuticals; potentiation of hepatotoxic pharmaceuticals or other product adulterations; and idiosyncratic reactions.
- *Hypertension/hypokalemia:* Herbal stimulants, including cola nut, caffeine, guarana, and most commonly, ephedra, can exacerbate already existing hypertension. Licorice has been reported to cause severe hypokalemia-induced hypertension at doses of up to 100 g daily. This reaction has only been reported rarely with licorice root and mostly with licorice candy, which is typically prepared with anise. There is, however, one case report of low-dose licorice root intake as part of a laxative tea causing hypokalemia. This may have been a result of the fluid loss owing to the laxative more than the physiologic effect of licorice. Asian ginseng (Panax ginseng) may exacerbate already existing hypertension. Yohimbe has been associated with hypertensive effects.
- *Mouth ulcers:* These can be caused by herbs rich in sesquiterpene lactones, such as feverfew (*Tanacetum parthenium*) and Missouri snake root (*Parthenium integrifolium*).
- *Hemorrhagic events:* A number of botanicals have the potential to contribute to bleeding events. Case reports

of subconjunctival hemorrhage, subdural hematomas, potentiation of bleeding effects of aspirin, and postsurgical bleeding complications have been associated with ginkgo (*Ginkgo biloba*), garlic (*Allium sativum*), and/or dong quai (*Angelica sinensis*). Bleeding abnormalities may occur with members of the legume family such as alfalfa or red clover, which contain coumarins. However, fermentation of these herbs is required to develop active coumarins. Such events have been reported for red clover. Feverfew may interfere with blood coagulation.

- *Exacerbation of gastroesophageal reflux disease (GERD):* There have been rare reports of peppermint (Mentha piperita) exacerbating GERD symptoms. It conversely is used to treat digestive upset.
- *Palpitations, cardiac arrhythmias, and tachycardia:* Sympathomimetic agents and central nervous stimulants commonly affect cardiac rhythm. Botanicals associated with such effects include: cola nut (*Cola nictida*), guarana (*Paullinia cupana*), lobelia (*Lobelia inflata*), and ma huang (*Ephedra sinensis*). Excessive intake of licorice candy (typically prepared from anise) may result in pseudoprimary aldosteronism with edema, hypertension, and hypokalemia. One case of near-fatal cardiac arrest has been reported. Excessive use of laxatives, which can cause fluid loss, has resulted in fatalities. Yohimbe has been associated with tachycardia.
- *Threatened miscarriage/abortion:* There have been a number of cases of attempted abortions using botanicals. Those most widely used include: black cohosh (*Actaea racemosa*), blue cohosh (*Caulophyllum thalictroides*), and pennyroyal (*Mentha pulegium*) oil.

Oncologists

Use of herbal medicines is prevalent among cancer patients. The seriousness of the disease leads patients to seek a variety of therapies regardless of the level of evidence supporting their use. Unfortunately, there are few well-designed trials examining the usefulness of botanical supplements for the direct treatment of cancer or in conjunction with conventional therapies, and what information exists is conflicting. Most commonly used are herbal therapies to enhance immune function, directly combat cancer, and yet others to provide palliative relief from side effects associated with conventional cancer therapies. There are two primary safety considerations regarding botanical therapies in cancer: (1) ensuring that potentially ineffective therapies are not substituted for potentially effective conventional therapies, and (2) making sure that botanical therapies do not lessen the effects of conventional therapies. Very few data regarding either exist.

Botanicals That Should Only Be Used by Qualified Health Professionals

The majority of botanicals that have remained on the commercial market have persisted because of their relatively high degree of safety when used by consumers without the guidance of a health professional. Most do not present a significant enough health risk to warrant prescription-only status. However, historically, relatively toxic botanicals (e.g., aconite, digitalis, and gelsemium) have been used by medical herbalists. Most of these have not remained in the commercial market as dietary supplements. The use of toxic such herbs should be limited to well-trained medical herbalists.[48] Recommendations regarding the use of botanicals that should only be used by skilled individuals can be found in the *Botanical Safety Handbook* (CRC Press).

CONCLUSION

With the increasing prevalence of the use of herbal products, and the fact that many consumers and patients are using herbal products in conjunction with conventional medications, it is becoming increasingly important for health care providers to be aware of potential adverse effects and interactions. Based on a review of the world's data, adverse effects caused by herbal medicine are relatively rare. A number of botanicals have compared favorably in clinical trials with conventional medications for the same indications, and a critical review of the literature demonstrates a remarkable safety record. For example, ginkgo (*Ginkgo biloba*) has been shown to be similarly effective to conventional nosotropics and better tolerated; whereas contrary to inaccurate media reporting, St. John's wort (*Hypericum perforatum*) has been shown to be equal to or more efficacious than standard antidepressant medications but with approximately half the rate of adverse events.[49–51] Another herb, kava kava (*Piper methysticum*) has demonstrated efficacy equal to many standard anxiolytics, with greater safety than the commonly prescribed benzodiazepines.[52]

Conversely, there are a number of safety concerns about which practitioners must remain aware. These include potentiating or antagonistic effects of herb–drug interactions (especially potential anticoagulant effects), some of which are predictable, although others are not; potential contaminations and adulterations of herbal products; and the potential for patients to forgo effective therapies. A review of the literature clearly shows that adverse effects due to herb–drug interactions are the most common. Understanding the in vivo pharmacologic effects of botanical medicines can help to increase the predictability of potential interactions. There are increasing resources designed for health care providers, including textbooks, online databases, and training programs. As use of herbal medicines grows, practitioners will be forced to obtain some level of education regarding their appropriate use. For many integrative medical practitioners, that time has already arrived, and this will lead to a greater understanding of how botanicals can best be used in conjunction with conventional medications, and therefore, how best to serve the patient.

INTEGRATING BOTANICAL MEDICINES INTO CLINICAL PRACTICE: ETHICAL CONSIDERATIONS AND GUIDELINES

Aviva Romm

Lack of general consensus among health practitioners regarding the safety and efficacy of botanical therapies

and their place in conventional medical care leaves many health professionals with the ethical dilemma of whether, and to what extent, to integrate herbal medicines into their practices, how much to support patient use, and the challenge of learning which products are efficacious and safe.[53] Practitioners are rightly reluctant to recommend or support botanical medicine use because they are uncertain as to which therapies are beneficial, which are merely harmless, and which are harmful. Most lack adequate training in their use unless specifically trained as herbalists. Unfortunately, lack of knowledge about herbal therapies, or disapproval of them, has been demonstrated to reduce patient disclosure of use to their primary care practitioners. It also prevents practitioners from serving adequately as advisors and advocates for their patients regarding safe and effective herb use, and the avoidance of potential herb–drug interactions.

ADDRESSING ETHICAL CONSIDERATIONS

Jeremy Sugarman, in the JAMA article, *Physicians' Ethical Obligations Regarding Alternative Medicine*, suggests that physicians facing ethical dilemmas about integrating CAM into their practices, or at least trying to decide how to address CAM use by patients, consider applying a broad ''set of inherent ethical principles of the medical profession: respect for persons, nonmaleficence, beneficence, and justice'' into their decision-making process.[54] These principles, well known to physicians, are:

1. *Respect for persons*, also referred to as *autonomy*, implies respecting the patients personal preferences, including the right to ''reject unwanted interventions and to make choices that are consonant with their values.''[54] Implicit in respect for autonomy is informed consent and shared decision-making—also a cornerstone of integrative medicine and CAM practices.
2. *Nonmaleficence* means not harming patients in the provision of medical care. In relationship to CAM, it becomes incumbent on the practitioner to elicit comprehensive information about the patient's CAM use in order to prevent harmful interactions between conventional and alternative therapies and to alert the patient to concerns the practitioner might have about a treatment.[4,54]
3. *Beneficence* suggests that patients have the right to effective interventions. Thus, if effective CAM therapies exist, patients have the right to be informed of them and practitioners have some ''limited obligation . . . to make patients aware of safe and effective alternative medicine modalities.''[54] This is, of course, limited by the availability and dependability of such information, as well as by the realistic time constraints that prevent practitioners from becoming fully knowledgeable about the range of therapies that exist. However, it is the responsibility of practitioners choosing to use CAM therapies, to be adequately knowledgeable about those therapies. Further, referral and consultation is appropriate if the patient will benefit and the referral is to a qualified practitioner.
4. *Justice* refers to equity in health care—meaning that patients should have ''fair access to alternative therapies that are known to be safe, effective, and appropriate for their conditions.'' In terms of CAM, the principle of justice encourages adequate research into CAM therapies so that practitioners may have a reliable base upon which they might recommend or reject various therapies.[54]

GUIDELINES

Once practitioners have decided that their patients have an ethical right to information on the safe and effective use of botanical therapies, or possibly even botanical products, how are they to advise patients about them? Wayne Jonas suggests that health practitioners follow a simple set of practical rules he calls the ''four Ps'': protect, permit, promote, and partner.[55] He defines these as follows:

- *Protect:* Determine whether the product or procedure is safe, low-cost, and nontoxic.
- *Permit:* Support the use of those therapies that are safe and affordable, even if they have not been definitely proved. Jonas suggests that such therapies may ''empower the patient and enhance nonspecific effects'' (''placebo'' effect).
- *Promote:* Encourage the use of proven practices, in some way making them safely available to patients.
- *Partnership:* Respect your patient's right to self-determination and work in partnership with the patient and her or his complementary medicine provider. Be actively engaged in gathering and assessing information that will allow you to make professional recommendations to your patient.

Karen Adams, in *Ethical Considerations of Complementary and Alternative Medical Therapies in Conventional Medical Settings*, suggests consideration be given to the following: (1) whether evidence supports both safety and efficacy; (2) whether evidence supports safety but is inconclusive about efficacy; (3) whether evidence supports efficacy but is inconclusive about safety; or (4) whether evidence indicates either serious risk or inefficacy.[53] She advises the following steps as guidelines:

> *If evidence supports both safety and efficacy, the physician should recommend the therapy but continue to monitor the patients conventionally. If evidence supports safety but is inconclusive about efficacy, the treatment should be tolerated and monitored for effectiveness. If evidence supports efficacy but is inconclusive about safety, the therapy still could be tolerated and monitored closely for safety. Finally, therapies for which evidence indicates either serious risk or inefficacy obviously should be avoided and patients actively discouraged from pursuing such a course of treatment.*[53]

The risk–benefit analysis shown in Box 4-7 should be considered when there is insufficient evidence for or against a particular treatment.

There are numerous medical practices that were once considered fringe, such as biofeedback, that are now a routine part of conventional medicine. As practitioners gain increased experience and confidence with a modality, and as both clinical and pharmacologic studies are done that continue to demonstrate the safety and

BOX 4-7

Factors in Risk–Benefit Analysis of Complementary and Alternative versus Conventional Medical Treatment

- Severity and acuteness of illness
- Curability with conventional treatment
- Degree of invasiveness, associated toxicities, and side effects of conventional treatment
- Quality of evidence and efficacy of the desired CAM treatment
- Degree of understanding of the risks and benefits of CAM treatment
- Knowledge and voluntary acceptance of those risks by the patient
- Persistence of the patient's intention to use CAM treatment

From Adams K, Cohen M, Eisenberg D, et al:. Ethical considerations of complementary and alternative medical therapies in conventional medical settings, Ann Int Med 137(8):660-664, 2002.

efficacy of the modality, the less fringe a practice seems. Botanical medicines have always been part of human and medical history; their use should not seem entirely foreign today.

SELECTING AND IDENTIFYING QUALITY HERBAL PRODUCTS

The quality, therapeutic efficacy, and safety of botanical products are of concern to practitioners, manufacturers, regulators, and consumers alike. This section is a primer on the standards practitioners may want to look for when selecting botanical medicine products. The first part of this section focuses on the characteristics of quality botanical products; the second part looks at the issue of phytoequivalence.

CHARACTERISTICS OF QUALITY BOTANICAL PRODUCTS

Aviva Romm

Regulations Governing Botanical Products

It is frequently stated that botanical dietary supplement products in the United States are not subject to any regulatory standards. This is far from the truth. The Dietary Supplement Health and Education Act (DSHEA) of 1994 defines dietary supplements and dietary ingredients, establishes a framework for product safety, outlines guidelines for literature displayed where supplements are sold, provides for use of claims and nutritional support statements, requires ingredient and nutrition labeling, and grants the FDA the authority to establish good manufacturing practice (GMP) regulations beyond those for food, which already apply to this class of goods.[56]

Dietary supplements must conform to federal regulations that control their manufacture, labeling, and marketing as well as state and local health and business regulations. In addition, all supplement products are required by law to provide certain information about their formulation.[57] For those who wish to be informed about regulations governing dietary supplements, visit the FDA website at http://www.cfsan.fda.gov/~dms/supplmnt.html. The National Institutes of Health Office of Dietary Supplements also provides a wealth of information about dietary supplements at http://dietary-supplements.info.nih.gov/. For those wishing to study herbal products in clinical trials, visit the National Center for Complementary and Alternative Medicine website at http://nccam.nih.gov/.

Manufacturing Quality Botanical Products

Ultimately, the quality of the starting materials is essential to the quality of the product, along with proper preparation and meaningful labeling. A number of manufacturing steps that can maximize the quality, safety, and efficacy of botanical products may include:

- Proper identification
- Proper harvest times and collection practices
- Use of proper plant part
- Analysis of purity
- Organoleptic analysis
- Chemical assay when appropriate
- Good manufacturing practices (GMPs)
- Proper preparation
- Proper drying conditions if using dried herbs
- Proper labeling and marketing
- Appropriate enforcement (FDA/FTC)

Batch-to-batch consistency is also an important measure of a product's quality, and perhaps one of the most clinically significant aspects a product. Thus, practitioners will want to purchase from companies that have internal standards that allow them to guarantee a consistent product (Box 4-8).

Proper Identification

Proper identification is essential to product safety and efficacy. The plant should be identified in the field by the harvester and checked in the manufacturing facility to ensure there has been no mislabeling of the herb between harvest and delivery to the manufacturer. Misidentification (not to mention substitution, contamination, and adulteration) can lead to hazardous consequences for the consumer should a toxic or contraindicated herb replace the desired herb. The classic case illustrating this problem is that of a pregnant woman who was unknowingly consuming an herb called *Periploca sepium* in place of *Eleutherococcus senticosus* throughout her pregnancy due to the misidentification or adulteration of a product, and whose baby suffered from androgenization.[58] Identity tested can include organoleptic analysis and chemical assay. With whole plant material, organoleptic analysis can often be adequate for identification; however, with powdered herbs, microscopy can be very useful in plant identification, and chemical assays can be necessary because identification of material can be more difficult when the whole herb form is no longer available.

BOX **4-8**

Choosing an Herbal Product Brand

With regard to choosing a brand, one recommendation is to purchase products from companies who are members of the American Herbal Products Association (AHPA). AHPA members agree to abide by a Code of Ethics that requires adherence not only to established regulations, but also to meaningful industry policies. Thus, certain business practices that are not mandated by any government agency are expected of all of these companies. One such measure, established as an industry regulation in 1992, called upon all of AHPA's members to agree to a single standardized common name for each of the herbs used in their products to ensure clear labeling for consumers. This policy has now been adopted as Federal law. Links to many of AHPA's members and a copy of the Association's Code of Ethics are available on the AHPA website: http://www.ahpa.org/. It is also generally recommended that you buy your herbal product from a reputable company. If the claims made on a particular product are outrageous and unbelievable, especially when compared with other products with the same or similar ingredients, it may be an indication to try another brand. Always feel free to contact the manufacturer. Those who are selling high quality products should be happy to answer all of your questions.

From American Herbal Products Association: Herbal FAQs, http://www.ahpa.com

Harvest Times and Collection Practices

Plant constituent profiles are not static; rather, the concentrations of individual constituents have peaks and nadirs at various times, both seasonally and even daily. Harvesting herbs with an understanding of their optimal harvest times can improve the quality of individual herbs for their optimal medicinal activity. Contemporary agricultural, analytical chemical, and traditional guidelines may be used to determine proper harvest times and practices for various herbs. Manufacturers producing quality herbal products start with raw materials that were properly harvested to preserve the desired properties and hence the desired chemical profile.

Plant Part

The chemical profile of an herb also varies greatly within the plant itself; the roots, stems, leaves, flowers, fruits, and seeds usually contain different constituents or the same ones in different amounts, which results in different biological activities. The root of dandelion, for example, is a bitter tonic and gentle laxative, whereas the leaf of dandelion is a powerful diuretic. The flowering tops of St. John's wort contain much higher quantities of the constituents believed responsible for the herb's antidepressant activity, whereas the leaves and stems possess much lower amounts; thus, a more active medicine is produced by manufacturers harvesting the uppermost flowering parts rather than the entire above-ground portion. Most herb books name the medicinal part of the plant, making it easy for the practitioner to identify whether they should be using root, leaf, etc.

However, not all manufacturers strictly include just the medicinal plant part (although by law they are required to state the plant part used on the product label); cost buying often dictates, meaning that the most desired plant part may be haphazardously harvested to include additional parts. For example, large amounts of stem may be included when only leaf is desired, or a great deal of stem and leaf when flower is desired. This can be nearly impossible to detect in powdered or extracted products (although it is often obvious with bulk whole herb); thus, it is important to question manufacturers about their practices, which can include strict specifications for the plant part used and acceptable amounts of foreign matter (undesired other plant parts). They may even be able to specify which pharmacopeial monograph, if any, applies to their product.

Purity

AHPA recommends specific maximum tolerated levels for dried raw agricultural commodities, including cut and powdered commodities, that are used as botanical ingredients in dietary supplements and that are subject to further processing, as follows:[57]

- *Total aerobic plate count:* 10^7 colony forming units/gram
- *Total yeasts and molds:* 10^5 colony forming units/gram
- *Total coliforms:* 10^4 colony forming units/gram
- *Salmonella:* absent in 10 grams
- *Escherichia coli:* not detected in one gram
- *Aflatoxins* B_1, B_2, G_1, and G_2: 20 μg/kg (ppb)
- *Aflatoxin* B_1: 5 μg/kg (ppb)

Practitioners may want to inquire as to whether a manufacturer uses irradiation as a technique to reduce microbial count, as this is a common practice that has no federal allowance for most herbs.

Good Manufacturing Practices

Supplements, including herbs, are legally classified as foods and are therefore required to be manufactured to the same high standards that are required of all foods. Good manufacturing practices establish guidelines that assure supplements are manufactured under sanitary conditions, resulting in properly identified products that are not contaminated or adulterated and are fit for consumption. Any supplement that does not conform to these basic guidelines is subject to regulatory action by the FDA.[57]

Proper Preparation

Herbs differ in their preparation requirements. Whether the herb is manufactured as a tea, capsule, or alcohol extract, for example, depends on how the herb is best extracted or prepared to maximize and preserve its medicinal activity. Both traditional practices and basic chemistry can help guide the decision of how an herb is prepared.

Labeling and Marketing

Supplement labels must provide consumers with nutritional information. Unlike foods, supplements must

state the quantity of each of the contained ingredients (except for ''proprietary blends'') that make up a product. All herbal products are required to identify the parts of each plant ingredient used, and label them with their accepted common names. The FDA specifies exactly what kind of claims are allowed on product labels and prohibits the use of any statement that would brand the product as a drug. Herbal supplements are not allowed to make statements regarding prevention, cure, mitigation, or treatment of diseases. Instead, their claims are limited to statements that are legally defined as ''statements of nutritional support'' that include ''structure/function statements.''[57] The FTC guidelines for claims substantiation can be found at http://www.ftc.gov/bcp/conline/pubs/buspubs/dietsupp.pdf.

The Role of the Herbalist in the Botanical Products Industry

Skilled herbalists with combined training in botany, organoleptic and macroscopic plant identification, product formulation, and clinical practice, can offer unique insights regarding product quality, efficacy, and strength to today's herbal industry. Perhaps the most illustrative example of this occurred a number of years ago when a large batch of plantains distributed to United States botanical products manufacturers was contaminated with digitalis. Several consumers were poisoned by this adulterated product. However, because of the identification skills of an herbalist employed by one of the companies that received the bad shipment, this company rejected the batch and therefore did not distribute harmful product.

Programs such as Bastyr University's bachelor of science in botanical medicine are attempting to train herbalists who are prepared to work in industry. Herbalists and herbalist-manufacturers, those botanical manufacturing companies run by herbalists, approach issues of product quality and efficacy informed by an amalgamation of information drawn from traditional practices, observation of therapeutic response, experiential knowledge of the plants, and contemporary scientific studies. This synthesis of knowledge may represent a significant contribution to the conversation on medicinal plant product standards. Cooperation between scientific researchers and botanical practitioners/small manufacturers may present novel approaches to understanding optimal conditions for growing, harvesting, preparing, storing, and delivering medicinal plant products.

Sustainability

Sustainability is of key importance to the survival of many important botanical medicine species, some of which have been lost historically due to overuse, such as the once relied upon sedative lady's slipper (Cypripedium pubescens), the gynecologic remedy false unicorn (Chamaelirium luteum), or the antimicrobial herb goldenseal (Hydrastis canadensis). Herbalists prioritize sustainability in attention to harvesting, cultivation, and choice of plants prescribed in the clinic; regularly inform their patients of the need for sustainability; and are highly knowledgeable about sustainable alternatives to at-risk and endangered species. Thus, the sustainability of herbs is also an important factor in selecting herbal products. Practitioners can become informed about which herbs are endangered, and make efforts to use only those herbs that are cultivated if on an endangered list, or use alternatives to these herbs.

Efficacy

Product efficacy can be determined by clinical observation, patient reporting, clinical trials, or a combination of these. Practitioner observation and patient reporting are subject to a host of biases; however, the collective clinical knowledge of herbal practitioners is an important and valuable source of information. As few herbs have been subjected to rigorous clinical trials, and even fewer for combination herbal products, practitioners wishing to rely entirely on rigorously tested herbs are going to be limited to a select number of products.

The Handbook of Clinically Tested Herbal Remedies Volumes 1 and 2, by Marilyn Barrett, provides comprehensive reviews of over 160 herbal products and 360 clinical herbal studies, as well as background information on botanical medicine regulations, botanical identification and analysis, and many other topics germane to this chapter. It is a useful resource for clinical practitioners wishing to use products that have trials behind them. However, lack of clinical trials does not mean a botanical medicine is inefficacious, and presence of a clinical trial does not mean that the same herb will perform identically when not manufactured to the exact specifications and given in a different dosage.

In countries such as the United Kingdom, Canada, and Australia that have Traditional Medicines categories as part of the governmental regulatory framework for botanical medicines, efficacy is determined by a combination of factors, including historical use, traditional use, contemporary clinical use within a given period of time (e.g., the past 15 to 30 years), and scientific evaluation (e.g., clinical trials). Increasingly, there are companies that offer professional lines of products, aware of the unique needs and concerns of botanical practitioners.

PART II

General Gynecologic and Menstrual Health Concerns

Menstrual Wellness and Menstrual Problems

5 CHAPTER

Aviva Romm, Bevin Clare, Jill E Stansbury, Linda Ryan, Ruth Trickey, Laurel Lee, Angela J. Hywood

The scientific study of menstruation has been hampered by the overpowering influence of traditions and social and cultural beliefs. We have all, men and women, been conditioned to view menstruation in a negative way. Perhaps, it is time to look at menstruation from another point of view. How many fine novels have been finished in a burst of creativity in the premenstrual period? How many great ideas have been born premenstrually?

—Clinical Gynecologic Endocrinology and Infertility[1]

MENSTRUAL HEALTH AND THE NORMAL MENSTRUAL CYCLE

Aviva Romm

This section reviews the historical and cultural beliefs and attitudes surrounding menstruation, ''the normal menstrual cycle,'' and provides an overview of the menstrual irregularities and conditions presented later in this chapter. This section also looks at practical ways to promote menstrual health. Subsequent sections of Chapter 7 address common menstrual problems.

A BRIEF HISTORY OF MENSTRUATION IN CULTURE AND MEDICINE

Menstruation has historically been cloaked by religious, social, and cultural myths and meaning. Menstrual blood and menstruating women have been surrounded by fear, taboo,* restrictions, and worship since ancient times. Cultural views on menstruation are diverse. The Beng people of the Ivory Coast believed that ''Menstrual blood is special because it carries in it a living being. It works like a tree. Before bearing fruit a tree must first bear flowers. Menstrual blood is like the flower.''[2] In stark contrast it has been referred to as ''the curse'' by Judeo-Christians and is considered a sign of uncleanliness, or even evil, in some cultures.[3] Menstrual blood was used as a panacea, a medicinal ingredient, an ingredient in casting spells, and even as a pesticide capable of making caterpillars drop from plants and insects die in the fields.[4] Menstruating women were variably considered to be possessed by evil spirits or magic.[5–7]

Medical attitudes regarding menstruation have fluctuated over the centuries, from menstruation and menstrual blood being perceived as a natural process—a woman's ''flowers,'' as menstruation was described not only by the Beng but in the *Treatise on the Diseases of Women, and Conditions of Women*, part of the medieval compendium known as *The Trotula*, which remained the definitive text on women's medicine for several centuries—to something capable of poisoning men and deforming children, as described by Pliny and others.[2,7] Hildegarde of Bingen, the famed German nun and healer (1098–1179) used the term *flowers;* however, she also attributes menstruation to ''Eve's sin in Paradise,'' reflecting both positive and negative attitudes toward menstruation. Hippocratic and Galenic medicine viewed menstruation as the basis of women's unique physiology. It was considered a necessary and healthy purgation upon which the health of the entire female body was dependent. Menstruation was seen as women's inherent constitutional ''coldness.'' The inabilities to ''cook'' their nutrients thoroughly led to an accumulation of waste in the body that could only be gotten rid of

*Interestingly, the word *taboo* is derived from a Polynesian word meaning both ''sacred'' and ''menstruating.''

through menstruation. Lack of menses (e.g., amenorrhea) was believed to lead to a pathologic systemic state. Normal menstruation, that is, the proper amount at the proper time, was considered to reflect a state of health.[2]

In contrast, however, around the first century BCE, Pliny, a physician and prolific medical writer, wrote that menstrual blood could drive men and dogs mad, make vines wither, sour wine, and discolor mirrors, among other powers.[5,7,8] Pliny's views, as well as others' of his time, represented menstruation as poisonous or noxious, views that would contribute to misogynist medical views of women that have persisted.[1,2,4] Democritus wrote that ''usually the growth of greenstuff is checked by contact with a woman; indeed, if she is also in the period of menstruation, she will kill the young produce merely by looking at it.''[6]

Negative attitudes about menstruation have not only influenced the practice of women's medicine, but also the medical education of women. Western medicine historically viewed menstruation as a disease and an opportunity to treat women as fragile and weak.[7] Well into the nineteenth century in the United States, the fact that women menstruated was considered proof of the inferiority of the female intellect. Menstruation was used as a justification for keeping women out of medical schools, based on the grounds that menstruating women needed increased rest—mentally and bodily.[5]

Women's health reform and self-help movements throughout the twentieth century have played a major role in transforming and reshaping women's, society's, and medicine's attitudes toward menstruation. It has become a more acceptable topic for conversation, evidenced in many ways, not in the least, by the mention of menstruation on television sitcoms, the openness of menstrual products advertisements on television and in print media, and articles in popular magazines. This is a positive trend allowing women to more openly seek information and medical care about menstruation and menstrual concerns. However, advertising also directly contributes to the perpetuation of cultural menstrual taboos—that menstruation is ''dirty,'' and suggestions that it should remain hidden. Educational films and advertisements from menstrual product manufacturers stress products' abilities to keep safe the secret that the girl is menstruating and to help her feel fresh and clean, perpetuating the message that menstruation is shameful and dirty.[9]

Women's own personal and cultural views on menstruation also vary substantially. Menstruation may be considered a happy event, or a sign of uncleanliness—both attitudes persisting even in a single culture.[10] A correlation has been asserted in feminist literature that a woman's attitudes toward menstruation and can influence her physical experience of menstrual symptoms.[7] In one study analyzing menstrual attitudes, women were asked to describe their menstrual periods. Terms were rated as positive (such as ''red friend,'' ''my buddy''), negative (such as ''the curse,'' ''pain in the ass''), or neutral (such as ''period,'' ''surfin' the crimson wave''). In the groups combined, most terms were either neutral (46%) or negative (37%). There was a tendency for women in the negative group to employ negative terms (52% of negative group women used solely negative terms versus 18% in the positive group), whereas 55% of women in the positive group employed neutral, not negative terms.[9] Women in the negative group used negative terms significantly more than did women in the positive group. Many women consider menstruation somewhat of an inconvenience, but nonetheless, a natural event. Increasingly, American women are reframing menstruation as a celebration of women's femininity and women's connection to the rhythms of the earth and the moon.

WHAT IS NORMAL MENSTRUATION?

Menstruation is a cyclic process occurring in most women between 12 and 50 years of age. It generally occurs without difficulty, although there may be some normal sense of inconvenience accompanying the period. The variation in the interval between menstrual periods, the duration of each menstrual period, the amount of blood loss, the associated discomforts or lack thereof, and the subjective psychoemotional experience of menstruation among women is so great as to make it difficult to define ''normal menstruation.'' There is a wide range of normal variation.

It is necessary to determine whether a pattern, symptom, or concern is normal for the individual woman in the context of her own gynecologic and menstrual history, as well as against objective measures. Certain characteristics of menstruation can be a reflection of an underlying pathologic process or may predispose a woman to the development of chronic disease.[11] For example, metrorrhagia predisposes to anemia, and the irregular menstrual cycles associated with PCOS (see PCOS) can predispose a woman to diabetes and consequently, heart disease. Women with long or highly irregular menstrual cycles have a significantly increased risk for developing type 2 DM that is not completely explained by obesity.[12] Persistent deviations from the woman's own norms, as well as major deviations from accepted standards, require further evaluation.

ONSET, FREQUENCY, AND DURATION OF MENSTRUATION

The onset of the first menses (menarche) typically occurs between the ages of 10 and 16 years old (see Puberty, Menarche, and Adolescence). The menstrual cycle is generally irregular and anovulatory for the first several years after menarche, reaching a regular length and duration by 5 to 7 years after menarche. Variations outside of this range are generally normal, but could be signs of precocious puberty or amenorrhea; sometimes symptoms of underlying medical disorders (see Puberty, Menarche, and Adolescence, as well as Amenorrhea).

A woman will experience from 300 to 400 menstrual cycles in her lifetime. Cycle length is controlled by the rate and quality of follicular growth and development, which varies in individual women.[1] Based on several observational longitudinal studies of thousands of women around the world, it was determined that at age

25, 40% of women had 25- and 28-day cycles, and from ages 25 to 35 60% had 25- to 28-day cycles. The average cycle length is 26 to 34 days.[13] Only 0.5% of women experience cycles shorter than 21 days and 0.9% cycles longer than 35 days. At least 20% of women experience irregular cycles.[1] The length of the follicular phase is the primary determining factor in cycle length.

Menstrual bleeding lasts 3 to 6 days in most women, although there is variation in cycle length from 2 to 12 days after the start of ovulatory cycles. Longer periods (>8 days) are associated with anoluvation.[13] The heaviest flow is consistently on day 2 of the cycle. Normal blood loss is considered 30 to 80 mL. Small clots are considered normal; large clots may suggest the need for further evaluation.[7]

The duration and amount of bleeding declines slightly (by about a half a day per cycle) in women over age 35. However, women approaching menopause often experience significantly heavier bleeding than younger women.[13]

Although some women describe their periods coming ''like clockwork,'' most describe some amount of irregularity over the course of menstrual life cycle, even if it is only occasional. The endocrine system is easily affected by numerous factors: stress, changes in amount of daily and nightly light exposure, sleep patterns, diet, travel, amount of exercise, illness, and so forth. It is normal for women to occasionally experience an irregular period, a lighter or heavier period, a ''crampy'' period, or even to miss a period in the absence of pregnancy or lactation. It is when irregularity recurs repeatedly, presents with an acute problem (e.g., sudden, heavy, or unremitting vaginal bleeding), or occurs in the absence of other explainable factors that one might suspect a disorder.

Women in their late thirties and forties often begin to experience some degree of irregularity of menstrual frequency, duration, and amount of blood loss because of a decline in ovarian function as they approach menopause. In their late thirties, women experience a shortening of their cycle because of increased production of FSH, a result of follicle numbers beginning to decline. However, between 2 and 8 years prior to menopause, the cycles again lengthen.[1] Approximately 50% of women experience a cycle of 120 days or longer in the year prior to menopause, and 20% experience a cycle of this length or longer within 2 to 4 years of their final period.[13] The average age of menopause in the United States is 51 years old.[14]

FREQUENCY AND TYPES OF MENSTRUAL DISORDERS

Menstrual dysfunction is defined in terms of bleeding patterns, for example, amenorrhea (lack of menstruations), menorrhagia (excessive bleeding during menstruation), or polymenorrhea (frequent menstruation); ovarian dysfunction for example, anovulation and luteal deficiency; pain (dysmenorrhea); and premenstrual syndrome. Irregular menstruation is estimated to range from 2% to 5% of the general population, and up to 66% among athletes.[15] In the United States, approximately 2.9 million office visits are made annually by women age 18 to 54 for menstrual problems.[7,16] Two-thirds of these women contact a doctor regarding menstrual problems each year, and 31% report spending a mean of 9.6 days in bed annually. Among young women, dysmenorrhea is the most common cause of time lost from work or school. The costs of menstrual disorders to US industry have been estimated to be 8% of the total wage bill, and the impact is particularly acute in industries that employ women predominantly.[16] Interestingly, it is estimated that primitive, hunter gatherer women, over the course of an average lifetime, experienced only one-third as many menstrual periods as do modern women because of later age at menarche, earlier and more frequent pregnancies, and breastfeeding, suggesting that modern women experience a significantly greater lifetime exposure to estrogen, which may be partially responsible for increased health risks. Traditionally, factors such as later menarche, earlier first pregnancy, breastfeeding, and earlier menopause may have played a protective effect against, for example, breast and gynecologic cancers.[16] Menstrual disorders also predispose women to other risks, for example, anemia, osteoporosis, cancer risks, diabetes, and cardiovascular disease.

In spite of the significance of menstruation in women's lives and the high incidence of menstrually related health problems in society, there is surprisingly little epidemiologic evidence on menstrual disorders and associated risk factors, and no prioritization of research in this area.[11,16]

Subsequent sections of this chapter address these dysfunctions either individually or as part of a larger syndrome in which they occur.

BOX 5-1

Terms and Definitions for Common Menstrual Disorders[7]

Amenorrhea: absence of menses
Anovulation: absence of ovulation
Dysfunctional uterine bleeding: prolonged, excessive, irregular uterine bleeding in the absence of an organic disorder
Dysmenorrhea: painful menstruation
Hypomenorrhea: scant but regular menstruation
Intermenstrual bleeding: bleeding at any time between normal menses
Menorrhagia: prolonged, excessive regular menstrual bleeding
Menometrorrhagia: irregular heavy bleeding
Oligomenorrhea: infrequent menstrual cycles, ≥35 days
Polycystic ovarian syndrome: a syndrome resulting from androgen excess and anovulation; may lead to irregular menses
Polymenorrhea: frequent menses, ≤21 days
Premenstrual syndrome: cyclic recurrence of psychoemotional and physical disorders during the luteal phase of the menstrual cycle

FACTORS AFFECTING THE MENSTRUAL CYCLE

Numerous factors influence the menstrual cycle, including a woman's nutritional status, stress levels, body weight, exercise patterns, attitudes and beliefs about menstruation, and environmental and workplace exposures. Investigation into these can sometimes explain dysfunction; corrections can often restore physiologic and emotional balance. A holistic approach to preventing and treating menstrual dysfunction should always include consideration of possible social and lifestyle issues.

Diet/Nutrition

Menstruation is influenced by the amount of energy provided by the diet as well as by the types of foods consumed. Lean women with a low body mass index (BMI), as well as obese women, have an increased likelihood of menstrual disorders. Women with highly restrictive dietary practices are more likely to experience menstrual dysregulation, particularly amenorrhea, anovulation, and a shorter luteal phase.[17–19] Recent studies suggest that reduced energy availability (increased energy expenditure with inadequate caloric intake) is the main cause of the central suppression of the hypothalamic pituitary-gonadal axis. As a consequence, not only will there be menstrual dysregulation but a higher potential for bone demineralization and increased risk of skeletal fragility, fractures, vertebral instability, curvature, and osteoporosis.[19,20] Thus, the importance of treating underlying dietary imbalances that can cause menstrual dysregulation becomes more significant.

Dietary fat restriction is associated with amenorrhea even in normal weight, nonathletic women.[11] A raw foods diet is commonly associated with low BMI, weight loss, and amenorrhea. In one study of 279 women on a raw foods diet, 30% of women under age 45 experienced amenorrhea.[21] There is a common belief among adolescent girls and women that a vegetarian diet leads to weight loss; thus, many adopt a vegetarian diet as part of an attempt to diet. It has been suggested that a vegetarian diet is associated with menstrual disorders, especially amenorrhea; however, it appears that healthy, weight-stable, vegetarian women consuming self-selected diets do not experience more menstrual disturbances than healthy, weight-stable nonvegetarians.[11,22] There does not appear to be a correlation between a higher intake of soy foods in the vegetarian diet and menstrual dysregulation, as has been commonly assumed.[22]

The consumption of fruits, fish, and vegetables plays a protective effect against dysmenorrhea in adolescent girls and women. The protective role of the fish seems to be due to omega-3 fatty acids. During menstruation, this fatty acid competes with the omega-6 fatty acids for the production of prostaglandins and leukotrienes. The prostaglandins generated from the omega-3 fatty acids lead to a reduction in myometrial contraction and vasoconstriction.[23]

Weight

Overall weight and changes in weight affect menstrual regularity. Ovarian suppression can occur as a result of sudden or moderate weight loss, leading to amenorrhea. This is most pronounced in cases of eating disorders and famine. This phenomenon is also seen in women who are 20% in 30% below their ideal body weight, which is common in athletes or women on restricted caloric intake diets.[11] Obesity, particularly truncal obesity, is also associated with menstrual disorders, notably amenorrhea associated with polycystic ovarian syndrome (PCOS), and an increase in incidence of diabetes and long-term health consequences. It appears that at both ends of the extreme spectra of weight, women are likely to have the longest menstrual cycles and anovulation.[11,24]

Caloric restriction itself, even before there is a loss of weight, can result in menstrual dysregulation. It was demonstrated in one study that girls who simply skip breakfast experience a higher degree of dysmenorrhea than girls who eat an adequate daily breakfast.[25] The effects of body weight on menstrual function may be a result of nutritional status, caloric intake, stress on eating habits and the effects on menses, psychiatric disorders associated with weight problems, or the mechanics of body fat on steroid hormone synthesis and estrogen metabolism.[11] Significantly, excessive exercise with menstrual irregularity can be an important sign of an eating disorder, psychological restraint issues around food consumption, higher perceived stress, and low self-esteem.[26,27]

Exercise

Moderate exercise from a young age is essential for optimal lifelong health including prevention of cardiovascular disease, osteoporosis, and depression. However, excessive exercise or exercise at elite levels for competitive athletes can predispose women to nutritional deficiency, inadequate energy intake, and low body weight, all of which increase risk of menstrual dysfunction. Women athletes have a higher overall incidence of menstrual disorders. Ballet dancers and runners have an increased rate of amenorrhea, anovulation, and luteal phase defects compared with nonathletes.[11] In one study examining the role of nutritional status, eating behaviors, and menstrual function in 23 nationally ranked female adolescent volleyball players, these women were found to be low in folate, iron, calcium, magnesium, zinc, B complex, vitamin C, and carbohydrate intake, compared with RDAs. Approximately 50% of the athletes reported actively ''dieting.'' Past or present amenorrhea was reported by 17% of the athletes and 13% and 48%, reported past or present oligomenorrhea and ''irregular'' menstrual cycles, respectively.[28] Among women age 29 to 31, daily vigorous sports activity was associated with increased cycle variability and cycle length. Even recreational exercise is associated with an increase in mean cycle length.[11]

Exercise is an independent factor separate from weight loss in relationship to cycle variation and presence

of amenorrhea. Cessation of training even in the absence of weight gain can restore cycle normalcy. The most likely mechanism of cycle irregularity due to moderate exercise is decreased GnRH and gonadotropin and reduced serum estrogen levels, along with a possible physiologic stress response mechanism. However, because of the increased likelihood of aberrant eating patterns in amenorrheic athletes, inadequate caloric intake and a negative energy balance also may be causative.[11] With a societal emphasis on a lean body, many young women use exercise as a means of weight control, frequently combined with rigorous dieting patterns; thus, exercise patterns should be evaluated in the context of ruling out eating disorders, and proper amounts of exercise encouraged to ensure its benefits.

Stress

Most women have experienced, at least once in their lives, the effects of stress on menstrual regularity: skipping a period or having a period come late or early during a particularly difficult time. There is some evidence regarding connections between socioemotional processes and menstrual functioning. Psychological stress is generally acknowledged in the medical literature to affect menstruation; however, studies on stress and menstrual function are limited, consisting mainly of studies of major life changes, catastrophic events such as war or imprisonment. Studies on the effects of girls leaving home to attend school, the military, or work suggest that separation from home and family increases the likelihood of amenorrhea, but these studies have lacked adequate comparison groups.[11] High levels of workplace demand, combined with low levels of perceived control, have been associated with a doubled risk for short menstrual cycle length (e.g., less than 24 days) Characteristics consistent with submission (i.e., introversion, anxiety, low perceived control, and inhibition of aggression) have been shown to be elevated among women seeking treatment for hirsutism and irregular menses compared with women without such conditions. However, this association could reflect the socioemotional consequences of these medical problems and their associated features.[29]

It is no surprise that delicate HPA and endocrine functions might be disrupted by personal upheaval and stress. Although the mechanisms of stress- and anxiety-related menstrual changes have not been fully elaborated, it is suspected that either central psychogenic disturbances cause changes in the hypothalamus that consequently affect prolactin and endogenous opiate levels, and that stress leads to a systemic physiologic response causing elevated basal cortisol levels, and consequently alterations in hypothalamic response and changes in LH with a reduced pulsatile frequency.[11,30]

Attitudes and Beliefs about Menstruation

In a survey-based study of college-aged women (n = 327) those who had extremely negative or extremely positive early menstrual experiences were strongly associated with correspondingly negative or positive current menstrual attitudes. There were additional associations between early menstrual experiences and measures of body image and health behaviors. Positive group participants reported more positive body image and better general health behaviors. Results suggest that early menstrual experiences may be related to menstrual experiences later in life.[9] Unfortunately, adolescent girls often receive inadequate information or negative messages regarding menstruation from an early age. Although they may receive information on the biological aspects of menstruation from parents, teachers, and other sources, they are often not prepared for the practical aspects of getting their periods, for example, what it feels like or how to take care of themselves while menstruating. Instead, girls are directly and indirectly instructed about (largely negative) cultural beliefs concerning menstruation and the ways in which they will be expected to behave in order to uphold these beliefs. Somaticization of these beliefs may translate into increased difficulty in the menstrual experience, particularly in the form of dysmenorrhea or premenstrual syndrome (PMS). Women with negative menstrual beliefs are more likely to seek menstrual suppression through pharmacologic means.[9]

Environmental/Work Exposures

Women whose work requires large amounts of physical labor may experience weight loss and subsequent menstrual irregularity. Workplace stress and noise also may contribute to menstrual dysregulation. Occupational chemical exposure has clearly been demonstrated to act on the ovaries; cytotoxic agents, for example, can induce ovarian failure including follicular loss, anovulation, oligomenorrhea, and amenorrhea.[11] Many environment pollutants to which women are nearly ubiquitously exposed are now also recognized to be endocrine disruptors.

Pheromones and Menstrual Synchrony

Studies on menstrual synchrony, when women who spend time in close proximity begin cycling together, have yielded conflicting results. Nonetheless, the phenomenon is well known among women who report menstruating at the same time, or close to, that of roommates, daughters, sisters, or close friends; hence, it is casually referred to as ''the dormitory effect.'' Animal and human studies have shown that social interactions can modify endocrine function. It is suspected that pheromones may reduce menstrual cycle variability among women and synchronize menstruation. Pheromones are airborne chemicals released by one individual that can affect another. Odorless compounds obtained from the axillae of women altered cycles of other women exposed to these compounds.[1] However, a wider range of environmental signals may influence menstrual synchrony.[11] One study on women's qualitative experience of menstrual synchrony suggests that the concept of menstrual synchrony frames menstruation as a natural, healthy phenomenon for women.[31]

Ethnicity

Ethnicity is a determinant of menstrual patterns. African-American girls, for example, are significantly more likely than European-American girls to experience heavy bleeding. It may be that stress accompanying socioeconomic differences plays a role in this difference.[32]

PROMOTING HEALTHY MENSTRUATION

The health care profession has an obligation to promote menstrual education. We must have an understanding of reproductive physiology in order to impart it to our patients, and we must be sensitive to the need to present a positive attitude regarding sexual and reproductive functions.

Clinical Gynecologic Endocrinology and Infertility[1]

Menstruation, in the absence of underlying pathology, need not be fraught with discomfort. Menstruation is something that girls should be taught about from the time they are young, including an understanding of what is happening to their bodies, how to eat, exercise, rest, and care for themselves to avoid what are often preventable menstrual complaints, and to embrace this aspect of their feminine experiences. Unfortunately, many girls, and women, remain unaware of the impact that basic lifestyle factors can have on the menstrual cycle and suffer unnecessarily from what can be debilitating physical, emotional, and psychological symptoms. Although some menstrual disorders have complex pathophysiologic etiologies that do not simply respond to lifestyle modification, practitioners treating clients with common menstrual complaints should always take a multifactorial approach that includes education about possible lifestyle contributors. The discussion below focuses on basic lifestyle strategies that specifically relate to menstrual health—or eumenorrhea—a healthy menstrual cycle.

Diet, Nutrition, and Body Weight

The impact of insufficient dietary energy intake, inadequate nutrition, underweight, overweight and dieting on menstruation, was discussed in the preceding section. Not only are diet and nutrition determinant of menstrual cycle function and regularity but also menstrual dysregulation can be predictive of bone mineral density (BMD) and osteoporosis risk, diabetes, and cardiovascular disease. What type of diet then *promotes* healthy menstruation and reduces the risk of later disease development? A whole-foods based, primarily organic diet with an emphasis on vegetarian protein sources (although not exclusively vegetarian), good-quality cold water fish, whole grains, fresh fruits, nuts, vegetables, and good-quality oil, is probably the optimal human diet. Particularly important in maintaining menstrual health seems to be maintenance of stable blood sugar and stable weight at an ideal individual level, and adequate intake of healthy fats. For women, diet and body weight are intimately tied to self-esteem and personal identity. The landscape upon which this plays out can be reproductive function. Therefore, nutritional and personal counseling may play a part in the treatment of menstrual problems when nutrition, eating habits, or body image are issues.

Avoiding or at least reducing the amount consumed of certain foods also may improve menstrual symptoms. For example, one report found that women with PMS consumed 275% more refined sugar, 79% more dairy products, 78% more sodium, and 62% more carbohydrates than women without PMS. They also consumed 77% less manganese and 53% less iron than symptom-free women. Another study found that consumption of caffeine-containing beverages increased the incidence and severity of PMS in college-age women.[33]

Conversely, the inclusion of certain foods and nutrients may prevent or reduce symptoms. In many cultures it is believed that cold foods should be avoided and only warm foods consumed during the menstrual cycle to prevent dysmenorrhea. Calcium, vitamin B_6, magnesium, vitamin E, vitamin A, and essential fatty acid supplementation may be helpful for menstrual dysregulation. These are discussed under specific conditions in subsequent sections of this chapter. Not only is proper nutrient intake essential, but proper digestion and assimilation is necessary for nutrient absorption and use.

Many women experience premenstrual cravings, particularly for sweets. Ensuring adequate nutrition often reduces cravings; however, it is perfectly fine to indulge cravings if nutritional needs have been met and the woman is at a healthy weight. As with all things, moderation is the key. Chocolate is a popular premenstrual craving: Although the relationship between chocolate and menstrually related skin problems remains controversial, many girls and women self-report that a reduction in chocolate consumption improves acne. Dark chocolate is rich in beneficial antioxidants, and many women find a small amount to be stimulating and stress relieving.

Encourage: Adequate nutritional and energy (caloric, fat) intake, consumption of fresh fruits and vegetables, leafy green vegetables, whole grains, vegetarian protein sources, cold water fish, nuts, good-quality oil (especially olive and walnut oils), essential fatty acids, maintenance of healthy weight and stable blood sugar; positive body image and self-esteem.

Discourage: Excessive consumption of refined flour products, sugar, caffeinated products, red meat, dairy products; excessive dieting, dramatic weight loss, underweight, and obesity.

Exercise

Exercise, especially when regular and frequent, can reduce both physical and emotional menstrual discomforts, improving mood and relieving physical symptoms. The mechanisms for this are not fully understood but may include a reduction in estrogen levels and catecholamine levels, improved glucose tolerance, and increased endorphin levels.[33] Moderate exercise also reduces the risk of bone demineralization associated with menstrual dysregulation, especially anovulatory cycles and amenorrhea. Excessive exercise, which is discussed in the preceding, should be discouraged, or at least nutritional and

energy requirements should be met and healthy body weight maintained.[15,18,20] Yoga and many forms of dance include movements and stretches that can be especially specific for relieving pelvic tension and discomfort associated with dysmenorrhea. Forms of movement that help women to positively experience their body can be helpful in overcoming negative personal attitudes.

Encourage: Moderate amounts of exercise; weight-bearing exercise for bone health, exercise that promotes relaxation and pelvic movement such as yoga and dance; exercise that improves self-perception and body image. Exercise must be accompanied by adequate caloric intake and maintenance of healthy body weight; positive body image and self-esteem.

Discourage: Excessive exercise, exercise as part of an attempt at caloric restriction in non-overweight women; rapid weight loss.

Stress

As discussed, stress can contribute to physiologic changes that lead to menstrual dysregulation, and menstrual dysregulation itself can increase a woman's stress levels. Women can be encouraged to manage time to reduce work load or personal stress, and seek outlets for stress such as meditation, yoga, journaling, counseling, or other healthy means. Learning self-empowerment techniques can be very useful for women with stress-related menstrual dysregulation. Adequate nutritional and caloric intake (especially avoiding hypoglycemia) can reduce stress and improve stress resistance. Reduction in caffeine consumption can also reduce stress. Getting adequate rest is essential. Herbal adaptogens and nervines can be used to improve stress resistance and promote relaxation. Improving attitudes about menstruation can improve reduce the perception of menstrual problems.[1]

Encourage: Stress reduction activities, positive self-image and self-esteem; seeking creative outlets for stress, healthy diet with adequate nutrient intake, ample rest and relaxation, yoga, meditation, exercise.

Discourage: Negative self-talk, overwork, poor self-image, poor menstrual attitudes.

Attitudes and Beliefs about Menstruation

How we perceive our menstrual cycles can affect how we feel when we menstruate. Talking with patients about their menstrual beliefs and attitudes can help clarify whether underlying negative beliefs might be playing a role. Sometimes simply educating a woman about menstruation can help dispel ideas of it as a ''bad'' or ''unclean'' event, and improve a woman's acceptance of this natural process. Women may find that setting aside designated time for themselves just before or during the first couple of days of their menses can improve their sense of well-being. This may include time for a bath and a cup of tea, journaling, a long walk or hike, curling up in bed with a good book, or any number of activities that an individual woman finds relaxing and replenishing to her spirit. Women often report that the time around their menses, is one of heightened intuitive perceptions. Women can be encouraged to record their thoughts, dreams, feelings, and so forth., in a journal designated for this purpose. Creating menstruation as a time of personal feminine power, and one that includes space for the woman to explore her creativity and experience replenishment and solitude can help reframe it from a negative to a positive experience, and this in itself may go a long way to improving menstrual problems. There are numerous books in the self-help and women's book market with ideas for celebrating menstruation, including celebrations of a girl's menarche to help her begin her menstrual journey with a healthy attitude and necessary knowledge and self-care skills.

Environmental Exposures

Forty years ago, biologist Rachel Carson, whose own life was lost to cancer, began the task of alerting the public to the serious and long-term risks of environmental contamination to biological organisms. This concern has continued to be reiterated by such scientists as Sandra Steingraber and Theo Colburn, who have written extensively on the subject of the environmental pollution on human health. Numerous chemicals have the ability to mimic estrogen (and likely other chemical messengers) in our bodies. They are part of a larger class of chemical called xenobiotics, many of which are endocrine disruptors. Because of the massive role of estrogen in women's reproductive physiology, women are highly susceptible to reproductive problems from endocrine disruptors. The DES tragedy is a striking example of the effects of endocrine disruption, which includes reproductive cancers, reproductive failure, and congenital deformities in children exposed during pregnancy.

Nothing short of massive industrial regulation and change in consumption patterns of modern society can turn the tide on this environmental and chemical tsunami. Even if production of all endocrine disruptors were to cease today, these chemicals are pernicious and persistent. They last indefinitely in the environment, and tend to sequester themselves in the fat tissue of living organisms. Breast milk is one of the most likely repositories for these toxins.

Women can do a great deal to minimize their exposure to endocrine disruptors. They are widely present in inorganic food sources and soft plastics. Eating organically is advisable. Dairy foods, because of their high fat content, much like breast milk, are also likely to be more highly contaminated, so it is best to consume only organic dairy products. Practitioners must advise patients about environmental safety issues and ideally, work to advocate for improved workplace and environmental conditions to reduce overall exposure.

Some concern has been raised that standard commercial menstrual products are contaminated with dioxin and/or other organochloride compounds that can lead to reproductive disease, most notably, cancers; asbestos, which is alleged to be included in these products to increase the amount of bleeding, requiring women to use more of the products; and rayon fibers that may cause toxic shock syndrome (TSS). There are numerous Internet articles dedicated to spreading warnings about this topic. The FDA has posted a response to this concern

in a paper, ''Tampons and Asbestos, Dioxin, & Toxic Shock Syndrome,'' segments of which are quoted below.

According to the FDA, no evidence of asbestos in tampons has been found nor have there been reports of increased bleeding from tampon use. The FDA states that before any tampon is marketed in the United States, FDA reviews its design and materials. Asbestos is not an ingredient in any US brand of tampon, nor is it associated with the fibers used in making tampons. Moreover, tampon manufacturing sites are subject to inspection by the FDA to assure that good manufacturing practices are being followed. Therefore, these inspections would likely identify any procedures that would expose tampons products to asbestos. If any tampon product were contaminated with asbestos, it would be as a result of tampering, which is a crime. Thus far, the FDA has received no reports of tampering. Anyone having knowledge of tampon tampering is urged to notify the FDA or a law enforcement officer.

On the topic of dioxin, the FDA states that:

> *State-of-the art testing of tampons and tampon materials that can detect even trace amounts of dioxin has shown that dioxin levels are at or below the detectable limit. FDA's risk assessment indicates that this exposure is many times less than normally present in the body from other environmental sources, so small that any risk of adverse health effects is considered negligible. A part per trillion is about the same as one teaspoon in a lake fifteen feet deep and a mile square. No risk to health would be expected from these trace amounts.*

This author finds this information less than reassuring given the limited amount that is known about endocrine disruptors, the very minute and nearly undetectable quantities required for a substance to act as an endocrine disruptor, and the very significant hazards from and persistence of dioxins in biological systems. The only acceptable exposure should be no exposure.

Tampons currently sold in the United States are made of cotton, rayon, or blends of rayon and cotton. Rayon is made from cellulose fibers derived from wood pulp. In this process, the wood pulp is bleached. At one time, bleaching wood pulp was a potential source of trace amounts of dioxin in tampons, but that bleaching method is no longer used. Rayon raw material used in US tampons is now produced using elemental chlorine-free or totally chlorine-free bleaching processes. Some elemental chlorine-free bleaching processes can theoretically generate dioxins at extremely low levels, and dioxins are occasionally detected in trace amounts in mill effluents and pulp. In practice, however, this method is considered to be dioxin free. Totally chlorine-free bleaching refers to use of bleaching agents that contain no chlorine. These methods are also dioxin free. Totally chlorine-free methods include, for example, use of hydrogen peroxide as the bleaching agent.

The Environmental Protection Agency (EPA) has worked with wood pulp producers to promote use of dioxin-free methods because dioxin is an environmental pollutant. Because of decades of pollution, dioxin can be found in the air, water, and ground. Therefore, whereas the methods used for manufacturing tampons today are considered to be dioxin-free processes, traces of dioxin may still be present in the cotton or wood pulp raw materials used to make tampons. Thus, there may be trace amounts of dioxin present from environmental sources in cotton, rayon, or rayon/cotton tampons.[34] Regarding rayon and TSS, the FDA states:

> *Although scientists have recognized an association between TSS and tampon use, the exact connection remains unclear. Research conducted by the CDC suggested that use of some high absorbency tampons increased the risk of TSS in menstruating women. A few specific tampon designs and high absorbency tampon materials were also found to have some association with increased risk of TSS. These products and materials are no longer used in tampons sold in the United States Tampons made with rayon do not appear to have a higher risk of TSS than cotton tampons of similar absorbency.*[34]

Many women, reasonably concerned about the risk of exposure to toxins in menstrual hygiene products, choose instead to purchase only disposable menstrual pads and tampons made from organic cotton and other organic fibers that are non–chlorine bleach manufactured. These offer the convenience of disposability and are more environmentally friendly than many of the larger commercial brands. Still, a smaller group of women prefer to use only washable cotton pads, menstrual sponges, and menstrual cups. Although less convenient than disposables, and possibly offensive to some women as they require handling of the menstrual blood, these are environmentally friendly choices. Careful cleaning of these products after use is essential to avoid risks of infection. In one study of colonization of microorganisms during menstruation among women using various menstrual products, cultures from those from users of sea sponges were found to have significantly higher colonization rates with *S. aureus, Escherichia coli*, and other *Enterobacteriaceae*. The association of sea sponges with a high rate of *S. aureus* colonization suggests that they are not an alternative to tampons for women seeking to decrease the risk of toxic shock syndrome.[35]

Menstruation and Lunar Cycles

Circatrigintan cycles refer to those cycles that occur in monthly rhythms. The most common of these are menstruation and the lunar cycle, which have historically been considered to correspond. The average menstrual cycle duration is 29.5 days; the lunar cycle is 28 days. Menstruation is referred to as ''the moon'' in any number of languages, from French to Mandingo.

There is anecdotal evidence that moonlight can help to synchronize the menstrual cycle. This author was able to identify only one clinical trial evaluating this phenomenon. A double-blind, prospective study during the fall of 1979 investigated the association between the menstrual cycles of 305 Brooklyn College undergraduates and their associates and the lunar cycles. All subjects were 19 to 35 years old and using neither oral contraceptives nor the IUD. Approximately one-third of the subjects had lunar period cycles (i.e., a mean cycle length of 29.5 ± 1 day). Almost two-thirds of the subjects started their October menstrual cycle in the light half of the lunar cycle, significantly more than would be expected by random

distribution. The author concluded that there is a lunar influence on ovulation.[36]

Natural treatment for infertility sometimes includes recommendations for having the woman adjust the lighting in her bedroom so that she is only exposed to the natural lighting from the moon, or that she mimic the cycle of the moon using lighting in her room to correspond with the moon's cycles as a way to synchronize ovulation and menstruation with the lunar cycles.

SUMMARY

Given the number of menstrual cycles a woman will experience in her lifetime, menstrual wellness and comfort are certainly desirable goals. Approaches to promoting menstrual wellness and reducing problems may include, for example, improving nutrition, ensuring enough exercise, and improving self-esteem and body image to reduce women's tendencies to overdiet and overexercise. Conversely, obesity needs to be addressed, as does its opposite, underweight, as both are associated with increased menstrual problems. Stress reduction, menstrual health education, and improving both women's individual and society's attitudes toward menstruation also may influence the psychological, physiologic, and endocrine factors that lead to menstrual dysregulation.

Environmental hazards predisposing not only to such problems as hormonal dysregulation and menstrual complaints but to serious and life-threatening conditions and reproductive disasters need to be addressed. The ancients linked the earth to women, Gaia representing both. The health of women may ultimately be linked to the health of our environment. Therefore, those concerned about women's health must necessarily also turn their attention to the health of our planet.

PUBERTY, MENARCHE, AND ADOLESCENCE

Aviva Romm

Puberty and adolescence have long been considered synonymous. They are, however, properly considered distinct entities with puberty defined as the sequence of physical, endocrine, and reproductive system changes that lead to the physical maturation of a girl into womanhood, and adolescence encompassing the psychological maturation that leads to readiness to assume adult responsibility.[37] Menarche is the onset of the first menstrual period.

The hypothalamic-pituitary-gonadal axis (HPG axis) is established in utero and is functional at a mature level prior to birth. The HPG axis becomes nearly dormant during early childhood (typically at 1 to 2 years of age) to be reawakened at the onset of puberty by a nocturnal pulsatile signal of luteinizing hormone (LH) that soon establishes a pulsatile pattern during the day as well. By an uncertain mechanism that may be associated with nutritional status in the female signaled by blood chemical information about carbohydrate or protein metabolism, there is a resurgence of not only LH but also GnRH (gonadotropin-releasing hormone) and FSH (follicle-stimulating hormone). GnRH causes morphologic changes in the ovarian follicles and a subsequent increase in estrogen production (steroidogenesis). A positive feedback system is created between estrogen and GnRH that persists until maturation is adequate to trigger ovulation, and eventually, when sexual maturation is complete, the ovary assumes the role that the HPG axis has played in the regulation of hormonal secretion and feedback.

Puberty is classically divided into four distinct stages associated with landmarks in sexual development: (1) growth spurt, (2) thelarche, (3) adrenarche, and (4) menarche that in total extend over a period of approximately 4.5 years. It is triggered largely by genetics but also appears to be influenced by geography, level of light exposure, nutritional status, general health, and psychological factors.[38] Body weight may be a significant factor in the onset of puberty, with girls who weigh more exhibiting earlier signs.

Beginning between the ages of 9 and 13 years (mean age 11.2 years), and as early as 8 years in girls of black/African descent, marking the earliest onset of pubertal changes, girls begin to experience a growth spurt that will typically persist for the duration of puberty and slightly beyond. Other than in infancy, this is the most significant episode of physical growth a female will experience in her lifetime, with girls growing approximately 6 to 12.5 cm (2.5 to 5 inches) in height and gaining 3.5 to 4.5 kg (8 to 20 pounds) during this time. In addition to increased height, bone density increases (in the presence of optimal nutrition, significant for the long-term prevention of osteoporosis), internal organ size increases, and most dramatically, there is an overall increased deposition of fat with the percent of body fat increasing from 15.7% to 26.7%. HGH (human growth hormone), released by the pituitary gland, is instrumental in this pubertal growth spurt, whereas IGFs (insulin-like growth factors) play an important role in the deposition of fat, thus leading to an increasingly mature female shape (i.e., hip and breast development). By just over age 17, at least 50% of women have achieved full adult height, but the velocity of the growth spurt significantly decreases after the menarche. Full development is nearly always achieved by age 21.

About a year after the growth spurt begins, breast development becomes evident. Female breast development is a result of increased fat deposition and branching of the ductile system stimulated by increased estrogen secretion. Breast development represents the onset of maturation of secondary sex characteristics. Breast growth in puberty begins with breast budding. During this time, a small amount of glandular tissue develops, there is breast enlargement, increased deposition of fat in the breast tissue. Eventually there is elevation of the areola and the nipple. Finally, after approximately 3 to 3.5 years, breast maturation leads to an adult breast contour with protrusion of the nipple from the areola, and a flat continuity between the areola and the breast tissue.

Adrenarche, the development of pubic hair, occurs prior to or concomitantly with thelarche, although in 20% of girls it precedes breast development. Initial hair growth is only slightly pigmented, sparse and fine, appearing on the labia majora. With maturation, the volume of hair growth increases and spreads to cover

the mons pubis. The hair becomes more darkly pigmented, coarser, and less straight. After approximately 2 years, at which time axillary hair growth begins, the genital pubic hair achieves its characteristic curly appearance and is distributed triangularly with a horizontal border at the level of the pubic bone. Androgens are primarily responsible for hair growth. During these stages, vaginal acidity is increasing and there is an increase in the number of normal vaginal flora.

Menarche, the onset of menstruation, is the final stage in the process of puberty, and occurs at a mean age in the United States of 12.2 years for black Americans and 12.8 years for white Americans. Menarche typically occurs 1 to 3 years after the onset of breast development. Initial menstrual cycles are anovulatory, with anovulatory periods lasting from 12 to 18 months. Fifty percent of girls with early onset of menarche typically have established ovulatory cycles after 1 year, whereas girls with late onset ovulation often take 8 to 12 years for all cycles to become ovulatory.[39] Menstrual cycles are typically variable for the first 2 to 3 years after menarche, but most cycles range from 21 to 45 days even in the first year of menstruation. Occasionally, cycles may be shorter or longer than this with no pathology. Menstrual bleeding generally lasts for 2 to 7 days. The individual's own pattern of normal cycles is typically established by the sixth gynecologic year.[39] The time leading up to menarche and the pubertal years is typically marked by varying levels emotional lability and behavioral changes, including ''euphoria, depression, mood swings with paradoxical and hysterical reactions, crying with ease, and a negative attitude toward school.''[40] Emotional and behavioral challenges usually taper off once the process of sexual maturation is completed and hormonal regulation is achieved.

SIGNIFICANCE OF AGE AT MENARCHE AND PATTERNS OF EARLY MENSTRUAL CYCLES ON LONG-TERM HEALTH

There has been media attention and concern given to the fact that girls appear to be entering puberty at earlier ages than historically. In fact, there is some disagreement in the literature as to whether this is the case. One author states that in white American females, the mean age of menarche has not changed in 50 years, although the author admits that population studies may obscure the actual rates, whereas others state that evidence from the United States points to a decline in the mean age of menarche from 14.7 years at the turn of the century to age 12.8 at the end of the twentieth century.[39,41] These latter data are allegedly corroborated by European data that demonstrate a decline in age of menarche of 3 months per decade over the past 150 years.[41] All authors agree that earlier menarche is noted in girls living in urban environments and relate this to heavier than average weight compared with cohorts in rural areas. Increased rates of obesity and exogenous estrogens may indeed play a significant role in the early onset of menarche, and in addition to the risks associated with being overweight, may have implications for increased adult rates of breast cancer development. In fact, early age at menarche (<12 years) is a recognized risk for breast cancer, with risk declining by 10% for each year after that in which menarche is delayed.[41] This is primarily thought to be associated with greater cumulative exposure to estrogen and progesterone, especially estradiol. This risk may be reduced by the fact that girls who begin menstruating earlier are more likely to experience adolescent childbearing.

Conversely, girls with higher estrogen levels may be less predisposed to osteoporosis owing to increased bone density accumulation in the pubertal period, as evidenced by lower rates of osteoporosis among black women compared with white women. Adolescent girls with suppressed estrogen levels should be carefully monitored for bone density and optimally all girls should consume high-calcium diets or take calcium supplements particularly in the few years after menarche when bone density accumulation is as great as 10% to 20% and ensures as much as 10 to 20 years of protection against age-related bone mass loss.[38]

Age at menarche may be an indicator of nutritional status. Poor nutritional status or excessively low body fat percentage can lead to delayed menarche and may be a result of socioeconomic status, excessive exercise or athletic activity, or an eating disorder such as anorexia nervosa or bulimia. Vegetarian diet or low fat or carbohydrate (energy) intake also may lead to delayed menses. Unlike malnourished girls, girls with later-onset menses with adequate nutrition do not necessarily achieve demonstrably lower height by adulthood than girls with earlier-onset menstruation; however, compromised nutritional status requires social and medical attention. The fact that skeletal growth is still occurring throughout the teenage years underscores the importance of good nutrition. Girls with eating disorders are at risk for numerous medical complications and require counseling and intervention. It should be remembered that overeating leading to obesity is the most common malnutrition problem among adolescents in the United States and has been increasing in epidemic proportions. Girls with eating disorders critically need help with understanding how to nourish their bodies, but also need support in establishing positive body images and self-esteem. Adolescent pregnancy can also have a dramatic and deleterious impact on growth and development, and if adolescent pregnancy is accompanied by being overweight it can predispose the girl to problems with weight and diabetes later in life owing to alterations in growth hormone and insulin patterns. Health professionals counseling girls about their menstrual cycles have a tremendous opportunity to also counsel girls about nutrition, sexuality, lifestyle management, and a wide array of psychosocial issues that can impact their lives and long-term health.

TALKING WITH GIRLS ABOUT MENSTRUAL HEALTH AND HYGIENE

Although our culture has certainly become more open about menstruation, with overt menstrual product advertisement or mention of PMS commonplace, many girls are still reticent when discussing the topic. Girls may be generally ignorant about what is happening to their bodies, and even the more knowledgeable girls may be

uncertain about such things as maintaining menstrual health and hygiene.

Learning to chart her menstrual cycles can be an important first step in a girl's increased self-awareness and is also an important way to keep track of whether the cycles are regular and normal. Although cycles may be irregular for the first few years after menarche, this does not mean that all irregularity is normal or healthy. Even within patterns of irregularity, most menstrual cycles will range from 21 to 45 days with deviations of slightly higher or lower than this on occasion. Most periods will last from 3 to 7 days. Wildly irregular cycles, excessively heavy periods, or oligomenorrhea can be indicative of serious health problems requiring further attention, including: polycystic ovarian syndrome (PCOS), thyroid disease, Cushing's disease, diabetes mellitus, premature ovarian failure, eating-disorder or exercise-induced amenorrhea, congenital adrenal hyperplasia, adrenal or ovarian tumors or prolactinomas, or other endocrine problems. Providing girls with calendars for recording their menstrual cycles, and instructing them on how to do this, including recording the days they are menstruating (Day 1 is considered the first day of the period and counting extends to the last day before the next period, whereupon the cycle starts again with Day 1), symptoms they might have prior to during or after menstruation (e.g., mood alterations, headaches, fatigue), and for how long the bleeding lasts and the amount of flow that is considered normal can provide them with information about themselves and is a fantastic and important gynecologic record.

A blood loss of 30 mL per cycle is considered normal, with a loss of greater than 80 mL considered abnormal, putting a girl at risk for anemia. However, there is little value in milliliter measurement as this is virtually impossible to calculate. More useful is keeping track of the number of menstrual pads changed daily and their level of saturation. Typically, a girl can expect to change her pad three to six times per day. If the pad is oversaturated, she might not be changing pads frequently enough, the pads may be of the wrong size or fit, or they may be slipping in her underwear. If after ruling out these factors, there is concern over excessive menstrual flow, evaluate further. Educating the girl about proper use of pads, how often to change them, and also about the different types of available products (e.g., tampons) and their use can help a girl to be more comfortable during her menses and also prevent the embarrassment that could come from overflowing a pad. Many girls, especially athletes, are curious about the use of tampons. This is an area in which education is particularly important. Although all tampons must now meet FDA regulatory limits on absorbency, 50% of all reported cases of TSS still occur in menstruating women. Current US FDA recommendations state that tampons should not be worn for 24 hours a day nor 7 days a week, and should be alternated with the use of pads.[39] Tampons should be changed at least every 4 to 8 hours; it is preferable to sleep with a pad rather than a tampon, and the last tampon at the end of menses must be remembered—it is relatively common for a girl or women to forget to remove a tampon at the end of the period. TSS should be treated as an acute medical emergency.

Encouraging girls to use the increasingly available selection of disposable menstrual hygiene products—both pads and tampons—that are made from organic cotton, encourages the use of more environmentally friendly products. Most major health food stores carry a selection of good alternatives to conventional commercial products.

MENSTRUAL IRREGULARITIES AND DIFFICULTIES IN THE ADOLESCENT FEMALE

Adolescent girls, like women, commonly experience menstrual complaints, the most common for girls being dysmenorrhea, mood changes, and acne. Irregular or abnormal bleeding, particularly menorrhagia or amenorrhea, also may occur, and should be evaluated medically if persistent. Each of these complaints is addressed separately throughout this book. Additionally, a specific overview of these complaints in relationship to the special considerations of adolescent girls and the use of botanicals with adolescents is presented in the following. In order to avoid redundancy, only a brief discussion of the botanicals is provided in this section. More detailed herbal information is provided further in this chapter and throughout the text.

EMOTIONAL AND PSYCHOLOGICAL CHALLENGES IN ADOLESCENCE

Adolescence is a challenging and confusing time for even the most stable of girls. Hormonal changes and fluctuations, physical changes leading to the sexualization of the body combined with confusing cultural messages about the role of the adolescent and sex, increasing pressures at school and the challenges of teen friendships, and problems at home (stress with parents, birth of a sibling, trouble with a sibling, parents experiencing marital discord or divorce, financial troubles, moving to a new location/home/school, death of an elderly relative such as a grandparent, or personal illness) can lead to enormous internal turbulence. It is critically important for girls at this age to have women confidants they can turn to for security, advice, reassurance, and accurate information. An anchor in the storm may be the best thing a teenage girl can have to help her stay healthy and focused on self-development rather than getting side-tracked by the many distractions available to adolescents. And this anchor needs to be available as early into puberty as possible-access to drugs and sexual experience starts in middle school for many US children. Health care providers can also provide an anchor for adolescent girls. One study, conducted in the late 1980s, looked at the major topics that teenagers wanted to discuss with their physicians. The top concerns expressed were: sexually transmitted diseases, birth control, fear of cancer, self-image, self-confidence, sexual function, and sexual abuse, yet most doctors were found only to discuss the topic of menstruation.[39]

By charting their cycles, girls can begin to identify patterns in their mood fluctuations and how they are associated with their menstrual cycle. This can help them

to recognize their emotions as cyclical changes related to hormones and not something inherently wrong with them. Teaching girls the value of good nutrition, particularly adequate protein and healthy carbohydrates combined with a good vitamin and mineral supplement, to keep sugar and caffeine consumption to a minimum, and to keep the blood sugar stable can reduce mood swings and show them that they have some control over their emotional lives. Adequate sleep (teenagers may require as much as 12 hours per day!) and moderate exercise are also important for keeping emotions level and can also support cognitive function. Journaling can be a useful tool for self-expression and may help girls to both record and vent some of the challenging emotions they feel and situations they face as they emerge into women. Finally, if emotional or behavioral conflicts are significant, girls may benefit from or require counseling, as might the family constellation. A healthy home life is an important stabilizing force as young girls emerge into women and sort through their own identity, personal and social roles, relationships, and responsibilities.

HERBS AND ADOLESCENT GIRLS: SAFE USE VERSUS WRONGFUL ADVERTISING

In 2000, a national advertising campaign was launched for an herbal product called Bloussant® Breast Enhancement Tablets. The fall 2001 issue of *Teen Vogue* and the September 2001 issue of *Seventeen* ran full and quarter-page ads, respectively, for this product. These advertisements feed into the already prevalent idea that bigger breast size is better that led nearly 4,000 females 18 and younger to have breast augmentation surgery in the year 2000 alone (representing 2% of all such surgeries that year), a 425% increase over 1997 rates. This represents a growing trend of misuse of herbal products by teenagers.[42] Marketing of herbal products to teens has become increasingly popular, and teens are receptive to this marketing, many of them believing that natural means safer.[43] In fact, the prevalence of use as determined by limited population surveys appears to mirror that of national use by adults with nearly have of all teens surveyed reporting CAM use, with the use of herbal products at approximately 12%.[43–45] Teens primarily appear to base their use on perceived parental or friend use, and primarily appear to use herbs without parental knowledge.[45] Many are concurrently using other pharmacologically active substances, including medications, other herbal products, or recreational drugs or alcohol. Common conditions for which teens use herbal products include PMS, urinary tract infections (UTIs), obesity, pregnancy, and enhancement of athletic performance or stamina. Adolescent girls are more likely than boys to seek health care, including CAM therapies, although the rate of supplement use is higher for adolescent male athletes than their female athletic counterparts (29% vs. 12%).[43]

Because little to no clinical research has been done on the safety of botanical medicines in the distinct population of adolescent females, extra care should be taken during this period of rapid growth and development and hormonal change. Further, the combined use of herbs and pharmaceutical drugs, not to mention recreational use of pharmaceutical or ''natural'' drugs is also largely unstudied, and may be an area in which teenagers either experiment or unknowingly use potentially harmful combinations. Teens may therefore be at additional risk compared with the adult population when using herbal remedies. Much like with young children or pregnant and lactating women, additional precautions should be taken to minimize the use of botanical therapies that might inappropriately affect the endocrine system during this developmental stage. Adolescents should be educated and cautioned about the use of products such as those for breast augmentation and athletic enhancement, and should be advised about the hazards of using such herbs as ephedra or other stimulant herbs for athletic performance or weight loss. Finally, adolescents should be encouraged to seek the help of a qualified herbal practitioner when choosing to use herbs for the treatment of health problems, and should be told to inform their primary care provider of the use of any herbal products, particularly if being prescribed a pharmaceutical drug or medical treatment. Adolescents should be informed that natural does not mean safe and that there are potential hazards associated with the use of herbal products. Practitioners should not make the broad assumption that herbs that are safe for adult women are always and entirely safe for adolescent girls, and considering the unknowns of herbs for this population; short-term therapies (i.e., for 3 months or less followed by a rest) may be preferable to using herbs for long courses of treatment. More research in this area is warranted.

COMMON PROBLEMS OF PUBERTY AND MENSTRUATION IN ADOLESCENT FEMALES AND THEIR BOTANICAL TREATMENTS

Mood Changes

The Botanical Practitioner's Perspective

Mood swings are common among adolescent girls and may be particularly prevalent in the week or days just prior to the onset of menstruation, not dissimilarly to PMS, or they may occur more frequently and unpredictably than monthly or cyclically. Frequently, girls start exhibiting mood swings as early as age 11, which many parents assume to simply be a behavioral problem rather than recognizing the beginning of hormonally mediated mood changes. Mood swings may be extreme, ranging from hysteria to euphoria in a matter of moments. Dramatic behavior is not uncommon. Girls also may find that their cognitive functioning is not as sharp, especially just prior to menstruation, making it more difficult to concentrate and perform in school, especially in the more linear subjects such as science and mathematics. Tests in school just prior to menstruation may be especially challenging for some girls. These emotional and cognitive changes are typically the result not only of hormonal influences but also of dietary inadequacies and sleep deficiency so common to adolescence. Declining blood sugar associated with hormonal changes along with inadequate consumption of high-quality protein

and carbohydrates and an over-reliance on simple sugar for energy can lead to marked decline in mood and concentration. Inadequate rest as a result of staying up late at night and getting up early for school can exacerbate poor mood or concentration problems (also see Premenstrual Syndrome).

Adolescent girls are also subject to hormonal dysregulation that can lead to irritability, depression, and anxiety as frequently occurs with PMS. This period of time can be trying for parents and is difficult for the girl herself, who may be unhappy and feel out of control. Therefore, a great deal of support, encouragement, and reassurance may be needed as part of the health consultation. Conventional treatment relies on medication—either to regulate hormones, regulate mood (e.g., birth control pills, antidepressants) or both. In some cases medication may be appropriate, but counseling, lifestyle support, and appropriate nutritional and herbal supplements are preferable first line approaches when possible versus starting an adolescent on a course of hormonal or psychiatric drugs, whose long-term effects in the adolescent population are also frequently not well studied or understood. If depression is severe or thoughts or fears of suicide have been expressed, psychological counseling and medical intervention are essential. See Table 5-1 for a summary of mood changing herbs.

Discussion of Botanical Protocol

A number of herbs can be used to calm and nourish the nervous system. The gentlest of those that are used for promoting short- and long-term relaxation with a high safety profile when used in correct dosages include chamomile (Fig. 5-1), passion flower, and lavender, all of which are mild and nonaddictive. Ashwagandha is used over time as a tonic for the nervous system, and may exhibit beneficial effects on immunity, hemoglobin levels, and may have uterine antispasmodic activity as well, making it particularly beneficial when there is also dysmenorrhea.[46–49] For significant irritability and emotional lability many herbalists include the herbs motherwort or blue vervain in formulas. These bitter nervine herbs are applied in much the same principle as herbs for liver qi stagnation are applied in TCM with the understanding that herbs that improve the smooth functioning of the liver (possibly through liver detoxification mechanisms) have a regulatory effect on the female endocrine system. St. John's wort is included when depression is a component of the emotional picture.[50] Additionally, bacopa, reputed for its ability to enhance cognitive function and retain newly learned information, is used to improve concentration while dong quai is used in formulas, when there is anemia.[49] Vitex is used when there is emotional lability associated with the menstrual cycle, particularly when there is also menstrual cycle irregularity.[46] It has a high safety profile, with no contraindications reported in the German Commission E Monographs, although it is generally considered contraindicated for use during pregnancy. Bohnert considers simultaneous use with hormone therapy and oral contraceptives to be contraindicated.[46–48,51] In rare cases, short-term use of Vitex has been seen clinically to worsen depression; if this is observed discontinue its use immediately (Box 5-2).

Additional Therapies

Nutritional supplementation can play a pivotal role in the improvement of mood and cognitive function. In addition to taking a high-quality vitamin and mineral

TABLE **5-1**

Summary of Herbs Used for Adolescent Mood Changes

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Promote relaxation; decrease emotional and psychological stress	Nervines	*Hypericum perforatum*	St. John's Wort
		Matricaria recutita	Chamomile
		Passiflora incarnata	Passion flower
		Lavendula officinalis	Lavender
		Leonurus cardiaca	Motherwort
		Verbena officinalis	Blue vervain
Support healthy HPA axis function	Adaptogens	*Bacopa moniera*	Bacopa
		Eleutherococcus senticosus	Eleuthero
		Panax quinquefolium	American ginseng
		Schizandra chinensis	Schizandra
		Withania somnifera	Ashwagandha
Improve hormonal regulation	Hormonal regulators; hepatic tonics	*Paeonia lateriflora*	Peony
		Taraxacum officinale	Dandelion
		Vitex agnus castus	Chaste berry
Improve nutritional status; nourish the blood; treat anemia	''Blood tonics''	*Angelica sinensis*	Dong quai
		Urtica dioica	Nettles
		Withania somnifera	Ashwagandha

Figure 5-1 Chamomile (*Matricaria recutita*). (Photo by Martin Wall.)

supplement (an adult dosage can be taken by girls 14 and over; younger girls can take a supplement designed for adolescents), adolescent girls can benefit from a high-quality essential fatty acid supplement containing both omega-3 and omega-6 fatty acids. The best supplements contain a combination of both plant-based essential fatty acids (derived from evening primrose oil or borage oil) and cold water fish oil. Standard daily supplementation can improve mood and mental function, and can be helpful when skin problems are present (see Acne). Additionally, teenage girls who are menstruating need an adequate regular intake of dietary iron. If the diet is poor or there is heavy menstrual bleeding, dietary iron should be supplemented. Floradix® Iron and Herbs is an excellent and highly absorbable, nonconstipating iron supplement derived primarily from plant sources. It can be taken daily. Attention should be paid to adequate rest and opportunities for self-expression (journaling, art work) and physical activity to release tension (martial arts, running, swimming, boxing, yoga) (Box 5-3).

Dysmenorrhea in Adolescent Girls

Cramping, and lower abdominal pain associated with the onset of menstruation, are the most common complaints of adolescent girls leading to missed days at school and self-medication with over-the-counter pain relievers and

BOX 5-2

Botanical Prescription for Adolescent Mood Changes

A typical protocol for when there is slight menstrual irregularity, irritability, and emotional lability is as follows:

- Give *Vitex agnus castus* (chaste tree) 5 mL once daily (usually given in the morning).
- Also give the following formula:

Chamomile	*(Matricaria recutita)*	25 mL
Ashwagandha	*(Withania somnifera)*	25 mL
Passion flower	*(Passiflora incarnata)*	25 mL
Motherwort	*(Leonurus cardiaca)*	20 mL
Lavender	*(Lavendula officinalis)*	5 mL
		Total: 100 mL

Dose: 5 mL twice daily or 2.5 mL as needed throughout the day not to exceed six doses.

If there is poor concentration or memory difficulty, take 5 mL *Bacopa moniera* (Bacopa) 1:1 one time daily or two 2.5-mL doses.

BOX 5-3

Treatment Summary for Adolescent Mood Changes

- Calm and nourish the nervous system with herbal nervines including skullcap, chamomile, lemon balm, St.John's Wort, milky oats, passion flower.
- Treat depression: herbal antidepressants, appropriate nutrition, exercise, and counseling.
- Relieve stress and support adrenal function with adaptogens.
- Improve hormonal regulation through botanicals with endocrine effects and through improved liver function and bowel elimination (when there is hyperestrogenism).
- Enhance cognitive function and improve concentration with botanical agents and nutrition.
- Maintain stable blood sugar, mood, and cognitive function with adequate protein and complex carbohydrates.
- Include a high-quality essential fatty acid supplement containing both omega-3 and omega-6 fatty acids to improve mood, mental function, and skin problems.
- Supplement dietary iron.
- Encourage adequate rest.
- Provide opportunities for self-expression (journaling, art work) and physical activity to release tension (martial arts, running, swimming, boxing, yoga).
- Provide psychological counseling and medical intervention when necessary.

anti-inflammatory drugs and herbal products. In adolescents dysmenorrhea is generally nonpathologic and coincides with ovulatory menstruation, as progesterone secretion from the ovary is associated with uterine muscle contractility. It may coincide with or occur independently of PMS. Severe dysmenorrhea should be evaluated, particularly in sexually active girls, to rule out endometriosis, pelvic infection, or other problems (also see Dysmenorrhea).

Conventional Treatment Approaches

Medical treatment for nonpathologic dysmenorrhea is generally medication for the symptomatic relief of discomfort.

The Botanical Practitioner's Perspective

Botanical medicines have a long history of use for the symptomatic treatment of dysmenorrhea and can be used as needed just prior to the onset of the expected cramping (1 or 2 days prior to menstruation) and through the first day or two of menstruation, after which cramping usually ceases on its own. Practitioners also often suggest the use of anti-inflammatory herbs and dietary strategies to help reduce the inflammatory processes caused by increased prostaglandin production sometimes associated with menstrual cramps. Finally, herbalists may recommend herbs that help to stimulate pelvic circulation and relieve pelvic congestion in order to reduce ischemia and related pain.

Botanical Protocol

See Table 5-2.

Discussion of Botanical Protocol

Cramp bark and black haw can be used interchangeably as single herbs for the symptomatic relief of uterine cramps.[52,53] Ginger is an antiinflammatory herb and traditionally used by herbalists for improving pelvic circulation.[46,54–56] It may be combined in tincture with other herbs or used alone beginning a few days before the expected menses and continued as needed. Dong quai also has demonstrated uterine antispasmodic activity.[49,50] Excessive use of either ginger or dong quai may increase uterine bleeding; their use should be avoided if there is menorrhagia. Evening primrose oil is taken in capsules up to 1500 mg per day throughout the month or beginning in mid-cycle through the beginning of the menses. When there is significant cramping, peony, an excellent uterine antispasmodic, and motherwort might be added to the formula, the latter as uterine tonic and nervine antispasmodic (Box 5-4).[49]

Additional Therapies

Increased arachidonic acid production is associated with increased inflammation and menstrual cramps. Reduction of red meat and dairy products in the diet may reduce the severity and frequency of menstrual cramps. Alternative sources of protein and calcium should be included in the diet to ensure adequate nutrition. Increased consumption of cold water fish such as

BOX 5-4

Botanical Prescription for Adolescent Dysmenorrhea

A typical formula for an adolescent with dysmenorrhea is as follows:

Cramp bark	(*Viburnum opulus*)	55 mL
Chamomile	(*Matricaria recutita*)	15 mL
Motherwort	(*Leonurus cardiaca*)	15 mL
Ginger	(*Zingiber officiniale*)	15 mL
		Total: 100 mL

Dose: 2 mL repeated as needed up to every 20 minutes for 2 hours, or 2.5 mL up to one dose every 2 hours prior to and through the onset of menses.
Also: Evening Primrose Oil Capsules: 1000 mg daily
Tea of chamomile or fresh ginger daily, as needed
Externally: Hot ginger fomentation over the uterus.

TABLE 5-2

Summary of Herbs Used for Adolescent Dysmenorrhea

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Relieve uterine cramps	Antispasmodics	*Actaea racemosa*	Black cohosh*
	Anti-inflammatories	*Dioscorea villosa*	Wild yam
		Leonurus cardiaca	Motherwort
		Matricaria recutita	Chamomile
		Viburnum spp.	Cramp bark, black haw
		Zingiber officiniale	Ginger
Improve pelvic circulation		*Angelica sinensis*	Dong quai
		Leonurus cardiaca	Motherwort
		Paeonia lateriflora	Peony
		Zingiber officiniale	Ginger

*Recently concerns have been raised over hepatoxicity associated with black cohosh.
See Plant Profiles: Black cohosh for a discussion of safety concerns.

salmon and supplementation with high-quality fish oil (often combined with evening primrose or borage oil) also may help in the reduction of inflammation and menstrual cramps. Supplementation with magnesium was demonstrated in an open study to help improve uterine muscle activity and reduce symptoms.[53] Regular exercise with the addition of yoga poses for promoting pelvic circulation may be helpful. Abdominal massage, hot packs or ginger fomentations, and the use of hot baths with relaxing essential oils such as lavender, rose, and sandalwood can provide comfort and temporary symptomatic of menstrual cramps (Box 5-5).

Menorrhagia in Adolescent Girls

The primary cause of menorrhagia, or excessive menstrual bleeding ranging from heavy periods to hemorrhage, with durations of several days to several weeks, in adolescent girls is anovulatory cycles owing to hyperproliferation of the uterine endometrium in the absence of adequate progesterone. Menorrhagia can lead to acute and chronic anemia, weakness, fatigue, and anxiety. Rarely menorrhagia can be caused by an uncommon congenital blood disorder called von Willebrand's disease (also see Dysfunctional Uterine Bleeding).

Conventional Treatment Approaches

Acute treatment involves stabilization of bleeding, treatment of acute blood loss, and treatment of anemia. Treatment also includes use of hormone therapy to stabilize estrogen levels and provide progesterone to stabilize the endometrium.

BOX 5-5

Treatment Summary for Dysmenorrhea in Adolescent Girls

- Use botanical antispasmodics to reduce uterine cramping and pain: cramp bark, black haw, black cohosh, wild yam
- Use anti-inflammatory herbs and dietary strategies to help reduce the inflammatory processes caused by increased prostaglandin production: ginger, evening primrose oil
- Use botanicals to stimulate pelvic circulation and relieve pelvic congestion in order to reduce ischemia and related pain: peony, motherwort, dong quai
- Reduce arachidonic acid production through an anti-inflammatory diet, (For example, reduction of red meat and dairy product consumption)
- Increase consumption of cold water fish such as salmon and supplement with a high-quality fish oil (often combined with evening primrose or borage oil) to reduce inflammation and menstrual cramps
- Supplement with magnesium
- Exercise regularly, especially yoga poses for promoting pelvic circulation
- Use abdominal massage, hot packs, or ginger fomentations
- Take hot baths with relaxing essential oils such as lavender, rose, and sandalwood

The Botanical Practitioner's Perspective

Ovulatory cycles may be stimulated with regular use of *Vitex agnus castus*, 5 mL once daily. Elevated PGEs may also lead to increased bleeding owing to reduced clotting and increased dilation of the blood vessels. Acute episodes of mild to moderate excessive bleeding may be controlled with uterine hemostatic herbs; significant excessive bleeding and hemorrhage requires medical intervention.

Botanical Protocol

Herbs may be used as hemostatics, progesterone production enhancers, and antiinflammatories in the reduction of PGE2. Vitex is one of the primary herbs to be considered for stimulating the ovary and encouraging ovulation, thus increasing progesterone secretion. It should be given in a 3 mL daily dose of a 1:3 extract.

Additional Therapies

As with dysmenorrhea, the addition of fish oils supplements may help in the reduction of menorrhagia.

Additionally, vitamin A deficiency has been found to be an important factor associated with menorrhagia. Vitamin A is a cofactor of 3 beta-dehydrogenase in steroidogenesis and deficiencies of this vitamin may result in impaired enzyme activity. The level of endogenous 17 beta-estradiol appears to be elevated with vitamin A therapy, and in one study, menorrhagia was alleviated in more than 92% of patients.[57] Iron supplementation is essential because menorrhagia is regularly associated with anemia (Box 5-6).

Amenorrhea in Adolescent Girls

Adolescent girls may experience either primary or secondary amenorrhea. Primary amenorrhea is the lack of

BOX 5-6

Treatment Summary for Menorrhagia in Adolescents

- Use uterine hemostatic herbs to control acute bleeding.
- Use *Vitex agnus castus* daily for 3 months to stimulate ovulation in anovulatory cycles.
- Treat anemia with botanical agents and nutritional supplements.
- Vitamin A deficiency has been found to be an important factor associated with menorrhagia; vitamin A supplementation* may be effective in preventing excessive bleeding in some women. Some fish oil products contain substantial vitamin A and may be adequate for supplementation.

*Vitamin A is tetrogenic and should not be taken as a supplement if pregnancy is suspected.

menses by age 16; secondary amenorrhea is cessation of menses for three cycles or 6 months in girls or women who have previously menstruated. Primary amenorrhea is specific to adolescent girls and has a broad range of possible causes requiring medical consultation.

Acne

Acne, often dismissed by the medical community as simply a consequence of adolescence, is actually the most common dermatologic condition, affecting at least 85% of all adolescents.[58] It not only has the potential to cause permanent physical scarring but may have a significant effect on psychoemotional and social well-being and quality of life. Acne in adolescents and adult women is addressed in the next section.

ACNE VULGARIS

Aviva Romm

Acne vulgaris, acne, is a common and chronic skin condition affecting the pilosebaceous unit. It affects 80% of people in the United States at some point in life, and at any given time in the United States affects an estimated 17 million people.[59] It is the most common dermatologic condition seen in clinical practice leading to more dermatologic visits than any other skin condition, and leading to absenteeism at school and work and to millions of dollars in annual treatment costs.[60–62] At least 85% of adolescents and young adults are affected by acne. Not only does severe acne potentially cause permanent physical scarring, it has a significant psychosocial impact on the sufferer, sometimes dramatically reducing quality of life, particularly, but not exclusively, in adolescent girls, where it can have a marked influence on self-esteem and lead to embarrassment, anger, anxiety, and depression.[63–66] Previously considered a condition of adolescence, it is now widely recognized to be a problem that can persist chronically or cyclically well into a woman's fourth decade of life.[67,68]

PATHOPHYSIOLOGY

The pilosebaceous unit consists of a hair follicle and its associated sebaceous gland. Acne is caused by the following constellation of four pathogenic factors at the pilosebaceous unit:

- Androgens act upon the sebaceous gland causing increased sebum production.
- Impaired desquamation of the follicle leads to plugged pores and an abnormal pattern of follicular hyperkeratinization.
- Increased sebum supports the proliferation of bacteria, most commonly *Propionibacterium acnes*.
- Release of inflammatory mediators by *P. acnes* into the follicle and surrounding dermal tissue.[69–71]

During adolescence androgen levels increase, explaining the prevalence of acne during this time. However, elevated androgen levels are not always a finding; in 60% of women with acne, serum androgen levels are normal but there is significantly elevated 5α-reductase at the sebaceous gland, indicating a heightened sensitivity to androgen. This also may explain the persistent or recurrent acne that might occur well into a woman's forties.[72] Increased 5α-reductase results in higher rates of conversion of androgens, specifically conversion of testosterone into its active metabolite dihydrotestosterone.[73] There is clearly an association between acne and menstruation with a premenstrual flare noted as common among 3394 women who completed a survey on the prevalence of acne in females in France.[74] Emotional stresses have also been demonstrated to increase acne outbreaks. Additionally, hyperandrogenic conditions including polycystic ovarian syndrome (PCOS), 21-hydroxylase deficiency, adrenal androgen excess, and some medications (e.g., steroids) are clearly implicated causes of acne.[70,72,73,75–77] *P. acnes* converts sebum to free fatty acids and individuals who are hypersensitive to these free fatty acids may experience the more uncommon forms of severe nodular acne.[73] Hyperinsulinemia also may play a role in the etiology of acne, evidenced by the increased glucose levels at the sebaceous gland of those with acne, and the prevalence of acne and PCOS in those with hyperinsulinemia, although a causal association is not conclusive.

SIGNS AND SYMPTOMS OF ACNE

The characteristic clinical manifestations of *acne vulgaris* are the appearance of comedones (''blackheads'') or pustules (''whiteheads'') typically appearing on the face, back, chest, and upper arms, the distribution of outbreaks making it among the most visible of dermatologic complaints. Inflammation may or may not be considerable. Diagnosis of hyperandrogenic and hyperinsulinemic states is essential to proper treatment. (See Polycystic Ovarian Syndrome.)

DIAGNOSIS

A diagnosis of acne is made upon visual inspection and exclusion of other causes. Acne may be dismissed as an unimportant consequence of adolescence or cyclic hormonal fluctuation; however, this may a gross underestimation of the significance of the problem.[63] In a 1994 study conducted by the AMA, 89% of adolescent girls reported worrying about their complexion and 50% believed it was the first thing people noticed about them.[78] Therefore, quick diagnosis and treatment from the time of onset of acne is important, particularly in the adolescent population when it tends to be the most severe and has the greatest social impact. Conventional therapy also calls for dermatologists to be adept at recognizing and treating resultant psychiatric disturbances in patients with acne.[61] Furthermore, the appearance of acne may be indicative of more serious problems, such as PCOS, which predisposes to obesity, diabetes, and cardiovascular problems.[77]

CONVENTIONAL TREATMENT

Acne vulgaris is not considered a curable disease by conventional medicine; however, symptoms are frequently well controlled and scarring prevented by a combination of systemic (internal) and topical therapies, with patients typically prescribed a combination of therapies

as suggested by the causes and severity of the case.[60,79,80] Effective treatments are aimed at treating the four pathogenic factors mentioned in the preceding. Combination therapies are considered to be the most effective.[60] However, in mild cases, topical treatment sometimes may be adequate.[81]

Oral Contraceptives

Oral contraceptives have demonstrable effects in improving hormonally mediated acne, however, women are often concerned about their side effects. Additionally, teenage girls may be concerned about social perceptions related to their use of OCs, including disapproval or misunderstanding of the reasons for the medication.[66] In addition to oral contraceptives, other androgen antagonists may be prescribed.[76] For a complete discussion of the treatment of polycystic ovarian syndrome, refer to that section of this text.

Oral Antibiotics and Retinoid Preparations

In addition to OCs, systemic treatments for acne include the use of oral antibiotics and retinoid preparations.[63,67,80,81] Isotretinoin is the only medication thus far to induce long-term, drug-free remission; however, its use internally has been clearly demonstrated to carry risks of teratogenicity. Therefore, it cannot be used during pregnancy and ongoing negative pregnancy tests should be obtained when women of childbearing age use this drug. Isotretinoin treatments for clearing acne have been associated with marked improvement in quality of life and psychological status in those with severe acne who have benefited from its use.[6] Unfortunately, there has also been substantial concern in recent years regarding its association with increased suicide rates among users.[63,81] Topical use is not associated with these risks and is considered effective and safe. Antibiotics can be effective at reducing inflammations however, antibiotic resistance is emerging as a new and important concern in their use as first line internal and topical therapies.[69] Internal therapies are aimed at reducing microbial colonization, treating hyperkeratosis, and reducing immune modulated and inflammatory responses.[70]

Topical Treatments

Commonly prescribed topical treatments include retinoids, benzoyl peroxide, and antibiotics. Table 5-3 addresses the various systemic and topical treatments currently in use, their actions, and adverse effects. Conventional medical therapy for the treatment of *acne vulgaris* may need to be maintained for months or well over a year. This is limited by the tolerability of systemic and local dermatologic agents, the stigma to adolescents of OC use, the long-term risks of OC and corticosteroid use, limited ability to control sebum production with medications, development of antibiotic resistance by *P. acnes*, and in women of childbearing age, interference of antibiotics with OCs and demonstrated teratogenicity of the most effective moderate to severe acne therapy-isotretinoin.

Botanical Treatment of Acne

Philosophical View

Botanical therapy for acne begins with the belief that the health of the skin is a reflection of the overall health of the organism. The skin, a major organ of elimination, is believed to bear an excess burden of elimination when other eliminatory and detoxification organs (e.g., bowels, lymph system, liver) are not functioning optimally or are overtaxed. Thus, topical treatments are almost universally accompanied by systemic treatments that address the health of these other systems. An entire category of herbs, known historically and to this day as *alteratives*, and referred to colloquially as *blood cleansers*, are included in the treatment of most skin condition for their perceived stimulatory effects on the lymph system and liver. Many herbalists rely on the use of gentle choleretics to stimulate bile flow and improve bowel regularity and frequency, and herbs improve hepatic function, the long-term result of which is often found to be improved skin health. It is likely that the mechanisms of action include hepatic detoxification and a reduction in excess circulating hormonal load (i.e., excess estrogen, testosterone) via increased bile conjugation and intestinal elimination. Herbalists typically include botanical antimicrobials and anti-inflammatories as topical and systemic therapeutic agents. Additionally, herbalists view the skin as the interface between the individual and the world, "...being the vehicle through which we express, communicate, and perceive. Thus the psychological and spiritual aspects of an individual will impact and be impacted by the skin,"[2] corroborating what medical science now recognizes as the impact of emotional stress on the health of the skin and the influence of skin problems on emotional health.

As more information on the role of herbs on endocrine functions emerges, herbs are increasingly being considered for treatment of hormonal dysregulation in acne, such as hyperandrogenism. Based on the suspected hormonal etiology of *Acne vulagaris* there clearly appears to be a role for herbal hormonal modulation as an alternative to OCs and corticosteroids. (See PCOS if this is a suspected or confirmed diagnosis, of which the acne is symptomatic.) Hyperinsulinemia also should be evaluated for and treated if present, as this may be an etiologic factor in hypersensitivity to androgens.

The botanical medicine practitioner takes a multifactorial approach by incorporating dietary and nutritional modifications, attention to the individual female's hormonal patterns, and the effects of stress on and from acne into a comprehensive treatment plan. Supporting evidence below focuses on herbs that directly target the skin through anti-inflammatory, antimicrobial, or hormonal effects. Table 5-4 provides suggestions for adjunct therapies that might be considered in conjunction with these direct acting agents, for example, the use of nervines or adaptogens.

It should be noted that immediate results are not expected when treating chronic acne. Improvement may take place over several weeks or longer, and when acne is associated with menstruation, over several cycles.

TABLE **5-3**

Common Pharmaceutical Approaches to Treating Acne[63,69,70,71]

PHARMACEUTICAL DRUG	ACTION/ADVERSE REACTIONS
Systemic Treatments	
Antibiotics: Tetracycline, Clarithromycin, Clindamycin, Doxycycline, Erythromycin	Reduce microbial colonization, anti-inflammatory for moderate to severe acne when topicals not adequate alone. Adverse effects of oral antibiotic use range from increased vaginal yeast infection, GI tract upset, and decreased efficacy of oral contraceptives due to decreased intestinal absorption of estrogens from gut microflora disruption, to antibiotic resistance, an increasingly prevalent problem.
Hormonal drugs: oral contraceptives/antiandrogen therapy	Reverse hyperandrogenic states; reduce hormonal pathogenesis associated with acne by lowering levels of circulation androgens thus the only treatment effective at actually controlling sebum production. May also decrease adrenal and ovarian androgen production. Women using OCs are at risk for the well-documented common and serious adverse effects associated with their use. OCs containing androgenic progestins may aggravate acne.
	Spironolactone is the most commonly used antiandrogenic drug; it may cause menstrual irregularity and breast tenderness. Low dose corticosteroids are sometimes used to control adrenal androgen production.
Isotretinoin (Accutane)	Strong anti-inflammatory for severe inflammatory acne; only medication that addresses all four pathogenic factors simultaneously; produces significant reduction in sebum production. Known teratogen; may cause anemia and/or thrombocytopenia; adverse skin reactions (including pruritus, excessive granulation, secondary staphylococcal skin infection), nosebleeds, vaginal dryness, arthralgias, abnormal liver function tests, depression, and rarely, more severe problems.
PHARMACEUTICAL DRUG	**ACTION**
Topical Treatments	
Tretinoin	A comedolytic agent; normalizes follicular keratinization; promotes drainage of existing comedones; prevents formation of new comedones; use may resultant in decreased inflammation. May take 3 to 4 months for improvement; can cause local irritation that may persist until after 3 weeks of use.
Topical antibiotics: Tetracycline, Clindamycin, Erythromycin	Treats mild to moderate inflammation; reduces bacterial colonization through chemotaxis suppression and reducing amount of free fatty acids in surface of skin. Local irritation can be a problem; topical use of clindamycin associated with severe GI reactions (including pain, bloody diarrhea, and colitis). Antibiotic resistance development is an increasing problem.
Benzoyl peroxide	Reduction of microbial colonization, anti-inflammatory activity; can cause local irritation, erythema, dryness, or allergic contact dermatitis. Also bleaches clothing and bed linens.
Azelaic acid	Treatment for mild to moderate acne. Bacteriocidal, bacteriostatic, anticomedonal, decreases keratinization of the hair follicle. Has a very favorable safety record with low rate of local adverse effects, and is appropriate for long-term use. No known interactions with other topical agents so may be effectively used in combination therapies.

(Continued)

TABLE 5-3

Common Pharmaceutical Approaches to Treating Acne[63,69,70,71]—cont'd

PHARMACEUTICAL DRUG	ACTION
Topical Treatments	
Retinoids	Vitamin A derivatives and analogs, they reduce keratinization by interacting with retinoic receptors. They modulate cellular differentiation and inflammation. Local irritation is typical of topical retinoids.
Isotrexin (a combination of isotretinoin and erythromycin)	Reduces number of lesions and inflammation

TABLE 5-4

Botanical Treatment Strategies for Acne

THERAPEUTIC GOAL	THERAPEUTIC STRATEGY	BOTANICAL NAME	COMMON NAME
Reduce inflammation	Anti-inflammatories	*Glycyrrhiza glabra*	Licorice
		Hamamelis virginiana	Witch hazel
		Lavendula officinalis	Lavender
		Matricaria recutita	Chamomile
		Scutellaria baicalensis	Skullcap
Reduce local infection	Antimicrobials	*Echinacea* spp.	Echinacea
		Lavendula officinalis	Lavender
		Berberis aquifolium	Oregon grape
		Melaleuca alternifolia	Tea tree
Relieve stress, anxiety, tension, depression	Nervines, Anxiolytics, Antidepressants	*Hypericum perforatum*	St. John's wort
		Melissa officinalis	Lemon balm
		Scutellaria lateriflora	Skullcap
		Verbena officinalis	Blue vervain
Improve stress/adrenal response; enhance immunity	Adaptogens	*Withania somnifera*	Ashwagandha
Improve eliminative functions through lymphatic and hepatic systems, etc.	Alteratives, lymphagogues, choleretics, hepatics	*Arctium lappa*	Burdock
		Calendula officinalis	Calendula
		Galium aparine	Cleavers
		Rumex crispus	Yellow dock
		Scrophularia nodosa	Figwort
		Taraxacum officinale	Dandelion
		Trifolium pratense	Red clover
Hormonal regulation	Hormonal regulating herbs,	*Vitex agnus castus*	Chaste berry
Treat constipation	Aperients (mild laxatives)	*Linum ussitissimum*	Flax seed
		Rumex crispus	
		Taraxacum officinale	
Topical applications	Antimicrobials; anti-inflammatories	See above	

Discussion of Botanicals

Given the prevalence of skin complaints, there is a remarkable paucity of studies on botanicals for their treatment. The following discussion reviews the traditional and contemporary clinical uses of herbs for the treatment of acne.

Burdock Root: Internal/Topical. A *comprehensive* database search for uses of burdock root yields a long list of articles demonstrating its historical and traditional use for the treatment of sores, boils, and abscesses. It is discussed in *King's American Dispensatory* as an alterative, aperient, and specific herb for impaired nutrition of the skin, specifically recommended for eczema, psoriasis, and dry scaly eruptions.[82] Burdock root is used as an alterative and gentle laxative. The root extract has mild antibiotic activity, attributed to its polyacetylene

constituents, which however, may not be present in commercially available dried material.[83,84] According to Wichtl, the European use of burdock as an herbal drug is nearly obsolete. The German Commission E did not support its therapeutic use owing to insufficient evidence.[85] No clinical studies using burdock have been identified in the literature. Nonetheless, it remains widely used by herbalists as a decoction or tincture to be taken internally for the treatment of skin conditions, including acne. However, there is controversy among herbalists about its efficacy for skin conditions, and some have reported exacerbations of inflammatory skin conditions. It is typically used internally, although it may be used topically as well.

Calendula: Internal/Topical. The effectiveness of calendula blossoms in the treatment of skin inflammations is well documented. Although the active principles have not been clearly defined, it contains both anti-inflammatory flavonoids and retinoids.[83,85] Calendula, a bitter, cooling herb, exerts systemic antiseptic and anti-inflammatory activity when used orally, and is considered specific for the treatment of sebaceous cysts and acne.[86,87] Limited uncontrolled studies on the antimicrobial activity of calendula have been conflicting, and tend to discount its efficacy, although it has demonstrated anti-inflammatory activity.[88] Its demonstrated effects include promoting epithelialization of surgical wounds, and bactericidal action against *S. aureus*.[32] Herbalists continue to rely on it, finding it highly effective clinically for skin inflammation and infection, used both internally as a decoction and topically as a wash, steam, or fomentation. It is considered specific when there are swollen lymph nodes, and used internally, is considered to promote lymphatic circulation and drainage.

Chamomile: Internal/Topical. Chamomile is indicated externally for treatment of inflammation of the skin and mucosa, used as a wash or steam. Its effects may be largely owing to the chamomile flavones, e.g., apigenin, that exert a local anti-inflammatory effect with topical application. Apigenin is not only adsorbed at the skin, but penetrates to deeper layers.[83] Although no reports on the use of chamomile for the treatment of acne were identified, several reports indicate beneficial effects from topical use of standardized chamomile creams in the treatment of eczema, with two trials showing chamomile cream to have equal, or superior effects to topical steroidal and nonsteroidal anti-inflammatory medications.[87,89,90] It is recommended in the German Commission E Monographs for inflammations and bacterial conditions of the skin. No studies were identified on its specific use for acne. Allergic irritating skin reactions have been reported with the use of chamomile flowers topically, but such reports are very rare.[83] Internal use is appropriate as an adjunct treatment for stress and anxiety associated with acne.

Chaste Berry: Internal. Chaste berry is sometimes recommended for the treatment of acne, and in particular, menstrually or hormonally related skin problems.*

*References 83, 90, 93, 98, 107, 108

Figure 5-2 Chinese skullcap (*Scutellaria baicalensis*). (Photo by Martin Wall.)

Its use for acne appears partly based on a study conducted in 1968 by Giss and Rotheberg demonstrating clinical effectiveness in a group of 118 men and women (70% were women, some with PMS), including recurrence of acne with lapses in herbal treatment and complete healing in 70% of patients who had previously been unresponsive to long-term conventional therapy. Mills and Bone suggest the therapeutic efficacy seen in this study may be attributed to the mild antiandrogenic effects of Vitex, although this remains unknown.[93] Low Dog, however, argues that it seems illogical to give chaste tree for the treatment of acne given that acne seems to be aggravated in the progesterone dominant luteal phase of the menstrual cycle when Vitex appears to increase LH and progesterone levels.[90] Clearly, there is a great deal still not understood about the interactions of herbs with the endocrine system. Vitex has a good safety profile and may be of benefit in some women with acne; however, at this time there appears to be no scientific justification of its routine use as an acne treatment.

Chinese Skullcap: Internal/Topical. *Scutellaria baicalensis*, or ''scute,'' is considered specific in TCM for clearing ''damp heat,'' a category of diagnosis in which acne may commonly fall. It is clinically remarkable for

reducing inflammation in dermatologic conditions and should be considered an important herb in formulations for treating acne and other skin conditions. It has also shown antimicrobial activity against a broad spectrum of microorganisms.[91] It can be used orally for its systemic anti-inflammatory effects and/or topically in cream or wash form as a local anti-inflammatory (Fig. 5-2).

Cleavers: Internal. Cleavers is used internally for the treatment of a wide range of skin conditions.[83,87] It is particularly indicated when there are enlarged lymph nodes, and for inflammatory, eruptive skin conditions.[84] Its use is based on traditional evidence.

Dandelion Root: Internal. Dandelion root is an alterative and perhaps one of the best-regarded tonics for the liver.[83] Traditionally, it has been included in formulae for skin conditions such as acne. No human clinical trials have been conducted to support the uses of dandelion root for skin conditions.[90,92] Its use as a bitter, cholagogue, and aperient to promote and enhance liver function, bile secretion, and bowel elimination, respectively, may suggest some of the mechanisms of action in treating acne.

Echinacea: Internal/Topical. Echinacea has been used traditionally to clear inflammatory skin problems. It was used in the treatment of boils, abscesses, and eruptive skin conditions. Echinacea is believed to exert its benefits in the treatment of skin conditions via enhancing the activity of the lymph system, improving local elimination and reducing inflammation.[93] Echinacea also may be applied locally (topically) for inflammatory skin conditions. The polysaccharides are being investigated as possible active ingredients in its external activity.[83] Echinacea has demonstrated important immunomodulatory effects. It may be included in internal use formulae for chronic acne, as a general anti-inflammatory and immunotonic herb. Echinacea has been used successfully as a local anti-inflammatory for minor wounds and may be considered as part of a rinse or cream-based topical preparation.[93]

Figwort: Internal. Figwort, an herb not commonly known outside of herbal and naturopathic practitioners, is an alterative used specifically in the treatment of skin conditions, usually reserved for those that are intractable, aggressive, or longstanding.[93] It is considered eliminative, having mild laxative, diuretic, as well as lymphatic activity. Hoffmann cites figwort as having cardiac stimulant activity, and cautions against its use in patients with tachycardia and those on cardiac glycosides, which it might potentiate.[84] It is otherwise unexpected to cause side effects when used at the recommended dosage.

Guggul: Internal. Guggul (equivalent to 25 mg gugulsterone) was found to decrease the number of inflammatory acne lesions by 68% in a small, randomized study ($n = 20$), compared with 65.2% with tetracycline (500 mg). The response in inflammatory lesions (papules, pustules, nodules, cystic lesions) was better than that in noninflammatory lesions (comedones). It is thought that the antilipolytic activity of gugulsterones reduces the output of sebum and inhibits the lipolysis of triglycerides by bacteria to free fatty acids.[94] The study design was not considered methodologically rigorous.[95]

Licorice: Internal. Licorice has demonstrated increased cortisol effects (primarily in ulcerative bowel conditions).[95–99] Glycyrrhizin, a saponin of licorice root, and its derivative, glycyrrhetinic acid (GA), have been found to inhibit 11-beta-hydroxysteroid dehydrogenase, the enzyme that catalyzes conversion of cortisol to cortisone. One study found that 2% GA combined with hydrocortisone enhanced the local effects of the hydrocortisone. Because GA is already touted as a topical anti-inflammatory for dermatitis and psoriasis, this may point to a potential concomitant use of GA with hydrocortisone not only to enhance local effects but also to reduce systemic adverse effects with acne treatments.[100] It is used by herbalists as part of internal formulae for the treatment of acne and other inflammatory skin conditions. Licorice has not been directly studied for its effects in the treatment of acne; however, it should be considered for patients who wish to switch from corticosteroid treatments to a more natural approach to acne treatment, which should be done under the supervision of an experienced practitioner.[97]

Oregon Grape Root: Internal/Topical. Oregon grape root has a long history of use for the treatment of

Figure 5-3 Oregon grape (*Berberis aquifolium*). (Photo by Martin Wall.)

a wide variety of chronic skin conditions, including acne, and was listed as a bitter tonic in the USP until 1916 and the National Formulary until 1947 as a bitter tonic, which as discussed, holds implications for its use in treating acne. One placebo-controlled clinical trial of nine male and female patients aged 12 to 30 years using a topical cream of 10% Oregon grape tincture in a 1:10 extract versus placebo, applied topically twice daily for 8 weeks, showed positive results with both groups demonstrating a reduction in skin oiliness and lesions, but only the Oregon grape group showing a decrease in sebum production. However, the study was considered too small and the preparation possibly too dilute to demonstrate a significant therapeutic effect.[101–103] Kraft lists Oregon grape as a primary treatment protocol for acne and seborrhea, citing its anti-inflammatory effects.[104] Mitchell suggests that when thinking of Oregon grape, one should think of the skin-digestive system connection. He states that most cases of acne, eczema, and psoriasis are eased symptomatically by using this herb (Fig. 5-3).[105]

Tea Tree: Topical. Tea tree oil is a popular external application for skin problems. It has antibacterial and antifungal activity, in vivo, against a number of organisms, although its antiviral activities have not been conclusively demonstrated. A randomized control trial (RCT) of a 5% tea tree oil lotion demonstrated effectiveness as a topical antiseptic in the treatment of acne, slightly less effective than benzoyl peroxide in treating acne, although with fewer side effects. One hundred twenty-four patients were randomized to receive either tea tree oil or 5% benzoyl peroxide lotion for 3 months. Both groups showed improvement in the number of inflamed lesions, the number of non-inflamed lesions, and skin oiliness. Side effects in the tea tree group included skin dryness, pruritus, stinging, burning, and redness.[83,106] The German Commission E Monographs include skin inflammations and wound healing as indications for its use.[85] As with other essential oils, allergic dermatitis is a common side effect of tea tree oil, both from direct application to the skin (contact), as well as from inhalation of the vapors and ingestion.[83,102] Skin irritation appears to increase with the age of the tea tree product, possibly as a result of oxidation products, thus product freshness and storage practices may influence the rates of dermatitis.[102]

Witch Hazel: Topical. The astringent and anti-inflammatory herb witch hazel has been used successfully for the treatment of dermatological conditions (inflammation and eczema) and may be used topically as a facial wash or in a cream base. Witch hazel distillate has demonstrated noteworthy effects in the treatment of topical inflammation after UV exposures, and witch hazel creams and ointments have shown anti-inflammatory effects in patients suffering from atopic neurodermatitis, psoriasis, and eczema in a total of six different clinical trials.[99]

Yellow Dock: Internal. Yellow dock is a mild laxative, cholagogue, and alterative. Herbalists consider it a valuable herb in the treatment of chronic skin conditions, especially when there is accompanying constipation or digestive sluggishness.[87,105]

Topical Applications

The topical application of herbs for acne treatment relies on those that are antimicrobial, astringent, and anti-inflammatory. Treatments may include the use of facial steams, washes, compresses, and creams. Topical use of neat (undiluted) essential oils is contraindicated owing to their irritating nature; their use may exacerbate the condition or cause tissue damage.

Differential Topical Treatment: Dry vs. Oily Skin

Practitioners must be sensitive to the skin type and preferences of individual patients when choosing topical medications.[69] Agents containing a higher volume of alcohol may be preferable to patients with oily skin and drying to those whose skin is already dry. Conversely, patients with dry skin may prefer moisturizing bases such as creams, ointments, or oils.

Facial Steams

Hot facial steams are helpful for opening the pores and allowing delivery of antiseptic volatile oils to the affected areas. The patient is instructed to bring a large pot of water to a boil, and while doing so have ready a large bath towel, the necessary essential oils, and a trivet. The trivet is placed in a sink and when the water comes to a boil, the pot is placed on it. The lid is quickly opened and three to five drops of essential oil are added and the lid quickly replaced. The patient is then to form a small tent over the head and sink and carefully remove the lid allowing the steam to bathe the face. The face should be kept at least 18 inches from the pot and care must be taken to avoid burning from the steam. The steam exposure should be maintained for 3 minutes, after which the patient should rinse the face with cool water or an astringent herbal infusion (e.g., witch hazel distillate). Lavender, tea tree, and rosemary essential oils are all excellent antimicrobials and may be used alone or in combination. This treatment can be repeated several times weekly, and may be accompanied by systemic treatment. Herbalists often use lavender as a mild soothing topical antiseptic. Although no clinical trials using the extract or flowers have been identified, its aromatic nature enhances topical applications and inhalation of the essential oil has been shown to induce relaxation.[85,87] Witch hazel may be used as a cool rinse after the steam to tonify the pores. Additionally, the steam water can be substituted with an infusion of any number of botanicals for the skin including a combination of the antiseptic and anti-inflammatory herbs: calendula, chamomile, lavender, and witch hazel to which the essential oils are added.

Botanical Formulae for Acne

See Boxes 5-7 to 5-10.

Nutritional Considerations

Diet is an important part of any herbal treatment protocol. Cultures maintaining traditional diets other than Western diets clearly have lower rates of acne.[109,110] Optimal nutrition with an emphasis on foods and nutrients that promote skin health as well as

BOX 5-7

Botanical Prescription for *Acne vulgaris*

Tincture for Internal Use

Chinese skullcap	(*Scutellaria baicalensis*)	20 mL
Oregon grape	(*Berberis aquifolium*)	10 mL
Echinacea	(*Echinacea* spp.)	20 mL
Dandelion	(*Taraxacum officinale*)	20 mL
Licorice	(*Glycyrrhiza glabra*)	20 mL
Ashwagandha	(*Withania somnifera*)	10 mL
		Total: 100 mL

Dose: 3 mL bid-tid depending upon severity. Provide formula for 12 weeks, then re-evaluate formula based on progress. The tincture can also be used at this dose during acute flare-ups only.

If acne is associated with the premenstrual period, give 5 mL *Vitex agnus castus* each morning from the end of the menstrual period to the beginning of the next, for 3 consecutive months.

Rationale: Chinese skullcap, Oregon grape, echinacea, licorice, and ashwagandha appear in the formula for their alterative and anti-inflammatory effects; Oregon grape and dandelion are choleretic, hepatic bitters; Oregon grape, echinacea, and licorice are anti-viral, and licorice and ashwagandha are adaptogens included for general HPA support.

Rinse for External Use

Prepare a strong infusion using equal parts of the following herbs:

Calendula blossoms	Lavender flowers	St. John's wort
Witch hazel bark	Rosemary leaf	

Steam or wash the face or affected areas with hot water, then rinse the face or other affected areas once or twice daily with this infusion (either warm or at room temperature). Repeat daily as needed. This infusion also may be used as a warm compress rather than as a rinse.

BOX 5-8

"Alterative" Prescription for Treating Acne

Tincture for Internal Use

Echinacea	(*Echinacea* spp.)	25 mL
Dandelion root	(*Taraxacum officinale*)	25 mL
Red clover	(*Trifolium pratense*)	25 mL
Cleavers	(*Galium aparine*)	25 mL
		Total: 100 mL

Dose: 5 mL bid.

BOX 5-9

Nervine Prescription

Tincture for Internal Use:

Chamomile	(*Matricaria recutita*)	30 mL
Lemon balm	(*Melissa officinalis*)	30 mL
Blue vervain	(*Verbena officinalis*)	30 mL
Lavender	(*Lavandula officinalis*)	10 mL
		Total: 100 mL

Dose: 2 to 5 mL tid, or 3 mL as needed.

These herbs can also be used as tea; taken one to two cups daily. Omit the vervain or motherwort if taken as a tea (both are bitter in tea).

*Blue vervain may be replaced with motherwort (*Leonurus cardiaca*).

BOX 5-10

Prescription for Constipation

Tincture or Infusion for Internal Use:

Dry Herb		Dried Herb	Tincture
Dandelion root	(*Taraxacum officinale*)	4 parts	40 mL
Yellow dock root	(*Rumex crispus*)	4 parts	40 mL
Anise seed	(*Pimpinella anisum*)	2 parts	20 mL
		Total: 10 parts	**100 mL**

Infusion Dose: Prepare as for standard infusion, one cup taken daily as warm tea in the morning.

Tincture Dose: 5 mL bid

those that minimize the load on the eliminative organs is recommended. Red meat should be minimized in the effort to reduce the overall inflammatory response. Specifically important is evaluating the diet for the presence of unhealthy oils and excessive refined carbohydrate intake.

Although there has been no scientifically proven correlation between chocolate consumption and acne, many adolescents and women report aggravated acne after consuming it in large amounts. Chocolate cravings also may indicate unmet nutritional needs, which should be met through diet and supplementation. Low Dog suggests that individuals should avoid those foods that they themselves believe to be aggravating.[90]

Treatment Summary for *Acne Vulgaris*

- The skin is a reflection of overall health, thus herbalists take a systemic approach along with the use of local, topical applications.
- Digestive eliminative functions can be improved with the use of aperients such as dandelion root, yellow dock root, and flax seed and should be considered when acne is associated with chronic constipation or sluggish digestion.
- Hormonal regulation is considered important when there is acne associated with menstrual problems and other hormonally related problems such as PCOS. Chaste berry is commonly used.
- Herbalists traditionally use herbs categorized as ''alteratives'' to improve lymphatic function and hepatic elimination, hormonal conjugation, and excretion. The most commonly used are burdock root, calendula, cleavers, yellow dock root, figwort, dandelion root, and red clover.
- An anti-inflammatory diet is recommended and anti-inflammatory herbs can be used internally and topically. These include licorice root, witch hazel, lavender, chamomile, and Chinese skullcap.
- Herbs can be used topically and internally to reduce infection and aid in reduction of inflammation. These include echinacea, lavender, Oregon grape, and tea tree.
- Stress can aggravate a tendency toward acne, and chronic acne can cause significant stress and depression. Herbal nervines, anxiolytics, and antidepressants can be included in formulae and include St. John's wort, lemon balm, skullcap, and blue vervain. Adaptogens can be used long term to improve the stress response, enhance immunity, regulate the HPA-axis, and reduce inflammation. Ashwagandha should be considered. Other adaptogens are discussed in Chapter 7.
- Topical applications include washes, steams, and compresses. They are usually comprised of antimicrobial and anti-inflammatory herbs.
- Important nutritional considerations include an emphasis on optimal nutrition with good quality oils, Brewer's yeast, vitamin A, zinc, vitamin B_6, and vitamin C.
- Stress reduction and counseling can be beneficial in cases of severe and chronic acne.

What to Expect with Treatment
Chronic acne typically requires 2 to 3 months of systemic and topical treatment before significant and consistent improvement is noticeable. Reduction in inflammation may be observable after several days of topical treatment with steams and skin rinses.

The following supplements have been shown to have a beneficial impact on acne:

- *Brewer's Yeast:* 2 to 3 g tid may reduce insulin sensitivity and in one study showed a clinical improvement in acne patients. This supplement is contraindicated for those taking MAO inhibitors as concomitant use may cause hypertension.[71]
- *Vitamin A:* Retinoic compounds are a mainstay of acne treatment. Use of vitamin A as a treatment for acne may require intake of high (100,000 IU/day for 1 month followed by 25,000 to 50,000 IU per day for 3 months) and possibly unsafe dosages leading to hypervitaminosis A and if the use is prolonged, vitamin A toxicity. Kohani states that doses of 25,000 IU daily are safe and effective for acne treatment. Foods high in vitamin A (carrots, squash, sweet potatoes, apricots) can also be consumed as a regular part of the diet. Vitamin E assists in retinal regulation in humans and when combined with zinc may enhance the efficacy of the lower daily dose of vitamin A.[109]

Warning: Vitamin A in large doses (>5,000 IU daily) is teratogenic. Supplementation in pregnant women or those planning to conceive should not exceed the normal amount present in a prenatal vitamin supplement and should only be taken as part of the prenatal vitamin. Extreme care should be taken in supplementation in those younger than 18 years old other than what is typical in a daily nutrient supplement.

- *Zinc:* Zinc is intrinsically important to the health of the skin, the healing of wounds, and to optimal immune functioning. There has been controversy over its effectiveness as an acne treatment with some studies demonstrating effectiveness and others not showing benefit. The recommended dose for adolescents is 25 mg zinc picolinate twice daily for 2 weeks and then once daily for 2 months, taking care *not to exceed these recommended dosages*.[71,109]
- Vitamin B_6 (pyridoxine) has been shown to be beneficial when there is premenstrual aggravation of acne. Vitamin B_6 plays a role in steroid hormone metabolism and in animal studies B_6 deficiency appears to increase testosterone uptake and sensitivity.[109]
- Vitamin C has been suggested at a dose of 250 mg tid as a natural anti-inflammatory.[109]

Additional Therapies

Hygiene

Although keeping the face clean can play an important role in maintaining healthy flora at the surface of the skin, overcleansing of the face does not improve acne, as poor facial cleansing does not cause it. In fact, excessive washing and scrubbing with abrasive cleansers can aggravate inflammation and damage the skin. Regular cleansing with antimicrobial soaps is also not recommended as they can encourage antibiotic resistance and destroy healthy skin flora, increasing susceptibility to secondary skin infections. Daily rinsing with warm water and a mild, natural ingredient soap, followed by a cool water rinse is an ample daily cleansing routine. Keeping the hair clean and off the face, keeping hands away from the face, and avoiding picking at pustules are all recommended. Avoid makeup that clogs the pores or is allergenic.

Stress Reduction and Counseling

The impact of acne on psychological and emotional health, and the influence of stress on acne have both

been made clear in this section. Stress reduction techniques and counseling can both be important parts of a treatment plan for those with acne, particularly adolescent girls, and particularly when acne is moderate to severe. Emotional and psychological support should not be overlooked.

AMENORRHEA

Aviva Romm, Bevin Clare

Amenorrhea is the absence of menses. It is divided into two categories: *primary amenorrhea*, the absence of menstruation by age 14 with no secondary sexual characteristics, or the absence of menstruation by age 16 regardless of the appearance of secondary sexual characteristics; and *secondary amenorrhea*, the absence of menstruation for a total of at least three previous menstrual cycle lengths, or at least 6 months in a previously menstruating woman in her reproductive years. Strict adherence to these criteria, however, should not lead to delay in medical evaluation in patients showing other signs of a medical condition warranting investigation.[111]

The prolonged absence of menstrual periods is considered normal only prior to puberty, during pregnancy, while breastfeeding, and after menopause. Primary amenorrhea is relatively uncommon, occurring in 0.3% of the population; secondary amenorrhea occurs in 1% to 3% of women, however, subgroups, for example college students and athletes experience higher rates, the former as high as 5% and the latter as high as 66%. In most cases, patients with amenorrhea have simple problems that can be readily resolved; however, amenorrhea can be a challenging clinical situation caused by serious underlying conditions. It is completely normal for a woman to miss an occasional period. This can occur owing to stress, travel, illness, or minor or major changes that occur in the course of life (a break-up with a boyfriend, a move, a new job, a divorce, and so forth).

PATHOPHYSIOLOGY

The absence of menstruation is a symptom of an underlying imbalance, disorder or disease, rather than a disease in itself. The ability to menstruate is ''regulated by a complex mechanism that integrates biophysical and biochemical information composed of interactive levels of hormonal signals, autocrine/paracrine factors, and target cell reactions.''* Further, the ability to menstruate is dependent upon a normal reproductive system. Genetic disorders, congenital abnormalities of the genital system (absence of the uterus or vagina, vaginal septum, cervical stenosis, imperforate hymen), endocrine disorders, pituitary or hypothalamic disorders, hyperthyroidism, hypothyroidism, defective enzyme systems, tumors, radiation or chemotherapy exposure, autoimmune diseases, smoking leading to premature ovarian failure, hypothyroidism, anorexia, abnormally low body fat or sudden weight loss (e.g., resulting from poverty, fad dieting, anorexia nervosa, bulimia, or very strenuous exercise), hypoglycemia, obesity, PCOS, emotional stress, medications, recent discontinuation of oral contraceptives, and past surgeries may cause amenorrhea. Most nonpregnant women with secondary amenorrhea have chronic anovulation, hypothyroidism, hyperprolactinemia, or weight loss and anorexia. Pituitary tumor is not uncommon in this category. Aside from pathologic and congenital etiologies of amenorrhea, eating disorders are a significant concern and common reason for lack of menstruation. Eating disorders can lead to severe and dangerous consequences and must be treated professionally as with any serious disease process.

*Speroff L, Glass R, Kase N: Clinical Gynecology, Endocrinology and Infertility.

SIGNS AND SYMPTOMS OF AMENORRHEA

Absence of periods may be accompanied by:
- Galactorrhea
- Symptoms of pregnancy
- Hirsutism (and other signs of androgen excess)
- Temperature intolerance
- Signs and symptoms of other disease

DIAGNOSIS

It is essential to take a comprehensive health and gynecologic history to include history of pediatric or adult cancer, thyroid or adrenal disorders, renal or liver disease, and history of exposure to medications, radiation, or chemotherapy. Pregnancy should be ruled out by pregnancy test rather than just by sexual history. An evaluation of recent or current stresses and lifestyle habits such as excessive exercise, dieting, or eating disorders is needed. A careful physical exam should assess for signs of congenital abnormality of the reproductive system. The patient should be assessed for the presence of galactorrhea, PCOS and androgenization. Menopause should also be ruled out. Obstetric history must be reviewed, particularly for postpartum hemorrhage, which can lead to pituitary disease and resultant amenorrhea.

Other relevant tests include thyroid stimulating hormone (TSH), prolactin (PRL) to rule out pituitary tumor, progesterone challenge, estrogen challenge with progesterone withdrawal, the latter two tests to evaluate for anovulation and genital tract defects. Additionally, tests for ovarian and adrenal function, chromosomal disorders, autoimmune disease, anemia, and clotting disorders may need to be conducted. Brain MRI may be necessary to determine whether there is a pituitary tumor. Computed tomography (CT) or ultrasound scanning may be used to look for a tumor in the ovaries or adrenal glands (Box 5-11).

Differential Diagnosis

See Tables 5-5 and 5-6.

CONVENTIONAL TREATMENT APPROACHES

Treatment will vary widely depending on the cause of amenorrhea and may range from a dietary program to hormones or surgery.

BOX 5-11

Tests That May Be Considered When Evaluating Amenorrhea[122]

- ACTH and cortisol
- Chromosome analysis
- DHEA-sulfate
- HCG level for pregnancy
- Imaging studies (head CT or MRI scan, pelvic ultrasound)
- Laparoscopy
- LH and FSH
- PAP smear for maturation index
- Progesterone challenge
- Prolactin
- Testosterone
- TSH, T3, and T4
- Urine 17-ketosteroids

TABLE 5-5

Differential Diagnosis of Primary Amenorrhea

Athletic (hypothalamic) amenorrhea	Medications
Adrenal disease or dysfunction	Ovarian cysts, scarring, tumors
Autoimmune disease	Obesity
Chronic illness	Physiologic delay
Congenital abnormalities of the reproductive organs or sexual differentiation	PCOS
Cushing's syndrome	Pituitary disorders/tumor
CNS disease	Prader-Willi syndrome; Turner syndrome
Hyperprolactinemia	Psychiatric disorders including chronic stress, depression, emotional trauma, anorexia nervosa or other eating disorder
Hypothalamic disorders	Weight loss (sudden); eating disorders

TABLE 5-6

Differential Diagnosis of Secondary Amenorrhea

Conditions listed under primary amenorrhea	Menopause
Anovulation	Pituitary insufficiency (Sheehan's syndrome)
Autoimmune conditions	Post OC syndrome
Cervical scarring and stenosis	Pregnancy
Endometrial sclerosis	

Primary Amenorrhea

If a teenage girl has not started menstruating by age 16 and all test results are normal, an examination is performed every 3 to 6 months to monitor the progression of puberty. Progesterone and possibly estrogen may be given to start her periods. Estrogen is given to induce the changes of puberty in girls who have not developed breasts or pubic and underarm hair and cannot develop them spontaneously.

Secondary Amenorrhea

Treatment of secondary amenorrhea may include progesterone supplements (hormone treatment) and oral contraceptives (ovulation inhibitors). Dietary and exercise modifications may also be part of a treatment plan. In many cases physicians will induce menstruation in nonpregnant women who have missed two or more consecutive menstrual periods to avoid increased risk of uterine cancer.

BOTANICAL TREATMENT OF AMENORRHEA

There is a long history of using herbs for the treatment of ''retention of the menses,'' as amenorrhea is referred to in medieval botanical texts. Although it may appear that this was a convenient euphemism for herbal abortion prescriptions, there is evidence from classical texts such as the *Trotula* that such recommendations were also legitimately intended for amenorrhea caused by a wide variety of etiologies. In fact, amenorrhea in the absence of pregnancy was considered a pathologic condition. Hippocrates and followers of the Hippocratic tradition believed that women eliminate harmful biological toxins through the process of regular menses. Amenorrhea was thought to lead to a dire pathologic build-up of these toxins; thus, the largest percentage of prescriptions for women's diseases in most early medieval texts, reflecting the Hippocratic tradition, were ''aids for provoking the menses.''[112]

In the Eclectic literature, amenorrhea is often described as a cold, atonic condition requiring warming stimulants and tonifying herbs, for example, ginger (*Zingiber officinalis*) (Fig. 5-4). It was described as sometimes being accompanied by a bearing down sensation or feeling of pressure, for which tonic, antispasmodic herbs were also given, for example, motherwort (*Leonurus cardiaca*) and black cohosh (*Actaea racemosa*). Contemporary practitioners recognize that the cause of amenorrhea must be carefully identified to formulate an accurate and appropriate treatment strategy. Experimental evidence in primates indicates that corticotropin-releasing hormone (CRH) inhibits gonadotropin secretion, and this is the likely pathway by which stress interferes with reproductive function.[111] Stress-related amenorrhea is treated herbally with a combination of nervines and adaptogens. Targeting androgen excess and associated hyperinsulinemia is necessary in treating amenorrhea resulting from PCOS (see Polycystic Ovarian Syndrome). Several studies have demonstrated reduction in prolactin levels with chaste tree berry (*Vitex agnus castus*), peony (*Paeonia lactiflora*), and licorice (*Glycyrrhiza glabra*).[113] This may be considered with hyperprolactinemia in the absence of pituitary tumors. Amenorrhea associated with serious underlying disorders requires medical attention. Herbal treatments may be

Figure 5-4 Amenorrhea/dysmenorrhea. Eclectic advertisement circa 1900.

used as adjunct therapies in some of these cases. General botanical treatment strategies also include the use of herbs for promoting hormonal regulation, improving pelvic circulation and uterine tone (emmenagogues, warming pelvic circulatory stimulants, and uterine tonics), and through relieving pelvic tension (antispasmodics). Some of the effects of traditional actions of herbs on the reproductive organs have been associated with herbal activities on various prostaglandin receptors, alpha-adrenergic receptors, and H_1 receptors.[114] Mills and Bone suggest that subtle hormonal effects are most likely responsible for the menstrual stimulating effects of herbs classified as emmenagogues. Herbs may also be included to improve nutrition when women are energy deficient, underweight, or anemic (e.g., dong quai, ashwagandha, nettles, rehmannia, raspberry leaf).

Almost no clinical research has been done on botanical treatments for amenorrhea. There is a limited number of studies demonstrating efficacy in the treatment of amenorrhea with TCM protocol.[115,116] The majority of evidence supporting the efficacy of herbs in stimulating menstrual flow is derived from contemporary herbalists' clinical practice, and from the misuse of emmenagogues as abortifacients. According to toxicology reports, rue is the plant most commonly misused to induce abortion.[117] Herbalists do not routinely use this herb for the treatment of amenorrhea and contemporary herbalists typically do not perform or endorse herbal abortion owing to the ethical and legal considerations, and the risks of the required volume of herbs and their toxicity in these doses, some of which are associated with a high morbidity and mortality rate.[114,117]

Weiss on Amenorrhea and the Use of Emmenagogues

According to Dr. Rudolph Fritz Weiss in his book *Herbal Medicines*, herbs tend to be more effective in treating secondary amenorrhea. Weiss points out that delayed puberty will generally not respond to botanical therapies; however, ''medicinal plants get very good results in secondary amenorrhea and in oligomenorrhea.'' He adds that '' Medicinal herbs... continue to have their place. Emmenagogues were very popular before hormone therapy. There remains the fact, based on experience, that emmenagogues will often restore normal menstrual flow and give very considerable subjective relief.'' All herbal emmenagogues are contraindicated in pregnancy.

In spite of lack of scientific evidence directly supporting the efficacy or safety of herbal emmenagogues, many women with nonpathologic bases for their amenorrhea prefer an herbal approach prior to using hormones for treatment, as do many women who have ''just missed a period or two'' and who do not technically have amenorrhea. The historical and clinical use of herbs for the treatment of amenorrhea suggests areas that warrant further study, particularly on the hormonal effects of these botanicals, and on the adjunct effects of herbs such as nervines for treatment.

Lifestyle modifications, for example, stress management or addressing weight gain or weight loss as necessary, are always included in a comprehensive treatment plan and may be suggested prior to initiation of herbal therapies. It is essential to rule out pregnancy before beginning an herbal program to ''bring on'' the menses as in high enough doses many are potentially toxic to the fetus, and some may to act as abortifacients (Table 5-7).

Discussion of Botanicals

Black Cohosh. Black cohosh has been described historically as a uterine tonic and antispasmodic for the treatment of amenorrhea. The Eclectics classified it as an emmenagogue and considered it specific when there was pelvic pressure, bearing down discomfort, pain, or amenorrhea resulting from exposure to cold.[118,119] Hoffmann describes black cohosh as a ''valuable relaxant and normalizer of the female reproductive system ... It may be used to good effect to treat painful or delayed menstruation.''[120] Black cohosh is not directly hormonal; it does not contain estrogens, and its mechanism of action is not entirely clear. However, it does not appear to be estrogenic.[121] There has been suggestion that black cohosh may have a role in the treatment of amenorrhea with ovarian failure; however, this use has not been

TABLE **5-7**

Summary of Botanical Treatment Strategies for Amenorrhea

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Stimulate pelvic circulation; improve uterine tone; promote menstruation	Emmenagogues	*Angelica sinensis*	Dong quai
		Artemisia vulgaris	Mugwort
		Caulophyllum thalictroides	Blue cohosh
		Cinnamomum spp.	Cinnamon
		Gossypium herbaceum	Cotton root
		Leonurus cardiaca	Motherwort
		Zingiber officinale	Ginger
Treat hormonal dysregulation, for example, hyperprolactinemia, insufficient progesterone	Hormonal modulators	*Angelica sinensis*	Dong quai
		Glycyrrhiza glabra	Licorice
		Paeonia lactiflora	Peony
		Vitex agnus-castus	Chaste berry
Treat emotional and psychological stress and depression	Nervines	*Avena sativa*	Milky oats
		Humulus lupulus	Hops
		Hypericum perforatum	St. John's wort
		Leonurus cardiaca	Motherwort
		Matricaria recutita	Chamomile
		Melissa oficinales	Lemon balm
		Pasiflora incarnata	Passion flower
		Scutellaria baicalensis	Skullcap
		Ziziphus spinosa	Ziziphus
Improve stress resistance	Adaptogens	*Eleutherococcus senticosus*	Eleuthera
		Panax ginseng	Ginseng
		Withania somnifera	Ashwagandha
Relieve pain/discomfort/pelvic pressure/bearing down sensations accompanying amenorrhea	Antispasmodics	*Actaea racimosa*	Black cohosh
		Dioscorea villosa	Wild yam
		Leonurus cardiaca	Motherwort
		Vibrunum spp.	Cramp bark, black haw
Improve general nutrition	Nutritive tonics	See Actions of Herbs	
	Adaptogens	Also, see Adaptogens	

directly evaluated.[122] Its effects on LH activity appear contradictory: In several studies black cohosh demonstrated a suppressive effect, whereas in others it has stimulated LH secretion, again, making its role in treating amenorrhea ambiguous. Its clinical use by the Eclectics and contemporary herbalists is also contradictory: Although it is considered by some to be emmenagogic, it is also used as a uterine antispasmodic in the prevention of miscarriage. Its effectiveness as a uterine antispasmodic is evidenced by its approval by the German Commission E for the treatment of dysmenorrhea. It is also approved for the treatment of premenstrual syndrome (PMS), and menopausal symptoms, with demonstrated effects in improving the emotional and psychological status of menopausal women in clinical trials.[123] (See Plant Profiles: Black Cohosh, for a discussion of warnings and mechanisms of action.)

Blue Cohosh

Blue cohosh was used by northeastern indigenous American tribes to encourage menstruation and facilitate childbirth. The Eclectic physicians adopted blue cohosh as a treatment for a variety of gynecologic complaints, among them the treatment of amenorrhea, especially, but not exclusively, resulting from cold.[124] Felter describes *Caulophyllum* as an emmenagogue to be used where there is amenorrhea owing to pelvic congestion with irritation.[118] It was listed as an official emmenagogue in the USP from 1882 to 1905, after which it was dropped, and the National Formulary from 1916 to 1950.[124,125] Eclectics relied on both the tincture of blue cohosh and a concentrated product of the glycosidic derivative *leontin*, which was particularly employed in the treatment of amenorrhea, being considered to give ''excellent and quick results.''[124] It was also used when there was excessive uterine, menstrual, or postnatal bleeding. Blue cohosh was also considered an antispasmodic and mild sedative in cases of anxiety and restlessness; however, it is not used for these indications in contemporary clinical practice. Herbalists today use blue cohosh for menstrual difficulties including amenorrhea and dysmenorrhea, whereas midwives widely use it to stimulate labor.[126] (See Chapter 11, Pregnancy: Botanical Medicine Use and Safety.) Blue cohosh is considered useful when there is uterine atony. Bone describes it as an ovarian tonic; however, this activity has not been demonstrated by scientific evaluation.[125] Its uterine stimulating activity is justified by its chemical constituents,

in vitro and in vivo studies, and clinical observation. Blue cohosh root contains the oxytocic quinolizidine alkaloids sparteine and N-methycystisine.[127,128] The liquid extract, hot water extract, saponin fraction, and isolated caulosaponin have all demonstrated utero-stimulant activity.[125] Toxicity symptoms (hyperthermia, hypertension, tachycardia, hyperventilation, diaphoresis, and weakness) have been reported from excessive dosing in abortion attempts.[125] Blue cohosh is contraindicated for use during early pregnancy owing to potential teratogenicity, and throughout pregnancy because of abortifacient activity.

Chaste Berry

The Eclectic physicians used chaste berry as an emmenagogue, and contemporary herbalists continue to use it for a wide variety of menstrual irregularities, including amenorrhea.[146] The German Commission E approved it for irregularities of the menstrual cycle, premenstrual complaints, and mastodynia.[123] No specific studies were identified using chaste berry for the treatment of amenorrhea; however, it has shown menstrual regulating effects in a number of trials. Sustained use of Vitex over several weeks during the immediate postpartum period was associated with early return of the menses. McKenna et al. suggest that use of Vitex may be of benefit in resorting ovulation and the menstrual cycle in the lactating mother who is ready to resume regular cycles and to conceive another child.[145] [*Note:* This is an opinion that this author (AJR) corroborates from clinical use in my midwifery practice where I have worked with women who have had lactation-related amenorrhea persisting between 10 and 18 months who wished to become pregnant with a subsequent child. Use of Vitex for 2 to 6 weeks, 5 mL twice daily, has resulted in resumed menstruation in several cases.] In vitro studies suggest a dopaminergic effect inhibiting release of prolactin from the anterior pituitary gland and several trials demonstrate regulation of the menstrual cycle, lengthening of the luteal phase of the menstrual cycle, and reducing PMS symptoms.[122,125] An anecdotal report describes three patients with amenorrhea resulting from anorexia nervosa, hormonal imbalance, or idiopathic causes who were treated with 40 drops daily of 0.2% dried extract of *Vitex agnus castus* fruit. Menstruation resumed in all three women after 5 weeks to 3 months. *Vitex agnus castus* extract inhibited prolactin release from rat pituitary cells; LH and FSH release were not affected.[122] Use of this herb is not recommended in conjunction with OCs, HRT, or progesterone drugs, as it may interfere with these.[125,147]

Cotton Root Bark

Cotton root bark was historically used by indigenous North American tribes as an emmenagogue and abortifacient. Its use as an emmenagogue was adopted by the Eclectic physicians, and as an abortifacient by southern physicians into the 1800s.[129,130] The plant has a profound history, reportedly used as an abortifacient by female slaves in the United States who were frequently victims of rape by their ''masters,'' and consequently, experienced unwanted pregnancies.[130] The plant was marketed by Lloyd Pharmaceuticals and Eli Lilly as an oxytocic, emmenagogic agent. The USP listed cotton root as a parturient from 1860 to 1880. Cotton root is listed in the 1983 British Herbal Pharmacopoeia as an emennagogue.[131] The pharmaceutical agent *gossypol*, investigated for its male and female anti-fertility potential, as well as for anticancer activity, is derived from the cotton seed (and is now also synthetically produced). Animal and in vitro studies confirm the antifertility effects of gossypol observed in clinical trials. Use of gossypol (20 to 60 mg daily, or 0.6 to 0.8 mg/kg, for up to 6 months) has been associated with the risk of hypokalemia and possible permanent sterility. Less common adverse reactions that have been reported mainly in clinical trials with gossypol include mild leukopenia and thrombocytopenia, fatigue, dry mouth and skin, gastrointestinal distress, minor alopecia, and mild hepatotoxic effects. Cardiotoxic and hepatotoxic effects have been reported in animals and in vitro with *gossypol*. Altered hormone levels and other metabolic effects have been reported mainly in animals and in vitro but are also reported in human studies as well.[132] *Gossypol* is present in the seed in 0.5% concentration, and in lesser concentrations throughout the plant. Low Dog suggests it may actually induce amenorrhea and endometrial atrophy thus resulting in infertility.[130] *Gossypol* has antiprogesterogenic activity; its action on the corpus luteum can cause abortion. Seed extract has demonstrated abortifacient effects in rat models, and marked malformations in uninterrupted pregnancies.[133] The root bark extract (not *gossypol*) is currently used by western herbalists as an emmenagogue in cases of amenorrhea and as a uterine antihemorrhagic. Midwives occasionally use it as a labor stimulant in postdates pregnancies (Chapter 16.) No studies were identified in the literature on use of whole plant extracts; thus, the safety of this herb cannot be accurately determined. It is clear, however, that this herb may have teratogenic effects if taken during early pregnancy, and may induce abortion or labor.

Dong Quai

Dong quai is one of the most important herbs used in TCM formulae for menstrual irregularities and amenorrhea. It has been used traditionally to treat conditions associated with the TCM diagnoses of ''blood stasis'' and ''blood vacuity'' (''emptiness,'' ''deficiency'').[134] Whole root has been shown to have a stimulatory effect on the uterus in vivo, and studies have demonstrated its ability to relax or coordinate uterine contractions depending upon uterine tone. He et al. found a decoction of *Angelica sinensis* effective in treating patients with ''energy-deficient'' amenorrhea.[115] No other clinical studies have been done to substantiate its use in the treatment of amenorrhea.[125,134] Chronic and high-dose use of dong quai has been cited by herbalists as a cause of increased menstrual bleeding and increased period frequency; therefore, many herbalists recommend its discontinued use during the menstrual period. It is regularly used by herbalists in Western herbal formulae to ''move'' the blood, improve nourishment, and stimulate the menses.

Ginger

In keeping with the belief that amenorrhea can be a result of ''cold'' conditions and brought on by exposure to cold, ginger is mentioned in the Eclectic text *Materia Medica and Clinical Perspectives* (1905) as a treatment for congestive dysmenorrhea and amenorrhea.[129] It was recommended that tincture be taken dilute in hot water. Bone and Hoffmann also cite its traditional use as an emmenagogue.[120,125] Contemporary herbalists continue to incorporate fresh or dried ginger root into amenorrhea formulas as an adjunct herb, largely believed to increase pelvic circulation, warmth, and relaxation. It is also used topically over the lower abdomen as a fomentation. No studies have evaluated ginger's activity as an emmenagogue. Studies have demonstrated its safety and efficacy in tea and capsule forms in treating nausea and vomiting of pregnancy (NVP) even during first trimester pregnancy, suggesting that it does not have a directly abortifacient effect in modest, therapeutic doses.[121,135–137] However, it is recommended that doses not exceed 2 g of dried ginger daily during gestation.[135]

Motherwort

Motherwort was regarded by herbalists and the Eclectics as an emmenagogic agent to be used in cases of amenorrhea associated with nervous disorders. It was considered useful both internally and as a fomentation over the lower abdominal region.[138] Early research on the extract demonstrated mild uterine stimulatory and antispasmodic activity.[125] The German Commission E supports its use for nervous cardiac disorders, as an adjunct therapy in the treatment of hyperthyroidism, and mentions its traditional use for amenorrhea.[123] Motherwort is widely used by herbalists for a variety of menstrual disorders including dysmenorrhea, amenorrhea, and PMS, finding it a reliable uterotonic and nervine, especially when there is anxiety or irritability. Because of its bitter taste, it is primarily used in tincture form.

*Mugwort (*and *Artemesia* spp.*)*

Named for the Greek Queen and healer Artemisia who is credited with discovering the use of wormwood for women's health problems, and perhaps as a tribute to the Greek goddess Artemis, protector of women and children, members of the Artemisia family have been used for centuries, at least, for the treatment of amenorrhea and as abortifacients. In fact, several species are mentioned in ancient Greek sources.[139] *A. absinthum* (wormwood) was used as an oxytocic by Soranus and by Dioscorides to induce menstruation, abortion, miscarriage, and placental delivery. *A. arborescens* (southernwood) was considered an emmenagogue by Dioscorides, although not by Soranus. It was regarded by Pliny to be used as a sitz bath for ''uterine inflammation.'' Galen also reported on the use of mugwort for amenorrhea.[112] It was popular in the sixteenth and seventeenth centuries for women's complaints, when it was referred to as *mater herbarum*.[139] The BHP lists *A. arborescens* as an emmenagogue.[140] *A. vulgaris* (mugwort) was used traditionally as a treatment for amenorrhea and also dysmenorrhea, and it is the *Artemisia* species most likely to be used by herbalists in the United States today for gynecologic concerns.[120,137,141] In the Unani herbal tradition of India, single-dose mugwort decoctions (10 g) are dispensed for the treatment of amenorrhea, and this herb is also used in Ayurvedic medicine for ''functional amenorrhea.''[137] It is included in the German Commission E as an unapproved herb because of lack of therapeutic claims. Its gynecologic uses include menstrual problems and irregular periods, as well as promoting circulation and as a sedative; abortifacient action has been reported.[123] This intensely bitter herb is popular among grassroots women herbalists in the United States as an emmenagogue, and is often combined with other emmenagogic herbs such as pennyroyal herb, yarrow, and ginger in tea, taken hot.[142] Other *Artemisias* are very high in the essential oil thujone, and may cause serious side effects if not used properly.[141] Mugwort contains only trace amount of thujone and no side effects are expected when this herb is used in therapeutic doses. However, it may cause sensitization or allergic dermatitis, particularly in patients sensitive to the pollen in the Asteraceae family.[120,137]

Schisandra

Schisandra has demonstrated adaptogenic and tonic effects in experimental models and is sold in the United States as an adaptogenic tonic for decreasing fatigue, and improving performance and endurance.[125,143] It is believed to strengthen uterine contractions and its use is cited in TCM to stimulate labor.[144,145] A 70%

Sage and the Power of Herbal Emmenagogues: A Cautionary Tale

In the early years of my midwifery practice, about 20 years ago, I knew a midwife who conveyed the following story to me. She had become pregnant with her third baby while still breastfeeding her second child, then 10 months old. She was excited about the pregnancy but wanted to wean the older baby, because she was fatigued. She'd read in an herb book at her local health food store that sage was effective at drying up breast milk, so she decided to try this method in order to wean her baby. She obtained dried culinary sage and prepared a cup of tea using 1 tablespoon of the dried herb to 1 cup boiling water. Approximately 30 minutes after drinking the tea, she experienced a sudden uterine hemorrhage that required an emergency D&C at the hospital. She had miscarried. She had no prior history of miscarriage, and carried her next pregnancy to term with no complications. This reminder of the powerful nature of herbs instilled in me a great respect for using caution with even modest doses of possible emmenagogues during pregnancy—even seemingly benign culinary ones such as sage!

schisandra combination extract of the fruit suspension, fruit, and fruit coat demonstrated uterine stimulant activity in the pregnant, nonpregnant, and postpartum rabbit uterus, whereas a tincture administered to rabbits caused increased uterine tension and contractility. Its mechanism of action is not known. It appears to possess oxytocic effects; however, there are no endocrine receptor studies of this herb.[145] No clinical research has been conducted on its effects as an emmenagogue. McKenna et al. note that the effects of schisandra as an ovulation stimulator may have unpredictable effects on lactation-induced amenorrhea. Schisandra has a good safety profile when used in appropriate doses and with consideration of TCM contraindications (presence of excess heat, rash, early signs of a cough, epilepsy, excessive exercise, hypertension, intracranial pressure, excessive mental excitement, peptic ulcer).[143–145]

A Word about False Unicorn: An Endangered Species

Chamaelirium luteum, false unicorn root, has traditionally been used numerous native American tribes as well as by the Eclectic physicians for the treatment of all manner of gynecologic conditions in which there was a lack of tone or vigor, and by the latter to regulate glandular activity. It has traditionally been used as a stimulant for the treatment of amenorrhea.[119,125,138] False unicorn is popular on Internet chat groups for women seeking CAM therapies, for the treatment of a wide variety of gynecologic difficulties, especially infertility. It is recognized as an ecologically at-risk botanical and it is very difficult to cultivate; thus, its general use should not be widely recommended. Alternative herbs should be used when possible.

White Peony

Paeoniflorin, a constituent of white peony root, has demonstrated inhibition of testosterone synthesis in vitro, without affecting estradiol synthesis. It reduces testosterone production by the ovaries but not the adrenal glands. In an ovarietctomized model, oral administration of a combination of white peony and licorice increased DHEA and serum estrogen concentration. It acts as a uterine smooth muscle relaxant in several animal species. In one case study, TJ-68, a Japanese traditional herbal formula containing *Paeonia lactiflora* and licorice demonstrated effectiveness in treating risperidone-induced amenorrhea and hyperprolactinemia.[116] This combination, which consists of 6 g each of dried white peony root and licorice, has also demonstrated efficacy in

Caution against the Use of Several Popular Herbs to Bring on the Menses: Rue, Pennyroyal, and Liferoot

American pennyroyal (*Hedeoma pulegiodes*), a member of the mint family, was considered specific by the Eclectics for ''Amenorrhea of long standing, with pallor and anemia and dark circles around the eyes; the patient complains of languor, lassitude, takes cold easily, has pain in back and limbs.''[118] It is probably the most notorious of the herbal emmenagogue-abortifacient genre of herbs owing to widely publicized adverse events and deaths caused by consumption of pennyroyal essential oil in attempted abortion. Pennyroyal oil is considered one of the most toxic of the essential oils because of the hepatic effects of pugelone, and the abortifacient dose is similar to the toxic dose.[120,141] The toxic effects of the oil have long been recognized: Felter states in 1922 that ''Oil of pennyroyal produces toxic effects when given in overdoses. A drachm caused severe headache, difficult swallowing, intense nausea, severe retching without emesis, intolerable bearing down, labor like pains, abdominal tenderness, constipation, dyspnea, semi paralysis of the limbs, and nervous weakness and prostration.'' Pennyroyal oil is no longer available in the herbal market because of its toxicity. In contrast, drinking the infusion of the leafy stems is considered safe.[141] However, there were two cases of acute liver damage reported in California in 1996 in infants given pennyroyal infusion; one case resulted in fatality.[141] The infusion was a popular diaphoretic among the Eclectics, used for the treatment of acute colds.[119] It is popular among grassroots herbalists for the treatment of amenorrhea, generally combined with other emmenagogic herbs.

Ruta graveolens: Although rue is an effective emmenagogue, the furanocoumarin content of the plant presents a toxicologically known risk.[136] The German Commission E does not support its use, stating that the known risks outweigh the benefit of the plant. Rue oil can cause contact dermatitis; phototoxicity, severe liver and kidney damage, and deaths of pregnant women attempting abortion have all been reported with its use. Therapeutic doses can cause melancholy, sleep disorders, dizziness, and spasms.[123] The use of this herb is not recommended on the basis of significant safety concerns.

Senecio aureus, S vulgaris, S. jabaea: Mitchell references the use Senecio species (Ragwort) for the treatment of amenorrhea, dysmenorrhea, metrorrhagia, and menorrhagia.[148] Based on information in popular herb books for women's health, women may use this herb for a variety of menstrual disorders. However, such use is not recommended because of the contents of PAs in *Senecio*, which has caused serious and occasionally fatal cases of venoocclusive disease in humans, and poisonings and deaths in animals. (Bovine and equine poisoning with this herb, whether from grazing or feed contamination, has been widely reported in the literature.)[137,141] The author cannot recommend the use of this herb on the basis of significant safety concerns.

BOX 5-12

Botanical Prescriptions for Amenorrhea

Tincture for Internal Use:

White peony	(*Paeonia lactiflora*)	20 mL
Motherwort	(*Leonurus cardiaca*)	20 mL
Dong quai	(*Angelica sinensis*)	20 mL
Black cohosh*	(*Actaea racemosa*)	20 mL
Ginger	(*Zingiber officinale*)	20 mL

Total: 100 mL

Dose: 5 mL twice daily until the onset of the menses.

Rationale: Peony is included as a hormonal regulator; motherwort is a bitter nervine, acting on the liver and reducing stress, tension, and irritability; dong quai is a blood nourisher and anti-inflammatory adaptogenic tonic. Both motherwort and dong quai are used to promote pelvic circulation and menstrual flow; black cohosh is an antispasmodic for the uterus, and ginger is anti-inflammatory, antispasmodic, and increases pelvic flow. It also improves the taste of the formula and is an ''activating'' herb in the formula.

Sample Infusion for Amenorrhea
From Herbal Remedies for Women: Amanda McQuade Crawford

Mugwort lf.	(*Artemisia vulgaris*)	1 part
Motherwort	(*Leonurus cardiaca*)	1 part
Peppermint	(*Mentha piperita*)	2 parts
Eleuthero	(*Eleutheracoccus senticosus*)	2 parts
Skullcap	(*Scutellaria lateriflora*)	2 parts
Licorice root	(*Glycyrrhiza glabra*)†	2 parts

Total: 10 parts

Indications: Amenorrhea caused by stress.

To prepare: Infusion using 28 g (1 ounce)/750 mL (3 cups) water steeped 10 to 15 minutes.

Dose: one cup three times daily for 10 to 12 days; then take a 1-week break. If menses does not occur, repeat using half the amount of herbs/3 cups of water. Repeat for up to 3 months.

Rationale: Mugwort and motherwort are included for their specifically emmenagogic actions, whereas eleuthero is included as a nourishing and tonic adaptogen to regulate the HPA axis. Skullcap is a gentle nervine; mint is a digestive tonic and improves the flavor of the formula, as does licorice, which is also an anti-inflammatory, adaptogen, and harmonizer of the entire formula.

Topical Applications
Ginger compress: Use in conjunction with internal treatment. Apply hot directly over the lower abdomen, several times per week until the onset of menses.

*See Plant Profiles: Black cohosh, for cautions when using this herb.

†If there is hypertension, omit the licorice and replace with 1 part each marshmallow and burdock roots.

Treatment Summary for Amenorrhea

- Rule out pregnancy prior to starting any treatment.
- Proper diagnosis of the cause of amenorrhea is essential, as causes may range from stress to hormonal dysregulation, which can be indicative of an underlying disorder such as PCOS. Treatment for primary versus secondary amenorrhea must also be determined.
- General botanical treatment includes the use of herbs for improving hormonal regulation, for example, chaste berry, when there is underlying hormonal dysregulation. Treatment of accompanying conditions (e.g., PCOS) should occur concurrently.
- Emphasis is placed on improving pelvic circulation and uterine tone via the use of warming pelvic stimulants and emmenagogues, and uterotonic herbs, as well as through pelvic movement and exercise, for example, belly dancing or yoga postures.
- Pelvic relaxation is effected through the use of antispasmodics.
- Stress-related factors contributing to amenorrhea are treated with a combination of nervines and adaptogens, for example, milky oats, hops, St. John's wort, motherwort, chamomile, passion flower, skullcap, eleuthero, ginseng, and ashwagandha.
- Adaptogens may be used to improve energy and nutrition when women are energy deficient, underweight, or anemic.
- Proper body weight should be achieved through attention to diet and avoiding excessive exercise. Body image issues sometimes can be addressed through counseling.

What to Expect with Amenorrhea Treatment
If amenorrhea is acute and owing to stress, travel, or other simple disruption of regular lifestyle rhythm, the use of emmenagogues and warming pelvic stimulants can bring on the menses within a couple of days of treatment. In chronic amenorrhea, duration of treatment is usually longer, commonly one or more expected menstrual cycles before the menses becomes regular. The treatment course will also depend on the nature of the underlying cause, for example, if it is PCOS, treatment will be ongoing and it may take 3 to 6 months to see lasting and significant effects.

clinical trials, lowering serum testosterone levels and inducing regular ovulation in one study, and improving testosterone levels and fertility in a group of PCOS patients.[125] It is commonly used by herbalists both in TCM formulae and in combination with Western herbs in individualized patient prescriptions. The effects of this herb suggest it for treatment of amenorrhea, particularly in women with PCOS, although further research is required (Box 5-12).

Additional Therapies

It is essential to address lifestyle, dietary, and psychobiological factors when treating a patient with amenorrhea.

BOX **5-13**

Eclectic Specific Condition Review—A Historical Perspective*—Amenorrhea
David Winston

- **Aconite root** (*Aconitum napellus*)†
  Amenorrhea caused by exposure to cold. Patient feels cold, shivers easily, although the skin may feel hot and dry to the touch.
- **Black Cohosh/Macrotys** (*Actaea racemosa*)
  Amenorrhea with muscular soreness, restlessness, and flushed face. If amenorrhea has been caused by exposure to cold, use with Aconite. If the condition has been caused by anxiety or shock, use with Pulsatilla.
- **Cotton Root bark** (*Gossypium* spp.)
  Delayed menses (not owing to pregnancy) with backache and sense of dragging in pelvis; amenorrhea with an atonic condition of uterus, with feeling of fullness and heaviness in pelvis, as though it needed force to start the flow.
- **Damiana herb** (*Turnera* spp.)
  Delayed or suppressed menstruation in young girls, irregular menses at the early stages of menarch.
- **Life root** (*Senecio aureus*)†
  Amenorrhea caused by poor uterine tonus or subtle hormonal irregularities.
- **Motherwort herb** (*Leonurus cardiaca*)
  Amenorrhea from cold, feelings of anxiety or palpitations.
- **Pennyroyal herb** (*Hedeoma pulegioides*)
  Amenorrhea from environmental stress (cold, damp). Menses suddenly stops during menstrual period.
- **Pulsatilla herb** (*Anemone* spp.)
  Delayed and scanty menstruation, with mental distress; nervousness, restlessness, fearful of imaginary danger; sense of weakness in back and hips at menstrual period; dark lines under eyes.
- **Roman Chamomile flowers** (*Anthemis nobile*)
  Dysmenorrhea and amenorrhea from cold.
- **Spikenard root** (*Aralia racemosa*)
  Suppression of menses from cold, poor pelvic circulation, or stress.
- **Tiger Lily—entire fresh plant** (*Lilium lancifolium*)
  Amenorrhea with burning pain in the ovaries. A sense of weight and downward pressure in the ovaries.
- **Water Smartweed herb** (*Polygonum hydropiper*)
  Suppression of menses from cold, atonicity or impaired circulation, pains in back and legs.
- **Yarrow herb** (*Achillea millefolium*)
  Atonic amenorrhea with chronic leukorrhea

*These herbs are presented for historical perspectives only.
†**Toxic.** Use with caution and careful supervision, under the guidance of a qualified practitioner.

Optimally, a patient should have at least 22% body fat, exercise within moderation, learn stress management, and not smoke. There is a substantial correlation between inadequate body weight, eating disorders, psychological disorders, and amenorrhea. These conditions can lead to severe and even fatal consequences when left untreated. Excessive exercise, whether as part of an athletic training program or as a result of addiction to an ''exercise high'' or a body-image disorder, can result in amenorrhea and other medical consequences. Patients should be referred to physicians, therapists, and nutritionists as appropriate.

There are still many negative connotations about menstruation and female sexuality in our society. Interestingly, the earliest reported case of anorexia and amenorrhea occurred around the year 1000 in Portugal, when Wilgefortis, the King's seventh daughter, in protest of an undesired arranged marriage, went into intense prayer. Her anorexic state was accompanied by loss of her sexual characteristics, and she was released from the marriage. (She was instead crucified by her father!) She became a symbol of a woman who freed herself of her female problems and unwanted men, and later became a patron saint of women with sexual problems or problems associated with childbirth. The association between eating disorders and the desire to separate from sexual development at puberty is well recognized today.[111] It is important to refer patients for counseling to discuss issues of sexuality and menstruation when problematic. Explain to your patient that there is nothing bad or wrong about menstruating; that it is a healthy, normal, physiologic process.

DYSMENORRHEA

Jill E. Stansbury, Aviva Romm

Dysmenorrhea (literally ''difficult menstruation'') is painful menstruation. The pain may be of varying intensity, and is characterized by pelvic discomfort and menstrual cramps that may be wave-like or constant, and which may radiate to the lower back, legs, and vulva. Dysmenorrhea is frequently accompanied by additional symptoms including backache, headache, dizziness, nausea, vomiting, and diarrhea. Discomfort may begin 12 to 24 hours before menses and persist for the first 48 to 72 hours of the period. Estimates of adolescent girls and women experiencing dysmenorrhea range from 45% to 95% internationally, with debilitating to incapacitating dysmenorrhea occurring in approximately 7% to 15% of women. Dysmenorrhea is a major cause of work and school absenteeism, as well as a significant reason for regular use of analgesics and NSAIDs.

Dysmenorrhea is categorized as either primary or secondary dysmenorrhea. Primary dysmenorrhea is pain in the absence of organic pathology. It mostly affects young women, and has an onset after the beginning of ovulatory menstrual cycles. Secondary dysmenorrhea is associated with underlying pathology, for example, endometriosis or ovarian cysts. It typically occurs in the third and fourth decades of life, and presents with painful periods that have often become increasingly severe. Dysmenorrhea is more prevalent in smokers. It typically improves in most women after a full-term pregnancy.

PATHOPHYSIOLOGY

Primary dysmenorrhea is caused by myometrial contraction induced by excessive cyclic prostaglandin $PGF2_{\alpha}$ production in the secretory endometrium. Dysmenorrheic women appear to produce as much as seven times more $PGF2_{\alpha}$ than asymptomatic women. Excessive prostaglandin also leads to increased intrauterine pressure. Concomitantly, this same form of prostaglandin causes smooth muscle contractility in other muscles, leading to other symptoms associated with dysmenorrhea. The greatest menstrual release of prostaglandins occurs in the first 48 hours, the time of greatest symptom intensity. The etiology of secondary dysmenorrhea is the presence of underlying pelvic pathology.

SIGNS AND SYMPTOMS

- Cramps, spasm, nagging discomfort in the uterus, pelvis and/or lower back, accompanying menstruation
- Pelvic heaviness, fullness, and aching, that is typically, worse when upright and active, and remits somewhat with rest and reclining postures, accompanying menstruation
- Headache, nausea, vomiting, or diarrhea may accompany dysmenorrhea

DIAGNOSIS

Primary and secondary dysmenorrheas are diagnosed by symptom picture, history of onset and occurrence, and the exclusion of underlying structural or pathologic abnormalities (Tables 5-8 and 5-9). Dysmenorrhea is markedly cyclical, with discomfort occurring just prior to or during the menstrual period.

DIFFERENTIAL DIAGNOSIS

See Tables 5-8 and 5-9.

CONVENTIONAL TREATMENT

Conventional treatment options are the prostaglandin synthetase inhibitors (PGSIs), NSAIDS, and oral contraceptives (OCs).

Prostaglandin Synthetase Inhibitors

Prostaglandin synthetase inhibitors (PGSIs) prevent the synthesis of prostaglandin, thus reducing uterine hypercontractility, pressure, ischemia, and pain. Improvement also occurs in concurrent symptoms including backache, nausea, vomiting, dizziness, leg pain, insomnia, and headache. There is also a reduction in the amount of menstrual blood flow. PGSIs are quick acting, can be taken once symptoms have begun, and are effective in reducing pain in about 80% of dysmenorrheic women. Side effects include GI upset, edema, and skin rash.

TABLE **5-8**

Differential Diagnosis of Primary Dysmenorrhea

Bowel obstruction	Ovarian cysts
Constipation	PID
Endometriosis	Renal inflammatory and infectious disorders
IBS	Renal colic
Intestinal ulcers	Uterine fibroids
Miscarriage	UTI
Musculoskeletal disorders	

TABLE **5-9**

Differentiating Primary and Secondary Dysmenorrhea

PRIMARY DYSMENORRHEA	SECONDARY DYSMENORRHEA
Occurs after menarche with the onset of ovulatory cycles	Occurs in 2nd to 4th decades of life
Occurs in relationship to the menses, usually just prior to and through the first 12 to 72 hours of the menses	May occur during the menses, or before or after the menses
Typically improves over time	Typically worsens over time

Oral Contraceptives

Oral contraceptives (OCs) also work on the principle of decreasing prostaglandin production. Long-term OC use has side-effects and is contraindicated in women who smoke, have high blood pressure, or blood clotting problems. Many women complain of unpleasant side effects with both short and long-term use, especially weight gain and depression.

Nonsteroidal Anti-Inflammatory Drugs

Several families of non-steroidal anti-inflammatory drugs (NSAIDs) are prescribed for the relief of dysmenorrhea, including indomethacin, ibuprofen, and naproxen, and the fenamate drugs. Common names are easily recognizable and include such drugs as Advil, Motrin, and Aleve. Although these drugs may bring quick and temporary relief, they often require increasing doses to maintain efficacy, and sometimes eventually cease to bring relief at all. Gastric bleeding is a problematic side-effect.

In all cases, although medication can bring needed pain relief, it does little to address the underlying causes of prostaglandin overproduction, thus offering little to improve the condition in any real or lasting way.

BOTANICAL TREATMENT OF DYSMENORRHEA

Botanical treatment is highly effective for treating the pain and reducing inflammation associated with both primary and secondary dysmenorrhea. The treatment of secondary dysmenorrhea requires attention to the underlying pathology.

Herbalists subdivide dysmenorrhea into two additional categories: congestive dysmenorrhea and spasmodic dysmenorrhea.[150] In the former, there is scant or difficult blood flow, a feeling of pressure, congestion, or dull aching in the pelvis, and a sense of stagnation or bogginess in the uterus felt by the woman. Treatment emphasizes the use of uterotonic and astringent herbs that promote uterine circulation, reduce uterine blood congestion and stagnation, and facilitate the expulsive action of the uterus.[150] Improving uterine blood circulation is also a conventional pharmacologic strategy, but the pharmaceutical agents commonly used may have side effects.[151] Herbs used may include blue cohosh, dong quai, ginger, and yarrow. Spasmodic dysmenorrhea presents with spastic, cramping pain. Treatment focuses on antispasmodics, anodynes, analgesics, and sedatives, commonly cramp bark and black haw, wild yam, and black cohosh. Most commonly, these strategies are combined in a composite approach.

Treatment with herbal antispasmodics and analgesics can bring significant prompt relief. The goal of the herbalist, however, is not to simply eliminate acute pain but to prevent chronicity of the problem. As with other conditions, the botanical practitioner applies a variety of therapeutic strategies to affect not only the local symptoms, but to reduce the systemic factors that lead to these. In the case of dysmenorrhea, herbs are incorporated for their antispasmodic, tonic, and analgesic effects, as well as for their ability to reduce excessive production and circulation of inflammatory mediators and normalize the hormones. Herbs are also incorporated to improve sluggish pelvic circulation and relieve engorgement and pressure. Herbalists take psychogenic factors into consideration, providing nervines and adaptogens when appropriate.[150] Hormonal dysregulation is evaluated and treated as necessary, as part of an overall protocol. Finally, if there is constipation, this is treated as well, to reduce pelvic discomfort and pressure and prevent hormonal dysregulation via adequate bile–bowel axis elimination of estrogens.

Treatment of acute and chronic dysmenorrhea relies upon a combination of the most effective herbs for this condition. Although certain single herb drugs, such as cramp bark may be used effectively for reduction of acute uterine spasms, a combination of uterine antispasmodics and tonics is usually prescribed. A number of herbs may actually act as both (e.g., cramp bark, black cohosh, blue cohosh), which may seem contradictory; however, uterine physiology actually depends upon a coordinated action of the uterine muscles, based on adequate contractile and relaxation ability.[150] A number of herbs seem, by their clinical actions, able to effect regulation of uterine activity.

Herbs are given with a variety of scheduling approaches as appropriate for the women's complaints, as follows:

- Throughout the month to treat chronic dysmenorrhea
- Every 3 to 4 hours for several days prior to the onset of the period to prevent or mitigate pain
- Frequently at the onset of the period to reduce acute pain. Treatment for acute pain is given in a schedule of frequent, small doses until relief is achieved, frequently as every 15 to 30 minutes if pain is severe (Table 5-10).

Discussion of Botanicals

Black Cohosh

Black cohosh is spasmolytic and anti-inflammatory to the smooth and skeletal muscles, making it particularly useful in the treatment of dysmenorrhea with associated aching discomfort in the lower back and legs. It was used by the Eclectics for this purpose, and continues to be used extensively for dysmenorrhea by modern herbalists as well.[152–154] The salicylates and gallic acid in black cohosh are analgesic and anti-inflammatory; this may help to reduce prostaglandin excess if given before the period.[150,155] Ferulic and isoferulic acids are inhibitors of leukotriene production.[7] Black cohosh is approved by the German Commission E for the treatment of premenstrual complaints and dysmenorrhea.[156,157] Black cohosh is indicated for muscular pains, nervous tension, and has been noted to have anti-inflammatory and analgesic effects.[154]

Blue Cohosh

Blue cohosh is indicated when there is dysmenorrhea owing to uterine atony. It was popular among the Eclectics, and continues to be used by herbalists as a uterine tonic, promoting effective uterine contractions and relieving spasticity, in conjunction with uterine spasmolytic.[150,158] Blue cohosh is an emmenagogue, and uterotonic. The quinolizidine alkaloids N-methylcysteine and sparteine are believed to responsible for caulophyllum's oxytocic, stimulatory effect on the uterine muscle.[154] Its steroidal saponins, caulosaponin, caulosapogenin, and caulophyllosaponin also may have an effect on the uterus. It typically constitutes only a small fraction (i.e., 20%) of a formula owing to its potential hypertensive activity and toxicity.

Chamomile

Chamomile is an effective antispasmodic and anti-inflammatory useful in the treatment of menstrual discomfort and bowel disorders.[154,157] Water extracts of chamomile have been shown to enhance uterine tone in isolated animal uterine samples. Other investigations have demonstrated chamomile to possess weak estrogenic and progesteronic activity. The antispasmodic activity of chamomile has been credited to a number of flavonol glycosides. Apigenin is the most mentioned of the over 20 flavonoids, and currently thought to be the strongest antispasmodic agent in *Matricaria*. German studies have shown that the flavonoids in chamomile are a stronger antispasmodic than papaverine, from the opium poppy. It is also a reliable nervine, used as a mild sedative.

TABLE **5-10**

Botanical Treatment Strategies for Dysmenorrhea

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Relieve pain and relax cramping	Uterine Antispasmodics, Analgesics	*Actaea racemosa*	Pulsatilla
		Anemone pulsatilla	Dong quai
		Angelica sinensis	Black cohosh
		Corydalis ambigua	Corydalis
		Dioscorea villosa	Wild yam
		Foeniculum vulgare	Fennel
		Leonurus cardiaca	Motherwort
		Matricaria recutita	Chamomile
		Paeonia lactiflora	Peony
		Piscidea piscipula	Jamaican dogwood
		Viburnum prunifolium	Cramp bark
		Viburnum opulus	Black haw
	Anti-inflammatories	*Glycyrrhiza glabra*	Licorice
		Zingiber officinalis	Ginger
	Utero-tonics	*Achillea millefolium*	Yarrow
	Uterine astringents/vascular decongestants	*Caulophyllum thalictroides*	Blue cohosh
		Leonurus cardiaca	Motherwort
		Mitchella repens	Partridge berry
		Rubus idaeus	Red raspberry
Improve Pelvic circulation	Circulatory stimulants; ''Blood movers''	*Angelica sinensis*	Dong quai
		Paeonia lactiflora	Peony
		Zingiber officinalis	Ginger
Support liver's function in hormonal conjugation, detoxification, and elimination	Hepatic alteratives	*Arctium lappa*	Burdock
		Berberis aquifolium	Oregon grape
		Taraxacum officinale	Dandelion root
Relieve constipation	Aperients/Laxatives	*Taraxacum officinale*	Dandelion root
		Rumex crispus	Yellow dock
Topical applications for pain relief		Heat	
		Ginger fomentations	
		Essential oil applications/baths: Chamomile EO, Caraway EO, Fennel EO, Peppermint EO	

This makes it especially valuable in the treatment of dysmenorrhea with concurrent diarrhea, bloating, and gas, as well as anxiety and irritability. Weiss recommends the tea be sipped hot for rapid reduction of menstrual cramps.[159] It is not considered one of the stronger uterine antispasmodics; however, it makes an excellent addition to formulae, is a pleasant infusion to sip when there is pain, and has a marked effect on GI discomfort.

Corydalis

Corydalis is a highly effective analgesic that may be used in the treatment of congestive and spasmolytic dysmenorrhea. It has also demonstrated analgesic effects in the treatment of neuralgia and headache. The analgesic potency is considered to be 1% to 10% of that of opium.[160] Although not commonly known by Western herbalists as a treatment for dysmenorrhea, this herb should be considered for acute spasms associated with dysmenorrhea, and also may be of use in treating associated headache and musculoskeletal discomfort.

Cramp Bark/Black Haw

Cramp bark and black haw are considered among the most important and reliable uterine antispasmodics and tonics by herbalists, midwives, and naturopathic physicians.[161] They were extensively used by the Eclectics for dysmenorrhea, with numerous references throughout the Eclectic literature on their efficacy.[150,152,161,162] The actions of the herbs are so similar that they are frequently used interchangeably. Owing to slight variations in their chemistry, there may be minor therapeutic differences and strength, but herbalists do not seem to consider these consequential. Both are considered effective uterine antispasmodics, used for sedating pain and relieving menstrual disorders, especially dysmenorrhea and amenorrhea.[150,157,161] They are also considered uterotonic. Studies have been limited. In vitro and in vivo experiments have repeatedly demonstrated its effectiveness as a spasmolytic for the uterine musculature, an effect which is producible with oral administration.[154,157,161] The mechanism of action is unknown, but the herb is

Figure 5-5 Cramp bark (*Viburnum opulus*). (Photo by Martin Wall.)

suspected to contain a number of constituents that act on the uterine musculature, most notably scopoletin and aesculetin, which are believed partly responsible for their spasmolytic activity.[157] Flavonoid constituents have also been identified, including amentoflavone. Amentoflavone has been noted to inhibit cAMP phosphodiesterase in human platelets. No clinical trials have been conducted using cramp bark or black haw. Cramp bark was listed as a sedative and antispasmodic in the USP from 1894 to 1916 and the NF from 1916 to 1960.[154,161] *V. opulus* and *V. prunifolium* are used in acute formulas, often combined with other sedating herbs, and are also used in formulae for longer-term treatment, combined with other uterotonic and hormone-regulating herbs (Fig. 5-5).

Dong Quai

Dong quai has been used in TCM for the treatment of gynecologic complaints, including dysmenorrhea, since at least the sixteenth century.[163] It is used for the treatment of the TCM diagnoses of ''blood stasis'' and ''blood vacuity,'' which are associated with the western diagnoses of amenorrhea, dysmenorrhea, uterine fibroids, and endometriosis.[161] In spite of its long history of use for these conditions, few clinical trials have been conducted. In a 1988 study, Gao et al. administered both ligustilide (an isolated constituent believed responsible for uterine relaxant activity) 150 mg three times daily, and dong quai aqueous extract tablets, 2 g three times daily for 3 to 7 days during menstruation to women with dysmenorrhea. The ligustilide group had an effectiveness rate of 77% compared with 38% for the dong quai extract. Reported side effects included nausea, dizziness, and an increase or decrease in menstrual flow. Dong quai's ability to relax smooth muscle is thought to be due to its volatile oil-containing fraction, especially the phthalides. The aqueous extract, which contains ferulic acid, appears to act as both a uterine stimulant and relaxant.[161] Dong quai may also reduce tissue congestion through enhanced blood and lymph circulation. Animal studies have shown *A. sinensis* to have a general analgesic and anti-inflammatory effect.[164] Dong quai also contains nicotinic acid, which is believed to have a blood vessel relaxing or vasodilating action. The vasodilatory effects mentioned in the preceding also appear due to the coumarin compounds in dong quai. Many women have found dong quai to improve menstrual cramps. Interestingly, several studies have shown dong quai to act as a muscle relaxant overall, but to stimulate the uterus briefly before relaxing it.[165,166] This curious action is likely the result of two chemical constituents in *Angelica* that have opposite actions on the uterus. Animal studies (rabbits, cats, dogs) have shown *Angelica* to increase the ''excitability'' of the uterus. Like other muscles, uterine spasms may occur when the uterine muscle is out of shape.[167] Because dong quai dilates the blood vessels and improves circulation in the uterus, regular use can sometimes make menstrual flow heavier.[167] Many herbalists recommend that dong quai be stopped during the actual menstrual period in individuals prone to heavy menses.[168] Dong quai is typically used in combination with other herbs, and is rarely used singly. Bone suggests its use in combination with *Corydalis, white peony*, and *Ligusticum* for the treatment of dysmenorrhea.[154]

Fennel

Fennel seeds have been used to promote menstruation, alleviate the symptoms of the female climacteric, and increase libido. Fennel essential oil (FEO) also possesses emmenagogue and galactagogue properties. Seeds of fennel are used in folk remedies for treatment of dysmenorrhea. This traditional usage might be related to the antispasmodic effects of FEO.[151] Recent research on fennel oil shows promise in the treatment of dysmenorrhea. A 3-month, three-cycle clinical trial of 30 women with dysmenorrhea compared the efficacy of mefenamic acid with a 2% fennel seed essence extract. The first cycle was a control cycle with no medications administered; in the second cycle women were treated with the pharmaceutical drug, and in the third cycle women received the fennel extract. Results were based on a self-scoring system. Both treatment groups showed improvement in symptoms compared with the control cycle. Mefenamic acid had a more potent effect than fennel on the second and third menstrual days; however, the difference on the other days was not significant. No complications were reported in mefenamic acid treated cycles, but five people (16.6%) withdrew from the study owing to fennel's odor, and one person (3.11%) reported a mild increase in the amount of her menstrual flow. The authors of the study concluded that essence of fennel can be used as a safe and effective herbal drug for primary dysmenorrhea; however, it may have a lower potency than mefenamic acid in the dosages used for this study.[169] In an in vitro study administration of different doses, FEO reduced the intensity of oxytocin and PGE2 induced contractions significantly (25 and 50 μg/mL for oxytocin and 10 and 20 g/mL PGE2, respectively). FEO also reduced the frequency of contractions induced by PGE2 but not with oxytocin. LD50 of FEO was obtained in the female rats by using moving average method. Oral administration (200 mg/kg) of fennel seed methanolic

extract exhibited inhibitory effects against acute and subacute inflammatory diseases and showed a central analgesic effect.[170] Estrogenic effects are attributed to the polymers of anethole (dianethole, photoanethole) and lend credence to claims of increased human milk production, promoting menstruation.[171]

Ginger

Ginger root is used both internally and topically as a warming circulatory stimulant and anti-inflammatory in the treatment of dysmenorrhea. The Eclectics used it for this purpose, and it is a common ingredient in herbal formulae for menstrual cramps to this day, taken as a hot tea, tincture, fomentation, or hot bath. Further, its positive effects in relieving nausea have been repeatedly demonstrated (see Plant Profiles: Ginger), making it an especially useful herb when there is dysmenorrhea accompanied by nausea and vomiting. Ginger exerts anti-inflammatory effects in the prostaglandin synthesis pathway, and its activity as a thromboxane synthetase inhibitor and prostacyclin agonist may be responsible for its analgesic effects in dysmenorrhea.[154]

Jamaican Dogwood

Jamaican dogwood is a highly reliable and strong uterine antispasmodic and analgesic for the treatment of acute and severe dysmenorrhea. It is traditionally used for all manner of neuralgic and muscular pains and spasms.[154] It is especially indicated when there is sharp and nearly unremitting menstrual pain, or when pain is causing inability to work or sleep. Herbal literature commonly warns that this herb is toxic in large doses. While this is not a problem at clinically recommended doses, recommended doses should not be exceeded.[154] Reported side effects include nausea, vomiting, and headache, although these are not commonly seen clinically.

Licorice

Herbalists often include licorice as an adjunct herb in formulae for dysmenorrhea, considering it a possible mediator of adrenal and sex hormones, and inflammation. A number of studies have demonstrated prostaglandin inhibition and improvement in dysmenorrhea with the TCM formula shakuyaku-kanzo-to, which consists of equal parts of licorice and peony (see Peony in the following).[172] These studies suggest the need for further research into the role of licorice in the treatment of dysmenorrhea.

Motherwort

Motherwort has been used traditionally for dysmenorrhea, both by herbalists and the Eclectics, and has demonstrated uterine spasmolytic and sedative effects.[154,157] Herbalists consider motherwort a uterine tonic as well, particularly valuable in improving uterine atony owing to pelvic congestion, improving circulation and relieving vascular congestion. Motherwort may reduce pain via a reduction in endogenous inflammatory mediators, enhancing the synthesis of prostaglandins via prostaglandin E9-ketoreductase, important in the synthesis of the desirable PGE2 series prostaglandins.[173] Motherwort may relieve vascular congestion in the pelvis and enhance general circulation. The constituent prehispanolone (a tetrahydrofuran) has been noted to inhibit platelet aggregation via PAF receptor antagonism.[174] Motherwort is a well-known childbirth and post partum botanical having galactagogiue and uterine tonic properties. Motherwort is a hypotensive nervine useful for headache, insomnia, and vertigo as well as gynecologic and obstetrical conditions.[175] It is specific for pelvic pain with concomitant heart palpitations, anxiety attacks, and stress.[152,159] Motherwort may improve uterine tone through a slight stimulating action. Motherwort has been shown to stimulate both H1 and alpha-adrenergic receptors.[176] Motherwort injections were recently shown to improve blood viscosity by decreasing platelet aggregation, fibrinogen content, and erythrocyte deformation. *Lectins* extracted from motherwort seeds are noted to affect red blood cell agglutination, and are credited with some of the blood flow enhancing effects.[177] Another species, the Chinese *Leonurus heterophyllus*, is noted to contain a constituent able to bind to platelet-activating factor (PAF) receptors.[174] In addition to lectins, motherwort contains phytosterols, flavonol and iridoid glycosides, and the alkaloid leonurine.[178–180] Motherwort is reported to have uterotonic effect throughout the European and Chinese literature and is supported by modern animal research.[181] *Leonurine* has caught the attention of pharmaceutical researchers and is able to be synthesized. Synthetic *leonurine* has also displayed uterotonic activity in both in vivo and in vitro experiments.[182] Motherwort contains phytosterols, flavonol, and iridoid glycosides, including leonuride. It contains the alkaloids leonurine, leonurinine, and stachydrine.[178,183] Motherwort also contains volatile oils, tannins, a bitter substance named *leonurin*, and vitamin C (Fig. 5-6).

Peony

Peony is an important herb in TCM for the treatment of dysmenorrhea and muscle cramping. Paeoniflorin has exhibited smooth muscle relaxant ability in in vitro models (rat stomach and uterus) and it has demonstrated in vivo activity, analgesic, and spasmolytic activity. Paeoniflorin also demonstrated inhibition of twitch responses in skeletal muscles, an effect that was potentiated in vitro and in vivo by the addition of glycyrrhizin from licorice.[160] Additionally, clinical trials have demonstrated positive results in the treatment of dysmenorrhea owing to ''qi and blood stasis'' (with licorice root), a reduction serum and free testosterone in women with PCOS (with licorice), and an improvement in clinical symptoms and reduction in size of fibroids in an open study of 100 women (with *P. suffructicosa, Poria cocos, Cinnamomum cassia*, and *Prunus persica*).[160,184] Several clinical trials have been conducted with the TCM herbal medicine shakuyaku-kanzo-to for the treatment of dysmenorrhea. The formula consists and an equal amount each of peony and licorice. It appears that this blend may exert its action against dysmenorrhea through preventing prostaglandin production.[172] This suggests that this herb and traditional herbal combinations may

Figure 5-6 Motherwort (*Leonurus cardiaca*). (Photo by Martin Wall.)

Figure 5-7 Wild yam (*Dioscorea villosa*). (Photo by Martin Wall.)

play a role not only in symptom reduction with primary dysmenorrhea but in treating the underlying causes associated with secondary dysmenorrhea. Peony may be used in decoction or tincture in traditional TCM formulae, or in combination with other herbs in Western botanical formulae.

Pulsatilla

Pulsatilla is considered specific for painful or inflammatory reproductive conditions, including dysmenorrhea.[154,185] Its sedative action is beneficial when there is nervous tension causing or accompanying dysmenorrhea, and it also exerts pronounced effects on uterine pain.[150] No pharmacologic or clinical trials were identified on this herb. Only the dried herb is used. Fresh plant contains an irritating component, protoanemonin. The German Commission E has not approved the use of Pulsatilla species on the basis of lack of evidence of efficacy. It warns against fresh plant use, which can cause severe irritation of the skin and mucosa, and in high doses can lead to renal and urinary side effects.[156,185] This plant is teratogenic and abortifacient in cattle, and should not be used during pregnancy.[185]

Wild Yam

Wild yam has been used historically to treat spastic, dyspeptic pain of abdomen, uterus, gallbladder, and still finds popular use as such among herbalists. It was highly popular among the Eclectic physicians as an antispasmodic treatment for dysmenorrhea with spasmodic, colicky pains, for which it was given every few hours. Wild yam continues to be one of the primary uterine antispasmodics used for dysmenorrhea by contemporary herbalists.[150] No contemporary research is available on its effects on the uterine muscle. An in vitro analysis in 1916 failed to show effects on the uterine muscle.[186] A 1997 report demonstrated that diosgenin, a constituent in wild yam, exerts intestinal anti-inflammatory activity when consumed as a dietary supplement (Fig. 5-7).[187]

Yarrow

Yarrow is used in traditional and folk herbal medicine to relieve menstrual pain. Wichtl compares its actions, both internally and topically, to chamomile flowers. Its sesquiterpene lactones lend antiphlogistic activity, whereas its spasmolytic activity is attributed to its flavonoids.[157] Research has been limited, but some

investigations have shown yarrow to act as an antispasmodic and anti-inflammatory making it useful for pain and uterine cramps.[188,189] Yarrow may be taken at a low dose all month, or more aggressively for menstrual cramps when symptomatic relief is needed.

Other Herbs

Bromelain

Cervical application of bromelain improved symptoms in nulliparous women with severe primary dysmenorrhea. Bromelain was applied locally to the cervix in a phosphate buffer solution (pH 5.6). The solution was slowly poured into the vagina via a rubber catheter attached to a 20-cc syringe with the patient in Trendelenburg position. The solution remained in the vagina for 10 minutes. Following the application of bromelain, there was some degree of cervical dilatation in each patient. The uterine isthmus was affected dependent on the phase of the menstrual cycle. All patients obtained instantaneous relief of their primary dysmenorrhea. An unspecified number of patients with disabling dysmenorrhea was treated with solution of bromelain. Of 64 patients treated, 40 obtained immediate relief. Only fair to poor results were achieved in patients with secondary dysmenorrhea due to other gynecologic diseases (Boxes 5-14 to 5-16).[7]

NUTRITIONAL CONSIDERATIONS

A multifactorial approach that incorporates an anti-inflammatory diet and the use of essential fatty acids is an indispensable aspect of botanical treatment for chronic dysmenorrhea.

A diet rich in whole grains, plenty of fruits and vegetable, legumes, fish, and poultry can help to minimize dysmenorrhea.

Fish Oil Supplementation and the Anti-Inflammatory Diet

Supplementation of the diet with omega-3 fatty acids, and following an anti-inflammatory diet are indicated to reduce the production of the inflammatory prostaglandin-2 series (i.e., $F_{2\alpha}$). Arachidonic acid, which is present in animal fats and dairy products, is converted into $F_{2\alpha}$, thus a reduction in red meat and dairy products is recommended. Supplementation of omega-3 fatty acids can be accomplished by increasing the amount of cold-water fish in the diet to two to three times per week or adding a fish oil supplement to supply EPA and DHA. One placebo-controlled, crossover RCT of adolescent girls (n = 42) with primary dysmenorrhea showed improvement of subjectively rated symptoms in 73% of girls taking a fish oil supplement with 720 mg DHA, 1080 mg EPA, along with 1.5 mg vitamin E (see vitamin E in the following) for 2 months.[186] A double-blind RCT demonstrated reduction in amount of analgesics needed in dysmenorrhea women after 45 and 90 days of treatment with an extract of Antarctic brill, compared with control and women taking omega-3 fish oil.[155,186] Salmon, tuna, and halibut contain linolenic acid, which helps to relax the muscles by manipulating production of the PG1, 2, and 3 series to increase the anti-inflammatory 1 and 3 series and decrease the pro-inflammatory 2 series.

BOX **5-14**

Botanical Prescriptions for Dysmenorrhea

Tincture for Acute Menstrual Cramps[1]

Take for acute pain during menses. Can be taken for several days prior to anticipated onset of menses.

Cramp bark, black haw	*(Viburnum opulus or prunifolium)*	30 mL
Wild yam	*(Dioscorea species)*	20 mL
Motherwort	*(Leonurus cardiaca)*	20 mL
Black cohosh*	*(Actaea racemosa)*	20 mL
Ginger	*(Zingiber officinalis)*	10 mL
		Total: 100 mL

Dose: 2 to 4 mL tid

For severe cramping pain, take the above tincture every 2 hours; add 1 mL Jamaican dogwood (*Piscidia piscipula*) every 2 hours, not to exceed six doses per day, or more than 2 days.

Tincture for Acute Menstrual Cramps[2]

For *severe*, acute cramps

Cramp bark, black haw	(*Viburnum* spp.)	50 mL
Jamaican dogwood	(*Piscidia piscipula*)	30 mL
Cordydalis	(*Corydalis ambigua*)	10 mL
Pulsatilla	(*Anemone pulsatilla*)	10 mL
		Total: 100 mL

Dose: Take 1.5 mL every 20 minutes for six doses, or 2 mL every 30 minutes for four doses to relieve acute pain. This can be repeated twice daily at least 4 hours apart but should not exceed this dose.

Rationale: The herbs in this formula are included for their combined analgesic and antispasmodic effects.

Uterine Tonic Tincture

Use throughout the menstrual cycle to improve uterine tone and prevent recurrence of dysmenorrhea. Take for a minimum of three menstrual cycles for improvement.

Motherwort	(*Leonurus cardiaca*)	20 mL
Peony	(*Paeonia lactiflora*)	20 mL
Licorice root	(*Glycyrrhiza glabra*)	20 mL
Dong quai	(*Angelica sinensis*)	15 mL
Oregon grape root	(*Berberis aquifolium*)	15 mL
Blue cohosh	(*Caulophyllum thalictroides*)	10 mL
		Total: 100 mL

Dose: 3 to 5 mL tid

Rationale: Motherwort is included as a uterotonic, antispasmodic, bitter nervine; the next three herbs in the formula, peony, licorice, and dong quai all possess anti-inflammatory actions, whereas peony and dong quai are also antispasmodic and are specific TCM herbs for dysmenorrhea. Oregon grape is used as a hepatic bitter to promote liver detoxification and as a choleretic to increase hormonal excretion via the bile-bowel axis. Blue cohosh is a specific uterine muscle tonic, whereas licorice is also included in the formula as a harmonizer and to improve the taste.

[†]See Plant Profiles: Black Cohosh for cautions when using this herb.

BOX 5-15

Antispasmodic Oil for Topical Application

Chamomile essential oil	Caraway EO
Fennel EO	Peppermint EO

Place ½ tsp of each essential oil into a 4-oz squeeze bottle of olive or Hypericum oil. Massage 1to 2 tsp into the lower abdomen and cover with heat for an analgesic, antispasmodic effect. To prevent a skin reaction test a single drop of essential oil on the inner wrist and wait 5 minutes before applying essential oils to larger skin surfaces.

BOX 5-16

Hot Ginger and Chamomile Fomentation

Prepare a strong infusion of chamomile and ginger tea using 2 tbs chamomile blossoms and 2 tbs fresh-grated ginger root/liter of boiling water. Steep 20 minutes and strain. Soak a cloth in the infusion, wring out, and apply as hot as can be tolerated. A hot water bottle and a warm towel can be applied over the fomentation to retain the heat. This can be repeated several times daily. Alternatively, the recipe can be doubled and added to a hot hip bath.

Seeds that contain linoleic acid such as pumpkin, flax, sesame, and sunflower also increase PGE3 levels.[7] Mercury contaminations in cold water fish is likely to be significantly higher than in high-quality fish oil screened for heavy metals.

Magnesium

An open trial of a small group of women with primary dysmenorrhea who were given 4.5 mg oral magnesium pidolate 7 days prior to the onset of menses through day 3 of menstruation showed a reduction in dysmenorrhea with no reported side effects. Magnesium also had a therapeutic effect on back pain and lower abdominal pain on the second and third days of the menstrual cycle in women with primary dysmenorrhea who were given magnesium or placebo beginning the day preceding menstruation and on the first 2 days of the menstrual cycle. Magnesium is a cofactor in delta-6 desaturase involved in anti-inflammatory prostaglandins (PGE1) and exerts a relaxing effect on the skeletal and smooth cramping. Magnesium is contraindicated in heart block and severe renal disease.[155] The recommended dose varies but is generally 300 to 600 mg three times daily for several days prior to the onset of the period.[186] Excessive doses can lead to serious toxicity.

Calcium

Two trials demonstrate the effectiveness of calcium in reducing cyclic uterine pain. Calcium supplementation was effective in reducing premenstrual pain (not menstrual) in a prospective, randomized, double-blind, placebo-controlled, parallel-group, multicenter clinical trial of premenstrual syndrome. Subjects (n = 497) were given 1200 mg calcium or placebo daily for three menstrual cycles. Subjective rating scales of 17 symptoms revealed significantly lower scores for all pain measures in the treatment group during the luteal phase of the third menstrual cycle, whereas scores did not change

Treatment Summary for Dysmenorrhea

- Herbalists categorize dysmenorrhea into congestive and spasmodic types. Both can occur concurrently, but identifying the characteristic features of the complaint can help to narrow treatment choices.
- Treatment of congestive dysmenorrhea emphasizes the use of uterotonic and astringent herbs. Herbs used may include blue cohosh, dong quai, ginger, and yarrow. Uterine tonics are used to improve pelvic and uterine circulation, relieve local congestion, and improve pelvic tone. Examples include yarrow, blue cohosh, motherwort, partridge berry, and red raspberry leaf. Herbs to move the circulation include dong quai, peony, and ginger.
- Spasmodic dysmenorrhea is treated with antispasmodics, analgesics, anodynes, and sedating herbs including, for example, cramp bark, black haw, wild yam, black cohosh, Jamaican dogwood, motherwort, dong quai, and pulsatilla, among many other choices.
- Emphasis is placed on reduction of inflammatory compounds that can cause dysmenorrhea. Anti-inflammatory diet and herbs (i.e., licorice, peony, ginger) can be beneficial, as can supplementation with omega-3 fatty acids with EPO, fish oils, or cold water fish.
- Topical applications can be used for soothing pain relief, and include ginger fomentations, massage with warm essential oils, and hot baths with essential oils.
- Supplementation with magnesium, calcium, and vitamin E has demonstrated varying levels of improved outcomes.
- Stress management, yoga, and exercise have also been shown to be beneficial in the treatment of dysmenorrhea.

What to Expect with Dysmenorrhea Treatment

Acute treatment with analgesics, antispasmodics, anodynes, and sedatives can bring relief within 2 hours of the onset of treatment. Prevention of acute dysmenorrhea, if begun 3 to 5 days prior to the onset of menstruation, can similarly be quickly effective, with pain offset at the next menstruation. Treating chronic dysmenorrhea may require several months' of use of anti-inflammatory herbs and adherence to an anti-inflammatory diet for women to be able to reduce dependence on acute pain relief treatment.

significantly in controls. In a prospective, randomized, double-blind, crossover trial targeted at investigating premenstrual syndrome, calcium carbonate supplementation (1000 mg/day for 3 months) was effective in reducing menstrual pain compared with placebo.[155]

Vitamin E

In a study of vitamin E for dysmenorrhea treatment, 68% of women ages 18 to 21 with spasmodic dysmenorrhea ($n = 100$) improved with 50 mg vitamin E three times daily following two cycles of treatment. After three cycles, 76% of the treated group had improvement; vitamin E can increase bleeding time, so use should be monitored in patients with blood clotting disorders or those taking anticoagulant medication. See fish oil (preceding) for a combined study with vitamin E.[155]

ADDITIONAL THERAPIES

Stress Management and Visualization

Stress management and visualization can be used to address dysmenorrhea. Teaching patients skills in these areas can be a useful adjunct to other strategies. Counseling may be beneficial for some women.

Yoga, Exercise, and Massage Therapy

Light general exercise in the form of walking, stretching, and pelvic exercise can improve pelvic circulation and reduce dysmenorrhea, both preventatively and acutely. Excessive exercise should be avoided. A number of yoga asanas (poses) are specifically indicated for improving pelvic circulation and reducing dysmenorrhea. Receiving massage therapy can also promote general relaxation and reduce musculoskeletal and pelvic tension (Box 5-17).

DYSFUNCTIONAL UTERINE BLEEDING

Linda Ryan

Dysfunctional uterine bleeding (DUB) is defined as excessive, prolonged, unpatterned endometrial bleeding in the absence of organic disease.[190,191] DUB is a subset of abnormal uterine bleeding (AUB), which encompasses all abnormal uterine bleeding regardless of cause.[192]

BOX 5-17

Eclectic Specific Condition Review: A Historical Perspective—Dysmenorrhea*

David Winston

- **Aletris root** *(Aletris farinosa)*
  Labor-like pains and a sense of weakness in the pelvic region, uterine prolapse with pain. Especially useful when a digestive tonic is also indicated.
- **Belladonna** *(Atropa belladonna)*†
  Painful menstruation, skin is cold and clammy, pain extreme, hands and feet ice cold.
- **Black cohosh/macrotys root** *(Actaea racemosa)*
  Muscular pain in the back, loins, and thighs, sense of soreness with dragging pains in the uterus. Dull, intermittent ovarian pain.
- **Black Haw bark** *(Viburnum prunifolium)*
  Cramps in legs; spasmodic dysmenorrhea, uterine colic, severe bearing-down, expulsive pains, painful menstrual disorders
- **Blue cohosh root** *(Caulophyllum thalictroides)*
  Spasmodic uterine pain with a feeling of fullness, weight, and pain extending to the legs. Uterus feels engorged.
- **Cramp Bark** *(Viburnum opulus)*
  Spasmodic uterine pains, expulsive pains. Pain in back and thighs.
- **Gelsemium herb/root** *(Gelsemium sempervirens)*†
  Ovarian pain during menstruation; nervous excitation, nervousness, elevation of temperature
- **Helonias root** *(Chamaelirium luteum)*
  Chronic uterine disorders, with mental depression and irritability; dysmenorrhea with pelvic fullness and heaviness, with a bearing-down sensation.
- **Jamaica dogwood bark** *(Piscicida erythrina)*
  Excruciating neuralgic menstrual pain with intestinal colic, ovarian neuralgia, difficulty sleeping caused by pain.
- **Mistletoe herb** *(Viscum album)*†
  Paroxysms of tearing, rheumatic, or neuralgic pains in dysmenorrhea.
- **Nux vomica seed** *(Strychnos nux-vomica)*†
  Uterine colic, sharp pain at the umbilicus, nausea, vomiting, patient is chilled. Alternate with Pulsatilla.
- **Partridge berry herb** *(Mitchella repens)*
  Chronic uterine congestion, dragging, uneasy sensations, ''weighty feeling'' over lower abdomen. Excellent uterine tonic.
- **Roman Chamomile flowers** *(Anthemis nobilis)*
  Dysmenorrhea and amenorrhea from cold.
- **Sweet Melilot herb** *(Melilotus alba, M. officinalis)*
  Dysmenorrhea associated with lameness in hip and along sciatic nerve; neuralgic pains.
- **Tiger Lily—entire fresh plant** *(Lilium lancifolium)*
  Neuralgic pain in the uterus extending down the inside of the thighs. Dysmenorrhea with uterine prolapse.

*These herbs are presented for historical purposes only.
†Toxic. Use with caution and careful supervision, under the guidance of a qualified practitioner.

After pathologic abnormalities, systemic disorders, or iatrogenic causes have been ruled out, *functional* (endocrinologic) causes are then considered, and resultant uterine bleeding is described by the term dys*functional* uterine bleeding.[193] Some authors further recommend limiting the definition of DUB to apply only to anovulatory cycles allowing for medical differentiation of excessive bleeding in ovulatory cycles to be classified as *functional menorrhagia*, a condition that involves disturbances in endometrial tissue prostaglandin synthesis, other forms of uterine pathology, or systemic causes.[194,195] For the purpose of examining a broader spectrum of support options, this discussion addresses DUB as irregular uterine bleeding without organic pathology.

DUB is a common diagnosis. It is estimated that 5% to 10% of women experience some form of DUB in their lifetime. DUB occurs most commonly at the beginning and end of the reproductive years; 20% of cases occur in adolescent girls, and more than 50% occur in women over age 45. It is estimated that 70% of cases of dysfunctional uterine bleeding occur in anovulatory or infrequent ovulatory cycles. Irregular uterine bleeding accounts for 20% of all gynecologic visits.[7] DUB may be accompanied by pain, can severely and negatively impact on quality of life, including limiting activity, as well as lead to fatigue and increased risk of illness if there is concomitant anemia.[196]

Most abnormal uterine bleeding is the dysfunctional type, but this diagnosis is made only when all other possibilities have been excluded. Primary presenting complaints may include:

- Menorrhagia (excessive bleeding, either in number of days, amount of blood, or both)
- Hypomenorrhea (scanty flow or brief number of days or both)
- Metrorrhagia (bleeding that occurs at times other than the menses)
- Menometrorrhagia (excessive bleeding at irregular intervals)
- Oligomenorrhea (bleeding occurs infrequently; prolonged time between cycles)
- Oligohypermenorrhea (infrequent and heavy)
- Oligohypomenorrhea (infrequent and scant)
- Polymenorrhea (bleeding occurs often; less than 21 days between cycles)
- Amenorrhea (absence or suppression of menstruation)

Occasionally, patients also exhibit signs and symptoms of hypovolemia, such as hypotension, tachycardia, diaphoresis, and pallor. Iron deficiency anemia is a common consequence of excessive menstrual flow, in quantity, duration, or frequency.[191]

Excessive bleeding can refer to amount or duration of blood loss. The average blood loss per normal menstrual cycle is 20 to 60 mL, with median expected blood loss of approximately 30 to 40 mL. Menstrual blood loss of 80 mL or more is considered excessive and increases the risk of iron-deficiency anemia.[198] This can initiate a chronic pattern of cyclical excessive bleeding, as iron deficiency can be an etiologic factor in abnormal uterine bleeding.[199] Prolonged bleeding is defined as bleeding lasting longer than 7 or 8 days; however, 10 days has been suggested as the maximum duration that distinguishes normal from abnormal bleeding.[198]

Heavy but regular menstrual bleeding may occur in normally ovulating women, and is usually a result of minor hormonal disturbances.[5] Many women who present with complaints of excessive menstrual bleeding have blood losses within the normal range.[200,201] Conversely, in one study, 40% of women with excessive uterine bleeding (>80 mL) reported that their periods were normal or even light. Some women with light periods viewed their bleeding as severe.[191,202] Practitioners routinely assess menstrual blood loss by inquiring about the number of sanitary pads or tampons that are used during the menstrual period. This is the most practical method of evaluation, as volumetric measurement of actual blood loss is not feasible. A clinically objective measurement is to assess blood hemoglobin and serum ferritin levels. Two-thirds of women with excessive menstrual bleeding develop iron-deficiency anemia.[203]

PATHOPHYSIOLOGY

Determining the ovulatory status helps narrow the etiologic possibilities contributing to dysfunctional uterine bleeding. Life stage may also provide some clue as to the etiology of DUB. A discussion of these factors follows (Box 5-18).

Additional factors that may influence the development of DUB and menstrual bleeding disorders include prenatal exposure to DES, BMI and dieting, perceived stress (blood coagulation factor activity may decline when an individual is under prolonged stress), cigarette smoking, obesity, mild hypothyroidism, inherited bleeding disorders, IUD devices (unless they contain progesterone), and use of aspirin or oral anticoagulants.[198]

Ovulatory Dysfunctional Uterine Bleeding

In normal ovulatory cycles, progesterone production from the corpus luteum converts the estrogen-primed proliferative endometrium to a secretory endometrium, which sheds cyclically if pregnancy does not occur. Ovulatory DUB is less common than anovulatory DUB, and the bleeding, although abnormally heavy, is usually regular. Ovulatory DUB may be owing to abnormalities in the 2-week luteal phase of menstruation that occurs prior to menstruation. It can also result from an ''atrophic endometrium'' that can result from a high progesterone:estrogen ratio. A lack of cell-building estrogen causes the endometrium to shed and bleed irregularly. This may occur in women who take over-the-counter progesterone creams or progesterone-only contraceptives.

Anovulatory Dysfunctional Uterine Bleeding

Any disruption in the cyclic release of GnRH, FSH, or LH can result in anovulation. This is most often owing to immaturity of the HPO axis just after menarche and decreased sensitivity of the ovary to gonadotropin stimulation in perimenopausal women. Most anovulatory DUB is due to estrogen withdrawal or estrogen breakthrough bleeding (EbB).

In anovulatory cycles, follicular growth occurs with stimulation from FSH; however, because estrogen

BOX 5-18

Overview of Possible Etiologies in Dysfunctional Uterine Bleeding (DUB)

- Hypothalamic-pituitary-ovarian (HPO) axis disorder. This is most commonly seen in the post pubertal period when normal hypothalamic function is not yet well established.[196]
- Hormone imbalance owing to insufficient estrogen production, or disordered estrogen to progesterone ratio.[192]
- Hormone imbalance resulting in excess estrogen, either from endogenous production or exogenous sources. Women with higher levels of estrogens often have prolonged intervals of amenorrhea followed by excessive episodes of bleeding.[234]
- Vascular fragility in cyclic angiogenesis. The continuous estrogen stimulation leads to a vascular, friable endometrium that may bleed intermittently or slough at irregular intervals.[235–237]
- Iron deficiency.
- Stress.[205,238]
- Excessively overweight women often have high estradiol levels because fat cells produce the aromatase enzyme that causes the body to make more estrogen.[239] A recent study concluded that obesity has been found to increase endometrial thickness independently.[240] Excessive endometrial thickness commonly results in menorrhagia when the lining is shed.
- Liver clearance of hormones—optimizing metabolic clearance of estradiol. If estrogen cannot be conjugated properly, it will not be excreted normally and levels will remain high.[192,205,232]
- Eating disorders—anorexia nervosa, bulimia. A study of 117 adolescent girls found a high percentage (43.7%) of those with menstrual dysfunction also had eating disorders.[241]
- Overexercise—In athletes or overexercisers.[242]
- Disordered prostaglandins.[195,201,243]
- Increase in fibrinolytic activity within the uterine cavity.[201]
- Thyroid conditions.[244]
  - Hypothyroidism—reduced levels of SHBG causes an increase in estrogen availability.
  - Hyperthyroidism—promotes increased conversion of androgens to estrogens.

levels remain below threshold there is a lack of LH surge and ovulation fails to occur. Consequently, no corpus luteum is formed and no progesterone is secreted. The endometrium continues its proliferative phase. When the follicle degenerates, estrogen levels drop and estrogen withdrawal bleeding occurs.[204] EbB may exhibit the pattern of normal menses, however, EbB generally occurs as scant (hypomenorrhea), irregular bleeding that may continue for a prolonged period. The low estrogen levels prevent excessive endometrial thickening between cycles, which accounts for the light-bleeding pattern.

EbB also occurs when unopposed estrogen levels are sustained, resulting in excessive endometrial proliferation and thickness. In the absence of progesterone, the endometrium does not develop the spiral arterioles of the secretory phase and the endometrial tissue eventually becomes fragile and breaks down erratically.[193,205,206]

SUMMARY OF ETIOLOGIES AS ASSOCIATED WITH LIFE STAGES

Adolescence

Owing to immaturity of the HPO-axis there is a pattern of erratic ovulation in adolescents. FSH acts on ovarian cells, producing estrogen; however, either the estradiol concentrations are not high enough to stimulate positive feedback of LH release, or the H–P complex fails to trigger the LH surge. Inadequate LH to induce ovulation results in the absence of luteal phase progesterone. This leads to a prolonged proliferative phase of the endometrium resulting in excessive thickness. Uncoordinated sloughing of endometrium occurs either in response to estrogen withdrawal or owing to insufficient blood supply for the excessive endometrial tissue. There is usually prolonged bleeding owing to a lack of chemical mediators (prostaglandins and thromboxane), that normally contribute to cessation of menses in the normal cycle. The presence of these chemicals is relative to the secretion of progesterone.[192]

Reproductive Age

Women of reproductive age more commonly experience DUB associated with ovulatory cycles that exhibit a luteal phase defect. The hormones do not support an adequate corpus luteum; therefore, progesterone secretions are insufficient. One study found that 70% of luteal phase defect patients had excessive prolactin levels.[207] Cycles are usually regular, but bleeding is prolonged and/or excessive. Low estrogen production and the consequent poor endometrial development typically results in estrogen withdrawal bleeding. In these cases, there are rising estrogens, although not enough to trigger LH, but enough to inhibit further FSH release, which, in turn, inhibits estrogen production by the ovaries. Excess, sustained estrogen levels resulting from anovulation is commonly associated with oligomenorrhea followed by acute, heavy ''estrogen breakthrough'' bleeding. An additional consideration for DUB in the reproductive years is excessive exercise. Studies of female athletes demonstrate a correlation between inadequate LH secretion by the pituitary gland and excessive exercise.[208]

Polycystic Ovarian Syndrome

Polycystic ovarian syndrome (PCOS) can contribute to DUB in women or reproductive age. In this condition, there is a hypersecretion of LH and suppression of FSH, which results in chronic anovulation. PCOS is associated with insulin resistance and common clinical presentations include hirsutism (from excess androgen

production), acne, elevated lipids, male-pattern baldness, and truncal obesity.

Other factors contributing to DUB in women of reproductive age include:
- Hypothyroidism
- Hyperthyroidism
- Diabetes mellitus
- Androgen excess disorders

Perimenopausal Years

During this stage, the ovaries become less responsive to gonadotropins and production of active follicles declines. In addition, the active follicles produced do not secrete sufficient estrogen to trigger the LH surge needed for ovulation and corpus luteum formation. DUB at this stage may be attributable to this anovulatory pattern.[209] Approximately 50% of all cases of DUB occur in women age 40 to 59 years old.[196]

Postmenopausal Years

In the absence of exogenous hormone therapy, postmenopausal bleeding is abnormal and women presenting with such should be investigated for neoplastic lesions. (See Table 5-12.)

DIAGNOSIS

Dysfunctional uterine bleeding is a diagnosis of exclusion. To accurately evaluate this condition it is important to determine when the menstrual pattern changed, determine whether or not pregnancy or pelvic infection is present, and particularly to document the frequency, duration, and amount of bleeding. Initial testing may include complete blood cell count, protime, activated partial thromboplastin time, iron profile, serum creatinine, TSH level, factor VIII level, von Willebrand factor antigen, ristocetin cofactor, platelet aggregation studies, a Pap smear, and a pregnancy test. Standard invasive diagnostic tests include the combination of hysteroscopy and curettage or guided biopsy, with the exception of adolescent patients, who generally do not require invasive diagnostics.[190,200] In women of childbearing age who are at high risk for endometrial cancer, the initial evaluation includes endometrial biopsy; saline-infusion sonohysterography or diagnostic hysteroscopy is performed if initial studies are inconclusive or the bleeding continues. Women of childbearing age who are at low risk for endometrial cancer may be assessed initially by transvaginal ultrasonography. Postmenopausal women with abnormal uterine bleeding should be offered dilatation and curettage; if they are poor candidates for general anesthesia or decline dilatation and curettage, they may be offered transvaginal ultrasonography or saline-infusion sonohysterography with directed endometrial biopsy.[210]

DIFFERENTIAL DIAGNOSIS

Disorders that need to be excluded are:
- Pregnancy; hydatidiform mole
- Coagulation defects—adolescents with acute menorrhagia have a 20% to 30% incidence of a coagulation disorder, such as, von Willebrand's disease, idiopathic thrombocytopenic purpurea (ITP), leukemia[203]
- Trauma to the vulva, vagina, or cervix
- Organic pathologies, such as, diabetes mellitus, hypothyroidism, hyperthyroidism, hypertension, liver or adrenal disorders, thrombocytopenia
- Carcinomas of the reproductive organs
- Polycystic ovarian syndrome (PCOS)
- Medications, such as, low dose estrogens, exogenous progestins or OTC progesterone creams, anticoagulants, NSAIDs, aspirin
- Infections, such as, cervicitis, STDs, salpingitis
- Structural disorders, such as, leiomyomas, endometriosis, polyps
- Drugs, nicotine
- High stress levels
- Obesity
- Excessive exercise[196]

CONVENTIONAL TREATMENT APPROACHES

Women with DUB are currently treated with a variety of approaches, including expectant management, iron replacement, medical therapy, and surgery. Surgery for DUB is generally reserved for situations in which the condition is life threatening, medical therapy is not effective or is not tolerated by the woman, or surgery is the woman's preference or the surgeon's recommendation. Types of surgery include hysterectomy and endometrial ablation (EA). Endometrial ablation is the targeted destruction or removal of the endometrium, leaving the uterus otherwise intact, and is performed using either hysteroscopically directed techniques (HEA) or a specialized device without hysteroscopic guidance (nonhysteroscopic EA or NHEA).[197] Hysterectomy carries a high complication rate but is associated with a high satisfaction rate.[211] Endometrial ablation therapy is an alternative to hysterectomy and allows for reduced surgical and recovery times, and does not require removal of the uterus.[191]

Medical therapies may include:
- Gestagens, estrogens, or combinations thereof.
- If contraception is needed, ovulation inhibitors are chosen.
- Nonsteroidal antirheumatics or antifibrinolytics are used if there are contraindications to the use of hormone therapy.
- Antifibrinolytic agents are used to prevent the proteolysis digestion of fibrinogen to fibrin and thus prevent the breakdown of blood clots. Aprotinin, isolated from bovine lung tissue, is a naturally occurring inhibitor of serine proteolytic enzymes.
- NSAIDs are used to decrease the production and use of prostaglandins.
- Iron supplementation and antiprostaglandin medications are recommended during bleeding episodes.
- Intravenous Premarin is given every 4 hours until the bleeding stops.
- High-dose estrogen therapy addresses DUB by maintaining the endometrial lining.
- Prostaglandin synthetase inhibitors (PGSIs), a nonhormonal treatment, associated with a 20% to 50% reduction in bleeding.[191]

- The levonorgestrel intrauterine contraceptive device may be recommended. Invasive therapies include:
  - Hysteroscopy
  - Dilatation and curettage
  - Endometrial ablation
  - Hysterectomy[212]

One study concluded because since none of the treatments for dysfunctional bleeding is superior to one of the others, and all treatments have advantages and disadvantages, counseling of patients with dysfunctional bleeding should incorporate a comprehensive review of the many options available to evaluate quality of life and risk–benefit ratio in relationship to patient preferences.[211] Surgical therapies generally may be avoided with appropriately applied hormonal therapies, particularly progesterones, and NSAIDs, allowing surgical intervention to be used in only severe, unresponsive, or life-threatening cases.[197,213]

WARNING! Severe bleeding can be life-threatening and must be treated acutely as an emergency.[214] Bleeding in excess of two menstrual pads soaked in 30 minutes is considered a hemorrhage and medical care should be sought. If there is excessive bleeding accompanied by orthostatic hypotension or a hematocrit less than 25%, hospitalization is required.

BOTANICAL TREATMENT OF DYSFUNCTIONAL UTERINE BLEEDING

Because DUB is a physiologic rather than pathologic problem, it is reasonable to attempt botanical and adjunct complementary therapies such as nutrition, stress reduction, and weight management prior to using more aggressive therapies. Once a diagnosis of DUB has been confirmed (underlying pathology ruled out) the primary botanical treatment goals are:

- Normalization of excessive or prolonged bleeding
- Correction of anemia, underlying nutritional deficiency
- Reduction of stress if stress related
- Correction of hormonal dysregulation

DUB treatment approaches can be divided into two categories:

1. Treatment of acute, non–life-threatening bleeding episodes
2. Treatment/prevention of chronic dysfunctional uterine bleeding

The role of the herbalist in cases of dysfunctional uterine bleeding is to address the primary complaints while working to restore hormonal balance. It is necessary to have an understanding of the underlying hormonal dysfunction in order to devise an appropriate therapeutic strategy. This can best be established by evaluating the woman's gynecologic and menstrual history, assessing her life cycle (i.e., postmenarchal, reproductive age, perimenopausal, postmenopausal). In most cases, the client will present with a diagnosis of DUB established by conventional diagnostic techniques. If this has not been done, it is strongly advised that the client have the condition medically investigated to rule out potentially grave pathology.

A systematic approach to choosing the most appropriate herbs for each individual case is to determine the key actions needed and to use those herbs known to reliably exert those actions. These herbs are then put into a formula (typically a tincture) according the specific needs of the individual client. Frequently, a client is given a formula to use in case of mild to moderate acute bleeding along with the formula(s) needed for addressing underlying dysfunction. Herbs may be used as hemostatics, progesterone production enhancers, and anti-inflammatories in the reduction of PGE2 (Table 5-11).

DISCUSSION OF BOTANICALS

The following discussion highlights several key herbs commonly used in the treatment of DUB. They specifically target hormonal and menstrual cycle regulation, and the treatment of mild to moderate acute excessive bleeding. Most evidence for antihemorrhagic activity is based on traditional use. Evidence for hormonal regulation can be extrapolated to DUB when there is a physiologic correlate, i.e., the use of chaste berry for DUB when it is related to luteal phase insufficiency. Readers should refer to the sections on PCOS, anemia, adaptogens, and nervines for additional and adjunct herbal treatments.

Botanicals for Hormonal Regulation

- Chaste berry
- Dong quai
- White peony

Chaste Berry

Herbalists have traditionally used chaste berry for a range of gynecologic applications, especially menstrual disturbances. Contemporary herbalists consider chaste berry an important herb for conditions resulting from unopposed estrogen, luteal phase defects, or latent hyperprolactinemia.[215] Bone specifically suggests the use of chaste berry for metrorrhagia from functional causes, menorrhagia, and polymenorrhea.[216] Increased serum prolactin levels are associated with menstrual irregularities. In vivo and in vitro experiments with chaste berry have demonstrated that extracts possess dopaminergic, prolactin-inhibiting activity, and thus suggest a role for the treatment of menstrual dysregulation.[217] Positive results on the treatment of secondary amenorrhea were seen in early clinical studies. In a clinical study of 52 women with luteal phase defects owing to latent prolactinemia, statistically significant changes were seen in the group taking the chaste berry extract. The prolactin release was reduced after 3 months, shortened luteal phases were normalized and deficits in the luteal progesterone synthesis were eliminated.[218] A study examined the use of *Vitex agnus castus* for menorrhagia and polymenorrhea over a 2-year period. Fifty-one women participated in the study, and of these 64% reported an improvement, which was noted within 2 to 3 months of commencing treatment. No side effects were reported.[219] A partially homeopathic preparation (containing *Vitex agnus castus*, *Caulophyllum thalictroides*, Cyclamen, Ignatia, Iris, and *Lilium tigrinum* in 53% ethanol) was effective in treating 13 women with hyperprolactinemia and menstrual cycle disorders, including secondary amenorrhea, polymenorrhea, menorrhagia, ovulation bleeding, and metrorrhagia. At the start of the study, 12 patients' baseline prolactin

TABLE **5-11**

Botanical Treatment Summary for DUB

THERAPEUTIC GOAL	THERAPEUTIC ACTION	BOTANICAL OPTIONS	COMMON NAME
Control of acute and excessive uterine bleeding	Antihemorrhagic, Uterine astringents	*Achillea millefolium*	Yarrow
		Capsella bursa-pastoris	Shepherd's purse
		Hamamelis virginiana	Witch hazel
		Panax notoginseng	Tienchi ginseng
		Trillium erectum	Birthwort, Birthroot, Bethroot
Hormonal regulation, especially of estrogen:progesterone	Hormonal modulatory herbs	*Chamaelirium luteum**	False unicorn
		Foeniculum vulgare	Fennel
		Actaea racemosa	Black cohosh
		Dioscorea villosa	Wild yam
		Vitex agnus-castus	Chaste berry
Promote uterine tone and efficient evacuation of uterine endometrium during menstruation	Uterine Tonics	*Angelica sinensis*	Donq quai
		Caulophyllum thalictroides	Blue cohosh
		*Chamaelirium luteum**	False unicorn
		Rubus idaeus	Red raspberry
Promote normal levels of estrogen and progesterone, improve luteal function and luteal phase of the cycle	Ovarian Tonics	*Caulophyllum thalictroides*	Blue cohosh
		Paeonia lactiflora	White peony
		Chamaelirium luteum[204,213]	False unicorn
Address iron-deficiency anemia[196]	Nutritive	*Angelica sinensis*	Dong quai
		Rehmannia glutinosa	Rehmannia
		Urtica dioica	Nettles
		Withania somnifera	Ashwagandha
		See Iron deficiency anemia	
Reduce underlying stress.	Nervines, sedatives, hypnotics	See nervines in Chapter 3	
Restore/Improve HPA axis function	Adrenal restoratives and tonics	*Eleutherococcus senticosus*	Eleuthero
		Glycyrrhiza glabra	Licorice
		Panax ginseng	Ginseng
		Schizandra chinensis	Schizandra
		Turnera diffusa	Damiana
		Withania somnifera	Ashwagandha
Treat chronic UTI; vaginal infection	Antimicrobials, urinary antiseptics		
	See UTI, Vaginal infection		
Optimizing the liver's ability to metabolize and eliminate hormones as part of improving hormonal dysregulation	Hepatic herbs		
	See Actions of Herbs		
Also see PCOS			

**Chamaelirium luteum*, false unicorn, is an endangered plant and should not be used unless from a cultivated source. It is included here for historical purposes, and to encourage cultivation of this valuable gynecologic herb.

levels ranged between 41.4 ng/mL and 93.5 ng/mL, and one was 514.9 ng/mL. Patients received 30 drops (equivalent to 33.4 mg *Vitex agnus castus*) of the preparation twice daily for 3 months. Prolactin levels significantly decreased in all patients over the course of treatment; in eight cases prolactin levels returned to normal or high normal. At the end of the study, all cases of dysfunctional uterine bleeding were resolved. No adverse effects were reported.[214] The German Commission E approved the use of chaste tree fruit for menstrual irregularities.[220] According to the American Herbal Products Association Botanical Safety Handbook, Vitex may counteract the effectiveness of birth control pills, and thus may not be appropriate to combine with OC therapies.[221]

Dong Quai

Dong quai is used in TCM formulae for conditions such as amenorrhea, irregular menstruation, menorrhagia, metrorrhagia, infertility, dysmenorrhea, PMS, menopause and as a general female reproductive tonic.[222] It has been shown to *inhibit* platelet aggregation and inhibition, and *increase* prothrombin time, and has been known clinically to *increase* uterine bleeding. This should only be used with caution for patients with DUB.[215,222] Should there be increased bleeding with use of this herb, it should be discontinued.

White Peony

See PCOS for a discussion of this herb.

Uterine Hemostatics/Antihemorrhagics

- Erigeron
- Shepherd's purse
- Tienchi ginseng
- Witch hazel
- Yarrow

Erigeron

Erigeron, or Canada fleabane, is a classic Eclectic herb for the treatment of uterine bleeding, still in use by herbalists, although not widespread.[225,226] It was described by Ellingwood as the agent to be given in cases of ''postpartum hemorrhage, abortion with alarming flow, menorrhagia with profuse flow of bright-red blood, dysmenorrhea with blood clots, bloody lochia increased by movements.. . .'' and numerous other hemorrhages, as well as for diarrhea.[226] Use is based purely on historical evidence and contemporary clinical observation. Use of this herb has not been evaluated by the German Commission E, nor the The American Herbal Products Association.[220,221]

Shepherd's Purse

This herb has a long history of use as an astringent and antihemorrhagic, and was specifically used for heavy uterine bleeding.[227] Nineteenth-century American Eclectic physicians used shepherd's purse to treat hematuria and menorrhagia.[226] During World War I, this herb was used to stop hemorrhaging when other medicines were not available. Treatment of heavy menstrual bleeding seems justified through empirical evidence. The hemostatic action of the extract may be owing to a peptide with oxytocin-like activity; however, its use for severe uterine bleeding is not recommended owing to unreliability. Interestingly, one study noted that the maximum activity of shepherd's purse extract was attained only 3 months after the manufacture date.[228] Clinical studies that correlate with pharmacological studies to humans have not been conducted. Ex vivo studies; demonstrated accelerated blood coagulation, however; a 1969 in vivo experiment did not demonstrate hemostatic activity.[216] Studies have shown that *Capsella* exerts a strong contractile effect on the uterus of guinea pigs. Clinically observed hemostatic action also may result from high oxalic and dicarboxylic acids; these phytochemicals have been shown to have a beneficial effect in the control of hemorrhage.[229] Because of its high oxalate content, care is advised for people with renal stones.[221] Shepherd's purse has been shown to be an important biomarker of environmental heavy metal contamination, because it appears to absorb heavy metals in large concentrations; therefore, care should be taken with long-term use.[230] The Commission E approved the internal use of shepherd's purse for symptomatic treatment of menorrhagia and metrorrhagia, hematuria, and topically for nosebleeds, superficial skin wounds, and bruising (Fig. 5-8).[220]

Tienchi Ginseng

Tienchi ginseng has been used traditionally in TCM for traumatic injury, bruising, and hemorrhage, and is included in protocol for uterine bleeding and menorrhagia. A comprehensive medical database search yields numerous studies evaluating the adaptogenic, antioxidant, immunologic, and cardiovascular effects of *P. notoginseng* and its saponins and ginsenosides. No studies of effects on uterine bleeding were identified. An animal study was conducted comparing the hemostatic activity of various *Panax notoginseng* preparations[231] in 62 male Wistar rats by administration of placebo (wheat flour), and alcohol, hydrophilic (water), and lipophilic (hexane) extracts of notoginseng. Rats were divided into five groups, and their tails were transected 5 mm from the tip. The alcohol extract group had the shortest bleeding time, which was significantly shorter than that of the control, placebo, and lipophilic extract groups. Alcohol extract provided better hemostatic effects than no treatment, placebo treatment, and treatment with lipophilic extract. Bone cites shortened clotting time in rabbits and good effects in visceral bleeding with tienchi.[224] *Panax notoginseng* has traditionally given as a powder or tablet in emergency to be taken with red wine. It is an ingredient in the traditional trauma formula Yunnan Paiyao.

Witch Hazel

Tannin-rich witch hazel is considered an astringent and hemostatic herb, and has been used traditionally for menorrhagia and metrorrhagia.[232] The German

Figure 5-8 Shepherd's purse (*Capsella bursa-pastoris*). (Photo by Martin Wall.)

Commission E and ESCOP monographs approve the use of this herb only for topical anti-inflammatory, astringent, and local hemostatic effects (e.g., for hemorrhoids). No studies were identified using witch hazel for the treatment of uterine bleeding. Oak Bark (*Quercus* spp.) has been used in much the same way, and similarly has no studied relating its use to uterine bleeding; however, its internal use is approved by the German Commission E for the treatment of diarrhea (Fig. 5-9).[220]

Yarrow

Yarrow has been used traditionally as a hemostatic and antihemorrhagic by both herbalists and the Eclectics.[216,225,227] Midwives and herbalists consider yarrow infusion one of the most reliable herbal uterine hemostatics available, employing it for DUB, uterine bleeding, and hematuria associated with UTI, and heavy bleeding with inevitable miscarriage. No studies were identified using yarrow for uterine bleeding (Fig. 5-10).

Other Uterine Hemostatics

The following herbs are also commonly used as uterine hemostatics/antihemorrhagics. Their use is based on traditional and empiric evidence and they are considered reliable and effective. Bayberry bark tincture is widely used by midwives for mild postpartum bleeding, generally in combination with equal parts of fresh shepherd's purse tincture (Boxes 5-19 and 5-20):

- Bayberry bark (*Myrica cerifera*)
- Lady's mantle (*Alchemilla vulgaris*)
- Oak bark (*Quercus* spp.)

Figure 5-10 Yarrow (*Achillea millefolium*). (Photo by Martin Wall.)

BOX 5-19

Sample Formula for Hormonal Dysregulation with Luteal Phase Defect

Chaste berry	*(Vitex agnus castus)*	30 mL
Eleuthero	*(Eleutherococcus senticosus)*	20 mL
White peony	*(Paeonia lateriflora)*	20 mL
Schizandra	*(Schizandra chinensis)*	20 mL
Licorice	*(Glycyrrhiza glabra)*	10 mL
		Total: 100 mL

Dose: 5 mL twice daily for up to 3 months; longer if needed.

Add nervines to protocol in a separate formula, or substitute *Schizandra chinensis* with 20 mL *Scutellaria lateriflora*.

BOX 5-20

Sample Great Flood Formula: for Acute Uterine Bleeding

This formula is an effective uterine hemostatic for *mild to moderate* bleeding only. For continuous or heavy bleeding, or any bleeding that soaks more than two menstrual (maxi) pads in 20 minutes, seek emergency medical care.

Yarrow	*(Achillea millefolium)*	30 mL
Shepherd's purse	*(Capsella bursa-pastoris)*	30 mL
Ladie's mantle	*(Alchemilla vulgaris)*	30 mL
Cinnamon	*(Cinnamomum zeylanicum)*	10 mL
		Total: 100 mL

Dose: Take 2.5 mL repeated every 15 minutes for up to 2 hours until bleeding abates. If bleeding continues beyond 2 hours or at any time becomes heavy, seek medical care. This formula can be taken preventatively immediately upon the start of menstruation during days 1 and 2.

CASE HISTORY: DYSFUNCTIONAL UTERINE BLEEDING

Kate is a 47-year-old female, gravida 2, para 2. Weight is excessive for height (185 lbs. 5′ 4″). Primary complaint is erratic, occasionally excessive menstrual bleeding. She was diagnosed with dysfunctional uterine bleeding by her OB/GYN who recommended hysterectomy and hormone replacement. Although she has no plans to have additional children, she is uncomfortable with the options presented to her.

Kate describes her cycle as erratic for the past 7 or 8 months (31 to 52 days), with some menses with very light flow with acute onset of excessive flow four of the past six cycles. Heavy days require 8 to 10 pad changes. Cycle lasts at least 7 to 10 days. Previous menstrual history was 28 to 31 days with normal flow for a maximum of 5 days. Denies any discomfort from cramping.

Additional complaints:

- Excessive stress owing to full-time job (high school math teacher), caring for elderly parent, financial difficulties, ''no time for herself''
- Constipation
- Fatigue, extreme at times
- Sleep onset insomnia
- Joints ache upon rising
- Bruises easily

Herbal Prescription for Dysfunctional Uterine Bleeding

Uterine Antihemorrhagic Herbal Formula

Tincture:

Shepherd's purse	(*Capsella bursa pastoris*)	20 mL
Tienchi ginseng	(*Panax notoginseng*)	40 mL
White peony	(*Paeonia lactiflora*)	40 mL
		Total: 100 mL

Dose: 5 mL in water qid at first indication that menses is about to start; continue until bleeding is controlled.

Also:

- *Vitex agnus-castus* 100 mL

Dose: 3 mL once per day upon rising starting on day 5 of menses continuing until the start of the next menses; repeat each cycle

- *Eleutherococcus senticosus* tablets: One tablet three times a day

Dietary recommendations: Boost iron levels, address low fiber intake and hypohydration, reduce proinflammatory prostaglandin production with dietary increase of EFAs and fish, eliminate hydrogenated products, address blood sugar management, and reduce caffeine intake. Include dietary phytoestrogens (soy, flax seed, red clover, and fennel teas).

At 3 weeks, patient reported reduced constipation and that her period was lighter the previously. At 8 weeks, patient reported having a ''tolerable'' cycle at 34 days with a lighter flow lasting 6 days. She also reported improved sense of well-being. She was prescribed a tablet formula of valerian, Zizyphus, and passion flower extracts to be taken as two tablets before bed, and repeat with one additional tablet if not asleep within 1 hour for persistent sleep difficulties. At 12 weeks, the patient reported an ''almost normal'' cycle starting at 30 days. Her heaviest flow on day 2 required only four pads, and the menses lasted for only 5 days. Patient reported good sleep for several consecutive days with improved energy levels. She has taken up a low-impact aerobics class and has lost 8 pounds over the past 6 weeks. Constipation returns occasionally, especially with stress, and she does not routinely use the flax meal preventatively. Practitioner plans to continue vitex for several more cycles and to begin weaning patient off of antihemorrhagic herbs as improvements become consistent but to have them on hand for use if needed.

Treatment Summary for Dysfunctional Uterine Bleeding

- Hemostatic and uterine tonic herbs are used to modulate mild to moderate acute episodes of excessive bleeding. Examples include yarrow, shepherd's purse, witch hazel, and tienchi ginseng. See Great Flood Formula in Box 7-20.
- Use of botanicals to normalize hormonal function and the HPO axis; chaste berry is a classic example. Other herbs may include peony, black cohosh, and fennel. Herbalists commonly include herbs for the support of liver function as well as proper bowel elimination part of a plan to regulate hormonal activity.
- Nutritive herbs should be included when there is anemia. Dong quai, Rehmannia, nettles, and ashwagandha should be considered.
- Chronic excessive bleeding can lead to significant stress; therefore, nervines and anxiolytics can be included in formulae. Examples are passion flower, motherwort, skullcap, and kava kava (with appropriate warnings as discussed in Plant Profiles: Kava kava). Adaptogens can play a role in helping to regulate the HPA axis, and also may be included.
- Associated or underlying causes such as UTI and vaginal infection should be addressed.
- The diet or supplementation should provide adequate vitamin K, essential fatty acids, vitamins C, E, and A, and iron, all of which play an important role in the regulation of hemostatic function and/or the prevention of anemia.
- Reduction of inflammation through an anti-inflammatory diet and the addition of EFA-rich foods and supplements may reduce the production of endogenous inflammatory compounds and thus play a role in the prevention and treatment of DUB.

What to Expect with DUB Treatment

Acute treatment is often effective for mild to moderate bleeding within a couple of hours of beginning treatment with uterine hemostatic herbs. Experienced practitioners also may find success with more severe bleeding, but this should only be undertaken with proper knowledge and medical supervision.

For chronic episodes of acute bleeding, as well as chronic bleeding, it can take several months to regulate hormones and achieve adequate control of bleeding and prevent recurrence of episodes. In many cases, small gains will be seen in the first couple of months of treatment, and the practitioner may feel the need to revise the formula to achieve more specific goals as care progresses. For example, in a woman with cramping, mood swings, and irregular dysfunctional uterine bleeding, one might achieve improvement in two of the three complaints using a single formula, and then decide to modify the formula to focus on the complaint that remains outstanding or is the most pronounced. Modification of formulae over the course of care is very common with herbal medicine.

Many women, particularly in the perimenopausal years, will achieve a high degree of success in modulating excessive bleeding, but may keep a formulae on hand, such as Great Flood, should there be an unexpected episode of uterine bleeding, as may occur as hormones shift into a menopausal state.

NUTRITIONAL CONSIDERATIONS

Vitamin K

Vitamin K is a cofactor for the enzyme responsible for chemical reactions that maintain blood clotting factors: prothrombin; Factors VII, IX, and X; and proteins C and S. Because vitamin K is supplied in the diet and by synthesis of intestinal bacteria, deficiencies are not common. Menorrhagia can be a symptom of vitamin K deficiency. Women at greatest risk for deficiency are those with poor diet or malabsorption, liver, or biliary diseases. Vitamin K is found in broccoli, Brussels sprouts, spinach, cauliflower, green leafy vegetables, and egg yolks.[233]

Essential Fatty Acids

As with dysmenorrhea, the addition of cold water fish to the diet, and fish oils supplements may help in the reduction of menorrhagia via reduction of inflammatory mediators in the prostaglandin pathway, whereas promoting production of anti-inflammatory prostaglandins.

Vitamins C, A, and E

Include nutrients to address integrity of the micro- and macrovascular system: whole-food sources of vitamin C (with bioflavonoids), vitamin E, and beta-carotene (instead of preformed vitamin A). Additionally, deficiency of vitamin A has been found to be an important factor associated with menorrhagia. Vitamin A is a cofactor of 3 beta-dehydrogenase in steroidogenesis and deficiencies of this vitamin may result in impaired enzyme activity. The level of endogenous 17-beta-estradiol appears to be elevated with vitamin A therapy, and in one study, menorrhagia was alleviated in more than 92% of patients (see Menarche: Adolescent Menorrhagia).

Iron

Iron supplementation is essential when there is anemia. Iron supplements are notoriously hard to digest and poorly bioavailable. Floradix Iron and Herbs® is an excellent source of bioavailable iron primarily derived from fruit and botanical sources. Take with vitamin C to enhance absorption (see Anemia).

ADDITIONAL THERAPIES

Stress reduction strategies can be incorporated to address stress associated with this condition. An exercise program appropriate for individual lifestyle and ability

BOX **5-21**

Eclectic Specific Condition Review: A Historical Perspective—Menorrhagia*
David Winston

- **Beth root** (*Trillium erectum*)
  Chronic passive uterine hemorrhage,
- **Canada fleabane herb** (*Conyza canadensis*)
  Passive uterine hemorrhage.
- **Carbo Ligni purified charcoal** (*Carbo vegetabilis*)
  Profuse menses, salty taste in the mouth, nausea, diarrhea, pallid (pale) tongue with peeled patches. The patient is very pale.
- **Cinnamon bark** (*Cassia cinamonum*)
  To arrest uterine hemorrhage, whether postpartum, menorrhagia, or metrorrhagia
  The essential oil of Cinnamon, combined with the essential oil of Canada Fleabane (formerly known as Erigeron) in an alcohol base, was known as Ellingwood's Compound.
- **Corn smut** (*Ustilago maydis*)†
  Menorrhagia with a discharge that forms dark stringy clots
- **Dogbane root** (*Apocynum cannabinum*)†
  Menorrhagia in which the flow lasts more than 6 to 7 days, is profuse, as well as reoccurring too frequently (polymenorrhagia). Fullness of the abdomen, edema of face and/or eyelids.
- **Fragrant sumach bark** (*Rhus aromaticum*)
  Profuse menstruation that occurs too frequently (polymenorrhagia).
- **Partridge berry herb** (*Mitchella repens*)
  Excessive bleeding caused by uterine atonicity with a sensation of fullness, tenderness, and pressure in the abdomen.
- **Shepherd's purse** (*Capsella bursa-pastoris*)
  Chronic menorrhagia; when the period occurs too frequently or is too long. The menstrual fluid is pale.
- **White ash bark** (*Fraxinus americana*)
  Uterine hypertrophy with profuse leukorrhea and profuse and too frequent menstruation.
- **Wild geranium root** (*Geranium maculation*)
  Profuse bleeding with fibroids and excessive vaginal discharge. Works well with Beth root.
- **Yarrow herb** (*Achillea millefolium*)
  Vaginal leukorrhea, profuse bleeding, blood bright red.
- **J.M. Scudder's Formula for Menorrhagia:**
  Veratrum tincture†
  Ipecac tincture*
- **A.F. Stephen's Formula for Menorrhagia:**
  Belladona tincture†
  Black Haw tincture
  Witch Hazel tincture

*These herbs are presented for historical perspective only.
†Toxic. Use with caution and careful supervision, under the guidance of a qualified practitioner.

may improve pelvic circulation, hormonal regulation, and decrease menstrual irregularities (Box 5-21).

PREMENSTRUAL SYMPTOMS, PREMENSTRUAL SYNDROME (PMS), AND PREMENSTRUAL DYSPHORIC DISORDER (PMDD)

Ruth Trickey

> *Is PMS due to an individual pathologic problem or is it due to cultural beliefs, beliefs that lead to the menstrual cycle being associated with a variety of negative reactions, or a combination of both? What if our societies and cultures had celebrated menstruation as a time of pleasure (and even public joy) rather than something private (to be hidden) and negative? Would we have PMS today? The answer may lie in the unravelling of the role of our shared beliefs about menstruation in society, rather than the functioning of those beliefs in individuals.*[245]
>
> **—Clinical Gynecologic Endocrinology and Infertility**

Premenstrual symptoms have been recognized at least since the time of Hippocrates; however, it wasn't until 1931 that the term premenstrual syndrome (PMS) first appeared in the medical literature. By the 1950s, the term Premenstrual Syndrome (PMS) was applied to the physical and psychological symptoms occurring for up to 2 weeks prior to menses with relief seen after the onset of the menstrual period. In the 1990s, criteria were included in the Appendix of the *Diagnostic and Statistical Manual for Mental Disorders*, third and then fourth edition, describing late luteal phase dysphoric disorder (LLPDD) and finally premenstrual dysphoric disorder (PMDD), a particularly severe form of premenstrual syndrome with an emphasis on the affective symptoms (Box 5-22). In April 2000, the American College of Obstetricians and Gynecologists published a Practice Bulletin on the topic of PMS, that included criteria for diagnosis and recommendations for the treatment of clinically significant premenstrual syndrome (Box 5-23).[246,247]

PMS is characterized by a wide range of symptoms (see Box 5-18) that recur in the luteal phase of the menstrual cycle (1 to 2 weeks prior to the next menstrual period) and that cease soon after menstruation commences. Surveys estimate that 30% to 85% of women report at least one premenstrual symptom during each menstrual cycle.[248] In its milder form, PMS is estimated to affect approximately 40% of women of reproductive age; in

BOX 5-22

ACOG Diagnostic Criteria for PMS[247]

Patient reports one of the following affective and somatic symptoms during the 5 days before menses in each of three prior menstrual cycles:

Affective symptoms

- Anxiety
- Breast tenderness
- Confusion
- Headache

Somatic symptoms

- Abdominal bloating
- Angry outbursts
- Depression
- Irritability
- Social withdrawal
- Swelling of extremities
- Symptoms are relieved within 4 days of menses onset without recurrence until at least cycle day 13
- Symptoms present in the absence of any pharmacologic therapy, hormone ingestion, or drug or alcohol abuse
- Symptoms occur reproducibly during two cycles of prospective recording
- Patient suffers from identifiable dysfunction in social or economic performance

BOX 5-23

DSM-IV Criteria for Premenstrual Dysphoric Disorder[272]

A. In most menstrual cycles of the past year, five (or more) of the following symptoms, which begin during the last week of the luteal phase (after ovulation) and end in the follicular phase (menses), were present most of the time and absent in the week post menses. At least one of the symptoms must be 1, 2, 3 or 4.
   1. Markedly depressed mood; hopelessness; self-deprecating thoughts
   2. Marked anxiety, tension, feeling ''keyed up'' or ''on edge''
   3. Marked affective lability (feeling suddenly sad or tearful; increased sensitivity to rejection)
   4. Persistent and marked anger, irritability, or increased interpersonal conflicts
   5. Decreased interest in usual activities
   6. Difficulty concentrating
   7. Lethargy, easy fatigability, or marked lack of energy
   8. Marked change in appetite, overeating or specific food cravings
   9. Hypersomnia or insomnia
   10. Sense of being overwhelmed or out of control
   11. Physical symptoms such as breast tenderness or swelling, headaches, joint or muscle pain, bloating, weight gain

B. The disturbance markedly interferes with work, school, usual social activities, and relationships with others.

C. The disturbance is not merely an exacerbation of the symptoms of another disorder, such as major depressive disorder, panic disorder, dysthymic disorder, or a personality disorder.

D. Criteria A, B, and C must be confirmed by prospective daily ratings during at least two consecutive symptomatic cycles.

its most severe form, it affects roughly 2.5% of women in this age group.[249] In 2% to 10% of cases, symptoms are significant enough to cause disruption in family, personal, or occupational function.[249] Between 3% and 8% develop a severe type of PMS termed premenstrual dysphoric disorder (PMDD).[250] PMDD is most likely to appear in the late twenties to mid-thirties. PMDD is primarily characterized by severe irritability, unprovoked anger, anxiety, and/or depression.[251]

Women can develop PMS at any time between puberty and menopause but tend to seek treatment more often in their thirties and forties. PMS symptoms do not persist following natural, surgical, or medically induced menopause.

More than the type of symptom, it is the timing during the menstrual cycle that is diagnostic of PMS and PMDD, although symptom severity (especially those related to mood changes) is the feature that distinguishes PMS and PMDD. Because PMDD differs from PMS in severity but not type of symptoms, there is considerable debate as to whether PMDD is a subset of PMS or constitutes a distinct entity. On the one hand, it has been suggested that PMDD is a media construct brought about by the popularization of PMS as a catchall diagnosis; on the other hand, it has been said that having a name and diagnosis for their intense premenstrual emotions actually provides a sense of relief and sanity to women with PMDD's characteristic symptoms. Women with PMDD have severe mood changes that occur premenstrually to the point of significant disruption in their abilities to perform daily tasks at work or in the home, unlike women with PMS, who may report the same symptoms but of a less disabling nature.[251] The mood changes seen in both PMDD and PMS must be differentiated from premenstrual magnification of an underlying psychiatric disorder or medical problem. Because differentiating between PMS and PMDD is difficult, and much of the literature considers PMDD a severe form of the psychoemotional manifestations of PMS, in this discussion PMDD is considered a subset of PMS (Box 5-24).

PATHOPHYSIOLOGY

The precise etiology of PMS remains unknown; however, there are many proposed theories. These include:

BOX **5-24**

Common Symptoms of PMS

Physical:
- Abdominal distention, bloating and discomfort
- Abnormal appetite, craving sweet foods, alcohol, and/or fatty foods
- Altered libido
- Breast swelling, pain, discomfort and/or breast lumps
- Change in bowel habit
- Cyclic weight gain
- Dizziness or fainting
- Headaches
- Fatigue and weakness
- Fluid retention
- Insomnia or excess sleepiness
- Joint pains and/or backache
- Palpitations
- Pelvic discomfort or pain
- Poor motor coordination
- Premenstrual acne/skin blemishes
- Tendency to have minor accidents
- Undesirable hair changes

Emotional and mental:
- Aggression
- Angry outbursts
- Anxiety
- Confusion
- Depression
- Feeling ''overwhelmed'' or ''out of control''
- Forgetfulness
- Hyperreactiveness
- Irritability
- Lack of concentration
- Loneliness
- Mood swings/moodiness
- Negative affect
- Nervous tension
- Poor judgment
- Restlessness
- Tearfulness

- Abnormal hormone levels/hormonal imbalance particularly excess estrogens and/or deficient progesterone; estrogens deficiency; endorphin/opiate deficiency; thyroid disorders
- Discrepancies in prostaglandins or neurotransmitters
- Latent hyperprolactinemia
- Disordered aldosterone function caused by excess estrogens
- Abnormal HPA axis functioning with diminished stress response and decreased cortisol response
- Nutrient deficiencies (especially B_6, vitamin E, vitamin A, calcium, and magnesium)
- Inappropriate diet (e.g., leading to blood sugar dysregulation; excessive caffeine intake)
- Environmental factors
- Stress (current relationship/marital/sexual difficulties; poor coping skills; workplace stress, and so forth)
- Psychosocial factors (e.g., negative attitudes about menstruation, sense of personal disempowerment or low self-esteem, history of sexual abuse)
- Cultural factors (negative attitudes about menstruation, cultural expectation that menstruation is accompanied by unpleasant symptoms)[245,249,252–257]

In spite of these numerous theories, no physiologic mechanisms have been identified as definitive causes of PMS. Elimination of ovarian function by hysterectomy and bilateral oophorectomy or by medical suppression of the cycle results in complete suppression of premenstrual symptoms, implying that they are triggered by cyclical fluctuation in endogenous estrogens and progesterone. The mechanism underlying an abnormal response to these hormones in some women is not clear.[258] Studies have failed to demonstrate any consistent or remarkable hormonal differences throughout the menstrual cycle or specific to the luteal phase in women with and without symptoms, including estrogens, progesterone, testosterone, FSH, LH, prolactin, endogenous opiates, and SHBG, both in terms of secretion and circulating levels.[245]

A recent hypothesis on the physiologic origins of PMS is that symptoms are related to central neurotransmitter changes occurring in response to normal fluctuations in hormone levels. Estrogens increase the production rate and receptor density of serotonin, dopamine, β-endorphins and noradrenaline, whereas progesterone may have the opposite effect and reduce these neurotransmitters.[259–263] In part, this seems to be related to the effects of estrogens and progesterone on monoamine oxidase (MAO) such that estrogens decrease, whereas progesterone increases MAO activity. In the presence of high levels of estrogens, the decreased activity of MAO reduces the catabolism of neurotransmitters and thus increases their availabilities in brain centers; conversely, high levels of progesterone (and progestogens) reverse this effect. It is hypothesized that women may have a greater susceptibility to changes in central neurotransmitters resulting from normal cyclical changes in sex steroids.[245] The largest body of evidence suggests that serotonin (5-HT) is the major neurotransmitter involved in PMS and PMDD, and that progesterone may be a key mediator of PMS. It has been found to increase 5-HT uptake in several brain regions, as well as increased 5-HT turnover. Decreased 5-HT activity has also been observed in the late luteal phase of the menstrual cycle, and this has been implicated in increased appetite, psychomotor activity, and depression. Other aspects of central nervous system physiology, including allopregnenalone, an allosteric receptor for GABA and a metabolite of progesterone, and the neurotransmitter glutamate are also responsive to cyclical variations in oestrogen and progesterone, and may be collectively or independently responsible for dysphoria and PMS symptoms.[262,263]

Interest has also focused on serotonin and the positive results seen with the use of SSRIs. Women with PMS have

been shown to have abnormal functioning of the serotonergic system that is related to altered serotonin levels as well as serotonin transmission.[264] The normal fluctuations in estrogen levels that occur in the second half of the cycle are thought to enhance or even trigger these abnormalities in susceptible women and lead to the alterations in mood seen in PMS. As described, increasing levels of estrogens in the luteal phase could inhibit the deactivation of noradrenaline and influence serotonergic pathways, thus contributing to symptoms of heightened mood such as aggression, irritability, and anxiety. Lower estrogen during the perimenopause seems to contribute to depression and also seems to be influenced by altered serotonergic activity.

Symptoms are also said to develop among women with PMDD because of altered sensitivity to these central neurotransmitters, especially serotonin, triggered by changes in the normal circulating levels of estradiol and progesterone.[265] Earlier suggestions have centered on other hormonal causes of PMS, including an estrogen to progesterone ratio imbalance in favor of estrogen; or to problems with progesterone receptors such that the receptors do not transport progesterone into cells.[266,267] These latter theories have not borne out using biochemical assays, and have largely gone out of favor.

Disruption of the hypothalamic-pituitary-adrenal axis has also been recently proposed as a cause of PMS and PMDD, and is an interesting and promising theory. It has been demonstrated that women with PMDD demonstrate a decreased effectiveness in their stress response, including a blunted cortisol response, blunted adrenal response, and decreased adrenal ACTH receptors compared with women who do not exhibit PMS symptoms.[268] These women have higher than normal circulating levels of allopregnenalone than their nonsymptomatic counterparts; however, they do not appear to break it down to a usable form under conditions of stress, indicating a diminished stress response. Allopregnenalone is a neuroactive metabolite of progesterone and a barbiturate-like modulator of central GABA.[269] The importance of progesterone as a neuroendocrine modulator in PMS has not been fully explored. Animal studies demonstrate that stressors repeated at 3- to 5-week intervals can generate adrenal hyporesponsivity or hypocortisolism, which in turn may contribute to stress-related pathology. The role of repeated dysphoric episodes occurring on a monthly basis in PMS can be regarded as potentially impacting stress physiology. Women with PMS appear to have an abnormal response to normal levels of progesterone, compared with nonsymptomatic women. Although the mechanism underlying the abnormal response to progesterone is unknown, as is the possible contribution of abnormalities in the stress axis to the symptomatology of PMS, recent data strongly suggest that PMS is characterized by stress axis physiology.[268,270]

The nature of PMS has been hotly debated and discussed, with opinions ranging from its etiology in biochemical imbalances to negative sociocultural issues influencing psychological expectations and biological responses to menstruation. Purely biochemical hypotheses may be criticized for pathologizing menstruation and ignoring social and cultural forces, whereas taking a purely sociobiological stance may ignore physical etiologies and suggest that women can merely reframe their attitudes toward menstruation and become symptom free. Many practitioners believe that the most effective approach is multifactorial and integrative, looking at biological, cultural, psychosocial, nutritional, and lifestyle factors that lead to premenstrual discomforts, PMS, and PMDD.[245,249] Further, it should be recognized that individual symptoms of PMS, for example, social withdrawal may to a certain extent reflect a natural inclination toward solitude and quiet during what many women consider a more sensitive, creative, and intuitive time, and should not be pathologized.

DIAGNOSIS

Several sets of diagnostic criteria have been developed for PMS and PMDD. The American Psychiatric Association (APA), the National Institute of Mental Health (NIMH), and the American College of Obstetricians and Gynecologists have all established diagnostic guidelines (see the following). The criteria from the APA are for PMDD. Because severity is subjective, it is difficult to definitively differentiate between premenstrual complaints, PMS, or PMDD—they really represent a spectrum of symptom severity. The diversity of PMS symptoms and syndromes is great, and the validity of the DSM-IV descriptive entities, as well as their clinical relevance should be seriously questioned, used as a guideline, and not be adhered to strictly.[271] At any given time, many individuals, both male and female, can identify symptoms in themselves that are characteristic of PMS/PMDD. PMS should not ultimately be considered a psychiatric disease but a constellation of symptoms that possibly occur as part of a complex interplay of biologic, psychologic, and societal factors.

The NIMH criteria require documentation of at least a 30% increase in severity of symptoms in the 5 days prior to menses over the 5 days prior to that. Using these two sets of criteria, approximately 5% of women are thought to experience disruptive PMS.[245]

A menstrual symptom diary that categorizes the classical symptoms of PMS is the preferred method to diagnose this syndrome (Box 5-25). The diary should be completed over at least two consecutive cycles and should show the typical variations in timing that suggest PMS—symptoms are absent for the week following the period, but appear at any time in the 2 weeks preceding menstruation, and then decline at the beginning or in the first days of the period. Symptoms should be apparent during at least two menstrual cycles for a positive diagnosis to be made.

Four distinct symptom patterns of PMS have been described (see Table 5-12). These categorizations provide useful information to assist with refining the treatment plan, although they are somewhat arbitrary and there is significant overlap in symptoms.[257] Some women report greater symptoms around ovulation and the week after; others are symptomatic in the premenstrual week only; whereas yet others report symptoms from ovulation through to the first days of the period.

BOX **5-25**

Menstrual Symptom Diary

NAME:_____ Age:_____ Month:_____

	Date																																		
	Day of cycle	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**	**36**
	Menstrual flow																																				
	PMS with mood changes																																				
A	Nervous tension																																				
A	Irritability																																				
A	Anxiety																																				
A	Insomnia																																				
A	Crying/sadness																																				
B	Depression																																				
B	Social withdrawal																																				
B	Lack of interest in life																																				
	PMS with food cravings																																				
	Craving sugar/carbs																																				
	Headache/migraine																																				
	Irritability if hungry																																				
	Fatigue																																				
	PMS with fluid retention																																				
	Breast fullness																																				
	Abdominal bloating																																				
	Weight gain																																				
	Swollen hands & feet																																				
	PMS with pain																																				
	Period pain																																				
	Breast pain																																				
	Aches and pain																																				
	PMS with depletion																																				
	Tiredness																																				
	Mental fatigue																																				
	Hot flushes																																				
	Headaches/migraines																																				

Grading of menstruation
0-none
1-slight
2-moderate
3-heavy
4-heavy and clots

Grading of symptoms
0-none
1-mild-only slightly aware of symptom
2-moderate-aware of symptom, but does not interfere with activities
3-severe-continually aware of symptom, but not disabling
4-very severe-disabling and unable to function

There is evidence that women often do not consult a physician if they have moderate to severe PMS or PMDD symptoms. Physicians also frequently fail to ask women if moderate to severe premenstrual symptoms affect their mood and well-being. Thus, the diagnosis of PMDD is often missed in primary care and gynecology settings.[263] Furthermore, whether or not a diagnosis is assigned may differ according the practitioner's gender; female physicians may be less likely to apply psychiatric labels to their female patients, and may be more apt to recognize contextual contributions to symptoms than male physicians.[273]

It should be remembered that whether a woman meets the criteria for a PMS or PMDD diagnosis is somewhat arbitrary. Lack of a diagnosable case should not be reason to invalidate a woman's experience of premenstrual symptoms and difficulties, nor should it be justification for withholding beneficial therapies. To deny women's experience based on lack of meeting diagnostic criteria would be to return to the days when it was suggested that premenstrual symptoms were merely psychosomatic, or ''all in their heads.'' Helping women to understand that there are both physiologic and social underpinnings to their experiences can give a name to their experiences, and help them contextualize, rather than personalize, their premenstrual states, and begin to find solutions. Women presenting with symptoms who do not meet diagnostic should be offered follow-up care, particularly in the case of possible PMDD.

DIFFERENTIAL DIAGNOSIS

PMS, PMDD, and premenstrual magnification of a preexisting complaint such as depression, irritable bowel syndrome, or certain autoimmune conditions can all present or worsen premenstrually. Many other conditions, such as diabetes, anemia, and abnormal thyroid function or other endocrine abnormalities, might mimic some of the features of PMS without actually worsening premenstrually and also should be excluded as a cause of the symptoms. A completed menstrual symptom diary that does not reveal the previously described pattern is indicative of diagnoses other than PMS. PMDD presents with the characteristic symptoms of irritability, anger, internal tension, dysphoria, and mood lability and should be suspected when symptoms are rated as very severe on the Menstrual Symptom Diary (Grade 4).[274] It is important to note, however, that although the use of the prospective menstrual symptom questionnaire can provide useful information on the type of symptoms, it is not always a reliable indicator of symptom severity. Trials have shown that questionnaires can be used to

TABLE 5-12

PMS Pattern Categories[245,257,270]

PATTERN	POSSIBLE ETIOLOGY	CHARACTERISTICS/SYMPTOMS
PMS-A Anxiety	Estrogen excess and/or progesterone insufficiency HPA-related diminished stress response Neurotransmitter related effects from normal hormonal changes associated with menstruation	Anxiety Insomnia Irritability Emotional lability
PMS-C Carbohydrate craving	Possible enhanced insulin binding effects	Sugar cravings Increased appetite (even ravenous) Headache Hypoglycemia Heart palpitations Sweating spontaneously
PMS-D Depression	Estrogen leading to increased neurotransmitter degradation	Depression Despair Crying Feelings of hopelessness Fatigue Insomnia Apathy Low libido
PMS-H Hyperhydration	Possible effects of increased aldosterone in the late luteal phase due to excess estrogen	Edema of hands and feet Weight gain Sense of ''bloating'' Clothes feel tighter Breast tenderness, or sense of engorgement

differentiate between women with and without symptoms suggestive of PMS, but that they are not sensitive predictors of severity or reliable tools to make a definitive diagnosis of PMDD.[275] Differentiation between PMS and PMDD usually relies on the clinical judgment of the consulting practitioner in conjunction with an evaluation of the symptoms against the criteria described in the appendix to the 1994 *Diagnostic and Statistical Manual of Mental Disorders Fourth Edition* (DSM-IV) Criteria for Premenstrual Dysphoric Disorder (see Box 5-24). Symptoms must be confirmed by prospective daily ratings during at least two consecutive symptomatic cycles. At least one of the symptoms must be severe depression; anxiety, mood lability, or anger, and the severity of the symptoms must be such that they disrupt daily life.

CONVENTIONAL TREATMENT APPROACHES

The medical treatment of PMS and PMDD includes OCs and other hormonal treatment strategies, NSAIDs, SSRIs, bromocriptine, antidepressants, and diuretics, as dwell as concentrating on symptom relief with specific symptom-related drug treatments. Most of these methods have failed to demonstrate definitive benefits over placebo, with the exception of antidepressants (particularly SSRIs) and GnRH and other ovulation suppressants, which have demonstrable benefit.[264]

Hormonal Treatments

Of the hormonal medications used to treat PMS, some prevent ovulation, whereas others affect the hormonal profile. OCs improve PMS symptoms in some women, have no effect in others, and may worsen symptoms in some. A monophasic pill is the most suitable option for women who experience PMS with mood changes, whereas a triphasic pill is more suitable when women have physical symptoms of breast pain and swelling.[276] Danazol is also prescribed to manipulate hormones. When taken on a daily basis this drug suppresses ovulation and is used for the treatment of breast pain and PMS.[277,278] This is generally an unpopular treatment because of side effects; however, reported improvements include a reduction in breast pain, fatigue, food cravings, and anxiety.

GnRH agonists have been trialed, sometimes in combination with the Pill for premenstrual symptoms.[279] These protocols, known as ''add-back'' therapy, require that a woman take the GnRH agonist combined with low doses of estrogens and progestogens. GnRH agonists alone are unpopular because many women are not prepared to exchange PMS for menopausal symptoms and reduced bone density and GnRH agonists alone did not help mood symptoms.[280] Add-back therapy showed more promise. This treatment is controversial and is reserved for severe and intractable cases of PMS.

Ponstan (mefenamic acid) has been used to treat mood swings, fatigue, headache, and the general aches and pains that accompany PMS.[281] The use of these NSAIDs should be restricted to a 7-day interval, making them unsuitable for the many women who experience PMS for more than 7 days before their period.[282] NSAIDs do not reverse the prostaglandin imbalance that causes excessive menstruation, pain, or PMS and has to be used indefinitely unless the cause/s of the imbalance are identified and rectified. This prospect is not appealing to many women, especially because these drugs have many side effects.

Diuretics

Diuretics will not improve most symptoms of PMS and have been shown to be useful only symptomatically for those women who gain weight premenstrually. Spironolactone has not demonstrated benefits over placebo in double-blind, placebo-controlled trials.[245]

Antidepressants

A number of recent trials have verified the effectiveness of the selective serotonin reuptake inhibitors (SSRIs) in the treatment of severe PMS or PMDD. Fluoxetine, sertraline, and citalopram given throughout the menstrual cycle have been shown to be well tolerated and effective.[264,283] Some of the SSRIs, such as citalopram, have also been shown to be effective when used during the luteal phase of the cycle only. Venlafaxine[284] (Effexor) a new-generation antidepressant that selectively inhibits serotonin and noradrenaline reuptake, has been evaluated for effectiveness in the treatment of PMDD and has been shown to be more efficacious than placebo.[285]

Despite their effectiveness, the SSRIs have considerable side effects, including gastrointestinal disturbances, headache, sedation, insomnia, weight gain, impaired memory, excessive perspiration, and sexual dysfunction. The tricyclic antidepressants have been used successfully, particularly nortriptyline and clomipramine. The benzodiazepine Alprazolam has also been suggested as a treatment for PMS and PMDD; however, dependence and tolerance occur quickly and make these types of drugs less attractive options for these conditions.

Dietary Supplements

Physicians have also prescribed vitamins B_6, A, and E; phenylalanine, L-tryptophan, calcium, magnesium; and herbal remedies, especially chaste berry extract. Among the treatment modalities that have not been shown to be effective in well-controlled studies are progesterone, thyroid hormones, lithium, and evening primrose oil.[264]

Surgery

Surgery to remove the ovaries is a controversial and radical option sometimes suggested; however, it is unacceptable to most women to trade the symptoms of PMS with those of premature menopause as well as the risk of loss of bone density; thus this option is reserved for severe and intractable cases.

BOTANICAL TREATMENT OF PMS AND PMDD

Botanical practice takes a multifactorial approach to PMS, addressing the patient's personal beliefs about menstruation, psychosocial situation, lifestyle factors, and incorporating a physiologic approach that treats both symptoms and underlying hormonal and HPA dysregulation. This integrative and comprehensive approach may be particularly relevant in PMS and PMDD, as the condition is considered to have physiologic, psychologic, and sociocultural origins.[249]

Physiologic treatment with herbs focuses on symptomatic relief (e.g., treatment of anxiety, irritability, depression, insomnia, acne, mastalgia, dysmenorrhea, and so forth) for mild premenstrual complaints, and a combination of the aforementioned symptomatic relief, hormonal modulation, and improving physiologic and emotional stress response in PMS. PMDD is treated slightly more aggressively with herbs for hormonal and stress response dysregulation, and mood dysphoria symptoms. Though some of these approaches are based on what are still theoretical grounds, a small number of trials, and significant practitioner experience provide at least preliminary justification for these strategies.

For many women, a complex plan with a combination herbal therapies is required to treat a constellation of symptoms, for example, when there are concomitant sugar cravings, dysmenorrhea, moderate to severe anxiety, or depression. Lasting improvements also require lifestyle, stress management, and personal/attitudinal changes. Patients should eliminate or at least minimize coffee, alcohol, and tobacco use, and should have a diet with frequent meals high in protein and with optimal intake of vitamins and minerals, and low in refined sugar. Excess sodium should be reduced when there is fluid retention, edema, or breast tenderness. Women should get regular exercise, and maintain a health body weight for their heights, ages, and activity levels. Stress management techniques should be practiced regularly. Women who feel self-empowered and in control of their lives experience PMS symptoms with less frequency than other women; women should seek support and counseling to create the necessary lifestyle changes that improve self-esteem (Table 5-13).[245,251]

The treatments discussed in the following are categorized by major PMS/PMDD symptoms. For comprehensive treatment of multiple symptoms, readers will want to refer to additional sections mentioned under Botanical Treatment Summary for PMS, for example, insomnia, dysmenorrhea, acne, and mastalgia, and include protocol from those sections into multiherb formulae.

Hormonal Modulation

Symptoms suggesting the need for hormonal modulation include:

- Mood swings
- Breast fullness or heaviness
- Fatigue
- Abdominal bloating

TABLE 5-13

Botanical Treatment Summary for PMS

THERAPEUTIC GOAL	THERAPEUTIC ACTION	BOTANICAL NAME	COMMON NAME
Hormonal regulation	Hormonal modulators	*Hypericum perforatum*	Chaste berry
Mood stabilization	Nervines	*Lavendula officinalis*	St. John's wort
Improve stress response		*Leonurus cardiaca*	Lavender
		Matricaria recutita	Motherwort
		Passiflora incarnata	Chamomile
		Scutellaria lateriflora	Passion flower
		Valeriana officinalis	Skullcap
		Vitex agnus castus	Valerian
	Adaptogens	*Eleutherococcus senticosus*	Eleuthero
			Ginseng
		Panax ginseng	American ginseng
		Panax quinquefolium.	Rhaponticum
		Rhaponticum carthimoides	Rhodiola
			Schizandra
		Rhodiola rosacae	Nettles
		Schizandra chinensis	Ashwagandha
		Urtica dioica	
		Withania somnifera	
	Antidepressants	*Hypericum perforatum*	St. John's wort
		Melissa officinalis	Lemon balm
		(Also see adaptogens)	
	Anxiolytics	*Eschscholtzia california*	California poppy
		Lavendula officinalis	Lavender
		Leonurus cardiaca	Motherwort
		Matricaria recutita	Chamomile
		Passiflora incarnata	Passion flower
		Piper methysticum	Kava kava
		Scutellaria laterifolia	Skullcap
		Valeriana officinalis	Valerian
		Verbena officinalis	Blue vervain
		Withania somnifera	Ashwagandha
	Hormonal regulators	*Vitex agnus castus*	Chaste berry
Regulate appetite; relieve sweet cravings; improve bowel function to reduce circulating estrogen load	Bitters	*Centaurium erythraea*	Centaury
		Gentiana lutea	Gentian
		Taraxacum officinalis	Dandelion root
Relieve fluid retention; may improve edema and breast fullness/tenderness.	Diuretics	*Taraxacum officinalis*	Dandelion leaf
Relief of PMS headache	See Premenstrual Migraine and Headache		
Relief of menstrually related pain	See Dysmenorrhea		
Relief of mastalgia	See Benign Breast Disorders and Breast Pain		
Treatment of premenstrual acne	See Acne		
Promote improved sleep	See Insomnia		

Hormonal modulation is a regular part of the treatment approach to PMS management. Chaste tree (*Vitex agnus castus*), taken daily throughout the cycle, is the principal herb used. Increased enterohepatic recycling of estrogens, achieved through dietary modification and herbal bitters (see Hepatics and Bitters) is often also suggested.

Mood Changes

Symptoms suggesting the need to address mood include:
- Fatigue
- Feeling ''overwhelmed''
- Anxiety
- Crying
- Depression

- Increased sense of vulnerability
- Insomnia
- Irritability and angry outbursts
- Lack of interest in daily life
- Nervous tension
- Sadness
- Social withdrawal
- Night waking

Many women respond to hormonal fluctuations with mild to severe mood changes, either with anxiety and heightened (negative) effect, or classic depressive symptoms in which withdrawal and fatigue predominate. Perimenopausal women often experience heightened depressive symptoms owing to declines in estrogen and serotonin. PMS depression, irritability, and fatigue also may occur when a woman is postpartum, breast-feeding, overexercising, underweight, or under stress. Treatment concentrates on hormonal modulation, as well as the use of anxiolytic, antidepressant, nervines, and stress modifying herbs (e.g., adaptogens).

Improve the Stress Response

Symptoms suggesting the need to modify the stress response include:

- Crying
- Fatigue
- Adrenal exhaustion
- Blood sugar dysregulation
- Labile mood
- Feeling ''out of control'' or ''overwhelmed''
- Headaches or migraines
- Hot flushes and night sweats
- Mental fatigue
- Poor word finding, memory loss
- Other symptoms of stress, for example, hair loss and insomnia

Maladaptive stress response in women susceptible to PMS may be an important trigger for premenstrual mood difficulties. Decreased levels of plasma adrenocorticotropic/hormones (ACTH) have been documented in PMS, and the suggestion that the dysphoria of atypical depressions such as postnatal depression, seasonal affective disorder, and PMS are caused by lower levels corticotropin-releasing hormone (CRH).[252,286] Herbal treatment for women who develop PMS in conjunction with exhaustion should combine hormone modulation with adaptogens, nervine tonics, and anxiolytic herbs to counteract the adverse effects of stress on the nervous system. Adaptogens not only assist in restoring a healthy response to stress but also have blood sugar regulatory effects (see Chapter 6 for more on adaptogens). Adequate rest, nutrition, and exercise can also improve stress response.

Premenstrual Pain

Symptoms suggesting the need for pain management include:

- Breast pain
- Headaches or migraines
- Dysmenorrhea
- Aches and pains

Some women experience increased sensitivity to pain premenstrually.

See related topics such as Premenstrual Migraine and Headache; Dysmenorrhea; and Benign Breast Disorder and Breast Pain for treatment options.

Sugar Cravings

Symptoms of PMS food cravings:

- Craving for sweets and refined carbohydrate
- Increased appetite
- Fatigue
- Headaches or migraines
- Irritability, especially when hungry

Sugar cravings are common prior to menses. Abnormal variations in blood sugar may be worsened by a magnesium deficiency, an imbalance in prostaglandins, or prolonged stress. Changes in serotonin levels are also associated with sugar and carbohydrate cravings. Herbalists often include bitters in herbal formulae for sugar cravings; however, the use of herbal treatments for PMS-C has not been evaluated. Herbal adaptogens have demonstrated the ability to regulate blood sugar, and may be of some help in premenstrual sugar cravings. Attention to diet may be the most beneficial approach, teaching women with PMS-C to maintain stable blood sugar by ensuring small frequent meals of high protein and high-quality complex carbohydrates, fresh fruits, and vegetables, and high energy snacks such as nuts and yogurt. Often when a high-quality diet is implemented, with the addition of a complex vitamin and mineral supplement, cravings dissipate. It is also perfectly reasonable for women who are within normal body weight and with healthy diets to indulge in a small amount of sweets premenstrually. When clients have chocolate cravings, encourage them to eat only very dark chocolate—it is much harder to overeat dark than milk chocolate. Nettles (*Urtica dioica*) is an herb often overlooked as an adaptogen; however, a number of herbalists specializing in women's herbal health care have found it remarkably effective in reducing sugar cravings when taken at the onset of a craving.

Premenstrual Syndrome with Fluid Retention

Symptoms of PMS fluid retention:

- Breast fullness
- Abdominal bloating
- Weight gain
- Swollen extremities

Fluid retention is believed to be caused by an increase in circulating aldosterone levels. Aldosterone may be elevated in response to decreased progesterone secretion, elevated estrogens, magnesium deficiency, or stress. Prolactin also may be implicated when breast symptoms predominate. When fluid retention, bloating, breast soreness or heaviness, and weight gain are prominent symptoms, salt and high sodium food (e.g., cheese) intake should be restricted and dietary potassium in the form of vegetables and fruits increased. Herbal diuretics may be considered, but diuresis, whether herbal or pharmaceutical, does not treat underlying causes. Chaste berry should be considered when

there is suspected elevated prolactin, and/or fluid retention accompanied by mastalgia. However, herbal treatments for PMS-H have not been evaluated.

Premenstrual Dysphoric Disorder

Symptoms of PMDD:
- Nervous tension
- Irrational and angry outbursts
- Depression
- Insomnia
- Anxiety
- Agoraphobia
- Social withdrawal
- Lack of interest in daily life

The herbal therapies and additional treatments outlined throughout this section, particularly in PMS with Mood Changes, are applicable to PMDD, although more aggressive treatment may be necessary and more frequent follow-up conducted with the patient. Herbal strategies include hormonal regulation, use of nervines, adaptogens, antidepressants, and anxiolytics.

DISCUSSION OF BOTANICALS

Aviva Romm

Hormonal Modulation

- Black cohosh
- Chaste berry
- Adaptogens

Black Cohosh

Black cohosh has a history of use by the Eclectic physicians for premenstrual and menstrual complaints. Most research has evaluated black cohosh efficacy in perimenopause, for which it has demonstrated positive effects in the treatment of neurovegetative complaints, including hot flashes, sweating, sleep disturbances, and depression.[287–293] Initially thought to have estrogen-like effects via its ability to modulate estrogen receptors, thus called a phtyo-SERM (selective estrogen receptor modulator), it is now thought to have serotinergic or dopaminergic effects rather than estrogenic action. It may be beneficial in PMS patients with headache and to those perimenopausal-type symptoms mentioned earlier that can occur premenstrually. The German Commission E approves the use of black cohosh for the treatment of premenstrual discomfort, dysmenorrhea, and neurovegetative symptoms of menopause.[254] See Plant Profiles: Black cohosh for additional information and warnings on black cohosh use.

Chaste Berry

Chaste berry has been used traditionally, and is still commonly used in Europe and the United States, to relieve symptoms of a number of gynecologic disorders, including those attributed to PMS. The berries are the most popular part of the plant used and contain a wide range of potentially active constituents, including essential oils, iridoids, and flavonoids.[258] In humans, it has been shown (at doses of 120 mg/d) to reduce levels of FSH and increase LH resulting in decreased estrogen and increased progesterone and prolactin levels.[249] Several studies have shown reduction of prolactin concentration after treatment with chaste berry. One proposed mechanism of action is that this herb (doses of approximately 480 mg/d) causes a decrease in prolactin, which leads to a reversal of LH suppression allowing full development of the corpus luteum, increasing progesterone levels, and reducing symptoms of PMS. However, chaste berry also appears to have dopamine-agonistic properties at higher doses.

No long-term randomized trials have compared medical treatments (e.g., OCs or antidepressants) with chaste berry. Numerous trials have evaluated the efficacy of chaste tree in the treatment of PMS. A multicenter study over 16 years assessed the efficacy of chaste berry (Agnolyt) in 1592 women suffering from PMS and related menstrual disorders. In 90% of patients, the doctor's evaluation was good or satisfactory, 33% became symptom free, whereas 51% recognized improvement. One third of those wanting to conceive became pregnant during treatment. A study involving 1500 women suffering from PMS were administered chaste berry extract. Of these women 1016 had corpus luteum insufficiency and 170 had fibroids. After treatment for an average of 166 days, 90% showed improvement in symptoms occurring on average 25 days after commencing treatment.[294]

A double-blind study involving 217 women tested Vitex against placebo for the treatment of premenstrual syndrome. For a period of 3 months, 105 women took chaste berry 300 mg tablets three times daily, whereas 112 women took placebos. The results of the study showed a dramatic improvement at the end of the first cycle for both groups with relative stability over the remaining two cycles. Vitex improved the symptom ''feel jittery or restless,'' but there was a difference observed between placebo and the herb for other symptoms. A study compared the efficacy of chaste berry to pyridoxine (B_6) in the treatment of PMS over three menstrual cycles. Ninety participants were given one capsule of Agnolyt (each capsule containing 3.5 to 4.2 mg of dried chaste berry), and one placebo capsule daily. The other 85 participants were given placebo twice daily from day 1 to 15 and then 100 mg bid of pyridoxine from days 16 to 35. When assessed by patients and the investigators, the chaste tree group achieved a significantly greater improvement in typical PMS complaints such as breast tenderness, edema, inner tension, headache, constipation, and depression compared with pyridoxine. Both preparations were well tolerated with only mild reactions reported in a few patients. Five patients from the chaste tree group became pregnant.[295]

Another double-blind, placebo controlled study examined the tolerability and efficacy of chaste berry extract for premenstrual mastalgia. The treatment or placebo was given over three menstrual cycles. Mastalgia during at least 5 days of the cycle before the treatment was the strict inclusion criteria. The results showed the intensity of the cyclical breast pain diminished in the chaste berry group and the herb was well tolerated.[296] In a prospective, multicenter trial the efficacy of a chaste berry was investigated in 43 patients with PMS. The patients took 20 mg Vitex extract daily for three menstrual cycles.

Symptoms in three posttreatment cycles were compared with baseline cycles before administration of the herb. A menstrual distress questionnaire was the tool used for self-assessment. At the end of the study, symptoms were reduced in the late luteal phase by 47.2%. Although symptoms gradually returned after treatment cessation, a difference from baseline remained for up to three cycles.[297] A multicentric open trial investigated the efficacy and tolerance of Vitex in 1634 patients suffering from PMS. A specific questionnaire was developed for determining the effect of chaste berry on the four characteristic PMS symptom complexes: depression, anxiety, craving, and fluid retention. After three menstrual cycles, 93% of patients reported a decrease in the number of symptoms or symptom complexes or even cessation of PMS complaints and 85% of physicians rated the treatment as good or very good. The severity and frequency of breast pain reduced after 3 months. The majority of patients assessed the tolerance of Vitex as good or very good. Adverse drug reactions were suspected in only 1.2% of patients, but none were serious.[47]

A randomized, double-blind, placebo-controlled trial compared chaste berry with placebo in 170 women with premenstrual syndrome over three menstrual cycles. Women undertook self-assessment of irritability, mood alteration, headache, breast fullness, and other menstrual symptoms and were also assessed for changes in clinical global impression. The study showed that chaste berry was an effective and well-tolerated treatment for the relief of PMS symptoms in 52% of the trial participants compared with 24% placebo.[299] As with all herbal remedies, a variety of chaste berry preparations are used that can differ substantially in terms of, for instance, concentration of active ingredients or bioavailability. Surveys of members of the National Institute of Medical Herbalists, and the American Herbalists Guild, showed that the tincture is the most popular preparation among herbalists, in a dose of 3 to 5 mL qd–bid, but fluid extracts and powdered herb preparations are also used.[258,300] Chaste berry is approved by the German Commission E for irregularities of the menstrual cycle, PMS, and mastodynia (Fig. 5-11).[254]

Figure 5-11 Chaste tree berry (*Vitex agnus castus*). (Photo by Martin Wall.)

Adaptogens

Although research has not been conducted specifically on the treatment of PMS with adaptogens, herbs in this category may have an important role to play in the treatment of affective mood symptoms and decreased stress resistance in the luteal phase of the menstrual cycle. For example, ashwagandha is an important nervine tonic and anxiolytic for women and is used as an adaptogen during episodes of prolonged stress. It can be used as an adjunct to other herbal treatment to reduce the effects of stress-induced hormonal changes, and has mild musculoskeletal relaxing activity.[301,302] Numerous clinical studies have confirmed that *Eleutherococcus* has the ability to improve physiologic responses to stress.[303] Apart from improving exhaustion-induced PMS symptoms, it can be used to improve mood in conjunction with nervine tonics, and as an adrenal adaptogen to improve hypothalamic-pituitary-adrenal axis activity. A discussion of adaptogens is found under Herbal Actions; thorough evidence for individual adaptogens is presented in Chapter 7. No clinical trials have evaluated the effects of adaptogens on PMS. Suggested adaptogens for PMS treatment include ashwagandha, ginseng, American ginseng, and eleuthero.

Anxiolytics, Nervines, and Antidepressants

- Kava kava
- Lavender
- Motherwort
- St. John's wort

Kava

Herbalists commonly use kava for anxiety and insomnia accompanying PMS. A systematic review and meta-analysis of the evidence for kava as an anxiolytic suggests that kava is effective compared with placebo.[304] Several small trials have demonstrated the efficacy of kava in treating menopause-related anxiety; however, no trials have evaluated kava for women with PMS symptoms.[249] Recently, concerns have arisen over the safety of kava owing to approximately 80 international case reports of hepatotoxicity allegedly related to kava consumption, leading several nations to ban kava sales. Although the evidence for kava-related liver disease is highly inconclusive, kava should not be taken by patients using other medications, known hepatotoxic substances, or with known liver disorders.[257] See Plant Profiles: Kava for a discussion of kava safety and contraindications.

Lavender

Lavender is an excellent herb for the anxiety, irritability, insomnia, and depression that accompany PMS. The essential oil constitutes 1% to 3% of the active components and has been shown to elicit feelings of happiness.[305] The German Commission E Monograph states the indications for lavender as mood and sleep disturbances, restlessness, and intestinal conditions of nervous origin.[254] It can be taken as a tea or tincture, or the essential oil indirectly inhaled through a diffuser, in a bath, via application to a pillow on which the patient will sleep, or diluted for use in a massage oil.

Motherwort

Motherwort was used by the Eclectics, and continues to be used by herbalists today for the treatment of nervous exhaustion, irritability, hysteria, and nervous excitability.[306] It is used clinically for the treatment of dysmenorrhea, and also has mild cardiotonic action, effectively reducing palpitations. Motherwort's combined actions make it a useful addition to PMS formulae, particularly when there is emotional lability and irritability, and if there is accompanying pain. It has a good safety profile. Due to its bitter taste, it is typically taken in tincture form. The German Commission E approves motherwort for nervous cardiac disorders.[254]

St. John's Wort

St. John's wort is prescribed for depressive symptoms of PMS or for PMDD. Trials have shown favorable results in depression, and St. John's wort has been compared favorably with both placebo and other antidepressants. A pilot study evaluating the effects of PMS St. John's wort demonstrated significant improvement in all outcome measures, with over two-thirds of the sample experiencing at least a 50% decline in symptom severity.[307] Antidepressant drugs for PMS are increasingly prescribed during the luteal phase of the cycle only; however, St. John's wort seems to be more effective when taken all month. In recent years, numerous double-blind, randomized trials have been conducted examining the efficacy of St. John's wort compared with placebo. Although one study failed to find any benefit over placebo, many others have found it to be an effective and well-tolerated herb for the treatment of mild to moderate depressive disorders.[308–310] In a large study of 2166 patients suffering from mild to moderate depression, between 83.7% and 88.6% improved after approximately 7 weeks of treatment. The drug tolerance was good or very good for 99% of all patients, and adverse drug reactions were only 0.41%.[311] A number of trials have compared *Hypericum* with common antidepressant medications, usually with favorable results. One double-blind, randomized trial compared the efficacy and side effects of St. John's wort and the antidepressant, sertraline, in 87 patients with major depression. Both treatments were effective and there were no important differences in changes in depression between the two groups at 12 weeks, with significantly more side effects in the sertraline group than in the St. John's wort group, suggesting St. John's wort is a good first-choice therapy.[312] Another trial compared St. John's wort, placebo, and sertraline. Neither sertraline nor St. John's wort were significantly different from placebo and neither was effective in moderately severe major depression, with 31.9% of the placebo-treated patients, 23.9% of the St. John's wort–treated patients, and 24.8% of sertraline-treated patients showing improvement.[313] Two randomized, controlled, double-blind trials compared St. John's wort and Prozac. In one, between 42% to 50% of the St. John's wort group and 52% to 58% of the Prozac group responded favorably, suggesting that St. John's wort is therapeutically equivalent to Prozac and is a rational alternative to synthetic antidepressants.[314] In the other trial, St. John's wort extract and fluoxetine were compared in 240 patients with mild to moderate depression. Both treatment groups were equivalent in terms of response, but the safety of St. John's wort was substantially superior to fluoxetine and fewer adverse events were reported.[315] A recent study examined the acute effects of St. John's wort on cognitive and psychomotor function compared with amitriptyline. Amitriptyline-impaired performance on a battery of psychological tests, whereas St. John's wort had neutral effects on performance in these tests.[316]

Additional important nervines and anxiolytics for the treatment of anxiety, insomnia, and irritability associated with PMS include:

Anxiolytics

California poppy
Chamomile
Passion flower
Skullcap
Valerian
Blue vervain

These herbs are discussed elsewhere throughout this book, and in Plant Profiles.

Anti-inflammatory Herbs

- Evening primrose
- Ginkgo

Evening Primrose Oil

Many practitioners use evening primrose oil (EPO) for PMS believing that its effects on reduction in inflammatory prostaglandins (PGE1) may improve PMS symptoms. Seven clinical trials have failed to find any improvement in PMS symptoms; however, it has been noted in the literature that small sample sizes in five of the trials may have prevented detection of modest benefit.[249] One paper reported positive outcomes for cardinal symptoms, but the trial had methodologic flaws.[258] It is typically recommended at a dose of 2 to 3 g/d.[249]

Ginkgo

A placebo-controlled trial demonstrated statistically significant positive results in reduction of breast pain and fluid retention, but no other symptoms of PMS, after treatment for two cycles.[257,258] Constituents may play a role in anti-inflammatory effects, antioxidant effects, or vascular smooth muscle relaxation. Further evaluation is needed to determine whether there is an important role for ginkgo in the treatment of these PMS symptoms.[249,258]

Bitters and Hepatic Tonics

Many herbalists consider the use of herbs that gently improve liver function important in formulas for hormonal regulation.

Herbal bitters, such as gentian, centaury, and dandelion are commonly used and also may be used to regulate blood sugar fluctuations associated with functional

Traditional Chinese Medicine and PMS

When it comes to the treatment of PMS in the clinic, many herbalists turn to the use of TCM, which offers a unique perspective on possible etiologies and treatment. The predominant patterns associated with PMS are *liver Qi stagnation and blood deficiency,* to which women are considered especially susceptible because of monthly blood loss. Further, anger, frustration, and irritability may actually cause liver qi stagnation, making this a self-perpetuating problem. Although TCM prescribing is always based on physical examination and determination of the specific imbalances of the individual, several classic formulas may be more generically applied.

***Xiao Yao Wan* (Free and Easy Wanderer)**
For liver qi stagnation: Indicated for premenstrual abdominal and breast distention, irritability, moodiness, depression, and clumsiness.

Ingredients: *Bupleurum falcatum* (9 g), *Angelica sinensis* (9 g), *Paeonia lactiflora* (12 g), *Atractylodes macrocephalae* (9 g), *Poria cocos* (15 g), *Glycyrrhiza uralensis* (6 g), *Zingiber officinalis* (three slices)
This formula is taken as a decoction or powder, and is available as a patent medicine. (See Safety of Herbal Medicine for Precautions with TCM Patent Medicines.)

***Angelica-Peony-Rehmannia* Decoction**
For liver-blood deficiency: Indicated when there is depression, weepiness, slight abdominal and breast distention, fatigue, poor memory, poor sleep, mild dizziness, pale complexion, and scant periods.
This formula is used to nourish the blood.

Ingredients: *Angelica sinensis* (9 g), *Paeonia lactfilora* (8 g), *Rehmannia glutinosa* (prepared-9 g), *Dioscorea oppositae* (6 g), *Fructus Cornii officinalis* (4 g), *Alismatic orientalis* (4 g), *Moutan radicis* (4 g), *Poria cocos* (8 g).

Ctirus reticulata (4.5 g), Bupleurum falcatum (6 g), Albizzia julibrissin (9 g)
To be taken as a decoction throughout the menstrual cycle.

(reactive) hypoglycemia and may improve symptoms when associated with PMS.[303]

Diuretics

Dandelion

Dandelion leaf can be considered for the symptomatic relief of fluid retention common before menstruation. Unlike most pharmaceuticals, it is potassium sparing. The usual dose of the dried leaf is 4 to 10 g three times daily by infusion; of the fluid extract, 4 to 10 mL three times daily.

CASE HISTORY: PREMENSTRUAL SYNDROME

Ruth Trickey

Julie is a 42-year-old woman presenting with prolonged and severe PMS. She describes her moods as swinging violently just around her periods and says she is ''unpleasant to be around, especially for her kids.'' On further questioning, she revealed a tendency to verbal abuse when premenstrual. She decided to have children late in life after a successful career and has had them close together so that the age gap is small. She is now a full-time mother and does not have the social or professional contacts she once enjoyed. Julie was seeking advice for self-diagnosed PMS but the severity of her symptoms indicated that a more appropriate diagnosis was PMDD. She had developed postnatal depression after the birth of her second child, but was offered little support from her medical practitioner who discouraged her from seeking counseling and put her on the antidepressant Prozac. She was taken off after a year but continued to have severe premenstrual mood changes, including depressive episodes, agoraphobia, low self-esteem, insomnia, and angry outbursts. This worsened as the children became older, and as she put it ''became more difficult to control.'' She described low energy levels, generalized body aching, poor adherence to a reasonable diet with abnormal sugar and salt cravings, headaches, and a tendency to catch numerous colds premenstrually. In addition, she developed stress and urge incontinence since the birth of her children. Although it was clear that counseling will go a long way to helping her deal with many of her emotional problems, she was unwilling to undertake this step and asked for herbal treatment instead. A treatment plan was discussed that consisted of hormone-regulating herbs combined with nervine tonics and nervine sedatives.

Her first treatment was as follows:

1. Chaste berry tablets 1000 mg, one tablet daily in morning continued throughout the cycle
2. An herbal tincture:

Botanical Prescription 1

Ashwagandha	(*Withania somnifera*)	30 mL
St. John's wort	(*Hypericum perforatum*)	20 mL
Kava kava	(*Piper methysticum*)	30 mL
Lavender	(*Lavandula officinalis*)	20 mL
		Total: 100 mL

Dose: 7 mL bid

3. Fish oil capsules, 1000 mg, two capsules twice daily

She was asked to restrict stimulants, sugar, and salt; substitute refined carbohydrates with complex carbohydrates; have a higher-protein intake in the evenings; and increase her dietary intake of essential fatty acids. In addition, she undertook a regular regimen of pelvic floor exercises and restricted the number of times she passed urine by not voiding at the first urge to do so. She was also asked to keep a menstrual symptom diary for every day of the cycle.

At her next visit, Julie reported a marked change in her mood premenstrually, with improved sleep and better relationships with her children. Her bladder control had improved in that the urge incontinence was better, but she still suffered from stress incontinence. A referral was arranged for a physiotherapist specializing in bladder control and Julie also decided to see a counselor. Her herbal prescription was continued and she was also given magnesium and vitamin B complex to be taken for 10 days before her period. This regimen was continued for three cycles.

One of the main issues in PMDD is the long-term management, especially following postnatal depression. Herbal treatment for depressive mood change needs to be protracted in many cases and may need to be continued for up to a year or even longer. A holistic approach incorporating dietary and lifestyle changes in conjunction with effective counseling is necessary so that herbal medication can be stopped with a high degree of confidence that symptoms will not recur. In addition, hormonal symptoms must be addressed. It is common for some form of PMS to be an ongoing and major concern for women who have suffered from PMDD and postnatal depression, especially when they are in their forties when PMS can classically worsen anyway. In Julie's case, she had already tried antidepressants and was fearful that herbal treatments might cause her the same problem; that is, she would manage while on the treatment, but her mood would deteriorate once more when the herbs were ceased. The determining factor would be whether her mood changes and physical symptoms respond well to herbs and lifestyle changes. Diet and regular exercise are essential.

Ongoing herbal treatment and supplements were:

Chaste berry:	1000 mg	one tablet every morning for another 6 months
St. John's wort:	1500 mg	two tablets every morning for 6 months
Fish oils:	1000 mg	one twice daily

In combination with an herbal mix of nervines for symptom control in the week premenstrually which included:

Botanical Prescription 2

Ashwagandha	(*Withania somnifera*)	30 mL
Kava kava	(*Piper methysticum*)	30 mL
Lavender	(*Lavandula officinalis*)	20 mL
Milk thistle	(*Silybum marianum*)	20 mL
		Total: 100 mL

Dose: 5 mL qd for 10 days premenstrually.

NUTRITIONAL CONSIDERATIONS

Diet, nutritional supplements, and exercise have been studied for PMS not PMDD, albeit in a limited number of investigations.[246,248] In a comprehensive review of the literature on PMS and nutritional supplementation by Stevinson and Ernst, only 13 reliable RCTs were identified.[248] In spite of the lack of literature demonstrating efficacy of many of the dietary changes commonly recommended for PMS, strategies such as improving fiber intake, reducing harmful fats, improving the intake of good-quality fats, proteins, fruits, and vegetables, ensuring proper nutrient intake, and reducing the consumption of coffee, sugar, and refined carbohydrates are all beneficial health practices and seem wise to recommend. Calcium carbonate, 1200 mg per day in divided doses, has been found in two controlled studies to reduce PMS symptoms.[317,318] Magnesium supplementation was found to be effective for the treatment of PMS in one placebo-controlled trial.[319] Vitamin E, 400 units per day, may be minimally effective for PMS.[2] Vitamin B_6, 50 to 100 mg per day, may be effective for PMS based on meta-analysis of inconsistent data.[246] Dietary recommendations, such as avoiding salt, chocolate, caffeine, and alcohol have never been subjected to either observational or controlled studies.[246] Low Dog cites a 1983 report that found that women with PMS consumed 275% more refined sugar, 79% more dairy products, 78% more sodium, 62% more refined carbohydrates, 77% less manganese, and 53% less iron that women without PMS.[257] Clearly, these data tell us that dietary modifications may play a significant role in improving PMS symptoms. Surprisingly, no comprehensive dietary modification strategies for PMS treatment have been evaluated to date.[249]

Reduction in Coffee and Sugar

Coffee and sugar consumption is higher in women who experience PMS than in those who do not. Based on the findings from a 1983 survey and two trials demonstrating that regular caffeine consumption is associated with a higher incidence of PMS, many practitioners recommend the reduction of caffeinated products in susceptible women. Many women self-report that a reduction in coffee consumption improves their symptoms.[249,251] Heavy sugar consumption may increase sodium and water retention, and increase magnesium excretion.[257] Blood sugar imbalances as a result of high sugar consumption can also negatively affect mood and lead to further sugar cravings.

Calcium

Ovarian hormones influence calcium, magnesium, and vitamin D metabolism. Estrogen regulates calcium metabolism, intestinal calcium absorption, and parathyroid gene expression and secretion, triggering fluctuations across the menstrual cycle. Alterations in calcium homeostasis (hypocalcemia and hypercalcemia) have long been associated with many affective disturbances. A number of clinical trials have suggested a positive relationship between calcium supplementation and improved mood and somatic symptoms in PMS (including food cravings, eater retention, pain, and negative affect) ranging from clearly beneficial to modest results.[318] Numerous researchers have concluded that unless contraindicated, calcium supplementation should be considered a sound treatment for PMS treatment. The recommended dosing schedule is 1200 to 1600 mg/day.[318,320]

Vitamin B_6

Pyridoxine deficiency is one hypothesized cause of PMS, and in Europe, B_6 supplementation is an accepted treatment. Vitamin B_6 is prescribed for PMS symptoms based on the rationale that it demonstrates positive effects on the neurotransmitters serotonin, epinephrine, histamine, dopamine, and taurine.[249] Positive effects have been observed in most trials for PMS with B_6 doses ranging from 50 to 600 mg daily or when B_6 (300 mg) is given in conjunction with other nutrients and a healthy diet.[321–324] Two comprehensive literature reviews suggest that B_6 is better than placebo in improving PMS symptoms; however, owing to the nature of the trials, evidence of its value remains inconclusive.[248,257] Sensory neuropathy is unlikely to occur when vitamin B_6 is given at doses of 50 to 100 mg/day for short periods of no more than 6 months; nonetheless, practitioners should be aware of this possibility and inform their patients of toxicity symptoms.[325] Given its low cost and the relative safety of appropriate doses, supplementation of B_6 in the form of a multivitamin may be reasonable for women with PMS and a suboptimal diet.[257,324]

Magnesium

Three small RCTs evaluated the effects of magnesium supplementation on PMS symptoms. Two concluded that supplementation improved symptoms; in one trial overall scores were positive, and there was improvement in negative effect; in the other the only area of significance improvement was fluid retention. The third trial showed improvement in anxiety when combined with B_6.[248] In one trial, studies included data on prostaglandin F2 alpha (PGF2) levels in menstrual blood. Women taking magnesium demonstrated significantly lower PGFS levels in their urine and reported a decrease in premenstrual pain. Magnesium is known to also promote muscle relaxation. A Cochrane database review on the literature on magnesium concludes that magnesium is more effective than placebo in the treatment of PMS-related pain.[249] Natural medicine practitioners typically recommend 400 to 800 mg/day.[257]

Tryptophan

There are some indications that premenstrual food cravings might be an attempt to increase the plasma ratio of tryptophan to other amino acids in order to improve symptoms via an increased central serotonergic activity.[326] There is also limited support (one placebo-controlled trial) for L-tryptophan, 6 g/day, from ovulation until day 3 of menses for the treatment of PMDD.[327] In addition, researchers have observed a reduction in premenstrual symptoms when women are given a dietary supplement that selectively increases tryptophan levels.[328] Dietary changes that can be reasonably expected to achieve a similar result include increased frequency of smaller volumes of food; no sugar or refined carbohydrates; regular complex carbohydrate and protein intake at each meal with increased consumption of fish, legumes, egg, lean meat, and/or low-fat yogurt.

Essential Fatty Acids

Dietary or supplemental omega-3 essential fatty acids, generally in the form of fish oils, are beneficial in depression and doses of up to 4000 mg daily are advisable.[329,330] However, studies on evening primrose oil have demonstrated no benefit in the treatment of PMS symptoms. (See Evening Primrose Oil, in Supportive Evidence for Botanicals.)

Reduction in Saturated Fat Consumption

This is commonly recommended in the herbal and naturopathic communities based on the belief that reducing enterohepatic recycling of estrogens can improve symptoms of PMS, and can be achieved by a reduction in saturated fat consumption, views that are somewhat supported by early literature on excess estrogens.[331–333] However, this approach assumes that excess estrogen is an etiologic factor in PMS, which has not been conclusively demonstrated by biochemical assays.[245]

Increasing Dietary Fiber

As with the previous recommendation, an increase in dietary fibers is thought to reduce excess estrogen by a reduction in reabsorption of estrogens from the intestine however, it is unclear how much of a role estrogen plays in PMS.[334–336] Vegetarians have significantly lower activity of the bacterial enzyme responsible for conversion of estrogen metabolites back into estrogens than meat eaters because they tend to have a higher fiber diet and a lower intake of fats. Lactobacillus acidophilus also reduces the activity of beta glucuronidase, suggesting a positive effect on estrogen excretion from eating yogurt and fermented milk products.[337,338] However, this practice has not been evaluated in the treatment of PMS, and like suggesting a low-fat diet, assumes that elevated estrogens is part of the pathophysiology of symptoms.[249,257]

ADDITIONAL THERAPIES

Numerous nonpharmacologic therapies may be beneficial in the treatment of PMS, including supportive or psychological therapy, exercise, and dietary supplementation. The most extensively reviewed interventions and approaches are reviewed in (Box 5-26); diet and nutrition were previously addressed.

Lifestyle

Exercise

Regular, moderate exercise improves mood and feelings of well-being. Women with PMS who exercise regularly and frequently have fewer symptoms than women who do not exercise. High exercisers experience fewer behavioral and mood changes, better concentration, and less pain.[248,339–341] One study of over 1800 women found that 50% used exercise as a self-help measure for alleviating PMS symptoms, and over 80% of these found it beneficial.[248] Aerobic exercise may help the physical symptoms of PMS.[339,342] Unfortunately, exercise is often overlooked as a treatment approach in conventional medicine.[248] Frequency of exercise, rather than intensity, appears more significant in prevention and

BOX 5-26

Summary of Nutritional and Additional Therapies for Premenstrual Symptoms, PMS, and PMDD

The interventions in this table are commonly recommended in clinical practice.

- Diet and nutrition
  - Reduction in coffee and sugar
  - Calcium
  - Vitamin B_6
  - Magnesium
  - Tryptophan
  - Essential fatty acids
  - Reduction in saturated fat consumption
  - Increasing dietary fiber
- Lifestyle
  - Exercise
  - Yoga
  - Massage therapy
  - Progressive relaxation and guided imagery
- Psychosocial
  - Cognitive therapies
  - Psychotherapy/Counseling
  - Celebrating menstruation

alleviation of physical and psychoemotional symptoms.[257] The mechanism behind this is proposed to be a reduction in estrogens and catecholamine levels, leading to improved glucose tolerance and endorphin levels.[257] Regular exercise also may increase a woman's sense of personal control and self-esteem, also shown to lead to a reduction in symptoms.

Yoga

After a 10-month empirical study to evaluate the effectiveness of specific yoga postures in relieving PMS symptoms (n = 40), the authors found significant scores on self-reported menstrual distress scales in women in the yoga-trained group versus the control group, which did not undergo yoga training.[249]

Massage Therapy

One RCT evaluated the effects of massage therapy in improving PMS. Progressive relaxation was used as the control. Some improvement in PMS was seen over baseline after one cycle of treatment; however, the study methodologies did not include intergroup comparisons, so conclusive evidence cannot be inferred.[248] Although massage might not prevent PMS, it may improve symptoms; massage therapy has been demonstrated to reduce stress, so for women with a high stress component to their PMS symptoms or musculoskeletal discomforts, regular massage may be beneficial.

Progressive Relaxation and Guided Imagery

Eliciting the relaxation response is a safe, and nonpharmacologic intervention in the treatment of PMS.[343] Women with PMS improved with progressive muscle relaxation in conjunction with guided imagery.[344] An interesting study of the use of foot, ear, and hand reflexology showed that those women who received pressure to actual reflex points responded significantly better than the women who were given treatment of incorrect reflex points.[345] Acupuncture and massage are also very effective techniques to relieve the severity of PMS.[346]

Psychosocial

Cognitive Therapies

Three published trials on cognitive therapy suggest that it is superior to a wait list (control) for improving premenstrual psychological and physical symptoms and functioning. Cognitive therapy was also found to be superior to group awareness and information-focused therapy.[246,347] Group coping skills training was found to be superior to relaxation training. However, relaxation therapy twice daily was found to be superior to daily PMS symptoms charting alone.[343] Diary symptom recording and communicating with family members about the connection between PMS and behavior are also considered supportive therapy, although they have not been well studied.[246]

Psychotherapy/Counseling

Women with low self-esteem, feelings of lack of control over their personal lives, and sense of personal disempowerment have a higher incidence of PMS symptoms. Psychotherapy and counseling have been shown to improve mild to moderate depression and anxiety as effectively as antidepressants. Various types of counseling and psychotherapy techniques are theoretically useful for women with PMS, although there have been few suitable studies to evaluate these techniques. One study looked at the effectiveness of cognitive behavioral therapy in PMS and found that it was useful in improving symptoms.[347]

PREMENSTRUAL HEADACHE AND MIGRAINE

Laurel Lee, Aviva Romm

Headaches and migraines are common conditions with substantial costs to individuals and society.[348] They are among the most common causes of emergency room visits and medical appointments, and also account for many lost days of school and work, and disruptions in family relationships.[349,350] In a survey of nearly 20,000 individuals, 53% reported that severe headaches caused substantial impairment in activities and required bed rest, and 51% reported that work or school activity was reduced by at least 50%.[350] Migraines cause more disability than tension headaches, with at least 20% of sufferers requiring at least 1 day of work absence per month, and cancellation of family and social activities.[351]

Data from several studies and surveys, including the American Migraine Study II, estimate the prevalence of migraine to be approximately 18.2% in females and 6.5% in males.[350,352] Prior to puberty, there is no gender difference in prevalence; however after puberty, women experience them significantly more frequently. Menstrual migraine (MM) has an onset at menarche in 33% of affected women.[352,353] The female:male

prevalence ratio is 2:1 at 20 years, and 3.3:1 between ages 42 and 44 years. This ratio decreases slightly but persists into menopause.[351] Prevalence is highest in middle life (ages 40 to 49).[350] In 7% to 14% of women with migraine, headache occurs only with menses. This is referred to as true menstrual migraine (TMM). Sixty percent of women with migraines throughout their cycle observe an association between increased headache onset and menses, referred to as menstrual migraine (MM), or menstrually triggered migraine.[351–354] In one study of 504 women with a history of migraine, 68.7% reported migraine occurrence with PMS, 29% reported menopausal symptoms, and 24.4% reported an association with OCs or HRT. Sixty-one percent reported experiencing migraine during pregnancy; 20.4% stated that they did not experience migraine during pregnancy. During pregnancy, headache symptoms improved in 17.8% of patients, remained unchanged in 27.8%, and worsened in 34%. Patients with onset of headache prior to age 20, or with menarche, are more likely to experience headaches with the menstrual cycle.[355] Although migraine prevalence typically decreases with advancing age, it may worsen at menopause.[352] Migraine prevalence appears to be higher in whites than blacks and is inversely proportional to income status.[350]

The headache classification committee of the International Headache Society recognizes 13 distinct headache categories.[349] This chapter focuses on headache and migraine associated with the menstrual cycle. Menstrual headaches include all headaches temporally related to the menses, whether occurring prior to, during, or after the period.[354] Migraine headaches can be classified as *classic migraine* (associated with visual aura), *common migraine* (no aura), and *complicated migraine* (associated with dramatic transient focal neurologic characteristics such as blindness, unilateral paresthesias, and so forth).[354] Tension headaches are the most prevalent types of headaches, and can be episodic or may occur chronically and daily. When occurring daily, they may be associated with depression. As with these other headaches, tension headaches are more common in women than men.[349]

The term *menstrual migraine* has not been universally defined.[356] True menstrual migraine (TMM) is defined as migraine that occurs regularly 1 to 2 days prior to menses to day 3 of the menstrual cycle and at no other time.[348] Menstrual associated migraine (MM) refers to attacks that occur at any time of the cycle, with increased frequency during menstruation.[348,352] Menstrual headache and migraine often occur in conjunction with other menstrually related symptoms, especially PMS, nausea, and dysmenorrhea; however, the presence of other symptoms is not a criteria for the diagnosis of a menstrual headache or migraine. Menstrual migraines of both types are frequently longer in duration, intractable to regular migraine treatments, and are typically not associated with migraine aura, even in patients who at other times of the month experience aura with migraine; however, migraine with aura is also increased 66% in the premenstrual and menstrual phase. Migraine and nonmigraine headaches are at least twice as common during the premenstrual and menstrual phases as between menses, and the highest incidence occurs on the day prior to and on the first few days of menstruation.[352]

PATHOPHYSIOLOGY

Headaches that specifically occur in relationship to the menstrual cycle, as well as menopause and pregnancy, appear to have their origins in the complex sex hormone fluctuations and interrelated neurotransmitter changes that occur during these times of intense hormonal change. The etiologies of PMS are similar to those implicated in premenstrual headache and migraine. [See Premenstrual Symptoms, Premenstrual Syndrome (PMS), and Premenstrual Dysphoric Disorder (PMDD).] Estrogens and progestins have powerful effects on central serotonergic and other neurotransmitters and receptors.

Estrogen withdrawal in the luteal phase, particularly in women with elevated estrogen levels in the follicular phase, has been shown to precipitate migraine and may be the primary cause of migraine as opposed to sustained high or low levels of estrogens. Estrogens given premenstrually delay the onset of migraine without preventing the onset of menstruation.[351,352] Women with menstrual migraines may have higher baseline estrogen levels than nonsufferers, and thus the extent of the decline may be the causative factor.[351] 5HT levels are reduced during the luteal phase in MM sufferers, and may be caused by catabolic changes, reduced synthesis, or estrogen withdrawal, which is itself associated with decreased peripheral 5HT, and increased blood vessel permeability to substance P, prolactin, and neurotransmitters.[351]

Opioid responsiveness also changes premenstrually, and may be associated with premenstrual decreases in both pain and stress control.[351] The hormone-mediated effects on the rhythm of CNS neurons and the serotonergic pain-modulating systems appear to play an important role in the etiology of menstrually related headaches, as do the effects of progesterone metabolites on neurosteroids, particularly at the GABA receptors.[351,352] Progesterone metabolites (e.g., allopregnenolone) may modulate anxiety, pain, stress response, and depression in sensitive individuals through interactions with endogenous benzodiazepine receptors.[352,357] Declining progesterone levels owing to luteal phase insufficiency may be, in part, responsible for increased prevalence of headache and migraine during the luteal phase and early menstrual period. Increased inflammatory prostaglandins associated with menstruation may be implicated in the etiology of MM, TMM, and premenstrual headaches because of neurogenic inflammation. Other associated symptoms include cramping, diarrhea, nausea, fainting, flushing, and difficulty concentrating.[351,352]

Menstrual migraineurs also have decreased nocturnal urinary melatonin immunoreactivity, a marker for nocturnal melatonin secretion. Melatonin exhibits a circadian pattern, with low concentrations during the day, and high concentrations at night. Melatonin promotes sleep and helps to establish patterns for biological rhythms, including hormone patterns. It may be that women with MM have delayed melatonin secretion or a sympathetic hypofunction, which has been associated with migraine.[352]

Pregnancy is associated with noncyclic rises in sex hormone levels; menopause is associated with noncyclic declining levels—both are associated with changes in previous migraine status.[353] Additionally, OC use during the reproductive years and HRT use in menopause may increase the intensity and prevalence of headaches in some women.[358]

Stress is also a common trigger of both headache (especially tension headache) and migraine. Migraine attacks frequently occur within 2 days of increased periods of exposure to stressors, or ''daily hassles,'' defined as ''the minor events of everyday life.'' Mood changes, including tension, irritability, annoyance, depression, or fatigue, significantly increase the likelihood of a migraine attack in women.[359] Stress has been demonstrated to exacerbate hormonally related stress intolerance, which in a vicious cycle can further dysregulate the endocrine system (i.e., stress can increase latent hyperprolactinemia); women with PMS symptoms may have endocrine and neurotransmitter-related reduction in stress tolerance.

In vitro fertilization and embryo transfer (IVF-ET) might also be associated with various degrees of headache, mostly observed in patients with a migraine headache background, and occurring specifically in the downregulation stage of treatment when very low levels of 17-β-E2 are observed.[360]

SYMPTOMS OF MIGRAINE

- Unilateral or bilateral head pain that is aching, throbbing, stabbing, or burning.
- May be preceded or accompanied by a visual ''aura'' or other visual disturbances such as flashing lights or visual field defects
- Extreme sensitivity to light, noise; craving for a dark, quiet environment
- Nausea, vomiting
- Pain aggravated by motion/movement
- Attacks may persist for 3 to 72 hours

DIAGNOSIS

History taking and review of a ''headache diary'' are the most accurate diagnostic tools for premenstrual headache and migraine; establishing the timing of headache/migraine allows for a definitive diagnosis. Possible serious underlying causes of headache should always be ruled out through differential diagnosis; however, insidious causes rarely cause headaches that occur with the periodicity of MM and TMM.

DIFFERENTIAL DIAGNOSIS

Less than 5% of headaches are the result of serious underlying causes.[349] Differentiation of TMM and MM is based on the appearance of TMM exclusively in the days immediately prior to or during the menstrual flow. Table 5-14 provides a differential assessment of headache patterns for migraine and tension headaches. Any headaches presenting with the warning signs in Box 5-27 require prompt medical evaluation.

CONVENTIONAL TREATMENT APPROACHES

Unfortunately, the treatment of migraine associated with changes in sex hormone levels is difficult and often refractory to conventional therapies.[358] The conventional medical approach includes a combination of preventative, nonpharmacologic, and pharmacologic interventions.

Prevention

Premenstrual migraine prophylaxis uses a combination of pharmacologic and nonpharmacologic measures, for example, stress reduction and pharmacologic agents. These are timed in accordance with the pattern of the

TABLE **5-14**

Differential Diagnosis of Tension versus Migraine Headache

SYMPTOM	TENSION HEADACHE	MIGRAINE
Onset	Gradual, triggered by stress	May be precipitated by aura, patient may waken with headache; many women report that migraines commonly begin in the late afternoon
Duration	8–12 hours, but may be episodic or chronic lasting days, weeks, or months	Typically 8–12 hours but may last 3 hours to 3 days
Frequency	Very variable from daily to only occasionally or rarely	1–2/month or less; some patients may have a migraine even weekly, but this is rare
Pain locus	Usually bilateral, frontal, or ''hatband''	Generally unilateral but may switch sides or become bilateral
Type of pain	Constant, nagging, severe	Throbbing, moderate to severe
Triggers	Stress	Stress, menses, foods, alcohol, OCs, HRT, menopause, pregnancy
Accompanying symptoms	Light, noise	Nausea, vomiting, photophobia, phonophobia

Adapted from *Women's Health: A Primary Care Clinical Guide*, ed. 2, Appleton and Lange, Stanford, CT, 1998.

BOX 5-27

Warning Signs for Dangerous Headaches[349]

If a patient reports any of these symptoms, immediate medical attention is advisable:
- No identifiable pattern of a benign headache
- Patient describes headache as ''the worst headache ever''
- Vomiting without nausea
- Personality or consciousness changes
- Abnormality upon physical exam (e.g., fever, neck pain/stiffness, neurologic signs)
- Seizure activity
- Onset of headache with exertion
- Sudden change in headache pattern
- Worsening symptoms

BOX 5-28

Common Migraine Triggers: Foods

Aged cheese
Alcohol
Avocado
Bacon
Bananas
Canned figs
Chicken livers
Chinese food (with MSG)
Chocolate
Citrus fruits
Coffee (including decaf)
Dry soup mixes (similar products—MSG)
Fermented sausages
Hot dogs
Nuts
Onions
Tea
Yogurt

Source: The National Headache Foundation, Chicago

headache diary and the use of preventative pharmacologic agents typically commences just before or with the onset of menses, with increasing doses of pharmaceutical agents as appropriate closer to the menses.[351] Specific interventions are discussed in the following. Prophylactic methods should be tried for several months to determine efficacy.[351]

Prevention also involves the avoidance of migraine triggers, which many migraine sufferers can self-identify or which they can learn to identify by keeping a headache diary that includes recall of associated factors.

Nonpharmacologic Treatment

- Stress management and behavioral modification techniques, for example, relaxation training, biofeedback, and cognitive-behavior approaches[361]
- Physical therapies for the prevention of migraine, including acupuncture and cervical manipulation[361]
- Avoidance of migraine triggers: In addition to stress, these include sleep deprivation, hunger, environmental factors, foods, fatigue, alcohol, caffeine, excess sleep, physical exertion, head trauma, travel, sexual activity, medications, smoking, and physiologically poor pillow.[362]
- Foods that have been implicated in migraine onset include: cheeses, chocolate citrus, hot dogs, MSG, aspartame, fatty foods, ice cream, and alcohol. Additionally, food allergies and sensitivities, as well as certain medications, may adversely affect serotonin levels and exacerbate the problem (Box 5-28).[362]

Pharmacologic Treatment

Conventional therapy relies heavily on pharmaceuticals to prevent or arrest headache/migraine.[363] The mechanism of action of medications proved effective in the treatment of migraines generally (not specifically MM or TMM) varies, and no single medication has demonstrated superiority. Mechanisms of action include specific serotonin receptor antagonism (5HT and $5HT_2$), platelet antagonism (e.g., aspirin), hormonal intervention, prevention of vasodilatation or vasoconstriction, enhancement of serotonergic transmission, leukotriene antagonism, prostaglandin-mediated actions, and monoamine-mediated actions.[361] The most commonly used types of medications include:
- SSRIs
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Ergot alkaloids
- Oral contraceptives
- Estrogen
- Progesterone
- Prostaglandin inhibitors
- Triptans (5HT agonists)

BOTANICAL TREATMENT OF HEADACHE AND MIGRAINE

The botanical approach to the treatment of headache and migraine, and specifically those that occur as a result of hormonal changes, includes:
- The direct use of herbal analgesics, sedatives, and antispasmodics for acute pain management and symptomatic relief
- The use of herbs to address endocrine related dysfunction
- Treatment of chronic stress, affected mood (depression, anxiety, irritability), and sleep disturbances with adaptogens, nervine tonics, herbal antidepressants
- Lifestyle modification to reduce exposure to triggers, including dietary modifications and stress reduction
- Dietary changes and nutritional supplements

The most commonly included herbs for the treatment of headache and migraine are listed in Table 5-16. Data in Discussion of Botanicals focuses on those herbs that have been specifically investigated for the treatment of headache.

DISCUSSION OF BOTANICALS

Anti-inflammatories

- Butterbur
- Feverfew

Butterbur

Butterbur or petasites, exhibits a marked anti-inflammatory effect that has demonstrated efficacy in the prevention of both asthma and migraines.[362,364–369] Its activity is largely attributed to inhibition of leukotriene biosynthesis; however, it also may be related to effects on calcium channel regulation.[367] Data from clinical trials support its efficacy in migraine prophylaxis. Doses in clinical trials have included 25, 50, 75, 100, and 150 mg given twice daily, usually for 2 to 4 months. Trials have consistently demonstrated that petasites significantly reduced the number of migraine attacks and migraine days per month over placebo.[364–369] In a study conducted by Lipton et al., 245 patients in a 5-month study received either 50 mg, 75 mg, or placebo twice daily. The 4-month mean attack count was reduced by 48% in patients who received 75 mg bid, whereas those receiving 50 mg twice daily presented with a 34% reduction and those who have taken placebo 26%.[367] In two controlled clinical trials, a total of 187 patients with migraine were exposed to doses of the special butterbur extract between 100 and 150 mg daily for at least 3 months. Compared with placebo, no significant differences were observed regarding adverse events rated to be at least possibly causally related to the product, except for mild GI discomforts, notably nausea and eructation (burping). These adverse effects are mild and transient, burping occurred in about 20% of study patients. A total of 188 patients (145 suffering from migraine, including 50 children and adolescents from 6 to 17 years of age) were treated with butterbur extract at various doses for several months in the framework of four postmarket surveillance studies, two which of have been finished. Excellent tolerability at doses from 50 to 150 mg has been reported, even for children from 6 years of age. About 90% of study patients rated global tolerability to be ''excellent'' or ''good.'' It is estimated that since 1992, approximately 450,000 individuals would have been exposed to the product according to sales figures, reflecting a total of approximately 75,000 patient years of exposure. A total of 75 reports of suspected adverse reactions from Germany and 18 spontaneous reports from other countries were received by the manufacturer from 1976 to June 30, 2002, representing a frequency of suspected adverse reactions of as low as 0.022%. Only 19 reports were determined to be possibly causally related to the administration of the butterbur root extract. The reported suspected adverse reactions with the highest frequency such as nausea, eructation, and stomach pain are considered a mild discomfort of the gastrointestinal system. However, the frequency of these suspected adverse reactions is less than 0.01%. Therefore, even the most frequently reported adverse reaction for the product can be assessed as ''very rare.''[366] Owing to the potential for hepatotoxicity from the PA content of butterbur, only PA-free products (or those containing up to the detectable limit of 0.08 ppm) should be used, and the herb should be avoided during pregnancy and lactation.[362,369]

Feverfew

Feverfew is an aromatic plant with a traditional history of use for the treatment of gynecologic complaints, and a recorded history of use for headache since the 1700s.[362,370] It is one of the few herbs with substantial scientific evidence for its efficacy in migraine prophylaxis. Most RCTs and surveys of individuals using feverfew for migraine prevention have documented beneficial results.[371–373] Not only has feverfew demonstrated a reduction in migraine frequency and pain intensity, but also a profound reduction has been observed in typical accompanying symptoms, including vomiting, nausea, photophobia, and phonophobia.[372] The combined data from six randomized clinical trials suggests that *Tanacetum* is an effective agent over placebo for preventing migraine, with only mild and transient side effects noted in a few cases.[375] According to a subsequent systematic review by Pittler, Vogler, and Ernst (2002) using the Jadad scoring system, only four trials evaluating feverfew efficacy for migraine met strict methodologic inclusion criteria. The review suggested that feverfew compared favorably with placebo; however, the trial with the highest methodologic quality found no significant difference between the herb and placebo.[376] The mechanism of action remains uncertain, but it is suspected to have an anti-inflammatory effect, possibly through its inhibition of granule secretion from platelets.[374] Feverfew does not, however, appear to interfere with normal clotting meachanisms.[362,374] Its pharmacologic activity is often attributed to its parthenolide content; however, although parthenolide may be a useful marker of activity in feverfew products, the active constituents have not yet been established.[370] Efficacy of ethanolic extracts has been questioned on the basis of clinical studies; preparations made from dried whole leaf are recommended.[370] No studies were identified that specifically evaluated this herb for the treatment of TMM or MM. *Tanacetum parthenium* also may reduce the severity of dysmenorrhea through anti-inflammatory mechanisms. Feverfew is recommended by ESCOP for the treatment of migraine.[377] Long-term safety has not been questioned, and continuous consumption by large numbers of individuals over 10 years did not cause toxicity. Occasional mouth ulcers have been reported; however, in the one clinical trial in which this was evaluated, mouth ulcers were reported with greater frequency in the placebo group consuming cabbage leaves. Patients allergic to members of the daisy family (Asteraceae) should using caution with this herb.[370] Feverfew should not be used during pregnancy owing to purported emmenagogic effects (Fig. 5-12).[362]

Antiemetics

- Ginger
- Peppermint

Figure 5-12 Feverfew (*Tanacetum parthenium*). (Photo by Martin Wall.)

Ginger

Ginger's use for the treatment of headaches and nausea dates back 2500 years in both China and India, and it is still used for headache treatment in these countries, as well as in East Africa.[378,379] Clinical trials have demonstrated the efficacy of ginger in the treatment of nausea: generally, postsurgically, and during pregnancy (NVP), and its use for nausea and vomiting is supported by ESCOP and the German Commission E (the latter, however, does not recommend its use during pregnancy).[377,379–382] Ginger exerts an anti-inflammatory effect through inhibition of cyclo-oxygenase and lipoxygenase enzymes of the prostaglandin and leukotriene synthesis pathways, and thus also may be of use in the prevention and relief of headache and migraine; however, it does not appear to exert direct analgesic effects.[381] One case report published in 1990 describes a case history of a 42-year-old woman who experienced an abortive effect on migraine taking 1.5 to 2.0 g/day of dried, powdered ginger root. The authors of the report attributed thromboxane and prostaglandin inhibition with the outcome.[383]

Peppermint

Peppermint is discussed in the next section on Analgesics.

Analgesics

- Corydalis
- Cramp bark/black haw
- Jamaican dogwood
- Kava kava
- Peppermint
- Pulsatilla/Pasque flower
- Willow

Analgesics play an important role in the symptomatic management of headache/migraine pain. They can be taken prior to the onset of headache, or acutely during headache. Effectiveness depends on adequate dosing. The most effective dosing strategy is typically to take small frequent doses of herbal extract until relief is achieved, for example, 1 to 3 mL of a tincture every 15 to 30 minutes, and then to repeat as needed to sustain relief, usually for a maximum of 2 hours. If relief is not achieved after 2 hours, the formula can be modified or the protocol can repeated again after a break of 2 hours. If pain was successfully relieved, but returns, the protocol also may be repeated after a rest of 2 hours. The protocol may be repeated up to three times daily. Caution is warranted with dosing for those herbs that have a toxic threshold. Note that doses that herbalists find clinically effective often exceed the recommended doses in safety charts. This is a confusing fact and often a conundrum for practitioners who of course want to avoid toxicity for patients and also legal liability by prescribing within suggested parameters. Unfortunately, dosing charts are often based on theoretic toxic effects or limited safety and clinical studies, and are not entirely dependable as the final word on safety. Nonetheless, they are a useful guide within which a modicum of flexibility may be allowed to achieve clinical fficacy, based on the individual patient's size and weight, tolerance, age, and status (i.e., pregnancy and nonparturient).

Corydalis

Corydalis is used in TCM, and called yanhusuo. It is an effective analgesic, sedative, and hypnotic, useful in the treatment of headache, insomnia, and dysmenorrhea. Thus, it is especially applicable for the treatment of headache and migraine associated with menstruation, and general menstrual pain. It combines well with anti-inflammatory herbs, antispasmodics, and anxiolytics.[384] Its action is attributed to the alkaloid tetrahyropalmatine, which lends sedative, hypnotic, and tranquilizing properties.[385] The mechanism of action appears to be blocking of postsynaptic dopaminergic receptors, but the CNS effects also may involve serotonin and noradrenaline.[384,385] In vitro and animal studies have confirmed the analgesic and sedative effects of this herb.[384]

Cramp Bark/Black Haw

Cramp bark/black haw are similar enough in effect to consider relatively interchangeable as spasmolytic and mild analgesic herbs. These salicylate-containing viburnums are generally considered for their effectiveness as uterine muscle relaxants in the treatment of dysmenorrhea (see Dysmenorrhea). Their mild sedating and

general spasmolytic actions also make them invaluable in the treatment of mild to moderate headache, and combined with Jamaican dogwood, for temporary relief in case of migraine.

Jamaican Dogwood

Jamaican dogwood is a highly reliable analgesic, antispasmodic, and CNS sedating herb, especially valuable in the treatment of headache, migraine, and dysmenorrhea, making it specific for women suffering from either or a combination. It is also used for cases of severe insomnia and anxiety.[362,374] It is quite a bit stronger than most of the other analgesic and sedative nervines; thus, it is advised to stay strictly within the recommended dosing schedule. No clinical studies using this herb were identified.

Kava Kava

Kava is approved by the German Commission E for the treatment of nervous anxiety, stress, and restlessness.[382] Its biological effects, owing to a mixture of compounds called kavalactones, are reported to include sedative, anxiolytic, antistress, analgesic, local anesthetic, anticonvulsant, and neuroprotective properties.[386] Kava's efficacy in the treatment of tension headache has not been evaluated specifically. However, it may be useful in preventing and treating underlying hyperexcitability and anxiety that appear to be triggers to tension headaches and menstrual migraines, and may provide reliable mild analgesic effects. The kavapyrones dihydromethysticin and dihydrokawain are muscle relaxants when given to animals. Animal and in vitro experiments support certain analgesic actions of kava. Both the aqueous and lipid soluble extracts of kava were tested for analgesia in mice. Both extracts were shown to elicit an analgesic response. Kava is contraindicated in patients with liver disorders and should not be taken concurrent with pharmaceutical medications. (See Plant Profiles: Kava kava.)

Peppermint

Peppermint oil has long been topically applied to the forehead and temples for the treatment of headache. *Mentha piperita* oil was equally effective as acetaminophen in relieving headache in a double-blind, placebo-controlled, crossover study with 40 patients. Each patient had four episodes of tension headaches. Topical peppermint oil application was equally effective as a 1-g oral acetaminophen dose in relieving headache, whereas their combination was significantly more effective than either treatment alone. The peppermint dose was 10% oil in ethanol applied to forehead and temples every 15 minutes for a total of three applications. Results were measured every 15 minutes for the first 60 minutes, at 15, 30, 45, and 60 minutes. Peppermint, acetaminophen, and their combination, significantly reduced headache intensity as compared with placebo; the combination resulted in the greatest reduction in pain and headache-related disability. No adverse effects were reported.[387] The effects of peppermint oil and eucalyptus oil preparations on neurophysiologic, physiologic, and experimental analgesimetric parameters were investigated in 32 healthy subjects in a double-blind, placebo-controlled, randomized crossover design. Four different test preparations were used. The test preparations were applied to large areas of the forehead and temples using a small sponge. The treatment effect of the preparations tested was evaluated by comparing baseline treatment measurements. The combination of peppermint oil, eucalyptus oil, and ethanol can increase cognitive performance while having a muscle-relaxing and mentally relaxing effect, but has little influence on pain sensitivity. However, a significant analgesic effect with reduction in sensitivity to headache is produced however by the combination of peppermint oil and ethanol. The essential plant oil preparations often used in empirical medicine can thus be shown by laboratory tests to exert significant effects on mechanisms associated with the pathophysiology of clinical headache syndromes.[388] Additionally, peppermint has demonstrated significant clinical effects in the treatment of nausea. Most studies have looked at postoperative benefits, but given the frequency of nausea and vomiting accompanying migraine, its use as an antinauseant/antiemetic also may be well applied here.

Pulsatilla

Pulsatilla, or pasque flower, is a strong, effective, and potentially toxic analgesic and sedative herb. It is included in this discussion because experienced herbalists and naturopathic physicians may recommend it for severe and intractable pain and insomnia. It is also used in the treatment of dysmenorrhea; in vitro it has been shown to reduce uterine contractions.[362] In dried form, this herb is expected to cause little harm when used in the proper dosage range; however, excessive (undefined amount) doses of the herb may cause severe gastritis, kidney, or urinary tract irritation (see Herbal Dosing Chart). In its fresh form, pulsatilla can cause serious irritation and blistering of the oral, esophageal, and gut mucosa. Pulsatilla also may be adulterated by the presence of other more toxic species of *Pulsatilla*. Therefore, this herb should be restricted to use ONLY by those trained in its use, and familiar with its identification and contraindications. It is fully contraindicated during pregnancy and lactation.[382] This herb is also contraindicated in depression, psychosis, and in children. Its use with pharmaceutical analgesics is not recommended.[389] No studies using this herb have been identified. Its use is not recommended by the German Commission E.[382]

Willow

Willow (and other salicylate-containing herbs) has been used as an analgesic for at least 2000 years, recommended by physicians such as Paracelsus and Hippocrates all the way up to the Eclectic physicians. Native Americans used numerous willow species for their analgesic, anthelmintic, and hemostatic properties.[390] The modern history of use focuses on the discovery and isolation of salicin from its bark and leaves. The popular use by herbalists of willow, and other salicylate containing herbs

such as wintergreen (*Gaultheria procumbens*), meadowsweet (*Filipendula ulmaria*, formerly *Spirea* spp., from whence the word ''aspirin'' is derived), lavender (*Lavendula officinalis*), and rosemary (*Rosmarinus officinalis*) as analgesics or anti-inflammatories for mild headache (meadowsweet is not typically used for headache) is mostly extrapolated from traditional use and reinforced by knowledge of their salicylate contents.[391,392] Surprisingly, no clinical trials have been conducted to assess the efficacy of these herbs for the treatment of headache. Two randomized, double-blind, placebo-controlled clinical trials, and two open trials, have demonstrated the efficacy of willow in treating lower back pain and osteoarthritis.[362,377,393] Inhibition of platelet aggregation was evaluated in two randomized, double-blind placebo controlled groups of patients with chronic low back pain. They were treated with willow back equivalent to 240 mg salicin (n = 19) or placebo (n = 16 for 28 days) a third group suffering from chronic ischemic heart disease was treated with 100 mg acetylsalicylate daily for the duration of the study period. AA induced platelet aggregation was measure ex vivo in blood samples and was minimally inhibited by the willow bark but to a much lesser extent than the acetylsalicylic acid.[377] Salicin did not induce gastric lesions in rats at a dose in which a comparable amount of sodium salicylate did.[377] Wintergreen herbs and other salicin containing herbs are similarly expected to be safer than salicylic acid.[392] White willow bark is approved by the German Commission E for the treatment of headaches, rheumatic ailments, and fever.[35] It is contraindicated in those patients with known salicylate allergy or hypersensitivity, and in those with glucose-6-phosphate deficiency (G6PD) in whom it can cause hemolytic anemia, although allergic reactions are considered improbable.[389,394] Willow bark is high in tannins, and therefore may interfere with nutrient absorption if used for prolonged periods, and theoretically, may interfere with (though potentiation) anticoagulant therapy. Its use in conjunction with pharmaceutical analgesics is not recommended.[389] However, salicylate-type side effects are not expected owing to the very low dose of salicylate provided by the herb. GI side effects may be owing to the presence of tannins (Fig. 5-13).[394]

Figure 5-13 Willow (*Salix nigra*). (Photo by Martin Wall.)

Nervines/Antispasmodics

- Black cohosh
- Lavender

Nervines and antispasmodics are used to reduce anxiety, emotional and musculoskeletal tension, and irritability, all of which have been shown to be headache and migraine triggers, and symptoms of PMS. Although few have been studied directly for their role in the treatment of headache and migraine, many play an adjunct role in combination herbal formulas for these problems. They also may be especially useful in promoting sleep during in the event of headache, and improving sleep overall to prevent fatigue that accompanies sleep disorders and may produce the end result of headache or migraine. Examples of commonly used nervines for the treatment of headache by herbalists are listed in Table 5-15.

Following are data on those nervines and antispasmodics that have been specifically evaluated for headache/migraine treatment.

Black Cohosh

Black cohosh was traditionally used for relief of a number of types of neuralgias, and many herbalists today include black cohosh in formulas in which there is emotional and/or musculoskeletal tension associated with gynecologic conditions. Research has focused on menopausal symptom relief and not on relief of premenstrual tension and headaches. Use of black cohosh to relieve menstrually related headaches is primarily based on case reports and traditional use. One double-blind, randomized, placebo-controlled trial evaluated a combination of soy, donq quai (*Angelica sinensis*), and black cohosh (*Actaea racemosa*) and found that the supplement successfully reduced migraine frequency. Following a 4-week placebo run-in period, patients were randomized to receive either a phytoestrogen supplement (n = 20) containing: 75 milligrams (mg) soy extract (40% isoflavones), 50 mg dong quai extract (standardized to 1% ligustilide),

TABLE **5-15**

Summary of Botanical Treatment Strategies for Headache and Migraine

THERAPEUTIC GOAL	THERAPEUTIC ACTION	BOTANICAL NAME	COMMON NAME
Reduce possible inflammatory response involved in headache etiology	Anti-inflammatories	*Petasites hybridus*	Butterbur
		Tanacetum parthenium	Feverfew
		Zingiber officinalis	Ginger
Relieve nausea; vomiting	Antiemetic	*Mentha piperita*	Ginger
		Zingiber officinale	Peppermint
Relieve headache/migraine pain	Analgesics	*Anemone pulsatilla*	Pulsatilla
		Corydalis ambigua	Corydalis
		Piscidea piscipula	Jamaican dogwood
		Piper methysticum	Kava kava
		Salix spp.	Willow
		Withania somnifera	Ashwagandha
Relieve stress, anxiety, musculoskeletal tension	Nervines/Antispasmodics	*Actaea racemosa*	Black cohosh
		Lavendula officinalis	Lavender
		Leonurus cardiaca	Motherwort
		Matricaria recutita	Chamomile
		Scutellaria laterflora	Skullcap
		Verbena officinalis	Blue vervain
		Viburnum spp.	Cramp bark, black haw
Promote sleep	Sedatives	*Anemone pulsatilla*	Pulsatilla
		Corydalis ambigua	Corydalis
		Eschscholtzia californica,	California poppy
		Humulus lupulus	Hops
		Matricaria recutita	Chamomile
		Passiflora incarnata,	Passion flower
		Piscidea erythrina	Jamaican dogwood
		Valeriana off.	Valerian
		Withania somnifera	Ashwagandha
Improve stress response	Adaptogens	*Eleutherococcus senticosus*	Eleuthero
		Panax ginseng	Ginseng
		Panax quinquefolium.	American ginseng
		Rhaponticum carthimoides	Rhaponticum
		Rhodiola rosacae	Rhodiola
		Schizandra chinensis	Schizandra
		Urtica dioica	Nettles
		Withania somnifera	Ashwaganda
Relieve depression and anxiety	Antidepressants/ Anxiolytics	*Hypericum perforatum*	St. John's wort
		Passiflora incarnata	Passion flower
		Piper methysticum	Kava kava
		Scutellaria laterflora	Skullcap
		Valeriana officinalis	Valerian
		Withania somnifera	Ashwagandha
Treat possible underlying hormonal dysregulation (e.g., estrogen withdrawal, luteal phase insufficiency)	Hormonal modulation	*Vitex agnus castus*	Chaste berry
TCM approaches to headache/migraine related to hormonal changes	Treat blood deficiency Treat liver qi stagnation	See Premenstrual Symptoms, Premenstrual Syndrome (PMS), and Premenstrual Dysphoric Disorder (PMDD)	

and 25 mg black cohosh (standardized to 8% triterpenes) or an identical-looking placebo ($n = 18$) twice daily for 24 weeks. Significant reductions in the primary outcome measure of mean number of menstrual migraine attacks (weeks 9 to 24) was observed in the supplemented group compared with placebo. Secondary outcomes including frequency of any migraine attack (weeks 20 to 24) mean headache severity score (weeks 20 to 24), self-medicated triptans doses (weeks 20 to 24), and doses of analgesics (weeks 20 to 24) were all significantly reduced compared with placebo.[395] Black cohosh has been demonstrated to have positive effects in the treatment of neurovegetative and psychological complaints associated with the hormonal changes of menopause, including sleep disorders and nervous irritability.[377] Onset of action is expected after 2 to 4 weeks of use, and that it be given a 12-week trial of use for maximal effects to be seen.[377] The German Commission E supports the use of this herb for the treatment of premenstrual discomfort, dysmenorrhea, and menopausal symptoms.[382] (See Plant Profiles: Black Cohosh for a discussion of cautions associated with the use of this herb.)

Lavender

Lavender is considered a mild sedative for restlessness, nervous exhaustion, and sleep disorders, and is approved by the German Commission E for these purposes.[382] It is also a mild antidepressant and anxiolytic.[374,396] The scent of the flowers, whether as one takes the tea, or the tincture diluted in water, is in itself uplifting.[374,397] Human and animal studies have indicated that linalool and lynalyl acetate are the active sedating compounds.[394] Considerable evidence from case reports and studies suggests the effectiveness of lavender oil in the treatment of pain; however, these studies tend to be small, and were not rigorous or controlled.[397] Although not a primary treatment for headache, lavender makes an excellent addition to internal use formulae for headache and migraine, and is also useful as a topical application to the temples (see the following) or in baths or other inhalation methods.

Sedatives

Botanical sedatives can be highly effective in promoting sleep and relieving pain during acute headache/migraine, especially when combined with analgesic and antispasmodic herbs. Many of the most appropriate sedatives for headache/migraine treatment are listed in Table 5-15.

Adaptogens

Stress and other affective moods are both a causative factor and a result of headache and migraine. Stress can lead to and exacerbate hormonal dysregulation. Adaptogens are especially appropriate for the long-term reduction and prevention of headache and migraine owing to stress, fatigue, irritability, and other affective moods, and should be considered whenever treating chronic premenstrual headache, MM, and TMM. They should be used long-term (for at least 12 weeks) before optimal results are evident. A number of adaptogens, for example, ashwagandha, also have mild sedative action and may be especially beneficial for treatment of headache and migraine. Adaptogens are listed in Table 5-15. Readers will want to refer to Chapter 7 for more data on adaptogens, as well as to discussions on adaptogens throughout this text.

Antidepressants/Anxiolytics

Like stress, anxiety and depression often accompany, precipitate, or are a result of headache and migraine. Therefore, anxiolytic and/or antidepressant herbs should be included in herbal protocol when indicated. Many herbs have multiple effects, for example, kava is an excellent anxiolytic and mild analgesic (see Plant Profiles: Kava for warnings and contraindications with kava), St. John's wort used long-term is both a tonic nervine and antidepressant.

External Treatments for Headache and Migraine

Peppermint and Lavender Oil Compresses

Dilute five drops each of peppermint and lavender essential oils in a bowl of cool water. Stir well to distribute the oil throughout the water, and dip a folded washcloth into the bowl. Apply the cloth to the forehead and temples, and if desired, another to the back of the neck, for pain and nausea. If warm water is preferred, then it may be substituted. Relax the head on a pillow for 10 minutes and breathe deeply during the application. Repeat two to three times per day as necessary. Herbal baths with essential oil (e.g., lavender) can also be very relaxing, and used prophylactically or for acute care.

Warm Ginger Compresses

For women who prefer heat to cold, warm ginger compresses can provide modest temporary relief of pain and nausea. Grate 1 tbl of fresh ginger into a bowl of boiling water. Cover and let steep for 5 minutes. Dip a folded washcloth into the preparation, and apply the cloth to the forehead and temples, and if desired, another to the back of the neck. Relax the head on a pillow for 10 minutes and breathe deeply during the application.

Tiger Balm Herbal Salve

Tiger balm is a topical medication used for almost a century to relieve pain and muscle tension. Tiger balm's active ingredients are camphor, menthol, cajuput, and clove oil. One RCT concluded that Tiger balm is as effective as any other commonly used analgesic.[398] Participants rubbed Tiger balm on their temples as soon as symptoms of headache presented. They repeated the application at 30 minutes and 1 hour. Patients with severe migraine headache were excluded from the study (Box 5-29).

NUTRITIONAL CONSIDERATIONS

Teach patients to:

- Avoid dietary triggers of headache/migraine (see Box 5-28).
- Maintain a diet that is low in proinflammatory precursors (e.g., arachidonic acid) by minimizing red meat and dairy (with the exception of some yogurt), and maximizing whole grains and complex

BOX **5-29**

Botanical Prescriptions

Botanical Prescription for Premenstrual Headache: Prevention

The following tincture can be taken throughout the month as a prophylactic remedy for headache/migraine. It can be accompanied by the tincture below for mild–moderate headache, as directed, for optimal prevention.

Tincture for Internal Use:

A general adaptogenic, anti-inflammatory, and anxiolytic formula:

Ashwagandha	(*Withania somnifera*)	30 mL
Feverfew	(*Tanacetum parthenium*)	20 mL
Skullcap	(*Scutellaria lateriflora*)	20 mL
Chamomile	(*Matricaria recutita*)	15 mL
Ginger	(*Zingiber officinale*)	15 mL
		Total: 100 mL

Dose: 3 to 5 mL bid–tid

Variations:

If there is anxiety: reduce chamomile and skullcap by 10 mL each and add 20 mL *Passiflora incarata*

If there is depression: reduce chamomile by 10 mL, skullcap by 5 mL, and add 15 mL *Hypericum perforatum*.

Botanical Prescription for Premenstrual Headache: Acute

This tincture can be taken at the onset of an acute headache and throughout, or preferably, it can be taken for several days prior to the typical time of onset for prophylactic pain treatment.

Mild to Moderate Pain

Black cohosh	(*Actaea racemosa*)	30 mL
Cramp bark/ black haw	(*Viburnum* spp.)	30 mL
Passion flower	(*Passiflora incarnata*)	15 mL
Motherwort	(*Leonurus cardiaca*)	15 mL
		Total: 100 mL

Dose: Prophylactically: 3 to 5 mL two to three times daily

Acute pain: 2 to 5 mL every 1 to 4 hours, up to 30 mL daily of total tincture

Severe Pain: To the above, consider adding Piscidea piscipula or Corydalis, 2 mL repeated as needed up to four doses over an hour, not to exceed 2 hours.

Relaxation Tea

Chamomile	(*Matricaria recutita*)	4 parts
Lemon balm	(*Melissa officinalis*)	3 parts
Lavender	(*Lavendula officinalis*)	2 parts
Spearmint	(*Mentha piperita*)	1 part

Mix these dried herbs together. Steep 2 tsp per cup of boiling water for 10 minutes (cover while steeping). Strain, sweeten lightly if desired, and drink hot, up to 3 cups daily.

carbohydrates, fish (especially cold water fish such as salmon and tuna), poultry, vegetarian protein sources (legumes, tofu, tempeh), and plenty of fresh fruits and vegetables.

- Maintain well regulated blood sugar by eating regularly (do not skip meals), getting adequate complex carbohydrates, and snacking on healthful choices. Avoid excessive (more than two times per week) consumption of refined flower products and sugar, as well as excessive salt intake, the latter that can lead to fluid retention and increased headache susceptibility.
- Minimize consumption of caffeinated products (coffee, black tea, soda, chocolate) (see Box 5-28).

Magnesium

Whether magnesium supplementation is beneficial in the prevention and treatment of migraine is inconclusive; however, several trials have suggested improvements with its use, especially for women who experience aura with menstrual migraines.[362] One study, reported in *Headache: The Journal of Head and Facial Pain*, reported that the incidences of magnesium deficiency in women with menstrual migraines was 45%, compared with 15% in nonmenstrual attacks, 14% during menstruation without migraine, and 15% between menstrual and migraine. The authors concluded that the high incidence of magnesium deficiency and the elevated calcium:magnesium ratio during menstrual migraine confirm previous suggestions of a possible role for magnesium deficiency in the development of menstrual migraine.[399] This study also confirms older studies that point to magnesium supplementation as a further means for menstrual migraine prophylaxis, and support the possibility that a lower migraine threshold could be related to magnesium deficiency.[400] Because magnesium supplementation is relatively safe and affordable, practitioners may feel that a trial of 200 mg magnesium salts twice daily or 400 mg four times daily is a sensible approach to migraine prophylaxis.[362,368]

Coenzyme Q10

Coenzyme Q10 is an essential element of the mitochondrial electron transport chain. A recent open trial by Rozen et al. assessed the efficacy of coenzyme Q10 as a preventive treatment for migraine. Thirty-two patients with migraine were treated with coenzyme Q10 at a dose of 150 mg/day. Thirty-one of 32 patients completed the study; 61.3% of patients had a greater than 50% reduction in number of days with migraine headache. The average number of days with migraine during the baseline period was 7.34 and this decreased to 2.95 after 3 months of therapy, which was a statistically significant response. Mean reduction in migraine frequency after 1 month of treatment was 13.1% and this increased to 55.3% by the end of 3 months. Mean migraine attack frequency was 4.85 during the baseline period and this decreased to 2.81 attacks by the end of the study period, which was a statistically significant response. There were no side effects noted with coenzyme Q10. Coenzyme Q was recently assessed in a double-blind trial by Sandor et al.[368] After 3 months,

patients receiving 100 mg of coenzyme Q had less attacks per month, days with headache and days with nausea. A total of 47.6% of those receiving coenzyme Q had more than 50% reduction in the frequency of pain, vs. 14.3% in the placebo group. One patient in the active group withdrew from the study owing to cutaneous allergy.[368]

Riboflavin, Magnesium, and Feverfew Combination

A randomized double-blind placebo-controlled trial was conducted to determine the efficacy of a combination of riboflavin, magnesium, and feverfew for migraine prophylaxis. A compound providing a daily dose of riboflavin 400 mg, magnesium 300 mg, and feverfew 100 mg was administered. The placebo contained 25 mg riboflavin. Previous studies of magnesium and feverfew for migraine prophylaxis have found conflicting results, and there has been only a single placebo-controlled trial of riboflavin. The study included a 1-month run-in phase and 3-month trial. The protocol allowed for 120 patients to be randomized, with a preplanned interim analysis of the data after 48 patients had completed the trial. Forty-nine patients completed the 3-month trial. For the primary outcome measure, a 50% or greater reduction in migraines, there was no difference between active and ''placebo'' groups, achieved by 10 (42%) and 11 (44%), respectively. Similarly, there was no significant difference in secondary outcome measures, for active versus placebo groups, respectively: 50% or greater reduction in migraine days (33% and 40%); or change in mean number of migraines, migraine days, migraine index, or triptan doses. Compared with baseline, however, both groups showed a significant reduction in number of migraines, migraine days, and migraine index. This effect exceeds that reported for placebo agents in previous migraine trials. Riboflavin 25 mg showed an effect comparable with a combination of riboflavin 400 mg, magnesium 300 mg, and feverfew 100 mg. The placebo response exceeds that reported for any other placebo in trials of migraine prophylaxis, and suggests that riboflavin 25 mg may be an active comparator.[401]

Magnesium, Coenzyme Q,[10] Riboflavin, and Vitamin B_{12} Combination

The therapeutic potential of magnesium, coenzyme Q,[10] riboflavin, and vitamin B^{12} can be cautiously inferred from some published open clinical trials; it should, however, be considered that double-blind randomized larger studies are needed to correctly estimate the impact of the placebo effect in these promising therapies.[402]

Vitamin D and Calcium

Two premenopausal women with a history of menstrually related migraines and premenstrual syndrome were treated with a combination of vitamin D and elemental calcium for late luteal phase symptoms. Both cited a major reduction in their headache attacks as well as premenstrual symptomatology within 2 months of therapy.[403]

Essential Fatty Acids

Evening primrose oil (EPO) is heavily promoted as a product for the treatment of PMS; however, trials have not demonstrated its benefits inconclusively. EPO contains two essential fatty acids—linoleic acid and gamma linoleic acid (GLA). Linoleic acid is needed for the synthesis of prostaglandin E, and GLA is needed for the synthesis of prostaglandin E1. Results of uncontrolled studies suggest abnormal essential fatty acid metabolism as an underlying problem in PMS. Resultant low levels of prostaglandins E1 may lead to increased sensitivity to prolactin and consequently, the problems associated with PMS.[404] EPO is considered generally safe, although side effects of occasional nausea, indigestion, and headache have been reported, as has the rare risk of inflammation, thrombosis (blood clot), and immunosuppression (reduced resistance to infection) with prolonged use of GLA use.

ADDITIONAL THERAPIES

Exercise

Exercise is beneficial for stress reduction and promoting mood elevation, and thus is an excellent adjunct preventative therapy when headache/migraine is mood or stress induced. (See Premenstrual Symptoms, PMS, and PMDD.)

Body Work

Spinal Manipulation and Massage Therapy

Spinal manipulation has been evaluated and shown some benefit in the treatment of menstrual headache and migraine.[362,405] Subjectively, many individuals report that regular massage reduces stress, anxiety, and associated health problems, and thus is a common sense therapy to include for the prevention of headache and migraine. However, there are minimal data pertaining to the benefits of these therapies for the treatment of these conditions.[363]

Behavioral Modification

Relaxation and biofeedback have also been shown to be effective in the treatment of tension headaches.[406,407]

POLYCYSTIC OVARY SYNDROME

Angela J. Hywood

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, spanning adolescence through menopause.[408,409] Previously considered a gynecologic problem diagnosed on the presence of a polycystic ovarian state evidenced by ultrasound, PCOS is now recognized as a complex endocrine disorder with multiple possible etiologies and clinical manifestations, only one of which may be the presence of polycystic ovaries.[410] PCOS is defined as hyperandrogenism and chronic anovulation in cases in which secondary causes of these signs have been excluded. It is characterized by oligo-ovulation, hyperandrogenism, insulin resistance, an increased LH:FSH ratio, decreased

Traditional Chinese Medicine and Premenstrual Headaches

TCM characterizes headaches that occur during the premenstrual time as caused by qi or blood stagnation, and offers formulae for their treatment. In TCM, anger, resentment, and frustration, especially when these emotions are pent up, can lead to liver-qi stagnation, that is, a lack of free flow of energy through the body. Liver-qi stagnation can transform into liver fire, which rises up and causes headache, or liver-blood stasis, which prevents blood from properly entering the uterus. Headaches after the period are considered to be a result of blood deficiency, and are treated with different herbs. Given the pressures, stresses, and frustrations that women may encounter in their daily lives, it is not surprising that premenstrual headaches are so common.

Liver fire headaches: characterized by severe throbbing in the temples or eyes, dizziness, visual disturbances, heavy menses, thirst, irritability, and dry stools and dark urine

Commonly combined herbs: *Gentiana scabra, Scutellaria baicalensis*, Gardenia, Alisma, Mutong, Rehmannia, Dong quai, Bupleurum, Licorice, and Tribulus. Taken as a decoction or prepared granules.

Blood stasis headaches: characterized by stabbing headaches in the temples or eyes prior to menses, dark, clotted menstrual blood, dysmenorrhea

Commonly combined herbs: Corydalis, Chinese motherwort, Peony (lactiflora), Dong quai, Rehmannia, Carthamus flowers, Peony (rubra), and *Salvia miltiorrhiza*

Blood deficiency headaches: characterized by dull headache during or after menses, palpitations, dizziness, fatigue, blurred vision, and pallor

Commonly combined herbs: Dong quai, Ligusticum, Peony (lactiflora), Rehmannia, Ginseng, Atractylodes, Poria, Licorice, Lycii fruit, and *Polygonum multiflorum*.

Treatment Summary for Premenstrual Headaches

- Reduce lifestyle factors that trigger headaches, for example, dietary factors and exposure to stressors.
- Use herbal analgesics, sedatives, and antispasmodics such as Jamaican dogwood, black cohosh, corydalis, lavender, motherwort, skullcap, California poppy, chamomile, and ashwagandha, among others, for acute symptomatic relief and prevention in prodromal headache stages.
- Use botanical anti-inflammatories such as butterbur, feverfew, and ginger, and consider and antiinflammatory diet.
- Use botanical treatments for endocrine dysregulation when it is related to headache etiology. Consider black cohosh, chaste berry, and dong quai.
- Treat chronic stress, affected mood, and sleep disturbances with adaptogens, nervine tonics, and botanical antidepressants, for example ashwagandha, passion flower, and St. John's wort.
- If there is nausea accompanying headaches use antiemetics such as ginger and peppermint.
- Consider TCM approaches such as treatment of blood deficiency and liver qi stagnation for chronic and intractable cases.
- Nutritional considerations, in addition to those mentioned above, include minimizing regular caffeine consumption (caffeine can actually help in some cases of acute headache), maintaining balanced and stable blood sugar, and supplementation with magnesium, co-enzyme Q-10, and riboflavin.

What to Expect with Premenstrual Headache Treatment

Acute headache often can be effectively and temporarily remedied within an hour or two with adequate doses of herbal analgesics, and sleep induced with herbal sedatives. Acute treatment may need to be repeated every few hours to maintain relief if headache persists or recurs in the course of a day.

Chronic headaches also can be effectively treated, but often require concurrent treatment of other conditions or underlying causes and attention to precipitating factors such as nutritional imbalances, hormonal dysregulation, and removal of stressors. Therefore chronic headache treatment may require several months of treatment before headaches are prevented. A formula for acute treatment can be provided for headaches that arise during the treatment period, and should be kept on hand for occasional use as needed.

sex hormone-binding globulin (SHBG), and hyperlipidemia. Patients may exhibit hirsutism, menstrual irregularities, DUB, obesity, anovulatory infertility, miscarriage, acne, alopecia, and affected mood (i.e., irritability, tension, or depression).[410–412] PCOS is estimated to affect up to 10% of women of reproductive age in the United States, or 5 million women, although data vary based on the population being studied.[409,412] PCOS is still considered in the gynecologic realm because patients typically seek gynecologic care for control of abnormal menstrual bleeding, anovulation, and infertility.[409,413] However, it is essential that practitioners expand their view of this condition to recognize the potential long-term and serious health implications associated with PCOS. Available data support significantly increased rates of type II diabetes mellitus, dyslipidemia, hypertension and cardiovascular disease, gestational diabetes, gestational hypertension, and endometrial cancer in women with PCOS.[409–411,414–416]

PATHOPHYSIOLOGY

The underlying primary cause of PCOS remains uncertain, and there are numerous proposed etiologies. Several genetic theories have been raised. A genetic predisposition (autosomal dominant) is suggested by familial clustering and increased incidence of female

hyperinsulinemia and male pattern baldness in male and female family members of women with anovulation, hyperandrogenism, and polycystic ovaries.[410] Positive findings have been identified in genes that regulate both steroidogenesis and insulin secretion. It is believed that insulin resistance may be due to aberrations in the insulin receptors. It has also been suggested that PCOS is a result of ''thrifty'' genes, an adaptive biological response providing advantages (e.g., increased muscle strength, moderate abdominal fatness, and decreased insulin sensitivity which is an energy-sparing mechanism) to women with this predisposition in times of nutrition shortage. However, a negative response of the mechanism is triggered under conditions of exposure to unlimited food supplies and sedentary lifestyle.[417]

Gestational factors have also been implicated in the development of this condition. In one study 235 women with PCOS were divided into two groups categorized according to a clinical presentation of either obese women with androgenization and elevated LH and testosterone, or thin to normal weight women with elevated LH but no androgenization. It was determined that women in the first group had above-average birth weight and were born to obese mothers; women in the second group were born after term (>40 weeks' gestation), reflecting the possibility that events occurring in fetal life may have long-term or irreversible effects on neuroendocrine function.[418,419]

The mechanisms of PCOS are better understood than the causes. In the normal menstrual cycle, gonadotrophin-releasing hormone (GnRH) is secreted from the hypothalamus in a pulsatile manner. GnRH reaches the pituitary gland where it stimulates the release of follicle stimulating hormone (FSH) and luteinizing hormone (LH). These hormones then act upon the ovaries, where they regulate production of steroid hormones and as a result, follicular development. LH stimulates production of androgen and progesterone by the theca cells and FSH stimulates the production of aromatase in the granulose cells, which are responsible for the conversion of androgen to estrogen. Local estrogen production nourishes the development of the follicle, whereas nonaromatized androgens inhibit follicular growth. The ovary generally regulates its own environment, with feedback mechanisms that cause the decline of FSH secretion as the follicle matures. When estrogen reaches a critical concentration in the general circulation, LH secretion surges, triggering ovulation. After ovulation, progesterone is secreted by the corpus luteum.[408] In PCOS, the GnRH pulsatile frequency is higher than normal, and there is increased circulating LH and decreased FSH. This imbalanced LH:FSH ratio leads to excessive production of androstenedione and testosterone, and in the absence of total suppression of FSH, continued follicular growth, but not to the point of maturity, and a resultant atresia of the developing follicles occurs. The classic polycystic ovary results from a state of chronic anovulation. Circulating estrogen levels are elevated owing to increased peripheral conversion of increased amounts of androstenedione to estrogen, primarily in the form of estrone. The chronic absence of progesterone allows an enhanced pulsatile secretion of GnRH, which contributes to the high LH, low FSH in a vicious cycle (Box 5-30).[410]

BOX 5-30

Summary of Hormonal Characteristics of PCOS

- Elevated LH
- Decreased FSH
- Overproduction of androstenedione,† testosterone,* dehydroepiandrosterone* (DHA), dehydroepiandrosterone** (DHAS), 17-hydroxyprogesterone (17-OHP), and estrone
- Hyperinsulinemia
- Inadequate progesterone stimulus owing to anovulatory state

*Mostly ovarian secretion
†Almost exclusively adrenal secretion

Elevated Androgens and Hyperactive CYP17 Enzyme

The ovaries and adrenals of women with PCOS are responsible for elevated androgen production. It is postulated that these women have a hyperactive production of CYP17 enzyme, responsible for forming androgens from DHEA-S at those sites, which is further exacerbated when there is obesity.[410] DHEA is found to be elevated in 50% of women with PCOS. The elevated DHEA is due to stimulation with ACTH, produced by the pituitary largely in response to stress. The excess DHEA then converts to androgens via adrenal metabolism. This contributes to the typically elevated androgen levels in PCOS. Elevated total and free testosterone levels correlate to the elevated LH levels. The serum total androstenedione is usually elevated to twice the normal range (20 to 80 ng/dL). High androgen levels in the ovary inhibit FSH; hence, they inhibit development and maturation of the follicles.[410,420] The skin and adipose tissue add to the complex etiology of PCOS. Women who develop hirsutism have increased sensitivity to androgen activity in the skin; hence, they develop abnormal patterns of hair growth. Aromatase and 17-beta-hydroxysteriod activities are increased in the fat cells and peripheral aromatization increases with body weight. The metabolism of estrogens by way of 2- hydroxylation and 17-alpha-oxidation is decreased. Estrogen levels increase as a result of peripheral aromatization of androstenedione. This cascade results in chronic hyper production of estrogen (estrogen dominance). Acne is seen in approximately one-third of all PCOS patients; also, most women with severe acne have PCOS.[412] Hirsutism occurs in 70% of women with PCOS in the United States, as opposed to only 10% to 20% of Japanese women diagnosed with the syndrome. This may explain the genetically determined differences in 5-alpha-reductase activity between cultures, or from a

holistic standpoint, may reflect differences in endocrine behavior in accordance with local diet and levels of physical fitness.

Estrogen Dominance

Hypothalamic pituitary ovarian (HPO) axis imbalance contributes significantly to the etiology of PCOS. The result of increased gonadotrophin releasing hormone (GnRH) output causes an elevation in the pulsatile output of LH and induces an elevated LH to FSH ratio (typically 2:1, respectively). Approximately 25% of PCOS patients also exhibit hyperprolactinemia. Hyperprolactinemia results from abnormal estrogen negative feedback from the pituitary gland. Elevated prolactin can contribute to elevated estrogen levels.

Insulin Resistance

In addition to aberrations in HPO axis behavior, insulin resistance, and resultant hyperinsulinemia are central to the picture of PCOS.[408,410] Insulin resistance is defined as reduced glucose response to a given amount of insulin, and is commonly referred to as Syndrome X. Hyperinsulinemia in hyperandrogenic anovulatory women is accompanied by upper-body obesity characterized by increased abdominal fat.[410,419] Central (android) obesity is associated with significantly increased cardiovascular risk factors including hypertension and poor cholesterol-lipoprotein profiles.[410] A waist:hip ratio of greater than 0.85 indicates android fat distribution.[410] Women with PCOS exhibit substantially increased impaired glucose tolerance (IGT) and a tendency toward non–insulin dependent diabetes (NIDDM) than other women of matched aged and weight.[421] The prevalence of impaired glucose tolerance is 31.1%, and that of type 2 diabetes is 7.5%, indicating that these women are at significantly increased risk for these conditions and their sequelae.[422] In addition to intrinsic endocrine factors, insulin resistance is caused by poor diet (especially excessive carbohydrate consumption) and stress. Hyperinsulinemia is not always a characteristic of hyperandrogenism but is uniquely associated with PCOS.[420] Thirty to forty percent of obese women with PCOS have impaired glucose tolerance or diabetes. However, women with anovulatory hyperandrogenism can present with normal insulin and glucose tolerance, indicating factors other than impaired glucose tolerance involved in the etiology.[420,423]

Acanthosis nigricans, velvety, darkly pigmented skin is considered a marker of insulin resistance in women with hirsutism. These pigmented lesions can also be found on the nape of the neck, in the axilla, inner thigh, and below the breast. Women with severe insulin resistance can develop HAIR-AR syndrome consisting of hyperandrogenism (HA), insulin resistance (IR) and *Acanthosis nigricans* (AR).[412] These women have elevated testosterone (>150 ng/dL) and fasting insulin levels of greater than 25 IU/dL. Insulin alters steroidogenesis secretion (independent of gonadal production) in PCOS, because insulin and insulin-like growth factor receptors are located within the ovarian tissue.

Stress

Stress appears to be a factor in the etiology of PCOS. The effects of stress on hormonal dysregulation, cortisol and blood sugar regulation, and adrenal function are well established. One animal study demonstrated that activation of the sympathetic nervous system precedes the induction of polycystic ovaries and that increased sympathetic activity plays a role in the development and maintenance of ovarian cysts. Further research on the role of stress and the development of PCOS is warranted.[424]

SIGNS AND SYMPTOMS OF PCOS

The symptomatology of PCOS is highly variable; therefore, close attention should be paid to the presenting clinical picture of the patient.[412] The most common reason for gynecologic evaluation is menstrual irregularity, most commonly oligo- or amenorrhea.[412,413] Women also commonly seek gynecologic care for infertility and signs of androgen excess.[413]

The following clinical features may be present in PCOS:

- Menstrual irregularity secondary to chronic anovulation or oligo-ovulation
- Dysfunctional uterine bleeding
- Anovulatory infertility
- Hirsutism
- Acne
- Alopecia
- Acaranthes nigricans
- Obesity (especially android-type)
- Mood disorders[425]
- Habitual abortion
- Ultrasound evidence of PCOS (not itself indicative of this syndrome)

Menstrual Irregularity

- Eight or fewer menstrual cycles per year
- Unpredictable menstrual cycles
- Amenorrhea for longer than 4 months in the absence of pregnancy or menopause
- Infertility
- History of ovarian cysts
- Irregular bleeding
- Excessive or heavy bleeding (DUB)

Hyperandrogenism

- Acne
- Acanthosis nigricans
- Alopecia
- Hirsutism
- Virilization

Obesity

- Seen in approximately 65% of patients with PCOS.[409]
- The body fat is centrally located (truncal, android).[410,419]
- A higher waist to hip ratio (>0.85) indicates an elevated risk of cardiovascular disease and diabetes.[410,412]
- BMI >30[412]
- Presents long-term complications of PCOS

Lipoprotein Profile

An abnormal lipoprotein profile is associated with impaired glucose tolerance, and is commonly seen in patients with PCOS. The typical PCOS lipoprotein profile includes:

- Elevated total cholesterol
- Elevated triglycerides
- Elevated low density lipoproteins (LDL)
- Low high density lipoproteins (HDL)
- Low apoprotein A-1

The culmination of these factors leads to a marked elevation in cardiovascular risk for the PCOS patient. Another metabolic observation that puts these women at higher cardiovascular risk is the incidence of impaired fibrinolysis, shown by elevated circulating levels of plasminogen activator inhibitor. This is associated with atherosclerosis and hypertension. When these factors are combined, PCOS women are at much higher risk of hypertension, atherosclerosis, and have a sevenfold risk of myocardial infarction.

An ultrasound will reveal ovaries enlarged two, up to five times, greater in size than normal, with bilateral micro cysts within each ovary, with generally more than five cysts per ovary. The size of each cyst is approximately 0.5 to 0.8 cm. As the number of cysts increases and the ovaries become larger, the clinical symptoms become more severe. Polycystic ovaries themselves may be normal and as a single sign are not diagnostic of hyperandrogenism, insulin resistance, or PCOS.

DIAGNOSIS

The major clinical criteria for PCOS include:

- Clinical or biochemical evidence of hyperandrogenism
- Oligo-ovulation or anovulation
- Exclusion of other known disorders (i.e., adrenal hyperplasia, hyperprolactinemia)

Additionally, any of the signs and symptoms presented above may be part of the diagnostic picture. Family history of diabetes or menstrual irregularity is significant.

BIOCHEMICAL AND ENDOCRINOLOGY EVALUATION

The following should be evaluated when establishing a definitive diagnosis of PCOS:

- Pituitary and ovarian hormone serum levels:
  - LH
  - FSH
  - Estradiol
  - Progesterone
  - Prolactin
  - β-HCG (to rule out pregnancy)
- Circulating androgens and related hormones:
  - Free testosterone and free androgen index (FAI): 17-hydroxyprogesterone
  - Sex hormone binding globulin (SHBG): 24-hour urinary free cortisol
  - Dehydroepiandrosterone sulfate (DHEA-S)
- Endometrial biopsy
- Glucose tolerance test

BOX 5-31

Risks and Consequences Associated with PCOS[410]

- Infertility
- Menstrual irregularities and DUB
- Hirsutism, acne, hair loss (alopecia)
- Endometrial cancer as a result of unopposed estrogen (and possible increased risk of breast cancer)
- Cardiovascular disease
- Diabetes

- Thyroid panel
- Blood lipid profile

Appropriate diagnosis and treatment are essential to prevention of the sequelae of this condition (Box 5-31).

DIFFERENTIAL DIAGNOSIS

Specific conditions that must be ruled out include:[412,419]

Common:
- Hyperprolactinemia
- Hypothalamic amenorrhea
- Non-PCOS insulin resistance
- Premature ovarian failure
- Obesity from other causes

Rare:
- Cushing's syndrome
- Hyperandrogenism
- Adrenal hyperplasia

Very Rare:
- Androgen-producing tumors

CONVENTIONAL TREATMENT APPROACHES

The overall goals of medical treatment are to:

1. Reduce androgen production and circulation
2. Protect the endometrium against unopposed estrogen
3. Achieve healthy body weight
4. Reduce cardiovascular disease risk
5. Reduce diabetes and hyperinsulinemia risks.[410,412]

More specifically, women are currently being treated for their presenting clinical symptoms, including irregular menses, hirsutism, and infertility, as well as according to complaints or desired outcome (e.g., persistent acne, achieving pregnancy).[420,423,426] Table 5-16 provides a comprehensive overview of medications commonly used to treat PCOS.

Irregular Menses

Oral contraceptive pills (OCPs) are commonly used to regulate the menses, and have been the mainstay of long-term PCOS treatment. They suppress pituitary LH, increase SHBG, and decrease androgen secretion. The combined pill often worsens insulin resistance and if the patient falls into the categories of being overweight or obese, this therapy is relatively contraindicated. Also, the long-term safety of OCs has been questioned.

TABLE **5-16**

Medications Commonly Used for the Treatment of PCOS[408–410,413,420,423]

MEDICATION	EFFECTS/USE
Oral contraceptives	Combined estrogen and progestin oral contraceptives are known to decrease the adrenal and ovarian production of steroid hormones and reduce hair growth by two-thirds in patients with PCOS and hirsutism. Progestin offers the benefit of lowering elevated LH levels, resulting in reduced ovarian testosterone production. The estrogen increases the liver's production of sex hormone binding globulin, also reducing free circulating testosterone levels. Estrogen inhibits the conversion of testosterone to DHT by inhibiting the enzyme alpha-5-reducatase. The use of oral contraceptives alone is only successful in 10 percent of cases and insulin resistance can be enhanced by the use of combined oral contraceptives.
Medroprogesterone acetate	Oral or intramuscular injection of medroprogesterone acetate has been used primarily for contraception and hirsutism. It affects the hypothalamic pituitary axis by decreasing the production of GnRH, hence reducing production of estrogen and testosterone. It also decreases the production of SHBG. If given orally, doses of 20 to 40 mg daily are suggested or if intramuscular injection is used, 150 mg is administered every 6 to 12 weeks. It is said to reduce hair production by 95% in responsive patients. Side effects include amenorrhea, headaches, fluid retention, weight gain, liver dysfunction, and depression.
Gonadotropin releasing hormone (GnRH) agonists	These drugs cause ovarian suppression to levels of castration in the patient with PCOS. The drug most commonly used from this class is Leuprolide acetate and is given by intramuscular injection every 28 days to suppress ovarian androgens. The oral contraceptive is used concurrently to replace estrogen in order to prevent bone loss and other menopause-like side effects this drug induces.
Glucocorticoids	Glucocorticoids such as dexamethasone are used for patients with adrenal or mixed adrenal and ovarian hyperproduction of androgens. A dose of 25 mg is given daily, which causes suppression of DHEA-S production. Excessive doses of this drug can suppress adrenal gland function and cause symptoms of Cushing's syndrome. The drug is used for both hirsutism and acne associated with PCOS.
Ketoconazole	This drug acts by inhibiting key steroid hormone synthesis via inhibition of cytochrome P450–dependent enzymes. As a result, when given at a dose of 200 mg per day, it can reduce the production of testosterone, androstenedione, and free testosterone. It also reduces the production of cortisol. Ketoconazole is a strong hepatotoxin.
Spironolactone	Spironolactone specifically inhibits aldosterone-binding sites in the kidney. Originally used as a potassium-sparing diuretic for the treatment of hypertension, Spironolactone is used for hirsutism to reduce androgens by inhibiting DHA at the intracellular receptor sites; suppressing testosterone synthesis by decreasing CYP enzymes; increasing androgen catabolism, and also inhibiting 5-alpha-reductase activity in the skin. Moderate improvement in hirsutism can be seen in 70% to 80% of PCOS women within 6 months on a dose of at least 100 mg for 6 months. The side effects of this drug include metrorrhagia, which occurs in 50% of women on doses greater than 200 mg per day. Other side effects include urticaria, mastodynia, and scalp hair loss. The patient's potassium and creatinine levels need to be monitored carefully while on this drug. It is essential that a woman uses contraception while on spironolactone, as it can cause feminization of a male fetus if she becomes pregnant.
Flutamide	Flutamide is a nonsteroidal antiandrogen first used for prostate cancer. Now used for PCOS, it acts by inhibiting the binding of androgens at target tissue. It also reduces elevated LH and FSH levels typically seem in PCOS and are often combined with the oral contraceptive pill. Side effects include dry skin, reduced libido, hot flashes, increased appetite, liver toxicity, breast tenderness, nausea, and headaches.
Finasteride	This drug is classified as a specific inhibitor of 5-alpha- reductase activity and reduces the hirsutism associated with PCOS. In clinical trials, most improvement was seen after 6 months on a dose of 7.5 mg per day taken orally. Finasteride is said not to cause menstrual irregularity, nor to suppress ovulation. It is often used in combination with an oral contraceptive, as it is said to be more effective this way. The oral contraceptive increases circulating SHBG, which further decreases the free testosterone. As with Spironolactone, this drug can cause feminization of a male fetus; hence, to needs to be used concurrently with contraception.

However, recent studies have indicated that a combination of OCs with metformin improved hyperinsulinemia and hyperandrogenism in nonobese women with PCOS.[408,409,420,423]

Hirsutism

Hirsutism is addressed with the administration of antiandrogens or spirolactone. The action of these drugs is to inhibit binding of dihydrotestosterone (DHT) to the receptors at the hair follicle site.[408,409]

Infertility

Clomiphene citrate is suggested to women with PCOS with diagnosed fertility challenges. Clomiphene citrate induces ovulation and does increase risk of multiple pregnancies. This drug acts by inhibiting estrogen negative feedback at the hypothalamus, thus enhancing the pituitary's production of FSH.[409]

Oral Hypoglycemic Agents: Metformin

Hyperandrogenism is said to be substantially relieved using metformin therapy, which leads to a decrease in insulin levels and results in improved reproductive function. Metformin is given orally at a dose of 500 mg three times daily. For obese women trying to conceive with PCOS, metformin is combined with clomiphene citrate for best results in restoring ovulation. The most common side effects of metformin are nausea, vomiting, diarrhea, bloating, and flatulence. One study confirmed that diabetics have substantially decreased cardiovascular risks with metformin treatment.[408,409,412,427–429]

Surgical Treatment

Ovarian wedge resections can be performed to reduce androstenedione levels and decrease plasma testosterone levels; however, in patients with hirsutism and PCOS, hair reduction was only noted to a figure of 16%.[410,423]

Weight Management

Numerous clinical studies have demonstrated that in women with obesity, insulin resistance, and PCOS, a weight loss of 5% to 10% of body weight can result in regulation in the menstrual cycle and a dramatic reduction in risk factors, likely through insulin regulation.[411,423,430–434] Richardson describes weight loss as the most successful and globally beneficial therapy for obese women with PCOS but also the most difficult to implement. Weight loss alone has led to achievement of pregnancy in 60% of cases without other medical intervention.[409] Weight loss may improve signs of hyperandrogenism and menstrual irregularity, hyperinsulinemia, restore ovulation and fertility, and improve gonadotrophin pulsatile secretion, and may prevent NIDDM and CV disease. Weight loss also decreases ovarian P450c17 alpha activity and reduces free serum testosterone in obese women with PCOS.[411,423,430–434] Encouragement of lifestyle changes, for example, weight loss and regular exercise, therefore, should be part of any treatment plan for overweight women with PCOS. It is interesting to note, however, that short-term caloric restriction does not reduce LH secretion, an apparent paradoxical effect in light of other findings, leaving questions unanswered as to the exact mechanisms of long-term weight loss, which demonstrates clear improvement of endocrinology markers.[434]

Strategies for weight loss include:

- Moderate weight loss over time (not rapid or drastic)
- Gentle exercise
- Consumption of low glycolic index carbohydrates, and reduced intake of fats and simple sugars
- Avoidance of hypoglycemia through frequent meals (4 to 6 times/day)[409]

In additional to the direct health benefits of weight loss, there is the additional and important improvement in body image, self-esteem, and a sense of personal control as a result. These improvements can lead to marked reduction in depression and other affective moods associated with PCOS.[409,425]

BOTANICAL TREATMENT OF PCOS

Little direct research has been done on the use of botanicals for the treatment of PCOS. Nonetheless, many women seek alternatives to reliance on conventional pharmaceutical interventions for this condition. Botanical treatment strategies for PCOS are best directed at stress reduction and management, and improvement of HPA axis response through the use of adaptogens. Adaptogens also play a positive role in glycemic regulation. In fact, the role of adaptogens should be given primary consideration. Vitex may play a role in hormonal regulation, particularly hyperprolactinemia and progesterone insufficiency. A small amount of Chinese research has been done on a TCM containing *Paeonia lactiflora* and *Glycyrrhiza glabra* for PCOS, and this is presented in the following. Adaptogens are discussed generally in the following, and at length elsewhere in this book (see index for ''Adaptogens,'' Chapter 7, as well as specific herbs in this category, and see Plant Profiles). The herbs discussed under supporting evidence may have direct benefit in the metabolic or endocrine disruption particular to PCOS. Protocol for the treatment of acne, infertility, amenorrhea, DUB, mood disorders, and other PCOS symptoms should be incorporated into treatment protocol for PCOS as needed. Refer to the relevant sections of this book for these additional treatment strategies. Weight loss should be a primary goal in the care of overweight women with PCOS, and counseling should be recommended as needed, especially when there is poor self-esteem, common with acne, obesity, and hirsutism, or for debilitating mood disorders (Table 5-17).

Discussion of Botanicals

Adaptogens and PCOS

- American ginseng
- Ashwagandha
- Eleuthera
- Ginseng
- Licorice
- Rhaponticum
- Rhodiola

TABLE 5-17

Summary of Botanicals Treatment Strategies for PCOS

THERAPEUTIC GOAL	THERAPEUTIC ACTION	BOTANICAL NAME	COMMON NAME
Improve stress response and HPA function	Adaptogens	*Eleutherococcus senticosus*	Eleuthero
		Glycyrrhiza glabra	Licorice
		Panax ginseng	Ginseng
		Panax quinquefolium.	American ginseng
		Rhaponticum carthimoides	Rhaponticum
		Rhodiola rosacae	Rhodiola
		Schizandra chinensis	Schizandra
		Withania somnifera	Ashwagandha
Hormonal regulation (increased progesterone secretion; LH:FSH regulation, decreased prolactin)	Hormonal regulators	*Glycyrrhiza glabra/ uralensis*	Licorice
		Paeonia laterflora	White peony
		Tribulus terrestris	Tribulus
		Verbena officinalis	Blue vervain
		Vitex agnus castus	Chaste berry
Glycemic regulation/improve lipid profile	Antihyperlipidemics	*Gymnema sylvestre*	Gymnema
Treatment of:			
Acne	See Acne		
Amenorrhea	See Amenorrhea		
Dysfunctional Uterine Bleeding	See Dysfunctional Uterine Bleeding		
Depression	See Depression		
Anxiety	See Anxiety		
Infertility	See Chapter 14		

• Schizandra

In response to stress, the adrenals release cortisol, inducing an elevation in prolactin (the ''stress hormone'') and increased androgen synthesis, which in turn leads to menstrual cycle dysregulation, especially anovulation, characteristic of PCOS. Physiologically, the HPA axis can be supported with adaptogens.[435] Combining adaptogenic herbs such as ginseng (*P. ginseng* or *P. quinquefolius*), eleuthera, and ashwagandha improve resistance to stress through modulate at the adrenal level. These herbs act to regulate the HPA axis and assist in general adaptation syndrome. Many adaptogens (e.g., *Panax* spp.) also have regulatory effects on blood sugar. Licorice is the only adaptogen that has been studied specifically for its effects on PCOS (see Peony; also see Adrenal Support).

Blue Vervain

Blue vervain is a favorite nervine of many herbalists specializing in gynecologic care, for its regulating effects on emotional irritability associated with hormonal fluctuations, especially with PMS. The German Commission E cites its uses for, among other things, irregular menstruation, nervous disorders and exhaustions, and complaints of the lower urinary tract; however, the efficacy for these claims remains unsubstantiated.[436] Many herbalists consider sluggishness of the liver, and attribute its hormonal action to stimulated liver function and subsequent actions on hormonal metabolism and elimination.

Chaste Berry

Chaste berry should be considered for hyperprolactinemia and low progesterone associated with PCOS. A review of the available literature on Vitex indicates evidence of efficacy for hyperprolactinemia, corpus luteum insufficiency, and infertility associated with corpus luteum insufficiency.[437] Hyperprolactinemia and latent hyperprolactinemia are frequent causes for cyclical disorders including corpus luteal insufficiency, which can lead to premenstrual syndrome (PMS), secondary amenorrhea, and premenstrual mastalgia. Vitex demonstrated the ability to regulate prolactin production through dopamine agonist activity at the hypothalamic-pituitary level.[437–439] The dopaminergic compounds in chaste berry have been identified as the diterpene, including rotundifuran and 6β,7β-diacetoxy-13-hydroxy-labda-8,14-diene. It may be extrapolated from pharmacologic studies that Vitex is indirectly progesterogenic, and may play a role in conditions where there is unopposed estrogen, an important factor in the association between PCOS and an increased risk of endometrial cancer.[439] No studies were identified evaluating the role of Vitex in PCOS treatment. Vitex studies are discussed in Plant Profiles: Chaste berry.

Gymnema

Gymnema is a traditional Indian herb used as an antidiabetic, hypoglycemic, lipid-lowering agent that supports weight reduction. Gymnema has a trophorestorative action of the beta cells of the pancreas. The leaf is the

plant part used medicinally. The key constituents of Gymnema include saponins and gymnemic acids. Gymnema is indicated in PCOS for its insulin-modulating activity, with added benefits in reducing elevated triglycerides. Key constituents suppress the perception of the sweet taste on the taste buds, so if taken before food, masks sweet detection and reduces desire for sweet foods and caloric intake for 90 minutes after administration.[440] Gymnema has demonstrated hypoglycemic activity in experimental models of diabetes, NIDDM, and hyperglycemia. Its mechanism of action includes the inhibition of glucose absorption in the intestine by the saponin fraction of the herb.[439]

Peony (white)

White peony is a frequently used gynecologic herb in TCM. Western herbalists use it for PCOS, hyperprolactinemia, endometriosis, ovarian failure, and androgen excess. *Paeonia* has been shown to positively influence low progesterone, reduce elevated androgens (testosterone), and modulate estrogen and prolactin. In vitro, the active constituent paeoniflorin has been shown to affect the ovarian follicle by its action on the aromatase enzyme.[436] Aromatase is necessary for follicle maturation, ovulation, corpus luteum function, steroid hormone synthesis, and the regulation of conversion of androgens to estrogens. The feedback mechanisms of the pituitary and hypothalamus rely on aromatase to regulate prolactin and GnRH. The traditional Chinese formula known as Shakuyaku-Kanzo-To or TJ-68, which is a decoction of *Glycyrrhiza glabra* and *Paeonia lactiflora*, has been subject to a number of clinical trials, all of which demonstrate activity in hormonal regulation of androgens. In one trial of Shakuyaku-Kanzo-To (TJ-68) eight women with hyperandrogenism and oligomenorrhea were given the formula for 2 to 8 weeks. This combination regulated LH to FSH ratios. Over this period of time, serum testosterone levels decreased to less than 50 ng/dL and this resulted in seven of the eight women regularly ovulating.[441] Another trial with TJ-68 involved 20 women diagnosed with PCOS. The formula was successful in lowering testosterone in 90% of the women, of which 25% went on to conceive.[442] It is suggested that TJ-68 acts directly on the ovary, increasing the activity of aromatase, which promotes the synthesis of estradiol from the testosterone, thus lowering serum testosterone levels. It also seems to regulate the LH to FSH ratio. Paeoniflorin has also demonstrated antihyperlipidemic and antihyperglycemic effects in animal models.[443,444] Licorice is contraindicated in patients with hypertension (Fig. 5-14).

Figure 5-14 Peony.

Sarei-to

One study reports on the use of the Chinese herbal medicine Sairei-to for the treatment of anovulatory PCOS patients. As a result of treatment, serum LH and the LH/FSH ratio significantly decreased and the ovulatory rate was 70.6%. Serum testosterone levels were within normal limits before the treatment, and did not significantly change during the treatment. The authors concluded that the preparation appears to have a steroidal effect.[445]

Tribulus

As a result of Bulgarian research, Tribulus has become a popular herb for the treatment of female and male endocrine disorders.[446] It is considered a general tonic, aphrodisiac, estrogen, and androgenic modulator, and is used to restore vitality, libido, and reduce the physiologic effects of stress. Bulgarian research has identified a steroidal saponin known as a furostanol saponin, calculated to no less than 45% protodioscin. The leaf is noted to be higher in the unique saponin rather than the fruit. Other active constituents include phytosterols and spirostanol glycosides. The tonic activities are exacted through intensifying protein synthesis and enhancing the activity of enzymes associated with energy metabolism.[440] Protodioscin, a steroidal saponin in Tribulus, has been proven to improve sexual desire via the conversion of protodioscine to DHEA (dehydroepiandrosterone).[447] It has also been observed that Tribulus grown in different soils does not consistently produce the important active furosterol, protodioscin. To ensure the desired clinical

BOX 5-32

Sample Botanical Prescriptions for PCOS

The first two formulae below are recommended by herbalist Amanda McQuade Crawford in her book *Herbal Remedies for Women* as a biphasic treatment for ovarian cysts. They are slightly modified to fit the dosage strategy used in this textbook.

Formula 1: Menstruation through Ovulation (Tincture)

Blue cohosh	*(Caulophyllum thalictroides)*	25 mL
Black cohosh	*(Actaea racemosa)*	20 mL
Yarrow	*(Achillea millefolium)*	5 mL
Wild yam	*(Dioscorea villosa)*	10 mL
Black haw	*(Viburnum prunifolium)*	10 mL
Milk thistle seed	*(Silybum marianum)*	20 mL
		Total: 100 mL

Dose: 5 mL three times daily.

Formula 2: Ovulation to the onset of Menstruation (Tincture)

Chaste berry	(*Vitex agnus-castus*)	30 mL
Black cohosh	(*Actaea racemosa*)	30 mL
Dandelion root	(*Taraxacum officinale*)	15 mL
Wild yam	(*Dioscorea villosa*)	15 mL
Black haw	(*Viburnum prunifolium*)	10 mL
		Total: 100 mL

Dose: 5 mL three times daily.

Hormonal Normalizing Formula for PCOS (Tincture)

This formula is designed to have a normalizing effect the HPO axis, and thereby a regulating effect for women with PCOS.

Chaste berry	(*Vitex agnus-castus*)	30 mL
White peony	(*Paeonia lactiflora*)	20 mL
Black cohosh	(*Actaea racemosa*)	20 mL
Dong quai	(*Angelica sinensis*)	20 mL
Hops	(*Humulus lupulus*)	10 mL
		Total: 100 mL

Dose: 5 mL three times daily.

For women prone to blood sugar dysregulation, also give 2.5 mL each daily of Gymnema and fennel tinctures.

results, it is recommended to use only the Bulgarian-grown Tribulus standardized to 40% furosterol saponins by UV analysis. It is not interchangeable with the Chinese or Indian Tribulus. It is best used on days 5 to 14 of the menstrual cycle to restore menstrual regularity (Box 5-32).

CASE HISTORY: PCOS

Sarah, aged 34, thinking about getting pregnant, presented with irregular menses. She was diagnosed with PCOS in the past 2 years. Up until 6 months prior to her naturopathic consultation, she has taken an oral contraceptive in combination with Levoxyl but suffered side effects of heightened emotional lability from these drugs. Her menstrual cycle varied in length from 50 to 70 days and she experienced midabdominal cramping for 24 hours prior to the onset of her menses. The flow was medium to light and lasted for 4 to 5 days, was a dark red in color, starting with brown spotting for 12 to 18 hours. She has had occasional menstrual clots. Her skin was affected badly from the PCOS and she experienced painful, deep cystic acne on her face, chest and back, which was worse for up to a week before the onset of each menses. She had taken two courses of isotretinoin (Accutane) within the past 5 years and regularly used tetracycline for treatment of her acne. Breast tenderness was an uncomfortable premenstrual feature. She had gained 23 pounds over the past 3 years, which she had difficulty losing despite exercise on a regular basis. She had a high carbohydrate diet and craved sugar intensely. She was a shift worker in a high stress and high responsibility occupation; she experienced fatigue daily. She was taking prescription thyroid medication for Hashimoto's thyroiditis, diagnosed 4 years prior, at which time she was also diagnosed as having secondary osteoporosis. Recent evaluation of her spinal density indicated osteopenia; her femoral density indicated osteoporosis; and total hip density indicated severe osteopenia.

Treatment Summary for PCOS

- Achieve a healthy weight.
- Modify the diet and lifestyle for heart protection.
- Control insulin resistance and hyperlipidemia through dietary modification and the use of herbal adaptogens such as eleuthera, licorice, ginseng, rhodiola, and schisandra, among others, and antihyperlipidemics, for example, Gymnema.
- Treat hormonal dysregulation with herbs such as licorice, peony, Tribulus, blue vervain, and chaste berry.
- Treat symptoms of PCOS such as acne, amenorrhea, dysfunctional uterine bleeding, depression, and anxiety. See relevant chapters for botanical and additional treatment strategies for these conditions and combine protocol accordingly.
- See Chapter 14 for the treatment of infertility associated with PCOS.

Additional Assessment

Hormonal evaluation showed a typical pattern of a 2:1 LH to FSH ratio, with elevated testosterone and hyperlipidemia.

Treatment Protocol

Chaste berry	(*Vitex agnus-castus*)	12.5 mL
Licorice	(*Glycrrhiza glabra*)	12.5 mL
White peony	(*Paeonia lactifolia*)	20 mL
Gymnema	(*Gymnema sylvestre*)	20 mL
Echinacea	(*Echinacea* spp.)	10 mL
Schisandra	(*Schisandra chinensis*)	20 mL
		Total: 100 mL

Dose: 8 mL twice daily

Additionally:
Tribulus concentrated extract, equivalent to fucosterol saponins (protodioscin) 300 to 400 mg per day on days 5 to 14 of the cycle to ensure cyclic regularity.

After five months on the herbal protocol, the patient's cycle regulated to a 32-day length with a consistent 15-day follicular phase and 17-day luteal phase. Problematic symptoms such as mastalgia, acne, and hirsutism diminished significantly during the 5-month program. The lipid profile has improved to within normal ranges and with the inclusion of a combined regimen of Gymnema, and dietary modification (low carbohydrate diet). She lost a total of 12% body weight in the 5 months. The client became pregnant in her second month of actively trying to conceive.

NUTRITIONAL CONSIDERATIONS

An extensive literature review specific to lifestyle factors and PCOS demonstrates that an essential treatment strategy for ameliorating the symptoms of PCOS and aiming to resolve the underlying metabolic derangements is the implementation of a weight loss program. Modulating the diet not only helps reduces hyperinsulinemia and normalizes female endocrine function, but also serves as a preventative against cardiovascular risk factors. Dietary modification is discussed under Weight Management (see the preceding).

Supplements

Chromium appears to have a beneficial role in the regulation of insulin action and its effects on carbohydrate, protein, and lipid metabolism, although not all studies have demonstrated favorable effects on blood glucose. Chromium appears well tolerated, with no toxicity even at 1000 μg/day, well above the typically recommended 200 μg/day dose.[448,449] Fish oil may be protective and beneficial for patients with PCOS and a dyslipidemic profile for its ability to reduce serum triglycerides in diabetics.[449]

ADDITIONAL THERAPIES

Stress Management

As discussed throughout this section, stress plays a direct role in HPA hormonal responses that affect the endocrine system and contribute to PCOS. Stress management strategies therefore are an important part of PCOS treatment.

Exercise

Implementing an exercise regime of approximately 30 minutes per day will assist weight loss and improve stress management. Light cardiovascular activity, even just a 30-minute walk daily, can also reduce CV disease risk.

Endocrine Disorders and Adrenal Support

6 CHAPTER

Mary Bove, Jillian E. Stansbury, Aviva Romm

THYROID DISORDERS: HYPOTHYROIDISM AND HYPERTHYROIDISM

Mary Bove

Thyroid disease is a disorder in women that, left untreated, can exact pronounced consequences on health and quality of life.[1,2] Thyroid dysfunction in women can alter menstrual regularity, affect reproduction, and lead to infertility, miscarriage, and affect intelligence in children born to women with untreated thyroid disorders during pregnancy.[3–7] Long-term, untreated thyroid conditions significantly increase the risk of cardiovascular disease, osteoporosis, reproductive cancer, and multisystem failure. Approximately 5% of Americans report having thyroid disease or taking thyroid medication, and numerous individuals have undiagnosed thyroid disorders.[2] The most common thyroid disorders are hypothyroidism, both clinical and subclinical, and hyperthyroidism. Detection and treatment of most thyroid disorders is straightforward and can prevent long-term and potentially disastrous sequelae that may occur in the absence of appropriate care.

HYPOTHYROIDISM

Hypothyroidism is a persistent insufficiency in thyroid hormone production leading to a generalized decrease in metabolic functions (Box 6-1). It is the most prevalent of the pathologic hormone deficiencies, and can reduce physical and mental functional ability, quality of life, and long-term health.[2,8] Hypothyroidism is classified on the basis of onset (congenital or acquired), endocrine dysfunction level (primary, secondary, or tertiary), and severity, which is classified as overt (clinical) or mild (subclinical) hypothyroidism.[8] The total frequency of hypothyroidism, including subclinical cases, among adult females from all age groups, ranges from 3.0% to 7.5%, with significantly higher rates in women over 60 years old.[1] Hypothyroidism occurs at a rate approximately 10 times higher in women than men.[9]

Pathophysiology

Hypothyroidism is classified as primary, secondary, or tertiary. Primary hypothyroidism is significantly more common than secondary, occurring at a rate of approximately 1000:1, and tertiary hypothyroidism, resulting from disease in the hypothalamus, is rare.[8,10] Myxoedema refers to severe or complicated cases of overt hypothyroidism with cretinism syndrome, and is extremely rare.[8] Those at increased risk of developing hypothyroidism include:[9]

- Postpartum women
- Women with family history of autoimmune thyroid disorders (AITD)
- Those with previous head, neck, or thyroid surgery or irradiation
- Those with other autoimmune endocrine disorders (e.g., type 1 diabetes mellitus, adrenal insufficiency, or ovarian failure)
- Those with nonendocrine autoimmune disorders (e.g., vitiligo, multiple sclerosis)
- Patients with primary pulmonary hypertension
- Those with Down's or Turner's syndromes

The following biological activities are particularly impaired by hypothyroidism:[8]

- Calorigenic modification
- Oxygen consumption throughout most tissues
- Protein, fat, and carbohydrate metabolism
- Augmentation of calcium ATPase activity in cardiac muscle
- Mitochondrial ATP production
- G-protein–coupled membrane receptor activity
- Organ-specific effects

The clinical manifestations of hypothyroidism (see Symptoms) are the result of effects occurring at the molecular level because of the impact of thyroid hormone insufficiency.[8]

Primary Hypothyroidism

Primary hypothyroidism is the most common form of hypothyroid disorder. It may be either congenital or acquired. Globally, the most common cause of congenital

BOX **6-1**

Thyroid Hormone: A Review of Its Synthesis and Release

Iodide, which is primary nutritionally derived, is concentrated by the thyroid gland, converted to organic iodine by thyroid peroxidase (TPO), and then incorporated into tyrosine in thyroglobulin in the thyroid. Tyrosines are iodinated at one (monoiodotyrosine) or two (di-iodotyrosine) sites and then joined to form the hormones thyroxine, (T4) and tri-iodothyronine (T3). Another source of T3 within the thyroid gland is the result of the outer ring deiodination of T4 by a selenium-based enzyme. T3 and T4 are cleaved from thyroglobulin by proteolytic lysosomes, resulting in release of free T3 and T4. The iodotyrosines (monoiodotyrosine and diiodotyrosine) are also released from thyroglobulin, but little reaches the bloodstream.

The T4 and T3 released from the thyroid reach the bloodstream where they are bound to thyroid hormone-binding serum proteins (primarily TBG and transthyretin) for transport. About 0.03% of the total serum T4 and 0.3% of the total serum T3 are free and in equilibrium with the bound hormones, and only free T4 and T3 are available to the peripheral tissues for thyroid hormone action. T3 is the metabolically active hormone.

Thyroid-stimulating hormone (TSH), or thyrotropin, controls all reactions necessary for the formation of T3 and T4 and is itself controlled by the pituitary gland through a negative feedback mechanism regulated by the circulating level of free T4 and free T3 and by conversion of T4 to T3 in the pituitary. Increased levels of free thyroid hormones inhibit TSH secretion from the pituitary decreased, whereas levels of T4 and T3 result in an increased TSH release from the pituitary. TSH secretion is also influenced by thyrotropin-releasing hormone (TRH) synthesized in the hypothalamus.

The thyroid produces about 20% of the circulating T3. The remaining 80% is produced by peripheral conversion of T4 primarily in the liver. A variation of this process also may produce reverse T3 (rT3), which has minimal metabolic activity. rT3 levels increase in chronic liver and renal disease, acute and chronic illness, starvation, carbohydrate-deficient diets, and possibly during extreme or prolonged stress. These states result in decreased production of the active hormone, T3, and in increased serum rT3 levels because of decreased rT3 clearance. The decreased production of T3 might be an adaptive response to illness, and can be seen in hypothyroidism.

hypothyroidism is endemic iodine deficiency; however, it may also result from thyroid gland agenesis, defective thyroid hormone biosynthesis, or rarely, hemangiomas, which also may occur in young children.[8,9] (Congenital hypothyroidism is not discussed in the remainder of this section.)

The most common form of primary hypothyroidism in areas of normal iodine intake is acquired primary hypothyroidism. It is most frequently a result of autoimmunity and is referred to as autoimmune thyroid disease (AITD) or autoimmune thyroiditis (Hashimoto's disease).[1,7,8] Antibodies are formed that bind to the thyroid (specifically against the thyroid peroxidase [TPO] enzyme, thyroglobulin, and TSH receptors) and prevent the manufacture of sufficient levels of thyroid hormone. In addition to binding to thyroid tissue, these antibodies also may bind to the adrenal glands, pancreas, and parietal cells of the stomach. Autoimmunity as an etiologic factor is supported by the presence of lymphatic infiltration of the thyroid gland and the presence of circulating thyroid autoantibodies in nearly all affected patients.[8] In fact, the most common risk factor for both hypothyroidism and hyperthyroidism is the presence of TPO autoantibodies.[1] Genetic predisposition (autosomal dominant inheritance) is a major factor in the etiology of AITD, accounting for as much as 79% of susceptibility to autoimmunity.[1,8] Hormonal and environmental factors appear to account for the remaining etiologies.[1] Autoimmune thyroiditis is increased in areas of high iodine intake, for example, in Iceland, suggesting an antigenic response.[1,8]

Other causes of hypothyroidism include iatrogenesis secondary to radiation or medications that interfere with thyroid function, genetic defects of the T3 hormone receptors and excessive consumption of goitrogens (substances that interfere with thyroid hormone production and release). Postpartum hypothyroidism is a transient form of hypothyroidism that affects 5% to 10% of postpartum women in the United States.[11] Transient hypothyroidism may occur secondary to subacute thyroiditis caused by infection. Primary hypothyroidism is often idiopathic, with no definable cause.[7]

The long-term consequences of untreated overt hypothyroidism are significant, and include elevated cholesterol and atherosclerosis, cardiac, renal, and neurologic diseases, increased susceptibility to infectious diseases, possibly increased rates of reproductive cancers, and ultimately, multiple organ failure if the disease progresses.[7,12,13] Hypothyroidism is readily detectable and treatable; therefore, these consequences should be almost entirely avoidable with screening and early treatment.

Subclinical Hypothyroidism. Subclinical hypothyroidism refers to patients with primary hypothyroidism with normal serum free thyroxine (free T4) and elevated thyroid-stimulating hormone (TSH).[2] These individuals may or may not be symptomatic. Low Dog suggests that *symptomatic euthyroid state* is a more appropriate label for these patients.[10]

The prevalence of subclinical hypothyroidism is highest in the United States among white women (5.8%), and is 5.3% and 1.2% among Hispanic-American and African-American women, respectively. Rates tend to increase significantly with age, reaching as high as 8% to 10% in women ages 45 to 74 years, and 17.4% in women over 75 years.[14]

There is strong evidence from high-quality longitudinal studies that subclinical hypothyroidism places women at significant risk for the later development of overt hypothyroidism, yet it frequently goes undetected and untreated.[2] Untreated subclinical hypothyroidism can lead to daily interference with optimal physical, neurologic, psychological, and emotional functioning, and can cause a diminished quality of life. Controversy exists regarding the routine screening and treatment of subclinical hypothyroidism for all women, a practice that has not been well studied or determined to be conclusively beneficial.[7–9] Its proponents argue that preventative treatment with thyroxine is relatively safe, effective, and inexpensive, and can prevent the development of overt hypothyroidism and its consequences.[7,8] Further, women who have been treated for subclinical hypothyroidism have retrospectively reported improvements in their physical and mental wellness.[7] Patients with subclinical hypothyroidism and abnormal lipid profiles may experience improvement within 1 month of thyroxine treatment.[7] Subtle and reversible changes in myocardial performance also have been reported in women with mild hypothyroidism.[8] Careful follow-up is essential, with periodic re-evaluation of relevant laboratory markers and symptoms. Because of the frequency of hypothyroidism in older women, routine screening and treatment may be justified in this population. Routine screening also may be prudent during pregnancy, because of the serious consequences of long-term cognitive dysfunction and decreased intelligence in the offspring of women with untreated prenatal hypothyroidism.[6]

BOX 6-2

Signs and Symptoms of Hypothyroidism

Ataxia
Bradycardia
Carpal tunnel syndrome
Cold intolerance
Constipation
Decreased energy
Decreased exercise tolerance
Delayed reflexes
Depression
Diastolic hypertension
Dry or brittle hair
Dry skin
Fatigue
Galactorrhea
Goiter
Hyperlipidemia
Infertility
Loss of libido
Low body temperature
Low-pitched or hoarse voice
Menstrual irregularities
Miscarriage
Muscle cramps
Muscle weakness
Periorbital edema
Poor memory
Psychomotor retardation
Slow speech
Somnolence
Water retention
Weight gain

Secondary Hypothyroidism

Secondary hypothyroidism can result from diseases that interfere with thyrotropin-releasing hormone (TRH) production by the hypothalamus, its delivery by the pituitary stalk, or with problems of pituitary thyrotropin production (e.g., pituitary adenomas, hypothalamic tumors, or their treatments such as surgery or radiation therapy). Head trauma, metastatic disease, and infection can also lead to secondary hypotyroidism.[8] Iatrogenic hypothyroidism is the second most common cause and is the result of radioactive iodine therapy or ablation treatment for Graves' disease and other forms of hyperthyroidism.

Signs and Symptoms

Any of the symptoms listed in Box 6-2 may be present in degrees ranging from mild (requiring careful discernment of the clinical picture) to severe. Hypothyroidism may also be asymptomatic, detectable only by laboratory screening. Hypothyroidism is commonly overlooked clinically because of the presence of these symptoms in any number of other diseases.

Diagnosis

Diagnosis of hypothyroidism should be sought on the basis of family history, clinical signs, age, and pregnancy status (because of risks for the fetus in cases of untreated maternal hypothyroidism). Diagnosis remains somewhat controversial because of variations in acceptable ranges of laboratory values among different labs and institutions. Because of this, thyroid dysfunction in a patient who complains of symptoms but presents with ''normal'' laboratory values should not be disregarded.

TSH measurement is commonly accepted as the most significant and sensitive measurement for hypothyroidism diagnosis. Elevated TSH identifies patients with primary hypothyroidism regardless of the cause or severity.[8] Primary hypothyroidism presents with a low serum T4 with attendant elevation of serum TSH. Subclinical hypothyroidism is marked by normal serum T4 levels

TABLE **6-1**

Biochemical Markers in Thyroid Dysfunction

THYROID DISORDER	TSH LEVEL	THYROID HORMONE LEVEL
Overt hypothyroidism	>5 mU/L	Low FT4
Subclinical hypothyroidism	>5 mU/L	Normal FT4
Overt hyperthyroidism	Low or undetectable	Elevated FT4 or FT3
Subclinical hyperthyroidism	Low or undetectable	Normal FT4 or FT3

Data from Helfand M: Screening for subclinical thyroid dysfunction in nonpregnant adults: a summary of the evidence for the U.S. Preventive Services Task Force, Ann Int Med 140(2):128-141, 2004.

with slight to moderately increased TSH levels and a normal FTI (Table 6-1). Laboratory tests are considered generally unnecessary to determine the underlying cause of primary hypothyroidism. Factors such as previous neck/thyroid irradiation or surgery, or other exposure to radiation (e.g., pharmaceutical exposure) postpartum status, or other known contributing factors is adequate. Autoimmune causes can be assumed on the basis of ruling out other possible etiologies.[8] An important note is that serum TSH levels may rise in the recovery phase of illness, mimicking values associated with hypothyroidism. Therefore, measurement of TSH after complete recovery is appropriate. Free T4 is required to give an accurate measurement of thyroid hormone activity, given that only 0.03% of total T4 hormone is unbound and reflects the thyroid hormone activity of T4. The remaining 99.97% of total T4 is bound to carrier proteins and is metabolically inactive. The fT4 or FTI in conjunction with a TSH can be used to categorize most cases of thyroid dysfunction. The exception occurs when FT4 remains normal but FT3 is abnormal, as may occur when there is a deficient conversion of T4 to T3.

Measurement of T3 is controversial. The conventional medical belief is that normal serum T3 levels are maintained until severe hypothyroidism occurs. Recently, however, many physicians have begun to evaluate T3 as a part of thyroid screening. Many test T3 levels only when patients are unresponsive to treatment with T4. T3 levels can be decreased in primary and secondary hypothyroidism as well as decreased serum TBG, by some medications, low carbohydrate diets, and euthyroid sick syndrome. Laboratory diagnosis of secondary hypothyroidism is marked by low T4 levels and low or normal TSH levels. Many patients need to have tests repeated several times to achieve an accurate and correct diagnosis.

Basal body temperature (BBT) testing has been suggested as a screening test for subclinical hypothyroidism. However, there are many factors other than thyroid hormones that affect BBT and thus by itself, low BBT is not a pathognomonic indicator of thyroid hormone status, although it does indicate lowered metabolic status.

Conventional Treatment

Treatment of hypothyroidism with thyroid extract has been practiced since 1891, when Murray first reported the use of sheep thyroid extract. Thyroid hormone was first crystallized in 1914, and initial testing with thyroxine began in 1927.[8] Exogenous thyroid hormone replacement remains the standard treatment, with thyroxine (T4) considered the treatment of choice based on its general efficacy and relatively small risk of adverse effects when given at the proper dose.[7,8] Conventional practice advocates the use of thyroxine alone over T3 and T4 combinations, the latter of which may provide T3 in excess of normal thyroid secretion.[7] However, many physicians find that the addition of T3 can be beneficial for patients not responding optimally to T4 alone.

Dosing of thyroid replacement therapies should be carefully monitored because of the narrow toxic-to-therapeutic ratio of thyroid hormone, with the patient maintaining on the lowest possible effective dose, which will be individually determined. The typical required daily dose is 1.5 μg/lb body weight, with doses for older adults at approximately 70% of that required for younger women.[7] It has been estimated by some researchers that as many as 20% of hypothyroid patients are receiving excessive doses. Adverse reactions to thyroxine are usually related to excessive dosing or increased thyroid hormone activity.[9] T3 supplementation may be implemented for patients unresponsive to T4 treatment alone.

No studies of controlled treatment of subclinical hypothyroidism have been conducted.[2]

Commonly used thyroid medications include:

- Synthroid and other synthetic preparations containing only T4
- Liotrix and Thyrolar: synthetic mixtures of T3 and T4 in similar ratios
- Cytomel: a synthetic T3 preparation
- Desiccated ''natural'' thyroid preparations (e.g., Armour thyroid): provide T4 and T3, plus amino acids and micronutrients. A popular criticism of natural thyroid preparations is that they lack consistency and reliability, and as stated, may provide T3 in excess.[7]

TABLE 6-2

Botanical Treatment Strategies for Hypothyroidism

THERAPEUTIC GOAL	THERAPEUTIC ACTION	BOTANICAL NAME	COMMON NAME
Stimulate thyroid hormone production/thyroid activity	Thyroid stimulating	*Bauhinia purpurea*	Bauhinia
		Coleus forskohlii	Coleus
		Commiphora mukul	Guggul
		Fucus vesiculosus	Bladderwrack
		Withania somnifera	Ashwagandha
Support metabolic function, reduce damage from oxidative stress, improve energy and vitality	Adaptogens	Adaptogen section below	
Supplement iodine in iodine deficiency-related cases	Iodine-rich	*Fucus vesiculosus*	Bladderwrack

Botanical Treatment

Traditionally, hypothyroidism would have been recognized and treated by herbal practitioners on the basis of its presenting metabolic deficiency symptoms, rather than as a discrete disease entity. The botanical practitioner recognized the patient picture as one of overall depletion. Herbalists today also view hypothyroidism with the goal of improving overall metabolism and the general integrity of the endocrine system. Many consider primary thyroid dysfunction to be a treatable condition with herbs and specific nutritional supplements (Table 6-2). Symptoms of hypothyroidism (e.g., constipation) may be treated with a symptom-specific protocol.

An adequate understanding of the influence of botanical medicines on the thyroid gland, thyroid hormone production, and metabolism is lacking, as are human studies on the use of herbs for hypothyroidism. In fact, there is limited evidence for the botanical treatment of this condition. In contrast, there is a long history of the successful and relatively safe use of thyroid hormone replacement therapy. Thus, unless a patient is responding poorly, conventional replacement therapy remains an excellent treatment choice. However, patients with borderline hypothyroidism may prefer and request alternatives to conventional therapy, and symptomatic euthyroid patients, or those with subclinical hypothyroidism, may be good candidates for botanical therapies that might support normalization of thyroid function. Note that botanicals that increase thyroid hormone levels are contraindicated in patients with hyperthyroidism; similarly herbs presented in the discussion of hyperthyroidism for the reduction of thyroid hormone levels are contraindicated for patients with hypothyroidism. Botanical therapies that increase thyroid function should not be combined with thyroid replacement therapies. Patients using botanical therapies to manage thyroid conditions should be monitored regularly (every 6 months) with thyroid testing.

Adaptogens

Adaptogenic herbs play a key role in regulating various metabolic processes through improvement in HPA functioning. Both hypothyroidism and hyperthyroidism are associated with enhanced oxidative stress. Adaptogenic herbs counter catabolic processes associated with stress on the body and increase the oxygen consumptive capacity to decrease metabolic markers associated with anaerobic metabolism. Additionally, adaptogens such as *Eleutherococcus senticosus* and many others have been demonstrated to improve fatigue, weakness, and debility.

Ashwagandha (*Withania somnifera*) is the only adaptogen for which a thyroid-related study was identified. In one study, the effects of daily administration of Ashwagandha root extract (1.4 g/kg body wt.) and *Bauhinia purpurea* bark extract (2.5 mg/kg body wt.) for 20 days on thyroid function in female mice were investigated. T3 and T4 concentrations were increased significantly by Bauhinia, and serum T4 concentration was enhanced by Withania. Both the plant extracts showed an increase in hepatic glucose-6-phosphatase (G-6-Pase) activity and antiperoxidative effects as indicated either by a decrease in hepatic lipid peroxidation (LPO) and/or by an increase in the activity of antioxidant enzyme(s). It appears that these plant extracts are capable of stimulating thyroid function in female mice.[15] The importance of *Withania somnifera* root extract in the regulation of thyroid function with special reference to type-I iodothyronine 5′-monodeiodinase activity in mouse liver was investigated. Although the extract (1.4 g/kg, p.o. for 20 days) increased serum T3 and T4 concentrations and hepatic glucose-6-phosphatase activity, hepatic iodothyronine 5′-monodeiodinase activity did not change significantly. Furthermore, the extract significantly reduced hepatic lipid peroxidation, whereas the activities of antioxidant enzymes such as superoxide dismutase and catalase were increased. It was concluded that the extract stimulates thyroid

activity and also reduces lipid peroxidation of hepatic tissue.[16]

Bladderwrack

Many herbalists and naturopathic physicians have relied on seaweed species in the treatment of hypothyroidism predicated on their iodine content. *Fucus vesiculosus*, or bladderwrack, for example, contains variable amounts of iodine, up to 600 mg/g. Much of the iodine content is organically bound, a more potent thyroid stimulating form than mineral bound iodine.[17] There are case reports of seaweed, especially bladderwrack, causing both hypothyroidism and hyperthyroidism, and evidence suggests thyroid activity. However, there are no studies of efficacy, dosing, or safety to support its use, and no standardization of iodine content.[18,19] Using seaweeds with the rationale that its iodine content is what is affecting treatment may be erroneous, as most thyroid insufficiency in the United States is not attributable to iodine deficiency. Further, excess iodine, as discussed, can contribute to or worsen hypothyroidism. Bladderwrack may interfere with thyroid replacement therapies such as thyroxine.[17] Bladderwrack also contains organically bound arsenic, which although rapidly excreted, should suggest caution when using large amounts.[19]

Coleus

Coleus spp. has been used for centuries in Ayurvedic medicine.[20] Forskolin stimulated thyroid function with increased thyroid hormone production in the isolated gland. However, in vitro, low forskolin concentrations inhibited thyroid function.[19] No other research on the use of this herb for thyroid conditions was identified.

Guggul

Guggul has shown thyroid stimulating activity, but not via the pituitary-TSH mechanism. It is thought to have a direct action on the thyroid gland. It acts on the peripheral conversion of T4 to T3 increasing T3 levels without changing T4 levels. By increasing thyroid metabolism and activity, guggul reduces LDL cholesterol in individuals with functional hypothyroidism, which may be related to the stimulation of T3 by guggulsterones.[21] The effect of a petroleum ether extract of *Commiphora mukul* was tested on mice thyroid gland grown in organotype of culture using modified Dulbecco's eagle medium. There was significant increase in the structure and function of thyroid cultivated explants using media containing the guggul extract with raised media T3 resin uptake, PBI, and free thyroxine index. It is inferred that extract of *Commiphora mukul* augment thyroid hormone synthesis and release.[22]

Tincture for Hypothyroidism

Coleus	(*Coleus forskohlii*)	20 mL
Ashwagandha	(*Withania somnifera*)	20 mL
Bladderwrack	(*Fucus vesiculosus*)	15 mL
Licorice	(*Glycyrrhiza glabra*)	10 mL
Guggul	(*Commiphora mukul*)	10 mL
Nettles	(*Urtica dioica*)	10 mL
Reishi mushroom	(*Ganoderma japonica*)	10 mL
Ginger	(*Zingiber officinalis*)	5 mL
		Total: 100 mL

Dose: 5 mL morning and noon

Nutritional Considerations

A variety of food antigens may induce antibodies that cross-react with the thyroid gland. A food elimination diet free of gluten containing grains and casein-containing dairy products may be helpful in the treatment of autoimmune hypothyroidism. The ingestion of goitrogens—foods that block iodine utilization—are best limited in those patents with goiter. These include such foods as turnips, cabbage, mustard, cassava root, soybean, peanuts, pine nuts, and millet. Cooking usually inactivates goitrogens.[23] Rich sources of iodine include ocean fish, sea vegetables (kelp, dulse, arame, hijiki, nori, wakame, kombu), and iodized salt, and should be included when there is iodine deficiency, but reduced when there is iodine excess.

Thyroid function may be supported nutritionally, even with the use of thyroid replacement therapy. Nutrients that may be beneficial supplements include selenium, zinc, tyrosine, and vitamins A, D, E, and C.[23] Good sources of zinc include seafood (especially oysters), beef, oatmeal, chicken, liver, spinach, nuts, and seeds. The richest food source of selenium is Brazil nuts, especially those that are unshelled.

Selenium is a cofactor in normal thyroid hormone production. Selenium deficiency decreases conversion of T4 to T3. People with selenium deficiency have elevated T4 and TSH. Patients with normal circulating hormone levels who display clinical hypothyroid symptoms may be selenium deficient; thus, selenium levels should be evaluated and supplementation provided if deficiency is present. In a double-blind, placebo-controlled trial of selenium supplementation of 100 μg/day for 3 months among older subjects showed an improvement in selenium indices, a decrease in T4, and a trend toward normalization of T3:T4 ratio.[10]

Zinc is involved with synthesis of hypothalamic thyrotropin-releasing hormone (TRH); a zinc deficiency may lower 5′-deiodinase function, thereby contributing to a lower conversion of T4 to T3. Supplementation with zinc acts to normalize the TRH-induced TSH reaction and increase conversion of T4 to T3. The recommended dose is zinc picolinate, 30 mg/day.[23]

Tyrosine is an amino acid used as a precursor for making thyroid hormone. Tyrosine deficiency can contribute to low thyroid function. Low protein diets may provide insufficient tyrosine for normal thyroid hormone production. Supplementation of tyrosine at a dose of 500 to 1500 mg daily has therapeutic benefits in hypothyroidism.

Treatment Summary

- Improve overall metabolism with diet, exercise, and herbs. Green tea is an excellent herb for gently boosting metabolism, and the adaptogens are a good long-term treatment.
- Remove stressors and improve adrenal and thyroid functioning with the use of adaptogens.
- Use botanicals to directly augment thyroid function.*
- Monitor progress with regular thyroid testing.
- Avoid foods that stimulate antigen cross-reactivity with the thyroid, such as gluten and casein.
- Avoid excessive intake of foods that act as goitrogens.
- Evaluate and ensure adequacy of dietary iodine intake: ocean-caught fish, iodized sea salt, and sea vegetables (kelp, wakame, nori) are good sources.
- Supplement with zinc, selenium, and vitamins A, C, D, and E.
- Initiate an exercise program to improve metabolism and prevent weight gain; dieting is discouraged as it can reduce metabolic function.

*Do not combine thyroid-stimulating herbal therapies with pharmaceutical thyroid medication. Consult with the patient's physician if the patient wants to make a switch between conventional and botanical therapies. In many cases, conventional treatment is the optimal choice.

Exercise

Regular daily exercise stimulates thyroid gland function and increases tissue sensitivity to thyroid hormone.[23] Exercise is especially important for dieting overweight hypothyroid patients, as dieting can often put the body into a lower metabolic rate as the body tries to conserve fuel. Adjunctive regular exercise prevents the metabolic rate from dropping with the decrease in caloric intake.

CASE HISTORY: HYPOTHYROIDISM

Eliza, 44-year-old woman, reports weight gain without an increase in dietary intake, fatigue, muscle weakness, frequent infections, poor healing skin lesions, and alopecia. Symptoms began about 6 months ago and over the last 5 weeks have increased in severity. She works 30 hours a week as a therapist, lives alone with her two cats, and loves to garden. She takes a daily multivitamin and mineral supplement plus 1000 mg daily of vitamin C.

Her maternal family history is positive for hypothyroidism, allergies, and depression, paternal history is positive for late-onset diabetes, stroke, and allergies. The patient reports a generally healthy diet of whole foods with light meats, eggs, tofu, and fish as her main proteins. She eats mostly organic vegetables and seasonal fruits along with whole grains breads and cereals. She eats some cheese and butter, but uses rice milk instead of cow milk. She drinks water, herb teas, and one cup of coffee each morning. She often skips breakfast, because she has no hunger in the morning.

She experiences sluggish bowels, often skipping a day or two each week and has frequent gas and bloating. She experiences recurrent sore throat and tonsillitis along with frequent sinus fullness and swollen glands in her neck. She claims to sleep well but wakes too early and often feels tired upon rising. She feels tired often in her day and experiences muscle fatigue. Her menstrual cycle length is every 32 days, with menses lasting 6 to 7 days and accompanied by heavy bleeding and clots for 2 days, and with dysmenorrhea on those first 2 days. Associated complaints include bloating, food cravings, irritability, weepiness, and depression for 5 to 7 days before her menses starts. She reports no children and never having been pregnant. She has no breast complaints and does a monthly self-breast exam. On physical exam, her BBT averages 96.4 over a 5-week period. Her normal blood pressure is 110/66, pulse 68, and she has reduced lower extremity reflexes. Her skin is slightly dry to the touch. Laboratory results demonstrate a TSH of 17.04 (0.32–5.00), Free T4 of 0.8 (0.8–1.8), Total T3 of 94 (60–180), T3 uptake of 36 (22–37). Thyroid antibodies, antimicrosomal antibody of 400 (<100) and anti-thyroglobulin antibodies are normal. She was diagnosed with Hashimoto's disease.

Treatment Protocol

Tincture to be taken internally:

Coleus	(*Coleus forskohlii*)	20 mL
Ashwagandha	(*Withania somnifera*)	20 mL
Bladderwrack	(*Fucus vesiculosus*)	15 mL
Licorice	(*Glycyrrhiza glabra*)	10 mL
Guggul	(*Commiphora mukul*)	10 mL
Nettles	(*Urtica dioica*)	10 mL
Reishi mushroom	(*Ganoderma japonica*)	10 mL
Ginger	(*Zingiber officinalis*)	5 mL
		Total: 100 mL

Dose: 5 mL morning and noon

Supplements

Include, along with the balanced diet:

- High-quality multivitamin supplement
- Selenium 100 μg, three times daily with meals
- Zinc 15 mg daily
- Tyrosine 500 mg daily

Additional Therapies

- Apply rose hip-myrrh essential oil blend daily to the thyroid area to stimulate thyroid function.

Patient was evaluated 3 months after starting treatments with the following lab values: TSH of 1.27, fT4 1.1, and fT3 4.0. The botanical medicine dose was adjusted to 3 mL AM and noon. The patient was instructed to continue all else and follow up in 6 months.

HYPERTHYROIDISM

Pathophysiology

Hyperthyroidism, or thyrotoxicosis, is the result of excessive levels of circulating thyroid hormones. It is characterized by elevated total T4, free T4, free T4 index, and/or T3 and T3 resin uptake. Low TSH and normal levels of T3 and T4 characterize subclinical hyperthyroidism, and it has the same causes as overt hyperthyroidism.[2] Graves' disease, an autoimmune disorder in which stimulatory anti-TSH receptor antibodies are formed, comprises the majority of hyperthyroid cases. In fact, the strongest risk factor for both hypothyroidism and hyperthyroidism is the presence of TPO antibodies.[1] These antibodies are directed toward the receptors in the cell membrane of the thyroid gland, causing the gland to increase growth, size, and function. Graves' disease is characterized by several common features, including thyrotoxicosis, goiter, exophthalmos, and pretibial myxedema. Graves' disease is eight times more common in women than men, typically presents between the ages of 20 and 40 years old, and the most common presentation is a diffuse nonpainful goiter. It may be more prevalent in some genetic HLA haplotypes.[24]

There are several types of thyroiditis that can cause hyperthyroidism, including Hashimoto's thyroiditis, subacute thyroiditis, painless thyroiditis, postpartum thyroiditis, and radiation thyroiditis. Other contributing factors include stress, smoking, and iodine supplements/excessive iodine intake, drug-induced hypothyroidism, higher pregnancy frequency, being postpartum, and microbial infections. Hyperthyroid patients have a significantly lower exposure to exogenous estrogens than euthyroid patients.[1]

Toxic adenoma is a solitary nodule within the thyroid that produces excessive amounts of thyroid hormones. It typically occurs in the middle-aged and older populations.[10]

Thyroid storm, or thyrotoxic crisis, can occur as a result of a serious stressor, such as surgery, infection, or trauma in a poorly managed case. The mortality rate is approximately 25% even with proper medical treatment.[10]

Hyperthyroidism and subclinical hyperthyroidism affect quality of life, producing symptoms mimicking adrenergic overactivity. Subclinical hyperthyroidism exerts significant effects on the cardiovascular system. It is associated with a higher heart rate and increased risk of supraventricular arrhythmias, and with an increased left ventricular mass, often accompanied by impaired diastolic function and sometimes by reduced systolic performance on effort and decreased exercise tolerance. These changes usually precede the onset of more severe cardiovascular disease, thus potentially contributing to increased cardiovascular morbidity and mortality. Subclinical hyperthyroidism may accelerate the development of osteoporosis and hence increased bone vulnerability to trauma, particularly in postmenopausal women with a pre-existing predisposition. Fortunately, subclinical hyperthyroidism and its symptoms are readily preventable, and reversible with timely treatment.[25]

BOX 6-3

Signs and Symptoms of Hyperthyroidism

Diaphoresis
Diarrhea
Exercise intolerance
Exophthalmia
Goiter
Hair loss
Heart palpitations
Heat intolerance
Increased appetite
Nervousness
Onycholysis (separation of the nail from the bed)
Personality/psychological changes
Pretibial myxedema
Skin changes
Tachycardia
Thyroid bruit (murmur)
Tremor
Weakness
Weight loss

Signs and Symptoms

Symptoms of hyperthyroidism are listed in Box 6-3. Menstrual symptoms associated with hyperthyroidism can vary, and may range from amenorrhea to oligomenorrhea, but menstrual cycles also may appear normal. Anxiety, nervousness, and depression rates are higher in hyperthyroid patients than in euthyroid controls.[2] Graves' disease is characterized by a triad of hyperthyroidism, exophthalmos, and pretibial myxedema. Hyperthyroidism symptoms in postmenopausal women present differently than in younger women. Symptoms are usually confined to a single organ system, particularly the cardiovascular or central nervous system. Goiter is usually absent in 40% of cases, and in older women, a co-occurring disease such as infection of coronary heart disease is usually predominant. The triad of weight loss, constipation, and appetite loss occurs in about 15% of older patients, whereas ophthalmic disease is rare. Practitioners may notice failure to thrive in older patients, with signs of heart disease, unexplained weight loss, and mental or psychological changes signaling possible hyperthyroidism.[7]

Diagnosis

Definitive laboratory diagnosis is based on elevated serum free T4, total T4, free thyroxine index, and T_3 resin uptake. If these are borderline elevated, the T3 should be checked as it is often elevated out of proportion to the T4. TSH is typically decreased. Test for Graves' disease using the serum TSH receptor antibodies (TSH-R-Ab) test. If nodular goiter presents, a thyroid scan to rule

out cancer is recommended.[26] As with hypothyroidism, controversy exists as to whether to routinely screen for subclinical hyperthyroidism. Proponents of screening advocate for the potential benefit via prevention of atrial fibrillation, osteoporotic fractures, and other complications of overt hyperthyroidism. Controlled studies of the treatment of subclinical disease have not been conducted.[2]

Conventional Treatment

The primary goal of conventional medicine is to limit the amount of thyroid hormone production by the thyroid gland.[11] Three main treatment methods are available: (1) antithyroid drug therapy, (2) surgery, or (3) radioactive iodine therapy. Although Graves' disease is an autoimmune disorder, conventional treatment of the disorder is aimed at managing the hyperthyroidism.

Antithyroid drug therapy seems to be most useful in young patients with mild disease. The drugs propylthiouracil, carbimazole, and methimazole may be given until spontaneous remission occurs. Twenty to forty percent of patients have spontaneous remission within 6 months to 15 years duration. There is a fifty to sixty percent relapse rate in patients treated with this method of therapy.[10,24]

Thyroidectomy is the treatment of choice for those patients with large or multinodular goiters. The patient is given antithyroid drugs for 6 weeks to bring the gland to a euthyroid state. The patient is also given potassium iodine for 2 weeks prior to surgery to diminish the vascularity of the gland and simplify the surgery. Subtotal thyroidectomy is preferred over total thyroidectomy. Patients generally require supplementation with thyroid hormone following surgery.

In radioactive iodine therapy, radioactive iodine is given in one dose, following which the gland shrinks and the patient becomes euthyroid over a period of 6 to 12 weeks. The major complication of this method of therapy is hypothyroidism, which develops in 80% of patients treated.[27]

In mild cases of hyperthyroidism, beta-blockers may be given to provide symptomatic relief of adrenergic symptoms, including arrhythmia, tremor, tachycardia, and anxiety. They also provide minimal prevention of peripheral conversion of T4 to T3. As beta-blockers have no effect on inhibition on the production or release of thyroid hormone, they are an adjunctive therapy alongside of one of the more invasive therapies described in the preceding.[10]

Botanical Treatment

Traditional Western botanical medicine practitioners have found several herbs effective in the treatment of hyperthyroidism, a number of which have demonstrated antithyroid activity, inhibiting the binding of TSH to thyroid tissue (Table 6-3). Additionally, a number of herbs are effective in the treatment of heart palpitations, anxiety, and adrenergic symptoms associated with hyperthyroidism. Note the treatment of mild hyperthyroidism only with botanical medicines is recommended.[10]

Herbs that increase thyroid activity, as discussed under hypothyroidism, should be avoided in the hypothyroid patient. Additionally, the use of ephedra is contraindicated in patients with hyperthyroidism, and herbs with high caffeine content should be avoided.[28] Increased consumption of goitrogens (leafy greens, cabbage, broccoli, and Brussels sprouts, as well as soy) can be part of a treatment strategy to reduce thyroid hormone.[10]

Thyroid hormone excess causes an increase in metabolism, and thus an increase in nutritional needs, excessive glucose metabolism, and increased oxidative stress and increased susceptibility to liver damage. Botanical medicines and nutritional supplements to reduce oxidative stress (adaptogens, antioxidants) and protect the liver (*Silybum marianum*) also should be included in the protocol (see Additional Therapies).

Bugleweed

Bugleweed (Fig. 6-1) has a long history of use by herbalists for the treatment of palpitations and anxiety.[10] It is widely recommended in medical herbalism texts: Priest describe it for the treatment of palpations, tachycardia, and dysregulation of the autonomic nervous system.

TABLE 6-3

Botanical Treatment Strategies for Hyperthyroidism

THERAPEUTIC GOAL	THERAPEUTIC ACTION	BOTANICAL NAME	COMMON NAME
Inhibit TSH binding	Antithyroid	*Lycopus* spp.	Bugleweed
		Lithospermum officinale	Club moss
		Melissa officinalis	Lemon balm
Relieve palpitations	Anti-arrhytmics	*Leonurus cardiaca*	Motherwort
Relieve anxiety	Anxiolytics	*Leonurus cardiaca*	Motherwort
		Melissa officinalis	Lemon balm
		See Nervines in index	

Figure 6-1 Bugleweed (*Lycopus* spp.). (Photo by Martin Wall.)

Formula for Hyperthyroidism		
Motherwort	(*Leonurus cardiaca*)	25 mL
Bugleweed	(*Lycopus* spp.)	25 mL
Lemon balm	(*Melissa officinalis*)	25 mL
Nettles	(*Urtica dioica*)	25 mL
		Total: 100 mL

Dose: This is a classic herbal formula for hyperthyroidism. The late Hein Zelstra, well-known herbal educator from Tunbridge Wells, UK, recommended an equal part mixture of 1:5 tincture these herbs given in 5 mL doses three times daily.

Weiss refers to bugleweed as having thyrostatic effects and suggests its use for the treatment of hyperthyroidism, whereas the British Herbal Pharmacopoeia (BHP) calls it a thyroxine antagonist.[29–31] Hoffmann reports it to be indicated for mild forms of hyperthyroidism, especially when symptoms include tightness of breathing, palpitations, and shaking.[32] Priest and Priest recommend combining bugleweed with motherwort for hyperthyroid cardiac reactions, a common practice among herbalists.[31]

In vivo and in vitro evidence has demonstrated that *Lycopus* spp. can be beneficial in the treatment of hyperthyroid symptoms.[10] Rosmarinic acid, ellagic acid, chlorogenic acid, and luteolin-7-beta-glucoside appear to be the active constituents leading to blocking of TSH receptors and inhibition of peripheral conversion of T4 to T3.[10,33] Aqueous, freeze-dried extracts of *Lycopus* spp., *Lithospermum officinale*, and *Melissa officinalis* have been studied in vivo and in vitro; preliminary results support their use in Graves' disease. This combination was shown to inhibit TSH effects on TSH receptor sites on thyroid cell membranes, block effects of antithyroid immunoglobulins on TSH receptors, and inhibit peripheral deiodination of T4 to T3.[34] No human clinical trials have been conducted using bugleweed.[10] The German Commission E recognizes the use of bugleweed for mild hyperthyroid conditions with neuroanatomic dysfunction based on pharmacologic studies only, and states that in rare cases high doses have resulted in thyroid enlargement, whereas sudden discontinuation of use has increased disease symptoms.[35]

Club Moss, Gromwell

Like bugleweed, *Lithospermum* has a long history of use for the treatment of hyperthyroid conditions. It was used by the Eclectic physicians for this purpose, and although less widely used than Lycopus, has been equally well studied.[10,36] Animal studies using *Lithospermum officinale* have demonstrated its ability to block TSH activity at the receptor level, block the release of TSH from the thyroid, and suppress the iodide pump. It also inhibits peripheral T4-deiodination and conversion to T3.[34,37] An in vitro study using freeze-dried extract demonstrated the ability to decrease antibody binding to thyroid tissue on Graves' disease.[34] No human clinical trials have evaluated the use of Lithospermum for hyperthyroid diseases.[10]

Lemon Balm

Lemon balm (Fig. 6-2), historically referred to as the ''gladdening herb,'' is calming to the nervous system and has been used since ancient times for this purpose. In vitro studies have confirmed this herb's ability to block TSH receptors and inhibit both binding of bovine TSH to human thyroid tissue, and binding of autoantibodies in Graves' disease.[34] The herb has a high safety profile and is appropriate for the treatment of mild hyperthyroidism, as well as associated anxiety and depression.[10]

Motherwort

Motherwort (Fig. 6-3) is classically used for the treatment of anxiety, depression, heart palpitations, and tachycardia, making it highly appropriate for symptomatic relief in hyperthyroid disease.[10,29,32] Chemical analytical and animal studies confirm the herbs sedative, anxiolytic, anti-arrhythmic, and antispasmodic effects.[10] The German Commission E supports the use of motherwort for the treatment of cardiac disorders associated

Figure 6-2 Lemon balm (*Melissa officinalis*). (Photo by Martin Wall.)

Figure 6-3 Motherwort (*Leonurus cardiaca*). (Photo by Martin Wall.)

with anxiety and for the symptomatic relief of hyperthyroidism.[36]

Nutritional Considerations

The risk of oxidative damage is increased in the hyperthyroid patient because of a higher metabolic rate. Lipid peroxidation is increased and activities of antioxidant enzymes are altered. Dietary changes involve an emphasis on goitrogens, foods that naturally block thyroid hormone synthesis, and the avoidance of certain foods, particularly those high in iodine content such as seaweeds. Dietary goitrogens include broccoli, cauliflower, Brussels sprouts, cabbage, kohlrabi, sweet potatoes, almonds, pine nuts, millet, peaches, and peanuts.[8]

- Include a complex daily antioxidant supplement.
- Flavonoid-containing substances have been shown to decrease serum T4 concentrations and inhibit both conversion of T4 to T3 and 5′-deiodinase activity.[38] Foods and botanical medicines that are high in flavonoid compounds include those fruits and vegetables of yellow-orange, red, and purple color, such as blueberries, purple grapes, and cherries. Botanical medicines that provide flovanoid compounds include hawthorne berry, astragalus, gingko, licorice, and chamomile.[39]
- Calcium metabolism is altered in hyperthyroidism, making Graves' patients more susceptible to osteoporosis.[7] Adequate prevention of osteoporosis should be an important part of the patient's treatment plan (see Chapter 19).
- Selenium deficiency substantially alters the conversion of T4 to T3 in peripheral tissues such as the liver and kidneys.[33,40] In a randomized, prospective, blinded study 36 patients with autoimmune thyroiditis were supplemented 200 μg of selenium for 3 months, thyroid-specific TPOAb concentrations significantly decreased from 100% to 63%, 9 of the 36 had complete normalization of TPOAb concentrations.[41]
- Zinc needs are increased in hyperthyroid patients because of greater urinary zinc excretion.

Additional Therapies

Stress reduction methods include biofeedback, meditation, tai chi, yoga and prayer therapy, and should be included in a plan for hyperthyroid treatment.

Treatment Summary

- Achieve symptomatic relief of heart palpitations and anxiety with herbs.
- Use herbs and antioxidant supplements to protect the liver against the oxidative stress effects of increased metabolism caused by this condition.
- Ensure adequate nutritional intake, metabolism is significantly increased in patients with hyperthyroidism.
- Increase intake of dietary goitrogens to help reduce excessive thyroid function.

Severe hyperthyroidism requires medical management

CASE HISTORY: HYPERTHYROIDISM

A 32-year-old woman presented with a 3-month history of chronic vaginal and nipple candidal infection. She is 8 months postpartum and breastfeeding her daughter, who has also had recurrent thrush for the past 3 months. She reports nearly constant anxiety, heart palpations several times a day, excessive thirst and hunger, irritability, fatigue, and hot flashes. She reports that it is difficult for her to relax and she is bothered by insomnia. She reports a normal first pregnancy and birth and no menstrual cycle since the pregnancy. She experiences frequent colds and sinus infections and is chronically congested in her nasal passages, with postnasal drip, and fullness in her left ear. She complains of frequent gas and bloating and reports two or three bowel movements daily, often unformed.

She used Nystatin oral suspension several times for the yeast, as prescribed by her primary care physician, and was taking a prenatal vitamin and EPA/DHA 500 mg two times a day. Her blood pressure was 124/78; pulse 92, respirations 20 per minute. Her physician observed that the woman had extreme nervousness about the well-being of the baby, how she is caring for the baby, and breastfeeding issues.

Laboratory Values

TSH: <0.01 (0.4–5.0), T4: 18.8 (4.5–12), FT I: 7.3 (1.4–3.7), T3 uptake: 39 (25–36), fT4: 5.1, (8–1.8) Total T3: 553 (80–180), and TSH-R antibodies positive.

She was diagnosed with hyperthyroidism (Graves' disease).

Treatment Protocol

Tincture to be taken internally:

Bugleweed	(*Lycopus* spp.)	20 mL
Club moss	(*Lithospermum officinale*)	20 mL
Lemon balm	(*Melissa officinalis*)	20 mL
Motherwort	(*Leonurus cardiaca*)	10 mL
Skullcap	(*Scutellaria lateriflora*)	10 mL
Valerian	(*Valeriana officinalis*)	10 mL
Eleuthero	(*Eleutherococcus senticosus*)	10 mL
		Total: 100 mL

Dose: 5 mL TID with meals
Also: Astragalus capsules 500 mg twice daily

Dietary recommendations were to increase dietary goitrogens, including broccoli, cauliflower, Brussels sprouts, cabbage, kohlrabi, sweet potatoes, almonds, pine nuts, millet, peaches, soy, and peanuts.

She was encouraged to practice daily yoga for half an hour, along with aerobic exercise four to five times a week.

Take a 20-minute warm bath at night with essential oils of lemon balm and lavender (5 to 7 drops each per bath).

The patient was evaluated with labs 2 month later showing TSH: <0.01, T3: 38, T4: 18.3, FTI: 5.9, Total T3: 433, and fT4: 3.4. She reports her average pulse as being 84 and her signs and symptoms are lessening.

Evaluation after 7 months of treatment shows TSH <0.01, T3: 110, fT4: 0.72, and FTI: 2.9.

STRESS, ADAPTATION, THE HYPOTHALAMIC-PITUITARY-ADRENAL-AXIS (HPA) AND WOMEN'S HEALTH

Jillian E. Stansbury, Aviva Romm

Viewed from the perspective of the evolution of the animal kingdom, sustained psychological stress is a recent invention, mostly limited to humans and other social primates.

—Robert Sapolsky, author, *Why Zebras Don't Get Ulcers*

Stress is a fact of life. However, for most of our biological history, stress was a short-term crisis, after which, according to Robert Sapolsky, author of *Why Zebras Don't Get Ulcers*, ''it's either over with or you're over with.''[43] Modern society, with its 24/7 work requirements and global Internet access, high level of stimulation and demand, and chronic (daily) repeated stresses, has opened us to a whole new realm of chronic, debilitating diseases. Western medicine is beginning to understand what has long been recognized by traditional medicine systems: that stress, or more traditionally viewed, one's relationship with and response to the world, has an impact on health.

What we now know scientifically is that the challenge of a small amount of stress, whether from positive or negative stressors (eustress/distress), can actually increase the overall health and performance of the individual organism, but that prolonged or repeated stress leads to wear and tear on the body—allostatic load—part of a deleterious picture leading to numerous health consequences. These may include reproductive disorders, endocrine dysregulation, insulin resistance (Syndrome X), obesity, chronic fatigue syndrome (CFS), cardiovascular disease, osteoporosis, impaired immunity and autoimmune disorders, cognitive impairment, thyroid disorders, chronic anxiety, postpartum depression, and major depression, to name a few of the big players.[43–48] It might not surprise readers that women are experiencing these conditions in increasing and significant numbers. Although stress is not the sole cause of these illnesses—as most illnesses have multifactorial etiologies—stress appears to be an underlying factor in many conditions. Unlike exposure to

environmental toxins and radiation, or traffic patterns, and other factors over which we have little control, it may be one factor whose effects we have the ability to minimize.

STRESS, HEALTH, AND DISEASE: THE PHYSIOLOGY AND PATHOPHYSIOLOGY OF STRESS AND THE STRESS RESPONSE

The groundwork for the scientific understanding of the physiology of mind–body interactions was first established in the 1930s by the work of Walter Cannon, and followed in the 1940s by the extensive work of Hans Selye, who first formally elaborated the concept of stress and its effects on physiology.[44,49–53] Selye is also credited with introducing the terms corticoids, glucocorticoids, and mineralocorticoids, and through his work demonstrated the ''triad of stress'': adrenal enlargement, GI ulcers, and thymus gland atrophy, in response to exposure to chronic stressors.[51] George Chrousos summarizes stress and the stress response as follows:

> *Life exists by maintaining a complex dynamic equilibrium, or homeostasis, that is constantly challenged by intrinsic or extrinsic adverse forces or stressors. Stress is, thus, defined as a state of threatened homeostasis, which is reestablished by a complex repertoire of physiologic and behavioral adaptive responses of the organism. The adaptive responses may be inadequate for the reestablishment of homeostasis or excessive and prolonged; in either case a healthy steady state is not attained, and pathology may ensue.*[49]

Stressors are threats to homeostasis and the adaptive responses are the counteracting forces intended to re-establish it.[43,48,52] Selye termed the adaptive stress response *general adaptation syndrome*, and demonstrated that it consisted of a consistent set of physiologic responses that included initial response to the stressor followed by an exhaustion phase, and eventually a recovery phase (Fig. 6-4).

More recently the stress response has been renamed allostasis, the ability of the organism to maintain stability, or homeostasis, through change.[44,52] McEwen elaborates:

> *The terms, ''allostasis'' and ''allostatic overload,'' allow for a more accurate definition of the overused word ''stress'' and provide a view of how the essential protective and adaptive effects of physiological mediators that maintain homeostasis—the body's optimal set points for important factors such as blood pressure, fluid balance, pH, glucose levels, oxygen levels, temperature, etc.—are also involved in the cumulative effects of daily life when they are mismanaged or overused. When mediators of allostasis, like cortisol and adrenaline, are released in response to stressors or to lifestyle factors such as diet, sleep, and exercise, they promote adaptation and are generally beneficial. However, when these mediators are not turned off when the stress is over, or when they are not turned on adequately during stress, or when they are overused by many stressors, there are cumulative changes that lead to a wear-and-tear, called ''allostatic load or overload,'' on the body and brain. The concept of allostasis refers to the network of interacting mediators by which stability, that is, homeostasis, is achieved through change. There are primary mediators of allostasis, such as, but not confined to, hormones of the hypothalamic-pituitary-adrenal (HPA) axis, catecholamines, and cytokines. These mediators interact with each other to create a network of reciprocal effects.*[44]

Our bodies possess complex and elegant mechanisms for responding to and recovering from acute exposure to stressors. The neuroendocrine system has evolved two primary pathways responsible for responding and adapting to potentially harmful or life-threatening encounters: the sympathoadrenal system (SAS) and hypothalamic-pituitary-adrenal axis (HPA). Both mediate a two-way brain-body communication that sets in motion a series of hormonal and neuroendocrine responses that ''switch on'' and ''switch off'' what has been commonly referred to as the ''fight or flight'' response.[43,52] In response to the alert system being switched on, the body's resources are mobilized for protective action: The heart rate increases and blood is diverted from digestion (who needs to digest when being chased by the proverbial saber tooth tiger?) into the periphery, especially the legs (yup, you want to be able to run away from the tiger!), the respiratory rate increases, blood pressure increases and urinary output decreases, the pupils dilate to increase sight, and other senses such as hearing and smell become keener, the mind becomes sharp and alert and vigilance is enhanced, appetite decreases, immunity is suppressed, and large amounts of sugar are delivered to the bloodstream via lypolysis and gluconeogenesis to fuel the energy needed for a massive response. Growth, reproduction, and sexual response are inhibited—resources are instead diverted to immediate life-saving needs, rather than toward what Sapolsky refers to as optimistic activities. In the recovery phase, interestingly, the body responds to the need for repair by increasing appetite and storing fat (primarily in the abdomen).[43]

Hormonal and neuroendocrine mediators and messengers from the sympathetic nervous system and HPA axis orchestrate all of these responses. At the first sign of threat, or even a perceived threat, the sympathetic nervous system goes into action. Epinephrine (adrenaline) and norepinephrine (noradrenalin) are released from the nerve endings of the adrenal glands and the rest of the body, respectively, and begin to stimulate the body to further reaction in a matter of seconds. The hypothalamus

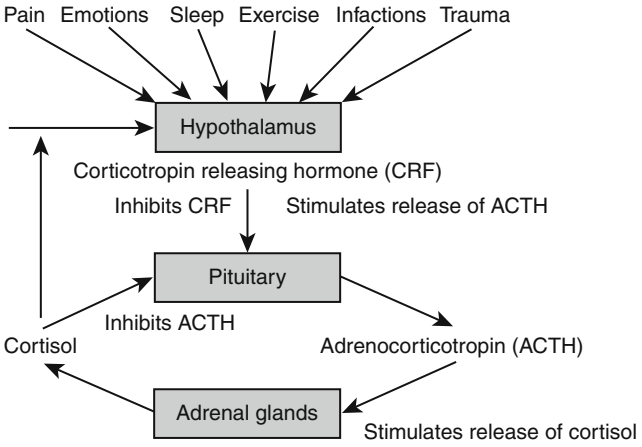


Figure 6-4 Stressors, the stress response, and the HPA axis. *(Courtesy of Robyn Klein)*

releases a substance called corticotrophin-releasing hormone (CRH), which triggers the release of ACTH (corticotrophin), which within a few minutes reaches the adrenal glands, where it causes the release of glucocorticoids (cortisol, corticosteroids). The pancreas releases glucagons, which with the glucocorticoids increase the levels of circulating glucose. Glucocorticoids do this via the promotion of protein and lipid degradation from muscle, skin, and fat. Energy is mobilized at the expense of storage. Other hormones are released as well. Prolactin is secreted by the pituitary, and plays a role in the suppression of reproduction during stress. Endorphins and enkephalins are released, blunting pain perception, while vasopressin (antidiuretic hormone) is released from the pituitary, and maintains blood pressure, forestalling for example, hypovolemic shock in the event of massive blood loss. Prostaglandins, PAF, and NO are all stimulated. The allostatic response also inhibits the release of numerous hormones, for example, estrogen, progesterone, and testosterone, as well as growth hormone and insulin.

Prolonged and repeated exposure to aversive events—as well as anticipation of aversive events (e.g., worry and anxiety about future or impending events such as an interview, an exam, paying the bills)—may lead to a sustained activation and dysregulation of the HPA axis.[43] In time, allostatic states place wear and tear on the regulatory systems of the brain and body, which can lead to HPA hyperfunctioning or hypofunctioning (respectively, the inability to turn off, or turn on the adaptive response) maladaptive responses thought to be causally linked to a number of disorders via glucocorticoid and other effects on the cardiovascular system, mobilization of bone stores of calcium, effects on weight and fat distribution, hormonal effects on the reproductive system, thyroid effects, and so forth.[43,44,47,52]

Women are more likely to experience menstrual irregularities, anovulation, infertility, osteoporosis, chronic fatigue, autoimmunity, and cardiovascular disease, Syndrome X, and diabetes, for example. Further, there is significant evidence that a history of childhood sexual or psychological abuse predisposes to HPA dysfunction later in life.[54] Excessive exercise (overtraining) also can lead to HPA dysfunction with increased fatigue and decreased immune response.[55] Irregular and inadequate food intake, regular hypoglycemic episodes, and yo-yo dieting also cause excessive stress and cause blood sugar imbalances that can lead to allostatic overload and eventually HPA dysregulation.

The medical profession does not define a category of illnesses that encompasses the effects of allostatic load. Prevention and treatment of stress and its effects on the HPA axis are not considered a part of preventative care or treatment for the numerous and serious stress-related diseases mentioned earlier, with limited exception. Adrenal disease is recognized only in its severest forms: Addison's disease and Shy-Drager syndrome. Yet the symptoms of HPA axis dysregulation are rampant in modern society. Aside from overt dysfunction and disease [reproductive disorders and endocrine dysregulation, insulin resistance (syndrome X) and obesity, chronic fatigue syndrome (CFS), cardiovascular disease, osteoporosis, impaired immunity and autoimmune disorders, thyroid disorders, cognitive impairment, chronic anxiety, and major depression], Americans are plagued by fatigue and exhaustion, insomnia, emotional frustration, digestive problems, weight problems, menstrual problems, infertility, menopausal problems, headaches, susceptibility to colds, musculoskeletal tension, allergies and asthma, atopic conditions, and numerous other problems that can be related to stress and chronic HPA hyperfunctioning or hypofunctioing.[43–47] The need to address chronic stress as part of the prevention and treatment of chronic illness is more than a lip service to a holistic approach—it is a significant part of a comprehensive medical and public health approach to reducing chronic health problems affecting all populations in the United States. It is also an integral aspect of herbal medicine care, as discussed in the following.

EUSTRESS AND DISTRESS

Interestingly, pleasant and pleasurable activities (sex, numerous mind-altering and energy-altering substances that are commonly used and abused, heavy exercise) also trigger the stress response. The primary factors distinguishing distress from eustress appear to be the quality and intensity of the stressor, termination of the stress response after a particular stressor has ceased, and the return of homeostasis.[52] Genetic predisposition, life history, and age also seem to play significant roles in the perception of stress and in the stress response.[43,52]

DIFFERENTIAL DIAGNOSIS

HPA dysfunction must be distinguished from specific chronic and acute diseases, as well as from frank adrenal disease. Patients complaining of chronic, recurrent symptoms should have serious underlying illness ruled out. HPA dysfunction then becomes a diagnosis based on exclusion of other possible causes.

CONVENTIONAL THERAPIES FOR HPA AXIS DYSFUNCTION

Although Selye's work was accepted as logical and well supported, and was validated by numerous subsequent researchers, conventional medicine does not recognize generalized HPA dysfunction as a discrete entity, much less propose methods for prevention and treatment. Patients presenting with weakness, fatigue, insomnia, anxiety, susceptibility to colds, stress symptoms and stress intolerance are typically prescribed antidepressants and anxiolytics. If hypertension and heart palpitations are most prominent, beta-blockers or other cardiovascular medications may be prescribed. If low adrenal function has affected progesterone or reproductive function, hormone replacement is typically offered. If dysglycemia and episodic blood sugar difficulties are the presenting symptoms, the case is often misunderstood. Vital signs and routine blood work, including blood glucose, may often be normal, and the individual is typically told all is fine, or perhaps offered psychiatric medications.

BOTANICAL APPROACHES TO STRESS AND HPA AXIS DYSREGULATION

Adaptogens reduce the cost of homeostasis/allostasis to the organism, preventing or delaying damaging effects caused by stress and aging. By helping to maintain a state of balance throughout the body, adaptogens hold the key to vitality.

—Donald Yance

Those using this book may notice the regular inclusion of adaptogens and nervine herbs in the treatment of conditions, which on the surface may appear unrelated to the nervous system or HPA axis. By now it is probably evident that the nervous, endocrine, reproductive, and immune systems are immutably interconnected—effects in one have a tremendous impact on the regulation of the others. Herbalists recognize the significant effects of stress on physiologic functioning as well as the role of illness increasing stress response. Therefore, many botanical protocols for chronic health problems include herbs that support the ability of the organism to respond to and withstand stress—or allostatic overload.

The primary class of herbs used to support and restore adrenal health and optimal HPA axis functioning is known as the adaptogens. Many are considered ''tonics'' in traditional medicine systems (e.g., ginseng in TCM, ashwagandha in Ayurveda). Lazarev, a Russian pharmacologist, researching the resistance of organisms to stress in experimental studies and initially testing pharmacologic drugs, first coined the term ''adaptogen'' in 1947. To be considered an adaptogen, the substance had to demonstrate the following:[53]

- Nonspecific effects in that the adaptogen increases resistance to a very broad spectrum of harmful factors (stressors) of different physical, chemical, and biological natures
- A normalizing effect, that is, it counteracts or prevents disturbances brought about by stressors
- It must be innocuous to have a broad range of therapeutic effects without causing any disturbance (other than very marginally) to the normal functioning of the organism

Lazarev, Brekhman, and other Russian researchers were using the terms *stress* and *stressors* in the classical sense as defined by the work of Selye, and were seeking to develop medications able to mobilize the intrinsic adaptive mechanisms to help individuals cope with and survive in situations of intense or prolonged stress while maintaining physical and mental work capacities. Adaptogens were considered to constitute a new class of metabolic regulators, of natural origin, which increased the organism's adaptive abilities to environmental factors, and prevented damage from these factors. Most studies of adaptogens were originally conducted in Russia and focused on *Eleutherococcus senticosus, Rhodiola rosea, Schisandra chinensis*, and *Bryonia alba*. These herbs were incorporated into official medical practice in the USSR and produced as standardized extracts in various forms. Having been found quite safe, they are still used in Russia in both self-care and physician-prescribed regimens.[48] By 1984, there were over 1500 studies in Russia alone on just three adaptogenic herbs (*Eleutherococcus, Rhodiola*, and *Schisandra*). Interest in adaptogens has also spread worldwide; the term *adaptogen,* for example, is recognized by the FDA as a functional term.[53]

A substance that reduces the state and severity of stress and counteracts the effect of stressor is an adaptogen.[56] Adaptogens contain phenolic compounds with a structural resemblance to catecholamines, suggesting an effect on the SAS, tetracyclic triterpenes similar to the corticosteroids that inactivate the stress system; and oxylipins, unsaturated trihydroxy or epoxy fatty acids resembling leukotrienes and lipoxines.[48] Adaptogens have a wide range of effects, and appear to act broadly on tissue involved in homeostatic regulatory systems (immune, endocrine, central nervous system [CNS]) rather than having specific targets. There is significant evidence that adaptogens increase exercise capacity, endurance, stamina, cognitive function, and mental alertness, and that they increase nonspecific immunity, stress resistance, relieve fatigue, and improve energy metabolism and tissue repair. Evidence also indicates that administration of adaptogens modulates ACTH and corticosteroid formation and normalizes levels of stress hormones.[53] They may be considered substances that allow the organism to resist stress at higher levels of challenge.

Adaptogens have been used historically as general tonic medicines, thought to gently strengthen the CNS in cases of fatigue, physical exertion, aging, weakness from disease and injury, and prolonged stress. They are considered to induce ''states of non-specifically increased resistance'' (SNIR). Many cultures have embraced the widespread use of such herbs in older adults and infirm; Panax in China and Asia, *Eleutherococcus* in Russia, and *Withania* in India. They have been historically and clinically reported to improve diabetes, blood pressure, and cardiac action, and relieve mental confusion, headache, and weakness among older adults. These plants are also credited with an affinity for the nervous system and an ability to relieve mental stress in cases of insomnia and anxiety disorders. Muscle fatigue, physical weakness, and immune deficiency were all thought to improve with the use of such herbs. Athletes, for example, sometimes benefit from the use of adaptogens, noting improved stamina and endurance. They also may be used to improve postsurgical healing and convalescence.[48]

It is generally recommended to give a course of adaptogens over a prolonged period of time, a minimum of 3 months generally, or on an ongoing basis for up to several years for severely depleted patients. Adaptogens may be used singly; however, it is preferable to combine them with other herbs to support, direct, and moderate their individual effects. Although adaptogens, by definition, lack serious side effects, their specific qualities may best be tempered by combination with other herbs. For example, Rhodiola or Schisandra taken alone are both quite drying and astringent, and can be tempered by combining them with herbs that are moistening and sweet, for example, licorice. Ginseng, particularly red ginseng, can be heating and stimulating. Looking at TCM formulas, one quickly notices that herbs such as ginseng are one of only several of many herbs included in the formula for

this very reason. Additionally, although adaptogens share many similar qualities, each individual herb possesses unique characteristics that distinguish it from the others; thus, prescribing should still be based on the individual patient. Adaptogens may be used prophylactically prior to times of physical, emotional, or mental stress, or restoratively, such as after a long illness or prolonged period of debility or stress.

The discussion that follows presents evidence on the most commonly used herbal adaptogens. Licorice, which may not be truly classified as an adaptogen, is included because of its marked cortisol-sparing, adrenal tonic effects. Calmative nervines that act as sympathetic relaxing agents such as *Matricaria recutita, Scutellaria lateriflora, Avena sativa,* and *Passiflora incarnata*, for example (Table 6-4), are indicated, as these may reduce stress-induced CRH stimulation of the adrenal output of cortisol and adrenaline. Parasympathomimetics directly or indirectly increase parasympathetic function, reducing sympathetic dominance. They are indicated for anxiety and stress, and to relieve symptoms that result from adrenergic stress.[57] Evidence for nervines and other herbs listed in Table 6-4 are found elsewhere throughout this text. For insomnia, sedatives may be included, as for chronic musculoskeletal problems, antispasmodics incorporated into formulae. Adaptogens also may be effectively combined with herbs for individual systems, for example, hawthorn for the cardiovascular system, or chaste berry for the reproductive system.

Ashwagandha

The roots of ashwagandha have long been used as ''rasayana'' drugs in Ayurvedic medicine to prevent or treat disease through the restoration of a healthy balance of life.[56] Ashwagandha is used in Ayurvedic medicine as a general restorative medicine, and to improve general health, longevity, and prevent disease. Ashwagandha is much less stimulating than ginseng, making it preferable for patients with irritability, anxiety, and insomnia, and as a gentle tonic herb for the nervous system.[58] The species name, somnifera, indicates the plant's traditional use for sleep induction. Ashwagandha is immunomodulatory and improves energy in patients experiencing stress-induced illness or exhaustion. It is indicated in inflammatory conditions, such as arthritis or other musculoskeletal disorders, and it is combined with other herbs in the treatment of cancer. Ashwagandha is used in Ayurveda and Unani systems of medicine for the

TABLE **6-4**

Botanical Treatments for Improving the Stress Response

HERBAL ACTION	BOTANICAL NAME	COMMON NAME
Adaptogens	*Eleutherococcus senticosus*	Eleuthero
	Panax ginseng	Ginseng
	Panax quinquefolius	American ginseng
	Rhaponticum carthimoides	Rhaponticum
	Rhodiola rosea	Rhodiola
	Schizandra chinensis	Schizandra
	Withania somnifera	Ashwagandha
Nervines	*Hypericum perforatum*	St. John's wort
	Lavandula officinalis	Lavender
	Leonurus cardiaca	Motherwort
	Matricaria recutita	Chamomile
	Passiflora incarnata	Passion flower
	Scutellaria lateriflora	Skullcap
	Valeriana officinalis	Valerian
Parasympathomimetics	*Anemone pulsatilla*	Pulsatilla
	Lobelia inflata	Lobelia
	Piper methysticum	Kava kava
Anxiolytics	*Avena sativa*	Milky oats
	Eschscholzia californica	California poppy
	Lavandula officinalis	Lavender
	Leonurus cardiaca	Motherwort
	Matricaria recutita	Chamomile
	Passiflora incarnata	Passion flower
	Piper methysticum	Kava kava
	Scutellaria lateriflora	Skullcap
	Valeriana officinalis	Valerian
	Verbena officinalis	Blue vervain
	Withania somnifera	Ashwagandha

treatment of pain, skin diseases, infection, inflammation, gastrointestinal disorders, rheumatism, and epilepsy. It is also used as a general tonic for the improvement of libido, liver health, mental state, cancer, heart disease, and the immune system.[59] In vivo studies support its use for anti-inflammatory, immunomodulatory, antioxidant, thyroid stimulating, anxiolytic, stress-reduction, memory enhancing, and antineoplastic effects (Table 6-5).[56,59–69] Ashwagandha is also reported to be hematopoietic, making it useful in the treatment of anemia.[70] Ashwagandha is combined with levodopa, tropane alkaloid–containing plants, and other herbs as a therapy for Parkinsonism.[71] Ashwagandha and other herbs may take the place of benzodiazepines and have a calming effect on the nervous system. Applications for ashwagandha based on traditional use, animal studies, and clinical evidence are listed in Box 6-4.

Overall, toxicity studies have demonstrated a high level of safety of ashwagandha and its extracts.[56,70] Safety is discussed further in Plant Profiles: Ashwagandha. The American Herbal Products Association has rated it a class 2b herb (not to be used during pregnancy); however, the evidence contraindicating its use during pregnancy is limited and questionable, and Ayurvedic practitioners have used it traditionally during pregnancy.[70,72] Because ashwagandha reverses cyclophosphamide-induced neutropenia, it may be prudent to avoid its use in patients with leukemia who are being treated with cyclophosphamide.[60]

Eleuthero

Eleuthero, a native of northeast Asia, is used in TCM for general weakness and debility, lassitude, anorexia, insomnia, and dream-disturbed sleep.[81] Its use as an adaptogen

TABLE 6-5

Effects and Supposed Mechanisms of Some Actions of Ashwagandha

EFFECTS	SUPPOSED MECHANISM OF ACTION
Adaptogenic and immunomodulatory activity	Steroidal lactones 5,20(R)-dihydroxy-6,7 alpha-epoxy-1-oxo-(5 alpha)-with a-2,24-dienolide and solasodine are known to possess adaptogenic and immunomodulating activity.[56,59,60,65]
Anticonvulsant activity	May be mediated via a GABA-ergic mechanism, likely through the barbiturate site on the macromolecule ionophore complex.[59,73]
Anti-inflammatory effect	May be mediated by decreased glycosaminoglycan synthesis. Ashwagandha extract increased phagocytosis and intracellular killing of peritoneal macrophages but did not increase the number of peripheral leukocytes.[63]
Antistress/antianxiety effects	Ashwagandha has demonstrated inhibition of stress-induced increases in dopaminergic receptor population in the corpus striatum.[74] Ashwagandha may have a GABA-mimetic action.[67,73,75,76]
Anticancer effects	Withaferin A is the primary antineoplastic agent. Its mechanisms of action are still unclear.[60] It has been found to arrest cellular division at metaphase, has shown inhibition of protein and nucleic acid syntheses in P388 cells in vitro, and RNA synthesis in Sarcoma 180 cells was inhibited. Withaferin A induces a G2/M block.[59,60] An immunostimulatory effect may be partially responsible for antineoplastic activity but this is uncertain, because in animal experiments withaferin A has shown both immunostimulatory and immunosuppressive activity.[60] Some studies have focused on the ability to reduce stress-induced oxidative damage.[63] Rat models have observed condensation and fragmentation of chromatin as quantitative markers, and other observable cellular changes to assess the cytoprotective properties of Withania.[77] Such researchers propose that Withania extracts may help prevent free radical induced cleavage of DNA. Withania somnifera has been shown to increase the percentage of cells containing neurites in human neuroblastoma cells, promote the growth of new dendrites, may aid in the repair of damaged neuronal circuits.[62] Withaferin is reported to have a radiosensitizing effect that has been noted in animal studies to reduce the toxicity of irradiation therapy, while improving the effects.[60] Antitumor effects of Withania have also been investigated.[78,79]
Memory-enhancing effects	Withania appears to mediate stress-induced disruption of memory formation and retention. Neuroelectric, physical stress, and scopolamine induced disruption of acquisition and retention of memory consolidation all appear to be significantly reduced with the administration of Withania extracts.[64] Animal experiments have noted Withania to provide protection to neuronal cell bodies when animals are subjected to stressful conditions.[80] Effects may also be due to increased cholinergic signal transduction cascade in the brain.
Sedative effects	May be due to the alkaloid somniferum
Cardiovascular effects	The steroidal lactones have a mild ionotropic and chronotropic effect on the heart.

originated in the former Soviet Union, in the latter half of the twentieth century, when it was researched and promoted by scientists as a substitute for Panax ginseng, which was more expensive and less accessible. Pharmacologic studies have suggested that its effects are at least equal to, and perhaps superior to those of Panax ginseng.[81]

Until recently referred to as Siberian ginseng, the herb is now properly referred to as Eleuthero, because of recognition that although the plants are from the same family, their actions arise from very different chemical constituents.[72] Eleuthero's actions much like ginseng, are considered immunomodulating, stress reducing, performance and energy enhancing, anabolic, and adaptogenic, hence the original misnomer.[81] The herb has demonstrated the ability to improve adrenal function, stress tolerance, enhance immune function and resistance to infection including influenza, and enhance selective memory.[18,28,53,76,82] The plant contains phenylpropionates (e.g., syringin, caffeic acid, sinapyl alcohol, coniferyl aldehyde), lignins (e.g., sesamin, syringoresinol and its glucoside), saponins (e.g., daucosterol, β-sitosterol, hederasaponin B), coumarins (e.g., isofraxidin and its glucoside), vitamins (e.g., vitamin E), and provitamins (provitamin A, i.e., beta-carotene). These molecules have demonstrated a wide range of pharmacologic activities and are associated with an extensive literature base.[83] Six secondary compounds found in Eleutherococcus have been shown to have various levels of activity, as shown in Table 6-6. Previously, many of these compounds were referred to as *eleutherosides;* however, as these compounds are not unique to this plant, and had been previously identified from other sources, the term eleutherosides is not properly applied to these constituents.[81,83]

Animal experiments have confirmed not only these actions but also the reduction of NK activity and the inhibition of corticosterone elevation induced by swimming stress in animal models.[84] Stress-induced gastric ulcers have been prevented in animal models, and positive results have been shown with reduction of serum lipid-peroxide levels and improved lipid metabolism.[81,85] In healthy volunteers, ingestion of fluid extracts led to markedly increased T-lymphocyte counts and studies have demonstrated overall improvements in cellular defense.[35,85] Studies on athletic performance and stress response have shown that Eleuthero improves the testosterone:cortisol ratio by over 28%, a marker of reduced stress response in athletes.[86] Clinical findings also have suggested that patients with moderate fatigue in chronic

BOX 6-4

Applications for Ashwagandha

Anxiety
Arthritis
Cancer (animal and in vitro data)
Cardiovascular effects (animal data)
Cyclophosphamide toxicity (animal data)
Debility
Epilepsy (animal data)
Growth and development
Immune system (animal data)
Infection (animal and in vitro data)
Inflammation (animal data)
Insomnia
Liver disease (animal data)
Memory (animal data)
Morphine withdrawal (animal data)
Muscle spasm (animal data)
Oxidation (animal data)
Pain (animal data)
Sedation (animal data)
Stamina (animal data)
Stress (animal data)
Thyroid stimulant (animal data)

TABLE 6-6

Eleutherococcus Constituents and Effects

EFFECTS	CONSTITUENT(S)
Antioxidant	Syringin, caffeic acid, caffeic acid ethyl aldehyde, coniferyl aldehyde
Anticancer	Sesamin, sitosterol, isofraxidin
Hypocholesterolemic	Sesamin, sitosterol, beta-sitosterol and beta-sitosterol 3-D-glucoside
Immunostimulatory	Sesamin, syringin
Choleretic	Isofraxidin
Reduce moderate insulin levels	Beta-sitosterol and its glucoside
Radioprotectant	Syringin
Anti-inflammatory and antipyretic activities	Beta-sitosterol
Antibacterial agent	Caffeic acid

Data from Wichtl M: Herbal Drugs and Phytopharmaceuticals: A Handbook for Practice on a Scientific Basis, ed 4, Stuttgart, 2004, Medpharm; Davydov M, Krikorian AD: Eleutherococcus senticosus (Rupr. & Maxim.) Maxim. (Araliaceae) as an adaptogen: a closer look, J Ethnopharmacol 72(3):345-393, 2000; Brekhman II, Dardymov IV: New substances of plant origin which increase nonspecific resistance, Annu Rev Pharmacol 9:419-430, 1969.

fatigue syndrome may benefit from use of Eleuthero, and that older adults may safely experience improvement in some aspects of mental health and social functioning after 4 weeks of therapy, although these differences attenuate with continued use.[87] Eleuthero also has been shown to cause reductions in cardiovascular stress response in healthy patients. Eleuthero is considered to have a high safety profile. Russian studies have noted a general absence of side effects and adverse reactions, and there are no expected significant herb–drug interactions; however, its use is not recommended for patients with hypertension or during acute phase of infection, although it may be combined with antibiotics for treatment of dysentery.[18,28,35,88] The German Commission E considers it an invigorating tonic to be used in cases of fatigue, decreased work capacity and concentration, and for convalescence.[35,81] It is not heating or stimulating to the degree of ginseng or Schisandra. In fact, herbalists consider it a generally neutral herb that can be used by anyone.[89,90]

Ginseng (*Panax ginseng; Panax quinquefolius*)

Ginseng species include *Panax ginseng* and *Panax quinquefolius,* Asian and American ginseng, respectively (Fig.6-5).

Figure 6-5 Ginseng (*Panax ginseng*). (Photo by Martin Wall.)

Panax notoginseng and *Panax pseudoginseng* are also ginsengs but are not discussed here. *Eleutherococcus senticosus*, formerly referred to as Siberian ginseng, is not, in fact, a ginseng. White and red ginsengs are both forms of *Panax ginseng*, white being unprocessed, and the red having been steam prepared.[91] In TCM, white and red ginseng are considered to have different actions, the former being much less stimulating, and the latter being used for deep deficiencies and to move the qi. Western herbalists consider American ginseng to be less heating and gentler than either Asian ginseng, especially compared with red ginseng. The word *Panax* is derived from the word *panacea* in deference to wide-ranging uses from immune support to energy enhancement to promotion of longevity. Ginsenosides are considered to be the pharmacologically active components of ginseng; however, as stated in Wichtl, ''the theory for its use in traditional medicine cannot be explained based on the criteria of western rational medicine.''[81,91]

Chinese medicine has included ginseng in its pharmacopoeias for as much has 5000 years. It is not considered a medication so much for specific conditions; rather, it is a tonic for improving overall energy and sense of well-being. It is, however, included in formulae for specific conditions, especially those associated with debility, fatigue, immunodeficiency, irritability and insomnia, decreased cognitive and memory functions, impotence or loss of libido, calming the nerves, and promoting the production of moisture in the body, and other conditions. The German Commission E approved its use as a tonic to combat feelings of lassitude and debility, lack of energy and ability to concentrate, and during convalescence.[35] Ginseng is one of the most extensively researched botanical medicines in the world.[91] This review of ginseng is by no means comprehensive, and primarily is intended to convey its overall effects in the context of this section. The actions most ascribed to ginseng are tonic and adaptogenic, demonstrating the ability to enhance nonspecific immunity, inhibit fatigue, and have antiaging effects (Box 6-5).* Randomized, double-blind, controlled trials have shown that (Korean) ginseng significantly improves quality of life and well-being measures while under stress, including alertness, relaxation, appetite, fatigue levels, sleep quality, recovery from the common cold and bronchitis, and significantly decreases systolic blood pressure compared with controls.[19]

Ginseng's adaptogenic effects are notable in the HPA axis. Ginseng improves recovery from chronic stress by improving corticoid response from the adrenal gland, and the corticotropin feedback loops with the HPA.[76,82] Animal studies have noted ginseng administration to enhance energy metabolism during exercise.[92] Panax ginseng has been noted to elevate testosterone when low, but not elevate it excessively when within the normal range. *Panax* ginseng has been investigated for immune modulating and anticancer activities.[93] Animal and human investigations have shown ginseng to possibly reduce the occurrence of cancer. Mice exposed to

*References 19, 76, 81, 82, 88, 91–110

BOX **6-5**

Summary of Ginseng's Beneficial Effects

- Improvement in physical stamina, exercise performance and well-being
- Improvement in mental performance, learning, memory
- Reduction in fatigue
- Improved stress response and functioning under stress
- Glucose regulation/blood sugar reduction in NIDDM
- Improve cardiac function in congestive heart failure
- Improved HDL levels
- Improvement for diminished libido, male fertility problems, erectile dysfunction
- Antioxidant activity
- Cancer prevention
- Improved recovery in infection, especially chronic bronchitis, and for the treatment of asthma, COPD, and dyspnea
- Psychological and physical complaints associated with menopause
- Improvement in metabolism; anabolic effects
- A tonic for older adults and during convalescence
- Reduction in preeclampsia in pregnant women compared to matched controls
- Neuralgia, convulsions, neurosis, anxiety, insomnia
- Improvement of bifida strains and inhibition of clostridia strains in human intestinal flora

carcinogens have fared better when treated with ginseng than untreated controls.[94] In one human trial, Panax was shown to be an effective therapy in the treatment of acute infectious bronchitis.[95] Ginseng may improve immune function, as evidenced by increased blood levels of basic immune cells including natural killer cells, lymphocytes, and macrophages, seen after the administration of ginseng preparations.[96–98]

Enhancing gonadotropin activity may be added to the list of the many uses for Panax. Gonadotropin levels have been shown to increase in men with low sperm counts taking ginseng extracts but not in men with normal sperm counts.[99] After 3 months of daily ginseng consumption, testosterone, dihydrotestosterone, and related sperm counts and sperm motility were noted to improve in the infertile men, whereas normal controls displayed only slight increases, with none of the controls developing abnormally high or excessive levels of hormones. Human clinical studies also observed an increase in libido and erectile function. The Chinese species, *Panax* ginseng, is also reported to be a sexual tonic and aphrodisiac useful in maintaining the reproductive organs and sexual desire into old age. Low sperm counts are a symptom of hypogonadism and/or hormonal imbalance. There are case reports of acute life-threatening hypopituitarism (postpartum Sheehan's syndrome) being successfully treated with *Panax* and *Glycyrrhiza*.[100]

Ginseng may improve the stress response by reducing the excessive sympathetic response that promotes a fight or flight cascade. Adrenal cortisol production and activity may be improved, along with corticotropin feedback loops with the use of adrenal tonic herbs such as Panax ginseng.[76] Blood sugar reductions have been demonstrated, with potential benefit for patients with type 2 diabetes mellitus.[101,102] Several human trials have shown clinically useful antianxiety effects with the use of ginseng preparations, without any adverse side effects reported.[103] Side effects, and drug interactions are not expected with proper use.[35] However, reported side effects in noncontrolled studies in which subjects have been using high doses of caffeine and taking products with additional ingredients, have included sleeplessness, anxiety, diarrhea, and skin problems.

Concerns about ginseng abuse syndrome (GAS) occurring with regular use have been entirely debunked, the progenitor of the concept himself retracting his conclusions.[91] Pregnancy use is contraindicated in the British Herbal Compendium to the British Herbal Pharmacopeia; however, ginseng is traditionally used during pregnancy in China, and studies have shown no teratogenicity, mutagenicity, or other adverse effects, and in fact one study demonstrated a reduction in pre-eclampsia compared with a control group.[91] Neither the American Herbal Products Association nor the German Commission E suggest restricted use during pregnancy; however, given that long-term safety studies are lacking, it is best to avoid except in TCM formulae specifically for pregnancy-related problems and under the supervision of a qualified TCM provider or herbalist skilled in obstetric herbal medicine.[28] Diabetic patients may need to adjust insulin doses; patients taking anticoagulant drugs are recommended to speak with their health care providers before taking ginseng.[28] Herbalists generally discourage the use of stimulants with ginseng, and also may contraindicate ginseng use in patients with hypertension, hyperthyroidism, or other ''excess'' states.

Licorice

Although licorice is sometimes categorized as an adaptogen, it does not strictly meet the criteria of one: Its actions are specific rather than nonspecific, and its use in certain patients in high doses or over a prolonged period is not always benign, and in fact can pose serious consequences. However, because of licorice's action on the adrenal glands, as well as on several conditions associated with HPA dysfunction, it raises questions about the potential role of licorice in the prevention and treatment of HPA dysfunction, and merits mention in this section. Peptic ulcer was one of the first conditions ever to be associated with an overactive stress response. Interestingly, licorice extract has demonstrated efficacy against *Helicobacter pylori,* including against clarithromycin-resistant strains.[91,111]

Licorice studies have demonstrated its positive effects in treating viral infection, particularly those caused by herpes simplex virus, an active infection associated with increased stress. A recent study demonstrated that licorice root extract might even interfere with the latency of the herpes virus.[112] Licorice components also have demonstrated the ability to modulate bone disorders in

menopausal women because of affinity to estradiol-17 beta. This potential exists with or without the presence of vitamin D.[91,113] (Licorice has also demonstrated estrogen-inhibitory effects.)[91] Licorice hydrophobic flavonoids have evidenced abdominal fat-lowering and hypoglycemic effects, possibly mediated via activation of peroxisome proliferator-activated receptor-gamma (PPAR-gamma).[114]

Researchers examined the effects of licorice on memory and learning in a mouse model and found promise as a memory enhancer in both exteroceptive and interoceptive behavioral models of memory. The anti-inflammatory and antioxidant properties of licorice may be contributing favorably to the memory enhancement effect. Because scopolamine-induced amnesia was reversed by licorice, it is possible that the beneficial effect on learning and memory may result from facilitation of cholinergic transmission in the brain.[73] In the treatment of postpartum anterior pituitary insufficiency, 10 patients demonstrated complete recovery with a decoction of licorice and ginseng.[91]

Licorice inhibits corticoid dehydrogenases, prolonging the half-life of cortisol in the body. The British Herbal Compendium cites licorice as having adrenocorticotropic activity, indicating it for adrenocorticoid insufficiency.[58] Thus, it is sometimes described by herbalists as an adrenal tonic, and cortisol sparing.[18,58,115]

Licorice is contraindicated by the German Commission E in patients with cholestatic liver disorders, liver cirrhosis, hypertension, hypokalemia, severe kidney insufficiency, and pregnancy.[35] It is also contraindicated in congestive heart failure and edema.[19] Licorice safety issues are discussed further in Plant Profiles and discussions of pregnancy and herb safety.

Rhaponticum

R. carthamoides has been used for centuries in Siberia as a folk medicine for the treatment of fatigue, anemia, and impotence, as well as for convalescence after illness.[116] In 1961 the liquid extract (1:1) was officially recognized and included in the Soviet Pharmacopoeia as a natural agent for overcoming fatigue, improving physical and mental productivity and stamina, and shortening recovery time after illness.[117] The roots and rhizomes are considered the plant's medicinal parts; the active ingredients are primarily phytoecdysterones (especially ecdysterone), although the plant also contains a number of other biologically active compounds, including flavonoids, sesquiterpene lactones, and polyines.[118,119] *R. carthamoides* extract standardized to 5% ecdysterone is considered the most potent form.[117,120] Several decades of research have demonstrated numerous pharmacologic effects in animal models and human studies.[117,121,122] It is a classic adaptogen with a wide range of activities, including normalizing effect on the central nervous and cardiovascular systems, sleep, appetite, moods (neurotic, asthenic, depressive, hypochondriac), mental and physical state, and the ability to function well under stress. It has marked anabolic activities, building lean muscle, reducing body fat, and improving work and athletic capacity and performance, improving mental acuteness, alleviating depression; is a tonic for the vital organ systems, and is erythropoietic and antioxidant, delaying the effects of aging.[117] Rhaponticum improves stress response and adaptability to physical and mental challenges, enhances mental and physical capacity for work under stressful conditions, inhibits disorders of energetic metabolism, maintains stable glycogen levels in the skeletal muscles, increases the blood supply to the muscles and brain, and shortens the recovery period after prolonged muscular workloads.[117,123] Rhaponticum favorably affects heart rate, improving arterial pressure, and hastening recovery after work load.[124,125] In trained athletes, Rhaponticum improves endurance, speed, recovery, and physiologic markers, and allows anabolic processes to outpace catabolic processes, leading to greater fitness, endurance, and performance.[117,124,126–129] Rhaponticum has also shown some preliminary beneficial outcomes in childbearing women, shortening the duration of labor and improving postpartum recovery.[117] A comprehensive list of rhaponticum's effects appears in Box 6-6.[116,117,122,129–138]

Rhodiola

Rhodiola rosea, also called golden root, Arctic root, and rose root, grows in arctic and mountain regions throughout Europe, Asia, and America.[139–141] Its use was first recorded by the Greek physician Dioscorides in 77 CE in *De Materia Medica*.[141] It has been used for centuries as a

BOX 6-6

Therapeutic Actions of *R. carthamoides*

- Increases protein synthesis, reduces adipose tissue, builds muscle mass
- Increases stamina, endurance and athletic performance, and work productivity
- Improves mental health, learning, and memory
- Improves additivity to cold climates
- Enhances immune activity
- Improves insulin sensitivity, stabilizes blood sugar, antidiabetic
- Reduces body fat/Increases lean muscle
- Lowers cholesterol, reduces atherosclerosis; cardiovascular restorative
- Antiarrhythmia
- Hepatoprotective/Regenerative
- Protects against the effects of steroids
- Enhances mitochondrial activity
- Antioxidant
- Stabilizes cell membranes
- Anticancer
- Antiepileptic
- Stimulates erythropoiesis, increasing erythrocytes and hemoglobin
- Renal protective
- Sexual enhancement
- Antidepressant; reduces alcohol cravings
- Anti-giardia; antifungal

traditional medicine in Russia, Scandinavia, and other countries for the treatment of fatigue, depression, anemia, impotence, GI ailments, infections, and nervous system disorders, and to promote physical endurance, longevity, and work productivity.[141,142] Rhodiola appeared in the scientific literature of Sweden, Norway, France, Germany, the Soviet Union, and Iceland as early as 1725.[141] Because most of the identified literature on this herb is from foreign language sources, I have relied largely upon secondary sources for this review.[140–142] *R. rosea* has been an accepted medicine in Russia since 1969 for the treatment of fatigue, somatic and infectious illness, psychiatric and neurologic conditions, and as a psychostimulant to increase memory, attention span, and productivity in healthy individuals. It is also officially registered in Sweden and Denmark and is widely used in Scandinavia as a general tonic and to increase mental work ability under stress.[141] Rhodiola is classified as an adaptogen.[139–142] It contains a range of antioxidant compounds, and its adaptogenic activities are attributed to its unique phenylpropanoids rosavin, rosarin, and rosidirin, and to phenylethanol derivatives p-tyrosyl and salidroside (also called rhodioloside), as well as to flavonoids, triterpenes, monoterpenes, and phenolic acids. Rosavins are the accepted marker compounds for water and alcohol extracts.[140,141] Research both from animal models and human clinical trials indicates a number of favorable effects associated with its use, including CNS stimulation, pronounced antistress effects, enhanced physical work and exercise performance, increased muscle strength, reduction in mental fatigue, and prevention of high altitude sickness.[139,142–145] Cardioprotective and anticancer effects also have been attributed to its intake.[139,142] Although research on Rhodiola has been extensive, it has also been described as ''fragmentary,'' with methods, statistics, and controls poorly defined.[139,145] Further, not all studies have yielded positive outcomes for efficacy, although this may be related to product, dose, and duration of administration. *Rhodiola rosea* extract exhibited an anti-inflammatory effect and protected muscle tissue during exercise.[146] Studies have demonstrated its ability to induce a general sense of well-being and reduce situational anxiety.[141,142] It has demonstrated improvement in depressive syndromes, mental and physical fatigues secondary to medical conditions, sexual dysfunction, thyroid hypofunction (without causing hyperthyroidism), thymus gland functioning, adrenal functioning, and menopause-related conditions.[141,142] Its mechanism of action is partly attributed to the herb's ability to influence levels of monoamines, including serotonin, dopamine, and norepinephrine in the cerebral cortex, brainstem, and hypothalamus through inhibition of degradation enzymes and facilitation of neurotransmitter support in the brain. It also appears to prevent catecholamine release and camp elevation in the myocardium, to prevent depletion of adrenal catecholamines by acute stress, and to induce opioid peptide biosynthesis and activation of central and peripheral opioid receptors.[140,147,148] Enhanced antitumor and antimetastatic activity has been demonstrated when *R. rosea* extract is combined with cyclophosphamide (an antitumor agent).[140,149]

Schisandra

This herb (spelled *schisandra* or *schizandra*) has an ancient history of use in China, where it is called wu wei zi, or five flavored fruit, because of it is said to possess the five flavors of classical Chinese medicine: sour, bitter, sweet, salty, and pungent. Because of this, it is held in high regard in the Chinese materia medica and is still widely used in TCM today.[91,150] In the first century classic herbal compendium, the *Divine Husbandman's Classic of the Materia Medica* (Shen Nong Ben Cao Jing), schisandra is classified among the superior medicines, purported to ''prolong the years of life without aging,'' increase energy (qi), treat fatigue, emaciation and langor, act as a male sexual tonic, and treat asthma.[91,150,151] It was also considered antihepatotoxic, antidiabetic, antitussive, and is a sedative, tonic, and treatment for cholera. In combination with other herbs, its applications become much broader.[91,151] The fruit is considered highly astringent, and is therefore used for a variety of secretory excesses, including night sweats, chronic diarrhea, and in males, spermatorrhea.[150] Official indications for the fruit include diabetes, frequent urination, night sweats, chronic cough, and dyspnea.[19,91] Schisandra was introduced from Eastern Russia into Europe in the 1850s.[91] Since the 1950s, research in the former Soviet Union has focused on its potential uses as an adaptogen, primarily to enhance concentration and increase endurance, and its use is integrated into conventional medical and pharmacy practice in Russia.[53,150] The primary active ingredients are lignans.[91,150,152] It is official in the pharmacopoeias of China, Japan, Korea, and Russia. Current research has focused on its effects in treating diabetes and liver damage related to hepatic disease, for example, hepatitis.[91,150] Hepatoprotective, antioxidant, antiproliferative and chemopreventive, anti-inflammatory, cardioprotective, and antimicrobial effects have all been demonstrated in in vivo and in vitro studies.[91,150,153] Hepatoprotective and performance/endurance enhancing effects have been demonstrated in human clinical studies.[91,154] Research into Schisandra's use as an adaptogen was inspired by its TCM use as a tonic for debility. Numerous clinical trials conducted in the 1950s showed improvement in activities requiring concentration, coordination, and endurance, a reduction in fatigue, and an increase in accuracy and work quality.[150] Uncontrolled trials suggest general improvements in mental efficiency in humans, with associated improvement in vision and hearing and skin receptor sensitivity.[155] Animal models have demonstrated adaptogenic effects, including increased renal and gonadal RNA, glycogen and enzyme levels in older models (rabbits) compared with younger animals.[19] In a double-blind, placebo-controlled RCT involving race and show-jump horses, treatment with schisandra reduced heart rate, respiratory frequency, and lactate levels, and increased plasma glucose and performance.[19,150] Treated horses also completed the race faster than controls.[150] Similar results demonstrating enhanced performance and recovery after exercise have

been found in other studies involving racehorses.[150] In an in vivo study with phenobarbital, ethanol, and ether intraperitoneal administration of schisandra reduced sleeping time, suggesting antidepressant activity.[19,150] Several other studies have also suggested antidepressant activity, both in animal and human clinical models. One rat study showed a significant increase in dopamine and its metabolites in the rat brain. Stimulating effects on the CNS have been reported, including restlessness, increased aggressiveness, and insomnia at higher doses.[150] Increased resistance to heat and frostbite have both been demonstrated, suggesting the ability of the herb to increase response to environmental stressors.[150] Schisandra is considered to have a high safety profile, and appears to be entirely free of toxicity when used in the recommended dosage range.[150] No clinical reports of overdosage in humans have been identified.[91] According to TCM, schisandra should not be used in cases of excess heat, or in the early stages of a rash or cough.[151] Patients with high gastric acidity or peptic ulcers may experience exacerbation.[150] It is also considered contraindicated in patients with epilepsy, hypertension, and intracranial pressure.[156] Side effects may include restlessness, insomnia, and dyspnea.[91,151] Schisandra may increase uterine contractility, and is used in TCM to induce or promote prolonged labor; therefore, its use is not recommended during pregnancy.[91,150,151]

ADDITIONAL THERAPIES

Dehydroepiandrosterone

Dehydroepiandrosterone (DHEA) and its active metabolite, DHEA sulfate (DHEAS), are endogenous hormones synthesized and excreted primarily by the adrenal cortex in response to ACTH. In women, the synthesis of DHEA and DHEAS occurs almost exclusively in the adrenal cortex. DHEA is classified as an androgen, and may be converted into other hormones, including estrogen and testosterone. DHEA and DHEAS serve as the precursors of approximately 75% of active estrogens in premenopausal women, and 100% of active estrogens after menopause. The levels of DHEA in the blood are typically 10 times those of cortisol.

DHEA is active in the CNS, and is taken up by the amygdala, hippocampus, thalamus, midbrain, and frontal cortex.[157] DHEA and DHEAS also appear to have neurotrophic effects, increasing the number of neurofilament-positive neurons and regulating the motility and growth of corticothalamic projections in cultured mouse embryo brain cells.[158] DHEA and DHEAS output is maximal between the ages of 20 and 30 years and then declines with age at a rate of approximately 2% per year, leaving a residual of 10% to 20% of the peak production by the eighth or ninth decade of life. The exact mechanism of action and clinical role of DHEA and DHEAS remain unclear. Epidemiologic data indicate an inverse relationship between serum DHEA and DHEAS levels and the frequency of cancer, cardiovascular disease (in men only), Alzheimer's disease and other age-related disorders, immune function, and progression of HIV infection.[158]

Beneficial effects of DHEA, based on animal studies, include improved immune function and memory and prevention of atherosclerosis, cancer, diabetes, and obesity. Clinically validated uses of DHEA include replacement therapy in patients with low serum DHEA levels secondary to chronic disease, adrenal exhaustion, or corticosteroid therapy; treating systemic lupus erythematosus (SLE), improving bone density in postmenopausal women; improving symptoms of severe depression; improving depressed mood and fatigue in patients with HIV infection; and increasing the rate of reepithelialization in patients undergoing autologous skin grafting for burns; however, such uses remain controversial.[158] Supporting clinical studies also suggest possible benefit in enhancing immune response and sense of well-being in older adults, and a reduction in some cardiovascular risk factors. Other uses for DHEA, for example, for retarding the aging process, improving cognition, promoting weight loss, increasing lean muscle mass, and slowing the progression of Parkinson's disease and Alzheimer's disease are clinically unsubstantiated.[158]

DHEA supplementation has been found to elevate serum testosterone, estrone, and estriol levels in postmenopausal women. DHEA may lead to an increase in progesterone production indirectly, because both DHEA and progesterone require pregnenolone as a precursor. If the body does not have to manufacture DHEA, more pregnenolone may be shunted to progesterone synthesis. Physiologic replacement dosages of oral DHEA in healthy women over 40 range from 5 to 30 mg/day, and are usually given once in the morning. This is generally adequate to raise serum DHEAS to the levels found in adults 20 to 30 years of age and impart the documented benefits of heightened sense of well-being and increased bone mineral density in postmenopausal women.[158] Higher doses may be necessary for increasing suppressed DHEA and DHEAS levels secondary to chronic disease, adrenal exhaustion, and corticosteroid therapy.[158] Pharmacologic dosages of 200 mg/day have been successfully used in patients with SLE. Dosages of 200 to 500 mg/day have been used in HIV-positive patients with depressed mood and fatigue.[158] With physiologic and supraphysiologic doses, the most common side effects include acne and mild hirsutism.[158,159] Rakel suggests that dosing not exceed 50 mg/day of an oral dose regimen in non–adrenal deficient patients.[23] As OTC sources of DHEA are not standardized, inconsistent dosing with insufficient daily dosing may be a problem.[23]

The long-term effects of significantly raised androgen levels in women using DHEA are unknown. A case control study of postmenopausal women not taking DHEA or hormone replacement therapy whose levels of endogenous DHEAS were in the highest quartile had a significantly higher risk of breast cancer than women whose levels of endogenous DHEAS were in the lowest quartile. The effects of long-term physiologic or supraphysiologic doses of DHEA on suppression of adrenal cortex are unknown; however, there does not appear to be feedback inhibition of DHEA or DHEAS secretion by the HPA axis.[158] Baseline DHEAS should be checked prior to

TABLE **6-7**

Condition/Botanical Medicine Summary Table

BOTANICAL	CONDITION/ACTION																			
	Adaptogen/tonic	Antidepressant	Antiinflam/neuralgia	Antioxidant	Anxiety/stress	Cardioprotective/hypocholesteroemic	Chemoprotective	Fatigue/exhaustion	Heart palpitations	Hematopoeitic/erythropoeitic	Hepatoprotective	HPA Dysregulation	Hyperthyroidism	Hypothyroidism	Immunomodulation	Insomnia/sleep disturbance	Libido/fertility	Memory/cognition	Metabolism/glucose reg	Nervine	Stamina/energy
Avena sativa					X			X								X	X			X	X
Bauhinia purpurea														X							
Coleus forskohlii														X							
Commiphora mukul														X							
Eleutherococcus senticosus	X	X	X	X	X	X	X	X				X			X			X	X		X
Eschscholzia californica					X															X	
Fucus vesiculosus														X							
Hypericum perforatum		X			X															X	
Lavandula officinalis		X			X															X	
Leonurus cardiaca					X				X				X							X	
Lithospermum off.													X								
Lobelia inflata																				X	
Lycopus spp.													X								
Matricaria recutita					X															X	
Melissa officinalis		X			X								X							X	
Panax ginseng	X	X		X	X		X	X	X		X	X		X	X	X	X	X	X		X
Panax quinquefolius	X	X			X		X	X				X							X		X
Passiflora incarnata					X															X	
Piper methysticum		X			X															X	
Rhaponticum carthimoides	X	X		X	X	X	X	X		X		X					X	X	X		X
Rhodiola rosea	X	X		X	X	X	X	X	X	X		X		X	X		X	X	X		X
Schizandra chinensis	X		X	X		X	X	X			X	X			X			X	X		X
Scutellaria lateriflora		X			X															X	
Valeriana officinalis					X															X	
Verbena officinalis					X															X	
Withania somnifera	X	X	X		X	X	X	X		X		X		X	X		X	X			X

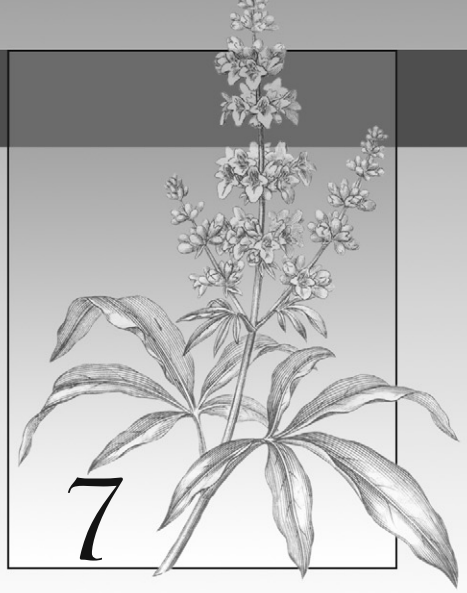
initiating therapy and the serum DHEAS level should be checked at least annually to ensure that it is in the normal range.[158] DHEA can affect (raising some, lowering others) serum levels of: calcium channel blockers, metformin, corticosteroids, insulin, and triazolam. Diet and exercise also can affect DHEA and DHEAS levels. DHEA supplementation is contraindicated in patients with a history (personal or family) of sex hormone–responsive cancers. DHEA supplementation should be avoided during pregnancy and lactation.[158]

Lifestyle and Reducing the Effects of Stress

Stress is an unavoidable fact of life. Its effects, however, can be mitigated. The effects of lifestyle on preventing and reducing stress, and consequently stress-related illness, cannot be overstated. The following are simple suggestions for managing stress:[43]

- Avoid emotional eating (overeating and undereating). Teach patients to eat healthy foods, in appropriate amounts for their body and lifestyle, when hungry. This will not only keep the body healthy, but will

also lead to weight stabilization. For many women, being overweight is both a result of stress and a cause of stress, leading to a vicious cycle.
- Encourage dietary changes that enrich nutrition and reduce empty calories.
- Take a complex multivitamin and mineral supplement to ensure adequate intake of trace nutrients.
- Drink enough fluids throughout the day.
- Get enough sleep and correct sleep. Sleeping adequate amounts is critical to keeping the neuroendocrine system healthy, reducing stress, and caring well for the body. However, sleeping at optimal hours for the body's hormonal and neurotransmitter systems is also important to health. Cortisol and melatonin, for example, both intrinsic to maintaining proper stress response, have secretory rhythms that are optimized by following diurnal sleep patterns, ideally by going to sleep by 11 PM and rising early in the morning. Although patients with jobs that require night work or women with young children might not be able to achieve this rhythm, lack of this rhythm may be a clue to HPA access disruption and related illnesses such patients are experiencing.
- Get moderate exercise.
- Engage in relaxation techniques, for example, yoga, tai chi, meditation, art ''therapy,'' journaling, and so forth.
- Avoid or minimize caffeine intake.
- Address work life, relationship, or environmental stressors through making changes, getting counseling, or other means that reduce exposure to life stressors and environmental hazards. Provide patient referral to marriage and family counselors, environmental groups, and so forth. as appropriate.
- Social support is one of the most important factors in stress response and life expectancy. Individuals living in isolation respond more poorly to stress and illness, recover more slowly, and have a lower life expectancy than individuals with an established social network and social support.



Conditions of the Reproductive Organs

Aviva Romm, Isla Burgess, David Winston, Suzanna M. Zick, Amanda McQuade Crawford

7 CHAPTER

UTERINE FIBROIDS

Aviva Romm, Isla Burgess

Uterine fibroids (properly called leiomyomata or myomas) are solid, well-defined benign monoclonal tumors of the smooth muscle cells of the uterus (Fig. 7-1).[1,2] They range in size from microscopic to many pounds in weight, and may be singular or clustered. Multiple myomas in the same uterus are not clonally related.[3] Fibroid size is described in comparison to a pregnant uterus (i.e., a fibroid the size of a 16-week pregnancy). As many as 20% to 40% of all women develop fibroids by age 40.[1] Approximately 17% of all hysterectomies performed in the United States are for uterine myomas, with a peak incidence of surgery occurring for women around age 45, making fibroids the primary annual cause of premenopausal hysterectomy in the United States.[3,4] They are rare in a premenarchal young women and shrinkage typically occurs in post-menopausal women with the natural decline in estrogen levels, unless stimulated by exogenous estrogen (foreign estrogens usually a result of environmental exposure, for example, from pesticides or plastics).[1] For unknown reasons, fibroids are two to three times more common in black women than white, Asian, and Hispanic women.[1,3] Fibroids are classified according to their site of growth in the uterine or surrounding tissue as submucosal, intramural, and subserous (see Figure 7-1). They also may occur in the cervix (cervical fibroids), between the uterine broad ligaments (interligamentous fibroids), or they may be attached to a stalk (pedunculated fibroids) and protrude into the uterine cavity (pedunculated submucosal fibroids) or through the cervix.[1,3]

The exact etiology of uterine fibroids remains undetermined.[5] Leiomyomas are hormone dependent. This is evidenced by the fact that they develop during hormonally active years and decline during menopause, fibroid tissue has an increased number of estrogen and progesterone receptors, fibroid tissue is hyperestrogenic, hypersensitive to estrogen, and does not possess the normal regulatory mechanism that limits estrogen response, the peak mitotic activity occurs during the luteal phase, and they respond to treatment with gonadotropin-releasing hormone (GnRH) agonists.[3,6–8] Growth factor also plays a role in leiomyomata development.[3,9] As estrogen and progesterone levels rise, insulin is released causing the transient hypoglycemia commonly experienced premenstrually. When plasma glucose levels fall, pituitary growth hormone is released, exerting bodywide effects. Its action on hepatocytes causes the release of insulin-like growth factors (IGFs). In a study by Vollenhoven et al., it is postulated that the net effect of these changes increases the bioavailability of free (bioactive) IGF, which may play a major role in promoting fibroid growth.[9] A further study by De Leo and Morgante states that concentrations of epidermal growth factor, insulin-like growth factor 1 (IGF 1), and platelet-derived growth factor (PDGF AB) are present in myomatous tissues together with their receptors.[6] Prolactin also may be a factor. Leiomyomata express a number of hormones, including parathyroid hormone–related protein (a growth factor), prolactin, and IGF.[3]

Factors that might increase fibroid development and growth include:

- Increased lifetime estrogen exposure due to early age at menarche, fewer pregnancies, increased follicular phase, or obesity[2,4]
- Exposure to exogenous estrogens [i.e., environmental exposure (plastics, pesticides, hormones through meat and dairy, etc.) or medical exposure (HRT, etc.)]
- Poor enterohepatic estrogen clearance
- Hypertension[2]
- Pelvic inflammatory disease[2,4]
- IUD use with infectious complications[2,4]
- Perineal talc use[2,4]

The use of oral contraceptives is not associated with any changes in fibroid size, and may even be protective; however, one study reported a slight increase in risk with a history of OC use beginning in the early teenage years.[2–4]

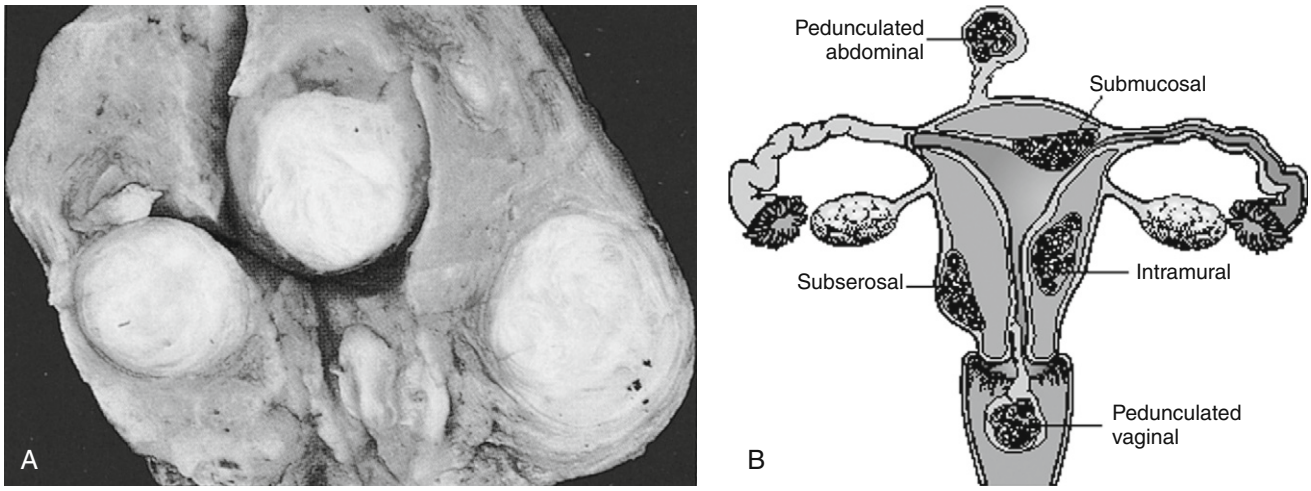


Figure 7-1 Uterine fibroids. (Salvo S: *Mosby's Pathology for Massage Therapists,* St. Louis, 2004, Mosby.)

PATHOPHYSIOLOGY

Myoma risk is inversely related to increasing parity and age at last pregnancy, and is decreased by smoking (due to its inhibition of estrogen) and increased by obesity (likely due to increased estrogen levels) and hypertension.[1–3,10] Fibroids occur in 1% to 2% of pregnancies. However, it is uncertain whether this relationship is entirely causal. Infertility, as well as early pregnancy loss, may be due to mechanical obstruction of implantation or distortion of the cervix or endometrium. Once a pregnancy is established, it is rare for myomata to interfere with its progress, and most proceed uncomplicated. However, a higher rate of cesarean section has been noted, and premature labor may result from very large myomata.[1] Degeneration of fibroids, caused by hemorrhagic infarction, may rarely occur during late pregnancy and is marked by pain, and also may be accompanied by rebound tenderness, fever, nausea, vomiting, and leukocytosis.[3] Treatment consists of rest and analgesia; surgery is a last resort.

Anemia and fatigue can be caused by excessive blood loss associated with fibroids. Pressure on the bowel or bladder can cause constipation, urinary frequency, and dyspareunia. Large fibroids may mask the diagnosis of serious gynecologic neoplasm. Rapidly growing fibroids may indicate a more serious pathology such as leiosarcoma and should be investigated. Malignancy is rarely associated with uterine fibroids; however, they occur with increased frequency in endometrial hyperplasia and are associated with a fourfold increased risk of developing endometrial cancer.[1]

SYMPTOMS

Most women with myomas are asymptomatic, never knowing that they have them unless informed of such by gynecologic examination. This was actually discovered based on ultrasound and autopsy results revealing that many more women had fibroids than had ever been diagnosed or treated for symptoms.[2] The most common symptoms are menorrhagia and the physical effects caused by large myomata such as increased pelvic pressure, frequent urination, difficulty with defecation, and dyspareunia with deep penetration.[1,3,5] Abnormal uterine bleeding is present in about 30% of all patients, and periods are typically heavy and prolonged, often with premenstrual and postmenstrual spotting.[2,4] Uterine bleeding caused by myomas can be associated with significant social, emotional, financial, and medical difficulties; women's concerns should be addressed. Some women experience dysmenorrhea.[2] Metrorrhagia, may occur, but should be evaluated with an endometrial biopsy to rule out other endometrial disease.[4] About 2% to 10% of women experience infertility as a result of fibroids, ostensibly due to abnormal uterine of tubal motility, interference with sperm movements, or abnormal uterine blood flow.[3,11] Fibroid degeneration, torsion, or compression of a nerve against the pelvis caused by encroachment by a fibroid can lead to significant pain.[4,11]

DIAGNOSIS

Diagnosis can be determined by:

- Pelvic bimanual examination: Large fibroids (greater than a 12- to 14-week gestation) can be manually palpated and felt as an enlarged uterus, lump, or mass.
- Ultrasound scan: It is useful to monitor size and growth rate of fibroids. Repeat scans should be done during the same phase of the menstrual cycle.
- Laparoscopy: This is important if the mass is indistinguishable from the ovaries.
- The differential diagnosis includes:[1]
  - Ovarian neoplasm
  - Tubo-ovarian inflammatory mass
  - Diverticulum inflammatory mass
  - Endometrial carcinoma

CONVENTIONAL TREATMENT

Unless fibroids are symptomatic, observation is the most prudent form of treatment and no other intervention

is necessary.[1,4] GnRH agonists (e.g., Leuprolide) have been used effectively to control symptoms and reduce myoma size through suppression of estrogen and progesterone production.[3,12] Mean uterine size decreases 30% to 64% after 3 to 6 months of treatment, and symptoms associated with fibroids are alleviated as a result. Possible side effects include hot flashes, headache, vaginal dryness and vaginitis, decreased libido, joint and muscle stiffness, and depression, and 30% of patients continue to have light, irregular vaginal bleeding.[3,12] Local allergic reaction occurs in about 10% of patients.[3] Bone loss occurs but is reversible, and a small number of women (2%) experience major vaginal hemorrhage 5 to 10 weeks after treatment commences. Steroid add-back therapy has been investigated to prevent bone loss in women requiring long-term GnRH therapy; however, because of the risk of osteoporosis, long-term therapy is inadvisable.[3,12]

Surgery should be reserved for women who are past childbearing, who are heavily symptomatic and not responsive to drug therapy, or who have suspected malignancies. Women wanting to preserve childbearing ability should be given the option of conservative therapy. GnRH therapy may be prescribed as pretreatment for surgical procedures to reduce fibroid size and bleeding. Myomectomy may be performed vaginally, hysteroscopically, or laparoscopically, and when performed skillfully, improves symptoms in 80% to 90% of patients. Between 15% and 30% experience fibroid regrowth after 5 years. Uterine scarring may occur from the procedure and affect fertility.[12] Endometrial ablation and uterine artery embolization (UAE) are additional options.[13,14] UAE is increasingly popular, and appears generally safe, but it is uncertain how long the treatment lasts and whether future fertility may be affected. The procedure involves injection of polyvinyl or gelatin particles into the uterine arteries to cut off blood supply to the fibroids, which leads to shrinkage over the next 3 to 12 months. Approximately 85% of patients gain relief from the procedure, which has been performed since 1995. However, it is not risk free. Adverse outcomes include infection, bleeding, and formation of emboli, as well as future fertility problems. For women intending to become pregnant in the future, myomectomy may still be the most certain conventional surgical intervention.[14] Hysterectomy is generally recommended when women are past childbearing age, are symptomatic, malignancy is suspected, or if other therapies are ineffective.[1,3,12]

BOTANICAL TREATMENT

Among Western herbalists specializing in gynecologic complaints, there is a common perception that although symptoms of uterine fibroids are not difficult to control with botanical medicines, and their growth can be arrested, they are difficult to eliminate entirely unless the fibroid is small at the onset of treatment (smaller than 12-week size). Many women are content to have symptom control over pharmaceutical or surgical intervention, as long as the fibroids present no mechanical problems.[15] Traditional Chinese medicine (TCM) has clearly defined diagnostic constructs, many herbal formulae, and well-developed adjunctive treatment protocols (e.g., acupuncture, moxibustion) for treating uterine fibroids and has claimed success in entirely eliminating uterine fibroids.

Western herbal treatment protocols include a variety of strategies (Table 7-1). These include weight reduction, promoting hormonal balance, specifically through the elimination of estrogens by enhancing liver detoxification mechanisms, promoting pelvic circulation while simultaneously controlling bleeding if necessary, and general improvement of uterine tone. These are integrated with the general recommendation to avoid excess exposure to xenoestrogens (environmental estrogens) and reduce overall estrogen levels, exposure to both being a risk factor for the development of uterine fibroids. Women with fibroids report greater frequency of red meat and pork intake, and less frequent green vegetable, fruit, and fish consumption.[4] Although there is little correlation between the development of uterine fibroids and cancer, numerous studies have demonstrated a connection between diet, estrogen levels, and hormone-dependent cancers, as well as a protective effect of fruit and vegetables against cancer.[4] No studies have evaluated the effects of US dairy consumption and the development of uterine fibroids. However, an association between dairy intake and increased risk of ovarian cancer has been reported.[16,17] Herbalists recommend that patients avoid foods that increase risk, and emphasize intake of those shown to facilitate estrogen biotransformation, for example, by increasing dietary fiber, and regular intake of complex carbohydrates as found in vegetables and grains.[11,18,19] Botanical strategies are aimed at reducing the estrogen burden through liver detoxification and improved elimination, promoting gynecologic health in general by improving pelvic circulation, reducing symptoms, and controlling fibroid size.

TCM treatment for fibroids has been evaluated through several preliminary studies, which are presented in the following section. Western botanical protocol for the treatment of uterine fibroids has not been subjected to controlled trials.[4] The Western botanical information presented in this chapter reflects the opinions of herbalists practicing in the United States, United Kingdom, Canada, Australia, and New Zealand, regarding the efficacy and safety of the primary herbs used to treat myomas. Given the general safety of the botanicals being discussed, and the lack of noninvasive long-term effective medical treatments for fibroids, it seems that investigation of the primary Western herbal protocols cited in Table 7-1 is warranted. Nervines, laxatives, adaptogens, and other herbs included in fibroid protocol are discussed elsewhere throughout this text. Stress reduction should not be overlooked as part of the treatment protocol for women with symptomatic fibroids, as chronic uterine bleeding can cause emotional, social, financial, and medical consequences.[2]

TABLE 7-1

Botanical Treatment Strategies for Uterine Fibroids

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Hormonal regulation; increase hormone biotransformation, conjugation, and improved elimination; displace with endogenous estrogen with estrogen receptor competitors.	Cholagogues Hepatic detoxification stimulants	*Berberis vulgaris* *Camellia sinensis* *Chelidonium majus* *Hypericum perforatum* *Schisandra chinensis*	Barberry Green tea Chelidonium St. John's wort Schisandra
Hormonal regulation; increase hormone biotransformation, conjugation, and improved elimination; displace with endogenous estrogen with estrogen receptor competitors.	Hormonal modulators	*Actaea racemosa* *Vitex agnus-castus*	Chaste tree Black cohosh
Hormonal regulation; increase hormone biotransformation, conjugation, and improved elimination; displace with endogenous estrogen with estrogen receptor competitors.	Phytoestrogens/SERMS	*Glycine max* *Trifolium pratense*	Soy Red clover
Hormonal regulation; increase hormone biotransformation, conjugation, and improved elimination; displace with endogenous estrogen with estrogen receptor competitors.	Laxatives (bulk, anthraquinone)	*Linum ussitissimum* *Rumex crispus* *Taraxacum officinale*	Flax seed Yellow dock Dandelion root
Improve uterine tone, reduce menorrhagic bleeding (Also see Menorrhagia in Dysfunctional Uterine Bleeding)	Uterine tonics	*Caulophyllum thalictroides* *Leonurus cardiaca* *Mitchella repens* *Rubus idaeus* *Viburnum opulus*	Blue cohosh Motherwort Partridge berry Red raspberry Cramp bark
Improve uterine tone, reduce menorrhagic bleeding (Also see Menorrhagia in Dysfunctional Uterine Bleeding)	Uterine astringents	*Achillea millefolium* *Alchemilla vulgaris* *Capsella bursa-pastoris* *Cinnamomum* spp. *Erigeron canadensis* *Geranium maculatum* *Hamamelis virginiana* *Myrica cerifera* *Rubus idaeus* *Trillium erectum*	Yarrow Lady's mantle Shepherd's purse Cinnamon Canada fleabane Cranesbill geranium Witch hazel Bayberry Red raspberry Birthroot, birthwort, Bethroot
Relieve pelvic stagnation and blood stasis, improve uterine circulation	Uterine circulatory stimulants	*Angelica sinensis* *Cinnamomum cassia* *Paeonia lactiflora* *Paeonia suffruticosa* *Prunus persicae* *Zingiber officinalis*	Dong quai Cinnamon White peony Peony Peach Ginger
Treat dysmenorrhea	Uterine antispasmodics See Dysmenorrhea		
Treat anemia	Iron-rich supplements and herbs See Anemia		

Traditional Chinese Medicine Treatment

Cinnamon and Peony

Traditional Chinese medicine has numerous well-developed treatment protocols and formulations, some of which have been used for several centuries for promoting gynecologic health in general and for treating uterine fibroids specifically. For a more comprehensive review of the Chinese treatments for gynecologic problems, readers are referred to the primary TCM literature. Generally speaking, TCM views uterine myomas as a

result of poor circulation of chi (energy) and blood through the pelvic region. Many formulas are designed to dispel pelvic stagnation and increase the flow of blood to uterine and ovarian tissues and facilitate the smooth flow of blood via menses. A classic TCM formula used for relieving blood stagnation is Cinnamon Twig and Poria Pill (gui zhi fu ling wan) consisting of: *Cinnamomum aromaticum* twigs, Poria cocos, *Paeonia lactiflora* root, *Paeonia suffruticosa* root, and *Prunus persica* seed. It should also be noted that in TCM, each herbal formula has specific diagnostic criteria for which it is used as well as clear contraindications and cautions. For maximum efficacy in using TCM protocols, a qualified herbal TCM practitioner should be consulted. In addition to herbal protocol for promoting gynecologic health and specifically treating uterine fibroids, TCM also employs numerous other modalities, which may include walking to promote circulation in general and abdominal circulation specifically, moxibustion, acupuncture, external application of compresses, and other such adjunctive therapies. Specific lifestyle recommendations also can be given such as the avoidance of cold foods and drink (in TCM coldness is said to cause congealment and stagnation) and constrictive clothing.[20]

Several studies have looked at the efficacy of the Cinnamon Twig and Poria Pill formula noted in the preceding section for the treatment of uterine fibroids. Specifically, the studies investigated the effectiveness of the Japanese version of this formula (Keishi-bukuryo-gan, KBG) in an open study on 110 premenopausal women with symptomatic uterine fibroids measuring less than 10 cm in diameter. They were treated with 22.5 g/day of a freeze-dried decoction of the herbs for 12 weeks. Twenty-one women were considered ''normal'' and 47 women much improved by the end of the trial. This herbal formula is frequently used to treat a range of gynecologic disorders including dysmenorrhea, cervical erosion, ovarian cysts, chronic salpingitis, and endometriosis, to name a few conditions.[15] There is research to suggest that the Paeonia species in this formula may act as an LH-releasing hormone (LH-RH) antagonist with weakly antiestrogenic effects in the presence of estrogen.[21] In another study, the authors applied individualized TCM formulations and treatments to treat 223 cases of uterine fibroids with a reported 72% reduction of menorrhagia in 160 women complaining of this symptom, 58% improvement in backache, and an overall effectiveness rate of 92.4%. Myomas were eliminated in 29 of 223 patients and markedly diminished in 42 patients. In 32 patients, no changes were seen and there were no positive results in 12.5% of patients.[15] If the TCM treatments were tailored to the individual patients, then this can be kept with the addition I made. If the treatment was specific, a similar level of detail as the previously reported study should be given for consistency of presentation.

In an interesting study by Mehl-Madrona et al., an integrated TCM-Western medicine pilot study was conducted to compare the cost and efficacy of a set of therapies typically used by CAM practitioners and conventional medicine on ability to reduce uterine fibroid size. All patients were premenopausal and age 24 to 45 years, educated, employed, and from a socioeconomic bracket that allowed them to pay cash for all treatments. None were on pharmaceutical treatment or hormonal contraceptives at the time of the study and all received a pelvic ultrasound before and again 6 months after treatment. Sonograms were obtained on patients who dropped out of the study as well, so sonograms were available on all patients. Uterine fibroids measured at least 6- to 8-week pregnancy size, with palpable fibroids 2 to 3 cm in diameter. Inclusion in the study required hemoglobin greater than 8 g/dL, with fibroid growth of less than 6 cm/year. CAM treatment included a combination of nutritional, herbal, acupuncture, bodywork, and psychological interventions. Acupuncture and herbal protocols were selected individually for the patient, using formulae and points traditionally indicated for the patient's patterns: symptoms, constitution (based on TCM pulse and tongue diagnosis), and condition. The comparison group used progestational agents, oral contraceptives, and NSAIDs. The results of this study demonstrated no statistically significant difference in change of symptoms between the two groups when measured after 6 months of treatment. Both experienced improvement in symptoms and fibroid size. Patients in the treatment group considered the pilot study a success because they were able to achieve results equivalent to pharmaceutical interventions using nonconventional methods.[15]

Hormonal Modulators

Chaste Berry

Chaste berry is the primary herb employed by herbalists and integrative medicine practitioners for hormonal modulation in the botanical treatment of fibroids.[4,22] It acts as a dopamine agonist, resulting in a reduction in prolactin release.[23] Prolactin may play a role in fibroid growth. No scientific evidence in the literature has been found for the use of chaste berry specifically in the treatment of fibroids, and although its use may result in reduction of apparent estrogen excess due to relative progesterone deficiency, increased progesterone levels have been shown to result in increased mitotic division in fibroid tissue. Wuttke et al. studied the putative estrogenic effects of a chaste berry extract and found it contained substances that replaced radiolabeled estradiol from a cytosolic estrogen receptor preparation, and appeared to be agonistic to ERβ. However, because the uterus expresses ERα, no effects on the uterine expression of estrogen were expected or have been experimentally observed.[23]

Phytoestrogens and Selective Estrogen Receptor Modules

Phytoestrogens are plant compounds with a similar molecular shape and structure to endogenous estrogen molecules, and which can bind competitively to estrogen receptors, preventing the binding of more potent estrogen and estrogen metabolites (see Part IV).[24] They appear to behave similarly to selective estrogen receptor modulators (SERMs). Low Dog explains their potential clinical application in conditions of estrogen excess, in

relationship to the role of phytoestrogens in breast cancer treatment:

> *By binding to estrogen receptors in the premenopausal woman, phytoestrogens ''turn down'' estrogen production through negative feedback at the level of the hypothalamus and pituitary gland...when endogenous estrogen levels are high, phytoestrogens may have an antiestrogenic activity by preventing estrogen from binding to the estrogen receptor through competitive inhibition.*[25]

Legumes, including soybeans and red clover, are rich in phytoestrogens.[26] In a study by Liu et al. methanol extracts of red clover (*Trifolium pratense*), chaste berry, and hops (*Humulus lupulus*) showed significant competitive binging to both ERα and ERβ. In the same study, dong quai (*Angelica sinensis*) and licorice (*Glycyrrhiza uralensis*) showed weak ER binding, whereas black cohosh did not exhibit any competitive binding. Controversy abounds as to the mechanisms of action of black cohosh, which do not appear to be directly phytoestrogenic.[27] Current research is suggesting a dopaminergic or serotonergic effect for this botanical.[25,27] The application of phytoestrogens may be a promising area for further investigation for the botanical treatment of fibroids, and should be considered in the development of botanical protocols.

Hormone Excretion and Biotransformation

Greater than 50% of all estrogen metabolism and conjugation occurs in the liver, suggesting a basis for the belief among herbalists that herbs that improve liver function may increase estrogen excretion and either treat or lower the risk for uterine fibroids.[4,22] Herbalists commonly include liver-specific herbs in formulae for treating fibroids. Several herbs actively effect phase 1 and phase 2 liver detoxification systems and CYP450, an enzyme system partially involved in the metabolism of estrogen. These effects and their relationship to uterine fibroid treatment, if any, have not been formally investigated but are often applied by modern herbal practitioners in putatively reducing estrogen burdens. Cholagogues, herbs which stimulate the release of bile from the gallbladder, also may be useful for clearing estrogen through increased bowel clearance resulting from their indirect laxative action. Examples of cholagogues include bayberry and chelidonium.[22]

Uterine Tonics, Astringents, and Hemostatics

Because bleeding is a common symptom of uterine fibroids, numerous antihemorrhagic herbs are used in botanical medicine protocols (see Menorrhagia in Dysfunctional Uterine Bleeding).[22] Yarrow dried plant infusion is perhaps one of the most widely used uterine antihemorrhagics, reliably reducing acute uterine bleeding, but conversely promoting menstrual flow when suppressed. It has been used since ancient times as a styptic.[25] Either dry or fresh plant can be used as a tea or tincture. Many herbalists believe that yarrow herb taken as tea is more quickly effective for stopping acute uterine bleeding than other preparations. Other traditionally used uterine antihemorrhagic herbs include lady's mantle, shepherd's purse (fresh only), cranesbill geranium, witch hazel, bayberry, red raspberry, and bethroot. These are all generally taken in tincture form in 2- to 4-mL doses repeated every 15 minutes as needed until bleeding subsides, or combined into larger formulae for the treatment or prevention of chronic menorrhagia. Shepherd's purse in particular has been used traditionally as a uterine antihemorrhagic. The 1986 Commission E monograph recommends daily oral doses of 10 to 15 g of crude herb (or equivalent in extract) for mild gynecologic bleeding.[28] Extracts of the drug contain a hemostyptic action, likely owing to the presence of a peptide that has demonstrated oxytocin-like activity in vitro.[28,29] Many modern Western herbalists believe that it is imperative to prepare Shepherd's purse from fresh, not dry, plant material. Lady's mantle's mechanism of action lies in its high tannin content, indicating it for bleeding, diarrhea, and wound healing, a likely mechanism for many of the other herbs used as uterine antihemorrhagics.[29] The combination of Cinnamomum and Erigeron was relied upon by the Eclectics for uterine hemorrhage, and is still employed by midwives today for the treatment of nonemergency postpartum bleeding, and by herbalists for the treatment of menorrhagia.[30,31] Red raspberry leaf is typically used more as a long-term uterine tonic than to arrest acute bleeding. Blue cohosh has been used historically for its utero-tonic actions. It is listed in the 1918 US Dispensatory for the treatment of menorrhagia and dysmenorrhea, and is still widely used by herbalists for these conditions.[32]

''Great Flood'' Formula (tincture)

Yarrow	(*Achillea millefolium*)	40 mL
Lady's mantle	(*Alchemilla vulgaris*)	20 mL
Bayberry bark	(*Myrica cerifera*)	15 mL
Shepherd's purse	(*Capsella bursa-pastoris*)	15 mL
Cinnamon	(*Cinnamomum cassia*)	10 mL
		Total: 100 mL

Dose: 2 to 4 mL as needed, repeated up to every 15 minutes for 1 hour until bleeding subsides or is arrested.

WARNING: Soaking more than two maxi-pads in 30 minutes is considered a uterine hemorrhage. If this occurs seek medical care immediately.

Relieving Uterine Stasis: Circulatory Stimulants

Improving pelvic circulation and relieving stasis is a common approach to fibroid treatment in both Western and traditional Chinese herbal medicine, based on the belief that relieving stagnation and congestion in the pelvis will facilitate the removal of ''blockages'' and growths (e.g., fibroid tissues), remove wastes, and promote greater health and nourishment of the pelvic organs in general.[11,18,20] Decreasing pelvic stagnation is also thought to help reduce uterine hemorrhage. Ginger and cinnamon are both traditionally used to increase circulation to the reproductive organs. Further, cinnamon has been used historically to reduce uterine bleeding, making it specific for the treatment of uterine fibroids with menorrhagia or metrorrhagia.[30,31] White peony, an ingredient in

Keishi-bukuryo-gan, discussed in the preceding, is a common herb used in TCM for the treatment of women's disorders, including menstrual dysfunction and uterine bleeding.[33] Red peony is often combined with white peony and peach seed to dispel blood stasis, and conditions associated with it, including excessive uterine bleeding, particularly with the presence of thick, purple clots.[33]

CASE HISTORY: UTERINE FIBROIDS

Latisha, a 44-year-old café worker presents with irregular heavy bleeding, strong mood swings, and insomnia. Uterine myomata had been diagnosed by ultrasound and are easily palpable at rest. She has overwhelming sweet cravings premenstrually, poor dietary habits, and no exercise. She is currently using a women's multivitamin and Ferrous gluconate tablets, but no other treatments. She experiences some flatulence associated with certain foods and regular constipation, especially when she ''forgets to eat.'' She has had several miscarriages, two terminations, and one live birth. Christine works late nights, does not sleep well, and describes herself as ''living on her nerves.'' Uterine fibroids were causing discomfort at night. She drinks several cups of coffee and several glasses of wine daily. Her blood pressure is 110/65. She describes herself as happy at home and likes her work but realizes it affects her health. Menstrual irregularities have developed over the past 5 years.

Treatment Protocol

- For promoting hormonal regulation:
  Vitex agnus-castus (chaste berry) tincture
  2.5 mL each morning and evening
- As a uterine tonic:

Lady's mantle	(*Alchemilla vulgaris*)	25 mL
Raspberry	(*Rubus idaeus*)	30 mL
Nettles	(*Urtica dioica*)	20 mL
White peony	(*Paeonia lactiflora*)	15 mL
Ginger	(*Zingiber officinalis*)	10 mL

Total: 100 mL

Dose: 3 mL bid for 3 months

She was also given a series of dietary guidelines (as described under Additional Therapies) and prescribed a strong chamomile infusion before bed. Her menstrual cycle became more regular over the proceeding 3 months, with a significant reduction in bleeding (1.5 days of medium to heavy bleeding reducing to mild to moderate).

After 3 months the above protocol was modified to:

- For promoting hormonal balance:
  Vitex agnus-castus (chaste berry) tincture
  As a uterine tonic and to promote pelvic circulation:

Red raspberry leaf	(*Rubus idaeus*)	40 mL
White peony	(*Paeonia lactiflora*)	40 mL
False unicorn	(*Chamaelirium luteum*)	15 mL
Ginger	(*Zingiber officinalis*)	5 mL

Total: 100 mL

Dose: 3 mL bid

She was told to take yarrow tea and was also given a botanical tincture for promoting sleep, to be taken 20 minutes before bed, and repeated as needed, as her insomnia was still problematic.

Ashwagandha	(*Withania somnifera*)	40 mL
Lemon Balm	(*Melissa officinalis*)	30 mL
Hops	(*Humulus lupulus*)	15 mL
Valerian	(*Valeriana officinalis*)	15 mL

Total: 100 mL

Dose: 5 mL each time

Her blood loss continued to be well controlled; she was sleeping better, experienced reduced sugar cravings, and was eating better. She felt light-headed just prior to and during her period but without extreme mood swings. She had no sensation of the fibroids at all when at rest. A reduction in symptoms of fibroids does not necessarily mean a reduction in fibroid size, but it does appear to have been the case with Christine. Without a follow-up ultrasound, this conclusion is unsupported.

NUTRITIONAL CONSIDERATIONS

Obesity/Weight Management

Obesity is a risk factor for fibroid development. Therefore, dietary and lifestyle strategies should be aimed at weight reduction and healthy weight maintenance.

Xenoestrogens/Endocrine Disruptors

Avoid xenoestrogen ingestion from pesticide and herbicide residue by eating organically cultivated foods and avoiding foods in plastic containers. Xenoestrogens are found most concentrated in the fat of meat, farmed fish, and nonorganic dairy products.[12] Eating primarily organic meat, dairy, and produce, washing fruits and vegetables thoroughly before eating, and minimizing the use of soft plastics, such as for food storage, can help reduce xenoestrogen intake.

Estrogen Biotransformation and Diet

Metabolism and detoxification of estrogen in the body ultimately determines its biological effects. Estrogen biotransformation occurs mainly in the liver through phase I hydroxylation and phase II methylation and glucuronidation, allowing estrogen to become a water-soluble, excretable compound.[11] This is predominantly excreted by the liver in bile (see Dietary Fiber). Phase I detoxification yields three estrogen metabolites with highly variable biological activity: 2-hydroxyestrone (2-HE), 16-alpha-hydroxyestrone (16α-HE), and 4-hydroxyestrone (4-HE). 2-HE is a beneficial estrogen metabolite in that among its effects, it competitively binds estrogen sites, blocking more potent estrogens. Conversely, 4-HE and 16α-HE are potent estrogens that may promote the growth of estrogen-sensitive tissue.[11] Dietary consumption of cruciferous vegetables, such as broccoli and cabbage, as well as green tea, garlic, and rosemary can increase the amount of 2-HE by modifying P450 activity in phase I, and have antioxidant effects as well.[11,34]

Dietary Fiber

Once estrogen metabolites are excreted by the liver in bile, the metabolites are soaked up by fiber in the small intestines and excreted via defecation. If the diet lacks fiber, bile, along with the estrogen metabolites are reabsorbed, adding an unnecessary estrogen burden to the body. Soluble fiber such as the lignins found in flax seeds also increases sex hormone binding globulin (SHBG), decreasing the amount of available active estrogen, as estrogen bound to SHBG is rendered inactive.[11] Brassicae vegetables such as cabbage and broccoli contain indole glucosinolates, which when chewed, are degraded by a plant enzyme into a variety of indole structures. When degraded in the body, these structures induce cytochrome P450 expression (CY1A1) in hepatic and extrahepatic tissue, leading to greater conversion of 2-hydroxyestrone (2-HE), and decreasing the availability of E1 for conversion to 16-HE, thereby reducing the estrogen burden overall.[25] This is partly associated with the anticancer effects associated with these foods.

Dietary Antioxidants

The conversion of estradiol to catechol estrogens via 4-hydroxylation stimulates an oxidant stress response induced by free radicals. This activity is markedly increased in fibroid tissue. Therefore, daily intake of foods containing the vitamins A, C, and E, and the minerals zinc, selenium, and a range of phytochemicals would be appropriate supportive treatment, as would inclusion of antioxidant adaptogen herbs.

ADDITIONAL THERAPIES

Exercise not only encourages weight reduction but also improves pelvic circulation, promotes uterine muscular tone, promotes regular bowel elimination, and reduces

Treatment Summary: Uterine Fibroids

- Achieve a healthy body weight and distribution.
- Promote hormonal regulation and elimination of excess estrogen. Avoid excess environmental (and dietary) estrogen exposure.
- Encourage an anti-inflammatory diet low in red meat and dairy products and high in fresh fish, green vegetables, and fresh fruit.
- Improve uterine tone and circulation with herbs and exercise (e.g., specific yoga postures, belly dancing).
- Treat/prevent symptoms, such as, bleeding and pain, with appropriate botanicals for acute and chronic problems.
- Treat anemia if necessary.
- Supplement with vitamins A, C, and E, and the minerals zinc and selenium.

What to expect with treatment

- Expect an immediate reduction in acute pain within 1 to 2 hours of the onset of treatment with analgesic, antispasmodic, and sedative herbs, and a reduction in bleeding within 1 to 4 hours with the use of herbal astringents and antihemorrhagic herbs.

Treatment Summary: Uterine Fibroids—cont'd

- Expect an overall reduction in symptom occurrence within two menstrual cycles after the onset of treatment.
- Expect to begin to see reduction in fibroid size within 3 to 6 months of onset of treatment.
- Fibroids may not be eliminated entirely but can be reduced significantly enough to prevent symptoms and mitigate the need for pharmaceutical and surgical interventions.
- If after two menstrual cycles symptom relief is not beginning to be achieved, the botanical protocol and compliance with and dietary strategies, and so forth, need to be evaluated and formulae possibly modified.

Eclectic Specific Condition Review: Uterine Fibroids—a Historical Perspective
David Winston

Fibroids were as common in the time of the Eclectic physicians as today. Small but palpable fibroids were treated via specific herbal medications, whereas large symptomatic tumors were often treated by surgery. The following is a review of the herbs classically used by Eclectic physicians to treat uterine fibroids.

- **Black Cohosh root (*Actaea racemosa*)**
  Fibroids with dragging pain in the uterus, back pain, patient feels hot and sweats easily.
- **Blue Cohosh root (*Caulophyllum thalictroides*)**
  For uterine pain with a feeling of fullness, weight, or pain in legs. Uterus feels sore and bruised.
- **Canada Fleabane herb (*Erigeron canadense*)**
  For profuse bleeding with fibroids and excessive vaginal discharge.
- **Cinnamon bark (*Cinnamomum cassia*)**
  For profuse bleeding with fibroids.
  The essential oil of cinnamon, combined with the essential oil of Canada fleabane in an alcohol base, was known as Ellingwood's Compound.
- **Collinsonia root, leaf, and flower (*Collinsonia canadensis*)**
  Fibroids with venous congestion of the uterus, uterine prolapse, chronic uterine irritation; best for small growths.
- **Cotton root bark (*Gossypium* spp.)**
  Uterine fibroids with hemorrhage, backache, large boggy uterus.
- **Goldenseal root (*Hydrastis canadensis*)**
  Atonic boggy uterine tissue with a tendency to excessive discharge and bleeding. Useful in the early stages of fibroid growth.
- **White Ash bark (*Fraxinus americana*)**
  Fast-growing uterine fibroids with subinvolution of uterus (not very effective for large, late-stage fibroids).
- **Wild Geranium root (*Geranium maculatum*)**
  Profuse bleeding with fibroids and excessive vaginal discharge. Can be used with beth root (*Trillium* spp.).

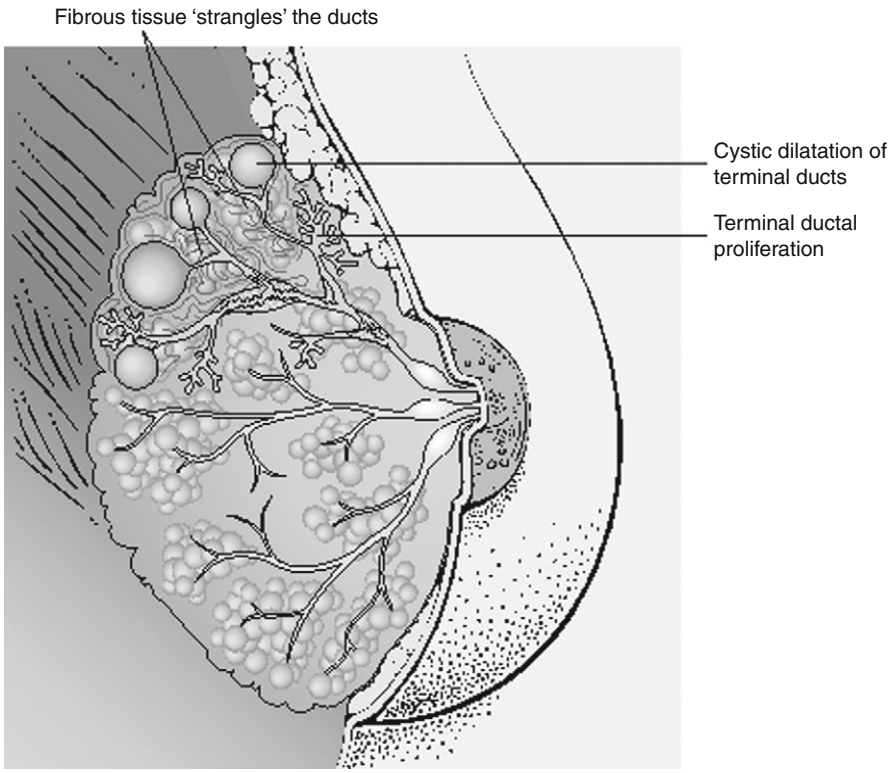


Figure 7-2 Comparison of normal and fibrocystic breast tissue. (Salvo S: *Mosby's Pathology for Massage Therapists,* St. Louis, 2004, Mosby.)

stress. Herbalists often recommend specific yoga postures or Kegel exercises to assist in improving pelvic circulation particularly.[35] Vigorous walking, hip circling, pelvic thrusts, and belly dancing can all be useful to improve pelvic circulation.

TREATMENT SUMMARY: UTERINE FIBROIDS

FIBROCYSTIC BREASTS AND BREAST PAIN

Suzanna M. Zick

Benign breast conditions are a common finding in clinical practice, with fibrocystic breast changes and fibroadenomas occurring in 60% to 90% of all women.[36] The hallmark of fibrocystic breast changes is that the cysts fluctuate in size and shape, may entirely disappear and reappear cyclically, and are associated with hormonal changes in the menstrual cycle. Women with this condition describe their breasts as feeling lumpy, ''ropey,'' and tender. The changes occur bilaterally. Fibroadenomas are mobile, solid, firm, rubbery masses that typically occur singly, and are not usually painful (Fig. 7-2). They are second only to fibrocystic changes as the most common of the benign breast conditions, and are commonly found in women in their 20s. Breast tenderness that accompanies the menstrual cycle is known as cystic mastalgia.[38,39] Cyclic mastalgia may be associated with other premenstrual complaints. The terms *benign breast disorder* and *benign breast disease* are unfortunate misnomers, as they are neither a disorder nor disease. In only a small percentage of cases are the atypical ductal and lobular hyperplasias associated with increased risk of breast carcinoma. Practitioners consulting with women for fibrocystic breast changes and other findings must be sensitive to a patient's increased anxiety about finding a breast lump, and provide clear information and calming reassurance both during the exam and while the patient awaits tests results if any were deemed necessary.

PATHOPHYSIOLOGY

Fibrocystic breast changes are an exaggerated response to cyclic ovarian hormones.[39] The etiology of fibroadenomas and cyclic mastalgia may also be hormonal, though in some cases, the cause of a fibroadenoma may be unclear. When this occurs in women over 30, removal of the mass is generally recommended.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

There are two primary aims when arriving at a diagnosis of fibrocystic breasts. The first is to rule out breast cancer, and the second is to determine if benign breast symptoms warrant treatment. A careful history, physical exam, and cancer risk assessment are indicated (Box 7-1 and Table 7-2).[36] A thorough breast exam is best performed after the menses, as examination prior to menses (when the pain is actually likely to be most acute) can obscure problematic lumps caused by normal breast tissue proliferation and nodularity from normal hormonal changes. If a suspicion of breast cancer remains after the history and physical, further diagnostic tests should be performed as appropriate.[36] Diagnosis of fibrocystic breasts can be made on the basis of cancer exclusion. For women experiencing

symptoms including pain, tenderness, swelling, inflammation, or nipple discharge, the comprehensive history and physical can be used to determine if the problem is cyclic or noncyclic in nature and whether it is associated with other signs and symptoms, including fever or premenstrual mood swings. It is also important to gently move aside the breast tissue and examine the chest wall and muscle to determine whether breast pain or muscle pain is the proper diagnosis.[40] Depending on the associated signs and symptoms, a diagnosis, including breast infection, muscle sprain/strain, premenstrual syndrome, or noncyclic mastalgia can be determined.

CONVENTIONAL TREATMENT

Conventional treatment for fibrocystic breasts includes encouraging women to wear loose fitting brassieres, decreased caffeine consumption, and smoking cessation, and a pharmacologic focus on hormonal modulation, including oral contraceptives (OCs), prolactin antagonists, and antiestrogen agents as well as diuretics for moderate premenstrual mastalgia; and analgesics such as ibuprofen, salicylates, and acetaminophen for pain.[36,38] Hormonal therapies often carry unwanted side effects, including weight gain, lipid profile changes, depression, and abnormal bleeding.[36] Although OCs reduce symptoms in up to 90% of women, symptoms return upon discontinuation.[36] Danazol, which suppresses the pituitary ovarian axis by inhibiting the output of both FSH and LH from the pituitary gland, is also used for mastalgia. Its side effects include virilization, muscle cramps, CPK elevations, and liver damage. Bromocriptine is also used for breast pain and nodularity but has several common side effects, including nausea, giddiness, and postural hypotension.[36] Reduction in dietary fat intake has been shown to reduce cyclic mastalgia.

BOX 7-1

Clinical Features of Benign Breast Changes

Breast tenderness and swelling
Nodularity
Breast pain (mastalgia)
Lumps
- Gross cysts
- Galactoceles
- Fibroadenomas

Nipple discharge
Breast infections
- Lactational or postpartum mastitis
- Acute mastitis associated with macrocystic breasts
- Chronic subareolar abscess

BOTANICAL TREATMENT

Botanical treatment for fibrocystic breasts has not been widely subject to scientific evaluation, in spite of this being a commonly treated condition in the herbal clinic. Treatment aims primarily at hormonal regulation through direct (i.e., HPA and HPO axes) and indirect (i.e., improved hormonal biotransformation and excretion) actions, and reduction of local congestion and symptomatic pain relief through topical applications (Table 7-3). The liver plays a central role in metabolizing and detoxifying sex hormones.[34] Consequently, herbal practitioners typically include herbs that are known or thought to enhance hepatic detoxification functions in formulae for treatment of fibrocystic breasts.[34] Such herbs, many of them considered ''bitters,'' include dandelion root, burdock, root, licorice root, Oregon grape root, fringe tree, motherwort, blue vervain, and celandine. These botanicals are usually included in ranges of 5% to 20% of formulae, in tincture or decoction forms. Although there has been little investigation of such herbs to establish their pharmacologic or physiologic action for such use, they are nonetheless a common part of the

TABLE 7-2

Risk for Development of Breast Cancer by Type of Benign Breast Disease

HISTOLOGIC PATTERN	APPROXIMATE RELATIVE RISK OF DEVELOPING BREAST CARCINOMA	PROPORTION OF BENIGN LESIONS*
Nonproliferative changes	No increased risk	70%
Proliferative disease without atypical hyperplasia	Twofold increased risk	27%
Proliferative disease with:		3%–4%
Atypical hyperplasia	Fivefold increased risk	
Atypical lobular hyperplasia	Fivefold increased risk	
Atypical ductal hyperplasia	Twofold increased risk	
Proliferative disease with atypia and family history**	11-fold increased risk	3%–4%

*As determined by biopsy
**Family history limited to mother, daughter, or sister with breast cancer

TABLE **7-3**

Summary of Botanical Treatment Strategies for Treatment of Fibrocystic Breasts

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Hormonal modulation	Herbs with putative or known hormonal activity	*Angelica sinensis*	Dong quai
		Caulophyllum thalictroides	Blue cohosh
		Glycyrrhiza glabra	Licorice
		Leonurus cardiaca	Motherwort
		Smilax ornata	Sarsaparilla
		Trifolium pratense	Red clover
		Verbena officinalis	Blue vervain
		Vitex agnus-castus	Chaste berry
Hormonal modulation	Essential fatty acids	*Linum usitatissimum*	Flax seed
		Oenothera biennis	Evening primrose
Enhanced clearance of estrogen by liver and bowel; improvement of liver function	Aperients Cholagogues Hepatics	*Calendula officinalis*	Calendula
		Ceanothus spp.	Red root
		Chelidonium majus	Celandine
		Chionanthus virginicus	Fringe tree
		Mahonia spp.	Oregon grape
		Taraxacum officinale	Dandelion root
Relief of local congestion and swelling through lymphatic clearance (topical/internal)	Lymphatics	*Galium aparine*	Cleavers
		Phytolacca americana	Poke root

protocol for many gynecologic concerns, including benign breast complaints, and their role in formulae should be considered and further evaluated.

Chaste Berry

Chaste berry is extensively recommended by herbal practitioners for cyclic breast pain and fibrocystic breasts, both when it presents independently and when associated with PMS. This traditional use is supported by clinical trials. Chaste berry may be used singly or in combination with other herbs that enhance hormonal regulation and hormone metabolism (e.g., herbs that promote liver function and hormonal conjugation and elimination). There have been three placebo-controlled, double-blind, randomized clinical trials (RCT) examining the effects and safety of a proprietary chaste berry extract–containing solution (VAC) on cyclic mastalgia. VAC is sold as Mastodynon®, and manufactured by Bionorica Arzneimittel GmbH (Neumark/Opf. Germany).[41] It contains 32.4 mg of chaste berry fruit extract/60 drops as well as a mixture of homeopathic ingredients, including Caulophyllum thalictroides, Cyclamen, Ignatia, Iris, and Lilium. This product is available as both a tablet (MR 1025 E1) and a liquid extract in Germany. German drug indications for the product include menstrual disorders based on a temporary or permanent corpus luteum insufficiency, infertility resulting from corpus luteum insufficiency, and menstrually related complaints, including mastodynia.[42] All three of the studies used the liquid solution, which contained 53% (v/v) alcohol, although the study by Wuttke et al. also used the tablets.[41,43] All three studies defined cyclic mastalgia as having at least 5 days of breast pain the previous cycle and treated women for three menstrual cycles with 30 drops two times daily of VAC (1.8 mL/equivalent to 32.4 mg extract of chaste berry drug). Researchers found that both the severity (assessed on a 1- to 100-mm visual analog scale [VAS]) and presence of breast pain (as measured by women's diaries) were significantly improved in the women who were assigned to the chaste berry groups compared with placebo after the first month of treatment. Although pain intensity was reduced by 30% in the chaste berry group compared with 11% in placebo after one cycle, pain intensity was even more reduced at the end of the second month of treatment, with 53% of women receiving chaste berry having decreased severity of breast pain compared with 25% of the placebo group ($p = 0.006$).[41] No further improvement was obtained with longer treatment periods. However, to reduce the number of days with severe pain women needed to receive VECS for three to four cycles before they had significantly fewer days with breast pain compared with the placebo group ($p = 0.21$).[41,44] Two of the studies also measured serum hormone levels including estradiol, progesterone, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and basal prolactin levels at baseline and in the premenstrual weeks of cycles 1, 2, and 3.[43,45] One study found a significant rise in prolactin levels and a decrease in progesterone levels,[45] whereas another study found no effect on FSH, LH, and progesterone, but did see a decrease in estradiol levels and a significant decrease in basal prolactin levels

(3.7 ng/mL tablets and 4.35 ng/mL liquid extracts) compared with placebo.[43] Adverse events were rare and did not differ from placebo in any of the RCTs.

Dong Quai and Blue Cohosh

Along with chaste berry, dong quai and blue cohosh are commonly employed by herbal clinicians to modulate hormone levels. Blue cohosh, as part of the German herbal formulation Mastodyn® (reviewed in the preceding), may provide some of the therapeutic benefit of that formulation. However, to date, no studies have demonstrated that blue cohosh has any effect on hormonal levels. Dong quai in vitro can weakly bind to estrogenic receptors and induce progesterone receptors. However, it did not stimulate vaginal cells or increase endometrial thickness and had no estrogenic effect showing no transactivation of either alpha- or beta-estrogen receptors.[27,46,47] Additionally, dong quai showed no significant effect on either hormonal levels or symptoms in an RCT in menopausal women.[48,49] Consequently, dong quai appears to have a limited if any effect on hormone levels. In a recent study, dong quai was found to have significant anti-inflammatory effects because of one of its constituents, ferulic acid.[50] Although this study is very preliminary, it may offer an alternative mechanism through which dong quai could be helping to decrease mastalgia in women with fibrocystic breasts. According to TCM theory, dong quai dissolves blockages and relieves blood stagnation, and is thus a common ingredient in formulae for mastalgia.

Flax Seed and Evening Primrose Oil

Flax seeds are the richest source of plant-based omega-3 fatty acids, with a-linolenic acid (ALA) being the primary fatty acid (18:3n-3).[51] These fatty acids are considered strongly anti-inflammatory, being precursors for the anti-inflammatory series prostaglandins (PGE3). Flax seeds are also rich in fibers called lignins. Like isoflavones in soy and other foods, lignins and their associated phenolic compounds are classified as phytoestrogens.[52,53] Flax seeds are an especially rich source of dietary lignins, with 75 to 800 times more than any other food source.[51,54] Research has shown lignins to be a promising agent for binding excess sex hormones, including testosterone and estrogens. Through both its anti-inflammatory and possible anti-estrogenic effects researchers believed that flax may prove a beneficial treatment for fibrocystic breasts. One study examined the effect of eating one muffin daily supplemented with 25 g of ground flax seeds in 127 women with mastalgia.[55] Women experienced a significant reduction of symptoms; however, the full results of this study were never published and thus it is unknown how long women needed to take the flax seed–enriched muffins, what symptoms were reduced, what the degree of symptom reduction was, or if there was any placebo control to assess for the considerable level of spontaneous remission (60% to 80%) of symptoms in women with breast pain over time.[55] Evening primrose oil (EPO), is a rich source of omega-6 essential fatty acids (EFAs). EFAs are precursors to either series 1 or 2 prostaglandins, depending on substrate availability. The more omega-6 EFAs there are in the diet, the more likely it is for the inflammatory series prostaglandins to be made; conversely, the less omega 6 EFAs there are in the diet, the more likely it is for anti-inflammatory series 1 prostaglandins to be produced. Because of EPO's potential anti-inflammatory properties, two randomized placebo-controlled, double-blind clinical trials and one open-labeled trial of EPO in both cyclic and noncyclic mastalgia have been conducted. One double-blind, placebo-controlled randomized study in 73 women with either cyclic or noncyclic mastalgia found that 1000 mg of EPO or placebo three times daily over 3 months significantly reduced symptoms of pain and tenderness in the women who received EPO compared with placebo.[56] In a similar study, 291 women with severe persistent breast pain given either placebo or 1000 mg EPO three times daily for 3 to 6 months found that 45% of women with cyclic pain improved. Further, 27% of women with noncyclic breast pain improved compared with 9% in the placebo group.[57] In a nonrandomized open-labeled study, 94 women with cyclic and 32 women with noncyclic mastalgia received 3 g of EPO for at least 4 months. Severity of pain was diminished in a ''clinically useful''[40] manner in 58%[49] of the women with cyclic mastalgia and 38%[12] of the women with noncyclic mastalgia taking EP. Unfortunately, all three of these studies are difficult to assess because of lack of reporting of how pain and symptoms were measured and how great the effect, and thus how clinically relevant the effect of EPO is in women with breast pain.[40] The recommended dose of flax oil to treat and prevent mastalgia and nodularity is two to four 500-mg capsules twice daily or 1 to 2 tablespoons of the oil daily. One to three grams daily is the recommended dose of ground seeds.[58] A typical dose of EPO is 1500 mg daily.

Red Clover

Red clover is rich in isoflavones, especially genistein and daidzein. Genistein and daidzein have weak estrogenic effects, which have led researchers to hypothesize that genistein may compete with stronger endogenous estrogens such as estradiol for estrogen receptors; although what effects this may have on breast tissue is unclear at this time. One unpublished study found that a red clover extract had a significant effect on improving mastalgia. No further information is available concerning this trial.[59]

Topical Applications

Castor Oil

Herbalists and naturopaths commonly recommend placing an absorbent cloth saturated with heated castor oil over the affected area of the breasts. The hot compress is typically applied for 1 hour for up to 5 days per week. The oil may be further medicated by the addition of essential oils as mentioned under poke root.

Poke Root

Poke root has traditionally been used to stimulate the immune system, relieve lymph congestion, and resolve

Botanical Protocol for the Treatment of Fibrocystic Breasts

Use the following combined protocol for at least 3 months for optimal results.

I. Prepare the Following Tincture:

Calendula	(*Calendula officinalis*)	20 mL
Chaste berry	(*Vitex agnus-castus*)	20 mL
Burdock root	(*Arctium lappa*)	20 mL
Sarsaparilla	(*Smilax ornata*)	20 mL
Dandelion root	(*Taraxacum officinale*)	20 mL

Total: 100 mL

Dose: 5 mL twice daily for 3 months

This tincture formula and infusion combination is designed to optimize liver function and promote the conjugation and elimination of excess estrogen and regulation of hormones.

II. Topical Application:

• Ginger and poke root compress

Prepare a strong infusion of ginger root using 2 tablespoons of fresh grated ginger root to 1 cup of liquid. Add 1 teaspoon of pokeroot tincture to the infusion, stir thoroughly, and soak a towel in the hot liquid. Apply for 15 minutes redippping the towel in the hot liquid to keep the compress hot. Repeat three or four times weekly for 3 months. The poke root may be omitted if practitioners are uncomfortable including it because of concerns about toxicity associated with the herb.

III. Nutritional Considerations

Eliminate caffeinated products. Reduce dairy consumption and exposure to environmental estrogens. A diet rich in essential fatty acids may be beneficial in hormonal regulation.

Vitamin E: 400–800 IU daily

Vitamin B_6: 50–100 mg daily

lumps and cysts, and by extension, has been widely applied topically for the treatment of fibrocystic breasts. Poke root oil is applied topically by rubbing in a small amount (1 tsp) of the oil throughout the affected breast(s) for at least 5 nights per week for 1 to 2 months. The addition of 5 to 7 drops each of rose geranium and sandalwood essential oils makes the oil slightly more stimulating to the local circulation and also adds a pleasant scent to the oil. All parts of the plant are toxic and can lead to contact dermatitis or even toxicity from handling large amounts. Internal use is not recommended without the supervision of a qualified practitioner.

CASE HISTORY: CYCLIC MASTALGIA

Tanya, 47-year-old perimenopausal woman consulted for increasingly painful cyclic mastalgia occurring 2 to 3 days prior to the onset of menses. Her pain had begun 2 years prior during a stressful time in her life at which time she also started having mild menstrual irregularities and bloating around the time of her periods. At that time, she started eating red meat again regularly and drinking several cups of caffeinated beverages daily. Tanya walks and rides an exercise bike 30 minutes daily five times weekly and has recently joined Weight Watchers and started eating cold water fish three to four times weekly as well as increasing her vegetable and fruit intake after finding out that she had high cholesterol (total cholesterol 251). She is drinking three to six glasses of water per day. She has some problems sleeping because of pain in her left hip and a history of GERD, and was recently diagnosed with mild depression. Tanya has a history of numerous sinus infections and vaginal yeast infections. She is taking Effexor (150 mg daily) for depression. Physical exam of the breast revealed bilateral tender spots on left lower quadrant that felt like ''bags of lentils.'' Patient claimed that she was aware of these areas due to self-breast exam and that it appeared to worsen around the time of her menstrual cycle.

She was prescribed the following tea for her to take after supper to help her sleep:

Passionflower	(*Passiflora incarnata*)	2 parts
Chamomile	(*Matricaria chamomilla*)	2 parts
Skullcap	(*Scutellaria lateriflora*)	1 part

Dose: Infuse 1 level tablespoon of dried herbs per cup of boiling water, covered, for 15 minutes. Strain. Drink 2 cups within 2 hours before going to bed.

For her mastalgia and menstrual irregularities, she was prescribed the following tincture:

Chaste berry	(*Vitex agnus-castus*)	20 mL
Burdock root	(*Arctium lappa*)	20 mL
Cleavers	(*Galium aparine*)	20 mL
Dong quai	(*Angelica sinensis*)	40 mL

Total: 100 mL

Dose: 3 mL, three times daily in water.

She returned 4 weeks later saying that her sleep had greatly improved. She also said that her GERD was about 75% improved. She estimated that she had about a 25% improvement in breast pain and tenderness. Her menstrual irregularities had not changed. The patient then returned 8 weeks later, and reported about a 75% improvement in breast tenderness and pain. She said that her last period was less irregular and closer to ''being on time.'' Her sleep remained improved.

NUTRITIONAL CONSIDERATIONS

Elimination of Coffee, Tea, and Other Caffeinated Products

An association between caffeine, or methylxanthines, and fibrocystic breast disease has been reported but remains controversial. In one study of a group of 102 women who had mammograms performed to measure the level of fibrocystic breast disease, a strong correlation was

found with both caffeine and total methylxanthine ingestion and fibrocystic breasts as determined by a series of questionnaires.[60] Similar results were found in a large case control study of 634 women.[61] Other studies, however, have found only weak associations. Normal fluctuations in hormonal effects on breast tissue and difficulty in consistently measuring caffeine or methylxanthine intake make it difficult to conclusively demonstrate a causal relationship.[62,63] In a review of the literature presented on AltMedex, the following studies are cited: A controlled clinical trial showed no clinically or statistically significant effects of alcohol- or methylxanthine-free diets on signs and symptoms of fibrocystic breast disease. One hundred sixty-two women with clinical and thermographic diagnoses of fibrocystic breast disease completed the study with evaluation at 6 months. It was concluded that abstinence from alcohol or methylxanthine-containing beverages is not likely to substantially reduce severity of fibrocystic breast disease within a few months.[64] A case control study examined the relationship between coffee consumption and the development of benign breast disease involving the analysis of 854 cases of histologically diagnosed benign breast disease and 1748 control subjects. No association between coffee consumption and benign breast disease was found; neither was a dose–response relationship between methylxanthine consumption and benign breast disease development noted. These results suggest no association between caffeine intake and the development of benign breast disease.[65] In a randomized study, 158 women with breast concerns were divided into two groups; one group abstained from consumption of methylxanthine-containing foods and beverages. The second group (controls) had no dietary restrictions. The patients were re-examined at 4 months for palpable breast findings. One hundred forty patients completed the study. There was a statistically significant decrease in clinically palpable breast findings in the abstaining group compared with controls, but the absolute change was minor and may be of little clinical significance. This study offered little support for the claim that caffeine-free diets are associated with clinically significant improvement in benign breast disease.[66] In a study of 66 patients, restriction of dietary caffeine ingestion can cause improvement in fibrocystic breast disease. Graphic stress telethermometry (GST) was performed as an objective monitor for fibrocystic breast. At baseline, an average score of 83.5 on GST was observed in these women. Following dietary methylxanthine restriction, these scores were observed to be an average of 69.5 at 2 months and 55.5 at 6 months. Forty-two of the 66 patients had decreases in GST scores of more than 20 points at 6 months. Eighty-five percent of the patients showed improvement in GST patterns at 6 months, 15% of patients showed no change, and none showed worsening in GST patterns. Subjectively, at 6 months, 22 of 66 patients reported marked improvement, 30 of 66 moderate improvement, 6 of 66 mild improvement, and 8 of 66 no change in symptoms of fibrocystic breast disease. At pretreatment, 78% of patients had 2+ or 3+ nodularity on palpation. At the 6-month examination, 89% of patients had no or 1+ nodularity on palpation (91% had improvement, 9% had no change, and none had worsening). In 85 US women with clinical and mammographically confirmed fibrocystic disease, complete abstention from methylxanthine consumption resulted in complete resolution of fibrocystic breast disease in 82.5% and significant improvement in 15% of the patients studied.[67]

Vitamin E and B_6 Supplementation

Supplementation with vitamin E (400 to 800 IU) may be beneficial for reducing mastalgia and nodularity of fibrocystic breasts and pyridoxine (vitamin B_6/50 to 100 mg) to reduce breast tenderness and pain.[68,69] Women are also encouraged to increase dietary fiber and complex carbohydrates, reduce dietary fat to 15% to 20% of their diet, and move toward a more plant-based diet, rich in phytoestrogens. A recent review examined various dietary therapies, and their potential effects in treating fibrocystic breasts.[38] The review found that some dietary therapies, including vitamin E and B_6, do not have adequate evidence to support their use in fibrocystic breasts. Studies were either of poor quality or had too few study participants to make definitive conclusions. Because of the dynamic nature and very high placebo response (20%) in fibrocystic breast complaints, only well-designed studies with large numbers of participants can address the efficacy of these treatments. Indeed, better-designed studies of vitamin E have all showed no significant effect on any parameter of fibrocystic breast. Studies on reducing caffeinated products from the diet have been variable, some showing positive outcome, others showing no benefit at all. This review found no studies that had examined the effect on fibrocystic breasts of low-fat diets, increased dietary fibers, soy isoflavones, or a more plant-based diet. However, there are considerable mechanistic data, including increasing unabsorbable estrogen conjugates for excretion, reducing the recirculation of estrogen, and positively affecting bowel microflora populations that support the use of these dietary strategies. The general health benefits of adjunct therapies such as adding vitamin E, reducing poor-quality fat intake, or reducing caffeine consumption suggest that these may be worthwhile strategies to try.[38]

ADDITIONAL THERAPIES

Exercise

It is important to evaluate whether women with breast pain are exercising appropriately and properly. Some women who believe that they are experiencing breast pain or tenderness are instead having chest wall pain, often resulting from inappropriate or overexercise, especially strength-building exercises that emphasize the pectoral muscles.[39] No studies have examined the impact of any type of exercise on the symptoms or nodularity of fibrocystic breasts. Consequently, it is difficult to know what duration, type, or frequency of exercise would most benefit women with fibrocystic breasts.

Clothing

Inadequate support of the breasts is thought to lead to suspensory ligament strain, which may cause or

contribute to pain and tenderness.[55] No randomized controlled studies have examined breast support and its relationship to breast pain.

Stress Reduction

No studies have examined the effect of stress, anxiety, depression, or sleep disturbances on fibrocystic symptoms. However, many other pain syndromes, including fibromyalgia and vulvar pain, are closely associated with levels of ''distress'' in a woman's life.[70] No randomized clinical trials have been conducted using acupuncture for fibrocystic breast symptoms; however, several open label trials have found that up to 95% of women's mastalgia was improved after acupuncture treatment.

TREATMENT SUMMARY FOR FIBROCYSTIC BREASTS AND BREAST PAIN

- Reduce endogenous and exogenous estrogen load through dietary modification, reduction in environmental exposure, and botanical modulation of HPA and HPO axis and biotransformation of hormones. Examples of herbal actions to accomplish this include adaptogens, hormonal modulators, cholagogues, and aperients.
- Use SERMS to competitively bind estrogen receptors.
- Relieve excess congestion in breast tissue via stimulation of local lymphatic drainage with lymphatics as well as diuretics to help eliminate excess fluids.
- Use topical applications for symptomatic pain relief and to stimulate local circulation and lymphatic flow.
- Avoid the use of caffeinated products, including coffee, black tea, chocolate, and caffeinated sodas.
- Supplement with vitamins E and B_6.
- Make certain that exercise is appropriate and not causing chest wall pain or strain.
- Make sure that the patient wears adequate breast support and appropriately sized brassieres.
- Acupuncture may be beneficial for relieving symptoms of fibrocystic breasts.

ENDOMETRIOSIS

Amanda McQuade Crawford, Aviva Romm

Endometriosis is one of the most common gynecologic problems in the United States and a leading gynecologic cause of both hospitalization and hysterectomy.[25,71,72] Women with symptomatic endometriosis face chronic and sometimes debilitating pain; asymptomatic and symptomatic women alike may experience significant fertility problems due to this condition. The least-biased estimate for the overall prevalence of endometriosis in reproductive-age women is about 10%.[73] Endometriosis is defined as the presence and growth of endometrial tissue in locations outside of the uterus. These cells may appear on the ovaries, fallopian tubes, bowel, bladder, peritoneal tissue, ligaments, or other structures in the abdominal cavity, and rarely may occur at other sites, including the nasal and respiratory passages leading to nosebleeds or pink frothy sputum at the time of the menses. Displaced endometrial tissue responds to cyclic hormonal changes, proliferating and shedding outside of the uterus. The bleeding is accompanied by inflammation caused by irritation of local tissue, such as, the peritoneum. Recurrent inflammation can cause scarring and adhesions that can cause pain and dysfunction of other affected sites. Endometriosis is common in women between menarche and menopause, and is associated with as many as 25% of cases of infertility; however, causality has not been definitively established.[3,73]

Endometriosis occurs across all socioeconomic and ethnic populations, is more common in women who experience early menstruation and fewer than two pregnancies, is associated with menstrual cycle length greater than 30 days, and is more prevalent in women with IUD use greater than 2 years (Box 7-2). Studies demonstrate that women who have experienced repeated vaginal and uterine infections have higher rates of endometriosis than the general population.[3] Women with a mother or sister with endometriosis are more likely to suffer from severe endometriosis, suggesting a genetic predisposition; however, milder forms do not always have familial association. The literature is conflicting on the relationship between oral contraceptive (OC) use and the risk of endometriosis. A 1993 review by Vercellini et al. showed that four prospective investigations found a nonsignificant reduction in risk of up to 20%.[74] Of three case control studies, two suggested an increased risk and one indicated a reduced risk of developing endometriosis with OC use. The 1994 analysis of the Oxford Family Planning Association OC study found a significantly reduced risk of endometriosis in current OC users. The researchers found that OCs were associated with a 60% reduction in endometriosis. The risk of endometriosis

BOX 7-2

Risk Factors for Endometriosis

Possible Risk Factors
Early menarche (before age 12)
Cycles <26 days (= higher frequency)
Heavy bleeds >7 days
IUD use
D&C history
Fewer than two pregnancies
Family history
High stress, especially linked to relationships or sexuality
High fat intake, especially heated fats, fried foods

Risk Reducing Factors
Full-term pregnancies
Breastfeeding
Avoiding caffeine, alcohol
Regular exercise (timing and type are important)

was significantly related to age with the highest risk occurring at ages 40 to 44 years when compared with women ages 25 to 29 years. On the other hand, the risk of endometriosis was elevated among women who formerly used the pill by almost twice the rate of women who had never used OCs.[75–77]

Multiple theories exist on the etiology of this condition, including retrograde menstrual flow, lymphatic flow theory, and de novo origin. In fact, Konickx et al. propose that mild endometriotic lesions are common and to some extent normal at varying times in all women, and that it is symptomatic, aggressive, or deeply infiltrating endometriosis that should be considered a disease.[78] Retrograde menstrual flow theory describes menstrual or endometrial tissue flowing backward through the fallopian tubes and into the abdominal cavity. Lymphatic flow theory suggests the spread of endometrial tissue throughout the body via the lymphatic system. Some researchers postulate that coelomic metaplasia, a de novo origin, might be induced by pathologic processes as a result of chemical exposure. A role for oxidative stress has also been suggested as one of the contributing factors for the development of endometriosis, possibly as part of a conglomeration of factors that pair immunologic and inflammatory factors in its etiology.[79,80]

There is substantial evidence that immunologic factors play a role in the pathogenesis of endometriosis and endometriosis-associated infertility, and that there is a bidirectional relationship between the endocrine and immune systems.[81] In early endometriosis, elevated levels of inflammatory mediators such as cytokines, lymphocytes, and macrophages can be identified in the peritoneal fluid. Immune alterations include increased number and activation of peritoneal macrophages, decreased T-cell reactivity and natural killer cell cytotoxicity, increased circulating antibodies, the presence of autoantibodies, and changes in the cytokine network. Decreased natural killer cell cytotoxicity leads to an increased likelihood of implantation of endometriotic tissue. In addition, macrophages and a complex network of locally produced cytokines modulate the growth and inflammatory behavior of ectopic endometrial implants.[79,82–84] There also may be a positive correlation between immunosuppression and disease progression in the presence of established disease.[85,86] Further, women with endometriosis appear to have higher rates of atopic conditions and susceptibility to opportunistic infections (e.g., candidiasis) than women who do not have endometriosis.[87]

Environmental exposures appear to play a certain role in the development of endometriosis via endocrine disruption. Studies demonstrate a link between dioxin exposure and the disease, with increased dioxin-like compounds found in the serum of women with peritoneal endometriosis and deep endometriotic (adenomyotic) nodules. A search of the BIOSIS database for endometriosis and dioxin yielded over 50 studies. The development of this condition is likely a result of the interplay of numerous factors; thus, it has been concluded by many researchers that endometriosis is, most likely, a condition with complex multifactorial origins.

BOX 7-3

Common Symptoms of Endometriosis

Abdominal pain
Back pain
Depression
Frequent or constant pain that is over site
Infertility
Insomnia, lethargy
Later on, pinched nerve pain
Ovulation pain
Pain on intercourse
Pain with bowel movement or urination
Pelvic burning, aching not limited to menstruation
PMS with dysmenorrhea and infertility
Rarely, bleeding after bowel movements or after intercourse
Referred pain in distant sites, especially shoulder blades or top of collar bone
Swollen abdomen, intestinal gas

SYMPTOMS

The following symptoms (Box 7-3), alone or in constellations, should alert a woman and her practitioner to the possibility of endometriosis: premenstrual pain, dysmenorrhea, dyspareunia, generalized pelvic pain throughout the month without other explanation, atypical periods, nausea, vomiting, exhaustion, bladder problems, frequent infections, dizziness, painful defecation, rectal pain, low backache, irritable bowels, or infertility. The far-reaching nature of these symptoms and their possible association with other conditions helps to explain why this condition is difficult to diagnose. Dysmenorrhea and painful intercourse become even more suggestive of endometriosis if they begin after a history of relatively pain-free menstruation and intercourse. Severity of pain is not indicative of the severity of the condition, with the exception of severe pain, which is associated with extensive endometriosis and adenomyosis (deeply infiltrating endometriosis.)[3,78] Other causes of pelvic and abdominal pain or bleeding must be ruled out.

DIAGNOSIS

Endometriosis is most commonly seen in women 30 to 40 years old and is rarely found in postmenopausal women. Endometriosis has been thought not to occur prior to menarche; however, the rates of this condition are increasing among teenagers.[3] The site of lesions, although widely variable, is generally the posterior cul de sac or ovaries. Diagnosis is based on pelvic examination, diagnostic ultrasound, or laparoscopy, with definitive diagnosis based on laparoscopy. CA-125 is a serum antigen found in endothelial cervical cancer that can also be found to be elevated in women with endometriosis. The diagnostic importance of the test for endometriosis is still uncertain; however, there appears to be some predictive value demonstrating which women

might benefit from specific treatments on the basis of CA-125 levels, and CA-125 levels may indicate whether improvement is occurring.[88] Endometriosis is staged based on the location(s) of the endometrial tissue as follows:

- Stage I, or minimal, disease (superficial endometriosis, filmy adhesions)
- Stage II, or mild, disease (superficial and deep endometriosis, filmy adhesions)
- Stage III, or moderate, disease (superficial and deep endometriosis, filmy and dense adhesions)
- Stage IV, or severe, disease (superficial and deep endometriosis, dense adhesions)

CONVENTIONAL TREATMENT APPROACHES

Medical treatment of endometriosis includes both pharmaceutical and surgical approaches. Pharmaceutical treatments provide only suppression of the disease; they do not exact a cure.[3] Decisions regarding treatment are based on endometriosis severity and staging, symptom picture, and ultimately, the woman's needs and goals, for example, desire for children in the future.[89] For women experiencing mild symptoms (or none) and for women who are close to menopause, the appropriate treatment may be to do nothing.[78] For women with mild to moderate symptoms, and those who desire pregnancy, the appropriate pharmacologic therapy should be considered, and if necessary, can be combined with conservative surgery. It should be noted that, in spite of medical treatment, endometriosis has a high recurrence rate of 5% to 20% unless total hysterectomy and bilateral oophorectomy are performed. With pharmacologic interventions, pain typically resumes upon cessation of medications, although initially with pain that is less intense than prior to treatment. Pain relief, pregnancy rates, and recurrence rates are similar with all treatment methods. The goal of pharmaceutical treatment is to interrupt patterns of endometrial stimulation and bleeding.[89] Pharmaceutical options include nonsteroidal anti-inflammatory drugs (NSAIDs) and hormonal therapies (progestins, GnRH analogs, Danazol, and oral contraceptives). NSAIDs (i.e., ibuprofen, naproxen) may be prescribed for mild to moderate pain. They are relatively safe for short-term symptomatic relief; however, long-term use can lead to health consequences, including gastrointestinal bleeding, and should be avoided in patients with a history of peptic ulcer disease or renal failure. It should be noted that none of these therapies demonstrates significant benefit over the others, and all are associated with a high recurrence rate (20%–50%) upon discontinuation of the therapy.[89] Progestins (medroxyprogesterone acetate, i.e., Depo-Provera) suppress the response of endometrial tissue to cyclic hormones, leading to atrophy of this tissue and decreased pain. They are typically better tolerated than oral contraceptives (OCs), with fewer side effects, and are less costly than Danazol and GnRH analogs. This is often considered the pharmaceutical treatment of choice for endometriosis, although the FDA no longer supports the use of Depo-Provera for this purpose. Side effects include weight gain, fluid retention, and breakthrough bleeding. Depression is a common significant side effect of medroxyprogesterone use. In high doses, medroxyprogesterone can adversely affect lipid profiles, and may lead to a state of hypoestrogenism, with subsequent potential for bone loss. Oral contraceptives are used to control pain in women not desiring pregnancy. The combined effect of estrogen and progesterone is to induce a state of ''pseudopregnancy,'' and appears to lead to a 90% rate of improved symptoms with long-term use. Side effects include all those typically associated with general OC use. Danazol, a synthetic testosterone, is used for the treatment of mild to moderate endometriosis in women who desire fertility but not necessarily in the immediate future. It induces a state of ''pseudomenopause,'' eliminating mid-cycle FSH and LH surges. Once considered the optimal treatment for endometriosis, it is now considered no more effective than any of the other pharmaceutical treatments. Possible side effects include weight gain, fluid retention, fatigue, decrease in breast size, hirsutism, atrophic vaginitis, hot flashes, muscle cramps, emotional fluctuations, voice changes, spotting, and decreased HDL cholesterol levels. In some patients it may cause hepatocellular damage; thus is contraindicated in patients with liver disease, and liver enzymes should be monitored in all patients during treatment. It is also contraindicated in patients with a history of hypertension, hyperlipidemia, congestive heart failure, renal impairment, and pregnancy.[3,25,89,90] Gonadotropin-releasing hormone analogues (GnRH-a, e.g., Leuprolide) also cause a suppression of endometriosis via a ''pseudomenopausal'' state. GnRH treatment does not carry the same risks of negative impact on serum lipids and lipoproteins compared with Danazol; however, it does interfere with calcium metabolism via stimulation of a hypoestrogenic state, and thus can cause osteoporosis. Even after only 6 months of use, a 6% to 8% loss in trabecular bone has been observed. It can take up to 2 years after cessation of treatment to replace this bone loss; thus a treatment is usually restricted to 6-month durations.[3,91]

Surgical options include conservative surgery (destruction and removal of endometriomas while maintaining reproductive function) and radical surgery (hysterectomy, generally accompanied by bilateral salpingo-oophorectomy). Conservative treatment involves the removal of endometriotic lesions and restoration of normal anatomical relationships via removal of adhesions to the greatest extent possible, with the goal of pain relief, and possible restoration of fertility when achieving pregnancy is desired and has been impaired by the condition. In approximately one-fourth of women treated surgically, however, there is no improvement in fertility even if the disease was considered mild. Procedures include knife excision, laser surgery, electrocautery, curettage, and laparotomy. The worse the disease, the worse the statistics for conceiving after surgery.[92,93] Recurrence of endometriosis after surgery is dependent on the skill of the surgeon and extent of disease, and as with other endometriosis treatments, rates may be as high as 20%. Hysterectomy will not remove lesions outside the uterus and is not considered a

successful treatment when used primarily to reduce the symptom of chronic pelvic pain. Surgery carries the risk of complications, especially adhesion formation and continuing pain. The total rate at which symptoms of chronic pelvic pain returned after drug treatment is estimated to be 5% to 15% at the end of 1 year, or up to 50% at the end of 5 years. Nonetheless, the risks of surgery or medication may be justifiable for severe pain that does not respond to other methods, especially if menopause is not expected for some time. There is a concern that diagnostic microsurgery may aggravate or cause the transfer of viable endometrial cells into general or lymphatic circulation, thereby causing the very condition being identified. Because of this, some wary clients choose natural treatment approaches for the condition without a certain diagnosis, believing that if the signs and symptoms respond, the holistic prescription was correct for the presumed diagnosis.

BOTANICAL TREATMENT

Herbalists share the conventional medical perspective that endometriosis has multifactorial causes. The botanical approach, however, takes into consideration immune dysregulation, inflammation, hormonal dysregulation, diet and nutritional status, lifestyle, exposure to exogenous estrogens, and the woman's emotional and psychological mechanisms for coping with this condition as components of a whole picture. Given that nonradical medical treatments for endometriosis are purely suppressive rather than curative, the high recurrence rate of endometriosis upon cessation of pharmaceutical treatment, and the potential for drug-related or surgical side effects, botanical medicines may provide women with a safe alternative for symptomatic pain relief, reduction of inflammation, prevention and reduction of recurrent vaginal and pelvic infections, stress reduction, and improvement of overall immunologic health (Table 7-4). By applying a comprehensive natural health care protocol, many cases of endometriosis can also be resolved. The herbal approach should also include as part of the protocol, herbs that address concomitant discomforts arising from the condition, such as irritable bowel complaints or depression.

Many herbs have multiple actions. Varying degrees of success have been obtained when improving as many of the known cofactors as possible. However, the mechanisms behind the success of herbal protocol are not well elucidated nor understood, and clinical successes are inconsistent. In fact, many Western herbalists consider endometriosis hard to completely ''cure,'' and ultimately focus on symptom control and overall health improvement. There are well-developed treatment protocols for the treatment of endometriosis in traditional Chinese medicine (TCM) that have been associated with successful treatment. By applying a comprehensive natural protocol, endometriosis may be entirely resolved in some cases, and made significantly less problematic in many. The following section discusses the general Western botanical treatment approaches for endometriosis as well as a brief overview of TCM approaches. Fertility treatments appear in a chapter devoted to that subject. Also see chronic pelvic/vaginal pain, vaginal infection, dysmenorrhea, and other relevant topics under separate headings.

The following factors have been noted in endometriosis patients, but this does not explain why all patients with SOME of these findings do not necessarily have the other syndromes associated with these factors (e.g., PMS):

- Estrogen excess
- Progesterone deficiency
- Magnesium deficiency
- Essential fatty acid deficiency
- High stress (often complicated by hypoglycemia)
- Hormone imbalance other than progesterone/estrogen ratio
- Excess dietary caffeine
- Excess alcohol consumption

Attention to these factors may help some women with symptom reduction and regression of size and infiltration of endometriotic tissue.

DISCUSSION OF BOTANICALS

For many women with endometriosis pain is the single most debilitating aspect of this condition (other than chronic fertility problems in women desiring pregnancy). Therefore, pain management should be an important focus in the care of women with this condition. Herbalists reliably employ a number of herbs for the treatment of pelvic and abdominal pain, many of which have a long history of traditional use for painful gynecologic conditions. These herbs can be used singly but are generally used in various combinations with other herbs in these categories, or as part of a larger protocol. Analgesic herbs are used for generalized or local pain of an aching or sharp quality and include black cohosh, black haw and cramp bark, chamomile, corydalis, pulsatilla, dong quai, ginger, and Jamaican dogwood. Corydalis, Jamaican dogwood, and pulsatilla are especially dependable for moderate to serious pain. Pulsatilla is considered specific for ovarian pain.[22] Antispasmodics are typically used for cramping pain, but also may be used for sharp or dull pain, aching, and drawing pains in the lower back and thighs, and include, such as wild yam, the viburnums (cramp bark and black haw), black cohosh, chamomile, and ginger. Dong quai's traditional TCM uses for gynecologic conditions, specifically for conditions of blood vacuity and stasis, the latter of which endometriosis may be considered among, along with its antispasmodic, anti-inflammatory, and immunomodulatory qualities, make it an important herb to consider.[25,50,94] Many antispasmodics and anti-inflammatories, such as wild yam, the viburnums, ginger, and chamomile are specific not only for uterine pain, but also for intestinal, bowel, and urinary pain and irritability, making them uniquely suitable for endometrial pain and accompanying bowel and bladder discomforts. This is important to keep in mind, because the pain of endometriosis is related to irritation of tissue by endometrium outside of its normal site in the uterus. Sedatives are useful when there is the need to induce deep rest or sleep to obtain pain relief, and include

TABLE 7-4

Botanical Treatment Strategies for Endometriosis

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Pain relief	Analgesics	*Anemone pulsatilla*	Pulsatilla
	Anodynes	*Angelica sinensis*	Dong quai
	Sedatives	*Actaea racemosa*	Black cohosh
		Corydalis ambigua	Corydalis
		Eschscholzia californica	California poppy
		Matricaria recutita	Chamomile
		Paeonia lactiflora	White peony
		Piper methysticum	Kava kava
		Piscidea piscipula	Jamaican dogwood
Pain relief	Anti-inflammatory	*Angelica sinensis*	Dong quai
		Calendula officinalis	Calendula
		Camellia chinensis	Green tea
		Echinacea spp.	Echinacea
		Glycyrrhiza officinale	Licorice
		Hypericum perforatum	St. John's wort
		Matricaria recutita	Chamomile
		Oenothera biennis	Evening primrose
		Paeonia lactiflora	White peony
		Prunus cerasus	Cherry
		Rehmannia glutinosa	Rehmannia
		Tanacetum parthenium	Feverfew
		Zingiber officinale	Ginger
Pain relief	Antispasmodics	*Dioscorea villosa*	Wild yam
		Actaea racemosa	Black cohosh
		Matricaria recutita	Chamomile
		Paeonia lactiflora	White peony
		Viburnum opulus	Cramp bark
		Viburnum prunifolium	Black haw
		Zingiber officinale	Ginger
Immunologic support, reduction in fatigue, depression and concomitant psycho-emotional symptoms	Immunostimulatory herbs Adaptogens	*Angelica sinensis*	Dong quai
		Astragalus membranaceus	Astragalus
		Calendula officinalis	Calendula
		Cordyceps sinensis	Cordyceps
		Echinacea spp.	Echinacea
		Eleutherococcus senticosus	Eleuthero
		Panax ginseng	Ginseng
		Panax quinquefolius	American ginseng
		Picrorrhiza kurrhoa	Picrorrhiza
		Rhaponticum carthimoides	Rhaponticum
		Rhodiola rosea	Rhodiola
		Schisandra chinensis	Schisandra
		Thuja arbor-vitae	Thuja
		Withania somnifera	Ashwagandha
Improve pelvic circulation and tone; reduce size and extent of endometriotic tissue	Emmenagogues Uterotonic herbs	*Achillea millefolium*	Yarrow
		Alchemilla vulgaris	Lady's mantle
		Caulophyllum thalictroides	Blue cohosh
Hormonal regulation: Indirect via enhanced clearance of estrogen by liver and bowel, improved hormone metabolism by liver, improvement of healthy hepatic function	Hepatic trophorestoratives Aperients Cholagogues Hepatics	*Calendula officinalis*	Calendula
		Chionanthus virginicus	Fringe tree
		Curcuma longa	Tumeric
		Rosmarinus officinalis	Rosemary
		Schisandra chinensis	Schisandra
		Silybum marianum	Milk thistle
		Taraxacum officinale	Dandelion
Hormonal regulation:Direct via known or putative hormonal actions	Hormonal regulators	*Gossypium herbaceum*	Cotton root
		Verbena officinalis	Blue vervain
		Vitex agnus-castus	Chaste tree
Improve pelvic and abdominal lymphatic circulation; enhance immunologic function	Lymphatics	*Calendula officinalis*	Calendula
Stress relief	Nervines	*Leonurus cardiaca*	Motherwort
		Verbena officinalis	Blue vervain

Also see chapters discussing vaginal infection, dysmenorrhea, UTI, and fertility problems for additional protocols.

Formulae for Dysmenorrhea

Formula for Treatment of Mild to Moderate Pain Associated with Dysmenorrhea

Black cohosh	(*Actaea racemosa*)	20 mL
Cramp bark	(*Viburnum opulus*)	20 mL
Chamomile	(*Matricaria recutita*)	15 mL
Dong quai	(*Angelica sinensis*)	15 mL
Wild yam	(*Dioscorea villosa*)	15 mL
Licorice	(*Glycyrrhiza glabra*)	10 mL
Ginger	(*Zingiber officinale*)	5 mL

Total: 100 mL

Dose: 2.5 to 4 mL every 2 to 4 hours during episodes of endometrial discomfort. This can also be given 3 mL three times daily prophylactically for women who experience predictable cyclic pain associated with endometriosis.

Formula for Treatment of Moderate to Severe Pain Associated with Dysmenorrhea

Black cohosh	(*Actaea racemosa*)	25 mL
Cramp bark	(*Viburnum opulus*)	25 mL
Wild yam	(*Dioscorea villosa*)	20 mL
Corydalis	(*Corydalis ambigua*)	15 mL
Jamaican dogwood	(*Piscidea piscipula*)	15 mL

Total: 100 mL

Dose: For severe acute pain take 2.5 mL every 15 minutes until pain begins to subside, or for up to 2 hours consecutively, then reduce dose to 2.5 to 5 mL every 2 to 4 hours as needed.

Sedative Formula for Severe Pain Associated with Endometriosis

Cramp bark	(*Viburnum opulus*)
California poppy	(*Eschscholzia californica*)
Jamaican dogwood	(*Piscidea piscipula*)

Dose: Combine equal parts of the above liquid extracts and take 2.5 mL every 15 minutes for 1 hour to induce sleep.

California poppy, a combination of black cohosh and cramp bark, or a combination of cramp bark and Jamaican dogwood. Valerian and hops are also useful sedatives. The successful use of these herbs for pain depends largely upon adequate dosing and frequency of administration.

Immunomodulation

The exact immunologic underpinnings of endometriosis remain uncertain. There appears to be a complex interplay of hyperimmune, autoimmune, and hypoimmune function at work, either variably or concurrently-leading only to the clear understanding that there is some level of immune dysregulation that accompanies this condition. The most appropriate response seems to be twofold: (1) to look at the unique constellation of symptoms presented by each individual woman, for example, whether she is depleted and susceptible to frequent colds and repeated vaginal infections or chronic atopic conditions—and to treat accordingly, and (2) to provide botanicals which support immune regulation—notably, the adaptogens. For women who evidence a state of immune depletion in combination with endometriosis some amount of immunostimulation may be appropriate to bolster the overall immune response, and may be provided through the use of herbs such as echinacea, astragalus, or *Picrorrhiza kurrhoa* in combination with adaptogens such as ashwagandha, American ginseng, rhaponticum, or rhodiola. These women also may benefit greatly from medicinal mushrooms such as Reishi and Cordyceps for immune support. For women with signs of hyperimmunity, atopic conditions such as eczema or chronic rhinitis, or autoimmunity, the use of immunosupportive anti-inflammatory adaptogens may be most appropriate, such as licorice, ashwagandha, and American ginseng. It is unknown and a matter of great debate as to whether immunostimulating herbs such as echinacea and astragalus are safe and appropriate for use when there is autoimmunity.[22] Using adaptogens for treating endometriosis makes sense in that their actions simultaneously influence and restore normalcy to the functions of the immune system and the HPA axis, both of which appear to have dysregulated function in this condition. The uterine endometrium is a complex structure of interspersed glandular tissue and endometrial stroma, closely associated with lymphoid tissue.[81] The inclusion of herbs that are traditionally thought to improve lymphatic circulation, such as calendula, echinacea, cleavers, and pokeroot, are commonly included in botanical protocol for endometriosis.

Anti-Inflammatories and Antioxidants

Inflammation is a hallmark of endometriosis, and as discussed, free radical damage may be part of the etiology of this disorder. It has been suggested that growth factors and inflammatory mediators produced by activated peritoneal leukocytes participate in the pathogenesis of endometriosis by facilitating endometrial cells growth at ectopic sites.[81] Elevated levels of inflammatory cells and mediators such as peritoneal macrophages, prostaglandins, proteolytic enzymes, complement fragments, IL-1, and tumor necrosis factor (TNF) have been identified in the peritoneal fluid of patients with endometriosis.[81] Numerous herbs that have been used traditionally for inflammatory types of conditions demonstrate significant anti-inflammatory and antioxidant effects and should be considered for use in formulations for treatment and symptomatic relief, along with herbs whose use for inflammation is only recently being discovered. These are discussed in the following.

Dong Quai

Dong quai has antispasmodic, analgesic, and tonic effects, and has demonstrated significant antioxidant and free radical scavenging actions, partially through inhibition of anion radical formation. Limited animal and in vitro studies have reported on the specific

immunomodulatory effects of dong quai, including a stimulation of phagocytic activity and interleukin-2 (IL-2) production, and an anti-inflammatory effect. There is evidence to suggest that the polysaccharide fraction of dong quai may contribute to these effects. Immunostimulatory and anti-inflammatory effects have also been documented for isolated ferulic acid. Dong quai has been traditionally used in Chinese medicine for the treatment of ''blood stasis,'' which encompasses a diagnosis of endometriosis.

Echinacea

Echinacea is widely used by herbalists for its immunostimulatory and anti-inflammatory effects, to support and promote the body's natural immune responses.[25,95,96] Antioxidant effects appear to include free radical scavenging mechanisms and transition metal chelating, whereas immunostimulating effects include enhanced phagocytosis, and the stimulation of cytokine and immunoglobulin production.[29,97]

Feverfew

Feverfew has been used for the treatment of menstrual complaints since at least the time of the ancient Greeks. In fact, its botanical name may reflect such use—*parthenos* means ''virgin'' in Greek.[98] It is mentioned by the Eclectic physicians for use in the treatment of menstrual irregularity.[99] Feverfew also has been used for the treatment of other inflammatory conditions, including headache, fever, psoriasis, and arthritis. Although studies have not been done on the use of this herb in the treatment of endometriosis, and indeed, it is not widely discussed for such use even in the herbal literature, its pharmacology and actions as an antinociceptive and anti-inflammatory suggest that consideration of such use is warranted.[100] Feverfew has exhibited inhibition of prostaglandin synthetase, which inhibits the conversion of arachidonic acid to inflammatory prostaglandins, inhibits mast cell degranulation and subsequent histamine and serotonin release, and has shown inhibition of other inflammatory cytokines such as TNF-α, IL-1, NFκB, and IFN-γ, as well as inhibiting peritoneal cyclooxygenase in animal models.[97]

Ginger

Herbalists use ginger root as an anti-inflammatory and antispasmodic herb for the treatment of numerous painful inflammatory conditions from arthritis to dysmenorrhea.[101,102] No studies have been identified for its use for painful gynecologic complaints. One trial of 120 women reported ginger to be an effective antiemetic for the treatment of postoperative nausea, with specific trials demonstrating its efficacy in reducing postlaparoscopic gynecologic procedures. However, two other trials demonstrated either no effect compared to placebo, or negative effect (increased nausea) with increased doses of ginger.[97] Ginger remains popular among Western and TCM herbalists as an antispasmodic treatment for dysmenorrhea.[25] It is taken in tincture form in combination with other herbs, in infusions, and also used externally as a poultice and in baths for pelvic discomfort.

Gotu Kola

Numerous studies support the traditional uses of the popular Ayurvedic herb gotu kola to promote wound healing, and as an anti-inflammatory and antimicrobial herb. Additionally, it has been demonstrated to have antiproliferative and antioxidant effects, and to prevent the formation of keloid scar tissue.[103–107] Its use as a neurogenerative and neurotrophoretorative adaptogen makes it particularly useful in the treatment of stress disorders, and may play some role in its mediation of other effects.[108] Given the association of these actions with the clinical and etiologic picture of endometriosis, this herb deserves consideration as part of a protocol for this condition both when botanical treatment is the primary modality, or to heal from surgical intervention and reduce adhesion and scar formation. Gotu kola is typically used in combination with other herbs as part of a comprehensive formula.

Green Tea

Green tea is rich in polyphenolic compounds, with catechins as its major component. Studies have shown that catechins possess diverse pharmacologic properties that include antioxidative, anti-inflammatory, anticarcinogenic, and antibacterial effects. Tea catechins are well absorbed in the gastrointestinal tract; thus drinking unfractionated green tea is the most simple and beneficial way to consume this herb.[109,110]

Licorice, Calendula, and St. John's Wort

Licorice root (*Glycyrrhiza glabra*) and calendula blossoms (*Calendula officinalis*) are used by herbalists as anti-inflammatory herbs, and may frequently be included in formulae for treating endometriosis. The aim of one recent study was to investigate whether standardized hydroalcoholic plant extracts such as calendula, St. John's wort, plantain (*Plantago lanceolata*), and licorice can suppress the activities of 5-lipoxygenase (5-LO) and cyclooxygenase-2 (COX-2), key enzymes in the formation of proinflammatory eicosanoids from arachidonic acid (AA). The researchers concluded that licorice extract might be a potential drug possessing anti-inflammatory activity devoid of the most troublesome (gastric) side effects seen for drugs used as COX-2 and 5-LO inhibitors. They purport that St. John's wort, plantain, and licorice extracts can be added to an already impressive list of botanicals with anti-inflammatory activity.[111]

Peony and Rehmannia

Two herbs commonly used in TCM formulae, peony and rehmannia, have demonstrated significant anti-inflammatory and antispasmodic activity. Both are specifically recommended by Mills and Bone for endometriosis, whereas Low Dog discusses the use of peony in the traditional Japanese medicine Shakuyaku-kanzo-to (which also contains the anti-inflammatory *Glycyrrhiza uralensis*).[22,25,108] Studies using the latter formula have demonstrated prostaglandin production inhibition in the uterine myometrium via phospholipase A2 inhibition, whereas other studies have demonstrated arachadonic acid inhibition, PAF inhibition, reduction in free

radical formation, and smooth muscle relaxation. Note that nearly all of the studies use these herbs in traditional formulae rather than in isolation, and that studies are conducted in animal models, and have focused on arthritis, ulcers, and other chronic inflammatory conditions. Licorice, a potent anti-inflammatory, is frequently included in TCM formulae that also contain peony and rehmannia, as is dong quai when these herbs are used for gynecologic conditions. It must be remembered that in TCM, herbs are not prescribed on the basis of a disease entity or a pharmacologic expectation of efficacy, but rather on an individual diagnostic approach using traditional parameters and categories.

Sour Cherries and Raspberry Fruit

Although not part of a traditional botanical approach to gynecologic problems, interesting new data suggests that sour cherry anthocyanins may have a beneficial role in the treatment of inflammatory pain. The antihyperalgesic effect may be related to the anti-inflammatory and antioxidant properties of anthocyanins and was found comparable to the commercial antioxidants and superior to vitamin E, at a test concentration of 125 μg/mL.[112] Anthocyanins from raspberries (*Rubus idaeus*) and sweet cherries (*Prunus avium*) demonstrated cyclooxygenase-I and cyclooxygenase-II inhibitory activities comparable to those of ibuprofen and naproxen at 10 μM concentrations.[113] The value of these findings in endometriosis is not known, but perhaps this is a worthy reminder that a diet rich in deep-colored berries and other fruits and vegetables may hold a key to improving health and preventing disease.

Hormonal Modulation

Predicated on the belief that steroid hormones are the primary regulators of the growth and activity of ectopic endometrial tissue, therapies aimed at hormonal modulation have been the foundation of conventional therapy for endometriosis, and have also featured prominently in botanical protocol.[81] Unfortunately, even less is known about the effects of botanical therapies on the endocrine system than about pharmaceutical medications. The goal of pharmaceutical therapies is to create an acyclic, low-estrogen environment that prevents bleeding, leads to atrophy of ectopic implants, and possibly minimizes retrograde bleeding. However, endometrial tissue may be histologically different than normal uterine endometrial tissue, and may respond differently to hormonal stimulation. Again, much remains unknown about this enigmatic condition.[81] Several botanicals are frequently used as hormonal modulators, in conjunction with other herbs discussed in this chapter. Little research is available on their application in endometriosis. But as part of a comprehensive protocol, many herbalists and naturopathic physicians report positive outcomes for achieving the goals established earlier in this paragraph. There is also some small discrepancy in the herbal literature as to which herbs should be avoided due to potential exacerbating hormonal effects. For example, Mills and Bone caution against the use of what they refer to as ''estrogen promoting herbs'' such as false unicorn (*Chamaelirium luteum*), the use of which should primarily be avoided in clinical practice due to its endangered status) and wild yam (*Dioscorea villosa*); however, wild yam is used widely for abdominal and pelvic cramping pain associated with the condition, whereas the late Silena Heron included these in endometriosis protocol and authors Hobbs and Keville, in *Women's Herbs, Women's Health*, mention wild yam as an antispasmodic specifically for endometriosis.[22] There would actually potentially be numerous plants in this category, ranging from fennel and hops to common foods such as legumes, most of which are rich in phytoestrogens, which would need to be avoided on this presupposition. One study on the estrogenic contents and activity of commonly used herbs found that soy, red clover, licorice, hops, and fo-ti have a large amount of measurable estrogen bioactivity not previously reported. Chaste tree berry, black cohosh, and dong quai did not have measurable activity with the methods used in the study.[114] Confusion stems largely from the fact that so much remains unknown about the endocrine effects of botanicals, and until more information is available, rational conclusion are hard to draw, suggesting that caution and observation of clinical response are required. Women with a predisposition to estrogen-dependent cancers are probably wise to avoid unnecessary and excess consumption of herbs with estrogenic effects. However, it should also be considered that herbs that competitively bind with estrogen receptors might actually displace endogenous estrogen with weaker, plant-based estrogens, actually decreasing a woman's overall estrogen response.

Blue Vervain

Blue vervain (Fig. 7-3) has a long history of use in traditional European herbalism as an emmenagogue and galactagogue, and a contemporary popularity among herbalists experienced in women's reproductive care for its regulating effects on gynecologic complaints, particularly for irritability associated with PMS. A BIOSIS database search and extensive review of the herbal literature references yields very little data on the medicinal uses of this plant, although historical references to its use as a treatment for rheumatism were identified.[29,115] A single study from 1974 on the effect of this herb on the uterus and its interactions with prostaglandins was identified but not obtainable. According to studies cited in Wichtl et al., hot water extracts of European verbena stimulates luteinizing hormone (LH) and FSH secretion. Other noted endocrine effects include antithyrotropic and abortifacient effects via inhibition of human chronic gonadotropin (hCG). Verbena has also demonstrated immunomodulatory effects, primarily through inhibition of phagocytosis by human granulocytes.[29] The German Commission E cites its uses, among other things, for irregular menstruation, nervous disorders and exhaustions, and complaints of the lower urinary tract; however, the efficacy for these claims remains unsubstantiated.[29] Many herbalists consider it an excellent herb for ''sluggishness of the liver,'' and attribute its hormonal action to stimulated liver function and subsequent actions on hormonal metabolism and elimination. It is typically

Figure 7-3 Blue vervain (*Verbena officinalis*). (Photo by Martin Wall.)

used as a small part of a larger general formula aimed at treating underlying causes of endometriosis.

Chaste Berry

Chaste berry has a reputation for its ability to regulate female menstrual cycles and relieve complaints and complications stemming from dysregulation of sex hormones. Clinical trials support the use of Vitex for menstrual irregularities (secondary amenorrhea, oligomenorrhea, polymenorrhea), relief of PMS symptoms, mastalgia, latent hyperprolactinemia, and infertility due to luteal phase dysfunction.[116] The effects of Vitex on estrogen levels remains uncertain, with one study (the full details of which were undisclosed) demonstrating its ability to elicit estrogen-like effects (increased uterine growth) in ovariectomized rats, and another reporting decreased estradiol levels, whereas other studies have reported no effects or were inconclusive.[116] Its efficacy in the treatment of endometriosis, for which is it widely used by herbalists, is supported by clinical observation, with no research identified for its use for this condition.

Cotton Root

Cotton is predominantly used as a uterine tonic and to stimulate uterine contractions. Gossypol, the active ingredient in the roots and seeds of cotton, has been used in the treatment of gynecologic disorders ranging from uterine myomas to menopausal bleeding, based on the discovery that regular cooking with cottonseed oil over long periods of time leads to amenorrhea and endometrial atrophy in females. Several studies over a 15-year period have demonstrated short-term efficacy of up to almost 90% in the treatment of endometriosis, and long-term effectiveness after 1 to 3 years of 54% to 63%. Treatment is typically accompanied by amenorrhea persisting for up to 6 months in 80% of women, and up to 1 year in 16% of women, with 4% experiencing amenorrhea lasting longer than 1 year.[117] Gossypol is reported to antagonize the actions of estrogen and progesterone, and may mimic a pseudomenopausal state.[117] A frequent side effect of gossypol treatment is hypokalemia, which is treated with administration of slow-releasing potassium salts. High-dose programs can lead to elevated liver enzymes, nausea, edema, and palpitations, as well as possible rash, reduced appetite, fatigue, and possible inhibition of thyroid function and mitochondrial energy metabolism. This compound is not available in the West, and would be considered a pharmaceutical drug rather than a botanical product were it made so. Studies on the use of cotton root bark, used, as a partus-preparator, emmenagogue, and abortifacient by Western herbalists, as an herbal extract for endometriosis have not been conducted.

St. John's Wort

According to modern clinical research, St. John's wort is commonly used for the treatment of mild to moderate depression and additionally has been shown to exhibit antiviral activity. In traditional herbal medicine currently and historically, it is used internally for anxiety and as a general nervous system tonic, whereas externally it is used as a primary application for scrapes and burns. Recent concerns regarding the interaction between St. John's wort and numerous pharmaceutical drugs have led to a host of contraindications for use of this herb. One such contraindication is the use of oral contraceptives, as it has been shown to induce the activity of cytochrome P450 3A4 (CYP3A4) and increase the clearance of numerous drugs and steroids, such as cortisol and ethinyl estradiol.[118] This interaction suggests the potential for use of St. John's wort to positively interfere with estrogen binding in states of estrogen excess, for example, in endometriosis. A limited number of studies have evaluated the estrogen-binding capacity of St. John's wort extracts. One study by Simmen et al. found that estrogen binding was 50% inhibited by the bioflavonoid I3,II8-biapigenin at micromolar concentration in the CNS.[119] Use of St. John's wort to deliberately modulate estrogen levels represents a potentially novel application for this botanical. This herb should also be considered in endometrioses treatment for its beneficial role in the treatment of mild to moderate depression, which may accompany this condition in women who suffer with it chronically.

Hepatics, Aperients, and Cholagogues

The use of herbs to improve hepatic function and affect the improved metabolism and elimination of excess hormones has been discussed throughout this text. Herbs for these purposes are commonly included in many gynecologic formulae in which there is estrogen dominance or excess, including endometriosis. Popular choices include calendula, fringe tree, tumeric, rosemary, schizandra, milk thistle, and dandelion root. Mechanisms of action are not clearly elucidated for many of these herbs, but likely include increased bile release leading to enhanced bowel elimination of estrogens, increased CYP450 activity, and improved liver health through antioxidant activity.

Uterotonics and Emmenagogues

Although the effect of uterotonic herbs, commonly included by herbalists in formulae for endometriosis, on endometrial tissue outside the uterus is dubious, uterotonic herbs may play a role in reducing retrograde menstruation via tonic and expulsive action, or other unknown mechanisms, for example, unidentified hormonal actions. Herbs that are commonly included as uterotonics in endometriosis formulae include blue cohosh, Lady's mantle, and yarrow.

CASE HISTORIES: ENDOMETRIOSIS

Endometriosis Patient #1

Lori, 35, is a highly stressed lawyer who smokes and experiences moderate to severe pain associated with endometriosis. She plans to quit smoking as soon as she gets a new job, marries, and moves this year. She hopes to have children soon after.

Tincture Formula I (ovulation through end of menses)

Chaste berry	(*Vitex agnus-castus*)	12.5 mL
Black haw	(*Viburnum prunifolium*)	25.5 mL
Blue vervain	(*Verbena officinalis*)	25.5 mL
Yarrow	(*Achillea millefolium*)	12.5 mL
Milky oats	(*Avena sativa*)	12.5 mL
Corydalis	(*Corydalis ambigua*)	12.5 mL
		Total: 100 mL

Dose: 5 mL diluted in ¼ cup water tid.

Tincture Formula II (end of menses to ovulation)

Chaste berry	(*Vitex agnus-castus*)	25 mL
Calendula	(*Calendula officinalis*)	12.5 mL
White peony	(*Paeonia lactiflora*)	20 mL
St. John's wort	(*Hypericum perforatum*)	30 mL
Partridge Berry	(*Mitchella repens*)	12.5 mL
		Total: 100 mL

Dose: 5 mL diluted in ¼ cup water tid.

Endometriosis Patient #2

Karen is a 21-year-old with no previous history of reproductive problems. After acute abdominal pain she was diagnosed with endometriosis by ultrasound, but decided against medication or surgery. She has abdominal pain and bloating, with spotting and heavy menstruation.

Tincture Formula I (ovulation through end of menses)

Chaste berry	(*Vitex agnus-castus*)	12.5 mL
Cramp bark	(*Viburnum opulus*)	25 mL
Blue vervain	(*Verbena officinalis*)	25.5 mL
Ashwagandha	(*Withania somnifera*)	25 mL
Black cohosh	(*Actaea racemosa*)	12.5 mL
		Total: 100 mL

Dose: 5 mL diluted in ¼ cup water tid.

Tincture Formula II (end of menses to ovulation)

Chaste berry	(*Vitex agnus-castus*)	20 mL
Blue Cohosh	(*Caulophyllum thalictroides*)	10 mL
Sarsaparilla	(*Smilax ornate*)	10 mL
Milk Thistle	(*Carduus marianus*)	20 mL
Partridge Berry	(*Mitchella repens*)	10 mL
Wild Yam	(*Dioscorea villosa*)	20 mL
Valerian	(*Valeriana officinalis*)	10 mL
		Total: 100 mL

Dose: 5 mL diluted in ¼ cup water tid.

NUTRITIONAL CONSIDERATIONS

In addition to a balanced whole foods diet, use high-quality oils, and minimize consumption of caffeine, sugar, alcohol, red meat, and large amounts of dairy. Also avoid excess refined carbohydrates, and address hypoglycemia with frequent small meals and snacks with high protein and complex carbohydrates. Adequate consumption of essential fatty acids is important; encourage two to three servings of salmon or other high-quality cold-water fish per week. Fatty acid–mediated mechanisms have demonstrated decreased cytokine-induced adhesion molecule expression, thereby reducing inflammatory leukocyte–endothelium interactions and modified lipid mediator synthesis, thus influencing the transendothelial migration of leukocytes and leukocyte trafficking in general. Even the metabolic repertoire of specific immunocompetent cells such as cytokine release or proliferation is modified by n-3 fatty acids. Beyond this these fatty acids regulate lipid homeostasis shifting the metabolic pathways toward energy supply, thus optimizing the function of immune cells. Because of the regulatory impact on different processes of inflammatory and immune cell activation n-3 fatty acids provide positive effects on various states of immune deficiencies and diseases with a hyperinflammatory character, among which selected examples are presented.[120]

Choose Between*:

Evening primrose oil: 3 g/day (may be cost prohibitive to some)

*When taking fatty acid supplements, it is important to increase antioxidant intake.

Omega-3: 600 mg EPA
Flax oil: ⅛ tsp to 1 tbl daily
Flax seed oil starting at ⅛ tsp doses, up to 1 tsp per dose or more as individuals can tolerate.

B vitamin supplementation may assist in hepatic metabolism of estrogens and are recommended as part of an overall multivitamin and mineral supplement.

ADDITIONAL THERAPIES

Lifestyle Management

Provide counseling to address psychosocial issues; suggest stress reduction techniques (e.g., yoga, meditation, counseling, visualization).

Exercise

Regular exercise, such as yoga, to reduce pelvic tension and improve suppleness, as well as relieve general tension and fatigue, should be encouraged.

Treatment Summary for Endometriosis
- Improve nonspecific immunity with adaptogens, immunomodulators.
- Reduce inflammation.
- Improve organ and tissue health where possible using uterine tonics.
- Decrease exposure to xenoestrogens.
- Decrease relative excess of estrogen.
- Increase liver function for hormone metabolism, from cholesterol synthesis to steroidal catabolism.
- Manage pain using antispasmodics.

CERVICAL DYSPLASIA: BOTANICAL AND NATUROPATHIC APPROACHES

Mary Bove and Aviva Romm

Cervical dysplasia describes cervical cells with an atypical appearance, loss of uniformity in cell structure, and loss of their normal architectural orientation. Each year between 250,000 and 1 million women in the United States are diagnosed with cervical dysplasia. It can occur at any age, but the mean ages are 25 to 35 years old. Atypia and dysplasia can be caused by inflammation, cervical intraepithelial neoplasia (CIN), or carcinoma in situ (CIS) (see Staging). Atypical cervical cells can be a precursor to invasive cervical cancer. Mild dysplasia is the most common form of cervical dysplasia, and up to 70% of these cases regress on their own, the cervical tissue returning to normal without treatment. Moderate and severe dysplasias are less likely to resolve spontaneously and have a higher rate of progression to cancer. The greater the abnormality of the cells as determined by staging, the higher the risk for developing cervical cancer. Cervical cancer is the third most common gynecological malignancy in US women (see Chapter 11). Cervical dysplasia is inversely related to the age of first intercourse; it is directly related to the number of sexual partners in the woman's lifetime, and the risk increases for the sexual partners of men whose previous partners had cervical cancer. The development of cervical dysplasia and cervical cancer is strongly associated with infection by human papillomavirus (HPV). There are many different types of HPV that are classified as high risk, most notably types 16 and 18. Contributing factors in the transformation of cells from dysplasia to neoplasm

Eclectic Specific Condition Review: Endometriosis
*David Winston**

Endometriosis, or adenomyosis externa, was not recognized as a disease by nineteenth-century physicians. It may have been much rarer than today or simply misdiagnosed as chronic menorrhagia with abdominal pain. Most Eclectic treatments would be to relieve pain and control bleeding, i.e., they are palliative rather than curative.

Blue Cohosh (*Caulophyllum thalictroides*)
Constant, cramp-like endometrial pain.

Canada Fleabane (*Erigeron canadense*)
For heavy endometrial bleeding.

Chaste Tree (*Vitex agnus-castus*)
For general reproductive support, to lower estrogen load, and reduce growth of endometrial tissue (modern clinical use).

Cinnamon (*Cassia cinnamomum*)
To arrest uterine hemorrhage, whether postpartum, menorrhagia, or metrorrhagia.
The essential oil of cinnamon, combined with the essential oil of Canada fleabane (formerly known as Erigeron) in alcohol oil base, was known as Ellingwood's Compound: 10 to 30 gtt of the mixture was put on a sugar cube and taken 1 to 2 per day to stop uterine bleeding.

Cotton Root (*Gossypium* spp.)
Endometriosis with excessive bleeding.

Gravel Root (*Eupatorium purpureum*)
Chronic uterine disease with painful dysmenorrhea.

Helonias Root (*Chamaelirium luteum*)
General reproductive support, and to normalize estrogen/progesterone balance and help eliminate feelings of pelvic engorgement and a bearing down sensation.

Jamaican Dogwood Bark (*Piscidia erythrina*)
Endometriosis of the fallopian tubes with nauseating pain, ashen skin color, and cold sweat.

Tiger Lily: entire fresh plant (*Lilium lancifolium*)
Neuralgic pain in the uterus, ovaries, and fallopian tubes. Excoriating (acid) leucorrhea. Nausea.

White Ash Bark (*Fraxinus americana*)
Decreases cell proliferation in uterine hypertrophy. Helps to restore uterus to normal position, size, and function. Dragging pains in the lower abdomen.

Wild Yam Rhizome (*Dioscorea villosa*)
Endometriosis of the fallopian tubes with painful cramping and ovarian colic.

*For historical purposes only.

are smoking, poor diet, oral contraceptive use, chronic cervicitis, herpes virus infection (HSV), HIV, exposure to DES, immune suppression, and exposure to environmental carcinogens.

DIAGNOSIS

Cervical dysplasia is usually asymptomatic and most commonly discovered upon routine Pap smear. In contrast, cervical cancer may be asymptomatic or present with abnormal vaginal bleeding. Pap testing has significantly reduced mortality from cervical cancer, a privilege of developed nations that if made available worldwide would nearly obliterate this disease. Current guidelines recommend that all women over aged 18 have a Pap test done every 1 to 3 years, depending on individual risk factors and medical history. With routine Pap smears, advanced morbidity and mortality from cervical cancer should be entirely preventable, particularly because it is a slowly progressing cancer allowing plenty of time for detection and treatment. Sadly, 50% of all women diagnosed with cervical cancer have not had a Pap smear in greater than 10 years. Any suspicious lesion should be biopsied directly. Colposcopy-directed biopsy usually provides enough clinical evidence for an accurate diagnosis. The diagnosis of cervical dysplasia is largely anxiety provoking for women because of the association between dysplasia and carcinoma. Therefore, it is important that practitioners take the time to thoroughly explain to each woman the level of concern that is warranted by her degree of dysplasia, and compassionately review options with her.

Staging of Cervical Dysplasia

The Bethesda System was developed by the CDC and NIH as a comprehensive, standardized scheme for classifying Pap smear results. It uses the term squamous intraepithelial lesion (SIL) to describe abnormal changes in the cells on the surface of the cervix. Changes are classified on a scale of low grade to high grade. It has largely replaced previous grading systems.

Bethesda System

- ASCUS (atypical squamous cells of undetermined significance): borderline, some abnormal cells
- LGSIL (low-grade squamous intraepithelial lesions): mild dysplasia and cellular changes associated with HPV
- HGSIL (high-grade squamous intraepithelial lesions): moderate to severe dysplasia, precancerous lesions, and carcinoma in situ (preinvasive cancer that involves only the epithelium)

CONVENTIONAL TREATMENT APPROACHES

Medical treatment depends on the severity of the lesions. For women with preinvasive cervical disease, treatments options include laser therapy, cryotherapy, loop electrical excision procedure (LEEP), and conization biopsy. Most physicians have abandoned laser and cryosurgery because of the inaccuracy of treatment compared to LEEP. The depth of the treatment and amount of collateral tissue damage is easier to control with a LEEP. The LEEP removes tissue precisely and cauterizes simultaneously. Cone biopsy is the removal of a cone-shaped amount of cervix the depth of the entire cervix. In both, the LEEP and the cone biopsy the physician is trying to obtain clean borders, meaning that there is no evidence remaining of cervical dysplastic cells. If the woman has progressed to cervical cancer treatment, it usually consists of a total hysterectomy and/or radiation treatment. Conventional treatment is an efficient solution, usually covered by insurance. However, conventional treatments often cause permanent scarring and do not address potential underlying causes. Scarring can interfere with women's ability to conceive by obstructing the endocervical canal with scar tissue, and damaging cervical crypts that are important in providing proper nutrition for advancing sperm and the proper formation of cervical mucus. The scarring also may interfere with cervical dilatation in labor. Further, conization can occasionally lead to ''incompetent cervix'' during pregnancy, necessitating cervical cerclage, in which a suture is inserted into the cervix to allow the woman to maintain pregnancy and prevent premature labor.

Because of the risks associated with sexually transmitted infections and subsequent cervical dysplasia, current sexual partners should be screened and treated for HPV as necessary. Adolescent girls should be educated about the risk factors for developing cervical dysplasia. The sociologic components of women's health also cannot be ignored. A history of sexual abuse, for example, is not an uncommon clinical finding in women with a history of cervical dysplasia.

BOTANICAL AND NATUROPATHIC TREATMENT

Intrinsic to both herbal and naturopathic treatment of cervical dysplasia is the belief that conventional therapy alone does not address a woman's underlying propensity to dysplasia, nor does it address preventable causes. This is significant as the 5-year return rate, with conventional therapies is as high as 75%. In contrast to conventional approaches, botanical and naturopathic treatments attempt to addresses multifactorial causes, treating the woman, not just her cervix. A disadvantage is that natural medicine protocols are demanding, inconvenient, and potentially costly, requiring multiple office visits. Naturopathic and botanical medicine practitioners emphasize a number of therapies including the use of immune enhancing, anti-inflammatory, hormone-regulating, and antiviral botanicals both for internal and topical treatments.[25,121] Adaptogens often feature prominently in a botanical program to address immune and endocrine function. Stress can depress immune response, which can increase viral activation. Recent lifestyle changes or stressors, even as seemingly benign as exposure to increased amounts of sunlight, may

suppress the immune system sufficiently to cause viral activation.[122] Environmental causes of gynecologic disease—ranging from exposure to excess exogenous estrogens to stress—must be addressed in the long-run for the benefit of all women. (See Endometriosis for a brief discussion of the role of exogenous estrogens on gynecologic health.)

Herbal and naturopathic treatment for the treatment of cervical dysplasia should occur in the context of a complementary relationship with a conventional care provider and in conjunction with appropriate medical care. The development of cervical cancer from dysplasia is highly preventable with proper integrated conventional and natural medical treatment.

An Herbalist's Approach to Cervical Dysplasia

Aviva Romm

Because mild cervical dysplasia has a high rate of spontaneous regression one approach of botanical practitioners is to encourage watchful waiting while using antiviral and immune supportive herbs internally to boost immunity and topically to reduce viral proliferation and inflammation and promote tissue healing. For persistent or more than mild cervical dysplasia, experienced gynecologic botanical practitioners favor the use of the LEEP procedure in combination with the postprocedural use of herbal suppositories and internal therapies to enhance immunity, reduce inflammation, and promote healing. Because stress may play both a contributory role in immune and endocrine dysregulation, and is often a consequence of a diagnosis of cervical dysplasia, long-term use (3 to 6 months) of adaptogens is also commonly recommended. Topical herbal applications consist of insertion of a medicated suppository 5 nights per week for as many as 12 weeks, with a repeat PAP at the end of 12 weeks. Several companies sell preformulated suppositories (see Resources at the end of this chapter). Alternatively, practitioners can make suppositories for patients using a suppository mold, or make a mold available to patients who wish to prepare their own. General instructions for preparing suppositories can be found in Chapter 3, with specific recipes for dysplasia treatment in the following pages. They can be prepared in large batches and kept refrigerated for the duration of treatment for use as needed. If after 3 months of botanical treatment the dysplasia has not improved or has progressed, further medical treatment should be pursued.

Although there are many similarities between botanical and naturopathic treatment of cervical dysplasia, the two approaches diverge over the use of escharotic treatments, a popular naturopathic approach. Escharotics can be caustic and irritating, and are much less controllable and reliable than the LEEP. The direct experience of herbalists with escharotic treatments does not endorse their use. There is no evidence for the efficacy of escharotic treatments for cervical dysplasia, and side effects seen with the LEEP, such as cramping and abdominal pain, may also be seen with escharotics. Additionally, escharotic treatment used topically on other tissue (e.g., for the treatment of breast tumors or skin cancers) has been associated with significant tissue damage in some cases. One observational study reports on dermatologic cases in which four patients had used escharotics in the treatment of basal cell carcinomas (skin cancer) in lieu of the recommended conventional treatment. One patient had a complete clinical response but had a residual tumor on follow-up biopsy. A second patient successfully eradicated all tumors but experienced severe scarring. A third patient disagreed with the physicians regarding her care and was lost to follow-up. One patient presented with a basal cell carcinoma that ''healed'' for several years following treatment with an escharotic agent but recurred deeply and required extensive resection. The lesion eventually metastasized. The researchers concluded that physicians should advise their patients against the use of escharotics. Low Dog states that although at this time there is only anecdotal evidence of the efficacy of escharotic treatments for cervical dysplasia, and because several of the herbs typically used possess antiviral and anti-inflammatory effects, further research is warranted.[25] Nonetheless, their use is popular among naturopathic physicians, and women may choose this option when looking for alternatives to conventional medical treatments. Thus, practitioners should be aware of their use.

Many licensed naturopaths specializing in the treatment of gynecologic complaints report excellent results and a high level of safety when using these preparations. No evidence for efficacy or safety for cervical dysplasia was identified in the literautre.[25] Naturopathic protocols, including the use of escharotics are described in detail in *Women's Encyclopedia of Naturopathic Medicine* by Tori Hudson. It remains a popular alternative that women may seek or be offered through their naturopathic care provider. It is strongly urged that only licensed NDs with adequate training and experience in the use of escharotic treatment for cervical dysplasia be consulted for this procedure.

Herbs commonly used internally and topically, both for herbal and naturopathic treatments are listed in Table 7-5. Evidence and discussion of adaptogens is found elsewhere in this volume. Readers are also referred to the chapter on cervical cancer for relevant botanical information as well as to Chapter 9.

Botanical Treatment Program for Cervical Dysplasia

Internal Formula for Immune Support: Antiviral, Anti-inflammatory, and Adaptogenic Effects

Reishi mushroom	(*Ganoderma lucidum*)	30 mL
Echinacea	(*Echinacea* spp.)	25 mL
St. John's wort	(*Hypericum perforatum*)	15 mL
Ginseng	(*Panax ginseng*)	15 mL
Licorice	(*Glycyrrhiza* spp.)	15 mL
		Total: 100 mL

Dose: 4 mL twice daily for 12 weeks, or as needed for the duration of treatment.

Suppository for Cervical Dysplasia/HPV Infection

Ingredients:

¼ cup cocoa butter
¼ cup coconut oil

TABLE 7-5

Botanical Treatment Strategies for Cervical Dysplasia

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL OPTIONS	COMMON NAME
Reduce viral infection	Antiviral	*Calendula officinalis*	Calendula
Prevent neoplasia	Antimicrobial	*Commiphora mol mol*	Myrrh
Reduce cervical inflammation and heal tissue	Antitumorigenic	*Echinacea* spp.	Echinacea
		Ganoderma lucidum	Reishi
		Hydrastis canadensis	Goldenseal
		Lavandula officinalis	Lavender
		Lomatium dissectum	Lomatium
		Origanum vulgare	Oregano
		Melaleuca alternifolia	Tea tree
		Sanguinaria canadensis	Blood root
		Thuja occidentalis	Thuja
		Thymus vulgaris	Thyme
		Usnea barbata	Usnea
Reduce viral infection	Demulcent	*Althea officinalis*	Marshmallow
Prevent neoplasia	Vulnerary	*Ananas comosus*	Pineapple (bromelain)
Reduce cervical inflammation and heal tissue	Anti-inflammatory	*Calendula officinalis*	Calendula
	Proteolytic	*Glycyrrhiza* spp.	Licorice
		Hydrastis canadensis	Goldenseal
Reduce viral infection	See Chapter 10		
Prevent neoplasia			
Reduce cervical inflammation and heal tissue			
Support immune response and HPA regulation	Adaptogens	See Stress, Adaptation, the Hypothalamic-Pituitary-Adrenal-Axis (HPA) and Women's Health	

1 tbl calendula oil or tincture
1 tsp each: thyme essential oil and lavender essential oil, and echinacea tincture
1 tbl each: dried goldenseal root powder and marshmallow root powder

Preparation instructions: See Special Preparations

Use: Insert one suppository on each of 5 consecutive nights per week for up to 12 weeks. It is advisable to wear a disposable cotton menstrual pad nightly during use, as the suppository will melt and leaking can cause staining of bedding or nightwear.

Combine the preceding protocol with the dietary and nutritional strategies described in the following as part of the naturopathic program. After 12 weeks, recheck the cervix with a Pap smear. If the degree of dysplasia has improved, repeat protocol for 8 to 12 additional weeks and recheck the cervix. If there has been no improvement, but also no worsening, make sure the patient has followed the protocol and repeat, modify the herbal protocol, or proceed with conventional medical care.

Alternatively, the naturopathic protocol can be followed as a botanical and nutritional protocol, omitting the escharotic treatment and using either the suppository described in the preceding or those described in the following.

Supplementation with vitamin C, beta-carotene, folic acid, selenum, zinc, vitamin E, calcium, and magnesium are commonly recommended. Essential fatty acids are also advised.

Low Dog states that a multivitamin with folate and B vitamins may be especially indicated for women with cervical abnormalities, citing one study evaluating the relationship between individual nutrients and persistent HPV infection, which showed that circulating levels of vitamin B_{12} were inversely correlated with persistent HPV infection after adjusting for numerous factors, and another study demonstrating that low serum homocysteine levels were highly predictive of invasive cervical cancer risk, possibly suggesting folate, B_{12}, or B_6 insufficiency.[25] Also see Cervical Cancer.

DISCUSSION OF BOTANICALS

Blood Root

The blood-red color of the sap from the roots of blood root led to its traditional use as a blood purifier. It was used as an emmenagogue, in the treatment of respiratory conditions, as a strong emetic, and for the treatment of fungal infections and ulcers.[124] By the eighteenth century, blood root was used topically to treat indolent chancres and tumors as an ingredient in the popular

''black salve,'' an escharotic treatment that was used topically for the treatment of tumors.[25] Extracts of sanguinarine, an alkaloid from the herb, have been shown to possess anti-inflammatory, antimicrobial, antioxidant, antiviral, antiproliferative, and apoptotic activities, and are under active research for the treatment of cancer.[125,126] Sanguinarine, an alkaloid compound fund in blood root, is a potent inhibitor of NF-kappa B activation.[25,125,126] Sanguinarine is an ingredient in dental hygiene products, for example, toothpaste, used for its antiplaque activity and in the treatment of gingivitis. There is controversy over the safety of its use in dental products, with contradictory research over whether it may cause malignant cell change and lead to the development of leukoplakia.[127–133] Most studies have concluded that the extract is safe for dental use; however, at least one study concludes that it should not be used until safety can be established. One study on reproductive and developmental toxicology conducted by orally administering blood root extract to rats and rabbits concluded that the oral intake of blood root extract has no selective effect on fertility or reproduction of fetal and neonatal development in either group.[134] The question of safety and effects of the herb on the oral mucosa remains relevant as the application to the cervix is similar in terms of direct treatment of epithelial tissue. The form used in black salve is the whole plant extract rather than isolated alkaloid for which cautions have been raised. At this time, evidence regarding the internal use of this herb for cervical dysplasia treatment is lacking, and serious caution is suggested regarding its topical use.

Bromelain

Bromelain is a complex mixture of proteinases derived from pineapple stems and fruit. Beneficial therapeutic effects of bromelain have been demonstrated in vitro, and in animal and human inflammatory disease models, including treatment of arthritis and inflammatory bowel disease, among others.[135,136] Bromelain inhibits plasma exudation through inhibiting the generation of bradykinin at the inflammatory site via depletion of the plasma kallikrein system, and possibly through other mechanisms, such as inhibition of the arachidonic acid pathway.[137–139] Beneficial anti-inflammatory effects have also been observed in patients suffering from HIV and cancer.[140–143] In one randomized study, 36 patients with Chlamydia infections were assigned either to a tetracycline-HCl plus bromelain (250 and 40 mg, respectively, four times per day) or a doxycycline (100 mg, twice daily) treatment for a period of 14 days. After 7 days, the pathogen was eliminated in 66.7% of the patients treated with tetracycline plus bromelain and in 55.6% of the patients receiving doxycycline. After the completion of the course of therapy, an infection with Chlamydia was no longer detectable in any patient of the two groups. The clinical effectiveness of the two therapies was considered to be good or very good in all cases. Adverse effects occurred in 11% (tetracycline + bromelain) and 16% (doxycycline) of the patients. Treatment of the sexual partner (with antibiotics) was also considered essential to the success of the study.[144] Bromelain is an important proteolytic ingredient in the treatment of cervical dysplasia.

Calendula

Calendula flowers are indicated for the topical treatment of minor inflammations of the skin and mucosa, to assist in the healing of minor wounds, and for the treatment of burns.[95,97] The most common topical applications include infusions used as washes, oil-based extractions, ointments, and the succus, or juice, which is high in enzymatic activity.[97,195] Hydroalcoholic extracts have demonstrated antibacterial and antifungal activity, as well as high virucidal action.[26,29] Calendula extracts have shown specific activity against HSV, HIV, and Trichomonas.[97,146] Anti-inflammatory and wound-healing effects have been demonstrated in vitro and in vivo, with topical anti-inflammatory effects attributed to the effects of the polysaccharide fractions of the plant.[149–151] Other important compounds are thought to be the major anti-inflammatory triterpenoid esters in the flower heads faradiol 3-O-laurate, palmitate and myristate.[152–154] In one study, freeze-dried extracts of St. John's wort, calendula, chamomile, and plantain were found to suppress both inflammatory effects and leukocyte infiltration in animal models.[155] Wound-healing effects also have been attributed to the angiogenic activity of the herb.[28] Calendula succus is used as a wash in the escharotic treatment, and as an ingredient in other topical applications for the treatment of cervical dysplasia, particularly in suppositories for vulnerary and anti-inflammatory effects after invasive gynecologic procedures (e.g., biopsy, LEEP). Calendula is used topically to hasten healing by reducing inflammation through an increase in granulation. No studies were identified using calendula for the treatment of HPV infection. Some concern exists as to whether use of calendula can lead to sensitization and potential for developing contact dermatitis; however, this risk appears to be insignificant, and in fact, the herb has been found to be highly effective for the prevention of acute dermatitis of grade 2 or higher in patients undergoing postoperative irradiation for breast cancer.[156] Known sensitivity to the Composita family can theoretically pose this risk; however, adverse effects from topical use have not been widely observed despite its widespread use.[97]

Goldenseal

Goldenseal is one of the five top-selling herbs in the United States, yet little scientific evidence is available regarding its efficacy.[157] Many herbalists consider goldenseal an indispensable antimicrobial herb, in addition to it being anti-inflammatory, immune enhancing, and antiproliferative, effects largely attributed the herb's berberine content.[158] These actions form the basis for its topical use in the treatment of cervical dysplasia. Although no research has been done specifically on the treatment of HPV with goldenseal, the herb has shown broad antimicrobial effects, with specific effects against *Chlamydia, S. aureus, E. coli, V. cholera, Trichomonas vaginalis, Giardia lamblia,* and *H. pylori*, as well as other organisms.[159–162] It has also demonstrated antifungal effects against

numerous organisms, including *Candida albicans*.[157] Its anti-inflammatory effects are attributed to its ability to interfere with the arachidonic acid pathway and cyclooxygenase generation, particularly COX-2 regulation and inhibition of phospholipase enzymes.[25,157] Berberine was demonstrated in vitro to have antiproliferative effects via inhibition of protein, DNA, RNA, and lipid synthesis in specific tumor cell lines; however, these effects were not borne out in vivo. Berberine extracts were able to induce apoptosis during S-phase of the cell cycle, and have demonstrated the ability to activate antitumor macrophages, in addition to several other anticancer in vitro effects.[157] In a study of the immunomodulatory effects of 6 weeks of orally administered goldenseal, the treated group showed an increase in the primary IgM response during the first 2 weeks of treatment, suggesting that goldenseal may enhance immune function by increasing antigen-specific immunoglobulin production.[163] Although direct effects against HPV are unknown, use of this herb in suppositories may be effective for reducing comorbid infection, allowing the body to direct its immune activity against the HPV, and through eliminating overgrowth of pathogenic microorganisms, allow the body to restore a healthy vaginal environment that may be less likely to support the growth of HPV. As with other herbs, goldenseal's anti-inflammatory effects may be beneficial in reducing cervical irritation or inflammation that might contribute to the development of dysplasia.

Licorice

Licorice is used in the treatment of cervical dysplasia, both topically and orally, for its antimicrobial, anti-inflammatory, immunomodulating, and antitumorigenic effects. It has been shown to inhibit prostaglandin and leukotriene synthesis in a similar way to corticosteroids such as prednisone.[164] It has also demonstrated specific antiviral activity against a wide range of viruses associated with chronic illness and latent infection. In one study, treatment of cells latently infected with Kaposi's sarcoma–associated herpes virus (KSHV) with glycyrrhizic acid (GL), a component of licorice, reduced synthesis of a viral latency protein and induced apoptosis of infected cells. This finding suggests a novel way to interrupt latency.[165] GL demonstrated activity against EBV replication in superinfected cells in a dose-dependent fashion in a novel way that differed that of the nucleoside analogs that inhibit viral DNA polymerase.[166] The mechanism underlying licorice's antiviral and antitumorigenic effects is poorly understood. One study looking at mechanisms was able to demonstrate that glycyrrhetinic acid (GA), an aglycone of GL, stimulates NO production and is able to upregulate iNOS expression through NF-κB transactivation in macrophages.[167] In vitro studies have demonstrated activity against HIV virus.[168] Licorice and its extracts have been shown to improve immune function in HIV patients by stabilizing helper and T-lymphocyte counts in comparison with the control groups in one study.[169] In another study, it increased T-helper cell levels, improved helper/suppressor cell ratios and improved liver function, and stopped the progression of HIV-positive patients to AIDS in comparison with the control group that did progress on to AIDS.[170,171] In yet another study, it showed a reduction of P24 antigen, an indicator of viral load.[172] The antiviral properties of these compounds have been found to be effective in hepatitis B and C where IV preparation has resulted in up to 40% going into complete remission.[173] Topical use of licorice extract on herpes reduces the healing time and pain associated with both genital herpes and cold sores.[174] Another component of licorice, deoxoglycyrrhetol (DG), also showed a remarkable improvement in anti-inflammatory, antiallergic, and antiulcer activities in animal experiments. Immunomodulating effects of GL, GA, and DG derivatives, which induce interferon-gamma and some other cytokines, have been demonstrated in relation with their antiviral activities.[175] Glycyrrhizin has been used for the treatment of chronic viral hepatitis. One study evaluated the mechanism by which glycyrrhizin inhibits complement. Glycyrrhizin inhibited the cytolytic activity of complement via the activation of both the classical and alternative pathways, whereas it had no effect on immune adherence, suggesting that it blocks C5 or a later stage of the complement cascade. Further analysis revealed that glycyrrhizin inhibits the lytic pathway in which the membrane attack complex (MAC) is formed. This mechanism suggests that glycyrrhizin may prevent tissue injury caused by MAC not only in chronic hepatitis, but in many autoimmune and inflammatory diseases as well.[176] Topical treatment of herpes simplex virus blisters with licorice extract may improve healing and prevent recurrence.[157] Although no studies were identified on the treatment of HPV with licorice or its extracts, other viral studies, as well as the herb's traditional uses, suggest that investigation into such use may be promising. See Plant Profiles: Licorice for warnings and contraindications to regular internal use of this herb.

Lomatium

Lomatium has been used historically by Native Americans, mostly as a treatment for respiratory illness.[177] It is considered antiviral, antibacterial, and antiseptic and is commonly used by naturopathic physicians and taken internally, for the treatment of cervical dysplasia. Lomatium has demonstrated in vivo and in vitro efficacy against HPV and HSV and has been investigated for its effects against HIV.[178–180] Its use has been described for the treatment of ''slow'' viruses with accompanying immune depression, and may commonly be combined with other herbs with immune-building effects.[181] Lomatium is also used topically for gum and mouth inflammations and as a douche for vaginal infections.[182]

Marshmallow

Marshmallow root (Fig. 7-4) is a polysaccharide-rich herb, loved by herbalists for its soothing, demulcent properties.[25] The mucilaginous quality of aqueous extracts and moistened powdered herb provides a protective, soothing coating to mucosa; thus, it is commonly included in preparations for throat, GI, and vaginal mucosal irritation.[97] Several studies have found the herb efficacious, in

Figure 7-4 Marshmallow (*Althea officinale*). (Photo by Martin Wall.)

combination with other specific herbs, for the treatment of cough, and the herb is approved for use by the German Commission E for the treatment of irritation of the oral and pharyngeal mucosa and mild inflammation of the gastric mucosa.[95] The root also exerts immune-enhancing and antibacterial effects.[25]

Myrrh

The tincture and powdered forms of this herb are used topically for the treatment of inflammatory mucosal conditions, usually of the oral and pharyngeal mucosa but also as an ingredient in vaginal suppositories. Local anesthetic, antibacterial, and antifungal activities also have been ascribed to the sesquiterpene fraction of the herb.[29] It is a common ingredient in oral hygiene preparations, for example, ointments, dentifrices, and toothpastes.[29] It is approved by the German Commission E for the topical treatment of mild inflammations of the oral and pharyngeal mucosa. Low Dog states that ''No data have been found to document antiviral activity [of myrrh], but in light of the antiseptic, cytoprotective, and anti-inflammatory effects of the herb it may offer some benefit'' in the treatment of cervical dysplasia.[25]

Oregano and Thyme

Both oregano and thyme essential oils are regularly included in vaginal suppositories for the treatment of vaginal infections, including HPV infection. They are also used topically as antimicrobials against numerous bacterial and fungal infections, for which they are considered highly effective ingredients.[183–185] One study reports on the efficacy of thyme as an antibacterial, and in another study oregano and clove oils were diluted and examined for their activity against enveloped and non-enveloped RNA and DNA viruses. Olive oil was also included as a control. Viruses were incubated with oil dilutions and enumerated by plaque assay. Antiviral activity of oregano and clove oils was demonstrated on two enveloped viruses of both the DNA and RNA types and the disintegration of virus envelope was visualized by negative staining using transmission electron microscopy.[185,186] Care should be taken in the use of essential oils topically; used undiluted (neat) they can be irritating to sensitive tissues such as cervical or vaginal mucosa.

Reishi

Reishi (Fig. 7-5) is a medicinal fungus with a long history of use as a Chinese folk medicine for promotion of health and longevity. Numerous in vitro and animal studies have demonstrated antitumor and immunomodulatory effects of Reishi mushrooms.[187] An OVID search for this herb yielded over 900 papers reporting on in vivo and in vitro effects. A wide range of antitumor and immunomodulatory mechanisms have been purported and observed, with the water extract and the polysaccharide fraction, as well as the alcohol extract or the triterpene fraction, and include enhanced function of antigen-presenting cells, the mononuclear phagocyte system, humoral immunity, and cellular immunity.[188,189] Reishi polysaccharide peptide (Gl-PP) has demonstrated antitumor effects in mice and potential antiangiogenesis, a reduction of Bcl-2 antiapoptotic protein expression and an increase of Bax proapoptotic protein expression; therefore, inducing cell apoptosis might be one of the mechanisms of action in inhibition of human carcinoma cells. High doses of Gl-PP resulted in a decrease in the secreted vascular endothelial growth factor (VEGF). Taken together, these findings support the hypothesis that the key attribute of the antiangiogenic potential of Gl-PP is that it may directly inhibit vascular endothelial cell proliferation or indirectly decrease growth factor expression of tumor cells.[190] It has been demonstrated that *G. lucidum* induces apoptosis, inhibits cell proliferation, and suppresses cell migration of highly invasive human prostate cancer cells PC-3.[191] Experimental results on cell-mediated immunity showed that *G. lucidum* could increase the percentage of CD5+, CD4+, and CD8+ T lymphocytes. Experimental results on humoral immunity in horses showed that *G. lucidum* could help horses to produce a significantly higher quantity of specific antibodies in a shorter time.[192] Although the pharmacology and clinical application of water extracts of *G. lucidum* have

Figure 7-5 Reishi (*Ganoderma lucidum*). (Photo by Martin Wall.)

been extensively documented, little is known regarding its alcohol extract. In the present study, the antitumor effect of an alcohol extract was investigated using MCF-7 breast cancer cells. The extract inhibited cell proliferation in a dose- and time-dependent manner, which might be mediated through upregulation of p21/Waf1 and downregulation of cyclin D1. Furthermore, this compound can directly induce apoptosis in MCF-7 cells, which might be mediated through upregulation of a pro-apoptotic Bax protein and not by the immune system. There are likely multiple mechanisms underlying the antitumor effects of *G. lucidum*.[193] *G. lucidum* also demonstrated antioxidant activity, free-radical scavenging, and chelating abilities.[194] No specific studies were identified on the use of *G. lucidum* for the treatment of HPV infection or cervical dysplasia; however, given the mechanisms of action of this herb, this may be a promising area of research, and certainly merits consideration of this herb in an immune-enhancing protocol.

Thuja

Thuja is used by many herbalists and naturopathic physicians for the treatment of genital and anal warts, and is commonly recommended in the naturopathic treatment of cervical dysplasia for its antiviral activity.[195] The main constituent is an essential oil consisting of α- and β-thujone, the content of which varies proportionally with the amount of ethanol used in producing the plant extract. If consumed internally, thujone can be neurotoxic, convulsant, and hallucinogenic. Long-term or excessive use of thujone-rich products can cause restlessness, vomiting, vertigo, tremors, renal damage, and convulsions.[196] Internal use of thuja decoctions and even very small doses of thuja oil (i.e., 20 drops per day for 5 days) as an abortifacient has been associated with neurotoxicity, convulsions, and death.[195] Additionally, thuja is associated with a substantial risk of inducing fetal malformation, and is absolutely contraindicated for use in pregnancy.[195] No research on the short- or long-term topical use of this herb was identified. Ingestion of thuja cannot be recommended because of potential for toxicity.

CHRONIC PELVIC PAIN

Aviva Romm

Chronic pelvic pain (CPP) is defined as pelvic pain lasting more than 6 months. Some authors add the additional criteria that the pain be noncyclic.[197] It is one of the most common presenting complaints in gynecologic practice, affecting as many as one in seven American women. CPP comprises up to 10% of outpatient gynecologic visits, accounts for 20% of laparoscopies, and results in 12% (75,000/year) of all hysterectomies performed annually in the United States.[198] Estimated annual direct medical costs for outpatient visits for CPP in the United States among women 18 to 50 years old is estimated to be $881.5 million. It is often an extremely frustrating condition for both patient and care provider because in many cases an etiology cannot be identified and there is no apparent pathology. Treatment of presumed underlying conditions is frequently ineffective, and the ''pain itself becomes the illness.''[198] Because the cause often cannot be identified, CPP is frequently attributed to psychogenic causes. Although these may play a role in CPP for some women with lack of an identifiable cause, this does not necessarily equate with a psychosomatic origin for this complaint.[199]

Common causes of chronic pelvic pain include endometriosis, pelvic inflammatory disease (PID), adhesions, ovarian remnant syndrome, pelvic congestion syndrome, and cyclic uterine pain, which may be caused by primary or secondary dysmenorrhea, uterine myomata, and adenomyosis. History of psychosexual trauma is common in women diagnosed with CPP.[200] Chronic pelvic pain is frequently associated with systemic inflammation, including autoimmune diseases. Peritoneal chronic inflammation is sometimes also associated. A study of chronic pain reveals that the immune system is intimately involved in the production, conduction, and exacerbation of pain and of its clinical features, such as hyperalgesia and allodynia.[201]

Not all pelvic pain is of gynecologic origin; other conditions must be ruled out. Genitourinary pain (e.g., due

to interstitial cystitis, urethral syndrome, or overactive bladder), gastrointestinal pain (e.g., irritable bowel syndrome, bowel obstruction, or bowel neoplasm), and neuromuscular pain are also common causes of CPP. CPP may be intermittent or continual. Pain is affected by physical and mental fatigue, as well as stress. It may lead to depression and anxiety, dyspareunia (painful sex/intercourse), and difficulties with sleep, decreased ability to work and enjoy normal activities, and may be a contributing factor in job loss, relationship dysfunction and divorce.[202–204]

SYMPTOMS

Symptoms associated with CPP include:

- Anxiety and depression.
- Constipation or diarrhea
- Dysmenorrhea
- Fatigue
- Leg pain radiating from the groin.
- Loss of interest in social activities
- Low back pain and a feeling of heaviness in the lower abdomen.
- Menstrual irregularity
- Persistent pain despite multiple treatments
- Reduced libido
- Sleep disruption
- Spasms of the vaginal and/or pelvic floor muscles
- Substance use/abuse
- Dyspareunia (painful and difficult intercourse/vaginal penetration)
- Family/relationship problems

DIAGNOSIS

Diagnosis of CPP is based on identifying the underlying cause(s). It also may be a diagnosis of exclusion, with no identifiable etiology. Careful attention should be paid to the history and physical examination, particularly a thorough pelvic examination to evaluate for tenderness, pelvic mass, adhesions, or prolapse. Testing may include ultrasound, laparoscopic examination, pregnancy test, CBC, vaginal and cervical cultures, Pap smear, evaluation for GI disorders, and urologic examination.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis in CPP is really a matter of identifying the possible causes of pain (Table 7-6) and treating the etiology while addressing the pain and concomitant

TABLE **7-6**

Common Causes of Chronic Pelvic Pain

CLASSIFICATION	CONDITIONS
Gynecologic	Abortion
	Adhesions
	Adnexal torsion
	Chronic salpingitis
	Dysmenorrhea
	Ectopic pregnancy
	Endometriosis
	Mittelschmerz
	Pelvic congestion
	Pelvic infection
	Ruptured ovarian cyst
	Salpingitis
	Uterine fibroids
	Uterine prolapse/pelvic relaxation
Gastrointestinal	Appendicitis
	Chronic appendicitis
	Constipation
	Diverticulosis
	Enterocolitis
	Gastroenteritis/Spastic colon
	Inflammatory bowel disease
	Irritable bowel syndrome
	Neoplasia
	Ulcerative colitis
Urologic	Chronic cystitis
	Detrusor hyperactivity
	Interstitial cystitis
	Ureteral calculus

Continued

TABLE 7-6

Common Causes of Chronic Pelvic Pain—cont'd

CLASSIFICATION	CONDITIONS
Musculoskeletal/Neurologic	Arthritis
	Coccydynia
	Conus medullaris lesions
	Degenerative joint disease
	Fibromyalgia
	Fractures
	Low back problems
	Multiple sclerosis
	Nerve entrapment syndromes
	Neuromuscular disorders
	Pelvic floor spasm
	Poor Posture
	Vertebral disk disorder
Psychogenic	Abuse
	Clinical depression
	Hypochondriasis
	Pain medication seeking
	Physical or sexual abuse
	Premenstrual dysphoric disorder
	Psychiatric disorders
	Psychosocial stress
	Sleep disturbances
	Substance abuse
Other	Hyperparathyroidism
	Calcium/magnesium deficiencies
	Trauma

Data from Forrest D: Common Gynecologic Pelvic Disorders. In Youngkin E, Davis M, eds. Women's Health: A Primary Care Clinical Guide, Stamford, Appleton and Lange,1998, pp. 313-362; Ryder R: Chronic pelvic pain, Am Fam Physician 54(7):2225-2232, 1995; Ostrzens A: Gynecology: Integrating Conventional, Complementary, and Natural Alternative Therapy, Philadelphia, Lippincott Williams & Wilkins, 2002.

symptoms. In patients under 30, the most common causes of pelvic pain include endometriosis and pelvic inflammatory disease; in older women, causes most likely include uterine myoma, adenomyosis, or pelvic relaxation. It is critical to rule out any serious or life-threatening causes, as well as to assess for depression, anxiety, and serious mental health disorders.

CONVENTIONAL TREATMENT APPROACHES

The choice of medical treatment for CPP depends on the etiology of the pain, thus necessitating careful diagnosis. Treatment of underlying conditions is the primary treatment strategy. However, in one-third of cases, no etiology is identified. Sympathetic and supportive care is critical, with reassurance and validation of the woman's symptoms essential, especially in the absence of an identifiable cause.[199] The pain should be treated as a real problem. Multidisciplinary team management of CPP may be the most productive strategy, including the expertise of a gynecologist, a psychologist with expertise in sexual and relationship counseling, and also possibly an acupuncturist for pain management, in addition to the appropriate specialists for the underlying cause.[199,205] Treatment with medication includes the use of NSAIDs, antidepressants for depression and sleep disorders, and hormonal therapies (i.e., oral contraceptives for management of cyclic pain or GnRH analogs for pain associated with endometriosis or uterine fibroids). Trigger point injections of local anesthetics has proved helpful for prolonged pain relief in some patients, as has TENS therapy.[206] Acupuncture has been used with good results in the treatment of dysmenorrhea, and may be beneficial in pain reduction for CPP.[206] Immune modification using steroids and disease-modifying antirheumatic drugs, such as hydroxychloroquine, are known to inhibit inflammatory cells and cytokines, such as interleukin-1, interleukin-6, and tumor necrosis factor, which are responsible for pain and tissue damage. These drugs are found to be effective in the treatment of chronic pelvic pain of an inflammatory nature and for symptomatic chronic inflammation of the vagina.[201,206] Surgical interventions include laparoscopy for the lysis of pelvic adhesions or removal of endometrial tissue, or hysterectomy.

Although hysterectomy without an associated pathology has not proved effective, it is nonetheless indicated as a reason for hysterectomy in 10% to 15% of those performed in the United States.[199] According to one study, 25% of hysterectomy patients reported persistent pain 1 year after surgery.[198]

BOTANICAL TREATMENT

Effective botanical treatment of CPP requires a clear understanding of possible etiologies and the appropriate treatment of the underlying cause of the pain. For patients with diagnosed gynecologic conditions associated with pelvic pain, readers are referred to the relevant chapters in this textbook, such as, dysmenorrhea, interstitial cystitis, uterine fibroids, endometriosis, and so forth. Treatments discussed in the following may be used as adjunct palliative therapies for pain, inflammation, and concomitant symptoms in these conditions.

In the absence of a clearly identified pathology, the practitioner can approach treatment symptomatically via specific botanical treatments for pain reduction, and attempt to address mechanisms that may be associated with CPP, for example, inflammation. One theory of CPP that was popular among physicians in the early- and mid-twentieth century, and that is still considered a possibility, is that of ''pelvic congestion syndrome.''[8,198,206,207] Women with this syndrome, which is poorly defined, are thought to exhibit many of the symptoms associated with CPP, including aching and dragging sensations in the lower back, lower abdomen, and pelvis, dysmenorrhea, and dyspareunia. The theory of pelvic congestion parallels Chinese medical theory regarding various forms of gynecologic pain. Pelvic vascular congestion is thought to be a dynamic vascular process, similar to migraine headache, with drug inducible [dihydroergotamine (DHE) injection] reversibility of vascular dilatation.[206] As with CPP, symptoms are commonly accompanied by depression, fatigue, and insomnia. Upon pelvic exam or laparoscopy, the uterus may be found to be enlarged and tender and the pelvic vessels engorged. However, there is no direct correlation between vessel engorgement and pain; some women have either pain without engorgement or vice versa.[8] Herbalists may include herbs in a formulae to tonify and astringe the uterus and pelvic vessels, ostensibly to reduce pelvic congestion. Psychogenic causes may contribute to CPP. Although this should not be overemphasized, it should also not be overlooked. Chronic pain can affect nearly every aspect of a patient's life: physically, mentally, emotionally, socially, and even economically. Because chronic pain can lead to depression and anxiety, as well as to sleep disturbance, which can create a vicious cycle of psychoemotional upset and increased pain, care should be taken to approach pain holistically, including in protocol herbs that are restorative to the nervous system, for example, adaptogens and nervines, and when needed, anxiolytics or antidepressants.

IBS and inflammatory bowel syndromes are highly associated with CPP. Herbs commonly used for the treatment of CPP are listed in Table 7-7. Many of these

TABLE **7-7**

Botanical Treatment Strategies for Chronic Pelvic Pain

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Pain relief	Analgesia	*Anemone pulsatilla*	Pulsatilla
		Actaea racemosa	Black cohosh
		Corydalis ambigua	Corydalis
		Eschscholzia californica	California poppy
		Piper methysticum	Kava kava
		Piscidea piscipula	Jamaican dogwood
		Viburnum spp.	Cramp bark, black haw
		Also see Dysmenorrhea	
Relief of pelvic muscle spasm	Antispasmodics	*Achillea millefolium*	Yarrow
		Angelica sinensis	Dong quai
		Dioscorea villosa	Wild yam
		Cannabis indica	Marijuana
		Actaea racemosa	Black cohosh
		Leonurus cardiaca	Motherwort
		Paeonia lactiflora	White peony
		Rehmannia glutinosa	Rehmannia
		Viburnum spp.	Cramp bark, black haw
		Zingiber officinale	Ginger
		Also see Dysmenorrhea	

Continued

TABLE 7-7

Botanical Treatment Strategies for Chronic Pelvic Pain—cont'd

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Treatment of depression and anxiety	Antidepressants Anxiolytics	*Hypericum perforatum* *Lavandula officinalis* *Leonurus cardiaca* *Matricaria recutita* *Melissa officinalis* *Piper methysticum* Also see Chapter 18	St. John's wort Lavender Motherwort Chamomile Lemon balm Kava kava
Nervous system support	Adaptogens	*Cordyceps sinensis* *Eleutherococcus senticosus* *Panax quinquefolius* *Rhodiola rosea* *Withania somnifera* Also see Stress, Adaptation, the Hypothalamic-Pituitary-Adrenal-Axis (HPA) and Women's Health	Cordyceps Eleuthero American ginseng Rhodiola Ashwagandha
Reduce inflammation	Anti-inflammatories	*Angelica sinensis* *Glycyrrhiza officinale* *Oenothera biennis oil* *Paeonia lactiflora* *Salix* spp *Tanacetum parthenium* *Zingiber officinale*	Dong quai Licorice Evening primrose White peony Willow Feverfew Ginger
Digestive support; treatment of IBS and inflammatory bowel syndrome	Antispasmodics	*Achillea millefolium* *Dioscorea villosa* *Matricaria recutita* *Mentha piperita*	Yarrow Wild yam Chamomile Peppermint
Digestive support; treatment of IBS and inflammatory bowel syndrome	Astringents	*Achillea millefolium* *Hydrastis canadensis*	Yarrow Goldenseal
Digestive support; treatment of IBS and inflammatory bowel syndrome	Carminatives	*Matricaria recutita* *Mentha piperita* *Pimpinella anisum*	Chamomile Peppermint Anise
Digestive support; treatment of IBS and inflammatory bowel syndrome	Demulcents	*Ulmus rubra* *Althea officinalis*	Slippery elm Marshmallow
Digestive support; treatment of IBS and inflammatory bowel syndrome	Laxatives	*Glycyrrhiza glabra* *Taraxacum officinale* *Rumex crispus*	Licorice Dandelion root Yellow dock
Treat insomnia/sleep disorders	Anxiolytics Nervines Sedatives	*Anemone pulsatilla* *Piper methysticum* *Eschscholzia californica* Also see Chapter 18	Pulsatilla Kava kava California poppy
Treat possible pelvic congestion syndrome	Uterine tonics Venotonics	*Aesculus hippocastanum* *Caulophyllum thalictroides* *Alchemilla vulgaris* *Hydrastis canadensis* *Mitchella repens* *Rubus idaeus* *Viburnum* spp.	Horse chestnut Blue cohosh Lady's mantle Goldenseal Partridge berry Red raspberry Cramp bark, black haw

herbs are discussed elsewhere in this book or in Plant Profiles.

Analgesia

The history of botanical medicine reveals many herbs that have been used for the treatment of a variety of types of pain.[208] Many traditional medicines have actions such as inhibition of platelet-activating factor, cyclooxygenase, prostaglandin formation, or arachidonic acid pathways.[209] Although not typically as fast-acting as conventional medications, repeated appropriate dosing over a short period of time, such as 1 to 2 hours, and continued as needed, often leads to satisfactory temporary alleviation of pain. Several herbs are reputed for their efficacy in the treatment of pain of gynecologic origin, as well as more generally (see Dysmenorrhea).

Black Cohosh

Black cohosh has historically been used by Northeast Native American tribes as an analgesic and as an emmenagogue.[210] The Eclectics used a resin of black cohosh specifically as a uterine tonic and in the treatment of dysmenorrhea and a number of other painful spasmodic or cramping gynecologic complaints.[211] It was also used in the treatment of deep muscle drawing in the legs, loins, and back, dull aching of the bowels, ovarian pains of a dull, aching quality, dragging uterine pain, and delayed menses with dull pain and muscle soreness. Felter specifically describes a condition called ''rheumatism of the uterus'' for which this herb was prescribed.[99] The plant's anti-inflammatory and analgesic properties are attributed to its aromatic acids, which appear to inhibit prostaglandin production. The herb is approved for use in Germany for the treatment of premenstrual discomfort and menstrual cycle pain.[25]

California Poppy

California poppy (Fig. 7-6) traditionally has been prescribed for reducing pain and producing calm sleep without the potential dangers of conventional opiate drugs. It may be useful for painful conditions in which there is irritation or stimulation of afferent pain fibers, in disturbed sleep, and for anxiety.[108] Its medical use as an analgesic and sedative in the United States dates as far back as the late nineteenth century, even being included in the Parke-Davis catalog for these purposes, and as an excellent alternative to morphine without its side effects.[108,211] Today, California poppy is widely used by herbalists in tincture form. Pharmacologic data demonstrate sedative activity in vivo, as well as GABAergic activity, sedative and anxiolytic action, and dose-dependent analgesia (when administered by injection). Two controlled clinical trials, the herb, combined with Corydalis cava, both standardized extracts, demonstrated normalization of disturbed sleep without carryover effects or addiction.[108]

Figure 7-6 California poppy (*Eschscholzia californica*). (Photo by Martin Wall.)

Corydalis

The Chinese botanical corydalis, is a strong and reliable analgesic. It is commonly used for headache, lumbar pain, abdominal pain, joint pain, menstrual pain, and other neurologic pain, making it specific for the symptoms associated with CPP. Alcohol and acetic acid extractions are the strongest, although powdered herb is considered effective as well. The mechanism of action of analgesia is thought to be inhibition of the reticular-activating system in the brainstem. Corydalis can increase the pain threshold significantly. Continuous use of corydalis results in tolerance and may theoretically lead to a cross-tolerance to morphine.[212,213] However, from a Chinese medical perspective the effects of corydalis are more than palliative as it is used to help promote pelvic circulation and therefore may treat underlying pelvic congestion. The alkaloids in this herb have sedative and hypnotic effects and act synergistically with barbiturates.[212] Chinese pharmaceutical companies have produced several preparations from corydalis alkaloids for use as analgesics. The available preparations include a 30-mg tablet containing all alkaloids and a 10% tincture used in doses of 5 mL three times daily.[212] Overdose leads to muscle relaxation and CNS depression. Corydalis is contraindicated in pregnancy.[32,212,213]

Cramp Bark and Black Haw

Cramp bark and black haw were similarly used for the treatment of pelvic pain, particularly of a spasmodic nature, and specifically when accompanied by a sensation of dragging pressure in the groin and drawing pain in the legs.[31,211]

Jamaican Dogwood

Jamaican dogwood is a reliable analgesic and spasmolytic herb with mild sedative properties. It was prescribed by the Eclectics for neuralgias, spasmodic complaints, migraines, dysmenorrhea, nervous tension, insomnia, and nervous excitability, although Felter cautioned about potential toxic effects (including convulsions) in large doses.[99] Ellingwood elaborated on its effects in quieting uterine pains of labor, promoting rest, and having a specifically relaxing influence, in addition to its general analgesic effects. He stated that the herb ''acts in close harmony with the vegetable uterine remedies, promoting the influence of Macrotys [*Actaea racemosa*-black cohosh], the viburnums...pulsatilla and dioscorea among others.''[30] The spasmolytic activity of Jamaican dogwood may be attributable to its isoflavone constituents; however, this plant has been only minimally studied.[154] Combined in equal parts with cramp bark or black cohosh, this author has found it a highly effective treatment for gynecologic and pelvic pain of neuromuscular origin, for dysmenorrhea, endometrial pain, urinary tract infection, and other pelvic pain. It also may be used postsurgically as an alternative to conventional pain medications. Regarding its toxicity, it is advisable that the recommended dosage range not be exceeded and that the herb not be used by pregnant women, or patients with bradycardia or cardiac insufficiency.[108]

Kava kava

Kava kava has been used traditionally as a muscle relaxant to reduce anxiety and may be considered for the treatment of muscle spasms associated with CPP. Both aqueous and lipid soluble extracts of kava have demonstrated antinociceptive activity through nonopiate receptor mechanisms.[158] It is commonly used by herbalists for the treatment of pain as well as anxiety. (See Plant Profiles: Kava Kava for safety considerations.)

Pulsatilla

Pulsatilla (Fig. 7-7), also called pasque flower, has analgesic and sedative properties. It is listed in the British Herbal Compendium for the treatment of painful spasmodic conditions of the female reproductive systems and dysmenorrhea. It is generally used in tincture form. Fresh herb contains potentially irritant and toxic compounds; therefore, only dried plant should be used, and the herb should not be used during pregnancy. Overdose can lead to gastric irritation, coma, and convulsions; thus, it is essential that patients stay within the proper dosage range, and use be monitored by an experienced practitioner.[25,108] This herb is more commonly prescribed by naturopathic practitioners than herbalists in the United States, although it is also used by European herbalists.

Figure 7-7 Pulsatilla (*Anemone pulsatilla*). (Photo by Martin Wall.)

Black Cohosh, Cramp Bark, and Black Haw

Black cohosh, cramp bark, and black haw are traditionally used as uterine antispasmodics and analgesics, and are discussed throughout this text for these properties (see Dysmenorrhea and Plant Profiles). This three-herb combination administered as a tincture is especially effective for the treatment of pelvic aching and pain. (See Plant Profiles: Black Cohosh for safety considerations with this herb.)

Dong Quai and Peony

Dong quai and peony, in addition to their significant analgesic and spasmolytic actions, are considered herbs that ''move blood'' and relieve stasis or stagnation in TCM.[92,214–216] The TCM concept of uterine stasis is consistent with the Western concept of pelvic congestion syndrome described in the preceding. Additionally these herbs, often used together in combination, and often with the addition of licorice (*Glycyrrhiza glabra* or

G. uralensis) are considered effective for the treatment of a number of gynecologic conditions that may be involved in the etiology of CPP, such as dysmenorrhea, polycystic ovarian syndrome (PCOS), and uterine fibroids. The Japanese traditional formula TJ-68, Shakuyaku-kanzo-to (Chinese: shao-yao-gan-cao-tang), which contains concentrated white peony root and licorice, has been approved by the Japanese government for clinical use in the treatment of pain and acute muscle spasm, including dysmenorrhea.[108]

Marijuana

One herb, not available widely (or at least, legally available) for clinical use that has clinically demonstrated significant uterine antispasmodic and analgesic effects is *Cannabis indica*, more commonly referred to as marijuana (Fig. 7-8). This controversial medicinal plant and recreationally used herb has a long history of use for relief of uterine spasms and dysmenorrhea, considered by the Eclectics to be a ''soothing uterine tonic.''[30] In fact, its use is ancient, with references and artifacts of its use found widely in Middle Eastern, Ayurvedic, and Semitic writings, continuing through to its medical use in Europe well into the late nineteenth century for the treatment of a variety of gynecologic and obstetric conditions, not limited to but including dysmenorrhea. A pharmaceutical product from the late nineteenth century, Dysmenine Compound, produced by the Keysall Pharmical Company, Kansas City, MO, contained *Cannabis, Cypripedium, Scutellaria, Pulsatilla, Viburnum prunifolium, Caulophyllum, Viburnum opulus*, and *Capsicum*. The compound was indicated for dysmenorrhea, menstrual colic, and cramps.[217] Indeed, this formula is not very different from one that might be prescribed by herbalists today (see sample formulae in the following); however, minus the now illegal cannabis and the ecologically endangered lady's slipper orchid (*Cypripedium*). Although it is not possible given the current legal–medical climate surrounding the use of Cannabis to prescribe this herb clinically, it is worthwhile to note its use and possible beneficial effects, as these have likely not escaped those who manage to procure it for self-medication for the treatment of chronic or cyclic pelvic pain. Russo et al., in *Women and Cannabis: Medicine, Science, and Sociology*, provide substantial evidence of its use. They cite Grinspoon and Bakalar in their 1993 book *Marihuana, the forbidden medicine*, who discuss numerous case studies of women using cannabis effectively to treat PMS, menstrual cramps, and labor pain, and when used at low doses, without cognitive impairments. They also cite an Australian study of the uses of cannabis for obstetric and gynecologic complaints in which 51% of respondents indicated use for PMS or dysmenorrhea. Discussing this herb's appropriate use with patients, outside the context of prescribing or condoning its use, is therefore possibly important and appropriate. The mechanisms of action appear to be primarily through anti-inflammatory activities. An interesting approach for inflammation-mediated pelvic pain is the use of the seeds of the hemp plants, which are notably rich in gamma-linolenic acid, in which women with PMS and dysmenorrhea have found to be low. In one study, a daily dose of 150 to 200 mg of over 12 weeks greatly improved PMS related symptoms; this dose could be provided by a 5-mL daily dose of hemp seed oil.[217]

Figure 7-8 Dysmenine compound—old pharmacy bottle. (Photo by Ethan Russo.)

Motherwort

Motherwort (*Leonurus cardiaca*) is a classic herb for the treatment of pelvic pain. Its actions appear to modulate both relaxant and contractile activity of the uterus, perhaps with an overall effect of regulating a balance between the two for effective uterine muscle activity. The commonly used Western species *L. cardiaca* has barely been evaluated for its effects in gynecology, whereas Chinese species have been evaluated in several investigations and have been found to have stimulating effects on the myometrium in vivo. The effect on the uterine smooth muscle may be related to alteration of the ion concentration in relation to myoelectric activity, resulting in the increase of myoelectric activity of pace setter cells as well as in the acceleration of depolarization of spike activity.[218] Leonurine, a plant alkaloid present in Chinese motherwort, has demonstrated some efficacy as a vascular smooth tone inhibitor, possibly through inhibition of Ca^{2+} influx and the release of intracellular Ca^{2+}.[219] It is uncertain whether these findings and effects can be extrapolated to effects on uterine vascular tone. Other studies have demonstrated interesting effects on mediators of the inflammatory and coagulation pathways in relationship to coronary blood flow and alleviation of stasis that may have some correlation to the use of this herb in both TCM and Western herbal medicine to alleviate pelvic congestion (in TCM ''blood stasis'' or ''stagnation''). In one study of 105 patients, 94.5% showed improvements in reduction in blood viscosity and fibrinogen content, important both for healthy blood flow but

also in the prevention of release of inflammatory compounds associated with clot formation.[220] A Russian study reported on the soporific activity of a combination of equal parts of valerian, motherwort, and hawthorn (*Crataegus* spp.) in tincture form. This combination prolonged the soporific effect of sodium ethaminal.[221] The effects of motherwort (*L. cardiaca*) for the treatment of spasmodic uterine pain and pelvic congestion are predicated on historical and contemporary clinical use, for which it remains a popular choice in gynecologic formulae.

Wild Yam and Ginger

Wild yam and ginger are considered important herbs to include in the treatment of CPP, especially when it is associated with irritable bowel–type complaints, as they are both effective not only for treating spasmodic uterine complaints and, in the case of ginger, inflammation, they exert these actions in the digestive system, thus addressing what may be causal associations, or concomitant conditions that are mutually exacerbating.[25,108] These herbs may be used in combination in capsule or tincture form, and may be included in formulae with other herbs.

Yarrow

Yarrow, a favorite herb of many herbalists, has the interesting characteristic of being considered an effective antispasmodic for painful, cramp-like conditions of psychosomatic origin in the lower pelvis in women when used as a sitz bath.[95] It is also used for dyspeptic complaints, including mild, spastic discomforts of the gastrointestinal tract. This combination of qualities makes it a particularly interesting herb to consider for the treatment of CPP, especially when of psychogenic origin and/or when occurring in conjunction or as a result of irritable bowel disorders.

Antidepressants and Anxiolytics

Herbs of note that possess both antidepressant or anxiolytic activity, as well as analgesic or antispasmodic activity, include St. John's wort, kava kava, motherwort, and ashwagandha, the latter of which is also a respected adaptogen and whose analgesic effects are discussed elsewhere in this text (see Plant Profiles). Gentle nervines that are commonly used as adjunct teas in the treatment of mild depression include chamomile, lemon balm, and lavender. Lavender also may be used externally in baths for its soothing aromatherapeutic effects, as well as for mild topical analgesia for the vulva.

Adaptogens

The use of adaptogens in the treatment of CPP is primarily for the reduction of stress and anxiety, modulation of inflammation, and improvement of sleep disorders. They are part of a long-term treatment plan rather than quick-acting for specific symptoms (see Chapter 6 and Plant Profiles). Ashwagandha has specific analgesic activity, and is among the most specific of choices for CPP.

Anti-inflammatories

Dong Quai

Dong quai possesses antispasmodic, analgesic, anti-inflammatory antioxidant, uterine tonic, as well as specific immunomodulatory effects (see Plant Profiles). Immunostimulatory and anti-inflammatory effects have been attributed to isolated ferulic acid. It has been used traditionally in Chinese medicine for the treatment of ''blood vacuity'' and ''blood stasis,'' which may be considered related to CPP.[94]

Evening Primrose Oil

It is thought that the use of evening primrose oil (EPO), with its high gamma linoleic acid content, may preferentially promote the synthesis of anti-inflammatory prostaglandin series over inflammatory prostaglandins. One critical review of the effects of EPO for the treatment of PMS concluded that there was no benefit. However, in a study of women (n = 40) who experienced symptoms of irritable bowel syndrome (IBS) just prior to and at the onset of menstruation, 53% reported an improvement in symptoms, whereas no improvement was seen in the placebo group. Improvement generally took 2 to 3 months to become apparent. Blood analysis at the beginning and end of treatment revealed significant improvement in fatty acid imbalances in the EPO-treated group.[158]

Feverfew

Feverfew has exhibited inhibition of prostaglandin synthetase preventing the conversion of arachidonic acid to prostaglandins, inhibits mast cell degranulation and subsequent histamine and serotonin release, and has shown inhibition of other inflammatory cytokines such as TNF-α, IL-1, NFκB, and IFN-γ, as well as inhibiting peritoneal cyclooxygenase in animal models.[97] These effects suggest possible application of this herb to treat pain related to inflammation in CPP.

Ginger

Herbalists commonly use ginger root as an anti-inflammatory and antispasmodic herb for the treatment of pelvic pain and congestion, as an infusion, and also in hip baths and hot compresses over the affected area. No studies have been identified for its use for gynecologic complaints. Ginger remains popular among Western and TCM herbalists as an antispasmodic treatment for dysmenorrhea; however, no clinical trials have been done to evaluate its efficacy.[25] Ginger's historical use for treatment of digestive disorders may be applicable for women with concurrent abdominal discomfort resulting from digestive complaints.

Licorice

Licorice root is commonly included in formulae when an anti-inflammatory herb is indicated. It may be considered an effective anti-inflammatory activity without many of the most troubling side effects seen for drugs used as COX-2 and 5-LO inhibitors.[111] However, high

doses of licorice may exacerbate hypertension (see Plant Profiles).

Peony and Rehmannia

Two herbs commonly used in TCM formulae, peony and rehmannia, have demonstrated significant anti-inflammatory and antispasmodic activity.[22,25,108] Studies using a traditional formula containing both herbs have demonstrated prostaglandin production inhibition in the uterine myometrium via phospholipase A2 inhibition, whereas other studies have demonstrated arachidonic acid inhibition, PAF inhibition, reduction in free radical formation, and smooth muscle relaxation. Note that nearly all of the studies use these herbs in traditional formulae rather than in isolation, and that studies are conducted in animal models, and have focused on arthritis, ulcers, and other chronic inflammatory conditions. Licorice is frequently included in TCM formulae that also contain peony and Rehmannia, as is dong quai when these herbs are used for gynecologic conditions.

Uterine Tonics: Venotonics

Treatment of pelvic congestion syndrome incorporates a combination of therapeutic actions, including anti-inflammatory, uterine tonics, and herbs used as vascular tonics. Uterine tonics, which historically have included herbs such as blue cohosh, goldenseal, lady's mantle, motherwort, partridge berry, red raspberry leaf, and cramp bark and black haw, are thought to exert their efforts by improving the overall tone of the uterine smooth musculature and vasculature. Goldenseal, for example, typically regarded for its antimicrobial effects, was used extensively by the Eclectics for the treatment of uterine bleeding resulting from a variety of conditions, including endometriosis, fibroids, and changes associated with menopause.[211] Although no clinical studies have been conducted using whole herb, in vitro trials using berberine, one of the primary alkaloids in goldenseal, have demonstrated both uterine smooth muscles stimulant and inhibitory activity.[22] Aqueous extracts of red raspberry leaf also have demonstrated both stimulatory and inhibitory effects on uterine smooth muscle.[108] In fact, this paradoxic effect is seen with several of the herbs commonly used as both uterine tonics and spasmolytics, for example, cramp bark and black haw. It is thought that the effect of these dual activities is a normalization of uterine activity, and the promotion of smooth, nonspasmodic uterine muscle activity, thus improving tone and reducing pain.[222,223]

Several herbs with venotonic activity should be considered for the treatment of pelvic congestion in CPP. Most notable are blue cohosh and horse chestnut. Blue cohosh has demonstrated uterine tonic, vasoconstrictive activity, and continues to be used for the treatment of many gynecologic formulae in which a uterine tonic is required. Historically, it has been used for labor induction, amenorrhea, dysmenorrhea, menorrhagia, and to induce abortion.[195,224] Blue cohosh is listed in the British Herbal Pharmacopoeia (1983) as a spasmolytic and emmenagogue.[225] It also may be used as an ovarian tonic and for the treatment of a variety of menstrual complaints, including menorrhagia, amenorrhea, dysmenorrhea, and pelvic congestion syndrome.[8] Horse chestnut is used to improve circulation through vascular tonification, to improve venous tone in venous insufficiency, and for the relief of aching discomfort in the lower limbs associated with varicosities and for complaints associated with chronic venous insufficiency (CVI).[22,100,157] Traditionally, it was used in the treatment of neuralgia and ''conditions of venous congestion particularly with dull, aching pain and fullness.''[22] One studied demonstrated safe use for 56 months without harmful effects. Horse chestnut extract is the third most widely sold herbal product in Germany, where it is used long-term in clinical practice apparently without adverse effects.[100] There appears to be very low risk associated with proper administration, although it is recommended that only product standardized to its presumed active ingredient, escin (aescin) be used, and not to exceed 12 weeks at recommended doses.[157] Adverse effects from use of horse chestnut seed extract have included GI upset and calf spasm most commonly, with headache, nausea, and pruritus occurring less commonly. Overall, adverse effects are extremely rare, in an observational study occurring at a rate of less than 0.6% in more than 5000 subjects.

FORMULAE FOR CPP TREATMENT

The following is a small selection of possible formulae to illustrate formulation strategies for CPP treatment. These various formulae can be used concurrently, or elements from several may be combined to create a unique formula for individual patients. Other herbs discussed above may be substituted if they are more specifically indicated to a particular patient's presenting picture. Further, CPP treatment, as discussed, almost invariably requires readers to refer to other relevant sections of this book for

Formulae for Chronic Pelvic Pain

General Tincture for CPP: Uterine Tonic/Antispasmodic

Blue cohosh	(*Caulophyllum thalictroides*)	20 mL
Cramp bark	(*Viburnum opulus*)	20 mL
Peony	(*Paeonia lactiflora*)	20 mL
Motherwort	(*Leonurus cardiaca*)	15 mL
Horse chestnut	(*Aesculus hippocastanum*)	15 mL
Yarrow	(*Achillea millefolium*)	10 mL

Total: 100 mL

Dose: 5 mL twice daily

This formula is an example of one that combines a variety of actions into a general formula that can be used long-term and daily for the treatment of CPP for women with spasmodic pain and pelvic congestion. It can be combined with a more analgesic formula for moderate to strong pain.

Formulae for Chronic Pelvic Pain—cont'd

Pelvic Analgesic and Antispasmodic Tincture: Moderate to Strong Pain

Cramp bark	(*Viburnum opulus*)	40 mL
Wild yam	(*Dioscorea villosa*)	20 mL
Jamaican dogwood	(*Piscidea piscipula*)	15 mL
Corydalis	(*Corydalis ambigua*)	15 mL
Yarrow	(*Achillea millefolium*)	10 mL

Total: 100 mL

Dose: 2.5 mL taken as needed, up to 6 doses per day. DO NOT EXCEED THIS DOSE.

Immune Support and Stress Reduction Tincture

Ashwagandha	(*Withania somnifera*)	30 mL
Milky oats	(*Avena sativa*)	20 mL
Blue vervain	(*Verbena officinalis*)	20 mL
Licorice	(*Glycyrrhiza glabra*)	15 mL
Lemon balm	(*Melissa officinalis*)	15 mL

Total: 100 mL

Dose: 5 mL twice daily for 3 to 6 months

This formula exemplifies the use of both adaptogens and gentle nervines to create a formula for everyday use to improve nervous irritability, reduce anxiety, and improve well-being. The formula is also anti-inflammatory. See Plant Profile: Licorice for precautions on regular intake of this herb.

Insomnia/Sleep Disturbance Formula

See Insomnia.

External Treatments for Chronic Pelvic Pain

Ginger-Yarrow Sitz Bath

Ingredients:

Fresh ginger root: 4-in. section, grated

1 oz dried yarrow blossoms

Instructions:

Bring 2 quarts of water to a boil in a large pot and remove from heat source. Add the above ingredients and cover tightly. Allow to steep for 20 to 30 minutes. Fill bathtub to patients waist height with water that is as hot as patient can comfortably tolerate. Strain the liquid into the tub, discarding the spent herbal matter. Soak. Repeat regularly as needed.

Medicated Analgesic Massage Ointment

To 2 ounces of a pre-made unmedicated ointment base (see Elan Botanicals in Resources) add:

15 mL tincture of *Viburnum opulus*

10 ml tincture of *Capsicum*

5 mL tincture of *Lobelia inflata*

Mix thoroughly (product may occasionally require mixing prior to use). Apply to lower back, pelvis, and backs of thighs as needed. Avoid contact with mucous membranes and eyes, because contact will cause burning.

treatment options, for example, dysmenorrhea or interstitial cystitis.

DIETARY CONSIDERATIONS

Dietary changes are indicated when the client suffers from digestive complaints such as constipation, bloating, flatulence, overweight, lethargy, excessive fatigue, or irritability accompanying CPP.[198] Achieving an optimal weight and stable blood sugar may lead to improvements in digestion and mood, and increasing dietary fiber and fluids can lead to reduction in constipation and bloating.[198] Additionally, a Mediterranean-type diet with the addition of high quality essential fatty acids can reduce the production of inflammatory mediators, and thus be beneficial in chronic pain reduction. Consider calcium and magnesium supplementation for relief of muscle spasm.

ADDITIONAL THERAPIES

Muscle Relaxation and Re-education, Biofeedback, and Electrical Stimulation

Muscle tension in the pelvis, hips, and lower back may be caused by, or lead to CPP. Helping a woman to identify and relax tension, become aware of and adjust her body mechanics and standing and sitting posture, and wear appropriate shoes to minimize postural problems can help to reduce pain caused by structural imbalances. Pelvic relaxation training techniques should be taught and practiced regularly. Much of this can be done at home, but physical therapy can be helpful if there is limited joint movement or muscular problems. Prolonged sitting or standing can aggravate CPP, so patients may need suggestions and supportive counseling for modifying jobs or activities that require positions that exacerbate the problem. Exercises such as running or high-impact aerobics also may be aggravating, and should be replaced with gentler, relaxing forms of exercise, for example, walking, tai chi, yoga, or dance.[226] Physical therapy for the treatment of musculoskeletal problems or postural problems can be beneficial for women with CPP.[227]

Biofeedback machines can be effective in helping women to identify and improve the effectiveness of pelvic muscle relaxation techniques for acquired muscle tension. The woman is instructed to visualize and practice muscle relaxation techniques while using a biofeedback device for feedback on the relaxation efforts.

Electrical stimulation using vaginal, rectal, or surface electrodes is used to produce rhythmic contraction and relaxation of the pelvic floor muscles. Electrical stimulation may give immediate reduction in the level of pain early in treatment, restore more normal muscle activity patterns over time, and also may help to disperse inflammatory mediators caused by chronic muscle spasm.[228–230]

Uterine Displacement–Mayan Uterine Massage

It has been suggested that uterine retrodisplacement can lead to symptoms of CPP.[198] Although the role of pelvic tension and improper posture in the etiology of CPP is accepted, conventional medicine does not address the potential for uterine displacement, other than prolapse associated with pelvic relaxation as an etiologic factor. Mayan uterine massage is a practice introduced into the United States by Rosita Arviga, after dedicated study with a Belizean shaman who specialized in this technique. Ms. Arviga trains and certifies people in this technique and it has grown in popularity because of many anecdotal reports of success for the treatment of vague but sometimes debilitating complaints such as CPP, as well as for many other gynecologic problems. The treatment is predicated on the belief that uterine displacement, which may occur as a result of childbearing, poor posture, sedentary lifestyle, improper carrying and work habits, etc., can lead to significant pelvic congestion, gynecologic, nervous, circulatory, and digestive problems. No studies have been done to objectively demonstrate efficacy. The practice appears generally noninvasive (it is an intervention); however, it should not be used for pregnant women.

TREATMENT SUMMARY FOR CHRONIC PELVIC PAIN

- Symptomatic pain relief can be achieved with herbal analgesics and antispasmodics. Sedatives can be used if pain interferes with sleep.
- Anxiety and depression commonly associated with CPP can be treated with botanical anxiolytics and antidepressants which may be combined with herbs for pain relief and sleep promotion.
- Reduce inflammation with herbs, an anti-inflammatory diet, including EFA supplementation.
- Treat underlying or associated digestive problems such as bloating, constipation, or IBS.
- Treat underlying or associated gynecologic or menstrual problems, for example, ovarian cysts, dysmenorrhea, or endometriosis.
- Treat underlying or associated urinary problems such as UTI or interstitial cystitis.
- Treat pelvic congestion syndrome with herbs that stimulate pelvic circulation.
- Use external treatments such as sitz baths and massage with analgesic essential oils to improve pelvic circulation and relieve pain.
- Employ muscle relaxation techniques, pelvic muscle re-education, biofeedback, or electrical stimulation to retrain muscle patterns and relieve pain.
- Mayan uterine massage may be a helpful technique for relieving pain and pelvic adhesions or uterine displacement.
- Achieve a healthy body weight, good posture, and adequate exercise.
- Supplement with calcium and magnesium for relief of muscle spasms.

SUMMARY

A number of conditions of the reproductive organs can be treated with botanical medicine. Table 7-8 includes a summary of the herbs used to treat these conditions.

TABLE **7-8**

Condition/Botanical Medicine Summary Table

	BENIGN BREAST DISORDER	CERVICAL DYSPLASIA	CHRONIC PELVIC PAIN	ENDOMETRIOSIS	UTERINE FIBROIDS
Achillea millefolium			X	X	X
Actaea racemosa			X	X	X
Aesculus hippocastanum			X		
Alchemilla vulgaris			X	X	X
Althea officinalis		X	X		
Ananas comosus		X			
Anemone pulsatilla			X	X	
Angelica sinensis	X		X	X	
Astragalus membranaceus				X	
Berberis vulgaris					X
Calendula officinalis	X	X		X	
Camellia chinensis				X	X
Cannabis indica			X		
Capsella bursa-pastoris					X
Caulophyllum thalictroides	X		X		X
Ceanothus spp.					
Chelidonium majus					X
Chionanthus virginicus	X			X	

Continued

TABLE 7-8

Condition/Botanical Medicine Summary Table—cont'd

	BENIGN BREAST DISORDER	CERVICAL DYSPLASIA	CHRONIC PELVIC PAIN	ENDOMETRIOSIS	UTERINE FIBROIDS
Cinnamomum spp and Erigeron					X
Commiphora mol mol					
Curcuma long				X	
Cordyceps sinensis				X	
Corydalis ambigua			X	X	
Dioscorea villosa				X	
Echinacea spp.		X		X	
Eleutherococcus senticosus	X	X	X	X	X
Eschscholzia californica			X	X	
Filipendula ulmaris			X		
Galium aparine	X				
Ganoderma lucidum		X			
Geranium maculatum					X
Glycyrrhiza glabra	X	X	X	X	
Gossypium herbaceum					
Hamamelis virginiana					X
Hydrastis canadensis		X	X		
Hypericum perforatum		X	X	X	X
Lavandula officinalis		X	X		
Leonurus cardiaca	X		X	X	X
Linum ussitissimum	X				X
Lomatium dissectum		X			
Mahonia aquifolium	X				
Matricaria recutita			X	X	
Melaleuca alternifolia		X			
Melilotus officinalis	X				
Melissa officinalis			X		
Mentha piperita			X		
Mitchella repens			X		X
Myrica cerifera					X
Oenothera biennis	X		X	X	
Origanum vulgar		X			
Panax ginseng				X	
Panax quinquefolius	X	X	X	X	X
Paeonia lactiflora			X	X	
Phytolacca americana	X				
Picrorrhiza kurrhoa				X	
Piper methysticum			X	X	
Piscidea piscipula			X	X	
Rehmannia glutinosa				X	
Rhaponticum carthimoides	X	X	X	X	X
Rhodiola rosea	X	X	X	X	X
Rosmarinus officinalis				X	
Rubus idaeus			X		X
Rumex crispus					
Sanguinaria canadensis		X			
Schisandra chinensis	X	X	X	X	X
Silybum marianus				X	
Tanacetum parthenium			X	X	
Taraxacum officinale	X			X	
Thuja occidentalis		X		X	
Thymus vulgaris		X			
Trifolium pratense	X				

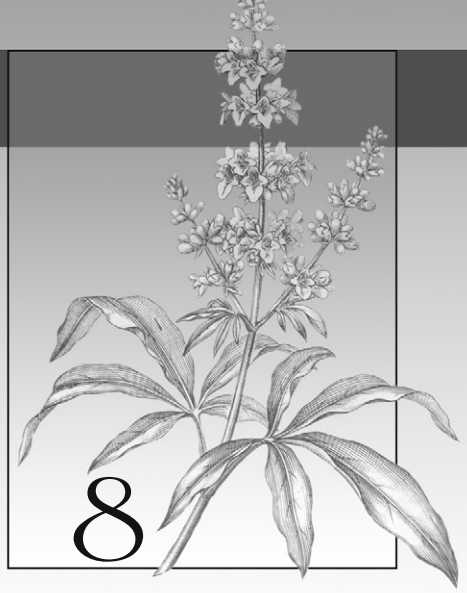
TABLE **7-8**

Condition/Botanical Medicine Summary Table—cont'd

	BENIGN BREAST DISORDER	CERVICAL DYSPLASIA	CHRONIC PELVIC PAIN	ENDOMETRIOSIS	UTERINE FIBROIDS
Trillium erectum					X
Ulmus rubra			X		
Usnea barbata		X			
Verbena officinalis	X			X	
Viburnum opulus			X	X	
Viburnum prunifolium					
Vitex agnus-castus	X			X	
Withania somnifera	X	X	X	X	X
Zingiber officinale			X	X	

Vaginal Infections and Sexually Transmitted Diseases

Aviva Romm, Bevin Clare, Lisa Alschuler, Christopher Hobbs, Roy Upton



8 CHAPTER

VULVOVAGINITIS AND COMMON VAGINAL INFECTIONS

Aviva Romm, Bevin Clare

The normal vaginal environment is a dynamic milieu with a constantly changing balance of *Lactobacillus acidophilus* and other endogenous flora, glycogen, estrogen, pH, and metabolic byproducts of flora and pathogens.[1] *L. acidophilus* produces hydrogen peroxide that limits the growth of pathogenic bacteria.[2] Disturbances in the vaginal environment can allow the proliferation of vaginitis-causing organisms. The term vulvovaginitis actually encompasses a variety of inflammatory lower genital tract disorders that may be secondary to infection, irritation, allergy, or systemic disease.[3] Vulvovaginitis is the most common reason for gynecologic visits, with over 10 million office visits for vaginal discharge annually.[4] It is usually characterized by vaginal discharge, vulvar itching and irritation, and sometimes vaginal odor.[5] Up to 90% of vaginitis is secondary to bacterial vaginosis (BV), vulvovaginal candidiasis (VVC), and trichomoniasis. The actual prevalence and causes of vaginitis, however, are hard to gauge because of the frequency of self-diagnosis and self-treatment.[1] In one survey of 105 women with chronic vaginal symptoms, 73% had self-treated with OTC products and 42% had used alternative therapies. On self-assessment, most women thought they had recurrent vulvovaginal candidiasis (RVVC), but upon diagnosis, only 28% were found positive for RVVC. Women with a prior diagnosis of vulvovaginal candidiasis (VVC), however, were able to accurately self-diagnose up to 82% of the time based solely on symptoms.[6] This may, however, be an overestimate, as in another study (questionnaire) of 634 women, only 11% were able to accurately recognize the classic symptoms of VVC.[6] Another study of women who thought they had VVC also found that self-assessment had limited accuracy, with only 33.7% of women with self-diagnosed yeast infection having microscopically confirmable cases.[7]

Two-thirds of patients with vaginal discharge have an infectious cause.[2] However, the presence of some amount of vaginal secretions can be normal, varying with age, the menstrual cycle, pregnancy, and the use of OCs.

Antibiotics, contraceptives, vaginal intercourse, receptive oral sex, stress, and hormones (e.g., HRT, endogenous hormonal dysregulation) can lead to overgrowth of pathogenic organisms.[1] Chemical vulvovaginitis can be caused by colored and perfumed soaps, toilet paper, bubble baths, panty liners, tampons, sanitary pads, and douches. Latex condoms, topical antifungal agents, and preservatives and other agents in lubricants can cause allergic reactions leading to vulvovaginitis.[2] In menopausal women, or those on antiestrogen therapies, decreased estrogen levels may lead to atrophic vaginitis, which if asymptomatic generally requires no treatment. Forty percent of postmenopausal women, however, are symptomatic; symptoms are readily treatable with topically applied lubricants, and the use of estrogen replacement therapies by topical or oral administration.

Although vaginal complaints may commonly be treated based on symptoms, studies have demonstrated a poor correlation between symptoms and diagnosis.[8,9] Therefore, the most accurate diagnoses and thus the most appropriate treatments, can best be made with testing methods specific for individual organisms. Acute singular episodes of vaginal infections are referred to as uncomplicated, whereas recurrent vaginal infections are considered complicated. Complicated cases are often more severe, resistant to treatment, and may be associated with underlying systemic causes, for example, in VVC, uncontrolled diabetes, or immunosuppression.[2]

The remainder of this section presents seperate discussions of the most common vaginal infections

TABLE **8-1**

Differential Symptoms and Signs of Common Vaginal Infections

	BACTERIAL VAGINOSIS	VULVOVAGINAL CANDIDIASIS	TRICHOMONIASIS
Discharge color	Thin off-white discharge	Curdy whitish to yellowish-white discharge	Yellow green or colorless copious discharge
Discharge odor	Malodorous discharge with a characteristic ''fishy'' odor that may be increased after sexual intercourse	May have no odor, or odor may be reminiscent of yeasted bread	Malodorous
Physical findings	Discharge and odor may be apparent; discharge may be adherent to vaginal walls; tissue typically appears normal	Vulvovaginal redness, swelling, and fissures; discharge appears thick, whitish, and adherent to vaginal walls	Vulvovaginal redness, swelling, ''strawberry'' cervix. Frothy and purulent discharge is visible
Vaginal pH (normal <4.5)	High (>4.5)	Normal	High (>4.5)

Adapted from Egan M, Lipsky M: Diagnosis of vaginitis, Amer Fam Phys 1095-1104, 2000.

(Table 8-1) followed by a discussion of the botanical treatment of vaginal infections. Table 8-2 provides a general overview of common causative organisms, agents, and conditions involved in vulvovaginitis. It should be remembered that multiple causes of vaginitis may occur concurrently.[2]

BACTERIAL VAGINOSIS

Bacterial vaginosis (BV) is a common form of infectious vaginitis caused by the polymicrobial proliferation of *Gardnerella vaginalis*, *Mycoplasma hominis*, and other anaerobes. It is associated with loss of normal lactobacilli.[2] BV accounts for at least 10% and as many as 50% of all cases of infectious vaginitis in women of childbearing age.[1,7] Determining the presence of BV can be difficult, however, because as many as 75% of women are asymptomatic.[1]

Symptoms

Some or all of these symptoms may be present in women with BV.

- Milky, homogenous discharge
- Possible vaginal irritation
- Malodorous vaginal discharge (characteristic ''fishy'' odor)

BV is also commonly asymptomatic.

Diagnosis

Diagnosis is based on the Amstel criteria, which is considered 90% accurate with three or four of the following findings: the presence of milky, homogenous discharge, vaginal pH greater than 4.5 positive whiff test (''fishy'' odor to the vaginal discharge), and the presence of clue cells on light microscopy of vaginal fluid. Odor is a symptom that is frequently associated with BV, due to amines produced from the breakdown products of amino acids produced by *Gardnerella vaginalis* in the presence of anaerobic bacteria. This also results in a rise in vaginal pH.[2]

Risks for Developing BV

Numerous factors, described in Table 8-3, are associated with the development of BV. It is uncertain whether BV is a sexually transmitted disease. The prevalence is higher in women with multiple sexual partners and in women seeking the services of STD clinics. Treatment of sexual partners of women with the infection has not definitely proved to be beneficial; however, urethral smears of male partners often show typical BV morphocytes.[1,2,5]

Risks Associated with BV

BV in pregnancy appears to be a risk factor for second trimester miscarriage, premature rupture of the membrane and premature labor, chorioamnionitis, and postcesarean and postpartum endometritis.[10,11] Women with BV have an increased incidence of abnormal Pap smears, pelvic inflammatory disease (PID), and endometritis. Further, the presence of BV in women undergoing invasive gynecologic procedures may increase the risk of serious infection including vaginal cuff cellulitis, PID, and endometrirtis.[1] Eliminating BV appears to decrease the risk of acquiring HIV infection; thus, it is suggested that women with BV be treated regardless of whether they are symptomatic.[5]

Conventional Treatment of BV

CDC guidelines recommend the treatment of all women with symptomatic BV.[5] Conventional treatment of BV is metronidazole (Flagyl) orally or vaginally (Metrogel), or Clindamycin. Proper treatment typically results in an 80% cure rate at 4 weeks, with recurrence rates of 15% to 50% in 3 months.[2] Treatment failure may

TABLE 8-2

Common Causative Organisms, Agents, and Conditions Involved in the Etiology of Vulvovaginitis

ORGANISM/AGENT/ CONDITION	EXAMPLES
Bacterial vaginosis (BV)	*Gardnerella vaginalis, Mycoplasma hominis*, other anaerobic microorganisms
Vulvovaginal candidiasis (VVC)	*Candida albicans, Candida tropicalis, Candida glabrata*, other *Candida* species
Trichomoniasis	*Trichomoniasis vaginalis*
Chemical vulvovaginitis	Feminine hygiene products: tampons, sanitary pads, douches, latex condoms, spermicides, colored and perfumed soaps, toilet paper, bubble baths
Allergic vulvovaginitis	Latex condoms, topical antifungal agents, and preservatives and other agents in lubricants
Atrophic vulvovaginitis	Estrogen deficiency due to menopause, anti-estrogenic therapies, or hormonal dysregulation
General causes/factors that might lead to or increase susceptibility to vulvovaginal infection and VVC	Antibiotics, oral contraceptives, use of diaphragms, spermicide, IUDs, frequent vaginal intercourse, receptive oral sex, stress, public hot tubs, hormones (e.g., imbalanced endogenous hormones, HRT), uncontrolled diabetes mellitus, immunosuppression (HIV/AIDS, steroids), pregnancy Sexual abuse must be ruled out in girls or young women with vulvovaginitis or recurrent vaginal infections.

TABLE 8-3

Factors Associated with the Development and Pathophysiology of Bacterial Vaginosis

TYPE OF RISK FACTOR	EXAMPLES
Personal risk factors	Use of: tampons, sponges, douches, intrauterine devices, sex toys Sexual practices: new or multiple sexual partners, receptive oral sex, latex condoms, contraceptive methods such as cervical cap, IUD, or spermicide Other risk factors: antibiotic use, oral contraceptives, smoking
Microbial factors	Initiating infectious agents; possibly a sexually transmitted infection Decline in lactobacillus numbers Rise in pH Lack of hydrogen peroxide produces lactobacillus strains

be caused by lack of successful recolonization of hydrogen peroxide producing strains of lactobacillus, antibiotic resistance, and possibly reinfection by male partners.

Metronidazole is also the prescribed treatment during pregnancy; however, it is contraindicated in the first trimester because of theoretic risks of teratogenicity. Thus, many pregnant women prefer to avoid exposure altogether.[10,11] Clindamycin is used as an alternative.[1]

Evidence on the use of antibiotics in pregnancy to reduce the risk of preterm labor and its associated morbidities is somewhat conflicting. A Cochrane review concluded that no evidence supports the screening of all women for BV, and Guidelines of the American College of Obstetricians and Gynecologists (ACOG) also does not recommend screening in asymptomatic patients.[12,13] According to a recent (2005) systematic review, no evidence supports the use of antibiotic treatment for either BV or *Trichomonas vaginalis* (see later in this section) for reducing preterm birth in low- or high-risk women.[14] Nonetheless, CDC Guidelines (2002) still recommend treatment of all pregnant women with Metronidazole or Clindamycin.[5]

VULVOVAGINAL CANDIDIASIS

Vulvovaginal candidiasis (VVC), commonly referred to as yeast infection, is the second most common cause of vaginitis in the United States. Approximately 75% of all women will experience an episode of VVC in their lifetime, with RVVC occurring in 5% of women.[1,3] It is most commonly caused by the fungus *Candida albicans*; however, other *Candida* species, such as *C. tropicalis* and *C. glabrata* are becoming increasingly common, possibly because of increased use of OTC antifungals, and they are also typically more resistant to antifungal treatments.[1] OTC antifungal treatments are among the top 10 selling OTC medications in the United States with an estimated $250 in annual sales.[6] Establishing Candida as a cause of vaginitis can be

difficult, because 50% of all women have Candida organisms as part of their normal vaginal flora.[1] Candida is not considered a sexually transmitted disease, and conventional medical practice does not include treatment of male partners unless uncircumcised or presenting with inflammation of the glans penis.[1] RVVC is defined as four or more episodes annually.[2] Recurrence may be a result of associated factors, intestinal microorganism reservoir, vaginal persistence, or sexual transmission.[1] Genital candidiasis is associated with antibiotic use, oral contraceptives and HRT, and other drugs that change the vaginal environment to favor proliferation of Candida. Vaginal yeast infections are also more common during pregnancy and menstruation, and in diabetics. Drugs and diseases that suppress the immune system can facilitate infection.

Causes and Risk Factors for Developing VVC

Reported risk factors include:
- Recent/repeated antibiotic use
- Diabetes mellitus
- HIV infections/AIDS
- Increased estrogen levels (e.g., hormonal dysregulation, HRT)
- Pregnancy
- Hyperglycemia

Additional factors may include anything that disrupts the normal balance of vaginal flora, which are listed in Table 8-2.

Symptoms

Women with VVC often develop mild to severe itching and irritation of the vulva and may have a vaginal discharge characteristically curd-like in appearance with a mild yeast-like odor. The vulva may be red, inflamed, and swollen and the tissue may become raw and fissured, particularly from scratching to relieve itch, which should be discouraged. Note that these symptoms are not specific only to VVC, and therefore other causes should also be ruled out. Physical findings in women with VVC include vulvar and/or vaginal erythema, edematous labia minora, appearance of vaginal thrush, and normal pH.

One or more of these symptoms are typically reported by patients with VVC:
- Vulvovaginal pruritus
- Vulvovaginal irritation
- Vulvovaginal swelling
- Dysuria
- Thick, whitish vaginal discharge
- Possible odor to vaginal discharge (characteristic ''yeasted bread–like'' odor)

Diagnosis

Definitive diagnosis of Candida can be based on positive microscopic findings.[6] Cultures are expensive, but obtaining a positive fungal culture can be important for the diagnosis and effective treatment of RVVC.[6] Candida vaginitis is associated with a normal vaginal pH (≤ 4.5). Identifying Candida by culture in the absence of symptoms is not an indication for treatment, because it is a part of the normal endogenous flora.

Conventional Treatment Approaches of VVC

Uncomplicated VVC is intermittent and infrequent, and in 80% to 90% of cases results in resolution of symptoms and negative culture after a short course of topical azole drugs.[5] Examples of azole-containing antifungal creams include: clotrimazole, miconazole, ketoconazole, and fluconazole. These are currently available OTC. The duration of treatment with these preparations may be 1, 3, or 7 days. Alternatively, ketoconazole, fluconazole (Diflucan), itraconazole, or Nystatin can be taken orally. Self-medication with OTC preparations should be advised only for women who have been diagnosed previously with vaginal Candida infection and who have a recurrence of the same symptoms. Any woman whose symptoms persist after using an OTC preparation or who has a recurrence of symptoms within 2 months should seek medical care. Treatment with azoles results in relief of symptoms and negative cultures among 80% to 90% of patients who complete therapy. Topical agents usually are free of systemic side effects, although local burning or irritation may occur. A maximum of 7 days of topical therapy is recommended during pregnancy. Oral agents lead to better compliance but have a greater risk for systemic toxicity, and occasionally may cause nausea, abdominal pain, dizziness, rash, or headaches.[15] Therapy with the oral azoles occasionally has been associated with abnormal elevations of liver enzymes. Occasionally, women who take oral contraceptives must stop using them for several months during treatment for vaginal candidiasis because they can worsen the infection. Women who are at unavoidable risk of vaginal candidiasis, such as those who have an impaired immune system or who are taking antibiotics for a long period of time, may need an antifungal drug or other preventive therapy. For women with complicated VVC (RVVC), a longer duration of therapy may be recommended, followed by a 6-month period of maintenance therapy.[5] Azole drugs may significantly interact with a number of drugs (e.g., astemizole, cisapride, H1-antihistamines interactions have been associated with cardiac dysrhythmia) owing to potent inhibition of cytochrome P3A4, leading to increased bioavailability of the interacting drug.[2]

TRICHOMONIASIS

Trichomoniasis vaginalis is a motile, flagellate protozoan. It is the third most common cause of vaginitis. Every year, approximately 180 million women worldwide are diagnosed with this infection annually, accounting for 10% to 25% of all vaginal infections.[1] Current belief is that *T. vaginalis* is almost exclusively acquired through sexual contact.[2] Male sexual partners are infected in 30% to 80% of cases.[1]

Symptoms

Symptomatic infection causes a characteristic frothy green malodorous discharge with a high pH (can be as

high as 6.0).[5] Additionally, there may be soreness and irritation in and around the vulva and vagina, dysuria, dyspareunia, bleeding upon intercourse, inability to tolerate speculum insertion because of pain, or a superficial rash on the upper thighs with a scalded appearance. The cervix may have a characteristic appearance, called petechial strawberry cervix, in up to 25% of cases.[1] Chronic asymptomatic infection can exist for decades in women; an infection also may present atypically.[2] In men, infection is mostly asymptomatic, or there may be a thin white or yellow purulent discharge with dysuria (nongonococcal urethritis).[2,5]

Diagnosis

Trichomoniasis can be diagnosed on the basis of simple microscopy, pH evaluation, and amine tests.[2] However, in as many as 50% of cases, microscopy yields negative findings in spite of strong evidence of *T. vaginalis* infection. In this case, PCR can be used to obtain a definitive diagnosis; however, it is more costly.

Risk Factors Associated with the Development of Trichomoniasis

Smoking, IUD use, and multiple sexual partners all increase the risk of contracting *T. vaginalis*.[1] Statistically, black unmarried women who smoke cigarettes, use illicit drugs, less educated teenagers, and those of low socioeconomic groups are more likely to be colonized with this organism, as are women who have had greater than five sexual partners in the past 5 years, have a history of gonorrhea or other STDs, and who have an early age at first intercourse.

Risks Associated with Trichomoniasis Infection

Trichomoniasis is associated with and may act as a vehicle of transmission for other sexually transmitted diseases, including HIV.[1,2,7] It is also associated with an increased risk of premature rupture of the membrane, premature birth, and low birth weight.[2,5]

Conventional Treatment of Trichomoniasis Infection

CDC treatment guidelines for treatment of *T. vaginalis* infection is oral metronidazole, which has a cure rate of 90% to 95%. Unlike with other vaginal infections, treatment is recommended regardless of whether a woman is symptomatic.[7] Treatment success may be increased with treatment of sexual partners. Sex is to be avoided until the patient and any sexual partners are cured. Follow-up is considered unnecessary in patients who are initially asymptomatic or who become asymptomatic after treatment is completed. Oral metronidazole is recommended for treatment of symptoms in pregnant women.[5] Treatment during pregnancy has not been shown to reduce the risk of preterm delivery.[7] Also, as stated, physicians and pregnant women may be hesitant to use this drug during pregnancy owing to potential risks of teratogenicity. A recent Cochrane review found no benefit from antimicrobial treatment for *T. vaginalis* during pregnancy, and in fact, implies possible harm from treatment on the basis that the largest trial was stopped early due to increased risk of preterm labor with metronidazole treatment.[14] As this is the only medication used to treat *T. vaginalis*, hypersensitivity and drug resistance are potential obstacles to therapy. Increasing dosage may overcome resistance, and a desensitization protocol is used in cases of hypersensitivity to the drug.[7] Additionally, other drugs are available in Europe but have not yet been approved by the FDA for use in the United States.[7]

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

Research and clinical experience indicate that women commonly seek OTC and alternative therapies for the treatment of vaginal infections and vulvovaginitis (Table 8-4). In one study, 105 patients, with a mean age of 36 years, and 50% with college degrees, referred by their gynecologists for evaluation of chronic vaginal symptoms, were interviewed about their OTC and alternative medicine use in the preceding year, it was found that 73% of patients had self-treated with OTC antifungal medications or povidone-iodine douching and 42% had tried alternative therapies including acidophilus pills orally (50%) or vaginally (11.4%), yogurt orally (20.5%) or vaginally (18.2%), vinegar douches (13.6%), and boric acid (13.6%).[16]

Vulvovaginitis may simply be an acute response to a temporary period of imbalance or recent exposure to precipitating factors, such as a period of stress at school or work, excessive consumption of sugar or alcohol at holiday time, or increased sexual activity with condom and spermicide use, affecting proper balance in local flora. In such cases, simple lifestyle modifications combined with topical applications are often adequate treatments. Recurrent vulvovaginitis may be part of a larger picture of chronic lifestyle imbalance, underlying conditions that disrupt the vaginal flora (e.g., bowel dysbiosis or hormonal dysregulation) or exposure to any of the many instigating causes mentioned earlier in this chapter (see Table 8-2). Complicated, recurrent vulvovaginitis can be more difficult to treat but can often be effectively addressed with a combination of local and systemic strategies and removal of underlying causes. Patients with intractable vulvovaginitis should be evaluated for serious underlying conditions such as immunosuppression or diabetes mellitus, and any botanical treatment should occur in conjunction with appropriate medical care. Although there is evidence in the medical literature to suggest that, with the exception of trichomoniasis, it is not necessary to treat sexual partners; empirical evidence from botanical clinical practice suggests that recurrence is less likely when all partners are treated. This should not be surprising, as with most vaginal infections, it has been found that men do harbor organisms in the urethra.

The goal of the botanical practitioner is to reduce or eliminate factors that encourage infection or overgrowth of pathogenic organisms, restore the normal vaginal environment and its flora, and relieve symptoms associated with infection. This chapter does not address hormonal dysregulation that may be associated with vulvovaginitis.

TABLE **8-4**

Botanical Treatment Strategies for Vulvovaginitis

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Eliminate/reduce infection	Antimicrobial	*Allium sativum*	Garlic
		Arctostaphylos uva ursi	Uva ursi
		Berberis aquifolium	Oregon grape
		Calendula officinalis	Calendula
		Coptis chinensis	Goldthread
		Glycyrrhiza glabra	Licorice
		Hydrastis canadensis	Goldenseal
		Melaleuca alternifolia	Tea tree
		Origanum vulgare	Oregano
		Thymus vulgaris	Thyme
		Usnea barbata	Usnea
Reduce swelling and irritation	Anti-inflammatory	*Althea officinalis*	Marshmallow
		Lavandula officinalis	Lavender
Reduce swelling and irritation	Demulcent	*Althea officinalis*	Marshmallow
		Symphytum officinale	Comfrey
		Ulmus rubra	Slippery elm
Heal and repair tissue	Vulnerary	*Althea officinalis*	Marshmallow
		Calendula officinalis	Calendula
		Symphytum officinale	Comfrey
		Ulmus rubra	Slippery elm
Reduce vaginal discharge	Astringent	*Arctostaphylos uva ursi*	Uva ursi
Improve vaginal lubrication and treat vaginal atrophy	Demulcent/emollient	See Chapter 18	
Improve vaginal lubrication and treat vaginal atrophy	Phytoestrogen		
Improve immunity and resistance	Adaptogens	See Chapter 6	

Antimicrobial Therapy

Antimicrobial herbs are used as primary treatments in cases of vulvovaginitis when due to infectious causes. For acute infections, they are generally used solely as topical applications. For recurrent cases, external application is combined with oral use. Internal treatment should focus on immune supporting and antimicrobial botanicals, including echinacea, garlic, goldenseal, Oregon grape root, Pau d'arco, astragalus, and various medicinal mushroom species such as maitake and reishi medicinal mushrooms. Also see Chapter 7 for a discussion on adaptogens and immune support.

Numerous herbs have exhibited both broad spectrum and specific antimicrobial activities. Although treatment approaches vary with each of the different infectious causes of vulvovaginitis, antimicrobial herbs are usually applied generically regardless of the infectious agent. There appears to be little, if any risk of resistance with herbal treatments; however, labs specializing in delivering services to CAM practitioners sometimes do sensitivity and specificity testing for natural agents with screening for vaginal infections. This is unnecessary except in chronic, recurrent, or intractable cases.

Garlic

Garlic is a popular antimicrobial botanical treatment for vaginal infections, effective when applied in fresh whole form. A single clove is carefully peeled and inserted whole at each application, usually at night, and left in during sleep. It is sometimes dipped in a small amount of vegetable oil to ease insertion. It also may be wrapped in a small piece of gauze or with a piece of string with a tail left hanging to ease removal. Otherwise, it can be removed manually. In vitro, garlic has demonstrated antimicrobial effects against a wide range of bacteria and fungi, including *E. coli, Proteus, Mycobacterium*, and *Candida* species.[17] In a study by Sandhu et al., 61 yeast strains, including 26 strains of *C. albicans* were isolated from the vaginal, cervix, and oral cavity of patients with vaginitis and were tested against aqueous garlic extracts. Garlic was fungistatic or fungicidal against all but two strains of *C. albicans*. In another in vitro study, an aqueous garlic extract effective against 22 strains of *C. albicans* isolated from women with active vaginitis. At body temperature, garlic had mostly fungicidal activity; below body temperature, the action was mostly fungistatic.[18,19] Cases of irritation and even chemical burn have been reported

after prolonged application of garlic to the skin or mucosa.[20]

Goldenseal, Goldthread, and Oregon Grape Root

Goldenseal, goldthread, and Oregon grape are all herbs that contain the alkaloid berberine, a major active component possessing antimicrobial activity.[21] In vitro studies demonstrate a rational use of the herb for its antibacterial properties.[22,23] Berberine has demonstrated specific activity against *C. albicans* and *C. tropicalis* as well as to a species of trichomoniasis, *T. mentagrophytes*, among other pathogens.[20,22] These herbs have been used historically and in modern herbal medicine with good reliability for the treatment of a variety of infectious conditions, both internally and topically. Goldenseal is considered by many herbalists to be the most effective of the three herbs. It is commonly included, as is Oregon grape root, as an ingredient in topical preparations for the treatment of vaginitis, added in powder or tincture form to suppositories or powder inserted vaginally in ''00'' capsules. Internal use of goldenseal, in addition to specific antimicrobial activity, may enhance immune response via stimulation of increased antibody production and may be suggested for oral use in intractable cases.[24] Goldthread has demonstrated significant antimicrobial activity against a wide range of Candida species.[25]

Oral consumption of these herbs is generally contraindicated for use in pregnancy. Goldenseal root is an endangered North American plant. Therefore, only cultivated root should be purchased for use. Oregon grape and goldthread can be substituted with confidence.[25]

Note: Berberine-containing herbs stain fabrics a very distinctive yellow color. Patients using any of these herbs in suppositories or other external treatments should be advised to avoid staining towels, clothing, and bed coverings. It is advisable to insert suppositories prior to bed, and to wear a menstrual pad to protect bedding.

Licorice

Licorice root is one of the most widely used herbs for the treatment of a range of inflammatory conditions. It has demonstrated effectiveness as a demulcent in the treatment of oral, gastric, and respiratory tract conditions, including ulcers and inflammation.[20] Although no research was identified on the use of this herb for vulvovaginitis, its effects on other mucosa would seem to substantiate this application. Additionally, licorice alcohol extracts have shown effectiveness against *E. coli*, and *Candida* and *Trichomoniasis* species in vitro. Alcohol extracts can easily be added to suppository blends for topical application.

Oregano and Thyme

The antimicrobial properties of essential oils have been known since antiquity. In vitro testing of essential oils against a wide variety of microorganisms, showed thyme and oregano to possess the strongest antimicrobial properties among many herbs that were tested.[26] Thyme essential oil has also found to be specifically effective against *Candida* spp.[27,28] Direct application of undiluted oil (neat oil) is not recommended as it is too caustic to the skin and sensitive mucosa. Rather, a small amount of essential oil can be added to suppository blends, diluted tincture may be added to peri-washes and sitz baths, and tea of these herbs may be used as a base to which other herbs may be added for peri-washes and sitz baths. See sample formulae in this chapter and Chapter 3.

Figure 8-1 Tea tree (*Melaleuca alternifolia*). (Photo by Martin Wall.)

Tea Tree

Tea tree oil (TTO) is derived from the leaves of the tea tree (Fig. 8-1), a native to Australia with a history of use of the leaves for the treatment of colds, coughs, and wounds by indigenous Australians, who spoke of healing lakes in which leaves of the tree had decayed. The medical use of the oil as an antiseptic was first documented in the 1920s, and led to its commercial production, which remained high throughout World War II.[29] Legend has it that it was provided to Australian soldiers fighting in World War II for use as an antiseptic and that harvesters were exempt from enlisting.[29] Reports of the effectiveness of TTO appeared in the literature from the 1940s through

Figure 8-2 Usnea (*Usnea barbata*). (Photo by Martin Wall.)

the 1980s, with a significant increasing interest in the medical value of TTO seen in the 1990s to the present, corresponding with interest in CAM generally. Current research, presented in a thorough review by Carson et al., supports its use as an antibacterial and antifungal, as well as an anti-inflammatory.[29] Limited studies have been done on TTO's use as an antiviral, but a few trials have indicated possible activity against enveloped and non-enveloped viruses.[29] A broad range of bacteria have demonstrated in vitro susceptibility to TTO, including those known to be associated with BV. A case report in which a woman successfully self-treated with TTO-containing suppositories also supports the use of TTO in BV.[30–35] At concentrations lower than 1%, TTO may be bacteriostatic rather than antibacterial.[29] Several studies have demonstrated efficacy against *C. albicans;* however, to date no clinical trials have been done. A rat model of vaginal candidiasis supports the use of TTO for VVC.[30] The organisms on which numerous TTO antifungal studies have focused.[32,35–37] Two studies demonstrated antiprotozoal activity of TTO, one specifically supporting anecdotal evidence that TTO is effective against *T. vaginalis*. The mechanisms of antimicrobial action are similar for bacteria and fungi and appear to involve cell membrane disruption with increased permeability to sodium-chloride and loss of intracellular material, inhibition of glucose-dependent respiration, mitochondrial membrane disruption, and inability to maintain homeostasis.[33,38–40] Perhaps what has attracted the most interest about this herb is that it has demonstrated activity against antibiotic-resistant bacteria. It has been used in Australia since the 1920s has not led to the development of resistant strains of microorganisms, nor have studies that have attempted to induce resistance with the exception of one case of induced in vitro resistance in *Staphylococcus aureus*.[41,42]

Usnea

Usnea lichens (Fig. 8-2) have a history of use that spans centuries and countries from ancient China to modern Turkey, from rural dwellers in South Africa to modern day naturopathic physicians and herbalists in the United States.[43,44] The lichen is rich in usnic acid, which has demonstrated in vitro antimicrobial activity against bacteria, viruses, protozoa. Additionally, it exhibits anti-inflammatory and analgesic activity.[25] Alcohol extract may be added to a suppository blend or diluted in water or tea (1 tbs tincture/cup of liquid) for use as a peri-wash or in sitz baths.

Uva Ursi

Uva ursi is used by midwives as a topical antiseptic and astringent to relieve vulvar and urethral irritation associated with vulvovaginitis. Leaf preparations have shown antimicrobial activity against *C. albicans, S. aureus, E. coli*, and other pathogens.[20] For vulvovaginitis, it is used topically as a peri-rinse or in sitz baths.

Symptomatic Relief and Tissue Repair

Irritation and superficial damage from vulvovaginitis can lead to significant discomfort as well as fissures and rawness of the vaginal tissue. The use of herbs as topical agents for reducing inflammation, irritation, and for promoting healing are an important part of any herbal protocol for this condition. Tissue repair is also especially important because inflamed and fissured vaginal tissue increases a woman's susceptibility to secondary infection, notably, with HIV. Herbs commonly used to promote local tissue repair and reduce discomfort fall into several categories including anti-inflammatories, vulneraries, demulcents, and astringents. Anti-inflammatories relieve local swelling, irritation, and pain; vulneraries work to heal wounds and irritated tissue, demulcents cool and soothe irritated tissue, and astringents tonify tissue and create a protective barrier on the surface, reducing further insult. Astringents can also be effective in drying up excessive secretions. Some of the many herbs with topical anti-inflammatory effects to consider using include licorice, marshmallow root, and lavender, all of which may be used in various combinations and preparations with other herbs to treat vaginitis.

Calendula

Calendula has demonstrated efficacy in the treatment of wounds, promoting tissue regeneration and re-epithelialization, and has also shown some antimicrobial activity (see the preceding). It is soothing as a tea, oil, or diluted tincture (1 tbs tincture to ¼ cup of water), and is an important ingredient in topical vulvovaginitis preparations.[45] ESCOP recommends calendula for the treatment of skin and mucosal inflammation and to aid wound healing.[46]

Comfrey Root

Comfrey root (Fig. 8-3) has a very long history of folk use for healing damaged skin, tissue, and broken bones. It is highly mucilaginous. It is thought that allantoin and rosmarinic acid are the constituents mainly responsible for comfrey's healing and anti-inflammatory actions.[47] Comfrey is indicated for topical use only. Use on broken skin or mucosa should be minimized but is reasonable for short durations (1 to 2 weeks at a time), and

Figure 8-3 Comfrey (*Symphytum officinale*). (Photo by Martin Wall.)

should not exceed 100 μg of pyrrolizidine alkaloids with 1,2 unsaturated necine structure daily for a maximum of to 4 to 6 weeks annually.[48] Comfrey infusion may be added to a peri-rinse or sitz-bath blend, or comfrey oil or finely powdered herb may be added to a suppository blend.

Lavender

Lavender has a folk tradition of use for topical treatment of mild wounds, for which it is still included by herbalists and midwives in topical preparations for vulvovaginitis.[47] Additionally, its fragrance imparts a pleasant scent to herbal preparations. It may be used as a rinse or sitz bath in tea form or using diluted tincture, or several drops of essential oil may be added to rinses, sitz baths, or suppositories.

Marshmallow Root

Marshmallow is demulcent and vulnerary. Marshmallow root contains a mucilage that covers the mucosa, protecting it from local irritation.[46] Topical application is soothing in sitz baths and peri-rinses, and the powdered herb, finely ground, helps give herbal suppositories firmness. Slippery elm bark powder can be substituted for marshmallow root powder in suppository blends.

Topical Preparations for Treating Vulvovaginitis

Sitz Baths, Peri-Washes, and Suppositories

The most common forms of topical applications used in the treatment of vulvovaginitis are sitz baths, peri-washes, and suppositories. Instructions for each of these preparations are found in Chapter 3.

Sitz baths may be done either in the bath tub with the water filled to hip height or in a purchased sitz bath, which is a small basin that fits over the bowl of the toilet and which may be purchased at most pharmacies. When prepared with anti-inflammatory and antimicrobial herbs, they provide a soothing relief to vulvar/urethral irritation. The bath water and herbs should be used only once, and prepared fresh each time. The water may be hot or tepid, according to the patient's comfort.

For a Soothing Sitz Bath: Combine equal parts of dried thyme, calendula, lavender, and uva ursi leaf. Place one ounce of the herb blend into a quart glass jar or pot with a close fitting lid. Cover with 1 quart of boiling water, close the vessel, and steep for 30 minutes. Strain the entire contents into a sitz bath filled with water to the desired level. Add 2 tablespoons of sea salt per bath and soak. Repeat up to twice daily for 2 weeks.

Peri-rinses provide an excellent alternative to sitz baths if there is a lack of time to soak, and also make a soothing, antiseptic rinse after using the toilet. They can be done anytime during the day if vulvar itching or irritation becomes uncomfortable (or unbearable as some women find it does!). The same infusion described for sitz baths can be used to fill peri-bottles, small, pointed-top squeeze bottles also available at most pharmacies. The peri-bottle can be kept filled and left near the toilet. Add 1 tsp of sea salt to each bottle. Use as frequently as needed, patting dry after each rinse.

Suppositories prepared with a blend of herbs specific for vulvovaginitis can provide effective, soothing relief, heal tissue, and have antiseptic action. They can either be custom purchased through naturopathic pharmacies, or must be made by the practitioner or the patient. Although this may cause some inconvenience, they can be prepared in large batches and kept in the freezer for many months and the refrigerator for many weeks, ready for use.

An effective suppository blend for BV and candidiasis includes a vulnerary herb, antimicrobial herbs, and a demulcent herb in a base of cocoa butter and coconut oil. The following is a highly reliable formula:

1 cup cocoa butter
½ cup coconut oil
3 tbs calendula oil
2 tsp thyme oil
1 tsp lavender oil
4 tbs marshmallow root powder finely ground
2 tbs goldenseal root powder

Suppositories are applied nightly for 7 to 14 days. It is advisable to wear a light pad and old underwear while sleeping because the suppository will melt at body temperature. The oils and herbs may stain bedding or clothes.

Why Douching Is Not Recommended

Women commonly douche because of the misperception that it ''cleans out'' the vaginal canal and can thus cure vaginal infections. A systematic review found that although douching may provide some symptomatic relief and initial reduction in infection, it may lead to rebound effects and other complications in the long run. Povidone iodine preparations, a common OTC choice for self-treatment, have been demonstrated to cause a ''rebound effect'' in which a higher than normal bacterial colonization is seen within weeks of last douching, which could actually increase the risk of bacterial vaginosis. Routine douching for hygiene has been shown to double the risk of acquiring vaginitis. Douching of all types can lead to increased risks of PID, endometritis, salpingitis, and ectopic pregnancy.[19]

CHRONIC VULVOVAGINITIS AND INTESTINAL PERMEABILITY

The roles of intestinal dysbiosis and permeability (leaky gut syndrome) should not be overlooked in the etiology of chronic or intractable cases of vaginitis. The body's ability to maintain control over the volume of microorganisms present in the intestinal and vaginal tracts is intimately connected to the health of the bowel and bowel flora. If the body is unable to sustain a healthy balance of microorganisms, those that normally inhabit our bodies without causing harm can overproliferate or migrate, becoming pathogenic. This is often the case with chronic vaginal infections. Further, when the body is in a chronic state of immune-mediated response and inflammation, normally controlled organisms may become opportunistic. Thus, a first line of botanical treatment for chronic vaginal infections, especially candidiasis, is improving the integrity of the bowel mucosa and helping to restore normal bowel flora. The former is done with many of the same anti-inflammatory, antimicrobial, and vulnerary herbs already mentioned, and a few additional botanicals. The most important of these include chamomile, marshmallow root, calendula, slippery elm, goldenseal, Oregon grape root, Dioscorea villosa (wild yam), and licorice root. These may be administered as teas, tinctures, or capsules. Essential fatty acids of both the omega-3 and -6 varieties should be supplemented for their anti-inflammatory action. Probiotics (see the following) are useful in restoring gut flora and can be taken as a supplement or as live, active culture yogurt.

Nutritional Considerations: Lactobacillus/Yogurt

The goal of treatment with lactobacillus supplements or yogurt, taken orally or applied vaginally, is recolonization of the vagina (and bowel with oral intake) with adequate numbers of healthy flora capable of controlling and resisting pathogenic infection. The success of this treatment requires products that contain the proper lactobacillus species and that these species be active. Additionally, oral yogurt therapy requires the survival of lactobacilli through the GI system and digestive processes, as it is thought that vaginal recolonization occurs as a result of migration of the microorganisms from the anus to the vaginal introitus.[19] Effective oral and topical yogurt therapy also requires that the lactobacilli be able to adhere to the vaginal epithelium. *L. acidophilus* is poorly adherent to the vaginal walls, and it also is not a major rectovaginal species. Although two clinical trials have demonstrated significant efficacy with oral and/or topical use, the use of other species of lactobacillus, such as *L. crispatus, L. jensenii*, *L. rhamnosus*, and *L. fermentum*, may be more effective.[20,49] A randomized crossover study with a washout period by Shalev et al. studied the effects of oral yogurt prophylaxis on a group of women (n = 46) with BV (n = 20) and candidal vaginitis (n = 18) or both (n = 8). The study showed a significant decrease in BV and no significant decrease in candidal infection. Only 28 participants were still enrolled in the study at 4 months and only 7 completed the protocol.[51] In an open crossover trial by Hilton et al., a randomized group of women (n = 33) with RVVC were assigned to either a 6-month protocol of daily oral intake of *L. acidophilus* containing yogurt or a yogurt-free diet. A threefold decrease was seen in candidal infections, substantiated by wet mount and potassium hydroxide. Interestingly, although only 13 women completed the yogurt treatment, 8 women in the yogurt arm refused to switch over to the yogurt-free diet.[51] Patients with lactose intolerance may experience GI complaints from oral yogurt intake. Topical treatment of BV with yogurt has been evaluated in several studies. In an unblinded study of 84 pregnant women with BV a program of yogurt douching twice daily for 7 days (n = 32) compared with acetic acid tampons (n = 20) or no treatment (n = 20), it was found after 2 months of treatment 88% of women in the yogurt group and 38% of women in the acetic acid group compared with 5% of women in the no treatment group were BV free. A multicenter, placebo-controlled RCT looking at the effects of lactobacillus vaginal tablets combined with estrogen as a delivery agent on BV demonstrated a 75% cure rate at 2 weeks and an 88% cure rate at 4 weeks compared with a 25% and 22% respective cure rates at corresponding times in the placebo group.[19]

Empiric evidence from herbal and midwifery practice suggests that live active culture yogurt may be more effective than acidophilus tablets or capsules, although any of the options is potentially effective. It is also provides some immediate relief of burning and itching to inflamed tissue. The easiest way to apply it is in the shower, placing one foot on the edge of the tub and using two fingers to insert the yogurt vaginally and around the vulva. Do not place fingers back in the yogurt after applying; rather place the appropriate amount (2 to 3 tbs) in a small container. The yogurt should be left on for 3 to 5 minutes, and then rinsed off, repeating up to two times daily depending upon the severity of the infection and irritation. Repeat for up to 2 weeks, although treatment is often effective within several days.

Additional Therapies

Boric Acid

Boric acid is a common OTC treatment for VVC and RVVC that is both self-prescribed and recommended by health practitioners.[1,19,52] Although it has not been widely studied, four studies have shown positive outcomes, even compared with conventional antifungal therapy, and it is considered an effective therapy for the treatment of vaginal candidiasis.[1,18,19,52,53] In one study, 92 women with chronic mycotic vaginal infections were followed with microscopic examination of the vaginal discharge during prolonged therapy with antifungal agents and boric acid. A microscopic picture unique to chronic mycotic vaginitis was observed, representing the cytologic reaction of the mucous membrane to chronic yeast infection. This diagnostic tool proved extremely effective in detecting both symptomatic and residual, subclinical mycotic infection and provided a highly predictive measure of the probability of relapse. The ineffectiveness of conventional antifungal agents appeared to be the main reason for chronic mycotic infections. In contrast, boric acid was effective in curing 98% of the patients who had previously failed to respond to the most commonly used antifungal agents and was clearly indicated as the treatment of choice for prophylaxis.[53] In a double-blinded, randomized study, 108 VVC-positive college students used boric acid or Nystatin capsules once daily for 2 weeks. Boric acid cure rates were 92% at 7 to 10 days posttreatment and 72% at 30 days, a statistically significant improvement over the Nystatin capsules, which only had a cure rate of 64% at 7 to 10 days posttreatment, and 50% at 30 days posttreatment.[54] In a case series of 40 patients with vulvovaginitis, 95% of patients remained symptom-free at 30 days post–boric acid treatment, and in another study, boric acid was tested against an azole-resistant strain of yeast, more commonly seen in women with recurrent yeast infections and yielded clinical improvement occurred in 81% of cases, with mycological eradication in 77% of the women.[19,55,56] The standard recommended dose and application is 600 mg of boric acid placed in a size ''0'' gelatin capsule and inserted vaginally. For acute treatment, one capsule is inserted nightly for 14 days, followed by a maintenance treatment of twice weekly insertion.[19,53] Some women report mild to moderate burning as the capsule dissolves. If intercourse occurs during the treatment period, males may report dyspareunia.[19] Serious side effects have not been reported from treatment.[53] Boric acid, available in drug stores, can be considered a safe, effective, accessible, and affordable treatment for vaginal candidiasis.

General Suggestions

Reducing exposure to the personal, sexual, chemical, and allergenic factors described in the preceding can be beneficial in preventing and reducing vulvovaginitis and infection. Wearing clean cotton underwear or ''breathable'' fabrics, changing underwear more often if there is copious vaginal discharge or dampness, sleeping without underwear, wearing loose-fitting pants, and observing hand-washing before and after genital contact may reduce the incidence and frequency of vulvovaginitis.[52] Wearing a thong may cause irritation or facilitate the transmission of anorectal organism to the vulvovaginal area. Regular bathing and showering with gentle soap, keeping the vulvar area dry, and regular use of sitz baths also may be helpful, the latter particularly in candidal vulvovaginitis.

Sex Education and Empowerment

It is optimal for women to abstain from sexual activity while undergoing treatment for vulvovaginitis. Not all women feel comfortable addressing intimate sexual matters with their partners; therefore, it may be important to help patients develop skills and confidence to tell partners what they need, encourage partners to obtain treatment when relevant, and make healthy sexual lifestyle choices that prevent infection.

TREATMENT SUMMARY FOR VULVOVAGINITIS

- Healthy vaginal flora and bowel flora must be promoted when there is chronic vulvovaginitis.
- Avoid precipitating factors, for example, anything that might trigger chemical or allergic reaction, or mechanical irritation (e.g., tampons, sexual activity) (see Table 8-2).
- For infectious vulvovaginitis, consider antimicrobial herbs including Calendula, garlic, goldenseal, oregano, thyme, tea tree, Pau d'arco, marshmallow, lavender, and Oregon grape root.
- For relief of irritation, itching, and inflammation use topical applications of calendula, marshmallow, comfrey, and lavender for their soothing, healing properties. Healing tissue can also reduce the spread of opportunistic infections such as HIV.
- Use topical or oral preparations containing live, active acidophilus cultures to restore normal bowel and vaginal flora.
- For chronic, recurrent vulvovaginitis, consider adding internal treatment for immune supporting and antimicrobial activity, including echinacea, goldenseal, Oregon grape root, and medicinal mushrooms. Also see Chapter 6 for a discussion on adaptogens and immune support.
- The role of intestinal permeability or ''leaky gut syndrome'' and other bowel disorders should be evaluated in the treatment of chronic vulvovaginitis.
- Limit or eliminate refined flour, refined sugar, dairy products, fruits, and fermented foods.
- Supplement with 5 to 10 mg of zinc daily in intractable cases of yeast infection.
- Use boric acid capsules as suppositories, especially for intractable BV.
- Loose fitting clothing made of natural fibers should be encouraged, especially during sleep.
- Avoid douching.
- Educate patient about vaginal hygiene and personal empowerment regarding healthy sexual behavior.
- When appropriate and possible, treat sexual partners.

GENITAL WARTS (CONDYLOMA AND HPV)

Lisa Alschuler

Condylomata acuminata, commonly referred to as genital warts, is a highly infectious sexually transmitted disease caused by the infectious agent human papillomavirus (HPV). More than 20 types of HPV have been identified as infective. Of these, types 6 and 11 typically produce visible genital warts. Warts typically occur at multiple sites in the urogenital, perineal, and perianal regions. They appear as soft, moist, small pink or gray polyps, although they can also appear flat and smooth or granulated. Polyps may enlarge to form pedunculated clusters the size of which can become so large as to affect urination, defecation, and normal vaginal delivery. Genital warts may be painful, friable, and pruritic; however, the majority are asymptomatic.

HPV types 16, 18, 31, 33, and 35 are strongly associated with cervical neoplasia, cervical intraepithelial dysplasia, and squamous cell carcinoma. Up to 80% of sexually active adults in the United States carry HPV; however, only 5% develop HPV lesions or cervical dysplasia. The outcome of HPV exposure depends on a number of factors, for example, HPV type, host immunity, and smoking status. The risk of infection increases with the number of sexual partners and is associated with unprotected sexual intercourse. Condoms are not adequate protection against transmission. Conditions of immunodeficiency, epithelial injury of the genital area, and pregnancy all increase the risk of HPV infection.

It is suspected that HPV remains dormant in the body once contracted; therefore, the goal of treatment is to minimize visible lesions and prevent progression to neoplasia, rather than eradicate the virus.[52]

DIAGNOSIS

Diagnosis of genital warts typically occurs during a woman's routine screening health examination. The health care provider may visibly assess HPV infection if characteristic lesions are present. Genital warts must be differentially diagnosed from the flat-topped *condyloma lata* of secondary syphilis. A diagnosis made by inspection can be confirmed by biopsy. Biopsy is indicated only if the diagnosis is uncertain, if the lesions do not respond to standard therapy, if the disease worsens during treatment, if the patient is immunocompromised, or if the warts appear to be pigmented, indurated, fixed, or ulcerated (signs of neoplasia or squamous cell carcinoma). Endocervical warts can be detected via colposcopy.

Although there are HPV nucleic acid tests available to identify the viral type, these tests are not routinely ordered. There are, in fact, no data that support the use of type-specific HPV nucleic acid tests in the routine diagnosis or management of genital warts.[57] The HPV nucleic acid tests are available primarily for research purposes and to determine possible risk for carcinoma in high-risk individuals.

HPV is classified as clinical, subclinical, or latent, depending upon the extent or absence of lesions.

CONVENTIONAL TREATMENT APPROACHES

The primary goal of conventional treatment is to remove visible symptomatic warts. Most patients respond to conventional treatment with wart-free periods. Without treatment, warts will spontaneously resolve, remain unchanged, or grow in size or number. The factors influencing these outcomes are not known. The main benefit of treatment is symptom improvement. A secondary likely benefit of treatment is the reduced risk of infectivity and decreased likelihood of complications associated with HPV infection. Current conventional treatment options do appear to reduce HPV DNA and thus infectivity. However, successful treatment of genital warts does not eradicate infectivity or the risk of recurrences of the disease. There are several standard, accepted conventional treatments.

Determination of the type of treatment is made after evaluation of wart size, location, morphology, patient preference, cost of treatment, adverse effects, and provider preference. Generally, a course of applied treatments is required to remove genital warts. First-line therapy for HPV may consist of the application of 0.5% podophyllotoxin (Podofilox 0.5% solution or gel) one to four times. Podophyllotoxin is an antimitotic agent. This treatment has been shown to be effective in 70% to 90% of men or women with exposed and accessible genital warts.[58,59] This treatment is typically well tolerated and self-administered, and produces minimal local irritation. Ten to twenty percent podophyllin resin ethanolic solution has also been used topically. However, podophyllin resin is less effective than podophyllotoxin. In one study, 94% of patients treated with podophyllotoxin were cured versus only 29% of patients treated with podophyllin resin.[59] Additionally podophyllin resin is commonly associated with local inflammation, erosion, pain, and burning. Finally, concern exists about the systemic absorption of the podophyllin resin and its systemic toxicity, particularly in pregnant women.

An alternative to podophyllotoxin is topical application of trichloroacetic acid (TCA) or bichloracetic acid (BCA). TCA and BCA are caustic agents that coagulate proteins, thus destroying the wart. A health care provider applies these agents. Treatment is repeated weekly until the lesions resolve. This treatment is generally effective but can cause inflammation at the site of application. If pain develops, soap or sodium bicarbonate must be applied to neutralize the acid.

Cryotherapy is another common treatment for exposed genital warts. Cryotherapy with liquid nitrogen or cryoprobe is typically done weekly or biweekly. Cryotherapy causes thermal-induced cytolysis. This therapy can be quite effective if applied properly; however, overtreatment can cause localized pain and blistering. Conversely, undertreatment is ineffective. Typical second-line therapeutic interventions include surgical removal of warts. There are several techniques of surgical removal. All techniques require local anesthesia. Surgical removal is a one-time treatment. However, surgery is more expensive and requires more time than

medical treatment options. Surgical treatment of genital warts is usually reserved for patients with a large number of lesions or for patients who have not responded to other treatments. Another second-line therapy is the intralesional injection of interferon. Many trials have confirmed the efficacy of this treatment. It causes the disappearance of all visible warts in approximately 43% of patients and visibly shrinks visible warts in an additional 25%.[60] However, interferon therapy is expensive and requires three treatments each week, usually for 4 to 6 weeks.

All conventional treatments are somewhat limited in their efficacy. In order to increase efficacy, it is common for health care providers to use combination therapy. However, combination therapy increases adverse effects. For this reason, some providers prefer to use different therapies sequentially. Warts that are not easily accessible, such as those located on the cervix, in the anal canal, or in the urethral meatus, are more difficult to treat. Liquid nitrogen or TCA (or BCA) are common treatments for warts located in these areas. Cervical warts must be closely monitored and high-grade squamous intraepithelial lesions (HGSIL) must be excluded before treatment for warts is begun. An important and universal aspect of the treatment of any type and location of genital warts is to examine and treat the sexual partners of the patient. In addition, women with genital warts should receive STD and Pap screenings annually until normal Pap tests have occurred for 36 consecutive months after treatment. After this time, a woman may elect to receive Pap screenings every 36 months. Women who are found to have HPV but who do not have any visible warts are not candidates for treatment as there are no treatments that are known to eradicate the infection. These women should, however, obtain annual Pap screenings. Additionally women with a Pap test indicative of low-grade SIL or ASCUS should obtain HPV DNA testing. If high-risk types of HPV DNA are found, these women should have colposcopy and biopsy to assess for more extensive dysplasia. Gardasil, an HPV vaccine, has recently been released and is recommended for women ages 14 to 26 years of age for the prevention of HPV infection, and thus is expected to lower cervical dysplasia and cervical cancer rates.

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

The herbalist's approach to genital warts may be in conjunction with or in place of conventional treatment. A comprehensive botanical approach supports the body's inherent abilities to resist infection and uncontrolled cellular proliferation caused by the virus. Herbs with antiviral actions are key components of the botanical protocol. Herbs with immunostimulatory actions, particularly activation of cell-mediated immunity, are of specific importance. Adaptogens (see Chapter 6) are also ideally included in a comprehensive botanical protocol to further support the immune system.

DISCUSSION OF BOTANICAL PROTOCOL

Treatment of HPV can be approached topically alone, but it is optimal to boost overall resistance using a combination of topical and internal therapies. For topical treatment, undiluted botanical extracts can be directly applied to warts using a cotton swab several times daily (use a fresh cotton swab for each application) for

TABLE **8-5**

Botanical Treatment Strategies for Human Papilloma Virus

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Reduce viral infection	Antiviral	*Allium sativum*	Garlic
Prevent neoplasia	Antimicrobial	*Astragalus membranaceus*	Astragalus
Reduce cervical inflammation and heal tissue	Antitumorigenic	*Calendula officinalis*	Calendula
		Commiphora mol-mol	Myrrh
		Echinacea spp.	Echinacea
		Ganoderma lucidum	Reishi
		Hypericum perforatum	St. John's wort
		Hydrastis canadensis	Goldenseal
		Lavandula officinalis	Lavender
		Lomatium dissectum	Lomatium
		Melissa officinalis	Lemon balm
		Origanum vulgare	Oregano
		Melaleuca alternifolia	Tea tree
		Thuja occidentalis	Thuja
		Thymus vulgaris	Thyme
		Usnea barbata	Usnea
Improve overall immune response via HPA axis support	Adaptogens	See Chapter 6 for a discussion of adaptogens.	

Protocol for the Treatment of HPV

Topical Treatment

Option 1. Combine the following tinctures and apply to lesions two to three times daily with a cotton swab for 6 to 12 weeks:

Thyme	(*Thymus vulgaris*)	30 mL
Goldenseal	(*Hydrastis canadensis*)	30 mL
Myrrh	(*Commiphora mol mol*)	20 mL
St. John's wort	(*Hypericum perforatum*)	20 mL
Thuja	(*Thuja occidentalis*)	10 mL

Total: 100 mL

Option 2. Combine the following tinctures and apply to lesions two to three times daily with a cotton swab for 6 to 12 weeks:

Tea tree	(*Melaleuca alternifolia*)	30 mL
Goldenseal	(*Hydrastis canadensis*)	30 mL
Oregano	(*Origanum vulgare*)	20 mL
Lemon balm	(*Melissa officinalis*)	20 mL
Licorice	(*Glycyrrhiza glabra*)	10 mL

Total: 100 mL

Note that applying undiluted tincture to sensitive mucosa can cause a burning sensation. If this is too irritating to the patient, first apply a small amount of calendula oil to the surrounding area, and then apply tincture carefully on the lesion.

Option 3. For suppositories, use either combination of the above tincture combinations in a suppository recipe. See Chapter 3 for general suppository instructions.

Combine external treatment with:

Antiviral Tincture: Internal Treatment

Combine the following tinctures:

Astragalus	(*Astragalus membranceus*)	25 mL
Reishi	(*Ganoderma lucidum*)	25 mL
Ashwagandha	(*Withania somnifera*)	25 mL
Echinacea	(*Echinacea* spp.)	15 mL
Usnea	(*Usnea barbata*)	10 mL

Total: 100 mL

Dose: 5 mL twice daily for up to 6 months for acute cases; 3 mL daily for maintenance and prophylaxis for up to 6 months posttreatment for an acute case.

6 to 12 weeks, as needed. Suppositories can be inserted vaginally or rectally for warts in those areas. They should be inserted nightly five times per week for 6 to 12 weeks. The patient should be re-evaluated periodically for HPV.

Astragalus

Astragalus has been used for centuries in Chinese medicine as a qi tonic, specifically for strengthening what is called the ''wei qi'' or the protective energy of the body. It has long been used to build energy, increase general immunity, improve digestion and improve longevity. Herbalists and naturopathic doctors commonly use astragalus for its immunostimulatory effects. Oral doses of astragalus have been found to increase IgE, IgA, and IgM antibody levels and lymphocyte levels in humans.[61] Of particular relevance to the treatment of genital warts was a randomized, controlled trial involving 531 patients with chronic cervicitis secondary to HPV, CMV, and HSV infections. This trial demonstrated that a liquid extract of astragalus root potentiated recombinant interferon in the treatment of cervicitis, particularly when resulting from HPV infection.[62] In addition to the immunostimulatory effect of astragalus, people who take it often experience increased physical stamina, increased mental alertness, and decreased fatigue.

Echinacea

The purified polysaccharide, arabinogalactan from *E. purpurea*, has been found to increase T-cell proliferation and the production of interferon by macrophages.[63] Additionally, unpurified fresh pressed juice of *E. purpurea* has been shown in vitro to induce macrophages to produce cytokines, which in turn create an antiviral effect against viruses, including the herpes virus. Clinical trials of echinacea are of mixed results. As an example, a year-long prospective, double-blind, placebo-controlled crossover trial ($n = 50$) examined the efficacy of a tablet form of *Echinacea purpurea* (Echinaforce) in the clinical course of genital herpes. The study found no statistically significant benefit in the clinical course of frequently recurrent genital herpes.[64] It is possible that this study failed to show benefit because of insufficient dosing and/or the use of a tablet form of echinacea. Certain constituents in echinacea species, namely alkenes and amides, possess potent antiviral activity (including against HSV). Ethanol extracts of these constituents and these extracts of echinacea have been shown to have the most potent antiviral activity.[65] Although clinical trials have not yet conclusively demonstrated significant antiviral and immune stimulation, previous and current naturopathic and herbal practice demonstrate these effects and hence many modern herbalists and naturopathic doctors use echinacea as part of their treatment of HPV.

Goldenseal

Although no research has been done specifically on the treatment of HPV with goldenseal, the herb has shown broad antimicrobial effects that suggest this herb may be beneficial as part of a topical herbal application for this infection.

Lemon Balm

Acutely, lemon balm extract is applied topically for its virostatic action. Lemon balm has demonstrated effects against a number of viruses including HSV and Influenza. Virostatic effects are attributable to the glycoside-bound phenolcarboxylic acid and its polymers. These constituents block cellular receptors responsible for viral adsorption, and thus viral replication.[66] Additionally oxidation products of caffeic acid, found in lemon balm, inhibit

protein biosynthesis in vitro, which may account for the antiviral activity of topical application.[67] These in vitro data have been confirmed in at least three human trials. One of the more recent trials was a prospective, double-blind, randomized trial (n = 66). The treatment group applied a standardized balm cream [1% Lo-701 dried extract from *Melissa officinalis* L. leaves (70:1)] four times daily to an active *Herpes labialis* lesion over a 5-day period. All patients suffered from recurrent *Herpes labialis*. However, there was a significant decrease in the intensity of herpetic symptoms by day 2 of treatment between the active vs. the placebo group (p = 0.042).[68] Lemon balm also has anxiolytic and sedative actions.[69]

Licorice

Although no studies were identified on the treatment of HPV with licorice or its extracts, other viral studies suggest, as well as the herb's traditional uses, that investigation into such use may be promising.

Oregano and Thyme

Both oregano and thyme essential oils are regularly included in vaginal suppositories for the treatment of vaginal infections, including HPV infection. One study reports on the efficacy of thyme as an antibacterial, and in another study oregano and clove oils were diluted and examined for their activity against enveloped and non-enveloped RNA and DNA viruses. Olive oil was also included as a control. Viruses were incubated with oil dilutions and enumerated by plaque assay. Antiviral activity of oregano and clove oils was demonstrated on two enveloped viruses of both the DNA and RNA types and the disintegration of virus envelope was visualized by negative staining using transmission electron microscopy.[70,71] Care should be taken in the use of essential oils topically; used undiluted (neat) they can be irritating to sensitive tissues such as cervical or vaginal mucosa. Tincture may be applied directly.

Thuja

Thuja (Fig. 8-4) is used for the treatment of genital and anal warts, and is commonly recommended in the naturopathic treatment of cervical dysplasia for its antiviral activity.[72] The main constituent is an essential oil consisting of α-thujone and β-thujone, the content of which varies proportionally with the amount of ethanol used in producing the plant extract. If consumed internally, thujone can be neurotoxic, convulsant, and hallucinogenic. Long-term or excessive use of thujone-rich products can cause restlessness, vomiting, vertigo, tremors, renal damage, and convulsions.[73] Internal use of thuja decoctions and even very small doses of thuja oil (e.g., 20 drops per day for 5 days) as an abortifacient has been associated with neurotoxicity, convulsions, and death.[72] Additionally, thuja is associated with a substantial risk of inducing fetal malformation, and is absolutely contraindicated for use in pregnancy.[72] No research on the short- or long-term topical use of this herb was identified. Ingestion of thuja cannot be recommended because of its significant potential for toxicity.

Figure 8-4 Thuja (*Thuja occidentalis*). (Photo by Martin Wall.)

Usnea

Usnea lichens have a history of use that spans centuries and countries from ancient China to modern Turkey, from rural dwellers in South Africa to modern-day naturopathic physicians and herbalists in the United States.[43,44] The lichen is rich in usnic acid, which has demonstrated in vitro antimicrobial activity against bacteria, viruses, and protozoa. Additionally, it exhibits anti-inflammatory and analgesic activity.[25] Alcohol extract may be added to a suppository blend or diluted in water or tea (1 tbs tincture/cup of liquid) for use as a peri-wash or in sitz baths.

NUTRITIONAL CONSIDERATIONS

The nutritional supplements recommended in Chapter 7 are appropriate for use when treating HPV infection.

TREATMENT SUMMARY FOR CONDYLOMATA

- Apply antiviral botanical agents directly to affected sites using a cotton swab. Use suppositories for cervical, vaginal, or rectal lesions.
- Support the body's inherent resistance using herbs with antiviral and immunostimulatory actions.

CASE HISTORY

Mary, a 27-year-old female patient presented for her annual gynecologic examination and Pap smear. She had no menstrual or vaginal symptoms. She was currently not sexually active but had recently ended a 2-year, monogamous, heterosexual relationship. Her Pap smear revealed cervical atypia (ASCUS). The patient was counseled about her management options, ranging from colposcopy to wait-and-retest in 3 months. The patient was very anxious but chose to wait and have her Pap redone in 3 months. The second Pap demonstrated cervical ASCUS once again. The patient was extremely anxious about this result and wanted to be tested for HPV. She refused a biopsy. An HPV nucleic acid test was done that revealed the presence noncancerous HPV. At this point, the patient continued to refuse colposcopy; however, she wanted to be on active treatment. She willingly agreed to engage in active naturopathic treatment for 3 months and then to undergo a repeat Pap smear. The following treatments were recommended to the patient:

- Increased consumption of dark leafy greens and broccoli to at least three servings weekly.
- Engage in relaxation activities regularly (the patient chose to attend a yoga class).
- Folic acid: 10 mg po daily

Tincture Formula:

Echinacea	(*Echinacea* spp.)	40 mL
Licorice	(*Glycyrrhiza glabra*)	20 mL
Lemon balm	(*Melissa officinalis*)	15 mL
St. John's wort	(*Hypericum perforatum*)	20 mL
Thuja*	(*Thuja occidentalis*)	5 mL
		Total: 100 mL

Dose: 5 mL three times daily

The patient was diligent with her protocol and tolerated treatment well. A repeat Pap smear done after 3 months of treatment was normal. The patient discontinued the folic acid and herbal tincture after this normal Pap smear result. A subsequent Pap smear 6 months later was also normal. All subsequent Pap smears up to the most recent one, done 24 months after her initial atypical Pap smear have been normal (no atypia present).

HERPES

Aviva Romm, Christopher Hobbs

Herpes simplex virus (HSV) is a member of the human herpes virus group that includes, for example, HSV-1, HSV-2, and Epstein-Barr virus (EBV). HSV is a recurrent viral infection that remains dormant in the nervous system with periods of reactivation characterized by individual or multiple clusters of fluid-filled vesicles at specifically affected sites. HSV-1 and -2 are the main types of herpes virus seen in general clinical practice. HSV-1 typically manifests above the waist and is referred to as Herpes labialis because of it primarily appearing on the lips in the form of ''cold sores.'' HSV-2, Herpes genitalis, typically appears on the genitals, although it also produces skin lesions. The vesicles rupture, leaving small, sometimes painful ulcers, which generally heal without scarring, although recurrent lesions at the same site may cause scarring. Coinfection with HSV-1 and -2 increases the frequency of HSV-2 outbreaks. Orogenital sex can lead to cross-contamination of these sites, with oral herpes being more likely transmitted to the genitals than the other way around. The incubation period for HSV-1 is 3 to 7 days and 3 to 5 days for HSV-2.

Approximately 75% of individuals in the United States are infected with HSV-1, and about 25% with HSV-2, with an estimated incidence of 500,000 to 1 million new cases annually.[74–76] Independent predictors of HSV-2 infection include sex (women are more likely to become infected and have more frequent outbreaks, whereas men are more likely to transmit infection), race (rates are higher among African Americans and Mexican Americans), increased age, less education, poverty, cocaine use, and multiple sexual partners.[74] Since the late 1970s, seroprevalence has quintupled among white teenagers and doubled among whites in their twenties. The virus is spread through contact with the lesions and through viral shedding. Sexual contact is the primary method of contamination; however, kissing and other contact with sores or shed virus in an asymptomatic individual can lead to infection. Casual contact, such as sharing of a drinking glass or cigarette has also been known to lead to infection. Ninety percent of affected individuals are unaware they have herpes.[77] HSV-2 infection significantly increases susceptibility to HIV infection.

Immunologic changes of pregnancy, particularly depression of T-cell response, appear to make pregnant women more susceptible to a number of viral infections, including HSV.[78] Primary herpes outbreaks in pregnancy, especially during the third trimester, pose great danger to a newborn, causing significant morbidity and mortality. Antibodies to HSV-2 have been detected in about 20% of pregnant women, with only about 5% aware they have herpes (see Herpes Simplex Virus in Pregnancy).

Prevention is always the best treatment. Practicing safe sex on all occasions regardless of whether lesions are visible, and avoiding contact with active lesions is essential. HSV may be shed in the saliva and genital secretions of asymptomatic individuals. Active lesions shed between 100 and 1000 times the amount of virus. Minor injury, for example, irritation from vaginal Candida infection, may increase the likelihood of viral transmission. Condoms do not guarantee protection, but do significantly reduce HSV-2 transmission, especially to women.[79] The virus is commonly passed from a person who does not know they have the virus because they have never had any symptoms.

PATHOPHYSIOLOGY

HSV travels along the peripheral nerve axons to the nerve cell bodies in the dorsal root ganglia and can exist in the

*To avoid possible toxicity resulting from thuja, replace with 5-mL thyme (*Thymus vulgaris*) tincture.

paraspinous ganglia indefinitely, sometimes in a completely inactive state. The virus can be reactivated and begin replicating in response to such factors as stress, depression, and anxiety, trauma to mucosa, fever, exposure to ultraviolet light (sun exposure), menstruation, poor sleep, spicy food, immunodeficiency, and other unknown factors. Migration to mucosal surfaces by way of the peripheral sensory nerves can lead to a cutaneous outbreak of lesions, which are often painful. Although the virus usually becomes dormant after an outbreak and before the next outbreak, if it occurs, an infected person, even if asymptomatic, can still pass the virus to another person. Asymptomatic viral ''shedding'' is common and occurs in cycles. Therefore, transmission of infection is possible at any time regardless of the presence of active lesions. The possibility of transmission between an infected and uninfected person in a monogamous relationship increases at the rate of about 10% a year. Women who have regular herpes outbreaks, or who have a sexual partner who has active outbreaks, should have routine Pap smears because herpes may predispose women to cervical cancer. Recent research suggests possible long-term consequences of harboring chronic HSV infection, such as development of rheumatoid arthritis.[80]

SYMPTOMS

The first episode of herpes after initial infection is known as the primary outbreak, characteristically appearing with flu-like symptoms such as fever, headache, and swollen lymph glands in the groin (Table 8-6). Primary outbreaks can last 2 to 3 weeks and can be severe enough in rare cases to require hospitalization. Recurrent herpes outbreaks are commonly heralded by a prodromal stage with characteristic feelings of tingling or itching in the genital area or around the mouth, pain and tingling in the groin, and possibly in the buttocks and backs of the thighs. Virus is already present on the skin in the prodromal phase, so this is considered a contagious phase although blisters are not yet visible. The prodromal phase typically lasts 1 to 3 days followed by vesicles, lesions, and scabbing lasting for up to 10 days before complete healing has occurred. Recurrent outbreaks are often mild and may present with pruritus, local tingling or pain, slight vaginal discharge but present with no generalized systemic symptoms. Small sores or vesicles can occur anywhere on the skin or mucous membranes of the mouth anogenital region, and are most common around the mouth and genital area. The vesicles break and become wet, finally crusting over. Healing is complete when new skin is formed under the scab, which falls off. Rarely, focal necrosis, ballooning degeneration of skin cells, and other histopathologic changes can result.

Most patients are mistakenly thought to be silent carriers. At least 90% of HSV-2 carriers are ignorant of their conditions with up to 60% to 75% having unrecognized signs and symptoms of genital herpes. Commonly, symptoms are falsely attributed to other more casual urogenital problems. Because herpes is a self-healing condition, with symptoms easily controlled with topical nonspecific agents, the diagnosis is not frequently made. The following are examples of the conditions to which female patients attribute what are actually symptoms of genital herpes outbreaks:[81]

- Vaginitis
- Allergies or reactions to medications, toilet paper, sanitary pads or other menstrual products, soaps, condoms
- Lack of lubrication during sex
- Excessively frequent sexual intercourse
- Irritation from tight jeans, g-string, bicycle seats
- Urinary tract infections
- Vaginal dryness
- Shaving burns
- Reactions to hair removal products
- Hemorrhoids or anal fissures

TABLE 8-6

Symptoms of Herpes According to Type of Outbreak

CATEGORY	CLINICAL MANIFESTATION
Primary outbreak	• This is the initial outbreak after infection; if patients do not notice vesicles, a primary outbreak may be dismissed as ''flu.''
	• Characterized by systemic infection commonly with fever and aching
	• May last 2 to 3 weeks
	• Frequently accompanied by lymphadenopathy
	• Appearance of clusters of vesicles on an erythematous base that develop into ulcers that crust over and heal
	• Severe primary outbreak can cause serious infection, including encephalitis, and may require hospitalization
	• Immunocompromised patients may develop especially severe symptoms
Recurrent episodes	• Symptoms of tingling and itching or perineal aching may precede the appearance of vesicles and lasts 1 to 3 days. Note that virus is already present on the skin during this stage.
	• Vesicles appear and last up to 10 days until full healing.
Subclinical infection	• Asymptomatic with viral shedding

Adapted from Roe V: Living with genital herpes: how effective is antiviral therapy? J Perinat Neonat Nurs 18(3):206-215, 2004.

DIAGNOSIS

When a patient presents with clusters of painful vesicles and inflammation of the surrounding area, herpes should be considered. The standard test for HSV infections is viral culture of vesicular fluid. Direct immunofluorescent

staining with conjugated monoclonal antibodies to HSV is faster, more expensive, and only about 80% to 90% as accurate as viral culture. Polymerase chain reaction (PCR) is the most accurate and most expensive test.[82]

Diagnosis in the neonate can be difficult at first because symptoms are sometimes nonspecific (e.g., fever, lethargy), with no other outward signs of infection. Less than 50% of newborns with disseminated disease or encephalitis have skin lesions.[83] If diagnosis is delayed, damage to the CNS or internal organs can be significant.

CONVENTIONAL TREATMENT APPROACHES

Antiviral therapy with drugs that selectively inhibit viral replication including acyclovir, famciclovir (Famvir), and valacyclovir (Valtrex) is the standard treatment. Acyclovir has been on the market for over 20 years, and has a reasonable safety profile, even when given during pregnancy. Teratogenicity has not been demonstrated, even during the first trimester. Famciclovir and valacyclovir are more absorbable and higher blood levels can be sustained, although their safety, especially during pregnancy, has not been as thoroughly tested as acyclovir.[76] Studies suggest that prophylactic administration of acyclovir during pregnancy can reduce shedding, shorten the duration of shedding, and reduce the cesarean rate, although these were small and not conclusive. The usual dose of acyclovir is 60 mg per kg of body weight per day in three doses intravenously for 14 days for localized skin disease, and 21 days for more severe infections.[84] Acyclovir has been associated with numerous side effects in its various dosage forms, including nausea and vomiting, diarrhea, headache, dizziness, fatigue, skin rash, edema, inguinal lymphadenopathy, anorexia, leg pain, medication taste, and sore throat from short-term oral administration, and nausea and vomiting, diarrhea, headache, dizziness, insomnia, irritability, depression, rash, acne, hair loss, arthralgia, fever, palpitations, sore throat, muscle cramps, menstrual abnormalities, and lymphadenopathy with long-term use.

HERPES SIMPLEX VIRUS IN PREGNANCY

It is estimated that 20% to 25% of pregnant women have genital herpes. With recurrent herpes, less than 0.1% of babies will contract the infection. Primary herpes outbreaks pose a much greater risk to the fetus/neonate with transmission rates as high as 50%. In asymptomatic cases the risk of transmission at birth is about 0.04%; in symptomatic cases, the risk is about 5%.

Primary herpes infection in pregnancy is associated with miscarriage, premature labor, intrauterine growth retardation, and neonatal infection. Neonatal infection most frequently occurs during labor and is associated with increased neonatal death, brain damage, seizures, cerebral palsy, blindness, and deafness.[85] Neonatal herpes affects about 1 in 15,000 newborns and the prognosis for disseminated disease with encephalitis is poor.[86] Because 90% of cases of neonatal herpes are a result of direct contact with lesions in the birth canal, cesarean section is routinely performed as the mode of delivery in active herpes outbreaks at the time of labor. Neonates are treated acyclovir or vidarabine, but this treatment is less effective once the infection has spread to the brain and internal organs.[87]

More recently, experiments have looked at using acyclovir for herpes prophylaxis in late pregnancy. Treatment has been shown to reduce recurrences after a primary infection, and reduce asymptomatic viral shedding as well as need for cesarean delivery; however, prophylaxis only partly prevents neonatal herpes infection, because it is not applicable to patients with no known clinical history but may excrete the virus.[86,88]

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

HSV infection is a major global health problem, and its association with HIV infection makes it imperative to develop effective prevention and treatment strategies. The efficacy of many topical pharmaceutical agents in treating herpes has been somewhat disappointing and inconsistent, and additionally, are costly.[89,90] Patients are often looking for safe and effective alternative measures to reduce the frequency of outbreaks and shorten their duration. It is also important to look for agents that will be effective at preventing the virus from inculcating into nerve cell bodies, proliferating, and taking up host residence. Botanicals represent a promising area for research.[16] Unfortunately, at present there are few well-designed human clinical trials looking at the effects of herbs on HSV. However a number of botanicals have demonstrated antiherpetic activity in vitro, offering some validation of the traditional use of herbs for infection. Several herbs have been shown to be topically healing for wounds, and as discussed in Chapter 7, have demonstrated efficacy in improving immune response and reducing stress. These latter categories are listed in Table 8-7 with brief descriptions of their applications to HSV treatment, but discussions of these herbs are found elsewhere throughout this book.

Clinically, patients using a combination of botanical and nutritional therapies report reduced frequency, severity, and length of outbreaks. Herbalists have found botanical medicines effective at relieving symptoms associated with outbreaks, preventing outbreaks, and reducing the frequency of outbreaks (Table 8-7). Some patients have reported going 10 years or more without an outbreak, even with a history or regularly recurrent outbreaks. Similarly, pregnant women have been shown to cease to have recurrent outbreaks during gestation, even with a history of regular recurrence in prior pregnancies (see Case History: Herpes Genitalis). It is unknown how botanicals affect asymptomatic shedding.

Symptomatic relief can be directed at systemic manifestations during a primary outbreak, mostly via analgesics to relieve discomfort and antivirals to control the degree of infection, and can be used topically to speed the healing of lesions and relieve discomfort associated with both primary and recurrent episodes. A number of herbs have been shown to have beneficial effects in supporting and enhancing immunity. Because host immune response plays a role in the outcome of herpes infection,

TABLE 8-7

Botanical Treatment Strategies for HSV-1 and HSV-2

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Pain relief for systemic aching and discomfort in primary outbreak	Analgesic	*Actaea racemosa*	Black cohosh
		Corydalis	Corydalis
		Piscidea erythrina	Jamaican dogwood
		Viburnum spp.	Cramp bark and black haw
Reduce systemic viral replication, inhibit viral attachment to cells; topical antiviral activity	Antiviral	*Aloe vera*	Aloe
		Calendula officinalis	Calendula
		Echinacea spp.	Echinacea
		Ganoderma lucidum	Reishi
		Glycyrrhiza glabra	Licorice
		Hypericum perforatum	St. John's wort
		Melissa officinalis	Lemon balm
		Salvia officinalis	Sage
		Thuja occidentalis	Thuja
		Uncaria tomentosa	Cat's claw
Wound-healing agents to promote granulation of new, healthy tissue	Vulnerary	*Aloe vera*	Aloe
		Calendula officinale	Calendula
		Symphytum officinale	Comfrey
Relieve local pain	Topical analgesic	*Hypericum perforatum*	St. John's wort
		Mentha piperita	Peppermint
		Piper methysticum	Kava kava
Relieve local pain	Anti-inflammatory	*Glycyrrhiza glabra*	Licorice
		Hypericum perforatum	St. John's wort
		Lavandula officinalis	Lavender
		Scutellaria baicalensis	Chinese skullcap
		Symphytum officinalis	Comfrey
Dry weeping lesions	Astringents	*Hamamelis virginiana*	Witch hazel
		Plantago spp.	Plantain
		Quercus alba	White oak bark
Dry weeping lesions	Antimicrobial powder	*Commiphora mol-mol*	Myrrh
Enhance immune response, increase general resistance	Immunomodulation	*Andrographis paniculata*	Andrographis
Enhance immune response, increase general resistance	Adaptogens	*Eleutherococcus senticosus*	Eleuthero
		Panax ginseng	Ginseng
		Panax quinquefolius	American ginseng
		Rhaponticum carthimoides	Rhaponticum
		Rhodiola rosea	Rhodiola
		Schizandra chinensis	Schizandra
		Withania somnifera	Ashwagandha
Improve stress response	Adaptogens	*Eleutherococcus senticosus*	Eleuthero
		Panax ginseng	Ginseng
		Panax quinquefolius	American ginseng
		Rhaponticum carthimoides	Rhaponticum
		Rhodiola rosea	Rhodiola
		Schizandra chinensis	Schizandra
		Withania somnifera	Ashwagandha
Improve stress response	Nervines	*Avena sativa*	Milky oats
		Eschscholzia californica	California poppy
		Lavandula officinalis	Lavender
		Leonurus cardiaca	Motherwort
		Melissa officinalis	Lemon balm
		Passiflora incarnata	Passion flower
		Scutellaria lateriflora	Skullcap
		Turnera diffusa	Damiana

with the immune system modulating infection both in the nervous system and the periphery, prevention focuses on supporting optimal immune response using adaptogens and the use of antivirals to reduce viral attachment and proliferation.[91] Additionally, herbs that improve the stress response (adaptogens) and relieve stress (nervines) are important, because stress is both a known precipitating factor for outbreaks and suppressive of immune function (see Chapter 6).

Analgesics

Analgesic herbs are used internally, typically as tinctures, either singly or in combination, for the symptomatic relief of generalized discomfort and aches in uncomplicated primary herpes outbreaks and for aching discomfort in the prodromal phase of recurrent outbreaks. Black cohosh, an antispasmodic and mild analgesic, was historically used specifically for aching, drawing discomfort in the buttocks and the backs of the thighs.[92] Cramp bark and black haw are reliable antispasmodic herbs with analgesic effects. Corydalis and Jamaican dogwood have strong analgesic and sedating effects. See Plant Profiles: Black cohosh, for safety considerations.

Antiviral Botanicals

The following herbs represent a selection of botanicals used for internal and/or topical antiviral therapy. All have shown some measure of antimicrobial activity in various studies and are a promising area of research for herpes treatment. Specific studies of the effects of herbs on HSV are presented in the following. These herbs may be used singly, but more commonly are used by herbal practitioners in combination with other antivirals, or in comprehensive, multiherb, multieffect formulae.

Aloe

Aloe has long been used by herbalists as a topical healing agent for wounds, burns, irritated skin, and sores. Two studies were conducted by Syed et al. examining the efficacy of topical aloe vera treatments on men experiencing primary outbreaks of genital herpes. In the first study, 120 men were randomized into three parallel groups receiving either 0.5% in hydrophilic cream, aloe vera gel, or placebo three times daily for 2 weeks. The shortest mean duration of healing occurred with aloe vera cream, followed by gel and then placebo with healing times of 4.8 days, 7.0 days, and 14.0 days, respectively. Percentages of cured patients were 70%, 45%, and 7.5%, respectively.[93] In the second study, 60 men were randomized into two groups receiving 0.5% aloe vera extract in a hydrophilic cream base or placebo. The trial had comparable favorable results to the previously discussed trial.[94] Additionally, in vitro testing has demonstrated virucidal effects of anthraquinones and anthraquinone derivatives such as emodin, a component of aloe.

Cat's Claw

The use of cat's claw, *una de gato*, by traditional healers of tropical South America extends back in history for an unknown length of time as part of oral tradition, where it was used to treat gastric ulcers, as an anti-inflammatory, antitumor, and antirheumatic, among other uses ranging from fevers and diarrhea to contraception and female genitourinary cancers. It is also used in the treatment of disharmony between body and spirit, or what we might call anxiety.[20] Inhibition of HSV-1 and -2 was demonstrated in vitro by a standardized extract of cat's claw. *H. genitalis* was significantly more susceptible to inactivation by the extract than *H. labialis*.[20] Cat's claw appears to selectively modulate ovarian hormone function and therefore should be used with care in women with hormonal dysregulation, particularly progesterone insufficiency. It is completely contraindicated in pregnancy.[20] The herb has demonstrated significant in vitro and in vivo immunostimulatory, immunoregulatory, and immunosuppressive, and anti-inflammatory effects, specifically, enhanced lymphocyte production and inhibition of tumor necrosis factor alpha (TNF-α) in a dose-dependent manner.[20] Therefore, it is cautioned any patients on immunomodulating therapies (e.g., immunosuppressant, hyperimmunoglobulin therapy, receiving vaccinations) avoid the use of cat's claw and caution be exercised in patients with autoimmune conditions. Use of cat's claw containing products is entirely contraindicated during pregnancy and lactation; however, it has been used traditionally in the immediate postpartum period for recovery after childbirth, and may facilitate milk supply through estrogen modulation.[20]

Echinacea

Echinacea is a popular herb used to prevent and mitigate viral infections, and also to prevent recurrent infection. It is commonly used as a tincture or decoction as part of a protocol for HSV infection. Midwives rely on it in pregnancy as one of the antivirals considered safe to use during that time. In a 5-month uncontrolled clinical study of 4598 patients, a salve prepared from the juice of the aerial portion of *Echinacea purpurea* was reported to have an 85% success rate in the treatment of a number of inflammatory skin conditions, among them Herpes simplex eruptions.[20] Echinacea is used by herbalists during pregnancy for the prevention of herpes outbreaks. Longitudinal use of echinacea in pregnancy was evaluated for safety and outcomes by Gallo et al. In a prospective study, 206 Canadian women, already taking echinacea-containing products, were compared with a matched cohort not taking echinacea. The products mostly contained *E. angustifolia* and *E. purpurea*, although one respondent took *E. pallida*. Thirty-eight percent took the tincture at a dose of up to 30 drops daily and 58% took tablets or capsules at a dose of 250 to 1000 mg/day. Echinacea use was primarily in the first trimester (54%); 8% used echinacea during all three trimesters. There were no statistical differences between pregnancy outcomes in the two groups nor were there statistically significant differences in the neonates.[95]

Lemon Balm

Lemon balm (Fig. 8-5) has classically been used as an uplifting herb for the treatment of stress and anxiety. Rich in volatile oils, in vitro and clinical research conducted over the past decade has demonstrated impressive

Figure 8-5 Lemon balm (*Melissa officinalis*). (Photo by Martin Wall.)

results using lemon balm ointment as a local therapy in the treatment and prevention of herpes outbreaks.[46,96,98] In one study, four different concentrations of volatile oils extracted from lemon balm were examined for the effects against HSV-2. At concentrations of 200 μg/mL, replication of HSV-2 was inhibited, indicating that the *M. officinalis L.* extract contains an anti-HSV-2 substance.[96] Another study, a double-blind, placebo-controlled, randomized trial, was carried out with the aim of proving efficacy of standardized and highly concentrated lemon balm cream for the therapy of herpes simplex labialis. Sixty-six patients with a history of recurrent herpes labialis (at least four episodes per year) in one center were treated topically; 34 of them with lemon balm cream and 32 with placebo. The cream had to be smeared on the affected area four times daily over 5 days. A combined symptom score of the values for complaints, size of affected area, and blisters at day 2 of therapy was formed as the primary target parameter. A significant difference seen in the combined symptom score on the second day of treatment is of particular importance because symptoms are usually worst at that time. In addition to reducing the duration of the healing period, the treatment led to prevention of spreading of the infection and had a rapid effect on common herpes symptoms including itching, tingling, burning, stabbing, swelling, tautness, and erythema. Some indication exists that the intervals between the periods with herpes might be prolonged with balm mint cream treatment. There is little reason to expect the development of resistance to treatment.[98] Commercial lemon balm extract concentrated creams for topical use are available over the counter and in herbal pharmacies.

Licorice

Numerous in vitro and in vivo studies have shown licorice preparations to have antiviral, antiherpetic, anti-inflammatory, antiulcer, anticarcinogenic, and a wide variety of immunomodulating effects.[99,100] Licorice root (Fig. 8-6) is taken singly or in combination as a tea, tincture, or powdered extract in capsules or tablets. It is also applied topically for local relief of swelling and irritation. The herb is indispensable for its inhibitory effects on the virus, its anti-inflammatory effects to reduce pain and swelling of lesions, and its immunomodulatory effects to enhance host resistance and reduce episodes of active lesions.[101] Glycyrrhizic acid has demonstrated lipoxygenase, cyclooxygenase, and protein kinase C inhibition. Active fractions include triterpenoids like glycyrrhizin and its aglycone glycyrrhizic acid, polyphenols, and immunomodulating heteropolysaccharides.[102,103] Licorice extract inhibited the growth and cytopathology of herpes, as well as inactivating herpes simplex virus particles irreversibly. In vivo, glycyrrhizin (GR), administered intraperitoneally could increase the survival rate of mice by 2.5 times (37.5%–39.0% to 81.8%–83.3%) that were infected by HSV-1 with herpetic encephalitis. GR also reduced HSV-1 replication in vivo.[104] Glycyrrhizic acid inhibits the growth of several DNA and RNA viruses in cell cultures and inactivates Herpes simplex 1 virus irreversibly.[101] A recent study shows that treatment of cells latently infected with Kaposi's sarcoma–associated herpes virus (KSHV), a member of the herpes family, with glycyrrhizic acid, a component of licorice, reduces synthesis of a viral latency protein and induces apoptosis of infected cells, suggesting a novel way to interrupt latency.[105]

Reishi

Considered an adaptogenic and immunomodulating herb, a number of studies have demonstrated activity of Reishi against HSV. One study, looking at the mechanisms of action of Reishi against HSV-1 and -2 found that the Ganoderma lucidum proteoglycan (GLPG), obtained by liquid fermentation of the mycelia, works by inhibiting viral replication by interfering with the early events of viral adsorption and entry into target cells.[106] Two protein-bound polysaccharides, a neutral protein-bound polysaccharide (NPBP) and an acidic protein-bound polysaccharide (APBP), isolated from water soluble substances of Reishi were also found to be effective against HSV-1 and -2. APBP was found to have a direct virucidal effect on HSV-1 and -2. APBP did not

Figure 8-6 Licorice root (*Glycyrrhiza glabra*). (Photo by Martin Wall.)

Figure 8-7 Sage (*Salvia officinalis*). (Photo by Martin Wall.)

induce interferon (IFN) or IFN-like materials in vitro and is not expected to induce a change from a normal state to an antiviral state. APBP in concentrations of 100 and 90 μg/mL inhibited up to 50% of the attachment of HSV-1 and -2 to cells and was also found to prevent penetration of both types of HSV into cells. These results show that the antiherpetic activity of APBP seems to be related to its binding with HSV-specific glycoproteins responsible for attachment and penetration, and APBP impedes the complex interactions of viruses with cell plasma membranes.[107] Virucidal effects of Reishi extracts have also been identified by other researchers.[108,109] A study by Oh et al. demonstrated potent synergistic antiviral effects against HSV-1 and -2 showed when combining APBP and acyclovir, suggesting the development of APBP as a new antiherpetic agent.[110] Reishi has also demonstrated beneficial effects in the treatment of herpes zoster, reducing postherpetic neuralgia.[111] Reishi is usually taken as a decoction or tablet. Although tinctures are also available, the polysaccharides are likely more bioavailable in whole or water-extracted forms.

Sage and Rhubarb Combination

Essential oil (EO) rich herbs, for example, thyme (*Thymus vulgaris*), tea tree, and lemon balm, and anthraquinone-rich herbs such as aloe and St. John's wort all contain antimicrobial activity, some specifically against HSV. A combination ointment containing sage (Fig. 8-7) and rhubarb extracts, the former EO rich and the latter anthraquinone-rich, and a product containing sage alone, were evaluated for their efficacy against HSV. A total of 149 patients participated: 145 (111 female, 34 male) of whom 64 received the rhubarb-sage cream, 40 the sage cream, and 41 Zovirax cream. They could be evaluated by intention-to-treat analysis. The dried rhubarb extract used was a standardized aqueous-ethanolic extract according to the German Pharmacopoeia and the dried sage extract an aqueous extract. The reference product was Zovirax cream with the active ingredient acyclovir. The mean time to healing in all cured patients was 7.6 days with the sage cream, 6.7 days with the rhubarb-sage cream, and 6.5 days with Zovirax cream. There were statistically significant differences in the course of the symptoms. For the parameter *swelling*, at the first

follow-up visit there was a significant advantage for Zovirax cream compared with sage cream, and for the parameter *pain*, at the second follow-up visit there was a significant difference in favor of the rhubarb-sage cream compared to the sage cream. The combined topical sage-rhubarb preparation proved to be as effective as topical acyclovir cream and tended to be more active than the sage cream.[89]

St. John's Wort

Hypericin and related compounds have been shown to have selective activity against viruses, both in vitro and in vivo, including HSV-1 and -2.[112,113] A prospective double-blind placebo-controlled study of St. John's wort extract compared with placebo was conducted on 110 patients with herpes genitalis. Patients were given a 90-day treatment protocol of 300 mg tid, and 600 mg tid on the days of herpes outbreaks. Symptoms were significantly and equally reduced compared with placebo, including severity of episodes, size of affected area, and numbers of vesicles.[20] Similar trials conducted by Koytchev et al. and Mannel et al. have yielded similar positive results.[20,114] Herbalists include St. John's wort in protocol for both internal and topical use for its positive effects on the nervous system, antiviral activity, and topically in tincture or salve, for its mild vulnerary and anti-inflammatory actions.

Tea Tree

Tea tree oil (TTO) has broad spectrum antimicrobial effects in vitro, and is specifically active against HSV. One in vitro study looked at the effects of both tea tree oil and eucalyptus oil (EUO) against HSV-1 and -2.[115] At non-cytotoxic concentrations of TTO, plaque formation was reduced by 98.2% and 93.0% for HSV-1 and -2, respectively. Noncytotoxic concentrations of EUO reduced virus titers by 57.9% for HSV-1 and 75.4% for HSV-2. Virus titers were reduced significantly with TTO, whereas EUO exhibited distinct but less antiviral activity. In order to determine the mode of antiviral action of both essential oils, either cells were pretreated before viral infection or viruses were incubated with TTO or EUO before infection, during adsorption or after penetration into the host cells. Plaque formation was clearly reduced, when herpes simplex virus was pretreated with the essential oils prior to adsorption. These results indicate that TTO and EUO affect the virus before or during adsorption, but not after penetration into the host cell. Thus, TTO and EUO are capable of exerting a direct antiviral effect on HSV. Although the active antiherpes components of Australian tea tree and eucalyptus oil are not yet known, their possible application as antiviral agents in recurrent herpes infection is promising.[115] A clinical trial by Carson et al. focused on the effects of topical application of tea tree oil on recurrent herpes labialis (RHL). Patients age 18 to 70 years (n = 18) with a self-reported history of RHL completed the study. Patients who had antiviral therapy in the previous month, long-term steroid therapy, immunocompromised status, pregnancy, lactation, or known TTO allergy were excluded. Participants presented as soon as possible after onset of a herpes outbreak and randomly received and applied either 6% TTO in an aqueous gel base or placebo gel five times daily and recorded treatments and any adverse effects in a diary. Subjects were assessed in the clinical daily except Sundays, with swabs collected for culture and PCR evaluation for HSV. Visits continued until vesicles were completely healed (re-epithelialized) and PCR was negative for HSV DNA on two consecutive days. Investigators were blinded to which patients were using which gels. Parameters measured included re-epithelization time, time to crust formation, duration of detectable virus by lab methods, and virus titer. Although most of the parameters did not reach statistical significance, re-epithelialization time was reduced comparable with other common topical treatments. The authors state that the study size may have been too small to draw complete conclusions, and that the study may have been confounded by the fact that eight of the nine patients in the TTO group began the study in the vesicular stage compared with only six in the placebo group. Nonetheless, they concluded that TTO may be a useful and more affordable acceptable alternative to patients and poses little risk of causing resistance.[29]

Immunomodulation and Adaptogenic Support

Andrographis

Andrographis, an Asian herb used in the Ayurvedic medicine and TCM, has been used traditionally as an anti-inflammatory, hepatoprotective, antiviral, antioxidant, and immune-enhancing herbal medicine.[116] In vitro and in vivo studies demonstrate immune enhancing activity and immunomodulating effects including its ability to stimulate both antigen-specific and nonspecific immunity, reduce inflammation, relieve fever and sore throat, and reduce incidence of common cold and upper respiratory infection in children and adults.[117–119] Andrographalide, a constituent of the herb, has demonstrated anticancer activity. One study demonstrated specific anti-HSV activity using isolate diterpenes from the herb.[120] Western herbal medicine uses this herb in combination with other immunomodulating herbs, and in multieffect comprehensive formulae for patients who experience recurrent herpes outbreaks and who also have a tendency toward frequent colds and infections generally, and who also may be run down and depleted. It is excellent combined with adaptogens for overall immune support.

Eleuthero

Eleuthero is an important traditional medicine in China and Russia, used to stimulate the immune system, for prophylaxis of infectious diseases, and to enhance stamina and performance. It is mentioned repeatedly in the literature for its antiviral effects.[121] An in vitro study by Glatthaar-Saalmuller et al. demonstrated specific activity against HSV virus. Given the ability of this herb to support general immunity, it is recommended in the prevention of recurrent herpes outbreaks, particularly for patients exhibiting general susceptibility to infection,

and when fatigue or stress precipitate episodes. It is regularly given in tincture or encapsulated forms, most often combined with other adaptogens, antivirals, and nervines. See Chapter 6 for a larger discussion in adaptogens and this herb.

Reishi

Reishi is an important adaptogen and immunomodulating herb. It was previously discussed extensively for its specific activities against HSV. The combination of immune supportive and anti-HSV activity makes this herb especially important to consider for patients who have recurrent herpes infection in the context of overall susceptibility to infection, fatigue, and general depletion.

Nervines

HSV outbreaks can be precipitated by stress. Nervines are therefore an important part of the treatment protocol in patients in whom stress is a chronic underlying factor. Not surprisingly, this may be the case for many individuals. Therefore, herbalists routinely include herbs that nourish the nervous system—nervous trophorestoratives (nervines)—with the aim of reducing stress, improving sleep, and promoting a sense of well-being in herbal protocol to prevent recurrent HSV. Nervines work more directly on the nervous system than adaptogens, which improve stress response through their actions on the HPA axis. A combination of adaptogens and nervines is excellent for both short- and long-term tonification of the nervous system. The herbs in this section are discussed more thoroughly in chapters on anxiety and insomnia, as well as in Plant Profiles. A brief description to help differentiate when each nervine might be selected follows.

California Poppy

California poppy is the most sedating of the herbs in this section. Traditionally, it has been used to treat pain, neuralgia, anxiety, stress, depression, migraines, and to promote sleep. It was used by medical practitioners in the late nineteenth century for its soporific and analgesic effects, with a liquid extract sold as a product by Parke-Davis.[45] A hydroethanolic extract has demonstrated affinity for the benzodiazepine receptor, and the sedative, anxiolytic effects of the herb were inhibited by a benzodiazepine receptor antagonist.[25] It should be considered when there is the need to promote sleep during periods of serious stress that threaten to precipitate a herpes outbreak. It also can be used as a muscle relaxant for general aches and pain during a primary herpes outbreak. It can be taken as a tea, but is commonly prescribed as a sedative in tincture form to be taken in small repeated doses every 15 to 30 minutes for 2 hours prior to attempting to sleep. California poppy is not addictive and does not cause the adverse effects associated with opiates.

Damiana

Damiana is a nervine tonic with an affinity for the reproductive system. A South and Central American native herb, it has been used traditionally as an herb for nervous debility, an aphrodisiac, for menstrual disorders, an emmenagogue, and for bladder irritability. It should be considered when there is nervousness, anxiety, and depression as well as sexual dysfunction. It is a mild stimulating tonic for the nervous system. It was official in the National Formulary from 1916 to 1942 as a stimulant and laxative.[45] It was described by Ellingwood as a valuable nerve tonic, particularly when there is sexual debility, and by Hoffmann as an excellent tonic for the nervous system. No clinical studies on this herb have been identified.[122,123]

Lavender

Lavender has a long history of use as a gentle sedative and antispasmodic, used to treat nervousness, restlessness, nervous exhaustion, sleep disorders, depression, and headache.[25,47] In Tibetan medicine, the flowers are used for the treatment of psychosis. Aromatherapy uses lavender oils to promote calm and relaxation, in forms available for inhalation including diffusers, pillow sprays, and bath oils. Herbalists may employ it in its aromatherapy forms alone or in combination with either tea, in which it is pleasant tasting, or tincture form. Lavender is commonly combined with chamomile and lemon balm for a gentle but effective calmative tea. In higher doses, a tincture combination of these same herbs is more sedating and can promote a relaxed sleep.

Lemon Balm

This herb has been used historically to lift the spirits, hence its nickname ''the gladdening herb.'' Surprisingly, little research has been conducted on its calming, sedating effects. The German Commission E supports the use of lemon balm for nervous sleeping disorders.[48] ESCOP lists its indications for internal use as tenseness, restlessness, and irritability.[46] Given its antiviral effects, it is commonly included in general formula for internal use in addition to topical use for treating HSV.

Milky Oats

Milky oats are considered a nervine tonic to be used when there is nervous exhaustion and related conditions including insomnia, chronic anxiety and stress, excitatory states, general debility, and depression.[45,48] Herbalists use milky oats to calm and regenerate the nervous system. A number of clinical trials demonstrate efficacy in the treatment of nicotine and opium addiction using extracts of the green milky oats.[45] It is typically taken for several months for maximum effects, and is considered nourishing rather than sedating. Tinctures should be made from fresh milky oats rather than dried tea.

Motherwort

Motherwort is widely regarded for its quick action as a calmative when there is nervousness, irritability, and anxiety. The German Commission E supports its use for nervous cardiac conditions and thyroid hyperfunction; however, its use as a nervine is derived from empirical and historical use.[47,48] Herbalists specializing in women's health favor it for irritability associated with hormonal changes, for example, in the treatment of

PMS or postnatal irritability, suggesting possible use for irritability and stress associated with menstruation, a known combination of precipitating factors for herpes outbreaks.

Passion Flower

Passion flower is a highly valued calmative nerve, used for nervous relentlessness, as a gentle sedative for sleep difficulties, and to reduce anxiety, neurasthenia, and nervous disorders. It is gentle enough to be favored for use in children.[47,48,124] ESCOP supports its use for tenseness, restlessness, and irritability with difficulty falling asleep.[46] Animal experiments corroborate traditional use for its sedative activity and extracts have demonstrated effects on EEG that support sedative action; however, because the herb is nearly always used in combination with other sedative herbs, no single-herb studies have been conducted that give proof of its efficacy as a monopreparation.[47] The herb may be taken as a tea or tincture, the latter preferred by herbalists for maximum efficacy. Numerous preparations containing passion flower, both as monopreparations and combinations, are available as sedative formulas in Germany. It is commonly combined with valerian root (*Valeriana officinalis*) and hops strobilus (*Humulus lupulus*).

Skullcap

Hoffmann describes skullcap as perhaps the most relevant nervine available to us in the Western materia medica.[123] It an excellent nervous trophorestorative used to soothe tension and restore calm. It is not immediate acting, and is generally used long term (up to 6 months) for optimal effects, in the treatment of nervous conditions associated with exhaustion, and in the treatment of PMS. A double-blind, placebo-controlled study of healthy subjects demonstrated noteworthy anxiolytic effects.[125] The identification and quantification of the flavonoid, baicalin in a 50% ethanol and its aglycone baicalein in a 95% ethanol extract, as well as the amino acids GABA in aqueous and ethanol extracts and glutamine in an aqueous extract was performed using HPLC suggests anxiolytic activity because baicalin and baicalein are known to bind to the benzodiazepine site of the GABAA receptor and because GABA is the main inhibitory neurotransmitter.[126] Skullcap is generally recommended as a tea or tincture, usually in combination with other herbs such as lavender, passionflower, and lemon balm; however, it also may be taken singly.

Vulneraries and Anti-Inflammatories

Vulneraries are herbs used to promote wound healing. Among herbs commonly used to heal herpes blisters are those mentioned earlier in this chapter, such as aloe, lemon balm, St. John's wort, sage and rhubarb combination, and so forth, and additionally, calendula and comfrey root. Calendula, an herb long relied on for its wound healing and antimicrobial abilities, has demonstrated antimicrobial has been shown to increase rate of cutaneous herpes lesions when combined with acyclovir, over acyclovir alone.[127] Comfrey is primarily used as an anti-inflammatory and to heal wounds, ulcers, and sores.[47] Any of these herbs may be used topically at the onset of blisters or once they have begun to crust over, and should be applied two to four times daily using a clean cotton swab for each application. Aloe may be used in the form of gel or cream, comfrey is used as a cream or ointment, and calendula and the others may be used in the form of tincture, oil, ointment, cream, or salve.

Topical Analgesics

A number of herbs have shown analgesic effects with topical application. Two studies specifically looked at topical pain management with herpes zoster, a relative of HSV that causes painful outbreaks along nerve dermatomes and often leads to significant postherpetic neuralgia. Both 100% geranium oil, applied directly to the affected area, and peppermint oil have demonstrated analgesic effects in a clinical trial and a case report, respectively. Geranium oil relieved pain dramatically in 25% of patients whose pain following shingles had lasted for 3 months or more and was not relieved by standard pain medications such as acetaminophen (Tylenol) or meperidine (Demerol). Fifty percent of patients showed some relief, and 25% did not benefit.[128] Other herbs used for topical analgesia include kava kava and St. John's wort.

Astringents

According to Schulz et al. virtually all substances with a protein-coagulating, astringent action can improve symptoms associated with herpetic lesions.[124] Those herbs commonly relied on as astringents include witch hazel extract; plantain leaf poultice, salve, or tincture; and white oak bark tincture. Many patients find witch hazel easily acceptable and accessible as it can be used in the readily available drug store form of the extract for external use. Witch hazel is approved by ESCOP and the German Commission E for use as a treatment of mild skin injuries and local inflammation of the skin and mucosa.[47,48] Plantain is approved by ESCOP for temporary, mild inflammations of mucosa (oral and pharyngeal are specified) and by German Commission E for inflammatory alterations of the skin.[47,48]

NUTRITIONAL CONSIDERATIONS

Reduce Arginine and Increase L-Lysine

In vitro evidence supports increasing dietary lysine and decreasing dietary arginine to prevent recurrent herpes outbreaks. Arginine is necessary for replication of HSV; it may actually stimulate cell replication, whereas L-lysine blocks arginine activity. L-lysine is shown in studies to decrease the severity of outbreaks and reduces recurrence, although it does not necessarily have an impact on healing time. Supplementation of 1 g daily is recommended preventatively or 1 g three times daily during an outbreak in addition to dietary modification.[119,129] Because of concerns over prolonged lysine supplementation and the risk of developing atherosclerosis, dietary adjustments may be optimal to regular lysine, supplementation that can be reserved for acute need.[119] However, nuts provide important and healthy fats to the diet; therefore, it is not

Botanical Treatment Protocol for Recurrent Herpes Simplex Virus

Combine the following botanical therapies both for internal and topical treatment, as appropriate for specific patients' needs.

This symbol *** in front of internal protocol in the following indicates that the formula is not considered safe for use during pregnancy. Special pregnancy protocols are noted as such. Topical protocol can be used freely during pregnancy, although thuja should be omitted even for topical use in pregnancy.

***** Immune Supporting/Antiviral Tincture**

For patients prone to regular recurrent outbreaks give the following formula as a prophylactic agent to boost the immune system and for its antiviral effects, for use daily. For patients with only periodic and predictable outbreaks, such as during periods of stress such as after the holidays or during exams or deadlines, give the following formula for 6 weeks prior to the time of anticipated stress and continue for 2 weeks after the stressful event or period. For women susceptible to herpes outbreaks at the time of menstruation, give daily until recurrent outbreaks become infrequent, and then take two to three times weekly.

Ashwagandha	(*Withania somnifera*)	20 mL
St. John's wort	(*Hypericum perforatum*)	20 mL
Licorice	(*Glycyrrhiza glabra*)	15 mL
Lemon balm	(*Melissa officinalis*)	15 mL
Echinacea	(*Echinacea* spp.)	15 mL
Andrographis	(*Andrographis paniculata*)	15 mL

Total: 100 mL

Dose: 5 mL twice daily

***** Herbal Infusion or Tincture (Alternative to Immune Supporting/Antiviral Tincture)**

Adapted from Amanda McQuade Crawford, *Herbal Remedies for Women*

		Dried Herbs	Tincture
St. John's wort	(*Hypericum perforatum*)	3 parts	30 mL
Calendula	(*Calendula officinalis*)	2 parts	15 mL
Damiana	(*Turnera diffusa*)	1 part	10 mL
Echinacea	(*Echinacea spp.*)	2 parts	15 mL
Wild indigo root	(*Baptisia tinctoria*)	½ part	10 mL
Eleuthero	(*Eleutherococcus senticosus*)	½ part	10 mL
Pulsatilla	(*Anemone pulsatilla*)	½ part	10 mL

Total: 100 mL

To prepare infusion: Steep 28 g (1 oz)/1 L of boiling water for 20 minutes. Strain.

Dose: Infusion: 1 teacup three times daily
Tincture: 5 mL three times daily

Take 5 days weekly for 1 to 3 months to reduce frequency and severity of outbreaks.

For both of the preceding formulas, if menstrual hormone irregularity triggers or exacerbates herpes outbreaks, give 5 mL of Vitex tincture daily, preferably in the morning, for 3 to 6 months.

Antiviral Formula for Use during Pregnancy

Most of the antiviral herbs discussed in this chapter have not been proven safe for use during pregnancy. However suppression of HSV outbreaks is particularly important during pregnancy owing to the potential consequences to the fetus of being exposure to lesions during vaginal delivery, and risks to the mother of a cesarean delivery as the alternative. It has been the experience of many midwives who, using a combination protocol of a simple internal antiviral formula, topical applications, and dietary and lifestyle modifications (e.g., stress reduction), can reduce the frequency of outbreaks during pregnancy and prevent the need for cesarean section. The following protocol is reliable and the herbs not contraindicated during pregnancy. The case history at the end of this chapter illustrates the successful treatment of HSV-2 during pregnancy.

Prepare the following herbs as an infusion:

Echinacea root	(*Echinacea angustifolia or purpurea*)	6 parts
Lemon balm	(*Melissa officinalis*)	4 parts

Steep 28 g (1 oz)/L of boiling water for 1 hour. Strain and drink two cups daily during the first trimester; increase to four cups daily during the third trimester. Use other formulas in this chapter, both internally (i.e., nervine formula) and topically, along with the dietary considerations.

Nervine Formula

For patients with stress-induced HSV outbreaks also give the following formula either daily on an ongoing basis, or for several weeks prior to and during times of anticipated stress.

Milky oats	(*Avena sativa*)	30 mL
Passion flower	(*Passiflora incarnata*)	30 mL
Blue vervain	(*Verbena officinalis*)	20 mL
Lavender	(*Lavandula officinalis*)	20 mL

Total: 100 mL

Dose: 3 to 5 mL two to three times daily, based on severity of stress.

Topical Treatment

Herbs from the following topical formulae can be combined or treatments can be alternated for various effects, for example, using tincture to heal lesions twice daily alternated with topical application of herbs to dry lesions.

(Continued)

Botanical Treatment Protocol for Recurrent Herpes Simplex Virus—cont'd

For painful lesions:

Mix the following combination in a 1 oz. amber or cobalt glass bottle. Shake hard before each use to mix the tinctures and oil. Apply using a cotton swab, 2 to 4 times daily:

Kava kava tincture	10 mL
Licorice tincture	10 mL
Peppermint or geranium oil	20 drops

To speed healing and as a topical antiviral:

Mix a combination of equal parts of the following tinctures in a 1-oz amber or cobalt glass bottle. Apply using a cotton swab, two to four times daily:

St. John's wort	*(Hypericum perforatum)*
Thuja (***)	*(Thuja occidentalis)*
Lemon balm	*(Melissa officinalis)*
Calendula	*(Calendula officinalis)*

Alternatively use lemon balm or St. John's wort ointments, available over the counter in shops that retail herbal products, or simply use witch hazel extract available at regular pharmacies.

Omit thuja during pregnancy. Replace with licorice or lavender tincture.

For weeping lesions:

Option 1: Mix equal parts of powders of myrrh and goldenseal and apply several times daily by packing the powder onto weeping ulcers. Note that goldenseal powder may well stain clothing so caution should be taken to avoid contact with garments, for example by using a panty liner in the underwear.

Option 2: Apply witch hazel extract onto weeping ulcers using a cotton swab, repeating two to four times daily.

To heal tissue once sores have begun to crust over:

Use a vulnerary containing comfrey, lemon balm extract, calendula, and an essential oil such as geranium or peppermint salve to quickly heal tissue.

Also see Nutritional Considerations for a high-lysine, low-arginine diet, and avoid outbreak triggers.

desirable to eliminate them entirely, especially during pregnancy. Therefore, moderation is advisable. Pregnant women should consult with their midwife or obstetrician when modifying their diet to ensure optimal health for themselves and their babies. See Box 8-1 for foods high in arginine and lysine. Lysine supplementation is not contraindicated during pregnancy.

Zinc

Supplementation with 25 mg daily has been shown to inhibit HSV replication in vitro and clinically has led to complete suppression of an outbreak or resolution within 24 hours and stimulates cell-mediated immunity, decreases frequency, and reduces severity of outbreaks. Supplementation is suggested for 6 weeks with 250 mg vitamin C. Topical use of zinc sulfate solution (0.01% to 0.025%) improves healing of HSV-1 blisters and prevents recurrence. Internal use of zinc as a supplement is not recommended during pregnancy.[119]

Vitamin C

Supplementation with 1000 mg vitamin C with bioflavonoids daily during the prodromal phase and then 5000 mg divided into five doses daily for 3 days after the onset of symptoms was shown to reduce blister. Healing time in herpes labialis from 10 days in the placebo group to 4.4 days in the group receiving supplementation.[119] Pregnant women should not exceed 4000 mg vitamin C supplementation daily, including vitamin C that is in a prenatal vitamin.

Vitamin E

Topical use of vitamin E oil shortens healing time and significantly reduces pain associated with HSV-1 lesions. Apply two to four times daily with a cotton swab.

BOX **8-1**

Food Sources of Lysine and Arginine

Foods high in lysine (emphasize these foods in the diet):

- Fresh fish
- Canned fish
- Chicken
- Turkey
- Milk
- Beef
- Cooked beans
- Eggs
- Cheese
- Soybeans

Foods high in arginine (minimize consumption of these foods):

- Chocolate
- Nuts and nut products:
  - Brazil nuts
  - Hazel nuts
  - Peanuts
  - Walnuts
  - Almonds
  - Cashews
  - Sunflower seeds
  - Peanut butter
- Gelatin
- Brown rice
- Wheat
- Oatmeal
- Raisins
- Coconut

ADDITIONAL THERAPIES

Chronic stress has the most significant impact on recurrent HSV, even more so than acute stress.[119] Regular practice of mind–body therapies that help to relieve stress are important in the prevention of recurrent HSV for many patients. Examples include meditation, yoga, biofeedback, and massage.

TREATMENT SUMMARY FOR HERPES

- Observe safe sex and common hygienic safety practices to reduce the likelihood of transmission of infection
- Reduce exposure to avoidable common stressors that trigger outbreaks, for example, excessive sunlight exposure
- Minimize unavoidable chronic stress and practice stress reduction techniques such as yoga and meditation
- Regulate hormones and reduce stressors related to menstruation if outbreaks are cyclically related
- Use adaptogens and nervines for improving immune and stress response
- Use antivirals internally and topically to prevent recurrence and reduce frequency of outbreaks
- Use topical astringents, anti-inflammatories, analgesics, and vitamin E to speed healing and reduce pain
- Reduce dietary arginine and increase lysine
- Supplement with zinc and vitamin C
- Pregnant women should make every effort to avoid outbreaks late in the third trimester, and should be evaluated for herpes infection in late pregnancy to be sure there are no active lesions during a vaginal birth.

What to expect with botanical treatment of herpes:

Patients can expect to shorten the duration, frequency, and severity of herpes outbreaks in as quickly as 24 hours with aggressive topical treatment in outbreaks that are caught early. Prevention of recurrence of herpes can be achieved quickly with the addition of dietary and lifestyle modifications accompanied by nervine, adaptogen, and antiviral therapy, internally and topically as appropriate and indicated. Some patients may continue to experience periodic and infrequent outbreaks during times of heightened stress, but these can largely be ameliorated with adherence to botanical and dietary protocol. Some patients experience complete remission of the virus, and may go indefinitely, even more than a decade, without a sign of an outbreak.

CASE HISTORY: HSV-2 IN PREGNANCY

Caroline is a 38-year-old mother of two children born by cesarean section because of history of recurrent herpes genitalis outbreaks, including at the time of delivery in both previous pregnancies. Currently 22 weeks pregnant with her third child, she is already being told by her obstetrician that she has almost no chance of a vaginal birth given the likelihood that she will again experience an outbreak close to labor given her frequently recurring outbreaks, sometimes as often because every 2 to 3 weeks. She is very discouraged by this, because she found the recovery from the c-sections challenging, and she would prefer to have a vaginal birth. She has been told by a birthing center that if she can remain free of herpes for several weeks prior to and at the time of labor, they will support her desire for a vaginal birth barring other problems. At the time, Caroline was working as a nurse, doing many night shifts to bring in extra money for her family and to have time available in the daylight hours for her daughter. She was chronically stressed and exhausted, and the anxiety about the potentially impending cesarean was exacerbating her stress level. She was eating a lot of fast foods, especially in the evening at the hospital, and drinking coffee regularly to combat fatigue. Her marriage and home life were otherwise good, and she was committed to making personal and dietary changes to see if she could prevent herpes outbreaks.

Caroline immediately went on a high-lysine and low-arginine diet, cut back her night hours, switching to weekends with the plan to phase out working by the middle of her third trimester (she had planned to stop working then anyway), committed to stop drinking coffee, and began the following herbal protocol:

- Infusion of equal parts of echinacea and burdock roots, two cups daily, prepared 28 g herb (1 oz)/1 L of boiling water and steep 2 hours
- Nervine tea, two cups daily consisting of chamomile, lemon balm, and lavender
- 2000 mg daily vitamin C
- Alternating applications of vitamin E and antiviral tincture (lemon balm, licorice, thyme, and St. John's wort in a witch hazel extract base) should tingling or lesions become apparent

Caroline had an outbreak 1 week after our initial visit, at 23 weeks pregnancy. This was not surprising, given that she had been under prolonged stress and had worked an especially long weekend, and had only just started the herbal protocol. This was the last outbreak she experienced during the pregnancy, and cultures at 38 and 40 weeks yielded negative results. Caroline gave birth vaginally, at the birthing center, after 3 days of difficult labor and antibiotics for prolonged rupture of membranes. She experienced a vaginal yeast infection after the birth but felt this was a mild inconvenience compared with the recovery she previously experienced postcesarean.

HIV INFECTION AND BOTANICAL THERAPIES

Aviva Romm

An estimated 19.2 million women worldwide are living with HIV infection or AIDS. Since the early 1990s, the proportion of AIDS cases in females aged 13 to 49 years has tripled from 7% to 25%. Appropriate treatment is essential to the wellness and longevity of HIV/AIDS patients. Conventional medical treatment, for example, highly active antiretroviral therapy (HAART), which consists of a combination of antiretroviral therapies, including protease and reverse transcriptase inhibitors, is showing tremendous promise.[130] Numerous HIV patients also use complementary and alternative therapies such as herbs and nutritional supplements in conjunction with their medical treatment, or in some cases, in lieu of

conventional therapies. This chapter looks at the statistics and demographics of CAM use for HIV/AIDS, reasons for use, risks and benefits associated with use, and provides a brief review of the literature based on two major reviews conducted by other researchers. There is a tremendous paucity of evidence on botanical therapies for HIV/AIDS; however, there is also a tremendous amount of human experience in the HIV community regarding natural therapies that may support conventional treatment, and also may eventually point the way to more effective integrative therapies.

A comprehensive overview of HIV/AIDS is beyond what can be adequately covered within the scope of this book. The author hopes that this chapter will provide a glimmer of insight into the nature of CAM use by individuals with HIV/AIDS and elucidate the need for both practitioner understanding of patient motivation for using CAM therapies with HIV/AIDS, and the tremendous need for further research in this area.

CAM USE IN THE HIV/AIDS POPULATION

In general, chronic disease is a positive predictive factor for CAM use; people with HIV are more likely to use CAM than those with other serious illnesses, including cancer.[131] Patients with chronic illness are highly likely to turn to CAM therapies, sometimes with a sense of desperation, seeking a sense of control over their health, and anything that will improve quality of life and reduce discomfort.[132] It is imperative that medical practitioners understand their patient's desire to use CAM therapies as part of their overall treatment, and help patients to obtain reliable, accurate information. These patients may be especially vulnerable to hype and scams in their deep desire to alleviate their suffering and improve their health. Misinformation about what therapies to use can be a problem. A study by Mills et al. illustrates the potential for misinformation and unnecessary products expenditure to patients.[133] Four male research assistants, posing as asymptomatic HIV-positive individuals, inquired of employees of all retail health food stores in a major Canadian city (32 stores) as to what is recommended for their condition. Eight store employees (25%) offered no advice; eight (25%) inquired whether the subjects were currently taking medications; six (19%) suggested visiting a physician; and eight (25%) suggested visiting a CAM provider. A total of 36 different products (mean 2.3 per employee) were recommended with considerable variability in product evidence and cost. There was considerable heterogeneity in advice on natural products provided by employees of natural food stores and, in general, these individuals had limited formal training in CAM. The products they recommended had limited evidence supporting their efficacy and in some instances were potentially harmful and had considerable costs. It is important for practitioners to develop patient education resources on CAM safety and efficacy, and for these to be made available in a variety of community settings in which HIV+ patients might seek such information.[134]

Several studies have looked at the overall population demographics of individuals with HIV/AIDS using CAM.[130,131,135–141] These studies have shown that at least 50% and as many as 68% of individuals with HIV/AIDS have used a CAM therapy at least once, and many use them regularly as part of, or in conjunction with, HIV/AIDS treatment. Only a limited number of studies have investigated CAM use specifically among women with HIV/AIDS. Women in this population reporting CAM use are generally older than 35 years of age, have a higher degree of education, and are more likely to be uninsured than those not using CAM therapies. Women living with HIV for greater than 4 years are significantly more likely to be CAM users than those with shorter disease duration.[130] Meneilly et al. reported that HIV-positive white women were more likely to use botanical therapies than black or Hispanic women with HIV/AIDS.[142] In a study of 391 women of mixed ethnicity, 18 to 50 years old with HIV/AIDS, about 60% of women reported using at least one CAM therapy. Approximately 16% reported using herbs, 22% used dietary supplements, 27% practiced religious healing, 10% used bodywork (e.g., message, yoga), and 1% practiced some type of psychic healing.[130] In another study, 53% of patients had recently used at least one type of CAM. Of these, 27% had used therapies with the potential for adverse effects and 36% had not discussed such use with their health care provider, a common problem with CAM use generally. Patients with a greater desire for medical information and involvement in medical decision making and with a negative attitude toward antiretroviral drugs were more likely to use CAM. Only 3% used CAM instead of conventional therapy.[136] Patients in one survey (n = 180) saw CAM providers with greater frequency than primary care physicians and nurse practitioners, and were likely to report CAM therapies to be either ''extremely'' or ''quite a bit'' helpful.[135]

WHY ARE HIV/AIDS PATIENTS TURNING TO CAM THERAPIES?

Most people with HIV/AIDS report using CAM therapies to manage health complications, especially control of conventional medication side effects, which can be significant enough to reduce compliance with conventional therapy.[139] Many also report using CAM to cope with emotional issues, such as depression and stress. Pain management is a significant reason for CAM use among HIV/AIDS patients.[141] Pain may result from direct effects of HIV on the peripheral or central nervous system, immune suppression, and resulting opportunistic infections, antiretroviral medications, and common problems unrelated to HIV disease or treatment, such as low back pain.[141]

Additional reasons for CAM use among those with HIV/AIDS include symptom management, as a way to prevent disease progression, forestall beginning the use of conventional therapies (often while monitoring for disease progression), gain freedom from medical regimens; and avoid stigmas associated with the use of conventional therapy, for example, the self-perception of ''being diseased,'' feeling dependent on conventional medications, or having to publicly and thus visibly fill prescriptions, take medications, or get medical care

where they might be seen by those who know them, for example, coworkers at sites at which medical care is offered by employers.[131] A recent Canadian study reports that people with HIV/AIDS are drawn to CAM as a health maintenance strategy, a healing strategy, an alternative to Western medicine, as a way of alleviating the side effects of drug therapies, a strategy for improving quality of life, a coping strategy, and as a statement of political resistance.[143]

Approximately 50% of CAM users are what has been referred to as ''pragmatic users.''[144] This means that although they use CAM often, their use is limited to short durations and specific reasons such as stress or treatment of a cold. Interestingly, many individuals express interest in using CAM, but may choose not to for a variety of reasons, including cost, skepticism, or lack of confidence in CAM therapies, inability to comply with complex protocols, lack of knowledge on how to obtain reliable information, lack of scientific data, and concerns about interactions with medications.[144] It appears that reducing viral load or ''curing'' HIV/AIDS is not a primary motivation, and in fact, in the underground HIV/AIDS community it seems that improving quality of life, maintaining optimal health in spite of the diagnosis, and preventing disease progression are the goals of CAM use, as well as management of drug side effects, and so forth, as already stated.

Desire to support a positive self-perception appears to be a reason that some individuals with HIV/AIDS seek CAM. Patients report that conventional medical visits often leave them feeling medicalized and diseased, whereas CAM therapists, such as acupuncturists, are more likely to reinforce a positive approach to disease management and instill greater hope that the patient can achieve some sense of well-being in the context of having HIV/AIDS.[131]

BENEFITS OF CAM THERAPY

Perhaps most significantly, patients have reported that the use of CAM therapies enables them to remain on conventional treatment protocol, which is often accompanied by minor to debilitating side effects including fatigue, nausea, diarrhea, vomiting, anemia, neuropathy, and pancreatitis.[131] Foote-Ardah found that patients were using acupuncture for relief of neuropathic pain, Chinese herbs for nausea, and marijuana to improve appetite and weight gain.[131] The psychoemotional well-being and sense of empowerment reported by individuals using CAM therapies for the treatment of HIV/AIDS, as well as the increased ability of patients to comply with pharmaceutical regimens as a result of using herbs, etc, represents an important benefit, as long as the CAM therapies do not interfere with the medication or are not themselves harmful. This in itself should be a central reason for conventional practitioners to support their patient's choice to use CAM therapies with no demonstrated harm, and should encourage research on the safety and efficacy of botanicals used as adjunct therapies for associated complaints of HIV/AIDS patients and for side effects of HIV/AIDS pharmacotherapy, as well as herb–drug interactions. Clearly a combination of the two models is desired by the majority of HIV patients and may represent a simple, safe, and empowering method of treating minor to major complaints and side effects while lending a sense of empowerment to those who may otherwise at times feel entirely dependent on medical care and with very few medical options.

RISKS OF CAM USE IN HIV/AIDS

The major risks of using botanicals for HIV/AIDS and AIDS-related conditions are inherent risks of using unsafe therapies, foregoing use of conventional treatment in favor of therapies that may be ineffective, delaying necessary medical therapies for too long, and interactions that may interfere with the efficacy or safety of conventional therapies. Further, unnecessary cost to the patient may be considered an associated risk. For some, the use of CAM to forestall beginning conventional therapy, in conjunction with evaluation of CD4 counts, has allowed them to maintain a sense of autonomy from medical dependence for as long as possible, and has been met with positive outcomes. Including delayed disease progression.[131] Other patients, however, have not fared as well, with attempts to avert medication with CAM therapies leading to the development of serious opportunistic infections.[131] Unfortunately, very little is known about the safety and efficacy of combining herbs and conventional HIV/AIDS pharmaceutical therapies, both directly for the reduction of viral load or enhancement of immunity, or for the treatment of side effects of medications or conditions associated with HIV/AIDS, such as fatigue, other infections, and depression.

EFFICACY OF BOTANICAL THERAPIES IN HIV/AIDS

There is an astounding paucity of research on the efficacy and safety of botanical therapies used for the treatment of HIV/AIDS. Two comprehensive reviews of the literature were identified, one by Mills et al. on CAM therapies and one by the Cochrane Collaboration specifically on botanical therapies. Mills et al. only identified three botanical trials that met their inclusion criteria. Two of the trials were of Chinese herbal preparations, the other of an extract of the boxwood plant (*Buxus sempervirens*). Another trial looked at the effectiveness of capsicum on AIDS-related peripheral neuropathy.[145]

The Cochrane Collaboration review identified a total of nine randomized placebo-controlled clinical trials, involving 499 individuals with HIV or AIDS, which met their inclusion criteria. A total of eight different herbal medicines were evaluated in these trials.[146] Herbal medicines were defined as preparations derived from plants, and could be extracts from a single herb or a compound of herbs. It should be noted that these are generally not herbal products that one can simply purchase at a natural foods store or obtain through a local herbalist. They are often more closely akin to pharmaceutical products. These were compared with no intervention, placebo, and antiretroviral therapies. Outcome measures included mortality, HIV

progression, new AIDS-defining event, number and types of adverse events, immunologic indicators (CD4 and white blood cell counts), viral load, and psychological status and quality of life. With limited exception (e.g., diarrhea), most of these trials looked at herbs and HIV/AIDS directly, rather than at supportive therapies for specific symptoms or associated problems, such as ginger for nausea or marijuana for appetite stimulation. Several trials are committed from the presentation below due to lack of efficacy or side effects, thus leaving a total of four trials that demonstrated efficacy and a lack of significant side effects compared to placebo.

IGM-1 (Chinese Herb Combination)

In a 1996 study by Burack et al., 30 patients with at least two HIV-related symptoms were randomly assigned to receive herbs (n = 15) or placebo (n = 15). The product, IGM-1, is a standardized preparation of 31 Chinese herbs developed by one of the investigators. Of 31 herbal ingredients in the 650-mg tablet, those present in high concentration included *Ganoderma lucidum, Isatis tinctoria, Astragalus membranaceus, Andrographis paniculata, Lonicera japonica, Milletia reticulata, Oldenlandia diffusa,* and *Laminaria japonica*. Overall life satisfaction appeared to be improved in patients treated with herbs compared with placebo. Patients receiving herbs reported a reduced number of symptoms. There was no significant reported difference in overall health perception, symptom severity, absolute CD4 count, anxiety or depression between the two groups. No adverse events were reported or identified in any of the patients randomized to herbs.[146,147]

''35'' Chinese Herb Combination

In a 1999 study by Weber et al., HIV-infected adults (n = 68) were randomized to receive a preparation of 35 Chinese herbs (n = 34) or placebo (n = 34). The preparation includes *Ganoderma lucidum, Isatis tinctoria, Milletia reticulata, Astragalus membranaceus, Tremella fuciformis, Andrographis paniculata, Lonicera japonica, Aquilaria agallocha, Epimedium macranthum, Oldenladia diffusa, Cistanche salsa, Lycium chinense fructus, Laminaria japonica, Angelica sinensis, Polygonum cuspidatum, Panax quinquefolium, Schizandra chinensis, Ligustrum lucidum, Atractylodes macrocephala, Rehmannia glutinosa, Salvia miltiorrhiza, Curcuma longa, Viola yedonensis, Citrus reticulata, Paeonia lactiflora, Polygonum multiflorum, Eucommia ulmoides, Amomum villosum, Glycyrrhiza uralensis, Prunella vulgaris, Cordyceps sinensis, Pogostemum cablin, Crataegus cuneata, Massa medica fermentata, Hordeum vulgare*, and *Oryza sativa*. Of those completing the study (24 in the herb group and 29 in the placebo group), there were no significant differences in CD4 cell counts and HIV-1 RNA load. There were no significant differences between the groups regarding new AIDS-defining events, number of reported symptoms, psychosocial measurements, or quality of life. There were more adverse effects in the herb group (19/24) than in the placebo group (11/29). Adverse events included diarrhea, increased number of daily bowel movements, abdominal pain, constipation, flatulence, and nausea. There was no evidence of toxicity from the study drugs, based on hematologic and blood chemistry analysis. The deaths of two patients in the herb group were attributed to severe immunodeficiency and pre-enrollment history of multiple severe opportunistic complications and not to the herbal preparation.[146,148]

SPV30-Boxwood

In a pilot trial in France, 43 asymptomatic HIV patients with CD4 cell counts between 250 and 500/mm^3 were divided into an SPV30 (n = 22) or placebo (n = 21) group. Patients receiving SPV30 were less likely to progress to AIDS-related complications or to decrease to a CD4 cell count of below 200/mm^3. There was a significant increase of CD4 cell count in people treated by SPV30 after 30 weeks compared with placebo. Based on these findings, 145 previously untreated participants with asymptomatic HIV infection and decreased CD4 cell count (250 to 500/mm^3) were randomized to SPV30 990 mg/day (n = 48), SPV30 1980 mg/day (n = 49), or placebo (n = 48).[149] There was a tendency for AIDS defining events such as candidiasis, herpes zoster, weight loss, and diarrhea to occur less frequently in the SPV30 group (combination of two dosages) than in the placebo group (RR 0.12, 95% CI 0.01 to 1.08; p = 0.06). There was no significant difference between either SPV30 990 mg/day or SPV30 1980 mg/day and placebo with respect to CD4 cell counts and viral load. The trial did not observe serious adverse effects, and biochemical parameters did not show abnormal changes in the participants.[146,149]

SP-303

SP-303 is a product containing a proanthocyanidin oligomer isolated and purified from the latex of Croton lechleri. Fifty-one patients with AIDS and diarrhea were randomized to either SP-303 or placebo. SP-303 reduced stool weight and abnormal stool frequency. The product was well tolerated and there were no adverse events reported in either group.[146,150]

The authors of the Cochrane review concluded that there is insufficient evidence to support the use of herbal medicines in HIV-infected individuals and AIDS patients.[146] It must be remembered that only a very few of the large number of herbs that are used for HIV/AIDS have been subject to any evaluation.

SAFETY ISSUES WITH HERBS AND HIV/AIDS THERAPY

There is no comprehensive list of herbs to be avoided by HIV/AIDS patients. The efficacy and safety of standard HIV/AIDS pharmacotherapy is dependent upon many delicate and complex mechanisms (e.g., cytochrome P450 metabolism), which may be affected by any number of substances, including botanical medicines. Several herbs are known to significantly interfere with the CYP450 system, most notably St. John's wort, which

is contraindicated with HIV/AIDS pharmacotherapy. Although there is only very low-level evidence that herbal products might interfere with protease inhibitors, garlic and St. John's wort may reduce HIV drug concentrations and lead to drug failure.[145] Caution and knowledge of potential interactions are needed when combining HIV/AIDS therapies and herbal medicines. Cooperation between conventional and CAM practitioners in the treatment of HIV/AIDS patients may help to increase the efficacy and sustainability of treatment protocol for patients while minimizing unwanted effects.

OVERVIEW OF IMMUNOMODULATING HERBS COMMONLY USED IN HIV/AIDS

Roy Upton

Herbs used in the treatment of HIV/AIDS are aimed at improving the integrity of the immune system. The herbs below are presented merely on an informational basis. They are generally used for tonic purposes, taken in any number of forms from concentrated extracts to use in soups. They are considered to have a high safety profile, although little research has been conducted on the effects of these herbs clinically in individuals with HIV/AIDS using conventional pharmacotherapy. Readers can refer to other topics in this textbook for HIV- and AIDS-related conditions, for example, nausea and vomiting of pregnancy for common antinausea herbs, vaginitis, insomnia, anxiety, or depression. Anecdotally, many HIV/AIDS patients have reported that, in conjunction with conventional therapies, various combinations of the following herbs, and others, along with heavy nutritional supplementation programs, have vastly improved their quality of life.

Astragalus

Astragalus (*Astragalus membranaceus*) is the one of the most widely used immune tonifying herbs of Chinese medicine. It is primarily used as a lung tonic, and may be helpful in increasing resistance against respiratory infections. It is also used as a digestive tonic. It has been shown to potentiate both thymus and spleen function, and to augment both humoral and cell-mediated immunity. Most studies evaluating the effects of astragalus on immunity have used cancer models and patients undergoing chemotherapy. The quality of astragalus products varies greatly. At least nine different species and one other genus (*Hedysarum*) of plant are traded as astragalus but not all contain the primary marker compound astragaloside IV.

Atractylodes

Atractylodes (*A. lanata*) is much like astragalus in improving digestive and assimilative functions. It increases energy, and has specific and nonspecific immune-stimulating activity. It can increase phagocytic activity, increase white blood cell counts, increase lymphocytic transformation, promote cellular immunity in general, and significantly increase immunoglobulin activity (IgG). It is also high in vitamin A.

Codonopsis

Codonopsis (*C. pilosulae*) is used similarly to ginseng as a tonic. It can increase both red and white blood cell counts and hemoglobin, increase phagocytic activity and promote lymphocytic transformation. It has also been reported to increase T-cell production.

Eleuthero

Eleuthero (*Eleutherococcus senticosus*) has primarily been valued for its adaptogenic properties and its ability to increase nonspecific resistance to physical and psychological stresses. Eleutherococcus increases macrophage activity in lymph tissue.

Licorice

Extracts of licorice (*Glycyrrhiza uralensis*) are widely used as part of an AIDS protocol in many clinics. Anti-AIDS activity that has been reported include reversal in P-24 antigen, reduction in the progression from ARC to AIDS in hemophiliacs, increases in overall lymphocytes, increase in natural killer (NK) cell activity, and a dose-dependent reduction in viral replication. Preparations used clinically include oral administration of crude licorice extracts as well as intravenous preparations. Although generally safe, excessive amounts of glycyrrhiza can cause fluid retention, heart palpitations, and contribute to hypertension.

Ligustrum

Ligustrum (*L. lucidum*) is widely used in China as an adjunctive therapy to chemotherapy and radiation therapy used in the treatment of cancer. It stimulates hematopoiesis, and has been shown to restore immune functioning to almost normal in cancer patients. Ligustrum specifically promotes lymphocytic transformation, increases leukocytes, and may decrease the immunosuppressive side effects of radiation and AZT.

Reishi

Reishi (*Ganoderma lucidum*) is one of the primary herbs of choice in any immune deficiency disease. It possesses a broad spectrum of immunostimulating activities, as well as anti-inflammatory and antiallergenic properties. Reishi contains more than 100 oxygenated triterpenes, many of which exhibit a marked effect on the activity of NK cells. It has been widely used for a variety of infectious disease such as bronchitis and hepatitis. It stimulates phagocytosis, increases T-cell activity and is a treatment for viral hepatitis. Reishi has been reported to increase CD4 cells in vivo. It is also used as an effective antidepressant.

Shiitake Mushroom

Shiitake mushrooms (*Lentinus edodes*) are rich in immunostimulating polysaccharides, and seem to exhibit a primary healing effect on the liver, being widely used

TABLE **8-8**

Condition/Botanical Medicine Summary Table

	ANALGESIC	ANTI-INFLAMMATORY	ANTIMICROBIAL	ASTRINGENT	DEMULCENT	IMMUNOMODULATOR	NERVINE	VULNERARY
Actaea racemosa	X							
Allium sativum			X					
Aloe vera		X			X			X
Althea officinalis								
Andrographis paniculata			X			X		
Arctostaphylos uva ursi			X					
Astragalus membranaceus						X		
Avena sativa					X		X	
Berberis aquifolium			X					
Calendula officinalis		X	X					X
Commiphora mol mol			X					
Coptis chinensis			X					
Corydalis	X							
Echinacea spp.			X			X		
Eleutherococcus senticosus						X		
Eschscholzia californica	X						X	
Ganoderma lucidum						X		
Glycyrrhiza glabra		X				X		X
Hamamelis virginiana		X		X				
Hydrastis canadensis			X					
Hypericum perforatum			X				X	
Lavandula officinalis			X					
Leonurus cardiaca							X	
Lomatium dissectum			X					
Melaleuca alternifolia			X					
Melissa officinalis			X				X	X
Mentha piperita	X	X						
Origanum vulgare			X					
Panax ginseng						X		
Panax quinquefolius						X		
Passiflora incarnata							X	
Piper methysticum	X						X	
Piscidea erythrina	X							
Plantago spp.		X		X	X			X
Quercus alba				X				
Rhaponticum carthimoides						X		
Rhodiola rosea						X		
Salvia officinalis			X					
Schizandra chinensis						X		
Scutellaria lateriflora							X	
Symphytum officinale		X						X
Thuja occidentalis			X					
Withania somnifera	X					X	X	

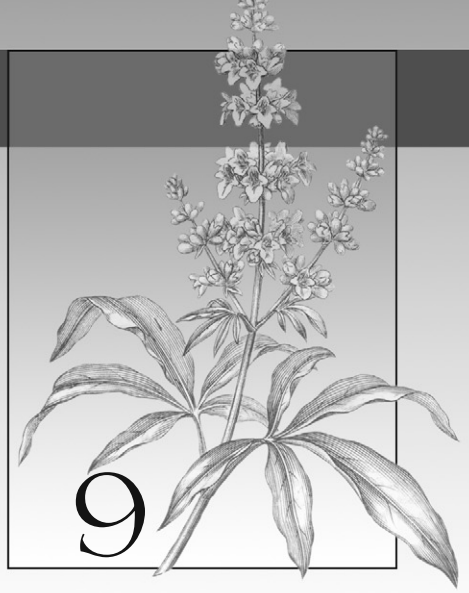
for hepatotoxicity, Hepatitis-B, and cirrhosis. For this purpose, a high-tech extract of the immature mycelium is used. It is rich in a broad spectrum of amino acids and B vitamins. One constituent, Lentinan, has been shown to possess a 97% inhibition rate against sarcoma 180 growth, and 80% inhibition of Ehrlich's Sarcoma in vitro.

SUMMARY

A number of vaginal infections and sexually transmitted diseases can be treated with botanical medicine. A variety of strategies are used including antimicrobial herbs, immunomodulating herbs for chronic recurrent infections, topical applications, and even botanicals for supprting the nervous system for stress related infections. Table 8-8 includes a summary of the herbs used to treat these conditions.

Urinary Complaints

Aviva Romm, Eric L. Yarnell, David Winston



9 CHAPTER

URINARY TRACT INFECTION

Aviva Romm

Urinary tract infection (UTI) refers to the presence of microbes anywhere in the urinary tract, ranging from the distal urethra to the kidney. UTI in the kidney is called pyelonephritis; in the bladder, cystitis; and in the urethra, urethritis. Infection is usually caused by bacteria, particularly *E. coli*, which accounts for 85% to 90% of all UTIs, but also may be caused by other bacteria, viral, and fungal infection. *Klebsiella, Proteus*, and *Pseudomonas* are commonly associated with UTI, particularly in recurrent cases. Urine itself is normally sterile, but the moist environment of the periurethral area, the proximity of the urethral orifice to the rectum, and the short length of the urethra provide a conducive environment for the growth and ascension of potential uropathogenic microorganisms into the urinary system. The presence of bacteria in the urine is called bacteriuria. In nonpregnant women bacteriuria in the absence of symptoms is not considered an indication for treatment; however, during pregnancy, bacteriuria is associated with increased risk of pyelonephritis as well as prematurity and possibly other complications; therefore, UTI in pregnancy requires special consideration.[1–3]

UTI INCIDENCE AND ETIOLOGY

It is estimated that several hundred million women suffer from UTI annually, with costs to health care providers amounting to over $6 billion annually worldwide, a figure that may even be an underestimate.[4] Additional costs to society of UTI are tremendous in terms of the personal suffering of millions of women annually, lost work days, and childcare costs. Over 56% of women will experience a UTI in their lifetimes, and among those experiencing uncomplicated acute UTI, as many as 20% will have a recurrence within 6 months. Overall UTI recurrence rate is between 27% and 48%.[4] Even with treatment, symptoms typically last for an average of 6 days, with nearly 2.5 days of limited activity. The rates of UTI are slightly higher in young, sexually active women because of mechanical factors affecting the urethra and the presence of uropathogenic organisms. UTI rates increase during pregnancy and with age, the former because of mechanical pressure of the growing uterus on the ureters and bladder preventing complete voiding, and the latter because of declining estrogen levels, declining mucin (a surface coating of the bladder epithelium that prevents bacterial adhesion), inability to void completely, incontinence, inadequate nutrition, and the occurrence of other disease and excessive catheter use as a result of medical procedures.

RISK FACTORS FOR URINARY TRACT INFECTION

A number of common factors appear to increase the risk of developing a UTI. As mentioned, sexual activity is associated with a higher incidence of symptomatic UTI; however, risk only seems to be increased in the presence of uropathogenic microorganisms, either from a woman's own reservoir of bowel microbes, or passed from a sexual partner. Urinating after sexual activity decreases the rates of infection. Evidence suggests that host genetic factors influence susceptibility to UTI. A maternal history of UTI is more often found among women who have experienced recurrent UTIs than among controls. Susceptible patients may have a genetically increased number of receptors on uroepithelial cells to which bacteria may adhere. Additionally, nonsecretors of specific blood group antigens, which are glycoproteins, are at increased risk of recurrent UTI. Mutations in host genes integral to the immune response (interferon receptors and others) also may affect susceptibility to UTI.[3] The use of oral contraceptives doubles the risk of UTI compared with no birth control, and the use of diaphragms and spermicides doubles the rate of UTI compared with OCs. Sexually transmitted infections and vaginitis can cause urethritis. Dehydration can increase bacterial growth leading to UTI. A history of antibiotic use is common in

women with a UTI; a possible mechanism that has been suggested is disruption of the vaginal flora and consequently overgrowth of pathogenic organisms. An interesting correlation exists between recurrent UTI and exposure to cold. A case-controlled study demonstrated a higher rate of UTI in women who reported cold hands, feet, or buttocks in women with UTI than controls. In a nonrandomized crossover study, cooling the feet of 29 healthy women with a history of recurrent UTI led to the development of UTI in five participants, compared with no UTI development in the control group.[1]

SYMPTOMS

UTI is commonly divided into lower UTI (urethritis and cystitis) and upper UTI (pyelonephritis), each with differing symptoms and treatments. Urethritis usually presents with a gradual onset, urethral irritation and inflammation, possibly changes in voiding patterns and dysuric symptoms, as well as possible vaginal discharge or bleeding. The most common symptoms of cystitis are frequent, painful urination, the urgent need to urinate, and suprapubic pressure, and malaise, with up to 40% presenting with blood in the urine (hematuria). Some women may exhibit mild to moderate vaginal bleeding associated with UTI.

Cystitis often has a sudden onset. Pregnant women may present with contractions and suprapubic pain, with dysuria possibly having been mistaken for normal polyuria of pregnancy. Women with lower UTI often complain of feeling achy, crampy, or ''just not feeling well.''

Pyelonephritis commonly has a gradual onset, although it can seem sudden if preceded by lower UTI, and is associated with not only urinary symptoms, but generalized symptoms such as fever, chills, nausea, malaise, and mild to extremely severe lower to middle back discomfort. Patients with pyelonephritis may appear quite ill. It is critical to differentiate between the symptoms of cystitis and pyelonephritis, as the latter requires more aggressive treatment and carries greater risks, particularly during pregnancy (Box 9-1). Cystitis may resolve spontaneously; however, effective treatment lessens the duration of symptoms and reduces the incidence of progression to upper UTI. Pyelonephritis is associated with substantial morbidity. Complications include acute papillary necrosis with possible development of urethral obstruction, septic shock, and perinephric abscess. Chronic pyelonephritis may lead to scarring with diminished renal function.

DIAGNOSIS

Diagnosis is based on a combination of clinical symptoms, physical examination, and laboratory findings. Diagnostic testing methods include urinalysis and culture and sensitivity. A proper urine specimen is obtained via a midstream catch. Vaginal cultures may rule out sexually transmitted disease and vaginal infection.

DIFFERENTIAL DIAGNOSIS

Primary differential diagnoses include urethritis, cystitis, and pyelonephritis.[2] In women with recurring infection, it is important to differentiate between relapse and reinfection. Additional considerations for acute or chronic UTI include:[5]

- Asymptomatic bacteriuria
- Chancroid
- Constipation
- Diabetes
- Dysfunctional uterine bleeding
- Dysmenorrhea
- Endometriosis
- Gonorrhea
- Interstitial cystitis
- Ovarian cysts
- Pelvic inflammatory disease
- Pregnancy
- Renal calculi
- Sexual assault
- Toxic shock syndrome
- Vaginitis
- Vulvovaginitis

BOX 9-1

Differential Diagnosis of Cystitis and Pyelonephritis

Cystitis
- Sudden onset typical
- Dysuria and symptoms associated with urination
- No fever, chills, nausea
- No costovertebral angle (CVAT) tenderness (flank pain)
- WBC count normal

Pyelonephritis
- Gradual onset typical
- Symptoms associated with urination may or may not be present
- Fever, chills, nausea
- + CVAT tenderness (flank pain)
- WBC count elevated

Adapted from Youngkin EQ, Davis MS: Women's Health: A Primary Care Clinical Guide, Stamford, CT, Appleton and Lange, 1994, p. 851.

CONVENTIONAL TREATMENT APPROACHES

Oral antibiotics effective against gram-negative aerobic coliform bacteria, particularly *E. coli*, is the principal treatment in patients with UTI. A 3-day course is typical in patients with an uncomplicated lower UTI or simple cystitis with symptoms for less than 48 hours. A bladder analgesic may be given if the patient has intense dysuria. Increased fluid intake is often recommended to promote dilute urine flow. Pregnant, otherwise healthy women with no evidence of an upper UTI may be treated with a 7- to 10-day course of a cephalosporin, such as cephalexin, even in the absence of upper urinary tract signs. Pregnant women are typically treated for all episodes of

bacteriuria, even in the absence of symptoms. Upper UTI requires antibiotic treatment and may require IV therapy and hospitalization. In most cases, pyelonephritis responds to antibiotic treatment in 48 to 72 hours.[5] Therapeutic approaches to treatment and prevention of urogenital infections have remained essentially unchanged for many years. Antibiotics and antifungals remain the mainstay of therapy. Several antibiotic therapies have become less effective because of antibiotic resistance, and the use of antibiotics in pregnancy often leads to vaginal yeast infection requiring treatment.[6]

Lifestyle changes may be recommended, such as teaching the client to void at the first urge to urinate, void after intercourse, drink adequate fluids, and avoid contraceptives associated with high UTI risk. Estrogen cream may be recommended for older women.[1,2] Other risk factors may include use of menstrual pads (i.e., rather than tampons), wiping the anogenital region from back to front after a bowel movement (front to back is the proper motion), wearing nonabsorbent underpants or pantyhose, and bubble baths with irritating soaps; however, none of these factors have been found to be significant in clinical trials.[1] Increasingly, conventional practitioners are recommending the use of cranberry juice and vitamin C for UTI treatment. These are discussed under Botanical Protocol.

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

Botanical medicine provides an excellent alternative to antibiotic use for reducing the duration and symptoms of lower UTI, preventing progression to upper UTI, and preventing recurrence. Lower UTI in nonpregnant women is often easily treated with simple protocol. Because of the risks associated with untreated pyelonephritis, it is recommended that patients with upper UTI be referred for medical care, and that botanical interventions be used in the context of complementary care. Care of pregnant women requires specific expertise in midwifery or obstetrics, as well as knowledge of herbs that are contraindicated in pregnancy, and must be done in consultation with an obstetric care provider. This section provides guidelines for the treatment of uncomplicated cystitis (Table 9-1).

Botanical treatment of lower UTI incorporates the use of urinary antiseptic and antimicrobial herbs with demulcent herbs (Table 9-2). Additionally, a diuretic may be included to assist the body in its attempt to increase the delivery of fluids through the bladder. Herbs for cramping and aching may be included if needed. Herbs are used in the context of an overall protocol to increase fluids and diuresis, and to relieve offending lifestyle causes (e.g., chronic vulvovaginitis, overgrowth of uropathogenic bowel flora, or use of birth control methods or sexual habits that may contribute to the problem). Rarely UTI can lead to vaginal bleeding, sometimes quite copious. If this occurs seek medical care.

Although not discussed in this chapter, herbal care also incorporates strategies for improving overall immunity in women with chronic recurrent UTI.

Calendula, Thyme, and Lavender

Calendula is typically used as a topical anti-inflammatory rinse with mild antimicrobial activity, either in the form of an infusion or diluted tincture, 1 tbs/125 mL water. Thyme and lavender are used topically for their antimicrobial activity and mild anti-inflammatory activity. in the form of peri-rinses for the treatment of urethritis associated with vulvo-vaginitis, and also for the reduction of rectal to urethral microbial spread. They can be used as infusions or the essential oils can be diluted in tea or warm water. Ingredients for a sample peri-rinse are provided in Table 9-1 (also see Chapter 3). Topical use of these herbs is considered safe during pregnancy.

Cranberry

The use of cranberries (Fig. 9-1) for the treatment of UTI dates back to the mid-nineteenth century when German chemists discovered that consumption of the berries produced a bacteriostatic acid in the urine. By 1900 in the United States, it was postulated that eating cranberries acidified the urine and prevented UTIs.[7] This mechanism of action has been questioned as studies have failed to consistently show acidification of the urine with consumption of cranberry juice. There are mixed results regarding the effect of cranberry juice, fruit, and extract on urine pH. It appears that cranberry does not consistently lower urine pH and it is uncertain whether any reduction in urine pH that does occur has an antibacterial effect.[8] However, the use of cranberry products continues to be a popular and empirically efficacious means of preventing and treating uncomplicated lower UTI. It is now accepted that the primary mechanism of action of cranberries is caused by two compounds in cranberries that each prevent fimbriated *E. coli* from adhering to uroepithelial cells in the urinary tract.[9–11] These compounds are also found in blueberries, which may also be used as part of the prevention and treatment of UTI.[12] Although cranberry has primarily been used against uropathogenic *E. coli*, recent evidence from in vitro studies suggests that it may have activity against other uropathogenic organisms, and also against *H. pylori*, responsible for gastric ulcers.[13] Cranberry also may prevent the formation of biofilms on epithelial mucosa, reservoirs of bacteria that are difficult to effectively treat with antibiotics.[8]

Based on a comprehensive review of the literature by the Cochrane Collaboration, there is some evidence from two good-quality RCTs that cranberry juice may decrease the number of symptomatic UTIs in women over a 12-month period. Based on the literature, there have been problems with noncompliance over long periods of administration, probably because of the taste of some cranberry products or possibly other side effects; and the optimum dosage and administration methods (e.g., juice or tablets) are unclear, necessitating further properly designed trials.[14] However, clinical experience with cranberry juice products in herbal practice suggests that compliance problems can be overcome by using palatable products. In two good-quality RCTs, cranberry products significantly reduced the incidence of UTIs at 12 months compared with placebo/control in women. One trial gave 7.5 g cranberry concentrate daily (in 50 mL); the other

TABLE 9-1

Sample Botanical Protocol for Cystitis

DAYS	HERBS	SUPPLEMENTS	OTHER
1–2	Prepare the following decoction either as a hot or cold water infusion:* • 6 g uva ursi leaf† • 6 g marshmallow root • 2 g dandelion leaf • 500 mL water Steep and strain. Dose: ½–1 cup every 4 hours depending upon severity of UTI. This preparation will keep refrigerated for 24 hours. 3 mL echinacea tincture every 2–4 hours depending upon severity of UTI • If there is discomfort and cramping associated with UTI in a nonpregnant patient, 3 mL each of cramp bark and wild yam tinctures may be mixed with the echinacea the dose increased to 5 mL every 2–4 hours.	500 mg vitamin C every 4 hours‡	• Every 2 hours drink 6–8 oz of spring water • Every 2 hours drink 6–8 oz of unsweetened cranberry juice. (The juice can be cranberry-apple for palatability, but should contain no added sugars.) Thus, the patient is taking 6–8 oz of fluid to increase urinary volume and flush the urinary tract. • Probiotic supplement • Urinate at first urge • Avoid sexual activity during treatment • Reduce dietary sugar intake other than fresh fruit. • Address/reduce any risk factors that might be present as discussed earlier in the chapter.
3–4	If symptoms have lessened, continue protocol but decrease all doses to ½ of the original volume. If symptoms have not lessened, continue as for Days 1–2, taking 1 ''00'' capsule of baking soda with each dose of the uva ursi containing infusion.	If symptoms have lessened, continue protocol but decrease all doses to ½ of the original volume. If symptoms have not lessened, continue as above.	If symptoms have lessened, continue protocol but decrease all doses to ½ of the original volume. If symptoms have lessened, continue as above.
5–7	If symptoms have lessened or have disappeared, continue protocol but decrease all doses to ¼ of the original volume. If symptoms have not lessened, seek medical care.	If symptoms have lessened, continue protocol but decrease all doses to ½ of the original volume.	If symptoms have lessened, continue protocol but decrease all doses to ½ of the original volume.
8–14	UTI frequently recurs in the weeks after treatment. This is most commonly a problem with antibiotic treatment, but even with herbs, prophylaxis is preferable to retreatment. On days 8–14 maintain all day 5–7 treatment, but omit the uva ursi blend infusion from the protocol. Repeat days 5–7 for several days is patient notices any inkling of recurrence. Patients with a tendency to UTI can periodically repeat Days 3–7 without the uva ursi blend infusion as prophylaxis on a semi-regular basis, for example, for 1 week per month. In many cases this prevents recurrent episodes entirely.		

Note: All of the protocol from each of the three columns should be followed concurrently. Symptoms usually begin to significantly resolve within 24–48 hours. If at any time symptoms worsen, or persist past 5 days, seek immediate medical care.

*Steep 1 hour or 4 hours, respectively

†See discussion of uva ursi use in pregnancy.

‡Pregnant women should not exceed 2000 mg of vitamin C supplementation daily because of risk of rebound scurvy in the infant.

Topical Treatment for Urethritis

Prepare a periurethral rinse:
7 g dried calendula blossoms
4 g dried lavender blossoms
3 g dried thyme leaf
Steep in 1 L of boiling water for 30 minutes. Cover while steeping. Strain and place in a peri-bottle to which has been added 1 tsp sea salt. Instruct patient to rinse the peri-urethral area with the tea after each urination and bowel movement (after wiping) and then pat dry gently.
Alternatively, the mix could be prepared by adding 1 tbs of calendula tincture and 5 drops each of thyme and lavender essential oils to 1 cup of warm water with 1 tsp sea salt, and use as per the instructions of the previous peri-rinse.

TABLE 9-2

Botanical Treatment Strategies for Simple Lower UTI

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Reduce infection	Antimicrobial	*Achillea millefolium*	Yarrow
		Arctostaphylos uva ursi	Uva ursi
		Calendula officinalis	Calendula
		Echinacea spp.	Echinacea
		Lavandula officinalis	Lavender
		Thymus vulgaris	Thyme
		Vaccinium macrocarpon	Cranberry
Relieve spasm in urinary tract smooth muscle	Antispasmodic	*Achillea millefolium*	Yarrow
		Actaea racemosa	Black cohosh
		Dioscorea villosa	Wild yam
		Piper methysticum	Kava kava
		Viburnum opulus	Cramp bark
		Viburnum prunifolium	Black haw
Relieve pain	Analgesic	*Anemone pulsatilla*	Pulsatilla
		Corydalis ambigua	Corydalis
		Eschscholzia californica	California poppy
		Piper methysticum	Kava kava
		Piscidea piscipula	Jamaican dogwood
		See Endometriosis, Chronic Pelvic Pain, and specific Plant Profiles for discussions of analgesic herbs	
Soothe urinary tract irritation and inflammation	Demulcent Anti-inflammatory	*Althea officinalis* *Solidago virga urea*	Marshmallow Goldenrod

Figure 9-1 Cranberry (*Vaccinium macrocarpon*). (Photo by Martin Wall.)

gave 1:30 concentrate given either in 250 mL juice or tablet form. There was no significant difference in the incidence of UTIs between cranberry juice vs. cranberry capsules.[14] The safety of cranberries and their general healthful properties, along with combined empiric evidence of numerous practitioners, suggests that it is reasonable for women with no other significant health problems to use cranberry products for the prevention of recurrent UTI.[15] A recent review article on cranberry summarizes that ''recent, randomized controlled trials demonstrate evidence of cranberry's utility in urinary tract infection prophylaxis. . . . Cranberry is a safe, well-tolerated herbal supplement that does not have significant drug interactions.''[16] Recommended daily doses of cranberry for the prevention of UTI vary. Based on the available literature, the therapeutic dose of cranberry juice is 30 to 300 mL daily or three 8-oz glasses of unsweetened juice daily, or one tablet (300 to 400 mg) of cranberry extract tablets twice daily.[8,16]

Echinacea

Echinacea is used in protocol for women with an acute UTI and for prevention of chronic UTI. Although Echinacea is not used to directly address the UTI, it is included as an adjunct for overall immune support. Echinacea is discussed extensively in Plant Profiles: Echinacea.

Uva Ursi

Uva ursi (Fig. 9-2) is one of the most commonly used urinary tract disinfectants in modern herbal medicine.[17] The leaves, taken as a cold or hot infusion, decoction, or tincture, are primarily used as an antiseptic in urinary tract infections.[7] Uva ursi is commonly combined with urinary demulcents, such as marshmallow root or corn silk, and also may be taken with an herbal diuretic, most commonly dandelion leaf, but goldenrod or birch

Antimicrobial Herbs

Two primary herbs used as antimicrobials in the treatment of lower UTI are cranberry fruit and uva ursi leaf. Some controversy exists in using these two herbs together based on the disputed belief that uva ursi must be used in an alkaline urinary environment for efficacy, and that cranberry products acidify the urine. Modern herbal practice and emerging evidence suggest that, in fact, there may be no reason to avoid combining these herbs. It appears that although an alkaline environment may enhance the efficacy of uva ursi, effectiveness as a antimicrobial is not depending on the urinary pH, and in fact, cranberry may not significantly reduce urinary pH. Herbalists have long combined these herbs in UTI treatment protocol with excellent outcomes.

Figure 9-2 Uva ursi (*Arctostaphylos uva ursi*). (Photo by Martin Wall.)

leaf may be used as well. Diuretics are contraindicated in pregnancy. Cold infusion reduces the tannin content of the product, making it easier for the digestive system to handle and reducing the nausea sometimes associated with its use; however, cold preparations might be inadvisable for immunocompromised patients because of the potential for microbial contamination from the herbs. Uva ursi is approved by the German Commission E for the treatment of inflammatory conditions of the urinary tract.[18] It is widely used in the treatment of uncomplicated acute and recurrent UTI, based on its astringent and antibacterial actions, and when antibiotics are not deemed essential.[19] Midwives include the herb as an astringent anti-inflammatory in sitz baths and perineal rinses for postnatal perineal healing and as part of treatment of vaginitis and urethritis. Unfortunately, there are few clinical trials and pharmacodynamic studies of uva ursi. In vitro studies using crude leaf preparations and extracts of uva ursi leaf have demonstrated mild antimicrobial activity against known UTI-causing organisms including *C. albicans, E. coli, S. aureus*, and *Proteus vulgaris*, and others.[20] Several studies have also demonstrated anti-inflammatory activity of the herb, particularly enhanced when extracts are used in combination with anti-inflammatory pharmaceutical drugs, such as prednisolone, indomethacin, or dexamethazone.[21,22] One double-blind, placebo-controlled, randomized study of 57 women utilized a combination extract of hydroalcoholic extract of uva ursi leaves, standardized to an unknown amount of arbutin and methylarbutin uva ursi with dandelion leaf (*Taraxacum officinalis*) to evaluate the efficacy of this combination for the prevention of recurrent urinary tract infection. Inclusion in the study required that otherwise healthy individuals had suffered at least three episodes of cystitis in the past year and at least one episode in the last 6 months prior to this study. Patients received either the extract ($n = 30$) or placebo ($n = 27$) three tablets three times daily for 1 month and were then followed for 12 months. At the end of the 12-month monitoring period, significantly more women in the placebo group experienced recurrent cystitis compared with the treatment group ($p < 0.05$). No adverse effects were reported.[17,23]

Some amount of disagreement can be found in the literature regarding the requirement of an alkaline pH environment for the efficacy of this herb. Some authors postulate that a reduced urinary pH inhibits the efficacy of the herb; others argue that increasing the alkalinity of the urinary environment enhances the efficacy of the herb, while still others state that activity is not dependent on urinary pH. Given the reliability of this herb generally, it is prudent to conclude that if uva ursi does not seem to be working, the addition of four ''00'' capsules of the equivalent of 1 tablespoon sodium or potassium bicarbonate may be taken once or twice daily, divided between uva ursi doses, to alkalinize the urine in such situations before making a final determination about efficacy.[15,19,24,25]

The question of whether this herb is safe for use in pregnancy is difficult to definitely answer based on the available evidence. The Botanical Safety Handbook gives this herb a Class 2b and 2d rating: Not to be used in pregnancy, a caution that is reiterated by many authorities.[17,18,26,27] However, the reasons for contraindication are variable and not well supported, ranging from alleged uterotonic and oxytocic activity to ''theoretical fetotoxicity.''[17,27] The original source of the concern of oxytocic activity appears to stem from Brinker, who reported that there is ''empirical'' evidence of oxytocic action with no further explanation.[28] Low Dog states that the herb has potential fetotoxicity because of its hydroquinone content. Studies using pure hydroquinone (i.e., not the whole herb or whole herb products) have produced microtubulin dysfunction in bone marrow, and exposure of human lymphocytes and cell lines to hydroquinone has been shown to cause genetic damage.[15] However, giving pure constituent is not the same as giving a whole herb, a perennial problem in assessing the safety of herbs with conventional pharmaceutical testing models. Although Tyler et al. state that mutagenicity may be associated with this herb, other researchers report on low potential for mutagenicity and negative Ames' test.[17] In animals administered 100 and 400 mg/

kg per day of arbutin, no signs of fetal toxicity were observed.[17] Uva ursi has been used by midwives as a mainstay treatment of acute symptomatic cystitis in pregnancy for over two decades in the United States with no adverse reports associated with its use.[29] Empiric observation demonstrates less recurrence of UTI with uva ursi versus treatment with antibiotics. The transference to infants of arbutin/hydroquinone from uva ursi use during lactation has not been researched and therefore is not recommended by German authorities; however, the risk remains speculative.[18] McKenna et al. recommend using only the lowest doses during lactation, observing the infant for side effects, and using under the guidance of a knowledgeable lactation expert.[7] It is always prudent to avoid the medical use of herbs during the first trimester unless absolutely necessary. In the case of uva ursi, it is advisable to avoid it entirely during the first trimester, and to use it only if it is the best option for treatment of UTI later in pregnancy, using only at a minimal effective dose and for minimal duration. Further research in this area is clearly needed, particularly given the volume and frequency of UTIs among pregnant women.

Yarrow

In vitro studies of the essential oil and methanol extracts of several species of yarrow found *Achillea millefolium* to be active against a number of pathogenic organisms including *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella enteritidis*, *Aspergillus*, and *Candida albicans*, and also to possess antioxidant activity.[30,31] Water extracts have also demonstrated antimicrobial activity.[32] Two studies, however, while identifying antimicrobial activity in a number of herbs, did not demonstrate antimicrobial activity of yarrow.[33,34] The German Commission E lists among its actions antibacterial, astringent, and spasmolytic. No other literature was identified evaluating use of yarrow for UTI. Herbalists typically recommend the tea, 1 cup two to four times daily, for its antimicrobial and mild diuretic effects. Mills and Bone assert that limited use in pregnancy has not been associated with adverse fetal outcomes. Evidence of increased fetal damage in animal studies exists, with unknown relevance to human consumption. Yarrow is generally contraindicated during pregnancy because of its potentially high thujone content and emmenagogic activity.[27,35]

Demulcent and Anti-inflammatory Herbs

Goldenrod

Goldenrod is an anti-inflammatory, diuretic herb and spasmolytic favored for its beneficial effects in the treatment of UTI, which have been successfully demonstrated in both animal and uncontrolled human trials.[19,36] It is described by the German Commission E monographs and ESCOP as used for irrigation therapy for diseases of the lower urinary tract, especially for inflammation, as well as for prevention and treatment of urinary calculi and renal gravel. The flavonoid (including quercetin), saponin, caffeic acid derivatives, and glycosides have been described as the active components.[32] Goldenrod is taken as an infusion, 3 to 4 g of dried herb/150 mL water, steeped 10 minutes, taken two to three times daily.[19,32] It is suggested to take in conjunction with copious fluids.[18,19,32] ESCOP contraindicates the use of European goldenrod in patients with edema because of impaired cardiac or renal function.[19] Patients with allergies to plants in the Compositae family should avoid use of this herb. No data are available on use during pregnancy and lactation.

Marshmallow Root

Marshmallow root is soothing and anti-inflammatory to the throat and GI system.[19] It is an excellent addition to water extracted uva ursi infusions and decoctions for its demulcent, soothing effects in the treatment of UTI.[35] The roots are rich in mucilage, which is composed largely of polysaccharides. Lack of studies on the pharmacodynamics of this herb in the urinary system make it impossible to conclude whether there are direct or indirect effects on the urinary epithelium of the urinary tract, but combination with uva ursi certainly reduces the possible irritation to the GI of the high-tannin content of that herb. Alcohol is not an effective menstruum for extraction of polysaccharides; therefore, only water-based extraction methods are used for this herb.

Antispasmodic Herbs

Discussions of specific antispasmodic herbs are found elsewhere in this book. All of the herbs listed in Table 9-2 as antispasmodics are used specifically for their unique ability to relieve spasms in the pelvic organs, mostly through their action on smooth muscle. Yarrow has mild antimicrobial activity. Kava kava has a reputation for marked action specifically on the bladder, and is especially valued for treatment of neurogenic bladder pain. Yarrow and kava kava are contraindicated in pregnancy and should be used with caution in lactation. See Plant Profiles: Kava kava for specific precautions with its use. Wild yam has been used historically for its ability to ease spasms in the hollow organs, and is considered a valuable herb for the treatment of cramping associated with lower UTI, as are cramp bark and black haw. Black cohosh is specifically indicated for pelvic discomfort and cramping that are also associated with drawing pains in the lower back and legs. See plant profiles: Black Cohosh, for safety consideration. Yarrow may be taken as a tea or infusion, alone or added to other UTI specific herbs, but otherwise these herbs, including yarrow, generally are included in tincture form with other herbs for UTI, typically as 10% to 50% of the formula.

NUTRITIONAL CONSIDERATIONS/ ADDITIONAL THERAPIES

Probiotics

There is limited research on the influence of diet on UTI. Midwives and herbalists commonly suggest a reduction in dietary sugar consumption and an increase in fluid intake, with the addition of cranberry juice, as discussed. Because urinary tract infections are often cause by bowel flora, which are pathogenic in the urinary tract, one train of thought is that modification

of bowel flora may lead to a reduction in recurrent UTI.[37–40] The use of probiotics to restore normal vaginal flora, and thus provide a competitive bacterial barrier to uropathogens is emerging as an area of research in the prevention of recurrent UTI.[1,13] Proponents of this approach use specific microorganism strains to restore the vaginal lactobacilli microflora such that the indigenous lactobacilli recover, or the patient retains some degree of acidic pH and protection against infection. The basis for use of probiotics emerged from clinical observations in 1973, when a study of healthy women showed an association between lactobacilli presence in the vagina and absence of UTI history. Results from a limited number of studies have demonstrated a significant reduction in recurrence rate of UTI using one or two capsules vaginally per week for 1 year, with no side effects or yeast infections. A two-strain combination is recommended for vaginal use: *L. rhamnosus* GR-1 is used for its anti-Gram negative activities and resistance to spermicide, and *L. fermentum* RC-14 is included for anti-Gram positive cocci activities and hydrogen peroxide production. Various protocols have been explored, such as administration postmenses, one or two capsules per week, or one capsule daily for 3 days.[37] Studies are needed to determine whether healthy people and those prone to recurrent urogenital infections benefit from daily ingestion of probiotics, such as *L. rhamnosus* GG, the most clinically documented probiotic strain for gut health. A study using this strain in fermented milk has suggested some reduction in UTI recurrences. The potential for intestinal probiotics to influence bladder and vaginal health through immune modulation has not been fully explored.[6] Researchers in one study concluded that dietary habits may be an important risk factor in UTI recurrence. One-hundred thirty-nine women from a health center for university students or from the staff of a university hospital (mean age: 30.5 years) with a diagnosis of an acute UTI were compared with 185 age-matched women with no episodes of UTIs during the past 5 years. Data on the women's dietary and other lifestyle habits were collected by questionnaire. A risk profile for UTI expressed in the form of adjusted odds ratios (ORs) with 95% CIs was modeled in logistic regression analysis for 107 case control pairs with all relevant information. Frequent consumption of fresh juices, especially berry juices, and fermented milk products containing probiotic bacteria (e.g., yogurt, cultured milk, cheese) was associated with a decreased risk of recurrence of UTI. A preference for berry juice over other juices, and consumption of fermented milk products three times weekly were both associated with a reduction in recurrent UTI.[12] The efficacy of probiotics depends on having the proper strains, prepared and stored to maintain their activity. According to Low Dog, a recent analysis of 20 probiotic products claiming to contain specific *Lactobacillus* species found 30% of products to be contaminated with other organisms, and 20% of products contained no viable species whatsoever.[15]

Vitamin C

Vitamin C has is used as a bacteriostatic and acidifying agent in the treatment of urinary tract infections. Studies have shown, however, that it actually does not significantly acidify the urine. It is likely, therefore, that it is having a bacteriostatic action through other mechanisms not yet fully elucidated. It was demonstrated by Carlsson et al. that large amounts of a bacteriostatic gas (NO) are formed in mildly acidified nitrite containing human urine and that NO formation is greatly enhanced by the addition of vitamin C. Moreover, mildly acidified nitrite-containing human urine showed antimicrobial activity against three of the most common urinary pathogens and this inhibitory effect was further increased after addition of ascorbic acid.[41]

CASE HISTORY 1: TREATMENT OF AN UNCOMPLICATED LOWER UTI IN A NONPREGNANT WOMAN

Lisa, a 32-year-old married mother of four young children, has a history of UTI since her teenage years. Throughout her adult years, infections have recurred regularly, and with more frequency during times of stress. She has always received antibiotic treatment in the past. She is overweight (5'2'' and 220 pounds), with no reported health problems and an unremarkable gynecologic history and no history of pyelonephritis or other renal problems. She has been a regular patient in a midwifery practice through the pregnancy and birth of her fourth child, now 3 months old and breastfeeding. Her pregnancies were uneventful, though likely with undiagnosed gestational diabetes. She had mild transient glucosuria, and large babies (on average, 9 lbs), the most recent birth resulting in a shoulder dystocia that was resolved with no consequences to mother or newborn. She has not been diagnosed with gestational diabetes, but was told that she could be at risk for the later development of adult onset diabetes. She has a family history of marked obesity (maternal, sister).

Lisa presents with an acute, severe UTI, which by 10 PM when she phoned the office on an emergency basis, had led to a complete inability to void accompanied by pain (8 on a scale of 1 to 10), nausea, and malaise. She is afebrile on self-reporting, and has no other symptoms, but is extremely anxious and does not want to go on another round of antibiotics, particularly while breastfeeding. Her husband had picked up an over-the-counter medication for her to take to help her void. She does not know the name of it but described it as a ''little blue pill'' that she has used several times before. It did not help and now she is concerned. She was reassured that her UTI was a solvable problem, but that given the hour we needed a strategy. Her husband agreed to make the 45-minute drive to the office to fill a prescription from the apothecary, and she began an herbal protocol immediately, with a 24-hour observation period: If symptoms improved she would continue with the botanical protocol; if they did not, or at any point worsened, she would obtain medical treatment.

Her protocol is a standard botanical UTI intervention as follows:

Days 1–2

Drink:
- One 6- to 8-oz glass of water or diluted, unsweetened cranberry juice alternating every hour throughout the day.
- ½ cup of uva ursi and marshmallow infusion four times daily (see the preceding for preparation)
- 500 mg vitamin C and 4 mL of echinacea tincture every 4 hours
- If necessary for spasmodic bladder, take 3-mL antispasmodic tincture, including equal parts of wild yam, cramp bark, and yarrow.

Avoid:
All sugar, including honey, maple syrup, and other natural sugars, in food products.

Days 3–5
Repeat above protocol but reduce all doses by 50% frequency.

Days 6–7
Repeat days 3–5, but take only ¼ cup of the decoction.

Lisa began the protocol immediately that night, and given the acute situation, woke repeatedly throughout the night to continue. By 4 AM she voided copiously, and by morning her symptoms had improved mildly but not significantly. She continued the protocol throughout the day with no further improvement. By 4 PM, suggested she take two ''OO'' capsules of baking soda with her next two doses of the uva ursi decoction, after which marked improvement ensued. By the next morning, she was voiding normally and beginning to feel symptom free. By day, 3 she was completely symptom free and continued the protocol until completed. She phoned 3 weeks later saying she was thrilled that she had not had her typical relapse and was able to avoid antibiotics. We discussed her tendency to UTI, as well as the possible association with diabetes, and she was encouraged to reduce the sugar consumption that was a regular part of her heavily carbohydrate-based vegetarian diet. She was also reminded of the importance of voiding soon after she felt the urge, rather than waiting until a convenient time when she was not busy with her small children, and to urinate before she sat down to nurse the baby, rather than holding it until the baby was finished.

CASE HISTORY 2: TREATMENT OF AN UNCOMPLICATED LOWER UTI IN A PREGNANT WOMAN AT 8 WEEKS' GESTATION

Note: The following case is from the late 1980s, prior to the publication of contraindications to the use of uva ursi during pregnancy and prior to ACDG recommendation for antibiotic treatment of all UTI in pregnancy. Should a pregnant woman experience recurrent infection, cranberry juice, increased fluids, and vitamin C, along with lifestyle changes, should be considered, or appropriate antibiotic therapy employed.

Michelle, age 24, phoned early in the morning with presenting symptoms of frequent urination, light, irregular uterine cramping, and blood-tinged vaginal mucus. She was 8 weeks pregnant with her first child, and planning a home birth with a midwife. She had no other medical problems. Vaginal examination revealed a closed cervix and speculum inspection revealed no evidence of blood in the vaginal canal or around the cervix. Her past history of frequent UTIs and current symptoms suggested that UTI might be the problem, and a urine dipstick provided preliminary confirmation. She suspected that she might be slightly dehydrated from the intense heat of summer, and she and her partner had also had sex the previous morning. Michelle wanted to avoid antibiotics if at all possible because of a history of vaginal candidal infections following past treatment for UTI, but understood that if symptoms persisted, antibiotics would be necessary. A 24-hour trial was agreed upon with support of her family doctor, with medical intervention to be sought should symptoms worsen or persist, and a prescription for an antibiotic made available.

Michelle immediately began an intensive regimen of cranberry juice concentrate diluted in water every 2 hours, alternated with an 8-oz glass of water every 2 hours, 500 mg vitamin C 4 times daily, and ¼ cup of uva ursi and marshmallow root infusion every 2 hours, prepared with 7 g each of the herbs steeped in 1 liter of boiling water. The herbs were left to sit in the infusion, the liquid being strained off for each dose.

Within 8 hours, symptoms began to improve, and all cramping and spotting had completely ceased by 24 hours. She decreased the dose and frequency of the uva ursi and marshmallow infusion to ½ the original recommendation for the next 24 hours, and after this remained on the cranberry juice preparation for 5 days, drinking three glasses per day, and maintaining a high water intake. She has no further episodes of recurrence and gave birth to a healthy child after a full-term pregnancy, with no complications, at home.

INTERSTITIAL CYSTITIS

Eric L. Yarnell

The syndrome of chronic urinary bladder inflammation, pelvic pain, and frequent urination was dubbed interstitial cystitis (IC) in the 19th century. There is no uniform or pathognomonic histopathologic lesion; rather, IC represents part of a spectrum of irritative pelvic syndromes not clearly resulting from infection.[42] Although some patients have ulcerations of the bladder epithelium, these occur in less than 10% of cases. Interstitial cystitis generally affects women beginning around 40 years of age, and also affects men.[43] Generally speaking, IC waxes and wanes but does not tend to spontaneously remit except in a minority of patients. Although anxiety, depression, and psychosocial distress (including inability to work owing to pain and frequency of urination) are common accompanying complications, the condition itself does not progress and has no known life-threatening complications.

PATHOPHYSIOLOGY

Interstitial cystitis is a multifactorial disorder with no definitively established etiology.[42] Connections to allergy

or autoimmunity are suspected based on features of the illness and associations with other allergic or autoimmune diseases. In the past decade, research attention has focused on the deterioration of the glycosaminoglycan layer of the bladder epithelium as well as the role of nitric oxide (NO).[44,45]

SYMPTOMS AND SIGNS

Signs and symptoms of interstitial cystitis include:

- History of progressive urinary frequency and nocturia
- No evidence of urinary tract infection
- Marked suprapubic pain when the bladder is full
- Pain in the urethra or perineum that is relieved on voiding.
- Hematuria, especially when urination has been delayed (e.g., due to bladder over distention)
- Patient often has a history of allergies
- Chronic pelvic pain
- Dyspareunia

Physical examination is usually normal, although there may be some suprapubic tenderness and bladder region tenderness when palpated transvaginally. Anxiety and stress often accompany the preceding symptoms.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

IC diagnosis is one of exclusion. Other causes of pelvic pain and urinary frequency, including infectious urethritis or cystitis, bladder polyps, bladder cancer, endometriosis, and vaginitis, must be ruled out. Although diagnosis is often presumed based on the clinical picture, cystoscopic examination can help to confirm the diagnosis.[42] The presence of glomerulations or a Hunner's ulcer strongly correlates with interstitial cystitis. Some also consider pain on bladder distention produced by intravesical instillation of water, saline, or potassium solutions, to be diagnostically significant.

CONVENTIONAL TREATMENT

One definitive review of IC sums up conventional treatments for the condition thus: ''Although the symptoms of IC can be controlled with one of a variety of treatments in the overwhelming majority of patients, there is little evidence that treatment accomplishes anything more than influencing the symptomatic expression of the disease, rather than curing the condition.''[42] There are three categories of standard therapy available: oral, intravesicular, and surgical.

Oral Treatment

Amitriptyline, a tricyclic antidepressant, is one of the most commonly prescribed oral medications for patients with interstitial cystitis. Although apparently effective in uncontrolled trials, no controlled trials have been reported.[42] The most common adverse effect of amitriptyline is sedation, and thus it is usually given at bedtime. It is contraindicated in patients with conduction disorders or arrhythmias, unstable angina, congestive heart failure, or orthostatic hypotension. Hydroxyzine and other H1 receptor antagonist antihistamines also have been used, although they are not supported by controlled clinical trials.[46] It can take 3 months to see a benefit from these drugs, and they tend to be most effective in patients with allergies.[47] The major adverse effect of these drugs is sedation. Pentosan sodium polysulfate is a synthetic glycosaminoglycan administered orally. It has been repeatedly shown to induce remission in approximately 30% of patients who take it, particularly if they have milder symptoms of shorter duration.[42,47] It may taken many months for benefits to appear, and many more for optimal effects. The most common adverse effects are nausea, rash, diarrhea, and reversible alopecia.[42] Rarely hemorrhage can occur. The final category of oral medications routinely prescribed for patients with interstitial cystitis are nonsteroidal anti-inflammatory drugs (NSAIDs) and opioid analgesics. Nonspecific NSAIDs and cyclooxygenase (COX)-2–specific NSAIDs appear to be equally effective for relief of pain related to interstitial cystitis, although they have not been proved effective for this condition in controlled trials. COX-2 inhibitors are considered safer than nonspecific NSAIDs, but are also dramatically more expensive. Ceiling effects are noted for both types—no added benefit is achieved above a certain dose.[42] Both types can cause gastrointestinal bleeding, although COX-2 inhibitors are less likely to do so. Both also have significant renal toxicity. Opioid analgesics, with the significant problems of sedation, respiratory depression, dependence, addiction, and other problems are generally considered a last resort in patients with chronic pain. Unlike NSAIDs, opioids do not have an efficacy ceiling.

Intravesicular Treatment

There are two major intravesicular therapies available: dimethyl sulfoxide (DMSO) and heparin. Less common intravesical therapies that will not be discussed here include silver nitrate, Clorpactin, and hyaluronic acid. DMSO was the first FDA-approved treatment for interstitial cystitis—interesting as it is a natural product and because no controlled clinical trial data supported its efficacy. Using a solution of 50% DMSO on an outpatient or self-administration basis, approximately 35% of patients go into remission after one to three cycles of treatment.[47] Unfortunately the treatment tends to lose efficacy over time. The main adverse effects are acute symptom flare-up for 24 hours after instillation (sometimes compensated for by prior instillation of a topical anesthetic or systemic opioid analgesic) and intense sulfurous odor of breath and body after use. Intravesical heparin requires long-term use (minimum 2 to 6 months) before benefits begin to be noticed, but they can be significant.[42] Benefits do not appear to be sustained unless treatment is continued more or less indefinitely. There is no systemic absorption of heparin administered in this fashion and thus no effect on coagulation or bone density.

Surgical Treatment

Hydrodistention is the most common surgical procedure for treatment of people with interstitial cystitis. It consists of anesthetizing the patient, and then distending the bladder with water and holding it in the enlarged state for a period of 15 or more minutes.[42] Symptoms are usually

immediately relieved after hydrodistention and remain in remission for up to 24 months. However, they almost always return. Repeat treatments can be effective. Controlled clinical trials have not been published. This procedure can help in the diagnosis of interstitial cystitis as it often makes glomerulations or Hunner's ulcers obvious. Perhaps surprisingly, there is no indication that this treatment results in long-term bladder dysfunction, although there is a significant risk of bladder rupture. For the fewer than 10% of patients who have severe symptoms not relieved by these therapies, more invasive surgery is contemplated.[42] These procedures include resection of Hunner's ulcers, neurotomies, cystectomies, augmentation cystoplasties, and neobladder construction. Results vary considerably and there are many possible adverse effects, necessitating a careful, thorough decision-making process before choosing this method of treatment.

BOTANICAL TREATMENT OF INTERSTITIAL CYSTITIS

A large number of medicinal plants are utilized clinically in patients with IC based on observed botanical actions (Table 9-3). There is a general absence of clinical trials for botanicals for the treatment of this condition. This parallels the fact that many of the pharmaceuticals prescribed for IC patients also have not been subjected to controlled clinical trials. The most important categories of herbs for treatment are mucilaginous or reflex demulcent herbs, anti-inflammatories, anodynes, pelvic lymphagogues, spasmolytics, astringents, anxiolytics, and bladder tonics. Herbs with these actions are aimed at treating underlying causes and pathophysiologic processes as well as alleviating symptoms. Immunologic support (e.g., via use of adaptogens; see Chapter 7) is a potentially important means to successful treatment in

TABLE 9-3

Botanical Treatment Strategies for Interstitial Cystitis

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Soothe inflammation, relieve pain	Demulcent/Mucilage	*Alcea rosea*	Hollyhock
		Althea officinalis	Marshmallow
		Elymus repens	Couch grass
		Ulmus rubra	Slippery elm
		Verbascum thapsus	Mullein
		Zea mays	Corn silk
Relieve inflammation and pain	Anti-inflammatory	Betula spp.	Birch
		Echinacea spp.	Echinacea
		Glycyrrhiza spp.	Licorice
		Melilotus officinalis	Sweetclover
		Populus tremuloides	Quaking aspen
		Solidago canadensis	Goldenrod
Relieve pain	Spasmolytic Anodyne Analgesic	*Cannabis sativa*	Marijuana
		Herniaria glabra	Rupturewort
		Lobelia inflata	Lobelia
		Paeonia brownii	Peony
		Piper methysticum	Kava kava
		Pulsatilla vulgaris	Pulsatilla
		Valeriana sitchensis	Pacific valerian
Relieve accompanying stress and anxiety	Anxiolytics	*Cannabis sativa*	Marijuana
		Passiflora incarnata	Passion flower
		Pulsatilla vulgaris	Pulsatilla
		Puper methysticum	Kava kava
		Scutellaria lateriflora	Scullcap
Improve bladder circulation, reduce local inflammation	Lymphagogue	*Fouquieria splendens*	Ocotillo
		Galium aparine	Cleavers
Improve bladder tone	Astringent Tonic	*Anemopsis californica*	Yerba mansa
		Chimaphila umbellate	Pipsissewa
		Ephedra viridis	Mormon tea
		Equisetum arvense	Horsetail
		Rhus aromatica	Sweet sumac
		Zea mays	Corn silk

patients exhibiting this condition in conjunction with a history of allergies or atopy.

Demulcent Herbs

Herbs rich in complex polysaccharides are believed to induce mucus secretion in the urinary tract after oral administration, possibly through neurological pathways.[48] Marshmallow leaf and root, hollyhock leaf and root, couch grass rhizome, slippery elm bark, and cornsilk stigmata are among the many herbs commonly used for this purpose. Many herbal practitioners believe that reflex demulcent herbs such as these may help restore or support the glycosaminoglycan layer and/or epithelium of the bladder, although restoration of the GAG layer is not a definitive treatment.[49,50] It is unknown if this action is truly operational in patients with interstitial cystitis, although many patients report at least some symptomatic relief while taking demulcent herbs. The demulcent herbs cited here have no known adverse effects. The usual preparation and dose of each is to stir approximately 1 tbs powder into 4 to 8 oz water, and drink this two to three times daily. This amount of powder also can be taken as capsules. Optionally, 5 to 10 mL of a glycerite can be administered three times daily. These herbs do not work well as tinctures because the polysaccharides are not very soluble in ethanol. These herbs should not be administered simultaneously with other herbs or drugs, because the polysaccharides may alter absorption of many agents.[51]

Anti-Inflammatory Herbs

Anti-inflammatory herbs are also likely to be important in any botanical approach for patients with IC. The botanical constituent quercetin is the best example supporting the potential benefit of anti-inflammatory herbs. The only botanical medicine that appears to have been studied in a modern clinical trial is the ubiquitous, anti-inflammatory, antioxidant flavonoid, quercetin. In an open trial, 1 g twice daily for 4 weeks brought symptomatic relief to 20 of 22 male and female volunteers with interstitial cystitis.[52] There were no adverse effects, although two people dropped out of the study. For acute symptoms, as much as 1 g five times a day of quercetin may be necessary. Often quercetin is combined with bromelain, a plant enzyme complex, on the theory that bromelain enhances absorption of quercetin and because bromelain itself has systemic anti-inflammatory activity that clearly affects the lower urinary tract.[53] A typical dose of bromelain is 500 to 1000 mg three times daily between meals. Taking bromelain with food causes it to act as a protease in the digestive tract and may reduce systemic absorption and activity. Many herbs influence multiple inflammatory pathways and also often have other effects on immune cells, as has been well established for echinacea.[54] Salicylate-containing herbs are commonly used in countering inflammation, with birch leaf and quaking aspen bark having some specific affinity for the genitourinary tract.[55] These herbs have an additional benefit in that they are analgesic. Any of these anti-inflammatory herbs may cause mild digestive upset. Birch and quaking aspen may theoretically inhibit platelet aggregation, although there is no clinical evidence of bleeding with these herbs or interaction with other antiplatelet or anticoagulant agents. Clinical research with the related herb willow cortex shows no significant effect on platelet aggregation in humans.[56] Two anti-inflammatory herbs hold a special place in the treatment of people with interstitial cystitis—*Glycyrrhiza glabra* (licorice) and *Glycyrrhiza uralensis* (gan cao) root. These plants have been studied in depth and found to have several actions that should have a beneficial effect on interstitial cystitis patients. Licorice and gan cao contain compounds that are anti-inflammatory, immunomodulating, antioxidant, and inhibit abnormal complement.[57–60] This coupled with the historical use of these herbs to treat inflammatory diseases and inflammatory autoimmune conditions makes them well suited as treatment for interstitial cystitis.

Spasmolytic and Anxiolytic Herbs

One herb that seems to be among the most commonly prescribed for people with interstitial cystitis is Kava kava (*Piper methysticum*) root. This herb has repeatedly been shown to be an effective anxiolytic in double-blind, placebo-controlled trials.[61] Safety concerns regarding kava kava are discussed in Plant Profiles: Kava kava.

Interstitial cystitis, like so many chronic conditions with an inflammatory component, involves the inseparably linked mind and body. To this end, an anxiolytic herb such as kava might be helpful in a psychoneuroimmunologic way. Indeed, a neurogenic hypothesis of the etiology and pathogenesis of interstitial cystitis has recently gained ground.[62] Many practitioners ascribe kava's benefits to the spasmolytic properties of the herb, a theory that correlates with the fact that the bladder of the interstitial cystitis patient often contracts when it reaches a certain, abnormally low point of fullness.[62]

A typical adult dose of kava tincture for IC treatment is 3 to 5 mL tid. Standardized extracts of this herb are not recommended for use because some use acetone as a solvent, and such concentrated extracts differ sufficiently from the natural state of the herb that cannot be ruled out as a possible cause of the handful of reports of hepatotoxicity. Kava is nonaddictive and nonsedating in small doses. It actually improved mental function compared with diazepam in a clinical trial.[63] Because of lack of information it should be avoided in pregnancy and lactation. Pending further study, it should be avoided in patients with pre-existing liver disease or those concomitantly taking hepatotoxic drugs.

Several other spasmolytic botanicals may also help reduce symptoms in patients with interstitial cystitis. These include rupturewort herb, lobelia herb and seed, and peony root. Rupturewort is a safe spasmolytic for use in milder cases but must be used fresh.[64] The dose of a fresh-plant tincture is 5 mL tid. If fresh material is available for cold infusion, steep 1 tbs in a cup of water and drink three cups per day. Lobelia is the next strongest spasmolytic and, in the proper dose, is also without adverse effects. Overdose will cause nausea or sometimes even vomiting in most people. The typical dose of

tincture is 0.5 to 1 mL tid. Peony or its Asian cousins *Paeonia lactiflora* (Chinese peony) and *P. suffruticosa* (tree peony) are in a similar class with lobelia in terms of strength and potential for toxicity. Peony root tends to be helpful for mood disturbances as well as being spasmolytic.[65] The same dose as lobelia is used with the same consequences occur with overdose (e.g., nausea).

Lymphagogue and Astringent Activity

Ocotillo is an unusual plant native to the southwestern United States and northern Mexico. There is no modern research on this plant, which clinically acts as the most specific pelvic lymphagogue the author has encountered. It seems to be helpful in all instances of chronic pelvic conditions characterized in traditional herbalism as being ''congested,'' including interstitial cystitis. Owing primarily to habitat loss and the fact that it is a slow-growing desert plant, ocotillo is potentially threatened in the wild. Therefore, it is important to find a source of sustainably harvested herb. The usual dose of tincture is 3 to 5 mL tid, or smaller doses when combined with other herbs in formulas. Sweet sumach bark of root belongs to the Anacardiaceae family along with its greatly feared cousin, *Rhus toxicodendron* (poison ivy). Sweet sumach does not contain urushiol and does not cause dermatitis. It is high in tannins and has an astringent effect that appears to be specific to the urinary tract.[66] Astringent herbs may be anti-inflammatory and may help tonify the bladder tissue in a way that has not yet been scientifically investigated. Sweet sumach does have a history of use in treating symptoms of interstitial cystitis. The usual dose of tincture is 1 to 2 mL tid. It may cause nausea, in which case it should be taken with food. Mormon tea stem and related native American species in the genus are also used as urinary tract astringents. These species, unlike their Asian cousins (particularly *Ephedra sinica* or ma huang), do not contain ephedrine or pseudoephedrine.[49] They are rich in tannins. Because Mormon tea is also diuretic, it may be irritating to some patients and should not be taken as a tea in most cases. In cases of acute pain episodes, a sitz bath made by adding a handful of Mormon tea herb to the bath water may help relieve symptoms. Mormon tea may cause nausea when taken internally; taking it with food usually eliminates this problem. Yerba mansa root grows exclusively in the desert southwest of the United States and northern Mexico. It also contains tannins and has a strong reputation in Southwestern herbal traditions as a mucus membrane tonic, mild antimicrobial, and as a mild diuretic.[49] It also has moderate anodyne effects. Although unrelated to goldenseal, it acts similarly to this useful plant.[49] Yerba mansa is considered specific for chronic inflammatory bladder conditions, although it has not been the subject of research.[49] The usual dose of tincture is 3 to 5 mL tid. It may cause nausea; taking it with food eliminates this problem. Owing to the limited distribution of this plant in the wild, care should be taken in obtaining it from a sustainable source. All astringent herbs should not be combined with alkaloid-rich herbs or most drugs, as tannins interfere with the absorption of these agents.[51]

Bladder Tonics

Several nonastringent herbs traditionally have been considered bladder tonics, meaning that they support the urinary bladder in a very general way. They have not been the subject of modern research to determine the mechanisms involved. Pipsissewa herb, horsetail herb, cleavers herb, and mullein root are four such herbs. All four are completely benign, even at large doses. Because they can be diuretic,[67] high doses may aggravate some patients with interstitial cystitis. Generally, they are used in lower doses for long periods of time combined with other herbs to promote general healing. Investigation of these widely used, gentle herbs is warranted to determine the degree of efficacy and their actions. A typical dose of tincture of any of these is 2 to 4 mL tid or less when combined with other herbs in formulas. Although these humble herbs do not conform well to the dominant pharmacologic model, their utilities cannot be overstated.

Anodyne/Analgesic Activity

A wide range of herbs are available to reduce pain associated with interstitial cystitis. Of course, the underlying causative aspects of this condition must be treated foremost to help eliminate the cause of pain, but sometimes it is necessary to suppress pain to make a person's life bearable. The simplest and safest botanical anodynes are herbs normally thought of for relieving insomnia and anxiety—the nervines. These include Pacific valerian root, passionflower leaf, and skullcap leaf and flower. All three are central-acting anodynes and are safe for regular use. There is little research on the analgesic mechanism of these herbs, although preliminary animal studies do support that they are active.[68] A typical dose of tincture of these herbs is 3 to 5 mL tid, although higher doses more frequently (up to 10 mL five times a day) are indicated for more serious pain. If sleep problems are a distinct element of a patient's case, nervines should be taken at bedtime. Some people may become drowsy when taking nervines during the day, but often there is no problem. Some studies show these herbs actually increase daytime alertness by improving sleep quality at night.[69] These same studies showed no signs of addiction and no interaction with alcohol, facts that are strongly supported by clinical experience. A much more potent, central-acting analgesic is pulsatilla leaf and flower. Although generally active orally, suggesting possible activity in the central nervous system, the widespread use of topical pulsatilla by native peoples for arthritis and related conditions suggests it also may have local anodyne effects.[70] Pulsatilla contains glycosides that although more toxic when fresh are also more active. This author feels that fresh pulsatilla is superior to dried, and simply recommends a lower dose to avoid adverse effects. A typical dose of fresh-plant tincture is three to five drops tid, or more frequently (up to every 2 hours) until the pain is alleviated. Signs of overdose include nausea, weakness, bradycardia, hypotension, mydriasis, paralysis, seizure, or coma. Pulsatilla is contraindicated in pregnancy and lactation.

A more controversial but effective analgesic is marijuana leaf and seed. Clearly, this herb is illegal in most

jurisdictions for political reasons, but some patients still consider using it on their own volition, making it important to understand it. Cannabinoids from marijuana have long been known to have central analgesic effects, probably mediated through cannabinoid receptors.[71,72] Tetrahydrocannabinol is not the most potent cannabinoid in many animal studies, suggesting the whole herb may be more effective or possibly broader in its activity.[73] This concept is supported by other evidence suggesting the whole plant is safer than its constituents in isolation.[74] Substantial evidence also shows that cannabinoids and flavonoid compounds in marijuana are anti-inflammatory.[75] Marijuana has not been specifically reported to alleviate pain or other symptoms in people with interstitial cystitis.

Relief of Inflammation with Edema

The final category of herbs sometimes used in patients with interstitial cystitis is those that have historically been used to relieve local inflammation with edema. Deer's tongue leaf and sweet clover herb are two examples. Deer's tongue has not been researched but has a strong history as a topical, local anti-edema herb. It is recommended as an addition to a sitz bath (approximately half a cup of leaves per bath) for relief of acute symptoms.[49] Sweet clover can be used similarly, although it is also safe for internal use with a typical tincture dose being 3 to 5 mL tid. Sweet clover and deer's tongue both contain coumarin, the non-anticoagulant antiedema compound which, when fermented, gives rise to the vitamin K antagonist compound dicoumarol. An ample body of literature supports the antiedema, anti-inflammatory, and other effects of coumarin.[48]

NUTRITIONAL CONSIDERATIONS

Avoidance of various foods in the diet has been suggested as helpful by many sources, although controlled trials are lacking. The mechanism by which food would exacerbate interstitial cystitis pathogenesis or symptoms has not been determined, although food allergy and leakage of irritating food chemicals (e.g., caffeine) excreted in the urine out of the bladder across a damaged bladder wall might explain this phenomenon. Because of the heterogeneity of response among patients, the most reasonable approach would be to have patients eliminate foods that individually seem to bother them and look for effects on symptoms. For patients who are uncertain, an elimination-challenge diet will likely produce better results than avoiding an arbitrary list of possible triggers that might miss what actually has the most damaging influence.

L-Arginine has been advocated as a potential therapy for interstitial cystitis patients because of the possible role of nitric oxide in the disease. An initial open trial found that 1.5 g daily was helpful at reducing voiding discomfort and pain over 6 months.[76] A subsequent open study using 3 to 10 g daily found no effect on symptoms or nitric oxide production over 5 weeks.[77] A double-blind trial involving 53 patients who took 1.5 g for 3 months found that it decreased pain intensity significantly compared with placebo, and just barely missed statistical significance in reducing pain frequency and urgency.[78] More research is needed by a trial of 1.5 g arginine daily is worth considering in most interstitial patients.

ADDITIONAL THERAPIES

Bladder Retraining

Bladder retraining is an important element of any treatment approach because treatment often does not significantly improve bladder capacity after long-term low-volume voiding.[47] It consists simply of determining the average time between urinations, then gradually having the patient increase the interval by small increments each month, usually by 10 to 15 minutes per month. This approach has resulted in more than doubling of voiding intervals in some patients. It should be noted, however, that it will probably only succeed if pain symptoms have first been alleviated.

Stress Reduction

Stress reduction methods of all varieties including regular light exercise, meditation, self-hypnosis, visualization, or regular have been recommended, although their efficacy has not been assessed.[79]

Sitz Baths, Perineal Massage, and Trigger Point Therapy

Warm sitz baths have also been advocated for pain relief without support from clinical trials. Perineal muscle massage and trigger point therapy have been advocated to relieve pain. In one case series involving 52 women and men (10 with interstitial cystitis and the rest with urgency-frequency syndrome), a series of manual trigger release techniques performed per anus and per vagina weekly or biweekly for 8 to 12 weeks resulted in moderate-to-marked improvement in 70% of participants with interstitial cystitis.[80] A similar set of techniques also has been reported to be helpful in a smaller series of four patients with interstitial cystitis.[81]

Acupuncture and TENS

Acupuncture and transcutaneous electrical nerve stimulation (TENS) are methods of pain reduction with preliminary support from clinical trials. Needling the spleen 6 point was associated with reduction in frequency, urgency, and dysuria in one case series.[82] A case series found that high or low frequency suprapubic TENS applied daily for 30 to 120 minutes was associated with good pain relief or remission of symptoms in 23% of patients with nonulcerative interstitial cystitis and 54% with ulcerative disease.[83] A combination of acupuncture and TENS resulted in only minor pain relief in an open trial.[84]

TREATMENT SUMMARY FOR INTERSTITIAL CYSTITIS

- Use mucilaginous or reflex demulcent herbs, anti-inflammatories, anodynes, pelvic lymphagogues, spasmolytics, astringents, anxiolytics, and bladder tonics.
- Teach bladder retraining exercises after pain symptoms have first been alleviated.
- Use stress reduction methods including regular light exercise, meditation, self-hypnosis, visualization, and warm sitz baths.
- Perineal muscle massage and trigger point therapy have been advocated to relieve pain.

TABLE **9-4**

Condition/Botanical Medicine Summary Table

	CONDITION								
BOTANICAL	ANTIMICROBIAL/ANTISEPTIC	ANTISPASMODIC	ANALGESIC/ANODYNE	ANTI-INFLAMMATORY	ANXIOLYTIC	ASTRINGENT/TONIC	DEMULCENT	DIURETIC	LYMPHAGOGUE
Achillea millefolium	X	X		X					
Actaea racemosa							X		
Alcea rosea	X			X			X		
Althea officinalis		X							
Anemone pulsatilla						X			
Anemopsis californica	X								
Arctostaphylos uva ursi				X					
Betula spp.				X					
Bromelain	X			X					
Calendula officinalis		X							
Cannabis sativa						X			
Chimaphila umbellate		X							
Corydalis ambigua			X						
Dioscorea villosa		X							
Echinacea spp.	X								
Elymus repens							X		
Ephedra viridis						X			
Equisetum arvense						X			
Eschscholzia californica		X	X						
Fouquieria splendens									X
Galium aparine									X
Glycyrrhiza spp.	X			X					
Herniaria glabra			X						
Lavandula officinalis	X				X				
Lobelia inflata		X							
Melilotus officinalis				X					
Paeonia brownii		X	X						
Passiflora incarnata		X	X		X				
Piper methysticum		X			X				
Piscidea piscipula			X						
Populus tremuloides				X					
Pulsatilla vulgaris		X							
Quercitin				X					
Rhus aromatica						X			
Scutellaria lateriflora					X				
Solidago canadensis				X					
Solidago virga urea				X					
Thymus vulgaris	X	X							
Ulmus rubra							X		
Vaccinium macrocarpon	X								
Valeriana sitchensis		X	X						
Verbascum thapsus								X	
Viburnum opulus		X							
Viburnum prunifolium		X							
Zea mays								X	

Eclectic Specific Condition Review: Interstitial Cystitis, a Historical Perspective

*David Winston**

Agrimony (*Agrimonia eupatoria*)
Pain extending from the kidneys to the ureters. Catarrhal conditions of the bladder, foul-smelling urine. Often used for ''chronic cystitis.''

Black willow (*Salix nigra*)
Inflammation of the bladder and ovaries, increased secretions from mucous membranes, especially if there is a fetid discharge.

Cleavers herb (*Galium aparine*)
Irritation of the urinary tract, with dysuria and painful urination, urinary irritation associated with uterine inflammation. Inflammation of the Bartholin's glands.

Gravel root (*Eupatorium purpureum*)
Scanty urine with dysuria, stinging, and burning pain in the urethra.

Hydrangea root bark (*Hydrangea arborescens*)
Irritation of the mucous membranes or urinary tract with a gleety discharge or urinary calculi, painful urination, spasmodic stricture of the urethra.

Kava root (*Piper methysticum*)
Irritation of the mucous membranes of the genitourinary tract with pain during urination. Chronic inflammation of the neck of the bladder, urethra, and vulva. The tea can be applied topically for itching or pain of the vulva (vulvodynia).

Marshmallow root (*Althea officinalis*)
A soothing urinary demulcent. Painful cystitis with a mucous discharge, urination painful, acidic, burning urine.

Parsley herb (*Apium graveolens*)
Cystitis wherein the specific gravity of the urine is high, urination is painful, and the mucous membranes are inflamed.

Partridge berry herb (*Mitchella repens*)
Frequent desire to urinate with difficulty voiding urine.

Pipsissewa herb (*Chimaphila umbellata*)
Frequent urination with stinging pain—chronic urinary or renal conditions with a mucopurulent discharge.

Saw palmetto berry (*Serenoa repens*)
Chronic irritation of the bladder, acid urine, uterine hypertrophy.

Water eryngo root (*Eryngium aquaticum*)
Frequent desire to urinate, burning sensation or burning pain in the urethra or bladder, worse at night, constant sexual urge caused by chronic irritation of the urinary tract.

White poplar bark (*Populus tremuloides*)
A sensation of heat and burning in the urethra. Tenesmic vesical irritation after urination.

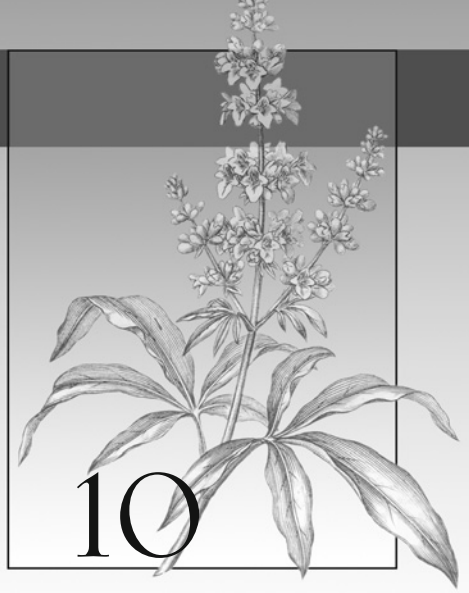
Wintergreen leaf (*Gautheria procumbens*)
Inflammation or irritation of the neck and base of the bladder and urethra. Urinary pain worse with sexual arousal.

*For historical purposes only.

- Avoid foods that might exacerbate interstitial cystitis pathogenesis or symptoms on an individual basis.
- Acupuncture and transcutaneous electrical nerve stimulation (TENS) are adjunct methods of pain reduction that can be considered.
- L-Arginine has been advocated as a potential therapy for interstitial cystitis patients.

Breast Cancer

Aviva Romm



10 CHAPTER

For the majority of women with breast cancer, complementary and alternative medicine (CAM) has become a standard part of their treatment and healing.[1]

THE BREASTS AND THE BREAST EXAM

Aviva Romm

ANATOMY OF THE BREASTS

The breasts of an adult woman are tear-shaped mammary glands (Fig. 10-1), technically developmentally modified sweat glands with the potential for milk production. A layer of subcutaneous adipose tissue surrounds the glands and extends throughout the breast itself, comprising 80% to 85% of the normal breast. The breasts are supported by and attached to the pectoral muscles of the thorax by ligaments. Each breast contains 12 to 25 circularly arranged lobes radiating around the nipple. Each lobe is comprised of numerous lobules containing clusters of alveolar glands that produce milk in a lactating woman. The alveolar glands transport the milk into lactiferous ducts that drain its respective lobe. Each lactiferous duct widens to form an ampulla, and then narrows prior to termination at openings in the nipple. A band of circular smooth muscle surrounds the base of the nipple, whereas longitudinal smooth muscle fibers extend this ring, encircling the lactiferous ducts as they converge toward the nipple. The adipose tissue and configuration of lobes determine the size and shape of the breast.

The darker-pigmented area around the nipple is called the areola. Its size and color varies from 2 to 6 cm in diameter and from pale pink to deep brown depending on age, parity, and skin pigmentation. The areola contains numerous small oil-producing glands called Montgomery's tubercles, which serve to lubricate the areola and become more pronounced during pregnancy.[3]

The breasts possess arterial blood supply and venous return, as well as a lymphatic drainage system divided into two main categories: superficial (including cutaneous) drainage and deep parenchymatous drainage. The lymph system serves to filter infection and protect the body from disease. Additionally, the breast has a nerve supply; the nipple is highly innervated, and for many women is a highly sensitive, erogenous organ.

Women's breast shape, size, and ''tone'' are as highly variable as are women themselves. Yet, because of a narrow range of acceptable breast appearance in Western culture, many women are dissatisfied with their breasts. According to the American Society for Plastic Surgery, nearly 250,000 breast augmentation procedures were performed in 2005. Breast augmentation for teenagers accounted for 3841 procedures in 2003. The number of breast augmentations increased 7% from 2002 to 2003. When physicians were asked the primary reason, their patients offered for wanting a breast augmentation, 91% said it was to improve the way they feel about themselves.[4]

CYCLIC INFLUENCES ON BREAST TISSUE

The breast tissue is highly influenced by the hormonal changes of the menstrual cycle. The three major hormones affecting the breast are estrogen, progesterone, and prolactin. Estrogens cause proliferation of mammary ducts, whereas progesterone causes growth of lobules and alveoli. Many women experience breast swelling, tenderness, and pain in the 10 days preceding menstruation, largely due to distention of the ducts, hyperemia, and edema of the interstitial tissue of the breasts. These changes regress, along with the symptoms, during menstruation and the postmenstrual phase.

During pregnancy, in response to progesterone, breast size and turgidity increase significantly, accompanied by deepening nipple and areolar pigmentation, nipple enlargement, areolar widening, and an increase in the number and size of Montgomery's tubercles. In response to hormonal signals, the alveoli enlarge and their lining cells, the acini cells, increase in number and size (hyperplasia and hypertrophy). The breast ductal system branches markedly. In late pregnancy, the fatty tissues of the breasts are almost completely replaced by cellular breast parenchyma. Secretion of colostrum may begin during pregnancy. After birth, the fully mature breasts secrete milk in response to prolactin.

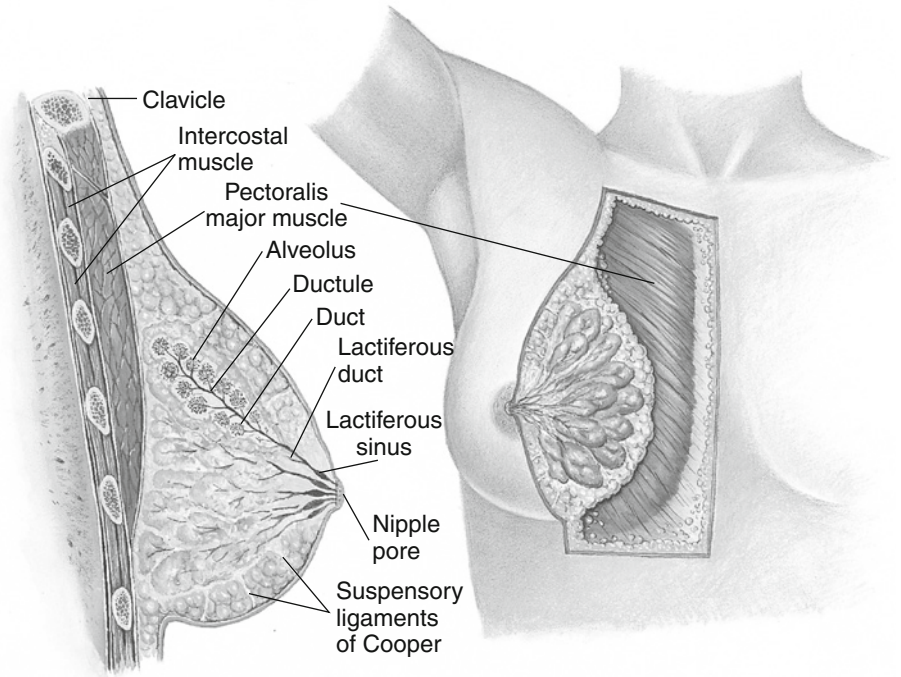


Figure 10-1 Anatomy of the female breast. (Seidel HM: *Mosby's Guide to Physical Examination,* ed 6, St. Louis, 2006, Mosby.)

During menopause, due to lack of hormonal stimulation, the breast undergoes a process of involution eventually regressing to an almost infantile state.

Fibrous Breast Tissue

Many women have fibrous breast tissue, which upon palpation may cause them to think they have abnormal breast tissue or a problematic lump. Fibrocystic breasts are discussed in Benign Breast Conditions. Women with fibrocystic breasts should also learn to perform breast self-examination (BSE). In addition, other normal masses may be present, for example, cysts that are not a cause for concern but that should be regularly evaluated for changes nonetheless. Women can learn to differentiate the usual pattern of lumps and identify new or unusual lumps. Information on the normal breast pattern from the patient may help her physician to differentiate between a new mass and a stable lump.

BREAST CANCER

Breast cancer is perhaps the single most important medical concern women face today. Although there has been an overall decrease in breast caner rates in the United States in recent decades, in 2007 there were greater than 180,000 new cases of invasive breast cancer and 40,910 breast cancer-related deaths. This is equivalent to a breast cancer diagnosis every 2 minutes.[2] Breast cancer is the leading cause of cancer in women, accounting for one-third of all cancer cases.[3] All women are affected by breast cancer—whether by literal diagnosis or a lifetime of worry about whether they will experience this disease.[2] It has been estimated that 50% of all women in the United States at some point in their lives will ask their physicians about a concerning lump or other worrisome breast finding with the anxiety that they have breast cancer. Many have known a friend, relative, or colleague who has gone through a possible or actual breast cancer diagnosis.

Breast cancer, from etiology to treatment, is a vast and complex topic with an enormous literature. There is controversy over screening methods, treatments, and the role of complementary and alternative therapies in the care of women with breast cancer. There are still many unknowns in cancer diagnosis, prevention, and treatment. It would be impossible to elucidate the entire topic of breast cancer, or even that of breast cancer and CAM, within the confines of a single chapter. It is hoped that this chapter will help the reader begin to understand the magnitude of breast cancer as a disease that effects all women, whether as a direct clinical reality or a lifelong concern, to understand nonmodifiable and modifiable breast cancer risk factors, to gain perspective on the complexity of issues women must sort through regarding screening and, if diagnosed, choices regarding their treatment, including whether and how to use CAM therapies. This chapter does not provide guidelines for the botanical treatment of breast cancer, although does direct readers to additional resources on evidence for botanicals commonly used in cancer treatment protocol.

RISK FACTORS FOR DEVELOPING BREAST CANCER

Breast cancer is the result of the complex interaction of multiple factors—hormonal, genetic, environmental, and lifestyle.[2] Breast cancer risk factors can be divided into nonmodifiable and modifiable risks. The former are heritable or genetic, although it is arguable that genetics can be favorably or negatively influenced by either beneficial

or harmful environmental exposures, diet, and therapies that target genetic processes such as transcription and tumor suppression, and thus to some extent, may be modifiable. Modifiable factors include diet, obesity, alcohol intake, and environmental exposures.

GENETICS

Germ line mutations are responsible for no greater than 10% of human breast cancers.[3] However, women with specific mutations have a much higher lifetime risk of developing breast cancer, are more likely to experience breast cancer at an earlier age than the average population, and may experience more severe forms of the disease, BRCA-1 and BRCA-2 are known as tumor suppressor genes. Women who have inherited a mutated BRCA-1 allele from either parent have a 60% to 85% lifetime likelihood of developing breast cancer (as well as a 33% chance of developing ovarian cancer). Women with this gene born after 1940 have an even higher risk, attributed to increased exposure to cancer-promoting environmental factors, and Ashkenazi Jewish women have an increased likelihood of carrying this mutation.[3] Mutation of the p53 tumor suppressor gene, such as occurs in the inherited Li-Fraumeni syndrome, is associated with an increased incidence of breast cancer and other cancers, as are PTEN tumor suppressor mutations. Heightened oncogene expression is seen in approximately 25% of breast cancer cases. Erb-2 (HER-2 neu), a member of the epidermal growth factor receptor (EGFR) superfamily, is a product of oncogene overexpression, and can contribute to malignant transformation of human breast epithelium.[3] Women with a genetic cancer predisposition are considered high risk for breast cancer and may receive recommendations for prophylactic cancer treatment including oophorectomy, elective mastectomy, and chemotherapy with tamoxifen, raloxifene, and/or aromatase inhibitors, discussed in the following.[2]

Endogenous Hormone Exposure

Breast cancer is a hormone-dependent disease manifesting as a malignant proliferation of clonal epithelial cells lining the ducts or lobules of the breast.[3] Its hormonal dependence is demonstrated by the fact that women who lack functioning ovaries and who never received hormone replacement (HR) do not develop breast cancer. Women are 150 times more likely to develop breast cancer than are men because of their greater exposure to estrogen and progesterone.[3] Although women may develop breast cancer at any age, there is a slight decline in breast cancer incidence after menopause accompanying naturally declining levels of estrogen and progesterone; however, statistically, as women age they have an increasing likelihood of being diagnosed with breast cancer, likely as a result of a lifetime of accumulated exposures (0.4% chance of diagnosis between 30 and 40 years of age; 4% chance between the ages of 70 and 80 years).[3,4]

Three life cycle events appear to significantly influence a woman's overall risk of developing breast cancer: age at menarche, age at first pregnancy, and age at menopause. Women who begin to menstruate at age 16 have 50% to 60% of the risk of developing breast cancer compared with those who experience menarche at age 12.[3] Having a full-term pregnancy by age 18 confers a 30% to 40% lower risk of developing breast caner compared with women who have no children, and menopause (natural or surgical) that occurs 10 years prior to the median age of 52 years old for menopause decreases lifetime breast cancer risk by approximately 35%.[3] Breastfeeding duration has been shown by meta-analysis to also confer substantial protection against breast cancer regardless of age at first pregnancy or number of pregnancies.[3] The risk reduction is directly correlated with a decreased amount of time during which breast tissue is exposed to endogenous estrogens. International variation in breast cancer rates has also supported the role of hormonal exposure as an etiologic factor in breast cancer. Asian women, for example, have been found to have significantly lower serum estrogen and progesterone levels, and have breast cancer rates of 10% to 20% of women in westernized nations (see discussion on diet and phytoestrogens).

Alcohol Intake

Even modest amounts of regular alcohol consumption (e.g., one glass of wine daily) has been associated with a 26% increased risk of breast cancer on the basis of multiple cohort studies.[2,3] Folic acid supplementation may modify this risk somewhat.[3] The risk of breast cancer needs to be weighed against the cardioprotective effects of modest alcohol intake.[3]

Dietary Fat Intake and Obesity

Dietary fat intake has been a focus of much research and debate. The dietary fat hypothesis, which proposed a correlation between amount of dietary fat intake and breast cancer incidence, is based on the observation that national per capita fat consumption is highly correlated with breast cancer mortality rates. However, per capita fat intake is also associated with economic prosperity, and this is accompanied by other factors that are also related to breast cancer risk, such as early menarche, low parity, later age at first birth, and lower levels of physical exercise.[5] Studies have failed to show a direct correlation between consumption of specific types of dietary fats, or the amount of fat in the diet, and breast cancer.[6] However, excessive caloric intake from any source in adolescent girls has been shown to lead to earlier menarche, whereas in older women can delay the onset of menopause, which as discussed are risk factors for breast cancer development.[3]

Obesity has been correlated with increased risk of all-cause mortality in women.[7] Postmenopausal weight gain and obesity have been shown to increase breast cancer risk by as much as 50%.[2] Increased risk results from prolonged and increased aromatase activity in the adipose tissue leading to increased conversion of fat to estrogen.[2,3,7] As many as 20% of all postmenopausal breast cancers and 27% of all cancers in women over 70 years of age may be attributable to obesity or moderate to significant weight gain after the fifth decade of life, and up to 50% of all postmenopausal deaths resulting from breast cancer may be attributable to obesity.[7] Obesity is

also a risk factor for poor breast cancer prognosis with larger tumor size, greater risk of metastases, poorer surgical outcome, and less efficient response to chemotherapy and radiation. The Cancer Prevention Study II concluded that as many as 18,000 deaths of women in the United States over 50 years old could be prevented if women maintained a body mass index (BMI) of less than 25 kg/m^2 throughout adulthood.[7] Weight loss and maintenance of weight in the BMI ranger of 19 to 25 kg/m^2 has been shown to reduce breast cancer risk by about 30%.[2]

Environmental Hormone Exposure

Exogenous hormone exposure may play a significant risk in the etiology of breast cancer. There is well-supported evidence that many commonly used chemicals and widespread environmental pollutants act as hormone disruptors.[8] Polycyclic aromatic hydrocarbons (PAHs) and polychlorinated biphenyls (PCBs), in conjunction with certain genetic polymorphisms involved in carcinogen activation and steroid hormone metabolism, cause mammary gland tumors in animals specifically by mimicking estrogen, or increasing susceptibility of the mammary gland to carcinogenesis.[9] Evidence regarding dioxins and organic solvents is sparse and methodologically limited but also suggestive of an association between breast cancer and exposure.[9] Scientist Rachel Carson suggested the role of environmental contamination in human cancers several decades ago, however, it is only in recent years that the role of exogenous hormones acting as hormone disruptors has begun to be seriously studied, and a great deal is unknown.

Although older studies suggested an association between oral contraceptive (OC) use and breast cancer, more recent meta-analyses imply little to no breast cancer risk from their use.[2,3] The Women's Health Initiative trial found a correlation between risk of breast cancer (and increased cardiovascular risk) and hormone replacement therapy (HRT), particularly with conjugated equine estrogens (CEE) plus progestins. Further, women with a prior breast cancer diagnosis have an increased rate of recurrence with HRT.[3] Minimizing unnecessary human exposure to known endocrine disruptors and other carcinogens should be high on our national medical and environmental research budgets.

Prior Radiation Exposure

Women with Hodgkin's lymphoma who were treated with thoracic radiation have a significantly higher risk of developing breast cancer caused by exposure.[2]

Lifetime vs. Age-Adjusted Risk of Developing Breast Cancer

The figure that one in eight women will develop breast cancer is slightly misleading and may create unnecessary fear in women. Based on statistics from 2002 to 2003 from the National Cancer Institute (NCI), 12.7% will be diagnosed with cancer in their lives, and it is from this figure that the ''one in eight'' statistic is derived. However, lifetime risk is a cumulative average and does not reflect a woman's risk at different ages. The age-adjusted risk gives women a more realistic, although still generalized, picture of their risk of developing breast cancer. According to the NCI's Surveillance, Epidemiology, and End Results statistics (http://seer.cancer.gov/), a woman's chance of being diagnosed with breast cancer is:

- From age 30 through age 39 — 0.43% (often expressed as 1 in 233)
- From age 40 through age 49 — 1.44% (often expressed as 1 in 69)
- From age 50 through age 59 — 2.63% (often expressed as 1 in 38)
- From age 60 through age 69 — 3.65% (often expressed as 1 in 27)

Of course, as discussed, many more factors than gender, age, and nationality contribute to breast cancer risk. To adjust for such factors as genetics, weight, and lifestyle, a number of statistical tools have been devised to calculate what might be closer to actual risk for any individual woman. The most widely used scale is the Gail model, which is available as a risk calculator via the National Cancer Institute website at http://www.cancer.gov/bcrisktool/for individuals and practitioners to use.[2,10,11] The tool is not a valid method of calculating breast cancer or recurrence risk in women who have already had a diagnosis of breast cancer, lobular carcinoma in situ (LCIS), or ductal carcinoma in situ (DCIS). One research group suggests that another model, the Rosner and Coldiz model, more accurately classifies women according to their risk stratification; however, it is not as widely used as the Gail model.[11]

Race/ethnicity and socioeconomic status have been associated with delayed diagnosis of breast cancer, and therefore may contribute to poorer outcomes. Breast cancer outcomes are also worse for uninsured and Medicaid patients than for privately insured patients.[12]

Breast Cancer in Pregnancy

During pregnancy breast tissue is stimulated by increased levels of estrogen, progesterone, prolactin, and human placental lactogen (HPL).[3] Breast cancer occurs at a rate of 1/3000 to 4000 pregnancies. Pregnant or lactating women should have any persistent breast or axillary lumps evaluated by a gynecologist. Too often breast lumps in this population are dismissed by women or health care professionals as the result of hormonal changes, unfortunately sometimes leading to detection of breast cancer only once it has become advanced.

CONVENTIONAL RISK REDUCTION STRATEGIES

Conventional breast cancer risk reduction strategies include:[2]

- For all women:
  - Lifestyle modification (maintaining a healthy BMI, exercise, alcohol avoidance)
  - Surveillance (clinical breast exam, mammography or other appropriate imaging, breast self-exam)
- For high-risk women:
  - Risk reducing surgery (oophorectomy or mastectomy)

- Chemoprevention with tamoxifen, raloxifene, and/or aromatase inhibitors

Surveillance

Breast Self-Exam

A recent review by the Cochrane group, the results of several large randomized trials, and a review by the US Preventative Services Task Force (USPSTF) all concluded that breast self-exam (BSE) does not reduce breast cancer specific mortality, and in fact, may increase the number of unnecessary biopsies women receive for benign findings.[4] Nonetheless, it is a noninvasive method that some women find self-empowering or reassuring to perform, and which may sometimes lead to the early detection of breast cancer.[3] Women should be informed about the potential risk of BSE findings leading to unnecessarily invasive testing and they should be taught to perform the BSE correctly to maximize the value of the exam.

Breast cancer is a leading cause of death in American women. Overall exposure to circulating and environmental estrogens, lifestyle factors, and genetic predisposition may all contribute to breast cancer development. The clinical practitioner should include a thorough breast exam as part of routine gynecologic care. It is a simple technique, and when done properly, can be an important part of overall cancer screening. In recent years, the value of the BSE has come under scrutiny, and large trials suggest that it is not helpful in reducing cancer mortality and may actually contribute to an overall higher rate of unnecessary breast biopsies. It is clear that if women wish to perform BSE, they should be taught to do so correctly. The Susan E. Komen Breast Cancer Foundation website (http://www.komen.org/bse/) offers a valuable video demonstration on the proper techniques for BSE, relevant to the health practitioner and patient alike. Additionally, numerous other websites provide invaluable resources on BSE for patients and care providers. The following discussion provides very general guidelines for BSE.

BOX 10-1

Breast Self-Exam

Breast Changes and Warning Signs

- A new lump or hard knot in the breast or armpit
- A lump or thickening that does not decrease in size after menstruation
- A change in the size, shape, or symmetry of the breast
- Thickening or swelling of the breast
- Dimpling, puckering, or indention in the breast
- Dimpling, skin irritation, or other change in the breast skin or nipple
- Redness or scaliness of the nipple or breast skin
- Nipple discharge, other than breast milk, in a lactating woman, especially if the discharge is bloody, clear and sticky, dark, or occurs without squeezing the nipple
- Nipple tenderness or pain
- Nipple retraction
- Any breast change that appears to be cause for concern

Differentiating Breast Lumps by Palpation

- Normal, noncancerous lumps such as cysts are typically soft, smooth, and moveable. They tend to fluctuate in size with the menstrual cycle. Also, if a lump, knot, or other ''difference'' is found in one breast, the woman should examine the other breast. If the lump or texture is symmetric between breasts, it is likely to be normal breast tissue.
- Questionable lumps are usually firm, irregular nodules that are fixed in place. They do not typically fluctuate in size with the menstrual cycle.

WARNING: A physician should evaluate persistent lumps or abnormalities as soon as possible.

When to Perform a Breast Self-Exam

Hormonal changes associated with the menstrual cycle normally increase breast lumpiness and swelling. These changes are particularly noticeable just prior to the menstrual period. Therefore, it is advisable to perform a BSE a few days to a week after menstruation has ended. Women using oral contraceptives are advised to perform their BSE each month on the day they begin a new package of pills.

Unfortunately, too many women do not carry out this simple technique. Selecting one day each month is the easiest reminder—encourage patients to circle this date on their calendars or post a reminder to themselves. It is easier to remember once it becomes routine. Pregnant women should continue to perform BSE throughout the pregnancy. An exam should also be performed by the care provider at the onset of pregnancy prior to the beginning of dramatic pregnancy-induced breast changes, and again later in the pregnancy and postnatally. Pregnancy does not preclude the development of breast cancer. The biggest problem with breast cancer during pregnancy is it going undetected due to lack of regular breast exams.

In 80% of all cases, breast lumps and changes do not signal breast cancer. However, women should report all unusual changes (Box 10-1) to their health care provider and seek a clinical evaluation. Many women put off telling their doctor out of fear. It can be reassuring for patients to know that at least 50% of all women will seek evaluation for a suspicious lump or breast change at some point in their life.

Performing the Breast Self-Exam

Breast self-examination requires examining the entire chest area and both breasts, as well as the axillary area. Although it does not matter in what order the steps of the BSE are performed, it is essential that all steps be performed so that no area remains overlooked. Therefore, women should perform the BSE systematically each time. A log or journal, with an entry after each exam, can help a woman keep track of her findings, and can help her to objectively track any changes she

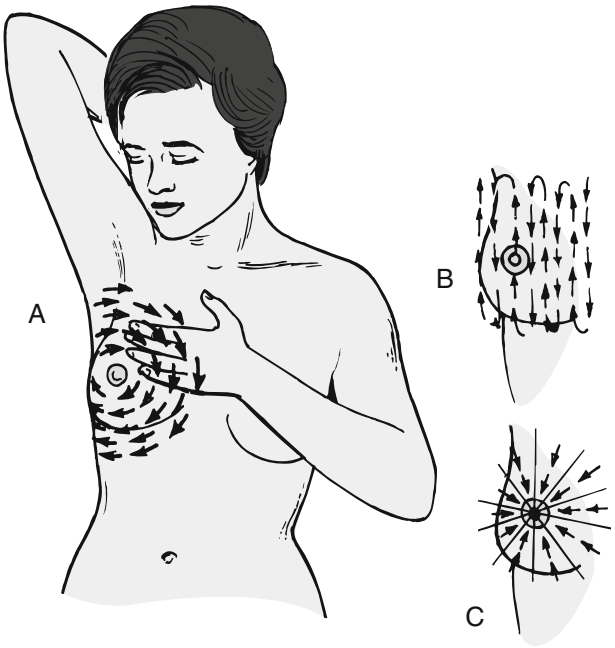


Figure 10-2 Comprehensive breast exam illustrations showing directions for three methods of BSE: A, Spiral. B, Square. C, Wedge. (Lowdermilk DL, Perry SE: *Maternity & Women's Health Care,* ed 9, St. Louis, 2007, Mosby.)

might notice. The instructions that follow are adapted from the American Cancer Society.

General Rules

- BSE should be done in a warm, comfortable, private place free from distractions. This allows women to be mindful of the exam, and the warmth allows the breast tissue to relax, facilitating the exam.
- BSE should be conducted using the pads, not the tips, of the three middle fingers.
- The right hand should be used to examine the left breast, the left hand to examine the right breast.
- The woman should examine all tissue from the mid-axillary line to the clavicle and to the sternum. Evidence suggests that a vertical pattern (Fig. 10-2) is most effective for covering the entire breast without missing any breast tissue.
- Three levels of pressure should be applied: light, medium, and firm.
- The breast should be examined in small ''massaging'' circles when using the patterns shown in Figure 10-2. The fingers should maintain contact with the breast at all times. Lifting the fingers could lead to an area being missed.
- BSE should be performed both lying down, and in an upright position. The upright portion of the exam can be done in the shower. Additionally, a visual inspection should be done in front of a mirror.
- A small amount of oil, soap, or powder may be applied to the fingers to reduce friction and allow the fingers to glide more smoothly over the skin.
- The following areas should be examined thoroughly with each BSE:
  - Outside: armpit to collar bone, and below the breast
  - Middle: the breast itself
  - Inside: the nipple area

Although cancerous growths are most likely to be found in the upper, outer breast quadrant or behind the nipple, they can occur in any area of the breast, chest, or lymph network (Box 10-2); therefore, a thorough exam is essential.

BOX 10-2

Palpating the Lymph Nodes

Lymph nodes are easily slightly enlarged by noncancerous processes, such as infection. Occasionally, a cancer may cause lymph node enlargement. Lymph node changes or enlargement should be reported to the woman's physician.

Figure 10-3 Exam lying down (Seidel HM: *Mosby's Guide to Physical Examination,* ed 6, St. Louis, 2006, Mosby.)

Step 1: Breast Self-Exam While Lying Down

Lie down with a pillow or folded towel under the right shoulder and place the right arm behind the head (Fig. 10-3). Check the entire breast and armpit area using the pads of the first three middle fingers on the left hand to feel for lumps, changes, or irregularities in the right breast.

1. With the pads of the fingers, use the vertical pattern. Press firmly enough to know how the breast feels. Examine each breast separately and feel for any new lumps, changes, or irregularities. A firm ridge in the lower curve of each breast is normal.
2. The exam should then be repeated on the left breast, using the finger pads of the right hand (the pillow or folded towel should also be moved under the left shoulder at this time).
3. The nipple should also be checked for changes. After making an initial examination noting changes of appearance, gently squeeze the nipple to check for discharge of fluid (Box 10-3). Check the color, consistency, and whether the discharge occurs spontaneously or by squeezing. Depress the nipple deep into the hollow beneath it noting unusual resistance, hardness, or lump beneath the nipple. Also check the nipple for cracking.

BOX **10-3**

Nipple Discharge

Most suspicious nipple discharges are found to be caused by noncancerous conditions. In approximately 10% of all cases, nipple discharge is caused by cancer. In women less than 30 years of age, less than 10% of nipple discharge is caused by cancer.

- Green or yellow discharge is usually normal.
- Bloody, dark, or clear and sticky discharge is considered abnormal.

WARNING: A physician should evaluate unusual nipple discharge.

Figure 10-4 Exam upright. (Seidel HM: *Mosby's Guide to Physical Examination,* ed 6, St. Louis, 2006, Mosby.)

Step 2: Breast Self-Exam Upright and Front of a Mirror

The upright position (Fig. 10-4) can facilitate examining the upper and outer portions of the breasts and armpit. The lying down portion can either precede or proceed the upright portion. Both a lying down and an upright exam should be performed at each monthly BSE. Examining the breasts in front of a mirror allows women to check for changes in shape, direction, or texture of the breasts. It should be done in a warm area with good lighting. The mirror should allow inspection of the torso from the waist to the neck.

1. Place the arms at the sides. Looking in the mirror, check the breasts for any changes in size, shape or position, dimpling or puckering of the skin, indented or misshapen nipples, other changes in the nipple, redness, swelling, or other irregularities.
2. Repeat this process with the hands on the hips, pressing firmly to flex the chest (pectoral muscles). Bend forward with the hands on the hips and note any irregularities.
3. Raise the arms overhead or put the hands behind the head. Turn to each side to check the breasts in profile. Note any changes in symmetry between the right and left breast. Remember, it is often normal for women to have one breast that is larger or a different shape than the other.

Step 3: Breast Self-Exam in the Shower (Optional but Optimal)

Palpating the breasts in the shower is helpful because the skin can be lubricated by soap. Some breast changes can be felt more easily when the skin is wet and soapy. The BSE can be performed in the shower on a monthly basis, or can be used to enhance the previous exams when trying to more thoroughly feel a lump or other tissue change. Follow the same steps as the lying-down exam.

Clinical Breast Exam

The clinical breast exam (CBE) is an important but often overlooked or deferred part of the routine physical exam. The clinical breast exam makes a small but important contribution to breast cancer detection, with approximately 5% to 10% of breast cancers identified solely by CBE, independent of mammography.[4] As with BSE, CBE should be properly performed using a vertical technique to maximize the likelihood of finding abnormal breast changes, and the breasts should be visualized with the woman in a variety of designated positions. One study reported that variations in CBE technique led to a 29% variation in sensitivity and a 33% variation in specificity.[4] The most important aspect of the CBE contributing to sensitivity is the amount of time taken to perform the exam.[4]

Mammography MRI, and Ultrasound

There are two basic categories of mammography: screening mammography done in asymptomatic patients with no breast abnormalities and diagnostic mammography done in patients with breast symptoms or abnormalities. Mammography employs a machine that compresses the breast while delivering low-dose radiation to the tissue to allow visualization of breast lesions or abnormalities. In low risk with no known breast abnormalities, two images are typically taken per breast at two different angles, although additional compression images or magnifications may be required, particularly if there are breast symptoms. Mammograms are usually done as an outpatient procedure.

Numerous RCTs performed since the 1960s have demonstrated decreased risk of breast cancer death in women randomized to receive mammography. Although a well-publicized meta-analysis questioned the value of mammography as a breast cancer screening test based on flaws identified in earlier studies, further meta-analysis by the USPSTF concluded that these flaws did not significantly affect outcomes, and recommended screening mammography every 1 to 2 years for women over 40 years of age and annually for women over age 70 with no comorbidities that that decrease life expectancy.[4,13–21]

Screening mammography is associated with reduced size and stage of breast cancer at diagnosis. Sensitivity is estimated to be between 60% and 90%.[4] Many mammography testing facilities have begun to use computer-aided detection systems designed to assist radiologists in interpreting; however, recent research has found that these tools actually decrease sensitivity and increase false positive results, and since their introduction, breast cancer detection rates have not changed substantially.[4,22]

There is no greater benefit to annual mammograms compared with every 2 years in women under 70 unless they are high risk for breast cancer or breast cancer recurrence.[13] High-risk women with a family history of breast cancer should begin screening when they are 10 years younger than the age at which their youngest relative to be diagnosed with breast cancer received a diagnosis. No trials to date have evaluated an age end point for screening mammography. Two trials have enrolled women over age 65; none have evaluated mammography in women over age 74 years.[13]

Mammography is the only imaging method that has been demonstrated through RCTS to be effective for breast cancer screening. Current recommendations call for screening mammography every 1 to 2 years beginning at age 40 for low-risk women, and annual screening for women over 70 in the absence of comorbid disease that lowers life expectancy.[13]

The risk of radiation exposure associated with mammography is of concern to many women. The Biological Effects of Ionizing Radiation (BEIR V) review estimated that the potential total annual added risk of breast cancer mortality resulting from mammography (300 mrad for two-view examination of both breasts) to be 41.9/100,000 for women age 25, 30.9/100,000 for women age 30; 21.4/100,000 for women age 35; 13.8/100,000 for women age 40; and 3.9/100,000 for women age 50 compared with an estimate of greater than 3000 deaths that would occur as a result of naturally occurring breast cancers among women who do not receive screening mammography.[23–25]

Concerns have also been raised about the possible short- and long-term detrimental effects of false positive mammograms on women's psychoemotional well-being. Based on a recent systematic review, a false-positive mammogram does increase anxiety, sometimes substantially, but usually only short-term, and may actually lead women in the United States to increase their diligence about receiving breast screening in the future.[26]

Mammography is less sensitive and results in a reduction of breast cancer–related deaths in younger women, likely a result of greater breast tissue density in younger women as well as faster rate of cancer growth.[4] For women with dense breasts, particularly women under 30, screening ultrasound is commonly recommended; however, the European Group for Breast Cancer Screening concluded that there is no evidence to support the use of screening ultrasound at any age.[27] In contrast, a prospective, uncontrolled study of 11,130 women with dense breasts screened with mammography, clinical examination, and bilateral whole breast ultrasound over approximately 2 years, screening breast ultrasound increased the number of women diagnosed with nonpalpable invasive cancers by 42%.[28] Another option is digital mammography which may be more sensitive in women under 50 with dense breasts; however it is expensive and not widely available.[22,28]

Recently MRI has been receiving attention as a breast cancer detection tool owing to its greater sensitivity in detecting breast cancer in high-risk women, and its ability to increase earlier diagnosis.[4] MRI, however, is also associated with a higher rate of false-positives than is mammography, and it is costly. The latest American Cancer Society recommends screening MRI in addition to mammograms for women who meet at least one of the following conditions:[29]

- They have a BRCA1 or BRCA2 mutation.
- They have a first-degree relative (parent, sibling, child) with a BRCA1 or BRCA2 mutation, even if they have yet to be tested themselves.
- Their lifetime risk of breast cancer has been scored at 20% to 25% or greater, based on one of several accepted risk assessment tools that look at family history and other factors.
- They had radiation to the chest between the ages of 10 and 30.
- They have Li-Fraumeni syndrome, Cowden syndrome, or Bannayan-Riley-Ruvalcaba syndrome, or may have one of these syndromes based on a history in a first-degree relative.

MRI should be considered an adjunct to mammography and CBE in the detection of breast cancer in high-risk women, or when there is a suspicious finding with these other routine screening methods.

Risk-Reducing Surgery

Although this is an aggressive option, risk-reducing surgery may be reasonable for women with a high risk hereditary predisposition to breast cancer. Prophylactic oophorectomy may be the preferred primary strategy for risk reduction prior to mastectomy as it is effective and is not associated with visible physical alteration and thus can spare women struggles with body image that accompany mastectomy.[2] Surgical menopause before age 35 is established as protective against breast cancer; however, it is also a risk factor for osteoporosis and cardiovascular disease.[10]

Chemoprevention

It should be noted that no chemopreventative strategy to date has demonstrated increased health or survival benefits.[2] Tamoxifen and raloxifene will only reduce the incidence of estrogen receptor positive cancers, and have no effect on estrogen receptor negative cancer.[10] Side effects can be considerable and often make it difficult to complete the 5-year course of prophylactic treatment. Nonetheless, these drugs have shown significant chemopreventive effects.

Risk of developing breast cancer, and hence the value of preventative therapy, must be weighed against the risks of medication adverse effects.

Tamoxifen

In 1998, the Food and Drug Administration (FDA) approved tamoxifen, a first-generation SERM with both estrogenic and antiestrogenic effects, as an effective breast caner prophylactic agent at a does of 20 mg/d for 5 years. Its estrogen receptor blocking effects make it effective against breast cancer.[2] Four prospective randomized trials and one meta-analysis of prophylactic tamoxifen use demonstrated a significant reduction in breast cancer occurrence at rates of 43% to 69% in

women across all age groups, and also reduces risk of second primary and contralateral breast cancer.[2,10,11] However, there was no mortality benefit in any of the trials' use of the drug is associated with both mild and serious adverse effects, including hot flashes, vaginal discharge, endometrial cancer (2 per 1000 women per year), stroke (doubled risk), and life-threatening thromboembolic disease (double to triple the risk of deep vein thrombosis and pulmonary embolism).[10] These risks are most prevalent in postmenopausal women and those with comorbidities.[2]

Raloxifene

Raloxifene is a second-generation SERM with mechanisms of action similar to tamoxifen, but which does not produce endometrial proliferation to the extent as tamoxifen and therefore does not carry the same risk of causing endometrial cancer, although otherwise its side effect profile is similar to tamoxifen.[2,10,11] Women taking raloxifene may also experience dyspareunia, weight gain, and musculoskeletal problems compared with those taking tamoxifen; however, those in the latter group are more likely to experience more vasomotor symptoms and leg cramps, although they report improved sexual functioning.[2] Raloxifene increases bone mineral density in postmenopausal women and is FDA approved for the prevention and treatment of osteoporosis (see Chapter 18), an advantage for those women taking it prophylactically for breast cancer risk. Raloxifene is not recommended for premenopausal women.[2,11]

Aromatase Inhibitors

Conversion of androgens to estrogen in peripheral adipose and muscular tissue is called aromatization. At menopause, when the ovaries cease to produce significant quantities of estrogen, aromatization becomes the primary source of estrogens in postmenopausal women. Aromatase inhibitors (AIs) are used to reduce this process and substantially reduce breast tissue estrogen exposure. At present, they have been studied only as adjuvant therapies for breast cancer treatment; no RCTs have been completed for breast cancer prophylaxis at the time of this writing.[2]

SIGNS AND SYMPTOMS OF BREAST CANCER

Early findings of breast cancer include a non-tender mass that may be firm to hard, and with poorly defined borders; however, there may be abnormal mammography findings in the absence of a palpable mass. In 70% of cases, a painless lump is the presenting complaint. Later, there may be nipple or skin retractions (peau d'orange), axillary lymphadenopathy, breast enlargement with signs of inflammation, and adherence of a mass to the chest wall or the skin. There can be breast pain; nipple discharge that is watery, serous, or sanguineous, nipple erosion, itching, or enlargement; changes in breast size, shape, and symmetry; and rarely, edema of the axilla or arm. When there is metastatic disease, there may be more generalized symptoms of weight loss and jaundice, and commonly there is back or bone pain, which can have severe consequences if accompanied by spinal cord compression.

Conditions to consider that may present with breast lumps or other breast changes include fibrocystic breasts, intraductal papilloma, lipoma, fat necrosis, mastitis (in lactating women), breast abscess, and phyllodes tumor.

DIAGNOSIS

Diagnosis of breast cancer requires a multidisciplinary team of experts. Initially, suspicion may be raised by the woman herself who detects a lump on breast self-examination (BSE) or a lump is found incidentally upon routine clinical breast exam by her midwife, gynecologist, internist, or family doctor, or by a radiologist reading a mammogram. At this point, the woman is referred for screening mammography, also done by a radiologist if she has not had imaging, and if a lump is confirmed by mammography, a biopsy is performed to obtain tissue samples that are analyzed for the presence of cancer cells by a pathologist. If breast cancer is confirmed, additional health professions are consulted, including but not limited to breast surgeons and oncologists.

Diagnostic Imaging

Abnormal radiographic findings include clustered microcalcifications, densities, or architectural distortions.[3] If a radiologic abnormality is detected, this should be considered contextually. If it is a nonpalpable lesion with a low index of suspicion in a low-risk woman, a follow-up mammogram in 3 to 6 months is considered reasonable.[3] If a probably benign lesion is identified, a stereotactic core or surgical biopsy may be recommended, and if the lesion is clearly suspicious, a surgical biopsy is usually performed.[3]

Diagnostic Procedures

Fine needle aspiration (FNA), open biopsy, and computerized stereotactic or ultrasound-guided needle biopsies are all current methods for obtaining cell/tissue samples that can be sent to a pathology lab for analysis, and if cancer cells are present, staging.

Laboratory Testing

Laboratory testing for breast cancer, in addition to tissue samples sent for pathology assessment, include looking for serum markers of breast cancer, especially those that may indicate disease severity, recurrence, or metastases.

Staging

Breast cancer staging is based in the TNM (tumor-node-metastasis) model and guides not only diagnosis, but treatment strategies as well. Tumor refers to the histological classification of the lesion and determines the type and severity of the tumor (grading); node refers to the number of lymph nodes involved. Sentinel lymph node biopsy is an importance advance in node staging, sparing women invasive lymph surgery when possible. *Metastases* refers to the number of tumor sites, and distance from the primary tumor. Additionally, the presence

of hormonally positive or negative receptors is determined. Comprehensive cancer diagnosis and treatment guidelines, including breast cancer staging, are available from the National Comprehensive Cancer Network at http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf.

Prognosis

There are numerous prognostic variables in breast cancer. Tumor staging is considered the most important of these. Additional variables include:[3]

- The presence of estrogen and/or progesterone receptors (associated with a lower relapse rate)
- Measures of tumor growth, including S-phase analysis (higher S-phase suggests a greater risk of relapse, but is also associated with a greater response to chemotherapy)
- Histologic classification of the tumor
- Expression of tumor markers (overexpression of erb-2 is associated with a poorer prognosis, as are p53 mutations)
- The presence of neovasculature is a associated with a poorer prognosis

Patterns of tumor gene expression are increasingly being recognized as significant in breast cancer prognosis, and certain patterns may reliably predict disease free internals and survival more accurately than any other prognostic variables.[3]

CONVENTIONAL BREAST CANCER TREATMENT

The mainstays of conventional cancer treatment include surgery, chemotherapy, radiation, and endocrine treatment. Breast cancer treatment is highly complex and well beyond the scope of this chapter to discuss. Readers are referred to the National Comprehensive Cancer Network (Box 10-4) for 2008 recommended breast cancer treatment guidelines. Women undergoing treatment require a central care coordinator and a strong support network.

CAM BREAST CANCER TREATMENT

How Many Women Are Turning to CAM for Breast Cancer Treatment?

Estimates are that between 34% and 60%, but as many as 83% of cancer patients use some form of CAM, with an estimated out-of-pocket cost of up to $7200/year in the United States.[1,30–33] Women with breast cancer use more CAM than individuals with other types of cancer, and more CAM therapies than women who do not have cancer.[32,34] In one study of CAM use among women with breast cancer, 72% of CAM users used two or more CAM approaches, 49% used three or more, and 15% used seven or more CAM approaches, including prayer/spiritual healing and psychotherapy/support groups.[35] Herbs, vitamins, massage, acupuncture, homeopathy, and mind–body healing, are among the therapies frequently used. Most women use complementary therapies in conjunction with conventional medical cancer treatment, although about 2% of women with breast cancer may choose to forego conventional therapy completely and use alternative therapies only.[36]

BOX 10-4

Resources for CAM/Herbal Medicine and Cancer

The University of Texas MD Anderson Cancer Center
http://www.mdanderson.org/topics/complementary/
http://www.mdanderson.org/departments/cimer/
National Comprehensive Cancer Network
http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf

Why Women are Choosing CAM Cancer Therapies

The primary reasons women cite for CAM use include desire to enhance their chance of survival, reduction of risk of disease recurrence, relief of disease symptoms, relief from psychological distress, enhancement of immunity, minimization of conventional treatment related side effects, and improvement of quality of life.[31,34,37] Some women report that CAM use gives them a feeling of hope and a sense of greater control over their life.[1,34] Increasing interest in CAM may also partially be a result of the limitations of conventional breast cancer treatment.[35]

Desperation can be a motivator toward CAM use, with cancer patients wanting to explore every possible option at their disposal.[38] The fear and confusion wrought by a breast cancer diagnosis, and the hope of finding a cure, can make women vulnerable to trying therapies that have no basis of safety or efficacy, and which may be ineffective at best, and costly and/or dangerous at worst.

Several studies have found that women who use CAM therapies as part of their breast cancer treatment plan are more likely to have higher levels of psychosocial stress and anxiety and to report poorer quality of life than those who choose conventional treatment alone.[34] This is a perplexing finding with several possible explanations. For example, women who use CAM therapies may be more personally reflective about their stresses, because it has been found that CAM users tend to be more spiritually involved in their illness and tend to try to gain a deeper holistic view of their illness than non-CAM users.[34] Women who self-medicate with various herbs or nutrients in addition to conventional therapy also may have previously undetected underlying disorders, such as women taking St. John's wort may have previously undiagnosed depression. Women who experience more psychological distress associated with their illness may be self-selective for CAM, which is seen as more supportive in nature than conventional care.[34]

The Complexity of Choosing CAM Therapies

In spite of the widespread use of CAM therapies among women with breast cancer, these therapies remain largely marginalized from mainstream cancer care. This appears to result from lack of a strong evidence base for many of

the therapies leading to concern over the risks of therapies and how they might interact or interfere with conventional treatments, and also to differences in how healing is conceptualized and quantified by conventional and CAM practitioners.[1,34] Lack of scientific evidence available on CAM therapies means that patients wishing to incorporate CAM into their care are left to rely on hearsay, Internet information, or anecdotal evidence. An Internet search for cancer and either complementary or alternative medicine yields more than 3.4 million websites.[36] Distinguishing accurate from unreliable information is nearly impossible for even the educated patient.[33] Many women ultimately do their own extensive medical literature research, which is difficult and time consuming for a lay person, and even there, the evidence is limited, confusing, and contradictory. This is frequently an exhausting and frustrating process on top of the emotional and physical toll of dealing with breast cancer and treatment, and many women find they have to turn to family or friends to help them with the burden of research. This may compound a sense of helplessness or conflict.

Available information on CAM and breast cancer is often contradictory, both regarding its safety and value, causing tremendous confusion. Further, because many oncologists and other physicians remain skeptical about the use of CAM in cancer care, women experience a gap between their conventional care and their desire to use CAM, or their actual use, that can lead to inner conflict and tension as an added burden in their care, and this stress may not be insignificant.[1] As a result, many women who wish to use CAM therapies, either to enhance their conventional treatment, support their immunity, or mitigate side effects of conventional therapies often forego CAM therapies while they are undergoing conventional treatment out of fear of harmful effects, particularly with chemotherapy.[1] Significantly, as many as 64.5% of patients do not disclose CAM use to their health care providers.[31] Reasons for this include fear of disapproval from the practitioner, patient perception that the practitioner lacks knowledge of CAM therapies and therefore there is no reason to discuss them, lack of expressed practitioner interest in the patient's possible use of CAM, and patient perceptions that herbs and supplements are not medications and therefore have no bearing on medical treatment.[39]

Given women's desire to include CAM in their breast cancer treatment plans, it is essential that oncologists and other members of the oncology care team be articulate in CAM options, helping women to navigate the complex and overwhelming array of available options, some of which may be beneficial, and many others which may be harmful, or at least be open to the conversation in order to honor their patient's desire to incorporate CAM into their care. It has been suggested that due to their widespread use, access to CAM therapies should be part of standard oncology treatment.[31] What is currently needed are models that bridge the gap between CAM and conventional therapies, allowing for an integrated, interdisciplinary model of care that allows women to comfortably and safely access and incorporate a variety of beneficial and safe treatment modalities into their breast cancer care while relieving women with breast cancer of the onus of responsibility for obtaining and deciphering all of their treatment information.[1]

Mistrust Between Conventional and CAM Practitioners

There is generally an enormous gap of mistrust separating oncologists and CAM practitioners. Alternative practitioners base their mistrust of conventional physicians and practices on the historical precedence of the evolution of conventional medicine in the United States and the subsequent marginalization of nonconventional practitioners, combined with a general mistrust of cancer treatments that have historically sometimes proved to be as harmful as they have been helpful.[39] Conventional practitioners maintain a mistrust of CAM practitioners and products in a milieu in which CAM is widely available and unregulated, allowing just about anyone to put up a shingle or market a product offering the hope of a cancer cure.[39] This latter environment is also highly problematic for those CAM practitioners who do possess substantial knowledge and training, but who remain unregulated because of lack of available credentialing pathways in the United States, and are thus categorically lumped into being labeled as quacks or ''snake oil salesmen'' rather than being integrated into the oncology care team.[39]

Differing conceptual paradigms of healing have only reinforced this gap, with a lack of a common language upon which to converse about the possibility of a cross-disciplinary or integrated model of cancer care. Fortunately, a growing number of oncologists and other physicians are beginning to recognize the import role CAM plays for women in their approach to treating and healing from breast cancer, and also the potential value of CAM therapies in relieving suffering and improving patient quality of life, as well as possibly improving medical outcomes. Nonconventional practitioners must recognize that most women with breast cancer want to take an integrated approach to their treatment, and do not wish to forego conventional care altogether. Unfortunately, alternative practitioner attitudes toward conventional cancer care may lead women who wish to take an integrative approach to feel guilty for doing so, or may encourage women to rely on unproved therapies, resulting in a delay in seeking appropriate conventional medical care. A cross-disciplinary, integrated approach would allow women to receive the best of both worlds in the safest and most effective manner, and require the cooperation and collaboration of both conventional and nonconventional health care providers to bridge the existing gap.

Incidence of Botanical Medicine Use for Breast Cancer

A survey conducted at eight clinical sites of the University of Texas MD Anderson Cancer Center (MDACC) found that the most frequently used CAM therapies were herbs and/or vitamins, with 62% of

women surveyed using them. Fewer than 53% of women discussed herbal use with their physicians, and fewer than a third considered herbal products to be medications.[31]

Limitations in Botanical Breast Cancer Treatment Research

Numerous herbs have shown anticancer activity and antitumor properties in vitro. Several herbs have been the source for anticancer compounds currently in use as cancer chemotherapy, such as vincristine and vinblastine from periwinkle (*Vinca* spp.) and taxanes from the Pacific yew tree, and botanicals continue to be a major source of research into novel natural compounds that might hold further promise in cancer treatment.

Although many studies using botanical products have had promising results, none have definitively demonstrated altered disease progression in patients with breast cancer.[37] Because of a bias against unconventional cancer therapies, funding and publishing of studies on CAM cancer therapies, including herbs, historically has been limited. Lack of involvement of nonconventional practitioners in research on herbs, either owing to exclusion by mainstream research institutions or lack of CAM practitioner training in research methodologies, may lead to studies that do not reflect the actual clinical use of herbs; for example, herbal products included in clinical trials may be of inadequate standards or used in inappropriate doses.[31,37] For many botanical products, lack of product characterization, standardization, reproducibility, safety, and basic information on pharmacology remain an obstacle to their use and acceptance by oncologists.[31,40] Several research institutions, such as the National Cancer Institute and the University of Texas MD Anderson Cancer Center, have placed botanical medicine and cancer among of their research priorities, and have acknowledged the importance of including nonconventional practitioners who use botanicals in establishing study designs.

Herbs Used in the Treatment of Breast Cancer

Based on preliminary in vitro research and the efficacy of botanical products in the treatment of a variety of medical conditions, it is reasonable to expect that herbal medicines may offer numerous possibilities as preventative and therapeutic interventions for patients with cancer (Box 10-5).[41] An extensive body of literature exists documenting the in vitro and in vivo effects of isolated chemical constituents and single botanical entities. Little research is being done, however, in the actual practice of clinical herbal medicine and even less in herbal medicine and cancer. Many herbal practitioners, mindful of their dubious legal position in the United States, do not treat cancer at all, and others who do tend to fulfill a supportive, adjunctive role rather than becoming the primary care provider.[41] As a consequence the records of botanical practitioners are often inaccessible, and lack of a standardized system of record keeping in the profession often leads to inadequate documentation of clinical botanical care. In reviewing the efficacy of herbal medicine in treating breast cancer, there is a dearth of reliable, reproducible evidence.[41]

BOX 10-5

Commonly Prescribed Herbs

Based on a clinical audit of a busy botanical medicine caner clinic in the United States, the following herbs were found to be the most commonly prescribed, in descending order:

- *Trifolium pratense* (Red clover flowering tops)
- *Glycyrrhiza glabra* (Licorice)
- *Taraxacum officinalis* (Dandelion root)
- *Schisandra chinensis* (Schisandra seed)
- *Zingiber officinalis* (Ginger root and rhizome)
- *Withania somnifera* (Ashwagandha root)
- *Citrus aurantium* (Sweet orange peel)
- *Camellia sinensis* (Green tea leaves)
- *Salvia miltorrhiza* (Dan shen root)
- *Uncaria tomentosa* (Cat's claw stem bark)
- *Urtica dioica* (Nettle leaves)
- *Salvia officinalis* (Sage leaves)
- *Trigonella foenum-graecum* (Fenugreek seed)
- *Arctium lappa* (Burdock root)
- *Astragalus membranaceous* (Milk vetch root)
- *Foeniculum vulgare* (Fennel seed)
- *Hypericum perforatum* (St. John's wort aerial parts)
- *Silybum marianum* (Milk thistle seed)
- *Ulmus rubra* (Slippery elm bark)

Data from Cabrera C: Treatment of breast cancer with herbal medicine and nutrition, 2004.

The following is brief discussion of the herbs and strategies most commonly cited in popular and medical literature for use in the botanical care of women with breast cancer.

Immunostimulation

One of the most commonly cited reasons women with breast cancer give for using herbs is to stimulate or enhance immune function. A number of herbs have immunostimulatory effects. Conventional cancer therapies are known to have adverse effects on immunity and low cell counts can interfere with treatment schedules.[37] Therefore, it makes sense that herbal therapies used to boost the immune system might be beneficial to patients undergoing conventional therapies. However, there is concern that these therapies may interfere with the tumor-killing effects of conventional treatments.[37] Further, the immune system is incredibly complex and there are numerous immunostimulatory effects that are irrelevant to cancer treatment. For example, immunologic functions related to inflammation and allergic reaction may have little to do with a beneficial cancer response, although stimulating natural killer (NK) cell functioning is an important response. Therefore, it is critically important that research be conducted on the immunologic end points of claims for botanical therapies used tomodify immune function and how these relate

to conventional treatment goals and interact with conventional therapies.[37] Herbs commonly used as immunostimulants include maitake and other medicinal mushrooms, astragalus, and many adaptogenic herbs, the latter of which are also used to modulate the stress response (see Chapter 7).

Medicinal Mushrooms

Medicinal mushrooms are among the most commonly prescribed anticancer natural products with data from controlled clinical trials suggesting possible benefit in cancer treatment.[42] Maitake mushroom (*Grifola frondosa*) is among those used. Medicinal mushrooms contain a class of polysaccharides known as beta-glucans that promote antitumor immunity related to antibody–Fc interactions by activating complement receptors. Mouse models have demonstrated that beta-glucans act synergistically with therapeutic antibodies such as trastuzumab or rituximab.[42]

Human data are limited, and at this time there is insufficient evidence to recommend for or against the use of oral maitake for any indication; however, they are commonly ingested as a food and appear safe for general consumption.

Antioxidants and Green Tea

As many as 25% to 84% of patients with cancer use antioxidant supplements. Both in vitro and in vivo research suggest an antitumor role for antioxidants, including inhibition of tumor cell growth, induction of cellular differentiation, alterations in cellular redoc, and enhanced effects of cytotoxic therapies. Chemotherapeutic agents such as alkylating agents, antimetabolites, and radiation lower antioxidant status, generating free radicals that have cytotoxic effects.[43] Cancer patients are often told not to take antioxidant herbs and supplements during the course conventional treatment because of the apprehension that antioxidants will reduce the efficacy of these therapies by eliminating the free radicals. However, adjunctive therapies such as mesna and amifostine, also antioxidants, are commonly given along with other chemotherapeutic agents and do not reduce their efficacy, although antioxidants do appear to reduce the frequency and severity of toxic effects associated with chemotherapy.[43] In 2005, antioxidants were the most popular CAM therapy used for treating breast cancer.[44]

Green tea, prepared from the leaves of *Camellia sinensis*, has been consumed as a beverage for nearly 50 centuries. Next to water, it is the most widely consumed beverage in the world.[45] Multiple lines of evidence, mostly from population-based studies, suggest that green tea consumption is associated with reduced risk of cancer, including breast cancer.[45–48] Epigallocatechin-3-gallate (EGCG), a major polyphenol found in green tea, is a widely studied chemopreventive agent with potential anticancer activity. Green tea polyphenols inhibit angiogenesis and metastasis, and induce growth arrest and apoptosis through regulation of multiple signaling pathways.[45] Apparently, EGCG functions as an antioxidant, preventing oxidative damage in healthy cells, but also as an antiangiogenic agent, preventing tumors from developing a blood supply needed to grow larger. Epidemiologic studies suggest that green tea compounds could protect against cancer, but data are inconsistent, and limitations in study design prevent generalizability of published findings.[49] Some limited evidence suggests that green tea may have down regulatory effects on circulating estrogen levels, proposed as possibly beneficial in estrogen-receptor positive breast cancers.[50] High consumption of green tea was closely associated with decreased numbers of axillary lymph node metastases among premenopausal Stage I and II breast cancer patients, and with increased expression of progesterone and estrogen receptors among postmenopausal ones.[51]

It is recommended that women consume at least four to five cups of green tea per day for chemoprotective effects. Tea is much lower in caffeine than coffee, and a healthy alternative. Decaffeinated green tea products provide a comparable level of antioxidants to caffeinated green tea and may be substituted by caffeine-sensitive individuals.[52]

Phytoestrogens and Breast Cancer

Phytoestrogens are plant-derived nonsteroidal estrogens that are structurally or functionally similar to endogenous estradiol.[53] The major classes of phytoestrogens discussed here are the isoflavones (daidzein and genistein) and the lignins (enterodiol and enterolactone). Phytoestrogens are able to bind to the estrogen receptor, and while stimulating it, do so at only a minimal fraction of the strength of endogenous 17β-estradiol. It is believed that this weaker binding actually acts as an antiestrogenic effect in the presence of a high endogenous amount of estrogen, preventing the stronger endogenous estrogen from binding to estrogen receptors.[52,54]

Soy is the richest dietary source of isoflavones, whereas flax is a major dietary source of lignins. Findings of low rates of breast cancer among Asian women who regularly consume soy products in their diets, and the fact that breast cancer rates begin to approximate those of US women when Asian women consume a Western diet, has stimulated a significant amount of research into the possible protective role of dietary phytoestrogens against breast cancer.[54,55] Conversely, trends in increased consumption of phytoestrogens as a dietary supplement as a result of the popularity of phytoestrogens based on these findings has raised serious concerns that their estrogenic effects may actually increase the risk or recurrence of breast cancer; thus, in spite of a great deal of research, the topic of phytoestrogens and breast cancer remains highly controversial.[54]

Research on the health benefits of soy foods and soy extracts and isolates is contradictory and confusing. Twenty-two case control and cohort studies examined the incidence of breast cancer among women with and without a diet high in phytoestrogens. A meta-analysis of 21 studies found a significantly reduced incidence of breast cancer among past phytoestrogen users. Increased radiologic density has been associated with a four- to sixfold increased risk of breast cancer.[56] Three clinical trials have demonstrated an inverse association between

dietary phytoestrogen intake breast density, two using similar isoflavones and one reporting on lignins.[57–59]

None of the available RCTs documents a protective effect of phytoestrogens on the clinical end points of breast cancer.[60] Women who were high soy consumers during adolescence demonstrate a 23% risk reduction compared with matched controls, and consuming soy in adult life as well increases the risk reduction to 47%. Phytoestrogens may induce differentiation of breast epithelium during early childhood and puberty, thus making the breast epithelium less sensitive to noxious agents such as chemical carcinogens. Breast epithelia may no longer be sensitive to phytoestrogens after pregnancy.[60] Eating little soy in adolescence but more in adult life does not confer any advantage.[61] This is clinically significant because it promotes the use of soy as an early preventative but it challenges the usefulness of soy products to treat breast cancer in women who have not grown up eating such foods. The value of soy supplementation postadolescence is of dubious value, and one study actually demonstrated increase breast density in women who consumed large amounts of soy as adults.

Controversy exists as to the clinical significance of all these findings, and there is as yet no consensus of scientific opinion. The variability in outcomes of studies looking at the protective effects of phytoestrogens may result from individual variability in phytoestrogen metabolism and bioavailability and content of isoflavones in supplements. Both isoflavone and lignin metabolism are dependent on gut flora. Individual differences in gut flora, bowel transit time, and genetic polymorphisms comprise variations that may encourage or inhibit the conversion of phytoestrogens into beneficial metabolites. A study by Setchell et al. analyzed 33 different phytoestrogens supplements for isoflavone content and found that there were considerable differences between the amount the manufacture claimed to be in the product and the actual content.[62] Dietary fiber content affects the absorption, reabsorption and excretion of estrogens and phytoestrogens.[63–65] Additionally as phytoestrogen metabolism is dependent on availability of specific gut flora, antibiotic use may interfere with metabolism of phytoestrogens.[54]

In summary, the relationship between phytoestrogens and breast cancer appears to be dependent on a number of variables, including age at exposure, individual variability in metabolism, endogenous hormone levels, form in which phytoestrogens are consumed (i.e., as foods or supplements), and whether soy products are fermented, which may increase bioavailability.[54,62,66] Adolescent exposure to soy foods appears to be one key to its protective effects against breast cancer.[67] Although it cannot be stated without a doubt that there is no increased breast cancer risk from a diet high in phytoestrogen-containing foods, there are no data indicating that prolonged use of a phytoestrogen-rich diet induces malignant growth of hormone-dependent tissue.[60] Including phytoestrogens-rich foods such as tofu, tempeh, soy milk, and flax seeds as part of an overall balanced diet is considered likely to be safe, and possibly even health promoting; however, supplemental intake of phytoestrogen products is not advisable, particularly for women with a history of breast cancer or breast cancer risk.[54]

Reduction of Side Effects of Conventional Therapies and Disease Symptoms

Patients commonly turn to CAM therapies for the reduction of side effects of conventional therapies and disease symptoms.[68] Acupuncture relieves nausea and vomiting associated with chemotherapy, postmastectomy massage reduces lymphedema, and mind–body therapies help relieve the stress and pain associated with breast cancer treatment.[37,68] A number of herbs may be considered for the reduction of nausea, pain, and anxiety associated with treatment. Ginger (*Zingiber officinalis*) has been shown to be effective in several trials in reducing nausea associated with chemotherapy and surgery. Its mechanism of action, although not entirely known, appears to be a possible anti–5-HT action, possible reduction of GI motility, and reduction of feedback to central chemoreceptors.[52] Although not all trials have demonstrated efficacy, given generally positive findings, a high level of safety, and low side effects profile, it may be considered safe for use in patients experiencing problems nausea and vomiting during cancer treatment. High doses may theoretically inhibit platelet function.[52] St. John's wort (*Hypericum perforatum*) is used to treat mild to moderate depression. Its mechanisms of action include inhibition of the reuptake of 5-HT, DA, NE, and GABA, and L-glutamine in vitro.[68] Because of its interaction with CYP 3A4 it has been shown to lower the efficacy of irinotecan and tamoxifen.[68] Kava kava (*Piper methysticum*) or passion flower (*Passiflora incarnata*) can be considered for patients with anxiety. The former has been associated with hepatotoxicity (see Plant Profiles: Kava kava). The latter is also used for insomnia and neuralgias, and has a very good safety profile, although it may potentiate centrally acting sedative drugs.

Black Cohosh

Women undergoing chemotherapy for breast cancer experience increased intensity of menopausal symptoms, particularly hot flashes. Black cohosh has commonly been recommended for reduction of this troublesome symptom, and although many women report it effective, research evidence suggests that it is no more effective than placebo for women undergoing chemotherapy-induced menopausal vasomotor symptoms.[69] See Plant Profiles: Black Cohosh, for safety considerations.

The Hoxsey Formula and Essiac

The Hoxsey formulas are a combination of an externally applied yellow or red salve, respectively, containing arsenic sulfide, sulfur, and talc or antimony trisulfide, zinc chloride, and bloodroot; and a cathartic, ''immune stimulating'' liquid ''tonic'' to be taken internally consisting of a mixture of licorice, red clover, burdock root, stillingia root, barberry, cascara, prickly ash bark, buckthorn bark, and potassium iodide. A similar formula intended for oral use, without the buckthorn bark and with more cascara sagrada and prickly ash, was listed in the 1926 United States National Formulary (5th ed, 1926) and the 1936

sixth edition as an official remedy known as ''Compound Fluidextract of Trifolium,'' and was first described in 1898 in the King's American Dispensatory. A 2002 survey of naturopathic physicians in the United States and Canada treating patients with breast cancer reported that the Hoxsey formula was used by 29% of the 161 responders treating localized breast cancer and 24% of the 72 responders treating metastatic breast cancer.[70] No toxicity associated with the Hoxsey tonic has been reported, but the potential of toxicity exists from some of its components. No peer-reviewed scientific studies have been published regarding the effectiveness of the treatment.[71] The topical applications are potentially caustic and damaging to the breast tissue.

Essiac—typically a combination of burdock root (*Arctium lappa*), Indian rhubarb (*Rheum palmatum*), sheep sorrel (*Rumex acetosella*), and the inner bark of slippery elm (*Ulmus fulva* or *U. rubra*)—has become one of the more popular herbal remedies for breast cancer treatment, secondary prevention, improving quality of life, and controlling negative side effects of conventional breast cancer treatment.[72] The formula may also variably include blessed thistle (*Cnicus benedictus*), red clover (*Tinfolium pratense*), kelp (*Laminaria digitata*), and watercress (*Rorippa nasturtium aquaticum*).[71] In vivo and animal studies have reported antioxidant effects, competitive estrogen receptor binding, immune stimulation, inhibition of cell proliferation including human cancer cells, and laxative and bile-stimulating activities. Results have been inconsistent and have required doses than recommended for general consumption to achieve. A phase II trial in collaboration with the British Columbia Cancer Agency was discontinued apparently because of difficulties in enrolling patients.

A cohort study ($n = 510$) by Zick et al. to determine the effects of Essiac on health-related quality of life (HR-QOL) between women who are new Essiac users (since breast cancer diagnosis) and those who have never used Essiac, with secondary endpoints of differences in depression, anxiety, fatigue, rate of adverse events, and prevalence of complications or benefits associated with Essiac during standard breast cancer treatment found that Essiac does not appear to improve HR-QOL or mood states and seemed to have a negative effect, with Essiac users doing worse than the non-Essiac users.[72] This might be attributed to the fact that the group of users comprised younger women with more advanced stages of breast cancer, and both of these subgroups of patients have been shown to be at a significantly increased risk for negative mood states and/or a decreased sense of well-being. The women were taking low doses (total daily dose 43.6 ± 30.8 mL) of Essiac that corresponded to the label directions found on most Essiac products. Friends were the most common source of information, and most women were taking Essiac to boost their immune systems or increase their chances of survival. Only two women reported minor adverse events, whereas numerous women reported beneficial effects of Essiac.[72]

In another study, researchers evaluated the effects of Essiac and another popular herbal product, Flor-Essence, on a line of human breast cancer cells. Exposure to the tonics produced a dose-dependent increase in ER activity but did not affect cell proliferation. The authors concluded that Flor-Essence and Essiac Herbal Tonics can stimulate the growth of human breast cancer cells through ER-mediated as well as ER-independent mechanisms of action.[73] According to Low Dog, there is no compelling evidence that these products reduce tumor size, prolong survival, or improve quality of life.

Escharotic Salves

Escharotic treatments have been used historically as topical applications, commonly called ''black salves'' intended to ''draw out'' the tumor from the underlying tissue. They frequently include bloodroot (*Sanguinaria canadensis*), an herb traditionally used as a blood purifier, and zinc chloride a caustic agent, although ingredients vary widely. Escharotic treatments are commonly used by patients wishing to avoid surgical lumpectomy, with the promise that they are effective and safe. However, they are more commonly neither. The damage done to breast tissue from the topical use of these salves can be significant and permanently disfiguring. Use of escharotic treatments sometimes has resulted in much more radical breast surgery than simple lumpectomy would have, both owing to the damaging effects of the salves, and also to delay in obtaining appropriate medical care. This author recommends that their use be entirely avoided in the treatment of breast cancer.

AFTER BREAST CANCER. . .

Only recently have the emotional, social, and even medical complexities of life after breast cancer begun to be recognized. Even the terminology remains uncertain—do women think of themselves as breast cancer survivors? Do they move on or spend their lives worrying about recurrence? Are there preventative strategies they can use to reduce their risk of recurrence? Currently there are probably more questions than answers. From a medical standpoint, the following follow-up guidelines are recommended:[3]

- History, symptom review, and physical exam (including CBE) should be performed every 3 to 6 months for 3 years; every 6 to 12 months for 2 years, and then annually
- BSE can be performed monthly
- Mammogram should be done annually
- Pelvic exam should be performed annually
- Patient should receive ongoing education about recurrence symptoms and ongoing care coordination

Many women continue to use herbal and nutritional supplements, along with a healthy lifestyle, throughout their lives to maintain health and prevent breast cancer recurrence.

PART III

Fertility and the Childbearing Cycle

Pregnancy and Botanical Medicine Use and Safety

Aviva Romm

11 CHAPTER

So eight days late, huh, you must be getting a little uncomfortable?. . . If you're anxious there are a few ways to help things along...actually there are things you can do. . .just some home remedies. . . .I've found that some of them are very effective...there's an herbal tea you can drink. . . .

—Obstetrician in Friends, The One Where Rachel Is Late

The charge that herbal medications are not well tested in pregnancy is true, but it is just as true that conventional medications are not well tested in pregnancy. The medication-related embryopathies with which we are familiar are nearly all associated with conventional prescription drugs: thalidomide, anticonvulsants, ACE inhibitors, misoprostol, lithium, and isotretinoin. The most common embryopathy affecting humans is fetal alcohol syndrome, which is not associated with an herbal medication. This observation does not mean that herbal medications are safe, but only underscores the need to be well informed when prescribing in pregnancy. Let's recommend medications in pregnancy that have been adequately studied, without assuming that all conventional medications are on one side of a divide and all herbal medications are on the other side.[1]

PREVALENCE OF HERB USE DURING PREGNANCY

Herbs have been applied in the treatment of difficulties arising during pregnancy and childbirth since time immemorial, with texts and treatises on the uses of herbs for childbearing problems dating at least back to ancient Egypt. Childbearing women commonly experience minor complaints for which the use of natural remedies may be preferable to the woman who perceives them as gentler and safer than OTC and prescription pharmaceuticals. The appropriate use of herbs medicinally during pregnancy requires specialized knowledge and a healthy dose of caution. This chapter presents a discussion of the prevalence of herb use during pregnancy and childbearing, possible risks, and general guidelines for responsible use. Subsequent chapters discuss the use of herbs for specific pregnancy concerns.

Herbal medicines are commonly used by pregnant women for a variety of complaints, as well as for nutritive and tonic purposes, such as the use of ginger to treat nausea and vomiting of pregnancy or the traditional use of raspberry leaf as a uterine tonic. There is considerable evidence of increasing herb prescribing by obstetric health professionals, particularly certified nurse-midwives (CNMs).[2] The introductory quote to this chapter suggests a mainstreaming of herb use even by obstetricians—enough so that it would be mentioned by an OB-GYN on the popular television sitcom *Friends* when one of the characters is seeking advice for her postdates pregnancy.

Epidemiologic studies and surveys from the United States, United Kingdom, and Australia estimate a range of approximately 7% to 45% of women using herbs during pregnancy.[2–5] A recent survey of 587 pregnant women by Glover et al. revealed that a total of 45.2% of participants in a rural obstetric population had used herbal medications (95.8% had used prescription and 92.6% had self-prescribed OTCs).[6] In another study,

a one-page questionnaire examining the use of all prescription and nonprescription medications, including herbal remedies, was sent to parturients expected to deliver within 20 weeks who had preregistered with the hospital's admissions office. Sixty-one percent of the women responded to the survey, with 7.1% reporting the use of herbal remedies. Only 14.6% of users considered herbs to be medications. Herbal medicine use was most prevalent (17.1%) in parturients in the 41- to 50-year age range (5.6% of parturients). In another study, approximately one-third of 463 postpartum women surveyed in the United States reported having used CAM therapies during pregnancy.[7] Of 734 pregnant women that responded to one survey, 46% used herbal remedies at the recommendation of their health care provider; 54% did so at the recommendation of a friend of family member.[2]

Botanical medicine use is likely even higher in communities observing traditional practices, for example, among Hispanic Americans or Asian Americans, where herb use is an inherent cultural practice. Internationally, traditional herb use during pregnancy is common. For example, a report from the King Edward VIII Hospital in South Africa demonstrated use of a specific traditional herbal formula among 55% of 229 patients randomly selected for interview upon admission in early labor.[8]

Articles and studies published in prominent nurse-midwifery and obstetric journals (i.e., *Journal of Nurse-Midwifery*, *Obstetrics and Gynecology*, and *Clinical Obstetrics and Gynecology*) indicate that a large number of CNMs use herbal medicines clinically or are interested in learning to do so.[9–12] A study of CNMs in North Carolina indicated that 90% of midwives recommend CAM therapies to patients, with 80% of respondents suggesting herbal therapies for labor stimulation.[9] A survey of 596 health care professionals in Leicestershire, United Kingdom, found that 34% of midwives and 18% of nurses used complementary therapies in their practices.[13] According to Jeanne Raisler, Associate Editor of the *Journal of Nurse Midwifery,* ''Herbal healing is probably the complementary therapy most widely used by midwives.''[12]

WHY ARE HERBS BEING USED DURING PREGNANCY?

One of the primary reasons women cite for stopping conventional medication during pregnancy is concern for risks to the fetus.[2] A recent report by Lo and Friedman indicates that greater than 90% of all conventional medications prescribed for pregnant women have not been proved safe for use during pregnancy.[14] The specter of the thalidomide and DES disasters are sufficiently recent to remind us of the hazards of ''safe'' pharmaceutical use during pregnancy. Many pregnant women turn botanical therapies to pharmaceutical medications believing them to be safer and gentler. Women planning natural birth also may feel that the use of herbs is more philosophically harmonious with their overall belief that childbearing is a natural experience and are more likely to use herbal preparations than those who are not preparing for natural birth.[2] Thus, the use of herbal medicines represents both a philosophic and medical choice.

Midwives recommend herbal medicines for a variety of reasons, including support of patient choice, a shared belief in the naturalness of birth and the use of herbs as a natural extension of this belief, and as a way to help pregnant and postpartum women avoid more invasive and costly medical interventions that may be perceived as overly aggressive or unnecessary.[15] For example, Tiran suggests that the possibility of cephalic version of breech presentation through the use of moxibustion (see Breech Presentation) may avoid the costs (and risks) of cesarean section and adequate management of nausea and vomiting of pregnancy (NVP) may reduce hospital admission for hyperemesis gravidarum.[16]

Midwives are in a key position to interface with pregnant clients about the use of botanical therapies. The philosophic compatibility between herbal medicine, midwifery, and nursing care philosophies reinforces a perceived ''rightness'' of botanical medicine use.[11,17,18] Unfortunately, few midwives are adequately trained in the use of botanical medicines during pregnancy. Education on the use—or at least safety and risks— of botanicals in the childbearing cycle should be a requisite part of training for all midwifery and obstetric care providers.

LACK OF TRAINING IN OBSTETRIC BOTANICAL MEDICINE USE

The medical and alternative literature on botanicals for pregnancy and birth often contains erroneous or inadequate information on the use of herbs during childbearing.[15,19,20] Herbs may be recommended, for example, with insufficient explanation of possible risks, without specified dosage ranges, and may be based on theoretic or academic knowledge rather than training or clinical experience. In one well-cited survey conducted by McFarlin and O'Rear of nurse-midwives on their use of herbal remedies during pregnancy, most midwives who responded reported that they had learned about the use of herbs by word of mouth.[21] Several articles report on the need for further training in botanicals for nurse-midwives, citing its absence from curricula.[12,16,22]

Lack of practitioner training in botanical medicines for pregnancy might mean that practitioners are inappropriately recommending botanical therapies to their patients, either by recommending herbs that might be contraindicated, recommending inappropriate doses, not identifying safe and high-quality botanical products for patients, or recommending inappropriate durations of use. Further, practitioners with limited knowledge cannot accurately evaluate advice patients might receive from other sources, such as the Internet, a common source of misleading information on herbs and pregnancy.[23] There is clearly a need to include education on obstetric botanical medicine use in the growing number of CAM education programs in medical and nursing programs. Adequate practitioner knowledge is critical to the well-being of both patients involved in the prenatal and lactation dyad.

HERBS MOST COMMONLY USED DURING PREGNANCY

The herbs cited in the medical literature as those most frequently used for pregnancy complaints varies slightly among studies, but includes echinacea, St. John's wort, ephedra, peppermint, spearmint, ginger root, raspberry leaf, fennel, wild yam, meadowsweet, blue cohosh, black cohosh, red raspberry leaf, castor oil, evening primrose, garlic, aloe, chamomile, peppermint, ginger, echinacea, pumpkin seeds, and ginseng. In one study, patients cited lower GI problems, anxiety, nausea and vomiting, and urinary tract problems as the most common reasons for using complementary therapies in pregnancy.[2,4,7,10,23] Midwives most frequently recommend herbs for nausea and vomiting, labor stimulation, perineal discomfort, lactation disorders, postpartum depression, preterm labor, postpartum hemorrhage, labor analgesia, and malpresentation.[9] Most of the herbs cited as commonly used are generally considered safe and gentle, even for use during pregnancy; however, several including blue cohosh, ephedra, aloe (internally), and St. John's wort (internally) are not appropriate and may even be harmful (see further discussions on blue cohosh throughout in this and subsequent sections of this chapter).

SAFETY, EVIDENCE, AND POTENTIAL ADVERSE EFFECTS OF BOTANICAL USE DURING PREGNANCY

Little is known scientifically about the risk of using herbs during pregnancy, as most have not been formally evaluated and ethical considerations severely limit human clinical investigation during pregnancy.[2,5,9,24,25] Much the same can be said for the use of many pharmaceuticals during pregnancy. Bone identifies five primary risks associated with the use of herbs during pregnancy:[26]

1. Toxicity to the mother, which might indirectly affect the fetus
2. Toxicity to the fetus
3. Teratogenesis
4. Increased miscarriage risk
5. Poor neonatal health

An additional potential risk is the consequences of delayed administration of necessary medical therapy in favor of herbs, regardless of their safety.[27] Most of what is currently known about botanical use during pregnancy is based on a significant body of historical, empirical, and observational evidence, and limited pharmacologic and animal studies. There has been little evidence of harm from the use of botanicals during pregnancy. When apparent adverse events have occurred, cause and effect have been difficult to establish because of a wide range of confounding factors.[23] Also, adverse events reports typically have involved the consumption of known toxic herbs, adulterations, or inappropriate use or dosage of botanical therapies. In general, there have also been relatively few case reports of adverse drug interactions involving herbal medicines.[28] Overall, most herbs have a high safety profile. Many practitioners take this as proof of safety, believing that whole herbs are inherently safer than concentrated pharmaceutical drugs.[10,11] However, lack of proof of harm is not synonymous with proof of safety. Some of the harmful effects of herbs may not be readily apparent until long after use has been discontinued, or may only occur with cumulative use.

There is a paucity of human clinical trials on the safety and efficacy of Western botanical therapies during pregnancy. Two human clinical trials evaluated raspberry leaf for its effects on labor outcome with positive findings, a study conducted on echinacea safety after varying lengths of pregnancy use found no harmful effects, and several studies have evaluated the safety and efficacy of ginger root for the reduction of NVP, finding it safe and effective.[29–31] Most often, the results of clinical trials are positive.[3] Nonetheless, many researchers feel that in the absence of proof of safety, herbs should be entirely avoided during pregnancy.[3] However, many midwives and pregnant women continue to use herbs based on satisfaction with their safety, efficacy, and outcomes, and on the knowledge that many pharmaceutical preparations recommended during pregnancy also carry unknown risks.

Controls over the manufacturing of herbs do not entirely protect consumers from the accidental or deliberate adulteration, sophistication, or contamination of herbal products, all of which can pose problems during pregnancy. In one study of 200 different herbal products, 83% were found to be contaminated with undeclared pharmaceuticals or heavy metals, including lead, arsenic, and mercury.[5] Adulteration occurs when one herb is accidentally or deliberately substituted for another. Rarely, toxic herbs have been found as adulterants in otherwise completely benign herbal products, for example, adulteration of skullcap (*Scutellaria lateriflora*) with the toxic *Teucrium*, or *Digitalis* spp. (foxglove) with common plantain (*Plantago* spp.). One case in the literature reports on the substitution of the herb *Periploca sepium* for *Eleutherococcus senticosus*.[26,32] This substitution resulted in a case of hyperandrogenization of the fetus (''hairy baby syndrome'') as a result of the mother mistakenly taking the adulterated product throughout her pregnancy. Chinese patent products and imported Asian herbal formulae should be viewed with utmost caution during pregnancy, as they are well known to contain adulterants, heavy metals, and added pharmaceutical medications frequently not listed on the label, all of which can pose a threat to the safety of the pregnant woman and her fetus.

Negative outcomes have been reported for a limited number of herbal products used by parturient women. Ernst provides a through review of these in *Herbal Medicinal Products during Pregnancy: Are They Safe?*[3] Causality remains uncertain. Adverse reports cited by Ernst and others include:[8,10,33]

- One case of ovarian hyperstimulation in a woman undergoing in vitro fertilization and taking Vitex agnus-castus
- One case of fetal alcohol syndrome in a 29-year-old Chinese woman taking an herbal product containing 19% alcohol, regularly throughout pregnancy, with negative report of other alcohol consumption

- One case of hypertension in a 3-week postpartum mother and neonate associated with maternal consumption of dong quai; hypertension disappeared within 48 hours of discontinuation of the herbal product
- Case report of a 15-month-old Chinese female with congenital deformity of an accessory phallic urethra arising in the vicinity of the anus
- Possible association between maternal consumption of blue cohosh as a partus preparator and neonatal cardiac arrest, neonatal congestive heart failure, and neonatal stroke in three respective cases
- Maternal hepatotoxicity allegedly from a Chinese herbal product called Shou-Wu-Pian
- Neonatal hepatotoxicity and death caused by liver failure in a female Swiss infant associated with maternal consumption of an herbal tea known to be high in pyrrolizidine alkaloids (PAs)
- Congenital meningoencephalocele and cerebellar agenesis in a baby born to a woman who had consumed a known toxic herb, *Tripterygium wilfordii* for rheumatoid arthritis throughout her pregnancy

Other herbal products that have been associated with increased complications include a possible correlation between a German sinus preparation (Sinupret) and increased rates of miscarriage, stillbirth, and malformations; increased rate of meconium-stained amniotic fluid with maternal use of castor oil; and increased meconium staining and possibly related fetal distress with use of a traditional South African herbal pregnancy formula called isihlambezo, and a case of a baby born with veno-occlusive disease after the mother consumed a coltsfoot-containing cough syrup throughout her pregnancy.[3,8]

USING HERBS DURING PREGNANCY

The most prudent approach to the use of herbs during pregnancy is to avoid all herbs during the first trimester unless medically indicated (i.e., severe NVP preventing adequate nutritional intake, threatened miscarriage) and used with proper guidance, and to otherwise only use herbs during the remainder of pregnancy if there is a compelling reason for their therapeutic use, greater safety in a botanical option than a pharmaceutical one, or lack of a suitable pharmaceutical alternative. Beverage and nutritive teas that are known to be safe in moderate amounts (e.g., red raspberry, spearmint, chamomile, lemon balm, nettles, and others), and ingestion of normal amounts of cooking spices are excepted from these restrictions; however, practitioners and pregnant women should be aware that herbs may be contaminated with heavy metals or adulterated. For example, an industry recall of the nutritive tonic herb nettles occurred some years ago owing to high lead content of a batch that had been released to the market. It is therefore best for pregnant women to use only organically grown and carefully cultivated herbs, and to avoid all products with a high likelihood of contamination or adulteration.

The following key points are essential to remember when using botanical medicines during pregnancy:

- Natural is not synonymous with safe.
- Many botanical medicines contain potent pharmacologic constituents.
- Many constituents consumed by the mother can pass through the placenta and reach the fetus.
- Physiologic and metabolic changes during pregnancy may influence the pharmacokinetics of herbs thus changing expected actions or safety, for example decreased bowel transit time may affect dosing, and renal and hepatic changes may affect the metabolism and excretion of herbal constituents.
- Actions that may be acceptable in the mother may be inappropriate, or even harmful, for the baby.
- Herbs can have unknown and idiosyncratic effects in the pregnant woman or her baby.
- Herbs with known teratogenic, mutagenic, or abortifacient properties should be avoided.
- Highly concentrated herbal products should be avoided.
- Long-term use and high doses of alcohol-based products (i.e., tinctures), especially during the first trimester, should be avoided.
- Herbs may affect the developing fetal endocrine and/or nervous system.
- Herbs can disrupt pregnancy and lead to miscarriage or premature labor.

CONTRAINDICATED HERBS FOR PREGNANCY AND LACTATION

There are several specific categories of herbs that are historically avoided during pregnancy to minimize risks to the maternal–embryo/fetal dyad. See Table 11-1 for a summary of these. A discussion follows, as well as an extensive list of contraindicated herbs for pregnancy and lactation.

Abortifacients and Emmenagogues

Abortifacients are those herbs that may induce miscarriage/abortion (Table 11-2). The amounts required to induce an abortion may pose toxicity risks to the mother, including kidney and liver damage. Because the risks of maternal intake of these herbs to the fetus are unknown, women who have attempted to abort unsuccessfully may require a follow-up clinical abortion. Abortifacients should be entirely avoided during pregnancy and herbal abortion is not a recommended method of intentional pregnancy termination.

Emmenagogues are defined in herbal medicine as herbs capable of stimulating the menstrual flow even when it is not due, and are also to be avoided during pregnancy. For centuries, they have been colloquially defined as ''herbs for delayed menses,'' sometimes a euphemism for eliminating an unwanted pregnancy. Many emmenagogic herbs are therefore also abortifacients. There is disagreement in the literature as to what actually constitutes an emmenagogue. Certain herbs such as chamomile are frequently and erroneously listed as emmenagogic. Other herbs, such as Dong quai and peony, are considered emmenagogic, and in fact do have uterine stimulatory activity, but are nonetheless used extensively in the Chinese and Japanese formulary for the prevention of miscarriage. Finally, the recorded data on other herbs are contradictory; for example, Ashwagandha has been described as an abortifacient yet

TABLE **11-1**

Herb Categories to Avoid during Pregnancy

CATEGORY	EXAMPLES
Abortifacients and emmenagogues	Tansy
	Thuja
	Safflower
	Scotch broom
	Rue
	Angelica
	Mugwort
	Wormwood
	Yarrow
	Pennyroyal essential oil
Essential oils and volatile oils*	Thuja
	Tansy
	Oregano
	Thyme
	Sage
	Peppermint
	Pennyroyal
Teratogens	*Lupinus* spp.
	Veratrum spp.
	Conium spp.
	Solanum spp.
	Nicotiana spp.
	Ferula spp.
	Trachymene spp.
	Datura
	Prunus spp.
	Sorghum
	Senecio spp.
Alkaloids*	Comfrey
	Coltsfoot
	Borage
	Goldenseal
	Barberry
	Oregon grape
Stimulating laxatives	Cascara sagrada
	Castor oil
	Buckthorn
	Aloes
	Rhubarb
Phytoestrogens	Hops
	Red clover
	Isoflavone extracts
Nervous system stimulants/ depressants	Ephedra
	Guarana
	Coffee
	Kava

Note: The herbs listed under each category are representative examples and are not exhaustive. Additional herbs may fall into any of these categories.

*Avoid internal use; external use may be acceptable under the guidance of an experienced botanical medicine practitioner.

TABLE **11-2**

Commonly Used Botanicals with Possible Abortifacient, Emmenagogue, or Oxytocic Activity

COMMON NAME	BOTANICAL NAME
Blue cohosh	*Caulophyllum thalictroides*
Coleus	*Coleus forskohlii*
Cotton root bark	*Gossypium* spp.
Eucalyptus	*Eucalyptus* spp.
Goldenseal	*Hydrastis canadensis*
Motherwort	*Leonurus cardiaca*
Mugwort	*Artemisia* spp.
Pennyroyal	*Mentha pulegium*
Tansy	*Tanacetum vulgare*
Yarrow	*Achillea millefolium*

was used historically to prevent miscarriage. Many herbs that are high in essential oil content are undisputed emmenagogues, although the presence of essential oils in an herb does not mean it acts as an emmenagogue.[26] Commonly accepted abortifacients and emmenagogic herbs include (but are not limited to) tansy, thuja, safflower, scotch broom, rue, angelica, mugwort, wormwood, yarrow, and essential oil of pennyroyal.[26]

Essential Oils and Volatile Oils

Essential oils and volatile oils are capable of crossing the placenta and reaching the fetus, and may have effects on the developing fetal nervous system. In significant doses, essential oils can be emmenagogic. Concentrated essential oils should never be taken internally during pregnancy and should not be used neat (undiluted) topically. Oils known to be specifically emmenagogic because of their essential oil content (e.g., thuja, pennyroyal, tansy) should be entirely avoided during pregnancy. Common herbs with high volatile oil content such as chamomile, lavender, spearmint, and peppermint, but which are considered generally safe during pregnancy, should be used in moderation; however, they have not been associated with adverse clinical outcomes.

Teratogens and Mutagens

The word *teratogen* has its origins in the Greek *terato*, meaning ''monster.'' Teratogens are substances that cause structural abnormalities in the fetus. The drug thalidomide was a powerful example of a teratogen, and its legacy has left an imprint on those who prescribe medications to pregnant women. There is extremely limited knowledge about which herbs are teratogenic. Most of what is known is derived primarily from animal studies, observation of teratogenesis in grazing cattle, and suspected teratogenicity in humans from ingestion of suspected harmful herbal products. Known teratogens include those plants in the *Lupinus, Veratrum, Conium,* and *Solanum* genuses; and suspected teratogenic

substances can be found in *Astragalus, Nicotiana, Ferula,* and *Trachymene* genuses. Plants in the *Datura, Prunus, Sorghum,* and *Senecio* genuses may also contain teratogenic substances.[26] The primary means for identifying the propensity for this type of reaction is through general toxicologic screenings or through pharmacovigilance programs. Birth defects that occur between conception and birth are caused by teratogenic agents, whereas mutagens cause direct changes in the nucleus of cells.

The potential for mutagenicity is discerned through in vitro assays, most notably Salmonella microsome test (Ames assay) or rodent tests and then followed by animal studies. In both types of tests, isolated compounds rather than complete herbal products are most often investigated. Unfortunately, simple in vitro toxicity screenings do not reveal much useful data as they often can not be extrapolated to human use. The presence of a mutagen in a product does not automatically contraindicate the use of the substance in pregnancy. There are many commonly consumed substances such as basil, black pepper, coffee, tomatoes, and potatoes that contain toxic compounds, including those with mutagenic or teratogenic potential. However, consumption of these in pregnancy is not contraindicated when consumed as a normal part of the diet.

Alkaloids

Alkaloids are a highly bioactive category of plant compounds, many of which may have adverse effects on the developing embryo/fetus. One such group is the pyrrolizidine alkaloids (PAs), known to cause veno-occlusive liver disease (VOD), an adverse outcome that has been observed in fetuses when the herb has been ingested regularly by their pregnant mothers (Table 11-3). Comfrey, coltsfoot, and borage herb (not borage oil) are the main herbs that have been implicated, containing varying amounts of PAs. They should therefore be avoided for internal use and should be used only short term topically when there is broken skin, as there is a minimal risk of transdermal absorption into the bloodstream. Germany has established limits for external application of toxic PAs to no more than 100 μg daily. In addition to causing VOD, PAs are carcinogenic and mutagenic. Botanicals containing toxic PAs should not be used in pregnancy or lactation. PAs have been reported to be secreted into the milk of nursing animals. Also, new mothers should be cautioned against excessive or frequent use of salves, oils, and balms made from herbs known to contain toxic PAs, such as comfrey (Symphytum officinale) for sore breasts associated with breastfeeding.

Oral consumption of berberine alkaloid–containing herbs is also typically best avoided during pregnancy. Although there are no documented reports of adverse events in pregnancy associated with their use, they have been implicated in neonatal jaundice when used in pregnancy.[34] Herbs in this category include goldenseal, goldthread, barberry, and Oregon grape root. Topical and vaginal applications appear to be safe for use during pregnancy.

TABLE 11-3

Botanicals Containing Pyrrolizidine Alkaloids (PAs)

COMMON NAME	BOTANICAL NOMENCLATURE
Borage*	*Borago officinalis*
Butterbur	*Petasites hybridus*
Coltsfoot	*Tussilago farfara*
Comfrey	*Symphytum officinalis*
Eyebright	*Euphrasia officinalis*
Life Root	*Senecio aureus*

*Borage oil does not contain PAs.

Laxatives

Stimulating laxatives, including *Cascara sagrada*, castor oil, buckthorn, aloes, and rhubarb are to be avoided. Senna is generally contraindicated by midwives and herbalists for use during pregnancy, though Bone and Mills state that is has not been associated with adverse effects and therefore should not be contraindicated in pregnancy.[26] Constipation is best addressed with gentle, nonstimulating bulk laxatives (e.g., flax, psyllium) and lifestyle approaches such as dietary changes and exercise.[26] Laxatives containing anthraquinone glycosides are considered overly stimulating during pregnancy, as their effects of increasing intestinal peristalsis can lead to sympathetic uterine stimulation. Yellow dock, however, is one anthraquinone-containing laxative that herbalists and midwives frequently except from this rule, as it is much gentler in effects and is commonly added to formulas for treating anemia because of its purported iron-fortifying actions.

Phytoestrogens

Numerous plants, including food plants, such as legumes, contain phytoestrogens, which are an integral part of a healthy diet. Asian diets, which include large amounts of tofu and other soy products, are particularly high in phytoestrogens, and abnormal levels of fetal and neonatal problems have not been observed when compared with other populations. Nonetheless, there is concern that high consumption of phytoestrogens during pregnancy may exert abnormal hormonal effects on the developing embryo or fetus, particularly in female embryogenesis, as occurred with the drug diethylstilbestrol (DES). Although phytoestrogens are dramatically weaker than DES, because of its unknown effects, it is best to avoid specifically supplementing the diet with concentrated phytoestrogen supplements. Additionally, herbs with known hormonal activity, including hops, red clover, and isoflavone extract supplements are best avoided for long-term use or in large doses during pregnancy.

Nervous System Stimulants/Depressants

Herbs that strongly affect the nervous system including stimulants such as ephedra, guarana, and large amounts of caffeine-containing herbs, including coffee and green

and black teas may have adverse effects on pregnancy and the developing embryonic and fetal nervous system, and should be avoided during pregnancy. Kava kava, a strong anxiolytic and sedative herb, has recently been implicated in cases of hepatotoxicity. Although many of the cases appear not to be causally related to the herb, the herb does appear to have idiosyncratic hepatotoxic effects, and should be avoided during pregnancy and lactation in favor of other, safer botanical options.

A WORD ABOUT *PARTUS PREPARATORS*

Partus preparators are herbs used during the last weeks of pregnancy to tone and prepare the uterus for labor. Historically, they have been used to facilitate a rapid and easy delivery. Herbs commonly used as partus preparators include blue cohosh (*Caulophyllum thalictroides*), black cohosh (*Actaea racemosa*), partridge berry (*Mitchella repens*), and spikenard (*Aralia racemosa*), among others. The use of such herbs to prepare women for labor begs the question of why one would use an herbal preparation to prepare the body for something it naturally knows how to do. Furthermore, the safety of these herbs prior to the onset of labor is questionable. Case reports have appeared in the literature suggesting an association between blue cohosh and profound cerebral ischemic episodes or myocardial infarction in the neonate.[35,36] Blue cohosh contains a number of potent alkaloids, including methylcysteine and anagyrine, the latter, which is known to have an effect on cardiac muscle activity. Other side effects of blue cohosh include maternal headache and nausea. Yet, as previously stated, the use of blue cohosh represents one of the widely applied botanical medicines by midwives, and one of those most commonly included in late pregnancy formulas self-prescribed by pregnant mothers. The risks associated with extended third trimester ingestion of blue cohosh specifically suggest that it should be avoided as a partus preparatory. It seems that it would be preferable, unless otherwise indicated for the health of the mother and baby, to focus attention on nonpharmacologic methods of preparing for labor.

CONTRAINDICATED HERB LISTS AND BOTANICAL SAFETY CLASSIFICATIONS

The herbal literature is rife with lists of herbs contraindicated in pregnancy and lactation. Limitations are inherent in most of these lists, particularly in their lack of specifics as to how and when each herb is contraindicated. Herbs may sometimes be broadly contraindicated in pregnancy yet in actuality be only contextually contraindicated; for example, they are absolutely contraindicated during the first and second trimesters but may be reasonably used during labor, or they may be safe in small doses for a very limited duration. Culinary herbs, appearing on many contraindicated lists, when used in moderation as food seasonings pose no harm to the fetus or mother. Herbs such as aloe vera, calendula, and even comfrey may be used topically with no risk but are to be avoided for internal use, yet are contraindicated on such lists with no differentiation, leading to confusion about safety. Certain contraindications have become pervasive myths, for example, the frequent contraindication of chamomile in pregnancy owing to its alleged action as an abortifacient.[37] In fact, chamomile provides an excellent example of how misapplication of a scientific finding can lead to unjustified contraindication of a safe herb. A study conducted in 1979 found teratogenic effects using a concentrated extract of α-bisabolol at high doses. No teratogenic effects were seen at lower doses and the dose of the oil constituent required to cause teratogenicity are far greater than it would ever be possible for someone drinking the tea to ever approximate. However, based on this single study, chamomile was erroneously contraindicated for consumption during pregnancy.[38]

Finally, herbs may be contraindicated based on theoretical reasons; for example, ashwagandha, which in traditional Ayurvedic medicine was used to prevent miscarriage, is contraindicated on the basis that it might cause uterine contractions, predicated on a single anecdotal report, with no details on duration or mode of use, nor dose, that has been reiterated several times in the scientific literature. To complicate matters, certain herbs that are contraindicated by Western herbalists and Western scientific research for use during pregnancy are regularly used in traditional medicine from non-Western cultures, for example, dong quai (*Angelica sinensis*) is prescribed as a blood tonic for pregnant women in China, and listed in China and Japan in official formulae for the prevention of miscarriage, yet is considered contraindicated in Western herbal medicine.

The *Botanical Safety Handbook* has categorized herbs for use in pregnancy and lactation as follows:[39]

- Category 2b: ''Not to be used during pregnancy unless otherwise directed by an expert qualified in the appropriate use of this substance''
- Category 2c: ''Not to be used while nursing or unless otherwise directed by an expert qualified in the appropriate use of this substance''

Table 11-4 is an amalgamation of contraindicated herb lists from *The Botanical Safety Handbook*, *The Natural Pregnancy Book*, and *Women's Health in Complementary and Integrative Medicine*, all compiled by authors with significant knowledge of botanical safety and obstetric botanical use. It is not exhaustive, leaving out many obscure herbs, and focusing on those herbs the clinician is likely to encounter, consider, or question. It also does not cover many herbs from traditional Chinese medicine or the Ayurvedic materia medica. Table 11-4 also includes categoric designations of caution and contraindication according to Mills and Bone, which are subsequently discussed.

Mills and Bone suggest that a descriptive classification scheme for the risk of herbs during pregnancy, similar to that used for drugs in pregnancy, would be more useful than contraindicated lists in helping practitioners sort through some of the inconsistencies in the literature.[26] They recommend the use of the Australian Therapeutic Goods Association (TGA) Classification for Drugs in Pregnancy (Table 11-5) as the guideline for a similar classification of herb use and safety during pregnancy and lactation, which they have begun to outline based on available evidence. They suggest that practitioners

TABLE 11-4

Herbs Contraindicated in Pregnancy with AHPA and Mills and Bone Safety Classifications

COMMON NAME COMMENTS	BOTANICAL NAME	BOTANICAL SAFETY HANDBOOK CLASSIFICATION	MILLS AND BONE CLASSIFICATION*	EXCEPTIONS
Achyranthes	*Acyranthes bidentata*	2b	NC	
Albizzia	*Albizzia julibrissin*	2b	NC	
Alder buckthorn	*Rhamnus frangula*	NC	NC	
Aloe (dried juice)	*Aloe* spp.	2b/2c	B3	Safe for topical use
Andrographis	*Andrographis paniculata*	2b	B3	
Angelica	*Angelica archangelica*	2b	NC	
Arnica	*Arnica Montana*	2b	X	Safe for topical use; unbroken skin only
Ashwagandha	*Withania somnifera*	2b	B1	Used in Ayurveda to prevent miscarriage
Barberry	*Berberis vulgaris*	2b	P/C	
Basil leaf	*Ocimum basilicum*	2b/2c	NC	Safe for normal culinary use
Bethroot	*Trillium* spp.	2b	NC	
Birthwort	*Aristolochia clematitis*	NC	NC	
Black Cohosh	*Actaea racemosa*	2b/2c	B2	Classically used to prevent miscarriage
Bladderwrack	*Fucus vesiculosus*	2b/2c	B2	
Blessed thistle	*Carbenia benedicta*	2b	NC	
Blood root	*Sanguinaria canadensis*	2b	NC	
Blue Cohosh	*Caulophyllum thalictroides*	2b	D	Possibly safe for short-term use during labor only, and with proper monitoring of fetal heart tones
Blue flag	*Iris versicolor*	2b	B1	
Blue vervain	*Verbena hastate*	2b	NC	
Borage	*Borago officinalis*	2a	NC	
Broom	*Sarothamnus scoparius*	NC	NC	
Buchu	*Barosma betulina*	2b	B2	
Buckthorn	*Rhamnus cathartica*	NC	NC	
Bugleweed	*Lycopus* spp.	NC	P/C L/X	
Butterbur	*Petasites hybridus*	NC	NC	
Butternut	*Juglans Canadensis*	NC	NC	
Calamus	*Acorus calamus*	NC	NC	
California poppy	*Eschscholzia californica*	2b	B2	
Cascara Sagrada	*Rhamnus purshiana*	2b/2c	B2	
Celandine	*Chelidonium majus*	2b	C	
Chaparral	*Larrea tridentate*	NC	C	
Cola	*Cola nitida*	NC	NC	
Coltsfoot	*Tussilago farfara*	2b/2c	NC	
Comfrey	*Symphytum officinale*	2a/2c	NC	Safe for topical application for short duration but avoid on large areas of broken skin
Corydalis	*Corydalis yanhusuo*	2b	NC	
Cotton root	*Gossypium herbaceum*	NC	NC	
Cowslip	*Primula veris*	NC	NC	
Damiana	*Turnera aphrodisiaca*	NC	NC	

L = lactation category, NC = not categorized, P = pregnancy category.
*Only for those herbs appearing on this list.

TABLE **11-4**

Herbs Contraindicated in Pregnancy with AHPA and Mills and Bone Safety Classifications—cont'd

COMMON NAME COMMENTS	BOTANICAL NAME	BOTANICAL SAFETY HANDBOOK CLASSIFICATION	MILLS AND BONE CLASSIFICATION*	EXCEPTIONS
Elecampane	*Inula helenium*	2b/2c	B2	
Ephedra (Ma Huang)	*Ephedra vulgaris*	2b/2c	B3	
Fenugreek	*Trigonella foenum-graecum*	2b	B3	
Feverfew	*Tanacetum parthenium*	2b	B3	
Gelsemium	*Gelsemium sempervirens*	NC	NC	
Ginkgo	*Ginkgo biloba*	NC	B1	
Ginseng	*Panax quinquefolius*	NC	A	Used during pregnancy in TCM
Goldenseal	*Hydrastis Canadensis*	2b	C	Safe for topical and suppository use
Gotu kola	*Hydrocotyle asiatica*	NC	B1	
Goat's rue	*Galega officinalis*	NC	B3	
Guarana	*Paullinia cupana*	NC	NC	
Guggul	*Commiphora mukul*	2b	C	
Hops	*Humulus lupulus*	NC	B2	
Horsetail	*Equisetum* spp.	NC	B2	
Ipecac	*Ipecac ipecacuanha*	2b	NC	
Juniper berries	*Juniperis communis*	2b	NC	
Kava	*Piper methysticum*	2b/2c	B1	
Licorice	*Glycyrrhiza glabra*	2b	A	Possibly safe for medically indicated uses for short duration
Lily of the valley	*Convallaria majalis*	NC	NC	
Lobelia	*Lobelia inflata*	2b	NC	
Male fern	*Dryopteris felix-mas*	2a/2c	NC	
Mistletoe	*Viscum album*	NC	NC	
Motherwort	*Leonurus cardiaca*	2b	B3	
Mugwort	*Artemisia vulgare*	2b	NC	
Nutmeg	*Myristica officinalis*	NC	NC	Safe for normal culinary use
Oregon grape root	*Mahonia aquifolium*	2b	C	Safe for topical use
Osha	*Ligusticum porten*	2b	NC	
Parsley	*Carum petroselinum*	2b	NC	Safe for normal culinary use
Pasqueflower	*Pulsatilla vulgaris*	NC	C	
Pennyroyal	*Mentha pulegium*	NC	NC	
Pau d'arco	*Tabebuia heptaphylla*	NC	D	Safe for topical application
Periwinkle	*Vinca* spp.	NC	NC	
Peruvian bark	*Cinchona* spp.	NC	NC	
Pleurisy root	*Asclepias tuberosa*	2b	NC	
Poke root	*Phytolacca decondra*	2b	D	
Prickly ash	*Zanthoxylum americanum*	2b	B2	
Red clover	*Trifolium pratense*	2b	NC	
Rosemary	*Rosmarinus officinalis*	2b	B1	Safe for culinary use
Rue	*Ruta graveolens*	2b	NC	
Rhubarb	*Rheum palmatum*	NC	NC	
Sage	*Salvia officinalis*	2b	C	

(Continued)

TABLE **11-4**

Herbs Contraindicated in Pregnancy with AHPA and Mills and Bone Safety Classifications—cont'd

COMMON NAME COMMENTS	BOTANICAL NAME	BOTANICAL SAFETY HANDBOOK CLASSIFICATION	MILLS AND BONE CLASSIFICATION*	EXCEPTIONS
Sarsaparilla	*Smilax officinale*	NC	NC	
Senna	*Cassia senna*	2b/2c	A	
Shepherd's purse	*Capsella bursa-pastoris*	2b	B3	
Spikenard	*Aralia racemosa*	2b	NC	
Stillingia	*Stillingia sylvatica*	NC	NC	
Sweet flag	*Acorus calamus*	2b	NC	
Tansy	*Tanacetum vulgare*	NC	D	
Thuja	*Thuja occidentalis*	2b	D	
Tumeric	*Curcuma longa*	2b	A	Safe for normal culinary use
Uva ursi	*Arctostaphylos uva ursi*	2b	C	See discussion under UTI
Wild indigo	*Baptisia tinctoria*	2b	NC	
Wormwood	*Artemisia absinthium*	2b/2c	D	
Yarrow	*Achillea millefolium*	2b	B3	Safe for topical application

TABLE **11-5**

The Australian TGA Classification for Drugs in Pregnancy

CATEGORY	DEFINITION
Category A	Drugs that have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.
Category B1	Drugs that have been taken by only a limited number of pregnancy women and women of childbearing age, without an increase in the frequency of malformations or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have not shown evidence of an increased occurrence of fetal damage.
Category B2	Drugs that have been taken by only a limited number of pregnancy women and women of childbearing age, without an increase in the frequency of malformations or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.
Category B3	Drugs that have been taken by only a limited number of pregnancy women and women of childbearing age, without an increase in the frequency of malformations or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have shown evidence of an increased occurrence of fetal damage, the significance of which is considered uncertain in humans.
Category C	Drugs that, owing to their pharmacologic effects, have caused or may be suspected of causing harmful effects in the human fetus or neonate without causing malformations. These effects may be reversible.
Category D	Drugs that have caused, are suspected to have caused, or may be expected to cause, an increased incidence of human fetal malformations or irreversible damage. These drugs also have adverse pharmacological effects.
Category X	Drugs that have such a high risk of causing permanent damage to the fetus that they should not be used in pregnancy or when there is a possibility of pregnancy.

Note: For drugs in B1, B2, or B3 categories, human data are lacking or inadequate and subcategorization is therefore based on available animal data. The allocation of a B category does NOT imply greater safety than the C category. Drugs in category D are NOT absolutely contraindicated in pregnancy (e.g., anticonvulsants). Moreover, in some cases the D category has been assigned on the basis of suspicion.

TABLE **11-6**

Mills and Bone Classification for Herbs in Pregnancy

CATEGORY	EXAMPLES
Category A	Bilberry fruit, Chamomile (German), Cranberry, Echinacea, Garlic, Ginger, Ginseng,* Licorice,* Raspberry leaf, Senna,* Turmeric
Category B1	Astragalus, Blue flag, Boswellia, Bupleurum, Burdock, Butcher's broom, Chaste tree, Codonopsis, Evening primrose oil, Ginkgo, Goat's rue, Gotu kola, Hawthorn, Kava, Myrrh, Passionflower, Rosemary, Schisandra, Siberian ginseng, St. John's wort, St. Mary's thistle, Valerian, Willow bark, Withania
Category B2	Bacopa, Black cohosh, Black haw, Black walnut, Bladderwrack, Buchu, Calendula, California poppy, Cascara, Celery seed, Chickweed, Cleavers, Corn silk, Couch grass, Cramp bark, Cranesbill root, Damiana, Dandelion, Devil's claw, Elder flowers, Elecampane, Euphorbia, Eyebright, False unicorn, Fringe tree, Gentian, Globe artichoke, Golden rod, Grindelia, Gymnema, Hops, Horsetail, Hydrangea, Lavender, Lemon balm, Lime flowers, Marshmallow, Mullein, Nettle, Peppermint, Prickly ash, Pygeum, Saw palmetto, Shatavari, Skullcap, Thyme, Wild lettuce, Willow herb, Yellow dock, Ziziphus seed
Category B3	Aloe, Andrographis, Bittersweet, Crataeva, Ephedra, Fennel, Fenugreek, Feverfew, Horsechestnut, Meadowsweet, Motherwort, Rehmannia, Shepherd's purse, Tribulus, White horehound, Wild cherry, Yarrow
Category C	Barberry and Indian barberry, Bearberry, Bugleweed, Chaparral, Dong quai, Golden seal, Greater celandine, Guggul, Oregon grape, Pasque flower, Sage, Tylophora
Category D	Blue cohosh, Cat's claw, Jamaica dogwood, Pau d'arco, Poke root, Tansy, Thuja, Wormwood
Category X	Arnica, Boldo

*Recent literature suggests that the regular use of large amounts of licorice in pregnancy, including licorice candy containing real licorice extract (not just licorice or anise flavor) may lead to preterm birth. These other herbs are also contraindicated for use during pregnancy on other lists. Strandberg T, Andersson S, Jarvenpaa A, et al.: Preterm birth and licorice consumption during pregnancy, Am J Epidemiol 156(9): 803-805, 2002.

might use these guidelines to choose at which level(s) they are comfortable prescribing botanical medicines for pregnant women. For example, only those herbs that are considered benign or have been demonstrated to be safe would meet the criteria for category 1 (e.g., red raspberry leaf, ginger, and echinacea); those herbs definitively contraindicated, for example, the internal use of comfrey or other PA-containing herbs would be relegated to categories D or below. More conservative practitioners would have the option of recommending only those herbs in category A; others might prescribe from categories A to B3, herbs from categories C would primarily be avoided throughout pregnancy and would be contraindicated during first trimester, and those from D to X would be contraindicated entirely throughout pregnancy. Much work is still needed to be done to classify herbs according to this scheme, and classifications may shift as new data become available.

Based on their review of the literature using sources similar to those accepted in this text, they have developed the categorization that appears in Table 11-6. Mills and Bone clearly take the approach that with proper use and knowledge of risks and contraindications, herbs can be safely applied therapeutically during pregnancy and lactation. Their classification, however, itself introduces further inconsistencies and sometimes contradicts other recognized lists of herbs contraindicated during pregnancy. For example, Mills and Bone include in Category A, ''Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed,'' licorice, which is contraindicated for use during pregnancy in lists provided by Low Dog and McGuffin et al., among others, and which has recently been associated with premature delivery after regular consumption of licorice candy during pregnancy.[38–40] Their support of the use of senna as a category A herb is another example.

What becomes clear is that there is still a tremendous amount to be learned about the effects of herbs used during pregnancy, and given the inconsistencies, it is best for practitioners and patients to use only those herbs with a proven safety record or to use herbs during pregnancy only when the risks of a conventional medical therapy clearly outweighs theoretical but unproved risks of an herb otherwise recognized as generally safe, with the exception of a limited number of gentle nutritive or medicinal herbs that may be used safely.

FORMS OF ADMINISTRATION APPROPRIATE DURING PREGNANCY

The forms in which herbs are administered (e.g., tincture, tea) can affect their strength and efficacy. During pregnancy, various forms can be chosen to maximize or minimize the volume and availability of more or less desirable constituents in a preparation, as well as exposure to other unwanted substances, for example, using

water-based extracts to minimize extraction of bioactive compounds, or avoiding excessive consumption of alcohol in an alcohol-based preparation. Chapter 3 provides a full discussion of forms of administration. The following brief discussion addresses the specific nuances of administration of herbs during pregnancy.

Internal Forms of Herbal Medicines

Internally used preparations that might be considered during pregnancy include teas and infusions, decoctions, syrups, tinctures (alcohol- and glycerin-based), capsules, and rarely, enemas. Each of the internal forms offers specific advantages and disadvantages. For example, infusions are alcohol extracts and are less effective at extracting many of the bioactive compounds that are more readily extracted when alcohol, which is hydroethanolic, is used as a solvent. Thus, water-based preparations are considered by many herbalists to be gentler and safer. Further, because water-based preparations are more dilute than, for example, concentrated alcohol extracts, one must consume a larger volume of the preparation to approximate a comparable dose of a more concentrated form of preparation, thus being a limiting factor to excessive dosing.

The sheer unpalatability of many herbs, particularly those that are considered very strong medicinally or even toxic, frequently serves as an inherent mechanism to prevent excessive consumption of a harmful herb. The heightened taste sensitivity frequently accompanying pregnancy further reinforces this—many pregnant women find excessive consumption of liquids nauseating and thus they are only able to consume limited amounts of strong-tasting medicinal teas during the gestational period. Water-based preparations also allow ease in evaporating off strong essential oils from teas that are even considered safe for general use (e.g., chamomile, mint), but that do contain essential oil fractions.

A clear disadvantage of water-based preparations is that the volume of liquid (e.g., tea, infusion) one must consume for an effective dose may be difficult to achieve for the aforementioned reasons. Decoctions are concentrated water-based preparations made by simmering or long steeping of a larger quantity of herbs to water than is used for tea. They can be further reduced by simmering to a concentrate to which a sweetener is added for flavor, thickening, and as a preservative, allowing tablespoon-sized doses rather than cup-sized doses of herbs to be administrated. This can be an effective solution; however, for women who must limit their sugar intake because of gestational or true diabetes, the added sugar must be taken into account.

Tinctures, which are hydroethanolic extractions, offer the advantage of being highly concentrated and are self-preserved, allowing the patient to take small dose sizes. They eliminate the effort of preparation inherent in using teas. Thus, they are easy to consume and convenient. Taste often can be masked either by the addition of vegetable glycerin or a flavoring extract, or by ''hiding'' the dose in a small quantity of fruit juice. These factors often lead to increased compliance with a botanical protocol. However, there are disadvantages to tinctures. Because the water–alcohol combination is such an effective solvent, the medicines contain a full array of plant compounds, some of which might be undesirable for consumption during pregnancy. Additionally, there are concerns regarding the use of alcohol during pregnancy, although the volume of alcohol per dose is typically very small (e.g., in a 5-mL dose of a 40% alcohol tincture, the patient is receiving 2 mL of alcohol; even at three doses per day, this is ⅕ of an ounce of alcohol per day). However, in the first trimester, it may be advisable to avoid alcohol entirely. The practitioner and the patient need to determine the risks and benefits of using tinctures during pregnancy on an individual basis. Many naturopathic physicians, herbalists, and midwives are quite comfortable with their use on a limited, as-needed basis.

Capsules and pills, unless made from liquid extracts of freshly milled herb, are notoriously not fresh, and many herbalists consider them less than reliable medicines, preferring the use of water- and alcohol-based extracts. A number of companies, however, do make high-quality pills and capsules, using plant extracts rather than simply dried herbs bound with fillers. Understanding of manufacturing practices is essential in determining the quality and reliability of any herbal product.

Because of the high level of absorption that occurs through the intestinal mucosa, enemas may be classified as a form of internal administration. Although they are rarely given during pregnancy (there is some risk that the use of an enema during pregnancy can stimulate uterine contractions through stimulation of bowel evacuation), they can be extremely useful in limited conditions, such as hyperemesis gravidarum, when the pregnant mother is unable to take or retain anything orally. The herbal enema can be effective in providing both fluids and medicine that is well tolerated and retained via this route of administration.

External Forms of Herbal Medicines

Externally administered forms of herbal preparations include medicated and extracted oils, baths, compresses, washes, peri-washes, vaginal suppositories, creams, salves, and ointments. There is little risk from the topical use of botanical extracts, whether water-, oil-, or alcohol-based during pregnancy, and when applied primarily to unbroken skin. One exception is the topical use of concentrated, undiluted (neat) essential oils, which should be avoided. Extracted nonessential oils, for example, calendula oil, and many highly diluted essential oils can be used safely topically for the treatment of skin infections (e.g., fungal infections), for massage to promote relaxation (e.g., three to five drops of lavender and rose essential oils diluted in 2 tablespoons of a carrier oil such as almond oil), or for muscle spasms and aches (e.g., three to five drops each of wintergreen oil and cinnamon oil in 4 tablespoons of almond oil). Certain essential oils, however, are contraindicated for use during pregnancy.

Certain constituents, such as the hepatotoxic pyrrolizidine alkaloids present in comfrey, are capable of passing into the bloodstream through the skin. Although the risk is minimal from this small amount of potential exposure,

it may be wise to avoid prolonged use of comfrey-containing products on large areas of broken skin during pregnancy.

Vaginal suppositories (see Chapter 3) often may be used safely during pregnancy for the treatment of vaginal infections, providing the herbs they contain are safe for such use during pregnancy. Herbs with suspected or known teratogenicity or mutagenicity, such as thuja, should be avoided, as well as those that might cause uterine stimulation. However, herbs that are typically contraindicated for oral consumption often may be used vaginally in late pregnancy for the treatment of vaginal infection. This should be done with knowledge of the individual herbs in the preparation, or in consultation with a qualified herbalist. Douches should be avoided during pregnancy because of risk of embolism; peri-washes may be used for a vulvar and perineal rinse.

SUMMARY

Herbs can provide substantial relief of common complaints and concerns that arise during pregnancy and childbirth. The power of herbs should be respected during pregnancy, and therefore, they should be used with caution. However, many herbs may be contraindicated on the basis of very limited findings, erroneous reports, or by association with a problem rather than a proven causal effect. Many herbs that have not been evaluated may, nonetheless, offer simple, safe, gentle, and effective solutions for many common pregnancy problems ranging from anemia to vaginitis. Practitioners need to be better educated about patients' choices when it comes to herbal medicines, and further research needs to be conducted not only into the safety and efficacy of herbs for both the mother and her baby, but also a comparative safety analysis should be done with herbs and pharmaceuticals commonly used during pregnancy, and often without proper proof of safety during the childbearing cycle.

Fertility Challenges

Angela J. Hywood

12 CHAPTER

Infertility is defined as the inability to conceive after 12 months of unprotected intercourse in a couple of reproductive age attempting to conceive. Approximately 90% of couples achieve conception within this time, and a further 15% of normally fertile couples take longer than 12 months to become pregnant. Research has shown that even couples in their late thirties have a 91% chance of conceiving naturally within 2 years, and recent studies estimate that an average of 25% to 40% of women have a live birth without treatment during the 3 years after the first infertility consultation, even without treatment.[1–3] Nevertheless, of the approximately 60 million women of reproductive age in the United States in 1995, about 1.2 million, or 2%, had had an infertility-related medical appointment within the previous year and an additional 13% had received infertility services at some time in their lives.[4] This number has increased in recent decades because of societal demographic changes, particularly the aging of the baby boom generation, leading to an increased size of the reproductive age population, and more couples delaying fertility for the sake of careers.[1]

Infertility is not synonymous with sterility and it is important to differentiate these terms. Sterility is defined the inability to achieve pregnancy and affects only 1% to 2% of couples.[2] Primary infertility refers to those who have never before conceived and secondary infertility to those who have achieved conception some time in the past (regardless of pregnancy outcome) and thereafter became infertile.[5]

FEMALE FACTORS AFFECTING FERTILITY

The main types of female infertility include ovulatory disorders (25%) and tubal disease (20% to 25%), including endometriosis (10%). Ovulatory factors are suspected when menstrual abnormalities are reported. Male infertility is the primary cause in approximately 25% of cases and contributes to an additional 15% to 25% of cases. Infertility results from unexplained causes in up to 20% of cases.[1] Thorough evaluation of the couple will point to a probable cause in 85% to 90% of cases.[2] Ovarian factors are primarily associated with follicular phase disruptions. An inadequate luteal phase is said to account for only 3% to 4% of fertility failure. Examples of all of the factors that account for fertility challenges are listed in Table 12-1.

Unexplained and coexisting factors account for approximately 10% of infertility cases and can be a result of environmental and/or occupational exposure to toxicity such as heavy metals, radiation, solvents, DES, smoking, and exogenous androgens and/or estrogens from environmental and food sources. Nutritional deficiency, stress, and age can all contribute to fertility problems. Abnormal body mass index (BMI), including being underweight or overweight, can cause amenorrhea and infertility. The fertility of a woman begins to significantly decline between the ages of 35 to 38 and sharply declines after the age of 40.

MALE FACTORS AFFECTING FERTILITY

Male factors affecting fertility include:

- Endocrine disorders of the hypothalamus, pituitary, adrenal glands, thyroid
- Anatomical disorders of the male reproductive tract
- Sperm abnormalities
- Abnormal spermatogenesis resulting from chromosomal, infection, radiation, or chemical exposure
- Abnormal motility resulting from Kartagener's syndrome (the absence of cilia), testicular varicoceles, or antibody production (male immune-mediated infertility)
- Sexual dysfunction, including erectile and ejaculatory dysfunction or decreased libido
- Unexplained factors
- Environmental and occupational toxicity such as exposure to heavy metal, DES, radiation, and exogenous androgens and estrogens
- Nutritional deficiency, particularly zinc and selenium
- Psychological stressors

TABLE **12-1**

Causes of Fertility Challenges

FACTOR	EXAMPLES
Ovulatory	Defects of the ovaries Anovulatory cycles Hyperprolactinemia Hypothalamic dysfunction Pituitary dysfunction Gonadal dysgenesis Premature ovarian failure Ovarian resistance
Metabolic	Thyroid disorders Adrenal disorders Liver disease Renal disease Androgen excess (adrenal or neoplastic causes)
Pelvic	Common infection (genitourinary infections such as *Chlamydia trachomatis*, *Ureaplasma urealyticum*, *Mycoplasma hominis*, and *Neisseria gonorrhoeae* causing inflammation, infections and scar tissue) Chronic inflammation manifesting as pelvic inflammatory disease (PID) Uterine or fallopian adhesions Endometriosis (attributed to 5% of cases of infertility) Fibroids Structural abnormalities
Cervical (evident in only about 3% of cases)	Factors are and can include: Hostile mucus (sperm antibodies, abnormal viscosity or pH) Cervicitis and infections Acquired surgical damage to the mucus producing endocervical glands (cone biopsy, laser ablation, cryotherapy) associated with cervical dysplasia or neoplasia
Immune-mediated	Lack of blocking antibodies Autoimmune disease such as SLE Immunophenotypes Anti-thyroid antibodies Antiphospholipid syndrome (APS)

Data from Kaider A, Kaider B, Janowicz P, et al.: Immunodiagnostic evaluation in women with reproductive failure, Am J Reprod Immunol 42(6):335-346, 1999.

DIAGNOSIS

Initial evaluation of infertility must include a thorough workup of both partners for male and female factors that might cause fertility problems.

Evaluation of Male Factors

Primary evaluation includes:
- A thorough medical history and physical examination
- Semen analysis

A secondary evaluation is recommended and usually includes more holistic measures:
- Genitourinary infection screening
- Heavy metal screening
- Male hormone panel
- Adrenal stress index (ASI)

Semen analysis can rule out the most likely abnormalities in male factors. Sperm count, motility, morphology, pH, and white blood cell count need to be reviewed. If the male has not had a semen analysis within the past 3 months prior to the initial visit to the practitioner, it is suggested that this test be recommended. Spermatogenesis takes approximately 74 days; hence, the viability of the sperm will depend on the environment over the 74-day time frame in which the sperm were developing. If, for example, the man was exposed to dangerous solvents, toxic heavy metals, or radiation, his sperm parameters may reflect abnormalities. The morphology is the most relevant parameter to review, as this indicates the most likely chance of that sperm resulting in conception and hence the actual sperm viability. The percentage morphology reflects the number of normally shaped sperm within the sample.

Several genitourinary infections are known to significantly affect both male and female fertility, including *Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma hominis,* and *Neisseria gonorrhoeae*. Subclinical infection can contribute to unexplained infertility. Not only can these genitourinary tract infections adversely affect fertility, but they also can potentially cause miscarriage and birth defects.

Evaluation of Female Factors

Primary evaluation should include:
- Thorough medical history and physical examination
- Expanded female hormonal panel
- Evaluation for thyroid disorders
- Evaluation for immunologic disorders, including autoimmune conditions
- Genitourinary infection screening as described above for male evaluation
- Cervical cytology

A secondary evaluation is recommended, especially for unidentified infertility:
- Heavy metal screening
- Salivary adrenal stress index (ASI)

In a tertiary evaluation for pelvic factors, minor surgery is often required. These tests require referral to a reproductive medical specialist. These tests and

procedures, although sometimes necessary, are invasive, painful, and expensive:

- Hysterosalpingogram for investigation of tubal patency, congenital malformations, polyps, and distal and proximal occlusions
- Transvaginal ultrasound for detection and monitoring of the developing follicle on the ovary
- Endometrial biopsy sampling to determine the maturation of the endometria
- Laparoscopy for detection of tubal abnormalities such as agglutinated fimbria or adhesions, tubal cysts, and endometriosis
- Serum tests for immune-mediated infertility

Mutual Fertility Testing

The post coital test (Sims-Huhner Test) is an evaluation of the sperm's interaction within cervical mucus postcoitally. This test is designed to evaluate the number of sperm that survive within the mucus and their duration of survival. This test can rule out parameters such as inadequate quantity and clarity of cervical mucus, spinnbarkeit of greater than 8 cm, and non-forward progressive sperm in the mucus. When the quality and quantity of mucus is good, yet the test results are abnormal, then further evaluation for cervical mucus antisperm antibodies is warranted. It is a debatable test for efficacy but is used to assess cervical hostility to sperm. Hostile mucus can result from the presence of sperm antibodies and/or an unfavorable pH of cervical mucus.

Noninvasive Home Evaluation and Patient Participation: Thermo-Symptal Monitoring and Mucus and Cervical Evaluation for Detection of Ovulation

As fertility evaluation can be physically invasive, traumatic, and cost prohibitive, there are some useful tests women can do themselves at home. One easy technique is Thermo-Symptal monitoring, which involves the monitoring and recording of the basal body temperature (BBT) and recording of cervical mucus secretions on a daily basis throughout the cycle. Although convenient and cost-effective, Thermo-Symptal monitoring requires consistent commitment and a learned awareness of the body's subtle signs of fertility. This awareness can help the couple refine conception timing and allow the woman sense of participation in her own program toward achieving pregnancy.

Basal Body Temperature Monitoring

The luteal phase of the cycle is characterized by the production of progesterone from the corpus luteum. Progesterone is a thermogenic hormone elevating the core body temperature in the luteal phase of the cycle. When adequate progesterone is produced as a result of ovulation having occurred, the BBT elevates and remains elevated for approximately 10 days after ovulation, until either menses occurs, in which the temperature will drop, or pregnancy is established, in which the temperature will continue to elevate to a third phase as the progesterone continues to be produced into the pregnancy. This elevation in temperature usually occurs 1 to 2 days after ovulation.

Interpretation of the Basal Body Temperature

In the follicular, preovulatory phase of the menstrual cycle in a healthy woman, the temperature reading is approximately 97°F. An increase in temperature greater than 97°F in the luteal phase, after day 13 or 14, is indicative of a normal ovulation in 90% of cases. If the temperature maintains above this temperature after 16 days, this is suggestive of pregnancy. The BBT is measured orally first thing upon waking in the morning, before any activity, with a specific fertility thermometer (thermocrystal basal thermometer). The temperature is best taken at the same time each day, after at least 6 hours of sleep. The routine should commence on the first day of her cycle, which corresponds to the first day of menstrual flow. Sleeping with an electric blanket, heated waterbeds, or other heating or cooling devices near the body may disrupt the BBT and adversely affect the reading; hence, they need to be avoided while monitoring BBT. BBT cannot be used by the couple to predict ovulation; it only confirms ovulation retrospectively by indicating the event of luteinization but is considered a relatively reliable assessment of the preovulatory phase. Therefore, used as a single tool, it proves to be of limited value. When BBT is monitored concurrently with cervical mucus observations, it can be a very informative and valuable tool for the couple.

Monitoring Cervical Mucus Changes

Daily monitoring of the texture, quality, and quantity of cervical mucus secretions can be useful to predict ovulation. Cervical mucus secretions change throughout the cycle under the influence of estrogen and progesterone. Approximately 2 or 3 days before ovulation occurs, the estrogen levels peak and the nature of the mucus changes from a pasty thick or milky consistency to a distinctive ''spinnbarkeit'': stretchy mucus (usually 6 to 10 cm) of wet consistency and opaque color. It resembles a similar texture and nature to raw egg white. At this stage of the cycle, the mucus is an optimal reservoir to nourish sperm and encourage their survival for conception. When seen under a microscope, fertile spinnbarkeit mucus dries into a distinctive crystalline fernlike pattern. Small, inexpensive ovulation predictor microscopes for home use are available to assist couples in predicting ovulation. Saliva is usually used on the microscope as an alternative to cervical mucus, because saliva mimics the ferning pattern of the spinnbarkeit at the ovulation time. When estrogen levels are lower in the early follicular phase and midluteal phase of the cycle, the mucus secretions are thin, milky, and sparse in nature. When a woman is monitoring cervical mucus, it is recommended she feel the texture of the mucus (at the vaginal opening) between the forefinger and thumb and not use toilet tissue to collect the sample. It absorbs moisture and may lead to misinterpretation of the mucus viscosity. Home test kits that measure urinary LH levels are available for ovulation prediction. These are single use tests and their disadvantage is the expense when used regularly.

The Texture and Shape of the Cervix

Some women experiencing infertility may produce inadequate quantities of cervical mucus or experience difficulty feeling the texture of the mucus. In this case, she can be taught to feel the texture of the cervix itself. When cervical tissue is not under the influence of peak estrogen levels it feels hard, cartilaginous (imagine feeling the end of the nose; this is a similar texture), and the cervical os is closed. At the time of the LH surge and estrogen peak, the cervix becomes soft, ''ripe,'' and palpable (imagine feeling the texture of the cheeks; this is a similar texture) and the cervical os is slightly open.

CONVENTIONAL TREATMENT APPROACHES

Despite developments in fertility knowledge and technologies, the overall prognosis for achieving childbirth with reproductive technologies is approximately 50%, and declines as women age. Each treatment option has overt and hidden costs, including emotional, physical, and financial burdens, often without justification because of lack of success. Couples entering fertility treatment need to be fully cognizant of the potential price of treatment in all of these areas, and the benefit vs. costs must be evaluated. Patients must also consider the high frequency and implications of a multiple pregnancy, a common outcome with assisted reproductive technologies. Psychological support should be available to all couples considering reproductive technologies, with no blame laid upon either partner, and a realistic appraisal of the chances for success and failure of treatment honestly provided. Reproductive expert Marcelle Cedars advises, ''The option of child-free living should also be included in any discussion. At times couples must be advised to stop treatment if the likelihood for success is quite low. Frequently this is a very difficult time for both the patient and the physician, but fruitless treatment should be avoided.''[1]

Ovulatory Factors

The conventional treatment of ovulatory factors is determined by the conclusive diagnosis made after clinical investigation. With conventional infertility therapy, the chances of conception are said to be 15% to 25% per cycle, depending on the degree of drug-induced ovarian stimulation. If failure to conceive after a maximum of 12 cycles persists, then assisted reproductive technology (ART) is recommended as the next option by allopathic medical reproductive specialists.

Ovarian Stimulation Therapy

Induction of ovulation is said to be successful in 90% to 95% of cases with administration of particular pharmaceutical drugs in a given scenario. Each given scenario depends on a specific set of circumstances, such as hormonal imbalances or failure of a prior drug approach.

In cases of elevated FSH, indicating ovarian failure, postmenopause or ovarian resistance, fertility cannot be restored using drugs. Options for these women include adoption, or embryo or egg donation. Success of pregnancy with embryo or egg donation is reported to be approximately 40%, but this does not reflect live birth statistics for the given scenario. This scenario also gives rise to multifactorial ethical, legal, financial, and psychosocial issues. In the case of chronic anovulation with normal FSH and normal prolactin levels, first line therapy is Clomiphene citrate, a nonsteroidal, antiestrogen drug. This drug is prescribed for women with oligomenorrhea, amenorrhea (including polycystic ovarian syndrome and psychogenic amenorrhea), and women who have sufficient estradiol levels or luteal phase deficiency (progesterone failure). This is administered orally at 50 to 250 mg daily orally on days 5 to 10 of the cycle. It is often combined with corticosteroids, estrogen, and midcycle human chorionic gonadotrophin (hcG) and followed up with monthly hormonal testing or ultrasound to establish the drug's efficacy in stimulating the follicle and ovulation. Clomiphene citrate is reported to be successful in stimulating ovulation in 70% of cases. The pregnancy rate from use of this drug is only 35%. In 50% of women who use Clomiphene citrate, it stimulates more than one follicle, and the incidence of multiple births is 8%. It is recommended that it not be used for longer than six cycles. Use for longer than 12 months may increase the risk of ovarian cancer. Side effects of Clomiphene citrate include hot flashes, breast tenderness, mood swings, visual problems, thick cervical mucus, luteal phase deficiency (although it is routinely prescribed for this problem), ovarian enlargement, abdominal-pelvis bloating, and discomfort. Ovarian hyperstimulation syndrome has been associated with this drug therapy.

Where there is failure to respond to Clomiphene citrate, or in patients with pituitary insufficiency and/or hypothalamic insufficiency, unexplained infertility, or endometriosis, a second line of treatment is used to induce ovarian stimulation: human menopausal gonadotropin (hMG), a pituitary peptide hormone. This is a combination of FSH and LH derived from the urine of menopausal women. Administration is by intramuscular injection one to two times per day at a dose of 75 to 600 IU/day. This drug regime is also used to stimulate the ovaries in preparation for assisted reproductive technology (ART) procedures such as in vitro fertilization (IVF), gamete intrafallopian transfer (GIFT), or zygote intrafallopian transfer (ZIFT). It is said to be successful in stimulating ovulation in 85% to 90% of cases. It increases the multiple pregnancy rates up to 20% and increases the risk of both ovarian hyperstimulation syndrome and ovarian cancer. Side effects include mood swings and ovarian hyperstimulation.

When the diagnosis of hypothalamic dysfunction has been established and ovarian stimulation using Clomiphene citrate fails, the addition of gonadotrophin releasing hormone (GnRH), a hormone produced by the hypothalamus is administered. This is infused by pump into the indwelling and one side effect is potential infection of the indwelling line. This step is said to restore ovulation in nearly all cases. Restoring ovulation does not necessarily result in a successful pregnancy.

When elevated prolactin levels are causing amenorrhea or luteal phase defects are confirmed (e.g., in PCOS), bromocriptine is used. In this circumstance, thyroid function is also evaluated, as primary

hypothyroidism can cause elevated prolactin levels. Many pharmaceutical drugs can also cause hyperprolactinemia as a side effect. This needs to be considered and ruled out. Hyperprolactinemia is treated using bromocriptine, a dopamine agonist. Administration is either oral or vaginally at doses of 2.5 mg twice daily or 0.5 mg twice a week. Bromocriptine does not increase the risk of inducing multiple pregnancies. Side effects include weakness, nausea, and nasal congestion.

Pelvic Factors

Endometriosis and the effects of salpingitis are the most common problems causing infertility related to pelvic factors. These affect the structural health of the fallopian tubes, as well as uterine and endometrial tissue. Salpingitis is usually caused by infections with microorganisms such as *Neisseria gonorrhea* and *Chlamydia trichomatosis;* other infective organisms include *Escherichia coli, Mycoplasma hominis,* and *Ureaplasma urealyticum*.[7] Bacterial vaginosis is common among these women. Antibiotic drugs are the usual treatment for these infections.[8] The treatment option for moderate and advanced endometriosis is usually surgical; at the time of a laparoscopy, resection and ablation is performed. Fibroids are usually left untouched and are only addressed if multiple miscarriages have been a problem. ART is available for those who are unable to conceive after surgery for common pelvic factors.

Cervical Factors

Inadequate cervical mucus midcycle is treated in one of two ways. Either low-dose estrogen is given mid to late in the follicular phase or human menopausal gonadotrophin (hMG) is given to stimulate ovarian production of estrogen. If this fails, the couples are recommended to artificial insemination (AI), one of the oldest of the fertility treatments still used. If cervicitis is a possible causal factor, the antibiotic doxycycline is administered. If surgery (commonly cone biopsy or laser ablation) or congenital issues render the endocervical glands absent or damaged, intrauterine insemination (IUI) procedures can result in pregnancy in 20% to 30% of cases within three cycles of treatment. Those who fail to have a positive outcome are offered the possibility of IVF, GIFT, or ZIFT.

Unexplained Infertility

When both partners' evaluations yield negative results, this is defined as unexplained infertility. This is found in only 10% of cases.[8] The main courses of treatment for couples with unexplained fertility include observation of the cycle and refining of timing techniques for intercourse, ovarian stimulation, IUI, GIFT, and IVF.

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

Botanical treatment of infertility cannot address overt physical impediments to fertility; however, it can provide treatment and support for numerous fertility-related problems, such as hormonal dysregulation, thyroid and adrenal disorders, genitourinary infections, immune dysregulation, and stress-related problems (Table 12-2). The herbal consultation also takes into account factors such as nutritional deficiency and occupational/environmental exposures. Most importantly, a holistic practitioner reviews the case as a totality of contributing factors, not simply a reproductive issue.

Fertility challenges should be approached as an opportunity for the couple to engage in an active treatment plan to improve their overall health, rather than just a quest for reproduction. Couples should be encouraged to participate in a 3- to 4-month period of preconception care, in which their overall health can be improved with the use of herbs, nutrition, and dietary and lifestyle modification. Thus, not only will they then improve their chance of natural conception, but they will be more likely to have a healthy, complication-free pregnancy and a healthy child. Additionally, for many couples, the attempt to conceive can become mechanical, lacking in passion, and plagued by a repeating cycle of expectation and disappointment. Ideally, botanical treatments for infertility attend to this problem, offering common sense and herbal strategies for restoring sensuality and passion to conception.

Herbal therapy requires a minimum commitment of 3 to 4 months to improve the fertility of a couple prior to conception, and in general, is ideally done when the couple is not concurrently taking any pharmaceutical fertility drug. Herbal medicines and nutritional supplements are prescribed for each individual situation, with appropriate dietary and lifestyle modification, stress management, and detoxification measures, if necessary (e.g., caused by environmental toxin exposure). The protocol should be revised on a regular basis (e.g., monthly) until conception occurs. If conception has not resulted after 12 months of holistic therapy, then other medical options may be considered. The treatment protocol in the remainder of this chapter focuses on botanical treatments for female fertility.

Herbs that enhance fertility might be divided into categories, and although they may overlap, they serve different purposes in nurturing reproductive health as well as general wellness. These categories include nutritive herbs that build the blood (e.g., rehmannia, dong quai) and support hepatic function (e.g., milk thistle), herbs that restore hormonal balance (e.g., chaste berry) and impart pelvic tone (e.g., shatavari), herbs that improve pelvic circulation (e.g., dong quai), and adaptogenic (e.g., ashwagandha), and nervine herbs (e.g., vervain), which help to reduce stress and improve the stress response.

Herbs can also be used externally in the form of essential oils to stimulate sexual desire (aphrodisiacs), and include amber, sandalwood, rose, jasmine, and ylang-ylang. A few drops can be carefully placed on the body (slightly diluted in a carrier oil such as almond oil), used in an atomizer to scent the air, sprinkled onto linens, or placed in a bath.

DISCUSSION OF BOTANICAL PROTOCOL

Black Cohosh

Black cohosh was thought to have estrogen-modulating activity and is used for both ovarian insufficiency

TABLE **12-2**

Botanical Treatment Strategies for Female Infertility

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Hormonal regulation	Pro-estrogenic	*Actaea racemosa*	Dong quai
Fertility tonic	Pro-progesterogenic	*Angelica sinensis*	Shatavari
	Reproductive tonic	*Asparagus racemosa*	Black cohosh
	Regulate prolactin	*Dioscorea villosa*	Wild yam
	Unknown activities	*Chamaelirium luteum*	False unicorn
		Paeonia lactiflora	White peony
		Serenoa repens	Saw palmetto
		Tribulus terrestris	Tribulus
		Vitex agnus-castus	Chaste berry
Support immune response	Antimicrobial	*Albizzia lebbeck*	Albizzia
Treat vaginal infection	Immunotonic	*Echinacea spp.*	Echinacea
Reduce inflammation	Anti-inflammatory	*Glycyrrhiza glabra*	Licorice
		Hydrastis canadensis	Goldenseal
Detoxification of environmental toxins	Promote phase 1 and Phase 2 detoxification	*Bupleurum falcatum*	Bupleurum
		Picrorrhiza kurroa	Picrorrhiza
	Support hepatic function	*Schisandra chinensis*	Schisandra
		Silybum marianum	Milk thistle
	Antioxidant activity	*Camellia sinensis*	Green tea
		Curcuma longa	Tumeric
		Ginkgo biloba	Ginkgo
		Rosmarinus officinalis	Rosemary
		Silybum marianum	Milk thistle
		Vitis viniera	Grape seed
Relieve stress	Nervines	*Avena sativa*	Milky oats
		Leonurus cardiaca	Motherwort
		Matricaria recutita	Chamomile
		Melissa officinalis	Lemon balm
		Scutellaria lateriflora	Skullcap
		Stachys betonica	Wood betony
			(Also see index for references to nervines throughout the text)
	Adaptogens	See Chapter 8	

affecting fertility and estrogen dominance affecting infertility (e.g., one factor in PCOS) (See Plant Profiles: Black cohosh for a discussion on the research and possible mechanisms of action). It has been described as a selective estrogen receptor modulator (SERM). It was a favorite herb of the native North American Indians and Eclectic physicians for amenorrhea, as a uterine tonic and a number of other gynecologic applications.[9–11] Black cohosh has been subjected to extensive clinical trials, demonstrating some estrogen-modulating activity and ability to reduce elevated LH levels, while not affecting FSH and prolactin in any way. In modern herbal applications, black cohosh is indicated for infertility associated with anovulation, PCOS, ovulatory pain, and secondary amenorrhea. Some common side effects have been noted, including a frontal headache with a dull, full, or bursting feeling and a low frequency of stomach complaints, including nausea and vomiting. These side effects are most likely with the high end of a therapeutic daily dose. Recent concerns have arisen that black cohosh may be associated with liver disease, including liver failure; therefore, caution should be observed with its use. (See Plant Profiles: Black cohosh.) It is recommended that this herb be avoided in pregnancy.

Chaste Berry

Chaste berry has a long history of use for regulating menstrual cycles, which may result from its ability to regulate prolactin levels, enhance corpus luteum development, and correct relative progesterone deficiency. Vitex is beneficial for ovulatory factors associated with infertility, in particular, modulating the anterior pituitary's production of luteinizing hormone (LH), while mildly inhibiting follicle stimulating hormone (FSH). Vitex has been shown to downregulate the production of excess prolactin in hyperprolactinemia via dopaminergic activity.[9,12] In an uncontrolled study, chaste berry reduced elevated prolactin levels in 80% of 34 women with hyperprolactinemia at a dosage of 30 to 40 mg per day for 1 month and improved symptoms of a variety of menstrual disorders,

including secondary amenorrhea, cystic hyperplasia of the endometrium, deficient corpus luteum function, metrorrhagia, polymenorrhea, and oligomenorrhea.[9] Chaste berry reduces thyroxin-releasing hormone (TRH)–induced prolactin release (essentially a pituitary–thyroid axis problem), normalizes shortened luteal phases, corrects luteal phase progesterone deficiencies, and reduces PMS symptoms in women with luteal phase defects caused by latent hyperprolactinemia. In two uncontrolled studies involving 45 infertile women with normal prolactin and pathologically low progesterone, 39 of the women achieved pregnancy after 3 months on chaste berry. In a second study involving 31 women with infertility, after 3 months 15 of these women were pregnant. Of these, seven women who became pregnant using chaste berry, seven previously had amenorrhea, four had luteal insufficiency, and four had been diagnosed with unexplained infertility.

Chaste berry should be considered a first-line botanical therapy for infertility associated with secondary amenorrhea, hyperprolactinemia, and luteal insufficiency, and should be given for a duration of at least 3 to 6 months. Chaste berry is particularly effective in restoring the menstrual cycle in a woman after years of taking oral contraceptive pills and improving low LH levels. The daily dose of chaste berry needed to improve ovulatory factors affecting fertility is 1 to 4 mL tincture or 500 to 1000 mg of dried berries daily. It is best taken as a single dose in the morning. Chaste berry is preferably not taken with other progesterone drugs and may interact antagonistically with pharmaceutical dopamine receptor antagonist drugs.

Dong Quai

Dong quai has been used in traditional Chinese medicine (TCM) as a female reproductive tonic, menstrual regulator, and remedy for amenorrhea for at least 20 centuries. Dong quai is regarded as a tonic for women with fatigue and low vitality. Traditional prescribing indicated dong quai for conditions of what is referred to as congealed blood evidenced by clots in the menstrual blood, endometriosis, and dark, sluggish menstrual flow, and is typically used in formulas to harmonize the blood. In one uncontrolled trial involving infertility resulting from tubal occlusion, a dong quai extract was administered via vaginal irrigation (douche) for up to 9 months. Approximately 80% of the women regained tubal patency and 53% became pregnant. The known constituents of dong quai include coumarins, essential oils, ferulic acids, psoralens, and vitamin B_{12} and folinic acid, the active form of folic acid. Dong quai does not have estrogenic activity.

Dong quai is contraindicated for women with heavy bleeding and those with a history of spontaneous miscarriage. This herb is contraindicated for use with warfarin and anticoagulant medications, as it may increase bleeding time.

False Unicorn

False unicorn has been used historically as a female reproductive tonic, particularly for infertility and atony of the female reproductive organs. It was used by the Eclectic physicians as a uterine tonic to promote tone and vigor of the reproductive organs. For infertility, false unicorn is used when there is insufficient cervical mucus and amenorrhea. It was considered useful for congestion or stagnation of the uterus and ovaries, in which the menstrual blood is dark, sluggish, and clotted. Although not well characterized phytochemically, the steroidal saponins chamaelirin and diosgenin have been identified in false unicorn, and are postulated to exert an estrogen-modulating activity via interaction with estrogen receptor sites of the hypothalamus. There is no known toxicity or contraindication to use of false unicorn; however, this plant is a threatened species because of excessive wild harvesting and may soon be endangered. Therefore, this herb should only be used if other steroidal saponin–containing herbs such as tribulus and wild yam do not deliver a desired result and only when absolutely indicated.

Goldenseal

Goldenseal was the chief herb used by the Eclectics as a mucus membrane tonic. It was used for acute and subacute inflammation of the mucus membranes, especially when accompanied by discharge or mucus catarrh. It is valuable for the treatment for inflammation and infection of the genitourinary tract. The constituents include isoquinoline alkaloids, hydrastine, berberine, hydrastinine, and canadine. Hydrastis is a valuable remedy for ulceration, inflammation, and erosion of the cervix, affecting both quality and quantity of the cervical mucus. It can be used in both topical and internal applications.

Shatavari

Shatavari is a traditional Ayurvedic herb. The root is used medicinally. In the Indian medicine system, shatavari is said to ''give her capacity to have a hundred husbands.''[13] In traditional Ayurvedic gynecologic prescribing, shatavari has been used as a nutritive tonic, general female reproductive tonic, fertility tonic, treatment for sexual debility, and as an aphrodisiac. It has also been used traditionally as a tonic for lactating women to improve the quality and quantity of breast milk. Pharmacologic research has found the key constituents of shatavari are steroidal saponins, including shatavarin-I, alkaloids, and mucilage. The presences of the steroidal saponins suggest shatavari's activity as an estrogen modulator and a menstrual cycle regulator. Shatavari has adaptogenic and immunomodulating properties and can be used as a very useful tonic herb for women with stress-induced and immune-mediated infertility. It has antibacterial action; hence, it should be considered a general reproductive tonic for any woman who has a history of genitourinary infections. There are no known contraindications to the use of shatavari. The daily dose is 4.5 to 8.5 mL of a dried plant extract.

Saw Palmetto

The Eclectic physicians used saw palmetto as a urinary and reproductive tract remedy for inflammation. It was widely used for ovarian pain, pelvic congestion, and

atrophy of the ovaries. It proves to be a useful herb to include for infertility in cases of pelvic factors associated with infertility and infertility caused by PCOS. It is known to inhibit the production of prolactin from the pituitary.[20] If there is a history of genitourinary infection or pelvic inflammatory disease (PID), Saw palmetto is a valuable herb. The daily dose is 2 to 4 mL of a dried plant extract.

Tribulus

There is little information on the traditional use of tribulus leaf. In Ayurvedic medicine, the fruit has been used for improving male fertility and male erectile function, uterine disorders, urinary disorders, kidney stones, gout, and gonorrhea. As a result of Bulgarian research, tribulus has become a popular herb for the treatment of infertility, menopause, and low libido. It acts as a general tonic, aphrodisiac, and is used to restore vitality, reduce the physiologic effects of stress, and is a powerful fertility tonic for both men and women.[9]

Open-label clinical trials have demonstrated improvements in both male and female infertility.[14] Bulgarian research has identified a unique steroidal saponin known as a furostanol saponin, calculated to no less than 45% protodioscin. The leaf is noted to be higher in the unique saponin than the fruit. Other active constituents include phytosterols and spirostanol glycosides. The results of studies and clinical trials with tribulus have been remarkable, both in animal and human models. When given at a dose of 750 mg per day for 5 days it increased serum FSH and estradiol when compared with baseline in females, and increased LH and testosterone in males, demonstrating an increase in sex hormone production for both men and women.[9] The steroidal saponins are thought to bind and weakly stimulate the hypothalamic estrogen receptor sites. The tonic activities of tribulus have been shown to act by intensifying protein synthesis and enhancing the activity of enzymes associated with energy metabolism. It increases iron absorption from the small intestines and inhibits lipid peroxidation during stress. This leads to more muscle strength and improved endurance and stamina.[9] Another stunning study showed that tribulus increased serum growth hormone, insulin, and aldosterone without exceeding normal values. Protodioscin, the steroidal saponin in tribulus, has been shown to improve sexual desire via the conversion of protodioscine to dehydroepiandrosterone (DHEA).[15] It has been observed that tribulus grown in different soils does not consistently produce the important active furosterol, protodiocin. To ensure the desired clinical results, it is recommended to use only Bulgarian-grown tribulus standardized to 40% furosterol saponins by UV analysis. It is not interchangeable with Chinese or Indian tribulus. When samples of these were analyzed, they were shown to contain only 3% steroidal saponins by UV analysis, and none of these steroidal saponins are the unique and desirable furosterols. Specific female fertility studies have been conducted with tribulus. In an open study with 36 infertile women who were given tribulus on days 5 to 14 of the menstrual cycle for 2 to 3 months, 6% became pregnant as a result of normalized ovulation, 61% demonstrated normalized ovulation and no pregnancy, and 33% demonstrated no effect from tribulus within the 2- to 3-month time frame of the study.[16] In this same study, another subgroup of women used tribulus concurrently with pharmaceutical ovarian stimulation with the drug epimestrol. Of the 62 women in this group, within 2 to 3 months, 39% had normalized ovulation and resultant pregnancy, 35% had normalized ovulation with no pregnancy, and the remaining 26% had no effect from the combined therapy. The results obtained from using tribulus concurrently with epimestrol were better than using the drug alone.

Although no increased frequency of fetal malformation or other harm has been observed in limited use by women during pregnancy, tribulus is considered contraindicated in pregnancy according to TCM, and in at least one animal study, decreased survival in the offspring of penned pregnant ewes fed the herb was observed.[14] Animal studies of the minor alkaloid fraction of tribulus indicate that it inhibits acetylcholine, depressing activity of the frog heart in situ. The aqueous fraction produced mild hypotension. In dogs, an alcoholic extract of the whole plant produced a sharp vasodepression through a cholinergic mechanism.[16] Ingestion of tribulus by sheep produced outbreaks of a locomotor disorder known as staggers, an asymmetric locomotor disorder in sheep produced by a central functional abnormality.[17] Ingestion of tribulus caused photosensitivity in animals. No human or animal teratogenicity data are available, and scientific evidence for the safe use of tribulus during pregnancy is not available. The daily dose of tribulus is equivalent to 40 g per day of dried leaf or a concentrated extract standardized to contain a minimum of furostanon saponins as protodioscin at 300 to 400 mg per day. It is best used on days 5 to 14 of the menstrual cycle for enhanced fertility. It is essential to ensure phytoequivalence for optimal therapeutic outcomes. It is advisable to discontinue tribulus use during the luteal phase of the menstrual cycle, and to absolutely not resume use if pregnancy is suspected.

White Peony

White peony is commonly used in traditional Chinese and Japanese medicine for gynecologic conditions. It is generally used for infertility associated with PCOS, hyperprolactinemia, endometriosis, ovarian failure, and androgen excess. Paeonia has been shown to positively influence low progesterone, reduce elevated androgens (testosterone), and modulate estrogen and prolactin. In vitro, the active constituent paeoniflorin has been shown to affect the ovarian follicle by its action on the aromatase enzyme. Aromatase is important for follicular maturation, ovulation and corpus luteum function, steroid hormone synthesis, and the regulation of conversion of androgens to estrogens. The biofeedback in the pituitary and hypothalamus rely on aromatase to regulate prolactin and gonadotrophin-releasing hormone (GnRH). Excess levels of prolactin and GnRH inhibit the activity of aromatase. In TCM, Paeonia is always used in combination with other herbs. A TCM formula that

contains Paeonia lactiflora and used in application for infertility is Keishi-bukuryo-gan (TJ-25) or Cinnamon and Hoelen Formula. One study with TJ-25 demonstrated, when used for 14 consecutive days in rats, increased plasma levels of LH by 94%, FSH by 67%, and estradiol by 50%. This formula is thought to be a GnRH antagonist and mildly antiestrogenic. When combined with Glycyrrhiza glabra, Paeonia lactiflora is effective at promoting fertility and improving pregnancy rates in cases of androgen excess, as learned from the TCM Licorice and Peony Formula.[18] This combination regulated LH to FSH ratios.

Wild Yam

Wild yam has been used traditionally for uterine and ovarian spasm, including dysmenorrhea. When used for infertility it is employed to optimize estrogen levels and improve the quality and quantity of cervical mucus, if the cervical mucus is too viscous or too sparse. The active constituents of wild yam include the steroidal saponins dioscin and gracilin and soquinuclidine alkaloids such as dioscorine and tannins. It is useful as an antispasmodic to sooth oviductal and fallopian tube spasm, which can interfere with conception and implantation. For optimal bioavailability, the herb relies on adequate gut flora to enable to conversion of the steroidal saponin aglycone diosin to diosgenin. It is currently speculated that the bowel flora consumes a glycoside molecule from diosin, liberating diosgenin. Diosgenin is absorbed through the mucous membranes of the bowel into the bloodstream. Diosgenin may exert its effect by interaction at the hypothalamic estrogen receptor sites, regulating the production of estrogen by encouraging an increased production of FSH from the pituitary. Wild yam has demonstrated an estrogenic activity in vitro, and was shown to enhance estradiol by binding to estrogen receptor cites. Wild yam has no known side effects, interactions, or contraindications.

Immune Support

Immunologic factors affecting fertility are prevalent. Most cases result in recurrent spontaneous miscarriage; however, in some cases immunologic concerns prevent conception. The development of antisperm antibodies is one such circumstance. In study of 1020 female patients with primary or secondary infertility, serum antisperm antibody, antiovarian antibody, antiendometrial antibody, and anti-hCG antibody levels were tested. Patients were treated with dexamethasone, vitamin E, and vitamin C for three cycles consecutively as one course. After one course of treatment with corticosteroids, the disappearance rates of the antibodies mentioned were over 90%, and the average pregnancy rate was up to 30%. Corticosteroid use is associated with significant side effects.[8] Herbs can be used either as an alternative first-line therapy or concurrently. An example of herb–drug synergy was seen when *Glycyrrhiza glabra* and cortisone ere successfully used together to minimize the dose dependence of the corticosteroid drug.[9] *Glycyrrhiza glabra* has a cortisol-sparing action, as well as anti-inflammatory and adrenal restorative actions. It is contraindicated in hypertension, and steroid doses need to be modulated.

Rehmannia glutinosa is also of benefit in immune-mediated infertility and subfertility. Constituents in cured (cooked in wine) rehmannia, known as di huang, have been shown to inhibit antibody formation and reduce allergic reaction. Rehmannia has been shown to reduce the suppressive side effects of corticosteroid drugs on endogenous levels of corticosteroids and would be a valuable adjunctive therapy for a woman with immune-mediated infertility if already taking this drug therapy. It is sweet and warm in property and has been used to regulate menstruation and promote blood production, and is preferred in this application over the raw Rehmannia.

Echinacea is a well-known traditional immune-enhancing herb. It was widely used by Native Americans and then adopted by the Eclectic physicians for general immune support and infections. It is beneficial in the preconception stage of an infertility protocol to help immune surveillance. Echinacea can be aptly described as an immune modulator, assisting in enhanced phagocytosis and immune recognition. This may just be the key factor needed to regulate or prevent the onset of an autoimmune issue preventing conception or continued pregnancy. This action of echinacea is thought to be as a result of the presence of alkyl amides within the Echinacea root.[19]

Albizzia is a traditional Ayurvedic herb with antiallergenic properties. It has been shown to stabilize mast cells, reducing levels of allergy-inducing antibodies.[20] Although not phytochemically well defined, albizzia is a useful herb to support women who are producing antisperm antibodies.

NUTRITIONAL CONSIDERATIONS

Diet can play a significant role in fertility. Specific nutrients enhance normal reproductive function and fertility, thus assist in resolving conception problems when these are insufficient in the diet. These include zinc (found in pumpkin and sunflower seeds, brewer's yeast, wheat germ, soybeans, eggs, seafoods, and meats), calcium (found in dairy products, leafy green vegetables, seaweeds, almonds, and blackstrap molasses), magnesium (found in whole grains, dark-green veggies, blackstrap molasses, nuts, and seafoods), vitamin C (found in citrus fruits, rose hips, cherries, currants, alfalfa sprouts, cantaloupe, strawberries, broccoli, peppers, and tomatoes), and folic acid (found in dark-green leafy vegetables, root vegetables, whole grains, milk, salmon, and brewer's yeast). Essential fatty acids, found in wild cold water fish, most vegetable oils, flaxseed oil, evening primrose oil, borage oil, black current oil, are important for conception. In women who are very thin, with scanty or irregular periods or anovulation may be able to achieve cycle regularity, ovulation, and conception by gaining enough weight to bring them into a normal weight for height range.

Between 1990 and 1993, Foresight, a British medical association for the promotion of preconception, conducted a study using a nutritional and lifestyle

modification preconception care program. The results were nothing less than remarkable. There was a tenfold reduction in the expected incidence of miscarriage and birth defects and over 80% success rate with unexplained infertility. It was evaluated that before the study was started, 60% of the women drank alcohol regularly and 57% of the women involved were previously smokers. Out of the 367 couples in the study, 327 (89%) of them successfully became pregnant and 327 children were born. All of these babies were born healthy. Among the 204 couples with infertility problems, 175 (86%) were able to achieve a healthy pregnancy.[21] One of the most significant aspects of these results was the involvement of both partners in the program—both female and male factors were concurrently addressed. In addition to nutritional supplementation, the study included lifestyle and social modifications, including the cessation of smoking, and coffee and alcohol consumption. Smoking cigarettes and coffee consumption have been linked to subfertility and delayed conception.[22–24] Based on the Foresight study, the suggested preconception care nutritional program is outlined in Table 12-3.[21]

ADDITIONAL THERAPIES

Stress Management and the Mind–Body Approach

There is a direct relationship between fertility and stress is as much an endocrine experience as an emotional reality. The human body has extensive hormonal responses to the environment, especially stress, which occur at the hypothalamic and pituitary levels. The anterior pituitary is responsible for regulation of the female menstrual cycle. In response to stress, the adrenals release the hormone cortisol, known to adversely affect the menstrual cycle. The effects of stress are mostly associated with long menstrual cycles and delayed ovulation. Stress and elevated cortisol have also been linked to elevated prolactin levels. Stress management strategies should include lifestyle modifications, including exercise, yoga, and emotional release techniques. Physiologically, the hypothalamic pituitary adrenal (HPA) axis can be supported with adrenal tonic herbs such as licorice and rehmannia, in combination with adaptogenic herbs such as eleuthero (*Eleutherococcus senticosus*) and ashwagandha. These herbs act to regulate the HPA axis and assist in general adaptation syndrome. There is also increasing evidence that a behavioral approach might be effective in infertility treatment. A study of 54 women who completed a behavioral treatment program based on ability to elicit a relaxation response demonstrated decreased anxiety, depression, and fatigue. Additionally, 34% of the women became pregnant within months of completing the program. Behavioral therapy should be considered as therapy itself, or in conjunction with other treatments, including ART.[25]

Addressing Environmental and Occupational Toxicity Associated with Infertility

Environmental and occupational toxicity has been linked to infertility, subfertility, spontaneous miscarriage, intrauterine growth retardation, and various birth defects, and is currently blamed for declining fertility. The particular

Formulas for Infertility: Various Associated Contributing Factors

Estrogen Balancing and Ovarian Tonic Formula (for follicular phase problems)

Chaste berry	(*Vitex agnus-castus*)	30 mL
Shatavari	(*Asparagus racemosa*)	30 mL
Schisandra	(*Schisandra chinensis*)	20 mL
Black cohosh	(*Actaea racemosa*)	10 mL
Wild yam	(*Dioscorea villosa*)	10 mL
		Total: 100 mL

Dose: 5 mL three times daily

Luteal Insufficiency Formula

White peony	(*Paeonia lactiflora*)	50 mL
Chaste berry	(*Vitex agnus-castus*)	15 mL
Licorice	(*Glycyrrhiza glabra*)	25 mL
Blue cohosh	(*Caulophyllum thalictroides*)	10 mL
		Total: 100 mL

Dose: 15 mL per day in the morning

Formula for Hyperprolactinemia

White peony	(*Paeonia lactiflora*)	25 mL
Ashwagandha	(*Withania somnifera*)	25 mL
Gymnema	(*Gymnema sylvestris*)	15 mL
Chaste berry	(*Vitex agnus-castus*)	12.5 mL
Licorice	(*Glycyrrhiza glabra*)	12.5 mL
		Total: 100 mL

Dose: 5 mL three times daily

Formula for Elevated LH

White peony	(*Paeonia lactiflora*)	65 mL
Black cohosh	(*Actaea racemosa*)	35 mL
		Total: 100 mL

Dose: 2 mL twice daily

Formula for Low LH

Tribulus*	(*Tribulus terrestris*)	60 mL
Chaste berry	(*Vitex agnus-castus*)	40 mL
		Total: 100 mL

Dose: 20 mL twice daily.

Formula for Elevated FSH

Tribulus	(*Tribulus terrestris*)	80 mL
Shatavari	(*Asparagus racemosus*)	10 mL
Chaste berry	(*Vitex agnus-castus*)	5 mL
Wild yam	(*Dioscorea villosa*)	5 mL
		Total: 100 mL

*Dose:*10 mL three times daily.

*Because of the high dose requirements of tribulus, a concentrated extract in a tablet preparation is often more desirable for optimal patient adherence.

Formulas for Infertility: Various Associated Contributing Factors—cont'd

Formula for Elevated Testosterone/Androgens

Tribulus*	(*Tribulus terrestris*)	75 mL
Schisandra	(*Schisandra chinensis*)	10 mL
White peony	(*Paeonia lactiflora*)	10 mL
Licorice	(*Glycyrrhiza glabra*)	5 mL
		Total: 100 mL

Dose: 10 mL three times daily.

Formula for Pelvic Factors/Uterine Tonic

White peony	(*Paeonia lactiflora*)	25 mL
Shatavari	(*Asparagus racemosus*)	25 mL
Saw palmetto	(*Serenoa repens*)	20 mL
False unicorn	(*Chamaelirium luteum*)	15 mL
Goldenseal	(*Hydrastis canadensis*)	15 mL
		Total: 100 mL

Dose: 5 mL three times daily

Formula for Cervical Factors (sperm antibodies, mucous membrane integrity)

Rehmannia	(*Rehmannia glutinosa*)	25 mL
Echinacea	(*Echinacea* spp.)	25 mL
Wild yam	(*Dioscorea villosa*)	20 mL
Saw palmetto	(*Serenoa repens*)	
		Total: 100 mL

Dose: 5 mL three times daily

TABLE 12-3

Preconception Care Nutritional Supplementation

NUTRIENT	DAILY DOSE
Beta carotene	6 mg
Vitamin E	500 IU
Vitamin D	200 IU
B_1, B_2, B_3, B_5	50 mg each
B_{12}	400 μg
B_6	Up to 250 mg
Biotin	200 μg
Choline	25 mg
Inositol	25 mg
PABA	25 mg
Folic acid	500 mg
Vitamin C	2000–3000 mg
Bioflavonoid	300 mg
Calcium	800 mg
Magnesium	400 mg
Potassium	15 mg
Iron	15 mg
Iodine	75 μg
Selenium	100–200 μg
Zinc	20–60 mg
Chromium	100–200 μg
Omega-3 essential fatty acids (as Evening primrose oil)	500–1000 mg
Omega-6 essential fatty acids (as fish oil or flaxseed oil)	500–1000 mg

toxins linked to infertility include heavy metals, pesticides, environmental estrogens, volatile organic solvents, and radiation.[26,27] Heavy metals most often linked to subfertility are lead, mercury, and cadmium.[26,28]

One study examined the association between occupational chemicals and radiation exposure in 281 infertile women compared with 216 fertile women. The study concluded there was an increased risk of infertility among women exposed to volatile organic solvents, chemical dust, pesticides, and video display terminals (radiation). The women exposed to volatile organic solvent and chemical dust had an increased incidence of ovulatory problems. Tubal factors and endometriosis were associated with solvents and chemical dusts. Endometriosis and cervical factor infertility were associated with exposure to video display terminals (radiation).[29]

Environmental contamination is widespread; therefore, exposure to toxins is virtually ubiquitous. Research suggests the involvement of oxidative stress and electron transfer as the underlying causes of drastic health concerns such as infertility. The treatment framework should include multifaceted preventative measures, such as botanical and nutritional antioxidant therapy and liver support.[30] Herbal therapy with a focus on liver support and improvement of phase 1 and 2 liver detoxification are helpful in the preconception period and during the infertility treatment to aid effective conjugation of sex hormones and toxins. Herbs such as *Silybum marianum, Schisandra chinensis, Picrorrhiza kurroa,* and *Burpleurum falcatum* have demonstrated hepatoprotective and hepatorestorative activity and assist with improvement of liver function and the detoxification processes in the body.[31] To protect against the damaging effects of radiation exposure, foods and herbs rich in antioxidants have been shown to protect and regulate gene activity. Herbs that exhibit antioxidant activity include *Ginkgo biloba*, *Vitis vinifera*, *Silybum marianum*, *Rosmarinus officinalis*, *Camellia sinensis*, and *Curcuma longa*.

Acupuncture and TCM

Acupuncture can be considered for women suffering from infertility and has been shown to be of benefit in those with luteal phase defects. In TCM, the diagnosis of kidney insufficiency is said to relate to luteal phase defects. Using acupuncture to regulate the kidney may help regulate the hypothalamus pituitary ovarian axis.[32,33]

CASE HISTORY

A young couple had been trying to conceive for 28 months before seeking holistic therapy. They had been through one failed IVF attempt 6 months earlier, which motivated them to explore other options. The female was 30 years old, and from medical evaluation, the fertility complications resulted from female factors. The

menstrual history has been normal with menarche at age 14 and a regular 34-day cycle. She was aware of texture changes to her cervical mucus and noted that she experienced fertile mucus on days 16 or 17 of the cycle each month and experienced cramps on the first day of her menses. Her general medical history included anxiety, depression, insomnia, and hypoglycemia.

Drug and Supplement History

She has been taking a prenatal folic acid B_{12} supplement but was never advised by her medical doctor to take any other supplements. A few years prior, she took Prozac but discontinued this therapy because of side effects. She managed her depression and anxiety with counseling and regular yoga.

Reproductive History

Her reproductive medical history was complex and included hyperprolactinemia, a moderate degree of pelvic endometriosis, and mild cervical erosion with chronic inflammatory changes. She had a history of pelvic inflammatory disease associated with a *Chlamydia* infection that had been treated with doxycycline. Blood tests indicated progesterone failure with a late LH surge and elevated prolactin levels. She experienced premenstrual breast tenderness and mood changes on a monthly basis.

A previous laparoscopy, performed before the initial IVF attempt, revealed endometriosis and endometrial adhesions; her left ovary was tethered to the left broad ligament. During this procedure, the endometriosis was excised and ablated. A hysterosalpingogram before the IVF attempt revealed inflammation and edema in the fallopian tubes and some fallopian blockage. High-pressure oil perturbation was performed and bilateral tubal paltency was then established; her fallopian tubes were clear and apparently functional as of 18 months.

A previous postcoital test indicted she had been diagnosed with ''hostile mucus,'' with very few sperm moving in the mucus upon postcoital evaluation. Antisperm antibodies were detected in her mucus.

Additional Assessment

The client had regular lifestyle exposure to significant levels of radiation, including interstate and overseas flights five to six times per year, daily use of a cellular phone, recent spinal x-rays because of lower back pain, and daily exposure to video display terminals from working on a computer. She drank alcohol moderately (two glasses two to three times per week) and consumed 16 oz of coffee on a daily basis. Her diet was high in animal protein.

Treatment Protocol

Black cohosh	(*Actaea racemosa*)	15 mL
Ginger	(*Zingiber officinale*)	15 mL
White peony	(*Paeonia lactiflora*)	15 mL
Chaste berry	(*Vitex agnus-castus*)	15 mL
Goldenseal	(*Hydrastis canadensis*)	15 mL
Rehmannia	(*Rehmannia glutinosa*)	10 mL
Albizzia	(*Albizzia lubbock*)	15 mL
		Total: 100 mL

Dose: 10 mL twice daily before food through the cycle.
Additionally:

- *Tribulus terrestris*, standardized to 100 mg furostanol saponins as protodioscin: two tablets twice daily on days 5 to 14 of the cycle
- Tablet formula of *Vitis vinifera* extract standardized to contain procyanidins 42.5 mg per tablets, *Camellia sinensis* extract standardized to contain catechins 83.35 mg per tablets; *Curcuma longa* extract standardized to contain curcuminoids 70.4 mf per tablets; *Rosmarinus officinalis* extract 1000 mg per tablet. Dose of three tablets per day was given.
- Tablet formula of *Echinacea angustifolia* extract containing alkyl amides 2.5 mg per tablets and *Echinacea purpurea* extract containing alkyl amides 2.65 mg per tablets. Dose of four tablets per day was given.
- Full preconception nutritional program, as per Foresight studies, including lifestyle modifications.
- Diet: high fish protein, high in brassicae and green leafy vegetables. Low starch, dairy, and refined carbohydrates. Organic produce was advised when possible. Coffee, caffeine, and alcohol were eliminated.

Rationale

The primary clinical concern was a past history of pelvic and fallopian inflammation, endometriosis, and hormonal imbalance. Considering her history of Chlamydia and endometriosis, the use of immune tonics and anti-inflammatories was essential. Black cohosh was included for hormonal modulation. Ginger was included for its anti-inflammatory and circulatory tonic action. White peony was included to regulate the LH surge and reduce the elevated prolactin in conjunction with chaste berry. Goldenseal was included for mucous membrane trophorestorative, anti-inflammatory action. Rehmannia was included as an anti-inflammatory, adrenal tonic, and immune support. Albizzia was included as an antiallergenic herb to address the immunologic complications with the antisperm antibodies. The couple was also advised to use barrier contraception (condom) to reduce her exposure to her partner's sperm during the preconception period of 4 months. Echinacea was used as a general immune modulator as her case demonstrated a need for nonspecific immune support. A combination of turmeric, rosemary, green tea, and grape seed was prescribed for antioxidant and anti-inflammatory activity. These herbs also aid the microvascular circulation to the uterus, ovaries, and fallopian tubes to promote healing. Tribulus was added as a general tonic, one known to promote fertility.

Follow-Up Appointments

- Second consultation (8 weeks later)
  During the weeks between consultations, an ordered test showed no heavy metal toxicity and no active genitourinary infection. The patient commented that her cycle has become shorter and was now 32 days, with no premenstrual breast tenderness, improved mood stability, and increased sense of relaxedness. Overall, she remarked on improvements in energy and sleep quality, increased ability

to focus, and she was positive and relaxed. Her treatment protocol remained unchanged.

- Third consultation (8 weeks later)
  On a second postcoital test, there was no evidence of antisperm antibodies. Her mucus was now healthy such that she could support a natural conception. There was no abdominal tenderness and no pain at menses. Hormonal re-evaluation was conducted and prolactin, estrogen, progesterone, LH, and FSH were within normal ranges. She continues on her protocol.

Conclusion of Care

She remained on the protocol for 3 more months at the end of which the couple successfully conceived. The total duration of treatment was 18 weeks, of which 12 weeks was focused on preconception care, during which time the couple was advised not to try to conceive and instead focus on resolving health concerns and prepare for a healthy, conscious conception. She went on to have a complication-free, healthy pregnancy and a natural, drug- and surgery-free home birth. She gave birth to a 7 lb 8 oz baby girl after 39.5 weeks gestation. The mother commented that she was healthier during her pregnancy than she had ever been and the experience of using a holistic approach to resolve her fertility challenges had taught them the fundamental principles of diet, health, and the subtle signs of her body's fertility. She now uses natural thermo-symptal charting as an awareness technique for natural contraception.

Pregnancy: First Trimester

Aviva Romm

13 CHAPTER

The state of a woman's health is indeed completely tied up with the culture in which she lives and her position in it, as well as in the way she lives her life as an individual. We cannot hope to reclaim our bodily wisdom and inherent ability to create health without first understanding the influence of our society on how we think and care for our bodies.[1]

—Dr. Christiane Northrup, obstetrician/gynecologist

PREGNANCY CARE AND PRENATAL WELLNESS

The past decades have tremendously improved the outcomes of high-risk pregnancies and birth, yet with these improvements have come the ubiquitous presence of technological intervention in nearly all aspects of normal childbearing as well. Yet, the safety and efficacy of the routine use of many interventions is not clear, with a striking lack of an evidence base for many.[2,3] Nonetheless, the number and frequency of interventions has risen steadily since the 1950s. Since 2003, cesarean section has been the most common hospital surgical procedure performed in the United States, with 1.2 million of these major abdominal surgeries each year, accounting for more than 25% of all US births at a national cost $14.6 billion in total charges. In spite of spending more money and using more technologies on obstetric care than any other country in the world, the United States ranks only 25th in birth outcome and infant mortality worldwide. Dr. Marsden Wagner, former Director of the World Health Organization's (WHO) European Regional Office, remarked at an international medical conference that hospital births ''endanger mothers and babies—primarily because of the impersonal procedures and overuse of technology and drugs.''[4]

The desire to avoid excessive technology and an inclination toward natural approaches to health, combined with many women's perceptions that obstetric care is grossly impersonal, has led women to seek alternatives to conventional obstetric care. Homebirth has become an increasingly popular option because of its astounding safety record and the intimate prenatal, birth, and postnatal care experience it offers women.[5–9] Many choose to self-medicate with alternative therapies, such as herbs, and turn to sources that may not be reliable for information. Although the treatment of common pregnancy complaints with gentle herbs and simple home remedies has generally proved safe, women are increasingly seeking advice through the Internet, books, and alternative practitioners for potentially serious problems than can arise during the childbearing cycle. Thus, it is essential for practitioners to become knowledgeable about natural therapies and willing to have an open dialog with their clients about their concerns and preferences in order to help pregnant women access intelligent and accurate information about the safety and efficacy of such therapies during the childbearing cycle, and to avoid harmful therapies and obtain appropriate medical care as needed.

DIET, NUTRITION, EXERCISE, LIFESTYLE AND PSYCHOEMOTIONAL HEALTH: CENTRAL TO OPTIMAL CHILDBEARING HEALTH

Health education and preventative care through diet and nutrition, exercise, and healthful lifestyle are the cornerstones of an optimal childbearing experience that may play the most pivotal roles, outside of genetics, in shaping pregnancy health, and as a result, significantly influencing the health of the baby. In addition to routine prenatal care, attention should be given to the psychoemotional wellness of the emerging mother, her changing identity as a woman, and her changing family status. Although a presentation of diet, nutrition, exercise, and lifestyle approaches to prenatal health is beyond the scope of this edition, as is a discussion of the psychological and emotional factors that support a healthy pregnancy, the importance of these factors cannot be overstated.

HERBS AS PART OF PREGNANCY WELLNESS

Schools of thought differ on whether herbs should be used routinely—or at all—during pregnancy. Some ascribe

to the belief that because most herbs have not been proven safe for use during pregnancy, they should be entirely avoided, whereas others see certain herbs more as foods that can provide an additional source of nutrition during pregnancy, or as tonics that can encourage and support optimal pregnancy health and uterine function.[10,11] Many consider the choice of whether herbs are appropriate for use during pregnancy to be circumstantial, for example, dependent upon the nature of the condition being treated and the risk benefit of herbs compared with medical intervention for that particular condition. Certain conditions are beyond the scope of herbal treatment, and practitioners should be keenly aware of the symptoms that herald such conditions and indicate the absolute need for medical care (Box 13-1).

It can be useful to see herbs on a continuum between food and medicine. There are many herbs whose constituents are mostly benign, nutritive substances such as carbohydrates vitamins, and minerals (Table 13-1).[12–17] Herbs such as nettles (*Urtica dioica*), milky oats (*Avena sativa*), and red raspberry leaf (*Rubus idaeus*) are examples. On the other hand, there are numerous herbs whose use in pregnancy is entirely contraindicated for safety reasons (see Chapter 12). Somewhere between these categories are herbs not appropriate for daily, routine intake, but which can be used if necessary for brief or more extended periods of time for specific conditions. In addition to common complaints of pregnancy, pregnant and lactating women are also subject to the run of the mill complaints and illnesses we all face—colds, indigestion, headache, etc.—for which they may seek herbal care. Many of these problems can be addressed safely and gently with the herbs listed in the following or discussed in subsections of this chapter.

BOX 13-1

Warning/Danger Signs during Pregnancy

The following signs at any stage of pregnancy suggest that there may be a problem requiring medical treatment and are beyond the scope of what botanical care can treat. A patient with any of these signs should be referred immediately to an obstetrician or midwife for assessment and appropriate medical intervention.
Warning signs:
- Vaginal bleeding
- Initial outbreak of herpes blisters during the pregnancy
- Severe pelvic or abdominal pain
- Persistent, severe mid-back pain
- Edema of the hands and face
- Severe headaches, blurry vision, or epigastric pain
- Rupture of membranes prior to 37 weeks pregnancy
- Regular uterine contractions prior to 37 weeks pregnancy
- Cessation of fetal movement

Table 13-1 provides an overview of a number of herbs that are generally considered safe for general use during pregnancy, reasons for use, and dose. The remainder of this chapter is dedicated to common pregnancy complaints and problems, and the herbs that are often used in their treatment.

THE ROLE OF HERBS IN THE PREVENTION AND TREATMENT OF MISCARRIAGE

Miscarriage, medically referred to as spontaneous abortion (SAb), is the spontaneous, unexpected, and often unexplained loss of a pregnancy before 20 weeks gestation. Miscarriage is the most common pregnancy complication; however, the exact incidence is unknown because the actual incidence of conception in the population is uncertain. One in seven clinically recognized pregnancies will miscarry, and in studies of women attempting to conceive, spontaneous abortion occurs in 10% to 15% of conceptions.[18–20] Based on studies of pregnancies achieved through assisted reproductive technologies, 50% of conceptions result in miscarriage. Miscarriage rate is related to maternal age, with rates under 2% for women under 30 years of age, and between 5% and 10% for women more than 40 years old. Miscarriage rates decline to less than 3% if there is a healthy fetus present at 8 weeks gestation (as visible upon ultrasonogram) in healthy women. *Note:* The term *fetus* is used throughout this chapter; however, the term *embryo* is the technically correct developmental term for any baby less than or equal to 8 weeks of gestation.

Although miscarriage may occasionally be welcome in the case of an undesired pregnancy, it is generally accompanied by a sense of loss, grief, or sadness, and a woman may experience self-doubt or self-reproach (e.g., ''Maybe I miscarried because of that glass of wine I had last week, or maybe it was because I was ambiguous about being pregnant.''). In addition to supportive physical care, women need emotionally sensitive care providers who can understand and empathize that the loss of a pregnancy may matter a great deal to the mother.

CAUSES OF MISCARRIAGE

Numerous factors contribute to miscarriage; however, the etiology of most individual miscarriages is never determined. Causes of miscarriage can originate with either parent or the conceptus. Investigation into specific causes of miscarriage in individual women is generally not pursued unless the woman miscarries recurrently. Causes include:
- Fetal Factors
- Maternal Factors
- Age
- Environmental Exposure
- Infection
- Physical and Congenital Abnormalities
- Endocrine Disorders
- Immunologic Factors
- Coagulation Disorders
- Nutritional Deficiencies
- Psychological Factors
- Paternal Factors

TABLE **13-1**

Herbs Demonstrated as Safe for General Use in Pregnancy Based on Clinical Studies

COMMON NAME	BOTANICAL NAME	REASON FOR USE	CLINICAL TRIALS IN PREGNANCY	TYPICAL DAILY DOSE	COMMENTS
Red raspberry leaf	*Rubus idaeus*	Mineral-rich nutritive tonic, uterine tonic to promote an expedient labor with minimal bleeding. Can also be used as an astringent in diarrhea.	Positive[12,13]	1.5–5 g/day in tea or infusion	Highly astringent herbs can theoretically interfere with intestinal nutrient absorption
Echinacea	*Echinacea* spp.	Reduce duration, recurrence of colds and URI	Positive[14]	5–20 mL tincture	The dose listed here and considered safe by herbalists is higher than that used in the study by Gallo et al.
Ginger	*Zingiber officinalis*	Antinauseant, antiemetic for NVP, hyperemesis gravidarum, and generally nausea	Positive[15,16]	Up to 1 g dried powder/day	Higher doses of ginger are traditionally considered emmenagogic Untreated hyperemesis gravidarum in pregnancy can cause serious adverse outcomes
Cranberry	*Vaccinium macrocarpon*	Prevent and relieve UTI	None identified	16–32 floz of juice/day	Untreated UTI in pregnancy can cause serious adverse outcomes
Chamomile	*Matricaria recutita*	Promote general relaxation, treat insomnia, treat flatulence	None identified	1–5 g/day in tea	No reasonable contraindications[17]

SIGNS AND SYMPTOMS OF MISCARRIAGE

Signs and symptoms of miscarriage include:

- Vaginal bleeding (brown or bright red ''spotting'' or bleeding)
- Abdominal cramping, pain, or contractions that becomes increasingly regular
- Passing of clots, tissue, or a gush of fluid
- Diminished subjective signs of pregnancy (e.g., nausea and vomiting of pregnancy, breast tenderness)
- Cervical dilatation

DIAGNOSIS

Diagnosis and staging of miscarriage is made primarily upon ultrasound findings and the presence of cervical dilatation. Ultrasonography is considered the most important and useful diagnostic tool for SAb. Passage of complete embryonic or fetal tissue, cessation of pregnancy symptoms, and negative hCG levels for pregnancy are indicative of miscarriage; however, self-diagnosis on the basis of passage of large amounts of ''tissue,'' abatement of pregnancy symptoms, and a negative home pregnancy test are not proof of miscarriage. What appears to be embryonic or fetal tissue can actually be clots, pregnancy symptoms can fluctuate, and home pregnancy tests can give false-negative results.

DIFFERENTIAL DIAGNOSIS

Bleeding in early pregnancy can be a sign of serious problems. Major causes of early pregnancy bleeding, other than miscarriage, that must be ruled out include ectopic pregnancy and cervical, vaginal, or uterine pathology (e.g., trauma, polyp, cervicitis, or neoplasia). Molar pregnancy (hydatidiform mole) also should be ruled out. Some women experience a small amount of bleeding on implantation, known as physiologic bleeding, which typically is not of concern.

CATEGORIES OF MISCARRIAGE

Miscarriage is divided into six primary categories. Which category a woman fits into dictates the care she will need to receive. If miscarriage is threatened, then measures to prevent miscarriage are appropriate and may be effective, whereas if miscarriage is inevitable, preventative measures will not be effective and supportive care and appropriate medical care for safely completing the miscarriage are warranted.

Threatened Abortion

The term *threatened abortion* is used when there is vaginal bleeding prior to 20 weeks gestation. This may be accompanied by abdominal aching or cramping. Upon vaginal examination, the cervix is found undilated. Incidence is 25% of pregnant women experiencing some quantity of vaginal bleeding; of these, 50% ultimately miscarry. When there is threatened abortion caused by a number of factors, including hormonal dysregulation or vaginal infection, for example, preventative strategies sometimes may avert a miscarriage; however, in the case of a nonviable fetus, miscarriage eventually progresses to inevitable abortion.

Inevitable Abortion

In inevitable abortion, there is both bleeding and lower abdominal cramping, accompanied by some degree of cervical dilatation. Bleeding may range from minimal to severe and even life threatening. Inevitable miscarriage should not be treated with strategies to prevent miscarriage; rather, confirmation that the baby is no longer alive should be obtained and, support for miscarriage completion should be provided. Most women miscarry spontaneously without complications or need for physical support, although emotional support may still be needed.

Incomplete Abortion

An incomplete abortion involves vaginal bleeding, cramping (contractions), cervical dilatation, and incomplete passage of the products of conception. A woman experiencing incomplete abortion frequently describes passage of clots or pieces of tissue, and reports vaginal bleeding. The cramping may be rhythmic or labor-like, although less intense than a full-term labor. At this point, the baby has already died and has either been passed or is part of the retained tissue. Treatment focuses on helping the woman to complete the miscarriage process by expelling any retained tissue, and emotional and physical healing.

Complete Abortion

With complete abortion, all of the uterine contents of pregnancy are expelled, after which cramping and bleeding subside, the cervix returns to an undilated state, and the uterus begins to involute. Other symptoms of pregnancy disappear, and a pregnancy test will yield a negative result. Only emotional support is generally required.

Missed Abortion

Missed abortion refers to a fetus that has died but is retained in the uterus, often with no signs of ensuing miscarriage. This condition may persist for several weeks before miscarriage spontaneously commences. In some cases, it will not commence without assistance. Left untreated beyond approximately 4 weeks, missed abortion can lead to serious maternal infection and rarely, disseminated intravascular coagulopathy (DIC) in the mother, which can be fatal. Medical care must be consulted.

Habitual (or Recurrent) Abortion

Habitual (or recurrent) abortion refers to a history of repeated miscarriage, defined as three or more successive pregnancy losses. Habitual miscarriage suggests the need for medical evaluation of a couple and ongoing care for what may be chronic problems (e.g., hormonal dysregulation, infection, etc.). Of women who experience a first miscarriage, only 1% experiences a second miscarriage; however, for women who have never had a live and birth who have had two or more miscarriages, the risk of subsequent miscarriage is in excess of 40%.

CONVENTIONAL TREATMENT APPROACHES

Initially, an ultrasound should be performed to determine whether a live fetus is present. A live baby is born in 94% of pregnancies in which there was a threatened miscarriage. Conventional treatment of threatened miscarriage ranges from a ''wait and watch'' (expectant) approach with reassurance to the use of bed rest, administration of progesterone, use of uterine muscle relaxant drugs (tocolytics), or other therapies when appropriate, such as specific treatments for SLE or APS:

- Expectant approach
- Bed rest
- Progesterone therapy
- Uterine muscle relaxants (tocolytics)

Conventional treatment of inevitable miscarriage includes hospital admission for pain medication if needed, and ultrasound to determine whether the fetus is alive or whether miscarriage is incomplete. In incomplete abortion where there has been substantial blood loss, appropriate emergency procedures are followed, including resuscitation if needed, administration of intravenous fluids, blood work, and treatment of shock and infection is present. A dilatation and evacuation is performed to empty the uterus of any remaining products of conception and medication for pain and infection prophylaxis is administered as appropriate. In cases of missed abortion, typically first identified during routine ultrasound examination, or attention to a discrepancy between maternal growth or subjective or objective pregnancy signs and time elapsed since the missed period, a wait and see attitude may be adopted for up to several days to 2 weeks (depending upon the time elapsed since the missed abortion first occurred) to see if completion of the abortion ensues spontaneously, or surgical removal

of the conception products may be scheduled to prevent the risk of hemorrhage and infection.

Women presenting with a history of miscarriage should be evaluated for the presence of any of the factors named earlier that are associated with miscarriage. Diabetes mellitus, thyroid diseases, and immunologic factors should be ruled out. Chromosomal evaluation of both partners should be performed, and an evaluation of the woman's reproductive anatomy should be performed. Presence of infection and infectious organisms should be ruled out, and if present, treated. Cervical incompetence often can be treated successfully with cervical cerclage, a suture placed in the cervical os in the first trimester of pregnancy.

RhoGAM should be administered within 72 hours of miscarriage to all women who are Rh− to prevent maternal sensitization and possible Rhesus isoimmunization of a fetus in a subsequent pregnancy.

Support and counseling should be provided, as miscarriage is frequently accompanied by feelings of guilt, shame, and grief. Practitioners should reassure couples that it is unlikely that anything either parent did caused pregnancy loss. Women with a history of repeated miscarriage may need significantly more counseling than women experiencing a first miscarriage.

BOTANICAL TREATMENT FOR MISCARRIAGE: THREATENED AND HABITUAL

This section provides botanical strategies for miscarriage prevention in the event of threatened miscarriage (Table 13-2), and basic support for habitual abortion when resulting from progesterone insufficiency. If fetal demise has been confirmed by ultrasound, readers may follow the protocol in the example in the case history at the end of the chapter. When there is incomplete or missed abortion, special attention needs to be given to the risk of infection and subsequent coagulopathy. Women who miscarry are at some increased risk for postmiscarriage anxiety and depression. Emotional support during and after a miscarriage, as well as during a subsequent pregnancy, is often necessary. Botanical treatments for postpartum depression (see Chapter 18) can be extrapolated for use when needed.

Warning: Appropriate treatment/prevention of miscarriage requires specialized obstetric knowledge and may require hospitalization, particularly if there is cervical length shortening or cervical dilatation when the fetus is close to a viable age, or if there is excessive bleeding. Miscarriage can lead to maternal hemorrhage, and if left incomplete, maternal infection. The care of an obstetrician or midwife should be sought in conjunction with botanical care for the treatment or prevention of miscarriage.

Whenever possible in the prevention of habitual miscarriage, the practitioner will want to try to establish an etiology. When it is not possible to establish an etiology for recurrent miscarriage, a thorough personal and medical history often provide clues to the direction the practitioner will take in establishing an herbal protocol. Both the etiology and botanical treatment of habitual miscarriage are often complex. Unfortunately, emerging theories and understanding of the immunologic, endocrine, and thrombopathic bases of miscarriage are often more advanced than can be matched by current research on botanicals. Most current protocol for miscarriage are based on traditional uses. This section highlights

Herbalist/Midwife Protocol for Habitual Miscarriage

This formulae is to be begun 3 months prior to conception and continued until at least 2 weeks past the latest week's gestation of previous miscarriages (e.g., if a previous miscarriage occurred at 8 weeks, continue the formula until at least 10 weeks).

Chaste berry	(*Vitex agnus castus*)	50 mL
Cramp bark	(*Viburnum opulus*)	30 mL
Partridge berry	(*Mitchella repens*)	20 mL

Total: 100 mL

Dose: 5 mL twice daily

TABLE **13-2**

Botanical Treatment Strategies for Miscarriage Prevention in the Event of Threatened Miscarriage and Habitual Abortion

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Relieve uterine contractions	Uterine antispasmodic	*Viburnum opulus*	Cramp bark
		Viburnum prunifolium	Black haw
		Dioscorea villosa	Wild yam
Increase progesterone	Progesterogenic	*Vitex agnus-castus*	Chaste berry
Improve uterine tone	Uterine tonics	*Chamaelirium luteum*	False unicorn
		Mitchella repens	Partridge berry

Herbalist/Midwife Protocol for Threatened Miscarriage with Cramping as the Primary Symptom

Cramp bark*	(*Viburnum opulus*)	70 mL
Wild yam	(*Dioscorea villosa*)	30 mL
		Total: 100 mL

Dose: 3 to 5 mL every 30 to 60 minutes for up to 4 hours depending upon severity and regularity of cramping. This protocol can be repeated up to twice daily for three consecutive days.

*Black haw (*Viburnum prunifolium*) may be used interchangeably with cramp bark.

Figure 13-1 Cramp bark (*Viburnum opulus*). (Photo by Martin Wall.)

miscarriage prevention with uterine irritability and progesterone insufficiency, which is treated with long-term use of chaste berry (*Vitex agnus-castus*) begun several months prior to conception and continued until several weeks past the time of prior miscarriage, and accompanied by cramp bark or black haw, and wild yam once pregnancy is established to prevent cramping. Uterine tonic herbs, particularly partridge berry (*Mitchella repens*) and false unicorn root (*Chamaelirium luteum*), are commonly included in formulae as well. False unicorn is an endangered herb, therefore, it is recommended to use only cultivated sources. Traditional Chinese medicine can play an important role in miscarriage prevention when there is habitual abortion, as its constitutional diagnostic model and corresponding herbal and dietary protocol can be specifically tailored to a woman's constitution and imbalances.

In case of threatened miscarriage, the Western herbal practitioner will need to address commonly overlooked factors, such as overwhelming stress, dehydration, or malnutrition. Urinary tract infection (or other infection) should be ruled out, and if present, treated (see Chapter 10). Women should attempt to achieve an optimal body weight prior to conception with underweight women, particularly trying to bring their weight to within a normal body mass index to ensure adequate hormone production. Herbs can be used primarily to reduce uterine contractions associated with threatened miscarriage. The most commonly used herbs include cramp bark (Fig. 13-1), black haw, and wild yam, either alone or in combination.

Black Haw, Cramp Bark, and Wild Yam

When there is uterine cramping in the absence of cervical dilatation, cramp bark (*Viburnum opulus*) and black haw (*Viburnum prunifolium*) are used to arrest uterine spasm.[49,50] These herbs, which can be used interchangeably or together for this purpose, have a long history of use as spasmolytics during pregnancy, especially for miscarriage, dating back well over a hundred years by Western herbalists, and even longer by Native American tribes.[49,50] Black haw was official in the United States Pharmacopoeia in 1882, its uses as an antispasmodic and preventative for miscarriage popularized by the Eclectic physicians. Cramp bark is included in the British Herbal Pharmacopoeia and is used by herbalists in the United Kingdom for miscarriage prevention.[17,49] The active principles are unknown; however, it is thought that at least four active substances, including scopoletin and aesculetin, which have been identified, have uterine spasmolytic activity.[51]

Another herb with a long history of use for relieving uterine contractions is wild yam (*Dioscorea villosa*). Although this herb has developed the erroneous reputation for use as a progesterone supplement, wild yam in fact contains no progesterone, nor can it be converted by the body into progestogenic substances. However, this does not preclude its efficacy and reliability as a uterine antispasmodic, combining well both cramp bark and black haw; although, no research was identified that either supports or refutes its traditional uses.[17]

Chaste Tree

Chaste tree (*Vitex agnus-castus*) is used by midwives and herbalists to prevent miscarriage associated with low progesterone, where it may exert its effects via enhancing corpus luteum function.[52,53] Although researchers are still uncertain as to the exact mechanism of action of vitex it appears to having a regulatory effect on luteinizing hormone (LH), follicle-stimulating hormone (FSH), and progesterone, as well as the ability to reduce elevated prolactin levels via dopaminergic activity, and has shown positive effects in improving premenstrual syndrome symptoms and luteal phase defects.[53–58] It is used alone and in conjunction with topical USP progesterone when the latter is prescribed by an obstetrician or midwife for miscarriage prevention. Placebo-controlled studies for teratogenicity and mutagenicity were conducted in rats, and even when the animals were administered 74 times the dose typically consumed by humans, no toxicity nor aberrations in fetal development were seen.[53] Although it is sometimes given acutely, for the herb to have efficacy as a miscarriage preventative, it is ideally given for at least 3 months prior to conception and continued well

into the first trimester to maintain stable progesterone levels. The most recent edition of the *Botanical Safety Handbook* provides no contraindications to use during pregnancy.

CASE HISTORY

This case history illustrates the versatility of herbs for treating miscarriage-related problems. The patient initially presented with a missed abortion, which she went on to complete with herbal support, and then she desired to maintain pregnancy after a history of several miscarriages.

Initial Appointment

Jan is a 30-year-old woman in dire emotional distress having been informed that day by her nurse-midwife that her 10-week-old fetus had died and that her pregnancy was no longer viable. The CNM and obstetrician told her it appeared that the baby had been dead for about 3 weeks, and recommended dilatation and curettage (D&C). Jan was concerned about the procedure, as this was her third miscarriage and she was afraid that the D&Cs might contribute to uterine scarring and cause problems in a future pregnancy, and she desperately wanted to have another child. Jan requested assistance in completing the miscarriage herbally and wanted help, should she become pregnant again, to prevent miscarriage.

Past Medical History

Jan had twins 4 years ago after an uneventful pregnancy, and has been unable to carry a pregnancy to completion since, having had 3 miscarriages. In the year after the birth of the twins, Jan gained 30 pounds (height is 5'8'' and current weight 210 pounds) and had a serious bout of depression for which she took antidepressants for about 1 year, and then discontinued. After a year of not understanding what was wrong with her, she went to an endocrinologist and was diagnosed with hypothyroidism, for which she was taking Synthroid. Her thyroid condition is well managed and her thyroid tests are normal. Though she has not been experiencing chronic depression, the miscarriages get her really down.

Treatment Protocol: Missed Abortion

The goal is to stimulate uterine contractions and promote the expulsion of the fetus from the uterus. Jan's cervix was closed and firm at the initial appointment. We discussed giving the protocol a strict time limit of 5 days, after which she agreed to have a D&C if the protocol was not effective. Her CNM and obstetrician agreed to support her in this choice.

1. To initiate cervical ripening, *Oenothera biennis*, in the form of evening primrose oil (EPO), was given orally as follows: two 500 mg capsules, twice daily, for a total of 2000 mg per day, for 2 days. Also, Jan was instructed to digitally apply 1500 mg EPO to the cervix. (The woman can do this herself, her partner can do it, or she can go to a midwife for the treatment; although the efficacy of this practice has not been demonstrated by clinical trials.
2. After 24 hours of EPO as above, Jan began taking an oral administration of the following tincture:

Cotton root bark	(*Gossypium herbaceum*)	40 mL
Black cohosh	(*Actaea racemosa*)	40 mL
Blue cohosh	(*Caulophyllum thalictroides*)	20 mL
		Total: 100 mL

   Instructions: Beginning in the morning, take 2.5 mL every hour for 4 hours, and then discontinue. She was instructed that if no contractions commenced, she was to repeat the next day as for day 1. If no contractions ensue on day 2, discontinue on the third day, and resume for two more days on days 4 and 5.
3. The client was instructed to keep on hand *Angelica archangelica*, *Hamamelis virginiania*, and hemostatic herbs should bleeding be heavy, and was given strict instructions on when to seek medical care.

Contractions began after the first 24 hours of the herbal protocol, and she continued the herbs until miscarriage seemed inevitable. She miscarried within the next 24 hours and was pleased with the results, and relieved to be through this part of her ordeal.

Treatment Protocol: Miscarriage Prevention

Eight months later the client, who has a history of progesterone insufficiency, as well as depression and irritability, became pregnant again. At this point she was placed on the following herbal protocol to prevent miscarriage:

Tinctures of:

Chaste berry	(*Vitex agnus castus*)	60 mL
Cramp bark	(*Viburnum opulus*)	30 mL
Wild yam	(*Dioscorea villosa*)	20 mL
		Total: 100 mL

Dose: 5 mL three times/day

Jan continued this protocol throughout the first trimester of her pregnancy. Late in her pregnancy, she sent a note saying, ''I have had a great pregnancy so far.'' The client carried this pregnancy to term and gave birth to a healthy baby boy.

NAUSEA AND VOMITING OF PREGNANCY AND HYPEREMESIS GRAVIDARUM

Nausea and vomiting of pregnancy (NVP), generally referred to as ''morning sickness,'' is a common pregnancy discomfort. Its association with pregnancy was documented on papyrus dating as far back as 2000 BCE. The earliest reference is in Soranus' *Gynecology* from the 2nd century CE.[59] Some degree of nausea, with or without vomiting, occurs in 50% to 90% of all pregnancies. It generally begins at about five to six weeks of gestation and usually abates by 16 to 18 weeks gestation. As many as 15% to 20% of pregnant women will continue to experience some degree of NVP into the third trimester, and approximately 5% will continue to experience it until birth.[60,61] The socioeconomic impact of NVP on time lost from either paid employment or household work is substantial, with one study reporting as many

as 8.6 million hours of paid employment and 5.8 million hours of household work lost each year because of NVP.[62] Additionally, women experiencing more extreme versions of NVP or hyperemesis gravidarum are vulnerable to social isolation, and possibly depression, as a result of their symptoms—they are simply too ill to engage in their normal social activities, or they isolate themselves in order to avoid the embarrassment of being caught vomiting publicly.[63]

Morning sickness is actually a misnomer for this condition, as the symptoms are not limited to the morning, and may occur at any time of day. In fact, in 80% of women, symptoms persist throughout the day. It has been jokingly said the condition is called morning sickness because it starts in the morning and lasts all day. Both the etiologies and role of NVP in pregnancy remain uncertain. Several physiologic etiologies have been proposed. It has been suggested that NVP actually serves a protective function for the pregnancy. Flaxman and Sherman propose, for example, that morning sickness causes women to avoid foods that might be dangerous to themselves or their embryos, especially foods that, prior to widespread refrigeration, were likely to be heavily laden with microorganisms and their toxins.[64] Studies have demonstrated that women who experience some degree of NVP are less likely to miscarry or experience stillbirth.[64,65]

SYMPTOMS OF NVP AND HYPEREMESIS GRAVIDARUM

The spectrum of symptoms and severity of NVP range from mild to severe nausea, gagging, and retching to vomiting, and from mild discomfort with minimal food and smell aversions to severe. Extreme NVP with unrelenting vomiting is called hyperemesis gravidarum, and is a medical condition, as opposed to NVP, which in its milder forms is actually considered normal.

Symptoms of hyperemesis gravidarum include persistent vomiting (and often dry heaving as well) accompanied by weight loss exceeding 5% of prepregnancy body weight and ketonuria unrelated to other causes.[66] It is generally incapacitating. It is estimated that hyperemesis occurs in 0.3% to 2% of pregnancies.[67] Hyperemesis typically persists into the second trimester, and may continue until the time of birth. Hospitalization for hyperemesis is common, peaking at approximately 9 weeks gestation and leveling off at around 20 weeks. The pathogenesis of hyperemesis is unknown. Symptoms generally resolve by midpregnancy regardless of treatment. When properly treated, hyperemesis gravidarum is associated with a very low morbidity and mortality rate. Without adequate treatment, the mother may experience micronutrient deficiency, Wernicke's encephalopathy caused by vitamin B_1 deficiency, and consequences of malnutrition, for example, propensity toward infection or slow healing wounds. There does not appear to be an increased risk of birth defects in babies born to mothers with hyperemesis gravidarum, and although women with hyperemesis gravidarum may experience substantial weight loss in early pregnancy, as long as overall pregnancy weight gain is normal, there does not appear to be any difference in birth weight in women with hyperemesis gravidarum.[68–71] Low birth weight is likely to occur in babies born to mothers who do not make up their pregnancy weight later in pregnancy.[67,68,72–74]

RISK FACTORS FOR NVP AND HYPEREMESIS GRAVIDARUM

In a study of the risk factors for NVP and hyperemesis, hyperthyroid disorders, psychiatric illness, previous molar pregnancy, pre-existing diabetes, gastrointestinal disorders, and asthma were all statistically significant risks, whereas maternal smoking and maternal age older than 30 were associated with decreased risk. Singleton female pregnancies, as well as multiple pregnancies, were associated with statistically significant increased risk of hyperemesis.[75] Women with gastroesophageal reflux disease (GERD) are more likely to experience NVP and hyperemesis. During pregnancy, esophageal, gastric, and small bowel motility are impaired as a result of smooth muscle relaxation fostered by increased levels of female sex hormones. This dysmotility could contribute to NVP. Hormonal changes leading to changes in lower esophageal tone may also lead NVP, in addition to heartburn.[76,77] Psychological factors, particularly feelings of ambivalence about the pregnancy, have been suggested as part of the etiology; however, this theory has not been borne out by psychological evaluation of women with this condition, and studies are confounded by the fact that the experience of hyperemesis can lead to feelings of ambivalence.[78] Elevated serum concentrations of estrogen and progesterone have been implicated as pathogenic factors, as have decreased prolactin levels and elevated human chorionic gonadotropin (hCG); however, none of these associations has been definitely demonstrated.[79] Other proposed pathogenic factors include abnormal gastric motility, nutrient deficiencies, alterations in lipid levels, changes in the autonomic nervous system, genetic factors, and infection with *Helicobacter pylori*.[80–83]

DIAGNOSIS

There is no specific diagnosis for NVP. Nausea, accompanied by a missed menstrual period, or other confirmation of pregnancy, is usually adequate. Hyperemesis gravidarum, likewise, is a clinical diagnosis. There is not a definitive point of demarcation separating a diagnosis of NVP from hyperemesis. The sheer persistence of the vomiting accompanied, as mentioned, by weight loss exceeding 5% of prepregnancy body weight and ketonuria unrelated to other causes is considered diagnostic.[66] Although NVP can cause significant inconvenience and changes in daily activities, hyperemesis is usually markedly debilitating, and many practitioners consider persistent vomiting and marked debility diagnostic of hyperemesis. Women with persistent vomiting are evaluated by ultrasound for the presence of trophoblastic disease (e.g., hydatidiform mole) and multiple pregnancy. Serum electrolyte levels, as well as FT4

are also checked. Differential diagnosis for nausea and vomiting is extensive; other pathologic causes ranging from endocrine disorders to neoplastic conditions should be ruled out, particularly for nausea and vomiting that commence after 10 weeks gestation. Concurrent signs such as abdominal pain, fever, headache, goiter, abnormal neurologic findings, diarrhea, constipation, or hypertension suggest a problem other than NVP or hyperemesis gravidarum. Nausea and vomiting that occur in the latter half of pregnancy could be associated with preeclampsia, HELLP syndrome (hemolysis, elevated liver function tests, low platelets), and fatty liver of pregnancy, and should be ruled out.

CONVENTIONAL TREATMENT OF NVP AND HYPEREMESIS GRAVIDARUM

Conventional treatment for both NVP and hyperemesis gravidarum includes supportive therapy, nonpharmacologic, and pharmacologic interventions. Nausea that is mild and self-limiting is considered normal, and does not require treatment.[63] The supportive and nonpharmacologic therapies used in conventional care are the same as those used in conjunction with botanical care, and are described under Nonpharmacologic Treatment of NVP and Hyperemesis gravidarum. Pharmacologic treatment may be necessary in severe or refractory cases, and after nonpharmacologic interventions have failed to bring relief or improvement, in order for women to function in their daily lives and gain nutrition without IV or enteral feeding methods.

The mainstay of pharmacologic treatment for these conditions is the use of antiemetic drugs.[68,84,85] Antiemetics have been shown to be more effective than placebo, and do not appear to increase birth defect risk; however, evidence of safety from well-designed trials is not substantial.[86] Thus, many women and doctors remain wary of their use, especially in the first trimester. Most women are content to wait out the normal, mild to moderate first trimester nausea without significant intervention as long as it does not interfere with their ability to function.

When pharmacologic intervention is required, it is advisable to start with drugs with minimal known side effects, and progress to other drugs only if these are ineffective and antiemetic therapy is necessary.[87] Antihistamines are also successfully used as antiemetics to control NVP.[86] A meta-analysis reviewed 24 controlled studies including over 200,000 first trimester exposures and found that these medications had a protective effect, with a reduction in birth defects.[85] A number of other antiemetic medications are used including several of the dopamine antagonists, appear to be helpful and are not associated with teratogenicity.[86]

Corticosteroids have been used for women with severe, unresponsive hyperemesis. The mechanisms of action are poorly understood, and the results of controlled trials have been contradictory.[86,88–92] Prolonged use of oral corticosteroids in pregnancy may increase the risk of preterm premature rupture of membranes (PPROM), as well as the risk of cleft palate, the latter when administered prior to 10 weeks of gestation.[93,94] Given the potential risks and undetermined benefits, ACOG advises against the use of corticosteroids for treatment of hyperemesis unless as a last resort.[95]

NONPHARMACOLOGIC TREATMENT OF NVP AND HYPEREMESIS GRAVIDARUM

Mazotta et al. conducted an extensive review of MEDLINE, the Cochrane Database of Systematic Reviews, and bibliographies and texts for the effectiveness of maternal therapies for NVP (including randomized controlled trials of drug treatment versus placebo or no therapy, or another drug therapy). The researchers focused on observational, controlled studies for adverse fetal effects, specifically, the incidence of major malformations, because treatment of NVP usually involves administration of medication during the first trimester. Physical outcome measures were evaluated. The findings indicated that some women prefer more ''natural,'' nonpharmacologic therapies for NVP, such as dietary and lifestyle changes, pyridoxine, ginger, and/or stimulation of the P6 Neiguan point (e.g., Seabands). Theoretically, these therapies are not considered harmful to the fetus.[96] The goals of nonpharmacologic treatment for both NVP and hyperemesis gravidarum include reducing the symptoms and enabling the mother to obtain nutrition from foods and fluids. Malnutrition and dehydration are both significant concerns when there is a near complete inability to eat or drink, or when there is persistent vomiting.

Nutrition: Food and Fluids

Trigger Avoidance

Women with hyperolfaction are especially prone to NVP and hyperemesis. Avoiding triggers of nausea and/or vomiting, for example, offending smells or tastes can be helpful. This can be difficult to effectively achieve as preferences and aversions are continually changing for the pregnant woman, and are highly individual. It is for this reason that simple comfort measures, such as dry crackers, ginger ale, and so forth, may only yield fleeting results. Many women with NVP find that most measures only work for a limited time, often for a few consecutive days, and that the very substance that led to some improvement may often then join the ranks of the offending agents. For some women, teeth brushing is a major trigger, stimulating gagging or vomiting. Avoiding brushing when nauseated can help, and using a toothpaste that is low-foaming and with a mild minty flavor can help minimize an adverse response. Some women find foregoing the toothpaste altogether for a time can be helpful. Using a child's sized toothbrush, and avoiding getting the brush, toothpaste, or ''spit'' in the back of the mouth can be helpful. Many women find the sight of certain foods distasteful enough to trigger nausea or vomiting; for example, the meat or fish department of the market. Avoiding these departments or having someone else do the grocery

shopping until intolerable nausea has passed, can reduce trigger exposure. Iron-containing supplements cause gastric irritation, and thus should be avoided until NVP or hyperemesis is overcome. Women with very severe NVP or hyperemesis may be triggered by even the thought or the mention of food. In such cases, avoiding exposure to all food images may be necessary. Additional triggers include stuffy rooms, odors (e.g., perfume, chemicals, smoke), heat, humidity, noise, and visual or physical motion (e.g., flickering lights, driving), and inadequate rest.[97,98]

Protein and Carbohydrates

Avoid hypoglycemia by eating small, regular meals or snacks, including immediately upon waking in the morning, and prior to bed and even during the night, if necessary. Women with mild to moderate nausea, with or without minimal vomiting, often respond to intake of dry, slightly salty foods, for example, crackers, toast, and pretzels, as well as high-protein foods.[41] Many women find that eating simple, carbohydrate-based meals, for example, a baked potato or plain pasta with a small amount of butter and salt, can be easily digested and allay nausea. A small amount of slightly sweetened yogurt is often a tolerable snack, and can easily be eaten at any time of day (or night).

Fluids

Fluids that pregnant women commonly find tolerable include cold water with a squeeze of lemon or lime; sparkling; water with lemon, lime, or orange flavor; ginger ale, and small amounts of grapefruit juice, lemonade, or purple grape juice. Clear broth, bouillon, or miso broth may also be tolerated by some women. Although it is critical that women with hyperemesis adequately replace lost fluids, drinking large amounts of fluids is, in itself, often a trigger for nausea and vomiting. Therefore, drinking very small amounts at a time, as little as several tablespoons of liquid every 15 minutes or so, is frequently more effective than trying to drink larger amounts of fluids. Women should also be encouraged to drink a couple of tablespoons of fluid after each episode or vomiting.

Nutritive Enemas

In severe cases, an enema containing Pedialyte can dramatically and quickly improve the mother's status, and preempt the need to hospitalize her for intravenous (IV) nutrition. This can be repeated up to several times daily for a few days as a supplement to the woman's nutritional intake. Quite often this is enough to raise her energy and fluid level so that appetite is restored and she is able to eat and drink on her own. Many women find this an option they prefer to try before a more invasive trip to the hospital becomes necessary.

Intravenous Fluid and Nutrient Replacement

Should oral fluid or food intake be impossible to achieve, and a nutritive enema either ineffective or an undesirable treatment to the mother, IV nutrition will be necessary. Infusion of intravenous Lactated Ringer's solution supplemented with electrolytes and vitamins can relieve symptoms of dehydration in 1 to 2 days.[61] Minerals including magnesium, phosphorus, and potassium need to be supplemented, and 100 mg IV thiamine for 2 to 3 days is recommended for women who have vomited for greater than 3 weeks.[61] Plasma sodium should be corrected at a careful rate to avoid osmotic demyelination syndrome, which can occur with too quick a replacement.

Nutrient Supplements

Pyridoxine (vitamin B_6), 10 to 25 mg by mouth, three to four times daily, has been demonstrated to improve mild to moderate nausea in women with NVP, although it does not seem to be effective in the treatment of vomiting.[84,100,101]

Acupuncture/Acupressure

A number of studies have been published demonstrating the effectiveness of acupuncture and acupressure for the suppression and relief of nausea and vomiting, including NVP.[102–106] Treatment has focused on what is referred to in TCM as the Neiguan point, pericardium 6 (P6), an acupuncture point on the underside of the wrist. Acupuncture has been systemically tested in a limited number of trials. A single-blind, randomized, controlled trial in which 593 women less than 14 weeks with nausea and vomiting were treated weekly for 4 weeks found no difference in vomiting but less nausea and dry retching in treatment women versus controls. Although acupuncture clearly seems to be effective, it requires administration by a trained acupuncturist, regular access to which is a limitation for many women, and shows no apparently greater benefit than acupressure, which women can self-administer. Further, acupuncture treatment requires ongoing visits, which incur a much greater cost than the one-time purchase of acupressure bands, which can be used repeatedly.[107]

In one study, researchers randomly assigned 33 women with hyperemesis gravidarum to acupuncture treatments on P6 or to mock treatments at a different location. After 2 days, all treatments were stopped for an additional 2 days to allow any effects to dissipate. The groups were then reversed for two additional days of treatment. Before treatment, all women were vomiting. On day 3, only 7 out of 17 women (41%) receiving active acupuncture were still vomiting compared with 12 out of 16 (75%) receiving mock treatment. After the active and mock treatment groups were switched, more of the women in the active treatment group ceased vomiting. The women in the active treatment group also reported decreased nausea.[46] In another study, reported in the *Journal of Reproductive Medicine*, 41 patients were treated with acustimulation of P6 with an acustimulation device at the Department of Maternal-Fetal Medicine at Eastern Virginia Medical School.[108] Prior to treatment, patients averaged a score of 4.2 on a nausea severity scale, with 5 being completely debilitating nausea. Posttreatment device effectiveness averaged 4.2, with significant or complete relief rated 5. All neonates were evaluated for congenital abnormalities and all neonates were

found to be normal. The researchers concluded that because current pharmacologic treatments for nausea in early pregnancy are not consistent, efficacious, or without unwanted side effects or increased teratogenic risks, acustimulation of P6 in pregnancy may prove to be a significant therapeutic alternative. Stimulation of the P6 Neiguan point, three fingers above the wrist on the palmar aspect of the forearm, has been shown to alleviate NVP by at least 50%. (P6 stimulation for 5 minutes four times daily, or as continuously as possible, may be administered by acupuncture, acupressure, manual pressure, Seabands, or possibly by a small TENS unit, Relief Band.) However, the small sample sizes and the failure of most trials to blind outcome assessment complicate interpretation of results. The acupuncture principles and practices for the treatment of nausea and vomiting using P6 and for the alleviation of pain also have been effectively and successfully extended to the treatment of postsurgical nausea and postsurgical pain relief.[109] Because acupressure stimulation is safe and inexpensive as well as simple for women to achieve on their own at home with the use of wrist bands (e.g., Seabands), it is a reasonable part of a protocol for the treatment of NVP and hyperemesis. For nausea and vomiting, pressure is applied to the P6 point on the inside of the wrist, about 2 to 3 fingerbreadths proximal to the wrist crease, between the tendons, about 1 cm deep. Manually, the woman or someone else applies pressure for 5 minutes every 4 hours. Alternately, pressure can be applied by wearing an elasticized band with a 1-cm round plastic protruding button that is centered over the acupuncture point.[107] The FDA has recently approved a wristband type, miniaturized, battery-operated transcutaneous electrical nerve stimulator designed to stimulate the P6 acupuncture site. Called the ReliefBand, it has been found to be helpful for mild to moderate nausea and vomiting but not for severe symptoms.[106] It is available over the Internet for less than $100, and clients with nausea and vomiting of pregnancy may want to pursue this option.[107]

When Is Hospitalization for NVP Recommended?

According to the American College of Obstetricians and Gynecologists, 2004 ''When a woman cannot tolerate liquids without vomiting and has not responded to outpatient management, hospitalization for evaluation and treatment is recommended. After the patient has been hospitalized on one occasion and a workup for other causes of severe vomiting has been undertaken, intravenous hydration, nutritional support, and modification of antiemetic therapy often can be accomplished at home. Nevertheless, the option of hospitalization for observation and further assessment should be preserved for patients who experience a change in vital signs or a change in affect or who continue to lose weight.''[95]

Hypnosis and Psychotherapy

A limited number of studies have demonstrated the efficacy of hypnosis in reducing NVP in some patients.[110] Psychotherapy is more likely to be beneficial if anxiety is playing a role in the etiology of the condition.[111] Because it is a safe intervention, and because many women become anxious, depressed, or isolated when dealing with protracted vomiting, some form of counseling is a reasonable part of a treatment plan if it can be afforded.

BOTANICAL TREATMENT OF NVP AND HYPEREMESIS GRAVIDARUM

According to Borrelli et al., the potential teratogenic effects of drugs administered during the critical embryogenic period of pregnancy drastically limit their use.[112] Because of this, many pregnant women turn to complementary and alternative therapies including vitamins, herbal products, homeopathic preparation, acupressure, and acupuncture.[112–114] A recent literature survey reports that the most commonly used botanicals for the treatment of morning sickness are ginger, chamomile, peppermint, and raspberry leaf.[115] Only ginger has been subjected to investigation of its safety and efficacy for NVP.

The botanical approach to treatment of NVP and Hyperemesis gravidarum, like conventional therapy, includes supportive, nonpharmacologic, and pharmacologic therapies, the latter in the form of antinauseant/antiemetic and antispasmodic herbs, and the use of gently herbs that support digestion (Table 13-3). The supportive and nonpharmacologic therapies used with

TABLE **13-3**

Botanical Treatment Strategies for NVP and Hyperemesis Gravidarum

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Reduce nausea and vomiting	Antinauseant	*Cannabis* spp.	Marijuana
	Antiemetic	*Mentha piperita*	Peppermint
		Zingiber officinalis	Ginger
Relieve stomach cramps	Antispasmodic	*Dioscorea villosa*	Wild yam
		Matricaria recutita	Chamomile
Support digestion/appetite	Digestive bitters	*Ballota nigra*	Black horehound
		Taraxacum officinale	Dandelion root

herbal interventions are the same as those used with conventional therapies, and are described under Nonpharmacologic Treatment of NVP and Hyperemesis Gravidarum. NVP can be challenging to treat with consistent effectiveness in any individual woman, because it is difficult to find a single remedy that works consistently, especially over a prolonged time period. Typically, women find relief from a specific protocol for a short duration, only to find themselves nauseated by the remedy that helped in the first place. Therefore, it is preferable to have a ''repertoire'' or options a woman can try, and suggest she rotate these to create some variety and not become resistant to any single approach.

The literature is unclear and contradictory regarding the safety of the herbs used for NVP during pregnancy, which is especially concerning as they are used most extensively during the first and early second trimesters when embryonic/fetal development is critical. Historical and anecdotal use suggests a high degree of safety, but as with as substances taken during pregnancy, care should be exercised. Specific safety data are presented with individual herbs.

Ginger

The best studied herb for NVP is *Zingiber officinalis* (Fig. 13-2).[145–150] A recent systematic literature search by Borrelli et al. identified six double-blind RCTs with a total of 675 participants and a prospective observational cohort study, which met the inclusion criteria for the review. The methodological quality of 4 of 5 of the RCTs was high according to the Jadad scale. The six studies are outlined in Table 13-4.

Four of the six RCTs ($n = 246$) showed superiority of ginger over placebo; the other two RCTs ($n = 429$) indicated that ginger was as effective as the reference drug (vitamin B_6) in relieving the severity of nausea and vomiting episodes, including one study by Fischer-Rasmussen et al. that demonstrated efficacy and was superior to placebo for the treatment of hyperemesis gravidarum.[116] The observational study and RCTs showed the absence of significant side effects or adverse effects on pregnancy outcomes. There were no spontaneous or case reports of adverse events during ginger treatment in pregnancy.[112] The evidence, both scientific and traditional, is that ginger is safe and effective for some women with mild or moderate nausea and vomiting of pregnancy.[107] It can be taken in the form of ginger ale, ginger tea sipped in small doses (to avoid nausea that may from drinking large amounts of any fluid), ginger capsules, or even candied ginger or spiced ginger cookies. It is generally recommended that women take on up to 1 g daily, as this is the largest amount that has been studied in clinical trials and been demonstrated as safe. Ginger ale must have real ginger in it, not just ginger flavoring, to be effective. The use of ginger is affordable and many women find this an acceptable approach, preferring to try this before resorting to conventional medications. The various routes of administration allow women to change how they are taking it regularly, which can help them avoid becoming sensitized to and nauseated from the ginger flavor. Occasionally, some women find the flavor unpleasant; adding peppermint leaf to the tea may improve the flavor for these women. Capsules allow women to avoid the smell and taste; however, some may find that eructation is unpleasant. As with all NVP remedies, there will be a great deal of individual variety determining what is palatable and tolerable.

Figure 13-2 Ginger root (*Zingiber officinale*). (Photo by Martin Wall.)

Peppermint

Peppermint has a long history of use as a digestive aid, for improving digestion after meals, and calming nausea, flatulence, and abdominal spasms. The role of peppermint in the treatment of NVP has not been investigated; however, some benefit has been shown for the treatment of postoperative nausea, and also for the treatment of esophageal dysmotility, a physiologic finding that is also postulated as part of the etiology of NVP.[76,151] Anecdotally, peppermint reportedly has a calmative effect on the stomach, in addition to reducing nausea, in women with NVP.[142] It is taken as a tea in small sips (often combined with ginger for a pleasant-tasting tea), in the form of peppermint-flavored candies, or peppermint oil indirectly inhaled as aromatherapy. For the latter, many pregnant women have found it effective to douse a small piece of cotton wool with peppermint oil, and place this in a small glass vial that can be carried around in the pocket, opened and whiffed as needed, for example, during car travel.[152] It is considered a safe and gentle remedy; however, peppermint herb is rich in volatile oils that can cross the placenta; thus, care should be taken to use only if necessary and in small amounts as a tea only, and not as a tincture or essential oil for ingestion. Neither the Botanical Safety Handbook, nor the German Commission E contradict the use of peppermint during pregnancy.[153,154]

Black Horehound

British trained herbalists commonly use black horehound in the treatment of motion sickness and NVP and with reports of great effects.[116] The safety of this herb during pregnancy has not been evaluated.

TABLE 13-4

Clinical Trials Demonstrating Efficacy of Ginger for NVP

AUTHOR	STUDY DESIGN	WEEKS GESTATION	DOSE	CONTROL	TREATMENT DURATION	MAIN OUTCOME
Fischer-Rasmussen, 1990[145]	Randomized, double-blind, cross-over	<20	250 mg 4x/day	Placebo	4 days	Based on a 4-point subjective scoring system for severity and relief of nausea and vomiting and weight loss measurement, ginger was better than placebo in alleviating or eliminating NVP
Vutyavanich, 2001[146]	Randomized, double-blind	<17	250 mg 4x/day	Placebo	4 days	Based on severity of nausea and vomiting (subjective reporting), number of vomiting episodes; occurrence of side and adverse effects on pregnancy, ginger was more effective than placebo in reducing the severity of nausea and vomiting
Keating, 2002[147]	Randomized, double-blind	<12	250 mg 4x/day	Placebo	2 weeks	Using a 10-point scale to evaluate the duration and severity of nausea and vomiting, ginger was more effective than placebo in reducing nausea and stopping vomiting
Sripramote, 2003[148]	Randomized, double-blind	<17	500 mg 3x/day	Vit B_6	3 days	Using a visual analog scale to evaluate severity of nausea, number of vomiting episodes, and occurrence of adverse effects ginger was found to significantly reduce nausea score, and fewer vomiting episodes were noted
Willetts, 2003[149]	Randomized, double-blind	<20	125 mg 3x/day	Placebo	4 days	Ginger was observed to be more effective than placebo in reducing nausea and retching. No effects on vomiting symptoms were reported.
Smith, 2004[150]	Randomized, double-blind	>8, <16	350 mg 3/day	Vit B_6	3 weeks	Ginger was found to be as effective as vitamin B_6 at days 7, 14, 21 in reducing nausea, dry retching, and vomiting compared with baseline.

Data from Borrelli F, Capasso R, Aviello G, et al.: Effectiveness and safety of ginger in the treatment of pregnancy-induced nausea and vomiting, Obstet Gynecol 105(4):849-856, 2005.

It is typically taken in small does (1 to 2 mL tincture three times/day), in combination with ginger, chamomile, or peppermint. It may also be added to a small amount of ginger ale or carbonated water (see dandelion root).

Wild Yam

Wild yam has been used in herbal medicine as an antispasmodic for not only the uterus and bladder, but for the stomach and intestines as well. The Eclectic physicians reported its use for the treatment of NVP, a use which has found its way into contemporary midwifery-botanical practice.[152,155,156] Steroidal saponins in the plant may exert estrogenic effects by binding with endogenous estrogen receptors in the hypothalamus; however, this has only been demonstrated in vitro. There is no evidence to contraindicate the use of this herb during pregnancy, nor research on its safety or efficacy during pregnancy. There are no reports in the literature of wild yam having emmenagogic effects.[143] It is typically taken in repeated doses of small amounts (e.g., 20 to 30 drops) in tincture form, sometimes combined dandelion root tincture (see the following) or added to ginger tea, when other remedies alone have failed.

Dandelion Root

Dandelion root is traditionally used as a gentle digestive bitter to improve digestion, increase bile flow choleretic, and relieve nausea and vomiting and improve appetite. The bitter constituents in dandelion increase bile flow, and act as an appetite stimulant.[143,144] There are no reports in the literature of dandelion being either safe or contraindicated during pregnancy.[143] Herbalist-midwives may recommend it taken alone in small doses (1 to 15 drops) as a tincture in water, or this same dose added to half a glass of ginger ale or lemon-flavored carbonated water. It has a mildly bitter taste, but dilute, is not typically offensive to pregnant women.

Cannabis

Cannabis (marijuana) has at least a 4000-year history of use as a medicinal plant, including extensive use for the treatment of gynecologic and obstetric conditions in many cultures throughout the world.[117–119] It was first described in Western medical literature by a physician in Ohio who used an extract of *Cannabis indica* to successfully remedy a near fatal case of hyperemesis gravidarum.[120] Cannabinoids, delivered in the form of pharmaceutical preparations (e.g., nabilone and delta(9)-tetrahydrocannabinol) or directly smoked by the patient, are effective in reducing chemotherapy-induced nausea, vomiting, and anorexia, and may significantly improve appetite and ability to eat and drink.[121–125] It is used extensively by patients undergoing treatment for cancer and HIV, and may provide novel therapies for other GI disorders, including gastric ulcers, irritable bowel syndrome, Crohn's disease, secretory diarrhea, paralytic ileus, and gastroesophageal reflux disease.[121–125] The 5-HT3–receptor antagonists, including cannabinoids, offer enhanced control of emesis while causing few side effects.[126] Marijuana use may improve treatment adherence in patients undergoing treatments with protocol that have a high rate of side effects, such as HIV and cancer chemotherapy.[127] Clinical trials that have looked at the efficacy of cannabis as an antiemetic have found it better than conventional antiemetics.[128] Not only does cannabis reduce nausea and vomiting, but it has a significant effect on improving appetite and caloric intake.[123,129–131] Patients with multiple sclerosis (MS) symptoms report reductions in nausea, and improved ability to eat and drink, among improvement in other MS-related symptoms.[132,133] In additional to its effects on central nervous system receptors, new research suggests the role of cannabinoids in the treatment of esophageal dysfunction, as one of its mechanisms of action.[134] There are strong indications that cannabis is better tolerated than THC alone, because cannabis contains several additional cannabinoids, like cannabidiol (CBD), which antagonize the psychotropic actions of THC, but do not inhibit the appetite-stimulating effect.[135]

Cannabis is reported to be the most widely used recreational drug in pregnancy, with use during pregnancy in developed nations estimated to be approximately 10% to 20%.[136,137] Not uncommonly, it is self-prescribed for nausea and vomiting of pregnancy.[107,138] A recent (2003–2004) survey of 84 female users of medicinal cannabis, recruited through two compassion societies in British Columbia, Canada, found that of the 79 respondents who had experienced pregnancy, 51 (65%) reported using cannabis during their pregnancies. Although 59 (77%) of the respondents who had been pregnant had experienced nausea and/or vomiting of pregnancy, 40 (68%) had used cannabis to treat the condition, and of these respondents, 37 (over 92%) rated cannabis as ''extremely effective'' or ''effective.''[138] It is widely used by Rastafarian women in Jamaica and elsewhere to treat NVP, as well as other complaints, for example, labor pain.[138] Because of its status as an illegal drug, as well as the general ethical issues that arise regarding conducting clinical studies during pregnancy, no formal clinical trials that examine the efficacy of this herb for use during pregnancy have been conducted.[137,138] Because of its widespread use, its safety during pregnancy has been the subject of significant investigation; however, according to Westfall et al., it is important to be cognizant when evaluating marijuana and pregnancy safety data, that data derived from recreational use may not be equivalent to that which might be derived from therapeutic use, in terms of adverse effects.[138] The influence of cannabis use during human pregnancy, and indeed, the medical use of marijuana generally, have been fraught with contradictions and controversies.[137] A recent Medline database search by Karila et al. conducted for articles indexed from 1970 to 2005 using the terms cannabis/marijuana, pregnancy, fetal development, newborn, prenatal exposure, neurobehavioral deficits, cognitive deficits, executive functions, cannabinoids, and reproduction suggested that cannabis use during pregnancy is related to diverse neurobehavioral and cognitive outcomes, including symptoms of inattention, impulsivity, deficits

in learning and memory, and a deficiency in aspects of executive functions.[136] However, composite learning scores in these studies were not lower than controls, and adverse effects on learning were not significant when home factors were included.[139] It is therefore difficult to ascribe direct effects on learning and behavior to maternal cannabis consumption during pregnancy.[138] A report by Park et al. states that few studies have been conclusive regarding the effects of cannabis use during pregnancy. Cannabis use has been correlated with low birth weight, prematurity, intrauterine growth retardation, presence of congenital abnormalities, perinatal death, and delayed time to commencement of respiration. However, increased evidence of increased meconium staining was observed in newborns of heavy marijuana users who were from low-risk pregnancy and socioeconomic categories.[137] Studies evaluating the use of cannabis during pregnancy have been confounded by the failure to separate the effects of alcohol versus marijuana on the newborn.[136,140] A large survey ($n = 12060$) of British women showed no significant different in growth of the babies among women who did vs. did not use cannabis during pregnancy, based on self-report. Another large survey ($n = 12885$) of women in Copenhagen, which controlled for both alcohol and tobacco use, showed similar findings. A multisite study in the United States ($n = 7470$ women) showed no correlation between maternal cannabis intake and adverse pregnancy outcome including premature birth, low birth weight, or placental abruption. A study of Jamaican births ($n = 9919$) showed no correlation between maternal cannabis use and perinatal morbidity or mortality. Side effects of use reported in the HIV community and general population include more side effects, feeling high, sedation, euphoria, dizziness, dysphoria or depression, hallucinations, paranoia, and arterial hypotension.[128] Chronic cannabis use has been reported to affect memory in patients using it to treat HIV chemotherapy-induced symptoms, and a study found that acutely, cannabis can impair driving response.[125,141] Clearly, cannabis has effects on brain activity, cognition, perception, and function. Herbalists consider cannabis to be a reliable antiemetic, antinauseant, antianorexic, and analgesic. It is also considered to have mild oxytocic effects.[142]

What remains unknown is the effects of small amounts of marijuana intake during pregnancy for the specific treatment of NVP, anorexia, and weight loss, both independently and as compared with no treatment or the use of conventional antiemetics. As it can be expected that some population of pregnant women entering the clinic with NVP will be self-medicating with cannabis, it is important to elicit honest communication from the patient using a nonjudgmental approach, in order to ascertain how much cannabis the woman is using and what effects she feels it is having. Drug adulterants such as ketamine and others are common in street product, and can pose serious and dangerous consequences to the mother and fetus.

NUTRITIONAL CONSIDERATIONS

See nonpharmacologic treatments.

Treatment Summary for NVP and Hyperemesis Gravidarum

The following treatments may be tried individually or in combination, according to the woman's needs, preferences, and severity of her condition.

Nonpharmacologic/Nutritional Treatments

- Avoid triggers
- Avoid hypoglycemia with small, frequent intake of foods and beverages
- High protein, low fat snacks
- Dry crackers, pretzels, pasta, baked potatoes, or other bland, slightly salty foods
- Carbonated beverages; beverages with lemon or lime; ginger ale, slightly salty clear broth or bouillon
- Supplementation with vitamin B_6 (10 or 25 mg three times per day) significantly reduced the severity of morning sickness.
- Acupuncture/acupressure at P6, or an individually designed professional acupuncture program
- Hypnosis or psychotherapy
- Nutritive enemas or parenteral nutrition in severe cases

Pharmacologic Treatments

- Antiemetics

There are NO drugs that are FDA-approved for the treatment of morning sickness. However, drugs such as dimenhydrinate, diphenhydramine, and melamine have been used. Prescription medications used include prochlorperazine (Compazine®), ondansetron (Zofran®), meclizine (Antivert®), promethazine (Phenergan®), and metoclopramide (Reglan®).

- Hospitalization when there is complete inability to eat or drink, or if there is persistent weight loss

Botanical Treatments

- Ginger root has demonstrated efficacy and safety, up to 1 g/day, for the treatment of NVP and hyperemesis
- Other herbs include peppermint, wild yam, dandelion root, chamomile, and black horehound. These have a traditional basis of safe and effective use and can be taken regularly throughout the day.
- Peppermint oil can be used as aromatherapy as needed.
- Marijuana is commonly used as self-medication for nausea, vomiting, and loss of appetite. Results of safety studies in pregnancy are contradictory and the legal status makes use controversial; nonetheless, practitioners should inquire about patient's use and advise safe use if the patient is likely to continue to use regardless of practitioner's recommendations (i.e., avoid potentially adulterated ''street'' products).

Pregnancy: Second Trimester

Elizabeth Mazanec, Aviva Romm, Mary Bove

14 CHAPTER

HEARTBURN (GASTROESOPHAGEAL REFLUX) IN PREGNANCY

Elizabeth Mazanec, Aviva Romm

Heartburn is caused by a reflux of gastric acids into the lower esophagus, usually occurring after meals or when lying down.[1] The gastric acids irritate the esophagus, causing a burning sensation behind the sternum that may extend into the neck and face, and may be accompanied by regurgitation, nausea, and hypersalivation. Inflammation and ulceration of the esophagus may result.[2] Up to two-thirds of women experience heartburn during pregnancy.[3] Only rarely it is an exacerbation of preexisting disease. Symptoms may begin as early as the first trimester and cease soon after birth. Most women first experience reflux symptoms after 5 months of gestation; however, many women report the onset of symptoms only when they become very bothersome, long after the symptoms actually began.[3] The prevalence and severity of heartburn progressively increases during pregnancy.[4]

The exact causes(s) of reflux during pregnancy include relaxed lower esophageal tone, secondary to hormonal changes during pregnancy, particularly the influence of progesterone, and mechanical pressure of the growing uterus on the stomach which contributes to reflux of gastric acids into the esophagus.[3] However, some studies have demonstrated that, in spite of increased intra-abdominal pressure as the uterus expands as pregnancy progresses, the high abdominal pressure and the low pressure in the esophagus are maintained by a compensatory increase in lower esophageal sphincter (LES) pressure, supporting the finding by Lind et al. that the LES pressure rose in response to abdominal compression in pregnant women without heartburn.[3] Other possible contributing factors include an alteration in gastrointestinal transit time. For example, some studies have suggested that ineffective esophageal motility (decreased amplitude of distal esophageal contractions) is the most common motility abnormality in GERD.[5]

DIAGNOSIS

A diagnosis of heartburn in pregnancy is generally based on clinical picture. The association of other signs and symptoms is important in ruling out underlying causes: anorexia, hiatus hernia, and gastric ulcers are the more common causes in pregnancy. Other systemic illnesses of the respiratory, cardiac, or GI tract that are associated with GI irritation or substernal pain need to be taken into account when forming a diagnosis. Preeclampsia must be ruled out on a pregnant woman in her third trimester complaining of epigastric or right upper quadrant abdominal discomfort.

CONVENTIONAL TREATMENT APPROACHES

Medical treatment in pregnancy focuses on symptomatic relief. Complications due to reflux in pregnancy are rare because of its short duration, and thus upper endoscopy and other diagnostic tests are not typically indicated.[3] Complications, however, can include esophagitis, bleeding, and stricture formation. Care should follow a ''step-up algorithm'' (start with simple and noninterventional strategies and add on as needed) beginning with lifestyle modifications and dietary changes. Antacids or sucralfate are considered the first-line drug therapies. If symptoms persist, histamine-2-receptor (H_2) antagonists can be used. Proton pump inhibitors (PPIs) are reserved for women with intractable symptoms or complicated reflux disease. Promotility agents may also be used. All but omeprazole are FDA category B drugs during pregnancy. Most drugs are excreted in breast milk. Of systemic agents, only the H_2 receptor antagonists, with the exception of nizatidine, are safe to use during lactation.[3]

There are limited data regarding the safety of antacids during pregnancy, and teratogenicity is a significant concern.[3] One retrospective case controlled study in the 1960s reported a significant increase in major and minor congenital abnormalities in infants exposed to antacids during the first trimester of pregnancy.[3]

TABLE **14-1**

Botanical Treatment Strategies for Heartburn

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Relieve esophageal irritation and inflammation	Demulcents	*Althea officinalis*	Marshmallow root
		Ulmus fulva	Slippery elm bark
Improve esophageal sphincter tone	Unknown	*Amygdalis communis*	Almonds

Analysis of individual antacids has shown no such associations, and most aluminum-, magnesium-, and calcium-containing antacids are considered acceptable in normal therapeutic doses during pregnancy.[3] One study ''found a higher rate of congenital anomalies in children of women who took an antacid in the first trimester.''[6] Side effects of antacids are diarrhea, constipation, headaches, and nausea. Compounds containing magnesium trisilicate can lead to fetal nephrolithiasis, hypotonia, respiratory distress, and cardiovascular impairment if used long-term and in high doses. Magnesium sulfate can slow or arrest labor and may cause convulsions. Magnesium-containing antacids should be avoided during the last few weeks of pregnancy. Antacids containing sodium bicarbonate should not be used during pregnancy because they can cause maternal or fetal metabolic alkalosis and fluid overload. Pregnant women receiving iron for iron deficiency anemia should be monitored carefully when antacids are used, because normal gastric acid secretions facilitate the absorption of iron, and iron and antacids should be taken at different times during the day to avoid problems.[3] There are also little data to support the efficacy of antacids during pregnancy.[6] According to Richter:

> *Medications for treating GERD are not routinely or rigorously tested in randomized, controlled trials in pregnant women because of ethical and medicolegal concerns. Most recommendations arise from case reports and cohort studies by physicians, pharmaceutical companies, or the FDA. Voluntary reporting by the manufacturers suffers from an unknown duration of follow up, absence of appropriate controls, and possible reporting bias.*[3]

Some believe that over-the-counter antacids should be avoided in pregnancy because they can lead to an excess intake of aluminum and salt and interfere with absorption of potassium, phosphorus, and calcium and drugs such as anticoagulants, salicylates, and vitamin E.[7] One small double-blind randomized control trial in pregnancy was identified for H_2-blockers. It found that 150 mg of Ranitidine taken twice daily improved symptoms over a placebo by 44% and supposedly demonstrated no risk. However, it mirrored the antacid alone group, which also had reduced symptoms of 44%.[8]

BOTANICAL TREATMENT

Herbal treatment for heartburn during pregnancy focuses on simple lifestyle and dietary modification, and the use of gentle herbs to soothe and protect the esophageal epithelium (Table 14-1). A mild antacid herb may also be included in more bothersome cases. Nervines (e.g., chamomile, skullcap, or passion flower) can be added to a protocol if heartburn is causing sleeping problems or if stress is contributing to digestive difficulties. Herbs for treating heartburn are best taken as teas or lozenges (e.g., slippery elm bark lozenges) rather than as tinctures, both to bathe the alimentary canal as they are ingested, and avoid the potentially irritating effects of alcohol in the tinctures. Further, demulcent herbs are best extracted in water for maximum efficacy (see Chapter 3).

General Recommendations for Preventing/ Relieving Heartburn

A number of foods have been associated with an increase in reflux, either by increasing gastric acid or relaxing lower esophageal sphincter pressure. Individuals with GERD may wish to experiment with avoiding all, or some, of these possibly offending items or practices:

- Fatty or spicy foods
- Coffee (decaffeinated or caffeinated), chocolate, and alcohol[9,10]
- Eating for at least 2 hours before lying down
- Tomato products, for example., tomato sauce, pizza
- Peppermint and ginger[11]
- Drinking more than one cup of fluids with a meal.

Other practices may help to improve symptoms:

- Eat small frequent meals (six to eight a day)
- Elevate the head of the bed 6 inches
- Chew gum

Interestingly, almost no clinical trials have been conducted demonstrating beneficial effects of eliminating offending foods or practices, including those listed in the preceding, with the exception of elevation of the head of the bed.[12] Nonetheless, many women report improvement with a combination of these changes.

Discussion of Botanicals

Almonds

Chewing raw almonds is a treatment relied on by many midwives for the reduction of heartburn. Instruct clients to thoroughly chew 8 to 10 raw almonds and swallow. This may be repeated several times daily. Almonds are

nutritive and there are no expected side effects or contraindications to the use of this food.

Marshmallow Root

Marshmallow root has similar properties to slippery elm—it is mucilaginous, soothing, and anti-inflammatory to epithelial surfaces. Evidence for the use of this herb stems largely from traditional use. Though this herb has been used for centuries, there are remarkably few clinical trials evaluating its safety or efficacy. It has no known expected toxic effects; however, it has been shown to lower blood sugar in animal studies. Caution should be observed when using this herb in combination with blood sugar lowering medications, though the risk is theoretical. It has been suggested theoretically that this herb might interfere with drug absorption. Although this has never been demonstrated clinically, it may be prudent to avoid taking this herb at the same time as taking other medicinal agents, and instead take marshmallow root and other medications several hours apart.[13] Herbalists, however, commonly combine marshmallow with other herbs for the digestive tract. Unlike slippery elm, marshmallow is not available in convenient lozenges; therefore, it must be prepared as an infusion, and sipped as needed throughout the day or during an acute episode of heartburn.

Slippery Elm

Ulmus rubra is a nutritive demulcent, rich in mucilaginous polysaccharides. Slippery elm's emollient actions have led to its traditional use for centuries for soothing irritated tissue, coating, and protecting the digestive tract.[13] Its high calcium content may have some antacid effects. The herb may be taken as a tea; however, it has a thick, mucus-like consistency that can be unpleasant to women with NVP. To avoid this, one to two teaspoons of slippery elm can be added to oatmeal instead; it is has a pleasant, slight maple syrup–like flavor and is easy to take this way. The easiest and most effective way to use the herb is in the form of slippery elm lozenges, which may be purchased in a conveniently prepared form (e.g., Thayer Slippery Elm Lozenges), are quite palatable, and may sucked on as needed up to 8 to 12 per day. Supporting evidence for the herb's benefits is drawn from traditional use, and extrapolation from effects of the mucilaginous constituent of the herb. There is no known toxicity, and in fact slippery elm has been used in some baby foods and adult nutritional foods.[13]

IRON DEFICIENCY ANEMIA

Aviva Romm

Iron is essential to multiple metabolic processes, including oxygen transport (e.g., critical to muscle and brain functioning), DNA synthesis, and electron transport. Iron balance in the body is carefully regulated to guarantee that sufficient iron is absorbed in order to compensate for body losses of iron. Either inadequate intake of absorbable dietary iron or excessive loss of iron from the body can cause iron deficiency. Menstrual losses are highly variable, ranging from 10 to 250 mL (4 to 100 mg of iron) per menses. Women require twice the iron intake of men to maintain normal stores, and can expect to lose approximately 500 mg of iron with each pregnancy without careful attention to adequate dietary intake and supplementation.[14] Iron deficiency anemia occurs when all of the body's iron stores have been entirely depleted. This chapter focuses on the iron needs of the pregnant and lactating woman.

Iron deficiency is the most common nutritional deficiency worldwide, affecting 20% of the world's population. It is considered the most common health problem faced by women worldwide, adjusted for all ages and economic groups.[15] Poor socioeconomic status does, however, further increase the risk of iron deficiency anemia.[16] It is estimated that worldwide, 20% to 50% of all maternal deaths are related to iron deficiency anemia.[17]

During pregnancy the blood volume expands by about 35% to 50%, with additional iron required to meet the needs of the fetus, placenta, and increased maternal tissue. In the second and third trimesters, iron requirements increase to three times the nonpregnant needs. Women who do not supplement iron during pregnancy are usually unable to maintain adequate iron stores throughout and are at increased risk for developing iron deficiency anemia. Women who have a history of iron deficiency anemia prior to pregnancy, low iron stores at the onset of pregnancy, or those with heavy menstrual blood loss, are at further risk for anemia during pregnancy.[14,18] Iron deficiency anemia decreases quality of life to due to symptoms of fatigue, weakness, loss of appetite, and increased susceptibility to infection (see Symptoms), and increases the risk of a number of problems including severe anemia from normal blood loss during labor requiring blood transfusions. Fetal iron stores in the first 6 months of life are dependent upon maternal stores during pregnancy.[18] Postpartum anemia is a contributing factor to postpartum depression.[18]

SYMPTOMS

Symptoms of iron deficiency anemia include:

- Easy fatigability
- Tachycardia
- Palpitations
- Tachypnea on exertion
- Pica (craving for specific foods or nonfood items, e.g., ice chips, laundry starch, dirt)
- Muscle dysfunction
- Appetite loss
- Constipation
- Poor scholastic performance
- Altered resistance to infection
- Altered behavior
- Smooth tongue*
- Brittle nails*
- Cheilosis (fissures at the corners of the mouth)*

Improving iron status noticeably and rapidly improves most of these symptoms.

*In severe iron deficiency

DIAGNOSIS

Iron deficiency anemia is diagnosed on the basis of simple, inexpensive screening tests. Hematocrit (Hct) and hemoglobin (Hb), both of which can often be done in-office by an obstetrician or midwife, are the most commonly ascertained values. The mean cell volume (MCV) is done to assess red blood cell (RBC) size to rule out anemia caused by nutritional deficiencies other than iron, for example, vitamin B_{12} deficiency, which causes macrocytic anemia. Hematocrit is a measure of the percentage of whole blood occupied by red blood cells, the oxygen and iron-carrying portions of the blood, and Hb is the concentration of iron-containing protein in the RBCs. The normal hematocrit in nonpregnant women ranges from 36% to 45%. However, in pregnant women, because of normally increased blood volume (physiologic hemodilution of pregnancy), values can be as low as 34% in singleton and 30% in twin or multiple pregnancy, even with normal stores of iron stores, and does not necessarily indicate a true anemia. Normal Hb for women ranges between 12 to 16 g/dL, with a drop down to 10.5 possibly normal in mid-pregnancy (weeks 16 to 28) owing to physiologic hemodilution.[14] Diagnosis also may be made on the basis of an increase in hemoglobin levels after supplementation has begun. Additional tests, including serum ferritin concentration, and transferrin levels can also be used to differentiate iron deficiency anemia from other forms of anemia. This is usually only necessary during pregnancy when anemia is refractory to treatment.

DIFFERENTIAL DIAGNOSIS

Iron deficiency anemia can be a result of chronic internal bleeding that can occur, for example, in the case of gastrointestinal disease (e.g., inflammatory bowel disease, celiac disease, peptic ulcer disease). Causes of microcytic anemia that must be ruled out include thalassemia, anemia of chronic disease, sideroblastic anemia, and lead poisoning.

CONVENTIONAL TREATMENT

Conventional treatment of iron deficiency anemia relies primarily on diet and iron supplements.

Diet

Red meat, poultry, and fish are good sources of heme iron, the most absorbable form. Iron deficiency anemia is lowest in areas where red meat is a dietary staple. Dietary sources of non-heme iron include blackstrap molasses, dried apricots, raisins, dark green leafy vegetables (e.g., kale, collards), kidney beans, lentils, mussels, oysters, pine nuts, pumpkin seeds, quinoa, tempeh, tofu, and wheat germ. Non-heme sources of iron are also an important part of the diet, though not as readily absorbable. A carefully planned diet rich in a variety of iron sources can allow vegetarians to meet their dietary iron needs.

Iron Supplements

Oral iron supplements are an inexpensive, generally safe, and simple way to treat iron deficiency. Because iron is best absorbed from the duodenum and proximal jejunum, time released and enteric coated preparations are not very effective, and they are also much more costly. Ascorbic acid increases the absorbability of non-heme iron. Taking 250 mg of vitamin C with iron supplement is therefore advisable. Phytates, oxalates, carbonates, calcium, and tannins, found in foods such as cereals, dietary fiber, tea, coffee, eggs, and milk, interfere with iron absorption; therefore, iron supplements should not be taken with food. Antacids also interfere with iron absorption, and should be given several hours prior to or after taking iron supplements. Antibiotics also interfere with iron absorption. Gastrointestinal (GI) side effects are common (10% to 20% of patients report GI side effects) with conventional iron supplements (see Botanical Treatment of Iron Deficiency Anemia for herbal alternatives). Constipation is a common complaint, as are nausea, vomiting, abdominal discomfort, and diarrhea. Elemental iron in the forms of ferrous sulfate, ferrous fumarate, or ferrous gluconate may be substituted with ferrous sulfate elixir, a liquid preparation that may cause fewer GI symptoms. Improvement can usually be observed starting approximately 7 days after the onset of iron supplementation. Also, though a less effective therapy, iron supplements may be taken with meals to avoid discomfort. The various forms of iron commonly used therapeutically appear to be equally effective. In severe cases where oral iron is unable to be tolerated, parenteral iron may be given. It is considered optimal to remain on iron supplements for approximately 6 months after iron levels return to normal in order to adequately replenish depleted iron stores. Low-dose iron supplementation (30 mg/day) throughout pregnancy is as effective as higher dose supplementation (e.g., 60 mg day) and less likely to cause side effects.[15] If a patient does not respond to iron therapy, the possibility of an underlying disorder or coexisting disease (e.g., GI bleeding, thalassemia, and so forth.) must be addressed. Malabsorption is also a common problem leading to refractory anemia.

BOTANICAL TREATMENT

The use of various forms of elemental iron have been a part of both folk and Western medical herbal tradition for at least the past few hundred years, whether in the form of iron nails stuck in apples to infuse the apples with iron for consumption by pioneer women, or the use of ferrum supplements by the Eclectic physicians. As stated earlier, side effects from iron supplements are common. For pregnant women who may be experiencing GI symptoms due to the pregnancy itself, such as nausea, vomiting, or constipation, regular elemental iron supplements may be intolerable. Although there is almost no evidence in the literature evaluating the efficacy or safety of herbs used as ''iron tonics,'' their use is popular amongst herbalists, midwives, and pregnant women (Table 14-2). Clinical observation has demonstrated a high level of efficacy and minimal side effects (see Case History) with a limited number of botanical supplements. The herbs in this section are those most commonly used in contemporary midwifery and herbal practice.

TABLE **14-2**

Botanical Treatment Strategies for Iron Deficiency Anemia

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Provide dietary/ supplemental iron	Iron tonic	*Medicago sativa*	Alfalfa
		Rumex crispus	Yellow dock
		Taraxacum officinale	Dandelion root
		Urtica dioica	Nettles
			Floradix Iron and Herbs
			Liquid chlorophyll
Treat blood and yin deficiency		*Angelica sinensis*	Dong quai
		Paeonia rubra	Peony

Floradix Iron and Herbs

This product is a popular, easily assimilable source of elemental iron and iron-rich herbs, including aqueous extracts of carrot, nettle wort, spinach, kelp, blackberry, cherry, and beet root concentrates, among other herbal and food ingredients. A 2-tsp (10-mL) daily dose provides 100% of the daily dose of pyridoxine (vitamin B_6), 125% cyanocobalamin (vitamin B_{12}), and 10 mg (56%) of iron. Many of the herbs in the product have not been evaluated for use during pregnancy; however, no adverse outcomes from use of the product have been identified. Most women find Floradix palatable and easy to digest.

Nettles

The leaf of the nettle plant, prepared as a strong infusion, is a popular tonic used by many herbalists for treating iron deficiency anemia, many of whom stand by it as one of their primary anemia treatments. The fresh leaves, which lose their sting when cooked, can also be eaten as an iron-rich green leafy vegetable, if one has access to them. The leaves are also rich in chlorophyll, for which they are commonly a commercial source, and a rich source of vitamin C.[22] As with other herbs used for the treatment of iron deficiency anemia, the amount of iron in any given dose has not been quantified; however, pregnant women and midwives report good results with symptoms of anemia, particularly fatigue. It is rarely used as a singular treatment but rather as part of a protocol for anemia. It has been suggested, although not demonstrated, that the astringency of this herb might interfere with iron absorption. A 1975 review article by Farnsworth et al. reported that stinging nettle was a potential abortifacient, and that its constituent 5-hydroxytryptamine was a uterine stimulant; however, frequent use of large doses of this herbal infusion in midwifery practice has demonstrated no evidence of such activity.[23]

Yellow Dock and Dandelion Root Iron Tonic

The use of yellow dock root, in combination with dandelion root, is perhaps one of the most popular Western herb tonics used by midwives.[19,20] It is typically prepared as a syrup with blackstrap molasses (see recipe), itself rich in iron (and calcium), to be taken daily, usually in a 1- to 2-tbl dose. In this form it is easily digestible, though some women report mild nausea if taken on an empty stomach. Yellow dock is listed in Dr. Duke's Phytochemical and Ethnobotanical Databases (http://www.ars-grin.gov/duke/) as an iron-containing herb; however, the amount of iron per any single dose of this herb is difficult to quantify and has not been evaluated in regard to its use as an iron supplement. The herb is touted by traditional herbalists, as is dandelion, not only for its iron content but also for its actions on the liver. It is believed to increase uptake of dietary iron. Neither the veracity of this claim nor possible mechanisms have been evaluated. The use of yellow dock as an iron tonic is presented in the 1918 edition of Remington's Dispensatory of the United States of America: The roots of this plant are said to possess the power to take up the iron present in the soil, and fix it in the form of organic compounds of iron. By watering the plants with a solution of iron carbonate, roots are said to be obtained that contain 1.5% of iron. Rumex is said to give good results in the treatment of chlorosis and anemia. The authors gave the dried and powdered root during meals in doses of 15 to 45 grains (1 to 3 g), in view

Dandelion-Yellow Dock Syrup for Iron Deficiency Anemia

Yellow dock root (*Rumex crispus*): ½ ounce (14 g)
Dandelion root (*Taraxacum officinale*): ½ ounce (14 g)
Directions: Prepare a decoction by simmering both herbs (1 oz/28 g total) in 4 cups of water, uncovered, until reduced to 1 cup. Strain the liquid thoroughly (discard the herb material) and add ½ cup blackstrap molasses, mixing until blended. Cool to room temperature. Keep refrigerated. The product will keep for up to 2 weeks refrigerated.
Dose: 1 to 2 tbl, up to twice daily depending upon the severity of the anemia.

of their good results they regard it as a valuable iron medicine. Dock root is given in powder or in decoction.[21] Note that yellow dock is sometimes considered contraindicated in pregnancy because it is a mild anthraquinone laxative; however, clinically it has not been observed to be associated with increased uterine activity. The gentle laxative effects (aperient) relieve anemia-associated constipation while building iron.

Alfalfa

In 1915, Dr. Richard Willstatter, a German chemist, was awarded the Nobel Prize in Chemistry for elucidating the structure of chlorophyll. Willstatter observed that the chlorophyll molecule bears a striking resemblance to hemoglobin, except that its centerpiece is a single atom of magnesium rather than iron. Today, commercial liquid chlorophyll is derived mostly from alfalfa, and is popularly used to improve iron levels in iron deficiency anemia. No data evaluating the efficacy or safety of chlorophyll use during pregnancy have been identified. In fact, little data exists on the safety or efficacy of alfalfa, though some preliminary studies have suggested possible beneficial effects in lowering cholesterol.[13] The herb may also have some hypoglycemic and antifungal effects.[13] Alfalfa is considered to have minimal risk when used as a food source (e.g., a normal serving of alfalfa sprouts) during pregnancy and lactation.[22] Animal studies (nonpregnant and lactating) have demonstrated no toxicity when alfalfa seeds or saponins are ingested in large quantities over an extended period of time (up to 6 weeks consumption of seeds and 8 weeks for saponins).[13] However, the herb, particularly the seeds and seed products (e.g., alfalfa sprouts) are contraindicated in patients with systemic lupus erythematosus (SLE), in whom it has been reported to cause exacerbations and pancytopenia.[13] The constituent thought to be responsible for this effect, l-canavanine, is not present in the leaf; however, lupus-like syndrome has been reported with consumption of leaf-containing tablets. This may be caused by adulteration of leaf products with l-canavanine–containing plant parts. Alfalfa contains the phytoestrogen coumestrol, which may have estrogenic properties. A 1975 paper by Farnsworth et al. on the antifertility effects of herbs stated that alfalfa has uterine stimulant activity; however, no other such findings have been reported in the literature or observed by clinical herbalists.[23] Alfalfa is rich in vitamin K, and thus is contraindicated with anticoagulant therapies (e.g., Warfarin) with which it may interfere. It may also interact with hypoglycemic drugs, lower blood glucose levels, interfere with lipid-lowering medications, and should not be taken with Thorazine. Clinically, liquid chlorophyll, combined with other iron-raising protocols, has been observed to rapidly improve hemoglobin more quickly than the protocol used alone, and without adverse effects (see Case History that follows).

Dong Quai and Peony

Blood deficiency, a traditional Chinese medicine diagnosis, akin to iron deficiency anemia, is characterized by fatigue, depression, dizziness, constipation with dry stools, and pale complexion. The traditional Chinese medical literature is replete with treatments for blood deficiency in pregnancy, prescriptions historically tailored to the unique needs of the individual woman. Herbs classically used to treat blood deficiency include dong quai and peony, the two primary ingredients in the classic dong quai and peony formula; however, the literature is scant in demonstrating hematopoeisis or improvements in iron status with its use. There is only a single case report in the literature of a hemodialysis patient who was anemic because of insufficient production of erythropoietin, who self-medicated with dong quai and peony decoction once weekly. The tea was prepared using approximately 12 g of dong quai and 52 g of shao yao decocted in three cups of water reduced to one cup by cooking. The patient was concurrently given recombinant human erythropoietin but appeared to be resistant to it. One month after starting the herbal tea, the hematocrit increased from 29.7% to 34.4%.[24] Because of possible hormonal effects and anticoagulant/antiplatelet activity, the herb is listed in several Western sources as contraindicated in pregnancy.[13,23,26] Data regarding the effect of dong quai preparations on the fetus are lacking.[24] It is recommended that this herb be used in pregnancy only under qualified supervision, and in traditional herbal preparations used for pregnancy.[24]

CASE HISTORY

Celeste is a 28-year-old woman who is 29 weeks pregnant with her second baby. She has a history of iron deficiency anemia for which she has been under the care of her obstetrician. In spite of 6 weeks of treatment, her hematocrit, which is 29, has not increased. Her physician doubled her iron supplement to 60 mg/day, and she is now experiencing side effects, including severe constipation for 2 weeks, nausea, and abdominal cramps. Her skin color has a slightly greenish tint around her mouth and under her eyes. She is deeply fatigued and has a poor appetite, as well as daily headaches.

Recommendations:

- Discontinue taking the prescription iron supplement.
- Take Floradix Iron and Herbs as instructed on the bottle.

After 1 week, Celeste was still constipated, so she was instructed to add the following to her plan:

For constipation:

- Take Yellow-Dock Dandelion Root Syrup (1 tbl each morning)
- Soak 4 dried prunes and 1 tablespoon bran per ½ cup warm, unfiltered apple juice until prunes are soft. Eat/drink entire portion once each morning for constipation.

Three weeks after the initial visit (31 weeks pregnant), Celeste's hematocrit had risen to 30, and she was having regular bowel movements—one soft, formed stool per day or every other day. It was recommended that she continue taking the preparations for constipation each morning for a couple of additional weeks. It was also recommended that she add 1 tbl liquid chlorophyll to her protocol daily, and take 250 mg vitamin C

with each dose of Floradix. It was felt somewhat urgent to quickly raise her hematocrit, as her due date was only 9 weeks away.

At 34 weeks pregnancy, Celeste's hematocrit was 32, and now that her bowels were regular, she was instructed to start eating beef stew three times per week (organic beef). At 36 weeks, Celeste's hematocrit was 34, and by 37 weeks it had risen to 35. Celeste gave birth at home, with the midwife who had assisted her in treating her anemia, at 38 weeks, to a healthy baby boy.

PRETERM LABOR AND UTERINE IRRITABILITY

Aviva Romm

Preterm labor occurs prior to the end of the 37th pregnancy week. Preterm birth is one of the leading causes of infant mortality and also long-term disability in the United States.[27–29] In spite of improvements in the outcome of prematurely born infants, the rate of premature delivery has continued to rise, largely as a result of assisted reproductive technologies (ARTs) and multiple pregnancies, although poor nutrition and lower socioeconomic status continue to play a major role. In 2004, 12.5% of all births in the United States occurred prior to 32 weeks gestation. Rates of preterm birth are highest among African-American women, adolescents, women older than 40, unmarried women, and women with lower socioeconomic status. Additional factors that contribute to premature labor include prior preterm birth, history of second trimester pregnancy loss, preterm premature rupture of the membranes (PPROM), multiple gestation, concurrent obstetric or medical complications, uteroplacental insufficiency, cigarette smoking, drug use, alcohol intake, lack of prenatal care, uterine abnormalities, infections, loop electrosurgical excision procedure (LEEP), and fetal congenital abnormalities.[29,30] Stress, dehydration, domestic violence, emotional abuse, closely spaced pregnancies, and jobs that require a long period of standing are also thought to be contributory to premature labor.[30,31] The following specific conditions are associated with premature labor: urinary tract infections, vaginal infections, sexually transmitted infections and possibly other infections, diabetes, hypertension, preeclampsia, and clotting disorders (thrombophilia).[31] Dietary patterns also play a role. Decreased frequency of eating is associated with an increased risk of premature labor. Women who consume three meals and two snacks daily throughout pregnancy appear less likely to experience premature onset of labor.[32] Low or no fish consumption, associated with inadequate intake of omega-3 fatty acids, is also associated with an increased risk of premature labor.[33] Other nutritional deficiencies, notably vitamin C, may also be related to increased risk of premature labor.[34]

Uterine irritability is a stressful and annoying pregnancy problem in which the pregnant woman experiences frequent uterine contractions ranging from mild to painful that generally come in an irregular pattern, although they may appear to mimic early labor. Women with uterine irritability have an increased risk of premature labor; however, the presence of an irritable uterus is not indicative of labor, and may simply be a source of ongoing concern to the mother, her family, and care providers, and a bother to the mother.

SIGNS AND SYMPTOMS

Women should be advised to contact their health care provides or go to the hospital immediately if they are experiencing the following:

- Contractions every 10 minutes or more frequently
- Rupture of membranes (ROM)
- Vaginal bleeding
- Pelvic pressure
- Low, dull backache
- Menstrual-like cramps
- Abdominal cramps with or without diarrhea

Unfortunately, diagnosis of early preterm labor is difficult and has a high false-positive rate, which may lead to possibly harmful interventions for thousands of women. Screening methods for preterm labor such as routine cervical assessment, transvaginal ultrasonography, fetal fibronectin (fFN) detection, and home uterine activity monitoring have not been shown to be beneficial at actually preventing preterm labor, although some of these methods may detect risk or early symptoms, and fFN testing can provide information on the likelihood of a woman entering labor in the two weeks after the test.[29]

Medical evaluation for the presence of premature labor includes assessment for the following signs:

- Uterine activity that is suggestive of a labor pattern (increasingly regular contractions coming with increasing frequency)
- Rupture of membranes
- Vaginal bleeding
- Cervical dilatation, effacement, and station

MEDICAL TREATMENT

Strategies to prevent preterm delivery have focused on early diagnosis of preterm labor symptoms and on clinical markers such as cervical change, uterine contractions, vaginal bleeding, and changes in fetal behavior. Bed rest and home uterine monitoring have not led to a reduction in preterm birth rates. Since, bed rest can lead to potential adverse effects on women and their families, clinicians should not routinely advise women to rest in bed to prevent preterm birth.[35] The medical priority is to halt the progression to premature birth whenever possible, while treating underlying medical contributing causes, and assure fetal lung maturity and the availability of proper neonatal care if preterm birth becomes inevitable. Medical treatments used to arrest premature labor include the use of tocolytic agents (e.g., terbutaline, magnesium sulfate, ritodrine, and nifedipine); corticosteroid therapy to stimulate fetal lung maturity, and treatment of underlying causes of premature labor, for example, antibiotics for specific infections. Complications of the use of these medications vary according to the drug, and include but are not limited to pulmonary edema, profound hypotension, muscular paralysis, cardiac arrest, respiratory depression, hypokalemia, hyperglycemia, arrhythmias, myocardial

ischemia, and maternal death. A risk–harm evaluation is done based on the week's gestation of the pregnancy, status of the fetus, and reason for premature labor when determining whether to arrest labor medically or to allow labor to proceed. If premature labor is diagnosed and is progressing, the pregnant woman is transferred to a care facility equipped to care for the premature newborn.

BOTANICAL TREATMENT

Women in active, progressing, premature labor require hospitalization for birth to guarantee the neonate access to appropriate medical care necessary for survival after birth. The use of botanicals is not adequate treatment if a woman has premature cervical dilatation, ruptured membranes, or regular contractions with signs of labor progress. However, women experiencing uterine irritability or threatened premature labor with mild irregular contractions only may respond effectively to botanical uterine spasmolytics. Active labor must be ruled out by a qualified obstetric care provider and the situation carefully and appropriately monitored. Uterine spasmolytics such as cramp bark (*Viburnum opulus*) and black haw (*Viburnum prunifolium*) can be given in repeated doses every 15 minutes with 2 to 3 mL of these herbs over a 2- to 3-hour period. This should yield a demonstrable reduction in uterine irritability. Other herbs that may be combined with the aforementioned to create an additive musculoskeletal relaxant effect include wild yam (*Dioscorea villosa*) and Jamaican dogwood (*Piscidea Erythrina*). The latter two herbs are considered appropriate for acute use only during pregnancy; long-term effects are unknown and possibly unsafe. However, no adverse effects are expected from acute use over a few hours time within recommended doses (Jamaican dogwood up to 2 mL every 30 minutes for 2 hours, combined with an equal amount of either cramp bark or black haw at each dose). These herbs are not recommended for use during the first trimester, and should not be used for more than three consecutive days as described. Midwives may also recommend warm baths to which have been added 5 to 7 drops of lavender oil for relaxation, visualization, and other mind–body techniques for stress reduction. Bathing is contraindicated if there has been ROM. Emotional support of the mother is essential, and herbs for anxiety may be given short term in small doses if necessary.

Premature labor can progress to birth in this short time; thus, these herbs should not be relied on if premature labor is occurring unless in an appropriate medical setting and in conjunction with medical observation and care; no studies have been conducted to examine the safety or efficacy of botanical treatments to arrest premature labor contractions.

Pregnancy: Third Trimester

Aviva Romm, Laurel Lee, Christopher Hobbs

15 CHAPTER

CONSTIPATION DURING PREGNANCY

Aviva Romm

Constipation is defined as having bowel movements fewer than three times per week. The stools are typically hard, dry, small in size, and difficult to eliminate. Constipation may be accompanied by straining, pain, bloating, cramping, and the sensation of a full bowel. It is a bothersome common complaint of pregnancy, particularly in the second and third trimesters. Women who are habitually constipated may become more so during pregnancy. The prevalence of constipation in pregnancy is reported to be 11% to 38%.[1] It has been generally accepted that decreased gastric motility in pregnancy is a result of increased circulating progesterone levels. More recent experimental evidence suggests that elevated estrogen concentrations are involved in delayed motility through an enhancement of nitric oxide release.[1,2] Slow transit time of food through the intestinal tract leads to increased water absorption and thereby to constipation. Dietary factors, particularly inadequate fiber intake and lack of exercise, contribute to constipation, as does increased pressure of the growing uterus on the rectum as pregnancy becomes advanced.[3] Ignoring the urge to have a bowel movement can also contribute to the problem. Iron-deficiency anemia can contribute to constipation, as can elemental iron supplements (see Chapter 16).

DIAGNOSIS

Constipation first presenting in pregnancy does not require an extensive evaluation, and is considered a normal pregnancy complaint.[4] Constipation accompanied by other symptoms, for example, blood in the stools, or unresponsive to treatments requires further investigation to rule out possible pathology.

CONVENTIONAL TREATMENT OF CONSTIPATION

Most patients respond to simple dietary and lifestyle measures. Treatment during pregnancy is similar to that for the general population; however, special care must be taken to avoid medications that may be harmful to the fetus or disrupt the pregnancy.[4]

The first line of treatments for constipation include:

- Increasing water consumption to eight glasses per day: Avoiding dehydration will keep the stools softer and make them easier to pass; liquids that contain caffeine (coffee, tea, cola) increase dehydration.
- Increasing dietary fiber to 20 to 35 g/day: High-fiber foods increase stool bulk and facilitate bowel evacuation; high-fiber food sources include fruits, vegetables, whole grains and bran cereals, and beans.
- Minimizing consumption of constipating food items, for example, ice cream, meats, cheese, and high-fat foods can increase constipation, especially in a low-fiber diet.
- Increasing daily activity: Even increased daily walking, as well as other forms of exercise, for unknown reasons, will prevent constipation.
- Encouraging use of the bathroom as soon as there is the urge to eliminate; putting off the need to have a bowel movement can actually blunt the sensation over time, leading to constipation.
- Trying to have a bowel movement at a regular time each day by sitting on the toilet and trying to relax each morning shortly after awakening. Some women, particularly in advanced pregnancy, find that putting their feet up on a stool while sitting on the toilet relieves pressure of the uterus on the lower intestines, facilitating a bowel movement.

Should these measures not be adequate to treat the problem, bulk laxative fiber supplements, or, if necessary, osmotic or stimulating laxatives can be used.

Fiber Supplementation: Bulk-Forming Laxatives

Fiber supplements, which are bulk-forming laxatives, are effective, safe, and without side effects when used in appropriate doses; however, limited studies are available on the use of laxatives in pregnancy.[1] In addition to

Treatment Summary for Constipation

- Increase fluid intake, especially water and noncaffeinated beverages.
- Increase consumption of high-fiber foods such as fruits, vegetables, whole grains, and beans.
- Decrease consumption of constipating foods, particularly those high in fat, such as cheese, milk, and ice cream.
- Increase exercise, even a brisk walk once daily.
- Do not ignore or delay the urge to have a bowel movement—when you've got to go, you've got to go!
- HERBS ARE NOT A SUBSTITUTE FOR DIETARY AND LIFESTYLE CHANGES!

TABLE **15-1**

FDA Categories for Drug Use during Pregnancy

CATEGORY	DESCRIPTION
A	Adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities.
B	Animal studies have revealed no evidence of harm to the fetus; however, there are no adequate and well-controlled studies in pregnant women OR Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus.
C	Animal studies have shown an adverse effect and there are no adequate and well-controlled studies in pregnant women OR No animal studies have been conducted and there are no adequate and well-controlled studies in pregnant women.
D	Studies, adequate well-controlled or observational, in pregnant women have demonstrated a risk to the fetus. However, the benefits of therapy may outweigh the potential risk.
X	Studies, adequate well-controlled or observational, in animals or pregnant women have demonstrated positive evidence of fetal abnormalities. The use of the product is contraindicated in women who are or may become pregnant.

Adapted from Meadows M: Pregnancy and the drug dilemma, FDA Consum 35(3):16-20, 2001.

softening the stool by keeping more fluid in the bowel lumen, the presence of the increased bulk is thought to stimulate intestinal peristalsis.[5] Examples include wheat fiber (e.g., wheat bran), psyllium, flax seed, and pectin, to 25 g per day.[6] Laxative effects may take 3 to 7 days to be noticeable. If side effects occur, switching to a different bulk laxative may help. Taken in excessive qualities they can lead to cramping, gas, diarrhea, and bloating.[4,6] Bulk laxatives have a pregnancy B category (Table 15-1).[4,6] Stool softeners are not recommended for use during pregnancy.

Osmotic Laxatives

Osmotic laxatives are indigestible sugars that work by increasing the amount of fluid that is retained in the bowel. Sorbitol, lactulose, and glycerin appear to be safe sources for use during pregnancy. Saline, phosphorus, and magnesium salt laxatives, including many prepackaged enemas, are not advisable during pregnancy because they can cause salt retention in the mother.[7]

Stimulant Laxatives

Stimulant laxatives are best used in pregnancy only after other measures have failed to relieve constipation. Examples of stimulant laxatives include senna, cascara sagrada, and aloes. Of these, only senna is considered safe (see senna discussion in the following) for use during pregnancy. Approved as an over-the-counter (OTC) medication, senna is an herb and is thus discussed in the following section with other botanicals. Stimulants are more likely to cause side effects of diarrhea and abdominal pain than are bulk laxatives.[8]

BOTANICAL TREATMENT FOR CONSTIPATION

Botanical treatment for constipation relies on a combination of the practical dietary and lifestyle changes presented on the preceding page, and gentle herbs that increase bulk and moisture in the bowel, or gently stimulate bowel activity. These herbs may be used singly, or in combination, and are combined with a carminative herb—one that relieves gas and griping—to prevent side effects sometimes associated with laxatives. Examples of carminatives that can be safely used for short durations during pregnancy include ginger root and anise seed. Stimulant laxatives are used only for short durations (up to 2 weeks) to avoid dependence. When using herbal bulking laxatives, it is important to make sure the patient is drinking plenty of water, because the bulk laxative will absorb large amounts of water from the colon. There have been few studies evaluating the safety or efficacy of natural laxatives in pregnancy. A number of herbal preparations available in health food and grocery stores contain herbs that are not appropriate or safe for use in pregnancy, including cascara sagrada, aloe, and buckthorn (see Case History 1). Aloe may be teratogenic, whereas the other herbs are associated with increased uterine activity. Practitioners should inquire of their pregnant patients whether they are using preparations containing these herbs if constipation is a problem and

TABLE 15-2

Botanical Treatment Strategies for Heartburn

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Relieve constipation	Bulk laxatives	*Linum usitatissimum*	Flax (Linseed)
		Plantago psyllium, P. ovata	Psyllium
	Lubricating laxatives	*Glycyrrhiza glabra*	Licorice
	Stimulating laxatives (aperients)	*Cassia senna; C. angustifolia*	Senna
		Rumex crispus	Yellow dock root

direct them to safer food-based, lifestyle, and herbal alternatives.

Foods and food agents commonly used to relieve constipation include wheat bran, which is a high-fiber source, prunes (soaked in water or apple juice until soft and plump), and fruits high in sorbitol, including apples, pears, apricots, and cherries. Molasses is both high in iron and a gentle laxative, and therefore excellent for constipation associated with anemia.[9] Commonly used herbs are listed in Table 15-2, and discussed below. In traditional Chinese medicine constipation is considered a symptom of blood deficiency, and may be treated with Dong Quai and Peony formula, discussed under iron deficiency anemia.

Discussion of Botanicals for Constipation during Pregnancy

Psyllium Seed and Husk

Psyllium seeds, as well as Ispaghula seeds, which have comparable activity, are bulk laxative agents.[10] Psyllium seeds shorten bowel transit time by increasing the intestinal contents and stimulating stretch receptors and thereby peristalsis. The whole seeds or husks are soaked in water or apple juice for several hours and then they are taken with a large amount of liquid. Bowel movements are usually achieved within 6 to 12 hours after taking the preparation.[5] Rarely, allergic reactions have occurred.[5] The preparation should not be taken by patients with swallowing difficulties because choking can occur.

Senna Leaf and Pod

Senna, a quick-acting, reliable stimulating laxative generally, is taken as a tea. Its mechanism of action is primarily via anthracoids (sennoside A and B), or anthraquinone glycosides. Senna is considered appropriate for use in acute cases, and is not considered an herb to be used regularly. When used alone it can elicit loose stool with significant griping, and is therefore traditionally combined with a small amount of ginger root, anise seed, fennel seed, spearmint, or peppermint for their carminative action (see Formula 1 in Box 15-2). There is significant disagreement in the literature regarding the safety of senna use during pregnancy. Modern herbalists have tended to consider it contraindicated for use during pregnancy, with the supposition that the markedly increased bowel peristalsis stimulated by the herb might lead to reflex uterine activity and thus may have indirect emmenagogic effects. The herb is commonly found on lists of herbs contraindicated during pregnancy. The *Botanical Safety Handbook* classifies senna as a Class 2b herb, not to be used during pregnancy or lactation unless otherwise directed by an expert qualified in the appropriate use of this substance.[14] According to the European Scientific Cooperative on Phytotherapy (ESCOP) there no reports of undesirable or damaging

BOX 15-1

Commonly Used Botanical Laxatives That Are Contraindicated during Pregnancy

Aloe	(*Aloe vera*)
Cascara	(*Frangula purshiana*)
Buckthorn	(*Rhamnus cathartica*)
Castor oil	(*Ricinus communis*)
Chinese rhubarb	(*Rheum palmatum*)

BOX 15-2

Formulas for Constipation

Formula 1: Laxative Tea (adapted from the German Standard Registration)[5]

Senna leaf	(*Cassia senna*)	15 g
Anise seed	(*Pimpinella anisum*)	3 g
Chamomile blossoms	(*Matricaria recutita*)	5 g
Spearmint leaf	*(Mentha spicata)*	5 g
		Total: 28 g (1 oz)

Directions: Prepare 1 to 2 teaspoons as an infusion. Steep for 10 minutes. Take 1 cup each evening.

Formula 2: Dandelion-Yellow Dock Syrup

Yellow dock root	(*Rumex crispus*)	14 g
Dandelion root	(*Taraxacum officinale*)	14 g

Directions: Prepare a decoction by simmering both herbs (1 oz/28 g total) in 4 cups of water, uncovered, until reduced to 1 cup. Strain the liquid thoroughly (discard the herb material) and add ½ cup blackstrap molasses, mixing until blended. Cool to room temperature. Keep refrigerated. The product will keep for up to 2 weeks refrigerated.

Dose: 1 to 2 tablespoons, up to twice daily.

effects during pregnancy or on the fetus when senna is used in accordance with the recommended dosing and use schedule. However, because of experimental data concerning a genotoxic risk from several anthracoids (emodin and aloe-emodin), the herb should be avoided during the first trimester or taken only under medical supervision.[15] Two studies reported that human and animal data do not support concerns that senna laxatives pose a genotoxic risk to humans when taken properly.[16–18] A review article reported that senna appears to be the most appropriate stimulant laxative to use during pregnancy.[19] Small amounts of active metabolites are excreted in the breast milk, and though these do not appear to have a laxative effect in the newborn, its use is not recommended during lactation.[15] The dose recommended by ESCOP is individualized to the smallest possible dose that produces a comfortable, soft, formed stool. Weiss states that small doses of 1 to 2 g soften the stools within 5 to 7 hours.[10] It is recommended that the herb be used only short-term for occasional constipation. Senna preparations are typically taken at bed time to produce a bowel movement the following morning.

Yellow Dock Root

Yellow dock is sometimes contraindicated during pregnancy because of its anthraquinone glycoside contents. Clinically, it is widely used by midwives as a gentle stimulating laxative because it is effective yet much milder than senna, which is generally avoided when possible. According to the *Botanical Safety Handbook*, this herb contains only a small amount of anthraquinone glycosides and has a mild laxative effect.[14] Limited maternal use has not been observed to cause any increase in fetal malformation or other harmful effects to the fetus.[20] The use of yellow dock for constipation is illustrated in yellow dock dandelion root syrup, and in the case history in iron deficiency anemia.

Licorice Root

Herbalists favor the use of licorice root for its intestinal moistening abilities. According to Wichtl et al., licorice root is included in laxative herbal tea formulas because it potentiates the activity of anthraquinone-containing herbs (e.g., senna), lowering the required dose of the anthraquinone laxative.[11] Because of its effects on glucorticoids, excessive doses (>50 g per day) over a prolonged period can result in hypokalemia, hypernatremia, edema, hypertension, and cardiac disorders, and in extreme cases, pseudoaldosteronism. Symptoms disappear within days of discontinuation of the herb.[11] Two recent reports on high-dose licorice consumption, in the form of licorice candy containing actual glycyrrhizin-containing licorice, during pregnancy, demonstrated no increase in maternal hypertension or low birth weight; however, both studies, demonstrated a significant increased in preterm (<37 weeks) delivery. In one study, the risk of preterm delivery was greater than double the risk of women not consuming licorice.[12,13] No studies demonstrate harm or adverse outcomes with short-term use of modest doses of licorice. It is recommended that licorice not be used in excessive doses or for prolonged periods during pregnancy, rather, as with senna, it be used for acute use for up to several days at a time.

CASE HISTORY 1:

Sara, a nurse, was pregnant with her second baby. Her husband, Jeff, is a physician. In addition to these pregnancies, Sara had experienced two miscarriages, one prior to her first live birth, and the second between the two pregnancies. At 10 weeks gestation, Sara was experiencing moderate constipation, so she decided to go to the local health food store and try a natural laxative. She purchased a pre-packaged mix containing a number of herbs including senna, cascara sagrada, and buckthorn. Concerned about the safety of these herbs she called her obstetrician for information. He told her that herbs do not do anything, and that it was fine to take them. Sara took the herbs for 5 days, after which time she began having cramping and spotting. She miscarried 3 days later. Although the miscarriage may have been entirely unrelated to the use of these herbs, this case illustrates a serious lack of knowledge on the part of the obstetrician and the need for medical education to include training at least in the herbs contraindicated in various circumstances, for example, pregnancy.

CASE HISTORY 2:

See the case history in Chapter 16 Iron Deficiency Anemia.

HYPERTENSION IN PREGNANCY

Laurel Lee, Aviva Romm

Hypertension is the most common medical problem of pregnancy, affecting 10% of all pregnant women.[21] The condition can lead to devastating outcomes with significantly increased risks of placental abruption, disseminated intravascular coagulation (DIC), cerebral hemorrhage, hepatic failure, and acute renal failure.[22] Hypertensive disorders of pregnancy are a significant cause of maternal and perinatal morbidity and mortality, and therefore require accurate diagnosis and proper medical management. CAM treatments for hypertensive disorders during pregnancy should *always* accompany proper medical management *in conjunction* with the care of an obstetrician.

Hypertensive disorders of pregnancy are divided into four categories according to the National High Blood Pressure Education Program (NHBPEP) 2000 Working Group:

1. Preeclampsia–eclampsia
2. Chronic hypertension
3. Preeclampsia superimposed on chronic hypertension
4. Gestational (transient) hypertension[22]

Hypertension itself is defined as a sustained increase in blood pressure >140/90. Elevated blood pressure should be documented on at least two consecutive occasions greater than 6 hours apart, using the appropriate-size blood pressure cuff, to make a diagnosis of hypertension. Diastolic pressure should be considered the number at which the Phase V Korotkoff sound is auscultated.

BOX **15-3**

Diagnosis of Hypertensive Disorders Complicating Pregnancy

Preeclampsia
Minimum Criteria:
- BP = 140/90 mm Hg after 20 weeks gestation
- Proteinuria = 300 mg/24 hours or = 1+ dipstick

Increased certainty of preeclampsia:
- BP = 160/110 mm Hg
- Proteinuria 2.0 g/24 hours or = 2 + dipstick
- Serum creatinine > 1.2 mg/dL unless known to be previously elevated
- Platelets < 100,000 mm
- Microangiopathic hemolysis (increased LDH)
- Elevated ALT or AST
- Persistent headache or other cerebral or visual disturbance
- Persistent epigastric pain

Eclampsia
- Seizures that cannot be attributed to other causes in a woman with preeclampsia. THIS IS A MEDICAL EMERGENCY!

Chronic Hypertension
- BP = 140/90 mm Hg before pregnancy or diagnosed before 20 weeks gestation *Or*
- Hypertension first diagnosed after 20 weeks gestation and persistent after 12 weeks postpartum

Preeclampsia Superimposed on Chronic Hypertension
- New-onset proteinuria = 300 mg/24 hours in hypertensive women but no proteinuria before 20 weeks gestation
- Sudden increase in proteinuria or blood pressure or platelet count <100.000/mm in women with hypertension and proteinuria before 20 weeks gestation

Gestational Hypertension (Transient Hypertension)
- BP = 140/90 mm Hg for first time during pregnancy
- No proteinuria
- BP return to normal <12 weeks postpartum
- Final diagnosis made only postpartum
- May have other signs of preeclampsia, for example, epigastric discomfort or thrombocytopenia
- 15% to 25% of women will go on to develop preeclampsia; gestational age at diagnosis of transient hypertension is inversely related to likelihood of developing preeclampsia

Note that edema is no longer considered a diagnostic criterion of preeclampsia as it is found in many normal pregnancies and is not a reliable indicator.

Patients should be told to avoid tobacco and caffeine for at least 30 minutes prior to a blood pressure reading, and should be encouraged to relax for 10 minutes prior to evaluation.[22] The definition of hypertension as a 30 mm Hg systolic and/or 15 mm Hg rise over baseline is now considered invalid, as it is recognized that up to 73% of all women in their first pregnancies experience a diastolic rise of this magnitude at some point in the pregnancy with no subsequent development of pathology.[23] Nonetheless, close observation of these women is recommended.[21] Each type of hypertensive disorder of pregnancy has specific diagnostic criteria (Box 15-3).

DESCRIPTIONS OF HYPERTENSIVE DISORDERS OF PREGNANCY BY CLASSIFICATION AND GENERAL CONVENTIONAL TREATMENT APPROACHES

A great deal of debate and uncertainty surrounds the etiology, classification, and medical treatment of pregnancy hypertensive disorders. The following discussion provides a brief overview of the salient points of each of the pregnancy hypertensive disorders and their specific medical treatments based on current recommendations.

Preeclampsia

Preeclampsia is a disease specific to pregnancy, with ''cure'' occurring only upon delivery of the placenta. The etiology of preeclampsia remains unknown, although there are numerous theories. It appears that it is a complex, multifactorial condition with genetic factors, immunologic factors, altered inflammatory pathways, insulin resistance (obesity, hyperlipidemia, glucose intolerance), endothelial dysfunction, macronutrient and micronutrient deficiencies, altered placental angiogenesis, and subclinical infections possibly participating in the risk of developing this condition.[21,24] Advanced maternal age, first pregnancy, poor nutrition, residence at high altitudes, and lack of adequate prenatal care have also been associated with increased risk.[24] There is a common thread in all cases: poor placental perfusion associated with maternal vasoconstriction and subsequent maternal multiorgan failure.[21]

Early identification of preeclampsia increases the likelihood of proper early management and reduction of poor prenatal outcome. Unfortunately, in spite of a great deal of investigation into serum markers that might help to identify women at risk of developing preeclampsia, no reliable markers have been found, nor is there a consistent standard for clinical identification of this potentially devastating condition.[21] Similarly, no preventative measures for preeclampsia have been identified with any certainty. Current pharmacotherapy is able to reduce blood pressure and prevent the development of eclampia (preeclampsia with seizures), but it cannot stop the progression of the condition once it is established. Fetal intrauterine growth restriction is a major consequence of this disease. Initial ultrasound at 18 to 20 weeks gestation documents baseline fetal growth. When a woman is diagnosed with preeclampsia, serial

ultrasounds at 28 to 32 weeks gestation and then monthly until term, are suggested for objective measurement. Fetal well-being tests such as non-stress tests (NST) and biophysical profile (BPP) are ordered in the third trimester. Fetal movement counts are helpful as a subjective measurement the woman can do at home. A variety of therapeutic strategies have been evaluated for the prevention and treatment of preeclampsia. These are discussed in the following.

Diuretics

Diuretics were once assumed to be a beneficial part of treatment of preeclampsia with its attendant hypertension and edema. However, women with preeclampsia are actually hypovolemic and hemoconcentrated; therefore, the use of diuretics may exacerbate the condition, and thus their use for this condition has been abandoned.[21]

Salt Restriction

There is no evidence that salt restriction is of any benefit in the prevention or treatment of preeclampsia.[25,26]

Antihypertensive Medication

Antihypertensive therapy for women with preeclampsia does not affect the underlying disease process or improve mother–baby outcome.[26] Further, antihypertensive medications have been associated with adverse side effects, including total placental hypoperfusion; thus, their use is reserved for the treatment of chronic and severe hypertension.[26]

Aspirin

Data from randomized trials and meta-analysis have been conflicting on the prophylactic and therapeutic effects of low-dose aspirin for preeclampsia. The use of aspirin is predicated on the fact that widely disseminated endothelial dysfunction and platelet disturbances are associated with the etiology of this condition. Low-dose aspirin is thought to be effective because of its thromboxane synthesis inhibition, with consequent reduction in platelet aggregation, as well as its ability to inhibit free radical formation (lipid peroxides) and support of resistance to angiotensin II in pregnant women with increased susceptibility to this vasoconstriction substance.[21,27,28] The most recent systematic review of all randomized trials to meet the reviewer's inclusion criteria (39 trials with a total of 30,563 women) showed a positive safety profile with a moderate, but significant, reduction in the risk of preeclampsia regardless of weeks gestation at trial entry or dose of aspirin. A 15% reduction in incidence of preeclampsia was observed, with an 8% reduction in preterm birth and a 14% reduction in risk of perinatal death.[29] In spite of disagreement of the value of aspirin for preeclampsia in earlier studies, all studies have demonstrated that aspirin use in recommended doses during pregnancy appears safe.[21] Recent evidence suggests that the earlier in pregnancy that the aspirin is started, the greater the benefit. The recommended dosage range for optimal effects is between 80 and 150 mg per day, specifically to be taken at bedtime.[30,31]

Calcium

Studies on the efficacy of calcium supplementation for prophylaxis and treatment of preeclampsia have been equivocal. A recent, large, multicenter, randomized prospective trial of 2 g of elemental calcium vs. placebo given to healthy, nulliparous pregnant women beginning in their second trimester showed no differences in the incidence or severity of hypertensive disorders.[32] However, a more recent trial demonstrated benefit for women who were at very high risk for developing preeclampsia.[33] A proposed mechanism is via prevention of a compensatory rise in parathyroid hormone associated with low serum calcium, and consequently, smooth muscle contraction; however, this remains theoretical.[21]

Vitamins C and E

Oxidative stress has been proposed as a mechanism associated with the development of preeclampsia. Further, studies have demonstrated decreased levels of antioxidant levels in women with preeclampsia. This has prompted evaluation into the use of vitamin C and E supplements as possibly prophylaxis and therapy. The risk of developing preeclampsia was seen to be lower in high-risk women begun on supplementation at 16 to 20 weeks gestation compared with placebo.[21] At this point, the role of antioxidants in this condition remains unclear. For women wishing to supplement vitamin C during pregnancy, it is recommended not to exceed 2000 mg per day to avoid the risk of sensitivity or neonatal rebound scurvy.

Chronic Hypertension

Chronic hypertension is defined as hypertension that predated pregnancy, or hypertension beginning prior to 20 weeks gestation. This diagnosis is not easy to establish in women who have not had care prior to pregnancy and because hypertension prior to 20 weeks gestation can also be indicative of preeclampsia that can occur early in pregnancy in a limited number of conditions.[21] Blood pressure levels are less suggestive of poor maternal or fetal outcomes, including fetal growth retardation, prematurity, preeclampsia, placental abruption, and maternal or perinatal morbidity and mortality than are the onset of proteinuria and symptoms of preeclampsia.[35,36] The health care professional may order electrocardiography, echocardiogram, ophthalmologic exam, and renal ultrasound. Women with mild hypertension (140 to 159 mm Hg systolic or 90 to 105 mm Hg diastolic) generally do well in pregnancy and, overall, do not need antihypertensive medication. In fact, women already taking antihypertensive medications may need to decrease the dose as some studies have shown decreased uteroplacental blood flow and fetal growth with medication.[37] Tapering or stopping antihypertensive medications is done under close observation. Antihypertensive therapies are given to reduce the risk of maternal stroke and cardiovascular complication in women with a diastolic BP of >105 mm Hg. Recommendation of antihypertensive treatment is done when blood pressure levels reach or exceed 160 mm Hg systolic or 100 to 106 mm Hg diastolic, when abnormal laboratory values are found, and certainly with a combination of both abnormal factors.

Oral antihypertensive medication with methyldopa or labetalol is typically recommended. Methyldopa does not appear to have negative effects on uteroplacental blood flow.[38] Some women, however, do not tolerate it well because of drowsiness. Labetalol, a combined alpha- and beta-blocker, is another choice and can also be prescribed postpartum when breastfeeding. Ideally, women with chronic hypertension need to be evaluated before pregnancy for severity of the hypertension, modification of lifestyle habits and target organ damage (heart, kidney). Women with significant renal impairment (serum creatinine 71.4 mg/dL) may have further deterioration in pregnancy. Women with cardiac abnormalities may have underlying diseases in addition to chronic hypertension. Most women with mild chronic hypertension (140/90 mm Hg) have no end-organ involvement and can have uncomplicated pregnancies.

Gestational (Transient) Hypertension

Elevated blood pressure appearing after 20 weeks without proteinuria and with normal laboratory values in a previously normotensive woman generally results in a good outcome.[21] However, gestational hypertension is considered a provisional term. Although most women will not develop subsequent problems, up to 25% will go on to develop symptoms of preeclampsia.[39] Women with gestational hypertension appear to be at significantly increased risk of maternal and perinatal morbidity, with elevated rates of preterm delivery, small for gestational age infants, and abruptio placenta compared significantly higher than in the general obstetrical population, and similar to rates reported for women with severe preeclampsia.[39] Thus, women with a diagnosis of gestational hypertension should be monitored closely, with weekly prenatal visits optimal. Ultrasound and fetal well-being tests are appropriate in the third trimester. If symptoms of preeclampsia develop, women are treated as is appropriate for that condition. If elevated blood pressure readings persist 12 weeks postpartum, a diagnosis of chronic hypertension is made retrospectively.

BOTANICAL TREATMENT OF HYPERTENSION IN PREGNANCY

Improperly treated pregnancy hypertensive disorders can have dire consequences to the mother and baby. It is not recommended that pregnant women attempt self-medication for pregnancy hypertension, nor that this be done by inexperienced practitioners. The best treatment is obstetric medical care accompanied, when appropriate, by prudent use of herbal medicines as adjunct therapy, under the guidance of an herbalist, naturopath, or midwife trained in the use of botanical medicines in pregnancy. Although popular for the treatment of hypertension in the nonpregnant population, herbal diuretics such as dandelion leaf (*Taraxacum officinale*) are not appropriate for the treatment of pregnancy hypertensive disorders, and may potentially cause exacerbation. The herbs discussed in the following are those commonly used for treating gestational and chronic hypertension that are considered generally safe for use during pregnancy. Botanical treatment for preeclampsia is not recommended and has not been investigated.

Cramp Bark and Black Haw

Cramp bark and black haw have been used by midwives as part of herbal antihypertensive protocol for gestational hypertension. Traditionally, they have been used as musculoskeletal relaxants during pregnancy, and to treat irritable uterus, prevent premature labor, and relieve incoordinate uterine contractions.[40,41] They are taken in tincture form, either alone or more typically with relaxing nervines and hawthorn, for this purpose in Table 15-3.

Garlic

Garlic has mild antihypertensive properties and inhibits platelet aggregation and inflammation. No studies have evaluated the efficacy or safety of garlic use for pregnancy hypertension. Garlic is a common food used during pregnancy worldwide, and in modest doses is not expected to cause any adverse effects. The German Commission E gives no contraindication to its use during pregnancy, nor does the *Botanical Safety Handbook,* which does however provide a caution about use during lactation because of active constituents passing through the breast milk.[42–44] (McKenna et al. note that the dose of constituents received through breast milk is actually quite small.)[43] A randomized control study of 100 primigravid women given either 800 mg/day of garlic tablets or placebo during third trimester pregnancy to evaluate the effect of garlic supplementation on preeclampsia found that pregnancy outcomes were comparable in both groups. There were no reports of side effects in

TABLE **15-3**

Botanical Treatment Strategies for Hypertension in Pregnancy

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Reduce blood pressure	Antihypertensives	*Allium sativum*	Garlic
		Crataegus spp.	Hawthorn
		Ganoderma lucidum	Reishi
		Viburnum spp.	Cramp bark, black haw
Stress reduction, relaxation	Nervines	*Lavandula officinalis*	Lavender
		Passiflora incarnata	Passion flower
		Viburnum spp.	Cramp bark, black haw

the garlic group other than garlic body odor, and nausea, nor reports of an incidence of adverse fetal outcomes or spontaneous abortion.[45] Garlic odor was identifiable in the amniotic fluid of a small group of pregnant women taking garlic supplements.[46] It is commonly recommended that because of its antithrombotic effects, garlic use should be discounted 7 days prior to surgery.[43] A recent Cochrane review evaluating the effects of garlic on preeclampsia and its related complications concluded that there is insufficient evidence to recommend increased garlic intake for preventing preeclampsia and its complications, and that side effects have not been reported with its use in pregnancy.[47] Although the actual risk of bleeding is uncertain, it is prudent to discontinue the medicinal use of garlic 3 weeks prior to the due date to minimize any increased risk of bleeding, as women with hypertensive disorders during pregnancy are more likely to enter labor early.

Hawthorn

Hawthorn has been used for treating a variety of cardiovascular conditions, and has noted antioxidant effects and antiplatelet aggregating effects, which may be of benefit in preventing pregnancy hypertension.[42,43,48] Other noted actions are an increase in the integrity of blood vessel wall, improvement in coronary blood flow, and positive effects on oxygen use.[43] There are no known contraindications or restrictions to the use of this herb during pregnancy or lactation.[42–44]

Reishi

Although not classically used for the treatment of hypertension in pregnancy, it is worth mentioning that the medicinal mushroom *Ganoderma lucidum* has demonstrated positive results in research looking at its antihypertensive effects, as well as effects against diabetes and hyperlipidemia.[49–51] One interesting study looked at the effects of reishi on glomerular function, and found that it was able to improve hemodynamic flow in glomerular disease and reduce proteinuria. The beneficial effect of *Ganoderma lucidum* appears to be multifactorial, including the modulation of immunocirculatory balance, antilipid, vasodilator, antiplatelet, and improved hemodynamics. Together with vitamins C and E, this herb helped to neutralize oxidative stress and suppress the toxic effect to the glomerular endothelial function.[52] Extracts of reishi polysaccharides have demonstrated significantly improved basal nitrous oxide (NO) release and endothelium-dependent relaxation but without affecting endogenous nitrous oxide synthase (NOS) activity. These results suggest that this herb has the potential to improve endothelium-dependent relaxation in mineralocorticoid hypertension.[53] In a study evaluating the clinical effects of lyophilized *G. lucidum* extract, 53 patients were divided into two groups: Group I consisted of essential hypertensive patients, and Group II consisted of mild hypertensive or normotensive patients. The patients were instructed to take six tablets containing 240 mg of the extract per day. Biochemical and hematologic examination were performed for 21 test items, and the following results were obtained.[1] In regard to hypertension, blood pressure significantly decreased in Group I, but did not in Group II, thus showing that *G. lucidum* has an ameliorating effect on hypertension.[2] In regard to biochemical and hematologic effects, the oral intake did not result in any change in the values of any of the 21 test items beyond the normal range, except that total cholesterol decreased slightly and fibrinogen increased slightly. It was therefore concluded that *G. lucidum* has blood pressure lowering effect on patients with essential hypertension and will not have any side effects on patients with essential or border line hypertension during 6 months oral intake.[54] No safety data on use during pregnancy was identified.[55] Reishi may be taken alone or in combination with other herbs, and may be taken as a liquid extract or in solid (pill) form (Box 15-4).

BOX 15-4

Protocol for Chronic or Gestational Hypertension

Tincture Formula for Cardiovascular Support

Hawthorn	*Crataegus oxyacantha*	40 mL
Cramp bark or black haw	*Viburnum* spp.	30 mL
Passion flower	*Passiflora incarnata*	30 mL
		Total: 100 mL

Dose: 5 mL twice daily

Also:

Garlic: One clove fresh garlic daily or garlic capsules (dose according to specific product)

Reishi: 2 mL tincture twice daily

Daily supplementation:

- 2 g calcium citrate with 500 mg magnesium citrate
- 1000 mg vitamin C
- 400 IU vitamin E

Diet: Emphasize a heart healthy diet of fresh fruits, especially dark colored berries rich in vascular protective, antioxidant anthocyanidin; vegetables, whole grains, and legumes, nuts, fresh fish, and poultry. Avoid high fat, fried, and processed foods.

Exercise: 30 minutes walking daily (unless otherwise prohibited)

Relaxation: Daily yoga, meditation, or biofeedback exercises.

Warm (not hot) baths: 2 to 3 times/week with ½ cup Epsom salts and 5 to 10 drops lavender essential oil added to the bath.

ADDITIONAL THERAPIES

Nutritional Considerations

A diet rich in calcium, magnesium, and potassium may lessen cardiovascular risk. A diet rich in fruits, vegetables, whole grains, legumes, nuts, good-quality oils, and low-fat foods is associated with decreased hypertension and may be especially beneficial for women with chronic hypertension. Essential fatty acids may be beneficial in

the prevention of pregnancy hypertension. Vascular sensitivity to angiotensin II was determined in the midtrimester of pregnancy in women after taking a diet with supplemented essential fatty acids and vitamins. The essential fatty acids linoleic and dihomo-gamma-linolenic acid were administered as evening primrose oil capsules (Efamol) for 1 week prior to the study. Vascular sensitivity was then determined in response to 4, 8, and 16 ng kg-1 min-1 angiotensin II. Vitamin supplements (Efavit) were given with the Efamol capsules. Seven women have been studied, and their vascular sensitivity compared with controls on normal diet. The vascular sensitivity was significantly reduced in all the patients on essential fatty acid supplements, and all values fell below the mean of the control group.[56]

Exercise and Stress Management

Exercise and relaxation practices have generally been shown to be beneficial in the reduction of hypertension as part of therapeutic lifestyle choices. Although the role of exercise and stress management in the prevention of preeclampsia is not established, it is certainly beneficial in the management of chronic hypertension. Regular walking, yoga, meditation, biofeedback, and other gentle techniques are safe during normal pregnancy.

GROUP B STREP (GBS) INFECTION IN PREGNANCY

Aviva Romm, Christopher Hobbs

In the 1970s, Group B Streptococcus (GBS), infection with *Streptococcus agalactiae*, emerged as a leading cause of pneumonia, sepsis, and meningitis in newborns.[57] GBS is a normal inhabitant of the intestinal tract and colonizes the vaginal tracts of many women; it can be demonstrated by culture of combined rectal and vaginal swabs in 15% to 40% of pregnant women on random sampling. Most bacterial transmission to the neonate occurs during birth via passage of the baby through the birth canal, or via ascendant bacteria during labor with ruptured membranes. Premature babies and babies of mothers with premature or prolonged rupture of membranes (PROM) are at higher risk of infection. GBS can also cross the membranes, so cesarean section is not protective and carries additional surgical risks to the mother. Infection is categorized as either early or late onset. Early-onset disease symptoms manifest within a few hours, and up to a week after birth. Antibiotic prophylaxis administered to the mother during labor, as is discussed in the following, is used to prevent early-onset infection in the neonate. Late-onset disease develops through contact with hospital nursery personnel and usually manifests in the first 3 months after birth. Up to 45% of health care workers carry the bacteria on their skin, and may transmit the infection to newborns.[58] Meticulous hand-washing practices in the hospital are essential for reduction of nosocomial disease transmission.

Although GBS transmission rates are high, the rate of neonatal sepsis is surprisingly low. Unfortunately, the mortality rate associated with early-onset disease can be as high as 50% in premature infants and approaches 25% even in otherwise healthy term infants.[58] Over 1600 cases of early-onset infections occur in newborns annually, with as many as 80 deaths per year.[57] Long-term sequelae of meningitis in survivors include mental retardation, and hearing or vision loss. The bacterium can also cause maternal bladder and uterine infections; increases the risk of premature labor and premature rupture of membranes (PROM) and stillbirth in pregnant women; and can lead to blood infections, skin or soft tissue infections, and pneumonia in the general population.

DIAGNOSIS

The gold standard test used in screening is a bacterial culture of a sample collection from a simultaneous vaginal and rectal swab. The best time to test for the presence of the organism is between the 35th and 37th weeks of pregnancy.[57] Testing at this time is as much as 50% more effective at predicting and preventing perinatal disease than screening earlier in pregnancy, although the numbers of organisms in any individual might fluctuate, making detectable levels variable. CDC guidelines published in 2002 recommend universal screening for pregnant mothers between 35 and 37 weeks gestation.[57] The FDA has recently approved a new ''quick'' test that can diagnose GBS in pregnant women in about an hour. Some studies have shown the test to be up to 94% sensitive, whereas other studies show less consistent results. Because GBS resistance to specific antibiotics has developed, especially to those used for penicillin-allergic women, culture and sensitivity testing is recommended.

CONVENTIONAL TREATMENT APPROACHES

The American College of Obstetricians and Gynecologists, the American Academy of Pediatrics, and the Centers for Disease Control and Prevention (CDC) published guidelines in 1996 recommending a risk-based (screening) approach, to determine when to recommend intravenous (IV) antibiotic prophylaxis during labor.[59,60] It was determined that women with the following risk factors should be offered (IV) antibiotics during labor and delivery, not before labor:

- fever during labor
- rupture of membranes 18 hours or more before delivery
- labor or rupture of membranes before 37 weeks

As of 2002, the CDC revised the 1996 guidelines, recommending routine screening for all pregnant women between 35 and 37 weeks gestation, and universal treatment for women who test positive for GBS during pregnancy (Box 15-5).

Women with negative vaginal and rectal GBS screening cultures within 5 weeks of delivery do not require intrapartum antimicrobial prophylaxis for GBS even if obstetric risk factors develop (i.e., delivery at <37 weeks' gestation, duration of membrane rupture >18 hours, or temperature >100.4° F [>38.0° C]).

The use of prophylactic perinatal IV antibiotics is attributed with a 70% reduction in the incidence of GBS disease during the last 10 years. In spite of this reduction in incidence, early-onset GBS-related diseases such as pneumonia and meningitis remain a cause of illness and death

BOX **15-5**

CDC 2002 GBS Treatment Guidelines[57]

- All pregnant women should be screened at 35 to 37 week gestation for vaginal and rectal GBS colonization. At the time of labor or rupture of membranes, intrapartum chemoprophylaxis should be given to all pregnant women identified as GBS carriers. Colonization during a previous pregnancy is not an indication for intrapartum prophylaxis in subsequent deliveries. Screening to detect GBS colonization in each pregnancy will determine the need for prophylaxis in that pregnancy.
- Women with GBS isolated from the urine in any concentration during their current pregnancy should receive intrapartum chemoprophylaxis because such women usually are heavily colonized with GBS and are at increased risk of delivering an infant with early-onset GBS disease. Prenatal culture-based screening at 35 to 37 week gestation is not necessary for women with GBS bacteriuria. Women with symptomatic or asymptomatic GBS urinary tract infection detected during pregnancy should be treated according to current standards of care for urinary tract infection during pregnancy.
- Women who have previously given birth to an infant with invasive GBS disease should receive intrapartum chemoprophylaxis; prenatal culture-based screening is not necessary for these women.
- If the result of GBS culture is not known at the onset of labor, intrapartum chemoprophylaxis should be administered to women with any of the following risk factors: gestation <37 weeks, duration of membrane rupture >18 hours, or a temperature of $>100.4^\circ$ F ($>38.0^\circ$ C). Women with known negative results from vaginal and rectal GBS screening cultures within 5 weeks of delivery do not require prophylaxis to prevent GBS disease even if any of the intrapartum risk factors develop.
- Women with threatened preterm (<37 week gestation) delivery should be assessed for need for intrapartum prophylaxis to prevent perinatal GBS disease.
- In the absence of GBS urinary tract infection, antimicrobial agents should not be used before the intrapartum period to treat GBS colonization. Such treatment is not effective in eliminating carriage or preventing neonatal disease and may cause adverse consequences.
- GBS-colonized women who have a planned cesarean delivery performed before rupture of membranes and onset of labor are at low risk for having an infant with early-onset GBS disease. These women should not routinely receive intrapartum chemoprophylaxis for perinatal GBS disease prevention.
- For intrapartum chemoprophylaxis, the following regimen is recommended for women without penicillin allergy: penicillin G, 5 million units intravenously initial dose, then 2.5 million units intravenously every 4 hours until delivery. Because of its narrow spectrum of activity, penicillin is the preferred agent. An alternative regimen is ampicillin; 2 g intravenously initial dose, then 1 g intravenously every 4 hours until delivery (AI). (See Box 15-2 in the original guidelines for details concerning these regimens.)
- Intrapartum chemoprophylaxis for penicillin-allergic women takes into account increasing resistance to clindamycin and erythromycin among GBS isolates. During prenatal care, history of penicillin allergy should be assessed to determine whether a patient is at high risk for anaphylaxis, that is, has a history of immediate hypersensitivity reactions to penicillin (e.g., anaphylaxis, angioedema, or urticaria) or history of asthma or other conditions that would make anaphylaxis more dangerous. Women who are not at high risk for anaphylaxis should be given cefazolin; 2 g intravenously initial dose, then 1 g intravenously every 8 hours until delivery. For women at high risk for anaphylaxis, clindamycin and erythromycin susceptibility testing, if available, should be performed on isolates obtained during GBS prenatal carriage screening. Women with clindamycin- and erythromycin-susceptible isolates should be given either clindamycin, 900 mg intravenously every 8 hours until delivery; OR erythromycin, 500 mg intravenously every 6 hours until delivery. If susceptibility testing is not possible, susceptibility results are not known, or isolates are resistant to erythromycin or clindamycin, the following regimen can be used for women with immediate penicillin hypersensitivity: vancomycin, 1 g intravenously every 12 hours until delivery.
- Routine use of antimicrobial prophylaxis for newborns whose mothers received intrapartum chemoprophylaxis for GBS infection is not recommended. However, therapeutic use of these agents is appropriate for infants with clinically suspected sepsis.

in newborns in the United States, with a rate of approximately 80 deaths annually.

An alternative conventional treatment to IV antibiotic prophylaxis that has been investigated in Europe but is not employed in the United States other than by midwives, is the use of chlorhexidine vaginal flushings. A randomized controlled study was conducted to investigate the efficacy of intrapartum vaginal flushings with chlorhexidine compared with ampicillin in preventing group B streptococcus transmission to neonates. The study evaluated outcomes of singleton pregnancies delivering vaginally. Rupture of membranes, when present, must not have occurred more than 6 hours prior. Women with any gestational complication, with a newborn previously affected by group B streptococcus sepsis or whose cervical dilatation was greater than 5 cm were

excluded. A total of 244 group B streptococcus-colonized mothers at term (screened at 36 to 38 weeks) were randomized to receive either 140 mL chlorhexidine 0.2% by vaginal flushings every 6 hours or ampicillin 2 g intravenously every 6 hours until delivery. Neonatal swabs were taken at birth, at three different sites (nose, ear, and gastric juice). A total of 108 women were treated with ampicillin and 109 with chlorhexidine. Their ages and gestational weeks at delivery were similar in the two groups. Nulliparous women were equally distributed between the two groups (ampicillin, 87%; chlorhexidine, 89%). Clinical data such as birth weight (ampicillin, 3,365 ± 390 g; chlorhexidine, 3,440 ± 452 g), Apgar scores at 1 minute (ampicillin, 8.4 ± 0.9; chlorhexidine, 8.2 ± 1.4), and at 5 min (ampicillin, 9.7 ± 0.6; chlorhexidine, 9.6 ± 1.1) were similar for the two groups, as was the rate of neonatal group B streptococcus colonization (chlorhexidine, 15.6%; ampicillin, 12%). *Escherichia coli*, on the other hand, was significantly more prevalent in the ampicillin (7.4%) than in the chlorhexidine group (1.8%, $p < 0.05$). Six neonates were transferred to the neonatal intensive care unit, including two cases of early-onset sepsis (one in each group). In this carefully screened target population, intrapartum vaginal flushings with chlorhexidine in colonized mothers displayed the same efficacy as ampicillin in preventing vertical transmission of group B streptococcus. Moreover, the rate of neonatal *E. coli* colonization was reduced by chlorhexidine.[61] Additional studies have demonstrated the efficacy of this practice, but for unknown reasons it has not been more widely investigated or employed in the United States.[62–65] This is an option that many midwives in the United States are beginning to employ in home birth settings; clearly more investigation of this option should be conducted to determine whether it is a safe and effective alternative to routine intranatal IV prophylaxis for neonatal GBS infection. Until then, IV antibiotic prophylaxis remains the recommended standard.

BOTANICAL TREATMENT OF GBS

Choosing to Use Botanical Therapies for Reducing GBS Infection during Pregnancy

Despite the 2002 revised protocol, many pregnant women prefer to avoid routine antibiotic prophylaxis for a variety of reasons including:

- philosophic reasons (i.e., they prefer to minimize medical intervention or want a ''natural'' approach),
- due to concern about sequelae (i.e., development of resistant infections, increased likelihood of neonatal Candida infection (thrush))
- or choice of birth setting (i.e., home birth, making it difficult if not impossible to access antibiotic prophylaxis in labor)

For women choosing to birth naturally at home, the use of prophylactic IV antibiotics in labor is sometimes not a realistic option—most home birth midwives do not administer IV medications. Home birth midwifery protocol therefore continues to follow the risk-assessment model, transporting to the hospital for IV antibiotic prophylaxis should indications arise, including rupture of membranes longer than 18 to 24 hours (length of time varies with the protocol of different medical and midwifery communities) or any signs of infection. GBS-positive women planning home births commonly seek herbal options prenatally for reducing their microbial load, hoping to avoid PROM, thus prolonging the length of time before the need to transport to the hospital during delivery.

Herbal treatment has been demonstrated to be effective in reducing GBS colonization if it is started 2 to 3 weeks before the onset of labor. Note that herbal prophylaxis is done during pregnancy and not as a substitute for intranatal antibiotic prophylaxis. It is common for women in this situation to also use herbs to augment labor in the event of PROM, to encourage birth to occur within the allotted 18- to 24-hour window. PROM is discussed elsewhere in this book.

Should women choose to follow an herbal protocol for reducing GBS colonization, it is imperative that the protocol be accompanied by retesting as close to the expected due date as possible but with enough time to receive results prior to labor. GBS-positive pregnant women should be made fully aware of the risks of GBS before laboring without antibiotic prophylaxis. Women should also be informed that, in cases in which antibiotics are declined intranatally for the mother, they might then be routinely administered to the baby if she transports to the hospital and if at any time during the pregnancy she had a positive GBS test. Faced with these choices, a woman may prefer to receive antibiotic prophylaxis herself rather than have it directly administered to the baby. Yet other facilities and practitioners will allow antibiotics to be deferred unless there is ROM for more than 24 hours, allowing a period of observation of the baby for signs of infection rather than routinely administering antibiotics intranatally or postnatally. Women who test GBS positive during pregnancy should discuss their concerns and options with their obstetric and pediatric care providers prenatally. There is no substitute for antibiotics in women with signs of infection and prolonged rupture of membranes (>24 hours rupture), and all newborns exhibiting signs of GBS infection *must* receive immediate and aggressive antibiotic therapy.

Given the potential narrow time frame between a positive GBS test at 35 to 37 weeks and the time of birth, especially considering the possible need for antibiotic follow-up and the increased risk of premature rupture of membranes and premature labor associated with GBS, midwives may consider an initial culture during pregnancy earlier than the recommended 35 to 37 weeks gestation, particularly in women with a history of chronic UTI or vaginal yeast infection. Although a positive result earlier in pregnancy is not predictive of risk of neonatal infection, earlier testing allows time to address the potential problem using botanical strategies, with a reculture during the predictive period. This approach is consistent with the preventative philosophies of both herbal medicine and midwifery care, and also allows adequate time for more aggressive medical intervention with antibiotics should this be optimal.

Botanical Protocol for GBS

Botanical treatment for GBS infection relies on the vaginal application of antimicrobial herbs, and the internal (oral) use of probiotics to normalize intestinal flora and reduce *S. agalactiae* colonization. When women have had a protracted history of GBS infection, with repeated urogenital infections or other signs of decreased immune response, for example, frequent colds, sore throats, and so forth., an internal herbal protocol to enhance immunity is sometimes recommended; however, options during pregnancy are somewhat limited.

Many herbs are known in Western herbalism for their antibacterial actions. These include garlic, oregano, myrrh, thyme, and tea tree oil, to name a few. After an exhaustive search of a number of key medical and chemical databases; however, no clinical trials looking at the clinical treatment or prevention of GBS infection with herbal medicine are available in the world literature. In vitro tests show *S. agalactiae* to be inhibited by a number of herbs, however, many of these are not safe for use during pregnancy.

Given the paucity of research available directly on this topic, and the long history of clinical efficacy of many botanicals in reducing a variety of infections, including vaginal infections, contemporary herbal practitioners tend to rely on traditional indications of herbs enhanced by contemporary understanding of disease pathology and herbal pharmacology for developing modern clinical applications. Those herbs most commonly used by herbalists, midwives, and naturopathic physicians for the treatment of GBS are listed in Table 15-4. Information on specific categories of herbal actions and exemplary herbs follows.

The basic approach for treating GBS is the nightly insertion of either vaginal suppositories or capsules of antimicrobial, anti-inflammatory, and vulnerary herbs

GBS

There is absolutely no substitute for antibiotics in women with a history of a positive GBS test and prolonged rupture of membranes (>24 hours rupture). All newborns exhibiting signs of GBS infection *must* receive immediate and aggressive antibiotic therapy.

TABLE **15-4**

Summary of Botanical Treatment Strategies for GBS

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Reduce microbial infection	Antibacterial	*Allium sativum*	Garlic
		Baptisia tinctoria	Wild indigo
		*Berberis vulgaris**	Barberry
		Chrysanthemum morifolium	Chrysanthemum
		*Coptis chinensis**	Goldthread
		Commiphora mol mol	Myrrh
		Echinacea purpurea	Echinacea
		Ganoderma lucidum	Reishi
		Gardenia augusta	Gardenia
		*Hydrastis canadensis**	Goldenseal
		Ligustrum lucidum	Ligustrum
		*Mahonia aquifolium**	Oregon grape root
		Melaleuca alternifolia	Tea tree
		Origanum vulgare	Oregano
		Thymus vulgaris	Thyme
		Usnea spp.	Usnea
Reduce local inflammation, support tissue integrity	Anti-inflammatory Vulnerary	*Althea officinalis*	Marshmallow
		Calendula officinalis	Calendula
		Glycyrrhiza glabra	Licorice
		Hypericum perforatum	St. John's wort
		Symphytum officinale	Comfrey root
	Astringent	*Achillea millefolium*	Yarrow
		Hamamelis virginiana	Witch hazel
		Quercus spp.	Oak bark

*Coptis, goldenseal, barberry, and Oregon grape root all contain berberine, which may theoretically increase the risk of neonatal jaundice; thus, they are contraindicated for oral use during pregnancy. These herbs may be used safely in vaginal preparations in the last 4 weeks of pregnancy.

for a minimum of 3 weeks prior to the onset of labor. The suppositories, which are the most effective delivery model, are typically inserted in the evening, prior to bed, the woman instructed to wear a panty liner to prevent damage to bedding and underclothes from leakage as the suppository melts in the vaginal canal. This melting allows the vaginal and cervical tissue to be slowly bathed in the herbs and emollient. This is repeated nightly for 14 days, a 2-day break allowed, and reculturing done. Some practitioners choose to alternate nightly between the use of a suppository and an inserted capsule or garlic clove. A single ''00'' capsule can be filled with goldenseal powder and the woman instructed to insert these into the vaginal fornix every other night for the same duration as the suppository protocol. Again, a panty liner is worn. Perianal rinses are also sometimes used if there is heavy colonization or history of repeated urogenital infection. Astringent herbs may be included in topical preparations if there is a great deal of tissue irritation, as they also help to improve tissue integrity and make the tissue less permeable to infection. *Douching should be avoided*, because it is not an optimally safe practice during pregnancy and may also drive microorganisms upward toward the uterus. The combination of actions of herbs reduces microbial load while reinforcing the integrity of the vaginal tissue, reducing the ability of organisms to colonize in fissures and irritated areas. Probiotics are used concurrently on a daily basis to maximize the body's ability to produce flora that prevents overgrowth of GBS and enhances the presence of normal vaginal flora. Satisfactorily low levels of the organism should be achieved at least 1 to 2 weeks before the onset of labor. Should GBS bacteriuria persist later than this, an antibiotic protocol can be offered, according to CDC guidelines.

Discussion of Botanical Protocol for GBS

Immunomodulators

This is an important therapeutic category for women with a history of repeated or intractable vaginal or urinary tract infections. These herbs are taken as decoctions or tinctures with the goal of strengthening the immune response. Herbs with low toxicity that can be given in therapeutic doses include medicinal mushrooms such as *Lentinus edodes* (shiitake), *Trametes versicolor* (turkey tails), and *Ganoderma lucidum* (reishi). They can be safely employed for extended use throughout the pregnancy and are taken at a dose of 6 to 12 g for decoction, 1 to 4 g of a 5:1 powdered extract as an instant tea or in caps, 1 to 4 bid. Echinacea is the only antimicrobial, immune-enhancing botanical to have a study specifically validating its safe use during pregnancy, and is the herb most confidently relied upon by most midwives for this purpose. Inefficacy of echinacea products in treating infections is most likely owing to poor-quality product or inadequate dosing. Liquid extracts of fresh echinacea, rather than dried, powdered, or encapsulated products should be used; strong infusions can also be made from high-quality dried plant material. The dose should approximate 5 mL daily for general prophylactic use and up to two to three times that quantity for aggressive reduction of GBS colonies. Garlic can also be used during pregnancy safely. Although it may be more of a theoretical than an actual concern, because of concerns of increased bleeding with high levels of garlic consumption, the practitioner may wish to discontinue its oral administration 2 weeks prior to the due date.

Topical Antimicrobial Treatment

Antimicrobial herbs most commonly included in suppositories for GBS treatment include goldenseal, thyme, oregano, calendula, tea tree, and usnea. They are used in combination in forms most appropriate to each herb, for example, powder, tincture, or essential oil. Discussion of these herbs is found in their individual plant profiles (see Plant Profiles). An example of a suppository recipe, designating proper forms, can be found in the case history for GBS at the end of this chapter, and a discussion of suppository preparation can be found in Chapter 3. Garlic cloves have a long history of use as suppositories for the treatment of vaginal infections. A single garlic clove (*not* a full bulb!) is carefully peeled to avoid nicking of the garlic flesh, dipped in a small amount of olive oil and inserted into the vaginal fornix and left overnight. Whereas the suppositories and capsule will melt and do not require removal, the clove may fall out on its own when the woman urinates in the morning, or it may need to be manually removed by the woman if it does not spontaneously drop out. The woman can be instructed to remove the clove with a clean finger; some patients may find this offensive, and can be directed to the previous strategies. Capsules are usually filled with only one or two herbs, usually stronger antimicrobials, in powder form. Perhaps most commonly applied is goldenseal root powder, which is inserted on alternate nights to the suppository, as described in the preceding.

NUTRITIONAL CONSIDERATIONS

Probiotics

A high-quality probiotic blend should be taken, two capsules in the morning with the meal, and one or two in the evening with the meal. The active dose is from 9 to 12 billion organisms per day. It is recommended that probiotic products not be taken while using antibiotics or strong doses of antibiotic or bacteriostatic herbs. Start the probiotic product as soon as the antibacterial medications or herbs are discontinued.

ADDITIONAL THERAPIES

Improper toilet hygiene (i.e., wiping back-to-front after a bowel movement) and anovaginal sexual contact, both of which can increase transmission of GBS to the vaginal canal, should be avoided.

CASE HISTORY

Lisa, a 22-year-old woman, 36 weeks pregnant, tested positive for vaginal group B streptococcal (GBS) infection with routine screening. She was asymptomatic with no accompanying history of vaginal infection or UTI.

She was planning a home birth and did not have ready access to intranatal antibiotics because of the political climate of home birth midwifery in her community. Home birth midwifery protocol with GBS is quite strict, and thus her midwife would require her to transport to the hospital for IV antibiotics within 18 hours of ROM, regardless of her stage of labor. Her midwife supported her choice to reduce GBS infection prenatally in the hopes of achieving a negative culture and keeping her birth options open. The following treatment protocol was maintained for 2 weeks, and then Lisa was recultured for GBS.

GBS Treatment Protocol

Nightly insertion of the following vaginal suppository blend for at least 5 nights per week, for 3 weeks (see Chapter 3):

- To ½ cup each of melted coconut oil and cocoa butter add:
  - 1 tbs calendula oil
  - ½ tsp each of rosemary, lavender, and rosemary essential oils
  - 2 tsp tincture of *Usnea barbara*
  - 2 tsp tincture of *Thymus vulgaris*
  - 2 tbs *Hydrastis Canadensis* powder
  - 1 tbs *Ulmus rubra* powder
  - 1 tbs *Commiphora mol mol* powder

Instructions: Begin at 36 weeks. Wear a light menstrual pad each night to protect underwear and bedding, as the oil and goldenseal powders can stain as the suppository melts.

Lisa continued protocol for two weeks at which time a vaginal culture for GBS was performed. Culture came back negative 3 days later. She continued the protocol for an additional week (3 weeks total). A final culture several days before she went into labor also yielded a negative GBS finding. She continued the protocol until 40 weeks, at which time she gave birth to a healthy 7 lb 7 oz boy, at home, after 18 hours of labor with no PROM. The baby was closely observed in the neonatal period, and showed no signs of infection.

Treatment Summary for GBS Prior to Labor Onset

- If GBS is detected prior to 36 weeks and woman has history of GBS, chronic vaginal candidiasis, or recurrent UTI, begin treatment with nutritional and botanical strategies to improve immunity:
- Zinc, vitamin A, folate, and vitamin C to adequate pregnancy amounts
- Assess hemoglobin and hematocrit to determine whether anemia is present and supplement iron if needed.
- Use Echinacea or other immunity-enhancing herbs daily, 2 to 5 mL tid for up to 6 weeks.
- Reduce stress through stress reduction exercises, modifying stressful situations, and use of nervines and adaptogens, as needed.
- Treat accompanying conditions such as UTI or vaginal infection.
- If greater than 36 weeks, use oral and topical antimicrobial agents to reduce colonization, heal vaginal tissue, and improve resistance to infection. Orally, consider echinacea, garlic extracts, and medicinal mushrooms as immunomodulators.
- Apply suppositories nightly for 2 weeks consecutively, and reculture. Specific herbs to consider for suppositories are presented in Table 15-4 and discussed in this section.
- In all cases include a high-dose active probiotic daily.

PRURITIC URTICARIAL PAPULES AND PLAQUES OF PREGNANCY (PUPPP)

Aviva Romm

Pruritic urticarial papules and plaques of pregnancy (PUPPP) is the most common specific dermatologic condition affecting pregnant women, with an incidence of 1/120 to 1/300 pregnancies.[69] Seventy-five percent of women who develop PUPPP are pregnant for the first time, and it is 8 to 12 times more likely to occur in women with multiple gestations.[70] PUPPP usually develops in the third trimester, although the condition may have its onset in the postpartum, and rarely earlier in pregnancy.[69] PUPPP is referred to as polymorphic eruption of pregnancy (in the United Kingdom), toxemic rash of pregnancy, and late-onset prurigo of pregnancy, although PUPPP is the name most commonly used in the United States.[71]

The condition presents as erythematous papules within the striae, usually of the abdomen and thighs, which eventually spread to the extremities and become hives (urticarial plaques). The periumbilical area, breasts, face, palms, and soles usually remain unaffected. The hallmark of this condition is pruritus (itching), which can be extreme, disturbing sleep and preventing normal daily activities. The pruritus of PUPPP can be so uncomfortable as to cause women to feel quite desperate. Pruritus may worsen immediately after delivery, but generally resolves by 10 to 15 days postpartum. Rarely, the condition may resolve prior to birth. Most women do not experience a recurrence with subsequent pregnancies; however, when a recurrence does occur, it is almost always much milder than the original case.[69] The condition is not associated with any adverse maternal, fetal, or neonatal outcomes.[69]

The exact etiology of PUPPP is unknown. One popular theory, supported by the fact that women with larger babies, multiples, or greater maternal weight gain are more likely to develop PUPPP, is that the abdominal stretching of pregnancy leads to an inflammatory response in the connective tissue.[69,71] More recently, a maternal response to fetal circulating antigens has been proposed as an etiologic theory, based on the fact that fetal skin tissue has been found in maternal lesions.[69,72,73]

DIAGNOSIS

There are no specific laboratory diagnostic methods for PUPPP. Diagnosis is made clinically and on the basis of exclusion of other conditions (see Differential Diagnosis). Histopathology and immunochemistry are noncontributory to the diagnosis.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis includes all conditions that may cause hives, and specifically, pemphigoid gestationis, adverse cutaneous drug reaction, allergic contact dermatitis, metabolic pruritus, and atopic dermatitis.

CONVENTIONAL MEDICAL TREATMENT FOR PUPPP

Treatment for PUPPP consists of high-potency topical steroids, ideally tapering these off after 7 days of therapy. Oral prednisone in doses of 10 to 40 mg/day has been used for severe cases when the pruritus is unbearable to the woman. Symptoms are often relieved after 24 hours of oral treatment. Oral antihistamines are generally ineffective. Early delivery is sometimes discussed when the symptoms are unbearable and treatment is ineffective; however, early delivery does not usually give relief of symptoms.[71] Fortunately, symptoms are usually greatly improved with several days of steroid treatment.[69] The safety of antenatal steroid use remains controversial; short-term or single course use is advisable, and the safety of use is greater in the third trimester than in the first trimester.

BOTANICAL TREATMENT OF PUPPP

Many women, either unable to achieve adequate relief with conventional therapies, or concerned about the safety of steroid use during pregnancy, prefer to try natural alternatives for treating PUPPP. Treatment strategies include:

- use of topical and oral anti-inflammatories
- nervines to improve sleep, which is often seriously impaired owing to physical discomfort
- nervines to relieve irritability from itching
- traditional ''hepatic alterative'' herbs, which have been empirically shown to improve a number of skin conditions and
- use of adaptogens as immunomodulators

In botanical therapy, the health of the skin is believed to reflect the health of the other eliminatory and detoxification organs (i.e., bowels, lymph system, liver). When these are not functioning optimally or are overtaxed, as may be a natural consequence of the increased burden of pregnancy on the body, it is believed this will manifest in skin problems, including inflammatory disorders. Topical treatments are therefore almost universally accompanied by systemic treatments.

Although the use of conventional antihistamines has not demonstrated efficacy in the treatment of PUPPP, nettle leaf, which appears to have antihistaminic activity, has been empirically observed to be helpful in the treatment of conditions with hives as a key feature, including PUPPP.

Herbs used to promote sleep are discussed later in Insomnia in Pregnancy.

Treatments are divided into those for topical and internal use, and are recommended to be used in combination. Effects may be expected after 2 to 3 days of regular use, although some women gain relief more quickly and for some it may take up to a week to notice results. Many women report that herbal treatments provide only temporary relief, requiring them to reapply topical remedies often; however, they find this an acceptable alternative to steroid use during pregnancy.

TABLE **15-5**

Botanical Treatment Strategies for PUPPP

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Relieve inflammation	Anti-inflammatory	*Aloe vera*	Aloe vera
		Avena sativa	Oatmeal
		Glycyrrhiza glabra	Licorice
		Hamamelis virginiana	Witch hazel
		Matricaria recutita	Chamomile
		Scutellaria baicalensis	Chinese skullcap
	Antihistaminic	*Urtica dioica*	Nettle leaf
	Hepatic Alternatives/ Aperients	*Rumex crispus*	Yellow dock
		Taraxacum officinale	Dandelion root
Prevent striae gravidarum		*Centella asiatica*	Gotu kola
Promote relaxation and sleep as needed	Nervine	*Avena sativa*	Milky oats
	Sedative	*Eschscholzia californica*	California poppy
		Passiflora incarnata	Passion flower
Immunomodulation	Adaptogen	*Withania somnifera*	Ashwagandha
		Ganoderma lucidum	Reishi
		Schisandra chinensis	Schisandra

The effects of using oral corticosteroids and herbs internally simultaneously during pregnancy has not been studied, therefore, owing to unknown safety, is not recommended. However, the use of oral steroids and topical herbal treatments, or conversely, oral herbal treatments and topical steroids may be acceptable. Women using oral medications for the treatment of PUPPP should inform their medical provides about their use of herbs prior to beginning an herbal protocol (Table 15-5).

Topical Applications

The vehicle via which topical applications are delivered in the case of PUPPP will depend entirely on the mother's response to any given preparation. PUPPP presents as itchy, irritating, and inflamed. The urticaric lesions may be discrete, but often, as the condition progress, become contiguous, requiring application of medicine to a large area. Salves may not be the best delivery mode as they may actually feel as if they are ''sealing in'' the hot, inflamed sensation. Similarly, applying tinctures directly to the skin is not advisable, although tinctures may be highly diluted in water or preferably witch hazel extract and used as compresses. Washes made of herbal teas can be used as compresses as well, although they are inconvenient to prepare daily. Similarly, herbal extracts can be added to aloe vera gel and applied this way. A highly absorbent cream base to which herbal extracts are added is perhaps the optimal delivery mode, as the cream is soothing and allows broad application of herbs, and the preparations are easy to make in large batches, store well, and are highly portable should travel or application at work be necessary. Topical applications will need to be reapplied multiple times per day, or as needed, for symptomatic relief. Women should be advised that products containing oil may stain clothing or bedding.

Chamomile

Chamomile has been approved by the German Commission E for the treatment of inflammatory skin conditions.[74] Although there appear to be no contraindications to its use topically or internally (with the exception of rare allergy), herbalists have noted that with some conditions, for example, pediatric eczema, chamomile oil extracts may actually exacerbate irritation. For patients wishing to use chamomile for topical treatment of PUPPP, a cream preparation is advised. Chamomile tea may also be taken internally as a relaxing, mild sleep-promoting tea or tincture.

Chinese Skullcap

Chinese skullcap, ''scute,'' is used in traditional Chinese medicine to clear heat and drain dampness, which, from a modern medical perspective, might be interpreted as treating inflammation.[75] The anti-inflammatory effects are attributed to the herbs flavonoids, and antioxidant and antihistamine activity.[75,76] Only recently is this herb finding its way into Western herbal medicine practice. Little published data was identified specifically on the use of Chinese skullcap for skin conditions; however, clinical evidence from herbal practice suggests a high degree of efficacy and safety in the treatment of inflammatory skin conditions including eczema and dermatitis. Tincture may be added to a cream base and applied topically, either alone or mixed with or herbs, for example, licorice root and St. John's wort extracts. Internal use of Chinese skullcap is not recommended during pregnancy because of teratogenicity in animal studies. It may be used internally, short term, during the postpartum should PUPPP arise during that period, or persists past the time of birth.[77]

Gotu Kola

Because one of the theories on the etiology of PUPPP is connective tissue damage as a result of abdominal stretching, with manifestation in the striae, it seems a reasonable consideration to minimize striae development if at all possible. A Cochrane Collaboration review of topical agents for stretch mark prevention identified two randomized trials involving a total of 130 women. One study, involving 80 women, indicated that, compared to placebo, massage with a cream (Trofolastin) containing *Centella asiatica* extract, alpha tocopherol and collagen-elastin hydrolysates was associated with less women developing stretch marks. A second study of 50 women compared massage using an ointment (Verum) containing tocopherol, panthenol, hyaluronic acid, elastin, and menthol with no treatment. Massage with the ointment was associated with fewer women developing stretch marks. The two papers reviewed may show that any cream massaged onto the abdomen, thighs, and breasts (areas most affected by stretch marks) may be of some benefit. There may be additional benefit from certain ingredients in the cream and the ointment described, but it is unknown which constituent(s) is beneficial. Neither preparation is widely available.[78] Gotu kola is widely used by herbalists for the treatment of connective tissue damage. Practitioners should be aware that a number of cases of contact dermatitis from topical use were identified in the literature (nonpregnant patients); therefore, caution is advised and patch testing recommended before general use.[79–81]

Oatmeal Baths

To apply oats topically, the rolled oats are moistened and the milk extracted and added to bath water or rubbed on the body in a bath or shower.[82] Two handfuls (about 1 cup) of rolled oats are placed into a large clean sock or rolled in a towel or bandana that can be tied at the top. The sac is taken into the bath or the shower, and as the oats soak up the water the cloth is squeezed firmly in the palm of the hand. A milky liquid will begin to be exuded, and it is this liquid that is allowed to fill the tub or rubbed over the body in the shower, and then rinsed off. This oat milk is very soothing and emollient. This can be repeated as needed even several times daily.

St. John's Wort

St. John's wort oil is a classic topical burn treatment.[83] Both St. John's wort extract and hyperforin have demonstrated inhibitory effects in epidermal immune response

when applied topically, and suggest a role for this soothing application in the treatment of inflammatory skin conditions. It is popularly used by herbalists for inflammatory and microbial skin conditions. St. John's wort demonstrates good cosmetic skin tolerance.[84,85]

Witch Hazel, Aloe Vera

Witch hazel extract, applied as a compress, has long been used as a topical agent for reducing inflammatory and pruritic skin conditions. It is recognized by ESCOP and approved by the German Commission E as a treatment for skin irritations and minor inflammatory dermatologic and mucosal conditions.[74,86] A comparative study looking at witch hazel versus cortisone for the treatment of erythema found it to be slightly less effective than cortisone but still noteworthy in its effects, whereas a study on the outcome of treatment of sunburn with witch hazel vs. no treatment found that it led to a significant reduction in erythema and visible skin damage. It has demonstrated a mild anti-inflammatory effect in patients suffering from atopic neurodermatitis and psoriasis.[86]

Aloe vera gel is a soothing topical liquid from the aloe vera plant. Popular for pain relief and healing from burns and other skin conditions for thousands of years, some women find temporary relief from the itching of PUPPP with topical application of the gel. Promising preliminary research suggests that aloe has immunostimulatory properties that may improve wound healing and dermatologic inflammation.[87] There is no contraindication to liberal topical use during pregnancy; aloe should not be used internally during pregnancy.

Internal Use

California Poppy, Passion Flower

See Insomnia in Pregnancy, as well as Plant Profiles, for discussion of the safety and efficacy of these herbs commonly used to treat sleep difficulties in pregnancy.

Dandelion Root, Yellow Dock

An entire category of herbs, known historically and to this day as ''alteratives,'' and referred to colloquially as ''blood cleansers,'' are included in the treatment of skin conditions many. Dandelion root is perhaps one of the most commonly used, and is popularly cited on ''mother blogs'' on the Internet as prescribed by midwives in the treatment of PUPPP. No human clinical trials have been conducted to support the use of dandelion root for skin conditions and there are no data in the scientific literature of dandelion either being safe or contraindicated during pregnancy.[88–90] Yellow dock is used similarly to dandelion root. Note that yellow dock is sometimes considered contraindicated in pregnancy because it is a mild anthraquinone laxative; however, clinically, it has not been observed to be associated with increased uterine activity or other adverse outcomes.

Licorice

Glycyrrhizin has exhibited a range of corticosteroid-like activities when injected in animals and humans, including inhibition of prostaglandin synthesis similar to cortisone. Compounds in the root inhibit 5-lipoxygenase formation and leukotriene biosynthesis in vitro.[91] It is commonly used by herbalists for a wide variety of inflammatory complaints ranging from gastrointestinal disorders, for which it is best studied, to inflammatory skin conditions such as eczema. Its use for PUPPP is empirically based. Two recent reports on high-dose licorice consumption throughout pregnancy, in the form of licorice candy containing actual licorice extract rather than licorice flavor, demonstrated no increase in maternal hypertension or low birth weight; however, both studies, demonstrated a significant increased in preterm (<37 weeks) delivery. In one study, the risk of preterm delivery was greater than double the risk of women not consuming licorice.[92,93] No studies demonstrate harm or adverse outcomes with short-term use of modest doses of licorice, including a study of 110 case reports on the use of glycyrrhizin injections for treating viral hepatitis during pregnancy that showed no adverse effects.[88] It is recommended that licorice not be used in excessive doses or for prolonged periods during pregnancy; however, use for up to a week at a time appears to be safe. A comparative study of the safety and efficacy of licorice vs. cortisone use during pregnancy for the treatment of PUPPP would be informative. Women with hypertension should not take licorice during pregnancy (see Plant Profiles for safety information).

Milky Oats

The tincture of milky oats is considered a reliable nerve tonic, especially for use when there is nervous exhaustion or general debility. The medicinal use of oats during pregnancy has not beem studied; however, taken as food, no adverse effects have been noted in pregnancy.[82] The tincture may be used alone, but it is more commonly taken in combination with other nervine or sedating herbs, for example, chamomile, St. John's wort, California poppy, passion flower, and lavender.

Nettle Leaf

Stinging nettle leaf has demonstrated significant anti-inflammatory activity; it is used for the treatment of rheumatoid arthritis and allergic rhinitis.[86] Herbalists have found nettle to be a reliable herb in the treatment of numerous systemic and dermatologic inflammatory conditions. It may be taken as tea or in freeze-dried capsules. No serious adverse effects were reported in five clinical studies with a total of 10,368 patients using hydroethanolic extracts corresponding to an equivalence of 9.7 g of dried leaf daily for periods ranging from 3 weeks to 12 months. Minor side effects included GI upset and allergic reaction (1.2% to 2.7% of cases).[86] Nettle leaf is one of the most commonly used herbs by midwives who commonly recommend it to help build iron levels (see Chapter 15). It has been suggested, although not demonstrated, that the astringency of this herb might interfere with iron absorption. A 1975 review article by Farnsworth et al. reported that stinging nettle was a potential abortifacient, and that its constituent 5-hydroxytryptamine was a uterine stimulant; however, frequent use of large doses of this herbal

infusion in midwifery practice has demonstrated no evidence of such activity.

Adaptogens

Adaptogens and their immunoregulatory properties are discussed extensively in Chapter 8.

Baking Soda Paste

Baking soda paste is reported by women on ''mother blogs'' (Internet) to relieve itching from PUPPP. Enough water is mixed with baking soda to form a paste and this is applied directly to affected areas.

NUTRITIONAL CONSIDERATIONS

Essential Fatty Acids

Some women report finding relief from the daily addition of essential fatty acids (EFAs) to their diets. A high-quality combination EFA product containing plant source oils and fish oils is recommended. Women supplementing with fish oils during pregnancy should not exceed daily recommended allowances for vitamins A and D and should only take products that exclude the presence of heavy metal contaminants.

VARICOSITIES IN PREGNANCY

Aviva Romm

Varicosities are exceedingly common during pregnancy, when they often appear for the first time. Forty percent of all pregnant women are affected.[94] They most commonly appear on the lower legs and rectum (hemorrhoids), although vulvar varicosities may also occur. The physiologic changes of pregnancy are responsible for the development of varicosities. These include hormonal changes that cause increased fragility of the blood vessel walls, along with increased iliac venous pressure owing to the enlarging uterus, leading to reflux of blood in the vessels and subsequent, rupture of valves, and the appearance of varicosities.[94] More recently, the ''weak-wall hypothesis'' proposes that varicosities arising in pregnancy are actually the result of an inherited predisposition to weakness in the vein wall that allows progressive venous dilation even at normal venous pressures, with valve failure occurring as a consequence.[95] Further, it is now recognized that the saphenous veins contain estrogen and progesterone receptors that may play a role in pregnancy-mediated varicose vein development, although the role of these receptors is not entirely known.[95,96]

Varicosities may be accompanied by throbbing, a feeling of heaviness, aching, heat, and pain, and with leg varicosities there may be ankle edema and phlebitis. Varicosities frequently regress in intensity during the postpartum; however, they may also persist, with continued symptoms and worsening of venous distention.[97] Hemorrhoids are predisposed to bleed and are further aggravated by constipation, which also commonly increases in pregnancy. Venous thrombosis is a complication that occurs in less than 10% of pregnancies, and which requires immediate medical management. In severe cases, and especially in the postpartum and as women age, chronic venous insufficiency, and venous ulceration can become problematic. These conditions, too, require medical care in conjunction with complementary therapies.

This chapter focuses on the treatment of uncomplicated superficial leg varicosities and hemorrhoids during pregnancy; thus, the range of herbs is limited to those herbs and supplements considered safe for use by pregnant women; the treatments in this chapter, however, can be applied to anyone with varicosities.

TREATMENT OF VARICOSITIES IN PREGNANCY

Supportive therapy for leg varicosities includes leg elevation, compression with support hose, sleeping in a left lateral decubitus (side-lying) position, regular exercise, and avoidance of long periods of standing or sitting.[95,97] Anticoagulant therapy is used when needed to prevent thromboses. Hemorrhoids are treated with topical antihemorrhoid preparations and avoidance of straining when having a bowel movement. Excessive periods or sitting or standing should be avoided. Surgical treatment for hemorrhoids is rarely required during pregnancy; when surgery is required for either hemorrhoids or leg varicosities, it is preferably done between pregnancies.[95] Most often, vulvar varicosities also require only supportive treatment; severe vulvar varicosities may require attention during vaginal birth to prevent them from rupturing and bleeding extensively.

BOTANICAL TREATMENT OF VARICOSITIES IN PREGNANCY

There is very little published evidence in either the herbal or scientific literature on the use of botanicals for the prevention or treatment of varicosities in pregnancy. Topical treatments that include horse chestnut and witch hazel extracts are commonly recommended. Black tea (tea bags) are commonly used by midwives as a highly astringent ''home remedy'' used topically for the treatment of hemorrhoids, both during pregnancy and postnatally. Other herbs that may be used topically include witch hazel, yarrow, and white oak bark. Arnica may sometimes be recommended for external use, but should not be used on broken or open skin. The use of nettle leaf infusion, taken regularly as a tea, is often recommended for its reputed hemostatic and venotonic actions. Horse chestnut is a popular herb in Europe, taken internally for the treatment of venous insufficiency. Bilberry is an important venotonic herb used internally with a good safety for pregnancy. Foods high in rutin and bioflavonoids are commonly used to improve vascular tone and integrity. The herbal approach to the treatment of hemorrhoids includes gentle measures to alleviate constipation if this is a concurrent problem, and thus minimize straining during bowel movements. Gotu kola, which is sometimes used for varicosities and venous disorders is not safe for internal use during pregnancy, and has been associated with contact dermatitus with topical use, so it is recommended that patch testing be done before applying liberally (Table 15-6).[98–101]

BOX **15-6**

Herbal Protocol for PUPPP

Topical Treatment
As needed daily, shower and apply the extracted milky liquid of rolled oats (*Avena sativa*). Pat dry and then rinse affected areas with witch hazel extract. Then apply the following cream daily, *repeated as needed* to maintain symptom relief:

Mix
3 oz cream base
10 mL each of the following tinctures:

St. John's wort	(*Hypericum perforatum*)
Skullcap	(*Scutellaria baicalensis*)
Licorice	(*Glycyrrhiza glabra*)

Internal Treatment
Tincture for Relief of PUPPP
Combine:

Nettle leaf tincture	(*Urtica dioica*)	30 mL
Licorice root	(*Glycyrrhiza glabra*)	30 mL
Dandelion root	(*Taraxacum officinale*)	20 mL
Passion flower	(*Passiflora incarnata*)	20 mL
		Total: 100 mL

Take 3 to 4 mL repeated up to four times daily.
Take an herbal nervine tea or tincture as needed

Treatment Summary

- Convention therapy includes the use of topical and oral corticosteroids, usually taken high dose (10 to 40 mg) for up to 1 week, and then tapering down as symptoms subside.
- Botanical therapy primarily consists of the use of topical and oral anti-inflammatory and nervine herbs.
- An anti-inflammatory diet supplemented with essential fatty acids may be helpful.

Arnica

Topical arnica applications are sometimes included in treatment protocol for varicosities. According to Schulz et al., it is uncertain whether arnica extracts are active topically and if so, by what mechanism.[102] Clinical herbalists, however, report on the remarkable and rapid ability of arnica flowers to reduce bruises and swellings when applied topically to the affected areas. No studies were identified on the use of arnica for the treatment of varicosities. The herb is most commonly applied as an oil or gel, is not applied to broken skin, and should not be used internally. The oil may be applied two to three times daily, either alone or in combination with other herbal preparations. As the rectal mucosa is highly vascular and absorptive, it is recommended that arnica be used for leg varicosities only, and that other herbs (e.g., witch hazel, black tea) be used to reduce hemorrhoids.

Bilberry

Bilberry, a relative of the blueberry, is used as a vasoprotective herb, one of its many virtues. It has demonstrated potent effects on vascular permeability in animal and in vitro models, and a number of positive human trials have been done, tough their methodologic quality was not strong.[98] Bilberry has been reported to be safe for internal use during pregnancy, and efficacious in the treatment of gestational hemorrhoids and venous insufficiency of pregnancy.[103] It is taken in two and three divided doses of 160 to 340 mg per day, depending upon the severity of the condition.[103] It may also be taken in liquid extract form. Bilberry can be taken prophylactically in women with a predisposition to varicosities or a family history of gestational varicosities.

Horse Chestnut

Horse chestnut seed extract (HCSE) preparations are widely prescribed in Europe for the treatment of venous insufficiency and vascular fragility. They are taken orally. A review of the scientific literature yields seven well-designed studies that support the superiority of HCSE over placebo and suggest that the herbal product may be equal to compression stockings in efficacy.[98] Although the herb is generally not recommended for use

TABLE **15-6**

Botanical Treatment Strategies for Varicosities

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Tone the vascular system	Astringent	*Aesculus hippocastanum*	Horse chestnut
	Venotonic	*Arnica montana*	Arnica
	Hemostatic	*Camellia sinensis*	Tea
		Hamamelis virginiana	Witch hazel
		Quercus alba	White oak bark
		Urtica dioica	Nettle leaf
		Vaccinium myrtillus	Bilberry
			Rutin and bioflavonoid-rich foods

in pregnancy, this is owing to lack of data rather than contraindication based on known adverse effects. No teratogenic effects have been observed in animals given very high doses of extract by oral route, although fetal body weights were reduced compared with controls.[104] Steiner et al. conducted a double-blind, placebo-controlled study of HSCE use during pregnancy. Fifty-two women with leg edema owing to pregnancy-induced venous insufficiency received 300 mg of Venostasin (240 to 290 mg of HSCE standardized to 50 mg escin) twice daily for 2 weeks. No adverse effects were observed (Fig. 15-1).[105]

Nettle Leaf

Nettle leaf is highly valued by herbalists for its purported venotonic actions, and is used by herbalists and midwives for the treatment of varicosities.[106] It is taken internally as a strong daily nutritive infusion. Its use is empirically based. No herbal or scientific studies were identified on the use of nettle leaf for the treatment of varicosities. Animal studies are lacking on the use of this herb in pregnancy. No harmful effects to the fetus have been identified. The lignins in nettle, as well as their intestinal transformation products, have been shown to bind sex hormone binding globulin (SHBG) in vitro; however, ethanol extract of the aerial parts of nettle did not demonstrate significant anti-implantation activity when given to female rats.[104]

Witch Hazel, Black Tea, White Oak, Yarrow

Witch hazel bark, black tea, and white oak bark are tannin-rich, highly astringent herbs commonly used as topical remedies for the treatment of hemorrhoids. Yarrow is also quite astringent, and although more commonly used for bleeding, may sometimes be included in topical preparations. These herbs are not intended for internal use in pregnancy (with the exception of small amounts of black tea as a beverage). They can be used in a variety of forms including as strong washes or diluted extracts applied with a cotton ball, or in herbal suppositories (see the following) to be inserted nightly to reduce local swelling and inflammation. Black tea bags are a very convenient and acceptable remedy, as they are easily accessibly, affordable, and simple to prepare. Women can be instructed to purchase commercial tea bags and steep 1 per application in ¼ cup of boiling water (as if making a cup of tea with a very small amount of water). When the tea has cooled, the liquid can be discarded and the tea bag slightly wrung out and the bag applied to the hemorrhoids. Women must be warned that the tea will permanently stain fabrics and bedding. Putting a menstrual pad in an old pair of underwear on to hold the tea bag in place for up to 30 minutes at a time is effective, or the woman can simply apply the tea bag manually for several minutes, sitting over the toilet or in the shower, two to three times daily (Fig. 15-2).

Food Sources of Rutin

Rutin is a naturally occurring flavonoid in many foods, especially buckwheat, apricots, cherries, grapes, grapefruit, plums, and oranges. It is often used in patients with capillary fragility, varicose veins, bruising, or hemorrhoids.[107]

Figure 15-1 Horse chestnut *(Aesculus hippocastanum*). (Photo by Martin Wall.)

Figure 15-2 Witch hazel (*Hamamelis virginiana*). (Photo by Martin Wall.)

Most clinical studies have used hydroxyetylrutosides (HER), a standardized mixture of rutinosides. In a study of 37 pregnant women given 300 mg rutoside three times daily for 8 weeks vs. placebo, rutoside reduced

symptom scores for pain, feelings of leg heaviness and tiredness, nocturnal cramps, and paraesthesias associated with varicosities compared with placebo in women with visible varices and these symptoms after 28 weeks gestation. Rutosides also have led to reduction of ankle size compared with placebo, in whom ankle size increased. Adverse effects are rare and transient. The most commonly reported adverse effects include dizziness, headache, dry mouth, tiredness, nausea, dyspepsia, diarrhea, constipation, and skin rash. Rutin appears to be safe during pregnancy. Its safety after 28 weeks of gestation has been confirmed in two human trials. Scientific evidence for the safe use of rutin during lactation is not available. Given the uncertainty of the safety of rutoside preparations, it is recommended that pregnant women consume foods rich in rutin and take a complete vitamin supplement with bioflavonoids, including rutin, rather than a rutoside product.[107]

INSOMNIA IN PREGNANCY

Aviva Romm

The International Classification of Sleep Disorders has proposed that the occurrence of either insomnia or excessive sleepiness that develops during pregnancy be called *pregnancy-associated sleep disorder* in recognition of the association of sleep disturbance with pregnancy and the self-limited nature of these problems.[108] In nonpregnant populations, sleeping less than 5 hours per night has been observed to adversely impact both mood and performance, and places individuals at increased risk of adverse events such as motor vehicle accidents.[108] Postpartum sleep deprivation may increase the risk for mood disorders ranging from postpartum depression to overt psychosis.[108] Disrupted sleep during pregnancy is associated with poorer obstetric outcomes, in particular length of labor and type of delivery. In a prospective, longitudinal follow-up of 131 pregnant women, Lee and Gay demonstrated that women who slept less than 6 hours at night had longer labors and were 4.5 times more likely to have cesarean deliveries.[109] Given the potential magnitude of adverse events associated with sleep disturbances, serious attention should be given to this complaint during pregnancy, and its effects on a woman's quality of life and health.

Physiologic, hormonal, and physical changes of pregnancy are responsible for a variety of sleep disorders. Women may experience insomnia, night waking, parasomnias [e.g., restless leg syndrome (RLS)], leg cramps, hypersomnia, or snoring.[109–111] The growing uterus and the pressure it places on the lower back diaphragm, stomach, and simply its weight, require pregnant women to adopt a variety of positions to accommodate in order to sleep comfortably and avoid associated discomforts for example, heartburn, or pressure on the inferior vena cava leading to paresthesias of the distal extremities and shortness of breath. Increased need to urinate during the night, exaggerated dreams, worries over the increased responsibilities of pregnancy and parenthood, anxieties over the birth, and many other concerns also can interfere with sleep and severely decrease its quantity and quality. The effects of estrogen and progesterone in pregnancy also alter the quality of sleep, although the extent to which this occurs as a result of hormones is not clear. However, indirectly, hormonal effects such as increased nasal congestion, can dramatically affect sleep.[109,112] Pregnancy may also exacerbate existing sleep disorders, or exacerbate medical conditions (e.g., acid reflux, asthma) that affect sleep. Chronic pain is a common cause of sleep disturbances, and may also be exacerbated during pregnancy (see Case History).

Sleep disorders of pregnancy have a predictable pattern relative to the trimesters. During the first trimester, sleep duration and quality at night are often decreased, although women to require more and report that they are apt to fall asleep much more easily than usual during the day, commonly with an increased desire to nap. The second trimester usually leads to a return of a woman's normal sleep patterns. In the third trimester, women show increased wake after sleep onset and decreased sleep quality, and frequently complained of restless sleep, leg cramps, and frightening dreams.[109–111] Some amount of night waking during pregnancy may be the body's natural and intrinsic way of preparing the mother for the inevitable night waking that accompany having a breastfeeding newborn and infant, and therefore, regardless of treatment, may be unavoidable.

Lack of sleep or poor sleep quality can affect a woman's sense of well-being during her waking hours, increase irritability, lead to depression, decrease appetite, can affect memory, and may affect concentration and functioning at normal daily tasks. As discussed earlier, significantly diminished sleep during pregnancy may also have a deleterious effect on the birth experience.[109]

MEDICAL TREATMENT OF INSOMNIA IN PREGNANCY

The exact incidence of sleep disorders in pregnancy is unknown, but it is estimated that as many as 90% of women experience them during the third trimester.[108,109] There are no clinical trials of various treatment

Treatment Summary for Varicosities and Hemorrhoids during Pregnancy

- Women with leg varicosities should be encouraged to take a brisk walk each day. This can also be beneficial for women with hemorrhoids accompanied by constipation, as regular exercise reduces constipation.
- When constipation accompanies hemorrhoids, dietary changes, and gentle herbal and nutritional approaches should be taken to relieve constipation to avoid unnecessary rectal pressure and straining to pass stools.
- Compression stockings can be used in the event of extensive, painful, or swollen leg varicosities.

Continued

Treatment Summary for Varicosities and Hemorrhoids during Pregnancy

- Leg elevation for 30 minutes twice daily temporarily relieves ankle edema and discomfort associated with varicosities.
- Topical applications can be used two to four times daily to relieve swelling associated with varicosities.
  - For leg varicosities, compresses of witch hazel extract or arnica ointment can be applied.
  - For hemorrhoids, black tea back compresses or other herbal extract compresses (e.g., witch hazel) can be applied as needed. A convenient way to apply witch hazel to hemorrhoids is with medication-saturated cosmetic pads. Women can take a stack of cosmetic pads, place them in a 4-oz wide mouth jar with a screw top, and fill the jar to cover the pads with witch hazel extract purchased from the pharmacy. A few drops of lavender essential oil can be added as well for its pleasant scent and soothing action when applied topically. A pad can be tucked in next to the hemorrhoids, and changed several times daily. This can be used in conjunction with, alternated with, or in lieu of the tea bags. Both are quite effective as reducing the hemorrhoids and relieving itching and irritation. The black tea is more effective than the former.
  - An herbal suppository can be inserted nightly to shrink hemorrhoids and relieve itching, burning, and irritation. Use 4 oz of cocoa butter and 2 tbs each of marshmallow root, white oak bark, and goldenseal powders, as well as 2 tbs of calendula oil, which is vulnerary. See Chapter 3 for instructions on making suppositories. These can be made in batches that can be stored in the refrigerator for several weeks and used as needed. Women should be informed that the oil can stain clothing and bedding, and therefore, a menstrual pad should be worn with nightly insertion of the suppository.
- Internally:
  - 120 to 360 mg bilberry extract two to three times daily, depending on the severity of the varicosities or hemorrhoids
  - Nettle infusion: 2 tbs dried organic nettle leaf steeped to 30 minutes in 1 cup of boiling water
  - Strain and drink the liquid. Take 2 cups daily.
  - 2 to 5 mL horse chestnut seed extract (HSCE) twice daily depending on severity of varicosities
  - 500 mg vitamin C with bioflavonoids twice daily

modalities in this group of patients.[110] It is important to identify etiological factors and to treat any associated or underlying medical conditions. RLS may represent folate or iron deficiency, hormonal changes of pregnancy, or more rarely, may be a sign of end-stage renal disease or peripheral neuropathy.[113] It is usually transient in pregnancy, occurring most commonly in the third trimester and disappearing by the time of birth.[113] Insomnia associated with a more serious psychiatric disorder, for example, severe depression, anxiety disorders, or bipolar disorder, may require specific pharmaceutical treatment. Risks associated with the use of pharmaceutical medications during pregnancy must be seriously considered.

The medical treatment of RLS in pregnant women is difficult, as most of the drugs commonly used for this problem are not safe for use during pregnancy. Nonpharmacologic treatments are recommended, such as leg stretching prior to sleep and support hose if varicosities are prominent. Iron supplementation is suggested, as this condition is associated with iron deficiency. Opioids are used sometimes in the second or third trimester in severe cases.[114]

GENERAL TREATMENT OF SLEEP DIFFICULTIES IN PREGNANCY

Sleep quality in pregnancy is often greatly improved by improving the sleep environment—both internally and externally—through simple, common sense measures. For example, during growth spurts, the fetus places significantly increased nutritional demands on the mother—night waking may simply be a result of hunger, but this frequently goes unrecognized by the mother, or hunger is ignored in the effort to avoid getting out of bed—with sleep nonetheless compromised. Placing a snack near the bed and having the mother eat freely during the night may, in itself, remedy sleep disturbances. Nutritional deficiencies may also affect sleep quality. This is discussed under Nutritional Considerations. It is common for people to use stimulants during the day, for example, increased caffeine (coffee, chocolate, tea, sodas) intake, when they are not getting adequate restful sleep at night. Unfortunately, such behavior can further exacerbate sleep difficulties, making it difficult to finally unwind when one is ready for sleep. Therefore, encouraging pregnant patients to engage in healthful activities, for example, taking a refreshing walk, using aromatherapy (e.g., peppermint oil in an infuser) in their work area to increase concentration, eat well and drink plenty of water, and avoid stimulant use as much as possible, can be beneficial in promoting sleep and at least won't make sleep efforts more difficult.

Pregnant women can be encouraged to incorporate the following simple suggestions for encouraging sleep into their daily ''sleep hygiene'' practices:

- Create an environment conducive to sleep: a comfortable space with adequate pillows to support the pregnant woman comfortably, the ability to darken the room completely, and block out extraneous disturbing sound
- A gentle yoga session done approximately an hour before bed, followed by a warm bath, can promote relaxation prior to sleep.
- Take a warm bath about an hour before bed. Add 5 to 7 drops of relaxing essential oils to the tub, for example, lavender and rose oils.
- Get into bed 30 minutes before intended sleep and read, or take some time to write in a journal.

- Play quiet, relaxing music in the room, especially if other noises prevent sleep, or if troublesome thoughts are keeping the woman awake.
- Use aromatherapy to create a relaxing ambience.
- If possible, have a partner give the pregnant woman a foot and leg massage as she is trying to go to sleep.
- Encourage the woman to identify hunger as a possible cause of sleep disturbance. Eating a light snack just before sleep, and having a snack at the bedside or readily available in the kitchen to eat during the night if hunger awakens her can make a huge difference. Tell women that even if they do not feel hungry, if they wake in the middle of the night and cannot fall back to sleep, try eating something light—this will often help even if hunger was not obvious. Snack suggestions include low fat organic yogurt, toast with nut butter, crackers, cereal with a small amount of milk, hard cheese, a banana.
- Use cognitive behavioral therapy to help a woman cope with troublesome thoughts if these are the prime culprit preventing sleep, and have the woman develop strategies for dealing with her primary concerns.
- Although napping is not an alternative to a good night's sleep, it is essential, whenever possible, for pregnant women to nap when they are unable to get adequate sleep at night.
- Avoid: Caffeine after late afternoon, disturbing television programs, watching television close to bed time and in bed, spicy meals in the evening, eating heavy foods within 2 hours of sleep, tension in the bedroom.

BOTANICAL TREATMENT OF INSOMNIA IN PREGNANCY

There is a limited range of safe conventional pharmaceutical options for treating insomnia during pregnancy, and interestingly, most pregnant women do not report sleep disorders to their physicians.[108] It is nonetheless a problem for which women commonly seek relief, and therefore frequently turn to natural products. It is essential that the normalcy of symptoms, for example, RLS, be established prior to treating. However, once it is determined that the sleep disturbance is a simple pregnancy discomfort, gentle herbal therapies may be tried. Several herbal medicines appear to be safe during pregnancy and provide modest improvement in sleep quality; however, experimental and clinical data on the use of these during pregnancy is, with minimal exception, lacking. General recommendations should incorporated prior to or in conjunction with botanical use. For women with severe sleep disorders but who are not willing to use pharmaceutical drugs, stronger herbs may be considered; however, because studies evaluating their safety during pregnancy are largely lacking, their use should be limited to short term, and first-trimester use should be avoided. Examples of such herbs include passion flower (*Passiflora incarnata*), skullcap (*Scutellaria lateriflora*), California poppy (*Eschscholzia californica*), and valerian (*Valeriana officinalis*). Herbs commonly used during pregnancy for difficulty falling asleep or poor sleep quality, and which have a good safety profile, are presented in the following; further discussion of the evidence for these herbs, as well as additional herbs for insomnia, is presented in Chapter 19. Readers are also directed to Chapter 19 for insomnia secondary to anxiety. Consult Plant Profiles for pregnancy-related safety information.

Teas are an excellent form for using sleep promoting aromatic herbs such as chamomile, lavender, and lemon balm; unfortunately, drinking tea close to bedtime often causes the pregnant woman to awaken within a couple of hours after falling asleep with the need to urinate, thus defeating the benefits of the herbs. Therefore, it is recommended that tea not be taken closer than 2 hours prior to bed, and that frequent small amounts of tincture be taken instead to build an effective dose over a period of 1 to 2 hours, with a dose of 2 mL of any single herb or a combination of any two or three, taken every 15 to 30 minutes for 1 to 2 hours prior to attempting to sleep (Table 15-7).

Chamomile

Chamomile is commonly taken as a tea, although may also be included in tincture formulae, as a gentle calming and sleep-inducing herb.[115] Clinical trials are generally lacking. Studies in mice and rats have shown anticonvulsant and CNS depressant effects respectively.[115,116] Chamomile is erroneously placed on lists of herbs contraindicated during pregnancy; however, this is based on a single 1979 study that found teratogenic effects using a concentrated extract of α-bisoprolol at high doses. No teratogenic effects were seen at lower doses and the dose of the oil constituent required to cause teratogenicity are far greater than it would ever be possible for someone drinking the tea to ever approximate.[117] No harmful effects have been reported from the use of chamomile during pregnancy or lactation.

Cramp Bark/Black Haw

Considered generally safe for use during pregnancy, these closely related herbs have a long history of use for the treatment of spasmodic muscle discomforts.[118] Although they have not been studied for the treatment of RLS during pregnancy, they have been used traditionally for spasmodic pain in the legs and back, and particularly in the calf.[118–120] Today, midwives and herbalists consider these herbs in the treatment of back pain, leg discomfort associated with RLS, and leg cramps, which may interfere with sleep, used in conjunction with appropriate relaxation techniques and nutritional supplementation.

Lavender

Lavender oil's effects on sleep have been evaluated in murine models. Mice exposed to repeated dosing have demonstrated a more rapid sleep onset with longer duration of sleep, and exposure of mice to a lavender atmosphere in a dark cage resulted in depression of motor activity.[121,122] Lavender oil has also been shown to inhibit the stimulant effects of caffeine.[121] In a clinical study on four benzodiazepine-dependent geriatric patients on stopping this treatment, there was a significant decrease

TABLE **15-7**

Herbs for Treating Sleep Disturbances during Pregnancy

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Promote sleep, relieve anxiety (generally considered safe during pregnancy)	Nervine Sedative Spasmolytic	*Lavandula officinalis* *Matricaria recutita* *Melissa officinalis*	Lavender Chamomile Lemon balm
Promote sleep, relieve anxiety (stronger herbs, see Chapter 19)	Nervine Sedative Spasmolytic	*Eschscholzia californica* *Passiflora incarnata* *Scutellaria lateriflora* *Valeriana officinalis*	California poppy Passion flower Skullcap Valerian
Relieve restless legs	Spasmolytic	*Viburnum opulus/Viburnum prunifolium*	Cramp bark/black haw

in sleep duration, which was restored to previous levels by substitution of aromatherapy with lavender oil.[123] In a study comparing single 3-minute inhalations of lavender and rosemary (mental stimulating effects) in 40 subjects, the lavender group showed increased beta power (EEG) suggesting drowsiness, they had less depressed mood, and reported feeling more relaxed and performed the math computations faster and more accurately.[124] Although data in pregnancy are lacking, lavender appears to be a safe and gentle herb for sleep promotion. The herb may be taken as a tea or tincture; the oil should never be taken internally but can be added to a warm bath (5 to 7 drops per tub of water) and the woman encouraged to soak for 20 minutes each night prior to sleep, or in an aromatherapy infuser placed near the bed. A recent article in the *New England Journal of Medicine* suggested a possible estrogenic effect in young boys regularly exposed to topical products containing lavender oils. Although the products were not characterized, and the case reports do not clearly implicate lavender use, practitioners should be aware that this is an emergence concern and that other essential oils have been associated with estrogenic effects. Short-term use may be preferable until further research in this area has been conducted; however, no adverse effects have been previously reported with the external use of lavender oil or lavender oil containing products in spite of widespread use (Fig. 15-3).[125]

Lemon Balm

Lemon balm is approved by the German Commission E for the treatment of insomnia of nervous origin.[126] Lemon balm is beneficial in moderating subjective mood in response to mild psychological stress and may be capable of inducing a mood-state compatible with inducing sleep.[115,127] No mutagenic or genotoxic effects have been observed in experimental models.[9] Patients with thyroid disorders or taking thyroid medications should avoid the use of lemon balm during pregnancy owing to theoretical risk of reduction of thyroid function from this herb (see Chapter 18).[117]

ADDITIONAL THERAPIES

Nutritional Considerations

In addition to addressing hunger as a possible cause of sleep disturbances (see general recommendations), certain nutritional deficiencies may be associated with insomnia and other sleep disorders, for example, leg cramps and RLS. Adequate intake of iron, folate, B vitamins, calcium, and magnesium are essential for optimal sleep during pregnancy and appropriate supplementation should be introduced when there are sleep disorders.

CASE HISTORY:

Perri had experienced chronic insomnia and back pain for years, which had been severely exacerbated by her first pregnancy 5 years ago. The back pain began after a car accident about 7 years ago, and is believed by her doctors to be caused by muscle spasm. Perri is a school teacher in otherwise good health with a stable home life. Now in the 14th week of her second pregnancy, she is anxious that her growing uterus will worsen both her back pain and insomnia. She did not want to use pain killers or the antidepressants she had previously been prescribed and had taken until she became pregnant with this baby. She consulted with an herbalist about alternatives that might be safe and effective for sleep promotion. After taking a careful history, the herbalist determined that the back pain was really the underlying cause of the sleep disorder, and decided to begin treatment by addressing the chronic pain; however, because of pregnancy, herbal options were limited to mild herbs. Perri was instructed to do the following daily:

- 15 minutes of gentle yoga stretched upon waking
- 15 minutes of gentle yoga 1 hour prior to bed.

Figure 15-3 Lavender (*Lavandula* spp.). (Photo by Martin Wall.)

- Warm bath 30 minutes prior to sleep each night. Seven drops of lavender essential oil are to be added to each tub.
- Perri was provided with an herbal ointment containing cramp bark, capsicum (*Capsicum officinalis*), and lobelia (*Lobelia inflata*) to be rubbed into the tight areas of her back twice daily (she will need to get her partner to apply this).
- Cramp bark tincture to be taken as follows:
  - 2 mL in warm water four times daily, including one dose 30 minutes prior to sleep
  - 5 mL of the following tincture to be taken in two divided doses (2.5 mL each) 1 hour and again 30 minutes prior to bed

Perri followed the above protocol for 3 weeks and came in for a subsequent appointment. She subjectively reported that her back pain had improved by about 80%, and that for the first time she was getting a full night's sleep. She could not be more pleased. She reported that the improved sleep made a huge difference in the experience of her back pain, and vice versa, the decreased pain allowed her to sleep more comfortably. No subsequent prescriptions were necessary, and Perri gave birth to a healthy, full-term baby boy after an uneventful pregnancy and birth.

BREECH PRESENTATION AND VERSION

Aviva Romm

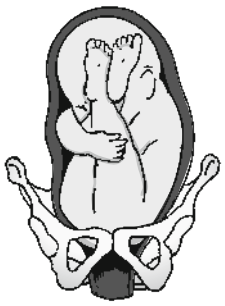
Breech presentation is when the fetus presents with the buttocks, knees, or feet rather than the head, toward the vaginal canal during pregnancy. It is common in early pregnancy when the fetus has ample room to move around. As the pregnancy progresses, the baby has less space to move around. The fetal head will tend to gravitate toward the pelvis and the baby will assume a position it often maintains until labor. By 32 weeks pregnancy, the prevalence of breech presentation is reduced to 16% and by term it is 3% to 4%. The likelihood that a baby in the breech position at 36 weeks will remain so until the time of birth is 25%; however, spontaneous version to a cephalic (head first) presentation may occur at any time. Preterm babies are more likely to present breech than those born at full term.

There are three classifications of breech presentation:

1. Frank breech, which is when the fetus has both hips flexed and both knees extended so its feet are near its head (Fig. 15-4). This occurs in 50% to 70% of breech presentations.
2. Footling or incomplete breech, in which the fetus has one or both hips or one or both knees not flexed. As a result, one or both feet present before the buttocks (Fig. 15-5). This occurs in 10% to 40% of breech presentations.
3. Complete breech refers to a fetus with both hips and both knees flexed. The feet are opposite the fetal trunk rather than the head, but do not present in advance of the buttocks (Fig. 15-6). This occurs in 5% to 10% of breech presentations.

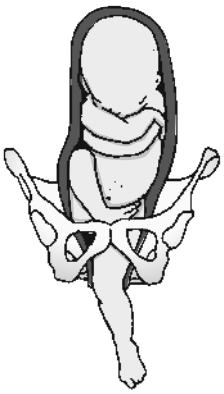
REASONS FOR BREECH PRESENTATION

In most cases a persistent breech position is nonpathologic in origin, being a random occurrence, or a combination of the dynamics between the maternal pelvic and fetal head shapes. Breech presentation itself presents little risk to the fetus. In some cases, however, persistent breech position is the result of a maternal, fetal, or placental problem. Maternal factors that may contribute to breech presentation include uterine abnormalities that change the normal shape of the uterus, for example, bicornate uterus or uterine fibroids; multiparity that leads to uterine and abdominal wall laxity, changing the shape of the uterus; and a deformed or contracted maternal pelvis. Placental abnormalities, for example, placenta previa, which prevent the fetal head from properly entering the pelvis can contribute to breech position, as can amniotic fluid volume abnormalities (polyhydramnios, oligohydramnios). Any factors that alter either the normal fetal shape or normal fetal mobility can contribute to breech presentation, and include fetal anomalies (e.g., anencephaly, hydrocephaly), multiple pregnancy (i.e., twins), short umbilical cord, and fetal



Frank breech

Figure 15-4 Frank breech. (Lowdermilk DL, Perry SE: *Maternity & Women's Health Care,* ed 9, St. Louis, 2007, Mosby.)



Single footling breech

Figure 15-5 Footling (incomplete) breech. (Lowdermilk DL, Perry SE: *Maternity & Women's Health Care,* ed 9, St. Louis, 2007, Mosby.)

Complete breech

Figure 15-6 Complete breech. (Lowdermilk DL, Perry SE: *Maternity & Women's Health Care,* ed 9, St. Louis, 2007, Mosby.)

demise. Previous breech birth is considered a risk factor for breech presentation in subsequent pregnancies.

RISKS OF BREECH PRESENTATION AND BREECH BIRTH

Breech presentation itself presents little risk to the fetus. Risk occurs when there are predisposing maternal, fetal, or placental factors that cause the baby to present breech. Breech birth does appear to increase the risk to the fetus.[128] The exact extent to which this is so is uncertain, as are the reasons. Prior to the 1950s, vaginal delivery was the preferred method for breech presentation in the United States. In 1970, cesarean rates for breech were 12%. By 2002, this rate had risen to 86.9%.[129] The American College of Obstetricians and Gynecologists Committee on Obstetric Practice currently recommends use of external cephalic version and planned cesarean delivery for persistent singleton breech presentation at term. This recommendation was amended to allow vaginal delivery of a term singleton breech if there is detailed patient informed consent, under hospital specific protocol guidelines for eligibility and labor management, and by a health care provider experienced in vaginal breech delivery.[129]

There is significant controversy regarding whether cesarean section is necessary or improves outcome, and just how great a risk there is with vaginal breech birth.[130] Several studies demonstrate decreased morbidity and mortality to the fetus with elective cesarean; however, this is accompanied by increased maternal morbidity. It has been suggested that the risk of breech birth is more attributable to the fact that most obstetricians are inexperienced in breech birth management because of the high use of cesarean delivery, than to inherent risks in the breech birth process, and that with skilled management, breech birth is a safe option in the absence of complicating factors.[131–134] The American College of Obstetricians and Gynecologists states

> *The number of practitioners with the skills and experience to perform vaginal breech delivery has decreased. Even in academic medical centers where faculty support for teaching vaginal breech delivery to residents remains high, there may be insufficient volume of vaginal breech deliveries to adequately teach this procedure.*[129]

To avoid the need for unnecessary cesarean section, obstetric and midwifery care providers recommended that attempts be made to turn the baby to a cephalic presentation prior to the onset of labor. This chapter focuses on the use of external cephalic version and moxibustion as two techniques that may be attempted with potential for success. Although this chapter addresses breech presentation as something to be changed, the author wishes to emphasize that breech presentation is most often a variation of normal rather than a pathologic condition, and that a discussion on changing the breech to a cephalic presentation is in no way meant to disparage vaginal breech birth.

SIGNS, SYMPTOMS, AND DIAGNOSIS OF BREECH PRESENTATION

With breech presentation, the mother is likely to report more upper abdominal discomfort, indigestion, and greater fetal movement in the upper, rather than lower, abdomen. The care provider may identity the breech presentation upon abdominal palpation. Ultrasound visualization is used as confirmation. Breech presentation is

sometimes first diagnosed upon vaginal examination in labor.

CONVENTIONAL TREATMENT OPTIONS FOR TURNING A BREECH PRESENTATION: EXTERNAL CEPHALIC VERSION

The primary method used to turn a breech baby to a cephalic presentation is external cephalic version (ECV). ECV is the manual transabdominal rotation of the fetus into a cephalic presentation. The practice was popular in the 1960s and 1970s but fell out of favor because of fetal deaths associated with the procedure. However, the practice was revived in the 1980s and is now considered a safe and effective means for avoiding cesarean section caused by breech presentation.[135–138] ACOG recommends ECV as a standard procedure for turning a breech to avoid cesarean section when the maternal–fetal dyad meets eligibility criteria.[129,139] CV is performed in the hospital with a surgical room set up should emergency cesarean be necessitated as a result of complications, which occasionally occur as a result of the procedure, including cord entanglement, fetal hypoxia, premature rupture of the membranes, separation of the placenta, and even fetal death.[140] The procedure may be performed with or without tocolysis (medications to relax the uterus) or anesthetic administered to the mother. Use of tocolysis or anesthetic may facilitate the procedure and reduces pain to the mother.[141,142] RhoGAM should be given to RH-negative mothers prior to attempting a version. The average success rate for the procedure is 58%. Efficacy is greater when the procedure is performed between 34 and 37 weeks, as compared with later in pregnancy, although the fetus may revert to its previous position, thus requiring that the procedure be repeated.

BOTANICAL TREATMENT OPTIONS FOR TURNING A BREECH PRESENTATION

Moxibustion for Breech Presentation

Moxibustion is a traditional Chinese medicine technique that involves the use of a cigar-shaped stick of compressed *Artemisia* herb, lit and indirectly applied as a heat source over the acupuncture point Bladder 67 (zhi yin) on the outer edge of the fifth (pinky) toenail, on each foot (the moxa is *not* applied directly to the skin). (see Fig. 15-7). The technique is repeated twice daily for 15 minutes on each foot for 7 to 10 days, and is discontinued when the fetus has felt to have turned. Fetal activity is observed to increase during the treatment period, followed by movement of the baby into a cephalic presentation. In a study by Cardini et al. published in *JAMA* in 1998, the authors reported that of 130 women with breech babies who received moxibustion beginning at 33 weeks gestation, 75.4% of babies were cephalic by 35 weeks gestation vs. 47.7% in the control group. Because no studies had previously been carried out on Western populations, pregnant Italian women at 33 to 35 weeks gestational age carrying a fetus in breech presentation were enrolled in a randomized controlled trial involving BL67 point stimulation and an observation group. A total of 240 were randomized to receive active treatment (acupuncture plus moxibustion) or be assigned to the observation group. Bilateral acupuncture plus moxibustion was applied at the BL67 acupoint (zhi yin). The primary outcome of the study was fetal presentation at delivery. Fourteen cases dropped out. The final analysis thus was made on 226 cases, 114 randomized to observation and 112 to acupuncture plus moxibustion. At delivery, the proportion of cephalic version was lower in the observation group (36.7%) than in the active-treatment group (53.6%). Hence, the proportion of cesarean sections indicated for breech presentation was significantly lower in the treatment group than in the observation group (52.3% vs. 66.7%).[143] Ewies and Olah report that moxa is a safe, painless, inexpensive, and easily administered option, but emphasize the small sample sizes of most studies, with lack of randomization.[144] The Cochrane Review reports no side effects associated with use of moxibustion in pregnancy.[145] Patients should be advised that the smell of burning moxibustion is similar to the smell of marijuana. This author has had several patients who had house guests or business associates who thought they were smoking cannabis. It may be suggested that clients use moxa outside or away from an area of business. One funny anecdote with moxa use is of a real estate agent who told a patient that if she wanted to sell her house, which was on the market during the time the patient was using moxibustion for breech version, she might want to smoke her marijuana somewhere else. The patient explained and demonstrated the moxa use to the realtor, and afterward completed her treatments outside, in spite of it being late autumn! She had a cesarean for a breech baby with her first pregnancy, and was delighted when, after 4 days of treatment at 37 weeks gestation, her baby changed to a

Figure 15-7 Moxibustion treatment. (Cassidy CM: *Contemporary Chinese Medicine and Acupuncture,* St. Louis, 2002, Churchill Livingstone.)

cephalic presentation and she gave birth vaginally at 39 weeks, to a vertex baby.

Although from a Western medical perspective, the mechanism of action is entirely unknown, the treatment appears to be entirely safe, is inexpensive, and is applied externally only. It is certainly a preferable alternative to external cephalic version or cesarean section for the management of persistent breech presentation. Because it is advised to be done from 34 weeks onward, treatment does not preclude the decision to perform external version or surgical delivery.

ADDITIONAL TECHNIQUES

Postural Management of Breech Presentation

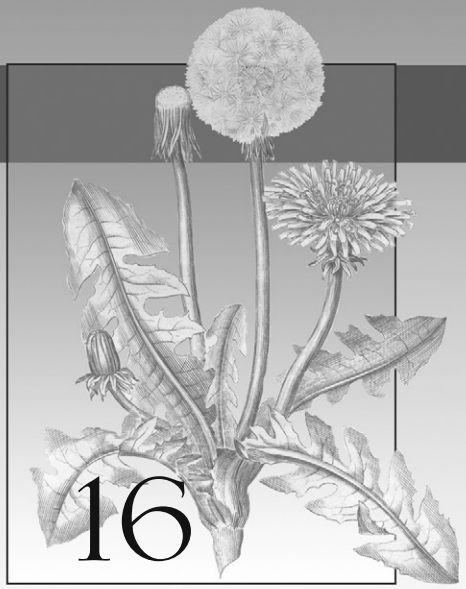
Five studies involving a total of 392 women were included in a Cochrane review on the efficacy of postural management for changing a breech to a cephalic presentation. Postural management includes the use of slant boards upon which the mother lies on her back, at a 45-degree angle with her head down, and other similar techniques that are thought to coax the baby to change position. The authors of the review concluded that there is insufficient evidence from well-controlled trials to support the use of postural management for breech presentation. The numbers of women studied to date, however, remains relatively small.[146]

Hypnosis

In a study by Mehl, 100 women with breech presentation between 37 weeks and term were compared with a similarly matched control group and achieved a version rate of 81% compared with 48% in the nonintervention group. It is thought that because psychophysiologic factors may influence breech presentation, relaxing the mother's abdominal musculature, or preparing her mentally and emotionally for delivery through the use of hypnotism or other techniques may assist in achieving cephalic version.[140] There are no studies in the literature on the use of hypnosis for breech version.[140]

Other

Small non-randomized, noncontrolled studies and case reports suggest that there may be some small benefit to a variety of techniques for changing breech position. These include yoga, chiropractic, and homeopathic methods, as well as the use of ginger paste applied in place of moxibustion to stimulate heat to BL67.[140] One of these methods has been systemically evaluated. Use of music applied to the mother's abdomen, a popular technique promoted on the Internet, has only been minimally studied in conjunction with the use of ECV with tocolytic drugs, making it difficult to evaluate the usefulness of the studies.[140]



Labor and Birth

Aviva Romm

16 CHAPTER

FACILITATING LABOR: INDUCTION, AUGMENTATION, AND DYSFUNCTIONAL LABOR

Labor induction refers to the medical stimulation of contractions prior to the onset of spontaneous labor to cause labor to commence.[1] One of the most commonly performed obstetrical procedures in the United States, rates of labor induction more than doubled between 1990 and 1998 from approximately 9.5% to 21%.[2,3] Reasons cited for this increase include widespread availability of cervical ripening agents, convenience to physicians, pressure from patients, and medico-legal constraints.[4] In spite of obstetric recognition that normal human gestation is 40 to 42 weeks (postterm pregnancy is defined as pregnancy past 42 weeks gestation), conservative obstetric practice frequently results in the suggestion, admonition—or insistence—by medical practitioners that their pregnant patients begin labor at, or close to, 40 weeks gestation. Data to support or refute the benefits of elective inductions are limited.[4] Risks to the mother and fetus include those related to the medications used, risks of iatrogenically induced prematurity, and the increased risk of operative delivery, which is more likely to occur as a consequence of labor induction.[5] According to a Cochrane review of outcomes of labor induction of fetal/neonatal death compared with awaiting spontaneous labor, or a policy of induction after 41 weeks gestation, including a total of 19 trials and over 8000 women, it was reported that there were intranatal and neonatal deaths when a labor induction policy was implemented after 41 completed weeks or later. However, such deaths were rare with either policy.[6] In a matched cohort study of 7683 women with elective induced labor compared with 7683 women with spontaneous labor, from 1996 through 1997, cesarean section rates (9.9% vs. 6.5%), instrumental delivery (31.6% vs. 29.1%), epidural analgesia (80% vs. 58%), and transfer of the baby to the neonatal ward (10.7% vs. 9.4%) were significantly more when labor was induced electively.[5] Studies from the United States have reported similar findings, with a doubling of operative delivery with induction.[7–10] Nulliparous women are especially at risk of cesarean section as a result of induction, and an unfavorable cervix at the time of induction appears to be the greatest contributing cause to need for operative delivery.[1,7] Elective induction leads to an estimated 12,000 excess cesarean sections per annum at a cost of over $100 million.[1] Overall, it is advisable to avoid elective induction unless medically indicated.[10]

Labor induction should only be undertaken when the benefits to either the mother or fetus outweigh the risks of maintaining the pregnancy.[1] Accepted indications for labor induction include:[1]

- Preeclampsia/eclampsia, and hypertensive disorders
- Maternal diabetes mellitus with a macrosomic infant ≥ 4000g
- Prelabor/premature rupture of membranes (P/PROM)
- Chorioamnionitis
- Intrauterine fetal growth restriction (IUGR)
- Isoimmunization
- Fetal death
- Post term pregnancy

Contraindications to labor induction include:[1]

- Prior classical uterine incision
- Active genital herpes infection
- Placenta or vasa previa
- Umbilical cord prolapse
- Certain fetal malpresentations (e.g., transverse lie)

Labor augmentation refers to the use of medications to stimulate contractions in an already commenced labor when contraction rate or intensity is inadequate to accomplish birth of the baby, or labor has slowed or stopped. Methods of augmenting labor commonly employed by medical professionals include administration of Pitocin via IV drip and artificial rupture of membranes (AROM). Dysfunctional labor is failure to progress in the presence of a normal labor pattern, or the contraction

pattern itself may be uncoordinated, leading to ineffectual labor. The results are protracted, stalled, or obstructed labor. Factors contributing to dysfunctional labor include but are not limited to pelvic abnormalities, fetal malpresentation, macrosomic fetus, and maternal sedation.

MEDICAL APPROACHES TO LABOR INDUCTION AND AUGMENTATION

The literature on the use of medical interventions for the induction and augmentation of labor is extensive, and far beyond the scope of this textbook to fully present. This section provides a brief synopsis of the most commonly used methods for induction and augmentation, their safety, and efficacy. Readers are encouraged to search the Cochrane Database, which has an extensive collection of articles (>400) reviewing methods of labor induction.

Oxytocin Induction

Synthetic oxytocin (Pitocin) is one of the most commonly used and most potent uterotonic agents available. It is given intravenously for purposes of induction (as an antihemorrhagic, it may be given intramuscularly), in the form of an infusion pump that allows exact dosing with various dosing protocols. Dosing is done incrementally, starting with small amounts and increasing until contractions come at 2- to 3-minute intervals, and typically not exceeding 40 mU/min. Oxytocin is more effective when administered in the presence of a ripened cervix (softening and ability to stretch), thus methods to induce ripening (i.e., prostaglandins suppositories or oral administration, cervical manipulation, amniotomy) may be used just prior to or in conjunction with oxytocin administration. Oxytocin use alone is less effective than prostaglandins for inducing labor. Labor induction with oxytocin is associated with an increased rate of cesarean section.[11] Any agent that increases uterine contractions can lead to hypercontractility of the uterus, and can interfere with blood flow to the uterus, and consequently the fetus, with ensuing fetal distress.[12] This is a less frequent complication with oxytocin than with misoprostol (see the following). There is some evidence to suggest that use of oxytocin may be associated with an increased incidence of fetal hyperbilirubinemia; however, it is unclear whether this is a direct result of oxytocin use, or associated with other pregnancy factors, such as preterm labor.[12]

High-dose oxytocin (40 mU) given over a prolonged period in hypotonic solution (>3 L), or in rapid infusion can lead to hyponatremia and hypotension, respectively, with resultant serious consequences.

Stripping the Membranes

Stripping the membranes, also called ''sweeping the membranes,'' is thought to release prostaglandin F2-alpha from the decidua and membranes, or prostaglandin E2 from the cervix, causing cervical ripening and instigating contractions. It is widely used by obstetricians and midwives, often done as a routine part of vaginal and cervical exams in women who are close to or past term, but often undocumented—possibly because it is not generally thought of as an invasive technique by many practitioners (although many midwives do consider it invasive, especially when done without the mother's permission).[1] In a meta-analysis of 22 trials, (n = 2797) 20 comparing sweeping of membranes with no treatment, three comparing sweeping with prostaglandins and one comparing sweeping with oxytocin, risk of caesarean section was similar between groups. Sweeping of the membranes, performed as a general policy in women at term, was associated with reduced duration of pregnancy and reduced frequency of pregnancy continuing beyond 41 weeks and 42 weeks. It is effective at preventing the need for formal induction in one out of eight women. No evidence of a difference in the risk of maternal or neonatal infection was observed. Discomfort during vaginal examination and other adverse effects (bleeding, irregular contractions) were more frequently reported by women allocated to sweeping. Studies comparing sweeping with prostaglandin administration are of limited sample size and do not provide evidence of benefit. The authors of the meta-analysis concluded that sweeping the membranes is effective in some women at inducing labor, and is generally safe in the absence of other complications, and reduces the need for other forms of induction; however, its rate of effectiveness seems limited.[13] Weekly membrane stripping appears to shorten the interval of time to spontaneous labor at term, although improvement in pregnancy outcome has not been demonstrated by large, randomized trials.[1] Risks of membrane stripping include premature rupture of membranes, infection, disruptions of occult placenta previa and rupture of vasa previa, though these are rare outcomes of this procedure.

Artificial Rupture of Membranes

Artificial rupture of the membranes (AROM), amniotomy, is performed when the cervix is partially dilated and effaced, and with the fetus in a vertex presentation with the head well applied to the cervix to avoid prolapse of the umbilical cord (or other presenting part). Fetal monitoring accompanies the procedure, as does evaluation of the color of the amniotic fluid to detect for the presence of meconium staining—a possible indication of fetal distress. A Cochrane review identified two trials comprising 50 and 260 women, respectively, that were considered eligible for inclusion in the review of amniotomy alone for labor induction. Conclusions were unable to be drawn on the use of amniotomy alone vs. no intervention, nor amniotomy alone vs. oxytocin alone. When compared with single-dose application of vaginal prostaglandins in women with a favorable cervix in a single center trial, a higher rate of oxytocin augmentation was required in the amniotomy alone group (44% compared with 15%). Combined use of amniotomy and intravenous oxytocin is more effective than amniotomy alone. Limited data suggest that the efficacy of oxytocin plus amniotomy is similar to that of prostaglandins alone.[14] Amniotomy is associated with an increase in caesarean section rate. With regard to neonatal outcomes, fewer babies are born with Apgar scores of less than seven,

but no statistically or clinically significant differences have been observed in other measures of neonatal morbidity, such as umbilical artery acid-base disturbances and admission to intensive care units.[15] Risks of amniotomy include intrauterine infection, umbilical cord prolapse, and disruption of an occult placenta previa or vasa previa with subsequent maternal hemorrhage. Serious complications, however, are rare.[12]

Prostaglandins

Although the exact mechanisms triggering the onset of labor remain unknown, the production of prostaglandins by the body is implicated in the commencement of cervical ripening and stimulation of uterine contractions. Administration of prostaglandins for labor induction is considered preferable to oxytocin use, as the latter does not lead to cervical ripening but only contractions. The use of prostaglandins for labor stimulation appears to decrease the need for obstetric analgesia, and increases the likelihood of birth without operative delivery within 12 to 24 hours of onset of treatment. These advantages, however, are accompanied by increased risk of uterine hyperstimulation with its increased risk of fetal distress and maternal uterine rupture—a surgical emergency. Prostaglandins used include PGE2 and PGF2α; PGE2 is considered safer and equally effective and therefore is the prostaglandin of choice.[12] The optimal route, frequency, and dose of prostaglandins have not been determined.[16–18] Dinoprostone, either in the form of Cervidil or Prepidil, both FDA-approved drugs for this purpose, is the agent of choice, and is most commonly administered by direct cervical application via vaginal route, as this has proved to be effective with the fewest side effects. Introduction of IV oxytocin approximately 12 hours after administration of dinoprostone is common practice to facilitate labor onset.

Misoprostol (Cytotec) is a synthetic PGE1 analog available as 100- and 200-μg tablets, which can be broken to provide 25- or 50-μg aliquots and can be administered orally or intravaginally. Misoprostol is approved by the FDA for the prevention and treatment of gastric ulcer disease related to chronic nonsteroidal anti-inflammatory drug use.[1] In most countries, it has not been licensed for use in pregnancy; however, off-label use is common because the drug is inexpensive, stable at room temperature (unlike other prostaglandin drugs), and effective in causing cervical ripening and uterine contractions. Misoprostol is highly effective at initiating labor; reduces the need for oxytocin administration, epidurals, and cesarean section; and shortens time to delivery by as much as 8.7 hours.[19] The use of misoprostol has been associated with uterine hyperstimulation, tetanic contractions, precipitous labor, and possibly an increased incidence of uterine rupture, which can be fatal for both mother and fetus.[19] Uterine hyperstimulation with fetal heart rate changes and meconium staining of the amniotic fluid—indicative of fetal distress—are increased with misoprostol use. The optimal dose and timing of misoprostol use remain unknown.

Oral misoprostol appears to be more effective than placebo and is at least as effective as vaginal dinoprostone. However, because of increased risk of uterine hyperstimulation and lack of certainty in dosing, vaginal administration, which is also effective, and associated with a slightly decreased risk of hyperstimulation and other side effects compared with the oral route, is considered preferable.[19] If misoprostol is used orally, the dose should not exceed 50 mcg.[19] In countries where misoprostol remains unlicensed for the induction of labor, practitioners may prefer to use a licensed product, for example, dinoprostone, for legal reasons.[19] Studies to date have not been large enough to determine the actual risk of uterine rupture, which has been anecdotally associated with misoprostol use.[20] Misoprostol, however, is contraindicated for women with a history of prior cesarean delivery or other previous major uterine surgery owing to increased risk of uterine rupture. Of particular concern also is the use of misoprostol in the home birth setting, where equipment for adequate measurement of uterine contractions is unavailable, as is rapid access to emergency surgery in the event of fetal distress or uterine rupture.

Mechanical Stimulation Methods

Mechanical methods of labor induction include use of a Foley balloon catheter and hygroscopic dilators. In the former method, a Foley balloon catheter is passed, uninflated, into the undilated cervix and then inflated; it may be used alone or in combination with pharmacologic methods of induction. The combination of balloon catheterization and prostaglandin administration appears to significantly increase the likelihood that a woman will deliver within 24 hours of the procedure; however, the benefit of the two methods combined has not been shown to be more effective than use of oral misoprostol alone. Hygroscopic dilators are inserted into the vaginal canal after application of a topical anesthetic, and gradually swell as they absorb moisture. The swelling, in addition to mechanical effects on the cervix leading to dilatation, may serve to disrupt the chorioamnionic decidual interface, causing lysosomal destruction resulting in prostaglandin release. Laminaria, made from seaweed, is a typical hygroscopic dilator; synthetic agents are also available. Hygroscopic dilators do not appear to be as clinically effective as PGE2 gels and are associated with an increased risk of maternal postpartum infection and neonatal infection.[1]

MEDICAL APPROACHES TO DYSFUNCTIONAL LABOR

The causes of and medical treatments for dysfunctional labor (dystocia) are extensive. This section provides only a brief overview of the pathophysiology and medical interventions. Labor is considered dysfunctional when any of the stages of labor is protracted with no progress made in cervical dilatation and fetal descent. During the latent phase of labor, it is recommended that women alternate rest or sleep with periods of activity (e.g., walking). Cervical effacement, uterine activity, and fetal status are periodically evaluated. Eight-five percent of women progress to the active phase of labor, 10% cease uterine activity, and approximately 5% require oxytocin

induction if it is necessary to expedite labor. If labor dysfunction arises during active phases, the underlying reason for arrest is ideally determined; for example, obstruction resulting from a macrosomic baby or contracted pelvis, or fetal head malposition (e.g., persistent asynclitism). Various methods may be used to facilitate labor, including amniotomy, oxytocin infusion, and epidural or other agents to relax pelvic musculature and allow the mother to rest. The fetus is monitored throughout. If fetal status remains normal and there is minimal risk of cord prolapse, ambulation may be allowed or encouraged. If labor does not progress normally with these, and possibly other interventions, or if fetal status becomes compromised, surgical delivery (cesarean section) ultimately must be performed.

BOTANICAL APPROACHES TO FACILITATING LABOR

Midwives use a wide variety of approaches to facilitate the onset and progress of labor when these are not occurring spontaneously or when otherwise indicated (Table 16-1). While midwives honor the fact that the timing and pace of labor and birth are highly individual, there are times when legal or medical restrictions require that women birth within certain time parameters, for example, by 41 weeks gestation or within 18 hours of ROM, for women to birth at home in certain states where home birth midwifery is licensed. These constraints require that midwives and their pregnant clients work creatively with a breadth of options in order to expedite labor and birth. Also, birth does not always progress smoothly, obstructed by any number of sometimes benign but nonetheless problematic factors such as malpresentation of the fetal head (persistent asynclitism), maternal fear, anxiety, pain, or pelvic tension. A combination of these factors is very common, as asynclitism can lead to uncoordinated contractions and maternal fatigue, which increase pain, tension, and anxiety—thus creating a vicious cycle that ultimately leads to medical intervention. Often, a combination of agents to alter the maternal response via uterine stimulation or maternal relaxation and noninvasive measures such as nipple stimulation, changes of maternal position, and relaxation techniques can facilitate labor. Rarely is any single technique used in isolation; rather, several techniques are more commonly employed, ideally in an orderly and rhythmic fashion to initiate a healthy, active labor pattern. Botanical choices are selected according to the individual needs and either physiologic or pathophysiologic response to labor, and are used in conjunction with options presented in the section Additional Methods for Facilitating Labor (Table 16-2).

The role of a knowledgeable, supportive care provider, serving as a labor facilitator—a midwife, understanding obstetrician, or doula—cannot be underestimated in its effects on facilitating a healthy labor and birth process. Further, in order to effectively intervene with natural, noninvasive strategies, it is essential that the care provider adequately understand the mechanics, physiology, and psychology of birth. For example, although many think that it is adequate to stimulate contractions in a stalled or dysfunctional labor using uterine stimulants, effective labor required a delicate balance between contraction and relaxation—this yields coordinated uterine contractions, cervical dilatation, and fetal descent. Therefore, it is often more effective to use both uterine

TABLE **16-1**

Botanical Treatment Strategies for Labor Induction, Augmentation, and Dysfunction

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Stimulate contractions	Uterine stimulant	*Caulophyllum thalictroides*	Blue cohosh
		Gossypium herbaceum	Cotton root
		Ricinus communis	Castor oil
		Rubus idaeus	Red raspberry leaf
Stimulate cervical ripening	Prostaglandin	*Oenothera biennis*	Evening primrose oil
Coordinate uterine activity	Uterine spasmolytic	*Actaea racemosa*	Black cohosh
		Leonurus cardiaca	Motherwort
		Viburnum spp.	Cramp bark/black haw
Promote smooth muscle relaxation	Uterine spasmolytic	*Actaea racemosa*	Black cohosh
		Leonurus cardiaca	Motherwort
		Viburnum spp.	Cramp bark/black haw
Relieve labor pain	Analgesic/sedative		Corydalis
			California poppy
			Jamaican dogwood
Relieve maternal anxiety and tension	Anxiolytic	*Eschscholzia californica*	California poppy
	Nervine	*Humulus lupulus*	Hops
		Leonurus cardiaca	Motherwort
		Matricaria recutita	Chamomile
		Passiflora incarnata	Passionflower
		Valeriana officinalis	Valerian

stimulant and uterine antispasmodic herbs in combination to achieve an effective labor pattern. Similarly, if a woman is exhausted and contractions are faltering, promoting sleep may actually achieve a better and faster outcome than stimulating contractions. Table 16-2 will help the reader to identify a combination strategy that might be applied to the individual woman. Practitioners must be knowledgeable about when medical intervention becomes required, and of course it is essential that the mother and fetus be adequately and properly monitored during labor, and efforts to stimulate labor. As discussed in the following, blue cohosh, for example, has been associated with rare adverse cardiovascular effects on the fetus, and more commonly with milder side effects as a result of maternal use.

The following section discusses herbs specifically used to stimulate contractions or used as spasmolytics specifically for labor. Analgesics, sedatives and nervine herbs are discussed widely throughout this book.

Castor Oil

Castor oil (Fig. 16-1) is a potent cathartic extracted from the castor bean. Use of this herb to stimulate labor appears to date back to ancient Egypt.[21] It remains a commonly used folk method to induce labor, and has made its way into obstetric practice, with its use common suggested by midwives. There are scant data evaluating its clinical efficacy. In a clinical trial, a single dose of castor oil was compared with no treatment. There was no evidence of a difference between caesarean section rates, meconium staining of the amniotic fluid, or Apgar score. No data were presented on neonatal or maternal mortality or morbidity. Nausea was a side effect in all women who ingested castor oil.[21] Overall, the trial was of poor methodologic quality and no determination can be made regarding efficacy for labor induction.

Blue Cohosh

Caulophyllum thalictroides (blue cohosh) (Fig. 16-2), a native of the eastern and central woodlands of the United States, has been used traditionally and historically as an anticonvulsant, antirheumatic, febrifuge, emetic, sedative, and most notably, a gynecologic aid.[22,23] It has been used for labor induction, amenorrhea, dysmenorrhea, menorrhagia, and to induce abortion.[22] Blue cohosh was official in the United States Pharmacopoeia from 1882 to 1905 for labor induction, and in the

TABLE 16-2

General Approaches to Labor Problems

LABOR PROBLEM	GENERAL STRATEGY	BOTANICAL STRATEGY	ADDITIONAL METHODS
Postdates pregnancy (> 41 weeks 6 days)	Stimulate labor	Uterine stimulants Prostaglandins	Nipple stimulation Sexual intercourse (if possible); orgasm Maternal activity (e.g., walking)
Obstetric pressure to induce (e.g., legal, hospital, or OB practice policy)	Stimulate labor	Uterine stimulants Prostaglandins	Nipple stimulation Sexual intercourse (if possible); orgasm Maternal activity (e.g., walking)
PROM	Stimulate labor	Uterine stimulants Prostaglandins	Nipple stimulation Sexual intercourse (if possible); orgasm Maternal activity (e.g., walking)
Labor stalled or ceased Prolonged labor Dysfunctional labor	If maternal exhaustion predominates	Uterine spasmolytics sedatives	Hot baths if no ROM or hot showers if ROM Promote sleep with massage, visualization, music
	If fetal malposition is present (i.e., asynclitism)	Uterine spasmolytics	Maternal pelvic relaxation with hot baths if no ROM or a hot shower Maternal position changes and movement
	If maternal anxiety or fear predominates	Anxiolytics Nervines	Verbal/emotional support
	If maternal pain predominates	Uterine spasmolytics Analgesics/sedatives	Verbal/emotional support Maternal pelvic relaxation with hot baths if no ROM or a hot shower Maternal position changes and movement

Figure 16-1 Castor plant (*Ricinus communis*). (Photo by Martin Wall.)

Figure 16-2 Blue cohosh (*Caulophyllum thalictroides*). (Photo by Martin Wall.)

National Formulary from 1916 to 1950.[24] It was a major ingredient in the popular Eclectic preparation Mother's Cordial, which also included *Mitchella repens, Rubus idaeus, Actaea racemosa*, and *Chamaelirium luteum*. At least one company (Herbalist and Alchemist, NJ) still makes this preparation; however, the blue cohosh has been removed as an ingredient in the product because of safety concerns. The practice of labor induction with blue cohosh remains a popular choice both among self-prescribers and obstetric professionals in the United States and abroad, with one large survey indicating widespread use among nurse-midwives.[25] Blue cohosh is listed in the British Herbal Pharmacopoeia (1983) as a spasmolytic and emmenagogue.[26] It may also be used as a uterine and ovarian tonic, and for the treatment of a variety of menstrual complaints, including menorrhagia, amenorrhea, dysmenorrhea, and pelvic congestion syndrome.[27,28] It is commonly used as a partus preparator to ease parturition, and for labor induction and augmentation.[27] It has also been used as an abortifacient.[27] Use of blue cohosh during pregnancy is a widespread practice among midwives and pregnant women.[25] Maternal ingestion has been associated with a range of fetal and neonatal side effects and adverse outcomes, including fetal tachycardia, increased meconium, profound neonatal congestive heart failure, and perinatal stroke.[25,29–31] There is one case report of a neonate born with complications including myocardial infarction and profound congestive heart failure to a mother who ingested blue cohosh as a partus preparator. The newborn remained critically ill for several weeks but eventually recovered. All other causes of myocardial infarction were excluded.[30] In another case report, a child was born with severe multi-organ failure associated with the use of a blue and black cohosh combination. The child required significant resuscitation at birth and sustained permanent CNS damage.[32] Neither the amount and duration nor preparation used were disclosed. The effects in both cases have been attributed to vasoactive glycosides in the herb. A 21-year-old woman developed symptoms of nicotinic toxicity, including tachycardia, diaphoresis, abdominal pain, vomiting, and muscle weakness and fasciculations after using blue cohosh in an attempt to induce an abortion. These symptoms likely resulted from methylcytosine known present in blue cohosh. The patient's symptoms resolved over 24 hours and she was discharged.[33]

Alkaloid and glycoside components in blue cohosh suggest possible mechanisms for these effects, as well as teratogenicity and mutagenicity.[33,34] Methylcysteine exhibited teratogenic activity in the rat embryo culture (REC), an in vitro method to detect potential teratogens. Taspine showed high embryotoxicity but no teratogenic activity in the REC.[34] Toxic effects of the plant's constituents include coronary vasoconstriction, tachycardia, hypotension, and respiratory distress.[24] However, Low Dog cautions that the quality of the case reports to date and the value of some of the testing methods used to establish toxicity may be questionable. For example, although REC tests have shown teratogenicity and embryotoxicity, ''neither the National Institute of Environmental Health Sciences nor the Environmental Protection Agency recognizes these tests as an appropriate screen for human reproductive risk.''[24] Similarly, it has been speculated that anagyrine, which produces known malformations in ruminant livestock, may do so only after metabolism by microflora in the ruminant gut.[24]

The *Botanical Safety Handbook* classifies this herb as 2b, not to be used during pregnancy; however, it states that *Caulophyllum* may be used as a parturient near term to induce childbirth under the supervision of a qualified practitioner.[35] Canadian regulations require that any products containing this herb be labeled as not for use in pregnancy.[35] Given the volume of blue cohosh use in the United States alone, and the general paucity of reports of its side effects, as well as a lack of comparison of side effects with conventional medications for labor augmentation (i.e., Pitocin, misoprostol), it remains uncertain how great a risk is posed by the use of blue cohosh, particularly for short-term labor augmentation as opposed to long-term use as a partus preparator. Low Dog states, ''The human case reports, flawed as they are, paint a picture that is consistent with the evidence provided by the in vitro and animal studies.''[24] The most conservative route is to avoid its use entirely as a *partus preparator*, and possibly at all during pregnancy, until safety information is established. Midwives and mothers choosing to use blue cohosh to augment labor should observe assiduous fetal heart monitoring during use and should discontinue use promptly if deviations are observed. No discussion on the safety of blue cohosh during lactation is reported in the literature.[27] One case report in the literature describes an infant born to a mother who had consumed anagyrine containing goat milk; however, as stated, it is not known whether activation of this compound requires metabolism in the ruminant gut.[24] Many direct-entry midwives have discontinued use of the herb because of safety concerns.[36]

The Use of Herbs as *Partus preparators* and for Labor Induction

The use of herbs for labor stimulation is popular, both with self-prescription among pregnant women and prescribing by midwives.[25,37–39] The pressure to give birth by a certain date in order to avoid artificial induction is the primary incentive behind such use, followed by the desire of pregnant women to avoid protracted pregnancy for personal comfort. In a study by Westfall and Benoit, a panel of 27 women was interviewed in the third trimester of pregnancy, and 23 of the same participants were reinterviewed postpartum (50 interviews total). Many of the women said they favored a natural birth and were opposed to labor induction at the time of the first interview. However, all but one of the ten women who went beyond 40 weeks gestation used self-help measures to stimulate labor. These women did not perceive prolonged pregnancy as a medical problem. Instead, they considered it an inconvenience, a worry to their friends, families, and maternity care providers, and a prolongation of physical discomfort.[40]

A national survey of 500 members of the American College of Nurse-Midwives and 48 nurse-midwifery programs was conducted by McFarlin et al.[25] to determine whether they were formally or informally educating students in the use of herbal preparations for cervical ripening, induction, or augmentation of labor. Ninety surveys were returned from CNMs who used herbal preparations to stimulate labor and 82 were returned from CNMs who did not. Of the CNMs who used herbal preparations to stimulate labor 93% used castor oil, 64% used blue cohosh, 63% used red raspberry leaf, 60% used evening primrose oil, and 45% used black cohosh. The most cited reason for using herbal preparations to stimulate labor was that they are ''natural,'' whereas the most common reason for not using herbal preparations was the lack of research or experience with the safety of these substances. Although 78% of the CNMs who used herbal preparations to stimulate labor directly prescribed them and 70% indirectly suggested them to clients, only 22% had included them within their written practice protocols. Seventy-five percent of the CNMs who used herbal preparations to stimulate labor used them first or instead of Pitocin. Twenty-one percent reported complications including precipitous labor, tetanic uterine contractions, nausea, and vomiting. CNMs who used herbal preparations to stimulate labor were more likely to deliver at home or in an in-hospital or out-of-hospital birthing center than CNMs who never used herbal preparations to stimulate labor.[25]

Initiation of labor may be medically necessitated in some cases of postdatism or in the advent of PROM. Labor augmentation is required when contractions in a previously active labor cease or become ineffective. The use of a variety of herbs and approaches, including some of those used to induce or augment labor, are commonly a part of the protocol for prolonged or dysfunctional labors. The herbs most commonly used for labor induction are blue cohosh (*Caulophyllum thalictroides*) and black cohosh (*Actaea racemosa*).

The use of herbs to prepare women for labor begs the question of why one would use an herbal preparation to prepare the body for something it naturally knows how to do, and seems antithetical to the principles upon which herbal medicine philosophy is built–to trust the body's innate wisdom. Although a small percentage of women truly need pharmacologic help with induction, most women can enter labor naturally and given proper support, experience labor and birth without the use of drugs for augmentation. The widespread use of blue cohosh to stimulate labor may be a problem in itself, but more importantly, it is symptomatic of a greater medico-sociologic problem. Health practitioners in the position to do so must help to educate their colleagues about the natural process of labor and a woman's (and baby's) ability to accomplish it successfully and safely, thus mitigating the need for unnecessary pharmacologic intervention.

Cotton Root

The historical use of cotton root bark as an emmenagogue and abortifacient is discussed in Chapter 5. Ellingwood considered cotton root specifically for uterine inertia, to increase uterine contractions and also prevent postpartum hemorrhage.[41] The plant was marketed by Lloyd Pharmaceuticals and Eli Lilly as an oxytocic, emmenagogic agent. The USP listed cotton root as a parturient from 1860 to 1880.[42] Cardiotoxic and hepatotoxic effects have been reported in animals and in vitro with

gossypol, an isolated chemical constituent used medically. Altered hormone levels and other metabolic effects have been mainly reported in animals and in vitro, but are reported in human studies as well.[43] Gossypol is present in the seed in 0.5% concentration, and in lesser concentrations throughout the plant. The root bark extract (not gossypol) is currently used by Western herbalists as an emmenagogue in cases of amenorrhea and as a uterine antihemorrhagic. It is increasingly used by midwives as an alternative or adjunct to blue cohosh as a labor stimulant in postterm pregnancies, for PROM, or for stalled labor. No studies were identified in the literature on use of whole plant extracts, nor the use of this herb for labor stimulation; thus, the safety and efficacy of this herb as a labor stimulant cannot be determined. This herb may have teratogenic effects if taken during early pregnancy, and may induce abortion, so it should not be used earlier in pregnancy than at the intended onset of labor. It is generally given in tincture form, usually in combination with other uterine stimulants, and often antispasmodic herbs. Repeated doses of 2 to 3 mL every 2 hours often result in contractions after four to six doses.

Red Raspberry

Red raspberry leaf is perhaps one of the most historically venerated herbal uterine tonics. It is used during pregnancy to strengthen the uterus, improve labor outcome, and prevent excessive bleeding after birth. Its use continues to be highly popular. One study indicates that approximately 63% of US midwives use this herb to stimulate labor.[25] Although it does not appear that raspberry leaf is very effective for labor stimulation or shortening the duration of labor, recent research has found that the consumption of raspberry leaf tea during pregnancy may in fact improve labor outcome and reduce the need for medical intervention at birth. The results of a double-blind, randomized, placebo-controlled trial consisting of 192 low-risk, nulliparous women who birthed their babies between May 1999 and February 2000 at a large tertiary-level hospital in Sydney, Australia found that raspberry leaf, taken in tablet form from 32 weeks' gestation until labor, caused no adverse effects for mother or baby, and although it did not shorten labor, a lower rate of forceps deliveries between the treatment group and the control group (19.3% vs. 30.4%) was observed.[44] Another study consisted of 108 mothers; 57 (52.8%) consumed raspberry leaf products, whereas 51 (47.2%) were in the control group. The findings suggested that raspberry leaf can be taken safely during pregnancy to shorten labor with no expected side effects for women or their babies. The study also reported a decreased likelihood of pre- and postterm gestation, and fewer obstetric interventions, including decreased amniotomy, caesarean section, forceps delivery, and vacuum extraction in the group that had taken raspberry leaf when compared with the control group.[45] Herbalists and midwives consider raspberry leaf to be a gentle, effective nutritive medicament, and recommended it be taken in the form of an infusion, 1 to 3 cups daily. Of all the herbs that might be considered for labor preparation, raspberry leaf products appear to be the safest.[24]

Evening Primrose Oil

Evening primrose oil (EPO) is a rich source of essential fatty acids, especially gamma linolenic acid (GLA), which function as precursors for prostaglandin synthesis. EPO is widely used by many midwives, both applied topically to the cervix and taken orally, to encourage cervical ripening in an effort to shorten labor and decrease the incidence of postterm pregnancies. Sparse data are available to support this use, although many midwives report it to be effective based on observational reports and anecdote (see Case History at the end of this chapter). One study was identified that investigated the effect of oral evening primrose oil on the length of pregnancy and selected intrapartum outcomes in low-risk nulliparous women. A two-group retrospective quasi-experimental design conducted on a sample of women who received care in a birth center, compared selected outcomes of 54 women taking evening primrose oil in their pregnancy with a control group of 54 women who did not. Findings suggested that the oral administration of EPO from the 37th gestational week until birth did not shorten gestation or decrease the overall length of labor. Further, in this study, the use of orally administered EPO may have been associated with an increase in the incidence of prolonged rupture of membranes, oxytocin augmentation, arrest of descent, and vacuum extraction.[46] Numerous studies of EPO have found no toxicity. Rare side effects include headache and gastrointestinal upset.[47]

Black Cohosh

Black cohosh was considered an excellent remedy to treat both ''false pains in the pregnant uterus, and aid true pains'' making ''labor easier and quicker and give a better getting up.''[48] One Eclectic physician gave a report to the Chicago Gynecologic Society of a study of 160 primiparous and multiparous women to whom he gave a combination of black cohosh and sarsaparilla during the last 4 weeks of pregnancy. By his account, the women experienced decreased length of labor, with minimal neuralgic cramping and irregular pain in the first stage, greater relaxation of the ''soft parts,'' energetic and rhythmic contractions throughout the remainder of labor, and decreased incidence of lacerations and good maintenance of contractions after delivery (he compared the effects with those of ergot).[49] Black cohosh was an ingredient in the popular Eclectic preparation Mother's Cordial, which was used as a labor preparatory blend in the late nineteenth and early twentieth centuries. It continues to be popular today, with one survey indicating that as many as 45% of nurse-midwives responding to a survey use it to stimulate labor. It is frequently combined with blue cohosh as a popular labor stimulant formula. It is spasmolytic and anti-inflammatory to the smooth and skeletal muscles, making it effective in the treatment of dysmenorrhea, and perhaps suggesting a mechanism for its observed efficacy in treating spasmodic pain in labor and incoordinate uterine contractions.[50,51] Black cohosh is approved by the German Commission E for the treatment of premenstrual complaints and dysmenorrhea.[52,53] It is indicated for muscular pains, nervous

tension, and has been noted to have anti-inflammatory and analgesic effects.[54,55] It is often used by midwives to relax spasmodic contractions and help coordinate uterine smooth muscle activity to promote effective contractions in combination with a more stimulating uterine tonic, for example, blue cohosh or cotton root bark (see Blue Cohosh for warnings regarding its use during pregnancy and labor). Several case reports have suggested a possible hepatotoxic effect of black cohosh. As of 2006, several Western nations, including Canada, have issued requirements that all black cohosh products be labeled with a warning about the risk of hepatotoxicity from consumption. The United States has not issued such a warning, based on prior findings that the herb appears reasonably safe. These findings and interpretations are discussed in Plant Profiles: Black Cohosh and should be thoroughly considered when considering whether to use black cohosh during pregnancy or labor. At this time, the safety of the herb for use during pregnancy and lactation is uncertain; long-term use (>2 days) is not advisable. Some herbalists report that patients sometimes experience a frontal headache with use of this herb. If this occurs, discontinue use; this side effect resolves with discontinuation.

Motherwort

Motherwort is considered a uterine spasmolytic and tonic, exerting both actions for the result of easing spastic uterine contractions, for example, in a protracted first stage of labor, while improving the resting tone of the uterine tissue. It is also a favored nervine and anxiolytic, including for panic disorders and to promote sleep. It is widely used by herbalists and midwives during labor, the puerperium, and for PMS-D. Its common name, motherwort, literally means ''healing herb for mothers,'' suggesting a long history of use for these purposes. Most evidence for the use of motherwort is based traditional medicine, and clinical observation.[23,53] No side effects are expected from appropriate use during labor; the herb is considered contraindicated earlier in pregnancy because of its history of use as an emmenegogue.[24] It is typically taken in tincture form.

Cramp Bark/Black Haw

Cramp bark, in small doses, was considered by the Eclectics to be an excellent partus preparator, easing irregular uterine contractions and ''greatly facilitating a speedy and uncomplicated normal labor.''[41] It was also used for after pains and prevention of post-partum hemorrhage, due to tonifying effects exerted on uterine smooth muscle. It was considered specific for erratic uterine cramping and pain.[41,56] These herbs are still widely used by contemporary midwives and herbalists for uterine cramping, with many finding it effective for spasmodic contractions and a protracted early labor. Either may be used in tincture form, alone or combined with other herbs as appropriate, for example, nervines or sedatives to promote rest during first stage. Evidence for the uterine antispasmodic effects of these herbs is presented in Plant Profiles: Cramp Bark/Black Haw. There are no adverse effects or side effects expected with use of this herb.

ADDITIONAL METHODS OF FACILITATING LABOR

Nipple Stimulation

Nipple stimulation is commonly recommended by midwives as part of a protocol to stimulate labor. The mother is instructed to apply traction and a pulling, rolling motion to the nipples either simultaneously or separately but sequentially, for 15 to 30 minutes at a time, and repeat this up to two or three times daily for several days if needed. It is more effective to have a partner apply the nipple stimulation, as it is difficult to achieve the required force on oneself. A 2005 Cochrane Review of the effects of breast stimulation on onset of labor identified six trials with a total of 719 women. Analysis of trials comparing nipple stimulation with no intervention found a significant reduction in the number of women not in labor at 72 hours. However, this result was only seen in women with a favorable cervix at the onset of stimulation. Interestingly, a major reduction in the rate of postpartum hemorrhage was reported (0.7% vs. 6%). There was no significant difference in the cesarean section rate (9% vs. 10%), nor in rates of meconium staining. There were no instances of uterine hyperstimulation. Three perinatal deaths were reported.[57] Chayen and Kim, in a clinical trial of 317 contraction stress tests using stimulation with an automatic breast pump, found that contractions were successfully achieved in 84.2% of cases, with uterine hyperstimulation observed in 4.1% of tests performed. They reposted that side effects and complications were minimal.[58] In another study by Chayen et al., nipple stimulation with an electric breast pump was compared with oxytocin infusion as a means of labor induction. The time from stimulation to the onset of regular uterine activity and to 200 Montevideo units of uterine activity and the time until entrance into the active phase of labor were significantly shorter in the nipple stimulation group. Once the women were in active labor, there was no difference between the groups in the length of labor or mode of birth. Although nipple stimulation is not as effective as oxytocin induction, it appears to be effective for many women, and may be considered a safe, effective alternative to try before turning to pharmaceutical or mechanical labor stimulation.[59]

Sexual Intercourse

Prostaglandins have been extensively studied for their role in stimulating the onset of labor, particularly, ripening the cervix. Human semen is a rich biological source of prostaglandins, with a high prostaglandin concentration. The use of intercourse to stimulate labor has become a modern ''folk'' tradition, and it is widely recommended among midwives when labor stimulation is required. The typical recommendation is intercourse two to three times daily, for 2 to 3 days in a row. Of course, this assumes the mother is in a heterosexual, sexually active relationship. The recommendation is generally made in conjunction with additional techniques for labor stimulation (e.g., nipple stimulation, herbs). It is uncertain whether any stimulating effects resulting from sexual intercourse

result from the mechanical stimulation of the lower uterine segment, the endogenous release of oxytocin as a result of orgasm, or the direct action of prostaglandins in semen. Furthermore, nipple stimulation may be part of the process of initiation if this occurs in the context of sexual activity. These various factors are very difficult to standardize for clinical studies in comparison with other interventions for labor induction.[60] A Cochrane Review identified one study of 28 women, from which the authors determined that no meaningful conclusions could be derived.[60] As long as the membranes are intact, there is not placenta previa, and the mother is comfortable with this approach, there is no harm in incorporating intercourse into efforts to stimulate labor.

Acupuncture

Acupuncture has been used in Asia and Europe to decrease the pain of labor, effect cervical ripening, and stimulate the onset of labor. It has been suggested that acupuncture neuronal stimulation may increase uterine contractility either by central oxytocin release or parasympathetic stimulation of the uterus. A Cochrane Review on the effects of acupuncture on labor stimulation found that although there are a number of studies looking at acupuncture labor effects, few are of high quality. Induction of labor using electro-acupuncture was reported by Yip in 1976 with a success rate of 67% of women ($n = 31$), with pregnancy duration ranging from 38 to 42 weeks. Another study ($n = 12$) using acupuncture with and without electrical stimulation had a success rate of 83% with an average time between induction and delivery of 13.1 hours. In a third study, 34 term and postterm women and seven women with intrauterine fetal deaths were induced using electroacupuncture. Labor was successfully induced in 32 (78%) women.[61] These and a limited number of additional observational studies to date suggest that acupuncture for induction of labor appears safe, has no known teratogenic effects, and may be effective.[61] The evidence regarding the clinical effectiveness of this technique is limited.

Homeopathy

Homeopathy is popularly used for labor induction. The homeopathic extract of *Caulophyllum thalictroides* is proposed to be useful in establishing labor, or when uterine contractions are short and irregular or there is an arrest of uterine contractions.[62] It is commonly recommended that pregnant women ingest one tablet daily for the last few days prior to the due date or desired onset of labor, or alternatively to dissolve a tablet in a glass of water and sip from the glass from time to time, or whenever a contraction is imminent. A double-blind placebo controlled matched cohort study by Beer et al. compared Caulophyllum with placebo in 40 women at term with PROM and no onset of contractions. Women were administered Caulophyllum or a placebo hourly for 7 hours. Each active tablet consisted of 250 mg Caulophyllum (trituration D4) and inert binders.[63] A study by Dorfman et al. compared five homeopathic therapies with placebo in 93 women from 36 weeks pregnant; 53 women were randomized to the treatment group and 40 to the placebo group. The trial examined the effect of the homeopathic therapy on length of labor and difficulty of labor. The information on any side effects arising from Caulophyllum was unclear and it was unclear as to how women assessed the tolerability of Caulophyllum. No data were provided on side effects.[64] The Cochrane Collaboration concluded that both trials were of weak methodologic quality and no meaningful conclusions can be drawn on the efficacy of Caulophyllum for inducing labor or improving labor-related outcomes.[65] Additionally, they comment that the use of Caulophyllum may not represent common homeopathic practice, in which the prescribing of a therapy is typically individualized.[65] However, it may represent common over-the-counter self-prescribing that is based on more common generic prescriptions, of which it should be noted that the adverse effects that may be associated with the use of the herb blue cohosh (*Caulophyllum thalictroides*), discussed in the preceding, are not expected with the homeopathic preparation, in which no identifiable chemical compounds remain.

Walking and Positional Changes

Controversy exists regarding the relationship between maternal position in labor and outcome, such as labor duration, subjective discomfort, and fetal outcome.[66] In cultures not influenced by Western society, women progress through the first stage of labor in upright positions and change position as they wish with no evidence of adverse effects to either the mother or fetus.[12,67,68] The technologic approach to birth endemic to Western culture with nearly ubiquitous reliance on interventions such as continuous fetal monitoring, epidural use, and continuous IV infusion, relegates women to a supine position during labor. Numerous studies have demonstrated that this position may increase the risk of adverse effects to both the mother and her passenger, as well as impinging on the effective progress of labor.[69] Effective contractions, and therefore effective fetal descent and prevention of dystocia, are essential to labor progress and can be facilitated with ambulation and positional changes in labor.[12] Further, moving around can increase a woman's sense of control in labor by providing a self-regulated distraction from the challenge of labor and also may decrease her need for analgesia.[69] The use of a variety of position, changes of position throughout labor as needed, and maternal ambulation in labor are considered by midwives to be fundamental to the prevention and management of labor dystocia, particularly when associated with remediable fetal malpresentation, such as asynclitism. Further, changes in maternal position, such as from supine to left lateral or hands-and-knees, can be effective in relieving fetal cord compression and therefore fetal distress associated with the supine position.[70–73] Midwives frequently encourage positions that are not only physiologic for the mother, her maximal comfort and labor effectiveness, and the position of the fetus, but also positions that facilitate optimal maternal support, such as access to massaging her lower back to relieve the pain of lower back labor (Fig. 16-3).

A limited number of studies evaluate the effects of maternal position on labor outcome, and most of these evaluate positions prescribed by obstetric care providers rather than those chosen by laboring women for themselves.[66] In a study by Carlson et al., it was observed that left to select their own positions, a total of 80 laboring patients selected from no less than 59 different positions during the course of labor, with a greater variety of positions chosen in early labor, but more positional changes occurring during second stage. The most commonly selected position for labor was lateral recumbent.[66] Outcome measures were not evaluated in this study. The hands-and-knees position during labor has been recommended on the theory that gravity and buoyancy may promote fetal head rotation to the anterior position and reduce persistent back pain and cause rotation of the fetal head when in a persistently posterior position. A Cochrane Review based on two studies found that the use of hands and knees position for 10 minutes twice daily to correct occipitoposterior position of the fetus in late pregnancy does not affect this change; however, it did not evaluate the use of this position during labor or for more extended lengths of time.[74] A study by Stremler et al. was conducted to evaluate the effect of maternal hands-and-knees positioning on fetal head rotation from occipitoposterior to occipitoanterior position, persistent back pain, and other perinatal outcomes. Thirteen labor units in university-affiliated hospitals participated in this multicenter randomized controlled trial. Study participants were 147 women laboring with a fetus at 37 weeks gestation and confirmed by ultrasound to be in occipitoposterior position. Seventy women were randomized to the intervention group (hands-and-knees positioning for at least 30 minutes over a 1-hour period during labor) and 77 to the control group (no hands-and-knees positioning). The primary outcome was occipitoanterior position determined by ultrasound following the 1-hour study period, and the secondary outcome was persistent back pain. Other outcomes included operative delivery, fetal head position at delivery, perineal trauma, Apgar scores, length of labor, and women's views with respect to positioning. Women randomized to the intervention group had significant reductions in persistent back pain. Eleven women (16%) allocated to use hands-and-knees positioning had fetal heads in occipitoanterior position following the 1-hour study period compared with five (7%) in the control group. Trends toward benefit for the intervention group were seen for several other outcomes, including operative delivery, fetal head position at delivery, 1-minute Apgar scores, and time to delivery. The authors concluded that maternal hands-and-knees positioning during labor with a fetus in occipitoposterior position reduces persistent back pain and is acceptable to laboring women and this option of a position for labor should be made available to women laboring with a fetus in occipitoposterior position.[75]

LABOR STIMULATION PROTOCOL

Midwives use a variety of protocol to stimulate labor. They are applied in a supportive atmosphere conducive to labor, with the primary labor support person(s) present and ideally, appropriate monitoring available for mother and fetuses (e.g., maternal blood pressure and labor progress, fetal heart tones). A typical protocol for initiating labor is presented immediately following in the case history. Other herbs may be added to the protocol, such as nervines if there is anxiety. Women are not encouraged to attempt to stimulate labor prior to 40 weeks, unless otherwise medically instructed, because of the risk of inducing premature labor. The labor initiation protocol is typically applied over an 8-hour time course, and if not

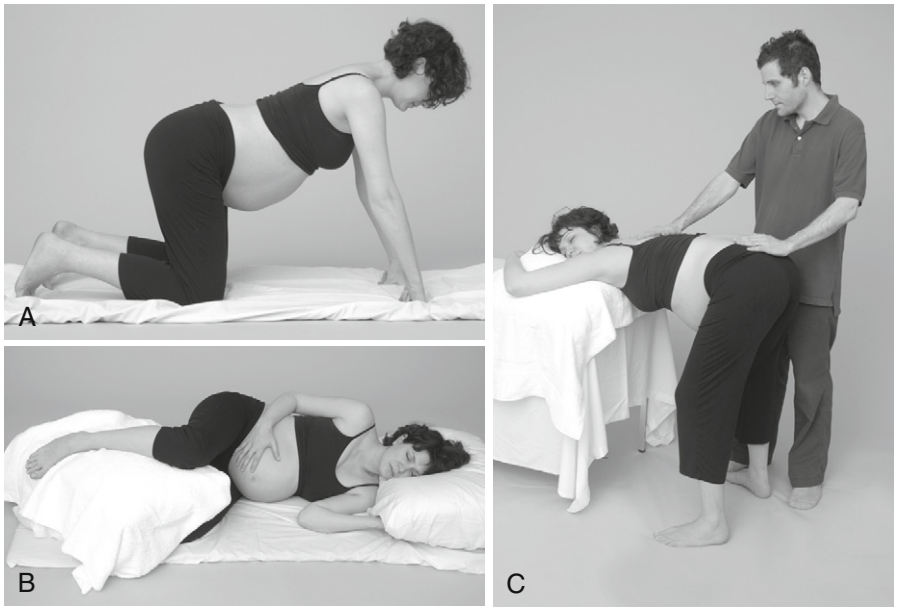


Figure 16-3 Positional changes to facilitate labor. A, Hands and knees position for labor. B, Left lateral recumbent position. C, Standing position with massage. (Stillerman E: *Prenatal Massage: A Textbook of Pregnancy, Labor, and Postpartum Bodywork,* St. Louis, 2008, Mosby.)

effective on the first attempt, it may be repeated the following day. It is not recommended to repeat this for more than two consecutive days. Some mothers find the castor oil intolerably nauseating; if so, repeat the abdominal massage and skip intake; some mothers may experience a frontal headache. This is most likely a result of the black cohosh. Discontinue the tincture for the following does and thereafter substitute cramp bark or black haw for the black cohosh.

CASE HISTORY:

Alison, a 38-year-old mother of two, was 34 weeks pregnant with her third baby when her midwives told her that her baby was getting too big and she should prepare herself for an early induction at 38 weeks or a cesarean delivery. Her previous baby, now age 8, was born by cesarean section at term after 30 hours of labor because of the baby's large size (9 lb 8 oz) and an ineffectual labor. She was not pleased about the idea of another cesarean, and therefore was excited to be preparing for a VBAC (vaginal birth after cesarean) in the hospital with a midwife and obstetrician practice. She had no medical risk factors, and was not diabetic. With her midwife's support, she found a direct entry midwife in the community who practiced herbal medicine, and contacted her to discuss possible alternative methods of initiating labor as early as 36 weeks. The midwife told Alison that 36 weeks is too early, but to discuss a reasonable goal with her primary care midwife and then they could discuss options. Alison came back to the herbalist-midwife with a reasonable due date of the beginning of the 38th week gestation. The herbalist midwife gave Alison a protocol, and agreed to help if all of the care providers involved in Alison's prenatal and delivery care supported the use of the herbs. All agreed. Alison's protocol was as follows:

- Beginning at 37 weeks gestation, for 1 week, apply 1500 mg of EPO to the cervix daily and take 1000 mg EPO orally. Alison was instructed that the cervical application could be accomplished by digital application or by using the oil as a lubricant during intercourse, which was also recommended several times weekly.
- On the first day of the 38th week, or in this case, the intended ''due date'' Alison was to follow a specific protocol for 8 hours and then discontinue.

8 AM

1.5 mL each Blue and Black Cohosh; 0.5 mL ginger root, in a combined tincture

30 minutes nipple stimulation

8:30 AM

Long walk (30 minutes)

9 AM

1.5 mL each Blue and Black Cohosh; 0.5 mL ginger root, in a combined tincture

9:30 AM

Massage selective acupressure points or acupuncture treatment for mother

10 AM

1.5 mL each Blue and Black Cohosh; 0.5 mL ginger root, in a combined tincture

Castor oil abdominal massage: Warm castor oil by running bottle under hot water or putting in a basin of hot water. Apply with effleurage style massage for 20 to 30 minutes.

10:30 AM

Hot shower or bath (the latter if membranes are intact)

11 AM

1.5 mL each Blue and Black Cohosh; 0.5 mL ginger root, in a combined tincture

Dose 1 Castor oil: 2 oz castor oil placed in blender with 4 oz orange juice, blend on high speed with pinch of baking soda to emulsify, and have mother drink down quickly (have mother sit and rest quietly, and if needed, suck a piece of candied ginger or a mint lozenge to quell nausea)

11:30 AM

Have mother rest

12 PM

Light lunch

1.5 mL each Blue and Black Cohosh; 0.5 mL ginger root, in a combined tincture

12:30 PM

Long walk if mother is not limited to ''bathroom range'' from castor oil

1 PM

1.5 mL each Blue and Black Cohosh; 0.5 mL ginger root, in a combined tincture

30 minutes nipple stimulation

1:30 PM

Dose 2 Castor oil: 2 oz castor oil placed in blender with 4 oz orange juice, blend on high speed with pinch of baking soda to emulsify and have mother drink down quickly (have mother sit and rest quietly, and if needed, suck a piece of candied ginger or a mint lozenge to quell nausea)

2 PM

1.5 mL each Blue and Black Cohosh; 0.5 mL ginger root, in a combined tincture

3 PM

1.5 mL each Blue and Black Cohosh; 0.5 mL ginger root, in a combined tincture

4 PM

1.5 mL each Blue and Black Cohosh; 0.5 mL ginger root, in a combined tincture

Alison was told that she should start the protocol after a good breakfast as early in the morning as possible, to absolutely discontinue the protocol at the end (do NOT take additional doses of the herbs) and then to try to have a good dinner, do something relaxing, and get to bed early, as labor rarely starts immediately with the protocol, but often starts as long as 8 to 12 hours after.

At 37 weeks, Alison went to her nurse-midwife who checked her cervix and found it to be uneffaced and undilated. By ultrasound, the baby's weight was estimated at approximately 8 lbs. Alison followed the instructions for using the EPO and went to her midwife for a follow-up appointment to determine whether any progress occurred with this treatment; she was found to be 50% effaced and 1 cm dilated. At the onset of 38 weeks, Alison followed the 8-hour protocol, ending at about 6 PM.

She had dinner with her family and then she and her husband went to a movie. She got to bed at about 11:30 PM and was awakened at about 2 AM with strong contractions. These persisted and by about 6 AM she could no longer tolerate the discomfort and felt the need to go to the hospital. In her mind, she was disappointed because with her previous labor she had labored for 30 hours and only progressed to 6 cm; now she felt she was giving up already and assumed she would have another cesarean. She arrived at the hospital about 45 minutes later, and was found to be 9 cm dilated. She birthed a healthy 8.5-lb baby boy within the hour, vaginally, and with no complications for the mother or baby. The family was entirely pleased and the nurse-midwife amazed at the efficacy of the herbal protocol. At 7 years old, the last time the herbalist-midwife saw the ''baby'' mother and child were in excellent health, and the mother still ecstatic over the birth experience.

PAIN IN LABOR

Knowledge is the most powerful thing as far as pain.[76]

The experience of pain in labor is a complex individual experience, and perhaps one of the greatest areas of anticipatory anxiety for pregnant women. Epidural anesthesia is currently used in almost two-thirds of all labors in the United States, a reflection of the immense desire of women to avoid the pain normally associated with labor.[77,78] Although epidural anesthesia can be an invaluable tool in the management of difficult labors and births, and many women report that epidural analgesia is very helpful, it is not without potential risks, including increased length of labor, need for operative vaginal delivery, likelihood of perineal laceration, increased incidence of maternal fever leading to increased use of neonatal antibiotics and sepsis evaluations, increased use of oxytocin augmentation, and possible increase in need for cesarean section.[76,78] There are little data evaluating the effects of epidural anesthesia on breastfeeding and mother–infant bonding; however, it has been observed that women who experience operative deliveries are more likely to experience postpartum depression, which can significantly affect mother–child interaction. Women are poorly informed about the potential side effects of epidural (and other) anesthesia, and what little information they are given is commonly provided in active labor, even at the height of a contraction, when it is impossible for a woman to make an informed choice.[78] Further, women are rarely offered nonpharmacologic alternatives for pain relief, in spite of the fact that numerous studies show that the use of doulas, continuous labor support, using various positions for labor, massage during labor, sterile water injections, acupuncture, and other modalities lessen labor pain.[78]

This chapter casts no judgment on the choice of women to receive epidural anesthesia for pain relief, and endorses its judicious use in difficult labors. It is every woman's right to choose how to birth, and to have access to all of the tools available for her to do so safely and with as much support, comfort, and confidence as possible. However, this chapter does encourage practitioners to give women the ability to make fully informed decisions by apprising them of nonpharmacologic and pharmacologic interventions equally, ideally prior to or during labor, with adequate information to make a realistic appraisal of risks and benefits. It also encourages birthing centers and hospitals to see alternative methods of pain management as safe, cost-effective means of caring for laboring patients than the routine use of interventions that can lead to unnecessary additional interventions and complications.

Unlike other chapters in this book, which emphasize the use of botanical therapies, this chapter provides an overview of the many possible options for pain management in labor that are commonly used by midwives and other practitioners, of which herbs are only a small part.

> *The non-pharmacologic approach to pain includes a wide variety of techniques to address not only the physical sensations of pain but also to prevent suffering by enhancing the psycho emotional and spiritual components of care. Pain is perceived as a side effect of a normal process, not a sign of damage, injury, or abnormality. Rather than making the pain disappear, the midwife and other caregivers assist the woman to cope with it, build her self-confidence, and maintain a sense of mastery and well-being.*[79]
>
> **—Penny Simkin and April Bolding**

ASSUMPTIONS ABOUT LABOR AND BIRTH: OBSTETRIC VS. MIDWIFERY BELIEFS

According to childbirth sociologist Carol Sakala, a prevalent assumption of the biomedical approach to labor pain is that many or most women require pain medication during labor.[76] In direct contrast, midwives assume that women intrinsically know how to birth, and that with adequate prenatal preparation and support during the birthing process, pain medication is often unnecessary.[76,80] Midwives recognize that a routine, homogenous approach to pain management in labor, even using nonpharmacologic methods, is inherently ineffective, and that care providers must be able to respond to the unique needs of individual laboring women with a variety of tools in their repertoire, and be creative and responsive in the moment.

Midwives believe that not only is education about the process of labor and birth essential, but so is a close and trusting relationship with their care provider, or in the least, a doula who can be both a support person and an advocate for the mother. Midwifery wisdom appears to be consistent with what women actually report as the most important factors leading to a feeling of satisfaction with birth, none of which include pain relief as important. A recent systematic review concluded that the four factors associated with satisfaction with the childbirth experience are:[78]

- Amount of support received
- Quality of relationship with care provider
- Involvement in decision making
- Personal expectations

Midwives, whose professional care is based on a mother-centered empowerment approach, and caregivers that

include CAM as part of the repertoire they offer mothers for labor support, are more likely to be perceived by patients as consistent with these factors.[81]

Hospital-based preparation (e.g., childbirth classes), commonly spend more time preparing women for the interventions they can expect as part of routine hospital practices than building their sense of personal empowerment and choice. Childbirth classes designed by midwives (e.g., Birthing from Within) in contrast, are more likely to emphasize skills and tools that can be used by the mother/couple to achieve as natural a birth as possible. Changing medical attitudes to embrace the possibility of natural birth as a routine childbirth practice will be necessary to expand the repertoire of nonpharmacologic interventions available to women birthing in medical institutions. It has been demonstrated in European hospitals that such attitude changes can lead to changes in practice that translate into reductions in unnecessary medical and surgical interventions, improving outcomes for both mother and baby.[82] ''Hospitals with low cesarean section rates have achieved this goal by embracing the belief that supportive labor care and the least intervention create the best opportunity for a good birth experience.''[82]

PSYCHOLOGICAL PREPARATION FOR LABOR

Every birth experience is unique and unpredictable. Preparing for labor is not dissimilar to preparing for a hiking trip. You train in advance, know the terrain, pack your gear, your trail mix and other provisions, stock your first aid kit, check the weather, and set out, prepared and expecting the best. Hopefully, you have good weather and a clear trail. But sometimes the unforeseen happens—the trails are closed because of rock slides, there is an unexpected thunder storm, or you slip and sprain your ankle. In the event of these problems, one takes an alternate route, breaks out the rain gear and seeks shelter, or abandons the trip and gets medical attention. So it is with birth. We make our plans, but sometimes the best laid plans are not what birth has in store—so we have to choose an alternate route. Empowerment and self-determination, tempered by flexibility, are perhaps the most important attributes with which women can enter labor.

Rarely does a woman give birth and later say ''that was easy.'' Even with quick and seemingly (to the observer) easy births, the mother goes through enormous physiologic, psychological, emotional, and perhaps even spiritual changes. At the least, a woman usually remarks that it was work. For most women labor is hard work, and a lot of it, perhaps for hours, perhaps protracted over days. Sometimes resources are available to help a woman cope with the intensity of it—a comforting partner, a midwife, doula, or obstetrician who can give reassurance, massage, or herbs if needed to relieve anxiety, fear, or pain—enabling the mother to endure a great deal of work to birth her baby. Other times, in the absence of such resources, or in spite of the best resources, medical intervention is needed in the form or pharmacologic pain relief or operative delivery.

Women led to believe that labor can be painless, fast, and easy, whether by using herbs, hypnotherapy, or the power of positive thinking are often sorely disappointed and ill-prepared as they get past the initial contractions. Although any of these tools may be useful adjuncts to a well-prepared woman, in the absence of preparation for a broad range of possible experiences, and acceptance that labor cannot entirely be controlled or planned, they may set a woman up for a sense of failure if things do not go according to plans, hopes, and expectations. Further, women who approach their prenatal preparation ''arming'' themselves with techniques to avoid pain in labor are probably not preparing effectively. The point of pain relief techniques is not necessarily to make labor ''pain free,'' but to give women tools to help them cope as they find their inner resources to get through labor. As practitioners, we can best help women and couples to prepare for labor and birth by honestly discussing the wide range of realities and possibilities inherent in the experience, and the options for maximizing coping skills. Helping women to become more comfortable and trusting in their bodies, more self-aware, more empowered to express their needs and preferences, and helping to create a safe place in which pregnant and laboring women can express their fears and pain are all powerful parts of labor preparation.

CONTINUOUS LABOR SUPPORT

The word ''continuous,'' as it relates to labor support, has been defined in various ways. In one study, in which staff nurses were the support providers, ''continuous'' was defined as ''a minimum of 80% of the time from randomization to delivery.'' In a meta-analysis of trials of labor support, ''continuous'' was defined as ''without interruption, except for toileting, from shortly after admission to the hospital or entry into the study, and during the birth of the child.'' Labor support with a midwife or doula usually includes continuous presence, emotional support (reassurance, encouragement, and guidance); physical comforting (assistance in carrying out coping techniques, use of touch, massage, heat and cold, hydrotherapy, positioning, and movement); information and guidance for the woman and her partner; facilitation of communication (assisting the woman to express her needs and wishes); and nonmedical information and advice, anticipatory guidance, and explanations of procedures.[79] Continuous support provided by another woman with birth experience consistently has been demonstrated to reduce labor pain and improve labor outcomes—a fact long known by traditional midwives worldwide. Perhaps the seminal studies on this were reported by Kennell et al., who found that the continuous presence of a supportive companion (doula) during labor and delivery in two studies in Guatemala shortened labor and reduced the need for cesarean section and other interventions. In a US hospital with modern obstetric practices, 412 healthy nulliparous women in labor were randomly assigned to a supported group ($n = 212$) that received the continuous support of a doula, or an observed group ($n = 200$) that was monitored by an inconspicuous observer. Two hundred four women

were assigned to a control group after delivery. Continuous labor support significantly reduced the rate of cesarean section deliveries (supported group, 8%; observed group, 13%; control group, 18%) and forceps deliveries. Epidural anesthesia for spontaneous vaginal deliveries varied across the three groups (supported group, 7.8%; observed group, 22.6%; control group, 55.3%). Oxytocin use, duration of labor, prolonged infant hospitalization, and maternal fever followed a similar pattern. The authors concluded that the beneficial effects of labor support underscore the need for a review of current obstetric practices.[83] A Cochrane meta-analysis found a decrease in operative vaginal deliveries, cesarean section, fewer requests for pain medication, and increased birth satisfaction when continuous labor support was given.[84] Interestingly, fear of labor in itself has been shown to decrease pain tolerance.[85] The support of a caring woman during pregnancy and in labor, herself educated and experienced in matters of birth, can be instrumental in dispelling and alleviating fear. Prenatally, midwives are aware that they can have a dual role in becoming both a trusted support person, but also someone who can help a woman to reframe or reprogram her misapprehensions and misconceptions about childbirth, so that the mother might enter labor with reduced anxiety.[76]

VARIOUS POSITIONS

Unrestricted, women will assume a variety of positions that they find conducive to labor and birth. Possible positions for labor and birth include semiseated, squatting, hands and knees, kneeling, side-lying, and standing. Women may birth in a shower, birthing tubs, on a bed, a birthing stool, or on the floor. Midwives have long assisted women in labor by having them change positions to facilitate rotation of the baby's head, downward descent of the baby, or having the mother shift positions to relieve discomfort when possible, such as laboring on the hands and knees to relieve lower back pressure and to rotate a baby from a posterior position, or rocking the hips during contractions to accomplish the same. Fourteen studies have been conducted in which women were randomized to various positions in labor; of these, two have shown a decrease in the use of analgesia. Randomizing women to specific birthing positions is not the same as individualizing birthing positions to optimize the mother's comfort, nor is it comparable with the mother intrinsically identifying the positions in which she is most comfortable laboring.

MASSAGE

Massage is a tool used almost ubiquitously by midwives throughout labor, whether of the lower back, gentle ''effleurage'' of the abdomen, or of the legs, neck and shoulders, or forehead (Fig. 16-4). Massage is tailored to the specific physical needs of the mother and her stage in labor; for example, during early labor, a deep foot massage can help a mother to sleep through contractions and get needed rest, in more advanced labor, firm lower back pressure might be welcomed, and during transition, light touch across the forehead can relieve tension. Even just simple touch can be a great comfort.[78] Massage can be used throughout labor, with women in a variety of positions from side-lying to standing, and requires no special equipment (although massage oil or hand cream can be used to prevent chaffing or irritation to the mother's skin). Training in specific massage techniques can be beneficial for optimal relief of discomfort, and is easy to teach the labor partner or for doulas and midwives to learn; however, it is not necessary to have special training to be effective and comforting.

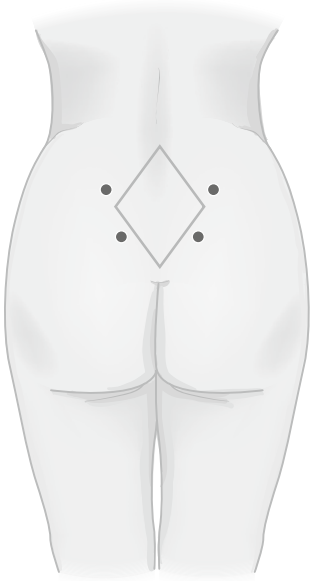


Figure 16-4 Sites for firm acupressure massage or sterile water injections. (Stillerman E: *Prenatal Massage: A Textbook of Pregnancy, Labor, and Postpartum Bodywork,* St. Louis, 2008, Mosby.)

A number of studies have explored the effects of massage on labor pain. In a study by Chang et al., 60 primiparas in labor were randomly assigned to either a massage or control group and tested using the self-reported Short-Form McGill Pain Questionnaire (SF-MPQ) at three phases of cervical dilation: phase 1 dilation (3 to 4 cm), phase 2 dilation (5 to 7 cm), and phase 3 dilation (8 to 10 cm). The massage group received standard nursing care and massage intervention, whereas the control group received standard nursing care only. The results of this study showed that in both groups, as cervical dilation increased, there were significant increases in pain intensity as measured by SF-MPQ; that massage lessened pain intensity at phase 1 and 2, but there were no significant differences between the groups at phase 3. The results of this study indicate that, although massage cannot change the characteristics of pain experienced by women in labor, it can effectively decrease labor pain intensity at phase 1 and 2 of cervical dilation during labor.[86] Another study evaluated a program of massage, controlled breathing, and visualization performed regularly by birth partners, from 36 weeks gestation and assisted by a trained professional, following hospital admission during labor and birth. The intervention was designed in light of experimental findings that repeated massage sessions over 14 days increases pain threshold, by an

interaction between oxytocin and opioid neurons.[87] A 4-week time frame was selected to coincide with a physiologic increase in maternal pain threshold. To detect the effects of massage during labor on maternal cortisol and catecholamines, cord venous blood was taken to measure plasma concentrations following birth. Twenty-five nulliparous and 10 multiparous women participated in the study. Cortisol values were similar to published studies following labor without massage, but pain scores on a Visual Analogue Scale (VAS), done at 90 minutes after birth were significantly lower than scores recorded 2 days. The mean score was 6.6. Previous studies suggest that a reduction from 8.5 to 7.5 would significantly reduce pharmacologic analgesia in labor.[87–89] A study by Field et al. of 28 average socioeconomic women from diverse ethnic backgrounds [Hispanic (57%), white (34%), black (9%)] were randomized to receive massage in addition to coaching or breathing, or to receive coaching and breathing in the absence of massage. Based on self-reporting using a Likert scale,[1–5] women in the massage group reported a pain reduction from 5.0 to 3.5, whereas the women in the control group actually reported an increase from 4.3 to 5.0.[90]

HYDROTHERAPY

Maternal anxiety and pain may prolong labor and contribute to fetal distress.[91] Hydrotherapy during labor can promote relaxation and decrease pain without the risks caused by other treatments. Hydrotherapy can include warm baths, birthing pools, or a hot shower, ideally with an adjustable flow spray nozzle with a firm massage setting. A pilot study by Benfield et al. on the psychophysiologic effects of hydrotherapy on maternal anxiety and pain during labor was conducted. Using a randomized, pretest-posttest control group design with repeated measures, 18 term parturients were assigned to a control or an experimental group. Experimental subjects were placed in a tub of 37° C water for 1 hour during early labor. The Wilcoxon two-sample test revealed statistically significant effects. At 15 minutes, bathers' anxiety and pain scores were decreased compared with nonbathers. At 60 minutes, bathers' pain scores were decreased compared with nonbathers. After 15 minutes of immersion, bathers had a significantly greater increase in plasma volume than nonbathers. No significant differences were found in urine catecholamines or maternal–fetal complications. The small sample limits conclusions, but the findings offer preliminary support for the therapeutic effects of bathing in labor for acute, short-term anxiety and pain reduction.[91]

A review of the literature suggests that a primary effect of immersion is a central blood volume bolus, which occurs almost immediately after bathing begins. Subjective maternal responses to bathing in labor have been favorable. No maternal or infant infections have been attributed to bathing by parturients with either intact or ruptured membranes. Maternal bathing in labor does not appear to affect infant Apgar scores or stress hormones at birth. No clear evidence exists to indicate that hydrotherapy increases cervical dilation, increases fetal descent, reduces uterine dyskinesia, shortens labor, decreases use of epidurals or analgesia, or decreases rates of operative delivery or hemorrhage. Study findings indicate support for using hydrotherapy for relief of rapid pain and anxiety in labor.[92] Midwives have observed that the overuse of water, especially full immersion in warm tubs for extended durations during labor, actually can lead to maternal exhaustion and delays in labor. Although there is no way to individualize the amount of time a woman spends in water during labor, personal midwifery experience suggests emphasizing the use of short baths or showers and massage in early labor, and using warm tubs and full immersion at longer lengths in later stages of active labor. Women may enter the water at any point in labor, but when there is cervical dilatation less than 5 cm, bathing may diminish the frequency or intensity of contractions, as may staying in the water for greater than 2 hours continuously.[93] Having the mother get out of the tub and walk around and cool off periodically may prevent prolonged labor. To prevent maternal dehydration during long immersions, fluid intake should be encouraged. Immersion in baths is contraindicated in labor when there is evidence of maternal infection, excessive vaginal bleeding, conditions requiring continuous fetal monitoring, with continuous oxytocin infusion, or a nonreassuring fetal heart rate pattern.

AROMATHERAPY

Many midwives and mothers report that soothing scents can enhance a sense of comfort and well-being in the laboring mother's environment. Scents may be chosen for their relaxing effects (e.g., lavender), soothing effects (e.g., lavender, vanilla), or stimulating effects (e.g., peppermint). Essential oils, distributed via diffuser or spray bottle, may be mixed into massage oil, added to a warm bath, or placed on a washcloth in the bottom of a hot shower. In one extensive observation study of 8058 mothers in childbirth, the largest research initiative in the use of aromatherapy within a health care setting. The study involved a wide range of participants, from mothers who experienced a low-risk, spontaneous labor and birth, to those whose labor was induced, and those who had vaginal operative delivery and cesarean section. The study took place over a period of 8 years, which enabled a more challenging test of the effect of aromatherapy on intrapartum midwifery practice and outcomes. In the study, a total of 10 essential oils were used, plus a carrier oil, which were administered to the participants via skin absorption and inhalation. The study found little direct evidence that the practice of aromatherapy per se reduces the need for pain relief during labor, or the incidence of operative delivery. But a key finding of this study suggests that two essential oils, clary sage and chamomile, are effective in alleviating pain. The evidence from this study suggests that aromatherapy can be effective in reducing maternal anxiety, fear, and/or pain during labor. The use of aromatherapy appeared to facilitate a further reduction in the use of systemic opioids in the study center, from 6% in 1990 to 0.4% in 1997 (per woman). Aromatherapy is an inexpensive care option. The study reports a minimal

incidence of associated symptoms. Out of 8058 mothers, 1%[100] recorded an associated symptom, all of which were mild in nature.[94]

HERBS FOR PAIN RELIEF

Independent midwives commonly use herbs for pain relief in labor when other, nonpharmacologic methods have not produced adequate results and the mother appears to be suffering. Although the analgesic and sedative actions of herbs are not as quick-acting or powerful as pharmaceuticals, their actions can be gently effective, most with minimal risk of serious side effects, and their use does not preclude subsequent administration of pharmaceutical intervention should it eventually be required. It is not usually expected that herbal medicines will entirely relieve the pain associated with labor, rather they are used to ''take the edge off,'' promote sleep when needed, and relax incoordinate uterine contractions that may be leading to ineffective and thereby unnecessarily painful labor. The herbs discussed in the following are those that are purely analgesic or sedating in action, and that are most commonly used by midwives for labor pain. These herbs are typically combined into formulae and given repeatedly over a short period of time (e.g., every 15 minutes for 1 hour until desired effect, i.e., sleep, pain relief, is achieved) and repeated as necessary. Maximum daily doses are provided in Table 16-3.

STERILE WATER INJECTIONS

Intracutaneous sterile water (ISW) injections made adjacent to the posterior superior iliac spines are believed to cause distention of the skin, which leads to stimulation of nociceptors and mechanoreceptors, creating a localized sensation that may act as a counterirritation to uterine contraction pain (see Fig. 17-4). A randomized controlled trial (n = 134) was conducted comparing the effectiveness of three nonpharmacologic approaches for relief of back pain: (1) intracutaneous sterile water injections (ISW); (2) transcutaneous electrical nerve stimulation (TENS); and (3) standard care, including back massage, whirlpool bath, and liberal mobilization. Women self-evaluated both intensity and affective dimensions of pain using visual analog scales. Their evaluations of control and satisfaction were assessed using adapted versions of the Labor Agentry Scale and the Labor and Delivery Satisfaction Index. The results indicated that women in the ISW group rated the intensity and unpleasantness of pain during the experimental period significantly lower than women in the standard care group or the TENS group. Mean pain intensity at 15 and 60 minutes after randomization was significantly reduced in the ISW group compared with the two other groups.[95]

In another study, 45 pregnant women in the first stage of labor presenting with lower back pain were randomized into two groups. One group received intracutaneous injections of sterile water in the lumbosacral region, whereas the other group was given corresponding subcutaneous injections of isotonic saline, regarded as a placebo treatment. In the group that received intracutaneous sterile water injections the mean pain score was significantly more reduced compared with the placebo group at 10, 45, and 90 minutes after the treatment. The midwives' blind estimation of the effectiveness of treatment was consistent with the subjective patient assessment. However, the requirement of meperidine was similar in the two groups. The analgesic method presented was found to be an effective treatment against lower back pain during the first stage of labor.[96]

BIOFEEDBACK

Biofeedback is a noninvasive system that utilizes monitoring instruments to provide visual or auditory feedback to patients based on physiologic responses of which they are usually unaware, for example, pulse or respiratory rate, allowing the patient to gain a sense of self-reliance in their ability to alter these parameters. In a study of 55 first-time mothers randomly assigned to either childbirth classes or childbirth classes plus biofeedback training, women who used biofeedback during labor reported significantly lower pain than women in the control group. Seventy percent of women in the control group requested epidural anesthesia, vs. only 40% in the biofeedback group.[97]

ACUPUNCTURE

Although the mechanisms of action remain unknown, findings from three randomized controlled trials (Western-based) have concluded that acupuncture during labor can reduce the use of pain medication in labor.[98] Numerous trials have been done in China with similar conclusions; however, the quality of these trials has not always met standards for inclusion in meta-analyses. According to the results of a systematic review by Lee and Ernst, three RCTs were identified, and their methodologic quality was generally good. Two RCTs compared adjunctive acupuncture with usual care only and reported a reduction of meperidine and/or epidural analgesia. One placebo acupuncture controlled trial showed a statistically significant difference in both subjective and objective outcome measures of pain. No adverse events were reported in any of the trials. The reviews concluded that the evidence for acupuncture as an adjunct to conventional pain control during labor is promising; however, they commented on the paucity of research upon which to assert a definitive conclusions.[99] Whether acupuncture in combination with other forms of nonpharmacologic support, for example, continuous labor support, massage, positional changes, and so forth, would be more effective than acupuncture used alone has not been evaluated.

HYPNOSIS

Two studies on the effects of hypnosis on pain in labor were identified. In one study, 82 first-time low-risk mothers were randomized to attend routine weekly prenatal classes plus individual hypnosis sessions focusing on relaxation and pain relief, or prenatal classes alone. Based on a linear analog scale, no significant difference in subjective reporting of pain relief was reported between the groups and there was no difference in rate of pharmacologic pain medication used in labor.[100] In a 1975 study, 60 primiparous women were randomly assigned

TABLE **16-3**

Herbs for Pain Relief in Labor

HERB	USE IN LABOR/EFFECT	CAUTIONS	FORM/DOSE FOR LABOR
Black cohosh (*Actaea racemosa*)	Relieve spastic uterine contractions; relieve lower back pain; relieve leg pain; general musculoskeletal relaxant	Concerns have recently been raised about the hepatotoxicity of black cohosh*; the actual risk has not been determined	Tincture 2 mL repeated every 15 to 60 minutes, up to 6 doses total in 24 hours, not to exceed 2 days use
California poppy (*Eschscholzia californica*)	Promote sleep	Sedating at excessively high doses	Tincture 1 to 2 mL repeated every 30 to 60 minutes, up to 6 doses total in 24 hours
Cannabis† (*Cannabis* spp.)	Relieve sensation of uterine pain; promote deep relaxation; relieve anxiety; general musculoskeletal relaxant; promote appetite	Not legally available; risk of positive drug test; risk of adulteration or contamination of product with harmful drugs; paranoia or increased anxiety in mother	Tincture; smoked in ''pin joint'' (very thin marijuana cigarette), 1 to 2 puffs as needed
Cramp bark (*Viburnum opulus*)	Relieve spastic uterine contractions; relieve lower back pain, general musculoskeletal relaxant	No expected adverse effects; possible mild hypotensive effects with large or repeated doses	Tincture 2 to 3 mL repeated every 15 to 60 minutes, up to 15 in 24 hours; not to exceed 2 consecutive days
Hops (*Humulus lupulus*)	Sedating; promotes sleep	Can be strongly sedating at higher doses; not recommended in patients with severe depression	Tincture 1 to 2 mL every 1 to 2 hours, up to 8 mL in 24 hours
Motherwort (*Leonurus cardiaca*)	Relieve spastic uterine contractions; relieve anxiety	No expected adverse effects	Tincture 1 to 3 mL repeated every 30 to 60 minutes, up to 15 mL in 24 hours
Passion flower (*Passiflora incarnata*)	Relieve anxiety, promote rest/sleep	No expected adverse effects	Tincture 1 to 3 mL repeated every 30 to 60 minutes, up to 15 mL in 24 hours

*See Plant Profiles: Black cohosh for a discussion of safety and possible hepatotoxicity.
†Because of illegality, this herb is not recommended for use unless under medical prescription.

to either hypnosis induction classes or relaxation and breathing exercise during childbirth classes. Ischemic pain thresholds were measured prior to labor and during labor with a standardized pain questionnaire. Women in the hypnosis group received less pain medication in labor than the control group.[97] Hypnotherapy is not widely used by midwives unless women have specific deep-seated fears about labor or past experiences that block effective preparation.

The Postpartum

Aviva Romm

17 CHAPTER

POSTPARTUM CARE OF THE MOTHER

On Crete, right after a baby is born, it is given chamomile tea. The mother's breasts and nipples are washed with chamomile tea before she nurses. When visitors come to the hospital to see the new baby, the first question they asked is ''has she/he drunk the chamomile yet?'' The tea is considered the perfect thing for both mother and child after the excitement of labor. Once the baby had had its first chamomile, it is a huge relief to everyone because it is a sign that they are healthy and now part of the clan. In the hospital near the village I live in part of the year, there is a special room for brewing chamomile for the new mothers and babies.[1]

—Patricia Kyritsi Howell, Herbalist

WHAT IS THE POSTPARTUM?

The postpartum (*puerperium*) is defined as the 6-week period of time beginning immediately after birth, during which the reproductive organs and maternal physiology return toward the pre-pregnant state. Catabolic processes cause the uterus to rapidly return from a weight of approximately 1000 g at the time of birth to approximately 50 g by the third postpartum week, through a process called involution. Although the vagina does not return entirely to its pre-pregnancy state, vaginal and pelvic tissue normally regains most of its pre-pregnant tone. The cardiovascular system likewise returns to its pre-pregnant level of vascular resistance and volume. Because of all of these changes in tissue size and fluid levels, women in the immediate week after birth experience marked diaphoresis and diuresis, accompanied by dramatic weight loss. In addition to these changes, women normally experience vaginal bleeding, the lochia, which begins as a menstrual-like discharge in the hours after birth, and tapers to a pale, thin, or mucousy fluid by three weeks after birth. Many women normally experience some lochial flow for up to 6 weeks or so postpartum. During the puerperium, women who choose to breastfeed also experience the physical changes (e.g., breast changes) that accompany lactation, whereas those who do not experience gradual drying of their milk supply with diminished breast engorgement over the first few postpartum days. Most women experience disturbance of sleep rhythm and regularity as a result of tending to their newborn, and emotional fluctuations as a result of hormonal and psychoemotional adjustments (see Postpartum Depression).

REDEFINING POSTPARTUM IN A WOMAN-CENTERED WAY

Many consider 6 weeks to be an arbitrary and terribly limited definition of time allocated for the postpartum, recognizing that it takes much longer than 6 weeks to fully physically and emotionally recover from the demands placed on a woman by pregnancy and birth, and much longer than this to adjust to the demands of motherhood. The postpartum is a time of enormous physical, emotional, psychological, and social change, whether associated with the birth of a first child or subsequent children. The adjustments are potentially much more difficult if there have been complications or loss associated with the birth. Each passage through birth and into motherhood is a journey into the unknown, with new hopes, fears, expectations, and demands. Although newborns are doted with kisses, praise, and gifts, most women receive little special attention and nurturing during this time, leaving many new mothers stressed, exhausted, or overwhelmed. The fact that women are no longer considered obstetric patients after 6 weeks also reflects the belief that women are expected to be physically recovered enough to resume their previous responsibilities. Defining the postpartum as a finite period of 6 weeks leads many new mothers to feel as if they are taking too long to ''get it together,'' or that they are overwhelmed by something that just should not be such a big deal.

Societal expectations also revolve around this arbitrarily allotted 6-week period. Many employers expect

BOX 17-1

Basic Needs of the New Mother

- Time to focus on the newborn and older children
- A good listener, and confidentially
- To feel protected, honored, and nurtured
- Reassurance that they are doing a good job
- Noncritical support and advice
- Praise and encouragement
- To have complaints and concerns taken seriously by family and care providers
- Time-out now and then for a bath, a shower, or a quiet moment
- Ample, healthy food
- Adequate rest
- Respect for their emotions

women to be back to work after 6 weeks; obstetricians' and midwives care packages end at 6 weeks; and even husbands, other relatives, and friends expect mom to be able to cope on her own by then. Yet most women, when given the opportunity to express their feelings about their postpartum experience say that they needed more help, support, care, guidance, and understanding than they received, and for much longer than 6 weeks after birth (Box 17-1). Most mothers say that they don't really begin to feel like their old selves for at least 6 to 8 months after birth, and many never feel quite like their old selves again. Most admit that they had feelings of profound joy as well as stress, anxiety, and confusion during those early days, weeks, and months of becoming a mother.

Postpartum women experience a significant rate of physical health problems; however, little attention has been given to research in this area beyond recent research into postpartum depression.[1,2] Substantial postpartum morbidity is known to exist and this is not routinely assessed as the postnatal assessment.[3] In a study of 11,701 postpartum women, nearly half had health problems within 3 months after the birth that continued for more than 6 weeks, and that they had never experienced before. The symptoms of ill health that they confronted sometimes lasted for months or years afterward, and many of them never told their doctors about their problems.[2] In general, the cursory nature of postnatal care does not facilitate the intimacy required for women to express the nature of their physical complaints, and thus most obstetricians have not recognized the extent to which postpartum women experience health complaints. Interestingly, recent studies have questioned the effectiveness of postpartum medical visits in meeting the postpartum health needs of mothers, and have concluded that ''the present six week postnatal examination does not appear to meet the health needs of women after childbirth: its content and timing should be reviewed.''[3]

Postpartum visits should focus on the challenges women face during this time, and should provide women with the opportunity to express their concerns and expectations, both physically and emotionally. In *Reactions to Motherhood: The Role of Post-Natal Care*, midwife Jean A. Ball states:

> *The main focus of postnatal care has traditionally been that of ensuring the physical recovery of the mother from the effects of pregnancy and labor and establishing infant feeding patterns.... The emotional and psychological needs of mothers have not received much attention until recently and there has been an assumption that these needs will automatically be met if the first two aspects of care are satisfied. The organization of postnatal care has accordingly been based upon this premise.*[4]

According to a study by Buchart et al., ''Listening to women is an essential element in the provision of flexible and responsive postnatal care that meets the felt needs of women and their families.''[5] By developing an open dialogue with women during pregnancy, care providers can help women to realistically prepare for the postpartum prior to birth, and overcome difficulties that might be inhibiting their recovery as well as their experience of motherhood. This chapter highlights the need for extensive family and social support for the mother after birth in the prevention of this potentially devastating problem. It must be recognized, however, that the need for such support is not limited to the prevention of PPD, but for the promotion of the overall wellness of the new mother, and by extension, her child and family. Indeed, many postpartum difficulties can be averted with adequate postpartum support of the mother, both from her immediate personal community (family, friends, coworkers, etc.) and from her health care providers.

Increasingly, the postpartum doula is becoming an important figure in the postpartum care of new mothers. In the United States, doula services are privately hired; however, in many European countries, postpartum visiting nurses are a common part of routine obstetric care. Beginning in the mid-1980s in the United States, postpartum mother care services, which now routinely employ certified doulas, began cropping up in major cities around the United States, providing in-home help and giving new mothers no-medical assistance and advice on such matters as breastfeeding and newborn care.

Unfortunately, the cost of such services is prohibitive to most. Optimally, doula care should be incorporated into maternal care services, as postpartum support has definitely been demonstrated to reduce postpartum morbidity, especially associated with depression (see Postpartum Depression).

THE USE OF HERBS FOR POSTPARTUM CARE

The use of medicinal herbs has been an intrinsic part of postpartum care in cultures throughout the world. Herbal teas and other preparations are given for a variety of reasons, including preventing infection, treating colic, and nourishing the mother and child. Herbs have been used both internally and topically to reduce bleeding, ease pain from cramping, increase breast milk production, heal and soothe the perineal area, and relax

the mother.[6–10] References to traditional herb use after birth abound in historical and sociological references, although the ethnobotany is often not specific. For example, women in Thailand have been known to drink a mixture of tamarind, salt, and water to ''strengthen the womb,'' whereas women of the Seri Indian tribe of Mexico drank ''seep willow tea'' to ''stop bleeding after birth.''[11] The Jicarillo women chewed the root of wild geranium to assist in ''expelling uterine blood.''[11] Herb use was common in Colombia and Jamaica, as it was in Southeast Asia.[12] In Burma, a paste of tumeric is rubbed onto the body to prevent blood stasis and encourage good circulation while expelling the afterbirth blood.[12] In Micronesia, women are given baths of tumeric paste after birth.[1] In both Ayurvedic and traditional Chinese medicine, herbs are a routine aspect of postpartum care, and have been for thousands of years.

There is little evidence on the number of women in the United States using herbs for postpartum complaints; however, it is likely consistent with the volume of herb use during pregnancy, or slightly higher, as the use of herbal teas for increasing lactation is very popular, and women and care providers are often less hesitant to use herbs outside of pregnancy. Numerous articles appearing in nursing, medical, and midwifery journals describe the use of herbs for postpartum care.[6–10] Chapters 12 and 18 discuss the safety of herb use during lactation. The remainder of this chapter presents information on treatments for common postpartum problems.

COMMON POSTPARTUM COMPLAINTS

After birth women experience a number of common physiologic changes that can lead to discomfort (e.g., sweating, engorged breasts, after birth pains), problems resulting from pregnancy or birth (e.g., hemorrhoids), and discomforts associated with breastfeeding (e.g., engorgement, sore nipples). Hemorrhoids are discussed in Chapter 5, and problems associated with lactation in Chapter 18.

After Pains

After pains are associated with the normal process of uterine involution—the return of the uterus to its pre-pregnant size. Involution involves the clamping down of the uterine myometrium, a process that is accompanied by menstrual cramp–like pain that varies from mild to very severe. Many women turn to nonsteroidal anti-inflammatory medications (NSAIDs) such as ibuprofen to relieve the discomfort, whereas others, preferring not to use pharmaceuticals while breastfeeding, turn to herbs. Herbs such as cramp bark (*Viburnum opulus*), black haw (*Viburnum prunifolium*), and motherwort (*Leonurus cardiaca*) are excellent choices as they are both antispasmodic and uterotonic.[13,14] This is important as uterine laxity might actually exacerbate the contractions as the uterus tries to involute. The herbs facilitate the physiologic process while providing relief of cramping and possibly, with the viburnums, mild analgesia. Simple teas such as catnip (*Nepeta cataria*) and chamomile (*Matricaria recutita*) have empirically been shown to be effective as teas, when combined with the preceding tinctures, providing and apparently synergistic effect when used together.[15] for mild cramping with tinctures of cramp bark, black haw, and/or motherwort added for severe discomfort.

A popular treatment among independent midwives for the relief of after pains, and for supporting recovery of the pelvic organs and ''qi'' of the body after childbirth is the use of the traditional Chinese medicine practice of moxibustion (Box 17-2). This technique, previously discussed for turning a breech baby when applied to acupuncture points on the small toe, is applied to the lower back and abdominal area over the uterus to warm the mother, reduced pain, and support involution. It is repeated once or twice daily, for 30 minutes, for the first week after birth, usually starting on day 2 or 3 postpartum.

Note that abdominal pain, especially if accompanied by fever or foul smelling vaginal discharge can be symptomatic of endometritis, a potentially life-threatening uterine infection requiring immediate antibiotics.

POSTPARTUM DEPRESSION

> *Postpartum depression is a crippling mood disorder, historically neglected in health care, leaving mothers to suffer in fear, confusion, and silence. Undiagnosed it can adversely affect the mother–infant relationship and lead to long-term emotional problems for the child. I have described it as 'a thief that steals motherhood.'*[16]
>
> **—Cheryl Tatano Beck**

Postpartum depression (PPD) is a potentially devastating mood disorder thought to affect approximately 15% but as many as 28% of new mothers, with an estimated 400,000 women suffering from this condition annually. Twenty-five percent of these women are likely to develop PPD in the first 3 months postpartum and 25% of these women are at increased risk of developing severe, chronic depression. PPD generally has a slow and insidious onset, beginning at 2 to 3 weeks postpartum; however, it can occur anytime in the first year postpartum, and may last up to a year or longer. Symptoms of PPD include irritability, depression, guilt, hopelessness, chronic exhaustion, despair, feelings of inadequacy, insomnia, agitation, loss of normal interests, joylessness, difficulty relaxing or concentrating, memory loss, confusion, inability to function, emotional numbness, inability to cope, irrational concern with baby's well-being, and thoughts of hurting oneself or baby (Box 17-3). Women with postpartum depression may become obsessed by the terrifying feeling that their depression and anxiety are interminable. They may feel extremely detached from their family, including husband, baby, and other children. They may be plagued by fear of hurting the baby, causing them panic and anxiety, leading them to distance themselves from the baby, and exacerbating feelings of inadequacy as a mother; thus, it has been described as ''a thief that steals motherhood.''[16,17]

Despite multiple visits to care providers in the postpartum period, postpartum depression often goes unrecognized by the obstetrician or midwife, with symptoms of

BOX **17-2**

Moxibustion for Essential Postpartum Care

In traditional Chinese medicine (TCM), heat is a significant part of healing for the woman who has recently given birth. One of the three major factors considered important for the health of postpartum women is ''sparing the exterior,'' which means protecting against wind and avoiding cold drafts. Childbirth is thought to deplete what is called the wei chi. The wei chi is the body's protective immune capacity, specifically found on the surface of the body and in the lungs. Special herbs are given to protect the woman and nourish the wei chi, and the woman is expected to remain indoors for one month after birth.

There is an area of the body known as the Ming Men. This literally translates as Life Gate, or Life Gate Fire, and correlates to the TCM concept of the kidneys, which are said to govern the functions of reproduction, sexuality, growth, and decline. It also controls the relaxation of the pelvis, which allows the baby to be born. Rest and heat are the two cardinal factors that facilitate proper closure of the Life Gate. Incomplete recovery is believed to lead to later chronic health problems and general weakness, which may become worse with each successive birth. Heat treatments, in the form of moxibustion, may be added to the postpartum care routine, to ensure optimal recovery.

Moxa is Chinese mugwort (folium *Artemisia argyria*), traditionally used internally for the treatment of gynecologic problems. For external use, it comes in the form of a rolled stick, much like a cigar, but completely covered by a fine linen paper. The end of this stick, when lit and held close to the skin, sends a deep, penetrating warmth in to area. The technique of moxibustion was featured in an article in the *Journal of the American Medical Association* (November 11, 1998), in which researchers concluded that the technique is reliable for turning babies from the breech to the head down position. No research has yet been published on its use for postpartum care, but midwives who incorporate this technique into their clinical practices, and mothers who have received this technique, can attest to its value.

To Give a Moxibustion Treatment

1. Have the mother lie in a comfortable position on her side or belly. Use pillows to support her if her breasts are sore or enlarged from breast feeding. Make sure the room is warm.
2. Provide some ventilation, but do not allow the mother to receive a chill or draft. A window may be slightly open on the opposite side of the room, or use ''little smoke'' moxa in cold weather. It is more difficult to light but does not emit as much smoke.
3. Peel the outer paper wrapper off of the moxa stick. Light the moxa stick with the inner paper left on it. Blow on the end until it is a burning ember. Roll off any excess ash in an ashtray or dish until the tip of the moxa becomes slightly cone shaped.
4. The area on the body you want to treat extends over the sacrum on the back, and the area from just above the pubic bone on the front to about an inch below the navel to 3 inches on either side of the midline of the lower abdomen.
5. Holding the moxa stick 1 to 2 inches over the correct area, begin to move the stick in tiny circles about 2 inches in diameter, until the area becomes warm and slightly pink. Then move to an adjacent spot until the whole area has been treated. Do not touch the mother with the moxa, and periodically knock ashes off into your ashtray or dish to prevent them from falling on her. Do not treat the point of burning or stinging pain, and instruct the mother to tell you if any area is becoming too hot.
6. Continue treating the back for 15 minutes, then ''massage the heat inward'' for several minutes before proceeding to treat the abdomen.
7. A woman may give herself a moxa treatment on the abdomen if none are available to do the treatment on her back.
8. To extinguish the moxa, place it upside down into a small dish of sand, run the tip until water until not lit, or use a specially made moxa extinguisher. Use fire safety precautions when treating with moxa.
9. Begin treatments the first day after birth, and continue daily for 1 to 2 weeks.

depression commonly dismissed as ''just the baby blues'' leaving women in need of treatment and care with none, and prolonging the terrible desperation they feel without an explanation.[16,18–20] Undiagnosed PPD can adversely affect the mother–infant relationship and lead to long-term emotional consequences for both.[16] For most women, a diagnosis of postpartum depression comes as a welcome relief—putting their experience into the context of an explainable illness for which there is treatment. It can provide a framework that helps them, as well as their family, begin to make sense of what is happening. It is essential that care providers learn to

BOX 17-3

Symptoms of Postpartum Depression

Agitation
Anxiety or panic attacks
Chronic exhaustion
Clumsiness
Confusion
Decreased appetite or extreme cravings
Depression
Despair
Difficulty relaxing or concentrating
Emotional numbness
Fear
Feelings of inadequacy
Frequent crying or inability to cry
Guilt
Hopelessness
Inability to cope
Inability to function
Insomnia
Irrational overconcern with baby's well-being
Irritability
Joylessness
Lack of attention to appearance
Loneliness
Loss of normal interests
Memory loss
Mood swings
Nightmares
Thoughts of hurting oneself or baby
Withdrawal from social contacts

recognize the many symptoms and manifestations of PPD to ensure that it is recognized and that women receive adequate support and treatment.[21]

ETIOLOGY AND RISK FACTORS FOR PPD

Despite its prevalence, the etiology of PPD remains unknown.[22] Smokers are at increased risk for PPD.[23] In a survey of 574 women in Ontario, of whom 9.9% were diagnosed with PPD, there was a higher rate of PPD among women with a prior history of depression, among women whose pregnancy was unplanned, among those who described the course of pregnancy as ''difficult,'' and among women who described their general health as ''not good.''[24] Women with a history of premenstrual dysphonic disorder (PMDD) may also be at increased risk.[25] Breastfeeding mothers may be significantly less likely to develop postpartum depression than non-breastfeeding mothers, and breastfeeding may have unknown protective biological factors against PPD.[23,26,27] A recent revision of the predictive factors for PPD lists prenatal depression, child care stress, life stress, lack of social/marital support, prenatal anxiety, low marital satisfaction/poor relationship, history of depression, a difficult infant temperament, maternity blues, low self-esteem, low socioeconomic status, single motherhood, and unplanned/unwanted pregnancy as the most important risk factors for PPD.[28–33]

Many hormones have been investigated for their possible causative roles, and PPD is commonly attributed to the rapid change in hormones in the postpartum period; however, the role of hormones in PPD remains inconclusive.[22,34] PPD has also been attributed to thyroid insufficiency (hypothyroidism), which is commonly found in the 2 to 5 months after birth. Recent research suggests that the abrupt physiologic drop in insulin levels that occurs during the postpartum period after the slow rise throughout pregnancy may induce mood disorders by affecting serotonin secretion in the brain. Low blood sugar can also have a dramatic effect on mood; therefore, postpartum women must ensure adequate caloric intake through a well-balanced diet to minimize the risk of depression resulting from hypoglycemia. It has been suggested that a carbohydrate-rich diet in the postpartum period may be a preventative or adjunctive treatment of postpartum mood disorders.[22] Inadequate intake of essential fatty acids, protein, B vitamins, zinc, and iron also have been associated with PPD. Women who have experienced significant blood loss at birth may be predisposed to depression caused by anemia and its accompanying increased fatigue, tendency to infection. Fatigue also appears to be highly correlated with PPD, especially persistent fatigue occurring by day 14 postpartum.[35]

Lack of social and emotional support during pregnancy, the labor and birth, and in the postpartum period have all been associated with an increased risk of developing PPD. One PPD study found that poor support with newborn care showed a positive correlation with PPD, whereas affiliation with a secular group was a positive preventative factor.[36] A study looking at the impact of a supportive partner in the treatment of PPD found a significant decrease in depressive symptoms in the group where the partner provided the mother with significant support, whereas another discovered that women with postpartum depression ''reported less practical and emotional support from their partners and saw themselves as having less social support overall.''[37] Clearly, adequate social support is an important variable in preventing postpartum depression. Even a therapist can lead to significant improvement in PPD. In one study, interpersonal psychotherapy was demonstrated to reduce depressive symptoms, improve adjustment, and was shown to be an alternative to drug therapy, especially for breastfeeding mothers.[38] It is important for women who are experiencing extreme or prolonged symptoms to seek help.

A study conducted in Switzerland found that among the most significant risk factors for postpartum depression are social or professional difficulties, deleterious life events, early mother–child separation, and negative birth experience.[39] Birth experience may have a dramatic impact on a woman's self-perception as she enters motherhood, yet is generally overlooked. Assisted delivery (cesarean, forceps, and vacuum extraction) may be associated with higher rates of postnatal depression, as are bottle-feeding, dissatisfaction with prenatal care, having unwanted people present at the birth, and lacking confidence to care for the baby themselves after they

leave the hospital.[40,41] A study by Edwards et al. indicated that there is an increase in rates of postpartum depression among women who have had cesarean sections, a finding that women themselves report.[42,43] Although this finding has been debated, clinical experience suggests that disappointment in the birth experience effect a new mother's self-confidence. Considering that 25% to 40% of American women now deliver by cesarean section, this certainly illuminates the need to both reduce cesarean rates and provide counseling and support for those women who have birthed operatively. Furthermore, one study indicates that women who were cared for by midwives had lower rates of depression in the postnatal period, whereas another study revealed a significantly lower rate of depression among the women who had given birth at home compared with hospital vaginal delivery.[44] Women reported that a sense of control and being informed about choices in their health care greatly improved their psychological state.

Few women experience all of the symptoms of PPD; some may exhibit only a few, some many. It is the duration, severity, and complexity of the symptoms that distinguishes postpartum depression from the common and normally occurring ''baby blues,'' which occurs in 50% to 70% of new mothers. Baby blues is thought to be a result of normal postnatal hormonal and other physiologic adjustments, and is self-limiting, usually beginning at about day 3 or 4 postpartum and lasting only up to about 14 days.[45] Symptoms include crying, irritability, fatigue, anxiety, and emotional lability.[16] Further, the baby blues tends to be punctuated by periods of elation, whereas postpartum depression lacks the elation and the periods of depression are more intense and prolonged. Women with baby blues require support and reassurance but no treatment is necessary, although attention to nutrition, sleep, and support are essential. If symptoms persist past 2 weeks, depression should be ruled out.

Postpartum psychosis is an extreme postpartum mood disorder, occurring in 1% to 2% per 1000 new mothers, usually having its onset a few weeks but up to 3 months after birth, occurring most often in primiparas, and being more likely to require hospitalization for treatment. Other mood disorders than can occur in the postpartum period include panic attacks, postpartum obsessive-compulsive disorder, postpartum traumatic stress disorder, and postpartum bipolar disorder.[16]

Any woman experiencing extreme depression, suicidal thoughts, or thoughts of harming her baby requires immediate professional help through her physician, an emergency hotline, or the local emergency room. Early identification and treatment of postpartum depression can decrease the duration and consequences of the condition for a woman and her family.

PREVENTION OF PPD

Many care providers are afraid to talk to women prenatally about postpartum depression, thinking it might frighten them. In fact, a woman will be better prepared to recognize the need for help and get it if she is informed that this could happen ahead of time. According to Jane Honikman, founder of Postpartum Support International, ''Ignorance and denial are the two greatest barriers to this problem.''[1] Many women enter pregnancy and become mothers with an unrealistic and romanticized picture of motherhood. There are also tremendous social pressures on women to conform to the image of being happy and grateful. Yet, new motherhood can also bring fatigue, feelings of being overwhelmed and inadequate, a sense of social isolation for women who have abandoned previous social or work activities to be home with the baby, and body image issues as a result of changes that occurred during pregnancy and accompanying lactation. Social pressures on mothers strongly contribute to many mothers' sense of inadequacy—leaving them feeling that ''everyone else does it better than I do, and is happy, why can't I?'' Single mothers face additional burdens, concerns, and fears unique to the task of raising a baby alone.

Talking about postpartum depression before birth can actually have a positive impact on reducing depression because it can help a mother develop realistic goals and expectations for herself for after the birth, and recognize the need to establish a support network for herself if she is not part of an actively supportive family or community. The need for family and community support, especially for women at risk for PPD, but for all new mothers, cannot be overestimated, and should be planned prior to the birth. The new mother's ability to get adequate rest, proper and ample nourishment, social interaction, time for self-care, support with breastfeeding, and access to a women skilled in newborn care and the needs of the new mother, for example, a doula, who can answer questions and reassure her should be established prior to birth. Women with a history of PPMD, depression, or previous episodes of postpartum depression after prior births, special care should be taken to assure support and even postpartum psychological or psychiatric care, and preventative measures taken during pregnancy to optimize nutrition, as this may help to allay symptoms (see Nutritional Considerations).

CONVENTIONAL TREATMENT APPROACHES

The biggest problem with treatment for postpartum depression is the uncertainty about causative factors. There is no consensus on the use of hormonal therapy in the treatment of PPD.[34] The safety of maternal use of psychotropic medications while breastfeeding is controversial. In 2001, expert consensus guidelines for the treatment of depression in women were published. The expert panel concluded that few studies published evaluate pharmacologic or nonpharmacologic treatments for PPD. Antidepressant medications and psychosocial interventions were recommended as first-line treatments regardless of the mother's breastfeeding status, with the exception of treatment of minor depression, for which the use of antidepressants was considered warranted only if the woman was not breastfeeding. A 2001 comprehensive review by Burt and colleagues that looked at the use of psychotropic medication in breastfeeding women since 1955 found no controlled studies evaluating safety.[46] In contrast, Hale suggests that many of these

drugs are well-studied and safe, although demonstrates that most do enter breast milk in varying quantities and may cause side effects in the infant, including sedation, somnolence, respiratory arrest, colic, jitteriness, and withdrawal.[47]

There is emerging data suggesting risk of antidepressants to the infants of nursing mothers using SSRIs; therefore, it is essential that a careful plan of treatment be considered for mothers committed to breastfeeding. Chambers et al. identified an association between maternal selective serotonin reuptake inhibitors (SSRIs) use in late pregnancy and persistent pulmonary hypertension (PPH) in the newborn. The authors stated, ''Although our study cannot establish causality, several possible mechanisms suggest a casual association is possible.''[48] Another physician writes:

> *Any drug that affects infant growth, in or ex utero, should be regarded with suspicion and should not be written up as a recommendable solution for postpartum depression, comparable with innocuous and effective methods such as psychotherapy, nurse home visits, and group therapy. The available evidence indicates that even when infant serum levels are low or undetectable, side effects may occur. There is an ample body of evidence that SSRIs taken during pregnancy cause neonates to suffer withdrawal symptoms, which all by itself is a matter for concern. Postpartum depression is an issue that should not be taken lightly, but, as history shows, the short-term benefits of drugs that have not been sufficiently studied do not weigh up against the tragic long-term disasters they might provoke.*[49]

Unfortunately, because untreated PPD can have significant and long-term consequences for mother, child, and family, a careful risk–benefit comparison must be done for use of medication versus nonpharmacologic treatment. In cases of severe PPD, medication may be unavoidable.

Nonpharmacologic treatments for PPD can be effective primary treatments depending upon the severity of symptoms and the woman's ability to comply, and can be used in conjunction with pharmacotherapy. Nonpharmacologic treatments include psychosocial supports, psychotherapy (individual and/or couple), group therapy, and/or medications. Attention to nutrition, fluid, sleep, and social support status, are essential.[34] Many women turn to alternative therapies for PPD, concerned about the risk of pharmacotherapy while nursing. Alternative therapies can constitute part of effective adjunct treatment for PPD.[50] Therapies to consider include nutritional and herbal supplements, aromatherapy, acupuncture, and both maternal and infant massage. These are discussed under Nutritional Considerations and Additional Therapies.

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

PPD is a complex condition because of its multifactorial causes. Although herbs can be tremendously beneficial, effective treatment depends on a holistic approach that includes the most appropriate choice of herbs in conjunction with nutritional, social, and psychological interventions. The impact of PPD on the mother, infant, and family should not be minimized, and medical interventions should be sought in severe cases, and even in milder cases if botanical therapies are not effective. It is difficult to know how much time to allot to determine whether herbs are bringing adequate improvement because they can take several weeks to make a noticeable impact. However, this is also the case with psychotropic drugs. It is essential that the practitioner remain in regular contact with the patient, and continually evaluate her status and progress to ascertain whether treatment is effective or it is necessary to use other interventions.

Herbal remedies are the primary pharmacologic therapy for the treatment of depression in many European countries, and are increasingly being recognized in the United States as safe and effective alternatives to many psychotherapeutic medications for mild to moderate depression and anxiety (Table 17-1). Herbs such as St. John's wort, kava kava, lavender, lemon balm, passion flower, and valerian have been used in the treatment of a number of mood disorders including depression, anxiety, restlessness, insomnia, and irritability.[51,52] Herbs, such as many adaptogens, can also be used to treat fatigue, nervous exhaustion, hormonal dysregulation, and blood sugar dysregulation. Unfortunately, almost no studies have been conducted on the safety and efficacy of herbs for the treatment of postpartum depression, or the safe use of herbs during lactation.

The application of herbs for the treatment of postpartum depression is largely extrapolated from traditional herbal treatments for general depression. The use of adaptogens in this context is predicated on their marked ability to improve the stress response, and via the HPA axis, to regulate cortisol and blood sugar levels, an important adaptation during times of increased and prolonged stress, as new motherhood is for many, and especially so for those at risk of PPD. Safety is an important concern when herbs are to be applied prophylactically during pregnancy for women with a history of PPD, and during lactation, especially for a prolonged period as is often necessary with PPD. Table 17-2 ranks these herbs according to the scale developed by Hale (Table 17-3) for the evaluation of drugs for the treatment of PPD during lactation and modified by this author for relevance to herbal medicine. When there is a history of previous PPD, it is best to focus on preventive nutritional strategies during pregnancy, as well as ensuring that proper social supports are in place, and reserving the use of herbs to the postpartum period for optimal safety to the fetus. Nutritional and social/psychological strategies can be continued postnatally, and herbal interventions begun immediately after birth with a history of PPD, or even prophylactically for a woman with significant risk factors for developing PPD. In women with no history or risk factors, or who present at their first appointment with symptoms, herbs can be started as needed.

Adaptogens

The role of adaptogens in improving stress resistance and response is extensively discussed in Chapter 6. No studies have been conducted on the use of these herbs for PPD; however, they are widely used by herbalists for the

TABLE 17-1

Botanical Treatment Strategies for Postpartum Depression

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Improve the stress response	Adaptogen		
Support and nourish the nervous system	Nervine tonic	*Withania somnifera*	Ashwagandha
		Panax quinquefolius	American Ginseng
		Verbena officinalis	Blue vervain
		Eleutherococcus senticocosus	Eleuthero
		Panax ginseng	Ginseng
		Avena sativa	Milky oats
		Hypericum perforatum	St. John's wort
Improve general relaxation and relieve stress	Nervine relaxant	*Verbena officinalis*	Blue vervain
		Matricaria recutita	Chamomile
		Lavandula officinalis	Lavender
		Melissa officinalis	Lemon balm
		Tilea spp.	Linden
		Avena sativa	Milky oats
		Leonurus cardiaca	Motherwort
		Passiflora incarnata	Passion flower
		Scutellaria lateriflora	Skullcap
Reduce anxiety	Anxiolytic	*Matricaria recutita*	Chamomile
		Piper methysticum	Kava kava
		Leonurus cardiaca	Motherwort
		Passiflora incarnata	Passion flower
		Hypericum perforatum	St. John's wort
		Valeriana officinalis	Valerian
		Zizyphus spinosa	Zizyphus
Alleviate depression	Antidepressant	*Eleutherococcus senticosus*	Eleuthero
		Panax ginseng	Ginseng
		Piper methysticum	Kava kava
		Rosmarinus officinalis	Rosemary
		Hypericum perforatum	St. John's wort
Promote sleep, relieve insomnia	Sedative	*Withania somnifera*	Ashwagandha
		Eschscholzia californica	California poppy
		Matricaria recutita	Chamomile
		Lavandula officinalis	Lavender
		Melissa officinalis	Lemon balm
		Passiflora incarnata	Passion flower
		Scutellaria lateriflora	Skullcap
		Valeriana officinalis	Valerian
Support steady hormonal states	Hormonal regulator	*Angelica archangelica*	Dong quai
		Paeonia lateriflora	Peony
		Vitex agnus-castus	Chaste berry
Build energy and stamina	Blood tonic	*Angelica sinensis*	Dong quai
		Panax ginseng	Ginseng
		Urtica dioica	Nettle
		Peony lactiflora	Peony
			Polygonum multiflorum
		Rehmannia glutinosa	Rehmannia
		Schisandra chinensis	Schisandra

treatment of general depression and no adverse effects are expected from their use during lactation. Use during pregnancy is generally not recommended. Women at high risk for developing PPD can begin the use of adaptogens in the days or weeks after birth to improve the ability to handle stress, withstand sleep deprivation, and also to improve nonspecific resistance. Ashwagandha may have anxiolytic activity.[53] Schisandra is used to calm the spirit, for insomnia, palpitations, and poor memory. Contradictory information exists on its safety in pregnancy. It is generally contraindicated in pregnancy owing to its potential for increasing uterine contractions.

TABLE 17-2

Safety of Herbs for PPD during Pregnancy and Lactation

HERB	RISK CATEGORY DURING LACTATION*	RISK DURING PREGNANCY†
American ginseng	See ginseng	
Ashwagandha	L1	B1
Blue vervain	No data	Unknown
California poppy	L2/L3	B2
Chamomile	L1/L2	A
Chaste berry	L2	B1
Dong quai	L2/L3	C
Eleuthero	See ginseng	
Ginseng	L1/L2	A
Kava kava	L3–L5	B1
Lavender	L1/L1	B2
Lemon balm	L1/L2	B2
Milky oats	L1/L2	B1
Motherwort	L1/L2	B3
Nettle	L1/L2	B2
Passion flower	L1/L2	B1
Peony	L2/L3	B1
Rosemary	L2	B1
Schisandra	No data	B1
Skullcap	L1/L2	B2
St. John's wort	L2/L3	B1

Data from Blumenthal M: The complete German Commission E monographs: therapeutic guide to herbal medicines, Austin, American Botanical Council, 1998; Mills E, Duguoa J, Perri D, et al.: Herbal Medicines in Pregnancy and Lactation: An Evidence-Based Approach, Boca Raton, Taylor and Francis, 2006; Mills S, Bone K: The Essential Guide to Herbal Safety, St. Louis, Churchill Livingstone, 2005; Basch E, Ulbricht C: Natural Standard Herb and Supplement Reference: Evidence-Based Clinical Reviews, St. Louis, Mosby, 2005.

*See Table 17-3 for ranking scheme.

†See Chapter 13 for Mills and Bone/TGA classification scheme for herb safety during pregnancy.

TABLE 17-3

Lactation Risk Categories

RISK CATEGORY		DESCRIPTION
L1	Safest	No adverse effects observed in infants of lactating mothers Controlled studies demonstrate no increased risk
L2	Safer	Limited studies demonstrate no increased risk Known constituent profile suggests no increased risk Extensive historical/traditional use profile suggests no evidence of risk
L3	Moderately safe	No controlled studies in breastfeeding women or controlled studies demonstrate minimal adverse effects
L4	Possible risk	Positive evidence of risk, but benefits may make risk acceptable
L5	Contraindicated	Significant documented risk Significant potential for risk based on known constituent profile

Adapted from Hale T: Medications and Mother's Milk: A Manual of Lactation Pharmacology, 10 ed. Amarillo, Pharmasoft Publishing, 2002.

However, no adverse effects on the fetus have been observed with maternal use, and in fact, some studies have demonstrated increased fetal weight and improved birth outcome with use of adaptogens. Although these herbs are considered compatible with lactation, it is best to avoid their use during pregnancy owing to inconclusive evidence of safety.[54]

Nervine Relaxants, Sedatives, Tonics, and Anxiolytics

St. John's wort is the most thoroughly studied herb for the treatment of depression. It is the primary medication used for depression in several European countries and it has become a popular alternative to pharmaceutical antidepressant medications in the United States. As of 2002, 34 controlled clinical trials of over 3000 patients have demonstrated the efficacy of this herb for treating mild to moderate depression (see Plant Profiles).[57] No studies have evaluated the herbs for either efficacy or safety in the treatment of PPD.[50] The herb is not contraindicated for use during pregnancy; however, safety studies are lacking. There is one published case report in which low levels of hyperforin were detected in the breast milk of a woman consuming 300 mg/day; however, no constituents of the herb were detectable in the baby's plasma and no adverse effects were observed in either.[58] Lactation and medication expert Hale states that recent data suggest transfer to milk is minimal and that St. John's wort appears to be safe for use during lactation.[47] Because of its potent ability to induce cytochrome P450 3A4, a major drug-metabolizing enzyme in the liver, St. John's wort is contraindicated with the use of other drugs, including MAOIs and SSRIs.[59]

Kava kava is traditionally used to promote a calm, relaxed mood and as a ceremonial and social drink by Pacific Islanders.[60] It used extensively in Europe and the United States as a treatment for anxiety and insomnia, both of which are associated with PPD.[61] Kava has been shown to improve general relaxation response time.[62] Studies have demonstrated kava to be a highly effective treatment for anxiety.[63] Kava has been shown to be significantly more effective than placebo in clinical trial participants with moderately severe, nonpsychotic

anxiety disorder, perhaps even more effective than benzodiazepines.[64] It has been generally well tolerated at recommended doses, although individuals taking higher doses of kava may experience fatigue, unsteadiness, appearance of intoxication, and skin changes.[64] As of 2000, however, approximately 60 adverse case reports suggesting a link between kava use and liver failure have led to the governments of at least eight countries removing kava from the general market. The German Commission E contraindicates the use of kava during pregnancy and lactation; however, no specific data on pregnancy and lactation exists. Ethnobotanical information suggests that the herb is avoided to maintain fertility and during pregnancy, but information on use during lactation is not reported.[60] Insufficient information on the use of kava during lactation makes it difficult to predict safety. The risk of hepatotoxicity from the herb vs. risks of conventional drugs for anxiety treatment, including addiction and infant sedation or toxicity must be investigated and evaluated.[60] However, until then and in light of recent concerns raised about kava and hepatotoxicity, it is prudent to avoid this herb during lactation. The herb is definitely contraindicated during pregnancy because of possible risk.

Motherwort is perhaps the classic historical herb for postpartum depression, anxiety with palpitations, and stress. The name of the herb itself mother wort—a healing herb for mothers—and its botanical *name Leonurus cardiaca*—heart of a lion—are evocative of its traditional healing uses. Today, the herb finds its way into many gynecologic formulae. It is used as a uterine tonic and antispasmodic, as a bitter to stimulate the liver, as a nervine and sedative, and in the treatment of stress, anxiety, and palpitations, including the latter in the treatment of hyperthyroidism. It is very popular for its perceived ability to modulate irritability and emotional lability. It may possess some hormonal activity, although this has not been thoroughly evaluated. Most of the evidence for this herb remains largely anecdotal.[65] It is approved by the German Commission E for nervous cardiac conditions and as an adjuvant for thyroid hyperfunction.[52] Motherwort is contraindicated in pregnancy but is safe during lactation.

Blue vervain has been used historically as a galactagogue and to treat nervous exhaustion; however, no studies have been done to confirm its efficacy.[52] Limited studies have demonstrated some effects on the endocrine system where it appears to stimulate FSH and LH. It may also have antithyrotropic effects and synergistic effects with prostaglandin E2, although the significance of these effects is unknown beyond possibly contributing to the herb's traditional use as an emmenagogue.[65] The herb is used by herbalists similarly to motherwort for its perceived ability to modulate irritability and emotional lability. It is contraindicated in pregnancy but is safe during lactation.

California poppy is used by herbalists as a mild sedative to promote sleep and reduce nervousness and anxiety in calming but not heavily sedating. It has demonstrated anxiolytic, mild sedative, and hypnotic effects. It should be considered when there is disturbed sleep (see Insomnia) or anxiety (see Anxiety). It was a popular drug in the late 1800s, when it was sold as a pharmaceutical product by Parke-Davis as a soporific (sleep-inducing) and analgesic agent. Extracts of California poppy inhibit catecholamine degradation and epinephrine synthesis. The former activity may be especially responsible for the herb's sedative and antidepressant activities. Sedative, anxiolytic, and muscle relaxant effects have been observed experimentally in animals injected with California poppy extracts. Two controlled clinical trials demonstrated normalization of sleep without carryover effects when combined with corydalis (*Corydalis cava*).[66]

Passion flower is approved by the German Commission for the treatment of nervous restlessness, and recommended by ESCOP for the treatment of tenseness, restlessness, irritability, and difficulty with falling asleep, indications for which herbalists generally prescribe this herb.[52,67] Pharmacodynamic studies and a limited number of clinical trials that have been conducted appear to support its empirical uses as an anxiolytic and sedative herb (see Plant Profiles).[67] Safety during pregnancy is not established; the herb is compatible with lactation.

Skullcap has been used traditionally as a relaxing nervine to support and calm the nervous system, for nervous exhaustion, excitability, irritability, overwork, sleep disorders, depression, and exhaustion from mental strain.[66] There is little pharmacologic or clinical research on this widely used herb, and there has been some controversy in the literature regarding its efficacy. A double-blind, placebo-controlled study of healthy subjects by Wolfson and Hoffmann demonstrated noteworthy anxiolytic effects.[68] Because of potential of adulteration with the hepatotoxic herb germander (*Teucrium chamaedrys*) it is best to avoid this herb during pregnancy; notwithstanding this concern, its use is safe during lactation. Obtaining the herb from a reliable source should largely mitigate the concern of adulteration.

Milky oats, chamomile, lavender, and lemon balm are all pleasant tasting, gentle nervines with a long history of use for the nursing mother, to promote relaxation, ensure ample breast milk, and as treatment both through the mother and directly to the baby for a fussy or colicky baby. They remain common ingredients in many ''mother's milk'' (galactagogue) formulas and are considered safe for use during both pregnancy and lactation. See Plant Profiles for detailed discussions of these herbs.

FORMULAS FOR POSTPARTUM DEPRESSION

The following examples of formulas for the treatment of various PPD symptoms and can be used both by nursing and non-nursing mothers. Formula can be modified for the individual needs of specific patients as required. Additionally, drinking herbal tea is a relaxing ritual for new mothers—a few minutes to sip a cup of hot tea can not only be medicinal but a needed moment for quiet and calm. A cup of hot tea can be taken while nursing or holding the baby, even if mom can't get a moment to herself. Mother's milk tea is a relaxing and delicious favorite of many women.

NUTRITIONAL CONSIDERATIONS

Important nutritional/dietary strategies include improving overall caloric intake through a well-balanced diet, ensuring adequate consumption of complex carbohydrates, and ensuring adequate intake of vitamins and minerals through foods, and supplemented with a multivitamin, mineral supplement for lactating women. Ample fluid intake is very important, especially for the lactating mother, who needs approximately 2 L per day. B-complex supplementation has been anecdotally reported to improve symptoms of depression and anxiety. Avoiding caffeine, chocolate, coffee, and caffeinated sodas, and keeping sugar consumption to a minimum may help erratic shifts in blood sugar, energy levels, and thus emotions.

Essential Fatty Acids

Essential fatty acids are critically important to a healthy functioning nervous system.[69,70] Evidence indicates an association between omega-3 polyunsaturated fatty acids (PUFAs) and depression.[71,72] The relationship between omega-3 PUFAs and depression is biologically plausible and is consistent across study designs, study groups, and diverse populations, which increases suggesting a causal relationship.[73] Four of six double-blind, placebo-controlled trials in depression, have reported therapeutic benefit from omega-3 fatty acids in either the primary or secondary statistical analysis, particularly when EPA is added on to existing psychotropic medication. The evidence to date supports the adjunctive use of omega-3 fatty acids in the management of treatment unresponsive depression.[74] Several studies suggest that docosahexaenoic acid (DHA) fatty acid supplements given to nursing mothers may reduce the incidence of postpartum depression and also improve early infant development. High EFA intake and high fish consumption have been inversely correlated with incidence of depression.[75,76] In fact, higher the intake of DHA by nursing mothers is related to a lower reported incidence of postpartum depression, with women in Singapore consuming 81 lb per year per woman and reporting 0.5% incidence of PPD compared to women in South Africa

Mother's Milk Tea

Combine the following herbs:

1 oz dried chamomile flowers	(*Matricaria recutita*)
1 oz dried catnip	(*Nepeta cataria*)
¼ oz fennel seeds	(*Foeniculum vulgare*)
⅛ dried lavender blossoms	(*Lavandula officinalis*)

Place 1 tablespoon of the dried herbs in a cup or teapot and cover with 1 cup of boiling water.
Cover the cup or pot and steep the herbs for 10 minutes. Strain and sweeten if desired.
Dose: 1 to 3 cups/day

For Irritability and Weepiness

For irritable nervous system, jumpiness and anxiety, quick angering, or frequent weepiness.

Blue vervain	(*Verbena officinalis*)	25 mL
Motherwort	(*Leonurus cardiaca*)	25 mL
Skullcap	(*Scutellaria lateriflora*)	25 mL
Nettles	(*Urtica dioica*)	25 mL
		Total: 100 mL

Dose: 3 to 4 mL in with water, 2 to 5 times daily

For General Depression with Irritability

Recommended by Simon Mill and Kerry Bone in *Principals and Practice of Phytotherapy*, specifically for the treatment of PPD caused by hormonal effects and adrenal depletion. They also recommend an addition of 2 mL of Vitex upon rising each day.

Ginseng	(*Panax ginseng*)	10 mL
St. John's wort	(*Hypericum perforatum*)	25 mL
Licorice	(*Glycyrrhiza glabra*)	15 mL
Ashwagandha	(*Withania somnifera*)	30 mL
Blue vervain	(*Verbena officinalis*)	20 mL
		Total: 100 mL

Dose: 5 mL in water, three times daily

For Depression with Anxiety

When anxiety is the predominant symptom accompanying depression.

Kava kava	(*Piper methysticum*)	20 mL
Ashwagandha	(*Withania somnifera*)	20 mL
St. John's wort	(*Hypericum perforatum*)	20 mL
Motherwort	(*Leonurus cardiaca*)	15 mL
Schisandra	(*Schisandra chinensis*)	15 mL
Licorice	(*Glycyrrhiza glabra*)	10 mL
		Total: 100 mL

Dose: 3 mL in water, two to four times daily

For Depression with Mild Sleep Difficulty

Primarily for insomnia and exhaustion related to insomnia.

Skullcap	(*Scutellaria lateriflora*)	20 mL
Passionflower	(*Passiflora incarnata*)	30 mL
Chamomile	(*Matricaria recutita*)	20 mL
Linden	(*Tilea* spp.)	20 mL
Lavender	(*Lavandula officinalis*)	10 mL
		Total: 100 mL

Dose: 3 to 4 mL in water, three to five times daily to promote a relaxed state throughout the day.
Can be taken 2 to 4 mL every 30 minutes for 2 hours before bed to promote sleep.

who consume on average 8.6 lb of fish per year per woman, and reporting an incidence of 24.5% PPD per year. Women in the use fall about halfway between these extremes in both fish consumption and PPD incidence.[72] The DHA content of mother's milk in the United States is among the lowest in the world—about 40 to 50 mg in US women, 200 mg in European women, and about 600 mg in Japanese women. Women who want to increase their DHA levels can take dietary supplements or eat more tuna, salmon, and other foods rich in DHA. To avoid mercury contamination, however, current guidelines suggest limiting fish to 12 oz of cooked fish per week during pregnancy and breastfeeding, and avoiding shark, swordfish, king mackerel, and tilefish. The dose of omega-3 PUFAs required for supplementation to prevent or treat postpartum depression is still not entirely clear. The recommended daily dose of 200 mg DHA has not been consistently sufficient in trials, whereas 1 g/day of EPA has shown more consistent benefit, and has been demonstrated to be superior in reliving symptoms such as delusion, hallucinations, and bizarre behavior in major depression. It is recommended that women supplement with 1 to 3 g/day of a fish oil supplement containing both DHA and EPA.[57] Twenty fish oil supplements tested for mercury levels by an independent lab were found to be free of detectable levels of mercury.[57] Many reputable fish oil companies will offer product information that address this concern for professionals and consumers.

ADDITIONAL THERAPIES

Massage for Mom and Baby

Therapeutic massage for the mother can provide an important opportunity for stress release and time to self-nourish on a regular basis, and can impart of feeling of being care for.[50] A study by Field et al. found that depressed teenage mothers receiving massage (10 sessions reported) experienced decreased depression and anxiety, had statistically significant behavior changes, and decreased salivary cortisol levels after a session.[77] Infant massage, which mothers can easily be trained to do, may also have benefits not only for the infant of the depressed mother via insuring contact and bonding that may become neglected with PPD, but also for the mother. Infants who receive massage regularly may sleep better and be less fussy, reducing potential stress, anxiety, and depression triggers for the mother, but also the act of giving infant massage can improve the mother's sense of connection and attachment to her baby while helping her to feel confident handling the baby and validated as a ''good mother'' for the effort she is making. A study by Onozawa et al. found that depression scores were reduced for both mothers with PPD and their infants as a result of regularly attending infant massage classes, and mother–infant interactions were improved.[78]

Aromatherapy

Scent can uplift the spirit, and its connection to memory and emotion has been well-documented. Several scents have been traditionally used to relieve depression; most notable among these is lavender oil. Although there is not data on the use of herbs to treat PPD, some evidence suggests the positive effects of lavender oil for the treatment of general depression.[50] The dilute oil may be used in a massage oil, or may be diffused in the room with an oil diffuser, sprinkled onto a pillow, or added to a bath. Care should be taken when oils are applied to the skin that they be dilute enough not to cause irritation. Usually several drops of essential oil to several tablespoons of carrier oil (e.g., almond oil) and 3 to 7 drops of undiluted essential oil added to a full bath are adequate.

CASE HISTORY: POSTPARTUM DEPRESSION

Anne began her prenatal care with a midwife, 9 weeks pregnant with her second child. At age 39, she had postponed this second pregnancy for 6 years largely out of fear of re-experiencing the postpartum depression that had debilitated her after the birth of her first child. Her first pregnancy had been uneventful, although she recalled losing a large amount of blood at birth. In the weeks and months postpartum, she reported symptoms of depression to her midwife, but these were dismissed as normal for the adjustment to motherhood. She tried St. John's wort with no noticeable improvement. At 1 year postpartum, the symptoms became severe, with suicidal thoughts. She had gained a significant amount of

Treatment Summary for Postpartum Depression

- PPD is a multifactorial problem requiring attention on many levels including social, psychological and emotional, nutritional, and biochemical. There is no single magic solution.
- Proper identification of women at risk and diagnosis of PPD is essential to the wellness of the mother, child, and family.
- Preventative strategies such as securing maternal parenting education and support for the postpartum period, and ensuring proper parental nutrition is essential.
- Essential fatty acid supplementation (1 to 3 g/day combined EPA and DHA) and adequate cold water fish consumption (up to 12 oz/week; avoid excess owing to potential for mercury toxicity) during pregnancy and in the postpartum may prevent or alleviate PPD.
- Ample complex carbohydrate intake in the postnatal period may be beneficial in preventing drastic drops in insulin level and thus maintain adequate levels of serotonin, and preventing PPD.
- Botanical therapies include the use of adaptogens, nervine tonics, antidepressant herbs, and nervine relaxant and sedatives (see Table 17-1).
- Additional therapies such as maternal massage, infant massage, and the use of lavender oil aromatherapy can be beneficial.

weight (50 lbs) over her prenatal and pregnancy weights, which added to her depression, and she was experiencing serious marital discord, so she sought the help of a psychiatrist. Anne spent over a year trying different prescription medications singly and in combinations. Finally, with a combination of three antidepressant drugs and a synthetic form of T3 hormone, she was symptom-free and remained so for several years. With the help of a prenatal psychiatry specialist, she was able to eventually wean off most of the drugs, which she did so she could become pregnant. She remained on a single antidepressant medication for the first couple of weeks of pregnancy and then discontinued this as well. She did not like the idea of being on pharmaceuticals at all, as this did not fit with her ''natural philosophies'' about medicine, and felt entirely uncomfortable using the drugs during pregnancy.

Upon beginning her relationship with a new midwife for this pregnancy, she had a tremendous amount of anxiety about the potential for repeated PPD. Her midwife worked with her to develop a plan that included postnatal support, about which her husband was educated during the course of the pregnancy, nutritional supplementation with an emphasis on essential fatty acid intake, a plan to begin using appropriate herbs immediately postpartum, and a back-up plan to access medical care if needed. She talked a great deal with her midwife about feelings of abandonment after her first pregnancy, and anger that her practitioner had not recognized the PPD. Her new midwife agreed to be available by pager for an extended postnatal period of time so that Anne would have the assurance that she was not going to feel isolated or alone, and that she could reach her midwife should she feel panicked. This was very reassuring to her throughout the pregnancy.

Anne's diet was revised to include fewer simple carbohydrates (she ate a good deal of refined and natural sugars) and more whole grains and ample protein. She was encouraged to get in the habit of eating often to prevent hypoglycemia. Her pregnancy was mostly uneventful with the exception of occasional migraines and severe itching, which were treated botanically. She gave birth to a healthy baby but again had a significant blood loss after the birth and was instructed in boosting her iron nutritionally and with Floradix Iron and Herbs for 6 weeks postnatally. Her midwife was in frequent contact with her, specifically inquiring about social and emotional aspects of her adjustment. Her husband was much more supportive. She took 3 g of a combination of DHA and EPA in the form of fish oil, and also 1500 mg of evening primrose oil daily. Immediately postpartum she also began taking the following tincture:

Motherwort	(*Leonurus cardiaca*)	25 mL
Eleuthero	(*Eleutherococcus senticosus*)	25 mL
Blue vervain	(*Verbena officinalis*)	20 mL
Passion flower	(*Passiflora incarnata*)	20 mL
Lavender	(*Lavandula officinalis*)	10 mL
		Total: 100 mL

Dose: 5 mL twice daily.

Anne remained on this protocol for 6 months postnatally and had no depression. She went off the formula at this point, but kept a 200 mL bottle on hand ''for emergencies.'' She resumed taking the formula at 8 months postpartum due to feeling ''overwhelmed,'' and remained on it for several more months, after which time she discontinued the formula and remained symptom free. She used no pharmaceutical drugs at any time in the postpartum period with her second child.

POSTPARTUM PERINEAL HEALING

> *Episiotomy is one of the most commonly performed procedures in obstetrics. In 2000, approximately 33% of women giving birth vaginally had an episiotomy. Historically, the purpose of this procedure was to facilitate completion of the second stage of labor to improve both maternal and neonatal outcomes. Maternal benefits were thought to include a reduced risk of perineal trauma, subsequent pelvic floor dysfunction and prolapse, urinary incontinence, fecal incontinence, and sexual dysfunction. Potential benefits to the fetus were thought to include a shortened second stage of labor resulting from more rapid spontaneous delivery or from instrumented vaginal delivery. Despite limited data, this procedure became virtually routine resulting in an underestimation of the potential adverse consequences of episiotomy, including extension to a third- or fourth-degree tear, anal sphincter dysfunction, and dyspareunia.*[79]
>
> **—American College of Obstetricians and Gynecologists**

The perineum is a muscular body at the inferior boundary of the pelvis, bordered superiorly by the muscles of the levator ani, and inferiorly by fascia. It is bordered by the vaginal introitus anteriorly and the rectal sphincter muscles and rectum posteriorly (Fig. 17-1). Because of the mechanical stresses of the baby's presenting part, particularly the head, on the perineum during birth, the perineum is subject to tearing during the second stage of labor (pushing). In the 1920s, episiotomy, the surgical cutting of the perineum, became a routine procedure for second state labor, predicated on the belief that the normal mechanical stresses of birth posed the risk of considerable overstretching of the pelvic floor muscles, predisposing women to long-term or permanent damage and risk of pelvic organ prolapse and incontinence. The final stitch placed in a repair job has often been referred to as the ''husband's knot,'' and it was not uncommon for an obstetrician to inform the new mother or her partner that she would be ''better than new'' after the repair! Medically, it is considered easier to repair a smooth surgical incision than a possibly jagged laceration that occurs naturally.

By the 1980s, episiotomy was being performed in rates in excess of 60% of all vaginal births.[80] More recently, emerging evidence of the lack of benefit of episiotomy, and associated risks, along with increased demand from maternal consumers that this procedure be avoided, has led to a significant decline in episiotomy rates to as low as 30% to 35% of all vaginal deliveries (against a backdrop of 27.5% of hospital deliveries now occurring by cesarean section).[81] As stated in the introductory quote, limited data supported the efficacy or safety of this procedure in preventing maternal damage as a result of normal

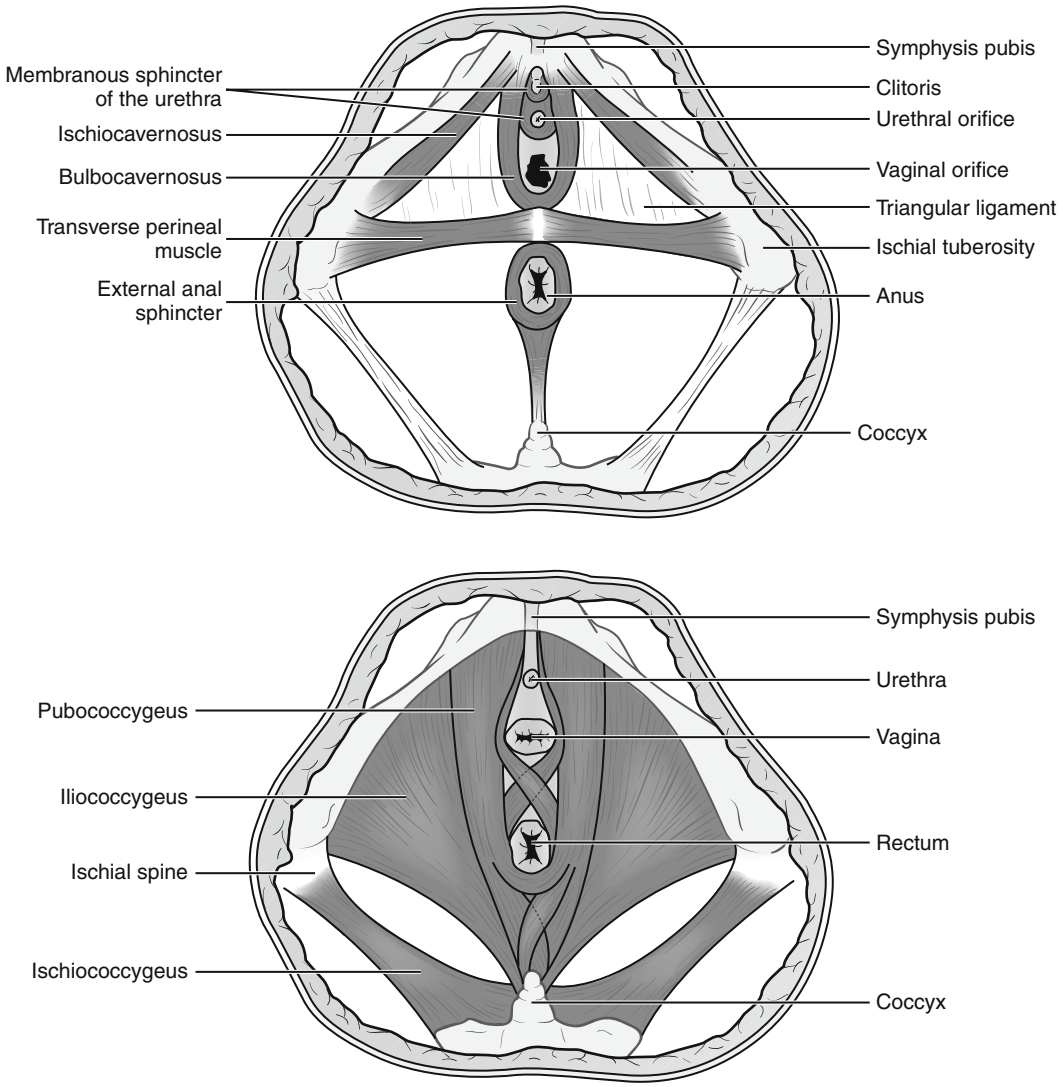


Figure 17-1 The female perineum and pelvic floor muscles. (Stillerman E: *Prenatal Massage: A Textbook of Pregnancy, Labor, and Postpartum Bodywork,* St. Louis, 2008, Mosby.)

vaginal childbirth, and the procedure itself has resulted in deleterious consequences for innumerable women, with soreness, itching, thickening, and scarring of the perineal tissue leading to lack of pliability and dyspareunia as common complaints.

Ironically, not only does routine episiotomy not reduce perineal trauma in most instances, episiotomy incisions frequently extend from first degree lacerations to third and fours degree lacerations, involving the pelvic floor musculature and rectum, and anal sphincter, with the emergence of the baby over the perineum. In fact, episiotomy is the overriding factor in the length of perineal tearing.[82] Bleeding is a common complication, and infection and permanent sphincter dysfunction not rare. Infection has led to anovaginal fistula, and rarely, infection has resulted in maternal mortality.[79]

It has a common obstetric myth that episiotomy is necessary in cases where expediting delivery in the second stage of labor is warranted for the safety of the fetus, or where the likelihood of spontaneous laceration to the mother seems high. Examples of these indications include ominous fetal heart rate, operative vaginal delivery such as forceps, shoulder dystocia, or a ''short'' perineal body. However, several trials suggest evidence supporting these claims is lacking. Two recent trials also failed to show evidence that episiotomy improved neonatal outcome, provided better protection of the perineum, or facilitated operative vaginal delivery.[83,84] Current evidence-based medicine does not support liberal or routine use of episiotomy. Although there is a role for episiotomy for a limited number maternal or fetal indications, such as avoiding severe maternal lacerations or facilitating or expediting emergency deliveries, a recent systematic evidence review found that prophylactic use of episiotomy does not appear to result in maternal or fetal benefit.[81] In fact, it appears to confer more harm than benefit.[80] Nonetheless, of those women who prefer elective caesarean section rather than vaginal delivery, 80% do so because of the fear of perineal damages.[85]

PREVENTION OF PERINEAL TEARS

Perineal tearing, even in the absence of episiotomy, is a common occurrence accompanying vaginal childbirth.

Tears are generally first- or second-degree tears, with third- or fourth-degree tears involving the musculature and rectum more likely to occur as a result of a tear that extends an episiotomy. Repair of natural tearing, as well as episiotomy, can lead to noticeable and prolonged discomfort and mild to moderate dysfunction for many women, depending upon the extent of the damage and the quality of the repair. A systematic review of the English language literature was conducted in 1998 to describe the current state of knowledge on reduction of genital tract trauma. A total of 77 papers and chapters were identified and placed into four categories after critical review: 25 randomized trials, four meta-analyses, four prospective studies, 36 retrospective studies, and eight descriptions of practice from textbooks.[86] The case for restricting episiotomy is conclusive—what remains uncertain is which techniques for preventing tears are effective. Midwives have consistently demonstrated reduced rates of perineal damage, with lower episiotomy rates, lower tear rates, and less damage to the perineum when either of the above occurs.[87,88] Techniques commonly employed include prenatal perineal massage, intranatal perineal massage, and application of hot compresses to the perineum during second state, as well as use of alternative positions to the lithotomy position, including standing, squatting, semirecumbent, and lateral positions. The contribution of maternal characteristics and attitudes to intact perineum has not been investigated to date.[86] Achieving an intact perineum, whether through avoidance of tearing or use of episiotomy can have significant effects on a woman's long-term health after birth. For example, a study by Signorello et al. reported that at 6 months postpartum about one-fourth of all primiparous women reported lessened sexual sensation, worsened sexual satisfaction, and less ability to achieve orgasm, as compared with these parameters before they gave birth. At 3 and 6 months postpartum, 41% and 22%, respectively, reported dyspareunia. Relative to women with an intact perineum, women with second-degree perineal trauma were 80% more likely and those with third- or fourth-degree perineal trauma were 270% more likely to report dyspareunia at 3 months postpartum.[89]

Prenatal Perineal Massage

Three trials (2434 women) comparing digital perineal massage with control were included in a review of antenatal massage and birth outcome by the Cochrane Collaboration. Antenatal perineal massage was associated with an overall reduction in the incidence of trauma requiring suturing. This reduction was statistically significant for women without previous vaginal birth only. Women who practiced perineal massage were less likely to have an episiotomy. Again, this reduction was statistically significant for women without previous vaginal birth only. No differences were seen in the incidence of first or second degree perineal tears or third- or fourth-degree perineal trauma. Only women who have previously birthed vaginally reported a statistically significant reduction in the incidence of pain at 3 months postpartum. No significant differences were observed in the incidence of instrumental deliveries, sexual satisfaction, or incontinence of urine, feces, or flatus for any women who practiced perineal massage compared with those who did not massage. The authors concluded that antenatal perineal massage reduces the likelihood of perineal trauma (mainly episiotomies) and the reporting of ongoing perineal pain and is generally well accepted by women. As such, women should be made aware of the likely benefit of perineal massage and provided with information on how to massage.[90] Another study evaluating the associations between perineal lacerations and 13 variables associated with the incidence of perineal lacerations concluded that perineal massage was beneficial not only to primiparous women but also to multipara who had episiotomies with their previous births.[91] Additional studies have demonstrated that women find prenatal perineal massage and acceptable practice.[92]

Birth Position, Practitioner Type, and Prevention of Perineal Trauma

In a study evaluating birth position and midwife versus obstetric outcomes in relation to intact perineum at birth, retrospective data from 2891 normal vaginal births were analyzed using multiple regression. A statistically significant association was found between birth position and perineal outcome, with a lateral position associated with the highest rate of intact perineum (intact rate 66.6%) and squatting for primiparas associated with the least favorable perineal outcome (intact rate 42%). Semirecumbent, standing, and ''all-fours'' positions led to outcomes of 36.3%, 42.7%, and 44.4%, respectively. The obstetrician group had an episiotomy rate greater than five times that of midwives, and generated tears requiring suturing 42.1% of the time, an average of 5 to 7 percentage points higher than midwives. In midwife supported births, an intact perineum was achieved 56% to 61% of the time, compared with 31.9% for obstetricians.[87] Additional studies have demonstrated improved perineal outcomes with birth in an upright position.[93] Midwives use a variety of techniques to support the perineum during birth. This study was an attempt to begin to understand which of these factors contribute to improved outcomes, and to what extent. However, it should be remembered that it may be the gestalt of factors together that is ultimately responsible for improved perineal outcome at birth.

Intranatal Perineal Massage and/or Hot Compresses during Birth

In one clinical trial done to evaluate these methods, neither intranatal perineal massage nor hot compresses during second stage of labor reduced the incidence of spontaneous perineal tearing as independent techniques. However, as these measures are not harmful and they provide comfort to many women, their use should not be excluded but should be based on whether they provide maternal comfort.[80]

''Easing the Baby Out'' and ''No Touching'' until Crowning of the Head

Techniques not used by the medical community, but widely reported by midwives include easing the baby

out gently rather than bearing down to push, and not touching the perineum until the baby's head is crowning.[94] The former practice encourages the mother to breathe with urges to push rather than using a Valsalva method, and, based on observation, appears to minimize pressure against the perineum as the head begins to emerge, and allows a slow emergence of the head, which may optimize perineal stretching over a fast delivery with the added force of maternal pushing behind it. Many midwives practice ''no touching'' rather than aggressive second-stage intranatal perineal massage or the practice of ''ironing'' the perineum, to thin and stretch it, as is commonly practiced in obstetrics. These techniques have not been studied systematically but may contribute to the improved perineal outcomes associated with midwifery care.

BOTANICAL TREATMENT FOR PERINEAL HEALING

For women who have experienced perineal trauma with birth, perineal healing is a concern (Table 17-4). Whether as a result of nonsurgical laceration or routine or medically necessitated episiotomy, if a surgical repair was done (stitches), postpartum perineal discomfort can be significant, with itching, soreness, tenderness, and even pain. Discomfort can sometimes persist for months after childbirth, interfering with normal activities, exercise, and sex. For some women, this has serious implications in their work life and marriage/sexual relationships. Severe perineal trauma at birth, even in the absence of episiotomy, can also lead to delayed return of sexual activity and perineal discomfort.

Astringent herbs such as yarrow, witch hazel, and white oak bark, vulnerary herbs such as calendula and comfrey, antiseptic herbs such as sage and myrrh, and a mild topical analgesic such as lavender can be made into strong decoctions, which can be applied to the perineum via a peri-wash or sitz bath. Alternatively, tinctures of these herbs can be diluted in water and similarly applied. These herbs can accelerate healing from perineal tears and episiotomy, reduce swelling and bruising, and alleviate pain and soreness. Peri-rinses can be used after each use of the toilet, and sitz baths can be taken one to two times daily as needed. These techniques are repeated up to 5 days postnatally. Sample recipes that are popular for use among midwives are described below. See Chapter 3 for instructions on preparing herbal baths, sitz baths, and peri-rinses. Studies on the activities of many of these herbs are found in specific Plant Profiles. With the exception of lavender, which has been studied minimally for this purpose, few studies have been conducted on the use of herbs specifically for postnatal perineal

Herbal Bath I

A blend of beautiful and fragrant blossoms that is soothing, healing, and antiseptic.
Mix these herbs:

Comfrey leaves	(*Symphytum officinalis*)	2 oz
Calendula flowers	(*Calendula officinalis*)	1 oz
Lavender flowers	(*Lavandula officinalis*)	1 oz
Sage leaf	(*Salvia officinalis*)	½ oz
Myrrh powder	(*Commiphora mol mol*)	½ oz
		Total: 5 oz

Also: ½ cup sea salt

Directions: Bring 4 quarts of water to a boil. Turn off heat, and place 1 oz of the above mix (not the salt) into the pot. Steep, covered, for 30 minutes. Strain the liquid thoroughly through a fine mesh strainer, and discard the herb material. Add 2 quarts of liquid to the tub, along with the 3½ cup of salt. Reserve the remaining liquid for another bath or alternatively, use the tea in a 4-oz peri-bottle, adding 1 tbs salt per bottle.

TABLE 17-4

Botanical Treatment Strategies for Perineal Healing

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Restore tone to tissue; promote healing, protect tissue from infection	Astringent	*Achillea millefolium*	Yarrow
		Arctostaphylos uva ursi	Uva ursi
		Hamamelis virginiana	Witch hazel
		Myrica cerifera	Bayberry bark
		Quercus spp.	Oak bark
Prevent infection	Antiseptic	*Allium sativum*	Garlic
		Commiphora mol mol	Myrrh
		Lavandula officinalis	Lavender
		Rosmarinus officinalis	Rosemary
		Salvia officinalis	Sage
		Thymus vulgaris	Thyme
Heal tissue	Vulnerary	*Calendula officinalis*	Calendula
		Symphytum officinale	Comfrey leaf

Herbal Bath II

Strongly antiseptic and astringent, this bath, or similar variations of it, is a popular postpartum treatment among home birth midwives. It can be used when there is tearing, bruising, abrasions (''skid marks''), or soreness.

Mix 1 oz each of the following dried herbs:

Comfrey leaf	(*Symphytum officinalis*)	1 oz
Yarrow blossoms	(*Achillea millefolium*)	1 oz
Sage leaf	(*Salvia officinalis*)	1 oz
Rosemary leaf	(*Rosmarinus officinalis*)	1 oz

Total: 4 oz

Also: Peel 1 large fresh bulb of garlic (*Allium sativum*) and obtain ½ cup of sea salt.

Directions: Peel all of the garlic cloves and place them in a blender with two cups of lukewarm water. Blend at high speed until a milky liquid is obtained and the garlic is completely pulverized. Strain through a fine mesh strainer. Bring 6 cups of water to a boil and turn off heat. Add 1 ounce total of the dried herb blend to the pot and steep for 30 minutes, covered. Strain the liquid thoroughly through a fine mesh strainer or cheesecloth and discard the herb material. Add 1 cup of the garlic ''milk'' and 4 cups of herb tea to the bath, along with ½ cup of salt. Reserve the remaining liquids for a subsequent bath. Do not use the garlic milk directly or in a peri-bottle—it is too irritating. However, the tea made be used as such, with the addition of 1 tbs sea salt per 4 oz peri-bottle.

healing. Anecdotally, women report these to be soothing, and look forward to repeating the baths and rinses. These applications are also effective in reducing hemorrhoids postnatally, and for this purpose, may additionally be used directly on the hemorrhoids in the form of compresses of the teas. When using compresses, omit the garlic, which is too irritating to be applied directly, and omit the sea salt, which is unnecessary.

Astringent and Antiseptic Tincture

Mix all tinctures and add ½ fl oz of the mix to 4 oz of warm water in a peri-bottle.

Witch hazel bark	(*Hamamelis virginiana*)	½ fl oz
Calendula	(*Calendula officinalis*)	½ fl oz
Lavender	(*Lavandula officinalis*)	½ fl oz
Myrrh tincture	(*Myrica cerifera*)	½ fl oz

Total: 2 fl oz

Lavender

Lavender herb and oil are traditionally used by herbalists for their antiseptic and mild analgesic properties when applied topically. It is commonly recommended by midwives and herbalists as an ingredient in postpartum sitz baths. Researchers at the Hinchingbrooke Hospital, Huntingdon, Cambridgeshire, undertook a blind randomized clinical trial using a total of 635 postnatal women to test these claims. The women were divided into three groups; the first group was given pure lavender oil, the second group being given synthetic lavender oil, and the third group were given an inert substance as bath additives to be used daily for 10 days following normal childbirth. Analysis of the total daily discomfort scores revealed no statistically significant difference between the three groups. However, on closer inspection, the outcomes showed that those women using lavender oil recorded lower mean discomfort scores on the third and fifth days than the two control groups, which is a time when the mother usually finds herself discharged home and perineal discomfort is high.[95]

Breastfeeding and Botanical Medicine

Sheila Humphrey, Aviva Romm

18 CHAPTER

BREASTFEEDING AND HERBS: A COMPREHENSIVE REVIEW OF SAFETY CONSIDERATIONS AND BREASTFEEDING CONCERNS FOR THE MOTHER–INFANT DYAD

Sheila Humphrey

Lactation is a healthy function of the postnatal female body; it benefits the woman and provides the child with the only known perfect food for humans—human milk.[1] The breast and breast milk are what the human baby is evolutionarily adapted to ''expect'' after birth. Breastfeeding is what the woman's body also ''expects'' after birth. Although a full description of benefits of breastfeeding is well beyond the scope of this chapter, the American Academy of Pediatrics (AAP) statement on breastfeeding provides a succinct summary (Box 18-1).[1]

As a society, encouraging breastfeeding of our young is one of the most important health measures we can take. The established risks of not breastfeeding include increased incidence of otitis media, GI infections, respiratory infections, juvenile diabetes, lymphoma, and lowered cognitive function for the baby; the mother is at increased risk for breast cancer, ovarian cancer, and osteoporosis. The beneficial effects of breastfeeding are generally dose related: Exclusive breastfeeding in the first 6 months, followed by significant breastfeeding for at least the first year and beyond is recognized as optimal.[1,2] This ''dose'' provides the gold standard of nutrition, with which all else must be compared. Benefits to both mother and child are now considered so extensive that the protection, promotion, and support of breastfeeding is a recognized global health activity in all countries; the WHO and UNICEF are but two global organizations that have consistently worked toward the goal of increasing breastfeeding rates and duration. Chemical risk to the breastfeeding dyad must be considered relative to the importance of breastfeeding in the optimal manner for the optimal duration.

HERBS AND BREASTFEEDING

Concerns involving herbs and breastfeeding have become commonplace among health care providers. Written information to date is often inadequate for counseling clients/patients: herbal product label information provides insufficient safety information, and reference texts generally present extremely limited data focused only on infant risk.[3–6] Few authors explain the rationale behind contraindications, nor do they provide documentation of adverse reactions, and the criteria for determining risk is typically not defined. Exceptions are McKenna et al.,[7] which features an introductory essay on the parameters of herb risk during lactation as well as more detailed discussion of lactation use for each monographed herb, and Mills and Bone,[8] with its extensive chapter on the safety of herbs during pregnancy and lactation. Some texts discourage or contraindicate all herb use during lactation, rendering such books particularly useless.[9] In sharp contrast, the Herbal PDR only rarely mentions that use of an herb may require caution during lactation, even when perhaps when it is merited. The German Commission E[3] as well as AHPA's *Botanical Safety Handbook*[10] provide generally reliable guidelines for the safe use of herbs during lactation.

Breastfeeding mothers, like all other women, have health needs that may at times require treatment, and breastfeeding mothers may choose botanical medicines as their treatment choice. Risk assessment must include those risks to the infant, the mother, and lactation itself. The risk analysis of the herbal medicine must be extended to include the comparison risk of using the relevant pharmaceutical drug.

Detailed information is now available on pharmaceutical drug use during lactation, providing the health care practitioner with sufficient information to counsel breastfeeding mothers. Most prescription drugs have been demonstrated to carry some degree of compatibility with breastfeeding.[11,12] Lactation pharmacology generally has

BOX **18-1**

American Academy of Pediatrics (AAP) Policy Statement on Breastfeeding

The AAP identifies breastfeeding as the ideal method of feeding and nurturing infants and recognizes breastfeeding as primary in achieving optimal infant and child health, growth, and development. The following are excerpts from the extensive AAP policy statement on breastfeeding, Breastfeeding and the Use of Human Milk, Section on Breastfeeding Pediatrics 115;496-506, 2005. The full text is available at http://www.pediatrics.org/cgi/content/full/115/2/496. Many of these recommendations are identical for high-risk infants, and a section devoted to the nursing of these babies is included in the AAP statement.

It should be noted that midwives and breastfeeding advocates have been purporting many of these policies for at least three decades.

Recommendations on Breastfeeding for Healthy Term Infants

1. Pediatricians and other health care professionals should recommend human milk for all infants in whom breastfeeding is not specifically contraindicated (for significant health reasons, i.e., infectious disease) and provide parents with complete, current information on the benefits and techniques of breastfeeding to ensure that their feeding decision is a fully informed one.
   - When direct breastfeeding is not possible, expressed human milk should be provided. Before advising against breastfeeding or recommending premature weaning, weigh the benefits of breastfeeding against the risks of not receiving human milk.
2. Peripartum policies and practices that optimize breastfeeding initiation and maintenance should be encouraged.
   - Education of both parents before and after delivery of the infant is an essential component of successful breastfeeding. Support and encouragement by the father can greatly assist the mother during the initiation process and subsequent periods when problems arise. Consistent with appropriate care for the mother, minimize or modify the course of maternal medications that have the potential for altering the infant's alertness and feeding behavior. Avoid procedures that may interfere with breastfeeding or that may traumatize the infant, including unnecessary, excessive, and overvigorous suctioning of the oral cavity, esophagus, and airways to avoid oropharyngeal mucosal injury that may lead to aversive feeding behavior.
3. Healthy infants should be placed and remain in direct skin-to-skin contact with their mothers immediately after delivery until the first feeding is accomplished.
   - The alert, healthy newborn infant is capable of latching on to a breast without specific assistance within the first hour after birth. The mother is an optimal heat source for the infant. Delay weighing, measuring, bathing, needlesticks, and eye prophylaxis until after the first feeding is completed. Infants affected by maternal medications may require assistance for effective latch-on. Except under unusual circumstances, the newborn infant should remain with the mother throughout the recovery period.
4. Supplements (water, glucose water, formula, and other fluids) should not be given to breastfeeding newborn infants unless ordered by a physician when a medical indication exists.
5. Pacifier use is best avoided during the initiation of breastfeeding and used only after breastfeeding is well established.
6. Pediatricians and parents should be aware that exclusive breastfeeding is sufficient to support optimal growth and development for approximately the first 6 months of life and provides continuing protection against diarrhea and respiratory tract infection. Breastfeeding should be continued for at least the first year of life and beyond for as long as mutually desired by mother and child.
   - Introduction of complementary feedings before 6 months of age generally does not increase total caloric intake or rate of growth and only substitutes foods that lack the protective components of human milk.
   - During the first 6 months of age, even in hot climates, water and juice are unnecessary for breastfed infants and may introduce contaminants or allergens.
   - Increased duration of breastfeeding confers significant health and developmental benefits for the child and the mother, especially in delaying return of fertility (thereby promoting optimal intervals between births).
   - There is no upper limit to the duration of breastfeeding and no evidence of psychologic or developmental harm from breastfeeding into the third year of life or longer.
7. Mother and infant should sleep in proximity to each other to facilitate breastfeeding.

Role of Pediatricians and Other Health Care Professionals in Protecting, Promoting, and Supporting Breastfeeding

General

- Promote, support, and protect breastfeeding enthusiastically. In consideration of the extensively published evidence for improved health and developmental outcomes in breastfed infants and their mothers, a strong position on behalf of breastfeeding is warranted.
- Promote breastfeeding as a cultural norm and encourage family and societal support for breastfeeding.

BOX **18-1**

American Academy of Pediatrics (AAP) Policy Statement on Breastfeeding—cont'd

- Recognize the effect of cultural diversity on breastfeeding attitudes and practices and encourage variations, if appropriate, that effectively promote and support breastfeeding in different cultures.

Education

- Become knowledgeable and skilled in the physiology and current clinical management of breastfeeding.
- Encourage development of formal training in breastfeeding, and lactation in medical schools, in residency and fellowship training programs, and for practicing pediatricians.
- Use every opportunity to provide age-appropriate breastfeeding education to children and adults in the medical setting and in outreach programs for student and parent groups.

Clinical Practice

- Work collaboratively with the obstetric community to ensure that women receive accurate and sufficient information throughout the perinatal period to make a fully informed decision about infant feeding.
- Work collaboratively with the dental community to ensure that women are encouraged to continue to breastfeed and use good oral health practices.
- Promote hospital policies and procedures that facilitate breastfeeding. Work actively toward eliminating hospital policies and practices that discourage breastfeeding (e.g., promotion of infant formula in hospitals including infant formula discharge packs and formula discount coupons, separation of mother and infant, inappropriate infant feeding images, and lack of adequate encouragement and support of breastfeeding by all health care staff). Encourage hospitals to provide in-depth training in breastfeeding for all health care staff (including physicians) and have lactation experts available at all times.
- Provide effective breast pumps and private lactation areas for all breastfeeding mothers (patients and staff) in ambulatory and inpatient areas of the hospital.
- Become familiar with local breastfeeding resources (e.g., WIC clinics, breastfeeding medical and nursing specialists, lactation educators and consultants, lay support groups, and breast-pump rental stations).
- Encourage adequate, routine insurance coverage for necessary breastfeeding services and supplies, including the time required by pediatricians and other licensed health care professionals to assess and manage breastfeeding and the cost for the rental of breast pumps.
- Develop and maintain effective communication and coordination with other health care professionals to ensure optimal breastfeeding education, support, and counseling.

Society

- Encourage the media to portray breastfeeding as positive and normative.
- Encourage employers to provide appropriate facilities and adequate time in the workplace for breastfeeding and/or milk expression.
- Encourage child care providers to support breastfeeding and the use of expressed human milk provided by the parent.
- Encourage development and approval of governmental policies and legislation that are supportive of a mother's choice to breastfeed.

Adapted from American Academy of Pediatrics Work Group on Breastfeeding: Breastfeeding and the use of human milk, Pediatrics 100(6):1035-1039, 1999.

shown limited drug entry into breast milk and few adverse reactions in the infant for most chemical entities. Weaning in order to use a medication is only rarely considered necessary.[11] Given this, herb safety cannot be evaluated in isolation from drug safety, and the relative safety of most herbs during lactation may be taken as an extension, because of the relatively limited side effects and adverse events from herbs as compared to pharmaceutical drugs.

Each mother–child nursing pair, or dyad, is considered a unit. Dyads are as unique as any individual, requiring information fitted to their own situation. Just as with drugs, categorical recommendations cannot be made about herbs. Ruth Lawrence, an internationally recognized expert in lactation, ended her discussion on herbs in a US government publication about risk with a simple summary statement: ''The medicinal use of herbs per se is not a contraindication to breastfeeding.''[13] Assessment of risk is possible but must be individualized using basic principles. This first requires an understanding of both lactation and lactation pharmacology.

HOW CHEMICALS ENTER BREAST MILK: WHAT WE KNOW

The science of lactation pharmacology and toxicology has greatly advanced over the last 20 years so that recognized principles of chemical entry into breast milk can be used to determine drug and environmental contaminant risk, even when some information is lacking.[12] Recognition of these principles has greatly advanced the

knowledge base and clinical practice of drug prescribing with breastfeeding women.

Almost any chemical a breastfeeding mother ingests that gains entry to her bloodstream will enter her milk to some degree; however, it appears that most substances will only gain entry in minute doses. The oft-quoted rule is 1% of the maternal dose of any medication will enter the milk, and with some exceptions, up to about 10%.[12,14] Pharmaceuticals, especially single-chemical preparations noted for their ''magic bullet'' effect on target systems, can have profound effects on the mother, yet it is the exception when the infant-received dose is large enough to elicit any pharmacological effect. In general, no adverse effects are noted when the milk dose of a substance is less than 10% of the mother's ingested dose. Such a dose is typically too small to elicit a pharmaceutical response. From ingestion to milk entry, the same pharmacologic principles for drugs apply to herbs, and there is no a priori reason to think that phytochemicals would be exceptional regarding milk entry.

The blood–breast barrier possesses unique permeability and selectivity regarding passage of any one chemical. Chemicals on the blood side must pass through the cell lining of the breast's alveoli in order to reach the milk. The amount of any chemical's entry into milk is determined by a number of pharmacokinetic factors: bioavailability, maternal serum levels, degree of protein binding in maternal serum, lipid solubility and the fat content of the milk, degree of ionization and milk pH, molecular size and weight, and the half-life in the maternal plasma compartment.

Bioavailability is an important first determinant of maternal serum levels and has proved useful in predicting the infant serum levels after milk ingestion. If a chemical is not absorbed into the bloodstream from the GI tract, then it cannot reach the breast. The most important factor affecting milk entry after oral availability is the mother's serum level, with breast milk levels almost always directly correlating to maternal serum levels. Chemical entry is primarily by diffusion through the alveolar cells, driven by equilibrium forces between the maternal plasma compartment and the maternal milk compartment. Chemicals do not usually ''get stuck'' in breast milk, though a few chemicals do sequester or concentrate in breast milk, most notably iodine and alkaloids. Unlike most minerals, iodine is actively transported into breast milk. Nonionized chemicals will more readily enter and leave the milk compartment than ionized chemicals. Due to a shift in pH, weakly basic chemicals such as alkaloids tend to concentrate in the slightly more acidic breast milk, resulting in ''trapping'' and higher milk:plasma ratios than is typical. The degree of protein binding is also a primary determinant of milk entry. Chemicals must be free in the plasma to diffuse into breast milk. Thus, coumadin, 99% bound to serum proteins, only enters milk in miniscule amounts (0.08 μmole/L), which have been shown to be of no pharmacologic consequence to the infant. Very large molecules, such as insulin and heparin, do not enter breast milk at all. Very small molecules, including ethanol and other volatiles, tend to diffuse more rapidly into and out of milk, with milk levels closely reflecting maternal serum levels. Lipid-soluble chemicals, such as most central nervous system drugs, also tend to enter into milk more readily, and can exhibit higher than expected levels. The blood–breast barrier somewhat resembles the blood–brain barrier in this regard.[12]

Factors Affecting Impact on Child by Substances Taken by the Mother during Lactation

1. Dose present in the milk (degree of entry)
2. Dose or volume of breast milk received by the child
3. Serum levels attained in the child depend on:
   a. oral availability in the child
   b. metabolism of that chemical by the infant
4. Age (and health) of the child determines elimination capabilities
5. Weight of the child will also determine the impact of the substance (a pediatric dose is always expressed in terms of weight)

Chemical entry into milk is restricted by a secretory epithelium with tight junctures between the alveolar cells of the mammary structure. However, colostrum, produced in the first 3 to 10 days postpartum, is produced before these tight junctures close. Until the alveolar cells swell with high-volume milk production, maternal proteins such as immunoglobulins and most chemicals in the serum have enhanced access to the milk compartment, passing freely between the alveolar cells. Lactation experts agree that relatively larger doses of chemicals enter milk during this time.[12,15] After this time, chemicals can only gain access to the milk compartment through the two cell membranes of the alveolar cells, usually by diffusion.

The amount of breast milk ingested by the child (nursing pattern) is probably the most important determinant of risk, and the most variable. The exclusively breastfeeding infant is ingesting a maximal volume of breast milk per body weight. An older infant may also be ingesting a similar volume of milk, but because the child now weighs considerably more at 6 months, possesses a GI tract ready to handle foods other than breast milk, and has a matured elimination capacity, the dose impact will be lessened. At the other end of the spectrum is the token-nursed infant receiving only one to two feedings at the breast per day, or the nursing toddler, who may nurse only occasionally.

Asking the mother the age of the child as well as nursing pattern will quickly place the dyad on the relative risk continuum. The age and weight of the child are largely predictive of the impact of any given herb/medication dose. Another important factor is the maturity of the child's metabolic and eliminative functions. The newborn is the most vulnerable to chemicals ingested by the mother, being born with immature gut, liver, and kidney function. By about the age of 2 weeks, however, the liver is able to effectively metabolize ingested

chemicals competently.[15] Kidney clearance capacity increases and becomes fully by 4 to 5 months of age. The adult half-life of a chemical is commonly used to give some measure of whether a drug is likely to accumulate in an infant, even though pediatric half-life is not known for most drugs. Chemicals with half-lives of over 24 hours are of greatest concern as they will accumulate in the infant.[12] For neonates with immature metabolic capacity and small body size, serum levels can rise to pharmacologically significant levels more quickly, even with drugs of shorter half-lives. Thus, great caution is required with premature and low birth-weight infants.[15]

Lactation pharmacology has developed to the point where generalizations about chemicals, synthetic or naturally occurring, are possible, and where a prediction of risk can be made for a particular mother–child pair. As the dose of breast milk as well as the size and health of a nursing child are highly variable, blanket statements or risk during breastfeeding are gross simplifications that cannot guide clinical practice, although a cautionary statement on an herbal or drug product label helps mothers regarding self-use.

RISKS

Risks of Medications

The American Association of Pediatrics, in 1994, 1997, and 2001, reviewed research and clinical information about drug use in lactation with the latest statement supporting the safety of the use of the vast majority of drugs during breastfeeding. Generally, only the most toxic drugs, such as cancer chemotherapeutics and long half-life radioactive iodine compounds, are absolutely contraindicated. Known adverse events are usually associated with premature or small for gestational weight babies, and such effects often reflect the known side effects in adults. Prediction of risk includes the nature and degree of adverse effects. Certain categories of drugs, such as antidepressants, may be of concern. Although clinical use of many of these substances is widespread, despite the AAP's concerns, most lack significant adverse effects.[12] The safety of antidepressant medications during lactation was discussed in Chapter 16.

Interestingly, synthetic hormonal substances such as the progestins are considered compatible with breastfeeding. Some experts are concerned about potential long-term effects on the infant yet no evidence of this has been found. Other hormonal preparations, such as synthetic thyroid preparations, are noncontroversial and have been used for decades. Synthetic estrogens are an exception; most practitioners report a decrease in milk supply with use of any amount of estrogen in birth control agents.

Measurement of the degree of milk entry of many types of pharmaceutical substances has led to the realization that few drugs can be expected to cause toxic effects in the infant. Animal lactation studies have been done for some, but not all drugs. Newer prescription drugs often lack studies. Yet, lack of specific lactation studies is not considered reason enough to contraindicate a drug. Indeed, many drugs lack even preliminary study of milk entry in animals or humans. The pharmacokinetic characterization of almost all pharmaceuticals does allow more precise prediction of milk entry, although few fall outside of the 1% to 10% milk entry rule predicted simply from maternal oral ingestion. The clinical evidence for use of most drugs has accumulated through publication of case studies, anecdotes, and experimental study of individuals or very small groups made up of a few mother–baby pairs (often fewer than 10). Typically, milk entry is only characterized for one stage of lactation. Very few drugs have been studied over long-term use, where the child has been exposed to the drug over weeks or months though some drugs are indeed administered in this way. Despite this narrow basis of experimental evidence or quantitative data on drugs during lactation, the increased prescription of medications during lactation has resulted in the documentation of few adverse reactions in children. It is worthy to note here that even drugs such as digoxin, a cardioactive alkaloid with a narrow therapeutic index, is considered compatible with breastfeeding, although close monitoring of mother and baby is necessary to ensure dose limitation.[11] As reassuring as this is to lactation experts, it is clear that the actual evidence for safety is quite limited when compared to the evidence for safety in adults. Thus, we know a lot about how a pharmaceutical is metabolized in the mother (pharmacokinetics), allowing tolerably accurate prediction of milk dose, yet have an almost nonexistent experimental base of information regarding actual milk entry or effects in large numbers of infants or over all stages of lactation. Quantification of milk entry and infant serum levels for most drugs is surprisingly limited.

In the Absence of Lactation Studies: Herbs vs. Medications

The powerful nature of pharmaceuticals that inherently generates side effects and drug interactions, as well as their use in complex medical situations results in a relatively high rate of adverse events associated with their use when compared with herbal medicines.[16] When comparing the merits of medications vs. herbs, the relatively narrow basis of evidence for safe use of medications during lactation must still be balanced by the fact that most medications are more completely studied, particularly regarding their metabolism and that more elaborate pharmacovigilance systems are in place to monitor their use.[17] However, information gained from traditional use cannot be ignored or discarded; traditional information is the basic study material for the scientific discipline of ethnopharmacology after all. Nor can drug data provided by the pharmaceutical industry be entirely trusted to always provide an objective measure of safety. Indeed, the PDR's statements regarding safety during lactation are singularly useless to guide clinical practice.[12,15] Regarding efficacy, the principle of proportionality should not be overlooked.[18] Are we talking about the mother having cancer or a cold? How important is efficacy in the risk–benefit analysis? The advantages of an herbal treatment that may not work as quickly or as well compared with a pharmaceutical must be balanced against the need for efficacy.

Herb Risks: Herbs with Pharmacokinetic Information

De Smet and Brouwers provide a systematic review of the state of herbal pharmacokinetics, evaluating the complexities of phytoconstituent bioavailability and pharmacokinetics, and providing a short list of plant constituents where serum levels have been measured.[18] The authors advocate pharmacokinetic study of herbs with narrow safety margins or those commonly used for life-threatening disorders, but point out that for herbs with wide safety margins, available in high-quality preparations and used for minor health disorders, the need for such characterization is unnecessary. Yet, bioavailability and serum levels are two measures that are of great utility in assessing herb safety during lactation, if for no other reason than to reassure the doubtful health practitioner. Assessment of herb risk during lactation is hindered by the fact that useful information such as serum levels, half-life, and protein binding are not yet characterized for many phytochemicals. Dose information for any one constituent, usually the ''active'' constituent, is often available for most controversial or well-researched herbs, and the simple application of the 1% rule to estimate maternal serum levels from oral dose will yield a ballpark estimate of milk entry for the chemical of toxicologic interest. Even if you assume a worse-case scenario and use 10% as the rule, this number is still likely to be very small. Hypericin and soy isoflavones are two examples where serum levels have been measured. Hypericin is a constituent of St. John's wort (*Hypericum perforatum*) that has been considered active, even though more recent studies indicate a number of other constituents may actually be responsible for the antidepressant activity. In any event, hypericin serum levels have been measured at 8.5 ng/mL following a dose of 900 mg/day of the dried herb.[19] This amount represents a very small dose available to diffuse into the milk. The soy isoflavone, genistein, was recently measured in breast milk at concentrations of 0.2 μmol/L in breast milk following ingestion of soy nuts containing a 20 mg of genistein.[20] Genistein entry into breast milk appears extremely limited in this study as serum levels were measured at 2.0 μmol/L plasma, representing a 1:10 milk:plasma ratio. This amount is tiny compared to what babies receive when fed soy formula.[21]

Another class of relatively well-studied herbs is the stimulant laxatives that breastfeeding women are cautioned about for good reason; diarrhea can result from local activity of constituents within the GI tract (compartmental effect). In a study described in Hale, sennosides A and B could not be detected in milk in one study of 20 breastfeeding women using Senokot tablets containing a dose of 8.6 mg sennosides/day.[12] Most (15/23) women in the study reported loose stool, of these, two had babies also had loose stools. In another study rhein, an active laxative metabolite of sennosides, was measured in 100 milk samples drawn from 20 women.[22] A daily dose of 15 mg sennosides were consumed for 3 days before sampling; 0 to 27 ng/mL was found, with over 90% of the milk samples containing less than 10 ng/mL of rhein. None of the infants had loose stools. However, the senna was combined with the bulking agent, *Plantago ovata*, which may have slowed or lowered absorption of the laxative constituents into the mothers' bloodstreams. In contrast to the German Commission E, senna and cascara are considered compatible with breastfeeding; this statement assumes the necessary short-term use of a standardized product in appropriate doses; occasional diarrhea has been noted in neonates but not older children.[11]

Herb Risk to the Child

Herbs that present a well-documented risk to adults [i.e., those containing aristolochic acid (AA) or toxic pyrrolizidine alkaloids (PAs)] logically can be expected to present some degree of risk to the breastfeeding child. However, most herbs of commerce lack serious side effects when used appropriately, and thus would not be expected to be able to produce them in infants in the tiny doses of phytoconstituents received in breast milk. Synthetic hormones such as progesterones, estrogens, thyroid replacements, and insulins are compatible with breastfeeding at least infant safety.[11] Thus, regarding, the proportional risk posed to the child by the relatively much weaker phytohormones would seem slight. This is not to say that adverse effects cannot occur. Herbs that do have adverse side effects when used appropriately or with narrow therapeutic safety range would be predicted to be much more likely to cause similar problems in the breastfeeding child. These herbs must be used with caution when breastfeeding, even in standardized or OTC forms. Yet, documented infant effects are rarely seen even in the more vulnerable neonates. And, in those instances where the infant has received the plant chemicals through breast milk alone, the adverse effects have been reversible. Appropriate use of herbs by mothers of nursing toddlers is not expected to pose a risk to the child. Still, the mother needs counseling on what appropriate use is, and what potential side effects should be watched for in the child. The strategy of using the medicinal and watching the child for expected side effects is advocated by lactation experts.[12,14] If side effects should appear in the infant, the dose is lowered or a different medicinal is used. Obviously, use of questionable herbs during lactation always needs a close look: Alternative approaches that may or may not include the use of other herbs need to be explored or recommended to the mother. A questionable herbal product should not be used by the nursing mother, regardless of the herb. This pragmatic aspect of herb safety cannot be ignored. Education on product selection should be part of any guidance provided to a mother.

The Pregnancy and Lactation Confusion

When reading herbal literature, it is important to determine whether precautions distinguish between pregnancy and lactation. Numerous authors do not make this distinction. To further complicate matters, many authors do not differentiate between self-directed use and supervised use of herbs; thus, it is not at all clear

under what use conditions such contraindications are thought necessary.

A prime example of confusing pregnancy and lactation precautions is seen in herbs where many authors contraindicate their use during ''pregnancy and lactation due to hormonal influences.''[6] For oxytocic or uterotonic herbs, this confounding of pregnancy and lactation is unfortunate as the following discussion shows. Note that ''oxytocic'' describes an agent capable of causing uterine contractions leading to the delivery of the fetus or placenta. Not all uterotonics are oxytocic, or capable of inducing true labor. ''Oxytocin'' is the hormone mainly responsible for labor resulting in birth; it is absolutely required for the milk ejection reflex (MER) to occur. Without oxytocin, there is no milk production. (It is worth noting here that women with a healthy pregnancy, who continue to nurse their child do not run an increased risk of premature labor.) Agents that are called oxytocic do not necessarily replace oxytocin, although many probably interact in some way at the oxytocin receptor. A synthetic form (Pitocin) is used to promote labor as well as trigger the MER after birth; it can act at peripheral receptor sites but cannot access the receptor sites within the CNS. At present, there is no information available on plant constituent interactions with oxytocin or its receptors in the brain or at peripheral sites. Although oxytocic herbs are properly contraindicated for self-use during pregnancy, there is a wealth of data on their usefulness in lactation. Galactagogues are herbs used with the intent of increasing milk production. Most herbal galactagogues common in clinical practice in Western countries have some degree of uterotonic or even oxytocin activity. Indeed, many of the hundreds of herbs traditionally used as oxytocics, i.e., speeding labor and delivery of both infant and placenta, are also traditionally used as galactogogues.[23–25] Recent lactation research has verified that frequent adequate milk removal is the primary mechanism by which milk production can be increased or maintained.[26] Adequate removal of milk immediately increases the rate of milk synthesis in that breast for the next several hours. Oxytocin is needed to remove milk and it is known that increasing the activity of the oxytocin system results in an increased milk flow from the breast, an immediate galactogogue effect. This boost in milk production can stimulate a flagging synthesis rate for a sustained galactogogue effect. Herbs with noted oxytocic effects have been noted to help trigger the MER as well as to increase milk flow. Both these actions can indeed aid lactation. However, a mother needing help with milk production is best served by consulting with a lactation specialist; judicious use of oxytocic herbs can play an important but complementary role.

Oxytocic activity is but one of many hormonal influences in which pregnancy cautions do not apply during lactation; indeed, hormonal activity risks during pregnancy may be what makes that herb helpful as a galactogogue. Although consumers should be able to easily identify such herbs, and thus avoid their unintentional use during lactation, health care providers should not mistake general consumer warnings as indicative of the need for all breastfeeding women to avoid supervised use when warranted.

Maternal Plant Use and Risks to the Infant

A study done in Minnesota examined the dietary habits of experienced breastfeeding mothers to determine what foods might be associated with colic symptoms in infants.[27] Researchers found a strong association between the consumption of cruciferous vegetables and the degree of crying and other colic symptoms. Clearly, constituents from the mother's diet are able to enter breast milk in sufficient quantity to cause the baby discomfort. It is worth noting that vegetables (foods) are consumed in much larger doses than most medicinal plants. No other systematic studies looking at food and adverse reactions in babies have apparently been done, although mothers are routinely told to avoid hot peppers, garlic, and onions by their doctors and others.

Capsaicin, the ''hot'' constituent in hot peppers, has been noted to cause problems with episodic consumption by the mother, including fussiness, diarrhea, and a red bottom in the baby. However, many mothers who eat hot peppers daily report no such problems. Additionally, infants accustomed to drinking ''spicy'' milk will readily eat spicy foods when introduced later in the first year. In the *Botanical Safety Handbook*, the authors classify garlic as an herb to use with caution, and cite references where infant ingestion of garlic resulted in death.[10] Clearly, the authors underestimated the dose difference between direct ingestion of a substance, and indirect ingestion of phytochemical constituents through breast milk. Although direct exposure of infants to large quantities of raw garlic may be potentially dangerous, the daily diet of many countries contains medicinal quantities of garlic, yet there are no documented adverse effects of garlic on nursing infants. Garlic is even used as a galactogogue in India. In one human trial, neither efficacy nor harm was demonstrated.[25] New lactation studies of garlic have been done, yielding no adverse effects.[28] Hale infers it is not known whether garlic constituents enter milk, which overlooks the pioneering work of Julie Mennella et al. who studied the effect of garlic on breastfeeding infants.[12] In an earlier study, these authors demonstrated greater interest and longer nursing times in infants whose mothers had ingested a dose of garlic. In a 1993 follow-up study in which mothers ingested garlic daily, the novelty wore off, and the infants went back to their usual nursing patterns. None of the infants suffered adverse effects during these tests. Given the widespread use of garlic as a food, and the existence of studies of garlic and breastfeeding infants, the maternal use of garlic to prevent or treat maternal breast candidiasis (thrush) should be considered a relatively safe and inexpensive alternative to certain medications, such as fluconazole, a powerful antifungal with potential serious adverse effects on the liver.

Allergy and Associated Risks of Direct Feeding on the Baby and Breastfeeding

The risk of allergic reaction to plant chemicals is real and most likely in the first months of life, yet significantly

reduced when exposure is restricted through breastfeeding. Not only are the range of plant chemicals reaching the bloodstream reduced but the dose received by the child is very small. Mothers with allergies or atopic and autoimmune diseases will need guidance with allergenic plants, for both her and the baby's protection. It is also important to determine the father's allergy history. When possible, initial use of simple rather than combination remedies will assist identification of the culprit if an allergy should occur in a mother or baby. Allergy, atopic, and autoimmune diseases are rampant in modern society, now in this third generation of widespread formula feeding experimentation. Besides being proved as a major preventative of allergenic and atopic disease,[15] exclusive breastfeeding in the first 6 months of life is also preventative against an enormous range of diseases of both childhood and adulthood;[1] direct feeding of substances (whether these are considered food, herbs, or drugs) other than breast milk is clearly an introduced risk.[1,29] The young baby's GI tract is not mature and is still quite ''leaky'' or permeable to ingested substances, even proteins. Early exposure of the GI tract and flora to foreign substances is thought to set the child up for subtle and frank infections as well as allergy. These effects may have permanent consequences.[14] Associated risks go hand in hand with premature direct feeding. It is possible to confuse a baby with bottle or pacifier nipples when used to administer a remedy or drug; replacing breast milk with other fluids will lessen his desire to nurse. (Young babies may only take 2 ounces at a time, an amount easily undermined with frequent ''tonic'' feeds.) For mothers already experiencing latching or other breastfeeding difficulties, these risks can become considerable, a fact that is not yet recognized in much of herbalist literature. Alternative treatment methods should be sought first. In some instances (e.g., colic), the mother can pass beneficial plant constituents through the milk without risking disruption of baby's pristine GI tract or throwing her breastfeeding relationship off-track. This wise and much safer method has been long known and is still used by mothers all over the world.

Herbs That Commonly Cause Adverse Effects in Infants: Coffee and Chocolate

Cases of adverse reactions to chemicals, whether drugs or herbs, usually involve newborns. Lawrence and Lawrence state that adverse drug reactions often can be traced to accumulation of the chemical in the infant, leading to adverse effects with increasing serum levels.[15] Just about the only herbs that are clearly and consistently able to cause adverse effects seen in infants are CNS-stimulant herbs, most commonly those that contain caffeine and other stimulant xanthine alkaloids: coffee, tea, chocolate, yerba mate, cola, and guarana. Even with its strongly alkaloidal nature, caffeine enters into milk in only tiny amounts. However, it tends to accumulate in the neonate, and can cause fussiness and hyperalertness. This effect is used with premature infants in whom tiny controlled doses of caffeine are given directly to prevent apnea. Despite the fact that mild adverse reactions have been documented in some newborns, caffeine is considered safe for use by breastfeeding mothers. Many mothers can ingest one to two cups of coffee per day without incident, even when breastfeeding neonates, although some babies, like some adults, are acutely sensitive to caffeine and react to any amount of caffeine even as they grow older. Mothers soon find out to what degree coffee, tea, or other caffeine-containing herbs are the cause of their baby's irritability and adjust their dose accordingly.[30]

Other Documented Adverse Reactions of Herbs during Breastfeeding

There is a body of literature describing adverse effects when young infants are directly fed herbal preparations or milk substitutes.[1,29] Yet, very few cases of adverse reactions are documented involving infants ingesting medicinal phytochemicals through breastfeeding, and those that do exist usually of involve herb ingestion during pregnancy as well. Farnsworth notes one case involving infant death attributed to the mother having used coltsfoot (*Tussilago farfara*) and butterbur (*Petasites officinalis*) during pregnancy as well as after birth while breastfeeding.[16] Both these plants contain hepatotoxic pyrrolizidine alkaloids. Without suggesting that the use of such herbs is hazard free during breastfeeding, it is reasonable to suggest that use during pregnancy alone could have produced significant liver damage before any amount was received through the milk. This case involved toxins that cause irreversible liver damage and death in adults, and underscores the need for contraindication of such substances in plant medicine more than that herbs per se are dangerous during breastfeeding. However, it remains entirely possible that the developing fetus as well as the newborn may be particularly susceptible to the toxic forms of pyrrolizidine alkaloids; there are other incidents of children being harmed through direct ingestion of these chemicals. There is no safe dose level established for children and a very stringent one set for adults in Germany. As the liver can sustain damage without immediate symptoms, it remains necessary to encourage nursing mothers to avoid consuming herbs with any amounts of these toxic substances that can cause irreversible adverse effects. Comfrey and borage are commonly used herbs known to contain various amounts of toxic PAs. The other widely recognized dangerous plant toxin is aristolochic acid, which is present in essentially all members of the Aristolochiaceae family. This toxin is associated with permanent and sometimes fatal kidney failure.[16,18] The limited elimination capacity of infants may place them at greater risk to this toxin.

The ''hairy baby'' story has entered the lactation textbooks, even though the original report has subsequently been shown to be incorrect.[15,16,31–33] A woman, thinking she was ingesting ginseng throughout pregnancy, was using twice the dose suggested by the label. She developed signs of androgenization during pregnancy, and the baby was born with significant hirsutism and other signs of androgenization. This incident reported ginseng as the likely culprit. A more thorough investigation showed that the package was actually labeled Siberian

ginseng (*Eleutherococcus senticosus*), and that the product was adulterated with the potentially toxic plant, *Periploca sepium*, although Farnsworth noted that in vitro hormonal studies of the adulterant did not show androgenic activity.[16] It was concluded that no likely cause of the hirsutism could be determined. This case has limited application in evaluating the risk of properly prepared herbal medicines during pregnancy or lactation. The ''hairy baby story,'' however, illustrates the number one deficiency in anecdotal reporting of adverse events involving herbs in medical literature: lack of verified identification of the actual substance consumed.

The first case identified in the literature that involves breastfeeding only was reported by Rosti et al.[34] In a letter published in *JAMA*, the authors tell how two mothers were taking high doses (2 L/day) of an herbal tea with the intention of stimulating lactation, twice the usual dosage of galactogogue teas considered appropriate. Assuming a typical tea, prepared in a standard infusion form, a more typical dose would be 1 L/day total at most. Both of their newborns presented with symptoms that included ''reduced growth, poor feeding and sucking, restlessness, emesis, hypotonia, lethargy, and weak cry.'' It is not clear how the babies could be both lethargic and restless at the same time. Poor breast milk intake alone could soon cause symptoms involving poor growth, suck and feeding, lethargy, low muscle tone, and a weak cry but would not explain restlessness or emesis. Obviously something was going on with these babies. The tea was reported to contain ''a variety of active ingredients'' that the authors listed as ''licorice, fennel, anise, and goat's rue.'' Symptoms resolved in both infants after the mothers discontinued the herbal teas.[34] Although it is common for mothers to ingest teas made from any or all of these ingredients without precipitating a visit to the emergency room, licorice (*Glycyrrhiza* spp.) and goat's rue (*Galega officinalis*) may be worth examining more closely, simply because of their capacities to induce side effects with excessive or prolonged use. Fennel (*Foeniculum vulgare*) and anise (*Pimpinella anisum*) both contain transanethole, a sweet-tasting compound thought capable of altering CNS activity, at least in high doses. It is quite possible that these babies may have simply been consuming breast milk containing too high a concentration of constituents, too early in the neonatal period, although a distinct lack of other similar adverse events points to other factors. First is the widespread use of such herbs where these mothers come from. In Italy, new mothers as a matter of course go out to buy galactogogue teas in pharmacies, whether they need them or not. Fennel and anise in particular, are favored there, as they have been for thousands of years. Goat's rue is very commonly used in France, a practice that dates back to antiquity as well. However, plant materials were not positively identified in the article, and adulteration of the presumed plant material is always a possibility, as occurred with the *Periploca* case. Given that fennel and anise both bear striking resemblance to a number of very toxic relatives (i.e., anise and the potentially toxic star anise have similar flavor), the question of plant identity must be raised. The letter does not indicate whether these women presented independently or were somehow connected. Since the letter's publication, no further corroborating cases involving any of these herbs have been published. Very little actual knowledge can be gained from such a letter, as the information was not scrutinized by plant or lactation experts and thus is incomplete and unverified.

A report involving the use of dong quai (*Angelica sinensis*) was published as a letter.[35] In this instance, a Chinese-American woman, 3 weeks postpartum, developed an acute onset of headache, weakness, lightheadedness, and vomiting and came to the emergency room for evaluation. In the ER she was found to be hypertensive (195/85). She had no history of hypertension, as verified from her medical record at birth. Blood chemistry and other studies were normal. Earlier that day, she had twice eaten a traditional postpartum soup made by her mother. The soup was reported as being made from *Angelica sinensis* rhizome that the grandmother had purchased in Malaysia before visiting her daughter. Within 12 hours of arrival at the ER, her blood pressure was once again within normal limits and other symptoms had disappeared. The next day, the baby was evaluated by a pediatrician and found to also have elevated blood pressure, which was treated by withholding breast milk. Within 48 hours, his blood pressure was normal. The authors clearly state that as they could not obtain a sample of the actual soup ingested, they could confirm neither the identity of the actual substance ingested, nor its dose. Use of other herbals or other medicines was denied by the mother. The authors did do the next best thing though, and obtained samples of the same product the mother purchased in Malaysia for analysis by a Chinese medicinal expert (unnamed) who said it was indistinguishable from *Angelica sinensis*. What is not mentioned in this article is the lack of any other cases in which ingestion of *Angelica sinensis* has led to high blood pressure. Indeed, the herb is known to be if anything, hypotensive in studies. Thus, the development of hypertension must be considered atypical. This is especially so given that it is a very widespread ancient tradition to use dong quai in postpartum soups for new mothers in Asia. A traditional Chinese medical practitioner in North America has commented that although most ordinary people would know when a new mother is already too ''hot'' and would not give the soup, it is entirely possible for such a mistake to be made. Further, botanicals imported from China are notorious for being contaminated—it is possible that it was not the herb, per se, but contaminants that, if at all, were associated with this episode.

External Use of Herbs on the Breast and Nipple

Products used to treat thrush or bacterial infections need to be nontoxic and nonallergenic to best ensure safety to the infant, who will be ingesting some share of such products.[31] The taste of an external substance can sometimes cause problems. Some babies refuse the breast upon tasting bitter substances and can quickly develop an aversion to the breast. To avoid this, babies must be nursed before external applications and the nipples rinsed before nursing if there are still obvious residues on the nipple.

It is possible that many substances in the cream may be absorbed into the breast tissue and thus enter the nearby milk ducts in relatively large amounts; wiping may not avert all potential problems with a questionable product. The use of potentially toxic herbs such as comfrey (which contains PAs) should clearly be seen as being an unnecessary risk to an infant, despite the herb's excellent healing properties. Safer alternatives, such as *Calendula officinalis*, should be selected. The use of essential oils on the breast and nipple is in general riskier than use of less-concentrated water-based herb preparations. Yet, tea tree oil is often suggested to treat nipple thrush, a practice that not only lacks evidence of efficacy but may be particularly unwise. First, babies exposed to tea tree oil near their faces and mouths may gag, or in a worst-case scenario, suffer respiratory collapse. This is a well-known phenomenon also known to occur with essential oils of peppermint, camphor, neroli, and cajeput, the last two being from close relatives of tea tree.[3] Tea tree oil can be irritating and sensitizing, leading to contact dermatitis, and there are two cases of toxicity associated with its use.[3] In one case, an adult developed petechiae and leukocytosis after ingesting about 7 cc of the essential oil; in another, a 17-month-old toddler developed ataxia and drowsiness after swallowing less than 10 cc of the essential oil.[12] Taken altogether, tea tree oil should not be used or suggested for nipple thrush and safer alternatives should be sought.

Risks to the Mother

The lactating breast is metabolically extremely active. All components of the milk are brought through the bloodstream and incorporated directly or assembled in the secretory cells. The breast has dermatologically unique areas—the areola and nipple. The nipples mark the boundary between mucous membranes of the internal ducts and external skin of the areola. The skin of the areola is very thin compared with other skin; both areas are extremely sensitive. It is known that breast sensitivity increases during lactation; this facilitates oxytocin release that is triggered in the brain by suckling. There is reason to believe that the lactating breast may be more unusually sensitive to externally applied substances, perhaps because of increased permeability of the skin.[25,36] It is known that very sensitive mothers can develop eczema from food residues in their babies' mouths. The permeability of the breast has not been directly studied, however. Care should be taken for the mother's safety when applying external products to the breast and nipple.

There are a number of reports of allergic reaction to herbs applied to the nipple, most often in an effort to heal sore nipples. One short communication gives two case histories that involved Roman chamomile *Chamaemelum nobile*. The herbal cream was applied to sore nipples and resulted in severe exudative eczema on the nipples and the areola.[37] In both cases, the mothers used a product marketed for sore nipples. One mother had used the product with her previous child without difficulty. Roman chamomile is much more frequently reported as a cause of allergic reactions than its relatively innocent cousin, German chamomile (*Matricaria recutita*).

Another case described the use of garlic on the breast, which resulted in skin burns.[36] Although the letter did not include this fact, garlic is a known allergen.[3] The mother was self-treating a rash on her breast that she thought was ''thrush,'' in and of itself a likely misdiagnosis. She placed fresh garlic on the rash and left the area covered for 4 days. The baby had access to the nipple and continued to nurse uninterrupted. The mother immediately experienced pain at the site, which continued for the entire time, but she did not remove the garlic plaster. When she presented to the emergency room, she was found to have third-degree burns to the site. Through the whole ordeal, the baby was not deterred from breastfeeding, and suffered no consequences. The authors do a first-rate job of differentiating between the risks and benefits of garlic ingestion vs. external application, clearly saying that this case has nothing to do with internal garlic use and cannot be used as an argument against it. They also do a good job of finding the rather numerous reports of fresh garlic having caused burns when used externally, and correctly point out that the mother's persistence of use contributed greatly to the event.

Risks and Benefits of Lactation-Modulating Herbs

The risk of herbs during lactation is, in the minds of most practitioners, limited to risk to the infant. Until very recently, both the herbal and pharmaceutical literature restricted consideration of risk to the infant and completely ignored the impact of a medicinal substance on milk supply or fertility.[3,10–12] There are some signs of this changing, perhaps related to the widespread successful use of herbal and pharmaceutical lactation modulators.

Hundreds of plants from all cultures are used as galactogogues.[25] Only a few of these are known and commonly used in the United States and Europe. Fenugreek (*Trigonella foenum-graecum*) (Fig. 18-1), blessed thistle (*Carduus marianum*), fennel, anise, nettle (*Urtica dioica*), alfalfa (*Medicago sativa*), marshmallow (*Althea officinalis*), and goat's rue have gained acceptance and see widespread, if mostly undocumented, use by lactation specialists. A well-recognized lactation consultant, Kathleen Huggins, wrote of her extensive use of fenugreek in helping hundreds of women increase milk supply.[38] Few side effects were experienced by either mother or baby, although isolated cases of diarrhea or allergic reaction in the mother were noted. Very rarely, an infant may experience diarrhea. Since that report, fenugreek use has become increasingly common and accepted. Combinations of fenugreek and blessed thistle have been recognized to help if taken in sufficient amounts; doses of up to 3 g/day of each have been found efficacious.[14] Mothers need to divide the doses and may find that gradual introduction over a few days avoids side effects. Fears of lowering blood sugar, an effect of fenugreek when consumed at 15 to 100 g/day are unfounded at this dose range.[39]

Formal studies are rare, however. One pilot study of fenugreek showed a positive effect on pumped milk volume in women.[40] The most commonly used

Figure 18-1 Fenugreek (*Trigonella foenum-graecum*). (Photo by Martin Wall.)

alternative pharmaceutical, metoclopramide, enters the blood–brain barrier and can cause maternal depression after extended use; domperidone does not enter the CNS and is relatively free of side effects, but because of its orphan status in the United States, it has limited availability.

This is truly a situation in which herbs can be viewed as preferable. Galactagogues are useful only when a true low supply issue exists; their role is secondary to basic lactation techniques to building milk supply. General marketing of herbal galactagogues to breastfeeding women is considered unethical, because it preys upon new mothers' often unfounded fears of inadequate milk. If a real problem exists, sole reliance on an herb may delay effective assistance without fixing the basic problem. It is critical to point out here that failure to establish a good supply in the early week or two of breastfeeding often results in a permanently reduced supply or weaning. Both herbs and pharmaceuticals can be very helpful in inducing and re-establishing lactation and are sometimes used in combination.[14]

It has become better known and accepted that many herbs and a few pharmaceuticals can modulate the process of lactation, affecting milk supply as well as the lactation amenorrhea state. Although herbalists may consider anything that increases milk to be a boon to nursing mothers, this is by no means a safe assumption.

Risks to Lactation

Herbal risks to milk production are not well discussed in the herbal literature. Most reference texts seem to focus entirely on the toxicity risk to the infant, and are not very consistent in identifying which herbs are traditionally used to increase or decrease milk. For example, the German Commission E entries for fennel make no mention of the herb's widespread use as a galactogogue, nor does it mention the use of sage for weaning.[3] The American Herbal Products Association's comprehensive review of a large number of herbs is to be commended for considering lactation separately from pregnancy, but likewise neglects to consider an herb's potential to increase or decrease milk production.[10] Feltrow and Avila, although contraindicating just about every other herb in their book, did not contraindicate dill, citing its traditional use as a galactogogue.[8] However, the idea that increasing supply is safe, that is always beneficial during breastfeeding, is simply not true. Some mothers may have an overactive milk ejection reflex and produce more milk than their babies can handle; the reasons for this development are unknown. But negative consequences are widely recognized by lactation specialists.[30] Herbalist lactation consultant, Mechelle Turner, suggests discontinuing prenatal alfalfa and nettles about 2 weeks before birth, so that their galactogogue influence will not cause or worsen oversupply problems in the early weeks of breastfeeding. Unintentional use of weaning herbs can also cause problems. ''Green drinks'' that contain parsley juice have been noted to lower supply. Use for oversupply, weaning, or unintentional lowering of milk supply has not been formally studied. These effects are reported in anecdotes gathered by lactation specialists but are in agreement with the traditional lactation use of these herbs. The mechanisms by which herbs may modulate synthesis or supply are far from understood, although for the galactagogues many potential mechanisms, and possibly active constituents, have been summarized in Bingel and Farnsworth's review of galactogogues.[25]

Herbs That Influence Prolactin

Endocrine stimulation of the breasts after birth drives the initial production of milk. In this stage, serum prolactin is high with even higher pulses released in response to a nursing session.[15] Later, autocrine control mechanisms prevail and each breast independently produces milk in response to milk removal.[26] Prolactin levels in later lactation are near normal between nursing sessions but spike after each feeding. Frequent and high prolactin spikes are associated with good milk supply as well as the maintenance of lactation amenorrhea.[15] Nonlactating women do not normally show elevated prolactin levels; indeed, hyperprolactinemia is generally seen as a stress response, and is associated with PMS symptoms and some associated infertility states (see Vitex in McKenna et al.).[7]

Herb influences on prolactin levels during human lactation have not been studied; studies done in this area

have used men or nonlactating women, with the exception of chaste berry (*Vitex agnus-castus*), which has been studied in lactating women.[41] Although the studies were done before the discovery of prolactin, and suffer from serious lactation study methodology flaws, the findings consistently indicated a galactogogue effect, in line with the herb's ancient and traditional use in Germany. Recent in vitro and in vivo animal studies found an antiprolactin and antigalactogogue effect after intraperitoneal injection with rats.[42–44] However, the question of dose has been raised. In one tantalizing study, low doses of a chaste berry extract raised prolactin, whereas high doses lowered prolactin in men.[45] It is far from clear just what effect chaste berry truly has on human lactation. It is well known, however, that it can be used to induce or re-establish normal ovulation in women with high prolactin levels. Mohr related that those lactating women who were instructed to continued using chaste berry tincture for more than 2 weeks reported an unexpectedly early return of the menstrual cycle.[41] This return of the menses and fertility after only a few weeks after birth needs to be seen as a loss of benefit to breastfeeding mothers; decreased risk of breast and ovarian cancer is related to the lower estrogen states that are especially prevalent during lactation amenorrhea. On the other hand, other breastfeeding mothers may find this same property of chaste berry of great benefit. Mothers of nursing toddlers may find their fertility is impaired but do not wish to actively wean their children. Chaste berry could restore fertility without the need for stressful mother-led weaning or the use of powerful fertility drugs.

Bugleweed (*Lycopus* spp.) and prolactin have a complex relationship in which at least some studies have found an antiprolactin effect mediated to some degree through its antithyroid actions.[46] Thus, it is generally contraindicated during breastfeeding. Given the many unknowns about bugleweed as well as prolactin, and the necessity of seeking expert medical guidance for situations involving the very complex but critical thyroid gland, general avoidance of this herb during lactation unless under the guidance of a qualified practitioner seems sensible.

HEALTH ISSUES AS SEEN IN THE CULTURAL CONTEXT OF THE BREASTFEEDING WOMAN

Herbal literature has shown little understanding of some health issues pertinent to breastfeeding women. Advice on herbs is generally presented in a vacuum, without consideration of larger cultural issues that are pressuring a breastfeeding mother. These may need to be countered first, to ensure the best protection and support for breastfeeding. Fatigue, depression, anxiety, and weight loss are common health concerns for women in Western cultures. Breastfeeding mothers are like other women and are afflicted with these health concerns. A breastfeeding mother is often isolated and overwhelmed in her role as mother and exclusive source of food for her baby. She often experiences great challenges in taking on her new role as mother, and can easily feel that breastfeeding is to blame for the fatigue, anxiety, and being over her usual weight. Modern Western culture places great importance to a mother getting back to ''normal'' quickly, even though this is not really possible. The fact is children change everything. Many mothers seek pharmacologic assistance to make these adjustments, and true to our culture's fondest beliefs, feel that the answer to their problems lies in a pill, whether it is a prescription or an herb capsule. And herein lies the dilemma: Mothers feel they must take ''something'' to fix problems that are better addressed through finding a network of supporters, sharing in discussions of parenting, breastfeeding with other mothers, or for some seeking counseling. Often, great improvement is experienced once improved communication of her needs is achieved with those closest to her. For example, cognitive therapy is proved to be as helpful as pharmaceutical antidepressants in the treatment of postpartum depression and may be more beneficial in the long term in preventing recurrence with the next child.[30]

Breastfeeding mothers are terribly sensitive to any information that suggests she is taking a risk in using any medicinal agent yet are culturally conditioned to greatly underestimate the risks inherent in formula use. Thus, she is easily led to wean if it is even hinted that this would be ''safer'' than using a medicinal or more typically, weaning to use a drug. Although few women wean in order to use an herb (other than tobacco), they may very easily be led to believe that the herbal option is always more dangerous than the pharmaceutical, given the current state of written information. On the other hand, some mothers will not consider anything but the herbal option, thus making it necessary for a rational decision to be made about a particular herb (Box 18-2). It is with these conditions in mind that the following discussion on controversial herbs is offered.

A Note about Alcohol and Tinctures

Tinctures are sometimes contraindicated during lactation out of concern for the infant receiving some alcohol through the milk. In pregnancy, any amount of alcohol can have negative consequences to the fetus, as exposure comes at a much more sensitive time in development. However, an occasional drink or regular light drinking (one or fewer drinks per day) is considered compatible with breastfeeding.[11,30] Heavier drinking (two or more drinks every day) may inhibit the milk ejection reflex.[30] Of course, heavy drinking renders the mother unfit for parenting, regardless of how the baby is fed.[14] Appropriate use of tinctures, on the other hand, would not be expected to represent this level of alcohol consumption. Tincture use during breastfeeding would seem to be a nonissue, because there is no evidence of harm from a mother enjoying a beer with dinner or a glass of wine or two at a party.[30]

Unsafe Compared with What? Psychoactive Herbs

Depression and anxiety are two issues that often lead a mother to the doctor's office. Antidepressants and anxiolytics have commonly been prescribed during lactation, although their use is not entirely accepted given the potential for alteration of brain chemistry in the infant.[11] However, some antidepressants enter the milk

BOX 18-2

Questions to Consider in Assessing Herb Use during Lactation

- Have you positively identified the herb(s) in the product to be taken? (The botanical Latin name should be on the package.)
- Have you ascertained the quality and reliability of the herbal product company being considered?
- What is the general nature of this herb? Does it have a wide margin of safety with no suggestion of toxicity? Are expected side effects mild and reversible? Is there any documented adverse effect of the herb on the breastfed child? Again, most herbs are not noted to cause problems in infants, nor expected to, although there are exceptions.
- How old is the baby and how much is she or he nursing? Is this a very young baby or a toddler? Is the baby exclusively breastfeeding or have other food plants already been introduced into the diet? Was this child born small-for-gestational age or premature? Does this child have health conditions, atopic disease, or allergies? Is the baby taking medications?
- What is the mother's medical history? Is this a safe herb for her? Does she use medications or dietary supplements that will require consideration of potential interactions? Does she or the father of the child have any relevant allergies?
- Is the mother intending to ingest it or use it externally? External use that does not involve the breast is mostly noncontroversial. Essential oils require more caution. Their use on the breast may not be appropriate.
- What are the risk–benefits of the herbs compared with the risks–benefits of the pharmaceutical alternative? And, does she run the risk of being told to wean in order to use the pharmaceutical alternative?
- Is the reason for taking the herb serious or chronic, or is it minor and self-limiting? In other words, what degree of harm is possible if the therapy does not work? If this is a breastfeeding problem, has she received help and guidance from a lactation specialist? For the sake of her breastfeeding relationship, this last question always should be answered, Yes!

supply to such a small extent that they cannot be detected in the baby's serum at all. These drugs are not absolutely contraindicated in lactation because the risks of formula are greater than any observed effects in the baby and untreated depression in the mother also has been shown to impact the baby's normal development.[14] Of course, such agents are not ever to be used lightly and at the lowest dose and shortest time possible. When needed, they should not be withheld or weaning forced.

St. John's wort (*Hypericum perforatum*) is an example of a well-studied herb for which considerable evidence has accumulated suggesting it is efficacious for the treatment of mild to moderate depression.[3,7,47] It is expected to be no more of a risk for infant health than any other antidepressant, and perhaps a better risk because it causes fewer side effects in the mother. Few if any effects would be expected in the baby. In a recent study, St. John's wort has been shown to have an acute negative effect on prolactin levels; within hours of ingestion, prolactin levels drop. However, after 2 weeks extending the same animal model, the herb has been found to increase prolactin levels well above those of the control group, SSRIs have been found to elicit the same drop in prolactin, with levels later returning to baseline.[48] However, no study of prolactin response in breastfeeding women exists, and the German Commission E report indicated no known problems with milk supply in this widely used herb.[3] If there are no other contraindications to the use of this herb (i.e., concomitant contraindicated medication use), there seems little reason to contraindicate it is a possible therapy for postpartum depression (see Postpartum Depression). There are also a number of other noncontroversial herbal alternatives for many nervous conditions. Valerian, passion flower, and oat straw are just a few of the psychoactive herbs that can be expected to be safe to use during breastfeeding. It is known that anxiolytics such as benzodiazepine can cause sedation in very young infants; necessary use is compatible with breastfeeding when the baby is closely monitored.[11] Nervine and sedative herbs are very mild compared with their pharmaceutical counterparts, and the amount of constituents entering breast milk unlikely to be sufficient to sedate a baby. Even though these would be expected to readily enter milk, no adverse events are known. Skullcap has been known to be contaminated with the toxic plant germander, so its use should be limited to reliable sources.

Weight Loss and the Infamous Ephedra Dilemma

Weight loss becomes an obsession that sets in with many mothers immediately after birth or within just a few weeks. Despite the biologically important gain of fat during pregnancy that prepares her body to feed the baby for many months, women are culturally guided to quickly return to a nonmaternal state of appearance. Herbal weight loss products abound in our culture, and mothers cannot help but encounter them. Breastfeeding mothers often approach breastfeeding counselors with questions about herbal weight loss products. Although recent bans on ephedra (*Ephedra sinica*) in dietary supplements has limited access to this herb, more obscure CNS-stimulant plants such as *Sida cordifolia* or *Citrus aurantium* are being substituted for ephedra.

Ephedra alkaloids are stimulants that are known to cause overstimulation and sleeplessness in breastfeeding babies.[30,49] As well, pseudoephedrine has recently been confirmed to lower milk supply by lowering prolactin levels at least on an acute basis.[12] In fact, some practitioners use pseudoephedrine in small doses to lower an overactive milk supply. It is interesting to note that the

German Commission E did not contraindicate ephedra in doses of up to 300 mg ephedrine per day during lactation, recognizing its utility for asthma while apparently finding little evidence for risk during lactation when used in a traditional episodic manner.[3] Given the stimulant nature of ephedra alkaloids and caffeine, combination products would be expected to yield an additive stimulant effect. Indeed, incidents of serious harm associated with the use of ephedra products typically involve such combination products.

This author has known mothers so desperate to lose weight that they said they would wean if they could not use a certain product. Many mothers have a very limited understanding of the risks of formula feeding or the benefits of breastfeeding. They may not know that breastfeeding will provide weight loss in a slow but permanent fashion; indeed, she can expect to lose more weight and keep it off by simply breastfeeding for a year compared with bottle-feeding mothers who dieted. Honest counsel on the risks and benefits of weight loss products, the benefits of breastfeeding for permanent weight loss, and the risks of weaning are essential. As of this time, ephedra containing weight loss products are no longer commercially available in the U.S.

COMMON LACTATION CONCERNS: ENGORGEMENT, CRACKED NIPPLES, MASTITIS, AND INSUFFICIENT BREAST MILK

Aviva Romm

Breastfeeding is, undoubtedly, the best nutritional option for the human infant. No substitute provides the essential nutrients needed by the baby, along with the immunologic protection and emotional nourishment provided by breastfeeding. Although not all women are able to breastfeed because of medical reasons, economic limitations, or lack of social support, many women quit breastfeeding because of common breastfeeding problems. Breast and nipple problems can detract terribly from the mother's experience of breastfeeding. Nipple pain can make breastfeeding nearly unbearable; both engorgement and mastitis can be extremely painful and worrisome, and mastitis presents acute illness that is debilitating; insufficient breast milk (or fear that the baby is not getting adequate nourishment) is tremendously anxiety provoking. It is the responsibility of women's health care providers to supply education and support should breastfeeding problems arise, and provide options for treatment that are safe and simple, enabling breastfeeding to continue whenever possible.

Herbal treatments for problems associated with breastfeeding can be identified in botanical writings as far back as ancient Egypt. Arabian physician Avicenna describe massaging the breast to improve insufficient milk production, and giving the mother black cumin, carrot, clover, dill, fennel, fenugreek, and leek mixed with fennel water, honey, and clarified butter. Herbs to induce lactation used by seventeenth-century midwives and physicians included aniseed, barley, cumin, dill, fennel, and flax—as well as the traditional well-known treatment—ale. Herbs such as St. John's wort, poppy oil, and red rose water, usually mixed in some form of oil or fat, were applied directly to the nipples for the treatment of sore, cracked nipples.[50] The medieval compendium of women's medicine, *The Trotula*, mentions applying plasters of vinegar and clay to the breasts for the pain of breast engorgement and mastitis.

Modern midwives have evolved a number of successful strategies for treating breastfeeding problems, and have a track record for long-term breastfeeding among their clients/patients. A number of the aforementioned herbs remain in use today.

SORE, CRACKED NIPPLES

Some amount of nipple soreness in the initial week of breastfeeding, especially with a first baby or with a long time span between pregnancies, is normal. The increased nipple sensitivity common to pregnancy usually begins to subside in the first week postpartum, but until then can lead to heightened discomfort. Normal sensitivity usually persists for 30 to 60 seconds once the baby latches on; pain caused by nipple trauma persists or worsens throughout a feeding. Prenatal nipple preparation has not been shown to be effective in the prevention of nipple pain or irritation after birth.

Nipples may become sore, cracked, and may even bleed, due to a variety of reasons including improper positioning of the breastfeeding baby on the nipple, thrush (*Candida albicans*) infection from the baby's mouth, or use of breast pads, which keep the nipple moist and can aggravate irritation or thrush. *Staphylococcus aureus* and other organisms are less commonly involved in nipple infection. Prevention is the best treatment. A midwife or lactation consultant should be contacted to assist in helping the mother position the baby properly on the breast if there is difficulty with nipple pain or trauma.

General Prevention and Treatment

- Ensure proper position of the baby at the breast; consult with a midwife or lactation consultant if needed.
- If nipples are sore or cracked, gently rinse and pat dry them after each feeding, and let air dry if possible for 10 minutes after each nursing.
- Avoid the use of breast pads, and whenever possible, spend time without a bra. This allows the nipple to remain dry between feedings and eliminates an otherwise friendly environment for microbial growth, especially in the breast pad.
- Treat oral thrush in the newborn to prevent spread to the nipples.
- Plastic breast shells can be worn to prevent irritation from clothing rubbing against the nipples.
- Wash nursing bras regularly if there is infection to avoid recontamination.

Medical Treatment

The medical treatment of breastfeeding-related nipple problems includes the general strategies listed in the preceding, as well as the addition of antibiotic ointments in the treatment of fungal or bacterial infection.

Such preparations are applied after each nursing, for 2 to 5 days, and are considered safe for use during breastfeeding. A lanolin ointment may be recommended in the absence of infection, though some women report sensitivity to lanolin and cannot use it. One report recommended that concentrated vitamin E oil preparations be avoided because they can be toxic to the baby in high doses.[51]

Herbal Treatment

In additional to the general treatment strategies described above, a number of topical herbal preparations are used to assist in the healing of irritated tissue, and as topical anti-inflammatory and antimicrobial agents (Table 18-1). Herbal applications for dry, cracked, painful nipples are usually applied as extracted oil or salve, carefully rubbed on the nipple several times daily after nursing. Excess remaining on the nipple can be wiped off prior to subsequent feeding. When there is infection, antimicrobial herbs may be used as tincture diluted in water (1:4), also after feeding, repeated throughout the day.

Discussion of Botanicals

Calendula

Calendula has a long history of use as a vulnerary herb. It is approved by ESCOP and the German Commission E for the treatment of minor inflammations of the skin and mucosa, and as an aid in the healing of minor wounds.[52] It is used as an oil extract and in salve for the treatment of inflamed, irritated, sore, or cracked nipples. Hydroethanolic extracts have exhibited antimicrobial and antifungal activity, and may be used as a topical rinse when there is infection.[52] There are no data in the scientific literature that supports or refutes the safety of use during lactation. There are no known or expected risks from minimal ingestion by via short-term maternal use on the nipple.

Chamomile

The use of chamomile is supported by the German Commission E and ESCOP for the treatment of skin inflammations and bacterial skin diseases.[3,52] There are no expected contraindications or side effects. Rarely, allergic sensitization has occurred from prolonged use of the herb; however, the risk appears very low, especially when *Matricaria* spp. is used.[52,53] The oil of *Matricaria* has demonstrated activity against *Candida albicans* at a concentration of 0.7%.[52] Several studies evaluating the efficacy of chamomile ointments and hydroethanolic extract in the treatment of topical inflammation and dermatitis have demonstrated improvement, either comparable or superior to cortisone.[52] It is frequently included in herbal salves for the nipples, in combination with other herbs discussed in this chapter.

Comfrey

Comfrey, also a traditional vulnerary, is generally considered safe for topical use in small amounts and for short durations on open skin. However, because of the potential for hepatotoxicity from pyrrolizidine alkaloids via ingestion by babies from the mother applying it to the nipples, this herb is NOT considered optimal for topical use on the nipples of breastfeeding mothers other than acutely. Residues should be thoroughly wiped off prior to nursing, and use should be limited to several days.

Goldenseal

Goldenseal is positively regarded by herbalists for its efficacy as a topical antimicrobial. There are no human clinical trials studying the antimicrobial effects of goldenseal. Goldenseal extract has shown in vitro and in vivo efficacy in the treatment of *Candida* infection on the mucous membranes.[7] It is commonly used in herbal salve to treat nipple infection and promote tissue healing.

TABLE **18-1**

Herbs Commonly Used to Treat Sore Nipples

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Heal cracks, fissures	Vulnerary	*Calendula officinalis*	Calendula
		Hypericum perforatum	Comfrey*
		Symphytum officinalis	St. John's wort
Moisten dry, cracked tissue	Emollient		Almond oil
			Cocoa butter
			Coconut oil
			Beeswax
Reduce irritation and inflammation	Antiinflammatory	*Calendula officinalis*	Calendula
		Hypericum perforatum	St. John's wort
		Symphytum officinalis	Comfrey
Treat fungal and bacterial infection	Antimicrobial	*Camellia sinensis*	Green tea
		Commiphora mol mol	Myrrh
		Hydrastis canadensis	Goldenseal
		Matricaria recutita	Chamomile
		Melaleuca alternifolia	Tea tree

*See comfrey discussion above for safety considerations.

Berberine is sometimes listed as contraindicated during lactation. This is based on evidence from animal studies that goldenseal has bilirubin displacing effects and may lead to neonatal jaundice, as well as on the observation that after ingestion of berberine containing herbs, babies with glucose-6-phosphate dehydrogenase deficiency (G6PD) developed hemolytic anemia and jaundice.[7] After these herbal products were banned for use by the Singapore government, the incidences of neonatal jaundice dropped; yet, they remained high among infants in southern China and Hong Kong, where they were not banned.[7] The issue of safety of goldenseal use during lactation remains inconclusive. Blumenthal et al. state that there are no known contraindication during lactation, but its use should be avoided during lactation until further research has been conducted.[54] No research has been conducted on the minimal amount that might be ingested by an infant from the use of goldenseal in salve on the mother's nipples. No adverse effects, nor neonatal jaundice, has been observed or reported from such use in midwifery practice.

Green Tea

A prospective, randomized trial was conducted of 65 primiparas with sore nipples who were breastfeeding after a vaginal delivery at 37 or more weeks gestation, who were 36 hours or less postpartum, and had combined mother–infant care. Participants were assigned randomly to one of six treatment groups with one of three regimens (tea bag compress, water compress, or no compress) randomly assigned to right or left sides. Participants applied the treatments at least four times a day, from Days 1 to 5 postpartum. Tea bag and water compresses were more effective than no treatment, with no statistically significant difference between the two types of compresses. The authors concluded that tea bag compresses are an inexpensive, effective treatment for sore nipples during the early postpartum period.[55] Additionally, green tea has demonstrated efficacy against methicillin-resistant *Staphylococcus aureus*.[56] Water extracts of green tea, or green tea bags, may be applied directly to the nipple. There are no known adverse effects or contraindications to use.

Myrrh

Local anesthetic, antibacterial, and antifungal effects have been reported with use of the sesquiterpene fractions of this herb.[57] It is almost always used as an ethanol extract, as it is not highly water soluble; it is also used in powdered form in ointments and directly on weeping, sore tissue. The German Commission E Monographs support its use for the topical treatment of mild inflammations of the oral and pharyngeal mucosa. The diluted tincture (1:4 with water) is dabbed on the affected area two to three times daily, or the mouth is rinsed with 5 to 10 drops of tincture diluted in a glass of water.[3] It may be used diluted and applied to the nipples several times daily, and is sometimes used as a rinse in the baby's mouth if this is the source of the thrush. Hans Schilcher, a German pediatrician, recommends its use as a treatment for oral thrush in *Phototherapy in Paediatrics: Handbook for Physicians and Pharmacists*.[58] There are no known safety contraindications to its use for mother or baby in this manner, with oral doses of up to 3 g/kg showing no major side effects.[56]

St. John's Wort

St. John's wort traditionally was used as a topical aid in the healing of cracked, dry nipples, and thrush. Both oil and ointment have demonstrated effectiveness in the treatment of burns and for the healing of skin injuries. Hypericum ointment standardized to 1.5% hyperforin reduced skin colonization of *Staphylococcus aureus* better than placebo in a prospective, randomized, placebo-controlled, double-blind study of the treatment of subacute atopic dermatitis. There are no known contraindications to use in this manner.

Tea Tree

Current research, presented in a thorough review by Carson et al., supports the use of tea tree oil (TTO) as an antibacterial and antifungal, as well as an anti-inflammatory.[59] Limited studies have been done on TTO's use as an antiviral, but a few trials have indicated possible activity against enveloped and nonenveloped viruses.[59] Several studies have demonstrated efficacy against *C. albicans*; however, to date, no clinical trials have been done. A rat model of vaginal candidiasis supports the use of TTO for VVC.[59] The mechanisms of antimicrobial action are similar for bacteria and fungi and appear to involve cell membrane disruption with increased permeability to sodium-chloride and loss of intracellular material, inhibition of glucose-dependent respiration, mitochondrial membrane disruption, and inability to maintain homeostasis.[60–63] Perhaps what has attracted the most interest in this herb is that it has demonstrated activity against antibiotic-resistant bacteria. Further, its use in Australia since the 1920s has not led to the development of resistant strains of microorganisms, nor have studies that have attempted to induce resistance, with the exception of one case of induced in vitro resistance in *Staphylococcus aureus*.[64,65] Tea tree oil applied directly to the nipple can be caustic and irritating, and should only be used highly diluted (1:10 with a carrier oil such as almond oil). Further, there is no established safe dose of this for babies. There are several reported cases of ataxia and drowsiness in young children who consumed 10 mL or less of the oil; therefore, TTO is not recommended for use as an oral rinse for babies with thrush, and if it is used to treat nipple thrush, the nipple should be rinsed off thoroughly before nursing.[56]

Breast Engorgement

National surveys in the United Kingdom have shown that painful breasts are the second most common reason for giving up breastfeeding in the first 2 weeks postpartum.[66] One factor contributing to pain is breast engorgement. Views differ as to how engorgement arises, although restrictive feeding patterns may be contributory.[66] Engorgement refers to swelling of the breast associated with breastfeeding. Engorgement is classified as early or late in onset, depending on when in the postpartum period it arises. Early engorgement occurs

because of edema, inflammation, and accumulated milk, whereas late engorgement is caused by accumulated milk only. Early engorgement typically occurs between 24 and 72 hours postpartum but may occur any time in the first postpartum week. Even a significant amount of engorgement may occur following birth, with a sense of fullness, warmth, and heaviness in the breasts, a normal physiologic change owing to an increase in the vascular supply.[66] In some women, milk production exceeds the baby's demand, and excess milk builds up, leading to distention of the alveolar sacs, and consequently hot, tender, swollen, and painful breasts. Edema may occur, if untreated, because of pressure of the surrounding tissue on lymph nodes, preventing their draining.

Early engorgement typically resolves over the first couple of weeks postpartum as the production of breast milk regulates to the breastfeeding demands of the baby. Engorgement can be extremely uncomfortable, as the breasts become markedly distended, hard, and hot to the touch. It can also make breastfeeding difficult as nipple protractility is reduced and latching on of the baby to the nipple can be challenging. The mother should be taught strategies to reduce engorgement, make the nipple more accessible to the newborn, reduce discomfort, and nurse regularly in order to establish the appropriate amount of milk production. Late engorgement occurs anytime during the breastfeeding period, but is most likely to occur in the first year. It commonly occurs if a feeding is missed, allowing milk to build up. It may lead to mastitis, in which there is a blocked milk duct preventing adequate emptying of the breast (see the following) and subsequent local or systemic inflammatory response and local infection. Treatment of early and late engorgement is the same.

General Prevention and Treatment

- The breast should be emptied regularly to prevent and treat engorgement. To facilitate latching on if the nipple is not protracted, the mother can reduce swelling of the areola by initially hand-expressing or pumping a small amount of milk and then putting the baby to the breast.
- Engorgement can be avoided by:
  - Allowing breast milk to freely flow out of the breast not being nursed while nursing on the other side (use a cloth diaper, receiving blanket, or towel to catch the running milk)
  - Avoiding tight-fitting bras
  - Nursing the baby often, on demand, and allow the breasts to be emptied as much as possible at each feeding
- Hot water running over the breasts can stimulate release of breast milk. Mothers can take a hot shower and let the water spray over the breasts, and let milk run freely out of the breasts; a hot bath will often also stimulate this reflex.
- Hot packs and cold packs both bring relief of discomfort. Women may try each and use the method that brings the greatest relief.
- Pumping the breasts other than to facilitate latching on during engorgement, should be avoided because it increases breast milk production beyond the baby's demand, and can increase engorgement.
- Massage appears to play a role in relieving discomfort. This was suggested by a randomized masked trial in 39 women in which application by massage of cabbage leaf extract (not otherwise effective) and placebo provided equivalent symptomatic relief.[67]

Medical Treatment

In addition to the practical strategies described in the preceding, analgesics may be considered for severe pain. The American Academy of Pediatrics considers acetaminophen and ibuprofen safe and effective for pain relief during breastfeeding.[68] Serrapeptase, a proteolytic enzyme product, is commonly used throughout Europe for the treatment of inflammatory and traumatic swelling, as an alternative to salicylates, ibuprofen, and other NSAIDs. Serrapeptase has been used in the treatment of fibrocystic breast disease and breast engorgement. In a double-blind, randomized, placebo-controlled study, 70 patients complaining of breast engorgement were randomly divided into a treatment group and a placebo group. Serrapeptase was superior to placebo in improving breast pain, breast swelling, and induration, with 85.7% of the patients receiving serrapeptase reporting moderate to marked improvement.[69] A review by the Cochrane database found that serrapeptase (Danzen) and bromelain/trypsin complex (OR 8.02, 95% CI 2.8–23.3) improved symptoms of engorgement, compared with placebo. Serrapeptase is available as an over-the-counter nutritional supplement. No data are available regarding its entry into milk or potential side effects in breastfeeding infants.[66]

Herbal Treatment

Midwives routinely use the common sense strategies described under General Prevention and Treatment. These are usually adequate to prevent or relieve engorgement. If there is mastitis, botanical treatment strategies are added (see the following). A popular folk remedy for the treatment of breast engorgement is the application of cabbage leaves to the swollen breasts. Fresh, refrigerated leaves are slightly crushed, for example, by rolling under a rolling pin, and are applied to the breast to draw out heat and inflammation. The leaves are left on until they become warm, and then are changed. This is repeated several times daily. According to a Cochrane review, cabbage leaves were no more effective than the use of gel packs for relieving discomfort.[66]

PLUGGED DUCTS AND MASTITIS

Milk ducts can become plugged, distended, inflamed, and tender owing to localized milk stasis. In mastitis, the plugged ducts are accompanied by infection. The differential diagnosis between plugged ducts and mastitis is the absence of signs of systemic infection including fever, local redness, and myalgia. Plugged ducts are most often easily treated by applying heat and gently expressing the blocked milk. Rarely, a galactocele may form

in which the milk congeals into a thick consistency and requires aspiration. Factors contributing to plugged ducts are similar to those for breast engorgement (see the preceding), and similar prevention strategies should be employed, including ensuring proper position of the baby on the nipple during feedings, and using gentle massage and heat to facilitate milk release from the duct. It may take several days to completely empty the duct and for residual soreness to resolve.

Mastitis is a breast infection affecting at least 1% to 3% of lactating women. Symptoms include a hard, tender, inflamed area of one breast, accompanied by fever which can become quite elevated (as high as 104° F). Women almost invariably complain of chills, achiness, and malaise. Infection is commonly caused by *Staphylococcus aureus*, *Streptococcus agalactiae*, and *Escherichia coli*. Fungal mastitis may also occur, typically owing to Candida infection, with sharp, shooting pains a common symptom. Risk factors for developing mastitis include cracked nipples or nipple sores, recent antibiotic use, use of antifungal nipple preparations within 3 weeks, and use of a manual breast pump. Diabetes, steroid use, and oral contraceptive use also increase the risk of Candida mastitis. Women with mastitis with a previous child have an increased likelihood of a repeated episode.[70] Breast abscess may occur in 5% to 11% of women with mastitis.[71] Relapse is common with mastitis; therefore, care must be taken to treat completely, and ensure adequate rest and nutrition, as well as avoiding contributing factors (e.g., tight brassieres, improper emptying of the breast).

General Treatment

- Encourage bed rest; minimize visitors and social activities to allow adequate rest.
- Drink copious amounts of fluids, especially water, up to 8 ounces every 2 hours.
- The breast should be emptied as completely as possible on the affected side. Breastfeeding on the affected side is encouraged. A breast pump may be used if needed for complete emptying.
- Avoid tight-fitting brassieres and sleeping in positions that lead to compression of the breast.
- Apply hot compresses to the breast to relieve pain and allow a hot shower to run over the breast to encourage draining of blocked ducts.
- Maintain adequate nourishment with grain and vegetable soups.

Medical Treatment

Medical treatment of mastitis includes regular complete emptying of the affected breast (breastfeeding, pumping), bed rest, pain management with anti-inflammatory medications (e.g., ibuprofen), and a 10- to 14-day course of antibiotics. The World Health Organization protocol suggests that breast milk be cultured and antibiotics prescribed according to sensitivity testing in cases in which there is no response to antibiotics in 48 hours, the infection is hospital acquired, there is relapse, or the case is severe.[72] Nystatin treatment is given to the mother and infant for Candida mastitis. Should abscess occur, draining may be accomplished with needle aspiration.[73] Women with unresponsive and intractable mastitis should also have other causes ruled out, such as breast cancer.

Herbal Treatment

Herbal treatment for mastitis consists of herbs to treat local inflammation and infection, and those to relieve systemic symptoms associated with fever such as myalgia and chills (Table 18-2). Improvements are usually seen within 12 to 24 hours, and complete recovery usually occurs in 48 hours. Should symptoms worsen, abscesses form, or treatment not lead to adequate results within 72 hours, medical treatment should be sought. Following the general instructions for plugged ducts and mastitis (see the preceding), along with herbal treatment, is essential for good results. As mastitis commonly recurs, general recommendations such as consuming adequate fluids, avoiding tight-fitting bras, and regularly emptying the breasts by breastfeeding are recommended beyond the duration of the infection as a general practice. Women with recurrent mastitis should be evaluated for adequate nutritional intake, particularly iron, protein, vitamin C, and zinc, because deficiencies of these nutrients can lead to susceptibility to infection. Adaptogens should be considered to enhance immunity, particularly if there is fatigue accompanying relapsing mastitis. Herbs to consider while breastfeeding include ashwagandha (*Withania somnifera*) and reishi mushroom (*Ganoderma lucidum*). Additional adaptogens were discussed in Chapter 6.

- Use compresses and tub soaks to apply moist heat to the breasts. Ginger root or chamomile infusion can be used as a compress. Hot water will suffice if nothing else is available.
- Apply a poultice of freshly grated raw white potato two to three times a day. This is a wonderful remedy because nearly everyone has a potato, and it is remarkably effective in reducing pain, blockage, and inflammation. Remove the poultice when it becomes warm, usually after about 20 minutes, and repeat with fresh grated potato several times daily.
- Take ½ to 1 teaspoon of echinacea tincture every 2 to 4 hours depending on the severity of the problem. Continue for at least 24 hours after all signs of illness are past. There are no known harmful effects related to Echinacea use during lactation.
- For high fever, hot elder blossom and spearmint infusion (5 g of each herb steeped for 20 minutes in a quart of boiling water, covered while steeping) can be taken, 2 cups consecutively, to help break a fever. The mother should stay warm under covers to avoid worsening of chill. These herbs are considered safe for short duration during lactation.
- Gentle antispasmodics such as lemon balm, chamomile, and catnip teas may be sipped to relieve muscle tension associated with fever. Cramp bark, passion flower, and hops tinctures may be used safely to relieve myalgia and promote sleep. There are no known harmful effects related to short-term use of these herbs during lactation.

TABLE **18-2**

Herbs Commonly Used to Treat Mastitis

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Relieve local inflammation	Anti-inflammatory	*Matricaria recutita*	Chamomile
		Zingiber officinale	Ginger
Relieve inflammation and treat infection	Antimicrobial	*Echinacea* spp.	Echinacea
Reduce fever	Febrifuge	*Mentha piperita*	Spearmint
		Sambucus nigra	Elder
Relieve flu-like symptoms	Antispasmodic	*Humulus lupulus*	Hops
	Analgesic	*Matricaria recutita*	Chamomile
		Melissa officinalis	Lemon balm
		Nepeta cataria	Catnip
		Passiflora incarnata	Passion flower
		Viburnum opulus	Cramp bark
Promote relaxation and sleep	Sedative	*Humulus lupulus*	Hops
		Matricaria recutita	Chamomile
		Melissa officinalis	Lemon balm
		Nepeta cataria	Catnip
		Passiflora incarnata	Passion flower
		Viburnum opulus	Cramp bark
Improve immunity; decrease susceptibility to infection	Adaptogens	*Ganoderma lucidum*	Reishi mushroom
		Withania somnifera	Ashwagandha

INSUFFICIENT BREAST MILK

Concern over the adequacy of the mother's milk supply is the primary reason that women discontinue breastfeeding in the first few months. Most often the woman is actually producing adequate quantities of milk—the baby's proper growth and development, as well as voiding patterns (urinary and stool frequency) are important indicators of adequate milk production and intake. Maternal concern over breast milk adequacy usually arises in response to the baby being fussy and wanting to nurse frequently—often because of a growth spurt in which the baby will nurse more to stimulate more milk production—and this is misinterpreted by the mother, her relatives or friends, or a physician who is not knowledgeable about breastfeeding trends and patterns—any of whom might recommend the mother give the baby supplemental feeding of formula or solids, and cause her to feel anxiety.

More rarely, milk supply truly is inadequate, with the baby demonstrating failure to thrive—either slow weight gain or weight loss. As maternal and infant factors other than inadequate milk supply can contribute to poor infant growth and development (e.g., maternal illness, significant stress, cigarette smoking, alcohol consumption, thyroid disorders and other hormonal problems, and certain medications, and infant neurologic disorders, reflux, congenital heart disease, and other conditions), a thorough examination of mother and infant should be performed, and a social history of the mother should be obtained to identify the cause. Proper positioning and sucking on the part of the baby is essential for both adequate milk production, and the baby actually receiving the milk. A baby with a short frenulum, for example, will not be able to suck properly; a baby with a congenital heart disease may fatigue easily while nursing, and may be unable to suck vigorously enough to maintain milk production. A lactation consultant can help to determine if the baby is latching on properly; a pediatrician should be consulted immediately if the baby appears to fatigue or develops cyanosis or apnea while nursing.

General Treatment

In a healthy woman, the following general strategies will often contribute to an increased milk supply:

- Increased sucking activity, either directly by the baby, or through use of a breast pump. Breast milk production works by demand and supply—the more demand, the greater the supply.
- Adequate food and fluid intake are essential for optimal milk production. Mothers should be directed to one of the many books (e.g., *What to Eat When You're Expecting*), which provide both guidelines and recipes for breastfeeding nutrition. Specific foods commonly recommended for increasing milk supply include oatmeal (cooked from rolled oats, not instant oatmeal) and barley soups and stews.
- Ensure that the baby is latching on properly while nursing.
- Several studies have suggested that increased skin-to-skin contact between mother and baby may prolong the duration and success of breastfeeding and should be considered when there are breastfeeding difficulties.[74,75]

BOX **18-3**

Recipe from *The Ladies' Dispensatory*

To increase milk abundantly:
Leaves of sea-purslane eaten with meat
Seed of agnus-castus drunk
French barley boiled with fennel seed, eaten often
Decoction of mallows drunk
Juice of sow-thistle drunk
Lettuce eaten often
Anise drunk
Dry dill seed drunk, or the decoction of the tops
Fennel eaten (Fig. 18-2)

Figure 18-2 Fennel (*Foeniculum vulgare*). (Photo by Martin Wall)

From Balaban C, Erlen J, Siderits R: *The Ladies' Dispensatory*, New York, 2003, Routledge.

- Adequate delivery of milk to the baby requires not only sufficient production but also an intact let-down reflex. Stress and inhibition can significantly interfere with milk let-down. A lactation consultant or midwife can help the mother to learn to relax during breastfeeding to improve let-down.
- Lactation consultants suggest the use of gentle breast massage techniques to increase milk supply.[76]
- Galactagogues are medications or herbs that aid in initiating and maintaining adequate milk production, and are particularly useful for women who are unable to produce adequate breast milk. They are also used when a woman wishes to breastfeed in cases of adoption or surrogate motherhood.[77] Pharmaceutical and botanical galactagogues are discussed in the following.

Medical Treatment

In addition to the general strategies described in the preceding, medical intervention includes the use of dopamine antagonists as galactagogues to augment lactation. Most exert their pharmacologic effects through interactions with dopamine receptors, resulting in increased prolactin levels and thereby augmenting milk supply. Metoclopramide (Reglan) is the preferred pharmaceutical agent because of its documented record of efficacy and safety in women and infants. Domperidone crosses the blood–brain barrier and enters the breast milk to a lesser extent than metoclopramide, decreasing the risk of toxicity to both mother and infant possibly making it an attractive alternative. Traditional antipsychotics, sulpiride and chlorpromazine, have been evaluated, but adverse events limit their use. Human growth hormone, thyrotrophin-releasing hormone (TRH), and oxytocin have also been studied. There are insufficient studies on the safety and efficacy of growth hormone in the infant, TRH is not commonly used for this purpose, and although it was highly effective at increasing milk production in limited studies, oxytocin is no longer available on the market.[77]

Herbal Treatment

The use of galactagogues to enhance milk production and relaxing herbs (nervines, anxiolytics) to promote let-down is as old as the proverbial hills, with traditional herbals and ''recipe'' books nearly ubiquitously containing recipes for these purposes (Box 18-3). The use of aromatic spices such as aniseed, caraway, cinnamon, dill, fennel, and fenugreek remains popular today.[56] Other commonly used galactagogues include chaste berry, barley, goat's rue, blessed thistle, oats, hops, nettle leaf, slippery elm bark, and marshmallow root, many of which are discussed in the following. Nervines and anxiolytics are important adjuncts to improving breast milk production and delivery to the baby. Specific herbs for this purpose are listed in Table 18-3; readers are directed to Plant Profiles for detailed discussions of their use and safety during lactation.

Discussion of Botanicals

Anise Seed, Fennel Seed, Caraway, and Dill

In the Netherlands, anise seed cookies are a traditional gift to bring to new mothers to ensure a plentiful milk supply.[76] Aromatic herbs including anise seed, fennel seed, dill, and caraway are traditionally used to improve milk supply.[56,76] They can be included in foods or taken as teas, and are common ingredients in tea products marketed as ''mother's milk'' blends. These herbs are approved by the German Commission E for another of their traditional uses—treatment of indigestion,

TABLE **18-3**

Herbs Commonly Used to Increase Milk Supply

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Increase breast milk production	Galactagogue	*Althea officinalis*	Marshmallow root
		Anethum graveolum	Dill
		Avena sativa	Oats
		Carum carvi	Caraway
		Cnicus benedictus	Blessed thistle
		Foeniculum vulgare	Fennel seed
		Galega officinalis	Goat's rue
		Hordeum vulgare	Barley
		Humulus lupulus	Hops
		Pimpinella anisum	Anise seed
		Trigonella foenum-graecum	Fenugreek
		Vitex agnus castus	Chaste berry
Promote relaxation to disinhibit let-down	Nervine Anxiolytic	*Humulus lupulus*	Hops
		Lavendula officinalis	Lavender
		Leonurus cardiaca	Motherwort
		Matricaria recutita	Chamomile
		Verbena officinalis	Blue vervain

Mother's Milk Support Tea

Combine the following herbs:

1 oz dried chamomile flowers	(*Matricaria recutita*)
1 oz dried catnip	(*Nepeta cataria*)
1/4 oz fennel seeds	(*Foeniculum vulgare*)
⅛ dried lavender blossoms	(*Lavendula officinalis*)

Place 1 tablespoon of the dried herbs in a cup or teapot and cover with 1 cup of boiling water. Cover the cup or pot and steep the herbs for 10 minutes. Strain and lightly sweeten if desired.

abdominal bloating, mild cramping, and flatulence.[3] ESCOP also supports similar uses for fennel, anise, and caraway. (dill is not discussed in the monographs.)[52] No trials have been conducted on the use of these herbs to promote lactation; however, they are generally considered a safe addition to the diet.[56] Little information is available on the culinary or medicinal use of fennel seed; however, one animal study observed an estrogenic effect (vaginal cornification and estrus) in female rats fed an oral preparation of an acetone extract of fennel seed (dose not available in abstract) for 10 days. Moderate doses increased the weight of the mammary glands and higher doses increased the weight of the oviduct, endometrium, myometrium, cervix, and vagina.[78] Trans-anethole from anise seed also has demonstrated estrogen activity in animal models.[52] Therefore, theoretically it may be prudent to avoid the use of these herbs in breastfeeding women with a history or risk of estrogen-dependent breast cancer. Note: It is the whole herbs that are used as galactagogues; essential oils are not safe for internal use. Star anise is not the same herb as anise seed, cannot be substituted, and has been associated with toxicity.

Blessed Thistle

Blessed thistle is an aromatic bitter used to stimulate digestive secretions and improve appetite.[3,57] It is a popular ingredient in galactogogue formulas, although not widely reported for its efficacy compared to fenugreek and the other aromatic seeds discussed in the preceding. The American Herbal Products Association considers it safe when used appropriately; its use is contraindicated in pregnancy.[10] Although cautions about possible allergic reactions in patients who are sensitive to plants in the Asteraceae family, no allergic reactions have been reported.[3] No research has been conducted on the use of blessed thistle for promoting lactation.

Chaste Berry

The use of chaste berry to promote breast milk production dates back to ancient Greece, recommended by both Dioscorides and Pliny.[56] Its efficacy as a galactogogue, however, is somewhat controversial against modern evidence that demonstrates that the efficacy of this herb for the treatment of other gynecologic complaints, including mastodynia and amenorrhea, is believed to be in part related to its prolactin-inhibiting effects, which would seem to be directly contradictory to the promotion of breast milk.[79–83] No modern studies of the efficacy of chaste berry on lactation have been conducted. A 1954 trial compared the use of chaste berry with vitamin B_1 and no treatment; however, because of the significant methodologic flaws of the study, no conclusions can be made. Animal studies using subcutaneous injection of

Vitex extract demonstrates decreased milk production. Low Dog and Micozzi state that lactogenic activity may be dose-dependent; however, the only study demonstrating lactogenic effect is that of 20 health males in whom prolactin secretion was increased at a dose of 120 mg and decreased at 480 mg.[56] Madaus, the manufacturer of the most widely studied Vitex product, Agnolyt, states that chaste berry is contraindicated for use during lactation, and lactation has been used as an exclusion criterion in other human clinical trails studying chaste berry.[56,84]

Fenugreek

Fenugreek is a traditionally used herbal galactagogue that continues to be discussed in contemporary medical and herbal literature and widely used by midwives, herbalists, lactation consultants, and the general public.[56,57,76,77] The seeds contain 40% mucilage along with coumarin compounds, diosgenin, and alkaloids such as trigonelline, gentianin, and carpaine, and make a pleasant tasting tea—the seeds themselves being generally regarded as safe (GRAS) and used as a food flavoring. Fenugreek is thought to act via stimulation of sweat production, enhancing milk secretion. (The breast is a modified sweat gland.) Anecdotal reports of its successful use as a galactogogue date back to 1945; however, clinical studies are lacking. In one remarkable anecdotal report, 1200 women reported increased milk production within 24 to 72 hours. Adverse effects are extremely rare and include diarrhea; a maple-like aroma in urine (fenugreek has a maple syrup–like flavor and scent), breast milk, or sweat; and aggravation of asthmatic symptoms.[85] One report states that this side effect could lead to a mistaken diagnosis of maple syrup urine disease, a rare metabolic disease, in the infant, so the infant's pediatrician should be informed of the mother's consumption of the herb.[86] There is a single oral report of a premature infant having a side effect of gastrointestinal bleeding. However, this is purely speculative because premature infants may have gastrointestinal bleeding secondary to infection. Caution is often advised when using in diabetic or hypoglycemic patients, because the herb has been shown to lower blood glucose; however, this does not appear to be a significant effect, with blood sugar changes only minimal, even in non–insulin-dependent diabetic patients.[86] Fenugreek is often used in conjunction with metoclopramide or domperidone.[85] The American Herbal Products Association gives this herb a high safety rating, and does not contraindicate its use during lactation. However, it cautions about keeping doses within 5 grams of seeds per day, although substantially larger doses (30 to 40 g/day) have been used safely with diabetic patients.[10,56] The German Commission E supports the use of fenugreek for loss of appetite.[3] It is typically taken in capsule or tea forms. Fenugreek tea should not be taken during pregnancy in medicinal amounts.[86]

Goat's Rue

Goat's rue has a long history of use as a galactogogue. It was reported to the French Academy in 1873 after it was observed that this herb increased milk production in cows, a fact that was later cited in *The Dispensatory of the United States of America,* 1918.[88] It has been used traditionally as an antidiabetogenic herb; however, evidence of efficacy is lacking. Scant evidence for its efficacy as a galactogogue is found in contemporary botanical literature, and some toxicity has been demonstrated in livestock fed the herb. Nonetheless, goat's rue is sometimes used by midwives and herbalists, and its use is commonly recommended on Internet sites. Case reports of maternal ingestion of a galactogogue tea containing goat's rue, licorice, fennel, and anise seed were associated with drowsiness, hypotonia, lethargy, emesis, and poor sucking in two newborns with no evidence of infection or other illness present. Symptoms resolved after maternal discontinuation of the tea and a 2-day hiatus from breastfeeding.[89] Given even the potential for toxicity, and safer alternatives, it may be prudent to reserve this herb for short-term use only, and only for cases when other herbs have not been effective.

Oats, Barley, and Marshmallow Root

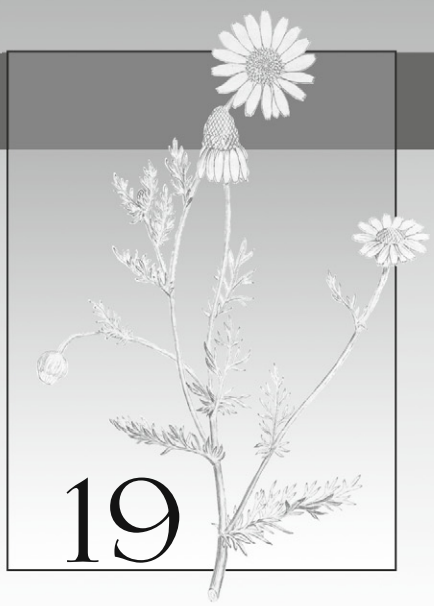
Mucilaginous herbs have long been used for their nutritive properties and to increase breast milk supply. Oats and barley are foods traditionally given to new mothers both as porridge and barley in stew. They are safe for daily consumption in food quantities. Marshmallow root is considered a safe herb when used as recommended.[35] It is typically included in galactogogue infusions. There are no known contraindications to the use of marshmallow root; however, the absorption of other medications taken simultaneously might be inhibited by marshmallow root.[52]

NUTRITIONAL CONSIDERATIONS

A full discourse on the nutritional needs of the mother during breastfeeding is beyond the scope of this book. However, it cannot be overstated that optimal nutrition, adequate fluid intake, unrestricted nursing patterns, minimization of stress, and avoidance of cigarette smoke are all first-line approaches to ensuring optimal breast milk production in otherwise healthy mothers.

PART IV

The Menopausal Years



19 CHAPTER

Menopausal Health

Aviva Romm, Susun S. Weed, Paula Gardiner, Bhaswati Bhattacharya, Clara A. Lennox, Roberta Lee, Wendy Grube, Robin DiPasquale, Margi Flint, David Winston

PERIMENOPAUSE AND MENOPAUSE: AN OVERVIEW

Aviva Romm

In other cultures women do not report severe symptoms of menopause and menopause is not managed medically. Relying solely on a medical perspective (or disease model) of menopause does not account for the impact of culture and other social influences and may ignore the variety of patient perspectives on the menopausal transition.[1]

It is estimated that by the year 2015, 50% of all women in the United States will be menopausal. Women's opinions and experience of menopause are changing. Until recent decades, menopause was a hushed topic for the 40 million American women going through ''the change.'' Times have changed and women today are openly looking for strategies to maintain their health and minimize discomforts. Women are also concerned about preventing the problems that commonly arise during and after menopause; for example, cardiovascular disease and osteoporosis, which may occur partly as a result of the decline in estrogen that is the hormonal hallmark of menopause. Although perimenopause—the commonly symptomatic phase leading to the permanant cessation of the menses—may be associated with varying degrees of discomfort from mild to severe, it is important to remember that this can be the beginning of a welcomed new phase of life for women. Social factors are sometimes more predictive than biologic factors of whether women will develop symptoms. A number of studies have found that women who report increased freedom, social status, and mobility after menopause are less likely to report negative symptoms.[2–6] In the United States, fear of aging and higher socioeconomic status are more frequently associated with negative menopausal symptoms than are body mass index or history of bilateral oophorectomy. A definition of menopause must take into account the impact of ''social/cultural factors in order to encompass the range of experiences that women experience at the menopause transition. This biocultural definition permits exploration of the worldwide differences in menopause within the framework of the human life cycle and appropriately accounts for the influence of medico-cultural definitions of the menopausal transition.''[1]

WHAT IS MENOPAUSE?

The term *menopause* is typically used to refer to what are actually three distinct phases: perimenopause, menopause, and postmenopause (Fig. 19-1). Perimenopause refers to the period of 2 to 8 years before the cessation of menstruation, during which regular cycles of ovulation and menses become irregular prior to terminating, a natural result of declining hormone levels, until one year after the cessation of menstruation. An elevated follicle stimulating hormone (FSH) level of 60 to 100 mIU/L on two tests done at least 1 month apart is considered indicative of menopause, although not definitive. Other hormonal indicators of the perimenopause are a luteinizing hormone (LH) level greater than 50 mIU/L and an estradiol level <50 pg/mL. The complete termination of menstrual bleeding for 12 months in the absence of another cause of amenorrhea heralds menopause and indicates that reproductive capabilities have ceased. Postmenopause is the time after complete cessation of menses. Despite ethnic, racial, and cultural variations, the median age around the world of 51 years for menopause indicates there are some common biological elements, although individuals range from ages 40 to

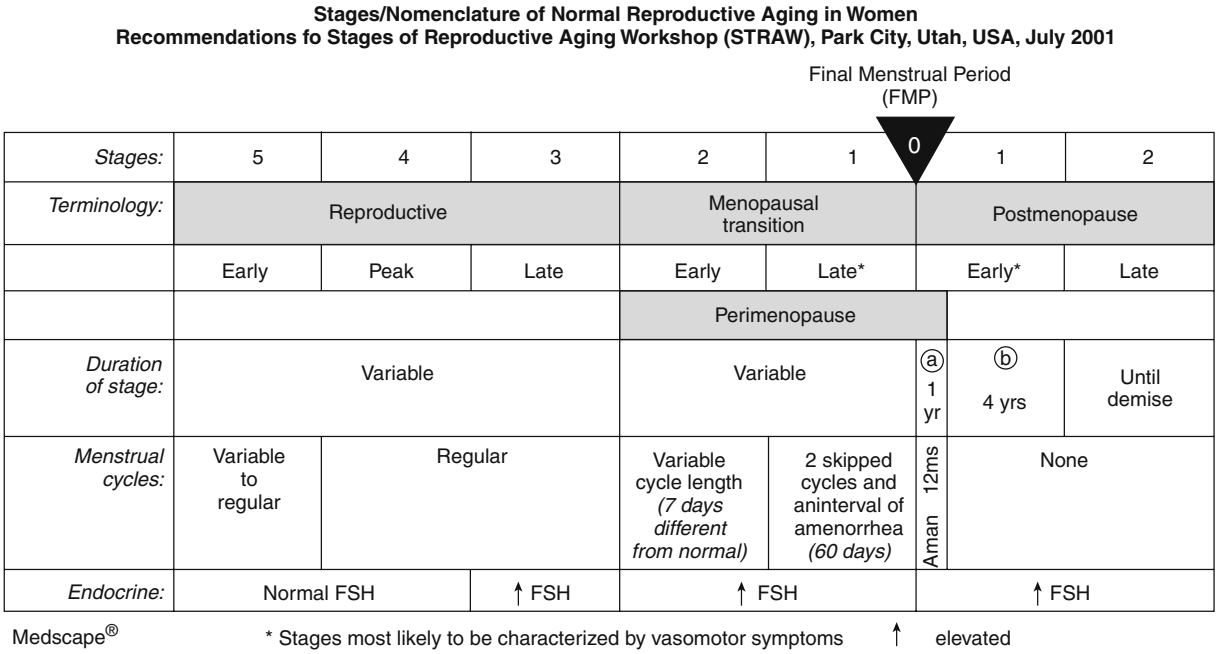


Figure 19-1 The STRAW staging system. (From Soules MR et al: Fertil Steril 2001; 76:874.)

58 years old. However, there is a great deal of cultural disparity related to symptoms that arise during this period. For example, according to the World Health Organization (WHO), menopausal vasomotor symptoms are not as problematic for women worldwide as they are for women in the United States and other Westernized nations. Along with diet and exercise patterns, cultural attitude differences toward menopause may play some role in these epidemiologic differences.[7]

> *Rather than view menopause as the end of a woman's life, it is important to remember that life expectancies in the developed countries around 80 give women an estimated equal number of years in the menopausal chapter of their lives as in the 25–35 years of fertility they experience. This positive emphasis on a woman's post-fertile years is celebrated by progressive women's health advocates. Terms such as the perimenopausal decline, past the prime of life, crone, and post-fertile do not address the new chapters of a woman's life that begin when her child-conceiving capacities have altered. The impact of patient-directed advertising and marketing that impedes the redefining of mid-life for women is disheartening. The implicit reference to women primarily as childbearers, mothers and caretakers for upbringing focuses away from the other roles women dream of in their lives: purposes, spiritual journeys and ambitions on nonreproductive levels that women also embody.*
>
> **—Bhaswhati Battycharya**

SYMPTOMS OF PERI/MENOPAUSE FOR WHICH WOMEN COMMONLY SEEK HERBAL CARE

Hot flashes, insomnia, memory problems, fatigue, heart palpitations, depression, anxiety, vaginal dryness, heavy vaginal bleeding, and incontinence are some of the most common problems for which women seek botanical therapies during the perimenopause and after. Women encounter new concerns about their heart and bones after menopause. Heart disease and osteoporosis raise the question of whether to use hormone replacement therapy (HRT) for protection. The chapters in this section present the reader with current botanical thinking, allowing practitioners to help their patients sort through the myriad of options available.

HERBAL STRATEGIES: AN OVERVIEW

Following is an introduction to the most common menopausal complaints and concerns, and the herbs most commonly used by menopausal women. The herbs are presented comprehensively throughout the remaining chapters in this section of the textbook, and many are also discussed further in Plant Profiles.

A number of botanicals are used in the symptomatic relief or treatment of peri- and postmenopausal complaints and problems—some of these, for example, soy, red clover, and black cohosh have become almost household names. Though the use of many herbs and supplements is supported by solid scientific, clinical, and historical evidence, caution is advised when considering and purschasing herbs and supplements marketed for menopause-related complaints. Menopause is a cash cow for the pharmaceutucal and supplement industries, which recognize the product sales potential in the vast number of women desiring relief from menopausal symptoms.

Botanical treatments must also be placed in the context of a holistic approach that recognizes and addresses social, emotional, psychological, and other factors that can impact women, and must be proactive in helping women to prevent the development of symptoms during this time in their lives, especially heart disease and osteoporosis.

Hot Flashes and Night Sweats

Approximately 75% of US women experience hot flashes; 15% have severe symptoms. This may lead to embarrassment, physical discomfort, and night waking, which can aggravate insomnia and related problems such as depression. Botanical therapies commonly used include motherwort (*Leonurus cardiaca*), sage (*Salvia officinalis*), black cohosh (*Actaea racemosa*), and red clover (*Trifolium pratense*).

Memory Problems

Memory difficulties may be a function of hormonal changes, and are worsened by lack of sleep and emotional stress. They can be extremely disconcerting, prompting many women to fear that they have Alzheimer's disease or another serious disorder. Botanical therapies commonly used include ginkgo (*Ginkgo biloba*), bacopa (*Bacopa moniera*), peony (*Paeonia lactiflora*), ginseng (*Panax ginseng*), and rosemary (*Rosmarinus officinalis*). Aromatherapy is also a popular option for stimulating cognition and memory.

Insomnia

Insomnia is a common and sometimes debilitating, problem for perimenopausal women, worsened by night waking caused by hot flashes and night sweats. Lack of sleep aggravates stress, memory loss, depression, and many physical discomforts. Botanical therapies commonly used to treat insomnia include skullcap (*Scutellaria lateriflora*), motherwort (*Leonurus cardiaca*), passionflower (*Passiflora incarnata*), lavender (*Lavandula angustifolia*), California poppy (*Eschscholzia californica*), kava kava (*Piper methysticum*), and valerian (*Valeriana officinalis*).

Heart Palpitations

Heart palpitations are common among otherwise healthy perimenopausal women, although cardiac and thyroid problems should be ruled out. Botanical therapies commonly used include motherwort (*Leonurus cardiaca*), hawthorn (*Crataegus laevigata*), lemon balm (*Melissa officinalis*), and black cohosh (*Actaea racemosa*).

Depression and Anxiety

Hormonal changes, worries about aging, personal concerns, loss of sleep, inadequate nutrition, memory problems, and other physical complaints can fuel feelings of frustration and depression, and new concerns about health can lead to anxiety. Botanical therapies commonly used include adaptogens [see Chapter 6 Stress, Adaptation, the Hypothalamic-Pituitary-Adrenal-Axis (HPA) and Women's Health], ashwagandha (*Withania somnifera*), eleuthero (*Eleutherococcus senticosus*), ginkgo (*Ginkgo biloba*), ginseng (*Panax ginseng*), dong quai (*Angelica sinensis*), motherwort (*Leonurus cardiaca*), St. John's wort (*Hypericum perforatum*), and blue vervain (*Verbena officinalis*).

Vaginal Dryness

Vaginal dryness, caused by reduced endogenous estrogen levels, is uncomfortable, increases susceptibility to infection, and has a negative impact on sexual experience with both physical and psychoemotional ramifications. Botanical therapies include topical emollient therapies to moisten and lubricate the vagina as well as internal botanical protocol to increase estrogen, such as red clover (*Trifolium pratense*), licorice (*Glycyrrhiza glabra*), calendula (*Calendula officinalis*), American ginseng (*Panax quinquefolium*), wild yam (*Dioscorea villosa*), and black cohosh (*Actaea racemosa*).

Heavy Bleeding

Many women experience at least one episode of heavy vaginal bleeding, or ''flooding,'' during perimenopause in the absence of pathology. Nonetheless, incidences of abnormal vaginal bleeding in a perimenopausal or menopausal woman should be investigated to rule out gynecologic cancer. Botanicals commonly used to manage dysfunctional uterine bleeding include yarrow (*Achillea millefolium*), lady's mantle (*Alchemilla vulgaris*), Tienchi ginseng (*Panax notoginseng*), and shepherd's purse (*Capsella bursa pastoris*), among others.

SUMMARY

Menopause is a time of tremendous physical, emotional, and social change for women. It can be a major life milestone for some—a time of psychoemotional reckoning, evaluation, introspection, and integration, as well as a time of starting a new phase in life. For some women, this is a smooth transition; for others, it is a rocky time, accompanied by varying degrees of symptoms, some physical, others emotional. It is also a time of increased vulnerability to developing heart disease and osteoporosis, both of which can lead to major future debility and hardship. Therefore, this is a time that practitioners working with women must be aware of and address the many nuances of change women face and the enormous opportunity for preventative care. Botanicals are but one option for helping to support or restore health and balance as women face the beginning of the rest of their lives.

REFRAMING MENOPAUSE: THE WISE WOMAN PERSPECTIVE

Susun S. Weed

Wise Woman Model:

The joy of menopause is the world's best-kept secret. Like venturing through the gateway to enter an ancient temple, in order to claim that joy a woman must be willing to pass beyond the monsters who guard its gate... as thousands of women from all cultures throughout history have whispered to each other, it is the most exciting passage a woman ever makes.[22]

Medical model:

[Menopause] is not a natural condition; it is an endocrine disorder and should be treated medically with the same seriousness we treat other endocrine disorders, such as diabetes or thyroid disease.[8]

—Theresa L. Crenshaw

The medical definition of menopause is the end of menstruation. However, this definition fails to recognize

women's experience: that menopause, like puberty, is not a moment, not an end, but a metamorphosis that may take 5 to 10 years.[1] Many practitioners—from both the scientific and alternative communities—define menopause as a state of loss, or an abnormal state. Menopause is described in disease terms as an endocrine disorder, estrogen deficiency, or simply hormonal imbalance. ''This insistence on viewing menopause as a disease. . .defines older women as aberrant.''[9] In contrast, the *Wise Woman Tradition* (woman-centered herbal medicine based on principles of nourishing the whole woman) defines menopause as a natural event occurring over several years, and during which the hormonal and nervous systems undergo cumulative and profound changes. In this woman-centered view, the menopausal years are an opportunity for conscious change and increased personal power, not a time of failure.

> *. . .the conventional view of menopause as a scary transition heralding 'the beginning of the end' couldn't be farther from the truth.*[10]

THE MEDICALIZATION OF MENOPAUSE

During the 1960s, with the popularization of hormone replacement, menopause became a treatable medical problem—and big business. Hormones became ''the cure,'' enabling women to remain ''forever female.'' The norm of care for middle- and upper-class white menopausal women in the United States from the mid-1960s to the present has been some form of hormonal supplementation: a combination of estrogen and progesterone for women who still have their uterus, estrogen for those without. It is now recognized that HRT increases the risk of endometrial and breast cancer.[11–13 15,16]

Given the volumes of press devoted to HRT, one might assume that most US women use hormonal therapies at menopause; however, this is not the truth. One survey found that 52% of women wanted to avoid the use of hormones and 58% preferred alternative therapies for menopausal symptoms.[17] Even before the recent cancellation of one large double-blind study of HRT, only half of all women over 50 had ever filled a prescription for estrogen or hormone replacement, and only one-third of those ever refilled the prescription. It is estimated that as many as 85% of the 37 million postmenopausal women [in the United States] do not want to use HRT.[18] With growing concerns over the safety of HRT, many women—and even some physicians—are turning to alternatives. An understanding of the appropriate use of herbal medicines to nourish women during this transitional time and address common complaints associated with menopause, can ease this transition and promote health for women entering their ''wisdom years.''

REFRAMING MENOPAUSE: WOMEN'S MYSTERY STORIES

Menopause is not simply an artifact of technology that has allowed us to expand our life expectancy and outlive our usefulness. Kristen Hawkes of the University of Utah studies hunter-gatherer cultures. Her ''grandmother hypothesis,'' based on observing the vigor and effectiveness of postmenopausal women in these cultures, demonstrates that postmenopausal women were critical to the health of their grandchildren, their community members, and the culture as a whole, and suggests that the presence of menopausal women in a society provides a survival advantage.[19] The most industrious members of the Hazda culture are women in their fifties, sixties, and seventies says Dr. Hawkes. ''The older woman knows the land, and its water, the seasons, the movements of the game, and the time to harvest each plant, she is not a sentiment, she is a requirement.''[19] ''Among many non-Western groups, the older woman enjoys increased status in the family and greater freedom in society at large. Menopause and the cessation of childbearing become positive events in a woman's life. . . .''[20] Reframing menopause from a ''problem'' to a ''gift'' is a direct help to most women. Women in cultures in which menopause is regarded as a gift have fewer problems with the physical and emotional changes that accompany it.[21] A vigorous life keeps women vital. Vigorous exercise and a whole foods diet can help us live longer; reframing menopause can help us enjoy each passing year: gray hair, wrinkles, and all.

Women's mysteries are the great events of a woman's life—menarche, pregnancy, lactation, menopause—and the stories and ceremonies associated with these life-changing times. Women's mystery stories reveal important and surprising truths from a woman-centered perspective that has been lacking in ''modern'' medicine. The stories, ceremonial themes, and herbal remedies that are shared here from these mystery teachings evoke and rely on the millions of careful observations and experiments made by wise women over hundreds of generations. The mystery stories of menopause are gifts to modern women from their foremothers, the ancient healers: women who were deeply intuitive and in tune with women's needs, emotional and spiritual as well as physical.

Using the mystery stories of menopause, we can ease a woman's menopausal distress by reframing her experience. Reframing is done in a variety of effective ways, including one-on-one counseling, peer group sessions, teaching, performance arts, storytelling, and through the written word. Reframing menopause allows women to think outside the box of victim-centered cultural beliefs. Because both orthodox and alternative practitioners in the United States believe that menopausal symptoms indicate a lack or an imbalance, they frequently prescribe hormones for healthy, but symptomatic, menopausal women. This makes it easy for women to remain in the role of victim: She is a victim of menopause, a victim of a body that is undependable and unable to age without medical intervention.

We have come to believe, patient and practitioner alike, that normal aging is a failure of our glands and that hormones—not just estrogen, but progesterone, testosterone, DHEA, and melatonin—are fountains of youth that will provide for us when our bodies fail. Reframing our view leads not only to a different attitude about normal menopausal symptoms, but to radically different treatments, in which herbs are not used as natural

hormones, but as sources of the rich variety of helpful phytochemicals available from nature. Reframing menopause gives women a greater sense of self-worth. We reframe ''loss of fertility'' into ''acquisition of postmenopausal zest.'' This gives women something to look forward, a reward for passing through the gates of menopause. One manifestation of this reframing is the ''Crone's Crowning Ceremony.'' This honoring ceremony, which celebrates a woman's passage through the menopausal years, has become increasingly popular in the United States, especially among ''the culturally creative'' and women engaged in natural lifestyles.[2,23]

We reframe mood swings and depression into ''menopausal women need more time alone,'' validating a core need experienced by many menopausal women. Taking quality alone time during menopause appears to be a critical factor for mental and physical health. Time out can give the menopausal woman an opportunity to try out new ways of dressing, being, serving her community. It provides the freedom to experiment, and the privacy to feel safe doing it. Quiet time alone in nature, or sitting in a comfortable chair listening to soothing music allows the hidden thoughts and feelings that have accumulated since menarche to arise. Menopause encourages us to sort through those ''holdings'' and discard those that are no longer needed.

Women also find ways to reframe the ''aggravating hot flash'' into a ''movement of energy.'' Women have described themselves riding hot flashes like a surfer on a wave, skiing them like a snowboarder on a fresh snowy slope, luxuriating in them like a hot bath, and enjoying them like an especially intense orgasm. Women who reframe their hot flashes often report that doing so gives them an increased sense of empowerment.

MENOPAUSE SUPPORT GROUPS

Menopause support groups help women form alliances and are a natural extension of the groups women tend to form throughout different stages of their lives, for example, alliances of young mothers at the playground sharing the joys and challenges of child rearing, or breast cancer support groups. Menopause support groups give women a safe place to tell their stories without interference or judgment. Support groups help women share remedies, ways of coping, and prevent isolation as women experience shifting roles in their personal lives, which may include having an ''empty nest,'' divorce, or changes in work or social life. Talking about and listening to others helps us to remember that we are not the only ones going through changes, that we are part of the web of women.

A WHOLE FOODS DIET FOR MENOPAUSE AND BEYOND

The healthiest diet for most women, before, during, and after menopause, is a whole foods diet including whole grains and beans, nuts, seeds, a variety of organic fruits and vegetables, organic lean meats, cold water fish, good-quality oils, and organic dairy products. A whole foods diet is heart-healthy and less likely to promote diabetes, cardiovascular, and nutritional deficiencies that become more common as we age.

Adequate, high-quality fat intake is essential; human steroid hormones are synthesized from cholesterol. Interestingly, studies have shown an inverse correlation between milk consumption and breast cancer. After tracking 4,697 Finnish women ages 15 to 90 for 25 years, researchers discovered that those ''women who habitually drank the most milk had only half the breast cancer risk of those who drank the least.''[25] A recent study done in the United States came to the same conclusion: Women who drank milk as children and continued to drink at least three glasses a day as adults had half the rate of breast cancer as those who drank little or no milk.[26] Is it possible that cholesterol-rich foods, eaten as part of a healthy whole foods diet are health promoting, and that hydrogenated and partially hydrogenated vegetable fats are the real culprits in heart disease?[27] A study of 61,000 Swedish women between the ages of 40 and 76 found that consumption of the monounsaturated fats, even from meat, milk, cheese, and butter, lowered the risk of breast cancer. For each 10 grams of monounsaturated fat [from dairy products and meat], the risk of breast cancer fell by 55%. For each 5 grams of polyunsaturated fat [from vegetable oil], the risk rose by 70%.[28] Studies on the relationship between dairy and cancer, however, are often conflicting, with other studies demonstrating a direct correlation between dairy consumption and ovarian cancer.

The healthiest women in the world may be the women of Greece. They have some of the lowest rates of heart disease and breast cancer in the world.[29] Their diets contain lavish amounts of olive oil, goat cheese, nuts, fresh vegetables, and meat. There is an inverse correlation between the amount of olive oil a Greek woman eats and her risk of breast cancer.[30]

HERBAL MEDICINES FOR THE MENOPAUSAL YEARS

Goals for helping women experience a healthy menopausal transition may include:

- Relief from or help with bothersome symptoms, for example, hot flashes, insomnia
- Maintenance and repair of bones; prevention of fractures
- Prevention of cardiovascular disease
- Prevention of breast cancer
- Prevention and treatment of incontinence, pelvic laxity, vaginal dryness, and sexual debility

The core approach to a healthy menopause achieves these goals through the use of nourishing herbal infusions, reframing counterproductive menopausal beliefs via counseling and/or group support, a whole foods diet that includes good-quality oils, calcium sources (e.g., organic yogurt), and healthy sources of phytoestrogens (not concentrated soy isolate supplements), and incorporates consistent, adequate exercise. Personal empowerment, time for reflection, and pursuing one's dreams are also important for ease during this transition.

Nourishing Herbal Infusions

Nourishing herbal infusions provide nutritional, phytochemical support for menopausal and postmenopausal women with low cost and little effort. There is generally

a high acceptance and follow-through rate among women of many ethnicities, cultures, education levels, and economic abilities.[3] When amply extracted into boiling water, herbs such stinging nettle, oat straw, and red clover release generous amounts of vitamins, minerals, proteins, phytoestrogens, and other important constituents.[31–33] If the menopausal and postmenopausal diet is not mineral-rich, the entire woman suffers, not just her bones, but her heart, blood vessels, and immune and nervous systems. Minerals may be difficult to get, even in an adequate diet.[32] Mineral values in commercial foodstuffs have decreased dramatically since the early part of the twentieth century.[32] Regular use of nourishing herbal infusions can help to close this gap.[32,34–36]

Cooked greens are also a rich source of minerals, as are edible seaweeds. Herbal vinegars are another great source of minerals and a way to encourage women to consume herbs daily, along with a healthful salad. Minerals are poorly absorbed from encapsulated herbs, and the amount taken is very small. Mineral-rich herbs are more like foods than medicines or drugs, and need to be consumed in dietary quantities—1 to 4 cups of infusion, not tea, or 1 to 3 tablespoons of infused vinegar daily. One cup of nourishing herbal infusion, prepared by steeping 35 g of dried herb in a liter of boiling water overnight, provides 100 to 400 mg of calcium. A tablespoon of medicinal herbal vinegar, prepared by macerating fresh herbs in vinegar for six weeks, may provide up to 50 to 100 mg of calcium.[37]

Supporting the Adrenals

Adrenal stress is often overlooked as a factor possibly contributing to a number of menopausal complaints including increased stress and irritability, panic attacks, emotional lability, fatigue, night waking, and possibly even night sweats.[38,39] Stinging nettle (*Urtica dioica*) is an excellent herbal ally. Fresh nettle leaves are eaten in soups, or as a cooked green or fresh or dried herb; 2 to 4 cups is a daily nourishing infusion. There is no scientific evidence exploring the effects of nettle on the adrenals; however, many herbalists corroborate the observation that nettle improves many symptoms associated with chronic stress and has rapid, reliable effects. Other adaptogenic herbs are also important for providing adrenal support. See Chapter 8 for a comprehensive discussion of adaptogens, as well as elsewhere throughout this book.

Supporting the Liver, Nourishing the Blood: A Vital Component of Menopausal Health

Traditional Chinese medicine (TCM) sees menopausal symptoms such as night sweats, hot flashes, memory loss, sleep disturbances, emotional swings, and even sometimes heart disease, as a result of liver qi stagnation, excess liver fire, and blood and *yin* deficiency.[40] Many herbs are used in TCM to treat these ''imbalances.'' Among the most commonly used by Western herbalists as analogues for the Chinese herbs for moving liver qi and cooling heat are dandelion (*Taraxacum officinale*), yellow dock root (*Rumex crispus*), burdock root (*Arctium lappa*), motherwort (*Leonurus cardiaca*), and bupleurum (*Bupleurum falcatum*). Dong quai (*Angelica sinensis*) is perhaps the most popularly used herb for nourishing the blood. For use of traditional Chinese herbs, women can be referred to acupuncturists and TCM herbalists.

Phytoestrogens and Menopause

Phytoestrogens are hormones made by plants for their own biological needs. They weakly activate estrogen receptors in mammals and are found in ordinary foodstuffs such as whole grains, many legumes (not just soy), root vegetables including carrots and yams, seeds (e.g., flax), and nuts, as well as in herbs.[42,43] A diet rich in phytoestrogens confers benefits such as reduction of breast cancer risk, with little effect on premenopausal women's cycles.[44–47] Phytoestrogens may also help prevent osteoporosis, high blood pressure, heart disease, and senility.[48,49] Phytoestrogens are ubiquitous in plants; only a totally plant-free diet would prevent exposure to them. Thus, phytoestrogenic foods are generally considered safe for long-term, daily use. Phytoestrogenic herbs and supplements, however, may not be safe for daily or long-term use for women at risk of developing estrogen-dependent cancers.[50]

A FEW WORDS ON EXERCISE

Although exercise alone is not sufficient to prevent heart attacks, osteoporosis, or fractures, it is vitally and tremendously important in their prevention and for the promotion of healthy hearts, healthy bones, and longevity.[51] Exercise not only strengthens bone, it also increases muscular flexibility and improves balance. A broken bone can cause a fall, but poor balance leads to more falls and more broken bones. Plus, of course, exercise improves the functioning of the heart, counters depression, and may even help prevent breast cancer. The amount of exercise needed varies, but 30 minutes daily is a goal most women can easily achieve and maintain. Any kind of exercise helps, but best results are found with a mix of strength building (such as weight training), simple walking—brisk if possible, and flexibility improvement with tai chi and yoga. Best of all, we are never too old and never too unfit to begin benefiting from some form of exercise.

SUMMARY

Menopause is a natural transition for most women. Reframing the menopause into a life—and age—affirming opportunity and transformation can improve women's experiences of this time. Emotional and nutritional supports—including nourishing herbal infusions and a whole foods–based, phytoestrogen-rich diet plus exercise—are often sufficient to alleviate mild to moderate acute symptoms and provide a basis for long-term health of bones, heart, and breasts, and the whole, wise woman.

Eclectic Specific Condition Review: Menopausal Symptoms

*David Winston**

- **Black Cohosh/Macrotias root (*Actaea racemosa*)** Hot flashes and sweating, with muscle aches, headaches, osteoarthritis, and nervousness. For black cloud depression, use with cactus.

Eclectic Specific Condition Review: Menopausal Symptoms—cont'd
*David Winston**

- **Blue Vervain herb (*Verbena officinalis*)**
  Menopausal anxiety, nervous tics, bruxism. Use with Motherwort and Pulsatilla.
- **Cactus stem (*Selenicereus grandiflorus*)**
  Hot flashes with melancholia (depression); irritable temper, neuralgia, and anxiety; palpitations; and other cardiac symptoms.
- **Chaste tree fruit (*Vitex agnus-castus*)**
  Hot flashes with a sense of ''skin crawling,'' dizziness, and depression.
- **Goldenseal root (*Hydrastis canadensis*)**
  Uterine hemorrhage associated with menopause and caused by inflammation and/or prolapse of the uterus.
- **Green milky oat (*Avena sativa*)**
  Vaginal dryness associated with menopause, menopausal anxiety.
- **Motherwort herb (*Leonurus cardiaca*)**
  Menopausal anxiety or insomnia, with palpitations or hyperthyroidism. Use with blue vervain and/or *pulsatilla*.
- **Passion flower herb (*Passiflora incarnata*)**
  Menopausal insomnia, with circular thinking ''can't shut the mind off,'' restless, agitated; use with motherwort and milky oat.
- **Pulsatilla herb (*Anemone* pulsatilla.)**
  Menopausal anxiety, depression, the patient easily cries, cold extremities, the pulse is small and fast.
- **Sage herb (*Salvia officinalis*)**
  Menopausal night sweats and sweating associated with hot flashes.

*For historical purposes only.

HORMONE REPLACEMENT THERAPY: RISKS, BENEFITS, ALTERNATIVES

Paula Gardiner

Hormone replacement therapy (HRT) is the cornerstone of allopathic treatment of menopausal symptoms. Since HRT was introduced 70 years ago, a steady flow of studies has produced evidence of both harmful and beneficial effects. Recent studies show HRT to be associated with an increased risk of breast cancer, myocardial infarction, cerebrovascular disease, and thromboembolic disease. Based on these new data, HRT prescribing practices are rapidly changing, as health care professionals are no longer recommending it as a ''preventative medicine.''

Today, the main reasons for prescribing HRT are relief of menopausal symptoms and prevention or management of osteoporosis. Strong evidence from both observational studies and RCTs show estrogen to be highly effective for controlling hot flashes and genitourinary symptoms.[54] Urogenital atrophy and vasomotor instability are improved with HRT.

The ''diagnosis'' of menopause is based on clinical history and physical exam. The cessation of menses for 12 months is usually accompanied by symptoms of estrogen loss. During perimenopause, the menstrual cycle can become erratic, as can the quantity and quality of the menstrual flow. By eliciting a good history, the client might note vasomotor symptoms, including hot flashes and night sweats. Hot flashes usually last 1 to 2 years but may persist for as long as 5 years. The severity of hot flashes increases with fatigue and stress. The most severe hot flashes usually occur at night and may adversely affect sleep. Other problems seen in perimenopausal and menopausal women are depression, decreased libido, irritability, nervousness, and insomnia, which may be related to poor sleep patterns associated with night sweats. Women may report difficulties with memory and concentration, or feeling fatigued or moody.

On physical exam, there are numerous changes in the female body accompanying the perimenopause. Women present with dry skin, smaller breast tissue, and smaller ovaries. With advancing age, the walls of the vagina become thinner, dryer, and less elastic. These changes can make sexual intercourse uncomfortable, leading to dyspareunia, or she may experience pain or urgency with urination. During menopause the bone density decreases, leading to increased risk of osteoporosis. Women are also at increased risk for heart disease, with decreases in high-density lipoprotein (HDL) cholesterol, glucose tolerance, and an increase in blood pressure.

There are changes in women's social fabric as well. Losing their ability to reproduce, some women see it is a time of sexual freedom, whereas for others a time of mourning and reflection. There is a transition in the woman's role as a mother, partner, or daughter.

In terms of preventative care, in addition to her pap smears, mammogram, and blood work (lipid profile), a DEXA scan can screen for osteoporosis. Some physicians find a follicle stimulating hormone (FSH) and luteinizing hormone (LH) level helpful for the diagnosis of menopause.

CONVENTIONAL TREATMENT APPROACHES

Until relatively recently, the allopathic gold standard of treatment for menopause has been HRT. Approximately 38% of postmenopausal women in the United States in 1995 used HRT, estrogen with or without progestin, to treat symptoms of menopause and prevent chronic conditions such as cardiovascular disease and osteoporosis.[55] In 2000, 46 million prescriptions were written for Premarin (conjugated equine estrogens), making it the second most frequently prescribed drug in the United States.[56] HRT was indicated for the classic symptoms of hot flashes and night sweats, which related to declining estrogen levels and are reported by 85% of US menopausal women.[57,58] HRT can effectively treat menopausal symptoms such as vasomotor instability (hot flashes), mood swings, concentration difficulties, dyspareunia, and vaginal irritation caused by dryness.[59]

For women with an intact uterus, HRT includes both an estrogenic agent and a progestin. Progestins are generally indicated to offset the increased risk of endometrial

cancer with the use of unopposed estrogen. For women using both an estrogenic agent and a progestin, there is a choice between cyclic and continuous dosing regimens. With the cyclic dosing regimens (intermittent high-dose progestin and estrogenic withdrawal), women can anticipate resuming a predictable (but artificial) menstrual cycle. With the continuous regimens (continual estrogen and low-dose progestin, without withdrawal), women can anticipate amenorrhea with occasional erratic spotting. Progestins are usually not recommended for women who have had a hysterectomy.[60]

The preventive effects of HRT on long-term health outcomes are now challenged by new data from clinical studies. In terms of beneficial effects, randomized clinical trials have proved that HRT is effective for vasomotor and urogenital symptoms.[61] A meta-analysis of estrogen treatment (oral or intravaginal) for urinary incontinence revealed a significant improvement in subjective symptoms, but no improvement in objective measures such as urodynamic testing.[62] It is unclear if HRT helps directly with depression and other nervous system disorders. A ''domino'' effect may occur; for example, relieving hot flashes may improve sleep, which may improve mood.[63]

Other allopathic treatments for hot flashes include a combination of ergotamine, belladonna alkaloids, and phenobarbital, which has been used for many years to relieve climacteric symptoms. Alpha-adrenergic agents, e.g., clonidine, are used for the relief of vasomotor symptoms. Physicians also prescribe serotonin reuptake inhibitors (SSRIs) to treat depression and mood disturbances related to menopause. ''Off-label'' use of megestrol acetate may help control hot flashes.

Osteoporosis

Another area where HRT was found to be helpful was for the treatment of osteoporosis. In the United States, 4 to 6 million women have osteoporosis. The consequence is that more than 250,000 hip fractures occur annually, with a health care cost of approximately $14 billion per year. Hip fracture carries a 10% to 20% risk of death within a year and a 25% chance of institutionalization.[64] After age 35 men and women start to lose approximately 1% of bone mass each year. However, bone loss is accelerated during the first 3 to 4 years after menopause. Estrogen therapy inhibits age-related bone loss after menopause by acting on osteoclasts (bone resorbing cells) and osteoblasts (bone-building cells) to decrease bone resorption. Estrogen also helps calcium to be absorbed in the gut. The daily dosage required to prevent bone loss is 0.625 mg of conjugated estrogen, but even 0.3 mg may suffice if taken with adequate calcium supplements.[59] Estrogen must be taken for at least 7 years to provide significant benefit and the risk of osteoporosis reverts back to baseline once the estrogen is discontinued.[54] Bone loss resumes within a year after stopping HRT, however, and bone turnover rises to the level of that in untreated women within 3 to 6 months.[65] Randomized controlled trials have shown that HRT reduces bone loss at clinically relevant sites such as the spine and neck of the femur.[66] The Women's Health Initiative (WHI) study was the first randomized controlled trial to show a reduction in hip fracture with HRT.[67] No herbal product studied has been proven effective in the prevention or treatment of osteoporosis.[68]

Nonhormonal therapies such as bisphosphates (e.g., Fosamax) and selective estrogen receptor modulators (SERMS) are as effective as HRT for preventing fractures. Bisphosphates inhibit osteoclast activity in the bone. Randomized controlled trials have demonstrated Fosamax efficacy increasing BMD and reducing fractures.[69] Etidronate (Didronel) is another bisphosphate. It is FDA-labeled for the treatment of Paget's disease, but has had an off-label use as a treatment for osteoporosis in patients who cannot tolerate Fosamax. Intranasal calcitonin is a polypeptide hormone that also inhibits osteoclastic activity; an intranasal form is now available for treatment of established osteoporosis. A selective estrogen receptor modulator, raloxifene (Evista), has been FDA labeled for prophylactic treatment of osteoporosis. For women whose main interest is prevention of osteoporosis, this agent offers an alternative to traditional HRT. Other selective estrogen receptor modulators pending FDA labeling include droloxifene and idoxifene.[59]

Colorectal Cancer

Observational studies have consistently suggested that HRT reduces the risk of colorectal cancer. The WHI study, however, was the first randomized controlled trial to confirm this, reporting six fewer colorectal cancers each year in every 10,000 women taking HRT compared with the placebo group.[67]

Cardiac Disease

Recent studies have cast doubt on the cardioprotective effects of HRT, the most frequently cited reason for starting women on HRT—further undermining conventional recommendations. Today, the results of the WHI have radically changed the way doctors are prescribing HRT. The WHI, the largest randomized trial of HRT, showed that long-term use of HRT poses more risks than benefits for healthy postmenopausal women. The WHI studied the use of estrogen plus progestin for prevention of coronary heart disease in 16,608 postmenopausal women age 50 to 79 years. After 5 years of follow-up, this arm of the study was stopped because of the adverse effects of the intervention. The researchers found that HRT increases the risk of several events: coronary heart disease events, invasive breast cancer, stroke, venous thromboembolic events, and pulmonary embolism.[67]

The Heart and Estrogen/Progestin Replacement Study (HERS) examined the effects of HRT in postmenopausal women with coronary artery disease. HERS was a large randomized controlled trial of 2763 women with an average follow-up time of 4.1 and 6.8 years. It showed no statistically significant difference between the HRT (estrogen plus medroxyprogesterone) group compared with the placebo group in either the primary outcomes (nonfatal myocardial infarction or coronary heart disease death) or in the secondary outcomes (coronary revascularization, unstable angina, congestive heart failure, resuscitated cardiac arrest, stroke or transient ischemic

attack, and peripheral arterial disease). However, further analysis showed a significant time trend, with more coronary heart disease events in the hormone group than in the placebo group during the first year of treatment and fewer in years 3 to 5. The recommendation after the HERS study was that postmenopausal HRT should not be used for reducing risk of coronary heart disease.[70] Thus, the WHI and HERS trials have shown that continuous treatment with 0.625 mg of conjugated equine oestrogens plus 2.5 mg of medroxyprogesterone increases the risk of heart disease events by 29% (37 vs. 30 per 10,000 person years) and stroke by 41% (29 vs. 21 per 10,000 person years).[67,70]

Thromboembolic Disease

Studies generally show an increased risk of deep venous thrombosis and pulmonary embolus in women taking HRT.[71,72] History of or risk factors for these conditions are contraindications to the use of HRT.

Endometrial Cancer

More than 30 observational studies have shown that unopposed estrogen therapy increases the risk of endometrial cancer. Progestin use in women with a uterus mitigates the risk of cancer associated with estrogen.[54]

Breast Cancer

A large meta-analysis of data from 51 observational studies reported that the risk of breast cancer increased by 2.3% for every year of use of HRT.[11] This increased risk does not become significant unless HRT is taken for more than 5 years. The risk of breast cancer falls after stopping HRT and returns to baseline within 5 years.

Because the WHI study stopped early, it could not examine the risk of death from breast cancer. However, it did confirm the excess risk of breast cancer with HRT. There was a 15% increase in invasive breast cancer in women taking estrogen plus progestogen for less than 5 years and a 53% increase in those taking it for more than 5 years. The study concluded that for every 10,000 women taking estrogen and progestogen, there would be eight more cases of invasive breast cancer a year.[11,67]

Mood and Cognitive Changes

Studies have also indicated that many cases of depression relate more to life stresses or ''mid-life crises'' than to the hormonal changes of menopause.[60] Menopause is not only a physical change but also a social transition. These transitions include an alteration in family roles, grown children leaving home; a changing social support network; a changing relationship with one's partner; parents or other close relative die; and changes in finances as one looks to retirement. Dysphorias, irritability, anger, memory loss, and losses of clarity of thought are among the most frequent symptoms reported by menopausal women, although the research data on the role of estrogen loss to depression and cognitive changes are mixed.[60] It is often the presence of mood- or memory-related symptoms that motivates a woman to request HRT. Physicians are now prescribing SSRIs to help women with these symptoms.

BOX 19-1

Relative and Absolute HRT Contraindications

Relative Contraindications
- Gallbladder conditions
- Uterine fibroids
- Poorly controlled high blood pressure
- Endometriosis
- Chronic liver dysfunction
- History of thrombotic disease
- Acute intermediate porphyria

Absolute Contraindications
- Breast cancer
- Estrogen-sensitive cancers
- Endometrial cancers
- Undiagnosed vaginal bleeding
- Active liver disease
- Active thrombotic disease

SIDE EFFECTS OF HRT

There are many reasons for noncompliance with HRT, but the most commonly cited include thrombotic complications, side effects on mood, and changes in the breasts.[60] Only about one in three women stay on HRT after a year, secondary to side effects. Adverse effects attributed to HRT include breast tenderness, breakthrough bleeding, and thromboembolic disorders. In addition, there are relative and absolute contraindications to the use of HRT (Box 19-1).

WOMEN'S OPINIONS OF HRT

Women's experiences of menopausal symptoms vary widely and have been found to relate to factors such as social class, ethnicity, and culture. The most common reason motivating women to take HRT is the relief of menopausal symptoms. Prior to the WHI, women who were trying HRT were having serious concerns about its use, and discontinuation was a major issue.[73,74] In 1995, a survey of women aged 50 to 80 found that 50% of women who had never used HRT believed that hormones were unnecessary, and 18% believed that menopause was a natural event not requiring medication. Safety concerns were expressed by nearly 30% of women who never used HRT, including fear of cancer (15.3%) and fear of side effects (12.9%).[75] Only a third to a half of women who leave their physician's office with a prescription for HRT are still taking it 1 year later. Women express concerns about the prospect of having menses indefinitely, the potential side effects of HRT, and the increased risk of cancer.[76,77] Forty percent of women discontinue HRT within 8 months of initial therapy or never fill the prescription.[78] Women who are currently using HRT are more likely to have had a hysterectomy than women who have never used HRT. In one survey of women who had undergone a hysterectomy, 50% of women were using HRT, 37% of women had used it in the past, and 24% of women never used HRT.[75]

NATURAL HORMONES

The most frequently prescribed estrogen in the traditional HRT regimen is conjugated equine estrogen (CEE). As public awareness of the source of CEE has grown, more women find this choice objectionable, whether out of concern for animal rights or out of an aversion to ingesting hormones that come from horse urine.[79] There has been a demand for natural sources of estrogen.

The three most common forms of estrogen produced by the body are estradiol (E2), estrone (E1), and estriol (E3). Estradiol, produced by the ovaries, is the most potent. Estrone becomes the most plentiful estrogen after menopause. Estriol is the weakest and is the estrogen that becomes more plentiful during pregnancy.[80] Estradiol can be produced from plants, and there is a growing market for such products. These estrogens are referred to as ''natural'' or ''bioidentical'' hormones, and are formulated by compounding pharmacies. There is little in the medical literature about these hormones. Additionally, among the lay public, there has been a growing demand for individually compounded hormone regimens. This demand is in response to the work of Wright and others who argue that HRT should mimic the ratios of E1, E2, and E3 naturally found in the body, or roughly 3%, 7%, and 90%, respectively.[80,81] This combination is known by the name of triestrogen or Tri-Est, which may consists of 1 mg estriol (E3), 0.125 mg estrone (E1), and 0.125 mg estradiol (E2) taken twice daily. This is equivalent to 0.625 mg CEE. There is also a product on the market called Bi-Est or biestrogen, which is estriol and estradiol. Bioidentical estrogens are compounded into sublingual troches, transdermal creams, and gels. Although only recently gaining popularity in the United States, these products have been used extensively in Europe where they are very popular. Although these estrogens are compounded in doses equivalent to prescription estrogens, and appear to have equivalent effects in regards to stimulation of the endometrium, there are, thus far, no studies that look at their safety or efficacy, particularly in regard to preventing or treating osteoporosis.[80] Although these are ''natural'' products, the safety of this estrogen and progesterone is being questioned following the publication of results from the Women's Health Initiative.

If many of the first-line measures are ineffective, such as clonidine, megestrol acetate, and antidepressants, low doses of bio-identical hormones may be initiated and titrated upward as needed for symptom control. Topical estrogen can be applied to the vagina for vaginal dryness or thinning, or painful intercourse.

PROGESTERONE

Progesterone plays a very important role in the shedding of the endometrium to avoid endometrial hyperplasia in postmenopausal women after they are exposed to estrogen in HRT. Therefore, it is now standard care to prescribe some form of progesterone with HRT in women with intact uteri. It is also believed that progesterone has additional benefits and risks. Synthetic progestins such as medroxyprogesterone and norethindrone have been shown to decrease vasomotor symptoms.[82,83] Reported androgenic effects of synthetic progestins include fluid retention, glucose metabolism, reduction of HDL cholesterol levels, headaches, and mood disturbance.[84] Furthermore, it was recently reported that women who were given HRT using a synthetic progestin had an increased rate of breast cancer compared with women who took estrogen alone.[15]

Natural progesterone taken by mouth is inactivated in the gastrointestinal tract. However, micronizing progesterone is a process designed to increase the half-life of progesterone and reduce its destruction in the gastrointestinal tract. Micronization decreases particle size and enhances the dissolution of progesterone.[84] Unlike synthetic progestins, micronized progesterone has not been shown to affect mood or lipid profile (or adversely affect pregnancy outcome).[84,85] The most commonly reported side effects are fatigue and sedation. Extensive use in Europe has shown that the micronized form can be taken once daily and is as effective as the synthetic progestins in controlling endometrial growth, while displaying significantly fewer metabolic side effects.[80,86]

A number of compounding pharmacies make natural progesterone products as alternatives to medroxyprogesterone acetate. Certain plants, including wild yam and soybeans, produce sterols called saponins that have chemical structures similar to progesterone. These sterols can be used as precursors for progesterone in the pharmacy. Most preparations that contain bioidentical progesterone contain United States Pharmacopeia (USP) grade progesterone, formulated from these plant sterols and manufactured by Pharmacia Upjohn (Peapack, NJ) and sold in bulk.[80] The hormone is not available from any natural source without extraction and synthesis. The body is not able to convert plants such as wild yam into progesterone on its own. Contrary to popular understanding, wild yam creams provide no active hormones because the sterols in plants cannot be converted into active steroidal compounds.[87] Only wild yam creams to which bioidentical progesterone has been added will exert a progesterogenic effect. Bioidentical progesterone is sold as a topical cream, a vaginal gel, and rectal or vaginal suppositories. The transdermal cream is formulated to contain 400 mg progesterone/oz and is easily absorbed into the skin. The usual dose is ¼ and ½ tsp once or twice a day. Recent research has cast doubt on whether the transdermal creams, even in prescription strengths, provide serum levels sufficient to protect the endometrium.[88]

In a double-blind placebo-controlled trial, 102 healthy women within 5 years of menopause applied 20 mg transdermal progesterone cream or placebo daily for 1 year. Each woman received daily multivitamins and 1200 mg of calcium and was seen every 4 months for review of symptoms. Improvement or resolution of vasomotor symptoms, as determined by review of weekly symptom diaries, was noted in 83% of treatment subjects and 19% placebo subjects. However, the number of women who showed gain in bone mineral density exceeding 1.2% did not differ.[89]

TABLE 19-1

Botanicals Commonly Used for Treating Menopausal Symptoms

BOTANICAL NAME	COMMON NAME	DOSE	SYMPTOM/PURPOSE
Actaea racemosa	Black Cohosh	40 to 200 mg dried root daily	For vasomotor complaints such as hot flashes, vaginal dryness
Angelica sinensis	Dong quai	200 mg standardized extract daily	For vasomotor complaints such as hot flashes, vaginal dryness
Panax ginseng	Ginseng	100 to 300 mg standardized extract daily	To improves energy and mood
Trifolium pratense	Red clover	40 mg daily	For vasomotor complaints such as hot flashes, vaginal dryness
Valeriana officinalis	Valerian	200 mg extract at bedtime	For sleep disturbances
Melissa officinalis	Lemon balm	1 to 3 cups daily of tea	To improve mood and insomnia, relieves anxiety

BOTANICAL ALTERNATIVES TO HRT

In the past several years, more than 100 OTC products targeted for menopausal women have reached the market, and women spend an estimated $600 million per year on these products. For nearly 70% of women, the transition into menopause is smooth;[90] however, many women seek advice for management of symptoms such as hot flashes or vaginal dryness. Women also seek information on the prevention of associated long-term health problems such as osteoporosis and coronary artery disease. It is essential that the practitioner address the whole woman. An individual assessment of her health risk factors and preferences for supportive care are chosen based on the symptoms she experiences, her risk of heart disease, breast cancer, and osteoporosis. This section addresses the clinical findings for botanicals commonly used as substitutes for HRT, or as treatments for menopausal concerns (Table 19-1). Specific menopausal concerns are also addressed in individual chapters.

Red Clover

Red clover was not traditionally used on a long-term basis for hot flashes, but today it is commonly used as an ''estrogen substitute'' for menopausal symptoms and the prevention of osteoporosis. Red clover contains phytoestrogenic isoflavones such as formononetin, biochanin A, daidzein, and genistein. Red clover has estrogenic properties on endometrial and breast cancer cells in vitro.[91,92] It is unknown whether long-term use has an estrogenic effect on the breast or endometrium. One small double-blind, randomized controlled pilot study looked at the effect of a 3-month course of a 33 mg red clover isoflavone supplement on endometrial cells taken between days 8 and 11 of the menstrual cycle. In this study of 30 late-reproductive age and perimenopausal women, there was no difference in endometrial index or thickness compared with the placebo groups.[93] Red clover extract is marketed as Promensil™ in Europe; it contains 40 mg isoflavones per tablet, which is approximately equivalent to the isoflavone content of a cup of soy milk and 5 cups of chickpeas. Promensil, a red clover isoflavone preparation, showed significant estrogenic activity, equivalent to 10 to 8 mol/L estradiol.[94] A 30-week small double-blind, randomized crossover trial of 43 perimenopausal and menopausal women with three hot flashes daily found no significant difference between Promensil (40 mg) or placebo to manage hot flashes.[95] A randomized, double-blind placebo-controlled prospective trial of 37 postmenopausal women with symptoms of estrogen deficiency was performed over a 12-week period. The women were randomized to three treatment groups: placebo, 40 mg, or 160 mg (isoflavone extract containing red clover isoflavones). There was no significant difference in the incidence of flashes among the three groups. There was no difference between the groups in Greene Menopause Symptom Scores, vaginal pH, levels of follicle stimulating hormone (FSH), sex hormone binding globulin (SHBG) or total cholesterol, liver function, or blood parameters. A statistically significant increase in high-density lipoprotein (HDL) cholesterol of 18.1% ($p = 0.038$) occurred in the 40-mg group.[96] Isoflavones have been found to increase arterial compliance in postmenopausal women,[97] thus presumably reducing heart disease risk. In another double-blind, randomized study, 60 postmenopausal women received either a commercially available red clover isoflavone supplement (80 mg/day) or placebo for 90 days. In this trial, red clover isoflavone supplementation significantly decreased the rate of menopausal symptoms and had a positive effect on vaginal cytology.[98] A recent meta-analysis and systematic review showed mixed benefits in reducing hot flashes compared to placebo.[99,100]

Although clinical research is lacking, the phytoestrogenic effects of red clover may, in theory, produce undesirable or unpredictable effects in the face of hormone-dependent tumors. Therefore, caution is advised in patients with estrogen receptor–positive neoplasia,[101] and patients taking hormonal or antihormonal medications such as tamoxifen.[101, 102] Use with caution in patients susceptible to bleeding problems or those taking anticoagulants.[101]

Dong Quai

For the past 3 years, sales of Rejuvex™, the most popular health remedy containing dong quai, have been extensive among hundreds of thousands of users in the United States.[103] In the Chinese Materia Medica, dong quai is

indicated for disorders of the women's reproductive system, including menopausal symptoms, dysmenorrhea and irregular periods, and menstrual cramps, and is used to ''strengthen the blood.'' The symptoms of ''deficient blood'' listed in Chinese texts are similar to those that Western medicine associates with menopause: menstrual flow abnormalities, nervousness, dizziness, insomnia, and forgetfulness.[60] Dong quai, traditionally prescribed as a tonic for women, is most commonly used as part of a mixture. It is sold in the United States for use alone or as part of newly formulated, nontraditional herbal combinations.

Its chemical constituents include furocoumarins, beta-sitosterol, flavonoids, and others. However, its presumed mechanism of action remains unknown. In a double-blind, randomized controlled study, 71 post-menopausal women age 40 to 65, were instructed to take three capsules three times daily, equivalent to taking 4.5 g of dong quai root daily (standardized to 0.5 mg/kg ferulic acid). There was no difference in Kupperman index scores, number of hot flashes, or endometrial thickness and vaginal maturation. A recent systematic review found dong quai to be ineffective in ameliorating menopausal symptoms at the dosages and preparation in the clinical trials reviewed.[99]

It would be valuable to study TCM formulas prescribed in accordance with TCM diagnostic methods. Dong quai does not contain the typically reported phytoestrogens, and the data on stimulation of estrogen receptor-positive breast cancer cells or binding to estrogen receptors are conflicting.[91,92,104] Dong quai contains coumarins and can cause bleeding when administered concurrently with warfarin; the furocoumarins contained in dong quai can cause photosensitization.

Black Cohosh

Black cohosh (Fig. 19-2) is widely used in Europe and has become increasingly popular in the United States as a treatment for menopausal symptoms (e.g., hot flashes and vaginal dryness). Since 1956, over 1.5 million women in Germany have used black cohosh extract, and in 1994 menopausal women in Germany, Scandinavia, and Austria used over 6.5 million monthly dosages of black cohosh extract.[105] It is an indigenous North American plant long used by Native American populations. Black cohosh contains several triterpenes and isoflavinoids. Other constituents are ascorbic acid, beta-carotene, butyric acid, calcium, chromium, selenium, thiamine, zinc, and salicylic acid. The German Commission E recommends it for premenstrual discomfort and dysmenorrheic as well as climacteric neurovegetative complaints.[106]

Studies of black cohosh's physiologic effects have had mixed results. Originally, it was believed that black cohosh had estrogenic effects, but now there is evidence to dispute this claim.[91,104,107,108] Data that suggest a nonestrogenic, or estrogen-antagonistic effect of the herb on human breast cancer cells may lead to the conclusion that treatment may be a safe natural remedy for menopausal symptoms in breast cancer, but the data are mixed.[109–111] There are no long-term safety studies using black cohosh in women who have had breast cancer.[112]

Figure 19-2 Black cohosh (*Actaea racemosa*). (Photo by Martin Wall.)

In numerous case studies, standardized black cohosh monodrug preparations have been used to treat menopausal symptoms, menstrual disorders (amenorrhea, oligomenorrhea, dysmenorrhea, polymenorrhea, PMS), and complaints during pregnancy. The literature describes the efficacy of black cohosh in approximately 1500 patients with menopausal disorders, citing distinct and clear improvements in the clinical picture and good to very good therapeutic responses.[107,113] By 1960, 1256 case reports in 111 published studies by gynecologists, general practitioners, internists, and neurologists had evaluated the use of black cohosh for the treatment of menopausal symptoms with positive effects and few side effects.[113] Most of the clinical trials assessing the use of black cohosh for menopausal complaints have been carried out using Remifemin® [Schaper & Brummer Gmb & Co., Salzgitter-Ringelheim, Germany]. Remifemin is standardized with respect to triterpene glycoside content, with each 20-mg tablet containing 1 mg of 27 deoxyactein; it is also available in a standardized liquid extract. Remifemin is the most clinically studied black cohosh product and has been the subject of more than 20 trials over the last 40 years. For an assessment tool, many studies have used the Kupperman

Menopausal Index, which is a weighted sum of 10 individual symptoms: hot flashes, outbreaks of sweating, sleep disorders, nervousness, irritability, dizziness, difficulty in concentration, joint pains, headaches, and palpitations.[114] The clinical trials are generally of poor methodically quality, small, and lack a control group. The results are mixed but most studies show benefit.[115–124] Recent systematic reviews demonstrate that majority of studies indicate that extract of black cohosh (*Actaea racemosa L.*) improves menopause-related symptoms.[99,125,126]

Black cohosh is not usually used on a long-term basis, and no clinical trials have lasted for more than 6 to 12 months. However, the safety profile is reassuring and black cohosh is well tolerated.[127,128] Tolerability of Remifemin appears to be good, with mild GI symptoms being the only significant adverse effect. Although black cohosh may be useful for menopausal symptoms, long-term use cannot be presumed to be safe until appropriate safety studies are conducted. Research by the German manufacturer has shown that black cohosh supplements have no effect on follicle-stimulating hormone, luteinizing hormone, estrone and estradiol, progesterone, sex hormone binding globulin, the vaginal maturation index, or endometrial thickness.[129] To date, four case reports of possible hepatotoxicity have been published, although previous safety reviews suggest that black cohosh is well tolerated and adverse events are rare when it is used appropriately.[99,126,130] Additionally, there is one case report of a woman with severe asthenia and very high blood levels of creatine phosphokinase and lactate dehydrogenase after using black cohosh.[131] (See Plant profiles: Black cohosh for a safety discussion.)

Evening Primrose Oil

Evening primrose oil, borage oil, and black currant seed oil produce seeds that contain gamma linolenic acid (GLA). A 6-month randomized double-blind placebo controlled trial was conducted with 56 menopausal women who reported having hot flashes three or more times a day. Participants were randomized to receive evening primrose oil 2000 mg with 40 mg vitamin E twice daily or placebo. Twenty-one women discontinued the study caused by a poor clinical response to the treatment, 10 taking evening primrose oil and 11 taking placebo. This study showed that evening primrose oil had no benefit over placebo in the alleviation of vasomotor symptoms.[132] A recent systematic review found no benefit.[99]

Panax Ginseng

Ginseng is reputed to be an aphrodisiac and to have estrogenic actions that improve menopausal symptoms. The Ginsana Corporation in Switzerland, the largest manufacturer of ginseng products worldwide, conducted a 16-week placebo-controlled trial in almost 400 postmenopausal women.[1,333] Although vasomotor complaints were not reduced, improvements were noted on scales used to rate depression and general health and well-being. Assessments of estrogenic effects, including the maturation index and measurement of plasma follicle-stimulating hormone and estradiol over a 16-week period, showed that there was no difference between the effects of ginseng and those of placebo.[133] A randomized, multicenter, double-blind, parallel study on symptomatic postmenopausal women assessed the effects of 16 weeks' treatment of standardized ginseng extract or placebo on quality of life and on physiologic parameters. To assess the efficacy of ginseng on postmenopausal symptoms, physiologic parameters [follicle-stimulating hormone (FSH) and estradiol levels, endometrial thickness, maturity index, and vaginal pH] were recorded at the same time points. Of the 384 randomized patients (mean age 53.5 ± 4.0 years), the questionnaires were completed by 193 women treated with ginseng and 191 treated with placebo. No differences were found between treatment subjects and placebo control is vasomotor symptoms, but significant improvements were reported on the quality measures for depression and well-being in favor of ginseng compared with placebo. Physiologic parameters such as FSH and estradiol levels, endometrial thickness, maturity indexes, and vaginal pH was not affected by the treatment.[134] In a double-blind placebo controlled study, 57 postmenopausal women were randomly assigned to 12 weeks treatment with Gincosan (320 mg/day), containing 120 mg Ginkgo biloba, and 200 mg Panax ginseng or placebo. The researchers found no significant effects of Gincosan treatment on ratings of mood, bodily symptoms of somatic anxiety, menopausal symptoms, or sleepiness or on any of the cognitive measures of attention, memory or frontal lobe function. Additionally, a recent systematic review found no benefit to using ginseng for menopause symptoms.[99] Ginseng's adverse reactions include nervousness, gastrointestinal upset or diarrhea, insomnia, dizziness, headache, euphoria, blood pressure effects, and vaginal bleeding.[135] Case reports link ingestion of ginseng with postmenopausal bleeding.[136,137] One case of postmenopausal bleeding occurred after topical use of a ginseng-containing face cream.[138]

Soy

Lower estrogen levels and longer menstrual cycles have been reported with soy-rich diets. Menopausal symptoms are reported to be less problematic in cultures (particularly Asian cultures) in which the diet is predominantly plant based and contains a lot of soy. Soy protein appears to be effective in reducing hot flashes, bone loss, and total and LDL cholesterol level.[139] The consumption of soy may reduce the frequency, severity, and incidence of hot flashes, but clinical studies and systematic reviews have showed mixed results.[140–146] The majority of phytoestrogens found in human diets are divided into two classes: isoflavones and lignins. Isoflavones are found predominantly in soy foods and other legumes such as chickpeas, pinto beans, and lima beans. Lignins are found in whole grains, seeds (particularly flax), and some fruits and vegetables. Soy supplement products are not recommended; whole food sources are optimal.

ADDITIONAL THERAPIES

For women with mild to moderate menopausal complaints, simple lifestyle modifications (Table 19-2) may

TABLE 19-2

Lifestyle Modification

TREATMENT	HOW IT HELPS
Diet	
High fiber	Decreases heart disease, decreases constipation, helps maintain weight
Low fat	Improves cholesterol, helps maintain weight
Rich in antioxidants	May decrease hot flashes and other menopausal symptoms
Increase soy	May decrease hot flashes, part of a heart-healthy diet
Exercise	
Cardiovascular	Decreases CAD risk, improves mood, aids sleep, helps maintain weight
Weight-bearing and strengthening	Improves bone health, may decrease hot flashes, helps maintain weight
Smoking cessation	Decreases heart disease, decreases smoking-related cancers, decreases osteoporosis risk, may decrease hot flashes
Decrease alcohol consumption	May decrease hot flashes, decreases osteoporosis risk
Maintain regular sexual activity	May decrease vaginal dryness (use it or lose it), may improve depressive symptoms

be enough to cope with the discomforts of this change without medications of any kind. Diet, exercise, and comfort measures can reduce hot flashes and other discomforts mildly to significantly.

Key dietary recommendations include the following:

- Diet: low fat and high fiber, increased variety of fruits and veggies (five servings a day)
- Whole grain foods
- Monounsaturated fats such as olive oil and canola oil
- Essential fatty acid and multivitamin supplement

Some have suggested that regular aerobic exercise lessens the frequency and severity of hot flashes.[147] Studies show that women who regularly exercise are less likely than their counterparts to experience severe hot flashes. In one observational study of 1323 women in Sweden, 15% of sedentary women experienced ''severe'' hot flashes, compared with only 5% of the subjects who exercised.[148]

There are many simple lifestyle changes women can make to help with hot flashes. The practice of wearing light, ''breathable'' cotton clothing helps, as does layering clothing. Other suggestions include keeping the ambient temperature of a room low; and avoiding hot, spicy foods, caffeine, and alcohol. Women also can benefit from stress reduction. In one study, women were taught ''paced breathing,'' a biofeedback technique that lowered their rate of hot flashes.[149] Diet and exercise also decrease bone loss. Other benefits can be derived from stopping smoking, decreasing soda and alcohol consumption, and improving dietary calcium intake.

Several studies have shown a benefit of calcium on improving bone density in both adults and children. There is no definitive evidence, however, that it lowers fracture risk. Calcium remains an important adjunct to the prevention and treatment of osteoporosis. Women should be encouraged to get their calcium through dietary intake of calcium-rich or fortified foods, but most women have trouble getting enough through diet. The aim for postmenopausal women should be a daily intake of 1000 to 1500 mg. Vitamin D supplementation should be a part of any osteoporosis prevention program. Studies have shown a decrease in fracture rates in older people treated with vitamin D, compared with those on placebo.[150,151] Present evidence suggests a daily dose of 400 to 800 IU may be required. Research has shown that people whose diets are rich in both magnesium and potassium have denser bones.[152]

CASE HISTORY:

Clare, a 50-year-old woman, presented with complaints of irritability, mood swings, hot flashes, and insomnia. She had had irregular periods for the past year, and now they had stopped for several months. ''Doc, I think that I am going crazy. Could I be going through menopause?'' She did not want to use HRT because her mother had a history of breast cancer.

Her medical history included a family history of breast cancer, hypertension, and diabetes. Clare had mild hypertension and Type 2 diabetes. She had no history of anxiety or depression. She had recently lost her job, and described being under extreme stress at home caused by financial hardship. Her husband was employed. Her son had broken his leg in a skiing accident.

She was currently taking Glucophage (500 mg bid), Atenolol (10 mg daily), a daily multivitamin, and calcium (1500 mg daily).

The following herbal protocol was recommended for anxiety and insomnia:

- Remifemin (standardized black cohosh) 40 mg bid
- Oat straw, chamomile, and lemon balm tea for sleep, as needed
- Sage aromatherapy mist to be sprayed near her bed or in her immediate vicinity for symptomatic relief of hot flashes

A follow-up in 3 months found Clare with symptoms much improved, and still taking the Remifemin.

HOT FLASHES AND NIGHT SWEATS

Bhaswati Bhattacharya and Aviva Romm

Approximately 75% of women in the United States experience hot flashes, one of the most common vasomotor symptoms of perimenopause. Hot flashes and night sweats typically accompany the onset of menstrual irregularity, as estrogen levels begin to decline. Women report a feeling of (sometimes intense) heat on the face, neck, and upper chest, which quickly progresses to a

generalized feeling of being overheated. The sensation lasts for 2 to 4 minutes and may be accompanied by sweating and palpitations. The episode is often followed by chills and shivering, particularly when episodes occur at night. Hot flashes may occur several times daily. Rarely, extremely frequent hot flashes occur—as often as hourly throughout the day and night.

Although some women experience hot flashes as a mild, transitory discomfort, or may even embrace them as an exhilarating sensation, reminding them of this powerful time of change in their lives, for many women, this is a severe symptom that can persist for up to 5 years, and rarely, as many as 15 years. Hot flashes may cause noteworthy social embarrassment when they occur in public settings. Stress often triggers a hot flash, thereby increasing the chance for socially embarrassing situations to arise.

Night sweats are a common source of significant sleep disturbance. Women may awake soaked from a night sweat. Sometimes, they are severe enough to necessitate a change of bedding, requiring the woman to wake fully, which further interrupts sleep. Severe sleep disturbance may be accompanied by daytime symptoms such as irritability, fatigue, depression, memory loss, and other disturbances in mental acuity. Sleep deprivation decreases functioning at daily tasks, increases the risk of accidents and injuries, and is an often-unrecognized source of marital tension, particularly when the partner's sleep also becomes disturbed by the woman's waking.[153]

Studies show that 72% to 80% of perimenopausal women consider hot flashes one of the most disturbing and disruptive symptoms they experience.[154] Addressing hot flashes in the history intake is pertinent, as not all women report hot flashes, sleep disturbances, and related symptoms unless specifically queried about their presence. Because not all women identify vasomotor symptoms as ''hot flashes,'' with descriptions of the symptoms varying based on education and cultural background, careful inquiry and creative questioning is important.

HOT FLASHES AROUND THE WORLD

According to the World Health Organization, menopausal vasomotor symptoms are not as problematic for women worldwide as they are for women in the United States and other Westernized nations.[155] Reported percentages are: Mayan women 0%, Hong Kong women 10% to 22%, Japanese women 17%, Thai women 23%, US women 45%, and Dutch women 80%. Cultural differences in attitudes toward menopause play a role in these epidemiologic differences; it is also postulated that the common denominator in reduced vasomotor symptoms also may result in part from disparities in phytoestrogen content of the diet and variations in amounts of exercise.[155]

HOT FLASH PHYSIOLOGY

Hot flashes occur as the result of a poorly understood hormonally mediated thermoregulatory response accompanying declining estrogen. This leads to inappropriate peripheral vasodilatation and the feeling of heat, followed by perspiration leading to rapid heat loss and cooling of the core body temperature to lower than normal. Shivering is the physiologic mechanism that occurs to restore normal body temperature.

Whether a woman chooses to use conventional therapy, herbs, massage, homeopathy, other modalities, or a combination, she knows her symptoms better than any other person and should be allowed her preferences, with proper advice and support.

Nonhormonal Treatments for Hot Flashes

Since the WHI study raised concerns about the safety of estrogen, women have been increasingly requesting nonhormonal treatments for menopausal symptoms.[156,157] Alpha-adrenergic agents such as clonidine have been used to relieve hot flashes and night sweats (especially at nighttime, as they may cause drowsiness). Its hypotensive effects also may limit its use for normotensive patients during the day.[158] Patients often experience edema and weight gain with continued use; rebound hypertension upon discontinuation is a potentially serious medical problem. Other nonhormonal treatments that are currently used and considered effective with relatively good safety profiles include SSRIs and gabapentin, a combination of ergotamine, belladonna alkaloids, and phenobarbital that has been used for many years to relieve climacteric symptoms, and ''off-label'' use of megestrol acetate, which also may help control hot flashes.[157,159–161] SSRIs have shown a 19% to 65% reduction in hot flashes, whereas clonidine has shown a reduction of 15% to 20%.[157] Gabapentin has been found to be more effective when combined with SSRIs than when used alone.[162]

Hormone Replacement Therapy

Estrogen and progestins are clearly effective in the reduction of hot flashes and have been a mainstay in the medical management of vasomotor symptoms; however, the use of HRT is accompanied by significant health risks. Should other alternative and conventional therapies prove ineffective in alleviating symptoms, and HRT be desired, some authors suggest that some of the personalized HRT prescriptions available through compounding pharmacies may minimize the risks associated with hormonal supplementation with equivalent efficacy.[163]

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

It is estimated that 50% to 75% of women use alternative therapies for the management of menopausal symptoms (Table 19-3), and the prevalence may be even higher in breast cancer patients.[164,165] Among the most commonly used botanical products are phytoestrogen-rich soy supplements, isoflavone-rich red clover products (e.g., Promensil), and black cohosh products (e.g., Remifemin). Herbal practitioners recommend herbs to ''regulate'' hormones and herbs for their ''cooling'' effects. Herbs rich in phytoestrogens and volatile oils, which may themselves exert estrogen-like or directly estrogenic effects (e.g., soy, red clover, sage, and hops), are highly favored for hot flashes and night sweats. Herbs are also used to treat concurrent symptoms (e.g., insomnia,

TABLE **19-3**

Herbs for Relief of Hot Flashes, Night Sweats, and Accompanying Symptoms

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Relieve hot flashes and night sweats	Serotinergic activity	*Angelica sinensis*	Dong quai
		Actaea racemosa	Black cohosh
		Glycine max	Soy
		Humulus lupulus	Hops
		Salvia officinalis	Sage
		Trifolium pratense	Red clover
Relieve hot flashes and night sweats	Phytoestrogen SERM		
Improve sleep	Nervine Sedative	See Chapter 19	
Improve mood/relieve fatigue, irritability	Adaptogen	See: • Chapter 6	
	Antidepressant	• Chapter 19	
	Nervine	• Chapter 19	

irritability, or depression), an essential component in improving a woman's overall sense of well-being while treating hot flashes. Holistic practitioners also encourage a variety of general comfort measures (see General Recommendations) to reduce the incidence of hot flashes and night sweats. Adaptogens can play a major role in hormonal regulation, as well as mediation of the sympathetic response, thereby providing underlying support to the system that can help to correct dysregulation. Important adaptogens to consider include ashwagandha (*Withania somnifera*), American ginseng (*Panax quinquefolim*), and eleuthero (*Eleutherococcus senticosus*), among others. Readers are directed to Chapter 8 for a complete discussion of adaptogens.

Traditional Chinese medicine offers botanical formulae that might be uniquely beneficial in addressing underlying imbalances of ''yin'' and ''yang,'' ''deficient heat,'' and ''kidney yin deficiency'' that are associated with the normal aging process, overwork, fatigue, and other contributors believed to cause hot flashes, night sweats, and related menopausal symptoms.

Phytoestrogens

The most commonly discussed plant compounds associated with perimenopausal therapies are the phytoestrogens. With a steroid ring structure similar to the estrogens, phytoestrogens are naturally occurring plant compounds that weakly bind to human estrogen receptors. Phytoestrogens are classified chemically into three main categories: isoflavones found in legumes such as soy, alfalfa, lentils, chickpeas, pinto beans, and lima beans; phytosterols such as coumestans, found in red clover, sunflower seeds, and bean sprouts; and lignins, found in flax seeds, fruits, vegetables, and whole grains. Lignins are converted by bacteria in the gut to enterodiol and enterolactone, and absorbed by the body to use for synthesizing the isoflavone subtypes: genistein, daidzein, and equol. Because they bind receptors weakly, phytoestrogens act as competitive agonists, blocking stronger estrogens from binding except at high concentrations. Genistein is clearly a bioactive molecule. It displays characteristics of a selective estrogen receptor (ER) modulator (SERM) rather than an estrogen, showing affinity for ERβ.[166]

Japanese women consuming a traditional Japanese diet, which is typically rich in soy products and vegetables, were found to have between 100 and 1000 times higher levels of urinary phytoestrogens than US and Finnish women eating omnivorous diets.[167] It has been proposed that phytoestrogens are a factor in the report of fewer hot flashes by Japanese women. However, trials evaluating the effects of soy supplements on hot flashes have not consistently found benefit. There is speculation that it is lifetime exposure to soy, as would occur in a traditional diet, that confers protective effects.[168] Of 12 clinical trials evaluating soy or soy isoflavones for the treatment of menopausal hot flashes, only four showed improvements.[163] A recent meta-analysis of evidence on phytoestrogen consumption and menopausal symptoms from 1966 to 2004 concluded that there is no benefit to phytoestrogens.[145] These inconsistent results may be related to methodologic issues with dietary monitoring or great variation in products used in the trials.[169,170] It should be noted that most of the clinical research on soy has involved the use of commercially processed soy proteins and not traditional soy foods, yet traditional soy foods are considered to be more effective than supplements.[168,169,171] Genistein, with few exceptions, is not a major isoflavone in most soy foods and products unless these have been fermented, as in traditional foods such as tempeh, natto, and to some extent, miso.[166] Further, only 30% to 50% of the adult population possesses the intestinal bacteria capable of converting the soybean isoflavone daidzein into the isoflavonoid equol.[169]

Although soy products (soy, miso, tempeh, natto) may only minimally reduce hot flashes, they do so in the context of providing other health benefits, including a beneficial effect on cholesterol and possible prevention

of osteoporosis. Caused by the long-term, large-scale exposure of humans to dietary soy without deleterious effects, regular consumption of fermented soy products is considered safe. Soy isoflavone supplementation has been recommended at a dose of 60 to 100 mg/day.[163] Whether to use phytoestrogens in women with estrogen-positive breast cancer is controversial and a legitimate concern. At this time, it is impossible to give a definitive recommendation. According to phytoestrogen expert Kenneth Setchell:

> findings for the prophylactic effect of the SERM raloxifene on breast cancer may offer some promise for soy in the latter group. To expect that soy and its constituent isoflavones will reverse or arrest chronic disease is asking too much of this small bean. The greatest potential for soy lies not in using it to treat pathologic changes that are usually irreversible, but in including it in the diet early in life, which will, by whatever mechanism, offer the potential for preventing chronic diseases.[166]

It should be remembered that many legumes are rich sources of phytoestrogens, and a varied diet is optimal.

Black Cohosh

Indigenous to North America, black cohosh has long been used for the treatment of menopause symptoms, mild depression, and its sedative and muscle-relaxant properties. Modern herbalists widely use this herb for the treatment of vasomotor symptoms, reporting positive results. The German Commission E approves the use of black cohosh for climeractic complaints associated with menopause, including hot flashes. It is the most widely studied herbal medicine for the treatment of menopausal complaints.[171] The bulk of clinical research on black cohosh for menopausal symptoms has used the isopropanolic extract Remifemin. Clinical trials have found noteworthy beneficial effects in the relief of hot flashes, night sweats, and other menopausal complaints, even comparable with the effects of conjugated estrogens, and statistically significant over the effects of placebo.[172–174] Unfortunately, the methodologic quality of the black cohosh trials is purportedly weak.[163] It was postulated that black cohosh is a selective estrogen receptor modulator (SERM); however, new data suggest a lack of estrogenic effects, with recent studies showing no changes in FSH, LH levels, SHBG, or estradiol levels, and a lack of endometrial proliferation, change in vaginal cytology, or increased risk development of breast cancer regrowth in survivors taking the herb for hot flashes.[91,172,175–177] It is now thought that perhaps black cohosh is working through a nonestrogenic, central mechanism, possibly through serotonergic or dopaminergic pathways; however, the exact mechanisms are unknown.[147,178] Clinically, black cohosh is used in a range from 20 to 80 mg twice daily of isopropanolic extract. There appears to be little risk of women with a history of ER+ breast cancer taking black cohosh; however, one study demonstrated an increased incidence of lung metastases in mice that developed breast cancer than in controls.[179] Recently raised concerns about possibly hepatotoxicity associated with black cohosh ingestion are discussed in Plant Profiles: Black Cohosh.

Dong Quai

The only randomized, double-blind placebo-controlled study of dong quai for hot flashes evaluated 71 postmenopausal women (mean age, 52 years) using 4.5 g/day dong quai root for 6 months. During the study, the hot flash incidence decreased by approximately 25% to 30% from baseline in the dong quai group, which was not significantly different from placebo.[103] Dong quai is commonly used in TCM for treating gynecologic conditions. However, unlike in this trial, it is never used singly; rather, it is included in individually tailored herbal formulae. Further, it is considered a warming herb, and in some women, may actually exacerbate hot flashes. Therefore, it is prescribed only for women in whom it is appropriate based on a TCM diagnosis, and used in combination with what are considered ''heat-clearing herbs'' (e.g., gardenia, *Gardenia jasminoides*).[180] Dong quai is contraindicated in women using warfarin. The herb may lead to increased vaginal or other bleeding. [This author (AR) managed the case of a menopausal woman taking a dietary supplement prescribed by an acupuncturist, consisting predominantly of dong quai, who experienced severe bleeding gums that ceased with 2 days of discontinuation of the product she had been on for 6 months and restarted on retrial.]

Hops

Hops, long used as a sedative by herbalists, is approved by the German Commission E for restlessness and sleep disorders. This, combined with its known estrogenic effects, which are considered greater than established phytoestrogens in vitro, caused by the presence of 8-prenylnaringenin, makes it an important herb to consider for treating hot flashes and night sweats.[91,163] Used in tea and tincture, often combined with herbs such as sage, passion flower, lavender, or other herbs to promote sleep, it is considered safe when used in moderate doses, although theoretically it may interfere with barbiturates and is thought by herbalists to exacerbate depression in some patients, although this is not a universally held concern.[181] There are no human clinical trials evaluating the efficacy or safety of this herb. With repeated consecutive doses, it will cause drowsiness; smaller single doses promote relaxation without drowsiness.

Red Clover

Red clover (Fig. 19-3) is a rich source of phytoestrogens: formononetin, biochanin A, genistein, coumestans, and daidzein. It has demonstrated estrogenic and progestational activity in ruminants as well as in in vitro receptor binding and cell proliferation studies.[91] Based on its constituents, it has been investigated for use in the treatment of menopausal symptoms. Promensil, a popular red clover product, is widely sold for its purported beneficial effects on hot flashes and other symptoms. To date, however, red clover clinical trials using 40 to 160 mg/day of red clover isoflavones have largely failed to provide evidence in favor of its use for reducing hot flashes or other menopausal symptoms.[96,181,182] One clinical trial that

Figure 19-3 Red clover (*Trifolium pratense*). (Photo by Martin Wall.)

Figure 19-4 Sage (*Saliva officinalis*). (Photo by Martin Wall.)

did demonstrate positive results was a randomized, double-blind placebo-controlled trial of 30 women with more than 12 months amenorrhea and experiencing more than five hot flashes per day. All received single blind placebo tablets for 4 weeks and were subsequently randomized to either placebo or Promensil (80 mg isoflavones) for a further 12 weeks. Efficacy was measured by the decrease in number of hot flashes per day and changes in the Greene Climacteric Scale Score. During the first 4 weeks of placebo, the frequency of hot flashes decreased by 16%. During the subsequent double-blind phase, a further, statistically significant decrease of 44% was seen in the isoflavones group, whereas no further reduction occurred within the placebo group. The Greene score decreased in the active group by 13% and remained unchanged in the placebo group.[184]

Sage

Sage (Fig. 19-4) is loved by herbalists for its ability to inhibit excessive sweating, and thereby finds its way into the materia medica of treatments for hot flashes and night sweats.[185] It is commonly recommended as a

Protocol and Formulas for Hot Flashes and Night Sweats

Protocol 1: Hot Flashes and Night Sweats with No Other Accompanying Symptoms

Use the cool down tincture throughout the day and again just prior to bed; take the tea 1 hour before bed for mild disturbances, or 2 to 3 cups/day if more troublesome. These can be taken together (the tincture can be added directly to the tea) or separately.

Cool Down Tincture

Mix the following tinctures:

Hops	(*Humulus lupulus*)	30 mL
American ginseng	(*Panax quinquefolium*)	30 mL
Lemon balm	(*Melissa officinalis*)	20 mL
Blue vervain	(*Verbena officinalis*)	10 mL
Lavender	(*Lavandula officinalis*)	10 mL
		Total: 100 mL

Protocol and Formulas for Hot Flashes and Night Sweats—cont'd

Dose: 2 to 4 mL tid to qid

Cool Down Tea

Sage leaf	(*Salvia officinalis*)	1 tsp
Spearmint leaf	(*Mentha spicata*)	½ tsp
Lavender flower	(*Lavandula officinalis*)	½ tsp

Steep 2 tsp/cup of boiling water for 10 minutes (keep covered while steeping to retain the important volatile oils). Strain. Take 2 to 3 cups/day.

Protocol 2: Hot Flashes and Night Sweats with Anxiety

Take 3 mL black cohosh* (or equivalent) bid with the tea or tincture.

Cool and Calm

Mix the following tinctures:

Hops	(*Humulus lupulus*)	20 mL
Skullcap	(*Scutellaria lateriflora*)	20 mL
Kava kava	(*Piper methysticum*)†	20 mL
Ashwagandha	(*Withania somnifera*)	20 mL
Licorice	(*Glycyrrhiza glabra*)‡	20 mL

Total: 100 mL

Dose: 2 to 4 mL tid

Take 3 mL black cohosh (or equivalent) bid with the tea or tincture.

Protocol 3. Hot Flashes, Night Sweats, and Insomnia/Irritability

Mix the following tinctures:

Hops	(*Humulus lupulus*)	30 mL
Passionflower	(*Passiflora incarnata*)	30 mL
Bupleurum	(*Bupleurum falcatum*)	15 mL
Ashwagandha	(*Withania somnifera*)	15 mL
Cramp bark/ black haw	(*Viburnum opulus/ prunifolium*)	10 mL

Total: 100 mL

Dose: 1 to 3 mL, for four doses, staggered over 1 to 2 hours prior to attempting sleep. Take a warm bath with lavender oil and practice progressive relaxation while going to sleep.

A small pillow filled with hops and lavender is an ancient sleep remedy.

Take 3 mL black cohosh (or equivalent) bid with the tea or tincture.

†Kava kava has been associated with hepatotoxicity in rare cases and should not be used by those with liver disease.

‡Licorice is contraindicated for patients with renal disease, hypertension, or hyperaldosteronism (see Plant Profiles).

*Recent concerns have been raised about black cohosh and rare cases of hepatotoxicity. The validity of the concern about black cohosh has not been corroborated by the FDA. See Plant Profiles: Black Cohosh.

tea, alone or with other herbs such as chamomile and lavender to also promote relaxation, to be taken 1 to 2 hours before bed, as well as 1 to 2 cups during the day. Only one trial of unknown quality was identified looking at sage specifically for hot flashes. In this study, the efficacy of a combination of *Salvia officinalis* and *Medicago sativa* (alfalfa) was tested in 30 menopausal women with hot flashes and night sweats. Symptoms completely disappeared in 20 women; of the remaining 10 women, four showed good improvement and the other six showed a reduction in symptoms. GnRH and TRH tests were performed in eight women to evaluate TSH and Prl responses before and after 3 months of therapy. The plants product induced a significant increase in Prl and TSH response to TRH. Basal levels of estradiol, LH, FSH, Prl, and TSH were unchanged. The authors concluded that the product seemed to have a slight central antidopaminergic action without side effects and is an effective agent in the treatment of menopausal symptoms. In an open study of two groups ($n = 40$, no control), given sage infusion (2.6 g or 4.5 g herb/day), the herb inhibited pilocarpine-induced sweating.[186] Herbalists also may encourage a perimenopausal patient to keep a spray bottle of sage tea on hand to use as a cooling spritz during the day and at night just before bed. Sage essential oil, 3 to 4 drops, diluted in 2 ounces of a lavender aromatherapy spray is also effective and pleasant for a quick cool down. Sage essential oil should never be taken internally!

ADDITIONAL THERAPIES

Nutritional Considerations

In spite of popular use, vitamin E (400 IU/4 weeks) has not been shown to be significantly more effective than placebo in the reduction of hot flashes. The study has been criticized for using too low a dose, with vitamin E proponents suggesting 800 IU to be a more appropriate dose for a trial.[163]

General Suggestions for Preventing Hot Flashes and Night Sweats

- Sip cool water with lemon throughout the day; stay well hydrated.
- Practice deep breathing techniques for relaxation to try to calm down when the heat starts to rise.
- Wear clothing in light layers and always keep a sweater on hand that is warm and dry should hot flashes be followed by chills and perspiration.
- Wear cotton or very light woolen knits—silk, thick woolens, and synthetic fibers retain heat. Similarly, sleep under cotton sheets and cotton quilts.
- Avoid spicy foods.
- Include tempeh, miso, and tofu in the diet two to three times a week, and other legumes two to three times a week (lentils, garbanzos, etc). Eat cold water fish for the essential fatty acids, and plenty of fresh fruits, vegetables, nuts, and seeds. Eat organic yogurt with fresh fruit as a cooling, calcium-rich snack.
- Avoid caffeine, except green tea (and the occasional piece of dark chocolate!).

- Keep alcohol to a minimum, with the exception of an occasional glass of red wine if desired (not more than 1 glass per week).
- Take a cool shower before bed.
- Keep a small fan near the bed and run on a low breeze to keep the air above the bed cool and circulating.
- Keep a set of sheets and change of night clothes near the bed to ease the burden of changing the bedding should a night sweat occur; take care to avoid chills.
- Carry a small spritz bottle with sage and lavender teas or lavender aromatherapy spray to which is added three to four drops of sage essential oil for quick cool downs.

DEPRESSION

Clara A. Lennox

Depression is clinically defined as a depressed mood, loss of pleasure in activities (or life), or loss of interest in nearly all activities, persisting for at least 2 weeks. It may be accompanied by symptoms such as sadness, poor self-esteem, anxiety, irritability, anger, social withdrawal, guilt, helplessness, hopelessness, multiple physical complaints or fears, obsessive thoughts, poor concentration, decreased libido, recurrent thoughts of death or suicide, or psychotic symptoms; and there also may be neurovegetative symptoms such as fatigue or loss of energy, sleep disturbance, appetite disturbance, or psychomotor retardation or agitation.[187]

The etiologies of depression are not fully understood but include both childhood events and the effects of current stressors on the individual.[188] Theories on the causes of depression include psychodynamic factors (e.g., poor self-esteem), cognitive origins (e.g., holding oneself to rigid rules and impossible standards), and genetic causes (e.g., family history is common; twin studies show up to a 90% chance of an identical twin also developing depression; and may involve neurotransmitters and neuroendocrine pathways).[187,189] Sociopolitical factors are suggested by the significant cohort effects found in epidemiologic studies, such as the discovery that people born between 1940 and 1950 seem to have more risk of depression, starting younger, than those born before 1940.[190]

The question about menopause itself as an etiology for depression has been hotly debated for years. The association between the two has been described since antiquity, and a causal relationship had been assumed. Factors implicating a hormonal role include worldwide data showing that the lifetime risk of depression in women is double that of men; the rate of depression in girls rises rapidly after puberty; women with cyclic premenstrual depression/anxiety symptoms (premenstrual dysphoric disorder) have elevated lifetime prevalence rates of major depression and postpartum depression; rates of depression in women decrease after menopause.[191,192] However, the prevalence of depressed mood is actually greater among young adults than midlife women, and although prevalence rates and symptoms of depression are similar in all societies worldwide, prevalence rates of menopausal symptoms differ widely.[193,194] In societies such as the Bantu women of South Africa, in which postmenopausal women attain a higher social position with more freedom and power, menopausal symptoms are few; in Japanese, Mayan, and Indian women, the prevalence of hot flashes is much lower; and Mexican women who spent their childhood years in Mexico before coming to the United States had a lower level of depressive symptoms and more satisfaction with life than those who were exposed to the United States in childhood, with higher scores on intrinsic strength factors such as mastery and resilience.[194–196] The importance of resolving this question can hardly be overstated, because according to the World Health Organization, depressive disorders are the fourth most important cause of disability worldwide and are expected to become the second most frequent cause of illness by the year 2020.[188,194] Further, mounting evidence suggests a role for depression in the development of coronary heart disease, increasingly a major contributor of morbidity and mortality in women.[197]

The preponderance of current medical evidence demonstrates that depressive disorders that meet DSM-IV criteria are not more frequent during menopause.[194] No association between depression and LH or FSH levels or estrone or testosterone levels has been identified.[194,198] A theory of subthreshold depression describes depressive symptoms that are less severe or fewer than required for classification of depression by the DSM-IV criteria;[194] the similarity between climacteric symptoms and depressive symptoms also may account for the apparent relationship between menopause and depression, leading to a postulated menopausally related mood syndrome, involving less severe depressed mood, anxiety, insomnia, irritability, fatigue, forgetfulness, decreased self-esteem, and decreased libido, possibly related to vasomotor symptoms.[200,201] Other factors strongly associated with depression in menopause include impaired health, vasomotor symptoms (hot flashes, sweats, insomnia), physical inactivity, a past history of depression and stressful life circumstances (problems with family, money, or work), or premenstrual dysphoric disorder.[193,194,199,200–206]

DIAGNOSIS

Types of depression are classified by the American Psychiatric Association's criteria, set forth in the DSM-IV-TR as follows:[190]

- *Major depression:* depressed mood and/or loss of interest or pleasure for at least 2 weeks, with at least four other symptoms (appetite disturbance; sleep disturbance; psychomotor retardation or agitation; fatigue or loss of energy; feelings of worthlessness or excessive or inappropriate guilt; diminished ability to think or concentrate, or indecisiveness; recurrent thoughts of de or suicidal ideation.[190] Symptoms should not be caused by the effects of a substance (alcohol or drugs—illegal or prescription) or a medical condition (e.g., hypothyroidism) or bereavement, which are classified separately.
- *Dysthymic disorder:* Symptoms are similar to major depression, but are persistent for at least 2 years and are less severe.[190]

- *Bipolar disorder* involves the occurrence of one or more manic episodes; often individuals also have had one or more episodes of major depression.
- *Seasonal affective disorder* (SAD) occurs in northern latitudes, as light exposure decreases in the fall; symptoms resolve as days lengthen in spring. Overeating (especially carbohydrates) and oversleeping are common.[187] These diagnoses may be applied only after other causes of depression have been eliminated.
- *Prescription drugs:* Numerous prescription drugs may cause depression as a side effect. Common culprits include beta-blockers, antihypertensives, tranquilizers, antiepileptics, corticosteroids, digoxin, H2-blockers, etc. Some antidepressants may exacerbate depression.
- *Drugs of abuse* (alcohol, etc.)
- *Toxic-metabolic conditions:* thyroid disease, diabetes mellitus, Cushing's syndrome, electrolyte/calcium imbalance
- *Neurologic conditions:* stroke, epilepsy, dementia, etc.
- *Infectious causes:* viral mononucleosis, hepatitis, HIV, syphilis, Lyme disease
- *Nutritional deficiency*
- *Other:* postsurgical, cancer, chronic fatigue syndrome, fibromyalgia, rheumatoid disease, etc.[187]

Psychosocial causes include domestic violence, bereavement, and personality disorders.[187] There are marked cultural, gender, and age differences in presentation. Many people with depression do not complain of sadness; in fact, they may describe anxiety or somatic symptoms as predominant. A diagnosis of depression should be considered in anyone complaining of fatigue, sleep or appetite problems, or multiple body symptoms. A careful medical, family, and social history, with detailed review of systems must be done; questions about organic causes and depressive symptoms in detail must be covered. If a diagnosis of depression is suspected, an evaluation of suicide risk must be made. Physical exam should address not only possible medical causes of depression but also specific somatic symptoms, providing reassurance about fears of covert illness. Mental status can be assessed during the history and exam, with specific questions about mood and memory. There are no lab tests for depression; blood work to rule out organic causes might include a CBC, blood sugar, BUN, creatinine, electrolytes, liver function tests, albumin, calcium, and TSH (thyrotropin).[187] Some of these would be required before starting psychotropic medications. Diagnostic questionnaires may be used to assess the severity of the depression and monitor clinical response to treatment.

CONVENTIONAL TREATMENT APPROACHES

An immediate referral to a psychiatrist should be made and confirmed by the practitioner in cases involving suicidal ideation, very severe depression, bipolar disease, paranoia, or psychosis.[187,194] Any underlying cause or contributing factor should be addressed (e.g., alcohol abuse, prescription drug side effect, hypothyroidism, domestic violence, etc.). Presuppositions should not be made about who is at risk for suicide based on demographics or educational levels; for example, suicide is a disproportionately high cause of mortality in physicians, particularly in female physicians.[207]

Hormone Replacement Therapy

Hormone replacement therapy (HRT) has been a standard treatment for many years, with equivocal findings as to effectiveness, tolerability, and safety. The history of HRT is quite instructive, as it illustrates many of the pitfalls of orthodox drug use. Initially, HRT was actually ERT-estrogen replacement therapy, and menopause was regarded as a deficiency state. In the 1960s and 1970s, many women were advised by their physicians to take estrogen; by 1975, medical reports were documenting an increased risk of endometrial cancer (5 to 15 times more likely).[208] At this point, for women who still had uteri, a synthetic progestin (usually Provera) was added for 10 days of the month (''sequential'' pattern), followed by a week of no ''hormone replacement'' during which withdrawal bleeding would occur. The risk of endometrial cancer was reduced, but other problems surfaced quickly. Women did not feel as well on HRT as they had on ERT.[191] Many women did not want to have bleeding every month indefinitely; the ''PMS'' side effects during the 10 days on the progestin and the return of menopausal symptoms on the week of no hormones made them miserable. The regimen was changed again to smaller doses of progestin to be taken every day, along with estrogen. Bleeding patterns changed from predictable to unpredictable, requiring endometrial biopsies and other even more invasive tests. Many women opted out of HRT, despite hypothetical benefits postulated by the medical establishment, mostly subsequently disproved. Data from 1992 showed that despite evidence supporting the benefits of HRT, only 15% of postmenopausal women currently use HRT.[5] Of those who begin HRT, fewer than 50% continue beyond 1 year.

The leading reasons for women's ''refusal or discontinuation of HRT are fear of malignancy, side effects such as vaginal bleeding, weight gain, *depressed mood*, and breast tenderness, and social reasons such as regarding menopause as a natural transition, not as a disease that requires treatment.''[104] As discussed in previous chapters, the controversy surrounding HRT use continues, with women concerned about its safety and eager for alternatives for the symptoms, including depression.

Estrogen has a modulating effect on serotonin, dopamine, and possibly norepinephrine,[201] likely explaining its antidepressant effects. Unfortunately, progestin, which also has a theoretical basis for antidepressant effect in that it increases monoamine oxidase levels, has been shown in several studies to worsen depression.[200,201] Pearlstein reminds us, ''The negative mood effects of progesterone are well-known in premenopausal women using oral contraceptives. Depressed mood has been reported in as many as 30 percent of OCP users and may occur less frequently with lower-dose OCPs.''[191] She also points out, ''Most controlled studies have reported that progesterone sequentially added to estrogen has a negative effect on mood.''[191] There are studies showing that estrogen alone does improve mood and control vasomotor symptoms, especially

during perimenopause and if the depressed mood is mild.[191,195,201,209,210]

Much of the data derive from studies involving white women who had chosen to use estrogen, who were younger, more likely to be married, less likely to live alone, and better educated; they were more physically active, thinner, had better cognitive function and functional status, and were more likely to have a primary care doctor; other studies were done on women who chose to seek help from menopause or psychiatric clinics, who had longstanding severe symptoms.[205,211] What do these studies tell us about the rest of us? There are a very small number of studies showing improvement in depressed mood with progestin or testosterone, but many are equivocal or describe worsening of mood symptoms.[191,201,210] Please note that the progesterone in most of these studies was almost always Provera, which is actually synthetic medroxyprogesterone, not human bioidentical progesterone, which is being studied now.

Many studies have found no evidence of effectiveness of HRT (estrogen plus progestin) on alleviating depressed mood.[205,212–215] A very interesting study showed no difference in psychological or psychiatric symptoms (including depression, insomnia, forgetfulness, irritability, lethargy, and sexual difficulties) in women who received estrogen or placebo implants.[213] Cognitive function was unrelated to menopause or HRT; sexual activity and satisfaction were almost identical in estrogen- and placebo-treated groups.[195] Two studies of positive mood and life satisfaction during the menopausal transition showed that life satisfaction was predicted by earlier attitudes; positively associated with feelings for partner and exercise; negatively associated with stress and smoking; and unaffected by menopause status, hormone levels, or HRT; ''the most important predictor of positive mood at the phase of late perimenopause or postmenopause was positive mood in the premenopause.''[216,217]

In addition to the lack of solid proof of efficacy, the risks of HRT that were well documented before 2002 included stroke, venous thromboembolism, worsening of hypertriglyceridemia, cholelithiasis, deterioration of liver function in women with liver disease, and increased pain in benign breast disease;[218] abnormal bleeding, weight gain, fluid retention, blood pressure elevation, glucose intolerance, and headache.[187] Caution was advised in women with sickle cell anemia, obesity, and tumors.[219] The most serious risk, however, is the increased risk of breast cancer, which becomes significant even after only 1 year of use;[220] by 10 years the relative risk of developing breast cancer is 30% higher in women taking estrogen;[218] ''adding a progestin may further increase risk substantially above this'';[218,221] and ''there was a 43% increase in deaths from breast cancer in patients who took HRT for more than 10 years.''[187] In 2002, results of two randomized trials of HRT (the WHI and the HERS trials) showed that it was not cardioprotective, and may increase risk of cardiovascular disease.[218,222,223] Premarin (conjugated equine estrogens) may be more risky than estradiol, because it causes levels of equilin estrogens that are many times higher than the levels of estrone and estradiol that occur,[224] but there is still no evidence that estradiol is effective. The summary of current evidence about the overall clinical relevance of currently prescribed HRT in treatment of depression is that it is unproven[225] to be effective, and proven to be hazardous.

Antidepressant Drugs

Antidepressant drugs are currently the mainstay of standard medical drug treatment of depression in menopause. Noticeable clinical improvement may take 3 to 4 weeks. There is little difference in efficacy among the varied categories of antidepressants; they are all equally effective; they differ in type and severity of side effects.[188]

The most popular category at present is the selective serotonin reuptake inhibitors (SSRIs), including fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), fluvoxamine (Luvox), and citalopram (Celexa).[187] They have energizing or activating effects, which can be useful in patients with low-energy symptoms, but can result in side effects such as anxiety, insomnia, agitation, and restlessness.[187] Paroxetine is effective for treatment of hot flashes, as is venlafaxine.[218] A major drawback to successful use of SSRIs is that sexual dysfunction occurs in nearly 60% of patients, is difficult to manage, involves loss of libido and orgasmic dysfunction in both men and women, and is often not mentioned unless the practitioner asks about it directly.[226] Serotonin syndrome (tremor, agitation, delirium, rigidity, myoclonus, hyperthermia, obtundation) is a potentially fatal consequence of combining SSRIs with other drugs that also increase serotonin,[226] especially in elders. SSRI inhibition of the liver cytochrome P450 isoenzymes causes slowing of hepatic drug metabolism and interactions with other drugs, including phenytoin (Dilantin), warfarin (Coumadin), cimetidine, barbiturates, macrolide antibiotics, antihistamines, benzodiazepines, beta-blockers, Tegretol, cyclosporine, diltiazem, digoxin, Haldol, Lithium, theophylline, tolbutamide, and many others.[227] Overdose is rarely fatal.[226] These drugs should not be stopped suddenly, or withdrawal symptoms (flu-like symptoms, malaise, dizziness, nausea, paresthesias, depression, sleep problems, etc.) may occur.[188,226]

Tricyclic antidepressants (TCAs) such as desipramine (Norpramin), nortriptyline (Pamelor or Aventyl), or doxepin (Adapin or Sinequan) are sedating, making them good choices for women with anxiety, panic, or insomnia symptoms.[187] Side effects are likely to be anticholinergic symptoms (dry mouth, constipation, sexual dysfunction, urinary retention, blurred vision, increased intraocular pressure, brain fog, sedation, heart block), postural hypotension, and weight gain.[187,226] A full-blown anticholinergic syndrome of agitation, delirium, and fever can occur, especially with antihistamines (including OTC sleep/allergy/cold medications) and other anticholinergic drugs.[187] Many other severe drug interactions include serotonin syndrome, hypertensive crisis (with clonidine), life-threatening arrhythmia (with quinolone antibiotics); and inhibition of CYP450 drugs.[227] Tardive dyskinesia may occur, and may be irreversible.[227] Overdoses are fatal with a 10-day supply of 200 mg/day.[226] Withdrawal symptoms may occur; taper slowly.

Trazodone (Desyrel) is sedating, very useful for anxiety, panic, insomnia, alcoholism, and aggressive behavior;[227] patients may respond in 1 week, with good effects in 2 weeks; some take up to 4 weeks.[227] It can be very effective for hot flashes that cause night sweats. It has few common side effects (other than drowsiness and headache) and much less sexual dysfunction, but it can cause serotonin syndrome and CYP450 drug interactions. Overdose can be fatal, especially in combination with other drugs. Nefazodone (Serzone) is similar, has complex effects on serotonin, and also less sexual dysfunction. There are reports of severe liver failure, all in women; somnolence occurs in 25% and dizziness in 17%; serious interactions occur with CYP450 drugs.[227]

Bupropion (Wellbutrin) is somewhat activating, so its side effects include anxiety, agitation, and insomnia; it has a fourfold to tenfold increase in risk of grand mal seizures, especially in patients with anorexia or bulimia; it can cause hepatocellular injury and increased risk of liver cancer, and interacts with CYP450 drugs.[227] Overdose can cause death.

Monoamine oxidase inhibitors (MAOIs; Nardil, Parnate, etc.) are drugs of last choice, when everything else has failed; in addition to more potentially fatal drug interactions than all the other antidepressants, they can interact with a substantial number of common foods (cheese, pepperoni, beer, red wine, bananas, avocados, coffee, colas, chocolate, and many more); there are cases of dependency and withdrawal; and overdoses can be fatal.[227]

Other Drugs

Clonidine can be effective for hot flashes;[218,219,228] it is used to treat migraine and hypertension, possibly acting as a peripheral vascular stabilizer.[219] Side effects include drowsiness, dry mouth, dizziness, and constipation. A small bedtime dose can be quite effective. Patches are available, but their use is limited by adhesive sensitivity.

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

In many indigenous medical systems, and for a substantial segment of Western herbal practitioners, beliefs about the causes and meanings or purposes of depression are radically different from those held commonly by orthodox medical practitioners. In addition to consideration of the individual's nutrition, exercise, and relaxation practices, work and family situations, use of drugs and medications, and exposure to toxins (physical, intellectual, emotional, spiritual), the major focus will be on the loss of inner balance and harmony, and on empowering the client to start to work on restoration.[230]

The illusion of separateness so pervasive in Western cultures is felt by many indigenous traditions to be a major cause of illness. This illusion allows us to ignore the reality that the whole of life is an integrated web, rooted both in earth and in the Divine,[231] one and inseparable; true ''interbeing,'' as Thich Nhat Hanh[232] would describe it. This includes humans, plants, rocks, water, animals, stars, and all that is, referred to with deep respect by Native Americans as ''all my relations.'' The mestizo poet Francisco X. Alarcon expresses this perfectly:

In *Xochitl In Cuicatl* [Nahuatl for ''flower'' and ''song,'' or ''poetry''][233]

every tree
a brother
every hill
a pyramid
a holy spot
every valley
a poem
in *xochitl*
in *cuicatl*
flower and song
every cloud
a prayer
every rain
drop
a miracle
every body
a seashore
a memory
at once lost
and found
we all together:
fireflies
in the night
dreaming up
the cosmos

A sense of lack of connectedness, of being in relationship with the entire universe, is for many, a cause of emotional disturbance, and recognizing this can be the means of its healing. Tibetan Buddhism attributes mental illness, including depression, to leading a life that runs counter to one's deepest spiritual self, especially if that self is resisted, denied, or repressed.[230] On the other hand, a deep sense of connectedness may cause depression in sensitive individuals. Those who have the strongest empathy for the planet and others may suffer emotionally in the face of ongoing worldwide environment, social, and political crises.[234]

The value of connectedness or interrelationship in healing depression includes several major considerations. If interbeing is accepted, then healing can take place via developing connections to Nature, and connecting with family, friends, and community.[235] Service to others, especially to the healing of the planet, can be a very powerful path to healing oneself.[235] An interdisciplinary medical literature review showed that ''interaction with the natural world positively affects multiple dimensions related to human health: physical, psychological-emotional, social, and spiritual,'' including less effect of stress on the autonomic nervous system, less pain, shorter surgical recovery time, improvement of deficits in attention, greater satisfaction with life, more positive social interactions, less aggressive behavior, and feelings of ''greater interdependence and connectedness.''[236] The botanical practitioner views the use of herbs as part of not only healing the body but as part of building a relationship with the natural world.

The following herbs represent only a fraction of those that are used worldwide to treat depression and its related symptoms (Table 19-4). These herbs may be used singly but are more often used in combinations specifically formulated for the unique needs of the patient. In addition to directly treating symptoms of depression, associated complaints such as chronic pain, insomnia, fatigue, and other predisposing health problems should be appropriately addressed through herbal formulae and other strategies.

TABLE 19-4

Herbs for Depression

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
	Antidepressant	*Hypericum perforatum*	St. John's wort
	Adaptogen	*Asparagus racemosa*	Shatavari
		Eleutherococcus senticosus	Eleuthero
		Withania somnifera	Ashwagandha
		Centella asiatica	Gotu kola
		Angelica sinensis	Dong quai
	Nervine	*Anemone pulsatilla*	Pulsatilla
		Lavendula officinalis	Lavender
		Leonurus cardiaca	Motherwort
	Stimulant	*Camellia sinensis*	Green tea
		Rosemarinus officinalis	Rosemary

Albizzia

In TCM, this is considered an herb to ''Nourish the Heart and Calm the Spirit''; the literal translation of the herb's common Chinese name is ''collective happiness bark.'' It is used for heartbreak, depression, insomnia, poor memory, bad temper, and irritability caused by constrained emotions, giving feelings of calm and peace, and lifting the spirit.[237,238] Studies show sedative properties (increased sleeping time in mice), strong antioxidant activity, improvement in learning and memory, increased levels of serotonin and GABA, anticonvulsive, and antianxiety activities.[239–243] Contemporary use is mainly by practitioners of TCM, but it is an herb that can be easily incorporated into Western botanical protocol in tincture and other forms.

Ashwagandha

A classic herb in Ayurvedic medicine and now regarded as one of the best adaptogenic tonics, ashwagandha has been used for over 3000 years to restore, enhance, and preserve energy, strength, memory, and vitality, counteracting the effects of stress on the mind and body, calming a turbulent mind, and promoting inner peace and clarity.[244,245] A review article describes the findings from 58 articles found in a search of four medical databases, concluding that ashwagandha has anti-inflammatory, antitumor, antistress, antioxidant, immunomodulatory, hematopoietic, and nutritive properties, and may be of benefit also to the endocrine, cardiopulmonary, and central nervous systems; it has little or no toxicity.[296] The review also pointed out that ashwagandha may be even more effective when given in combination with other herbs (as is usually the case in its traditional use). In addition to this extensive review, there are articles supporting the anxiolytic and antidepressant activities of ashwagandha, found to be comparable to that of lorazepam and imipramine; reversal of chemotherapy-induced neutropenia, anticonvulsant activity, improvement or protection of memory from known disruptors, and adaptogenic effects.[242–255] Mild GI side effects may occur. It is an excellent choice in depression with anxiety and panic, a racing mind, insomnia, exhaustion, heavy bleeding, stress, and low libido.[245] It is also used for helping memory and learning, for malnutrition and anemia, arthritis, inflammation, bronchospasm, immune enhancement, alcoholism, and reproductive system disorders; improvement in libido occurs gradually after at least a month of use.[244] Ashwagandha may be taken in tincture, decoction, or powdered in capsules. Traditionally, the powder is prepared by boiling in milk with a small amount of sugar or honey.

Bacopa

Bacopa is one of the most important Ayurvedic herbs for depression, emotional stress, mental exhaustion, forgetfulness, and anxiety.[256–259] Its effects on cognitive function (improvement in learning and memory) have been documented in numerous studies, as has its antioxidant activity in the brain and its ability to regulate brainwave activity and serotonin.[260–263] One study shows significant antidepressant effect, comparable to imipramine, in a rodent model.[264] Three review articles summarize its documented effectiveness in enhancing learning and memory.[247,265,266] Two studies show protection of brain function from the adverse effects of morphine and phenytoin.[267,268] Two studies found adaptogenic effects, protective against stress-induced physical and biochemical changes.[269,270] In view of the growing body of research, its use is increasing among Western herbalists, who combine it in tincture form with other herbs for memory and mood enhancement.

Black Cohosh

Black cohosh was a favorite remedy of the Eclectics, who used it for nervous irritation, hysteria, melancholia, and epilepsy related to menstrual cycles, and for obstetric purposes.[271] The therapeutic efficacy of black cohosh for menopausal symptoms, including hot flashes and mood disorders, has been demonstrated in a number of trials.[272] A double-blind, randomized, multicenter study showed black cohosh to be equipotent to estrogen and superior to placebo in reducing climacteric symptoms, with beneficial effects on serum markers of bone metabolism, no

effect on endometrial thickness, and increased vaginal superficial cells.[122] An excellent review monograph by McKenna reviews the history and clinical studies, concluding that black cohosh is safe (low toxicity, few and mild side effects), well tolerated, and effective for menopausal symptoms, including anxiety and depression.[273] A recent review reiterated that adverse effects are extremely uncommon, and that there are no known significant adverse drug interactions.[274] Current concerns about the possible hepatotoxicity of black cohosh are are discussed in Plant Profiles. Possible dopaminergic activity is being investigated, with early evidence supporting this.[275] Safety concerns have been studied extensively, with findings of no estrogenic effect, no increased growth of human breast cancer cells, and even actual inhibition of some breast cancer cell lines, with enhancement of the effect of tamoxifen.[104,276–281] Two comprehensive reviews reported that adverse events were rare, mild, and reversible; few reports of severe events were not sufficiently substantiated.[282,283] Contemporary use involves taking preparations of the black cohosh root or rhizome orally, often in tablet form, but also as a tincture.[284] It may be combined in a formula with other herbs to address individual needs.

Dong Quai

Dong quai is classified as a ''blood tonic'' in TCM, and as such is listed in TCM formulas for depression.[238] Lesley Tierra describes current TCM use of dong quai as one ingredient in formulas for stagnant liver qi, considered to be the root cause of depression.[285] However, TCM texts describe it as contraindicated for yin deficiency with heat signs, a classic TCM description of menopause.[285] When there is deficiency heat, it should be avoided or combined with appropriate herbs to mitigate its warming qualities.

Eleuthero

Eleuthero has been used in TCM for more than 2000 years as an important adaptogen and to treat depression, anxiety, insomnia, mental strain, stress, and energy depletion.[286,287] Eleuthero has demonstrated adaptogenic and endurance-enhancing effects,[288] immunomodulatory and immunostimulatory effects, radiation protection, improvement in cognitive function and well-being, and stress reduction.[289–296] Many herbalists add Eleuthero to their treatment protocols for depression with mental exhaustion, for rejuvenating the nervous system and restoring energy levels, in keeping with its traditional use.[297]

Ginkgo

Ginkgo may be beneficial in addressing a number of factors that can contribute to the experience of depression in women, particularly during the perimenopausal and menopausal years, including cognitive function changes, anxiety, and decreased sexual function, as addressed in the following.

Ginkgo's efficacy in preserving and improving cognitive function in elders or the cognitively impaired has been systematically demonstrated, especially for increasing accuracy and speed (working memory), improving complex attention, and significantly increasing speed of performance and mental fluency, including a number of critical reviews; meta-analyses; and well-designed randomized, double-blind, placebo-controlled clinical trials.[297–305] Clinical studies and EEG data have shown cognitive-activating ability and significant efficacy similar to that of conventional nootropic drugs (tacrine, nimodipine) and probably similar to Aricept, but at a tenth of the cost![306–309] In addition, the frequency of adverse effects was lowest with ginkgo.[309] Please note that almost all of the research has involved one specific type of ginkgo extract or its equivalent; one study concluded that EEG data showed that other products did not result in similar homogeneous CNS effects.[307] Recent studies have also shown significant improvement in cognitively intact older adults,[310] and dose-dependent improvement in memory and attention in healthy young adults, particularly when combined with Panax ginseng or *Bacopa monniera*.[311–314] The critical review by Kleijnen and Knipschild found that ginkgo led to clinically significant improvement in fatigue, depressed mood, and anxiety in patients with chronic cerebral insufficiency.[299] A study in similar patients by Vorberg also concluded that ginkgo improved symptoms of depression.[315] A trial by Lesser showed that many people over the age of 50 whose depression is unresponsive to antidepressants may have cerebrovascular insufficiency.[316] A randomized, double-blind placebo-controlled study demonstrated impressive improvement in resistant depression by adding ginkgo to the patients' conventional antidepressant; effectiveness was determined by a highly significant drop in scores on the Hamilton Depression Scale (HAMD) from 14 to 7 after 4 weeks of treatment, and then down to 4.5 at 9 weeks, whereas the placebo group decreased by only 1 point in 8 weeks.[317] Huguet's study showed the decrease in serotonin receptor sites associated with aging, and the restoration of binding sites by treatment with ginkgo.[318]

A review article on alternative therapies for menopause quotes data that ginkgo helps relieve anxiety and depression among postmenopausal women.[319] A more recent study (randomized, placebo-controlled, double-blind, crossover) described improvement in self-rated mood in healthy young adults taking ginkgo vs. placebo.[320] Using polysomnography (sleep EEG) to monitor sleep patterns, a pilot study was able to demonstrate that ginkgo significantly improved several sleep parameters in patients with major depression on a tricyclic antidepressant.[321] The addition of ginkgo to Haldol also resulted in improvement in patients with treatment-resistant chronic schizophrenia.[322]

There are now several studies showing that ginkgo can ameliorate sexual dysfunction, but this topic remains controversial. One open study also describes improvement in symptoms of antidepressant-induced sexual dysfunction by using adjuvant ginkgo, with particularly good results in women.[323,324] In support of this theory, a case report was published describing one patient with a rare side effect of SSRI treatment, genital anesthesia; her symptoms failed to improve on conventional therapy or

yohimbine but did resolve promptly with ginkgo.[325] Another case report tells of a woman who developed decreased libido and complete inability to achieve orgasm on Luvox; after 2 months on 240 mg of ginkgo per day, her symptoms resolved, and have remained under control for over a year, unless she tries to cut back the dose.[189]

A Cochrane Database Systematic Review done in 2002 concluded that data from the massive number of studies showed no significant difference between ginkgo and placebo in the proportion of participants experiencing adverse effects.[326] The biggest safety issue with ginkgo is the persistent question of whether or not it increases the risk of bleeding, particularly with Coumadin or aspirin. One study (1 year, 309 patients) reported one stroke and one subdural hematoma, both in the placebo group.[305] Considering that ginkgo is highly popular in Europe as an antiasthmatic and circulatory agent, and that in 1988 German physicians wrote 5.4 million prescriptions[327] for it, one might expect that if it caused serious bleeding it would be obvious by now. The question may have been answered by a new study (randomized, double-blind, placebo-controlled, crossover) of outpatients on stable, long-term warfarin, who were given ginkgo or placebo; there was no change in INR or geometric mean dosage of warfarin during all treatment periods.[328] Another study showed no EKG changes with short-term ginkgo in healthy volunteers.[329]

One safety issue, which is seldom raised, is that of the presence of a neurotoxin, ginkgo toxin, in the leaves and other plant parts; heating inactivates it during the extraction process.[306] Perhaps this is an indication that this is one of the few herbs, which are safest when taken in standardized extract form.

Ginkgo is used by herbalists all over the planet for many indications, including asthma, vascular disorders, memory problems, sexual dysfunction, macular degeneration, and tinnitus; it is often added to therapeutic protocols for depression, especially in people over the age of 45 with attention and memory symptoms, and is considered to be an important tonic herb for the brain.[10,297,330]

Gotu Kola

Gotu kola is used by Ayurvedic, TCM, and Western herbal practitioners for the treatment of depression, anxiety, stress, memory, and mental fatigue.[258,331] A summary of the research documenting effectiveness as an adaptogen and for improving learning and memory was published in 1997.[247,332–335] Other studies show sedative and antidepressant activity, comparable to imipramine and attenuation of the acoustic startle response (supporting anxiolytic claims).[336–338] It is used for memory enhancement, as a sedative nervine, and as an antispasmodic. It is considered to be a ''balancing tonic'' that both increases energy and relaxes the body, especially useful for insomnia.[339]

Lavender

Used in ancient Greek, Persian, Arab, and Roman medicine as a bath additive for the purification of body and spirit, it was also prized in Tibetan and Ayurvedic medicine.[340] Called ''the broom of the brain,'' it was mentioned in an eighth century BCE Indian/Tibetan medical text as an ingredient in psychiatric formulas (as an edible butter; still in use in Tibetan medicine) for insanity and psychoses.[340] Lavender is listed in the Ayurvedic Pharmacopoeia for depressive states with digestive dysfunction; it is also used as an antispasmodic, sedative, and antirheumatic.[340] European use of lavender as a soothing treatment for emotional overload is well described in Gerard's herbal of 1597, in which he said that lavender ''doth help the passion and panting of the heart.''[341] Felter stated that it was used by the Eclectics for colic, headache, hysteria, and ''nervous individuals who faint easily and have hysterical seizures,'' and also for nervous irritability in children.[342] EEG studies demonstrate that lavender has a relaxing effect (increased alpha and frontal beta), with decreased anxiety and tension, and significant decreases in State Anxiety scores; it promotes drowsiness and induces sleep.[343–347] Cardiac response patterns have also been used to demonstrate the relaxing properties of lavender.[348] In one study on hospitalized children with HIV, all the children reported relief of pain, some completely; their use of analgesic drugs was decreased; muscle spasms caused by encephalopathy and chronic chest pain that had been previously unresponsive to conventional analgesia were eased; and painful neuropathy was alleviated almost completely.[349,350] A study of foot massage with or without lavender essential oil was done on 100 patients in a CCU, 50% of whom were intubated; a control group rested in a curtained-off area; 90% of those in the massage-with-lavender group showed a significant reduction in heart rate, compared with 58% of those in the massage-only group and 41% of the controls.[349,351] One RCT on a small number of hospitalized patients with rheumatoid arthritis used a 10-minute upper neck and shoulder massage, with or without lavender, on 2 consecutive nights; analgesia use was decreased; patients reported better sleep or ability to roll over.[349,352] A RCT on 122 CCU patients showed that the aromatherapy group felt ''less anxious and more positive'' after massage with lavender, compared with massage only or with the control group; conscious patients who were able to respond also felt more able to cope; a modified assessment tool developed specifically for ICU patients who are unable to respond verbally was also used.[349,353] Other studies demonstrate lavender's sedative and mood-enhancing properties.[306,354] In contemporary botanical medicine, lavender is felt to have an amphoteric or balancing capacity, cooling and sedating (analgesic, antipyretic, sedating, anti-inflammatory) or warming and stimulating (diaphoretic, anti-infective, antidepressant) as needed.[355] Consequently, it is especially useful for depression with mood swings.[356] Varieties with different balances of chemical constituents (chemovars) have slightly different effects.[306] It is also used to treat anxiety, stress, spasms, cramps, pain, insomnia, and headache, and to enhance meditation and spiritual practices.[339] This is another good friend to have on the windowsill or in the garden.[357]

Motherwort

This herb, native to Europe and Asia, was used throughout its original range for female reproductive disorders and heart symptoms.[340] The ancient Greeks gave motherwort to pregnant women suffering from anxiety.[339] The English herbalist Gerard (late sixteenth century) noted its effectiveness in treating cardiac weakness. His successor, Culpepper, emphasized motherwort's ability to make the mind cheerful.[340] Ellingwood describes its use by the Eclectics for menstrual disorders, especially with nervousness and palpitations, considering it to be an emmenagogue, antispasmodic, nervine, laxative, and cardiotonic.[271] A number of Native American tribes used it for similar indications.[340,358] The Japanese prize their species of motherwort as an ''herb of life,'' using it to enhance longevity.[339] Studies show mild sedative effects, direct myocardial action (including slowing of tachyarrhythmias),* relaxation of vascular tone, lowering of lipids, inhibition of uterine fibroids, improvement of insomnia, muscle spasms, and headache; and protection during cerebral ischemia.[292,339,362,363]

Western botanical practitioners use motherwort for strengthening the heart and treating anxiety, PMS, menstrual problems, infertility, postpartum depression, irritability, and climacteric symptoms, especially when accompanied by palpitations; also to improve circulation, lower lipid levels, and reduce platelet aggregation.[339,364] David Hoffmann describes it as ''a useful relaxing tonic for aiding in menopausal changes,'' and ''an excellent tonic for the heart, strengthening without straining. It is a specific for over-rapid heartbeat brought about by anxiety. . . .''[284] Tori Hudson ND, a naturopathic physician specializing in women's health, adds it to her general menopause formula to control mood swings.[365]

Rosemary

A randomized clinical study showed that smelling rosemary essential oil for 3 minutes resulted in a significant decrease in State Anxiety scores, and a reported feeling of more alertness, confirmed by appropriate EEG changes.[345,369] Herbalists use it widely in tea and tincture form, as well as aromatherapy (i.e., in baths) to relieve symptoms of depression and improve cognition. It also can be included in foods, particularly taken raw, steeped in olive oil and use on bread and salads, or cooked into soups.

Shatavari

Shatavari translates as ''she who has a hundred husbands,'' and is a major Ayurvedic tonic adaptogen, traditionally used to promote physical and mental health, improve the body's defense mechanisms, and enhance longevity, especially for females; it is used for menopausal symptoms and for depression.[255,256] It is also used in TCM formulas for depression.[238] Studies support its efficacy as an adaptogen, protecting against a variety of stressors.[251,255] Shatavari is used mainly by Ayurvedic practitioners. Anne McIntyre refers to it as the most important rejuvenative tonic for women, an excellent remedy in menopause, calming, helping to relieve stress and anxiety.[370]

*References 102, 292, 339, 340, 359–362.

Figure 19-5 St. John's wort (*Hypericum perforatum*). (Photo by Martin Wall.)

St. John's Wort

St. John's wort's (Fig. 19-5) association with mood disturbance and the nervous system has a long historical precedence: medical use was documented by ancient Greek medical herbalists, including Hippocrates, who recommended it for ''nervous unrest;'' by Dioscorides, and Galen, for nerve pain; it is also used in Ayurvedic medicine.[287,340,371] The aerial flowering parts have been used in traditional European medicine for centuries internally to treat neuralgia, anxiety, neurosis, and depression.[340] The Eclectics used it internally to treat spinal injury pain, hysteria, and nervous affections with depression, and externally for pain, bruises, sprains, etc.[342] A number of studies have revealed that St. John's wort has a series of bioactive compounds with effects on a number of neurotransmitters, including serotonin, dopamine, norepinephrine, GABA, and glutamate.[372–374] It also affects the function of the hypothalamic-pituitary-adrenal axis.[375] Reduced activity of the latter is known to be associated with atypical depression, somatoform disorder, neurasthenia, and fibromyalgia.[376] An interesting recent study investigated a number of extracts, found strong activity in all but one, and then discovered that the inactive extract lacked the flavonoid rutin; addition of rutin then resulted in a strong pharmacologic effect, comparable with that of the other extracts.[377] Its spectrum of CNS activities is felt to be caused by the synergy of its beautifully balanced components, rather than to a single ''active ingredient.''[189,306,378] The major focus of contemporary investigation has been on St. John's wort's antidepressant activity, for which there is now considerable evidence. The first meta-analysis by Linde et al. in 1996 reviewed 23 randomized clinical trials, with 1757 outpatients with mild to moderate depression; hypericum was found to be significantly superior to placebo, and efficacy was similar to standard antidepressants (TCAs).[379] Two more meta-analyses in 1999 and 2000 came to the same conclusions.[380,381] This was followed by a Cochrane Database

review in 2000, involving 27 trials and 2291 patients, with the same findings; two meta-analyses, in 2001 and 2002, both finding St. John's wort to be significantly more effective than placebo for mild to moderate depression, similar to standard antidepressants (still TCAs); and two very recent reviews with the same conclusions.[382–386] One multicenter randomized, double-blind, placebo-controlled clinical trial was stopped early because convincing treatment efficacy could already be demonstrated; the conclusion was that hypericum extract is an effective drug for the treatment of mild to moderate major depression.[387] A very large multicenter study of 2166 patients with mild to moderate depression, 75% of whom were women, with an average age of 50 years, were found to have a clinically relevant improvement in symptoms with two dose levels of hypericum, with 83% to 89% responding.[388] Another double-blind, randomized, placebo-controlled trial with 375 patients showed a significantly greater reduction in total score on the Hamilton Depression Scale, and significantly more patients with treatment response or remission.[389] Two studies comparing hypericum with SSRIs did not find a difference in efficacy between 900 mg/day of St. John's wort and 75 mg/day of sertraline (30 patients); compared with fluoxetine, hypericum had significantly superior scores and responder rates (240 patients); however, there have been sharp criticisms of both studies.[390,391] A trial that was attempted by Massachusetts General Hospital, but that was closed prematurely by the sponsor, compared hypericum 900 mg/day with fluoxetine 20 mg/day and placebo; data showed a trend toward significance, for both hypericum and fluoxetine.[392] A fourth trial (70 patients, randomized, controlled, double-blind) concluded that hypericum is therapeutically equivalent to fluoxetine.[393] It is important to keep in mind that there is no difference in efficacy among the varied categories of antidepressants; they are all equally effective; they differ in type and severity of side effects.[188] It is useful when contemplating this mass of data to consider the results of a review conducted of clinical trial data for the nine antidepressant drugs approved by the FDA between 1985 and 2000; this reviewed 10,030 patients with depression, in 52 trials; the findings were that fewer than half (48%, 45 out of 93) of the antidepressant treatment arms showed superiority to placebo![394] A study on treatment for menopausal symptoms found that after 12 weeks of treatment, climacteric complaints diminished or disappeared completely in 76% (patient evaluation) to 79% (physician evaluation).[395] A sleep polysomnography (EEG) study in healthy older women showed improved sleep quality (increased deep sleep without interference with REM sleep), no sedative effect, and improved well-being.[396] Other studies have shown possible effectiveness in reducing alcohol cravings and treating anxiety, PMS, stress, learning and memory, chronic fatigue syndrome, and obsessive-compulsive disorder.[397–406] In addition, other documented activities include antiviral and antibacterial, anti-inflammatory (COX-2), and anticancer effects.[407–410]

A 1996 review of clinical trials involving 3250 patients showed only allergic reactions (0.5%), GI upset (0.6%), and fatigue (0.4%); since then, side effects have been consistently reported to be far less severe or frequent than with standard antidepressant drugs, with no cardiac effects or sedation (no impairment of psychomotor performance, attention, or driving).[411–415] One review concluded that its tolerability is so much better than antidepressant drugs that it might be an especially useful option in older people.[416] In 1998, Hippius was able to state, ''Overall, for a total of around 3.8 million patients treated during the period 1991 to 1996. . .there have been only 32 spontaneous reports of side effects recorded by the German reporting system.''[417] The issue of phototoxicity, which surfaced after several cases occurred during intravenous high-dose hypericin (presumed ''active ingredient,'' not whole-herb extract), has been laid to rest by two careful studies showing that oral whole-herb extracts of hypericum (LI 160), even in high doses (12 tablets a day, which is 10 times the usual dose), cause only limited photosensitivity. (UVA sensitivity increased only after the highest dose; solar light sensitivity did not increase at all.) This finding was replicated in a very recent study finding no phototoxic potential in humans in typical clinical doses (up to 1800 mg/day), confirming the prior review conclusion that it would require an oral dose of hypericum 30 to 50 times

Herbal Formulas for Treating Depression

Depression with Cognitive Dysfunction (i.e., memory loss)

St. John's wort	(*Hypericum perfoliatum*)	20 mL
Motherwort	(*Leonurus cardiaca*)	20 mL
Bacopa	(*Bacopa monnieri*)	20 mL
Eleuthero	(*Eleutherococcus senticosus*)	30 mL
Rosemary	(*Rosmarinus officinalis*)	10 mL

Total: 100 mL

This formula includes herbs with antidepressant and mentally stimulating effects with cerebrovascular blood flow enhancing action to improve memory, learning, and mood.

Dose: 5 mL twice daily. Use for at least 3 to 6 months for best results.

Tiger Today, Butterfly Tonight
(Modified depression formula from Amanda McQuade Crawford from *The Herbal Menopause Book*)

Black cohosh	(*Actaea racemosa*)	25 mL
St. John's wort	(*Hypericum perfoliatum*)	25 mL
Eleuthero	(*Eleutherococcus senticosus*)	25 mL
Lavender	(*Lavandula officinalis*)	10 mL
Blue vervain	(*Verbena officinalis*)	10 mL
Licorice	(*Glycyrrhiza glabra*)	5 mL

Total: 100 mL

This formula is designed to regulate the HPA axis, improve stress adaptation responses, lift the spirits, directly treat depression, and help regulate hormonal activity.

Dose: 5 mL twice daily. Use for at least 3 to 6 months for best results.

greater than the recommended daily dose taken at one time to lead to severe phototoxic reactions in humans.[418–420]

A clinically relevant safety issue is that of interactions with other drugs. Recent work has documented that hypericum, like many drugs and foods, potentiates several enzymes in the CYP450 series, affecting the metabolism of multiple categories of drugs, including lowering serum concentrations of warfarin, digoxin, theophylline, indinavir (HIV protease inhibitor), and cyclosporine and irinotecan (post/transplant immunosuppressants).[421–426] One case report described digoxin toxicity after stopping an herbal tea containing hypericum.[427] Another study showed lowered plasma concentrations of simvastatin but not of pravastatin, caused by differences in CYP3A4 involvement.[428] It is important to remind ourselves that fluoxetine (and even grapefruit juice!) is a potent inhibitor of CYP450, which could increase levels of other drugs.[306]

The other issue involving drug interactions is the possibility of developing a potentially life-threatening serotonin syndrome (agitation, hyperthermia, tachycardia, diaphoresis, rigidity) from adding St. John's wort to SSRIs. [Please note that this is a known risk of SSRIs combined with other drugs, especially in older people.] Several cases of this in older patients combining hypericum with SSRIs have been reported.[429]

There are a small number of case reports of episodes of mania and hypomania in bipolar patients who use St. John's wort; caution is advised.[414] At least one component is measurable in breast milk.[430]

St. John's wort is now the number one antidepressant prescribed by German physicians, almost 3 million prescriptions annually.[287,431] Even using standardized extract (the most expensive version) the cost is considerably less than the SSRIs.[386] Among botanical practitioners, it is used to lighten the mood, lifting the spirit, relaxing tension and anxiety, and improving sleep and energy levels; especially for PMDD, PMS, menopausal symptoms, dysmenorrhea, and SAD.[189,297,368] In addition, it is used as an antiviral, antibacterial, and for nerve pain or trauma, wounds, and burns.[189]

NUTRITIONAL CONSIDERATIONS

Diet and nutrition can play a major role in depression, both as a cause and a treatment; it is the foundation of prevention.[431] There is ample research to document the nutritional inadequacies of the US diet, and the contribution these deficiencies make to the worsening of depression.[315,432,433] Common deficiencies include vitamins A, C, D, E, and the B vitamins; the minerals calcium, magnesium, potassium, zinc, and selenium; fiber, complex carbohydrates, clean water, and essential fatty acids.[319] The opposite problem, that of dietary excesses, is contributing equally to the miserable nutritional situation.[319] Notorious excesses include caloric intake from excess carbohydrates, sugar, alcohol, and caffeine, all of which may contribute to depression.[319] Many nutrients have proven roles in both the etiology and treatment of depressive symptoms, most notably the B vitamins, but also vitamins D and E and the minerals calcium, iron, potassium, magnesium,[319] selenium, and zinc; and essential fatty acids, especially the omega-3s.* The B vitamins function as a team, and work best when supplemented as B complexes rather than isolated B vitamins; this avoids potential neurotoxic side effects.[330,437] Good-quality high-potency multivitamins and multiminerals are cost-effective ways of achieving desired results while continuing to improve diet habits.[10,433]

SAMe

A number of dietary supplements have been shown to improve outcomes in the treatment of depression. SAMe (S-adenosylmethionine) is an essential compound required by all body tissues; it has been used in Europe for decades, with extensive documentation of efficacy comparable to tricyclic antidepressant drugs in clinical trials, including 13 RCTs and 1 meta-analysis.[431,433,435,436] A review of 28 high-quality SAMe studies for evidence on treatment of depression, osteoarthritis, and liver disease published by the Agency for Healthcare Research and Quality found SAMe superior to placebo in reducing symptoms of depression. It has been shown to boost levels of neurotransmitters, including serotonin, norepinephrine, and dopamine, and improve nerve cell function.[435] Improvements may begin within 2 weeks.[435,436] It requires adequate levels of B vitamins, especially folate and B_{12}.[435] Treatment dosage is 400 to 1200 mg/day. According to Low Dog, the patient should be started on 200 mg/day for 5 days, which is increased by 200 mg/day every 3 to 5 days. Side effects include GI upset, agitation, and insomnia. This supplement is contraindicated in patients with bipolar disorder.[163]

Omega-3 Fatty Acids

Omega-3 fatty acids may play an important role in the prevention and treatment of depression. A number of studies have suggested efficacy in the treatment of a variety of psychological disturbances and psychiatric disorders, ranging from impulsivity and aggression to PMS, postpartum depression, and general clinical depression.[438–441] Epidemiologically, there are lower rates of depression in cultures in which there is significant dietary (fish) consumption of omega-3 fatty acids compared with those with less fish in the diet.[442] Unfortunately, few well-controlled studies have been conducted evaluating efficacy. However, given the potential overall benefits essential fatty acids on the nervous and cardiovascular systems, and the safety of supplementation, it seems reasonable to include essential fatty acids in a treatment protocol for depression.[163] Commercial supplements from fish oils have been found to be free of mercury and other heavy metal contamination by the Food and Drug Administration (FDA) and consumer labs. The daily recommended dose is 1 to 3 g. Doses higher than his have not been found to have added benefits.

ADDITIONAL THERAPIES

It is crucial to initially address underlying issues contributing to depression and associated conditions,

*References 10, 201, 319, 330, 432–435.

including psychosocial factors, lifestyle issues, spiritual stressors, etc. Simply substituting the prescription medication for an herbal medication does not qualify as ''holistic'' medicine. The preferred holistic strategy in all cases would be prevention, and the partial list of possibilities discussed in this section would be applicable to that aim as well as to treatment of an illness that results from failure of prevention.

Exercise

Exercise has been shown to be effective for both the treatment and prevention of depression, and the data are even stronger for women than men.[192,443] In treatment of older patients with major depression, supervised exercise was as effective as the antidepressant drug Sertraline.[444] Moderate exercise was more effective than vigorous exercise in decreasing the anxiety and stress components of depression, and in improving self-esteem.[192] A randomized, placebo-controlled trial showed that a program as simple as a brisk 20-minute walk outdoors at a target heart rate 60% max, 5 days a week (with increased light exposure and vitamins—see the following) was effective in improving mood, self-esteem, and sense of well-being, and decreasing depressive-symptom scores, and with an impressively high level of adherence by the study participants.[192] In multiple studies, exercisers' moods were found to be significantly more positive, regardless of menopausal state;[290] scores were lower on somatic symptoms and memory/concentration difficulties and significantly higher on well-being, positive mood, and libido.[319,445,446] In addition to aerobic exercise, strength training offers many of the same benefits.[10,447] Yoga and tai chi practices yield not only all the benefits of other exercise programs[435] but also improvement in flexibility and balance, and achievement of ''relaxation/stress management'' benefits; in addition, they may include a meditation component that enhances the latter effect.[431]

Relaxation and Stress Management

Relaxation training and stress management techniques have been demonstrated to be effective in many clinical studies, and should be considered in every prevention or treatment program.[230] Possible components include progressive relaxation, abdominal breathing, meditation,[448] imagery, and biofeedback. Relaxation response (mental focusing, diaphragmatic breathing, breath awareness) has been shown in randomized, controlled prospective clinical trials to produce significant improvement in hot flashes, tension/anxiety, and depression.[319,449–451] Yoga and tai chi have profound effects, via physical positions, breathing exercises, meditation, and spiritual practices; studies document successful outcomes in treatment of anxiety disorders, depression, PDD, menopause, and sleep disorders.[258,435]

Light Therapy

Light therapy has been studied repeatedly and found to be effective not only for SAD but also for nonseasonal depressions and eating disorders.[192,431] This is consistent with data showing that in Finland and Sweden the best single predictor of general well-being was the amount of light and length of day, and a London study of women without SAD that found a stronger correlation between mood and outdoor light levels than with menstrual cycle phases![192] Adding bright light to an exercise program gave better reduction of depressive symptoms than the same exercise program with normal lighting.[192] Light exposure in the morning has been shown to deepen sleep, via reinforcement of circadian rhythms.[452] In the Brown study, walking briskly outdoors 5 days a week for 20 minutes (plus vitamins—see the following) resulted in a significant improvement in mood, self-esteem, and sense of well-being, and decrease in depressive-symptom scores, and with an impressively high level of adherence by the study participants.[192]

Counseling

The role of counseling in treatment of depression has been well substantiated in a variety of modes—individual, family, self-help, group, and sex therapies. It has been progressively marginalized in the orthodox medical community, as drug prescription has become fashionable, but professional help sorting through the individual, family, societal, and planetary influences on our affective disorders can shorten the precious time we spend mired in psychic mud, freeing us to move again toward our life goals. Once again, it is important to stress that immediate, confirmed referral to a psychiatrist is mandatory in cases of suicidal ideation, paranoia, psychosis, or very severe depression.[194,201]

Many other possibilities also may be helpful, with a partial list including art therapy, music therapy, spirituality or religion, massage, laughter, hypnosis, solitude, journaling, self-nurturing, and acupuncture. An important and often-overlooked consideration is that of the influence of one's home and work surroundings on mood and health; attention to healing environments and to space clearing techniques may contribute considerably to restoration of well-being.

It is not expected that anyone would incorporate all of these wildly varied types of approaches into her treatment strategy for depression. An informed practitioner should be able to suggest a varied and colorful palette of choices, based on careful evaluation of the individual, who can be assisted to select one or more that resonate with her own sense of self. Initial strategies should be reevaluated jointly by the individual and her practitioner, with additions and substitutions as needed, until the desired outcome is attained. At that point, a maintenance plan to prevent recurrence must be instituted, to avoid contributing to the dismal relapse statistics.[187,453,454] Because humans are an integral part of a local and planetary ecosystem, all choices should be evaluated carefully for their potential to damage the health of humans, other species, or the ecosystem (Precautionary Principle).[455]

Affirmation for the Great Initiation of Perimenopause[456]

My time of initiation is upon me
and though
my apprehension quickens
I hold steady to the certainty

that my pain
is but a narrow gateway
through which I must pass—
a gateway that generations
of kinswomen
have passed before me
and a gateway that many more will pass behind me.
For as the moon wanes
and the tides ebb
I know that I too
must follow the cycle of nature.
And so I soothe my anxious moments
and I redirect my depressed spirit
for now is the time
to be gentle with the process
of returning home.

ANXIETY IN MENOPAUSE

Roberta Lee

Anxiety is defined as ''excessive worry involving a variety of issues related to health, family, money, or work in which the concerns seem pervasive, repetitive and out of proportion to actual life circumstances.''[457] Many individuals experiencing anxiety may fail to recognize the symptoms in themselves, and may present to a practitioner with the following signs and symptoms: easy fatigability, difficulty concentrating, irritability, muscle tenderness, muscle tension, restlessness, and sleep disturbance. The most frequently reported clinical symptoms of general anxiety are diaphoresis, headache, and trembling.[457]

General anxiety disorders are one of the most common medical conditions. According to the National Institute of Mental Health, the 1-year prevalence rate is 13.3% of the population.[190] In menopause, although symptoms of anxiety are reported frequently, according to the North American Menopause society, ''there are no psychological studies supporting the belief that natural menopause contributes to true anxiety or depression.''[458] Similarly, longitudinal studies evaluating the frequency of anxiety in menopause show no increase in rate of anxiety or depression.[459] However, anxiety has been noted to peak in a mild form just before menopause.[460]

The pathophysiology of generalized anxiety (GAD) is multifactorial and remains incompletely understood. Studies in humans and animals have attempted to pinpoint general areas in the brain that seem to play a critical role in anxiety, but consensus has not been reached. Functional imaging studies suggest a number of areas in the brain of patients that have been diagnosed with GAD, including the occipital cortex, limbic system, and basal ganglia, show altered metabolism after benzodiazepine therapy.[461]

The binding functions of several neurotransmitter receptors appear deregulated in GAD and include the gamma-aminobutyric acid neurotransmitter (GABA-A) and benzodiazepine receptors.[462] The noradrenergic system appears involved, but studies detailing the exact mechanism have not been consistent. However, higher levels of catecholamines have been correlated in anxiety,[463] as have elevated levels of the neurotransmitter 5-hydroxytryptamine. Other neuropeptides such as cholecystokinin, corticotrophin-releasing factor, tachykinins (including substance P) as well as neuroactive steroids such as dehydroepiandrosterone (DHEA) are also implicated, but again, their relationship to GAD is not well defined.[461]

Numerous studies evaluating depression and anxiety in relation to gender have shown an increased rate of depression and anxiety in women over men beginning in adolescence.[459] Although there seems to be some biochemical evidence for a hormonal role in the development of mood disorders, correlated increases during menopause do not appear evident. Several longitudinal studies in Europe and North America have observed cohorts of women through menopause and most studies have reported no increase in moderate or severe depression, nor anxiety with menopause.[459] Factors correlated with increased anxiety in menopause are more strongly correlated with women who are more symptomatic[464] (e.g., experience more hot flashes and night sweats), have a prior history of mood disorders, lower socioeconomic status,[464] poor marital adjustment,[465] unemployment,[464] and lower educational level.[466] Therefore, experts in women's health have attributed anxiety in menopause to sleep deprivation as a secondary occurrence to night sweats and menopausally related discomforts, or personal perceptions involving the physiologic changes associated with menopause.[10] Sometimes, anxiety can be a secondary phenomenon accompanying depression.[458]

DIAGNOSIS

As with many psychological presentations the symptoms of anxiety can overlap with very serious medical conditions and a full medical workup is suggested by a health care professional to prevent overlooking this as a contributing factor. Table 19-5 presents a simplified list of common medical conditions associated with anxiety.

CONVENTIONAL TREATMENT APPROACHES

Many conventional medications are available for the treatment of anxiety. These include antidepressants such as tricyclic antidepressants or the newer serotonin re-uptake inhibitors (SSRIs). The use of SSRIs has steadily increased from 2% in 1992 to 19% in 1997, but loss of libido, restlessness, or sedation are frequent side effects for which this class of medications is often discontinued.[467] For short-term treatment, the use of benzodiazepines is a consideration, but they are associated with sedation and habituation (tolerance).

Another option is the medication BuSpar® or buspirone. An azapirone, it is in a different pharmacologic class from the benzodiazepines. Buspirone has not been reported to be associated with tolerance. However, in comparison with the tricyclic antidepressants or SSRIs, its therapeutic effects are mild. Therefore, it is considered useful for mild anxiety. It also takes approximately 4 weeks to reach a therapeutic level. In 4 of 11 placebo-controlled studies comparing buspirone with placebo or a benzodiazepine, after 4 weeks of treatment, buspirone showed

TABLE 19-5

Medical Conditions Often Associated with Symptoms of Anxiety

TYPE OF CONDITION	EXAMPLES
Cardiovascular	Acute myocardial infarction (heart attack)
	Angina
	Arrhythmias
	Hypertension
	Mitral valve prolapse
Endocrine	Hyperthyroidism
	Hypothyroidism
	Parathyroid disease
	Adrenal disorders
	Hypoglycemia
Gastrointestinal	Irritable bowel syndrome
Vitamin deficiency states	Vitamin B_{12} deficiency
Toxic conditions	Alcohol and drug withdrawal
	Mercury
	Arsenic
	Caffeine and caffeine withdrawal
Neurologic	Brain tumor
	Seizure disorder
Respiratory	Asthma
	Pulmonary embolism
	Chronic obstructive pulmonary disease

Adapted from Kaplan H, Sadock B: Anxiety Disorders in Kaplan and Sadock's Synopsis of Psychiatry, 8 ed. Baltimore, Williams & Wilkins, 1998.

no benefit.[467] Further discussions of these options are beyond the scope of this chapter; those interested in this aspect of treatment should consult a general psychiatric text.

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

Menopause is a transition with a variety of clinical manifestations that are highly individual. The presence of anxiety, or symptoms that present masking anxiety, may be one of the first clinical signs indicating that this physiologic transition is occurring. Botanical remedies used in an integrative approach to menopausal anxiety may be an alternative for some who cannot tolerate the adverse effects of prescriptive medicines or in those who prefer more natural remedies. Herbalists have recognized a number of botanical preparations as nervines and categorized them as nerve tonics (preparations that tone or rehabilitate the nervous system), nerve sedatives (relax the nervous system), nerve stimulants (increase vitality without provoking the nervous system or creating agitation), or nerve demulcents (sooth and heal may physically "protect" the nerve endings).[468] Use of the botanicals classified in this way may include a combination of botanicals, in tincture or extract, from the different categories based on historical and anecdotal clinical experience of the practitioner. In other instances, treatment may include the use of a bath containing the herb(s) in combination with a tea or other form of oral preparation. Similarly, in many traditional cultures (e.g., Chinese, East Indian, etc.) preparations are used in combinations as formulas to support (regenerate), soothe, and calm with the common philosophical objective that treating a variety of facets of the disease or imbalance may hasten healing by synergism of the group of plants selected. This philosophy is different than the biomedical approach of using singular pharmacologic agents to treat an illness.

The herbs discussed in Table 19-6 are anxiolytics. However, practitioners are encouraged to draw from a wide selection of herbs, including nervines, adaptogens, and sedatives to create an optimal formulation for the individual woman with anxiety.

Black Cohosh

Black cohosh has been used for more than four decades in Europe to treat symptoms associated with menopause, including anxiety.[113] Although it is reported to reduce the symptoms of menopause, which include hot flashes, mood disorders, diaphoresis, palpitations, and vaginal dryness, there have been no trials showing its efficacy for anxiety alone. One study done in 1987 randomized 80 menopausal women to Remifemin (four pills daily), 0.625 of conjugated estrogens or placebo for 12 weeks. The Kupperman Index and Hamilton Anxiety scores were significantly lower in the groups treated with black cohosh.[469] Borreli and Ernst published a brief systematic review of controlled trials of black cohosh and its effects on menopausal symptoms. Four trials were included and the conclusion was that "the evidence was not compelling enough to support improvement."[470] However, many of the trials have been small with generally suggestive outcomes. In many of the studies, the standardized measurement used to assess symptom improvement was the Kupperman Index, which is considered outmoded as a standardized instrument for menopausal symptoms. The index omits some important symptoms classically associated with menopause, making the assessment of black cohosh in these studies harder to evaluate.[471] The use of this botanical primarily for anxiety in menopause is based primarily on traditional or theoretical use.

The mechanism of action for improvement of neurovegetative symptoms (including mood disorders) by black cohosh is not clear. Initially caused by the reported presence of formononetin, estrogenic receptor binding activity with lowering levels of follicle stimulating hormone (FSH) levels was considered the basis of the pharmacologic effectiveness of black cohosh.[472] The majority of subsequent studies both in animals and in vitro have demonstrated mixed results, and it is now believed that there is no estrogenic activity to black cohosh.[91,104,473] A recently identified compound found in black cohosh, fukinolic acid, has been shown to have weak estrogenic effects but does not fully explain the estrogen-like the activity of this botanical.[474]

TABLE **19-6**

Herbs for Anxiety

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Relieve anxiety	Anxiolytic	*Actaea racemosa*	Black cohosh
		Lavandula officinalis	Lavender
		Passiflora incarnata	Passion flower
		Piper methysticum	Kava kava
		Valeriana officinalis	Valerian
Relieve anxiety	Nervine	*Avena sativa*	Milky Oats
		Hypericum perforatum	St. John's wort
		Matricaria recutita	Chamomile
		Melissa officinalis	Lemon balm
		Scutellaria lateriflora	Skullcap
		Turner diffusa	Damiana
Relieve anxiety	Sedative	*Corydalis* spp.	Corydalis
		Eschscholzia californica	California poppy
		Humulus luplus	Hops
		Passiflora incarnata	Passion flower
		Valeriana officinalis	Valerian
		Ziziphus spinosa	Ziziphus
Relieve anxiety	Adaptogen	*Withania somnifera*	Ashwagandha
Relieve palpitations associated with anxiety		*Leonurus cardiaca*	Motherwort

Current recommendations for dosing range from 40 to 80 mg daily, although most clinical trials have used 80 mg daily. A recent clinical trial compared the efficacy of two different doses of a proprietary product of black cohosh (40 vs. 127 mg daily), which showed similar efficacy profiles.[176] It is not clear if black cohosh is safe in individuals with hormone-sensitive conditions such as breast cancer or endometriosis caused by the conflicting reports on estrogenic activity. The *ABC Clinical Guide to Herbs* states that ''Despite earlier concerns about the possible estrogenicity of black cohosh, and thus a possible contraindication for women with estrogen-positive breast cancer. . .it is clearly established that black cohosh is not estrogenic. Thus, no such contraindication is warranted.''[472] Occasional gastrointestinal effects[475] have been reported as well as vertigo headache, nausea, vomiting, impaired vision, and circulation with overdoses.[113,475] There are no known drug interactions.[476] Concerns regarding the possible hepatotoxicty of this herb are discussed in Plant Profiles: Black Cohosh.

Kava Kava

Kava is an excellent alternative for those wishing to avoid using conventional medications. This plant, used for many centuries in the Pacific island cultures as an indigenous botanical signifying special events and people,[477] has been found to reduce anxiety in a number of small clinical trials. Seven clinical trials have been done evaluating the efficacy of kava in anxiety, and in all kava was found to be superior to placebo.[478] Major criticisms of these trials have been small-size, ill-defined patient populations, or failure to meet the DSM-IV criteria for generalized anxiety. Several trials have been done specifically addressing anxiety in menopausal women. In these trials, not only was a reduction in anxiety statistically significant, but many of the neurovegetative symptoms associated with menopause were also improved as well.[479–481]

The active constituents responsible for kava's effectiveness in reducing anxiety are the kava lactones. These are a group of 15 lactones, maximally concentrated in the lateral roots of the kava plant. These lipophilic compounds exert their effects in several areas: at the GABA-A receptors,[482] and at receptor sites that regulate serotonin,[483] noradrenaline,[484] and dopamine.[485] Kava also may act at the limbic structures, reducing anxiety without causing sedation.[486] However, the exact mechanisms of how kava lactones exert their effects have not been entirely determined. The actual lactone content in the root varies between 3% and 20%.[487] Until recently, the reported adverse effects of kava have been mild or negligible, except for a dermatologic condition reported with chronic use. This dermatologic disorder, called kava dermopathy, is only seen with prolonged and excessive use of kava (doses of 400 mg for more than 3 months).[488] It is reversible with reduced intake or cessation. Until the last several years, rare reports of drug interactions, mostly involving sedation, have occurred with the concomitant use of other pharmaceutical drugs that share similar mechanisms of action with the kavalactones. However, by 2002, approximately 28 cases of severe liver toxicity associated with kava intake were reported in Europe (four in Switzerland and 24 in Germany).[489] The adverse effects reported included cholestatic hepatitis, jaundice,

increased liver enzymes, liver cell impairment, severe hepatitis with confluent necrosis, and irreversible liver damage requiring transplantation of the liver (four cases). In the United States, five cases of liver dysfunction have been reported associated with the use of kava. The reviews of the adverse case reports emphasize that in many of the reports the individuals were concurrently using medications known to be hepatotoxic.[490] In several cases other causes of hepatitis, such as viral infections or use of alcohol, could not be excluded. Currently, caused by the recent adverse effect reports, kava has been removed from unrestricted use in several countries including France, England, Germany, and Canada.[472] In the United States in March 2001, the Food and Drug administration issued a public warning in response to the hepatotoxic case reports.

Currently, the recommendations are a daily dose equivalent of 60 to 120 mg of kavalactones in a semisolid or dry extract (with not less than 30% kavalactone content).[472] Because of concerns over hepatotoxicity, it is recommended that those patients who have known liver disease, who are taking hepatotoxic medications, or frequently using alcohol should be advised to consult a health care professional before considering use of kava. In light of the recent reports on hepatotoxicity, it has been advised that use beyond 1 month be monitored by a health care professional.[472] Consumers should be advised of the rare but potential risk for liver problems (see Plant Profiles: Kava Kava) Kava taken along with alcohol, barbiturates, drugs affecting mental activity or other substances acting on the central nervous system may increase inebriation or the effect of the drug.[472] Kava should not be used during pregnancy or while nursing.[475]

Lavender

Lavender has been used in aromatherapy as an anxiolytic.[491] There have been one randomized trial, two controlled trials, and one case series evaluating efficacy of lavender herb as an anxiolytic. The largest randomized trial consisting of 122 intensive care unit patients used a lavender oil massage, grapeseed oil massage, or undisturbed rest for three sessions lasting 30 minutes at least 24 hours apart. The finding showed initial benefit in the first session but dissipated in later sessions.[353] In general, although the evidence for lavender as an anxiolytic aromatherapy agent is generally positive, the trials are considered flawed enough methodologically to make the evidence weak.[492] The mechanism of action for anxiolytic activity has been attributed to linalool. In mice linalool, a constituent of lavender, reduced motor activity caused by a dose-related binding of glutamate. Glutamate is an excitatory CNS neurotransmitter.[493] However, there are over 100 constituents in lavender, including linalool, perillyl alcohol, linalyl acetate, camphor, limoner triterpenes, coumarins, cineole, and flavonoids, which also may have some activity.[492] Lavender oil is quickly absorbed when topically applied and has a peak of 19 minutes; it disappears from the blood within 90 minutes.[494] In general, lavender is well tolerated with minimal adverse effects. There have been cases of mild dermatitis[495] with topical use, nausea[496] with oral use, CNS depression[497] with aromatherapy, and reversible neutropenia[498] with high oral doses of perillyl alcohol.

Passion Flower

Historical uses have been as an analgesic, anticonvulsant, for chronic pain, perimenopausal hot flashes, and tension to name a few.[499] It generally has been used in combination with other herbs, making it difficult to evaluate on its own. Few clinical trials have been done assessing its anxiolytic potential. One pilot evaluating passionflower (45 drops/daily) against oxazepam (30 mg/daily) for 4 weeks showed reduction in anxiety comparable with benzodiazepine. There were fewer difficulties with impairment in job performance noted in the passionflower arm.[500] Another trial with a mixture of passionflower, valerian, Crataegus, Ballota, Cola, and Paullinia showed improved Hamilton anxiety scores compared with placebo for 28 days.[501] There are other botanical preparations that have a historic use for anxiety but do not have clinical trials evaluating efficacy. The basis for use has been derived either from use in other traditional medical systems or use in Western herbalism.

Valerian

Valerian's use as a sedative and sleep aid in Europe dates back to the time of Hippocrates.[492] It is currently used in Western botanical medicine as a sedative. Since 1982, there have been 20 clinical studies on Valerian for insomnia ranging from 1 night to 4 weeks in duration. The majority of studies consistently report improvement of sleep with valerian. Five blinded or randomized clinical studies evaluated valerian for anxiety; two were combination preparations (most concluded that valerian significantly lowered the Hamilton Anxiety scores).[472,502] A major criticism of many of the studies were inadequate descriptions of randomization, blinding, and in some inadequate power to statistically detect significant differences.[502–504] The studies ranged from 2 to 4 weeks with the dosing ranging from 50 mg (in combination with other botanicals) to 300 mg daily. The mechanism of action with respect to action as an anxiolytic is attributed to the valepotriates and their breakdown products,[472] but valerian root contains as many as 150 compounds. Recently, it is thought that synergistic action by multiple compounds may exert a sedative effect.[505] Animal models suggest that valerianic acid may inhibit enzymes that break down GABA, and that increases GABA levels may produce sedating or CNS depressant effects.[506] Valerian has a characteristic odor that many find unpleasant, and is attributed to isovaleric acid. It is poorly absorbed by mouth. Mexican and Indian sources of valerian have reportedly high concentrations of valepotriates, which may be toxic and should be avoided.[507] General adverse effects have included headaches and stomach upset, but adverse reports are rare. In one case, a combination of valerian and skullcap plus other herbs, which may have adulterated the sample, caused an elevation of liver enzymes (hepatotoxicity). It was

undetermined in this case whether valerian contributed to this pathology.[50]

ADDITIONAL THERAPIES

Mind–Body Medicine

Psychotherapy has been shown to be effective in the treatment of GAD, with or without medical intervention. Behavioral therapy and cognitive behavior therapy (CBT) are two commonly used techniques that allow patients to identify their behavioral patterns and learn to change their thinking, reactions, and behaviors to create new response patterns.

Relaxation Techniques

Numerous relaxation techniques can help patients identify and shift anxiety patterns. These include visualization, massage, aromatherapy, sound therapy, and hypnosis, to name a few. Biofeedback also has been shown to be useful in the treatment of anxiety disorders. Exercise also can be a beneficial relaxation technique for some patients.

TREATMENT SUMMARY FOR ANXIETY IN MENOPAUSE

- Consider botanicals as an alternative for some who cannot tolerate the adverse effects of prescriptive medicines or in those who prefer more natural remedies.
- Choose from a variety of nervine categories and specific herbs according to patient indications.

INSOMNIA

Aviva Romm

Insomnia is dissatisfaction with one's quantity, quality, or timing of sleep; sleep disturbance occurring at least three times per week for at least 1 month; and is often associated with daytime dysfunction, impairing regular activities at home or work.[509,510] It commonly manifests as the inability to fall asleep (prolonged sleep latency), sleep interrupted by periods of wakefulness, or early morning waking. Insomnia is divided into two main categories: primary (extrinsic) insomnia resulting from psychosocial problems, poor sleep hygiene (discussed in the following), situational stresses, or substance misuse or abuse, and secondary (intrinsic) insomnia, caused by psychophysiologic problems or comorbidities; for example, sleep apnea, restless leg syndrome, shift work disorder, and circadian rhythm disorders.[509] It is estimated that between 10% and 50% of Americans report insomnia at any given time.[509,510] It may be transient, short term, or long term.[510]

Common causes of insomnia include sleep rhythm reversals, nightmares, restless leg syndrome (RLS), nocturnal leg cramps, snoring, sleep apnea, pain (i.e., arthritis or other chronic pain), dyspnea (e.g., caused by congestive heart failure), allergies, psychological stress, depression, anxiety, panic disorder, urinary frequency, gastroesophageal reflux, and hyperthyroidism.[509,511] Use of substances such as alcohol, caffeine, and nicotine, as well as many prescription and OTC medications can cause or exacerbate insomnia. Sleep disturbances are more common in women than men, and sleep disorders are more likely to occur at specific times during the female reproductive life cycle; for example, with symptomatic premenstrual periods, physical discomforts associated with pregnancy as well as nocturnal hypoglycemia in pregnancy, hormonal changes and neurovegetative complaints (e.g., hot flashes) associated with menopause, and old age, the latter possibly caused by decreased melatonin production.[512,513]

Rest is a critical biological need; patients with insomnia experience significant consequences caused by lack of restorative sleep, including fatigue, exhaustion, depression, irritability, cognitive disturbances, decreased job performance, and even an increased rate of accidents, such as motor vehicle accidents.

DIAGNOSIS

The diagnosis of insomnia is typically based on subjective reporting by the patient, and when possible, reporting by the patient's bed partner, who may be able to objectively convey information about the nature of the sleep disturbance.[512] A careful history and routine physical exam are conducted to rule out or determine whether there are associated or underlying problems. The type of insomnia (difficulty with sleep onset, sleep maintenance, or early awakening) can be indicative of associated disorders (Table 19-7). It is important to query the patient about

TABLE **19-7**

Type of Sleep Disturbance and Associated Conditions

SLEEP DISTURBANCE	POSSIBLE CAUSES
Delayed sleep onset	Retiring to bed prematurely Poor sleep hygiene Anxiety Mood disorders, including depression and bipolar disorder Restless leg syndrome Pain/neuropathy Dyspnea or respiratory disorders
Stimulants (e.g., caffeine, medications, drugs)	
Sleep maintenance	Excessive time in bed Mood disorders Sleep apnea Dyspnea or respiratory disorders Pain Neurologic disease
Early waking	Major depression Learned or conditioned waking Required waking for work, school, family responsibilities

Adapted from Becker P: Insomnia: prevalence, impact, pathogenesis, differential diagnosis, and evaluation, Psychiatr Clin North Am 29:855-870, 2006.

possible precipitants of sleep problems, such as relationship or work-related problems and other stressors, whether there is a family history of sleep problems, whether there have been any recent life events that may have led to the sleep disturbance (e.g., recent loss of a loved one, loss of a job, trauma, posttraumatic stress), or any circumstances that might perpetuate sleep disturbances; for example, working in bed, eating in bed prior to sleep, watching television in bed, having unrealistic expectations (e.g., that one must have 8 hours of sleep each night to feel rested), trying too hard to sleep and remaining in bed when sleep will not come easily, sleeping with a partner who snores or sleeps restlessly, or having arguments with a spouse or partner in bed. Patients should be questioned about physical problems that may cause them to wake during the night; for example, dyspnea, indigestion, pain, or restless or cramping legs. Sleep studies are rarely necessary for the diagnosis of common sleep disturbances.

CONVENTIONAL TREATMENT APPROACHES

Conventional treatment strategies are aimed at the needs of the individual patient. A range of therapies from nonpharmacologic to drug based are available, and treatments encompass the many possible etiologies of sleep disorders. Nonpharmacologic strategies include promotion of sleep hygiene (Box 19-2), cognitive behavioral therapies, stimulus control therapies (e.g., patients are taught to avoid sleep incompatible behaviors such as watching television in bed and are taught to get out of bed rather than lay there trying to fall asleep if sleep does not come easily), and temporal control therapies (deliberately waking at the same time each day and getting out of bed regardless of how much sleep was obtained the previous night and avoidance of naps). Pharmacologic interventions include antidepressant and anxiolytic medications, sedatives, narcotics, and the use of dopamine agonists for the control of RLS symptoms.

Nonpharmacologic Treatment Strategies

Nonpharmacologic therapies have proved effective and reliable for many patients with primary and secondary insomnia, whether of psychiatric or medical origin, compared with placebo and pharmacologic interventions, with none of the side effects associated with medications.[509,511,514] Therefore, when possible, it is preferable to attempt nonpharmacologic methods first, progressing to medications as needed.

BOX 19-2

Sleep Hygiene

Sleep hygiene refers to a set of practices that promote restful, effective sleep. These include:

- Wait until you are sleepy to go to bed.
- If you are not asleep after 20 minutes, get out of the bed and do something relaxing; for example, read.
- Use rituals that help you relax each night before bed; for example, take a warm bath.
- Get up at the same time each morning.
- Avoid taking naps if possible.
- Keep a regular schedule for meals, medications, chores, and other activities.
- Do not eat, watch TV, use the computer, or talk on the phone in bed—use bed only for sleep (and sex).
- Do not have caffeine after lunch.
- Do not have a beer, a glass of wine, or any other alcohol within 6 hours of bedtime.
- Do not have a cigarette or any other source of nicotine before bedtime.
- Do not go to bed hungry, but do not eat a big meal near bedtime.
- Avoid rigorous exercise within 6 hours of bedtime.
- Unclutter and clear your bedroom of desks, computers, and other work items.
- Check for potential allergens such as mold, dust, pollen, and mites.
- Ensure that your bed gives proper support. Sagging, lumpy, and overly soft or hard mattresses frequently cause sleep difficulties. Uncomfortable pillows also can be disruptive to sleep.
- Ensure sufficient exercise during the day; adequate exercise helps to promote restful sleep.
- Journal writing at bedtime is a fabulous way to process emotions, feelings, and the day's events, and clears the heart and mind before sleep.
- Use relaxation and stress-reducing techniques before bed, such as yoga, meditation, contemplation and prayer, listening to soothing music, or tuning into the night sky and moon.
- Because irregular sleeping habits lead to sleep problems, create a regular bedtime and stick to it.
- Examine attitudes about not sleeping, especially the emotions and thoughts that arise while not sleeping.
- Make your bedroom quiet, dark, and a little bit cool.

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

Practitioners may want to consider using botanical therapies in conjunction with nonpharmacologic strategies for the relief of sleep disorders prior to turning to pharmaceuticals. Many patients prefer a natural approach, related to concerns about dependency and side effects associated with conventional sleep medications.[515] The herbs presented in this section are those commonly used for general sleep promotion. To be effective, however, it is essential to also treat concurrent or underlying problems that prevent sleep. Readers are referred to relevant chapters for the treatment of anxiety, depression, premenstrual tension, pelvic pain, or menopausal symptoms. A number of the herbs herein simultaneously address more than one of these concerns; for example, hops may relieve hot flashes and promote sleep, California poppy may relieve restless legs and promote sleep, and kava kava, among others, has been shown to relieve anxiety and also promotes a tranquil state that is conducive to sleep. Adaptogens, principal herbs for the treatment of fatigue, are discussed in Chapter 8, and

TABLE 19-8

Herbs for Insomnia

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Sleep promotion	Tranquilizer	*Eschscholzia californica*	California poppy
		Lavandula officinalis	Lavender
		Leonurus cardiaca	Motherwort
		Matricaria recutita	Chamomile
		Melissa officinalis	Lemon balm
		Passiflora incarnata	Passion flower
		Piper methysticum	Kava kava
Sleep promotion	Sedative	*Eschscholzia californica*	California poppy
		Humulus lupulus	Hops
		Lavandula officinalis	Lavender
		Matricaria recutita	Chamomile
		Melissa officinalis	Lemon balm
		Passiflora incarnata	Passion flower
		Piper methysticum	Kava kava
		Scutellaria lateriflora	Skullcap
		Valeriana officinalis	Valerian
Sleep promotion	Hypnotic	*Eschscholzia californica*	California poppy
		Humulus lupulus	Hops
		Piper methysticum	Kava kava
		Valeriana officinalis	Valerian
Sleep promotion	Anxiolytic	*Humulus lupulus*	Hops
		Leonurus cardiaca	Motherwort
		Passiflora incarnata	Passion flower
		Piper methysticum	Kava kava
		Scutellaria lateriflora	Skullcap
		Valeriana officinalis	Valerian

provide important benefits for patients suffering from the effects of sleep deprivation or disturbance.

Herbs for sleep promotion may be taken 30 and 60 minutes before bed. However, herbalists commonly report that herbs for sleep problems associated with chronic anxiety yield the best results when taken several times throughout the day rather than only prior to bedtime. It may take several weeks of taking the herbs to notice consistent improvement. The dosage range for most formulae is 2 to 5 mL three to four times daily, with an additional dose of 2 mL taken every half hour for two to four doses in the few hours prior to bedtime. Dosing may be repeated in the night if the patient wakes and is unable to return to sleep. Herbal teas for relaxation also may be taken prior to bedtime; however, the need to urinate from drinking tea is apt to lead to waking and thus can be counterproductive. It is not advisable to combine botanical sedatives, tranquilizers, and anxiolytics with conventional pharmaceuticals caused by possible interactions and potentiation of sedative action.

A clarification of nomenclature related to sleep promotion is necessary, as the terms sedative, hypnotic, and tranquilizer are not synonymous.[516] Tranquilization refers to an emotional calming that may or may not lead to sleep but that does not promote drowsiness; sedation refers to a reduction in cognitive function that is favorable to sleep promotion, and a hypotonic directly promotes sleep. Readers will note some overlap in the Table 19-8 herbs categorically. Table 19-9 elucidates the strength of each of the herbs in this chapter based on this nomenclature. Readers will note a dose dependent relationship with herbs and strength of effect.

TABLE 19-9

Ranking Levels of Botanicals for Sleep Promotion

HERB	RANK
California poppy	1 to 3
Hops	2 to 5
Lavender	1
Chamomile	1
Lemon balm	1
Motherwort	1 to 3
Passion flower	1 to 4
Kava kava	2 to 5
Skullcap	1 to 3
Valerian	2 to 4

These herbs are ranked on a scale of 1 to 5. A 1 denotes general relaxation that facilitates sleep rather than sedation (tranquilization), whereas a 5 is a hypnotic. The range in between denotes sedation. A range suggests that the effects of the herb are dose dependent.

Valerian

Valerian has been used for sleep disorders, nervous conditions, anxiety, musculoskeletal tension, and pain for at least 2000 years.[505] The ESCOP Monographs indicate valerian for the relief of temporary mild nervous tension and/or difficulty falling asleep, uses that are corroborated by the German Commission E and the World Health Organization.[106,186] The WHO further describes valerian as gentler alternative or substitute for stronger sedatives; for example, benzodiazepines and for the treatment of anxiety-related sleep disturbances.[517] A systematic review by Stevinson and Ernst identified nine clinical trials evaluating the efficacy of valerian for sleep promotion. Of these, three found strong evidence of efficacy in reducing sleep latency and improving sleep quality.[518,519] Valerian contains sesquiterpenes of the volatile oils (e.g., valeric acid), iridoids (e.g., valepotriates), alkaloids, furanofuran lignins, and free amino acids such as g-aminobutyric acid (GABA), tyrosine, arginine, and glutamine.[505] The valeric acid and valepotriates are commonly cited as the active ingredients in valerian, and although it has been demonstrated that they possess direct sedative effects, it is likely that all of the active constituents of valerian function in a synergistic manner to produce a clinical response.[185,520] Animal studies suggest the inhibition of enzymes that degrade GABA as one possible mechanism of action. Valerian is considered more effective when used chronically rather than acutely as a sleep aid. It is a reasonable mild alternative to benzodiazepines and does not lead to sleepiness or grogginess upon waking. It is well tolerated by most patients, although herbalists have reported paradoxic effects (stimulation) in as many as 10% of patients. Vivid dreams have been reported as the most common side effect of valerian use.[531] Theoretical dose-related physical impairment may occur within the first few hours after ingestion; thus, it is advised that patients do not drive or operate heavy machinery while taking valerian. Chronic use over years may lead to withdrawal symptoms if the herb is discontinued abruptly.[472] Although there are no known contraindications, caution is advised in combining sedative herbs with sedative pharmaceuticals. It is considered safe when used appropriately at a dose of 2 to 3 g of crude herb per cup, one to several times daily, 1 to 3 mL tincture one to several times daily, or 10 to 15 mL of tincture 30 to 60 minutes before bed.[106,163] Valerian may be used as a single herb preparation; however, several trials have demonstrated efficacy of multiherb products including valerian, hops, and lemon balm.[472] Valerian root is considered contraindicated in pregnancy caused by lack of demonstrated safety and the mutagenic potential of valepotriates, although the actual valepotriate content of commercial products has been found to be extremely low.[472,505]

Hops

Hops, a primary ingredient in beer, has long been used for its sedative effects. Historically, it was taken internally as well as stuffed into herbal pillows to be slept on for a sedating effect.[163,186] Hops is approved by the German Commission E for mood disturbances, restlessness, anxiety, and sleep disturbances and by ESCOP for tenseness, restlessness, and sleep disorders.[106,186] Hops may have CNS depressant effects. Animal studies suggest sedative, hypnotic, and spasmolytic effects; however, there is a dearth of good-quality human clinical trials on the use of hops for the treatment of sleep disturbances.[186,522,523] Recent research has focused more on the phytoestrogenic uses of hops. Hops has a long history of safe use, few anecdotal adverse events reports,[523] and is considered safe when used in recommended doses. It is generally recommended, based on theoretical grounds of drug potentiation, that hops not be combined with herbs that effect the CNS, including barbiturates, antidepressants, sedatives, and antipsychotics.[163,523] Neither ESCOP nor the German Commission E provide contraindication to use nor report on drug interactions.[106,186] For insomnia and sleep disturbances, hops is often combined with other sedative herbs, including passionflower, skullcap, or valerian. Caution is advised when driving or operating heavy machinery. Use of hops is not advised during pregnancy or by women with a history of estrogen-sensitive cancers.

Passion Flower

Passion flower is a folk remedy used for anxiety. In Brazil; it is called ''maracuja'' and its juice is used as a popular beverage. Valued by the Eclectic physicians for its use in treating insomnia, passion flower is a useful adjunct in the management of nervous disorders that impact sleep, and is popular among herbalists to include in formulas for general sleep disturbances, perimenopausal sleep disturbances, depression, and anxiety.[185,524] It has not been associated with acute or chronic toxicity. Animal studies have confirmed sleep-inducing effects of the herb; however, there is a complete lack of human clinical trials.[516,525] The pharmacologic profile of the extracts suggests that large doses may result in central nervous system depression and bradycardia, prolonged QT interval, and ventricular tachycardia.[526] In a Cochrane Database review, two studies evaluating two distinct passion flower formulations, were not able to differentiate passiflora from benzodiazepines for any of the outcome measures. The authors reported that the lack of statistical difference may be interpreted in two ways: (1) the medications were equally effective, or (2) the absence of difference may explained caused by Type 2 error (sample sizes not large enough or insufficient number of studies for inclusion).[527] ESCOP endorses its use in the treatment of tenseness, restlessness, and irritability, and difficulty in falling asleep.[186] The German Commission E supports its use for the treatment of nervous restlessness.[106] There are no known side effects or contraindications to use, although the theoretic contraindication of sedative herbs with sedative pharmaceuticals is generally applied.

Skullcap

Skullcap has a long historical reputation of use as an anxiolytic, antiseizure, and sedative herb, and is commonly used both for nervous disorders and sleep problems. However, there is surprisingly little clinical

research on this herb. Studies with *S. baicalensis*, a species commonly used in TCM as an anti-inflammatory, antibacterial, antiviral, and anti-atherosclerotic herb, have demonstrated binding of several alleged active flavonoids, including baicalin and its aglycone baicalein, to the benzodiazepine site of the GABA-A receptor.[528] A recent animal study demonstrated significant anxiolytic activity of *S. lateriflora* crude herb administered as aqueous and hydroethanolic extracts.[528] Extracts were analyzed and compared with valerian and passionflower extract for constituents that might indicate anxiolytic or sedative activity. GABA and glutamine were identified in varying amounts, although it remains uncertain at this time just how much these amino acids contribute to the actions of skullcap.[528] Hepatotoxic reactions have been reported after ingestion of preparations allegedly containing skullcap. Adulteration of skullcap herb by *Teucrium* spp., a known hepatotoxic herb, is recognized, and is most likely the culprit in supposed skullcap-associated hepatotoxicity, rather than skullcap itself. Marketplace standards are (ideally) applied to prevent this from occurring. Nonetheless, it is this possibility of adulteration with Teucrium that leads to the contraindication of skullcap during pregnancy. One source reported symptoms of giddiness, stupor, confusion, and seizures associated with overdose of skullcap tincture; similar findings have not been otherwise reported in the herbal literature.[529]

California Poppy

California poppy, an herb indigenous to California and used by Native Americans as a sedative, hypnotic, and analgesic, remains widely popular among herbal practitioners today as a reliable treatment for sleep disorders, especially overexcitement and sleeplessness, and also as an antispasmodic when there is muscular tension, restlessness, and pain.[163,530,531] Of interest is that the liquid extract of this herb was included in the Parke-Davis catalog in 1890, in which it was referred to as an ''excellent soporific and analgesic, above all harmless.''[531] Its efficacy was compared to morphine but without the side effects associated with that drug (e.g., constipation, addiction).[531] Animal studies have demonstrated binding of alkaloids in California poppy to GABA receptors. Sedative effects have been demonstrated at higher doses, whereas anxiolytic effects are predominant at lower dose ranges.[532] These effects are may be mediated by interactions of California poppy with benzodiazepine receptors. In vitro and animal studies have demonstrated spasmolytic effects on smooth muscle.[533] A combination formula containing California poppy (80%) and Corydalis (20%) extracts demonstrated in vitro ability to interact with opiate receptors, suggesting an analgesic activity, and in a two controlled clinical trials normalized disturbed sleep patterns without carryover effects or dependency.[531]

Kava Kava

Kava kava is used in its native South Pacific Islands as a sedative, aphrodisiac, recreational, and religious beverage.[516] It has earned a reputation as a useful botanical for the treatment of anxiety, sleep disorders, restlessness, and as a muscle relaxant.[472] Practitioners might consider it for anxiety-related sleep disorders, muscle twitching, and restless legs that interfere with sleep. Short-term studies suggest that kava kava is effective for insomnia, particularly in improving sleep quality and decreasing the amount of time needed to fall asleep, and that the kava-methysticine pyrones act centrally as antispasmodics and anticonvulsants.[516,521] The mechanisms of action proposed for kava kava include decreased levels of glutamate, an excitatory neurotransmitter, activation of dopaminergic neurons, interaction with GABA receptors, direct action on muscles leading to relaxation, elevation of dopamine and serotonin levels via inhibition of monoamine uptake, and cellular actions similar to mood stabilizers.[534–540] The German Commission E contraindicates kava kava in patients with endogenous depression.[106] Some individuals do not like the feeling they get when taking kava kava, reporting a sensation of numbness that is unpleasant. Suggesting a lower dose may prevent this feeling, but some patients may just not tolerate kava kava well. There is a possible potentiation of the effects of alcohol, barbiturates, and other substances affecting the CNS when used with kava; therefore, simultaneous use is inadvisable.[472] Issues regarding kava kava and hepatotoxicity are discussed in Plant Profiles: Kava Kava. Patients with prior or current liver disease, or those taking medications that carry a risk of hepatotoxicity, should not use this herb without the supervision of a medical doctor.

Chamomile

Chamomile is noted both for its effects on the gastrointestinal (GI) system for the treatment of spasms and dyspepsia, and as a tranquilizer and mild sedative. It appears that inhalation of the essential oil containing vapor when drinking the tea may play an important role in the sedative effects of this herb.[541] Constituents including flavonoids and apigenins may bind to benzodiazepine receptors in the CNS.[542] Animal studies demonstrate anticonvulsant and CNS depressant activity, whereas human studies are lacking.[516] Chamomile is a gentle herb considered safe for children and pregnancy and lactating women, immortalized by Beatrix Potter when Peter Rabbit's mother gives it to the naughty Peter to promote sleep. There are no contraindications to use or known interactions.

Lemon Balm

A recent randomized controlled clinical trial found lemon balm to be ''beneficial in moderating subjective mood in response to mild psychological stress.''[543] Although sleep measurements were not made in this study, the findings suggest changes supportive of sleep induction. ESCOP supports the use of lemon balm as a sedative for tenseness, restlessness, and irritability, as well as the symptomatic relief of minor digestive complaints, for example, spasms.[186] The German Commission E supports its use for nervous sleeping disorders.[106] Like chamomile, lemon balm is considered a gentle herb to be taken as a tea, also rich in volatile oils that calm the

mood, and it also may be taken in tincture form.[541] It has been traditionally called ''the gladdening herb,'' which has lent to its modern use as not only a tranquilizer and mild hypnotic but as an anxiolytic and mild antidepressant. There are no contraindications to use or known interactions.

Lavender

Lavender is a mild sedative used for restlessness, nervous exhaustion, and sleep disorders.[185] It approved by the German Commission E for the treatment of mood disturbances and functional abdominal complaints; for example, nervous stomach irritations, is used as a tranquilizing herb in the form of tea, included in tinctures, and as an aromatherapy agent.[106] It is a gentle herb with no reported side effects or expected drug interactions. A relaxing bath can be taken prior to bed using five to seven drops of lavender essential oil added to a tub of hot water, or several drops. Alternatively, or additionally, an aromatherapy atomizer containing lavender oil can be sprayed near the sleeping area to promote a sense of calm. The essential oil is not to be taken internally.

Motherwort

Motherwort has been used traditionally as a nervine, tranquilizer, and mild sedative for irritability and tension. Its use is approved by the German Commission E for the treatment of nervous cardiac conditions and thyroid hyperfunction.[106] It is an excellent addition to formulae for sleep disorders in perimenopausal women experiencing anxiety or heart palpitations, and for patients with subclinical hyperthyroid function. Any patients experiencing heart palpitations or other cardiac symptoms, or hyperthyroid function, should seek the care of a qualified medical practitioner prior to self-medication with motherwort to rule out serious underlying disorder.

Protocol for Sleep Troubles

For patients with sleep troubles seeking a natural approach, a combination of nonpharmacologic strategies and appropriate botanicals can be effective. The following formulae are examples of how herbs might be combined to address a variety of sleep-related problems. Patients can expect results within a couple of weeks after beginning a therapy, although some may experience rather immediate benefits.

Difficulty Falling Asleep

Tea: Combine equal parts of the following bulk herbs. Prepare by steeping 2 tsp of herbs in 1 cup of boiling water for 10 minutes. It is important to steep the tea in a covered vessel to preserve the medicinal volatile oils.

Lavender	(*Lavandula officinalis*)	1 part
Chamomile	(*Matricaria recutita*)	1 part
Lemon balm	(*Melissa officinalis*)	1 part

Total: 3 parts

Dose: Drink 1 to 4 cups daily, but discontinue drinking about 30 minutes prior to bed to avoid night waking from the need to urinate.

Tincture:

California poppy	(*Eschscholzia californica*)	20 mL
Hops	(*Humulus lupulus*)	20 mL
Passion flower	(*Passiflora incarnate*)	20 mL
Valerian	(*Valeriana officinalis*)	10 mL
Skullcap	(*Scutellaria lateriflora*)	10 mL

Total: 100 mL

Dose: Take 2 to 4 mL for four doses starting 2 hours prior to bedtime. Repeat one to three doses during the night if night waking is a problem. For individuals for whom hops is contraindicated, omit the hops and increase the California poppy and passion flower each by 10 mL. For those who cannot tolerate valerian, omit and increase the passion flower by 10 mL.

Inability to Sleep Associated with Anxiety

Tincture:

Passion flower	(*Passiflora incarnate*)	30 mL
California poppy	(*Eschscholzia californica*)	25 mL
Motherwort	(*Leonurus cardiaca*)	15 mL
Kava kava	(*Piper methysticum*)	15 mL
Skullcap	(*Scutellaria lateriflora*)	15 mL

Total: 100 mL

Dose: Take 2 to 4 mL three to four times daily, and two to four doses within the 2 hours prior to bedtime.

Difficulty Sleeping Caused by Musculoskeletal Pain or Restless Legs

Tincture:

Cramp bark	(*Viburnum opulus*)	30 mL
California poppy	(*Eschscholzia californica*)	25 mL
Corydalis	(*Corydalis ambigua*)	15 mL
Hops	(*Humulus lupulus*)	15 mL
Kava kava	(*Piper methysticum*)	15 mL

Total: 100 mL

Dose: Take 2 to 4 mL as needed for pain relief, up to six doses daily.

Difficulty Sleeping Associated with Perimenopausal Complaints

Tincture:

Black cohosh	(*Actaea racemosa*)	30 mL
Hops	(*Humulus lupulus*)	20 mL
Motherwort	(*Leonurus cardiaca*)	15 mL
Passion flower	(*Passiflora incarnate*)	15 mL
Sage	(*Salvia officinalis*)	10 mL
Lavender	(*Lavandula officinalis*)	10 mL

Total: 100 mL

Dose: 3 to 5 mL as needed in the evening and prior to sleep, up to four doses daily.

NUTRITIONAL CONSIDERATIONS

- L-tryptophan was a popular supplement for sleep promotion. Though its use was banned in 1989 caused by association with eosinophilia-myalgia syndrome, it continues to be sold over the counter. Although its use as a supplement is not recommended, L-tryptophan is naturally occurring in milk. Its safety and efficacy in this form has not been evaluated.[509]
- Melatonin, also an endogenous neurotransmitter involved in sleep regulation, is a popular sleep aid, promoted for treating insomnia due to circadian rhythm disturbances and preventing jet lag. It is thought that it is the natural decline in melatonin levels as we age that is partially responsible for increasing insomnia in the elderly. A number of substances, including tobacco, alcohol, NSAIDs, calcium channel blockers, benzodiazepines, fluoxetine, and steroids decrease melatonin production. The primary side effect associated with melatonin use is drowsiness. It is typically take in 0.3- to 0.5-mg doses. It is contraindicated in prepubertal and pregnant women caused by interference with luteinizing hormone.[509]
- Magnesium supplementation may be effective in promoting high-quality, uninterrupted sleep.[163]
- Vitamin B_6 supplementation may reduce symptoms of insomnia, depression, and irritability. B_6 is involved in the production of the neurotransmitter serotonin, an endogenous chemical responsible for sleep regulation.[163]
- Iron-deficiency anemia has been associated with restless leg syndrome; women experiencing this discomfort should have their iron and ferritin levels checked to rule out anemia.
- Some women, especially during pregnancy, report that nocturnal leg cramps are improved when they take a calcium and magnesium supplement. A dose of 800 to 1200 mg calcium and 400 to 600 mg magnesium daily is recommended.

PREVENTION OF CARDIOVASCULAR DISEASE IN POSTMENOPAUSAL WOMEN

Wendy Grube

Cardiovascular disease (CVD) is the leading cause of major illness and death among women over the age of 50 in the United States, amounting to 2.5 million hospitalizations and 500,000 deaths each year.[544] Coronary artery disease (CAD), myocardial infarction (MI), and stroke (cerebrovascular accident or CVA) are the most common disorders in this category of disease. According to the National Institute on Aging, one in ten women age 45 to 64 will suffer from CVD. Although women perceive a greater risk from breast cancer, the actual lifetime risk of death associated with breast cancer is 1 in 25, versus a 1 in 3 risk of death from CVD. More women die from CVD than from all cancers, accidents, and diabetes together.[544] CVD occurs at a later age in women as compared with men, and carries with it a worse prognosis. Approximately 80% of deaths from CVD in women under 65 years old occur during the first MI, and 63% of these women never have a symptom before the fatal event. During the first year after an MI, 44% of those who survive die, and 64% never completely recover.[544,545]

Many risk factors, both modifiable and nonmodifiable, have been identified as contributing to CVD. The National Heart, Lung, and Blood Institute lists the following:[545]

- Age: After menopause, women lose the protective effects of estrogen and experience an increased risk of coronary disease. Estrogen also has been found to affect cholesterol levels, homocysteine levels (involved with inflammatory process), clotting mechanisms, and it inhibits platelet aggregation as well as diminishes the viscosity of blood. In general, women experience CHD 10 years later than men because they are protected by the effects of estrogen until after menopause.[544]
- History of CVD, stroke, or peripheral vascular disease
- Family history of premature CVD
- Dyslipidemia: According to the National Institute on Aging, cholesterol levels in women begin to rise somewhat after the age of 20, and again more rapidly after the age of 40. This increase in total cholesterol continues until the age of 60, with no observed difference by race or ethnicity. Women with high levels of HDL (high-density lipoproteins) have lower risk for CHD, with HDL offering a greater predictive value for women than men. Elevated triglyceride levels also indicate an elevated risk for heart disease.[544,546]
- *Cigarette smoking:* Data from the Nurses' Health Study show that women who were heavy smokers had more than six times the risk of CHD than nonsmokers, and after quitting for 3 to 5 years, were able to reduce their risk of CHD to almost within the range for nonsmokers. Smoking has been found to decrease estrogen levels in women, along with the cardioprotective effects of this hormone.[546]
- *Hypertension:* This is the most significant risk factor for stroke, and also contributes greatly to risk of heart disease. Although rates of hypertension for all women has been declining, black women are more likely to suffer from this disorder than white, Asian, or Hispanic women.[546]
- *Diabetes mellitus:* This disease increases a woman's risk of heart disease by three times, and is felt to reduce the protective effect of estrogen. Those women with diabetes who experience a myocardial infarction are more likely to die, compared to women without diabetes or men.[544–546]
- *Obesity (especially central):* Obesity has been defined as a body mass index (BMI) >30. The proportion of women who fall into this category has been increasing steadily over the past 40 years, with an increase in prevalence among black women (37.6%) over white women (23.5%) in 1994.[546]
- *Lifestyle—diet, physical activity, psychosocial factors, alcohol:* A diet high in saturated and trans-saturated fats are felt to increase the risk for CHD. Vigorous physical activity reduces cholesterol levels as well as obesity and hypertension, and most likely contributes to decreased incidence of CHD through these mechanisms. Psychological factors that may contribute to

CHD in women include stress and stressful life events, anger, hostility, hopelessness, depression, social support/networks, education, occupation and job control, and chronic fatigue.[546]

- *Homocysteine and C-reactive protein (CRP):* Increased levels of these biochemical markers have been associated with an increased risk of CVD.[545,546]

Modifiable risk factors include cigarette smoking, alcohol use, and lifestyle (diet, physical activity, and psychosocial factors). Nonmodifiable factors include age, gender, and family history.

SYMPTOMS

The major presenting symptom of CAD in women is angina, which may be accompanied by palpitations, shortness of breath, dyspnea on exertion, nausea, sweating, and fatigue. Associated CAD pain may occur in locations such as the jaw, arms and shoulders, or back. This profile of symptoms often leads to nonrecognition of their cardiac origin, leading to delayed medical recognition and treatment. Statistically, women receive less medical attention for their symptoms of coronary disease than men.[544]

DIAGNOSIS

Unfortunately, the diagnosis of CAD usually follows symptoms of angina that occur after years of plaque development, or an acute cardiovascular event, such as a myocardial infarction. In the past, women who presented with chest pain were evaluated less aggressively than men, most likely caused by an erroneous belief that angina in women was benign. In the contemporary medical system, a woman complaining of chest pain may expect to undergo the following:

1. *Detailed history and characteristics of the chest pain:* onset, location, duration, characteristics, concomitant symptoms, aggravating or relieving factors, and any self-treatment. Chest pain associated with angina is usually described as a feeling of retrosternal burning, heaviness, or ''crushing'' sensation, which may radiate to the back, arm, neck, or jaw, lasting over 1 minute but less than 10 minutes. In the event of an MI, the pain is similar, but usually lasts 30 minutes to 2 hours, and may be associated with nausea and vomiting, sweating, dizziness, weakness, or shortness of breath. It may have occurred after an episode of physical exertion or anxiety, and is relieved by narcotic analgesics.[547]
2. *Focused examination:* evaluation of all peripheral pulses, auscultation of the carotid arteries for bruits, awareness of any existing jugular venous distention, and recording of blood pressure while the patient is sitting, lying, and standing.[547]
3. *Diagnostic tests*: These usually include an electrocardiogram (ECG), nuclear scanning, and angiography to evaluate how many vessels are affected, and to what degree. A ''stress test'' or exercise ECG may be used to evaluate the heart's ability to respond adequately to the increased oxygen demands required by vigorous physical exertion. Nuclear scanning measures an ''ejection fraction,'' or the ability of the left ventricle to pump blood effectively. Angiography (cardiac catheterization), is the actual viewing of the coronary arteries via a catheter, through which stents or balloons can be placed to hold the artery open, or fibrinolytic medications can be distributed to unblock an affected artery. A comprehensive 12-lead ECG is used to look for diminished coronary artery blood flow (ischemia) or resulting injury to the surrounding cardiac tissue. Ischemia of heart tissue results in changes of the electrical conduction (depolarization and repolarization) of the cells. This creates an enlargement and inversion of the T wave on ECG. When actual injury occurs, there is visible ST-segment elevation, followed by a significant Q-wave after infarction (necrosis) occurs. The ECG is accompanied by serial cardiac enzyme levels, which can support the diagnosis of MI and assist in determining when the event occurred.[547]

If the woman is not experiencing an acute coronary event such as an MI, routine screening for risk factors will take place. This includes: continued monitoring of blood pressure and identification of hypertension when it exists; lipid testing to detect elevated total cholesterol and, more significantly, LDL (low-density lipoprotein) cholesterol, as well as triglycerides. At times, other potential risk factors may be screened for by checking serum homocysteine, C-reactive protein, or lipoprotein-a.[548]

CONVENTIONAL MEDICAL MANAGEMENT OF CAD

Management strategies for CAD (Table 19-10) revolve around the reduction of risk factors identified during the diagnostic process, and the prevention of a myocardial infarction or sudden death.[547] These approaches include attempted correction of hypertension, dyslipidemias, elevated serum glucose levels in diabetics, and risk of thrombus formation.

Medications

Medications used for the management of CAD in women include diuretics for hypertension, exogenous hormones and statins for lipid improvement, insulin and oral hypoglycemics for blood glucose control, antiplatelet drugs to prevent thromboembolic events, beta-blockers plus ACE inhibitors to reduce morbidity and mortality related to MI, vasodilators to reduce afterload and/or preload, and calcium channel blockers, with some of the aforementioned medications, to relax peripheral vascular resistance. The overall goal is to relieve the work the heart has to do while maximizing efficiency in order to reduce the oxygen consumption requirements of the heart.

Hormonal Replacement Therapy

Traditionally, the hormones most widely used and studied were conjugated equine estrogens plus medroxyprogesterone acetate, a synthetic progestin derived from wild yam. In the past, various observational studies indicated a 35% to 80% decrease in CAD in women using estrogen replacement therapy (ERT). However the use of estrogen alone, without adding a progestin, in a woman with

TABLE **19-10**

Conventional Management of CAD in Postmenopausal Women

DISORDER	MANAGEMENT
Dyslipidemia	Some studies have shown decreased incidence of CAD in women using hormonal replacement therapy (HRT). HRT raises HDL cholesterol by 10% while decreasing LDL cholesterol by 10%; however, it also raises triglycerides by 25%, and carries up to a fourfold risk of a thromboembolic event, and a small early risk of MI and CVA. This risk of thromboembolic disease has been found in clinical trials to persist for 4 years after discontinuation of HRT use. Because of the lack of clinical evidence demonstrating cardiovascular benefit from HRT use, hormonal supplementation is no longer recommended for management of dyslipidemia.
Goals:	
Women without CAD	
Low risk (<2 risk factors)	
LDL <160 mg/dL	
Ideal LDL <130 mg/dL	
Higher risk (≥2 risk factors)	
LDL <130 mg/dL	
Women with CAD	Pharmaceutical management includes statins, niacin, fibrate, or combination of the three:
LDL <100 mg/dL	
Other lipid goals:	• LDL ≥190 mg/dL in postmenopausal women with <2 risk factors
HDL >35 mg/dL	• LDL ≥160 mg/dL in postmenopausal women with ≥2 risk factors
Triglycerides <200 mg/dL	• Elevated triglyceride levels
	Statins have shown a 29% risk reduction of CHD in women; however, adverse effects may include liver and renal dysfunction.
Hypertension	Lifestyle modification, to include weight loss, physical exercise, and moderation in alcohol and salt intake.
Goal: <140/90 mm Hg	
Ideal: <120/80 mm Hg	Individualized pharmaceutical intervention is advised in the following instances:
	Blood pressure elevation of ≥140/90 mm Hg after 3 months of lifestyle change
	Systolic BP ≥160 mm Hg initially
	Diastolic BP ≥100 mm Hg initially
Diabetes	American Diabetes Association Diet
Blood glucose goals:	Weight loss and physical exercise
Preprandial: 80 to 120 mg/dL	Pharmaceuticals (insulin or oral medication) as indicated to achieve blood glucose goals
Bedtime: 100 to 140 mg/dL	
Hemoglobin A1C goal: <7%	
Thromboembolic events *women with established CVD*	Atherosclerotic CVD: use aspirin 80–325 mg a day
	Women who cannot take aspirin: use antiplatelet medications
Reinfarction and sudden death, *overall mortality in women after MI*	Hospitalized women with an evolving MI and no contraindications may start a β-blocker within hours of admission, or within the following few days after the event, and should be continued indefinitely.
	Women with left ventricular dysfunction may be started on an ACE inhibitor for 6 weeks, and then stopped.

a uterus was found to increase her risk of endometrial hyperplasia and cancer. The Postmenopausal Estrogen/Progestin Intervention (PEPI) trial results showed beneficial effects of estrogen on HDL, LDL, and fibrinogen levels as compared with placebo (in 875 healthy postmenopausal women).[549] A study using postmenopausal women with established heart disease, the Heart and Estrogen/Progestin Replacement Study (HERS), showed no significant differences between groups of women who used hormones and placebo in primary or secondary cardiovascular outcomes after 4.1 years. The HERS study also indicated an increase risk of cardiovascular disease events in the first year of HRT use, followed by less events in years 4 and 5.8 Another trial, the Women's Health Initiative (WHI), an NIH-sponsored multicenter study of health postmenopausal women, showed an significant increased risk of CAD, stroke, venous thromboembolism, and biliary tract surgery, and a nonsignificant risk of breast cancer. It is now recommended that HRT be prescribed for a short duration (3 to 5 years) for the control of vasomotor symptoms, and should not be used for primary or secondary prevention of CHD.[545]

Statins

Statins are drugs used to lower cholesterol and LDL levels, and are categorized as HMG-CoA reductase inhibitors. They block the production of cholesterol in the liver, and increase the speed of breakdown of LDL, resulting in LDL level lowering by 25% to 45%, triglyceride lowering by 10% to 30%, and HDL increasing by 8% to 10%. They are also effective due to anti-inflammatory effects. Common mild side effects include headache, myalgia, abdominal pain, and gastrointestinal symptoms such as dyspepsia, constipation, or diarrhea. Rhabdomyolysis and its associated renal dysfunction have been reported in 0.1% to 0.5% of patients using statins, and elevated liver enzymes also may occur.[550]

Hypoglycemics

Hypoglycemics include insulin and oral drugs used to lower serum glucose levels. Persons with Type 1 diabetes

lack endogenous insulin, and must be given exogenous insulin to prevent diabetic ketoacidosis and death. Persons with Type 2 diabetes may have some endogenous insulin, however may suffer from insulin resistance. Oral agents act on glucose utilization and liver storage and production of glucose. Occasionally, persons with Type 2 diabetes require insulin as well as oral agents. The goal of therapy is to normalize blood glucose levels, preventing the progression of the disease to target organs, such as the coronary arteries. The most common adverse effect is hypoglycemia.

Antiplatelet Drugs

Aspirin is the primary antiplatelet drug used to prevent clot formation in persons known to have CAD. It works by interfering with platelet aggregation. Common side effects include gastrointestinal discomfort and bleeding. Warfarin or clopidogrel can be used if aspirin is contraindicated.[545] Antiplatelet medications are only recommended in patients with prior events or risk factors for disease; they are not recommended prophylactically for otherwise healthy individuals.

Beta-Blockers

In women who have experienced an MI, beta-blockers are usually initiated within hours of the event unless contraindications exist, such as severe bradycardia, high-degree heart block, acute heart failure, asthma or peripheral vascular disease. Essentially, these drugs decrease the workload of the heart by slowing heart rate, decreasing conduction, velocity, and contractility. They effectively reduce angina and the incidence of rhythm disturbances, and also decrease blood pressure over time by diminishing peripheral vascular resistance. Passive bronchial constriction may occur because of beta-adrenergic receptors located in the lungs being affected by this class of drugs. Effects on the liver include a rise in total cholesterol, decrease in HDL, and elevation of triglycerides. Decreased insulin secretion by the pancreas also may be an effect of beta-blockers. Other adverse effects include urinary frequency, male impotence, and diarrhea.

Angiotensin-Converting Enzyme Inhibitors

Angiotensin-converting enzyme (ACE) inhibitors are used in the case of heart failure, and function to reduce cardiac preload and afterload, as well as peripheral vascular resistance and blood pressure through decreased sodium and water retention. They are started as soon as possible after an MI, with the goal of reducing the likelihood of heart failure or extension of the infarction. They are also used in the management of left ventricular dysfunction and heart failure. Common adverse reactions include hypotension and dry cough, with rarer effects, including rash (with captopril), neutropenia with high doses, renal impairment, and concomitant collagen diseases. Angiotensin receptors blockers are used with similar effects to the ACE inhibitors, without the side effects, as bradykinin, a vasodilator maintained by the ACE-inhibitors, is not maintained by this latter class of drugs, and it is the effects of bradykinin in the lungs that are thought to cause cough.

Niacin

Niacin is currently considered one of the most effective drugs for elevating HDL cholesterol, and is commonly combined with statins to increase the rate of improvement in cholesterol levels. Flushing is the major side effect but can be minimized by taking a baby aspirin 30 minutes prior to taking niacin. Niacin is contraindicated in patients with liver disease, and may transiently lead to an elevation in liver function test results even in healthy patients. Niacin may make glycemic control more difficult in diabetic patients and may aggravate arthritis associated with gout.

Procedural Interventions

Procedural interventions for the treatment of CAD include percutaneous transluminal coronary angioplasty, with placement of a stent in the coronary artery to maintain patency of the vessel combined with antiplatelet therapy, and coronary artery bypass graft surgery.

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

Heart disease is perhaps the most overt example of pathology representing a confluence of influences that conspire to create disease: diet, exercise, sleep, stress and coping mechanisms, spirituality, culture, family, and environmental conditions—all of which also can work in concert to affect healing.

Botanical medicine offers a number of herbs that have been used historically and traditionally for the treatment of cardiovascular disease. Every medical and herbal student learns the story of William Withering, who learned of the cure for dropsy (edema caused by CHF) from a local herb woman, and from which the modern mainstay drug digoxin was derived. However, determining the appropriate role for botanical therapies in treating the patient with CVD can be difficult. A number of herbs with cardiovascular effects have now been well studied, and have been found to improve cardiovascular wellness. Several have been demonstrated to have actions that parallel those of conventional pharmaceuticals, often with fewer adverse effects. For example, garlic, fenugreek, and guggul have demonstrated positive effects on cholesterol levels, whereas hawthorn has been shown to have positive inotropic effects and be beneficial in the prevention of CHF, and none have remarkable adverse effects associated with their use. However, whether these herbs are a suitable substitute for patients with heart disease is undetermined. There are, for example, a number of effective herbal diuretics, most notably dandelion leaf, which is rich in potassium and therefore may offer diuresis without potassium depletion. Unfortunately, its diuretic effects are more difficult to predict, control, and quantify than a standard pharmaceutical dose of a diuretic; therefore, although pharmaceutical diuretics certainly have more side effects, they may be easier to control in terms of dose and results. Because the potential for interactions exists between herbs and drugs, and because the effects on both patient safety and medication efficacy—either of the herb or the drug—when taken combined is largely unknown, it is advisable not to combine the two.

Therefore, for patients dependent on medications for basic cardiac functioning, it is probably best to take a conventional pharmaceutical treatment route; however, for patients in need of CVD prevention, or with only mild disease, that is., moderate hypertension, and who wish to avoid medications, a trial of botanical medicines along with therapeutic lifestyle change might be entirely safe and appropriate. Such decisions need to be made individually for each patient. Close monitoring of patients is important.

The importance of therapeutic lifestyle changes in altering the course of cardiovascular disease also cannot be overemphasized. Even walking briskly for as little as 3 hours per week can reduce a woman's risk of heart attack by about 40%![163] Similarly, dietary changes, stress reduction, treatment for depression, and perhaps most significantly, smoking cessation, can be life saving. Therapeutic lifestyle changes are always the first line approach in any nonemergent medical setting, as well as in the herbal clinic. The possible actions of herbs and their effects on the cardiovascular system are presented in Table 19-11 and are discussed in the following. This section focuses on those herbs used directly to prevent and treat mild cardiovascular disease. Treatment of concurrent problems, for example, diabetes, polycystic ovarian syndrome (PCOS), or insulin resistance, which are known to increase risk of cardiovascular problems, is essential.

For botanical options for stress, readers are directed to other chapters for discussions on herbs for treating depression, relieving anxiety, promoting sleep, and improving the stress response.

Patients with a history of cardiovascular disease, a suspected cardiovascular problem, or who are currently being treated for cardiovascular disease, are advised to work in conjunction with a physician when using botanicals. It is generally recommended that cardiotonic herbs (e.g., hawthorn) and cardioactive herbs (containing cardioactive glycosides) (e.g., lily of the valley) not be combined with cardioactive medications caused by possible potentiation of actions.

Black Cohosh

Traditionally, black cohosh was used by the Eclectics for a wide range of disorders, including emotional complaints associated with the perimenopause, as well as cardiovascular symptoms such as palpitations, arrhythmias, and hypertension caused by ''nervous stimulation'' of the heart. It was used in the treatment for angina and cardiac arrhytmias.[551] Primarily used for management of vasomotor symptoms commonly associated with the perimenopause, black cohosh also appears to increase the blood flow through peripheral vessels at doses of 0.5 mg/kg.[551] Animal studies have demonstrated a dose-dependent hypotensive effect; however, this has never been observed in human studies.[551] The primary use of black cohosh in a contemporary herbal approach to CVD is in combination with other herbs for its anxiolytic effects, relaxation of nonpathologic palpitations, and for concomitant relief of menopausal complaints. It is commonly given in tincture or capsule form. Recently raised concerns regarding the possible risks of hepatotoxicity associated with black cohosh use are discussed in Plant Profiles: Black Cohosh.

Coleus

Valued by herbalists for its hypotensive actions, coleus also may contribute to the prevention of CHD through its antiplatelet activity.[552] Its constituent forskolin has been subject to in vitro and in vivo (by injection) investigation and has demonstrated hypotensive activity,

TABLE **19-11**

Herbs Used in the Prevention and Management of CAD in Women

THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Anticholesterolemic	*Allium sativum*	Garlic
	Commiphora mukul	Guggul
	Cynara scolymus	Globe artichoke
	Salvia miltiorrhiza (dan shen)	Salvia
	Trigonella foenum-graecum	Fenugreek
Antihypertensive	*Allium sativum*	Garlic
	Actaea racemosa	Black cohosh
	Coleus forskohlii	Coleus
	Viburnum opulus	Cramp bark
Positive inotrope, cardiotonic	*Crataegus oxyacantha*	Hawthorn
Antithrombotic	*Allium sativum*	Garlic
	Angelica sinensis	Dong quai
	Salvia miltiorrhiza (dan shen)	Salvia
Relieve palpitations	*Leonurus cardiaca*	Motherwort
	Crataegus oxyacantha	Hawthorn
Prevent CHF	*Crataegus oxyacantha*	Hawthorn
	Convallaria majalis	Lily of the valley

positive inotropic action on isolated heart muscle, and increased cerebral blood flow with vasodilatation. No clinical studies have been conducted using coleus. Although a closely related species is used in traditional Ayurvedic medicine, this species is used only as a condiment.[531] Coleus extracts containing a quantified level of forskolin are recommended, and it is not advisable to use this herb with other cardiac medications or without the advice or a qualified practitioner.[531] This herb, like the others in this section, should not be used with conventional cardiac medications. It is used in the form of a hydroethanolic extract, and is generally included as less than 20% of an herbal formula.

Cramp Bark

Considered a ''vasorelaxant,'' this herb has been identified as having possible usefulness as an adjunct in the treatment of hypertension.[552,553] No clinical trials have evaluated the effects of cramp bark on blood pressure or cardiovascular measures. It is a highly respected musculoskeletal relaxant and is commonly combined in formula for the treatment of stress, chronic pain, and insomnia.

Dong Quai

Animal and in vitro studies have found that dong quai may exert a cardioprotective effect, increasing myocardial blood supply, decreasing myocardial oxygen consumption, and reducing oxidative damage to ischemic myocardial tissue. In addition, studies have shown that it can act to inhibit platelet aggregation, increase prothrombin time, decrease peripheral vascular resistance and arterial blood pressure, and inhibit experimentally induced arrhythmias and ventricular fibrillation. Butylidenephthalide and sodium ferulate have been found to inhibit platelet aggregation in vivo and in vitro, primarily by interrupting arachidonic acid metabolism. Ferulic acid has been shown to increase coronary blood flow in vitro, and sodium ferulate may have antiarrhythmic affects. In addition, butylidenephthalide has shown hypotensive effects in vivo. Most of these proposed cardiovascular and hemorrheologic effects of dong quai or its constituents are consistent with the TCM use of this herb to ''quicken the blood.'' Only three human controlled clinical trials evaluating dong quai's effects on cardiovascular disease were identified. The studies, of variable quality (e.g., one study lacks a placebo arm), show some vasodilatory effects and possible improvement in post ischemic stroke neurologic and hematologic perameters.[554]

Fenugreek

A systematic review by Thompson, Coon, and Ernst identified five randomized clinical trials using fenugreek for control of hypertension. The trials involved a total of 140 patients; all but one trial was conducted in India. Although the methodologic quality of the studies was considered generally poor in four of the trials, statistically significant reductions occurred in total serum cholesterol of between 15% and 33% compared with baseline. Commonly reported side effects included mild gastrointestinal symptoms, although none was severe enough to cause participant withdrawal.[555] This herb, like the others in this section, should not be used with conventional cardiac medications. Fenugreek has a pleasant taste to most, and is used as tea, in tincture, or finely ground in capsules of even in foods.

Garlic

Garlic has an extensive reputation for prevention and treatment of cardiovascular disorders. The fresh or dried cloves are used. (The cloves are secondary bulbs and make up the larger bulb.)[106] Approved by the German Commission E for the prevention of dyslipidemias in aging and the treatment of hyperlipidemia, it is popularly used for the treatment of mild hypertension and the prevention of atherosclerosis and CAD. The primary active constituent is considered to be allicin, produced when the clove is chopped or crushed.[556] Garlic has been shown to inhibit enzymes involved in lipid synthesis, decrease platelet aggregation, prevent lipid peroxidation of oxidized erythrocytes and LDL, increase antioxidant status, and inhibit angiotensin-converting enzyme (ACE). Numerous studies point to the fact that garlic reduces cholesterol, inhibits platelet aggregation, reduces blood pressure, and increases antioxidant status.[557] Like statins, garlic appears to inhibit cholesterol biosynthesis through inhibition of HMG-CoA reductase.[557–564] Forty-four percent of the clinical trials conducted since 1993 have indicated a reduction in total cholesterol, and the most profound effect has been observed in garlic's ability to reduce platelet aggregation. Inconsistent results have been seen in the area of blood pressure and oxidative-stress reduction, with very few studies addressing these. Negative findings from some clinical trials may have resulted from variations in the garlic preparations used, short trial durations, and other methodologic limitations.[557] Although the WHO cautions against the use of garlic in patients taking warfarin and other anticoagulant medications, clinical trials and adverse events reports thus far do not support these concerns. However, increased clotting time has been reported in patients taking garlic supplements; therefore, it is recommended that garlic supplementation be discontinued for at least one week prior to any surgical procedures, and it is prudent for patients on anticoagulant therapies to avoid garlic other than in common food quantities.[472] One clinical trial of HIV patients ($n = 9$) on saquinavir found significantly decreased serum levels of the medication after garlic ingestion.[565] Garlic breath and GI complaints are the most commonly reported adverse effects; contact dermatitis has been reported with prolonged exposure. The German Commission E and ESCOP both state that there are no known contraindications to garlic use.[106,186] This herb, like the others in this section, should not be used with conventional cardiac medications. Garlic make be eaten fresh in the diet in any number of foods, or may be taken in a variety of extracts, capsules, or other products available on the market. Which products are most efficacious remains a matter of some debate, with several types of preparations yielding positive results in clinical trials.[472]

Globe Artichoke

Prized for centuries as a medicinal plant used to ''tonify the liver,'' globe artichoke extracts have been shown to produce various pharmacologic effects, including marked choleretic activity and inhibition of cholesterol biosynthesis and LDL oxidation.[566] It is considered safe when used in food or therapeutic amounts, and is not known to interact with foods, drugs, or lab tests. The only adverse reaction noted is allergic response, primarily in persons allergic to the Asteraceae/Compositae family of plants. It is not recommended for use when there is obstruction of the bile duct, and should be used with caution when gallstones are present. Of two clinical trials (n = 187), one (n = 44) showed some reduction in total serum cholesterol in patients with a baseline of over 5.4 mmol/L, and the other showed reductions in total serum cholesterol of 18.5% for artichoke and 8.6% for placebo.[567] This herb, like the others in this section, should not be used with conventional cardiac medications.

Guggul

Resin from the guggul tree, a native of western India, has been used in Ayurvedic medicine since at least 600 BCE. In 1986, guggul oleoresin was approved in India for marketing as a lipid-lowering agent. Studies have shown that gugulsterones are antagonist ligands for the bile acid receptor farnesoid X receptor (FXR), which is an important regulator of cholesterol homeostasis.[568,569] A review by Thompson, Coon, and Ernst identified six randomized clinical trials of guggul, involving 388 patients with different diagnoses. Five of the studies were conducted in India and one in the United States; four were placebo controlled; and one compared guggul with two reference compounds. Results suggest reductions in total serum cholesterol from 10% to 27% compared with baseline levels. A statistically significant decrease in lipid peroxide levels was reported in one study, with no corresponding change in the placebo-treated group.[555] Because guggul is associated with numerous side effects, including abdominal discomfort, diarrhea, headache, hypersensitivity rash, nausea, and hiccups. The herb is typically recommended in a standardized form, gugulipid, standardized to 25 mg gugulsterones per tablet, with an oral dose of 75 mg in three divided doses daily, or two tablets twice daily.[570] It is estimated that the onset of action is approximately 2 to 4 weeks. The use of guggul may decrease the bioavailability of propranolol, diltiazem, and thyroid medication, and caution is advised with concomitant use.[570] This herb, like the others in this section, should not be used with conventional cardiac medications.

Hawthorn

Hawthorn, widely accepted in Europe as a treatment for mild congestive heart failure and minor arrhythmias, is one of the most important herbs in the materia medica for the prevention and treatment of cardiovascular disease.[163] Some consider it so beneficial that is has been called a ''food for the heart'' and suggested that everyone over 50 should take hawthorn daily! Much like red wine and green tea, hawthorn is rich in flavonoids (with the glycosides catechin and epicatechin) and oligomeric proanthocyanidins (OPCs), although amines and triterpene saponins are found as well.[472,571] It is thought to possess cardiotonic, coronary vasodilatory, and hypotensive actions. Traditionally, hawthorn has been in the treatment of heart failure, myocardial weakness, paroxysmal tachycardia, hypertension, and arteriosclerosis. The pharmacologic actions of leaf with flowers include increase in cardiac contractility, increase in coronary blood flow and myocardial circulation, protection from ischemic damage and decrease of peripheral vascular resistance. There have been no reported adverse reactions to the use of berries; however, there have been reports of nausea and gastrointestinal discomfort, as well as palpitations, headache, dizziness, sleeplessness, agitation and some circulatory disturbances when preparations containing the leaves and flowers have been taken, even in recommended therapeutic doses.[571] Presently, hawthorn is used as a cardiac tonic for mild heart disorders including CAD and angina, arrhythmias, hypertension, myocardial weakness, and prevention of arterial degeneration, well supported by scientific literature. Hoffman combines hawthorn with lime blossom, mistletoe, and yarrow in a formula to manage hypertension and circulatory system disorders.[530] In addition to the use of this plant as a cardiac tonic, it has been traditionally used as a diuretic. Current research supports the use of hawthorn extracts for the treatment of CAD and angina, ischemia-induced arrhythmias, dyslipidemias, hypertension, and early-stage congestive heart failure. Modes of action suggested by animal and in vitro studies include positive inotropic activity (increased cAMP, similar to cardiac glycosides), reducing peripheral vascular resistance and increased coronary and peripheral blood flow, increased integrity of vessel walls, decreased oxygen demand by the myocardium, protection against myocardial damage through antioxidative properties, protection against arrhythmias (through lengthening the refractory period), and anti-inflammatory effects. There is also some evidence through animal studies that hawthorn may lower serum lipid levels and improve hypertension, perhaps through the release of the potent vasodilator nitric oxide. Inhibition of platelet aggregation has been an additional observed effect of hawthorn in vitro. Although most of the science we have on hawthorn is from animal and in vitro studies, there have been extensive human trials investigating the use of hawthorn in early congestive heart failure. Preliminary studies by the German pharmaceutical company Schwalbe using an extract of hawthorn leaves and flowers (WS® 1442) indicated the product was safe and effective to treat CHF in humans. Standardized to contain 18.75% oligomeric procyanidins, this product was found to increase exercise tolerance and decrease symptoms of CHF. Zapfe, in a recent randomized, double-blinded, placebo-controlled study using WS® 1442 on 40 patients (75% women) with New York Heart Association (NYHA) class II mild, chronic CHF, confirmed a 10% improvement in exercise tolerance compared with a 15% reduction in the placebo group.[472,571] This herb, like the others in this section, should not be used with conventional cardiac medications.

Lily of the Valley

Lily of the valley is a cardioactive herb mostly used in European herbal medicine.[572] Its actions are considered similar to those of digitalis, although it is significantly less cumulative and apparently has a vastly broader therapeutic window. The plant contains approximately 40 glycosides, the principal three being convallatoxin, convalloside, and lokunjoside.[572] Cardiac glycosides improve the efficiency of the myocardium without increasing the need for oxygen, thus lessening the workload on the heart. Although US herbal practitioners seem wary of its use caused by concerns over potential toxicity, UK herbalists continue to use it, respectfully, primarily for the treatment of mild heart failure and bradycardia, considering it to complement well with hawthorn.[36] It has a rapid onset and a very short half-life.[573] Evans' reports that the toxicity of this herb is often overemphasized, citing publication in the United States of 2,639 case reports of ingestion, with 6.1% of patients experiencing symptoms, but only 3 showing severe side effects.[574] Lily of the valley, however, can induce side effects associated with cardiac glycosides including nausea and vomiting, although reported to be rare and mild.[36] This is a scheduled herb in the United Kingdom, and should be prepared as a 1:10 tincture and given only in low doses. This herb, like the others in this section, should not be used with conventional cardiac medications. This herb should be used only by a professional trained and skilled in its application, and in conjunction with medical evaluation of cardiac effects.

Motherwort

Ever since Gerard wrote his famous herbal text in the late sixteenth century, motherwort has had a reputation of usefulness in cardiac disorders, and although beneficial for men and women alike, has had an association as a "women's herb." Motherwort is approved by the German Commission E for heart palpitations occurring with anxiety. Direct myocardial action of motherwort was noted by Newall in 1992, with stimulation of both alpha and beta adrenoceptors and inhibition of calcium chloride effects. Another exploratory study by Bradley noted alkaloids contained in this plant depress the central nervous system and lower blood pressure. No modern studies have evaluated this herb clinically. Overall, however, this herb is little studied. It is quite safe and may be used in tinctures for anxiety, palpitations, and as a general cardiotonic, the latter especially when combined with hawthorn. As tea, motherwort is quite bitter, but some herbalists prepare a motherwort infused honey, a teaspoon of which can be added to other teas.

Change of Heart Cordial

This cordial was created by herbalist Amanda McQuade Crawford to safely prevent or reduce hypertension, calm heart palpitations, support the hormonal changes of menopause, and to calm and relax the nerves.

Combine:

Hawthorn tincture	(*Crataegus oxyacantha*)	4 oz
Motherwort tincture	(*Leonurus cardiaca*)	2 oz
Chaste berry	(*Vitex agnus-castus*)	2 oz
Blackstrap molasses		2 oz
Blackberry juice concentrate		2 oz

Dose: 1 tsp twice daily diluted in water, juice, or tea; 12 oz will last 30 days.

Salvia (Danshen)

Danshen, the root of Salvia miltiorrhiza, has a long history of use in TCM as a blood moving herb, activating circulation and dispersing "stasis."[575,576] It continues to be widely used in China and, to a lesser extent, in Japan, the United States, and other European countries for the treatment of cardiovascular and cerebrovascular diseases. In China, the specific clinical use is angina pectoris, hyperlipidemia, and acute ischemic stroke.[577] It is thought to be capable of improving microcirculation, causing coronary vasodilatation, suppressing the formation of thromboxane, inhibiting platelet adhesion and aggregation, and protecting against myocardial ischemia, and is used alone and in combination with other herbs for the treatment of CAD.[576] It is conspicuously advertised in the *Chinese Journal of Cardiology*, which is the official publication of the Chinese Society of Cardiology.[576] Animal experiments evaluating cardiovascular effects report prevention of intrauterine growth retardation (compound product), blood pressure reduction, reduction of low-density lipoprotein oxidation and atherosclerosis, prevention of oxidative stress, protection from liver fibrosis and renal failure, and vasodilatation.[578–583] Although the effects of danshen have not been investigated in human clinical trials, several herb–drug interactions reported in the literature, when combining danshen with warfarin suggest strong antiplatelet activity, and also emphasizes the need to avoid combining danshen with anticoagulant therapies.[576,584] The traditional dose of dried root is 6 to 15 g daily in decoction.[575] Reported adverse effects are pruritus, gastric discomfort, and appetite reduction.[575] In addition to cautions regarding combining danshen with anticoagulant and antiplatelet medications (including aspirin), it should not be combined with benzodiazepines caused by possible potentiation on depressant CNS effects. Because it is commonly included in TCM herbal formula, and is even found in certain Chinese cigarette brands, practitioners should be aware that patients may be taking this herb unbeknown to them.[576,585]

NUTRITIONAL CONSIDERATIONS

The American Heart Association considered the following guidelines part of a heart-healthy lifestyle:

- Reducing saturated and trans fatty acids in the diet
- Minimizing the intake of food and beverages with added sugars
- Emphasizing physical activity and weight control
- Eating a diet rich in vegetables, fruits, and whole-grain foods
- Avoiding use of and exposure to tobacco products

- Achieving and maintaining healthy cholesterol, blood pressure, and blood glucose levels

Eat, Drink, and Be Healthy: The Harvard Medical School Guide to Healthy Eating by Walter Willett, is an excellent resource for patients learning how to eat well. Willett lays out the following seven ''most important dietary changes'' patients can make toward heart and overall health:

- *Watch weight:* The healthier the body weight for that patient, and the more stable the body weight, the lower are a patient's chances of cardiovascular disease, diabetes, and of being diagnosed with postmenopausal breast cancer, endometrium cancer, and colon cancer.
- *Eat fewer ''bad fats'' and more ''good fats'':* Reducing dietary fat is not enough to protect the heart. Fats from nuts, seeds, grains, fish, and liquid oils (including olive, canola, soybean, corn, sunflower, peanut, and other vegetable oils) are healthy choices that allow the body to increase high-density lipoprotein (HDL), and reduce low-density lipoprotein (LDL)—which does increase cardiovascular health.
- *Eat fewer refined-grain carbohydrates and more whole-grain carbohydrates:* Eating whole-grain foods is clearly better for long-term good health and offers protection against diabetes, heart disease, cancer, and gastrointestinal problems such as diverticulosis and constipation—the latter a known risk factor for colon cancer.
- *Choose healthier sources of proteins:* The best sources of protein are beans and nuts, along with fish, poultry, and eggs. It separates vegetable and animal protein sources and makes the latter optional for people who want to follow a vegetarian diet.
- *Eat plenty of vegetables and fruits:* A diet rich in fruits and vegetables will lower blood pressure, and protect against heart attack, stroke, gastrointestinal problems, and reduced the incidence of aging-related problems cataracts and macular degeneration.
- *Use alcohol in moderation:* Evidence strongly points to one drink a day for women and one or two a day for men, preferably red wine, for reducing the chances of having a heart attack or dying from heart disease by about a third and also decreasing the risk of ischemic stroke. For those who prefer not to drink alcohol, or for medical or personal history reasons are unable to, similar benefits can be gained by exercise
- *Take a multivitamin for insurance:* Several of the ingredients in a standard multivitamin—especially vitamins B_6 and B_{12}, folic acid, and vitamin D—are essential players in preventing heart disease, cancer, osteoporosis, and other chronic diseases. At about a nickel a day, a multivitamin is a cheap and effective genuine ''life insurance'' policy. It will not make up for the sins of an unhealthy diet, but it can fill in the nutritional holes that can plague even the most conscientious eaters.

Shen: The Heart and Mind in TCM

In TCM, there is the concept of Shen, which may be thought of as the mind or spirit, but which is said to reside in the heart. As women age, it is believed, their yin becomes more deficient, leading to perturbations of Shen, which might include symptoms such as insomnia, irritability, and heart palpitations. Such disturbances are preferably prevented, but are also treated with TCM formulae for the heart.

Antioxidants: Alpha-Lipoic Acid, Vitamins C and E, and Beta Carotene

Although studies to date have been inconclusive regarding the use of antioxidants in the prevention of atherosclerosis, because the physiology of the disease involves oxidation, there have been proposed mechanisms by which these substances may be effective: removing reactive oxygen species, and improving the endothelial nitric oxide (NO) bioavailability. A 40% reduction in CVD risk was found in women with high vitamin E intake in the large Nurses' Health Study. In individuals with known CAD, a prospective study found vitamin E to reduce the risk of nonfatal MI. Another large prospective study, the α-Tocopherol, β-Carotene Cancer Prevention Study, failed to find a decrease in CAD in men over an 8-year period of time. Physicians taking 50 mg of β-carotene every other day also had no decrease in CAD in the Physicians' Health Study.[586]

Niacin

Niacin is currently considered the most effective drug for elevating HDL cholesterol, and is commonly combined with statins to increase the rate of improvement in cholesterol levels. Flushing is the major side effect, but can be minimized by taking a baby aspirin 30 minutes prior to taking niacin. Niacin is contraindicated in patients with liver disease, and may transiently lead to an elevation in liver function test results even in healthy patients. Niacin may make glycemic control more difficult in diabetic patients and may aggravate arthritis associated with gout.

Magnesium and Potassium

Low serum magnesium has been associated with an increased risk of heart disease, particularly hypertension, ischemic heart disease, CHF, sudden cardiac death, atherosclerosis, and associated risk factors such as insulin resistance and diabetes. Daily supplementation of 400 mg is recommended, in addition to a magnesium-rich diet, and is especially important for patients on thiazide diuretics, which lead to urinary magnesium loss. Potassium has overall protective effects on the cardiovascular system, and lowers blood pressure and prevents stroke. A diet rich in fruits and vegetables provides substantial potassium. Patients on high-sodium diets who are unable to reduce their sodium intake may receive additional protective benefits in cardioprotection by consuming a high-potassium diet.

Arginine

This semi-essential amino acid appears to encourage production of NO derived in the endothelium. Animal studies so far have demonstrated the ability of L-arginine to

Is There More to Chocolate than Good Taste?

Chocolate is now estimated to be the most significant source of dietary antioxidants in the Western world. A 100-g bar of milk chocolate contains 170 mg of flavonoid antioxidants, procyanidins, and flavonols. Cocoa is especially rich in flavonoids, and dark chocolate has the highest flavonoid content of all—comparable to green tea and red wine. Consumption of chocolate has been often hypothesized to reduce the risk of cardiovascular disease (CVD) caused by chocolate's high levels of stearic acid and antioxidant flavonoids. However, debate still lingers regarding the true long-term beneficial cardiovascular effects of chocolate overall. A review from 1966 through 2005 for experimental, observational, and clinical studies of relations between cocoa, cacao, chocolate, stearic acid, flavonoids (including flavonols, catechins, epicatechins, and procynadins) and the risk of cardiovascular disease (coronary heart disease (CHD), stroke) yielded a total of 136 well-designed studies. The body of short-term randomized feeding trials suggests cocoa and chocolate may exert beneficial effects on cardiovascular risk via effects on lowering blood pressure, anti-inflammation, antiplatelet function, higher HDL, decreased LDL oxidation.

It appears that one of the great culinary pleasures in life may actually also be part of a heart-healthy diet, in moderation, of course![587]

prevent lesions from forming in the endothelium of vessels, as well as diminishing ischemic and reperfusion injury in acute MIs. In humans, is it associated with increased exercise capacity in persons with CAD, decreased anginal episodes, and may play a role in prevention of atherosclerosis.

Coenzyme Q10

This lipid-soluble antioxidant may decrease oxidation of LDL cholesterol and plays an active role in the manufacturing of ATD, vital for energy in the myocardium. Human clinical trials show patients who received CoQ10 had better exercise tolerance and less angina. Cardiac function after coronary bypass graft surgery was better in those patients who received pretreatment with CoQ10 1 week prior to surgery.

Folic Acid, Vitamins B_{12} and B_6

Necessary for the metabolism of homocysteine, these vitamins may be crucial to minimize the homocysteine-associated endothelial dysfunction.

Omega-3 Fatty Acids

Studies have indicated that these substances may play a direct role in the reduction of atherosclerosis, with positive effects on endothelial function and vascular tone, even at physiologic doses. They are felt to inhibit platelet aggregation, lower levels of fibrinogen and promote healthier endothelial function. The American Heart Association recommends at least two servings of fish weekly, particularly salmon. Mercury-free fish oil capsules are available for those concerned about mercury contamination in fish, a very legitimate concern, and are a safer option for pregnant women and children, who are advised not to consume fish regularly because of the high risk of receiving toxic levels of mercury through dietary intake.

Grape Skin Products and Red Wine

Resveratrol, grape skin extract found in grape products along with flavonoids and proanthocyanidins, has been found to contain antioxidant and anti-inflammatory activity. It also has demonstrated the ability to inhibit platelet aggregation and promote vasodilatation.[586]

ADDITIONAL THERAPIES

Smoking Cessation

Perhaps the most significant contribution an individual can make to prevent CHD is the cessation of smoking (see risk factors for CHD).

Exercise

Individuals at risk for CHD need to establish an exercise program that is individually appropriate and feasible. Yoga, tai chi, aerobic walking, dancing, swimming, etc. all provide physical activity necessary for cardiovascular fitness.

Mind–Body

Meditation and deep relaxation techniques assist in management of daily life stresses, which contribute to the development of CHD. Stress and depression are associated with an increased risk of heart disease.

CASE STUDY:

Carol is a 51-year-old mother of two children who experienced her last menstrual period 14 months ago. She experiences rare, mild hot flashes and no night sweats, but continues to be mostly troubled by palpitations associated with a feeling of anxiety. She has difficulty falling asleep most nights, stating that she lies in bed and cannot shut her mind off. She sleeps for 5 to 6 hours night. Carol has been thinking about HRT, but is afraid because of her mother's history of embolic disease and hyperlipidemia. Carol's history is unremarkable for major acute disease but positive for episodic migraine with visual field cut occurring only premenstrually, and mild Raynaud's disease. Both of her parents have mild hypertension; mother with elevated cholesterol and angina, osteoporosis with severe osteoarthritis, and a history of a thrombophilia requiring lifetime anticoagulation.

Carol works full time as a nurse in a busy hospital clinic, and states she enjoys her job but is just too busy at times. She has one child in college and one in high school, both demanding considerable attention periodically. She also spends a great deal of her time caring for her mother, who has difficulty with ambulation caused by severe degenerative joint disease from osteoarthritis. She is married, and relates a good supportive relationship

with her husband. She does not smoke, and drinks about two to three glasses of white wine a week. She describes herself as ''active, happy, but too busy and stressed. I worry a lot.'' She has no history of endocrine dysfunction; however she has steadily been gaining weight (10 to 12 lb) since menopause, and is worried about a possible thyroid abnormality, even though all lab tests are normal.

Carol complains of episodic palpitations, associated with a feeling of chest tightness at times. These occur about three to ten times a day, both day and night. A feeling of anxiety may accompany them. She denies shortness of breath, nausea, or diaphoresis. She also complains of chronic shoulder and neck tension, and occasional tension headache, which she treats with NSAIDs.

Medications/Supplements

Carol occasionally uses NSAIDs for headache and prophylactically for migraine (she is unable to use triptans caused by Raynaud's). She occasionally takes a multivitamin and used echinacea at the onset of colds.

Diet

Carol eats mostly fast foods. She eats on the run, from job to activities, to parents. She often eats fried chicken sandwiches, French fries, and colas; she rarely has a salad. She does not have time to cook much during the week.

Assessment

1. Postmenopausal woman with:
   a. Palpitations
   b. Stress
   c. Insomnia
   d. Weight gain
2. History of migraines with focal neurological symptoms
3. History of Raynaud's disorder
4. Family history of osteoporosis, thrombophilia, hyperlipidemia, and hypertension

Plan

1. *Botanical Tincture Formula 1: Daytime*

Hawthorn	(*Crataegus oxyacantha*)	40 mL
Motherwort	(*Leonurus cardiaca*)	20 mL
Skullcap	(*Scutellaria lateriflora*)	20 mL

Total: 100 mL

Dose: 5 mL tid
The formula is intended to provide gentle cardiac and nervous system support, and help with stress relief.

2. *Botanical Tincture Formula 2: Evening*

Valerian	(*Valeriana officinalis*)	40 mL
Passionflower	(*Passiflora incarnata*)	40 mL
Kava Kava	(*Piper methysticum*)	20 mL

Total: 100 mL

Dose: 5 mL 30 to 60 minutes prior to bedtime
This formula is designed to help reduce anxiety and tension, both emotional and musculoskeletal, and promote sleep.

3. *Supplements:* Daily multivitamin with adequate Bs and folic acid, omega-3 fatty acids (fish oil capsules), and concentrated blueberry extract daily (antioxidant)
4. *Diet modification:* Increase green, leafy vegetables, soy foods, and garlic in diet. Meats should be lean, broiled (not fried). Reduce overall carbohydrate load and add more vegetables in general. Substitute red wine for white, as long as no migraine results. Snacks should be fresh fruit and nuts.
5. *Exercise:* Start with walking for 30 minutes three times per week. Work toward a 15-minute-mile (aerobic) walk. Simple upper body weight exercise with professional direction (gym). Consider yoga three times per week.
6. *Mind–Body:* Advised meditation or relaxation exercises on a daily basis. Warm baths with lavender essential oil (5 to 7 drops per bath) at bedtime, and write in a journal for stress relief each night around 30 minutes before bed.

Follow-up

Phone call 1 week; return visit 1 month. Carol experienced restful sleep within 2 days of beginning the botanical formulas. Within 2 weeks of regular use, she experienced significantly fewer palpitations, and less anxiety associated with her daily life and work. She walks only about two to three times a week because of the weather (winter), but is joining a gym for consistent exercise opportunities (mostly because of concern over her weight) and expert direction. She still struggles with her diet because of the time factor but is making adjustments gradually. After taking a class on relaxation techniques, she manages to incorporate this into her morning and evening schedule on a daily basis. She loves the baths, and journal writing has helped her gain perspective on her life, use her creative writing skills, and prepare for sleep.

OSTEOPOROSIS, BONE HEALTH, AND MENOPAUSE

Robin DiPasquale

Osteoporosis is defined as a skeletal disorder characterized by compromised bone density predisposing an individual to increased risk of fractures.[588] It is the most common bone disease affecting humans, and disproportionately affects postmenopausal women. Osteoporosis is now considered one of the most important diseases women face, affecting as many as 18% (approximately 12 million) of US women over 50, with another 37% to 50% (approximately 5 million) having osteopenia, bone loss that is less advanced than osteoporosis.[588–590] White women are at greatest risk for osteoporosis, although all races are affected, as are men in lesser but still significant numbers.

Peak bone mineral density (BMD) is typically achieved by about age 30, after which time bone loss begins to outweigh bone formation, a process that accelerates with menopause. In the 5 to 7 years immediately following menopause, women may lose as much as 20% of their BMD, largely as a result of declining estrogen levels and the resultant loss of the positive effects of estrogen on

bone formation and protection against bone loss.[590] Aging itself is also associated with changes that contribute to bone loss; for example, inefficient kidney function that leads to poor calcium reabsorption, which in turn leads to hyperparathyroidism and increased bone mineral loss. By age 80, at which time risk of falls and fractures is markedly increased, women may have lost as much as 30% of their BMD.[588] The risk of osteoporotic fractures doubles every 7 or 8 years after age 50.[588]

Osteoporosis is often a silent condition; the first sign of the disease is commonly a fracture.[588,590] Major sites for osteoporotic fractures include the hip, wrist, and vertebrae, but other sites, for example, thoracic fractures, may occur, leading to restriction of lung function and digestive problems. Most nonvertebral fractures occur as the result of a fall; however, vertebral fractures commonly occur spontaneously, often with simple activities such as stepping off a curb or sitting down in the seat of car, or without a provoking cause.

Fractures resulting from osteoporosis account for substantial morbidity and mortality.[591] As many as 25% of women who sustain a hip fracture will die within one year of the incident, and 50% of women who sustain a hip fracture do not return to their full functional status, becoming dependent on others for their daily needs, with 25% to 30% requiring long-term care.[588,590–592] In addition to the physical, emotional, and psychological costs to individuals, including loss of function, pain, dependence, and loss of self-esteem and negative changes in body image, this condition carries a considerable financial and social price for both family and society.[590,591] It is estimated that the directly attributable costs of osteoporosis in the United States may be as high as $10 billion annually, excluding the costs of long-term home care, a figure expected to grow as the US population ages over the next couple of decades.[589]

Osteoporosis is classified as either type 1 or type 2 osteoporosis, reflecting regional BMD loss, patterns of fracture, hormonal changes, and causal mechanisms.[589,590] Type 1 osteoporosis typically affects women within the first 10 years after menopause and is characterized by fractures that occur at sites rich in cancellous bone, such as crush fractures of the vertebrae and Colles' fracture of the distal forearm. Type 2 osteoporosis is associated with age-related changes, such as secondary hyperparathyroidism, impaired vitamin D metabolism, and impaired osteoblast function, vitamin D deficiency, inadequate calcium intake, and impaired bone formation, which occur as a late consequence of estrogen-deficiency osteoporosis. Type 2 osteoporosis is characterized by fractures at sites containing substantial portions of both cortical and cancellous bone including the hip, proximal humerus, proximal tibia, and pelvis. Anterior wedging of the vertebra of the dorsal spine is also common.[590]

Risk factors for developing osteoporosis include:

- Family history of osteoporosis or hip fracture in a parent
- Advanced age (risk begins to increase >50 years old and is greatest at ~80 years old)
- Low BMD (demonstrated by DEXA scan—see Diagnosis)
- Prior fracture
- Thinness [body weight <127 lb (57.7 kg) or body mass index (BMI) <21]
- Smoking in any amount
- Low calcium or vitamin D intake
- More than two alcoholic beverages daily
- Oral or intramuscular glucocorticoid use for >3 months
- Low levels of physical activity
- Increased fall risk[588,591]
- Warfarin use >1 year[593]

Factors that increase fall risk include impaired vision, dementia, poor health or frailty, low physical activity, problems with balance, history of syncope or seizures, and history of recent falls.[588,591] Medications include antihypertensives, anticholinergics, sedatives, and analgesics. Polypharmacy also may increase the risk of falls as can via potential drug interactions. The greater the number of risk factors, the greater the risk of falling, with four combined risk factors leading to an 80% increased risk of falling.[588]

A number of disease states and additional factors can lead to osteoporosis, commonly as a result of increased bone loss, or problems with mineral excretion, absorption, or deposition. Examples include but are not limited to:

- *Genetic disorders:* osteogenesis imperfecta; thalassemia; hemochromatosis
- *Calcium balance disorders:* hypercalciuria; vitamin D deficiency
- *Endocrinopathies:* cortisol excess; Cushing's syndrome; gonadal insufficiency; hyperthyroidism; Type 1 diabetes mellitus; primary hyperparathyroidism
- *Gastrointestinal disorders* that prevent calcium absorption
- *Chronic renal disease*
- *Medications:* oral or intramuscular glucocorticoids for >3 months; excessive thyroxin intake; long-term phenytoin use; heparin; cytotoxic agents; GnRH agonists; immunosuppressives[588]

Bone health cannot be viewed in isolation from the environment in which we live. The depletion of vital nutrients in our food, sedentary lifestyles, and increased levels of stress all diminish bone density. Our elderly population is faced with the major challenge of being socially marginalized, frequently living alone, consuming diets inadequate in nutrients essential for bone health as well as having few to depend on for assistance getting up and down flights of stairs or other activities of daily living (ADL) that predispose to risk of fracture.

It is significant to note that optimal bone building and prevention of osteoporosis begins in childhood, and is well under way in the teen years. Ninety percent of bone density is achieved by the age of 20, and bone remodeling continues to be optimal until about the age of 35. Education about osteoporosis prevention is ideally begun early in life when girls are still actively laying down vital bone matrix. Adolescents also face unique threats to bone health; for example, inadequate nutrition and consumption of large amounts of soft drinks that can compromise nutrition and predispose to later development of osteoporosis.[594,595] A specific area of concern for development of healthy bones in adolescent girls is

the attempt to conform to the cultural idealization of thinness, which leads to dieting, a decrease in caloric intake, and a decrease in nutrient intake. Emotional and psychological stress also may interfere with bone development in the teen years. Attention to lifestyle beginning at a young age may be among the most important strategies we take in the prevention of this devastating disease.

DIAGNOSIS

It is recommended by the North American Menopause Society that BMD be measured in:[588]

- Postmenopausal women with medical causes of bone loss regardless of age
- Postmenopausal women at least 65 years of age regardless of additional risk factors

In 1994, the World Health Organization (WHO) developed an international standard for evaluating bone strength.[596] The North American Menopause Society supports the WHO definition of osteoporosis in postmenopausal women as a BMD-T score of less than or equal to standard deviations (SD) in the following the mean at the total hip, femoral neck, or lumbar spine (posterior-anterior measurement, not lateral). The BMD-T score is derived by comparing the current BMD of the patient to the mean peak BMD of a normal young adult population of the same gender. For women, the reference standard is white women age 20 to 29 years old, as this is the age at which physiologic bone density is at or near its peak. If the patient's body habitus (e.g., obesity) or medical conditions (e.g., arthritis) make such measurements difficult or invalid, then the density of the distal one-third of the radius bone may be considered a valid diagnostic site.[588] Osteopenia, suggestive of early BMD loss, is defined as BMD 1.0 to 2.5 SD in the following mean. Osteoporosis is also clinically diagnosed regardless of T-score based on the presence of a fragility fracture.[588]

Dual energy x-ray absorptiometry (DEXA) is the gold standard screening test for osteoporosis and for assessing bone mineral density. A first DEXA is generally taken between the ages of 40 to 50 as a baseline. This baseline can then be referenced at further points along the menopausal transition. The National Osteoporosis Foundation recommendations for DEXA screening are:

- Postmenopausal women under 65 with one or more of the following risk factors:
- Oral steroids
- Thyroid problems
- Eating disorders
- Amenorrhea 3 months or longer
- Family history of osteoporosis
- Smoking
- Alcoholism
- Very thin/small body frame
- Low calcium intake
- Postmenopausal women who have had a past bone fracture
- Any woman over 65 years old
- Premenopausal women with any of these risk factors

Serum and urine markers of bone turnover, although sometimes used to assess therapeutic response to treatment, are not reliable for the diagnosis of osteopenia and osteoporosis, and are not especially clinically useful.[588]

Monitoring weight and height is a simple, important clinical screening method for evaluating bone health. A decrease in height or weight, especially postmenopausally, may be indicative of decreasing BMD and should lead to further evaluation. Assessment for chronic back pain is also essential, as this may be the only clinical indication of vertebral fractures. Kyphosis is an important indication of bone loss and possible vertebral fracture.

CONVENTIONAL TREATMENT

The primary goal in the prevention and treatment of osteoporosis is the deterrence of fractures via minimizing or stopping bone loss, maintaining bone strength, and reducing or eliminating factors that increase fracture risk.[588] Conventional medical approaches include nonpharmacologic and pharmacologic treatments. The treatment of secondary medical conditions (e.g., predisposing diseases, medications) that can lead to osteoporosis (see the preceding) is not discussed in the following.

Nonpharmacologic Approaches

Nutrition

Calcium. The role of calcium in establishing bone mineral density during childhood and adolescence is well established, as is the important role of calcium supplementation during pregnancy and lactation. It is optimal to obtain calcium from dietary sources; however, because most diets do not supply an adequate amount, supplementation is advised at the recommended daily allowance (RDA) of between 1200 and 1500 mg daily from adolescence through perimenopause.[588]

Substantial epidemiologic data have been amassed assessing the relation between calcium intake and bone density. The efficacy of calcium supplementation to prevent and treat osteoporosis in later life has been controversial.[589] Most researchers and clinicians support a valuable role for supplementation.[588,589,593,597] Reviews of over 20 studies on postmenopausal women have concluded that calcium supplementation can decrease bone loss by ~1% per year.[593] In a meta-analysis of 13 trials, calcium-induced significant mean gains (or slowed loss) of 0.6% at the forearm, 3% at the spine, and 2.6% at the femoral neck. A more recent meta-analysis found that in 15 trials, calcium changes were 1.66% at the lumbar spine and 1.64% at the hip.[593] Case-controlled studies and some double-blind, placebo-controlled studies, but not all, have corroborated the finding that 500 to 1000 mg of daily calcium supplementation may offset postmenopausal bone loss for at least 3 years in women age 40 to 70 years old. Calcium supplemented postmenopausal women also demonstrate lower levels of serum PTH and alkaline phosphatase concentrations decreased and urinary hydroxyproline excretion, all markers of bone turnover.[589,590]

The beneficial effect of calcium intake on bone mass may be greatest in older and late postmenopausal women, and in women with low baseline calcium intakes.[593] Calcium supplementation also appears to

improve the efficacy of antiresorptive therapy, for example, hormone replacement therapy (HRT), on bone mass.[588,589,593,597] It is estimated that approximately 1500 mg/day calcium would be needed to counteract bone loss associated with the estrogen depletion that occurs postmenopausally.[588,589]

Many forms of calcium supplements are available. Calcium citrate is the most bioavailable and leads to greater inhibition of PTH compared with calcium carbonate.[589] Also, the absorption of calcium citrate is independent of stomach acid levels, which commonly decline with age, whereas calcium carbonate requires adequate stomach acid for absorption and is thus better absorbed when taken with meals.[589] The primary advantage of calcium carbonate is that the amount of calcium per pill is higher; therefore, fewer pills are required.

Food sources of calcium include dairy products, dark green leafy vegetables, tofu, sesame seeds, almonds, sardines (bones included), and seaweeds. Calcium absorption can be inhibited by foods high in oxalic acid (e.g., spinach) and phytate-rich foods, for example, wheat bran.[588] Calcium supplementation at the RDA is not expected to cause kidney stones; however, supplementation is contraindicated in women with renal calculi.[588]

Vitamin D. Vitamin D is actually a hormone precursor, essential for the intestinal absorption of calcium and bone mineral deposition.[589] Genetics may play up to a 75% role in the ability to effectively synthesize vitamin D and thereby appears to contribute significantly to the 80% supposed role of genetics in determining peak bone mineral density in children and young adults.[589] Vitamin D synthesis begins in the skin upon exposure to ultraviolet light; further synthesis occurs in the liver, and finally the kidney where the active form, calcitriol, is produced. Aging can decrease the skin's ability to synthesize provitamin D, and age also tends to decrease time spent exposed to sunlight as well as consumption of milk fortified with vitamin D. Individuals living in northern latitudes are also more prone to vitamin D insufficiency caused by overall less sun exposure than those living in southern climates. Use of sunscreen further decreases vitamin D synthesis.

Reduction of both hip and other nonvertebral fractures, as well as delays in bone loss, have been demonstrated in trials supplementing 700 to 800 IU of vitamin D with 500 mg calcium daily; thus, many experts are recommending supplementation of 700 to 800 IU vitamin D daily with calcium for women over 65 and for those at risk for osteoporosis.[590,591,593,597,598] Studies using vitamin D supplements alone have had less impressive results. Sources of vitamin D include sunlight, fortified dairy, fish liver oils, butter, and oily fish.[588] *At recommended doses*, vitamin D is considered safe, well-tolerated, and with no expected serious adverse effects.[589] Vitamin D analogues (see Calcitriol, in the following) have been shown to have greater benefit in osteoporosis.

Vitamin K. Vitamin K is a fat-soluble vitamin found in dark green leafy vegetables, fruits, and vegetable oils with small amounts in dairy products and grains, and a subset of vitamin K found in fermented dairy and soy products, fish, meat, liver, and eggs.[593] Vitamin K is required for the synthesis of osteocalcin, the matrix that provides structure to bone, as well as for preventing excess urinary calcium excretion.[593] Studies have demonstrated that adequate vitamin K intake is associated with positive effects on bone turnover, and that daily supplementation is associated with a reduced postmenopausal bone loss, particular of the hip.[588,593] Caused by limited current evidence, there are insufficient data to recommend the required level of vitamin K supplementation for optimal bone health.[593] A daily dose of 1 mg/day of vitamin K (phylloquinone) is recommended based on a single trial using a 3-year supplementation of this dose with of calcium and vitamin D and demonstrated reduced hip bone loss.[588,593] A healthy diet, high in fruits and vegetables, ensures adequate vitamin K for most people.[593] Vitamin K supplementation interferes with the effectiveness of warfarin and is thus contraindicated for patients taking this medication.

Vitamin C. Vitamin C is an essential cofactor for collagen formation and synthesis of hydroxyproline and hydroxylysine. Low consumption of vitamin C has been epidemiologically associated with lower bone mass and a faster rate of BMD loss; however, there are no clinical trials evaluating the role of vitamin C in osteoporosis.[593] Recommended intakes of five or more servings of fruits and vegetables daily should provide adequate vitamin C for bone health.

Fluoride. Since the late 1930s, it has been known that fluoride can increase BMD. It is now readily available in commonly ingested substances—fluorinated water, juices made with fluorinated water, toothpaste, and mouthwash, for example. It is highly absorbable in the stomach. In large doses, fluoride actually causes bone to become excessively brittle, but at supplemental doses of 50 mg/day, along with calcium supplementation, can promote bone strength and decrease vertebral and femoral osteoporotic fractures, by increasing osteoblast recruitment and decreasing osteoclast activity, and by forming fluoroxyapatite a more densely packed bone matrix than the normal hydroxyapatite.[589,599] Toxicity, skeletal problems, and GI side effects are dose dependent and are especially associated with plain fluoride and monoflurophophsate.[592] Slow release tablets do not cause GI side effects.

Vitamin A. Excess consumption of vitamin A in the form of retinol equivalents (RE) at doses greater than 1500 micrograms daily has been associated with a doubling of the rate of hip fractures one study in the United States and Sweden but not in Iceland or other US studies. Beta-carotene supplementation has not been associated with an increase in osteoporosis or other fractures.[593] Patients at risk for osteoporosis should avoid excessive supplementation with vitamin A from retinol.

Protein. The Framingham osteoporosis study, a longitudinal cohort trial, demonstrated that adequate protein intake in women over 75 years could help minimize bone loss.[600] Also, protein supplementation of 20 g/day in patients with a mean age of 82 years hospitalized for hip fracture have been shown to have dramatically shorter hospital stays of a mean of 69 days versus 102 days for placebo and improved clinical outcome.[588]

Isoflavones

A significant amount of data from numerous studies on cultured bone cells and rat models of postmenopausal osteoporosis support a significant bone-sparing effect of the soy isoflavones, genistein, and daidzein; however, although a small number of human studies have shown promising results, these have been variable, with some authors reporting no benefits at all.[588] Human clinical studies have generally been of short duration and with relatively small sample sizes, making it difficult to observe significant and accurate bone changes.[601] Overall, the cumulative data suggest that diets rich in phytoestrogens have bone-sparing effects in the long term, however, the extent of the benefits and the exact mechanisms of action are currently undetermined.[601] No studies have been conducted to evaluate the effects of isoflavone intake on fracture rate.[601] Given the safety of legumes in the diet as a high-quality protein source, and the possible benefits, it seems reasonable for menopausal women to include traditional soy products and other beans as a regular part of the daily diet.

Ipriflavone

Ipriflavone (IP) is a synthetic derivative of naturally occurring isoflavone, manufactured from daidzein. It has been shown to inhibit osteoclast formation without suppressing the rate of bone formation.[602] IP also shows bone-forming activity through proliferation of osteoblast cell lines and inhibition of parathyroid hormone activity.[603] More than 60 human study trials have been published in the last 10 years evaluating ipriflavone for prevention and treatment of osteoporosis, and it is a popular nonprescription supplement. Before 2001, many of the studies showed promising outcomes. Throughout nine Italian sites, 196 subjects were randomly assigned to either ipriflavone 200 mg tid with food or placebo. All subjects were also give 1000 mg/d calcium carbonate or gluconolactate. Bone mineral density (BMD) by X-ray of at least one standard deviation in the following mean was a requirement for inclusion. After 2 years, the placebo group showed a decline in BMD, whereas the IP group maintained bone mass.[604] Two studies were able to show a slight increase, primarily in vertebral bone, when using IP, after two years and one year respectively.[605,606] One additional study looked at 91 postmenopausal women who were divided into early menopause (<5 years) or late menopause (>5 years). After 6 months of treatment with IP, the late menopause group had a statistically significant increase in BMD at the lumbar spine while the placebo and early menopause group showed no statistically significant differences.

In 2001, the Multi-Center European Fracture Study, which consisted of four European sites, 205 and 52 Belgian subjects, 197 Danish subjects, and 20 Italian subjects, published its 3-year outcome. Women ages 45 to 75, with a natural menopause of at least one year and with BMD at least 2 SDs the mean for perimenopause were given 200 mg of ipriflavone 3 times daily or placebo. All subjects were also given a 500 mg/d calcium supplement. BMD was determined by DEXA at onset and every 6 months throughout the 3 years and bone resorption markers were evaluated every 6 months as well. After 36 months, there was no statistically significant difference between the BMD and the bone resorption markers in IP and placebo group. Overall, there is conflicting data on the benefits of ipriflavone for prevention or treatment of bone loss. There are enough studies, however, showing that IP helps prevent bone loss at menopause to merit continued study.

Ipriflavone is associated with a variety of side effects. Gastrointestinal symptoms have been reported and lesser side effects include rash, headache, depression, drowsiness, and tachycardia. A decrease in lymphocytes was shown with the ipriflavone group during IP treatment.[607]

Questions have arisen as to the safety of long-term use of ipriflavone because of its estrogen-like effects. Two studies have demonstrated no changes in serum LH and FSH levels, prolactin, and estradiol, nor changes in vaginal cytology between ipriflavone and placebo, with the estrogen arm of the study demonstrating a considerable increase in superficial vaginal cells.[163] The recommended dose is 200 mg three times daily, except in patients with renal insufficiency in which case is creatinine clearance is between 40 and 80 mL/min, the dose should not exceed 400 mg/day and if the creatinine clearance is less than 40 mL/min, the dose should be no more than 200 mg/day. In one large study, ipriflavone use was associated with a significant incidence of lymphopenia, which resolved within 12 to 24 months of discontinuation of use.[163]

Exercise

A Cochrane Database Review of 18 randomized controlled trials, including a total of 1423 subjects from North America, Europe, and Asia, reported that aerobics, weight bearing, and resistance exercises were all effective in enhancing the BMD of the spine. The analysis also showed walking to be effective in improving BMD of the spine and hip. The review results showed some evidence that the slowing of bone loss was most effective with exercise done for 1 year or longer.[608]

A second meta-analysis was undertaken looking at aerobic exercise on bone density at the hip in postmenopausal women. Six studies were evaluated with the conclusion that aerobic exercise has a moderately positive effect, 67% of the exercise groups demonstrating benefits vs. the nonexercise groups. It was noted, however, that the activity should probably be weight bearing to optimize bone density.[609]

Elite and professional athletes have demonstrated greater than 12% higher BMD of the hip and almost 9% greater BMD of the spine than controls, even many years after discontinuing competitive training.[589] The benefits of exercise appear to be independent of estrogen levels.[589] The Surgeon General's Guidelines for moderate physical exercise, written in 1996, recommends some form of workout 5 or more days per week with moderate intensity of the activity, including a slight increase in breathing and little or no sweating, for 30 minutes or more per session. It may be necessary for patients to start off more slowly, progressively increasing their time toward

this goal. For elderly women with osteoporosis, moderate exercise also may play an important role in preventing fall risk by improving strength and balance, with up to a 75% reduction in falls according to the 2006 North American Menopause Society Position Statement on the Management of Osteoporosis in Postmenopausal Women.[588]

Smoking Cessation

Cigarette smoking is reported to have definite deleterious effects on BMD, increasing the risk of fractures.[588] Smoking cessation can be very difficult for patients to achieve, but given the availability of a wide-range of tools and the numerous deleterious effects of smoking in addition to BMD loss, attention should be given to helping willing patients achieve this goal.

Alcohol Reduction

Alcohol consumption of greater than seven drinks per week is associated with an increased overall risk of falls as established by the Framingham Heart Study.[588]

Pharmacologic Therapies

Following are the descriptions of the major categories of drug therapies that are generally recommended for osteoporosis treatment.

Bisphosphonates

Alendronate (Fosamax) and Risedronate (Actonel) are members of a class of antiresorptive drugs called bisphosphonates, approved in the United States for the treatment of osteoporosis and demonstrated to be effective in the prevention of vertebral and nonvertebral fractures. Bisphosphonates are a group of synthetic analogues of pyrophosphate, absorbed into the hydroxyapatite of bone, known to act as nonhormonal inhibitors of bone resorption. In a randomized controlled trial of more than 2000 women with previous vertebral fracture, Alendronate reduced the risk of hip and wrist fractures by 50%.[610] Multiple other trials have found that at a dose of 10 mg daily, BMD is increased and risk and incident of fracture is decreased.

Esophageal and gastric irritation are common side effects of these medications, and patients are required to drink water and remain in an upright position for 30 minutes after ingestion to prevent irritation. Severe side effects include esophageal erosion and esophagitis.[611] Weekly dosing schedules are available for these drugs; all fracture data are from studies in which there was a daily dosing protocol.[588] This class of drugs is contraindicated in patients with a creatinine clearance of 30 mL/min or greater. Discontinuation of therapy after 4 to 5 years of continuous use is followed by initially BMD stability but an eventual return to pretreatment levels over time.[588]

Calcitonin

Salmon calcitonin is an antiresorptive agent that acts by inhibiting osteoclast activity. Calcitonin may increase 1,25 (OH)2 D, as well as intestinal calcium absorption, all leading to an increase in bone mineral density (BMD) and reported reductions in vertebral fractures of up to 66%.[612] It may be administered either intranasally or by subcutaneous injection. In two studies, it was shown to reduce vertebral but nonvertebral fractures.[591] It has a low side effect profile, although in one study was shown to cause headache and increase menopausal symptoms.[591] Intranasal use has been associated with some gastrointestinal discomfort, facial flushing, rash, and dry nasal mucosa.[163]

Calcitriol

Calcitriol is an analogue of 1,25-dihydroxycholecalciferol, Vitamin D3, the active form of vitamin D. Vitamin D analogs have been found to be effective at reducing fractures compared to placebo and vitamin D in postmenopausal women.[591] One study suggested an increased risk of hypercalcemia with calcitriol compared with vitamin D; however, alphacalcitriol, another vitamin D analog, was not associated with this risk.[591]

Hormone Replacement Therapy

The beneficial effects of estrogen replacement therapy (ERT) on BMD and fracture prevention are well established.[588,590,591] Estrogen appears to act both directly and indirectly on bone. Direct actions occurs through osteoblast stimulation and inhibition of osteoclast activity, and indirect action occurs via antagonizing actions of estrogen on cytokines, which stimulate osteoclast activity.[589]

A 2002 meta-analysis of 57 RCTs found consistent improvements in BMD with estrogen replacement or estrogen and progesterone replacement therapies over placebo. In trials of 2 years of length, the mean difference in BMD was 6.8% at the lumbar spine and 4.1% at the femoral neck.[590] Although trials such as the Women's Health Initiative Study and the Postmenopausal Estrogen/Progestin Intervention Trial have demonstrated the harmful effects of estrogen replacement, including increased incidence of cancer (with the exception of colon cancer) and cardiovascular disease, the benefits of hormone replacement on BMD were clearly shown.[588,590,613] Of note is that rates of BMD loss do not differ significantly between women stopping HRT and women who never underwent treatment with HRT.

Until recently, the minimum effective dose of estrogen has been considered to be 0.625 mg/d conjugated equine estrogen (CEE), 0.05 mg/d transdermal estrogen, or equivalent. Recent promising research has demonstrated positive effects of estrogen on BMD with doses as low as 0.3 mg/d orally or 0.025 mg/d transdermally, with no changes in endometrial thickness, however, it is unclear whether, for most women, the potential risks of higher doses of HRT outweigh the benefits.[590,591]

Selective Estrogen Receptor Modulators

Selective estrogen receptor modulator (SERM) is a term for compounds that can bind to and stimulate estrogen receptors but whose effects on target tissue differ from those of estrogen.[589] Selective estrogen receptor modulation retains the action of estrogen on certain receptors, for example, in the cardiovascular system and skeletal

systems, without activating uterine and breast estrogen receptors. Their development was pursued in the treatment of osteoporosis as an alterative to HRT with its potentially serious adverse effects of breast and endometrial cancers. SERMs have been shown to selectively decrease bone resorption.[614] One of the most prescribed SERMs is raloxifene, which acts primarily as an antiresorptive, inducing a positive shift in calcium balance in postmenopausal women. Two large RCTs in postmenopausal women with osteoporosis found that raloxifene reduced vertebral fractures compared with placebo after 36 months but found no significant difference in nonvertebral fractures after up to 8 years. Another small RCT found no significant difference between raloxifene and placebo in fractures over 1 year. The two large RCTs found that raloxifene reduced the risk of breast cancer. The first large RCT found that raloxifene increased the number of women with venous thromboembolic events compared with placebo. The second large RCT found that raloxifene increased the risk of fatal stroke.[591]

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

Aviva Romm, Robin DiPasquale

There is very little evidence of a strong role for botanicals in the treatment of osteoporosis; however, practitioners can play a significant role in promoting healthy lifestyle choices and changes that lead to prevention of the disease (Table 19-12). Isoflavonoes were discussed previously, with specific herbal sources presented in brief in the following. There also may be a role for herbs as SERMs. There is a vital folk tradition of using infusions and herbal vinegars to build bone; however, these products have not been evaluated for mineral content or clinical efficacy, although appear largely harmless.

Phytoestrogens: Soy, Red Clover, and Alfalfa

Phytoestrogens were discussed previous under nonpharmacologic interventions for osteoporosis. They are found relatively abundantly in legumes, especially in soy products, alfalfa, and red clover. Although studies have yielded mixed results, there appears to be some modest but beneficial protection against spinal bone loss with the incorporation of soy into the diet.[601] Red clover contains the isoflavone biochanin A, primarily in the foliage. Alfalfa is high in genistein, daidzein, and coumestrol. Freshly ground flax seeds, rich in lignins, about 1 to 3 tsp per day, can be sprinkled on food after cooking, or put into beverages such as juice or smoothies, providing a regular source of lignins in the diet along with those found in fresh fruits, vegetables, and whole grains. One study using Rimostil (a red clover product), which did not have a control group, randomized the patients into three dosage levels, 28.5, 57, or 85.5 mg of phytoestrogen per day. The bone mineral density of the proximal radius and ulna, bones of the wrist, rose 4.1% in a 6-month period with a dose of 57 mg/day. The 85.5 mg/day group rose 3%, whereas the 28.5 mg/day response was not significant.[615]

Black Cohosh

In two different animal studies (in ovariectomized rats) using extracts of black cohosh, positive results were seen in parameters that correlate with bone loss, pyridinoline and deoxypyrimidine rates and osteocalcin and leptin rates respectively. Further, in the study by Seidlova-Wuttke et al., the black cohosh extract BNO 1055 exerted estrogenic activity in the bone but not the uterus. In the study by Nisslein and Freudenstein, results were found to be similar in quality and magnitude to raloxifene.[122,616,617] In a double-blind, placebo-controlled study on black cohosh on 62 menopausal women treated for 6 months with either placebo or BNO 1055, a black cohosh extract, beneficial results were seen on bone parameters with no evidence of increased endometrial thickness.[122] Recent reports on black cohosh have speculated whether its mechanisms of action was in part related to SERM activity; however, it is most likely that black cohosh exerts its influence through non-hormonal pathways, possibly through mechanisms involving neurotransmitters.[172] Black cohosh safety is discussed in Plant Profiles: Black Cohosh.

Nutritive Herbs: Milky Oats, Horsetail, Nettles, and Dandelion Leaf

There is a rich contemporary folk herbal tradition of using nutritive herbs for the prevention and treatment of osteoporosis via supplementation of minerals such as calcium, potassium, and silica. These preparations are typically taken as either foods or strong aqueous

TABLE **19-12**

Herbs Used in the Prevention of Osteoporosis

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Reduce bone loss	Phytoestrogen	*Glycine max*	Soy
		Medicago sativa	Alfalfa
		Trifolium pratense	Red clover
Bone mineralization	Nutritive	*Avena sativa*	Milky oats
		Camilla sinensis	Green tea
		Equisetum arvense	Horsetail
		Taraxacum officinale	Dandelion leaf
		Urtica spp.	Nettles

preparations (8- to 10-hour length for steeping decoctions), and also may be steeped in vinegar for an extended period of time and used by the tablespoon in salad dressings and over other foods. Four herbs particularly stand out as those included as part of the treatment protocol of osteoporosis given by contemporary herbalists and naturopaths: nettles, horsetail, milky oats, and dandelion. Although there have been no studies to demonstrate efficacy in osteoporosis prevention and treatment, they are considered relatively benign herbs and gentle tonics.

Nettles

Nettles are reported to be high in vitamin A (as carotenoids), B complex, C, D, K, and in the minerals calcium, magnesium, manganese, boron, chromium, phosphorus, iron, potassium, and silica, as well as chlorophyll. It is the upper part of the plant that is used, taken as a cooked green vegetable (not raw because of the stinging hairs!), as a strong infusion, or made into herbal vinegar.

Milky Oats

Oats contain vitamins B, C, D, E, K, and carotenes as well as many minerals, including calcium, magnesium, chromium, and silica. The milky oat pods are harvested before their full maturity and are used as tincture or infusion, although eating oatmeal as a breakfast cereal is probably the most effective way to derive nutrients from this herbal food.[163]

Horsetail

Horsetail also has the common name scouring-rush because of its high silica content, which was considered by pioneers as abrasive enough to scour wood and pewter. This silica, along with calcium, magnesium, bioflavonoid, carotenoids, chromium, potassium, iron, and copper, is only bioavailable at a certain stage of the plant's maturity before it opens to an angle of 90 degrees. It is taken as a fresh infusion, a decoction, or a vinegar extract for optimal mineral extraction. Capsules can be used, and are best with freeze-dried plant material. The vinegar extract is made by chopping the fresh plant, filling a jar with the chopped plant material, pouring organic apple cider vinegar to cover the plant and fill the jar and stepping for 2 to 3 weeks, shaking once daily. The herbal vinegar is strained from the plant material and stored in a cool dark place or refrigerated.

Dandelion

Dandelion leaves are vitamin and mineral rich, as are many leafy greens. The leaves are especially rich in calcium, magnesium, manganese, boron, and iron, as well as potassium. They are eaten raw in salads or steamed as a potherb. They also can be prepared as a vinegar extraction, along with horsetail, nettles, and many other leafy greens.

SUMMARY

Adequate nutrition and exercise from a young age are essential for the prevention of bone loss and maintenance of bone mass throughout the life cycle. Healthy living may therefore be the most important resource we have for osteoporosis prevention for future generations. Optimal nutritional intake especially calcium and vitamin D, and protein throughout a woman's life are necessary for bone strength and health. Avoiding cigarette smoking and reducing risk factors for falls is also significant. Finally, a number of nonpharmacologic and pharmacologic strategies are available that can prevent BMD loss and improve bone strength, prior to, during, and after menopause.

VAGINAL DRYNESS AND ATROPHY

Margi Flint

Vaginal dryness and atrophy occur as a result of the estrogen decline associated with menopause. These changes are frequently accompanied by vaginal itching and irritation, vaginal bleeding (especially postcoital), increased risk of vaginal infections, painful intercourse (dyspareunia), decreased arousal, and uterine prolapse. Sexual dysfunction is a significant aspect of vaginal atrophy and dryness. In a large prospective cohort study of women ages 40 to 55 years, the overall prevalence of vaginal dryness was 13.1%, but the prevalence was lower in the early menopausal transition, and increased across the transition.[618]

DIAGNOSIS

Diagnosis is based upon subjective symptom reporting by the client and physical findings including thinning of vaginal tissue, disappearance of vaginal rugae so that the vaginal canal appears smooth, pale vaginal tissue, and possibly petechial hemorrhages or blood-tinged vaginal discharge. Vaginal pH, which is usually less than 4.5 in the reproductive years, increased to 6.0 to 7.5 in postmenopausal women not taking estrogen, possibly increasing risk of vaginal infection. Differential diagnosis should rule out other causes of vaginal bleeding, itching, irritation, including sexually transmitted infections, malignancy, Sjögren's syndrome, or diabetes. A number of medications can lead to symptoms of vaginal dryness. Urethral dryness, atrophy, and irritation also can accompany vaginal atrophy and dryness. This can lead to discomfort and increased susceptibility to UTI, which should be prevented or treated as part of the protocol.

CONVENTIONAL TREATMENT APPROACHES

Estrogen supplementation is the primary conventional treatment. ERT can be taken orally or absorbed vaginally from a cream or vaginal ring. Estrogen helps maintain the muscle tone of the vagina and urethra, reducing vaginal irritation. It prevents drying and thinning of the vaginal tissues and can improve that which has already occurred.

Side effects, particularly from oral estrogen, include headaches, nausea, vaginal discharge, fluid retention, weight gain, breast tenderness, spotting or darkening of the skin particularly on the face, deep venous

thrombosis, pulmonary emboli, an increased growth of pre-existing uterine fibroids, or a worsening of endometriosis. Topical applications can be used without progesterone supplementation. The risks of hormone replacement therapy (HRT) are discussed earlier in this section. Creams, pessaries, tablets, and the estradiol vaginal ring seem to be equally effective. One trial found significant side effects following use of conjugated equine estrogen cream when compared with tablets, including uterine bleeding, mastalgia, and perineal pain. Another trial found significant endometrial hyperstimulation following use of estrogen cream when compared with the ring. As a treatment choice, women appeared to favor the estradiol-releasing vaginal ring for ease of use, comfort, and overall product satisfaction.[92,619–627]

Palliative treatment in the form of vaginal lubricants and moisturizers can make intercourse more comfortable and temporarily reduce vaginal dryness and irritation. Commonly recommended agents include: Replens, Astroglide, and K-Y Personal Lubricant, among others.[628–630]

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

Herbal medicine focuses on a combination of strategies to address vaginal atrophy and dryness with an overall goal of supporting tissue integrity and therefore vaginal health, comfort, and the ability to experience sexual pleasure (Table 19-13). Systemically, an emphasis is placed on phytoestrogens-rich foods and botanical supplements to bolster declining estrogen levels. Topical emollients, in the form of salves and suppositories, are used to reduce local inflammation and irritation, and vulneraries are used to heal tissue. Also, attention to a women's sexual health is an essential aspect of treating vaginal dryness and atrophy. This can be done through education, counseling, and the use of herbs both internally and topically to enhance sexual arousal and comfort.

Phytoestrogens

Adding phytoestrogen-rich herbs, or those with estrogen-like activity, is one botanical strategy for improving troublesome vaginal symptoms. Herbs to consider include wild yam, soy, hops, flaxseeds, alfalfa, ginseng, red clover, damiana. Although black cohosh has commonly been considered phytoestrogenic, as discussed previously, newer research suggests that is not, and that its effects on neurovegetative symptoms are occurring through neurotransmitter rather than hormonal effects. The risks and benefits of phytoestrogens are thoroughly discussed earlier in this textbook.

Vulneraries to Heal Tissue

The vaginal mucosa is receptive to topical moistening. Vaginal salve containing comfrey oil may increase epithelial cell growth and tissue integrity.[628] Other botanicals, such as St. John's wort and calendula, also contribute to cell regeneration and help to fight infection. Topical application of vitamin E (400 IU) included in vaginal salves and suppositories can help reduce irritation, inflammation, and promote healing.

Lubrication

Herbal salves also can be used as vaginal lubricants for increasing comfort and pleasure during sex; however, many women prefer a more liquid oil preparation than a salve. Herbs similar to those used for salves are also used in lubricants, often with pleasantly scented essential oils added for their aesthetic and aphrodisiac qualities; for example, sandalwood, vanilla, rose, or chocolate scents.

TABLE **19-13**

Herbs for Vaginal Dryness and Atrophy

THERAPEUTIC GOAL	THERAPEUTIC ACTIVITY	BOTANICAL NAME	COMMON NAME
Support tissue integrity, epithelial thickness, moisture, and tone	Phytoestrogen, Estrogen-like effects	*Dioscorea villosa*	Wild yam
		Glycine max	Soy
		Humulus lupulus	Hops
		Linum usitatissimum	Flax seeds
		Medicago sativa	Alfalfa
		Panax ginseng	Ginseng
		Trifolium pratense	Red clover
		Turnera diffusa	Damiana
Soothe, moisten, and heal tissue	Vulnerary	*Calendula officinalis*	Calendula
		Hypericum perforatum	St. John's wort
		Lavandula officinalis	Lavender
		Symphytum officinale	Comfrey
Soothe, moisten, and heal tissue	Emollient	*Calendula officinalis*	Calendula
		Hypericum perforatum	St. John's wort
		Lavandula officinalis	Lavender
		Symphytum officinale	Comfrey

Care should be taken to use high-quality essential oils in very small amounts, and avoid these in women prone to skin sensitivity from the use of perfumes. The preparation of a vaginal lubricant is described in the following.

Alfalfa

Alfalfa, a phytoestrogen-rich plant, containing genistein, biochanin A, and daidzein, may have a beneficial effect on estrogen and is sometimes recommended as part of a protocol for the treatment of vaginal atrophy and dryness.[631]

Calendula

The medicinal uses of calendula have been recorded since the earliest days of botanical writing. Herbalists still widely use calendula in clinical practice for the treatment of skin and mucosal injuries and abrasions, for which it is also recommended by ESCOP and the German Commission E.[106,186] Calendula cream applied morning and night helps soothe vaginal tissue, heals minor abrasions, and discourages infection. Topically, calendula flower oil is used as an anti-inflammatory and for poorly healing wounds. Some evidence suggests the water-soluble flavonoids might be responsible for the wound-healing effects. Calendula also shows some evidence of antibacterial, antiviral, and antitumor activity.[185]

Comfrey

Comfrey moistens, heals, and soothes irritated and inflamed tissue. Its mucilaginous nature lends well to its emollient effects on the vaginal tissue. Comfrey contains a number of constituents, notably allantoin and rosmarinic acid, as well as tannins and mucilage, which show evidence of anti-inflammatory activity and tissue healing activity.[185] Note that PAs from comfrey, associated with venoocclusive liver disease, may be absorbed transvaginally in small amounts; caution should be observed if topical comfrey products are used daily for prolonged periods of time, although adverse effects are not expected. The German Commission E approves the topical use of comfrey on unbroken skin only, not to exceed 4 to 6 weeks in duration, and not to exceed 100 μg equivalents of PAs daily.

Damiana

Traditionally used as a gentle stimulant and aphrodisiac, damiana has been suggested as an herb for the treatment of vaginal dryness, possibly with estrogenic effects.[92] A study was conducted by Polan et al. using a human endometrial adenocarcinoma cell line, Ishikawa, which contains an alkaline phosphatase (AP) enzyme sensitive to estrogen stimulation, to determine whether ArginMax or the *Panax ginseng* extract it contains has any estrogenic activity. ArginMax for Women, a nutritional supplement for optimization of sexual health, contains L-arginine, ginseng, ginkgo, damiana, multivitamins, and minerals. The authors found that neither ArginMax nor *Panax ginseng* at any of the concentrations tested had any estrogenic activity.[633] However, an open study by Ito et al. (34 subjects received ArginMax and 43 received a placebo) found that after 4 weeks, 73.5% of the ArginMax group improved in satisfaction with their overall sex life, compared with 37.2% of the placebo group. Notable improvements were also observed in sexual desire, reduction of vaginal dryness, frequency of sexual intercourse and orgasm, and clitoral sensation. No significant side effects were noted.[634] The herb is also taken as a tea or in tincture form, usually in combination with other herbs. It also may be prepared as an elixir.

Ginseng

Ginseng plays an important role in traditional Chinese medicine in nourishing the fluids of the body through its ability to nourish ''blood and yin,'' which are considered to diminish with age. Combined with other herbs, notably licorice, ginseng is included in many formulas for dryness in the body, and is also an important ingredient in many gynecologic formulas. Low Dog sites two case reports indicating a benefit in vaginal dryness. In one case, a woman reported improvement in symptoms of vaginal dryness after extended use of an oral ginseng, which was confirmed by microscopic evaluation of the epithelium. In another case, there was evidence of estrogen-like effects from a topical cream containing ginseng.[163] Safety has not been assessed for effects on uterine endothelium.

Hops

Hops' estrogenic effects are attributed to the presence of 8-prenylnaringenin.[91,635,636] It has demonstrated strong estrogen receptor-binding bioactivity.[91,92,637,638] Hops is an herb to consider for the treatment of vaginal dryness and atrophy, in addition to its potential use in the treatment of hot flashes, night sweats, and insomnia, the latter caused by its sedating action.[91,163,639,640] Used in tea and tincture, often combined with other herbs, it is considered safe when used in moderate doses, although theoretically it may interfere with barbiturates and is thought by herbalists to exacerbate depression in some patients, although this is not a universally held concern.[181] There are no human clinical trials evaluating the efficacy or safety of this herb; however, it has a long history of use and is a primary ingredient in beer. With repeated consecutive doses, it will cause drowsiness; smaller single doses promote relaxation without drowsiness (see Insomnia).

Lavender

Lavender is used topically for pain, neuralgia, sores, and to improve local circulation; however, these uses have not been substantially evaluated.[106,185] Lavender oil is commonly added to vaginal suppository and lubricant formulas for its soothing, antiseptic qualities, as well as its pleasant scent.

Red Clover

Red clover, (leaf, stem, and flower) contains phytoestrogenic isoflavones such as formononetin, biochanin A, daidzein, and genistein and has demonstrable phytoestrogenic activity that makes it an important herb to consider for menopausal complaints, including vaginal

atrophy and dryness.[638,639] Although not traditionally used on a long-term basis, it has become a popular herb for long-term use for the treatment of menopausal complaints. Long-term use raises questions about the safety of red clover's estrogenic properties on endometrial and breast cancer cells in vitro, as well as possible preventive effects.[91,92] In a double-blind, randomized study of 60 postmenopausal women receiving either a commercially available red clover isoflavone supplement (80 mg/day) or placebo for 90 days, the red clover isoflavone supplementation significantly decreased the rate of menopausal symptoms and had a positive effect on vaginal cytology.[98] It is recommended in either a strong daily infusion, in the form of red clover sprouts, or most commonly, as a standardized supplement.

Soy

Traditional soy foods (i.e., tofu, tempeh, miso, and small amounts of soy milk) are a rich source of phytoestrogens recommended for the prevention and treatment of menopausal symptoms, largely on the basis that Asian women, whose diet consists of regular consumption of soy foods, experience fewer menopausal complaints than their Western counterparts, and the known estrogen-like effects of phytoestrogens. Soy may reduce symptoms such as hot flashes and vaginal dryness. In one study, soy plus flax seed resulted in a marked increase in vaginal cell maturation in postmenopausal women.[181] Twenty grams a day is easily reached with two servings of soy products.[98] Soy is discussed extensively in Hormone Replacement Therapy.

St. John's Wort

Herbal practitioners use St. John's wort topically in ways similar to, and often in combination with, calendula for its topical anti-inflammatory effects and for healing superficial wounds and inflammation.[185]

Wild Yam

Wild yam has commonly been prescribed based on the erroneous assumption that it acts in the body as progesterone based on the fact that progesterone, androgens, and cortisol have been chemically manufactured from the Mexican wild yam. However, the body is unable to manufacture these hormones directly from the plant. Any progesterogenic effects associated with wild yam products are caused by the fact that many are blended with USP progesterone. Wild yam may have the ability to modulate estrogen levels and improve the quality and quantity of cervical mucus production, however, at this time there is insufficient evidence to support the theoretical use of wild yam as a treatment for vaginal dryness and atrophy, other than the use of topical emollient agents in which the oil base is serving as a direct vaginal lubricant. Interestingly, a recent study found that although the exact mechanism is not clear, the addition of 390 g/day of yams to the diet (approximately equal to the weight of 2 medium-sized potatoes), for 30 days improved the status of sex hormones, lipids, and antioxidants. The authors concluded that these effects might reduce the risk of breast cancer and cardiovascular diseases in postmenopausal women.[641] The effects were specific to yams, which are different than sweet potatoes.[641]

Vaginal Lubricant

This vaginal lubricant is intended for topical use. It can be inserted vaginally and applied to the labia daily. It also can be applied liberally prior to intercourse. Clients can be taught to prepare this product themselves, or it can be prepared by the practitioner and stored in a cool place (i.e., refrigerated) for up to 1 year. Warm to room temperature prior to insertion. The following recipe makes 8 oz.

Preparing the salve:

1. Sterilize four 2-oz glass wide mouth jars with plastic caps. Be sure the jars and caps are completely dry before using.
2. Place in a double boiler:
   - 0.8 oz grated beeswax
   - ¼ cup herbal oils made from dried black cohosh and comfrey roots, calendula flowers, and wild yam root powder
   - ¼ cup coconut oil
   - ¼ cup jojoba oil
3. After heating the above and allowing cooling, add:
   - 1 tbs wheat germ oil
   - 1 tbs liquid vitamin E in the form of d-alpha tocopherol
   - 1 tsp emulsified vitamin A
   - Pure certified therapeutic essential oils as follows:
     - 30 drops lavender
     - 30 drops rose geranium essential oil
     - 10 drops Rosa Damascena (Bulgarian. Buy Otto, not absolute)
4. Cap immediately. Keep out of direct sunlight and away from heat accept body heat. Use clean fingers or applicator to rub onto labia and into the vaginal canal.

NUTRITIONAL CONSIDERATIONS

Increase organically grown phytosterol-rich foods especially beans and legumes, in the diet.

Vitamin and Mineral Supplements

- Zinc (20 mg daily) with food can improve immunity and healing of tissue.
- Vitamin E (400 to 800 IU) with food can reduce inflammation and promote healthy tissue.
- Cold-water fish oil supplement, EPA, and DHA. (EPA 180 to 3000 mg and docosahexaenoic acid DHA 120 to 1200 mg)
- Vitamin A (3000 to 10,000 IU)
- Essential fatty acids (flax seed, 45 g with 150 mL of water) plus gamma linolenic acid (evening primrose oil) 2000 to 4000 mg, again, for the reduction of inflammation and promotion of tissue integrity.

ADDITIONAL THERAPIES

As with most conditions, herbal practitioners take a holistic approach to vaginal atrophy and dryness. The following recommendations are included as part of a comprehensive approach.

Exercise

Awaken the vagina. Practice pelvic floor exercises to promote optimal blood perfusion and circulation to the vaginal tissue.[641] See a physical therapist specializing in women's health to gain personal instruction on the proper practice of pelvic floor exercises.

Counseling

Women have unique psychological concerns regarding their sexuality. These include the attitudes of society toward aging and sexual relationships, or lack thereof.

Provide Education and Information on Restoring Sexual Pleasure

Women who are experiencing vaginal dryness and atrophy may be experiencing profound conflict and difficulty around their sexual relationship. Further, women who are healing and resuming sexual activity after extended abstinence or sexual difficulty may be anxious about pain, discomfort, or the return of symptoms. Again, counseling, support, and education in this area are essential and should be part of the process, either through the primary care provider or through appropriate referral.

TABLE 19-14

Factors Influencing Female Sexual Function

FACTOR	EXAMPLES
Biologic/Physiologic factors	Neurologic disease Cancer Urologic or gynecologic disorders Medications Endocrine abnormality
Psychological factors	Depression/anxiety Prior sexual or physical abuse Substance abuse
Interpersonal factors	Relationship quality and conflict Lack of privacy Partner performance and technique Lack of partner
Sociocultural factors	Inadequate education Conflict with religious, personal, or family values Societal taboos

From Amato P: Categories of female sexual dysfunction, Obstet Gynecol Clin North Am 33:527-534, 2006. Adapted from www.femalesexualdysfunctiononline.org/slides. Accessed October 2006.

LOW LIBIDO AND SEXUAL DYSFUNCTION IN THE PERIMENOPAUSAL WOMAN

***Aviva Romm*[6]**

> *Sexual relationships are some of the most important social and biological relationships in human life. Next to thirst, hunger and sleep, the sexual urge is the most powerful biological drive. This physiological instinct, so essential to the survival of the species, is one of the mainsprings of human motivation, and its fulfillment or disappointment is closely related to happiness or misery. Normal sexual function involves the successful integration of biological, psychological and interpersonal influences.*[642]
>
> **—Binu Tharakan and Bala Manyam**

"Female sexual response is a complex, nonlinear progression from desire to arousal to orgasm."[643] Sexual response in women is highly variable and multifaceted, including a complex interplay of physiologic, psychological, and interpersonal components.[644] It naturally fluctuates with stress, fatigue, the menstrual cycle, illness, and other factors (Table 19-14). Low libido becomes increasingly common during women's midlife (the fifties and sixties), and for a smaller percentage of women, as early as in their thirties. Female sexual dysfunction (FSD) is a medical condition defined as persistent or recurrent reduction in libido, aversion to sexual activity, difficulty becoming aroused, inability to achieve orgasm, or dyspareunia (painful intercourse).[645] A variety of terms have been used to describe disorders of sexual desire and arousal, including sexual avoidance, low libido, inhibited sexual desire, hypoactive sexual desire, hypoactive sexual desire disorder (HSDD), female sexual arousal disorder, and sexual aversion disorder.[646]

It has been estimated, and widely purported, based on a study of sexual behavior in a demographically representative cohort of US women, that as many as 43% of women experience some form of sexual dysfunction, with one report estimating as high as 76% of women.[647–650] It has been suggested, however, that even the 43% figure is an overestimation, and that the entity FSD is an invention of the pharmaceutical industry for economic gain. According to a recent article in the *British Medical Journal*, "The Marketing of a Disease: Female Sexual Dysfunction," "widespread and growing scientific disagreement exists over both its definition and prevalence. In addition, the meaningful benefits of experimental drugs for women's sexual difficulties are questionable, and the financial conflicts of interest of experts who endorse the notion of a highly prevalent medical condition are extensive."[648]

In spite of some controversy over the extent or exact definition of FSD, the decline in libido in midlife that many women experience is a well-recognized phenomenon. Decreased sexual desire is one of the most common problems seen in a primary care or OB/GYN office, and is multifactorial in origin.[646,651] Reasons for decline in libido include:[652]

- Irregular ovarian function and declining hormone levels associated with the perimenopause and menopause

- Changes in anatomy (vaginal prolapse, atrophy, or dryness), neurological function, and vascular responsiveness
- Psychosocial changes that accompany aging
- Relationship dynamics
- Personal sexual beliefs, expectations, and prior sexual experiences

Loss of libido can indicate the presence of underlying disorders; for example, diabetes, cardiovascular disease, pituitary tumors, depression, chronic pelvic pain, interstitial cystitis, and chronic renal disease.[643,653–655] Women whose partners have erectile dysfunction may suffer from increased rates of female sexual dysfunction.[656] Previous pelvic or bladder surgery may predispose to sexual dysfunction. Many medications, including antihypertensives, antidepressants (especially SSRIs), and tranquilizers can adversely affect libido. Antihistamines can reduce vaginal lubrication and thereby affect sexual response and comfort. In women in their thirties and forties, declines in libido are more likely to have psychoemotional origins rather than physiologic underpinnings. Low libido, for example may be a sign of relationship/marital discord or a reaction to negative sexual experience.[653] At any age, low libido is more likely to occur in those with poor physical and emotional health and is highly associated with negative experiences in sexual relationships and overall well-being.[647] Sexual dysfunction can be categorized into subtypes including hypoactive sexual desire disorder, sexual arousal disorder, orgasmic disorder, and sexual pain disorder.[645,657,658]

Physiologic declines in reproductive function (i.e., menopause and the cessation of fertility) typically precede loss of sexual interest by a couple of decades; for many women, it is extremely frustrating as they enter a time in their lives when they first might be able to experience greater sexual freedom and lack of concern over unwanted pregnancy. Other women see menopause as a painful loss of their youth and femininity, negatively affecting their self-perception and their sexuality, while others see (or use) loss of libido as an excuse to avoid sexual activity (e.g., in an unhappy marriage).[652] For some women and couples, loss of sexual interest may not be problematic at all, and unless there is an underlying disorder does not necessitate treatment.

FEMALE SEXUAL RESPONSE

In the 1960s, Masters and Johnson proposed a model of female sexual response that outlined a linear progression through four phases: excitement, plateau, orgasm, and resolution.[646] Kaplan updated this to a three-phase model consisting of desire, arousal, and orgasm, which forms the foundation of the DSM-IV classification of female sexual dysfunction. Basson has more recently suggested a multifactorially stimulated, circular, psychophysiologic model that recognizes emotional intimacy and physical satisfaction as goals in the female sexual experience.[644,646,658] Classifications of female sexual dysfunction have been expanded to include psychogenic and organic causes of desire, arousal, orgasm, and sexual pain disorders.[645] An essential element of the FSD diagnostic system is ''personal distress'' as part of the criterion.[645]

The Physiology of Women's Sexual Response

The sexual response is a complex interplay of psychological, emotional, visual, ''scentual,'' tactile, and physiologic stimuli. Erotic feelings are coupled to vascular changes that are characteristic of female sexual excitement.

- Vasocongestion of deep vaginal tissues leads to secretion of clear, slippery vaginal mucus within less than a minute of sexual arousal. This fluid serves a lubricating function for penile movement, neutralizes normal vagina acidity, and supports sperm survival.
- Vasocongestion not only affects vaginal tissue, but also causes flushing across the chest, back, and neck in as many as 75% of women.
- Vasocongestion of the breast tissue causes engorgement of the areola and results in nipple erection characteristic of sexual arousal.
- The labia majora respond according to parity. In women who have not borne children, they become flatter and thinner during arousal and orgasm. Women who have previously given birth have an extensively developed vascular network in the labia majora, which becomes engorged to two to three times its normal size caused by vasocongestion with arousal. The labia darken to a deep red or purple color during the height of arousal.
- The inner portion of the vagina distends as arousal continues, forming a receptacle for semen; the uterus becomes engorged and uplifted.
- The clitoris enlarges and becomes more sensitive to touch and pressure but is covered by the engorged prepuce. The clitoris appears and disappears under the prepuce as arousal continues. Immediately prior to orgasm the clitoris turns upward 180 degrees and retracts behind the symphysis pubis in a flattened position.
- During orgasm, the inner third of the vagina continues to distend while the pelvic floor muscles rhythmically contract. After orgasm, unless there are psychoemotional conflicts about the sexual experience, the resolution phase results in mental and physical relaxation, accompanied by a feeling of well-being.[653]

Phases of the Sexual Response

1. Desire and Arousal (sometimes referred to as Excitement)
   Activation of the central nervous system (CNS), desire, causes specific changes in blood flow-arousal. During the latter part of arousal—also called the plateau phase—retraction of the clitoris and engorgement of the labia occurs, and muscle tension increases.
2. Orgasm
   During orgasm muscular contractions of the levator ani, muscles occur at precise intervals. Vaginal and uterine contractions occur followed by massive release of muscle tension.
3. Resolution
   Resolution is characterized as a gradual, pleasant diminishment of sexual tension and response, lasting a variable amount in time in different women.[652]

DIAGNOSIS

Lack of training of physicians in female sexual issues and sexual dysfunction commonly leads to an under recognition of FSD.[646] Although numerous models and screening tools have been proposed, there is not a universally accepted tool to define FSD, and a combination of clinical evaluation, patient history, and screening surveys are used to establish a diagnosis.

CONVENTIONAL TREATMENT APPROACHES

Conventional treatment of FSD includes psychological and pharmacologic approaches, the latter primarily using hormone replacement therapy (estrogen, androgens), sildenafil, and tiblone.[646,651] Many treatments that are used in practice are not supported by adequate evidence.[651,659] The adverse effects of HRT should be weighed against potential side effects and risks associated with use; the long-term use of testosterone in women has not been thoroughly investigated and can lead to symptoms of masculinization over time, including deepening of the voice and hair growth changes.[651,659] Local estrogen application relieves vaginal dryness and dyspareunia. The recent discoveries of the side effects of hormone therapy necessitate careful evaluation of the indication for hormone therapy, and the duration of treatment is recommended to be as short as possible. Sildenafil has shown a positive effect on FSD only in women with arousal problems without desire problems.[659] There appears to be limited controlled research on the efficacy of psychophysiologic approaches to FSD.[660] Although psychological treatment for some subtypes of sexual dysfunction have been shown to be helpful, these are commonly overlooked or dismissed in the medical visit.

THE BOTANICAL PRACTITIONER'S PERSPECTIVE

Numerous herbal products on the market boast the ability to improve sexual function and treat sexual dysfunction, as evidences by a visit to a local vitamin and supplement shop or health food store.[661] Rowland and Tai recently catalogued those botanical products offered at two major national health food chains and found that ginseng, Muira puama, saw palmetto, Tribulus, and ginkgo were the most popular.[661] Of these, all are used for male dysfunction, and all but yohimbe are used for female dysfunction.[661] Other ingredients, to name a few of the dozens identified, include horny goat weed, kava kava, yerba mate, deer antler, guarana, nettles sarsaparilla, and cayenne.[661]

Demand for products to treat sexual dysfunction is not a modern phenomenon—the history of herbal medicine is replete with herbal aphrodisiacs from charms and love potions, to elaborate traditional medicines and elixirs.[662] Ayurvedic medicine contains ancient texts and treatises focused solely on the treatment of sexual dysfunction and the support and restoration of healthy sexuality and sexual pleasure.[642] Few studies have been conducted to validate botanical therapies for FSD, with a slightly greater number of studies available on the botanical treatment of male sexual dysfunction.[663] Conventional medicine also has focused more on the treatment of male sexual dysfunction. However, there is a rich materia medica of traditional herbs to consider in the treatment of decreased sexual desire, FSD, and some of the factors that contribute to sexual function difficulties; for example, vaginal dryness or anxiety associated with sexual activity and performance. Further, herbal therapies may have a role in the treatment of associated or other contributory problems such as fatigue and depression (see related chapters). Finally, traditional Chinese medicine (TCM) and Ayurvedic medicine offer several historically important female tonics. These are also included in the following discussion.

Proprietary Products

Several herbal products including ArginMax (a proprietary blend of L-arginine, ginseng, ginkgo, damiana, calcium, iron, and 14 vitamins), Zestra (containing borage seed oil, evening primrose oil, angelica root abstract, and *Coleus forskohlii* extract), Kyo-Green (a powdered drink of barley leaves and wheat grass with anti-inflammatory and antioxidant properties), and ginkgo (*Ginkgobiloba*) have been evaluated in peer-reviewed, published studies for the treatment of FSD.[664] Used daily, the supplement claims to enhance a woman's sexual response by increasing blood flow and promoting relaxation. In a double-blind, placebo-controlled study of women older than 21 years of age with an interest in improving their sex lives participated; 4 weeks of ArginMax use was associated with an improvement in sexual desire, sexual satisfaction, reduction of vaginal dryness, increased frequency of sexual intercourse, and improved clitoral sensation over placebo.[634] In an open-label trial of women with lack of libido, 80% of the women reported improved sexual function after Kyo-Green use.[664] The topical preparations Vigorelle (ingredients include damiana leaf, suma root, motherwort, wild yam, ginkgo, peppermint leaf, L-arginine, and vitamins A and C), and Pro Sensual (ingredients include natural mint, orange, and clove oil) claim to enhance a woman's sexual responses by increasing blood flow to her sexual organs. None have peer-reviewed data to support this claim.[664] The author has no experience with these products and includes them merely for the familiarity of the practitioner whose patients may be taking them or requesting information about them.

Decreased Libido

Damiana is an herb with a long history of folk use as an aphrodisiac, particularly in Latin American, and it continues to be popular among herbalists today. The Aztecs described it as a sexual stimulant at least 300 years ago.[661] The herb is purported to have progestin receptor binding activity; however, it appears to be neither an agonist nor an antagonist, it may also exert some of its action via antidepressant and nervous system stimulant activity.[92,661]

The Quechua Indians of Peru's central highlands consider maca a highly nutritious food that promotes

mental acuity, physical vitality, endurance, and stamina. It is also well-known as an aphrodisiac tonic that enhances sexual desire and performance, and is especially reputed to increase fertility. Maca is often eaten by Peruvian women wishing to get pregnant.[665] Dried maca root is rich in essential amino acids, iodine, iron, and magnesium, as well as sterols that may possess a wide range of activities, including aphrodisiac properties.[661] It has been used to treat menstrual and menopausal complaints as well.

Tribulus terrestris has been widely used in Ayurvedic medicine as a sexual stimulant for both men and women, to improve libido and performance. It is also popular among athletes for improving sports stamina and performance.[661] Tribulus appears to support the production of steroid hormones, including DEHA and androstenedione, possibly explaining its reported effects.[661] It may stimulate LH production, which in men, stimulates testosterone production in the testes, and in women, estrogen production in the ovaries; however, these are speculative mechanisms.[661]

The effects of damiana, maca, and Tribulus on sexual function are plausible; however, there is a paucity of studies, particularly relating to female sexual complaints. Side effects are not anticipated with use of these herbs, although very small amounts of cyanide have been detected in damiana and could cause renal or hepatic damage, although this is not reported in the literature.[661]

Milky oats was used by the Eclectics to treat what was termed *sexual neurasthenia*, a lack of sexual energy causing lack of libido.

Ginkgo is also used to treat sexual dysfunction in men and women. Study results have been mixed. In an open-label trial of women experiencing antidepressant-induced sexual dysfunction, ginkgo improved sexual function; however, there were no significant differences between ginkgo and placebo, both improved sexual function.[666] This study did show that women are more responsive to the sexually enhancing effects of the herb than men with success rates of 91% compared with 76%.[667] It is postulated that the ginkgo's ability to improve peripheral vascular circulation may be the explanation for its supposed effects in improving sexual response.[661]

Warming and stimulating herbs, for example, cinnamon and ginger, are thought to stimulate sexual appetite, and are therefore commonly included in formulas intended to stimulate sexual desire.

Vaginal Dryness

Vaginal dryness is most often a function of age and declining estrogen levels. It is also associated with cyclic fluctuations in hormonal cycles, candidiasis, inadequate intake of dietary essential fatty acids, and rarely, it is associated with the autoimmune condition Sjögren's syndrome. Intake of phytoestrogenic foods and herbs to support estrogen, as well as the use of topical emollients to moisten vaginal tissue locally and heal tissue that might be irritated or damaged caused by chronic dryness, may help to relieve vaginal dryness as well as more immediately relieve discomfort during sex. Treatments for vaginal dryness are elaborated on in the Vaginal Dryness and Atrophy section of this chapter. Shatavari root and Chinese asparagus, two herbs with very similar activity are used in Ayurvedic and Chinese medicine respectively as herbs to increase vaginal mucus. Long-term use, along with other yin tonics can help to reestablish normal vaginal secretions. In TCM, Chinese asparagus is considered a yin tonic, as is licorice rhizome, which also may be considered for vaginal dryness. Licorice contains isoflavones, which act as phytoestrogens. Vulnerary herbs such as calendula and comfrey can be used topically in suppositories, ointments, or vaginal lubricant creams to relieve irritation and inflammation associated with vaginal dryness, and to promote tissue healing.

Depression and Sexual Dysfunction

Damiana is an herb with a long folk history of use as an aphrodisiac, particularly in Latin America. The herb is considered a phytoprogestin, and also may exert some of its action via antidepressant and nervous system stimulant activity.[92] Ginkgo extract claims include increased pelvic blood flow and nerve transmission. As mentioned earlier, ginkgo improved sexual function in an open label trial; however, improvement was not greater than placebo.

Painful Intercourse

Painful intercourse can be caused by lack of lubrication, sexual trauma, vulvodynia, vaginismus, uterine fibroids, STDs, cervicitis, and uterine prolapse.

Orgasmic Dysfunction

Anorgasmia is an inability to achieve orgasm. Ginkgo and damiana should be considered for improving orgasmic function.[661] Muira puama has been suggested for improving low libido and anorgasmia in women; however, studies are limited. A study by Waynberg and Brewer demonstrated the prosexual effects of a commercial Muira puama and ginkgo product (Herbal vX) in women complaining of low libido. Compared with pretest evaluation, 65% of the women reported improvements in frequency and intensity of sex drive, sexual fantasies, and ability to achieve orgasm. Side effects possibly include sour stomach and headache.[667]

Sexual Anxiety

Fear of not being loved, fear of pregnancy or acquiring sexually transmitted infections, previous sexual trauma, fear of inadequacy, poor body image, lack of self-esteem, and guilt related to personal or religious beliefs related to sex can all contribute to anxiety associated with sexual encounters. Herbs can help relieve the anxiety; however, counseling or therapy is needed to get to the root of the problem and provide behavioral modification techniques and new patterning. Milky oats, ashwagandha, and skullcap are all excellent nervous system tonics and restoratives that should be considered when there is anxiety related to sex. Passion flower also can be considered in formulae for anxiety.

BOX 19-3

TCM and Low Libido

According to Oriental medicine, the ''kidneys'' govern sexual vitality and mental energy. Aging, stress, overwork, loud noise, cold temperature exposure, especially to the lower back (e.g., draft), drinking and eating icy foods, overusing stimulants, including caffeine, and fatigue may exhaust the kidneys and libido.

Female Sexual Tonics

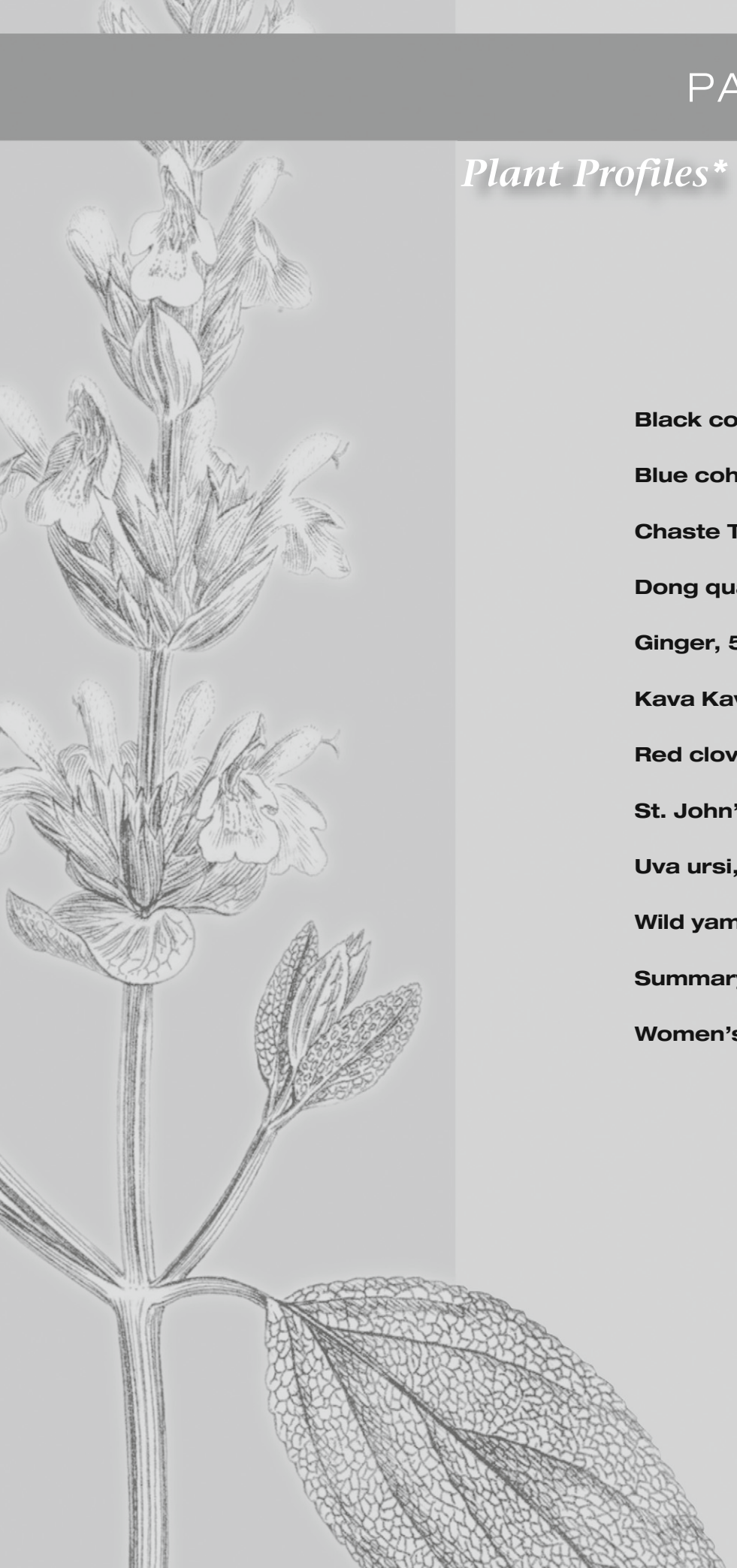
In Chinese medicine, herbs that build the blood (xue) are used to strengthen and nourish the female reproductive system.[180] Herbs in this category include processed rehmannia, dong quai, He Shou Wu, and white peony. Other female reproductive tonics include the classic Ayurvedic herb for women—shatavari—and the Chinese asparagus root, which possesses very similar activity. Epimedium is among the classic kidney tonics (Box 19-3) used in TCM for kidney deficiency and related sexual problems.

ADDITIONAL THERAPIES

Individual and relationship counseling, behavioral modification, and sex therapy are all important adjuncts to the treatment of debilitating sexual problems. There are nearly innumerable resources, ranging from books and tapes to seminars designed to help improve women's understanding of their sexuality and thereby to increase sexual pleasure and satisfaction. Competent and experienced sex therapists can help clients to identify effective resources.

PART V

*Plant Profiles**



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Blue cohosh, 528

Chaste Tree, 531

Dong quai, 534

Ginger, 536

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Red clover, 542

St. John's wort, 544

Uva ursi, 547

Wild yam, 550

Summary Table of Herbs for Women's Health, 553

INTRODUCTION TO PLANT PROFILES

These plant profiles are intended to serve as ''monographs in brief.'' The herbs were selected specifically because they are used frequently in gynecology and obstetrics and there is some amount of controversy surrounding their use or safety. Included in this chapter are profiles on:

- Black cohosh
- Blue cohosh
- Chaste berry
- Dong quai
- Ginger
- Kava
- Red clover
- St. John's wort
- Uva ursi
- Wild yam

In addition, a comprehensive table of all of the herbs in this text is presented at the end of this section for the convenience of the reader who may wish to quickly reference *in toto*, the clinical use and safety information for the herbs in this textbook as applied to women's health conditions. A separate table on herb–drug interactions appears in the appendices. For the sake of simplicity the data in the Plant Profiles and Summary Table of *Herbs for Women's Health* are not individually referenced. Rather, readers are directed to the following sources from which information for the plant profiles was drawn:

TEXTBOOKS AND MONOGRAPHS

Barnes J, Anderson LA, Phillipson JD: Herbal Medicine, 3 ed, 2007.

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McKenna DJ, Jones K, Hughes K, Humphrey S: Botanical Medicines: The Desk Reference for Major Herbal Supplements, 2002.

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Moerman D: Native American Ethnobotany, 2000.

Schulz V, Hansel R, Blumenthal M, Tyler VE: Rational Phytotherapy, 2004.

Upton R: American Herbal Pharmacopoeias and Therapeutic Compendium Series.

Weiss R, Fintelmann V: Herbal Medicine, 2 ed, 2000.

WHO: The World Health Organization Monographs. Geneva: WHO.

Wichtl M: Herbal Drugs and Phytopharmaceuticals: a Handbook for Practice on a Scientific Basis, 2004.

WEBSITES/DATABASES

AltMedDex. The US Pharmacopoeia herbal monographs: http://www.micromedexx.com

Cochrane Collaboration: http://www.compmed.umm.edu/Cochrane/Registry.html

Natural Medicines Comprehensive Database: http://www.naturaldatabase.com

National Library of Medline (PubMed): http://www.ncbi.nlm.nih.gov/entrez/query.fcgi

Ovid: http://www.ovid.com/

Readers interested in further expanding their depth of knowledge on botanicals are encouraged to obtain these additional references.

The author wishes to thank Roy Upton of the American Herbal Pharmacopoeia for generously allowing liberal use of information from monographs from the series American Herbal Pharmacopoeia and Therapeutics Compendium, and for assisting in the template for this chapter.

BLACK COHOSH

Botanical name: *Actaea racemosa* syn. *Cimicifuga racemosa*
Family name: Ranunculaceae
Synonyms: Black bugbane; Black snakeroot
Part used: Root, rhizome

Black cohosh has gone through numerous taxonomic reclassifications, and until recently has been listed as *Cimicifuga racemosa*. As of 2002 it was reclassified and renamed *Actaea racemosa*. Black cohosh is of a different genus than blue cohosh (*Caulophyllum thalictroides*), having in common only the word *cohosh* in their common names, supposedly derived from the Algonquin word for knotty root. They are not medicinally related or interchangeable, although both are used for gynecologic and obstetric complaints.

Black Cohosh (*Actaea racemosa*). (Photo by Martin Wall.)

MAJOR CHEMICAL CONSTITUENTS

Numerous triterpene glycosides (e.g., actein, cimicifugoside, cimigoside, 23-epi-26 deoxyactein, cimiracemoside A); aromatic acids (e.g., ferulic acid, isoferulic acid, acyl caffeic acid, fukinolic acid, salicylic acid); tannins, volatile oils, resin, phytosterols, starch, and sucrose. More recent studies suggest that black cohosh, contrary to prior alleged identification of isoflavones in the plant, does not contain isoflavones (e.g., biochanin A, formononetin). Kaempferol has been found in extracts of the leaf. The salicylic acid is in such as low concentration as to be unlikely to cause any allergic reactions in those sensitive to this agent. A unique bitter principle also has been identified.

PRINCIPAL USES

- Perimenopause; for the treatment of neurovegetative symptoms
- Antispasmodic, analgesic, and antirheumatic for the treatment of myalgia, rheumatism, and rheumatoid arthritis
- Uterine antispasmodic for the symptomatic treatment dysmenorrhea and other gynecologic pain; also used by midwives in combination with other herbs to treat pain and spasmodicity in dysfunctional labor
- Mild sedative, in combination with other herbs for the treatment of insomnia
- Osteoporosis

TRADITIONAL AND HISTORICAL USES

Black cohosh is an indigenous North American herb that was used widely by eastern Native American tribes including the Cherokee, Iroquois, Penobscot, and MicMac for gynecologic complaints and pain, including rheumatic pain, and also in the treatment of hives, constipation, colds, coughs, fatigue, sore throat, and snakebite. It appears in the botanical literature as early as the 1680s, and it was described by von Linne in 1749 as an herb primarily for female debility and pain relief, but also as a diaphoretic, stomachic, expectorant, cardiac tonic, and uterine tonic. Black cohosh was largely popularized by the Eclectics, who called it Macrotys, and who used it extensively for women's ''muscular pains, uterine pains with tenderness, false pains, irregular pains, rheumatism of the uterus, dysmenorrhea.'' They also recognized its value as a superb sedative. It was considered to have particular affinities for the uterus, heart, and circulatory system, supposedly improving (cardiac) contractile force; however, this indication has not been widely studied nor borne out by limited scientific evaluation of the plant. It was considered a reliable herb to aid in birth and relieve pain afterward, given in small doses before, during, and after labor. Its effects for the treatment of all manner of musculoskeletal and neuralgic pains were widely reputed. Listed in the USP from 1820 until 1920, it was and continues to be one of the most popular herbal medicines sold in Western nations.

CLINICAL INDICATIONS

Black cohosh is the most widely sold and used herb in western nations for the treatment of perimenopausal neurovegetative complaints. It is commonly used for such by herbal practitioners and research has largely centered on its use for these purposes. Herbal practitioners also use black cohosh as a reliable anti-inflammatory, antispasmodic, and analgesic for all manner of neuromuscular complaints, for premenstrual headache, as well as for treating spasmodic or paroxysmal coughs. Plant Profile Black Cohosh Table 2 lists the uses of this herb by contemporary herbalists and naturopathic physicians.

TABLE 1

Black Cohosh for Gynecologic and Obstetric Problems: Eclectic Medical Uses

Treat uterine and ovarian neuralgia
Antispasmodic for generalized and uterine ''rheumatic'' pains
Uterine irritability
Irritated and congested pelvic conditions
Amenorrhea
Dysmenorrhea
Hysteria
Relieves irregular pains and uterine contractions
Partus accelerator
Partus preparator
Postpartum hemorrhage
Relaxes the soft parts of the parturient canal and facilitates delivery
Relieves insomnia, relieves reflex irritability thus quieting morning sickness
Relieves spasmodic pains of early labor and due to its relaxing effects, reduces laceration at birth
Maintains uterine contraction after birth

TABLE 2

Common Uses of Black Cohosh in Modern Herbal Practice

Dysmenorrhea
Ovarian pain
Neurovegetative menopausal symptoms: hot flashes, reduction of sweating, headache, heart palpitations, anxiety, nervousness, insomnia, irritability, depression (for the latter in combination with *Hypericum perforatum* (St. John's wort), and possibly vaginal dryness and atrophy
Musculoskeletal pain; i.e., myalgia, sciatica, arthritis, neuralgia
Premenstrual migraine
Cough
Osteoporosis

Possible additional indications include
Uterine contractions in threatened miscarriage (see Use in Pregnancy and Lactation)

IN VITRO, ANIMAL, AND CLINICAL DATA

Black cohosh has been used widely to treat menopausal complaints in Europe for over 50 years. However, in spite of numerous studies, few that are without methodologic flaws have emerged to solidly demonstrate efficacy. Two reviews of human studies on the effectiveness of black cohosh for alleviating menopausal symptoms concluded that it is safe and effective, with pronounced effects on the central nervous system. In a study of hot flashes caused by tamoxifen in breast cancer survivors, it was found to reduce the number and severity of hot flashes (almost half the patients in the intervention group were *free* of hot flushes, whereas severe flashes were reported by 24.4% of the intervention group and 73.9% of the usual-care group), with assessment at 2-month intervals over 1 year. Yet other studies have found no benefit in the treatment of these symptoms. A 6-month randomized, double-blind, controlled study (by the manufacturer of the extract) showed efficacy, tolerability, and lack of systemic estrogenic effect (no change in vaginal cytology or relevant hormone levels) with two dose levels of black cohosh.

The data on estrogenic effects of black cohosh are very contradictory, demonstrating everything along the spectrum from positive estrogenic effects to no effects to antiestrogenic effects; selective estrogen receptor modulation to no estrogen receptor binding whatsoever. Although on balance, it does not appear that there is estrogenic activity associated with use of this herb, it is prudent for women with a history of estrogen-sensitive cancer to avoid use of this herb.

In vitro and in vivo evidence from animal trials has clearly demonstrated anti-inflammatory effects with black cohosh extract, supporting its traditional use as an herb for the treatment of rheumatism and rheumatoid arthritis.

Osteoprotective effects have been demonstrated with black cohosh in postmenopausal women. In a double-blind study of 62 postmenopausal women, the effects of a *Cimicifuga racemosa* extract on markers of bone metabolism, hormones, sex hormone–binding globulin (SHBG), lipometabolism, vaginal maturity, and routine laboratory parameters were compared with those of conjugated estrogens (CE) and placebo over 12 weeks. Markers of bone turnover, estradiol, follicle-stimulating hormone (FSH), leuteinizing hormone (LH), sex hormone binding globulin (SHBG), triglycerides, total cholesterol, high-density cholesterol, low-density cholesterol, and routine clinical chemistry parameters were determined from blood samples. Vaginal ''maturity index'' was determined from vaginal smears. The analyses of bone turnover markers indicated beneficial effects with stimulated osteoblast activity with mild estrogen-like activity on vaginal tissue with the black cohosh extract. Although these findings are preliminary, this represents an area of possible new and interesting research on this herb.

MECHANISMS OF ACTION

There is considerable interest in understanding the mechanisms of black cohosh. Nonetheless, in spite of its popularity, its mechanisms have not been elucidated. Studies on estrogenic activity have been contradictory. In spite of initial studies suggesting estrogenic effects, many recent studies demonstrate lack of systemic estrogenic effects and even antiestrogenic effects, with no changes in LH, FSH, prolactin, and SHBG, and no changes in endometrial or vaginal proliferation. SERM activity has also been postulated, however, some studies also demonstrate lack of binding to estrogen receptors. Recent in vitro and animal research suggests possible serotinergic

effects, and receptor binding assays suggest a possible dopaminergic mechanism of action.

RATINGS

- German Commission E Monograph: Black cohosh is approved for the treatment of premenstrual discomfort, dysmenorrhea, and menopausal complaints. As stated, it is not recommended for use for longer than 6 month durations. The prescribed dosage is 40 mg herb daily or equivalent tincture made with 40% to 60% ethanol.
- Botanical Safety Handbook Rating 2b, 2c

PREPARATIONS USED CLINICALLY

- Capsules/dried herb
- Tincture/liquid extract
- Standardized extract (i.e., Remifemin®, standardized to 1 mg triterpene glycosides per tablet)

DOSAGE

Dried Root and Rhizome

Dose recommendations vary from as low as 40 to 200 mg daily to 1 to 3 g daily

Tincture

0.4 to 2 mL daily of 60% ethanolic extract

Fluid Extract (1:1)

20 drops twice daily

Standardized Products

Remifemin®, and standardized products standardized to 1 mg triterpene glycosides per tablet. The typical dose is two tablets twice daily, although two to three times this amount of herb has been used in clinical trials, and half this amount of herb (one tablet twice daily) has been shown to be efficacious for the relief of menopausal symptoms in positive trials.

Herbal practitioners frequently recommend black cohosh tincture at the higher end of the doses specified in the preceding. Clinical trial length using doses in the specified ranges have been for up to 12 weeks. See the safety discussion that follows.

SAFETY INFORMATION: HERB–DRUG INTERACTIONS, TOXICITY, AND CONTRAINDICATIONS

Taking a serious and concerted look at the relative safety of black cohosh products for the treatment of menopausal symptoms, particularly for women in whom HRT is contraindicated, Low Dog et al. conducted a careful review of published and unpublished safety data extending well over 100 years. Analysis of more recent adverse events systems databases yields records demonstrating a high level of safety. The FDA Special Nutrition Adverse Events Monitoring System (SN/AEMS), shows only nine adverse reports reported prior to October 20, 1998; of these, only one—headaches and elevated blood pressure—was caused by black cohosh as a solo agent. The WHO Collaborating Center also maintains a database of adverse events reports, with summary clinical reports and some medical detail. As of July 31, 2000, a total of only 35 adverse events relating to all forms of black cohosh constituents and root products had been reported. Of these, the events were mostly related to general symptoms, ''suggesting a good tolerability of *Cimicifuga* preparations.''

More recently, concerns have arisen because of the report of a small number of hepatic complications associated with black cohosh use. Two cases of hepatitis and two cases of liver failure have been reported in women taking black cohosh extracts. One case was autoimmune hepatitis in a woman taking black cohosh for 3 weeks along with several prescription drugs. The second was a case of hepatitis after 1 week of black cohosh ingestion. The cases of liver failure were acute and occurred after 3 and 5 months of black cohosh administration. None of the cases was causally linked to black cohosh. In a systematic review of clinical trials, published case reports and pharmacovigilance reporting center data, Huntley and Ernst concluded that black cohosh is generally safe. If products are taken for a limited amount of time and in the recommended dosage range, the risk of adverse events is slight and the events are rare and usually mild and transient, with gastrointestinal upset and rashes being the most common events reported. When higher doses than those recommended are used, dizziness, headaches, nausea, and vomiting may be seen. Discontinuation of the herb resolves the symptoms. The European Medicines Agency (EMEA) recently assessed the case reports of hepatotoxicity associated with ingestion of *C. racemosa* root extracts (EMEA/HMPC/88766/2006) and concluded that the cases reported in the literature as well as the pharmacovigilance reports are mostly poorly documented and that these adverse events should be interpreted with caution. Although a recent animal study did show hepatocellular toxicity at high concentrations of herb, and minimal hapatocellular mitochondrial changes even at lower doses, the authors conclude that toxic concentrations seen in this study are likely not able to be reached in humans treated with the recommended doses. They conclude that ethanolic black cohosh extract is associated with hepatic mitochondrial toxicity both in vivo in rats and in vitro using cell cultures and isolated rat liver mitochondria, but that this toxicity is not clinically relevant for most patients but may become important in patients with underlying risk factors.

There are no expected herb–drug interactions, and even in combination with HRT, minimal side effects have been observed. No mutagenicity (Ames test) has been found and the herb has a very low toxicity risk based on animal toxicity studies. One case of nocturnal seizures was reported in a 45-year-old woman taking a combination of black cohosh, chaste tree, and evening primrose oil for menstrual irregularity. Her sister had also been taking this combination for duration of 1 to 2 years with no reported side effects. The woman's seizures abated upon discontinuation of the herb, no other pathology was identified, and the seizures were not directly attributed to the herbs in combination or singly. The limited number of other adverse events that

have reported (a thorough review of which is provided by Low Dog et al.) suggest that these may be owing to the use of the herb in combination with other herbal products or dietary supplements, or other ingredients in such combinations.

For short-term use, black cohosh clearly has a high safety profile. Long-term use of the herb, however, as a treatment for menopausal complaints, has been and continues to be debated because of concern over risk of estrogenic effects and cancer. The *German Commission E Monographs* rends a limited duration of 6 months for black cohosh use with no specific rationale provided for this caution. Bone states that ''Black cohosh may be taken long term within the recommended dose, although the Commission E recommends not more than 6 months, perhaps because controlled studies over longer periods are lacking.'' According to Blumenthal, Professor Hans Schilcher, vice president of the Commission E, explains that the limitation is based not upon concerns about the safety of long-term black cohosh use, and in fact, the German Commission E had considered approval the herb for use over an unlimited duration without safety concerns, but based the more conservative recommendation on the ''desire to ensure that women return to their health-care provider for periodic examinations at six month intervals.'' This follows prescription recommendations similar to those for HRT prescription in Germany, which are given for this same reason and seem a prudent standard of practice.

Preclinical human, animal, and in vitro studies have given mixed results on the estrogenic activity of black cohosh, although recent 6- and 12-month human clinical trials have indicated a lack of estrogenic effects. Questions persist regarding the estrogenic effects of black cohosh and safety for use in women with a history of or risk of uterine and breast cancer. Effects on vaginal epithelium have been variable and remain inconclusive. Because no trial has been conducted for a duration greater than 6 months, and it may take this long to see marked proliferation, lack of demonstration of cell proliferation in shorter trials is not a conclusive finding. Although reduction of LH has been demonstrated in animal studies (ovariectomized rodents), human clinical trials have consistently failed to show an effect on FSH and LH levels, leading to the current belief that black cohosh's mechanism of action is nonestrogenic. Further, black cohosh has shown antiproliferative activity in vitro on breast cancer cells under conditions testing for estrogenic activity and actually enhanced the antiestrogenic effects of tamoxifen in a trial combining the two agents. It appears, by all data available at this time, that this herb does not increase or predispose to breast cancer risk and is not contraindicated in such cases. Reviews examining the estrogenic effects of black cohosh have indicated that data from in vitro studies are mixed but leans toward lack of estrogenic activity or estrogenicity.

It appears that black cohosh is safe and possibly effective for some of the neurovegetative and psychological effects of menopause, as well as for numerous other complaints, particularly musculoskeletal and gynecologic pain. It also appears that the efficacy of this plant is not caused by direct estrogenic effects, and the herb has a significantly greater safety profile than HRT, especially for women who cannot use HRT because of cancer risk. A common pattern is for women to use black cohosh preparations for 1 to 2 years for the treatment of menopausal symptoms, then to discontinue use after this duration or with improvement of symptoms. It would appear that such use at this duration is beneficial with minimal risk compared with conventional hormonal preparations, and can be confidently used in the care and treatment of menopausal women; however, because of lack of long-term clinical studies, long-term safety is not conclusive. Clearly all women at risk for medical conditions should be re-evaluated by their primary care provider at regular interval, and patients should be queried for use of black cohosh and other herbs. Short-term use of black cohosh for acute conditions and within recommended doses appears to be a safe practice.

The safety of long term use of black cohosh cannot be established based on either traditional use, which was typically short-term, or on current research and literature. However, according to Low Dog et al., ''practitioners should be reassured that *Cimicifuga* appears to be a safe option for women who wish to take it for relief of menopausal symptoms.''

No drug or supplement interactions have been reported for black cohosh. Reviews of clinical trials and other safety data have indicated that black cohosh is generally safe. Although black cohosh does not appear to have any estrogenic activity, until further evidence is available, the herb should be avoided by those with estrogen-dependent cancers. Risk of hepatotoxicity from black cohosh use, particularly if of limited duration and within recommended dosage ranges, appears to be extremely minimal; however, patients with prior history of hepatic problems should avoid the use of black cohosh. Any patients taking black cohosh who experience any of the following signs or symptoms of possible hepatic injury should discontinue use of the herb immediately, and consult their physician: fatigue, appetite loss, yellow discoloration of the skin and/or eyes, severe epigastric pain with nausea and vomiting, and dark urine.

USE AND SAFETY IN PREGNANCY AND LACTATION

Limited scientific literature is available on the safety of black cohosh during pregnancy and lactation, although it is traditionally used to ease labor. Black cohosh is generally contraindicated by most contemporary authors for use during pregnancy and lactation. The American Herbal Products *Botanical Safety Handbook* takes a slightly more liberal position and assigns black cohosh a pregnancy Class 2b rating, herbs not to be used during pregnancy unless otherwise directed by an expert qualified in the use of the described substance, and a lactation Class 2c rating, herbs not to be used while nursing unless otherwise directed by an expert qualified in the use of the described substance.

Contraindication of black cohosh during pregnancy appears to be based largely on historical records of this herb's ability to affect uterine activity, with reports of its

use both as a uterine stimulant (emmenagogue) and uterine relaxant by the Eclectic physicians. Numerous published Eclectics (Cook, Ellingwood, Felter, Howe, King, and others) regularly used black cohosh during pregnancy for the treatment of threatened miscarriage and premature labor, and for relaxation of a rigid *os uteri* during labor, suggesting its action as a uterine antispasmodic. Although this was not necessarily the first choice of treatment (*Viburnum prunifolium* being specifically indicated for threatened miscarriage), it was clearly used often and with comfort during pregnancy. In a seeming contradiction, however, it was also used as a *partus preparator*, an herb used in the last weeks of pregnancy to prepare the uterus for labor, as well as an herb to stimulate labor and effect an expedient delivery. It was considered a gentle and safe alternative to ergot at the time and still used in the form of ergonovine. Black cohosh was considered specifically able to effect regular and effective uterine contractions while eliminating irregular or nonproductive pain in labor. It was also used for postpartum uterine pain and the treatment of uterine subinvolution.

It is black cohosh's reputation as an herb for initiating labor that has led to modern contraindications regarding its use during pregnancy. However, it appears that this may be an exaggerated concern that fails to take into account several factors, including the facts that the herb was equally used to relieve uterine contractions, its effects appear to be dose-dependent (with lower doses specifically leading to antispasmodic activity and significantly higher doses leading to increased uterine tone), Eclectic physicians used it to induce labor in significantly higher doses than herbalists and midwives presently use it clinically, and although it was frequently written about as a single herb, it was often combined with other herbs, such as *Caulophyllum thalictroides* (blue cohosh) or *Gossypium herbaceum* (cotton root), both known uterine contractants used to stimulate or enhance uterine contractions. It was considered only a very weak oxytocic, capable of inducing labor and abortion only in large doses. Reports on black cohosh from Eclectic physicians suggest very few adverse events associated with its use in pregnancy and birth, in spite of widespread use. One report among the Eclectics of ''free use'' during pregnancy correlated it with ''premonitions of abortion'' (allegedly threatened uterine contractions), but the author noted that this was the exception. Ellingwood, in 1919, mentioned six cases of the use of black cohosh during labor followed by severe uterine hemorrhage at birth.

Another confounding factor in the literature that appears to have contributed to the modern case against using black cohosh as a uterine antispasmodic during pregnancy is the fact that, as was the case with the Eclectics, the herb continues to be combined with blue cohosh, which has known cardiac glycosides and has been associated with several case reports of neonatal complications, including a case of myocardial infarction in a newborn whose mother took a combination of blue and black cohosh as a *partus preparator* during the last weeks of her pregnancy.

Black cohosh continues to be used by midwives for the prevention and treatment of threatened miscarriage when there are uterine contractions. It is also used as a *partus preparator* and an aid in difficult labors to impart uterine relaxation, effective rhythmic uterine contractions when there is dysfunctional labor, and to relax a rigid cervical os. Few clinical trials have been done on the uses of black cohosh outside of menopause, but Upton reports on a case series by Görlich published in 1962 involving the use of black cohosh in 258 women with various gynecologic and obstetric complaints. Among the case series are 18 cases of morning sickness successfully treated with black cohosh (only two requiring antiemetic medications) and successful prevention of miscarriage in six women with threatened miscarriage and a prior history of miscarriage. Considering the thousands of case reports cited by the Eclectics for use of this herb during pregnancy, it appears that further research is warranted for the application of this herb for threatened miscarriage and difficulties in labor for women who prefer an alternative to pharmaceutical drugs; and there may be some margin of safety when used appropriately, as suggested by the *Botanical Safety Handbook*, under the guidance of a qualified practitioner. Self-medication with this herb is not recommended, and neither the safety of this herb for the mother and fetus, nor safe dosing strategies for its use during pregnancy have been established.

Very little information is available on the safety of this herb for breastfeeding babies and its effects on milk production. Limited ethnobotanical evidence points to its postpartum use by the Iroquois to promote milk flow. A NAPRALERT search conducted by McKenna et al. yielded no records of adverse effects on lactation, and the same authors report that there is no evidence from human or animal studies regarding the transmission of constituents of black cohosh into breast milk. Further, McKenna et al. cite no reports of negative effects on the neonate associated with use of the herb during labor or the early postpartum period. The *German Commission E Monographs* do not contraindicate the use of this herb during lactation, and the herb does not appear to affect prolactin levels, although the herb's effects on prolactin have not been tested in lactating women.

Given concerns over estrogenicity and hepatotoxicity—however unlikely these are to be an actual problem with use—it is prudent avoid this herb for any more than short-duration acute use during labor to relieve pain and spasmodic uterine contractions associated with dysfunctional labor.

BLUE COHOSH

Botanical name: *Caulophyllum thalictroides*
Family: Berberidaceae
Synonyms: Papoose root, squaw root
Part used: Root, rhizome

MAJOR CHEMICAL CONSTITUENTS

The major chemical constituents are quinolizidine alkaloids including thalictroidine, *N*-methlycytisine, anagyrine, magnoflorine sparteine, baptifoline, and caulophyllumine, and the saponins caulosaponin and caulophyllosaponin.[1–4]

PRINCIPAL USES

- Emmenagogue for delayed menses and amenorrhea
- Abortifacient in unwanted pregnancy
- Uterine stimulant/tonic in conjunction with other herbs for the treatment of a variety of gynecologic complaints including uterine leiomyomata, ''pelvic congestion syndrome,'' and dysfunctional uterine bleeding, postdates pregnancy, dysfunctional labor to stimulate uterine contractions
- *Partus preparator* to prepare the uterus for labor and ''ensure'' an easier labor (discussed in the following)

TRADITIONAL AND HISTORICAL USES

Caulophyllum thalictroides (blue cohosh), a native of the eastern and central woodlands of the United States, is reported to have been used traditionally and historically as an anticonvulsant, antirheumatic, febrifuge, emetic, sedative, and most notably, a gynecologic aid.[5,6] Interestingly, in modern clinical practice, blue cohosh is used almost exclusively for gynecologic and obstetric purposes. It is not commonly used for anticonvulsant, sedative, or antirheumatic actions, whereas the unrelated herb *Actaea racemosa* syn. *Cimicifuga racemosa* is used for these purposes, as well as a uterine antispasmodic for the treatment of painful gynecologic conditions such as dysmenorrhea. It is this author's suspicion that some of the uses of black cohosh have been overlaid on blue cohosh in the historical literature because of the similar common name, confounding an interpretation of the traditional uses of blue cohosh.

Blue cohosh has been used for labor induction, amenorrhea, dysmenorrhea, menorrhagia, and the induction of abortion.[5] Blue cohosh was official in the United States Pharmacopoeia from 1882 to 1905 for labor induction, and in the National Formulary from 1916 to 1950. It was a major ingredient in the popular Eclectic preparation Mother's Cordial, which also included *Mitchella repens, Rubus idaeus, Cimicifuga racemosa,* and *Chamaelirium luteum*. At least one company (Herbalist and Alchemist, NJ) still makes this preparation; however, the blue cohosh has been removed as an ingredient in the product because of safety concerns. The practice of labor induction with blue cohosh remains a popular choice both among self-prescribers and obstetric professionals in the United States and abroad, with large surveys indicating widespread use among nurse-midwives.[7]

Blue cohosh (*Caulophyllum thalictroides*). (Photo by Martin Wall.)

CLINICAL INDICATIONS

Blue cohosh is listed in the British Herbal Pharmacopoeia (1983) as a spasmolytic and emmenagogue. It also may be used as a uterine and ovarian tonic, and for the treatment of a variety of menstrual complaints, including menorrhagia, amenorrhea, dysmenorrhea, and pelvic congestion syndrome. It is commonly used as a *partus preparator* to ease parturition, and for labor induction and augmentation. It has also been used as an abortifacient.

IN VITRO, ANIMAL, AND CLINICAL DATA

Uterine stimulant properties were observed using blue cohosh extract on isolated guinea pig tissue; however, subsequent in vivo studies with cats, dogs, and rabbits failed to demonstrate uterine activity. Smooth muscle stimulation has been seen in vitro on small intestine and in vivo on coronary blood vessels of small animals using caulosaponin. Caulosaponin has also demonstrated an oxytocic effect on tissue from rat uteri, in vitro constriction of carotid vessels, myocardial toxicity, and intestinal spasmogenicity on isolated intestinal tissue. Methylcystine has a nicotinic-like action resulting in blood pressure increases, respiratory stimulation, and increased intestinal motility. Clinical studies using blue cohosh are absent.

MECHANISMS OF ACTION

See Use in Pregnancy and Lactation.

RATINGS

- Botanical Safety Handbook classification 2b: Not to be used during pregnancy. However, *Caulophyllum* may be used as a parturient near term to induce childbirth under the supervision of a qualified practitioner.[17] Canadian regulations require that any products containing this herb be labeled as not for use in pregnancy.

PREPARATIONS USED CLINICALLY

- Capsules/dried herb
- Tincture
- Decoction (rarely)

DOSAGE

- 0.3 to 3 g/day of dried root (or dried root prepared as decoction)
- 0.5 to 3 mL/day of a 1:2 liquid extract (or equivalent)[8]

USE IN PREGNANCY AND LACTATION

Use of blue cohosh during pregnancy to ''prepare'' the uterus for parturition is a widespread practice among midwives and pregnant women.[7] Although this practice is rarely associated with significant adverse outcomes, maternal ingestion has been associated with a range of fetal and neonatal side effects, including fetal tachycardia and increased meconium, as well as several case reports of profound neonatal congestive heart failure and perinatal stroke.[7,9–12] There is one case report of a neonate born with complications including myocardial infarction and profound congestive heart failure to a mother who ingested blue cohosh capsules as a *partus preparator*. The newborn remained critically ill for several months, and at 2 years old required continued digoxin therapy for poor ventricular function. All other causes of myocardial infarction were excluded.[11,13] In another case report a child was born with severe multiorgan failure associated with the use of a blue and black cohosh combination. The child required significant resuscitation at birth and sustained permanent CNS damage.[12] Neither the amount nor duration used were disclosed. It should be noted that midwives attempted to resuscitate this newborn at home for 30 minutes prior to contacting emergency services. The effects in both cases have been attributed to vasoactive glycosides in the herb. A 21-year-old woman developed symptoms of nicotinic toxicity, including tachycardia, diaphoresis, abdominal pain, vomiting and muscle weakness, and fasciculations after using blue cohosh in an attempt to induce an abortion. These symptoms likely resulted from methylcysteine, which is known to be present in blue cohosh. The patient's symptoms resolved after 24 hours and she was discharged.[14]

Alkaloid and glycoside components in blue cohosh suggest possible mechanisms for these effects, as well as teratogenicity and mutagenicity, however, the case reports involving neonatal adverse events are inconclusive.[1,14] *N*-methylcytisine exhibited teratogenic activity in the rat embryo culture (REC), an in vitro method to detect potential teratogens. Taspine showed high embryotoxicity, but no teratogenic activity, in the REC.[15] Toxic effects of the plant's constituents include coronary vasoconstriction, tachycardia, hypotension, and respiratory distress; however, one author cautions that the quality of the case reports to date, and the value of some of the testing methods used to establish toxicity may be questionable. For example, although REC tests have shown teratogenicity and embryotoxicity, ''neither the National Institute of Environmental Health Sciences nor the Environmental Protection Agency recognizes these tests as an appropriate screen for human reproductive risk.''[16] Similarly it has been speculated that anagyrine, which produces known malformations in ruminant livestock, may do so only after metabolism by microflora in the ruminant gut.

The *Botanical Safety Handbook* classifies this herb as 2b, not to be used during pregnancy; however, it states that *Caulophyllum* may be used as a parturient near term to induce childbirth under the supervision of a qualified practitioner.[17] Canadian regulations require that any products containing this herb be labeled as not for use in pregnancy. Given the volume of blue cohosh use in the United States alone, and the general paucity of reports of its side effects, as well as a lack of comparison of side effects with conventional medications for labor augmentation (i.e., pitocin, misoprostel), it remains uncertain how great a risk is posed by the use of blue cohosh, particularly for short-term labor augmentation as opposed to long-term use as a *partus preparator*. Nonetheless, physician–herbalist Tieraona Low Dog states, ''The human case reports, flawed as they are, paint a picture that is consistent with the evidence provided by the in vitro and animal studies.''[16]

The most conservative route is to avoid its use entirely as a *partus preparator*, and possibly at all during pregnancy, until further safety information is established. Midwives and mothers choosing to use blue cohosh to augment labor should consider continuous fetal heart evaluation during use and discontinue use promptly if abnormal patterns are observed. No discussion on the safety of blue cohosh during lactation is reported in the literature. One case report in the literature describes an infant born with skeletal dysplasia and vascular anomalies to a mother who had consumed anagyrine containing goat milk; however, as stated, it is not known whether activation of this compound requires metabolism in the ruminant gut.[18]

Blue cohosh should never be used during the first or second trimesters of pregnancy. The most conservative—and safest—route is to avoid the use of blue cohosh as a *partus preparator,* and possibly at all during pregnancy, until further safety information is established. The safety of its use to augment labor has not been established; any such use should be accompanied by the supervision of a health professional skilled in midwifery or obstetric and herbal care.

SAFETY INFORMATION: HERB DRUG INTERACTIONS, TOXICITY, AND CONTRAINDICATIONS

Because of its potential vasoconstrictive activities, its use is cautioned in patients with hypertension, cardiovascular disease, and those on hypertensive medications. There have been no documented reports of drug interactions with blue cohosh,[19] although blue cohosh powder may be irritating to the mucus membranes. Caulosaponin may be cardiotoxic, causing constriction of the coronary vessels, and methylcysteine could theoretically increase blood pressure in excessive doses; however, this has not been documented.

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CHASTE TREE

Botanical name: *Vitex agnus-castus*
Synonyms: Vitex, Chasteberry, Monk's pepper
Family: Verbenaceae
Part used: Fruit

MAJOR CHEMICAL CONSTITUENTS

The principal constituents are two labdane diterpenoids, including rotundifuran, vitexilactone, as well as vitexilactam A; flavonoids, including casticin, penduletin, chrysosplenol, isoorientin, and isovitexin; iridoids, including aucubin and agnuside; fatty oils, including caprinic acid, palmitic acid, and stearic acid as well as possibly linolenic acid; and essential oils.

PRINCIPAL USES

- Menstrual dysregulation
- Premenstrual symptoms/premenstrual syndrome (PMS)
- Luteal phase dysfunction
- Fertility problems
- Mastodynia/mastalgia
- Hyperprolactinemia
- Habitual miscarriage (see Use in Pregnancy and Lactation)
- Insufficient lactation
- Acne

TRADITIONAL AND HISTORICAL USES

Vitex agnus-castus is a deciduous shrub native to Mediterranean Europe and Central Asia. It has a long history of use for gynecologic complaints, as well as an alleged history of use as an aphrodisiac among monks (hence the common names monk's pepper and chaste tree/berry). It is mentioned early in history by Greek philosopher and naturalist Plato (circa 428–348 BCE), who described the herb's aphrodisiac effects. The ability of chaste tree fruit to stimulate menstrual flow was reported by Lonicerus in 1582. It was mentioned in ancient herbals for the treatment of reproductive pain. For unknown reasons, chaste tree is not found in many Western herbals until the middle of the 1900s. Prior to that time it was not considered a primary herb in the US medical botany, Eclectic, or herbal literature. It is mentioned briefly by Felter and Lloyd in *King's American Dispensatory* as a galactogogue, emmenagogue, and aphrodisiac.

CLINICAL INDICATIONS

Chaste tree is one of the most popular herbs in Europe, the United States, and other Western nations for the treatment of a number of gynecologic complaints. Its primary uses include the treatment of menstrual irregularities, especially secondary amenorrhea, oligomenorrhea, and dysmenorrhea; premenstrual symptoms and PMS; luteal phase dysfunction caused by luteal insufficiency, infertility (particularly secondary to endometriosis or anovulation), cyclic mastalgia, hyperprolactinemia, habitual miscarriage (attributed to progesterone insufficiency), insufficient lactation, and acne. Subclinical hyperprolactinemia has been suggested as a possible cause of endometriosis in some women, and is associated with amenorrhea and other menstrual irregularities, and cyclic mastalgia. Chaste tree has been shown to increase progesterone levels and lengthen the hyperthermic phase of the basal metabolic temperature curve when taken daily for a minimum of three consecutive months.

Chaste tree (*Vitex agnus-castus*). (Photo by Martin Wall.)

MECHANISMS OF ACTION

The pharmacodynamics of chaste tree are not yet entirely understood. Dopaminergic activity, and consequently prolactin-lowering effects, have been demonstrated in preclinical studies and animal studies in vitro and in vivo, lending credence to the traditional uses of this herb in the treatment of menstrual irregularities; however, it appears contradictory to the herb's use as a lactagogue (see Use in Pregnancy and Lactation). There is also evidence that suggests mediation of the herb's effects via luteinizing hormone (LH), follicle-stimulating hormone (FSH), estrogen, and progesterone.

IN VITRO, ANIMAL, AND CLINICAL DATA

In vitro and animal studies have demonstrated binding of chaste tree extract and isolated constituents to dopamine (D2) receptors in a dose dependent manner, with a number of studies demonstrating subsequent reductions in prolactin release or levels. In vitro studies have suggested that chaste tree may exert benefits in PMS via a direct endorphin-like effect on opioid receptors as well as indirectly via estrogenic effects, which may lead to an increase in endogenous opioid levels. A weak binding of chaste tree extract components to serotonin receptors has been seen in animal models, hinting at another possible mediating effect of this herb on PMS. Elevations in progesterone levels have been seen with the herb. Ligand binding assays demonstrate competitive binding to estrogen receptors of both the α and β subtypes, although

estrogenic effects have not been seen consistently in in vitro assays using methanol extracts of the herb.

Clinical studies using chaste tree have focused on PMS and cyclic mastalgia. One of the strongest trials was a randomized, double-blind placebo-controlled trial of 170 women with PMS who received a chaste tree extract of 20 mg standardized to casticin daily for 3 months, at the end of which they reported significant improvements in PMS symptoms, including irritability, mood alteration, headache, breast fullness, and bloating compared with the placebo. Other, less robust clinical trials have also shown positive outcomes in the reduction of PMS symptoms. In a double-blind placebo-controlled study of 37 women with luteal insufficiency and latent hyperprolactinemia, the luteal phase was increased from 3.4 to 5.5 days to 10.5 days in the group taking chaste tree extract ($n = 17$) compared with the control group ($n = 20$). Results of two separate randomized, double-blind placebo-controlled trials ($n = 104$, $n = 97$) have provided evidence of efficacy for the treatment of mastalgia, with significant improvements in chaste berry groups compared with controls. Small trials, including randomized, double-blind placebo-controlled trials and several open uncontrolled studies, have shown achievement of pregnancy, and in cases with hyperprolactinemia, reported decreases in prolactin levels compared with baseline. Interestingly, in two studies looking at parameters not related to pregnancy, a total of 28 women in vitex groups only became pregnant; of these, 19 reported having some difficulty in achieving pregnancy prior to taking the herb. Preliminary reports suggest positive findings in the treatment of acne. Not all trials of chaste tree have shown consistently beneficial effects in the treatment of gynecologic conditions or improvements from baseline hormonal parameters; however, there have been a number of promising results, including the examples presented herein. Because gynecologic problems remain a significant cause of discomfort and distress to women, and represent significant social and economic costs to women and society (e.g., work absenteeism), further rigorous studies are needed to determine whether the use of chaste tree for common gynecologic complaints is supported by substantial evidence. In spite of limited trials, herbal practitioners and women continue to rely on this herb, reporting many positive outcomes.

RATINGS

- German Commission E: The German Commission E has approved the use of chaste tree for menstrual cycle irregularities, premenstrual disturbances, and mastodynia.
- Botanical Safety Handbook* class 1: Herbs that can be safely consumed when used appropriately.

*This is based on the revised edition, in publication. The prior 2b rating was based on theoretical emmenagogic effect because of the herb's historical use for menstrual regulation and the treatment of amenorrhea. The 2d rating was reported by Upton in the *American Herbal Pharmacopoeia* and *Therapeutic Monographs: Chaste Tree Fruit* to be an unsubstantiated rating, with no reports of inference with oral contraceptives (or any other) in the pharmacologic literature, clinical reviews, or herbal literature.

PREPARATIONS USED CLINICALLY

- Tablets
- Capsules
- Tincture

DOSAGE

As with many herbs, dose discrepancies exist for chaste tree in the herbal and scientific literature. Ranges are provided in the following reflecting these inconsistencies.

- Powder: 30 to 40 mg once daily, up to 500 to 1000 mg daily
- Tincture: 0.2 mL two to three times daily, up to 3 to 5 mL 1:5 tincture in 50% to 70% ethanol taken daily. Herbal practitioners commonly recommend taking the daily dose upon waking in the morning.

SAFETY INFORMATION: HERB DRUG INTERACTIONS, TOXICITY, AND CONTRAINDICATIONS

A number of transient side effects have been associated with the use of chaste tree. The most common are gastrointestinal complaints/nausea; acne, skin reactions, or urticaria; menstrual cycle changes, including intermenstrual bleeding; and headache. The adverse events following use of chaste tree are mild and reversible. The most frequent adverse events are nausea, headache, gastrointestinal disturbances, menstrual disorders, acne, pruritus, and erythematous rash. No herb–drug interactions have been reported. On theoretical grounds, it is thought prudent to avoid use of chaste berry in conjunction with dopamine agonists and antagonists. Case reports from herbalists have demonstrated that rarely, women with a history of depression taking chaste tree for the treatment of menstrual irregularity experience an exacerbation of depressive symptoms. This is also a reversible adverse effect, but one that practitioners and patients should be aware of prior to commencing use. A review of clinical trials, postmarket surveillance studies, surveys, spontaneous reporting schemes, manufacturers, and herbalist organizations indicate a high level of safety for this herb. See the following for safety during pregnancy and lactation.

USE IN PREGNANCY AND LACTATION

It has been postulated that increased progesterone levels as a result of improved luteal function associated with the use of chaste tree may partially explain positive results seen by herbal practitioners and midwives when using this herb for the prevention of subsequent miscarriage in women with a history of prior repeated miscarriages. No trials have been conducted to evaluate these claims, and specific data on the use and safety of chaste tree during pregnancy are lacking. Improvements in fertility were discussed earlier in this section. In studies in which pregnancy has been achieved while taking chaste tree, no follow-up studies have been conducted on the pregnancy outcomes or newborn health in those who did not discontinue the herb upon becoming pregnant. Reproductive toxicity studies in female rats at up to 80 times the concentration used clinically in humans

showed no difference in offspring compared with controls, and no teratogenicity was seen in the offspring of rabbit dams given up to 74 times the recommended daily dose for humans. A nonsignificant increase in the number of resorptions and placental weight was seen in groups receiving the highest dose, and it is not known whether this was attributable to the alcohol, the herb, or spontaneous events. As stated, the *Botanical Safety Handbook* gives chaste tree a Class 1: rating, suggesting an ease on prior restrictions during pregnancy.

Historically and traditionally, the herb has been used to increase milk supply in breastfeeding mothers. Although research has shown prolactin-lowering effects that suggest quite the opposite result, effects may be dose dependent. Chaste tree has been reported to increase milk production without changing the composition of the breast milk. There is no known risk to consumption of chaste tree during lactation; however, use is commonly discouraged because of lack of evidence for or against safety.

DONG QUAI

Botanical name: *Angelica sinensis*
Family name: Apiaceae
Synonyms: Dang gui, Tang kuei
Part used: Root (whole root, root head, root body, root tail)

MAJOR CHEMICAL CONSTITUENTS

Important compounds in dong quai include alkylphthalides present in the essential oil fractions of the plant and ferulic acid. The plant also contains additional essential oils, amino acids, lipids, aromatic compounds, polysaccharides, monoterpenes, and diterpenes. Vitamins A, B_1, B_{12}, E, biotin, and nicotinic acid, as well as a number of trace minerals, are found in the root.

PRINCIPAL GYNECOLOGIC AND OBSTETRIC USES

- Anti-inflammatory, analgesic, and antispasmodic for the treatment of dysmenorrhea and endometriosis
- Menstrual irregularities, i.e., amenorrhea
- Uterine atony
- Infertility
- In TCM used to ''nourish the blood,'' ''regulate qi,'' and treat ''blood stasis'' and ''blood vacuity,'' which may be considered to include the Western medical diagnoses of dysmenorrhea, amenorrhea, endometriosis, and uterine fibroids

Other uses:

- Fatigue
- Convalescence
- Improve circulation
- Cardiovascular protective effects

TRADITIONAL AND HISTORICAL USES

Dong quai is one of the oldest and most respected herbs in the Chinese pharmacopoeia, used since at least the first century to ''nourish the blood and qi'' and restore a state of well-being. Although not used exclusively for gynecologic complaints, its popularity as a woman's herb in the Western world stems from its traditional Chinese medicine (TCM) uses for the treatment of dysmenorrhea, amenorrhea, other menstrual irregularities, and uterine complaints. Traditionally, the herb is not used alone, but in combination formulae specific to various conditions. In addition to the aforementioned indications, it was used in pregnancy formulae to ''quiet the fetus'' in cases of threatened miscarriage, and in the postnatal period in soups to strengthen the blood and restore strength; however, in the West it is typically contraindicated during pregnancy (see Use in Pregnancy and Lactation).

CLINICAL INDICATIONS

Dong quai is a popular herb in contemporary western herbal medicine used in the treatment of a variety of gynecologic complaints, particularly for menstrual irregularities and endometriosis. Herbalists consider dong quai a ''uterine tonic'' based on its traditional uses and also on in vivo and in vitro animal studies demonstrating both stimulating and relaxing activity on uterine tissue. Its reported efficacy in the treatment of dysmenorrhea and endometriosis most likely lies in its effects as an anti-inflammatory, antispasmodic, and analgesic. It is also thought to improve blood flow generally, specifically in the pelvis; thus it is used to relieve pelvic congestion syndrome and associated pelvic pain and uterine fibroids, which some herbalists consider associated with pelvic congestion and poor uterine circulation. Although it is sometimes touted as an herb for perimenopausal symptoms, alone it is traditionally considered a ''heating'' herb, which would actually exacerbate symptoms such as night sweats, hot flashes, irritability, and insomnia. However, in TCM these symptoms are also associated with yin and blood deficiency; thus in appropriately combined formulas, it can be used for the treatment of perimenopausal complaints.

Dong quai (*Angelica sinensis*). (Photo by Martin Wall.)

IN VITRO, ANIMAL, AND CLINICAL DATA

Few studies have been done with dong quai as a single agent looking at its effects on gynecologic conditions for which it is traditionally indicated and for which modern herbal practitioners often use it. Further, many of the studies that have been done looking at dong quai are not in English language journals, limiting review of the literature and also raising questions about the standards used for clinical studies. Limited preclinical trials and human studies have shown efficacy in the treatment of dysmenorrhea and infertility resulting from tubal occlusion. Questions have arisen about whether dong quai has

estrogenic effects. To date this has not been determined, with one clinical trial of 71 symptomatic perimenopausal women showing no significant changes in vaginal cell maturation or endometrial thickness after 24 weeks of a daily dose of 4.5 g of crude herb; however, a longer trial may be needed to demonstrate changes in vaginal and epithelial tissue. Numerous preclinical trials have demonstrated the herb's dual ability to both relax and stimulate uterine smooth muscle. Dong quai has been shown to relax the vascular smooth muscle as well as uterine and intestinal smooth muscle, which may support its role in alleviating the symptoms of dysmenorrhea and endometriosis. Its stimulating effect is not usually corroborated with a clinical condition, but may explain its popularity as a uterine tonic for uterine atony and ''boggy'' uterus associated with uterine fibroids. Pharmacologic studies in animals suggest that dong quai may exert effects on the cardiovascular system, including increased myocardial perfusion, decreased myocardial oxygen consumption, increased blood flow, decreased afterload, inhibition of platelet aggregation, and inhibition of arrhythmias. Human clinical evidence suggesting hypotensive and cardiovascular protective effects of dong quai, however, is weak, with numerous methodologic flaws. Limited evidence suggests that the herb may have hemorrhologic effects, including decreased platelet aggregation and increased PT time.

MECHANISMS OF ACTION

The mechanisms of action for this herb are poorly elucidated. It is thought that the volatile components of the oil may be responsible for the uterine and other smooth muscle spasmolytic effects, whereas the nonvolatile components are excitatory. The spasmolytic effects may result from histamine receptor blocking activity and calcium ion channel effects of the phthalides; however, this has not been fully determined.

RATINGS

- Botanical Safety Handbook class 2b: Not to be used during pregnancy unless otherwise directed by an expert qualified in the use of the described substance.

The editor's note in the BSH states that both stimulating and relaxing effects on the uterus have been reported for this herb, but that no contraindication during pregnancy is noted in any of the authoritative reference books used in compiling the BSH. Canadian regulations require a bilingual label warning against dong quai use during pregnancy.

PREPARATIONS USED CLINICALLY

- Dried root in capsules and pills
- Dried root boiled into decoctions
- Tincture and standardized extract

DOSAGE

- Dried root products: 3.5 to 4 g/day
- Dried root in decoction: 6 to 12 g/day
- Tincture: 3 to 5 mL three times/day
- Standardized extract (to 1% ligustilide): 200 mg three times/day

SAFETY INFORMATION: HERB DRUG INTERACTIONS, TOXICITY, AND CONTRAINDICATIONS

Dong quai is associated with few side effects and a high level of safety in the general literature. In a survey conducted by the American Herbalists' Guild of its professional membership, 44% of those who responded reported having observed side effects, including worsening of endometriosis, bleeding gums with prolonged use over months, increased and sometimes excessive menstrual flow, breast tenderness, headaches, and irritability. All side effects are reversible with discontinuation of use. The increased bleeding seen with use of the herb is predictable given clinical studies demonstrating decreased platelet aggregation and increased PT time. Because of these effects, dong quai is contraindicated prior to surgery, with most practitioners suggesting a 2-week holiday from the herb prior to major procedures. The herb is also theoretically contraindicated for use in conjunction with anticoagulant medical therapy, i.e., warfarin.

USE IN PREGNANCY AND LACTATION

In spite of customary use in TCM formulae for miscarriage prevention, dong quai is generally considered contraindicated in all trimesters of pregnancy because of possible anticoagulant and uterotonic effects. The BSH states that it is not to be used during pregnancy unless otherwise directed by an expert qualified in its use. Anecdotal reports suggest that solo administration of the herb during pregnancy may be associated with miscarriage. Data regarding fetotoxicity, mutagenicity, and teratogenicity are lacking. Personal experience, including challenge and re-challenge in three nursing mothers has suggested that consumption of dong quai decoctions in formulae by lactating mothers may lead to a rash in the newborn. Dong quai is clinically associated with increased bleeding. Herbalists typically contraindicate its use during the menses, during pregnancy, in cases of abnormal uterine bleeding, and in conjunction with anticoagulant medications. It is also typically contraindicated in pregnancy because of possible uterine stimulatory effects; however, it is used in TCM in customary formulations to prevent miscarriage. It has been seen to cause skin rash in the infant of nursing mothers consuming the decocted herb in the neonatal period.

GINGER

Botanical name: *Zingiber officinalis*
Family name: Zingiberacaea
Part used: Rhizome

Ginger (*Zingiber officinalis*). (Photo by Martin Wall.)

MAJOR CHEMICAL CONSTITUENTS

The major chemical constituents are volatile oils, including β-bisabolene and zingiberene, sesquiterpenes, including zingiberol, zingiberenol, the oleoresin shaogol, numerous monoterpene hydrocarbons, alcohols, and aldehydes, oleoresins, free fatty acids including palmitic acid, oleic acid, linoleic acid, caprylic acid, capric acid, lauric acid, myristic acid, steric acid, and starch and amino acids.

PRINCIPAL USES

- Antiemetic for nausea and vomiting of pregnancy (NVP) and *hyperemesis gravidarum*
- Antiemetic and antianorectic for nausea and appetite loss associated with cancer and HIV chemotherapeutic treatments
- Anti-inflammatory and antispasmodic for dysmenorrhea, uterine fibroids, and chronic pelvic pain
- Antiinflammatory for headache
- Digestive complaints associated with endometriosis and chronic pelvic pain
- Flavoring for herbal formulae
- Possible chemopreventative and cytotoxic activity in cancer treatment

TRADITIONAL AND HISTORICAL USES

Ginger has been used traditionally from Asia to the Caribbean for its antispasmodic, carminative, and diaphoretic properties. It has been used in traditional Chinese medicine (TCM), for example, since at least the ninth century for the treatment of nausea, diarrhea, and digestive complaints. Ginger was included in the United States Pharmacopoeia (USP) and the National Formulary as a carminative, stimulant, and aromatic herb. Because of geographic/climatic distribution of the herb, its use was not reported in northern European traditional herbalism, but its place in modern Western herbalism has become firmly established, as described in this profile.

CLINICAL INDICATIONS

Modern use of ginger has focused on its efficacy as an antiemetic for the treatment of nausea and vomiting in a variety of contexts, including during pregnancy and for patients undergoing chemotherapy. It has also been used for the treatment of appetite loss in cases of HIV, cancer, and the side effects of medications for their treatment. Herbal practitioners also widely use ginger for the treatment of gynecologic pain, including dysmenorrhea, pain associated with uterine fibroids, and chronic pelvic pain. It is also used for the treatment of premenstrual headaches and for the relief of diarrhea and cramping bowel pain that often accompanies dysmenorrhea, PMS, and endometriosis.

IN VITRO, ANIMAL, AND CLINICAL DATA

Ginger has been shown to have antiemetic effects in animal and human studies, possibly through an antiserotinergic effect. In seemingly contradictory animal studies, the herb has been shown to both increase stomach acid production, possibly interfering with the effects of antacid medications, and to significantly reduce gastric secretions and provide gastric mucosal protection with a reduction in gastric ulcers comparable to the effects provided by NSAIDs. At 62 mg/kg ginger extract has demonstrated protective effects against stress ulcer induction in rats, although to a lesser extent than cimetidine. The antiplatelet effects of ginger are also controversial. Although the herb does inhibit prostaglandin, thromboxane, and leukotriene synthesis, inhibition of platelet synthesis has been inconsistent among studies. Ginger has demonstrated anti-inflammatory activity in vitro, with COX-2 inhibition and resultant reductions of severe arthritis, paw and joint swelling in rats treated with ginger oil. Fresh ginger juice has a hypoglycemic effect in nondiabetic and diabetic rabbits and rats, with the effect more pronounced in diabetic animals.

MECHANISMS OF ACTION

The aromatic principles of ginger are considered responsible for its medicinal actions, including enzymatic inhibition of prostaglandin, thromboxane, and leukotriene synthesis. The mechanisms of action on nausea and vomiting remain uncertain, with studies demonstrating

increased gastric motility contradictory to those showing no motility. Another theory is that the herb acts via a centrally mediated effect on 5-hydroxytryptamine-3 ($5\text{-}HT_3$), an effect that has been demonstrated in vitro. There is some evidence that ginger increases stomach acid production, thus possibly interfering with antacid medications.

RATINGS

- Botanical Safety Handbook class 1: Herbs that can be safely consumed when used appropriately.
- No significant adverse events in clinical trials
- No case reports with significant adverse events and high probability of causality
- No identified concerns for use during pregnancy or lactation
- No innately toxic constituents
- History of safe traditional use
- Toxicity associated with excessive use is not a basis for exclusion from this class
- Idiosyncratic, minor, or self-limiting side effects are not bases for exclusion from this class.
- German Commission E Monographs: Approved for the treatment of dyspeptic complaints and prevention of the symptoms of motion sickness.

PREPARATIONS USED CLINICALLY

- Tea
- Powder
- Tincture
- Also taken as ginger candy, dried crystallized ginger, ginger syrup, and in foods (i.e., soup broth)

DOSAGE

- Tea: 1 tbs grated raw root per 1 cup of boiling water, 3 to 4 cups daily
- Powder: 1 to 2 g daily
- Tincture: 1.5 to 3 mL three times per day

SAFETY INFORMATION: HERB DRUG INTERACTIONS, TOXICITY, AND CONTRAINDICATIONS

Ginger has a long history of safe use both as a culinary and medicinal herb. It is considered safe when used as recommended, including when used within the prescribed pregnancy dose. Dose should not exceed 1 g daily in pregnancy, and 4 g per day for the general population. Theoretical herb drug interactions have been proposed (Table 1). Concerns have been expressed that ginger might increase the risk of bleeding, for example, with surgery, owing to platelet activating factor (PAF) inhibition; therefore, it is recommended that patients taking ginger should discontinue use 1 to 2 weeks prior to surgical procedures. Patients using oral hypoglycemic medications may require a dose adjustment as ginger may have hypoglycemic effects. Limited evidence suggests that ginger may interfere with antacids, sulcralfate, H2 antagonists, and proton pump inhibitors (PPIs) by

TABLE 1

Herb–Drug Interactions with Ginger

DRUG	ACTUAL OR THEORETICAL	INTERACTION
Antacids, gastric acid inhibiting drugs	Theoretical	Ginger may increase stomach acid production, therefore interfering with the actions of antacids, sucralfate, H2 antagonists, and proton pump inhibitors (PPIs). Ginger also may have a gastroprotective effect.
Anticoagulants, antiplatelet drugs	Theoretical	Because ginger has been observed to inhibit both PAF and thromboxane synthetase, it has been proposed that ginger may increase bleeding time and increase the risk of bleeding with anticoagulant and thrombolytic medications. However, this is not supported by case reports, adverse events reports, or the clinical literature.
NSAIDs	Theoretical	Also caused by inhibition of thromboxane synthetase, theoretical interaction with NSAIDs has been proposed, also leading to increased bleeding risk and potentiation of effects.
CNS depressants	Theoretical	Large doses of ginger have been reported to lead to CNS depression; thus, there is a theoretical risk of interaction.
Cardiac drugs, including β-blockers, digoxin, and positive inotropes	Theoretical	Inotropic effects of ginger have been proposed; and thus a theoretical risk of interaction with cardiac drugs. However, this has not been observed clinically.
Oral hypoglycemic agents	Theoretical	Ginger has demonstrated hypoglycemic effects; thus, a dose-adjustment of oral hypoglycemic medications may be required for those taking this herb.

increasing stomach acid production. Patients with gastric and duodenal ulcers are therefore sometimes advised to avoid using ginger other than for culinary purposes for this reason; however, animal experiments suggest a protective effect against gastric ulcers.

Patients with known allergy or hypersensitive to members of the *Zingiberacae* family, or those allergic to Balsam of Peru, may experience sensitivity or contact dermatitis with use of ginger. Ginger powder taken unencapsulated has been known to cause heartburn-like symptoms, and raw ginger taken in large boluses and poorly masticated has been reported in the literature to cause ileus in a limited number of case reports.

USE IN PREGNANCY AND LACTATION

A literature review identified six double-blind RCTs with a total of 675 participants and a prospective observational cohort study ($n = 187$) met all specified inclusion criteria. The methodologic quality of 4 of 5 RCTs was high. Four of the 6 RCTs ($n = 246$) showed superiority of ginger over placebo; the other 2 RCTs ($n = 429$) indicated that ginger was as effective as the reference drug (vitamin B_6) in relieving the severity of nausea and vomiting episodes. The observational study and RCTs (including follow-up periods) showed the absence of significant side effects or adverse effects on pregnancy outcomes. There were no spontaneous or case reports of adverse events during ginger treatment in pregnancy.

In a study of pregnant women who called the Motherisk Program and who were taking ginger during the first trimester of pregnancy were enrolled in the study, the women were compared with a group of women who were exposed to nonteratogenic drugs that were not antiemetic medications. The women were followed to ascertain the outcome of the pregnancy and the health of their infants. They were also asked on a scale of 0 to 10 how effective the ginger was for their symptoms of NVP. Out of 187 pregnancies, there were 181 live births, two stillbirths, three spontaneous abortions, and one therapeutic abortion. The mean birth weight was 3542 g ± 543 g the mean gestational age was 39 ± 2 weeks, and there were three major malformations. There were no statistical differences in the outcomes between the ginger group and the comparison group with the exception of more infants weighing less than 2500 g in the comparison group (12 vs. 3, $p < 0.001$). These results suggest that ginger does not appear to increase the rates of major malformations above the baseline rate of 1% to 3% and that it has a mild effect in the treatment of NVP. Ginger has not been shown to cause teratogenesis in rat pregnancy models.

Perhaps one limit to the potential effectiveness of ginger as an antiemetic is suggested by a study that found tremendous variability in the contents of ginger products on the market, most notably the type of ginger used. Another limitation is that the studies cited in the literature review are time limited, whereas NVP and *hyperemesis gravidarum* are persistent problems of long duration (weeks to months) for which no remedy provides consistent, lasting relief.

Some studies reported side effects such as headache, diarrhea, and drowsiness, but there were no differences in pregnancy outcomes among women taking placebo, vitamin B_6, or ginger. Sipping ginger tea may actually aggravate nausea and vomiting in women who are triggered by larger volumes of fluid, as might swallowing ginger capsules; therefore, these women may be best served simply sipping tea, avoiding taking capsules on an empty stomach, or using other products such as ginger-flavored hard candies made with real ginger, crystallized ginger, or ginger ale made with real ginger.

Although several of the mentioned studies do not specify dose and product, in one of the most recent studies participants were randomly assigned to take a capsule containing 350 mg of ginger or one containing 25 mg of vitamin B_6 three times a day for 3 weeks.

KAVA KAVA

Botanical name: *Piper methysticum*
Family name: Piperacaea
Synonyms: Kava, kava pepper, kawa, awa
Part used: Peeled dry rhizome

MAJOR CHEMICAL CONSTITUENTS

The main constituents of kava kava rhizome include kavalactones (kavapyrones) kawain, dihydrokawain, methysticin, and dihyrdromethysticin; the alkaloids and amides 1-cinnamoylpyrrolidine, 1-(*m*-methoxycinnamoyl)-pyrrolidine, and cepharadione A; chalcones, flavonoids, steroids (sitosterol, stigmasterol, and stigmastanol); esters (e.g., bornyl cinnamate); aliphatic alcohols; and long chain fatty acids. Dried material should contain at least 3.5% kavalactones and good-quality rhizomes up to 8.3% kavalactones.

PRINCIPAL GYNECOLOGIC AND OBSTETRIC USES

- Sedative and short-term mood elevator for anxiety and associated sleep disorders
- Neurovegetative complaints associated with perimenopause and menopause
- Analgesic, antispasmodic, and neurotonic for dysuria, neurogenic bladder pain, and genital/pelvic pain
- Antispasmoic and nerve tonic for hyperactive bladder
- Rarely, used for topical analgesia in postpartum perineal repair and healing of episiotomy/lacerations.

ADDITIONAL USES

- Analgesic and antispasmodic for neuromuscular tension
- Analgesic for neuralgia
- Anticonvulsant

TRADITIONAL AND HISTORICAL USES

Kava kava use is deeply rooted in the ceremonial and daily recreational traditions of South Pacific Islanders, particularly Polynesia, Melanesia, and Micronesia, together known as Oceania, with heavy use found in Fiji, Samoa, and Tonga. Use spread to Australia via missionaries from the South Pacific, and it was traditionally also very popular in Hawaii, although a death penalty instituted for its use there eventually led to decreased consumption among Hawaiians. Legends abound regarding ''the kava,'' which is believed to be the child of their god of good seasons and rain, and patron deity of farmers. Kava kava use is accompanied by specific rituals, including the use of a special kava bowl (*tanoa*), strainer (*tau'anga*), and cup (*ipu*), also believed to be gifts from the gods accompanying the herb. Kava kava was traditionally taken as a beverage prepared as a cold infusion. The root is chewed, grated, powdered, or macerated and placed inside the kava bowl to which cold water is then added. This mash is steeped and strained repeatedly, then poured into cups for drinking. Kava kava is used in formal ceremonies such as political events, marriages, and births; at important and official meetings such as contract signings; and also more casually and informally on social occasions; and even recreationally, for example, at the start of the day by old men, or at the end of a long work day. Reports say that is has also been used to cure illness, help soothe arguments, and even as part of ceremonies at which disputes are resolved or differences between enemies are reconciled. One might say it is considered the beverage of hospitality in the South Pacific.

Kava Kava (*Piper methysticum*). (Photo by Martin Wall.)

Traditional medicinal indications for kava kava use include use as an intoxicant, a nervine, and neuromuscular restorative (e.g., calming the nerves, inducing relaxation and sleep, relieving headache, counteracting fatigue or weakness, and restoring muscle strength in asthma and rheumatism). It was used as a diaphoretic in the treatment of chills and head colds, and for asthma. Another important medicinal use was as a diuretic, particularly for difficulty urinating and the treatment of chronic cystitis, syphilis, and gonorrhea.

It was first described and named *Piper methysticum,* meaning ''intoxicating pepper'' in 1786, and was not highly used as a medicinal plant in Western botanical medicine. It was recognized by the Eclectics in the late nineteenth century as a local anesthetic, CNS depressant, and cardiac stimulant, and as a treatment for gonorrhea. In the early twentieth century the Eclectics cited its use for neuralgic conditions of the eyes, ears, and teeth, for edema, and for gastric atony and postsurgical anorexia. The herb was listed in the 20th to 24th editions of *The United States Dispensatory of the United States of America* (1918–1947) and the fluid extract had official status in the 4th and 5th editions of the *National Formulary* (1888–1926).

CLINICAL INDICATIONS

Herbal practitioners regard kava kava as a highly reliable anxiolytic, antispasmodic, analgesic, and neuroprotective herb, with mild topical anesthetic action. Treatment of anxiety and anxiety disorders is the most common clinical indication for kava kava; however it is also widely used for the treatment of neuromuscular tension, neuralgia, neurovegetative complaints associated with perimenopause and menopause, dysuria, urogenital pain, and hyperactive bladder.

IN VITRO, ANIMAL, AND CLINICAL DATA

The anxiolytic effects of kava kava have been the focus of most clinical trials, and results have generally supported the benefits of kava kava and kavalactones in the treatment of anxiety and anxiety disorders.

A Cochrane systematic review of kava kava monopreparations for the treatment of anxiety identified 12 double-blind placebo-controlled RCTs (n = 700) that met all inclusion criteria, all but one of which used a product standardized to 70% kavalactones, and produced by the same manufacturer. Data from seven trials (n = 380) assessed a common outcome measure—the total score on the HAM-A—and 74% of these patients (n = 282) were diagnosed according to the criteria of the American Psychiatric Association DSM-III-R and DSM-IV. All trials used the HAM-A total score at baseline as an inclusion criterion, and four trials included patients if the total score was 19 or above. One trial included only women with anxiety resulting from climacteric syndrome. The results of the meta-analysis suggest a significant reduction of the HAM-A total score in patients receiving kava kava extract compared with placebo. The results of the five studies that were not submitted to meta-analysis largely support these findings. Five other systematic reviews support these findings. Numerous pharmacologic studies have been conducted with kava kava extracts and isolated kavalactones. The most important findings suggest that kava kava and its preparations possess anxiolytic, anticonvulsive, neuroprotective, sedative, and local anesthetic effects. Kava kava has been demonstrated in animal and human clinical trials to improve sleep parameters. In a human clinical trial (n = 12) kava kava extract was shown to reduce sleep latency, improve deep sleep, and subjects reported a subjective sense of increased quality of sleep, with improved cognitive function compared with oxazepam, which led to impaired function. Additional human clinical trials have demonstrated improvements in cognitive function and performance with kava kava intake. Kava kava and isolated constituents have demonstrated topical analgesic effects in several animal studies. In one study, a 0.5% solution of kavain had an anesthetic effect equivalent to that of cocaine. The effect of a 3% solution of either compound had a comparable effect on the endurance of total anesthesia, extending it from 5.3 minutes for kavain and from 6.5 minutes for cocaine to approximately 31 minutes for both substances. Animal studies have demonstrated dose dependent muscle relaxant capabilities as well as anticonvulsant effects.

MECHANISMS OF ACTION

Animal studies demonstrate CNS penetration of kavalactones shortly after oral administration of extracts of the herb, with a half-life of 1 hour. Although the exact mechanisms of kava kava are not entirely elucidated, a number of sites of action have been proposed, including specific inhibition of voltage-dependent Na^+ and Ca^{2+} channels, indirect effects on GABA and benzodiazepine receptors, specific binding to cortical neurons, stimulation of the limbic system, and an ability to antagonize clonic strychnine convulsions. Effects on dopamine and serotonin receptors have been inconsistent, but some activity has been noted, including an increase in parkinson-like symptoms in patients taking high-dose kava kava. The muscle relaxing effects of kavalactones is attributed to a centrally induced attenuation of the a- and g-spinal motor systems directed by supraspinal sites. Peritoneal administration of aqueous extracts of kava kava has led to tolerance in animal models.

RATINGS

- Botanical Safety Handbook Safety rating 2b: Not to be used during pregnancy
  - Adverse event data in humans exist and have probability of causality
- Botanical Safety Handbook Safety rating 2c: Not to be used while nursing
  - Potential hepatotoxicity or neurotoxicity
  - Adverse event data in humans exist and have probability of causality
- Botanical Safety Handbook Safety rating 2d: Other specific use restrictions as noted
  - Information exists for unsafe use by specific populations
- German Commission E Monographs:
  - Approved for the treatment of nervous anxiety, stress, and restlessness
- Safety:
  - It is contraindicated in pregnancy, lactation, and endogenous depression.
  - Extended use can cause yellow discoloration of hair, skin, and nails. Discontinue if this occurs.
  - Do not use for more than 3 months without medical advice.
  - May adversely affect motor reflexes and judgment for driving and/or operating heavy machinery.
  - Potentiation of central acting substances (i.e., alcohol, barbiturates, and psychopharmacologic agents) is possible.

PREPARATIONS USED CLINICALLY

- Tablets, capsules of dried rhizome
- Liquid extract
- Standardized preparations

DOSAGE

- Tablets, capsules of dried rhizome
- 1.5 to 3 g daily, equivalent to 60 to 120 mg kavalactones daily
- Liquid extract

- 3 to 6 mL daily
- Standardized preparations
- 60 to 200 mg kavalactones daily. 60 mg kavalactones two to four times/day

Standardized product should be used to control the amount of kavalactones consumed, both for efficacy and safety purposes. Duration of use should not exceed 3 months.

SAFETY INFORMATION: HERB DRUG INTERACTIONS, TOXICITY, AND CONTRAINDICATIONS

A 1997 peer-reviewed appraisal of kava kava safety based on a comprehensive review of the scientific and historical ethnobotanical literature determined that

> *When used in normal therapeutic doses, kava appears to offer safe and effective anti-anxiety and muscle relaxant actions without depressing centers of higher thought. The safe use of kava as a dietary supplement in cultures that do not have historical experiences with its use depends on responsible manufacturing, marketing, individual consumption patterns, and education.*

Since that time, 79 adverse event reports of hepatotoxicity reportedly associated with oral use of kava kava preparations have been reported worldwide, with most in Europe, but also in Canada and the United States, and have led to rigorous investigation of the safety of this herb. Although in most cases prescription pharmaceutical medications were being taken in conjunction with kava kava, there was regular alcohol intake, or prior hepatic disease existed. Several cases of severe hepatic damage, including fulminant hepatic failure, apparently occurred de novo. These cases subsequently led to the withdrawal or restriction of sales of kava kava products from many national commercial markets, particularly in Europe. In the Cochrane systematic review discussed previously, six of twelve trials reported adverse events experienced by patients receiving kava kava extract. Stomach complaints, restlessness, drowsiness, tremor, headache, and tiredness were reported most frequently. Four trials comprising 30% of patients in the reviewed trials report the absence of adverse events while taking kava kava extract. None of the trials reported any hepatotoxic events. Seven of the reviewed trials measured liver enzyme levels as safety parameters and report no clinically significant changes.

Warnings about kava kava and performance safety are common. It has been proposed that *Piper methysticum* may cause cytotoxic cell death by interfering with hepatocellular mitochondrial function. Performance safety and basic performance under the influence of kava kava were tested in a randomized double-blind crossover study (n = 18) in which healthy subjects were simultaneously given 400 mg kava kava extract (containing 240 mg kavalactones daily) and 4.5 mg bromazepam twice daily over a period of 14 days. This was compared with the effects of the substances administered individually. Stress tolerance, vigilance, and motor coordination were not changed from baseline when only kava kava was taken, whereas the performance of subjects taking bromazepam and the kava-bromazepan combination deteriorated equally. Nonetheless, several cases of individuals being cited for ''driving under the influence'' after having used kava kava have been reported, and it is generally recommended that individuals not drive or operate machinery or equipment while using this herb.

Kava kava is reported as being generally well tolerated in clinical trials with few reported herb–drug interactions. Potential interaction with benzodiazepines, serotinergic- and dopaminergic-acting medications, and medications that act on sodium ion channels have been proposed. Kava kava should not be used with selective serotonin reuptake inhibitors, tricyclic antidepressants, barbiturates, benzodiazepines, or antipsychotic medications. Kava kava may potentiate the effects of alcohol; thus they should not be taken simultaneously beyond the normal amount present in kava kava extracts.

Kava dermopathy, and ichthyosiform condition, is a well-known side effect of frequent, high-dose kava kava consumption. In fact, in Oceania, this yellowish, scaly skin condition is common among kava kava users, and is reversible upon discontinuation of kava kava intake. Allergic skin reactions also have been associated with kava kava use. Extrapyrimidal symptoms, including torticollis; involuntary neck, head, and trunk movements; oral and lingual dyskinesia; and impairments in movement and visual coordination have been reported occasionally by kava kava users in the absence of cognitive impairment.

Common side effects associated with kava kava use, including stomach complaints, restlessness, drowsiness, tremor, headache, and tiredness were reported most frequently. In the Cochrane review, four trials comprising 30% of patients in the reviewed trials reported the absence of adverse events with kava kava extract.

Kava kava use has been associated with rare but severe liver damage. Kava kava consumption should be discontinued immediately and a qualified health professional should be sought if any of the following signs of hepatotoxicity occur: unusual fatigue, weakness, loss of appetite, unintentional weight loss, yellow discoloration of the skin or ocular conjunctiva, dark urine, or discolored stools. Individuals with a history of liver disease and those taking medications that can cause liver damage should not take kava kava.

USE IN PREGNANCY AND LACTATION

Information on the safety of kava during pregnancy and lactation is limited. Although there is no evidence of mutagenic, teratogenic, or genotoxic potential using standard assays of kava kava, or the synthetic product kavain with identical actions in animal models, use of this herb is entirely contraindicated during pregnancy because of potential hepatotoxic and CNS effects on the maternal–embryonic/fetal dyad. Similarly it is contraindicated for use during lactation and for children under 18 years old.

Kava kava should be avoided entirely during pregnancy and lactation because of uncertainty about hepatic safety and also because of the possible hazards of potential CNS effects of this herb on the unborn baby.

RED CLOVER

Botanical name: *Trifolium pratense*
Family name: Leguminosae
Synonyms: Meadow clover, purple clover, trefoil
Part used: Flowering tops and leaf

MAJOR CHEMICAL CONSTITUENTS

Isoflavondoids including biochanin A, daidzein, formononetin, genistein, and others; flavonoids including kaempferol, quercetin and others; coumarins; carbohydrates, saponins, salicylic acid, and trace vitamins and minerals.

PRINCIPAL USES

- Prevention and treatment of menopausal symptoms including hot flashes and vaginal dryness
- Hormone replacement therapy substitute
- Prevention and treatment of osteoporosis
- Hypercholesterolemia
- Acne and chronic skin disease

TRADITIONAL AND HISTORICAL USES

Red clover has been used traditionally as an alterative or ''blood purifying'' herb. As such, it has been included in the treatment of acute and chronic skin diseases, including acne, eczema, and psoriasis, and it is commonly found in herbal formulae for treating cancer, including the infamous Hoxsey formula. Numerous so-called ''trifolium compounds'' were marketed as blood purifiers to ''help clear the body of toxins.'' Red clover was listed in the National Formulary as a skin remedy until 1946. It has also been used traditionally for the treatment of upper respiratory conditions including acute and chronic cough, asthma, and pertussis. In recent years it has become an exceedingly popular herb for the treatment of menopausal complaints including hot flashes, vaginal dryness, and osteoporosis.

CLINICAL INDICATIONS

Red clover is one of the most popular herbal products in Europe and the United States for the prevention and treatment of menopausal complaints, particularly hot flashes. It is also used to prevent and treat vaginal dryness, osteoporosis, and hypercholesterolemia. Promensil, a commonly used red clover product, is used in many of the red clover clinical trials.

IN VITRO, ANIMAL, AND CLINICAL DATA

Results of human clinical trials to date are conflicting. High-quality human clinical trials supporting the use of red clover (for any conditions) are limited. A small number of positive trials suggest a reduction in menopausal symptoms, particularly hot flashes; improved bone density; reduction in serum lipids; and improvement in arterial compliance. However, study designs have often been weak or contain methodologic flaws including lack of power calculations, unclear statistical significance versus placebo, small sample sizes, lack of control groups, and lack of dietary records to account for other dietary isoflavones that might confound study results.

Red clover (*Trifolium pratense*). (Photo by Martin Wall.)

MECHANISMS OF ACTION

The basis of action of this herb is its phytoestrogen constituents, which exhibit both agonist and antagonist binding with endogenous estrogen receptors.

RATINGS

- Botanical Safety Handbook Class 2b and 2d rating: Not to be used in pregnancy

PREPARATIONS USED CLINICALLY

- Dried blossoms and aerial parts
- Tincture
- Isoflavone extracts

DOSAGE

- Dried blossoms: 4 g in infusion 3x daily
- Tincture: 1.5 to 3 mL 3x daily
- Red clover isoflavones: 40 to 160 mg red clover isoflavones daily

SAFETY INFORMATION: HERB DRUG INTERACTIONS, TOXICITY, AND CONTRAINDICATIONS

Red clover is widely used in Europe and the United States for the prevention and treatment of menopausal complaints with a very high safety profile. Although there are a limited number of human clinical trials using this

herb, even those looking at effects up to a year show excellent tolerance and no significant adverse effects. It is theoretically contraindicated for women taking HRT due to possible competition with the drugs. Red clover has also been contraindicated with heparin, ticlopidine, and warfarin, based on its coumadin content. However, unless red clover herb is fermented, it is unexpected to have any anticoagulant effects.

It is unclear whether red clover is safe for consumption by women with a history of estrogen-receptor (ER) positive cancer. Although it may have competitive binding effects with stronger endogenous estrogens, and thus may actually reduce risks associated with elevated estrogen levels, an in vitro study demonstrated that red clover was equipotent to estradiol in its ability to stimulate cell proliferation in estrogen receptor–positive breast cancer cells. Regular consumption of soy has been associated with a decreased risk of breast cancer, but the results cannot necessarily be extrapolated, as soy contains additional compounds not found in red clover. Further, isoflavones can variably act as ER agonists or antagonists. Until more conclusive evidence is available, it is possible for women with a history of ER positive breast cancer to avoid using red clover.

Concerns have also arisen over the safety of consuming red clover due to the risk of uterine cancer associated with unopposed estrogen. Preliminary studies of less than 6 months have found no increases in endometrial thickness based on ultrasound examination. No changes in GnRH, SHBG, FSH, LH, vaginal cytology, or endometrial thickness have been seen in studies of women taking the red clover compared with placebo, even over 1 year. Nonetheless, as with those with breast cancer, women with a history of endometrial hyperplasia might be prudent to avoid regular consumption of red clover supplements.

USE IN PREGNANCY AND LACTATION

Because of its estrogenic properties, red clover is not recommended for regular or high-dose consumption during pregnancy and lactation. Infertility and abortion have been observed in cattle grazing extensively on red clover. The Botanical Safety Handbook Class 2b rating, not to be used in pregnancy

ST. JOHN'S WORT

Botanical name: *Hypercium perforatum*
Family name: Clusiacaea
Synonyms: St. Joan's wort
Part used: Flowers, upper 6 to 8 inches of the aerial portion of the herb, including leaf and flower

St. John's wort (*Hypericum perforatum*). (Photo by Martin Wall.)

MAJOR CHEMICAL CONSTITUENTS

Hypericin, pseudohypericin, isohypericin, hyperforin; flavonols including kaempferol and quercetin; flavones, glycosides, bioflavonoids, catechins; phenols including caffeic acid, p-coumaric acid, ferulic acid, and vanillic avid; volatile oils, carotenoids, nicotinic avid, isovalerinic acid, palmitic acid, and a number of volatile oils.

PRINCIPAL USES

- Mild to moderate depression
- Mild sedative and nerve tonic for excitability, anxiety, and nervous irritability
- Mild sedative/analgesic for neuralgia and sciatica
- Antiviral for both internal and topical prevention and treatment of *Herpes simplex* virus (HSV)
- Neurovegetative menopausal complaints
- Topical wound healing, for example, postpartum perineal healing, hemorrhoids, sore. cracked nipples during lactation, and vaginal abrasions in vaginitis and perimenopausal vaginal atrophy and associate vaginal dryness
- Cystitis, urinary frequency and urgency, interstitial cystitis

TRADITIONAL AND HISTORICAL USES

St. John's wort (SJW) has been a famed vulnerary and antidepressant herb since the Greco-Roman times. In ancient medical history, however, depression was not the likely diagnosis—a patient was said to have been afflicted by evil spirits or other psychic malady.

In our modern era, mounting evidence from clinical trials, especially those conducted in the 1980s and 1990s, established the efficacy and safety of standardized SJW extracts for treating mild to moderate depression, and practically overnight, SJW became a ''household alternative'' for the treatment of depression as well as a multimillion dollar boon for the natural products industry. Although SJW remains a top-selling herb, reports of potentially serious herb–drug interactions, as well as widely publicized but poorly conducted studies questioning its efficacy have led to some decline in its popularity as a treatment for depression.

CLINICAL INDICATIONS

SJW is indicated for mild to moderate depression. Herbalists also prescribe SJW as a mild sedative and nerve tonic for excitability, anxiety, and nervous irritability, for pain relief for neuralgia and sciatica, as an antiviral for both internal and topical prevention and treatment of *Herpes simplex* virus (HSV), and for neurovegetative menopausal complaints, particularly anxiety and sleep difficulties, typically in combination with other herbs. It is commonly included as a vulnerary—or wound healing herb—in formulae for the treatment of cuts, scrapes, and puncture wounds, as well as to soothe and heal the perineum with or without perineal lacerations after childbirth, to soothe and reduce hemorrhoids, and for the treatment of vaginal abrasions in vaginitis and those that can occur with perimenopausal vaginal atrophy and vaginal dryness. Herbal practitioners may also include SJW in formulae for the treatment of cystitis, urinary frequency and urgency, and interstitial cystitis.

MECHANISMS OF ACTION

The precise mechanisms of action for the antidepressant effects of SJW are not understood. In vitro studies using hyperforin have demonstrated significant binding of GABA A and GABA B, adenosine, MAO, and benzodiazepine receptors. Only GABA A and GABA B receptor activity is likely to be achieved in concentrations to elicit a biological effect after oral administration in humans. Early studies focused on the inhibitory activity of hypericin on MAO receptors; however, most studies have demonstrated only weak binding if at all. It appears that there might be some effects in inhibition of synaptosomal uptake of serotonin (5-HT), dopamine, and noradrenaline, with an upregulation of 5-HT in rat cortex, with some increase in dopamine and noradrenaline. Studies have shown possible decrease in tryptophan degradation; tryptophan is a 5-HT precursor. Another possible explanation for the antidepressant effect of

SJW is via inhibition of interleukin-6 (IL-6) by hyperforin and via inhibition of substance P mediated effects on depression.

Antiviral effects of SJW are attributed in part to the flavonoid and catechin fractions of the herb. Both hypericin and psuedohypericin have demonstrated in vitro inhibition of HSV Types 1 and 2, *Varicella zoster* virus, and HIV type 1 via a photoactivation process that is not yet elucidated.

Tannins in SJW have a mild astringent effect and may help to explain some of the vulnerary effects, as well as use in the treatment of hemorrhoids. A quercetin-like compound in SJW has been attributed with possible analgesic effects of the herb. SJW extract has also been observed to suppress inflammation and leukocyte infiltration in murine models. Hypericin has demonstrated in vitro ability to inhibit tumor necrosis factor induced activation of NF-kappa B and the release of arachadonic acid, as well as inhibition of 5-lipoxygenase and COX-1. SJW may have free-radical scavenging activity; however, this has not been a consistent finding in studies.

RATINGS

- Botanical Safety Handbook rating 2d: Not for use during phototherapy; interaction Class C. Herbs for which clinically significant interactions are known to occur
- German Commission E: Internal uses include the treatment of psychovegetative disturbances, depressive moods, anxiety and/or nervous unrest. External: Oil-based preparations for the treatment of acute and contused injuries, myalgia, and first-degree burns.

PREPARATIONS USED CLINICALLY

- Dried herb in tea and capsules
- Tincture
- Standardized extract
- Oil extract for topical use

DOSAGE

- Dried herb: 2 to 4 g as an infusion three times daily
- Tincture: 2 to 4 mL 3x daily
- Clinical trial doses: 240 to 1800 mg daily standardized to varying concentrations of hypericin and hyperforin for a minimum of 4 to 6 weeks. Dosing in depression clinical trials suggests a starting dose of 300 mg of SJW standardized to 0.3% hypericin (and possibly also to 2–5% hypericin) 3x daily with a maintenance dose of 300 to 600 mg per day.
- Topical use as needed

SAFETY INFORMATION: HERB DRUG INTERACTIONS, TOXICITY, AND CONTRAINDICATIONS

St. John's wort is considered a generally well-tolerated herb, even when taken continuously for up to 8 weeks. Adverse reactions are usually mild and included skin reactions, GI symptoms, fatigue, sedation, restlessness, dizziness, dry mouth, and headache with few side effects, most notably photosensitivity and mania, reported in clinical trials. Studies of chronic toxicity in animals have shown only nonspecific symptoms such as weight loss. Rarely, skin reactions such as pruritus and rash have been reported, with a drug monitoring study of 3250 patients showing 17 allergic reactions.

A European review of adverse reactions from 1991 to 1999 involving nearly 8 million people documented only 95 adverse reactions. Three case reports in the literature suggest the possibility of phototoxicity; in patients taking SJW. Two of the cases involved patients receiving laser or UVB treatments. Phase 1 trials of IV and oral hypericin in adult patients with HIV demonstrated severe cutaneous phototoxic reactions in 11 of 23 subjects, and a variety photosensitivity reactions in 14 of 19 hepatitis C patients. Several additional studies have confirmed similar findings particularly at high doses of hypericin or high UVA light. One study did not find phototoxic effects. Patients receiving UV treatment are advised to avoid SJW use during treatment and those with fair skin are advised to avoid sun exposure of skin while taking SJW internally or topically.

Anorgasmia has been reported in 25% of patients taking 900 to 1500 mg SJW daily for 8 weeks versus 32% taking sertraline and 16% taking placebo, in additional to 2 published case reports of sexual dysfunction in patients taking the herb for mood disorders. Frequent urination was also seen in 27% of patients taking 900 to 1500 mg SJW daily for 8 weeks vs. 21% taking sertraline and 11% taking placebo.

SJW, through its actions on the hepatic metabolism of drugs, specifically via induction of the cytochrome system, *may* lead to changes in the plasma level of a number of drugs, preventing a patient from achieving appropriate therapeutic levels. There is evidence from clinical trials and case reports that SJW may interact with the following medications:

- Antiarrhythmics/calcium channel blockers: May lead to decreased plasma levels of digoxin, verapamil, and nifedipine
- Anticonvulsants: May lead to decreased plasma levels phenytoin
- Anticoagulants: May lead to decreased plasma levels warfarin
- Antidepressants: May lead to decreased plasma levels amitriptyline (a tricyclic antidepressant) and the SSRIs paroxetine, fluoxetine, and trazadone. Serotonin syndrome can result from reduced serum levels of SSRIs.
- Antihistamines: Fexofenadine (single dose may increase while continued use may decrease plasma level of drug)
- Antipsychotics and anxiolytics: May lead to decreased plasma levels of buspirone, quitazepam, midazolam, and alprazolam
- Antiulcer agents: May lead to decreased plasma levels of omeprazole
- Antivirals: May lead to decreased plasma levels of indinavir
- Chemotherapeutic agents: May lead to decreased plasma levels of irinotecan and imatinib
- Hormonal contraceptives: May lead to decreased plasma levels of hormonal birth control/oral contraceptives

- Immunosuppressants: May lead to decreased plasma levels of cyclosporine and tacrolimus
- Reverse transcriptase inhibitors: May lead to decreased plasma levels of nevirapine
- Skeletal muscle relaxants: May lead to decreased plasma levels of chlorzoxazone
- Statins: May lead to decreased plasma levels of simvastatin

WARNING

Patients taking cyclosporine for the prevention of transplant rejection or other medical reasons should avoid the concurrent use of SJW as it has been shown to interfere with immunosuppressant medications.

Patients taking medications metabolized by CYP450 should avoid SJW or consult with the physician prior to use.

Caution is advised with SJW use for patients with fair skin, receiving photosensitizing drugs, or receiving UV treatments. At recommended doses of whole plant extracts, the risk of photosensitization appears to be quite low.

Activation may occur in patients with a history of mania, bipolar disorder, and other mood disorders.

SJW is suggested for the treatment of patients with mild to moderate depression, not severe depression or suicidality.

Cases of possible serotonin syndrome has been reported in patients taking SJW.

USE IN PREGNANCY AND LACTATION

Because of lack of clinical trials and safety data, SJW is not commonly recommended for the treatment of mood disorders during pregnancy. Its use is more often reserved for topical treatment of vaginitis, in the treatment of perineal tears, and for the treatment of sore, cracked nipples during lactation.

It is becoming increasingly well established that untreated depression in pregnant women and new mothers can have significant health and social consequences for their offspring. Comparative studies on the efficacy and safety of SJW compared to pharmaceutical antidepressants for the treatment of prenatal and postpartum depression are needed.

Murine and rat studies on the prenatal consumption of SJW have been generally associated with normal gestation and fetal development. In one study, male offspring in a SJW exposed group had a statistically significant lower birth weight than the placebo group, however, by three days after birth the difference was not statistically significant. The males in the SJW group also demonstrated a statistically significant temporary delay in the appearance of upper incisors. In another rat study females were given a methanol extract of SJW standardized to 0.3% hypericin at 100 or 1000 mg/kg or placebo by gavage for 2 weeks prior to conception, throughout gestation, and/or for 3 weeks during lactation. Histological evidence of hepatic and renal changes was seen in the SJW exposed group, with more severe lesions in the rat pups whose dams received higher doses and the offspring of those receiving both SJW in both pregnancy and lactation. No significant impact on cognitive behaviors have been seen in the offspring of mice given SJW throughout gestation. A slight increase in in vitro uterotonic activity has been reported with SJW use.

Overall there is a lack of toxicity studies conducted on SJW use during pregnancy. A limited number of human case reports indicated healthy pregnancies and infants when SJW was used prenatally. In a small prospective cohort safety study of breastfeeding women (n = 33) who took SJW products during pregnancy and who contacted a toxicology advise service, compared to 101 matched controls who had also contacted the service but had not taken SJW, there were no maternal adverse effects, no statistically significant differences in women reporting decreased breast milk volume, and no medical problems in the offspring. Two of the infants born to mothers taking SJW experience colic, drowsiness, or lethargy compared with the other group; a number of these infants were also reported to have been exposed to conventional antidepressant medications while breastfeeding. Limitations to this report include lack of product identification or quantification in this report, and the number of women taking SJW while pregnant was small.

Hyperforin was detected in low concentrations in the breast milk who took 300 mg of SJW three times daily starting at 5 months postpartum for the treatment of postpartum depression. No adverse effects were seen in her baby. The clinical significance to the infant of SJW in breast milk is unknown; no adverse effects have been reported. Use of topical applications of SJW oil or salve as treatment for sore, cracked nipples, particularly if well-absorbed with any excess wiped off prior to nursing does not appear harmful to the infant. See warnings in the preceding regarding interactions with immunosuppressant and other medications.

The safety of SJW taken internally during pregnancy and breastfeeding, both in terms of effects on the mother and her child, are unknown at this time. Because of this, the herb is generally not recommended for internal consumption during pregnancy and lactation. Given the widespread incidence of depression in society, and the relatively high incidence and serious consequences of postpartum depression on the health of mother, baby, and their relationship, as well as the family overall, research in to SJW for prophylaxis and treatment of depression during the childbearing years should be explored in carefully controlled studies.

UVA URSI

Botanical name: *Arctostaphylos uva ursi*
Family: Ericaceae
Synonyms: Bearberry, Kinnikinnik
Part used: Dried leaf

Uva ursi (*Arctostaphylos uva ursi*). (Photo by Martin Wall.)

MAJOR CHEMICAL CONSTITUENTS

The primary medicinally active constituent is arbutin, a phenolic glycoside that generates hydroquinone as a result of glycolysis. Tannins, and flavonoids are also present. A small amount of free hydroquinone is found in the leaves. P-coumaric acid and caffeic acid, compounds with known antibacterial properties, and salicylic acid, a known bacteriostatic and anti-inflammatory agent, may be of significance. Uva ursi contains the flavonoid quercetin and the triterpenes ursolic acid, among many other constituents.

PRINCIPAL USES

- Urinary tract antiseptic, bacteriostatic, anti-inflammatory, and astringent in the treatment of cystitis, urethritis, dysuria, and pyelonephritis.
- Topical astringent applied for postpartum vulvovaginal healing

TRADITIONAL AND HISTORICAL USES

Uva ursi was used by numerous native tribes of the northern United States and Canada as a diuretic or for treatment of inflammation of the genitourinary tract. It appears to have been introduced into European medical practice in the thirteenth century as a treatment for conditions of the bladder and kidney, and as such has remained in use since. Goethe is reported to have been prescribed and successfully treated for kidney stones with this herb. Early US medical botanists reported on its usefulness in the treatment of genitourinary disorders and by the late nineteenth century it was widely used by Eclectic physicians as an astringent tonic for chronic diarrhea, dysentery, and menorrhagia, as well as for genitourinary disorders and diabetes. It has had an official entry in pharmacopoeias of numerous western nations since the eighteenth century, including the British Herbal Pharmacopoeia, the National Formulary and the United States Dispensatory. It can still be found in the pharmacopoeias of numerous countries including Austria, Czechoslovakia, Egypt, France, Germany, Hungary, Japan, Russia, Switzerland, and others.

IN VITRO, ANIMAL, AND CLINICAL DATA

Uva ursi remains one of the most important and commonly used urinary tract disinfectants in modern herbal medicine, widely used in the treatment of uncomplicated acute and recurrent urinary tract infections. Midwives include the herb as an astringent anti-inflammatory in sitz baths and perineal rinses for postnatal perineal healing and as part of treatment of vaginitis and urethritis. There are few clinical trials or pharmacodynamic studies of uva ursi. In vitro studies using crude leaf preparations and extracts of uva ursi leaf have demonstrated mild antimicrobial activity against known UTI causing organisms, including but not limited to *C. albicans, E. coli, S. aureus,* and *Proteus vulgaris*, and others. Several studies have also demonstrated antiinflammatory activity of the herb, particularly enhanced when extracts are used in combination with anti-inflammatory pharmaceutical drugs, for example, prednisolone, indomethacin, or dexamethazone.

MECHANISMS OF ACTION

The mechanisms of action of uva ursi are not fully elucidated. It appears, however, that arbutin, and its aglycone, hydroquinone—a urinary disinfectant—are primarily responsible for the herb's antimicrobial activity. Hydroquinones are primarily hydrolyzed in the kidney because tannins prevent enzymatic activity that would normally lead to its conversion in the gut; it also appears that arbutin might be hydrolyzed in the urinary tract as a result of β-glucosidase activity stimulated by pathogenic infection. Arbutin is rapidly absorbed after consumption of tea and extract preparations, with urinary excretion of metabolites within a few hours and up to 24 hours. Antibacterial actions may be most prominent in an alkaline (pH 8) urinary environment; however, activity is not necessarily dependent on elevated urinary pH.

RATINGS

- German Commission E: Approved for the treatment of inflammatory conditions of the urinary tract.

- Botanical Safety Handbook Class 2b and 2d rating: Not to be used in pregnancy, a caution that is reiterated by most authorities.

PREPARATIONS USED CLINICALLY

- Cold water infusion
- Hot water infusion
- Tincture

Uva ursi shows greater antibacterial activity in an alkaline environment; some authors suggest giving it along with sodium bicarbonate or substantially increasing fresh fruit and vegetable consumption during treatment to alkalinize the urine; others suggest avoiding the use of acidifying agents during treatment. Alkalinization of the urine seems not to be a prerequisite to the antiseptic properties of hydroquinone released from arbutin. Some amount of disagreement can be found in the literature regarding the requirement of an alkaline pH environment for the efficacy of this herb. Some authors postulate that a reduced urinary pH inhibits the efficacy of the herb; others argue that increasing the alkalinity of the urinary environment enhances the efficacy of the herb, while still others state that activity is not depend on urinary pH. Given the reliability of this herb generally, it is prudent to conclude that if uva ursi does not seem to be working, the addition of 2 ''00'' capsules of sodium or potassium bicarbonate may be taken once or twice daily with uva ursi doses, to alkalinize the urine in such situations before making a final determination about efficacy. Some authors recommend discontinuing use of the herb after 7 days; however, the European Scientific Cooperative on Phytotherapy (ESCOP) recommends treatment be continued until complete disappearance of symptoms, up to a maximum of 2 weeks.

DOSAGE

Doses should provide the equivalent of 400 to 840 mg arbutin daily, divided over two to four doses.

- Hot or cold infusion: 1.5 to 4 g dried leaves to 150 mL water as a cold infusion steeped for 2 hours or as a hot infusion steeped 30 minutes, and taken up to four times daily.
- Tincture: 2 to 4 mL three to four times daily of a 1:5 preparation.

USE IN PREGNANCY AND LACTATION

Pregnancy

The Botanical Safety Handbook gives this herb a class 2b and 2d rating: Not to be used in pregnancy, a caution which is reiterated by numerous authorities. However, the reasons for contraindication are variable and not well supported, ranging from alleged uterotonic and oxytocic activity to ''theoretical fetotoxicity.'' The risk of oxytoxic effect is based on a single unreferenced anecdotal report by Brinker in *Herb Contraindications and Drug Interactions*, and has not been substantiated clinically. Limited evidence suggest that the herb has potentially fetotoxicity owing to its hydroquinone content. Studies using pure hydroquinone (i.e., not the herb in bulk or extract form) have produced microtubulin dysfunction in bone marrow, and exposure of human lymphocytes and cell lines and pure hydroquinone has been shown to cause genetic damage. Low potential for mutagenicity and negative Ames test have also been reported. In animals administered 100 and 400 mg/kg sc per day of arbutin, no signs of fetal toxicity were observed. Uva ursi has been used by midwives in the United States as a primary treatment of acute symptomatic cystitis in pregnancy for at least two decades, with no adverse reports associated with its use.

Lactation

The transfer to infants of arbutin/hydroquinone from uva ursi use during lactation has not been researched and therefore is not recommended; however, the risk remains speculative. It is recommended that this herb be used only in the lowest doses during lactation, observing the infant for side effects, and using under the guidance of a qualified health professional.

SAFETY INFORMATION: SIDE EFFECTS, CONTRAINDICATIONS, TOXICITY, AND HERB-DRUG INTERACTIONS

Used as per directed dose and duration, uva ursi appears to have a good safety profile.

Side Effects

- Nausea and vomiting have been reported with use, but are not common.
- Excessive ingestion of arbutin may cause tinnitus, delirium, convulsions, collapse, and death.

Contraindications

- Kidney disorders
- Pregnancy and lactation (discussed in the preceding)
- Children under 12 years old
- Bowel inflammation

No justification is given for the caution against use in children.

High tannin levels may interfere with iron absorption in the gut and may aggravate highly inflamed or ulcerated GI conditions.

Toxicity

Several authorities claim that arbutin-containing preparations should not be taken for longer than a consecutive week, nor should they be taken more than 5 times annually without medical consultation. No explanation for this recommendation is given though it is likely due to concern regarding hydroquinone consumption. Contrary to this, the European Scientific Cooperative on Phytotherapy (ESCOP) recommends treatment be continued until complete disappearance of symptoms, up to a maximum of 2 weeks. Uva ursi is a known inhibitor of melanin synthesis, and in excessive

doses could result in retinal damage. Used acutely according to general dosing recommendations, this herb is expected to have very low carcinogenicity, though carcinogenicity has been observed in mouse and rat models given pure hydroquinone.

Herb–Drug Interactions

- The only expected drug interaction is possible potentiation of prednisolone and related anti-inflammatory drugs by 50% methanolic extract.

WILD YAM

Botanical name: *Dioscorea villosa*
Family name: Dioscoreacaea
Synonyms: Colic root, rheumatism root
Part used: Root and rhizome

MAJOR CHEMICAL CONSTITUENTS

Glycoside and steroidal saponins, including diosgenin and dioscin, alkaloids, tannins, phytosterols, and starch

PRINCIPAL USES

- Spasmolytic in the treatment of uterine cramping, dysmenorrhea, and chronic pelvic pain
- Spasmolytic in cases of urinary tract infection (UTI) and interstitial cystitis
- Antiemetic in nausea and vomiting of pregnancy (NVP) and *hyperemesis gravidarum*
- Antispasmodic for irritable uterus or threatened miscarriage with uterine contractions
- Intrapartum use for painful labor with dysfunctional uterine contractions
- Postnatally for afterbirth pains
- Proposed estrogenic effects owing to theoretical ability of steroidal saponins in the plant to bind to estrogen receptors, thus used in the treatment of a variety of perimenopausal and menopausal complaints.

TRADITIONAL AND HISTORICAL USES

Wild yam was used by Native Americans and Eclectic physicians for a wide variety of complaints relating to spasmodic contractions of the hollow viscera ranging from bilious colic to dysmenorrhea. It was included in the National Formulary (NF) from 1916 to 1942 as a diaphoretic and expectorant. In the past decade it has enjoyed a resurgence in popularity based on the erroneous assumption that because it contains steroidal saponins used in the manufacture of progesterone for oral contraceptive pills (OCPs), it could be taken as an herb to increase progesterone levels and thus treat a variety of gynecologic complaints. It is found in topical creams for vaginal dryness. Any increase in progesterone associated with using topical creams, was due to the inclusion of USP grade synthetic progesterone to these products. Its alleged hormonal activity has also led to the inclusion of this herb in breast-enhancing products.

CLINICAL INDICATIONS

Wild yam is reported by herbal practitioners to be a reliable spasmolytic herb in the treatment uterine cramping, dysmenorrhea, chronic pelvic pain (CPP), urinary tract infection (UTI) and interstitial cystitis, particularly as an adjunct in combination with other herbs specific to those complaints. It is also sometimes used by midwives as an antiemetic in the treatment of troublesome nausea and vomiting of pregnancy (NVP) and *hyperemesis gravidarum*, and as an antispasmodic for irritable uterus or threatened miscarriage with uterine contractions. It is also occasionally used as an adjunct antispasmodic herb painful labor with dysfunctional uterine contractions and in the postpartum period for afterbirth pains.

Wild yam (*Dioscorea villosa*). (Photo by Martin Wall.)

There is a paucity of studies on the clinical effects of wild yam, and no studies evaluating antispasmodic activity were identified.

IN VITRO, ANIMAL, AND CLINICAL DATA

A 2001 double-blind placebo-controlled crossover study of the effects of a wild yam cream in 23 healthy women suffering from troublesome symptoms of menopause was conducted. After a 4-week baseline period, each woman was given active cream and matching placebo for 3 months in random order. Diaries were completed over the baseline period and for 1 week each month thereafter, and blood and saliva samples were collected at baseline and at 3 and 6 months, for measurement of lipids and hormones. The average age of the subjects was 53.3 *** 1.1 years and average time since last period 4.3 *** 0.9 years. At baseline, the average body mass index was 27.3 *** 0.8, cholesterol level 5.7 *** 0.2 mmol/L and follicle stimulating hormone (FSH) level 74.2 5.1 IU/L; estradiol levels were undetectable in the majority of cases. After 3 months of treatment, no significant side effects were reported with either active treatment or placebo, and there were no changes in weight, systolic or diastolic blood pressure, or levels of total serum cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, FSH, glucose, estradiol, or serum or salivary progesterone. Symptom scores showed a minor effect of both placebo and active treatment on diurnal flushing number and severity and total non-flushing symptom

scores, and on nocturnal sweating after placebo, but no statistical difference between placebo and active creams. A randomized, controlled trial of 13 menopausal women given two capsules three times daily for 3 months of an herbal combination containing wild yam root in doses lower than recommended, along with burdock root (*Arctium lappa*), licorice root (*Glycyrrhiza glabra*), motherwort (*Leonurus cardiaca*), and angelica root (*Angelica archangelica*) demonstrated statistically nonsignificant decreases in menopausal symptoms in the active treatment group. Diosgenin, a component of wild yam, has been shown in several studies to reduce total serum cholesterol levels, likely as a result of reduced intestinal cholesterol and an effect potentiated by taking the herb with vitamin C. No hormonal effects, including no changes in DHEA, estrogen, and progesterone levels, or FSH or LH levels, have been observed. In one study of ovariectomized mice receiving 20 to 40 mg/kg of diosgenin injected subcutaneously daily for 15 days, mammary gland epithelial stimulation was observed without progesteronic effects, however, the effects of oral wild yam on breast tissue have not been studied in animal or human trials.

Is Eating Yams Where the Where the Health Benefits for Women Occur?

Interestingly, in a study by Wu et al, 24 apparently healthy postmenopausal women were recruited to replace their staple food (rice for the most part) with 390 g of yam (*Dioscorea alata*) in two of three meals per day for 30 days and 22 completed the study. Fasting blood and first morning urine samples were collected before and after yam intervention for the analyses of blood lipids, sex hormones, urinary estrogen metabolites and oxidant stress biomarker. The design was a one arm, pre-post study. A similar study of postmenopausal women (n = 19) fed 240 g of sweet potato for 41 days was included as a control study. Serum levels of estrone, estradiol, and SHBG were analyzed for this control group. After yam ingestion, there were significant increases in serum concentrations of estrone (26%), sex hormone-binding globulin (SHBG) (9.5%), and near significant increase in estradiol (27%). No significant changes were observed in serum concentrations of dehydroepiandrosterone sulfate, androstenedione, testosterone, follicular stimulating hormone, and luteinizing hormone. Free androgen index estimated from the ratio of serum concentrations of total testosterone to SHBG decreased. Urinary concentrations of the genotoxic metabolite of estrogen, 16-hydroxyestrone decreased significantly by 37%. Plasma cholesterol concentration decreased significantly by 5.9%. The researchers concluded that ingestion of yams as a staple part of the diet might reduce the risk of breast cancer and cardiovascular diseases in postmenopausal women. This is quite different than using wild yam as an herbal supplement, but nonetheless, worthy of further research. And as yams are such a nourishing food, unless one is on a diabetic diet, they are a healthy inclusion in most diets.

MECHANISMS OF ACTION

The belief that wild yam acts as a precursor to human sex hormones was widely popularized in the early 1990s based on research John Lee, a proponent of the benefits of progesterone replacement for a variety of menopausal complaints. However, the steroidal saponins found in wild yam are not biologically converted to human sex steroids in the body, nor does the plant itself contain progesterone or estrogen, and claims of it having hormonal activity appear to be erroneous based on clinical research (see the preceding). Mechanisms for the antispasmodic effects of this herb have not been elucidated nor substantiated.

RATINGS

Botanical Safety Handbook class 1: Herbs that can be safely consumed when used appropriately.

- No significant adverse events in clinical trials
- No case reports with significant adverse events and high probability of causality [need to select causality assessment references
- No identified concerns for use during pregnancy or lactation
- No innately toxic constituents
- History of safe traditional use
- Toxicity associated with excessive use is not a basis for exclusion from this class
- Idiosyncratic, minor or self-limiting side effects are not bases for exclusion from this class.

PREPARATIONS USED CLINICALLY

- Dried root in capsules
- Tincture

DOSAGE

- Dried root in capsules: 250 mg one to three times daily
- Tincture: 2 to 4 mL three to five times daily

SAFETY INFORMATION: HERB–DRUG INTERACTIONS, TOXICITY, AND CONTRAINDICATIONS

Wild yam appears to be generally safe when used internally or topically, as recommended Topical application of wild yam extract in women suffering from menopausal symptoms appears to be free of side effects, but appears to have little effect on menopausal symptoms. The herb is sometimes contraindicated for those using hormonal contraception and those with hormone dependent cancers, but this is based on the supposition of hormonal activity of the herb, which is not currently supported by the scientific literature.

Anecdotal reports state that large doses (amounts unspecified) may result in emesis. Positive interactions may be found in association with added benefits of lipid reduction when combined with lipid-lowering medications.

USE IN PREGNANCY AND LACTATION

Wild yam was used by the Eclectic medical physicians for the treatment of NVP and by Native American tribes to ease childbirth, suggesting some historical expectation of its safety during pregnancy. It remains in contemporary use by midwives for use as an antiemetic in nausea and vomiting of pregnancy (NVP) and *hyperemesis gravidarum*, as an antispasmodic for irritable uterus or threatened miscarriage with uterine contractions [in combination with other herbs such as cramp bark (*Viburnum opulus*) and black haw (*Viburnum prunifolium*)], occasionally for intrapartum use for painful labor with dysfunctional uterine contractions, again with cramp bark and black haw or other herbs, and postnatally for afterbirth pains, often combined with motherwort. Although the Botanical Safety Handbook categorizes wild yam as a Class 1 herbs that can be safely consumed when used appropriately, no data exist on the safety of this herb during pregnancy or lactation. One limited report suggests the possibility of induction of uterine contractions associated with this herb, this is not a finding consistent with the traditional observations or contemporary literature on this herb. Although concerns of hormonal activity are unfounded based on the scientific literature, care should be taken when using any herb during pregnancy and lactation.

SUMMARY

Scientific data do not lend credibility to the popular use of wild yam as a hormonal precursor or supplement. There is no research into the traditional and contemporary use of this herb as an antispasmodic for the hollow viscera. The herb appears safe when used as recommended both internally and topically. Although no significant reports of adverse events in pregnancy and lactation are found in the literature, care should be taken when using any herbs in this context.

PLANT PROFILES: SUMMARY TABLE OF HERBS FOR WOMEN'S HEALTH

The following table provides a quick reference to dose, indications, and major safety issues for the pharmacopoeia of herbs for women's health presented in this textbook. The table is not meant to be an exhaustive presentation of the scientific data for each herb; readers are encouraged to refer to the primary reference monographs and books from which this data was drawn. These resources were listed in the introduction to Part V: Plant Profiles. A great many herbs lack scientific research addressing clinical efficacy, mechanisms of action, and safety. Others have extensive research behind them. The data in this table does not attempt to address the scientific research for each herb; this is presented as relevant in the chapters within this textbook where the herb is mentioned in its clinical context. Only major safety issues are presented in the following. Allergic reactions, for example, are not addressed unless significant for a specific herb, as many individuals are allergic to plants in any number of families, for example, grasses, and thus may have a reaction to herbs in that family. Pregnancy data are listed only when specifically known to be safe or contraindicated. If not listed, it can be assumed that the data during pregnancy are not established due to lack of research. Readers are referred to Chapters 12 and 19 for specific information on the safety of specific herbs during the childbearing cycle. Many herb–drug interactions remain unknown, and the scientific literature is rife with examples of theoretical herb–drug interactions that may not have an actual clinical basis. Other interactions may, in fact, be positive, allowing the patient to use lower doses of potentially toxic medications, or helping patients to avoid the side effects of many commonly used medications. Nonetheless, caution and proper supervision are advised when taking herbs and pharmaceutical drugs simultaneously. Widely known contraindications or severe adverse effects that are well established are listed in bold. Practitioners will have to determine how to weigh single case reports on an individual basis.

KEY

The following abbreviations are intended to simplify use of the chart for readers:

KS: Known Safe:
Known to be safe and well tolerated when used as recommended.

KSw/C: Known Safe with Cautions:
Based on current information, this herb is considered generally safe and well tolerated, with no expected adverse effects when used within the recommended doses and duration and as indicated; however, there are cautions based on animal data or clinical reports of adverse effects, contraindications, or herb–drug interactions. A brief explanation of the adverse effects follows this abbreviation.

LS: Likely Safe:
Based on current information, no known contraindications or major adverse effects are expected; likely safe when used within recommended doses.

LSw/C: Known Safe with Cautions:
Based on current information, this herb is considered generally safe and well tolerated, with no expected adverse effects when used within the recommended doses and duration and as indicated; however, the safety data on this herb are limited and there are cautions based on animal data or clinical reports of adverse effects, contraindications, or herb–drug interactions. A brief explanation of the adverse effects follows this abbreviation.

KS or LS/LD: Known Safe or Likely Safe/Limited Data:
This designation is for herbs with a long history of traditional use and that are generally known to be well tolerated and without major contraindications, side effects, or expected interactions but for which no data are available in the resources used for this table.

LSP/L: Likely Safe During Pregnancy and Lactation:
This rating is given to those herbs that are considered safe for use as a culinary herb in modest amounts, or when there is specific evidence of safety during pregnancy and/or lactation.

Ø P or ØP/L: Not for Use During Pregnancy/Not for Use During Pregnancy and Lactation:
This is based on known contraindications due either to constituents that are present in the herb and may be harmful to the fetus or infant, or to known adverse effects in animals or human clinical reports. External use is exempted from this contraindication unless specified.

H-D!: Herb–Drug Interactions:
This symbol appears if there is a known or highly suspected herb–drug interaction. Any herbs appearing with this symbol should be used under the supervision of a qualified health care provider. If a risk is theoretic, the word *possible* is included in the wording of the caution.

RHT: Reported Human Toxicity:
This notation identifies an herb with important reported human toxicity when the whole plant is used as recommended. Commonly, hepatotoxicity is reported. Reports may be from case histories or trials. This notation does not imply causality but does suggest an added level of caution with use. Individuals considering use of an herb marked with RHT should consult a qualified health professional prior to taking the herb. Any herbs marked RHT should not be used internally during pregnancy.

COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
Albizzia	*Albizzia lebbeck*	Stem Bark	N/A	4–8 mL/day	Anti-allergic Antimicrobial Hypocholesterolemic Mild mood enhancement	Depression, grief Eczema Fertility problems Inflammation Irritability Memory deficits Pruritus	**LS/LD** ⊘ ***P***
Alfalfa	*Medicago sativa*	Above-ground parts	5–10 g/3x/day	5–10 mL/ 3x/day	Nutritive Phytoestrogen	Iron-deficiency anemia Osteoporosis prevention Vaginal dryness and atrophy	**KSw/C** • In large amounts, alfalfa seeds may exacerbate systemic lupus erythamatosus (SLE) in patients with SLE. • Case report of pancytopenia with use of the seeds; not an expected adverse effect with the leafy parts
Aloe vera	*Aloe* spp.	Gel from leaf	Topical use		Anti-inflammatory Vulnerary Antiviral	HSV 1 and 2 (topical) Sore, cracked nipples in lactating mothers PUPPP Vulvovaginitis	**KSw/C** • Case report of delayed wound healing following complicated gynecologic surgery • Case report of photodermatitis with use after dermabrasion treatment
American ginseng	*Panax quinquefolius*	Root	3–6 g/day	3–12 mL/day	Adaptogen	Debility Fatigue HPA dysregulation HSV Memory deficits Mild depression PCOS Stress Stress-related illness	**KSw/C** **H-D!** • Diabetics may need to adjust insulin doses because of the reported hypoglycemic effect of the herb. • Adverse events associated with American ginseng use include headache, weakness, apathy, aversion to cold, distended abdomen, vomiting, and delayed menstruation.

							• One study showed it significantly induced the growth of an estrogen-receptor-positive breast cancer cell line (MCF-7) in vitro; however, there was no evidence of estrogenic activity in the α- or β-estrogen receptors and no increase in uterine weight was observed. • May potentiate warfarin action
Anise	*Pimpinella anisum*	Seed	1–5 g/2–3x/day	1–3 mL/ 2–3x/day	Spasmolytic Carminative Flavoring Lactagogue	Flatulence, intestinal cramping Increase milk supply	**KSw/C** **LSP/L-culinary use** • Contact dermatitis with large exposure to seeds and oil • Do not substitute with star anise, which has known toxicity.
Ashwagandha	*Withania somnifera*	Root	3–6 g powder/day	4–10 mL/day	Adaptogen Sedative (mild) Analgesic Anti-inflammatory Hematopoietic	Acute and chronic pain Anxiety Depression Fatigue, lassitude Frequent colds Headache HPA dysregulation HSV Insomnia Hypothyroidism Iron-deficiency anemia Mental/emotional exhaustion Musculoskeletal pain PCOS PMS Postpartum depression PUPPP Stress Stress-related illness	**LS** **H-D!** ⊘ ***P*** • Possible respiratory depression in excessive doses • Possible additive effects with sedative herbs and medications
Astragalus	*Astragalus membranaceus*	Root	9–30 g/day	5–10 mL/day	Immunomodulator Adaptogen Qi tonic Cardiotonic Hypotensive	Convalescence (e.g., postpartum, postsurgical) Endometriosis Fatigue	**KSw/C** **H-D!** • Traditionally, use is not recommended during acute

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
						HSV Susceptibility to infection	infection and acute inflammatory conditions • Caution in diabetics because of possible hypoglycemic effects • Caution with patients on anticoagulant therapy because of possible increase in bleeding risk
Bacopa	*Bacopa moniera*		N/A	4–7 mL/day	Adaptogen	Depression Memory	**LS/LD**
Barberry	*Berberis vulgaris*	Bark	1–2/3x/day	1–2 mL/ 3x/day	Hepatic	Uterine fibroids	**LSw/C/LD** ⊘ ***P/L*** • Not recommended for use in individuals with liver disease, elevated liver enzymes, jaundice, or biliary disease
Barley	*Hordeum vulgare*	Seed (grain)			Nutritive Demulcent Lipid lowering	Increase milk supply Hypercholesterolemia	**KSw/C** • Contraindicated in patients with celiac disease
Bayberry bark	*Myrica cerifera*	Bark	1-2/3x/day	1–2 mL/ 3x/day	Astringent	DUB Menorrhagia Leukorrhea Postnatal perineal care Uterine fibroids	**LS/LD** ⊘ ***P***
Bethroot	*Trillium erectum*	Root	0.5–2/day	1–4 mL/day	Astringent Uterine tonic	DUB Menorrhagia Leukorrhea Uterine fibroids	**LS/LD** ⊘ ***P***
Bilberry	*Vaccinium myrtillus*	Fruit	50–115 mg fresh fruit daily 80–480 mg standardized to 25% anthocyanoside daily of extract in three divided doses		Vasoprotective Urinary complaints	Varicosities (treat/prevent) Treatment of UTI (see cranberry)	**KSw/C** **H-D!** • Possible decreased platelet aggregation and increased bleeding time in preclinical studies, so caution is advised with anticoagulant therapies. • Caution advised for diabetic patients because of possible hypoglycemic effects

							• Bilberry anthocyanin extract given to pregnant women at doses of 80 or 160 mg 2 to 3 times/day for 3 months for the treatment of lower-limb venous stasis and acute-phase hemorrhoids led to no adverse effects.
Birch	*Betula spp.*	Bark	2–3 g/day	1–2 mL/day	Anti-inflammatory Diuretic	Interstitial cystitis	**LS/LD**
Black cohosh	*Actaea racemosa syn. Cimicifuga racemosa*	Root	20–40 mg twice daily	Tincture: 0.4–mL Liquid extract up to 20 drops/day	Spasmolytic Antihypertensive Possible serotonergic or dopaminergic action SERM activity has been proposed, but this is not currently considered a likely mechanism of action. Possible antiproliferative effects	Amenorrhea Anxiety Breast cancer Chronic pelvic pain DUB Dysfunctional labor/labor augmentation Dysmenorrhea Endometriosis Hypertension Osteoporosis prevention Musculoskeletal pain or spasms Painful labor PMS Uterine fibroids Vasomotor and vegetative complaints of perimenopause and menopause Vaginal dryness and atrophy	**LSw/C** **RHT** ⊘ ***P/L*** • Generally well tolerated as directed for up to 6 months • Possible hepatotoxicity associated with herb; warnings now accompany products sold in Europe and Canada; FDA has not required warning labels as of this date. • Headache, dizziness, nausea in excessive doses. • Theoretical risk of stimulation in ER-sensitive cancers; therefore, should be used under supervision of a qualified care provider.
Black haw	*Viburnum prunifolium*	Bark	N/A	3–10 mL/day	Spasmolytic Hypotensive	Abdominal pain associated with endometriosis and chronic pelvic pain After-birth pains Chronic pelvic pain Dysmenorrhea Endometriosis Hypertension Incoordinate uterine contractions Irritable uterus	**KS/LD** • Long history of traditional use for threatened miscarriage, uterine irritability, and painful labor suggests possible safety during pregnancy. • Acute toxicity studies in animals at high doses lead to respiratory paralysis and death by cardiac arrest at doses of 5 to 7 g of extract administered sub-cutaneously.

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
						Painful labor Premature labor (threatened) Threatened miscarriage Uterine fibroids	
Black horehound	*Ballota nigra*	Herb	2–4 g 3x/day as an infusion	1–2 mL 3x/day	Antiemetic Sedative	NVP	**LS/LD** • No known major side effects and no reported herb–drug interactions.
Bladderwrack	*Fucus vesiculosus*	Herb	5–10/3x/day	4–8 mL/ 3x/day	Thyroid stimulant Weight reducing Demulcent	Hypothyroidism because of iodine deficiency	**LSw/C** ⊘ ***P/L*** • Excess intake may lead to hyperthyroidism. • May contain concentrated heavy metals found in the ocean • High sodium content may make use inadvisable for patients with heart or renal failure. • Not for medicinal use during pregnancy and lactation (modest food use acceptable) because iodides can cross the placenta and enter into breast milk.
Blessed thistle	*Cnicus benedictus*	Herb	1.5–3 g/ 3x/day	7.5–10 mL/ 3x/day	Lactagogue Appetite stimulant Emmenagogue	Increase milk supply Anorexia	**LSw/C/LD** **H-D!** ⊘ ***P*** • Gastric irritation and vomiting at high doses • Possible reduction in the efficacy of antacids, H2-receptor antagonists, PPIs, and sucralfate if taken with blessed thistle. • Possible decrease in platelet aggregation and increase in bleeding time

							• Tannins in the herb theoretically increase risk of gastric and esophageal cancer, hepatotoxicity, and nephrotoxicity if taken chronically.
Blood root	*Sanguinaria canadensis*	Root	Topical use only		Antimicrobial Antitumorigenic	Cervical dysplasia	⊘ ***P/L*** • No toxic effects documented from topical use; however, all use during pregnancy is contraindicated because of possible absorption and toxicity to the fetus. • Topically, the herb has been shown to be nonirritant and nonallergenic.
Blue cohosh	*Caulophyllum thalictroides*	Root	0.3–1 g/ 3x/day	0.5–2.5 mL/ 3x/day	Uterine and ovarian tonic Emmenagogue Oxytocic	Amenorrhea Benign breast disorder Chronic pelvic pain DUB Dysfunctional labor/ labor augmentation Dysmenorrhea Endometriosis Hypomenorrhea Oligomenorrhea Ovarian cysts Postdates pregnancy Uterine fibroids	⊘***P*** **RHT** • Overdose can cause symptoms similar to nicotine poisoning • Maternal use during pregnancy has been associated with case reports of neonatal MI, cerebral ischemia, increased meconium, and fetal tachycardia. Should be used only by skilled midwives and obstetric care providers
Blue flag	*Iris versicolor*	Rhizome	0.6–2g/ 2x/day	1–2 mL/ 3x/day	Dermatologic Anti-inflammatory	Interstitial cystitis	⊘ ***P/L*** **RHT** • Whether this herb is safe for internal consumption is a matter of question, because isolated components have been reported to be toxic in humans and livestock. • Use of fresh plant has been reported to cause nausea and vomiting. • Volatile oils in the plant have been reported to cause irritation of the throat and eyes, as well as headache.

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
Blue vervain	*Verbena* spp.	Herb	2–4 g/ 1–3x/day	2–4 mL/ 1–3x/day	Nervine Spasmolytic Uterine stimulant Possibly lactagogue	Benign breast disorder Endometriosis Irritability Depression Improve let-down reflex/Increase milk supply Mental/emotional exhaustion Headache PMS-like symptoms	**LS/LD** ⊘***P*** • Small amounts of verbalin stimulate the uterus in a frog model; the herb is contraindicated in pregnancy because of possible abortifacient/oxytocic activity.
Bugleweed	*Lycopus virginiana*	Herb	N/A	1–3/1–2x/day	TSH antagonist Sedative (mild)	Anxiety Hyperthyroidism Night sweats Palpitations Possibly Graves' disease	⊘ ***P/L*** • Possible thyroid suppression • Do not give concurrently with thyroid medications.
Bupleurum	*Bupleurum falcatum*	Root	1.5–12 g/day	3–7 mL/day	Anti-inflammatory Hepatoprotective Constrained Liver Qi Sedative (mild)	Dysmenorrhea Irritability and emotional lability Pre/menstrual Headache PMS	⊘ ***P*** • Flatulence, nausea, vomiting • Sedation • Cases of hepatotoxicity have occurred after consumption of TCM formulae containing Bupleurum; however, the formulae also contained other herbs and no causality has been established with this herb.
Burdock	*Arctium lappa*	Root	3–18 g/day	3–5 mL/ 2–3x/day	Alterative Aperient Antimicrobial	Acne Eczema PUPPS	**KSw/C/LD** ⊘ **P—first trimester** • Caution advised in diabetic patients because of possible hypoglycemic effects of the herb • Three case reports of allergic dermatitis associated with topical use. • Limited clinical evidence in HIV patients suggested possible additive effects with estrogens

							• In vivo uterine stimulant activity has been reported; this has not been observed clinically; however, medicinal use of burdock should be avoided during the first trimester.
Butterbur	*Petasites hybridus*	Aerial parts, rhizome, root	Recommended in PA-free standardized form. PA intake is not to exceed 1 μg daily, and not to exceed intake for greater than 4–6 weeks/year.		Anti-inflammatory Spasmolytic	Migraine headache	**LS/LD** **RHT** ⊘ ***P/L*** • PAs found in this herb are known to be hepatotoxic, carcinogenic, and mutagenic. • PA-free products used for short duration (up to 4 months) and in the recommended dosage are likely safe; however, there are limited safety data on this herb. As product quality may vary, it is possible that toxic amounts of PAs may be present in poorly processed products.
Calendula	*Calendula officinalis*	Flower	1–4 g/3x/day	0.3–1.2 mL/day	Vulnerary Anti-inflammatory Antimicrobial Lymphatic	Acne, inflammatory skin conditions Benign breast disorder Cervical dysplasia Endometriosis Hemorrhoids HSV (topical) Nipple thrush and cracked nipples Vulvovaginitis Lymphadenopathy Postpartum perineal care Urinary tract infection Vaginal dryness and atrophy (topical)	**Internal use: LSw/C/LD** **Topical use: KSw/C** ⊘ **P-internal use** • Allergic sensitivity has been reported, including cross-sensitivity in patients with latex allergy • Because calendula was traditionally used to affect the menstrual cycle, and in vitro uterotonic activity has been reported, internal consumption during pregnancy is not recommended. • May contain spermatocide activity
California poppy	*Eschscholzia californica*	Herb	N/A	2–4 mL/ 2–3x/day	Sedative (mild) Anxiolytic Analgesic	Anxiety Chronic pelvic pain Dysmenorrhea Endometriosis	**LS/LD** ⊘ ***P***

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
						Insomnia Musculoskeletal tension Migraine/headache PMS	
Canada fleabane/ Erigeron	*Erigeron canadense*	Aerial parts	N/A	1–2 mL 2–4x/day	Antihemorrhagic Astringent	Uterine fibroids DUB Menorrhagia	**LS/LD** ⊘ ***P***
Caraway	*Carum carvi*	Seed	2–5 g/2x/day	2–3 mL/ 2x/day	Lactagogue	Increase milk supply	**LS/LD** ⊘ ***P*** • Do not use caraway oil internally.
Castor	*Ricinus castor*	Oil extracted from seed	This herb is toxic for internal use. The pharmaceutical grade oil is used internally up to 4 oz spread over two doses as a laxative and uterine stimulant to induce labor		Stimulating laxative	Labor induction	⊘ ***P/L*** • Castor is a highly toxic plant and should not be taken internally other than in commercially prepared oil extract products. • Castor is contraindicated in pregnancy other than to stimulate labor. • Causes diarrhea
Cat's claw	*Uncaria tomentosa*	2–30 g/day in decoction	2–4 mL/2x day		Antimicrobial Anti-inflammatory Immunostimulant	HSV	**LD** ⊘ **P/L-internal use** **H-D!** • Contraindicated with concurrent administration of immunosuppressive medications, passive vaccines, immunoglobulin therapy, cryoprecipitates, and fresh plasma products. • It should not be taken by patients who have recently received or are awaiting organ or bone marrow transplantation.

							• Should not be taken by women trying to conceive—it is traditionally used as a contraceptive agent.
Catnip	*Nepeta cataria*	Leaf	5 g/3x/day	2–4 mL/ 3x/day	Spasmolytic Nervine Sedative (mild)	After-birth pains Dysmenorrhea Insomnia Nervousness	**KS/LD**
Celandine	*Chelidonium majus*	Aerial part, root	1–2 g/3x/day	1–2 mL/ 3x/day	Spasmolytic Laxative Immunomodulatory Anti-inflammatory Alterative Hepatic/biliary action	Uterine fibroids Endometriosis Hemorrhoids	**LD** **RHT** ⊘ ***P/L*** • Internal consumption of celandine has been associated with a total of 47 case reports of adverse events to the WHO Uppsala Monitoring Center up to the end of June 2005, including several case reports of hepatotoxicity including symptoms such as hepatitis, jaundice, and elevated liver enzymes. In 2003, the Australian government's Therapeutic Goods Administration recommended that *C. majus* preparations intended for oral intake be labeled with a warning to seek the advice of a health care professional before using celandine if there is a history of liver disease and to discontinue use if symptoms of liver disease occur. • Nausea, abdominal pain, diarrhea, discolored stool, and vomiting may result from use.
Centaury	*Centaurium erythraea*	Herb	2–4 g/3x/day	2–4 mL/ 3x/day	Hepatic	PMS	**LD**
Chamomile	*Matricaria recutita*	Flowers	2–8 g/3x/day	1–4 mL/ 3x/day	Nervine Anti-inflammatory Spasmolytic Carminative Sedative (mild)	Acne (topical) Amenorrhea Anxiety Dysmenorrhea Chronic pelvic pain Endometriosis GI spasm; Abdominal pain	**KS/LD** • Skin rash occasionally with topical application • While chamomile is commonly cited as a contraindicated herb during pregnancy, this is based on a study conducted in 1979 that

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
						associated with endometriosis and chronic pelvic pain Headache Insomnia PMS-related digestive symptoms Restlessness Topical for skin inflammation	found teratogenic effects using a concentrated extract of α-bisoprolol at high doses. No teratogenic effects were seen at lower doses and the dose of the oil constituent required to cause teratogenicity are far greater than it would ever be possible for someone drinking the tea to ever approximate.
Chaste berry	*Vitex agnus-castus*	Fruit	0–40 mg/day up to 500–1000 mg daily	0.2 mL/ 2–3x/day up to 3–5 mL/day	Dopaminergic agonist (↓FSH) Prolactin inhibitor Indirect progestogenic activity Galactogogue	Teenage acne Benign breast disorder Corpus luteal insufficiency Endometriosis Fertility problems Habitual miscarriage Increase milk supply Mastalgia Relieve PMS symptoms Sometimes used for treatment of symptoms of perimenopause Hyperprolactinemia PCOS Menstrual irregularities Uterine fibroids	**KSwC/LD** ⊘ ***P*** **H-D!** • Adverse effects include nausea, headache, acne, and GI symptoms. • According to a German postmarket surveillance study, a total of 23 women became pregnant while using chaste tree, of 1634 women taking the herb, 19 of the 23 reported having been previously unsuccessful in trying to conceive. • Theoretical inhibition of breast milk though traditionally used to increase breast milk supply • May exacerbate depression in some women with progesterone deficiency or PMS-D • Possible interference with dopaminergic drugs
Chinese Skullcap	*Scutellaria baicalensis*	Aerial portions	N/A	4–7 mL/ 1–2x/day	Anti-inflammatory Antimicrobial	Acne HSV PUPPP	**LS/LD**

Cinnamon	*Cinnamomum zeylanicum*	Bark	0.5–1 g/3x/day	Liquid extract: 0.5–1.5 mL/day Tincture: 2–4 mL/day	Astringent Carminative Flavoring	DUB Menorrhagia Uterine fibroids	**KS/LD** **H-D!** • Caustic with prolonged exposure to skin and mucosa • Because of possible hypoglycemic action, caution is advised in diabetics. • No known contraindications to cinnamon during pregnancy as long as not significant greater than food amounts
Cleavers	*Galium aparine*	Herb	N/A	4–10 mL/day	Alterative	Acne Benign breast disorder	**KS/LD**
Coleus	*Coleus forskolii*	Root	N/A	1.5–4 mL/day	Antihypertensive Cardiotonic Spasmolytic Antiplatelet	Congestive heart failure Hypertension Hypothyroidism Ischemic heart disease	**LSw/C/LD** ⃠ ***P/L*** • Not for use without medical supervision • Not to be used by patients with bleeding/clotting disorders • Do not combine with BP, cardiac, peptic ulcer, or antiplatelet medications.
Comfrey	*Symphytum officinale*	Root and leaf	External use only		Vulnerary Demulcent	Postpartum perineal care Nipple thrush and cracked nipples Vulvovaginitis Vaginal dryness and atrophy (topical)	**LSw/C** ⃠ **P/L-internal or extended topical** • Comfrey products are safe for topical application. While there is some transdermal absorption of PAs, which can be hepatotoxic when taken internally, the amount absorbed when used on unbroken skin is likely to be insignificant, and even on broken skin, minimal. Nonetheless, regular use on broken skin is not recommended. The German Commission E recommends not exceeding 1000 μg/day of PAs transdermally, and not using topical applications of comfrey products for greater than 4 to 6 weeks total per year.

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
Coptis	*Coptis chinensis*	Rhizome	2–4 g/3x/day	2–4 mL/ 3x/day	Antimicrobial	Vulvovaginitis GBS	**LSw/C/LD** ⊘ ***P/L*** • See Barberry. • As with other berberine-containing herbs (e.g., barberry, goldenseal), internal use is generally not recommended during pregnancy; however, topical use in suppositories appears to be safe.
Corn silk	*Zea mays*	Stigma, style	4–8 g/in infusion 3x/day	5–15 mL/ 3x/day	Demulcent Mucilage Diuretic	Interstitial cystitis	**KS/LD** • An isolated crystalline component from corn silk has been shown to have hypotensive and uterine-stimulating activity in rabbits, likely because of cholinergic effects. Although the herb is not typically contraindicated during pregnancy, it is prudent to be cautious given this observation.
Corydalis	*Corydalis ambigua*	Rhizome	5–10 g/day	5–20 mL/day	Analgesic Antispasmodic	Chronic pelvic pain Dysmenorrhea Endometriosis HSV 1 and 2—pain HA	⊘ ***P*** **H-D!** • Possible additive effects with antiarrhythmic medications • Oral administration of 1 to 50 mg/kg of gindarin to rats from the first to the second day of gestation led to significant embryotoxicity.
Cotton root	*Gossypium herbaceum*	Root	N/A	2–4 mL/ 2x/day	Abortifacient Emmenagogue	Amenorrhea Endometriosis Dysfunctional labor/labor augmentation Uterine fibroids	⊘ **P/LD** • Because of the known abortifacient activity of this herb, it is contraindicated during pregnancy.

Cordyceps	*Cordyceps sinensis*		3–15 g/day	N/A		Endometriosis	
Couch grass	*Elymus repens*	Rhizome	4–8 g/day in decoction	5–15 mL/ 3x/day	Demulcent Mucilage Antimicrobial	UTI Interstitial cystitis	**LS/LD**
Cramp bark/black haw	*Viburnum opulus/V. prunifolium*	Root	N/A	3–10 mL/day	Spasmolytic Antihypertensive	Abdominal pain associated with endometriosis and chronic pelvic pain After-birth pains Chronic pelvic pain Dysmenorrhea Endometriosis Hypertension Incoordinate uterine contractions Irritable uterus Painful labor Premature labor (threatened) Restless legs Threatened miscarriage Uterine fibroids	**KS/LD** • Long history of traditional use for threatened miscarriage, uterine irritability, and painful labor suggests possible safety during pregnancy.
Cranberry	*Vaccinium macrocarpon*	Fruit	300 mL cranberry juice daily for up to 6 months or equivalent capsules		Urinary antiseptic	Urinary tract infection Reduction of odor associated with urinary incontinence	**KSw/C** **H-D!** • In clinical trials, there is a high dropout rate of cranberry juice users because of taste. • Contrary to some claims, it is unlikely that regular consumption of cranberry juice will lead to the development of uric acid or oxalate stones; however, individuals who tend to form such stones may wish to avoid regular consumption and/or consumption of large amounts of cranberry juice. • There are several reports of interaction with warfarin. • There are no known contraindications to the use of cranberry juice during pregnancy and lactation.

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
Cranesbill geranium	*Geranium maculatum*	Leaf	N/A	2–5 mL/day	Astringent	Menorrhagia Uterine fibroids	**LS/LD** • Because of high tannin content, use cautiously in inflammatory and ulcerative GI conditions.
Damiana	*Turnera diffusa*	Leaf	2–4 g/3x/day	2–4 mL/day	Nervine Aphrodisiac	Anxiety Depression Low libido Vaginal dryness and atrophy	**LD** ⊘ ***P/L*** • Mild stimulating effects may possibly lead to insomnia • Because of possible cyanogenetic constituents, use during pregnancy and lactation is not recommended.
Dandelion	*Taraxacum officinale*	Leaf	4–10 g/ 3x/day	Liquid extract: 4–10 mL/ 3 x/day Tincture: 2–5 mL/ 3 x/day Fresh juice: 5–10 mL/ 2x/day	Diuretic Bitter tonic Choleretic	Acne Constipation Mastalgia PMS symptoms UTI	**KS/LD** • Contraindicated in bile duct and intestinal obstructions • Diuresis is not appropriate during pregnancy; use of dandelion leaf as a food is acceptable. • Dandelion leaf should be treated as a prescription diuretic in terms of precautions with other medications; dandelion is K+ rich.
Dandelion	*Taraxacum officinale*	Root	2–8 g/3x/day	Liquid extract: 2–8 mL/day Tincture: 5–10 mL/day	Aperient Alterative Bitter tonic	Benign breast disorders Endometriosis NVP/Related anorexia Uterine fibroids Acne Constipation PUPPS	**KS/LD** • Contraindicated for patients with gallbladder obstruction and obstructive ileus • No known contraindications during pregnancy when used in amounts comparable to food use
Dong quai	*Angelica sinensis*	Root	3–9 g/day	5–15 mL/day	Reproductive tonic Antithrombotic Anti-inflammatory	Amenorrhea Benign breast disorder Chronic pelvic pain Constipation	**KSw/C** ⊘ ***P/L*** • Increased bleeding

					TCM: yin and blood deficiency, blood moving	Dysmenorrhea Endometriosis Hypomenorrhea Fertility problems Irregular menstruation Menstrual migraines Oligomenorrhea/ Uterine fibroids Vasomotor complaints of perimenopause and menopause Weakness, fatigue, lassitude	• Not to be taken with blood-thinning medications • In TCM, dong quai is always combined with other herbs. • GI symptoms, including nausea, laxative effects, vomiting, and bloating may occur. • Photosensitivity with severe reactions may occur because of furocoumarin, psoralen, and bergapten contents. • Dong quai may have hypotensive action. A limited body of research suggests possible interference with antiarrhythmic medications, beta-blockers, and calcium channel blockers. • Avoid during pregnancy unless under the care of a qualified TCM practitioner. • Two case reports of rash in breastfeeding infants of mothers who took dong quai, including reappearance with discontinuation and retrial
Echinacea	*Echinacea* spp.	Root Herb	1–3 g/3x/day	Liquid extract 0.5–1 mL/ 3x/day Tincture: 2–5 mL/ 3x/day	Immunomodulating Anti-inflammatory Antimicrobial Alternative Lymphatic	Acne Cervical dysplasia Endometriosis GBS HSV 1 and 2 Interstitial cystitis Lymphadenopathy Mastitis Recurrent UTI Upper respiratory Infection Vulvaginitis HSV	**KS** • Transitory tingling of the tongue is a normal effect of this herb. • Possible allergy when flowering tops are included in allergic patients; use of root product only usually prevents allergy • Should not be taken by transplant patients or patients taking immunomodulatory medications • There is no clear evidence from either basic science of human reports that echinacea causes significant hepatotoxicity.

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							• Oral intake of echinacea is considered safe during pregnancy based on preliminary studies.
Eleuthero	*Eleutherococcus senticosus*	Root	0.6–3 g daily for up to 3 months	2–16 mL/day up to 1 month	Adaptogen Immunomodulator	Convalescence Depression Exhaustion Fatigue, lassitude HSV Illness exacerbated by stress Improve mental stamina Improve physical stamina Physical or nervous Stress	**KS** • Insomnia has been rarely observed in clinical studies. • Some sources recommend a limitation on the duration of use from 1 to 3 months; however, this is based on the need to reevaluate for possible health conditions rather than risks associated with the herb. • Contrary to some reports, there does not appear to be a significant need for concern over the development of hypertension from the use of Eleuthero. • Eleuthero has been known to be adulterated with Periploca sepium, a plant that contains cardioactive glycosides and was associated with a case of fetal androgenization (''hairy baby syndrome'') in a woman who unknowingly consumed an adulterated product during pregnancy.
Evening primrose	*Oenothera biennis*	Oil from seeds	Taken as a dietary supplement oil, 1500 mg/day		Anti-inflammatory Rich in essential fatty acids (EFAs), especially GLA	Benign breast disorder Chronic pelvic pain Dysfunctional labor/labor augmentation Endometriosis	**KSw/C/LD** • Contraindicated in patients with seizure disorders, as use of the oil may trigger undiagnosed temporal lobe epilepsy, particularly in

						Migraines PMS symptoms Improves quality of breast milk	schizophrenic patients, or those taking epileptogenic medications • Possible GI upset • No teratogenicity has been demonstrated during pregnancy; however, data are limited. As linoleic and gamalenic acids are components of breast milk, it seems safe for breastfeeding mothers to consume EPO; however, again, data are limited and concerns have been raised whether maternal consumption would cause excess consumption in the breastfeeding infant.
False unicorn root	*Chamaelirium luteum*	Root	1–2 g/3x/day	Liquid extract: 1–2 mL/ 3x/day Tincture: 2–5 mL/ 3x/day	Uterine tonic Ovarian tonic	Amenorrhea Irregular menstruation Fertility problems Ovarian pain PCOS Threatened miscarriage Uterine atony	**LD** • Although this herb has traditionally been used to improve fertility, there are no safety data on intake during pregnancy. The herb possesses uterotonic activity. Therefore, the herb should be discontinued when pregnancy has been achieved and care taken in women with a prior history of first-trimester miscarriage. • This plant is considered endangered and therefore should only by used from cultivated sources.
Fennel	*Foeniculum vulgare*	Seeds	2.5 g/2x/day in tea	2–4 mL/ 2x/day	Lactagogue Spasmolytic Estrogenic Carminative	DUB Increase milk supply PMS-related digestive symptoms	**LSw/C/LD** • Essential oil not for internal use • Not for medicinal use during pregnancy because of possible estrogenic effects • Caution is recommended in women with a history or risk of estrogen receptor–positive cancer.

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
Fenugreek	Trigonella foenum-graecum	Seed	1–6 g/ 3x/day	2–4 mL/ 3x/day	Lactagogue Aphrodisiac Flavoring Lipid-lowering effects	Increase milk supply Low libido in menopausal years Hypercholesterolemia	**Sw/C** ⊘ ***P*** • Caution in diabetics because of hypoglycemic effects • Caution in patients taking hypokalemic agents, cardiac glycoside medications, or with cardiac disease because of risk of hypokalemia from consumption • Theoretical risk of increased bleeding, so caution advised in patients taking anticoagulants • Possible estrogenic activity requires caution when combined with estrogenic medications, oral contraceptives, etc. • Possible reduction in serum thyroid hormone concentrations; therefore, caution is required for patients with hypothyroidism. • Not for medicinal use during pregnancy because of possible hypoglycemic and hypothyroid effects • Possible potentiation of MAOIs in patients taking these medications • If nursing mother consumes a large amount, the baby's urine may have a maple syrup–like odor that could be confused with maple syrup urine disease. • Possible interference with iron absorption with long-term use

Feverfew	*Tanacetum parthenium*	Leaf	Freeze-dried: .05 g/1x after meals Dried: 5–200 g/day	Liquid extract; 6.25 mg/ 3x/day Tincture: 1–40 drops every 2–43 hours	Anti-inflammatory Emmenagogue	Amenorrhea Dysmenorrhea PMS, tension and migraine headaches	**LSw/C** ⊘ ***P/L*** • Contact dermatitis (including oral ulcers/sore mouth) from fresh leaves • Reported side effects include GI complaints, tingling sensation on the tongue, headache, diarrhea, nausea, abdominal pain, flatulence, dizziness, and skin rash • No adverse effects seen in rats and pigs receiving 100 to 150 times the human dose daily • Because of reported abortifacient activity, feverfew is contraindicated during pregnancy. It has been reported to induce uterine contractions in full-term pregnant women.
Figwort	*Scrophularia nodosa*	Aerial parts	2–8g/day	Liquid extract; 2–8 mL/day Tincture 2–4 mL/day	Anti-inflammatory Dermatologic	Acne	**LD**
Flax seed	*Linum usitatissimum*	Seed	10–50 g seeds/day	N/A	Phytoestrogen Nutritional supplements: EFA source (Omega-3) Laxative Lipid lowering effects 1–3 Tbs/day 1000 mg/tid	Benign breast disorder Hot flashes Constipation Vaginal dryness and atrophy Hypercholesterolemia Uterine fibroids	**LSw/C** ⊘ ***P*** • Avoid in patients with bleeding disorders and those on anticoagulant/antiplatelet therapies • May interfere with absorption of medications, so take 2 hours apart from other medications. • Use cautiously in patients with irritable bowel disorders, chronic diarrhea, or diverticulitis. • Caution advised in patients with diabetes because of case series showing elevated glucose levels in patients taking omega-3 fatty acids, which are found in flax seeds.

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							• Drink plenty of water when taking soaked or ground flax seed to prevent constipation and bowel obstruction. • Has uncertain effects on triglyceride levels (may raise or lower), so avoid in patients with hypertriglyceridemia. • Immature flax seeds are neurotoxic and should not be taken. Symptoms of toxicity include ataxia, tachycardia, and weakness. • Possible interactions with NSAIDs, mood stabilizers, oral hypoglycemic agents including insulin, antihyperlipidemic agents, oral contraceptives, and hormone replacement therapy, and antihypertensive drugs. • Animal studies show possible harmful effects when taken during pregnancy and lactation, including increased levels of LH and testosterone, increased epididymal weight, and decreased prostate weight in males, and altered mammary structure, delayed or early onset puberty depending on dose, puberty, and reduced or lengthened number of estrus cycles in females exposed to flax seeds in utero.
Fringe tree	*Chionanthus virginicus*	Root bark	N/A	2–5 mL/day	Cholagogue/ choleretic Laxative	Benign breast disorder Endometriosis	**LD**

Garlic	*Allium sativum*	Bulb	2–4 g/3x/day	2–4 mL/ 3x/day	Antimicrobial (fresh) Antihypertensive Antiatherosclerotic Lipid lowering	CAD Trichomoniasis Vulvovaginitis GBS Hypertension Atherosclerosis Hypercholesterolemia Postpartum perineal care	**KSw/C** • Direct or prolonged exposure to skin can lead to irritation and ulceration. • GI upset when taken raw internally; also garlic odor from ingesting fresh garlic • Possible interactions with anticoagulant and antiplatelet medications • Possible increased bleeding time; therefore, discontinuation 2 weeks prior to surgery is recommended. • In vitro increase in uterine activity; therefore, caution when taking medicinally in pregnancy; no expected adverse effects when taken as a food in pregnancy • Altered odor of breast milk in breastfeeding mothers consuming garlic has led to alterations in infant feeding in a blinded, placebo-controlled study. Amniotic fluid odor is also influenced by maternal garlic consumption. • There are no known adverse clinical or experimental effects of garlic on pregnancy or lactation.
Gentian	*Gentiana lutea*	Rhizome	0.6–2 g/ 3x/day	1–4 mL/ 3x/day	Hepatic	PMS	**KS/LD** ⊘ ***P/L*** • Contraindicated in pregnancy and lactation because of mutagenic effects seen on Ames test
Ginger	*Zingiber officinale*	Rhizome	0.25–1 g/ 3x/day	1.5–3 mL/ 3x/day	Antinauseant Antiemetic Anti-inflammatory Spasmolytic Carminative Antiplatelet Flavoring	Digestive complaints associated with endometriosis and chronic pelvic pain Amenorrhea Dysmenorrhea	**KSw/C** • May increase absorption of other medications • Contraindicated in patients with gallstones • Caution in patients with peptic ulcer disease or GERD

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
						NVP Nausea with HIV, chemotherapy Pelvic pain and congestion Reduce nausea associated with herbs and medications Uterine fibroids	• Contraindicated in patients with bleeding disorders, on medications for bleeding disorders, and pre- and post-surgery • During pregnancy dose should not exceed 1 g/day because of possible abortifacient activity; doses up to this amount considered safe for the treatment of NVP
Ginkgo	*Ginkgo biloba*	Leaf	120–240 mg extract/day	120–240 mg extract/day in 2–3 divided doses	Cognition enhancing Anti-platelet activating factor (PAF) Antioxidant Circulatory stimulant	Dysmenorrhea Headache Memory loss and cognitive decline Pelvic congestion	**LSw/C** ⊘ ***P/L*** • Possible GI upset, headache, dizziness • Case reports of spontaneous bleeding have led to a high level of caution pre- and post-surgery and in patients on antiplatelet/anticoagulant therapies.
Ginseng	*Panax ginseng*	Root	1–9 g/day day in 2–3 divided doses	1–6 mL/day	Adaptogen TCM: Tonify qi, Spleen, Stomach, Heart	Endometriosis Fatigue, poor stamina PCOS Poor concentration Physical, mental fatigue Susceptibility to colds, infection Convalescence Vaginal dryness and atrophy	**KSw/C** ⊘ ***P/L*** • Generally well tolerated in most clinical trials • Caution advised in diabetic patients because of possible hypoglycemic effects • May cause or exacerbate hypertension, insomnia, anxiety, palpitations, and tachycardia in some individuals. Patients with any of these as pre-existing conditions should avoid ginseng use unless under the supervision of a qualified TCM practitioner.

							• Limited case reports of epistaxis, increased vaginal bleeding, and a single report of reduced effectiveness of warfarin. Based on these reports, caution has been advised for patients on antiplatelet/anticoagulant medications and pre- and post-surgically. • Although no adverse effects, mutagenicity, or teratogenicity have been reported, and the herb is traditionally used during pregnancy and for postpartum convalescence, it is generally recommended that ginseng only be used under the supervision of a qualified health professional during pregnancy.
Globe artichoke	*Cynara scolymus*	Fruit	250–750 mg of cymarin daily or 4–9 g leaves daily	3–8 mL daily	Lipid-lowering	Hypercholesterolemia	**LS/LD** • Considered well tolerated, with no known contraindications or major adverse effects • Individuals may experience nonspecific GI complaints when taking globe artichoke. • Likely safe when taken for short periods. • Because of lack of toxicity data, excessive use should be avoided in pregnancy and lactation.
Goat's rue	*Galega officinalis*	Herb	3–6 g/day of dried herb in infusion	4–8 mL/day	Lactagogue	Increase milk supply	⊘ **P/LD** • Goat's rue has caused poisoning and death in sheep; however, there is no evidence of human poisoning by goat's rue reported in the literature. Oral administration of goat's rue to pregnant ewes at various stages of gestation

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							produced no noticeable damage in the offspring. • Caution is advised in diabetic patients, because goat's rue may enhance the hypoglycemic effects of hypoglycemic drugs; however, there are no documented cases of this effect. • Goat's rue taken with mineral salts increased milk production in lactating women in a controlled trial from 1968; however, no safety or toxicity studies have been done on use during lactation.
Golden rod	*Solidago virgaurea*	Herb	3–5 g/ 2–3x/day	2–3 mL/ 2–3x/day	Diuretic Anti-inflammatory	Interstitial cystitis Urinary tract infection	**LS/LD** • Possible sensitivity in patients allergic to plants in the Composite family, and specifically to golden rod; contact dermatitis
Goldenseal	*Hydrastis canadensis*	Root/rhizome	0.5–1 g/ 3x/day	Liquid extract: 0.3–1 mL/ 2–3x/day Tincture: 2–4 mL/ 2–3x/day	Antimicrobial Anti-inflammatory Astringent Antihemorrhagic	Cervical dysplasia GBS Menorrhagia Pelvic congestion Vaginal discharge Vaginal infection Vulvovaginitis Nipple thrush	**LSw/C/LD** **H-D!** • There is limited research on goldenseal herb; however, much is known about isolated constituents from the herb, most notably, berberine and hydrastine. • Although one cannot extrapolate the effects of isolated constituents to the whole plant, cautions are suggested when using this herb regularly or in high doses.

- Consumption of isolated berberine alkaloids in goldenseal is toxic.
- High doses of hydrastine have caused elevated blood pressure following intravenous administration in animal studies; lower doses of berberine and hydrastine have hypotensive effects. Caution is suggested in use with hypertensive patients, and those on antihypertensive medications.
- No reported clinical herb–drug interactions.
- In vitro berberine has been reported to decrease the anticoagulant effects of heparin in dog and human blood, and although no sedative activity has been reported, increased barbiturate sleeping time has been reported.
- Berberine is reported to increase coronary blood flow, and at high doses is reported to inhibit cardiac muscle activity.
- Caution is advised in patients with cardiac arrhythmias.
- Antihistamine and antimuscarine activity has been reported.
- The use of goldenseal during pregnancy is controversial. Typically contraindicated, this is based on limited reports of increased activity of the in vitro increase of uterine stimulant activity on guinea pig and rat uterine tissue from

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							the isolated fraction canadine. However, the total alkaloid fraction of goldenseal has demonstrated anticonvulsant activity in vitro. The issue of contraindication in pregnancy appears to have less to do with the effects of the herb as a uterine tonic and more on the potential toxicity of long-term intake of the alkaloids. At this time, goldenseal is not recommended for regular or high-dose intake during pregnancy; however, based on current literature, it is premature to entirely contraindicate its use during pregnancy and lactation. • This herb is considered ecologically endangered; therefore, only products made from cultivated herb should be used.
Gotu kola	*Centella asiatica*	Herb	60–120 mg/day	20–40 mL/day	Nervine tonic Connective tissue repair	Anxiety, stress Fatigue Improve memory, cognitive function Chronic venous insufficiency and varicosities PUPPP/prevent striae	**LS/LD** **H-D!** • Well tolerated when taken for up to 6 to 12 months for chronic insufficiency and wound healing • Numerous case reports of allergic reactions and contact dermatitis

Green tea	*Centella asiatica*	Leaf	1–4 cups/day	Antiviral Antioxidant Antidyslipidemic	HSV Endometriosis Varicosities, hemorrhoids Osteoporosis prevention Uterine fibroids Improve mood. memory, concentration Nipple thrush and cracked nipples Reduce LDL, raise HDL	• Limited reports of adverse effects of gastric irritation and nausea have been reported. • Conflicting reports state both possible lipid-lowering and lipid-elevating effects with this herb. • Animal studies suggest possible sedating effects • Caution in diabetics based on animal evidence of possible ability to raise blood glucose • Safety unknown during pregnancy and lactation **KSw/C** • Diuresis • >500 mg/day of caffeine is associated with insomnia, palpitations, anxiety, agitation, delirium, psychosis, and detrusor muscle instability. Withdrawal commonly accompanies cessation of chronic use. • Preliminary research suggests a possible reduction in estrogen associated with regular green tea consumption. • Regular consumption of high tannin beverages may interfere with iron absorption. • Numerous interactions with caffeine and medications are known; the effects on green tea as a source of herb–drug interactions has not been well studied. • Regular caffeine consumption is best avoided in pregnancy, especially first trimester, because caffeine crosses the placenta. Consumption of >400 mg day of caffeine during pregnancy has been associated with increased

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							rates of SIDS; >1100 mg/day has been associated with congenital birth defects. • Caffeine is readily transferred into breast milk and may lead to sleep disturbances in infants. Infants of breastfeeding mothers consuming >500 mg caffeine/day have been reported to have tremors and cardiac dysrhythmias. • Green tea extracts and other concentrated green tea products are not recommended and are not considered safe during pregnancy and lactation.
Gromwell	*Lithospermum off.*	Herb	N/A	2–4 mL/day	LD	Hyperthyroidism	**LD**
Guggul	*Commiphora mukul*	Resin	500–1000 g guggulipid standardized to 2.5% guggulsteones or/2–3 day or an equivalent dose of prepared guggulsteone 25 mg 3/day		Antidyslipidemic Anti-platelet aggregation Antioxidant	Reduce LDL, raise HDL Atherosclerosis prevention Acne	**LSw/C** **H-D!** ⊘ ***P/L*** • Considered safe when used in recommended doses for up to 6 months. • Reversible inhibition of platelet aggregation; possible interference with anticoagulant and antiplatelet medications; discontinue 1 week prior to surgery. • Mild thyroid stimulation; not recommended in patients with thyroid disorders • Possible hypersensitivity reactions • May increase bioavailability of propranolol (beta-blocker) and

							decrease the bioavailability of diltiazem (calcium channel blocker) • Adverse effects include GI upset and headache • Not recommended during pregnancy because of possible abortive effects; not recommended during lactation.
Gymnema	*Gymnema sylvestris*	Leaf	200 mg 2–3x/day	2 mL/ 2–3x/day	Antidiabetic Hypoglycemic Hypocholesterolemic	PCOS	**LS/LD** ⊘ ***P/L*** • No known adverse effects or herb–drug interactions have been associated with this herb other than the possible glucose-lowering effects and possible potentiation of hypoglycemic agents and antihyperlipidemic effects and possible potentiation of lipid-lowering drugs.
Hawthorn	*Crataegus oxyacantha*	Fruit	0.3–1 g/ 3x/day	Liquid extract: 0.5–1 mL/ 3x/day Tincture: 1–2 mL/ 3x/day	Cardiotonic Antihypertensive Peripheral vasodilator	Cardiac insufficiency Heart palpitations with anxiety Hypertension Tachycardia	**KSw/C** • Hawthorn is exceptionally well tolerated and safe as recommended. • Theoretical concerns over potentiation of the actions of other cardiovascular medications; however, this has not been demonstrated clinically, including in a trial comparing digoxin alone compared with digoxin plus hawthorn. Potentiation of inotropic effects without toxicity was observed in guinea pig hearts. Use of the herb concurrently with cardiac glycosides has been suggested as a means to lower cardiac glycoside dose and toxicity. • Theoretical potentiation of effect on medications with coronary dilatory effects based on animal studies. • Rare reported side effects include nausea, headache, dizziness, and palpitations.

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							• Unspecified hawthorn extracts have demonstrated reduction in uterine tissue tone and motility in vitro. The clinical significance of this is unknown in pregnancy.
Hollyhock	*Alcea rosea*		N/A	1–3 mL/ 2x/day	Demulcent, mucilage	Interstitial cystitis	**LS/LD**
Hops	*Humulus lupulus*	Strobile	0.5–2 g/ 2–4x/day	Liquid extract: 0.5–3 mL/ 3x/day Tincture: 1–2 mL/ 3x/day	Sedative (mild) Anxiolytic Spasmolytic Estrogenic	Amenorrhea Anxiety Chronic pelvic pain Dysmenorrhea Headache Insomnia Lactation—improve let down reflex/Increase milk supply	**KSw/C** **H-D!** ⊘ ***P*** • May exacerbate depression in some patients. Do not use concurrently with anti-depressant medications or in patients with moderate to severe depression. • High doses may be significantly sedating. • Direct estrogenic effects of phytoestrogens have been observed in vitro. Caution is advised in patients with ER-positive cancer and those using hormonal contraception or HRT. • Hops may increase serum glucose levels; therefore, caution is advised in diabetic patients. • Not for use during pregnancy
Horse chestnut	*Aesculus hippocastanum*	Seed	0.2–1 g/3x/day	Extracts = to 50–150 mg triterpenes (aescin) in divided doses	Venotonic Anti-inflammatory	Chronic venous insufficiency, varicosities, hemorrhoids Chronic pelvic pain Pelvic congestion syndrome Vaginal dryness and atrophy	**LS** • Possible GI irritation • No documented herb–drug interactions • Improperly prepared products may contain escin, which has theoretical additive effects with anticoagulant and antiplatelet drugs.

							• Limited data suggest no adverse reactions or toxicity during pregnancy and possible safety for the treatment of venous insufficiency and varicosities.
Horsetail	*Equisetum arvense*	Herb	50–75 mg escin twice daily from standardized product; equivalent to 300 mg standardized product/day	Extracts equivalent to 50–150 mg triterpenes/day	Diuretic Urinary astringent Anti-inflammatory	Interstitial cystitis Urinary tract infection Osteoporosis prevention	**LSw/C** ⊘ ***P/L*** **H-D!** • Horsetail is generally very well tolerated with few reports of adverse effects. • Theoretical herb–drug interactions include: —Thiamine depletion because of thiaminase in the herb —Adverse effects with cardiac glycosides, diuretics, steroids, and laxatives because of potassium-depleting effects of horsetail [a] The nicotine content in horsetail is theoretically suggested to cause side effects associated with nicotine use and has theoretically suggested ability to have additive effects with other CNS stimulants. • Not for internal use during pregnancy
Jamaican dogwood	*Piscidea erythrina*	Root bark	1–2 g/ 3x/day	2–8 mL/day	Analgesic Sedative Spasmolytic	Chronic pelvic pain Dysmenorrhea Endometriosis Headache/Migraine Insomnia	**LSw/C** **LD** • Rotenone, a constituent in Jamaican dogwood, is a known toxin. Symptoms of overdose may include numbness, tremors, salivation, and sweating. In vivo oral doses of up to 1.5 mg/kg have not been shown to be toxic in animal studies. • Caution is advised in patients with hypotension, cardiac insufficiency, and bradycardia.

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							• Jamaican dogwood has been reported to have a potent depressant effect on the uterus in vivo and in vitro, possibly equivalent to papaverine. • Use is generally not recommended in pregnancy because of limited safety data; however, cautious use under the supervision of a qualified practitioner may be acceptable for a limited number of conditions. Use is not recommended during the first trimester of pregnancy.
Kava	*Piper methysticum*	Root	1.5–3 = to 60–120 mg kavalactones/day	Liquid extract 3–6 mL/day Standardized preparations: 100–200 kavalactones/day; 60 mg kavalactones 2–4x/day	Anxiolytic Analgesic Sedative Spasmolytic	Anxiety; tension Chronic pelvic pain Endometriosis Headache Hot flashes Insomnia Interstitial cystitis Musculoskeletal tension PMS symptoms Urinary tract infection	**LSw/C** **H-D!** ⊘ ***P/L*** • Associated with risk of hepatotoxicity; contraindicated in patients with history of liver disease. Periodic evaluation of liver enzymes may be prudent with chronic use. • Should not be taken in conjunction with CNS-affecting drugs medications/ substances because of possible potentiation; possible interaction with benzodiazepines Possible extrapyramidal effects with kava use. • Kava dermopathy may occur with abuse; it is reversible on discontinuation.

Ladies' mantle	*Alchemilla vulgaris*	Herb	2–4 g/3x/day	2–4 mL/ 3x/day	Astringent Uterotonic	Menorrhagia Chronic pelvic pain Endometriosis Uterine fibroids	**LS/LD**
Lavender	*Lavandula officinalis* *Lavandula angustifolia*	Flower	1–3 g/2–3x/day	2–4 mL 1–2x/day	Antimicrobial Anxiolytic Sedative (mild) Antiseptic Spasmolytic Antidepressant (mild) Carminative	Acne (topical) Anxiety Cervical dysplasia Headache Insomnia Irritability Mild depression PMS Postpartum perineal care (topical) Restlessness Vulvovaginitis (topical) Vaginal dryness and atrophy (topical)	**LSw/C** **H-D!** • Theoretical additive effects with CNS depressants, antidepressant drugs, and antiseizure medications • Possible lipid-lowering effects that may be additive with lipid-lowering medications • Essential oil for topical use only • Because of the ability of volatile oils to cross the placenta and the CNS effects of lavender, use of not more than an occasional cup of beverage tea with lavender is recommended during the first trimester.
Lemon balm	*Melissa officinalis*	Leaf	1.5–4.5 g/ 2–3x/day	2–4 mL/ 2–3x/day	Nervine Spasmolytic Anxiolytic Antiviral	Anxiety Depression (mild) Headache Hot flashes HSV Hyperthyroidism Insomnia	**KS** • Possible TSH/thyroxin antagonist effects
Licorice	*Glycyrrhiza glabra*	Root	1–4 g/2x/day	0.6–2 mL/ 2-3x/day	Adaptogen Anti-inflammatory Antitussive Antiviral	Cardiac insufficiency Constipation HSV Interstitial cystitis PCOS (with peony) Urinary tract infection Vulvovaginitis (topical) PUPPS	**H-D!** ⊘ ***P/L*** • Serious side effects include hypertension, symptoms of hyperaldosteronism, electrolyte imbalances (and associated sequelae), and hormonal dysregulation including elevated prolactin and estrogen levels in women, which may affect fertility or menstrual regularity. • Hypokalemia with chronic use/overdose; also blocked aldosterone/renin response, lethargy, hypertension,

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							headache, sodium retention, and in rare cases pulmonary hypertension and CHF (not caused by the DGL form) • Caution should be exercised with patients on digoxin because of potential decreases in potassium associated with licorice intake. • May reduce the effects of diuretics such as hydrochlorothiazide and spironolactone, affecting blood pressure and CHF control, and may cause hypokalemia when combined with furosemide, insulin, or kayexelate. • May theoretically interfere with hormonal contraceptives and HRT • Contraindicated in patients with hypertension or mineralocorticoid disorders • Increased risk of premature labor when used regularly during pregnancy. Generally not recommended for use during pregnancy; exceptions may be considered for short term under supervision of a qualified practitioner for specific conditions.
Lily of the valley	*Convallaria majalis*	Flower	N/A	0.5–1 mL/ 2x/day	Cardiotonic	Cardiac insufficiency	**H-D!** ⊘ ***P/L*** • Side effects associated with cardiac glycosides including vomiting, diarrhea, nausea,

							visual disturbances, hypotension, serious arrhythmias, and sinoatrial block. • Risk of interactions/potentiation with other cardiac glycoside drugs
Linden (Lime blossom)	*Tilea* spp.	Flower	2–4 g/2x/day	1–2 mL/2x/day	Sedative (mild) Spasmolytic Diuretic	Anxiety Hypertension Headache Insomnia See which other uses in text	**LS/LD** • There are limited data on the safety and efficacy of linden, an herb with a long history of use in European herbal medicine. Prior allegations that the herb should be avoided in patients with a cardiac disorder do not appear to have any scientific basis.
Lobelia	*Lobelia inflata*	Herb	0.2–0.6 g/3x/day	Liquid extract: 0.2–0.6 mL/3x/day Tincture: 0.6–2 mL/3x/day	Spasmolytic Sedative Analgesic	Insomnia Acute anxiety Dysmenorrhea (severe) Endometrial pain Cervical dilatation* Interstitial cystitis	⊘ ***P/L*** • Lobelia acts on nicotinic receptors and may cause respiratory stimulation in low doses and respiratory depression in high doses. • Tachycardia may occur at higher doses; if it does, discontinue and resume only at a lower dose with close monitoring, if at all. • Other side effects include nausea, vomiting, dizziness, hypotension, diaphoresis, and palpitations. • Some midwives use this herb to relax the cervix during a difficult labor with failure to progress; there are no data on the efficacy or safety of this practice. The herb should not be used in pregnancy prior to labor and should only be used in labor, if at all, under the supervision of a qualified practitioner.
Marijuana	*Cannabis* spp.	Leaf Flower Resin	Dose not specified		Sedative Spasmolytic Anodyne	Chemotherapy: nausea Chronic pelvic pain Dysmenorrhea Endometrial pain	**LS** • Sedation • Decreased reflexes • Risks associated with smoking

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
					Appetite stimulant	Interstitial cystitis HIV-pain, appetite Insomnia NVP	• Risks of dependency • Because of illegality, use is not recommended.
Marshmallow	*Althaea officinalis*	Root	2–5 g/ 3x/day	2–5 mL/ 3x/day	Demulcent Anti-inflammatory	Increase milk supply Interstitial cystitis Urinary tract infection Vulvovaginitis	**KS/LD** • There are no reported side-effects or herb–drug interactions with marshmallow. The high mucilage content has been purported to possibly reduce the absorption of other medications.
Meadowsweet	*Filipendula ulmaria*	Herb	4–6 g/3x/day	Liquid extract: 1.5–6 mL/ 3x/day Tincture: 3–4 mL/3x/day	Anti-inflammatory Antacid Urinary antiseptic	*See how used in book*	**H-D!** ⊘ ***P/L*** • Avoid in patients with salicylate sensitivity, G6PD deficiency, and bleeding disorders. • Toxicity and fetal malformations have been seen in animal studies; therefore, use of this herb is contraindicated during pregnancy and lactation.
Milk thistle	*Silybum marianum*	Seed	12–15 g/day	2–4 mL/ 2–3x/day	Hepatoprotective Antioxidant	*See how used in book* PUPPP	**KSw/C** **H-D!** • Well tolerated with no expected side effects with the exception of reports of hypersensitivity reactions • Rarely, headache, pruritus, or GI upset have been reported. • Hypoglycemic effects have been reported; thus, caution is advised in diabetic patients. • Possible herb–drug interactions include interference with medications metabolized by CYP450 via

							inhibition of the enzyme, theoretical decreased clearance of glucoronidated agents, increased clearance of estrogens, and increased efficacy of chemotherapeutic drugs, including platinums and anthracyclines. • Two separate clinical trials of milk thistle in pregnant women yielded positive results with no evidence of harmful effects on the pregnancy or offspring. In one study, 400 mg silymarin was used to treat mothers for 60 days for intrahepatic cholestasis. The women experienced improvements in symptoms and blood work. In another study, a 15-day trial of milk thistle was shown to attenuate pruritus associated with intrahepatic cholestasis.
Milky oats	*Avena sativa*	Milky Seed	N/A	3–5 mL/ 2–3x/day	Nervine	Increase milk supply Insomnia Nervous exhaustion PUPPP Stress, tension, irritability	**KS/LD**
Motherwort	*Leonurus cardiaca*	Herb	2–4 g/3x/day	Liquid extract: 2–4 mL/ 3x/day Tincture: 2–6 mL/ 3x/day	Nervine Spasmolytic Uterine tonic Hypotensive Cardiotonic Bitter	Amenorrhea Benign breast disorder Anxiety, stress, irritability Dysmenorrhea Dysfunctional labor/labor augmentation Endometriosis Hypertension Improve let-down reflex/Increase milk supply	**LS/LD** ⊘ ***P*** • No adverse effects or herb–drug interactions are expected. There is a general lack of clinical and safety data on this herb, although there is a significant record of historical use. • No warnings or cautions have been reported in association with the purported cardioactivity of the herb, which was found to have

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
						Irregular menstruation Menstrual headache Palpitations (e.g., because of stress, hyperthyroidism) PMS Uterine fibroids	inhibitory effects on myocardial function. • Motherwort is traditionally not recommended for use during pregnancy because of purported uterotonic effects. Leonorine, a constituent, is reported to have uterotonic effects, and stachydrine, another constituent is reported to have oxytocic effects.
Mugwort	*Artemisia vulgaris*	Aerial parts	1–3 g/ 2x/day	1–2 mL/ 2x/day	Emmenagogue	Amenorrhea	**LD** ⊘ ***P***
Mullein leaf	*Verbascum thapsus*	Leaf	3–6 g/day	2–4 mL/ 2–3x/day	Demulcent, mucilage	Interstitial cystitis	**LS/LD**
Myrrh	*Commiphora molmol*	Resin	N/A	1–2.5 mL/day	Antimicrobial Anti-inflammatory Antitumorigenic Vulnerary	Cervical dysplasia Hypothyroidism HSV ulcers (topical) Vulvovaginitis (topical) GBS Postpartum perineal care	**LS/LD** ⊘ ***P*** • Prolonged topical use may cause contact dermatitis—limit topical use to 7 days consecutively.
Nettles	*Urtica dioica*	Leaf	2–4 g/ 3x/day	Liquid extract: 3–4 mL/ 3x/day Tincture: 2–6 mL/ 3x/day Fresh juice: 1–15 mL/ 3x/day	Nutritive Vascular tonic Antiallergic Diuretic	Acne Fatigue Anemia DUB Iron-deficiency anemia Menstrual irregularities Pelvic congestion Sugar, caffeine cravings Osteoporosis prevention Varicosities	**KS/LD** • Nettles has a long historic use as a food and tonic. It is considered well tolerated but is almost entirely lacking in clinical data. • Uterotonic activity has been reported in vivo in pregnant and nonpregnant murine models, with betaine and serotonin considered the active ingredients. The clinical relevance of this is unknown. Although this has been a

							purported basis for contraindication of use during pregnancy, nettle has been consumed in large quantities by pregnant women as a uterine tonic with no reported increase in uterine activity, miscarriage, or malformations in the offspring.
Ocotillo			N/A	2–4 mL/ 2x/day			**LD**
Oregano	*Origanum vulgare*	Leaf	Used topically as a diluted essential oil		Antiviral Antimicrobial	Cervical dysplasia GBS	**KSw/C** ⊘ ***P*** • Oregano is considered safe when used in amounts comparable with use in foods. • The essential oil is for topical use only. Prolonged topical use may lead to contact dermatitis. • Not for internal medicinal use during pregnancy and lactation, because the volatile oils can cross the placenta and breast milk.
Oregon grape root	*Berberis aquifolium syn. Mahonia aquifolium*	Root	1.5–3 g/ 2–3 mL/day	2.5–5 g/ 2–3x/day	Antimicrobial Anti-inflammatory Bitter	Acne (topical/internal) Benign breast disorder GBS Nipple thrush PUPPS (topical) Urinary tract infection Vulvovaginitis (topical)	**LSw/C** • See goldenseal for cautions associated with berberine, found in Oregon grape root.
Osha	*Lomatium dissectum*	Root	1–3 g/2x/day	1–3 mL/ 2x/day	Antiviral	Cervical dysplasia	**LD** ⊘ ***P***
Partridge berry	*Mitchella repends*		N/A	2–4 mL/ 2x/day	Uterine astringent/tonic	Chronic pelvic pain Dysmenorrhea Uterine fibroids	**LS/LD**
Passion flower	*Passiflora incarnata*	Herb	4–8 g/day	1–4 mL/ 3x/day	Sedative (mild) Analgesic Antispasmodic Anxiolytic	Anxiety, stress, tension Dysmenorrhea Endometrial pain Headache Insomnia Nervous irritability PMS	**KSw/C/LD** • No known contraindications or herb–drug interactions reported in the literature; excessive doses may theoretically cause sedation.

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							• At the highest concentrations of extract, passion flower increased spontaneous uterine contractions on isolated rat uteri, and caused a statistically significant reduction in tissue response to acetylcholine when compared with control.
Pau d'arco	*Tabebuia impetiginosa*	Bark	250 mg/x/day	3–7 mL/day	Antimicrobial	Vaginal infections (topical) Vulvovaginitis (topical)	**LSw/C** ⊘ ***P/L*** • Safe when used for topical use, including for acute use as a suppository during pregnancy.
Peony	*Paeonia lactiflora*	Root	3–6 g/day	3–5 mL/ 1–2x/day	Spasmolytic	Amenorrhea Dysmenorrhea Endometriosis Fertility problems Interstitial cystitis Iron-deficiency anemia PCOS Threatened miscarriage Uterine fibroids	**LSw/C** • Possible anticoagulant activity; caution should be used with patients with bleeding problems or on anticoagulant/ antiplatelet medications.
Peppermint	*Mentha piperita*	Leaf	3–5 g/1–3x day as tea	0.5–2 mL/ 1–2x day	Antiemetic	Digestive complaints associated with PMS NVP	**KS** • Contraindicated in patients with esophageal reflux disease • Caution recommended for patients with salicylate allergy • Caution recommended for patients with gallstones • EO not for internal use • For use as a beverage tea only during the first trimester of pregnancy, because the volatile oils can cross the placenta.
Picrorrhiza	*Picrorrhiza kurrhoa*	Root	N/A	2–4 mL/ 2–3x/day	Anti-inflammatory Immunomodulatory Hepatoprotective Antioxidant	Benign breast disorder	**LSw/C/LD** ⊘ ***P*** • Side effects include GI symptoms and skin rash.

Pipsissewa	*Chimaphila umbellata*	Aerial parts	N/A	2–3 mL/ 2–3x/day	Astringent tonic	Interstitial cystitis	**LS/LD**
Poke root	*Phytolacca americana*	Root	For topical use only		Lymphatic Anti-inflammatory Alterative Cytotoxic	Benign breast disorder	⊘ ***P/L*** • Known toxicity associated with internal use of all parts of the plant with both internal and topical use. Peripheral blood changes have been observed with ingestion, including eosinophilia. • Toxicity symptoms include nausea, vomiting, cramping, weakness, diarrhea, hematemesis, hypotension, and tachycardia. • Limited topical use under qualified supervision only • Not for internal or topical use at any time during pregnancy or lactation
Psyllium	*Plantago ovata*	Seed	20–35 g/day	N/A	Bulk laxative	Constipation	**LSw/C** • Serious allergic reactions have been reported after ingestion. • Bowel obstruction has been reported after ingestion, particularly in individuals who have had prior bowel surgery or when psyllium has been taken with inadequate quantities of water. • GI side effects include bloating, gas, and diarrhea, as well as constipation (as a result of obstruction). • Caution is suggested in diabetic patients because of the hypoglycemia effects of psyllium. • Pregnancy and lactation warnings include those described above for this herb. No other known contra-indications exist during pregnancy for any of the trimesters; however, pregnancy safety studies are lacking.

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
Pulsatilla (Pasque flower)	*Anemone pulsatilla*	Herb	0.12–0.3 g/ 3x/day	Liquid extract: 0/12–0.3 mL/ 3x/day Tincture: 0.3–1 mL/ 3x/day	Analgesic	Chronic pelvic pain Dysmenorrhea Endometriosis Migraines Interstitial cystitis	**LSw/C/LD** ⊘ ***P/L*** • Only preparations made from DRIED plant material should be used—fresh plant is toxic. • Increased uterine activity has been documented.
Quaking aspen	*Populus tremelloids*	Bark	1–4 g/2–3x/ day as a decoction	1–3 mL/ 2x/day	Anti-inflammatory Astringent Antiseptic	Interstitial cystitis	**LD** • The high salicylates and tannin levels in this herb suggest that use during pregnancy is not appropriate; however, there are no studies of pregnancy/lactation safety with this herb, and dearth of research on this herb generally.
Red clover	*Trifolium pratense*	Flower Herb	3–5 g/ 3x/day	1–2 mL/ 3x/day	Phytoestrogen (isoflavones) Alterative Spasmolytic	Acne Benign breast disorder Osteoporosis prevention Uterine fibroids Vasomotor complaints of perimenopause and menopause Vaginal dryness and atrophy	**KSw/C** • Some consider caution advisable for patients with a risk/history of ER-positive cancer. • Standardized isoflavone products should not be used during pregnancy and lactation because of the potential for estrogenic activity. • Possible cautionary use when taking hormonal contraceptives or HRT. Red clover may enhance estrogenic effects via estrogen receptor binding.
Red raspberry	*Rubus idaeus*	Leaf	4-8 g/ 3x/day	4-8 mL/ 3x/day	Uterine tonic Astringent Partus preparator Nutritive	Chronic pelvic pain Pregnancy uterine tonic Dysmenorrhea	**KS** • The safety of red raspberry leaf during pregnancy has been demonstrated.

						Uterine fibroids DUB Dysfunctional labor/labor augmentation	• There are no known contraindications or expected side-effects or herb–drug interactions; however, any herb with a high-tannin content can theoretically interfere with nutrient absorption, particularly iron, when taken in high doses or for extended periods. • Some women report nausea when taking raspberry leaf tea during the first trimester of pregnancy, likely because of the astringency of the herb.
Red root, New Jersey Tea	*Ceanothus americanus*	Root	N/A	2–4 mL/ 1–2x/day	Astringent Lymphatic Antiviral	Cervical dysplasia Fibrocystic breasts	**LSw/C** ⊘ ***P/L*** • Not to be used for patients with coagulation disorders or those taking anticoagulant/ antiplatelet medications
Rehmannia	*Rehmannia glutinosa*	Root	2–6 g/day	4–12 mL/day	Anti-inflammatory Antihemorrhagic	DUB Endometriosis	**LSw/C** • Digestive complaints have been reported. • Caution is advised in patients with immune dysfunction, autoimmune disorders, and those taking immuno-suppressive medications. • Safety in pregnancy is not established. There is no expected contraindication in lactation.
Reishi	*Ganoderma lucidum*	Fruiting body and mycelium	6–12 g/day	10 mL/ 3x/day	Adaptogen Immunomodulator Cardiotonic	Cervical dysplasia Frequent colds, susceptibility to infection GBS HSV 1 and 2 Hypertension Palpitations Prevent atherosclerosis Stress	**LSw/C** • Side effects are uncommon; rashes are one of the most common side effects. • Caution is advised in patients with immune dysfunction, autoimmune disorders and those taking immunosuppressive medications. • Safety in pregnancy is not established. There is no expected contraindication in lactation.

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
Rhaponticum	*Rhaponticum carthimoides*		N/A			Benign breast disorder Cervical dysplasia Chronic pelvic pain Endometriosis PCOS PMS Uterine fibroids	
Rhodiola	*Rhodiola rosea*		50–500 mg/ day x 2 weeks		Adaptogen Cardiotonic/ cardioprotective	Benign breast disorder Cervical dysplasia Chronic pelvic pain Endometriosis PCOS PMS Uterine fibroids Cardiovascular protection	**LS/LD** • Limited data show this to be a well-tolerated herb with no expected side effects or herb–drug interactions • Safety in pregnancy is not established. There is no expected contraindication in lactation.
Rosemary	*Rosmarinus officinalis*	Leaf	2–4 g/ 3x/day	Liquid extract: 2–4 mL/ 3x/day	Spasmolytic Circulatory stimulant Antioxidant Antimicrobial Anti-inflammatory	Endometriosis Depression Headache Memory difficulties with menopause Vaginal infection (topical) Postpartum perineal care (bath)	**KSw/C** ⊘ ***P*** • Overall, this herb is reported to have low toxicity. • Because of reputed abortifacient effects and ability to affect the menstrual cycle, this herb is not recommended for internal use during pregnancy beyond the normal amount found in food use. • Essential oil is for topical use only; extended topical use may lead to irritation.
Sage	*Salvia officinalis*	Leaf	1–4 g/ 3x/day	Tincture: 1–4 mL/ 3x/day	Anhidrotic Estrogenic Emmenagogue Astringent Antiseptic Carminative/ spasmolytic	Hot flashes/Night sweats Inhibits breast milk secretion Postpartum perineal care (topical) Vulvovaginitis (topical)	**LSw/C** ⊘ ***P/L*** • Sage products should not be used internally during pregnancy beyond minimal amounts found as seasoning in foods. The herb is strongly abortifacient and emmenagogic.

							• Sage oil is toxic and is not meant for internal consumption.
Salvia	*Salvia miltiorrhiza*	Root	2–6 g/day dried root	1–4 mL/ 3x/day	Antithrombotic Antihypertensive	Hypertension, CAD	⊘ ***P/L*** • Contraindicated for patients with bleeding disorders or on anticoagulant/antiplatelet medications • May increase risk of bleeding and should be discontinued 1 week prior to surgical procedures.
Sarsaparilla	*Smilax ornata*	Root	1–4 g 3x/day as decoction	N/A	Anti-inflammatory Hepatoprotective	Benign breast disorder	**LD** • No side effects or drug interactions have been reported; overall, there are limited data on this herb.
Saw palmetto	*Serenoa repens*	Serenoa serrulata	320 mg lipophilic compounds (160 mg 2x/day)		Antiandrogenic Estrogenic	Acne (adult) Fertility problems PCOS	⊘ ***P/L*** **H-D!** • Not for use with adolescents because of possible hormonal effects; treatment of acne may be an exception under qualified supervision. • May cause GI upset • Possible interference with hormonal contraception and HRT
Schisandra	*Schisandra chinensis*	Fruit	1.5–15 g/day	3–7 g/ 1–2x/day	Adaptogen Nervine Hepatoprotective Antioxidant Oxytocic	Benign breast disorder Fatigue Frequent colds, susceptibility to infection Stress-related illness Improve stamina Depression (mild) DUB PCOS PMS Improve memory Insomnia Uterine fibroids Labor augmentation	• Not for use in pregnancy because of potential for stimulating to uterine contractions • Caution recommended with barbiturates which may be potentiated; may antagonize the effects of stimulants
Senna	*Senna alexandrina*	Leaf	3–12 pods in 150 g warm water for 6–12 hours	0.5–2 mL	Laxative	Constipation	**LSw/C** • Contraindicated in patients with intestinal obstruction,

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							stenosis, atony inflammatory bowel diseases, appendicitis, and undiagnosed GI disorders • Contraindicated in patients with electrolyte disturbances and dehydration • Excessive use can lead to dependency. • Long-term use can lead to hypokalemia with resultant cardiac and neuromuscular dysfunction, particularly when combined with cardiac glycosides, diuretics, or steroids. • Although there have been no documented adverse effects from the use of senna during pregnancy or lactation, use during pregnancy and lactation is generally not recommended because of potentially genotoxic anthracoids (emodin and physcione) contained in the herb.
Shatavari	*Asparagus racemosa*	Root	N/A	4–7 mL/ 1–2x/day	Adaptogen Aphrodisiac/tonic Lactagogue	Decreased libido Depression Fatigues, lassitude Fertility problems Insufficient breast milk Oligomenorrhea Susceptibility to infection	⊘ ***P*** • Because of the high saponin content, this herb is not recommended for patients with cholestasis, fat malabsorption, and upper GI irritation, or inflammation. Gastric irritation and reflux are possible side effects. • In a murine model using oral administration of the herb, Kupffer cell enlargement, liver

							congestion, bile plugs, mild cellular degeneration, fibrosis, and leukocytic infiltration were observed. • Although this herb is used traditionally to promote fertility, it is also used as an abortifacient; therefore, use in pregnancy is not recommended and if used as a fertility agent, use should be discontinued upon conception. There is no known increase in harmful effects on the fetus from limited use in women.
Shepherd's purse	*Capsella bursa-pastoris*	Herb	2–5 g/ 3x/day	2–4 mL/ 3x/day	Antihemorrhagic	DUB Menorrhea, metrorrhagia Uterine fibroids	**LSw/C/LD** ⊘ ***P*** • There is a general lack of safety and toxicity data available for this herb. Low toxicity was shown in a single murine study in vitro of intraperitoneally and subcutaneously injected extract, at doses of 1.5 g/kg and 31.5 g/kg, respectively. Toxicity signs included sedation, pupil dilatation, hind limb paralysis, dyspnea, and death because of respiratory paralysis. • Generally contraindicated in pregnancy because of reported oxytocin activity, possibly a result of tyramine contained in the plant
Skullcap	*Scutellaria lateriflora*	Herb	1–2 g/ 3x/day	Tincture: 1–2 mL/ 3x/day	Nervine Sedative (mild)	Anxiety, stress, tension Headache Insomnia PMS-related symptoms	**LSw/C/LD** • There is a general lack of safety and toxicity data for skullcap, with no reported contraindications or herb–drug interactions. • Adulterations of skullcap with the toxic herb *Teucrium* have occurred; thus, caution is advised and a reliable product

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							source should be obtained. This is of particular importance in pregnancy. Ingestion of *Teucrium* has led to reports of hepatitis. • Overdose of skullcap tincture may lead to the following symptoms: giddiness, stupor, confusion, and seizures. This is most likely a result of adulteration with Teucrium.
Slippery elm	*Ulmus rubra*	Inner bark	2–5 g/ 1–3x/day	5 mL 3x/day	Demulcent	Acid reflux Interstitial cystitis Vaginal infections (topical in suppository mix)	**KS/LD** • There are no known contraindications or toxicity issues associated with slippery elm use. • Any contraindications to use of slippery elm during pregnancy are a vestige of the use of slippery elm sticks to dilate the cervix mechanically to induce abortion. Oral intake of slippery elm is not known to be abortifacient and is considered safe during pregnancy. • Slippery elm was traditionally used as a supplement for newborns, and also to increase the supply and quality of breast milk. There are no expected contraindications to use during lactation.
Soy	*Glycine max*	Fruit	Used as a food from sources such as tofu, soy milk, and tempeh		Phytoestrogen	Hot flashes Osteoporosis prevention Uterine fibroids	**KSw/C** • Gas, indigestion • Possible goitrogenic effects (>30 g/day)

						Vaginal dryness and atrophy	• Fermented products contraindicated with MAOIs • Concentrated soy products are not recommended for use during pregnancy and lactation because of possible estrogenic effects.
St. John's wort	*Hypericum perforatum*	Herb/ flower	2–4 g/ 3x/day	2–4 mL/ 3x/day	Antidepressant Antiviral Nervine Vulnerary	Cervical dysplasia Chronic pelvic pain Depression Endometriosis HSV (internal and topical) Insomnia PMS Psychological complaints associated with perimenopause Neuromuscular pain Vulvovaginitis Postpartum perineal care Nipple thrush and cracked nipples Vaginal dryness and atrophy (topical)	**LSw/C** **H-D!** • Not for treatment of severe depression • Potential herb–drug interactions with anticoagulants (e.g., warfarin), immunosuppressives (e.g., cyclosporine), oral contraceptives, indinavir and other HIV medications, digoxin, and other drugs metabolized by the CYP450 oxidase system, and SSRIs • Theoretical effects on serum hormone levels because of actions on CYP450 metabolism • Photosensitivity has been reported in patients taking high doses of hypericin; caution should be observed for patients using high-dose St. John's wort or taking the herb for a prolonged duration. • Safety during pregnancy has not been established. • The detrimental effect of untreated depression on the mother and fetus are increasingly well accepted. There is no known contraindication to use during lactation. Prenatal and postpartum depression should be treated by a qualified health professional. • Safety during pregnancy and lactation is discussed in detail

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							in Plant Profiles: St. John's Wort.
Sweet sumach	*Rhus aromatica*	Leaf	3–5 g/1-3x/day in infusion	2–4 mL/ 1–3x/day	Astringent tonic	Interstitial cystitis	**LD**
Tea tree	*Melaleuca alternifolia*	Leaf	Used topically as an essential oil		Antimicrobial	Acne Cervical dysplasia GBS Nipple thrush and cracked nipples Vaginal infection Vulvovaginitis	**KSw/C** • Not for internal use • Prolonged topical use may cause irritation.
Thuja	*Thuja occidentalis*	Leaf	N/A	1.5–2.5 mL/day	Antimicrobial	Cervical dysplasia HPV infection HSV (topical)	⊘ ***P/L*** • Known neurotoxicity • Not for internal use • Avoid even topical use during pregnancy and lactation.
Thyme	*Thymus vulgaris*	Leaf	1–2 g/ 1–2x/day	1–2 mL/ 1–3x/day	Antimicrobial	Cervical dysplasia GBS HPV infection HSV infection Vulvovaginitis	**LSw/C** ⊘ ***P/L*** • Not for internal use during pregnancy (topical and suppository use is acceptable) other than amounts typically consumed in foods • Not to exceed 10 g dried leaf containing 0.03% thymol/day • Thyme oil is highly toxic and not intended for internal use (dilute use in suppositories is acceptable).
Tribulus	*Tribulus terrestris*	Aerial parts	N/A	3–5 mL/ 2x/day	Tonic Aphrodisiac Estrogenic	Fertility problems Menstrual irregularities PCOS	**LS/LD** ⊘ ***P/L*** • Tribulus is used as a fertility agent in both men and women. Because it has demonstrated an increase in fetal damage in animal studies, discontinuation

							immediately upon conception is recommended. No increase in frequency of malformation or other harmful fetal effects have been seen in women using it to increase fertility; however, studies are very limited and animal evidence of harm is significant. • In vivo mouse studies have suggested a very low toxicity from this herb. Staggers (a neuromuscular disease), cholestasis, and photosensitivity have all been observed in sheep that have consumed tribulus. • The high saponin content may cause gastric irritation and reflux as side effects.
Turmeric	*Curcuma longa*	Rhizome	750 mg–3 g/ day in divided doses	N/A	Anti-inflammatory	Endometriosis	**KSw/C** **H-D!** ⃠ ***P*** • Overall, turmeric has a very good safety profile, even in high doses. • High doses and prolonged use may be associated with gastric irritation and are not recommended for individuals with peptic ulcer disease or gastric hyperacidity. • Turmeric should not be taken by individuals with bile duct obstruction, gallstones, or those taking immunosuppressant medications. • In vitro studies demonstrate inhibition of platelet aggregation and thus the herb may potentiate the effects of anticoagulant/antiplatelet medications. Caution is also advised with discontinuation

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							of the herb 1 week prior to surgical procedures. • Curcumin potently inhibits CYP450 in rats. There are no human data. • Curcumin (200 mg/kg) protected against doxorubicin myocardial toxicity in rats. • Because of lipid-lowering effects, turmeric may potentiate the effects of lipid-lowering medications. • It is traditionally considered emmenagogic; therefore, it is not recommended for internal use in pregnancy in doses higher than those typically found in food.
Usnea	*Usnea barbata*	Herb (lichen)	N/A	2–4 mL/ 2–3x/day	Antimicrobial	Cervical dysplasia GBS Trichomoniasis Vaginal infection	**LS/LD** • Safety in pregnancy is not established; therefore, use topically (including in vaginal suppositories) only.
Uva ursi	*Arctostaphylos uva ursi*	Leaf	Up to 12 daily in divided doses	2–4 mL/ 2–4x/day	Urinary antiseptic Astringent Anti-inflammatory	Urinary tract infection Vulvovaginitis Postnatal perineal care	**LSw/C** • Many references state that uva ursi is not to be used in pregnancy; however, there is no evidence direct evidence to support this claim. See Plant Profiles: Uva Ursi. • Not for use >7 days consecutively. • Some authorities claim that the herb is most effective when urinary pH is alkaline; therefore, it is often given with 2 ''00'' capsules of baking soda.

Valerian	*Valeriana officinalis*	Root	1–3 g/2-3x/day	3–5 mL/ 3x/day	Sedative Anxiolytic Spasmolytic Carminative	Anxiety Gastric distress related to endometriosis or PMS Headache Insomnia	**LSw/C** **H-D!** ⊘ ***P*** • Valerian effects possibly enhanced by alcohol consumption—avoid excessive alcohol consumption concurrently with this herb. • Intake of valerian preparations is not recommended within 2 hours of driving or operating machinery because of possibly impaired response time. • Herbalists have reported a paradoxic effect of stimulation rather than relaxation in a small percentage of patients using valerian. • In vitro experiments suggest that valerian may inhibit CYP 450 activity. • Caution is recommended when using in combination with CNS-depressing medications. • Even overdose with large quantities of the herb have not led to fatality; however, side-effects have included tremor, GI upset, chest tightness, and when injected, cardiac disturbance, blurred vision, and excitability, among other less significant symptoms. • The safety of valerian during pregnancy and lactation has not been established. In a limited number of cases of valerian intoxication during pregnancy, no teratogenic effects have been observed. Degradation products of valepotriates have demonstrated cytotoxicity and mutagenicity in vitro, but have

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
							not caused birth defects in a limited number of animal studies. They are poorly absorbed.
White oak bark	*Quercus alba*	Bark	Topical use only		Astringent	Postnatal perineal care Varicosities and hemorrhoids (topical)	• Topical use only for use during pregnancy for the treatment of varicosities, hemorrhoids, and postnatal perineal care
Wild yam	*Dioscorea villosa*	Root	2–4 g/day in divided doses	2–4 mL/day in 3–5 divided doses	Spasmolytic Anti-inflammatory Possible estrogenic effects	Chronic pelvic pain Dysmenorrhea Endometriosis Fertility problems Interstitial cystitis NVP Threatened miscarriage Urinary tract infection Vaginal dryness and atrophy	**LSw/C** **H-D!** • Possible GI complaints with long-term use of high doses • Although hormonal effects are not supported by scientific research, internal use is not recommended in individuals with a history of sex hormone–dependent cancers. • Possible/theoretical interactions with steroids, hormonal contraception, HRT, and lipid-lowering agents (potentiation) • Caution is advised in avoiding products that may have been adulterated with progesterone.
Willow	*Salix* spp.	Bark	1–3 g/3x/day up = to 60–120 mg salicin/day	1–3 mL/ 3xday	Analgesic Anti-inflammatory	Headache	**LSw/C** **H-D!** ⊘ ***P/L*** • Minor adverse effects include GI upset, dizziness, sweating, and rash. Adverse effects associated with salicylates may be associated with this herb.

							• Precautions similar to those with other salicylate containing medications are advised, including avoiding if there is salicylate sensitivity, asthma, peptic ulcer disease, gout, bleeding disorders, and kidney or liver disease. • Drug interactions associated with salicylates are theoretically possible with the use of willow bark. • The safety of willow bark during pregnancy is not known, and in fact, the safety of aspirin in pregnancy is somewhat uncertain. Salicylates excreted in breast milk have been observed to cause skin rash in the breastfeeding infant.
Witch hazel	*Hamamelis virginiana*	Bark	2g/3x/day	2–4 mL/ 3x/day	Astringent Anti-inflammatory	Acne DUB Hemorrhoids (topical) Menorrhagia Postnatal perineal care PUPPP Uterine fibroids Varicosities (topical)	**LSw/C** ⊘ ***P*** • Data on the internal use of witch hazel are limited. No side effects or contraindications are reported for this herb other than possible GI irritation in some individuals, and excessive ingestion is not recommended because of the high tannin content of the herb. • No problems are expected with the topical use of witch hazel during pregnancy and lactation. Internal use is not recommended.
Yarrow	*Achillea millefolium*	Herb/ flower	2–5 g/ 3x/day	2–4 mL/ 3x/day	Antimicrobial Antihemorrhagic Urinary antiseptic Astringent Vulnerary Spasmolytic	Benign breast disorder Endometriosis Chronic pelvic pain DUB Dysmenorrhea Hemorrhoids Menorrhagia Pelvic congestion	**LSw/C/LD** ⊘ ***P*** • Limited safety and clinical data available; considered to have low toxicity with toxic principles in too low a concentration to be clinically significant in humans

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COMMON NAME	BOTANICAL NAME	PART USED	DRIED HERB (IN CAPSULES, TEA, INFUSION, DECOCTION)	TINCTURE	ACTIONS	WOMEN'S HEALTH INDICATIONS DESCRIBED IN THIS BOOK	SAFETY CONCERNS
						Postnatal perineal care Urinary tract infection Uterine fibroids Vulvovaginitis	• Contraindicated in those with known allergy to plants in the Composite family • Not for internal use during pregnancy because of thujone content and purported abortifacient activity
Yellow dock	*Rumex crispus*	Root	3–5 g/ 3x/day	2–4 mL/ 3x/day	Aperient Alternative	Acne Constipation Iron-deficiency anemia	**LSw/C/LD** • Limited data available for this herb; excessive and prolonged use of laxatives may lead to abdominal cramping, diarrhea, and hypokalemia. • Avoid if there is intestinal obstruction, as with all laxatives. • Although no safety data exist for use during pregnancy and lactation, caution is advised during pregnancy because of anthraquinone contents, because anthraquinones can be passed into the breast milk.
Yellow sweet clover	*Melilotus officinalis*	Aerial parts	2–4 g/day in tea form to no greater than 3–30 mg coumarin daily	2–4 mL/day	Anti-inflammatory	Benign breast disorder Interstitial cystitis	**LD**
Yerba mansa	*Anemopsis californica*	Root	N/A	3–5 mL/day	Astringent tonic Antimicrobial	Interstitial cystitis Vulvovaginitis	**LS/LD**
Yohimbe	*Pausinystalia yohimbe*	Bark	16–20 g yohimbine hydrochloride (standardized) per day		Aphrodisiac CNS stimulant	Low libido	**H-D!** ⊘ ***P/L*** • Multiple adverse effects are associated with use. Side effects include nausea, vomiting, tachycardia, hypertension, hypotension,

							dizziness, and irritability. Toxicity is associated with lupus-like syndrome. • Avoid in patients with renal disease, hypertension, CAD, PTSD, panic disorder, ulcers (active), bipolar disorder, and hepatic insufficiency. • Multiple possible herb–drug interactions include drugs metabolized by CYP450, alcohol, androgenic and antiandrogenic drugs, benzodiazepines, antihypertensive medications, MAOIs, opioid antagonists, sympathomimetics, as well as other theoretic contraindications. • Not for long-term use • Should only be used by trained practitioners.
Ziziphus	*Ziziphus spinosa*	Seed	5–10 g/day	5–10 mL/day	Sedative (mild) Anxiolytic Hypotensive Antihidrotic	Insomnia Anxiety Irritability Nervous exhaustion Palpitations Night sweats	**LS/LD** • Low toxicity in in vivo mouse models. Limited human clinical and safety data. • Commonly used in Traditional Chinese Medicine, including in formulas used during pregnancy. • No reported contraindications or herb–drug interactions

*The data from this table are derived from the same sources listed in the introduction to this chapter.

Common and Botanical Medicine Names Quick Reference Dose Chart

APPENDIX I

HERB		DOSAGE RANGE	
COMMON NAME	**BOTANICAL NAME**	**DRIED HERB (OR INFUSED/ DECOCTED) G/DOSE/X DAY**	**TINCTURE ML/DOSE/X DAY**
American ginseng	*Panax quinquefolium*	3–6 g/day	3–12 mL/day
Anise seed	*Pimpinella anisum*	1–5 g/2–3x/day	1–3 mL/2–3x/day
Ashwagandha	*Withania somnifera*	3–6 g powder/day	4–10 mL/day
Astragalus	*Astraglaus menbranaceus*	9–30 g/day	5–10 mL/day
Bacopa	*Bacopa moniera*	N/A	4–7 mL/day
Barberry	*Berberis vulgaris*	1–2/3x/day	1–2 mL/3x/day
Bayberry	*Myrica cerifera*	1–2/3x/day	1–2 mL/3x/day
Beth root	*Trillium erectum*	0.5-2/day	1–4 mL/day
Birch	*Betula spp*	2–3 g/day	1–2 mL/day
Black cohosh	*Actaea racemosa*	0.04–0.2, up to 1–3 g/day	Tincture: 0.4 mL liquid extract up to 20 drops/day
Black haw	*Viburnum prunifolium*	N/A	3–10 mL/day
Bladderwrack	*Fucus vesiculosus*	5–10/3x/day	Liquid extract: 4–8/3x/day
Blood root	*Sanguinaria canadensis*	Topical use only	
Blue cohosh	*Caulophyllum thalictroides*	0.3–1 g/3x/day	0.5–2.5 mL/3x/day
Blue flag	*Iris versicolor*	0.6–2 g/2x/day	1–2 mL/3x/day
Blue vervain	*Verbena officinalis*	2–4 g/1–3x/day	2–4 mL/1–3x/day
Bugle weed	*Lycopus* spp.	N/A	1–3/1–2x/day
Bupleurum	*Bupleurum falcatum*	1.5–12 g/day	3–7 mL/day
Burdock root	*Arctium lappa*	3–18 g/day	3–5 mL/2–3x/day
Butterbur	*Petasites hybridus*	Recommended in PA-free standardized form	
Calendula	*Calendula officinalis*	1–4/3g/day	0.3–1.2 mL/day
California poppy	*Eschscholtzia californica*	N/A	2–4 mL/2–3x/day
Celandine (Greater)	*Chelidonium majus*	1–2 g/3x/day	1–2 mL/3x/day
Centaury	*Centaurium erythraea*	2–4 g/3x/day	2–4 mL/3x/day
Chamomile	*Matricaria recutita*	2–8 g/3x/day	1–4 mL/3x/day
Chaste berry	*Vitex agnus-castus*	30–40 mg/day up to 500–1000 mg daily	0.2 mL/2–3x/day up to 3–5 mL/day
Chinese skullcap	*Scutellaria baicalensis*	N/A	4–7 mL/1–2x/day
Cinnamon	*Cinnammomom* spp.	0.5–1 g/3x/day	Liquid extract: 0.5–1.5 mL/day Tincture: 2–4 mL/day
Cleavers	*Galium aparine*	N/A	4–10 mL/day
Coleus	*Coleus forskohlii*	N/A	1.5-4 mL/day
Corn silk	*Zea mays*	4–8 g/in infusion 3x/day	5–15 mL/3x/day
Corydalis	*Corydalis ambigua*	5–10 g/day	5–20 mL/day
Cotton root	*Gossypium herbaceum*	N/A	2–4 mL/2x/day
Cordyceps	*Cordyceps sinensis*	3–15 g/day	N/A
Couch grass	*Elymus repens*	4–8 g/day in decoction	5–15 mL/3x/day
Cramp bark	*Viburnum oplulus*	N/A	3–10 mL/day
Cranberry	*Vaccinium macrocarpon*	300 mL cranberry juice daily for up to 6 months	

HERB		DOSAGE RANGE	
COMMON NAME	**BOTANICAL NAME**	**DRIED HERB (OR INFUSED/ DECOCTED) G/DOSE/X DAY**	**TINCTURE ML/DOSE/X DAY**
Cranesbill geranium	*Geranium maculatum*	N/A	2–5 mL/day
Daminana	*Turnera diffusa*	2–4 g/3	2–4
Dandelion leaf	*Taraxacum officinale*	4–10 g/3x/day	Liquid extract: 4–10 mL/3x/day Tincture: 2–5 mL/3x/day Fresh juice: 5–10 mL/2x/day
Dandelion root	*Taraxacum officinale*	2–8 g/3x/day	Liquid extract: 2–8 mL/day Tincture: 5–10 mL/day
Dong qual	*Angelica sinensis*	3–9 g/day	5–15 mL/day
Echinacea	*Echinacea* spp.	1–3 g/3x/day	Liquid extract 0.5–1 mL/3x/day Tincture: 2–5 mL/3x/day
Eleuthero	*Eleutherococcus senticosus*	0.6–3 g daily for up to 3 months	2–16 mL/day up to 1 month
Evening primrose	*Oenethera biennis*	Taken as a dietary supplement oil, 1500 mg/day	
False unicorn	*Chamaelirium luteum*	1–2 g/3x/day	Liquid extract: 1–2 mL/3x/day Tincture: 2–5 mL/3x/day
Fennel	*Foeniculum vulgare*	2.5 g/2 x/day in tea	2–4 mL/2x/day
Fenugreek	*Trigonella foenum-graecum*	1–6 g/3x/day	2–4 mL/3x/day
Feverfew	*Tanacetum parthenium*	Freeze-dried: 0.05 g/1x after meals Dried: 5–200 g/day	Liquid extract; 6.25 mg/3x/day Tincture: 1–40 drops every 2–43 hours
Figwort	*Scrophularia nodosa*	2–8 g/day	Liquid extract; 2–8 mL/day Tincture 2–4 mL/day
Fringe tree	*Chionanthus virginicus*	N/A	2–5 mL/day
Garlic	*Allium sativum*	2–4 g/3x/day	2–4 mL/3x/day
Gentian	*Gentiana lutea*	0.6–2 g/3x/day	1–4 mL/3x/day
Ginger	*Zingiber officinale*	0.25–1 g/3x/day	1.5–3 mL/3x/day
Ginkgo	*Ginkgo biloba*	120–240 mg extract	120–240 mg extract/day in 2–3 divided doses
Ginseng	*Panax ginseng*	1–9 g/day day in 2–3 divided doses	1–6 mL/day
Golden rod	*Solidago canadensis*	3–5 g/2–3x/day	2–3 mL/2–3x/day
Goldenseal	*Hydrastis canadensis*	0.5–1 g/3x/day	Liquid extract: 0.3–1 mL/2–3x/day Tincture: 2–4 mL/2–3x/day
Green tea	*Camellia chinensis*	1-4 cups/day	
Gromwell	*Lithospermum off.*	N/A	2–4 mL/day
Guggul	*Commiphora mukul*	500–1000 g guggulipid standardized to 2.5% guggulsteones or/2–3 day or an equivalent dose of prepared guggulsteone 25 mg 3x/day	
Gymnema	*Gymnema sylvestre*	200 mg 2–3x/day	2 mL/2–3x/day
Hawthorn	*Crataegus monogyna*	0.3–1 g/3x/day	Liquid extract: 0.5–1 mL/3x/day Tincture: 1–2 mL/3x/day
Hops	*Humulus lupulus*	0.5–2 g/2–4x/day	Liquid extract: 0.5–3 mL/3x/day Tincture: 1–2 mL/3x/day
Horse chestnut	*Aesculus hippocastanum*	0.2–1 g/3x/day	Extracts = to 50–150 mg triterpenes (aescin) in divided doses
Hollyhock	*Alcea rosea*	N/A	1–3 mL/2x/day
Horsetail	*Equisetum arvense*	50–75 mg escin twice daily from standardized product; equivalent to 300 mg standardized product/day	Extracts equivalent to 50–150 mg triterpenes/day
Jamaican dogwood	*Piscidea piscipula*	1–2 g/3x/day	2–8 mL/day
Kava kava	*Piper methysticum*	1.5–3 = to 60–120 mg kava lactones/day	Liquid extract 3–6 mL/day Standardized preparations:100–200 kava lactones/day; 60 mg kava lactones 2–4x/day
Lades' mantle	*Alchemilla vulgaris*	2–4 g/3x/day	2–4 mL/3x/day
Lavender	*Lavendula officinalis*	1–3 g/2–3	2–4/1–2

HERB		DOSAGE RANGE	
COMMON NAME	**BOTANICAL NAME**	**DRIED HERB (OR INFUSED/ DECOCTED) G/DOSE/X DAY**	**TINCTURE ML/DOSE/X DAY**
Lemon balm	*Melissa officinalis*	1.5–4.5 g/2–3x/day	2–4 mL/2–3x/day
Licorice	*Glycyrrhiza glabra*	1–4 g/2x/day	0.6–2 mL/2–3x/day
Flax	*Linum ussitissimum*	10–50 g seeds/day	N/A
Lobelia	*Lobelia inflata*	0.2–0.6 g/3x/day	Liquid extract: 0.2–0.6 mL/3x/ day Tincture: 0.6–2 mL/3x/day
Marijuana	*Cannabis sativa*	*Dose not specified*	
Marshmallow root	*Althea officinalis*	2–5 g/3x/day	2–5 mL/3x/day
Meadowsweet	*Filipendula ulmaris*	4–6 g/3x/day	Liquid extract: 1.5–6 mL/3x/ day Tincture: 3–4 mL/3x/day
Milk thistle	*Silybum marianus*	12–15 g/day	2–4 mL/2–3x/day
Milky oats	*Avena sativa*	N/A	3–5 mL/2–3x/day
Motherwort	*Leonurus cardiaca*	2–4 g/3x/day	Liquid extract: 2–4 mL/3x/day Tincture: 2–6 mL/3x/day
Mugwort	*Artemisia vulgaris*	1–3 g/2x/day	1–2 mL/2x/day
Mullein leaf	*Verbascum thapsus*	3–6 g/day	2–4 mL/2–3x/day
Myrrh	*Commiphora mol mol*	N/A	1–2.5 mL/day
Nettle leaf	*Urtica dioica*	2–4 g/3x/day	Liquid extract: 3–4 mL/3x/day Tincture: 2–6 mL/3x/day Fresh juice: 1–15 mL/3x/day
Ocotillo	*Fouquieria splendens*	N/A	2–4 mL/2x/day
Oregano	*Origanum vulgaris*	Used topically as an essential oil	
Oregon grape	*Mahonia aquifolium*	1.5–3 g/2–3 mL/day	2.5–5 g/2–3x/day
Osha	*Lomatium dissectum*	1–3 g/2x/day	1–3 mL/2x/day
Partridge berry	*Mitchella repens*	N/A	2–4 mL/2x/day
Passion flower	*Passiflora incarnata*	4–8 g/day	1–4 mL/3x/day
Peony	*Paeonia lactiflora*	3–6 g/day	3–5 mL/1–2x/day
Peppermint	*Mentha piperita*	3–5 g/1–3x/day as tea	0.5–2 mL/1–2xday
Picrorrhiza	*Picrorrhiza kurrhoa*	N/A	2–4 mL/2–3x/day
Poke root	*Phytolacca americana*	For topical use only	
Pulsatilla	*Anemone pulsatilla*	0.12–0.3 g/3x/day	Liquid extract: 0/12–0.3 mL/ 3x/day Tincture: 0.3–1 mL/3x/day
Quaking aspen	*Populus tremuloides*	N/A	1–3 mL/2x/day
Red clover	*Trifolium pratense*	3–5 g/3x/day	1–2 mL/3x/day
Red raspberry	*Rubus idaeus*	4–8 g/3x/day	4–8 mL/3x/day
Red root	*Ceanothus americanus*	N/A	2–4 mL/1–2x/day
Rehmannia	*Rehamannia glutinosa*	2–6 g/day	4–12 mL/day
Reishi	*Ganoderma lucidum*	6–12g/day	10 mL/3x/day
Rhaponticum	*Rhaponticum carthimoides*	N/A	
Rhodiola	*Rhodiola rosea*	50–500 mg/day x 2 weeks	
Rosemary	*Rosmarinus officinalis*	2–4 g/3x/day	Liquid extract: 2–4 mL/3x/day
Sage	*Salvia officinalis*	1–4 g/3x/day	Tincture: 1–4 mL/3x/day
Saw palmetto	*Serenoa repens*	320 mg lipophilic compounds (160 mg/2x/day)	
Schizandra	*Schizandra chinensis*	1.5–15 g/day	3–7 g/1–2x/day
Shatavari	*Asparagus racemosa*	N/A	4–7 mL/1–2x/day
Shepherd's purse	*Capsella bursa-pastoris*	2–5 g/3x/day	2–4 mL/3x/day
Skullcap	*Scutellaria lateriflora*	1–2 g/3x/day	Tincture: 1–2 mL/3x/day
Slippery elm	*Ulmus rubra*	2–5 g/1–3x/day	Not typically taken in these forms
St. John's wort	*Hypericum perforatum*	2–4 g/3x/day	2–4 mL/3x/day
Tea tree	*Melaleuca alternifolia*	N/A	Used topically as an essential oil
Thuja*	*Thuja occidentalis*	N/A	1.5–2.5/day
Thyme	*Thymus vulgaris*	1–4 g/3x/day	2–3mL/1–3x/day
Tienchi ginseng	*Panax notoginseng*	2–9 g/day	4–18 mL/day
Tribulus	*Tribulus terrestris*	N/A	3–5 mL/2x/day
Tumeric	*Curcuma long*	750 mg 3 g/day in divided doses	N/A
Usnea	*Usnea barbata*	N/A	2–4 mL/2–3x/day
Uva ursi	*Arctostaphylos uva ursi*	Up to 12 daily in divided doses	2–4 mL/2–4x/day

HERB		DOSAGE RANGE	
COMMON NAME	**BOTANICAL NAME**	**DRIED HERB (OR INFUSED/ DECOCTED) G/DOSE/X DAY**	**TINCTURE ML/DOSE/X DAY**
Valerian	*Valeriana officinalis*	1–3g/3x/day	3–5 mL/3x/day
Wild yam	*Dioscorea villosa*	2–4 g/day in divided doses	2–4 mL/day in 3–5 divided doses
Willow	*Salix* spp.	1–3 g/3x/day up = to 60–120 mg salicin/day	1–3 mL/3x/day
Witch hazel	*Hamamelis virginiana*	2 g/3x/day	2–4 mL/3x/day
Yarrow	*Achillea millefolium*	2–5 g/3x/day	2–4/3x/day
Yellow dock	*Rumex crispus*	3–5 g/3x/day	2–4 mL/3x/day
Yellow sweet clover	*Melilotus officinalis*	2–4 g/day in tea form to no greater than 3–30 mg coumarin daily	
Yerba mansa	*Anemopsis californica*	N/A	3–5 mL
Zizyphus	*Zizyphus spinosa*	5–10 g/day	5–10 mL/day[1]

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CHAPTER 6

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CHAPTER 7

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Further-Reading

Resources

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CHAPTER 8

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CHAPTER 16

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CHAPTER 19

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Plant Profiles

1. Wu W-H, Liu L-Y, Chung C-J, Jou HJ, Wang TA: Estrogenic effect of yam ingestion in healthy postmenopausal women, J Am Coll Nutr 24(4):235-243, 2005.

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