CHAPTER 13

Menopause

Ivy M. Alexander
Linda C. Andrist

Menopause, which is often thought of as the closure of reproductive capability, has emerged as one of the predominant health issues for midlife women. A major reason that menopause is receiving so much attention is the increasing numbers of women reaching midlife, which encompasses the perimenopausal years (ages 35 to 50 years) to menopause (ages 50 to 60 years) (Davis & Huber, 2004; Fogel & Woods, 2008). The baby boom generation—that is, people born between 1945 and 1960—is the largest middle-aged cohort ever recorded. In 2004, women who reached age 65 had an average 20 years of life expectancy (Administration on Aging, 2008). Because the life span continues to increase, women will live one-third of their lives after menopause.

The emphasis on the end of reproduction ignores the myriad issues facing women at midlife. Midlife brings with it many changes, such as children leaving home, illness or death of parents, and career changes. Transitions that accompany midlife include adjusting to the idea of mortality, adapting to changes in family relationships, becoming more authentic, and assessing and appreciating one's life experiences (Sampselle, Harris, Harlow, & Sowers, 2002).

During midlife, women continue to grow and develop psychologically. Increasingly, menopause is being understood as another life stage with potential for growth and development. The challenges experienced during this transition may serve as the basis for personal reflection and growth (Busch, Barth-Olofsson, Rosenhagen, & Collins, 2003).

Many researchers have elucidated women's unique growth and development. For example, Gilligan (1982) found that relationships were a priority for women. Jordan and colleagues (1991) found that women develop in relationship with others, and development means increasing complexity, connection, and mutuality. Collins (1990) recognized the uniqueness of African American women's experience. The major premise in many of the

published works is the importance of recognizing the variation in women's development based on culture, race, and socioeconomic variables.

To that end, Sampselle et al. (2002) conducted focus groups with 32 Caucasian and African American women who were in midlife to identify factors that enhanced their well-being, and to determine whether these factors differed between the two groups. These researchers found that Caucasian participants were concerned about menopause as a sign of aging and the loss of youthful appearance, whereas the African American women were welcoming of menopause as a normal event. All of the women identified childbearing and child launching as major stages in women's lives. The potential for further personal development was enhanced by fewer childcare demands, and women felt few feelings of loss.

Quinn (1991) developed a theoretical model, known as "Integrating a New Me," through a qualitative study with 12 women. Four processes that women experienced were identified:

- Tuning into me: The beginning of the awareness of entering perimenopause
- Facing a paradox of feelings: Both positive and negative feelings about situations such as getting older, reproduction, physical vulnerability, and uncertainty about the future
- Contrasting impressions: The processing of conflicting information, women developing their own symbolic meaning through integrating interactions with others, and their own self-appraisal
- Making adjustments: The changes and alterations that women make in response to their emotional, physical, and life changes in daily living

Arnold (2005) interviewed 23 women about the transition in moving from their 40s to their 50s. The women described these changes as "stepping out of the mold" of society's "rules" about how they should behave, and "letting go" of material things as well as previous expectations they had of themselves. "I feel competent and no longer have to prove my abilities" (p. 12). "Walking in balance" was a theme that women described as "characterizing self as peaceful, accepting, and in line with their interests and needs" (p. 13). They described themselves as "moving in new directions," finding a new zest for life and interests for creative self-expression. At this stage of their lives, they were "redefining relationships" with family and particularly female friends. Finally they expressed a freedom "to be" strong resourceful women.

Building on Sheehy's (1976, 1995) work, Wilmoth (1996) proposed a conceptual framework that includes disassembling, evaluating, and reassembling, as a means to find one's own truth. Disassembling entails taking apart our psychological lives and examining them from a new perspective. This phase includes a natural mourning process for lost youth, loss of procreative abilities, and lost opportunities, and is similar to Quinn's first process. The evaluation process that accompanies disassembling requires that women look into themselves to see who they are and whether they like themselves. Wilmoth argues that the context of each woman's experience depends on her lived experience and life situation—hence the variation in women's experiences. Reassembling incorporates a coming of age and a movement toward mastery.

Ballard, Kuh, and Wadsworth (2001) described the menopause transition as a status passage based on a longitudinal study, which includes five stages: (1) expectations of symptoms, (2) experience of symptoms and loss of control, (3) confirmation of the menopause, (4) regaining control, and (5) freedom from menstruation.

All of the aforementioned models include three major phases: assessment, adjusting to change, and acceptance. It is noteworthy that many researchers have found that menopause itself—that is, the cessation of menstruation—is just one event in the overall context of women's lives during midlife.

The Medicalization of Menopause: A Historical Perspective

Menopause is a remarkable example of the medicalization of women's bodies. The biomedical model of the twentieth century perpetuated menopause as a deficiency disease (MacPherson, 1981) or endocrinopathy (Utian, 1987). Science attempted to establish hormone therapy (HT; **Table 13-1**) as the panacea for prevention of diseases in old age, and pharmaceutical corporations aggressively marketed their products as representing "the fountain of youth."

In 1938, researchers in England produced the first synthetic estrogen, diethylstilbestrol, which was heralded as the cure for postmenopausal symptoms. Premarin, a medication

TABLE 13-1 Recommended Hormone Therapy Terminology*

Term	Abbreviation/Explanation
Estrogen therapy alone	ET
Estrogen/progestogen therapy	EPT
Continuous-combined daily estrogen/progestogen therapy	HT; encompassing term for ET/EPT
Hormone therapy	CC-EPT
Continuous-sequential estrogen/progestogen therapy (estrogen daily, progestogen added on a set sequence)	CS-EPT
Preparations of ET or EPT that have a systemic—not solely vaginal—effect	Systemic ET/EPT
Preparations of ET that have a predominantly vaginal—not systemic—effect	Local ET
Progestogen	Encompassing term for progesterone and progestin

*The North American Menopause Society (NAMS) has urged clinicians, researchers, and the media to standardize terminology, which it considers essential for ensuring accurate communication. Note that the word "replacement" has been deleted from the terms "hormone replacement therapy" and "estrogen replacement therapy."

Source: Adapted from NAMS, 2003.

introduced by Wyeth-Ayerst in 1942, was the first nonsynthetic estrogen produced from the urine of pregnant mares. Although this therapy was prescribed for many women, the use of HT did not increase significantly until the 1960s, particularly after the publication of *Feminine Forever* by gynecologist Robert Wilson (1966). The major message in this highly popular book—100,000 copies of which were sold in the first seven months after its publication—was that after menopause women would become eunuchs with withered breasts and begin a "living decay" (Wilson, p. 43). Estrogen use, which was then referred to as hormone replacement therapy (HRT), promised women the fountain of youth and was praised by Wilson as "one of the greatest biological revolutions in the history of civilization" (Wilson, p. 16). Interestingly, Wilson's work was funded by the pharmaceutical manufacturers Ayerst, Searle, and Upjohn.

Between the years 1967 and 1975, sales of Premarin (conjugated equine estrogens [CEE]) tripled. By the time its association with endometrial cancer became known, Premarin was the fifth most popular drug in the United States. In 1975, researchers began to link estrogen use with an increased incidence of endometrial cancer, and the sales of Premarin dropped dramatically. By 1979, the National Institute on Aging convened a consensus conference and agreed that "women using estrogens should take them only for the shortest possible time, in the lowest possible dose," because HRT increases the risk for endometrial cancer (U.S. Department of Health, Education, and Welfare, 1979, p. 1). Additionally, the committee concluded that HT was effective only for hot flashes and vaginal dryness (National Women's Health Network, 2000). It is noteworthy that this is the same recommendation put forward by the North American Menopause Society (NAMS) in 2003.

During the 1980s, epidemiological data demonstrated that the addition of a progestogen to estrogen therapy (ET) lowered the risk of endometrial cancer. Once again, HT increased in popularity. When researchers demonstrated that HT could decrease the risk of osteoporosis in the early 1980s (Weiss, Ure, Ballard, William, & Daling, 1980), the promotion of HT changed from an emphasis on symptom relief to prevention of disease in old age. By the late 1980s, several observational studies had shown that HT was protective against heart disease. Indeed, until the release of the findings of the Women's Health Initiative (WHI) in 2002, clinicians continued recommending HT to nearly all postmenopausal women for long-term prevention of heart disease. The U.S. Preventive Services Task Force (USPSTF) made the recommendation in the 1990s that all women should be counseled about and consider preventive HT (USPSTF, 1996). The USPSTF did not, however, offer a recommendation about whether women should actually take HT. Studies linking estrogen use and breast cancer were glossed over, and women were told that the risk of heart disease outweighed the risk of breast cancer. Studies were published linking the use of HT and reduced risk of Alzheimer's disease, memory loss, skin integrity, and colon cancer.

The WHI is the largest clinical trial ever to be conducted on health risks of postmenopausal women. As part of this study, nearly 17,000 women were randomized into HT or placebo groups between 1993 and 1998. The estrogen with progestogen arm of the study was halted in 2002, after a mean of 5.2 years of follow-up, because the health risks outweighed the benefits. These deleterious outcomes included increased risk of breast cancer, coronary events,

stroke, and pulmonary embolism (Rossouw et al., 2002). In March 2004, the estrogen arm of the study was also stopped because researchers found an increased risk of stroke. The study group reported that estrogen did not appear to increase or decrease heart disease or breast cancer (Anderson et al., 2004; National Institutes of Health [NIH], 2004). Results from the WHI established that ET prevents osteoporosis-related hip fractures and protects the spine and small bones against the development of osteoporosis. While CEE preparations are still indicated for the prevention of postmenopausal osteoporosis, most experts recommend the use of nonestrogen medications for this purpose (Liu, 2004).

Some experts have pointed out the limitations of the WHI results, such as the age of participants. The mean age of women participating in the study was 63 years, which is significantly older than newly menopausal women. The study also used only one HT product, Prempro, which contains CEE and medroxyprogesterone acetate (MPA). Although findings from the WHI may apply to all HT products, additional clinical trials are needed to clarify the risks and benefits of other products. Finally, the WHI did not address quality of life issues for women with moderate to severe vasomotor symptoms related to menopause. In fact, these women were excluded from the study. For these reasons, it remains difficult to evaluate differences in HT response between women who initiate HT before the cessation of menses and those who begin later (Wysocki, Alexander, Schnare, Moore, & Freeman, 2003).

Women's use of postmenopausal HT declined shortly after the results of the WHI were published; some resources reported that only 16% of women reinitiated HT, with women with diabetes, hyperlipidemia, or cardiovascular disease and those who were taking ET alone being more likely to restart HT (Newton et al., 2008). A meta-analysis of 30 clinical trials (26,708 women) and data from the Nurses' Health Study (121,700 women) demonstrated that the timing of initiating HT is an important factor, at least in terms of preventing heart disease. Women who started HT nearer to the menopause obtained a greater benefit from this therapy (Grodstein, Manson, & Stampfer, 2006; Salpeter, Wash, Greyber, Ormiston, & Salpeter, 2004).

NAMS released position statements on the use of HT in menopausal women in 2004, 2007, and 2008, based on all of the studies subsequent to the WHI. The 2008 paper has specific recommendations:

- HT is not indicated for the sole purpose of preventing cardiovascular disease. Beginning HT in women age 50 to 59 years or within 10 years of menopause to treat menopausal symptoms should not increase CHD risk. A growing body of evidence suggests that beginning HT at that time may decrease this risk.
- ET taken for fewer than 5 years seems to have little effect on the risk for breast cancer.
- HT is not recommended for prevention of cognitive aging or dementia.
- Although there have been no randomized clinical trials (RCTs) involving the lowest effective doses of ET and EPT, using the lowest dose that results in effectiveness should be the therapeutic goal for individual women.
- Duration of use must be individualized and based on the woman's profile and risk–benefit ratio.

- All women with an intact uterus should receive systemic progestogen with estrogen to decrease the risk of endometrial carcinoma (NAMS, 2008).

The evolution of the use of HT for the prevention of disease has been challenged based on RCTs, and epidemiological and observational data. The opening page of the NAMS's 2008 publication *Menopause Practice: A Clinician's Guide*, third edition, begins with these words: "Menopause is a normal, natural event …" (p. 9). This shift from the 1980s view of menopause as pathologic, along with the increase in research on women's experiences of menopause, indicates a paradigm shift is occurring, which is effectively dismantling the concept of menopause as a disease. Nurse researchers, in particular, have demonstrated that menopause is a normal developmental stage in women's lives. Some women will need HT to increase their quality of life, but practice is no longer standard treatment for all women during midlife.

Natural Menopause

Menopause is defined as the point in time in which there has been a cessation of menstruation for at least 12 consecutive months. Menopause occurs in response to normal physiologic changes in the hypothalamic–pituitary–ovarian axis (see Chapter 5 for a detailed description of the menstrual cycle). During the perimenopausal period, which spans approximately 2 to 8 years prior to the last menstrual period, and for the 12 months of amenorrhea preceding menopause, fewer ovarian follicles develop in each menstrual cycle. The follicles that do develop are less responsive to follicle-stimulating hormone (FSH), and the ovaries produce less estradiol, progesterone, and androgens. Thus the usual negative feedback effect from elevated estrogen and progesterone levels on hypothalamic production of gonadotropin-releasing hormone (GnRH) is lost, and the anterior pituitary production of FSH and leuteinizing hormone (LH) continues. Irregular menstrual cycles—characterized by longer or shorter cycles, heavier or lighter flow, periods of amenorrhea, and worsening or newly developing premenstrual symptoms—are common during this time. Eventually, ovarian follicle production stops, estrogen and progesterone levels remain low, FSH and LH levels remain high, and menstruation ceases. The postmenopausal period refers to the first 5 years or so following menopause when hormonal fluctuations often continue to occur (NAMS, 2007; Soules et al., 2001; Utian, 1999a, 1999b, 2001).

A woman is born with approximately 1.2 million ovarian follicles. Throughout her life, some of these follicles are used during ovulation, but most are lost through atresia until menopause when about 1000 follicles remain.

Although it sounds like a smooth process, the perimenopausal transition is anything but smooth for most women. Hormone levels can fluctuate wildly from day to day, causing many of the symptoms associated with the perimenopause and menopause transition (**Table 13-2**). Hormone fluctuation is related to many factors including the reduced number of responsive ovarian follicles.

Contrary to popular belief, women continue to produce estrogen and androgens after menopause. Three types of estrogen of exist. Estradiol (E_2), which is the most potent of

TABLE 13-2 Symptoms Associated with Perimenopause and Menopause

Acne	Hot flashes/flushes	Headache
Arthralgia	Irregular menses/bleeding	Poor concentration
Asthenia	Irritability/mood disturbances	Recurrent cystitis
Decreased libido	Mastalgia	Recurrent vaginitis
Decreased vaginal lubrication	Myalgia	Skin dryness/atrophy
Depression	Nervousness/anxiety	Sleep disturbances/insomnia
Dizziness	Night sweats	Stress urinary incontinence*
Dry eyes	Nocturia	Urinary frequency
Dry/thinning hair	Odor	Urinary urgency
Dyspareunia	Palpitations	Vaginal atrophy
Dysuria	Paresthesia	Vaginal/vulvar burning
Fatigue	Forgetfulness	Vaginal/vulvar irritation
Hirsutism/virilization	Formication	Vaginal/vulvar pruritis

*Data are inconclusive.

Sources: Alexander et al., 2003; Avis et al., 2001; Greendale, Lee, & Arriola, 1999; Jacobs Institute on Women's Health, 2003; McKinlay, 1996.

the three, is the main estrogen produced during the reproductive years; it is present in low amounts in the postmenopausal years following peripheral conversion of androstenedione. Estriol (E_3) is secreted by the placenta and synthesized from androgens produced by the fetus during pregnancy, and is present in nonpregnant women in small amounts as a by-product of estradiol and estrone. Estrone (E_1), the weakest estrogen, is the primary estrogen present in postmenopausal women, children, and men. In the postmenopausal period, estrone is produced by adipose conversion of androstenedione secreted by the adrenals (95%) and, to a lesser extent, the ovaries (5%), as well as by metabolism of estradiol.

Although the ovaries no longer produce functional follicles after menopause, the corticostromal and hilar cells of the stromal tissue are steroidogenic and produce significant levels of both androstenedione and testosterone for many years. Circulating levels of androstenedione in postmenopausal women are approximately half those of premenopausal women. Conversely, circulating levels of testosterone remain relatively constant in women who are either premenopausal or postmenopausal, partly due to the presence of high FSH and LH levels, which stimulate the ovarian stromal tissues to increase their testosterone production.

Natural menopause occurs for most women between the ages of 48 and 55 years. Fifty-one is the average age for women in the Western world (Soules et al., 2001; Utian, 1999b). The age at menopause is difficult to predict for an individual woman, but does correlate with the age when her mother or older sisters had menopause (Cramer, Xu, & Harlow, 1995; de

Bruin et al., 2001). A number of factors that may affect the age at menopause have been studied, such as parity, age at menarche, obesity, height, and oral contraceptive use (Bromberger et al., 1997; Cooper, Sandler, & Bohlig, 1999; Dvornyk et al., 2006; Gold et al., 2001; Santoro et al., 2007; Santoro et al., 2004; van Noord, Dubas, Dorland, Boersma, & te Velde, 1997). In contrast, studies of gene mutations and models to predict age for menopause have had limited success (Hefler et al., 2006; Huber et al., 2006). Smoking has consistently been found to have a relationship with age at menopause, and is associated with menopause occurring 1½ years earlier among smokers versus nonsmokers (Bromberger et al., 1997; Cooper et al.; Gold et al.; van Noord, Dubas, Dorland, Boersma, & te Velde). Menstrual cycle changes, including length of cycle, amount of bleeding, and 2- and 3-month periods of amenorrhea are associated with a shorter time to menopause (Garcia et al., 2005; Harlow et al., 2006). Cycle lengths less than 21 days have been associated with the early stages of the menopause transition (Van Voorhis, Santoro, Harlow, Crawford, & Randolph, 2008). A combination of symptoms—including irregular cycles, changed hormone levels, age, and smoking—was identified to be predictive in the Study of Women's Health Across the Nation (SWAN) (Santoro et al., 2007).

Ethnicity also may have an effect on age at menopause. A few studies have found that African American women experience menopause slightly earlier than other women, with an average age at menopause of 49.6 years and a median age of 49.3 or 50 years (Bromberger et al., 1997; Palmer, Rosenberg, Wise, Horton, & Adams-Campbell, 2003). However, no significant difference in age at menopause was identified in black versus white women (average age = 51.4 years for both groups) in the SWAN study (Gold et al., 2001). Interestingly, the SWAN study did identify statistically significant differences in average age at menopause among Hispanics (51.0 years) and Japanese Americans (51.8 years), as compared with Caucasians (51.4 years). Body size could also be a factor (Santoro et al., 2004), because women with higher body weights often have more adipose tissue, which stores androstenedione and converts it to estrogen (Speroff, Glass, & Kase, 1999).

A serum blood test for anti-Müllerian hormone (AMH) may be the preferred predictor in the future. Research has identified that AMH, which reflects the number of follicles, may be helpful in identifying when women older than the age of 30 can expect to be postmenopausal (van Disseldorp et al., 2008). More research is needed to determine exactly how this measure, which is currently used for infertility evaluations, might be applied for predicting menopause.

Menopause from Other Causes

Menopause can also occur due to several other causes (NAMS, 2007; Utian, 1999a). Induced menopause occurs following either surgical excision of both ovaries (bilateral oophorectomy) or ovarian function ablation caused by medication, chemotherapy, or radiation. Although menstruation and fertility cease immediately following surgical menopause, both may persist for several months after ablative treatments are given. Premature menopause is menopause that occurs before the age of 40. It often follows the pattern of natural menopause, and results in the permanent loss of menstruation and fertility. Idiopathic ovarian insufficiency or prema-

ture ovarian failure (POF) also occurs in women younger than 40 years old; however, unlike premature menopause, POF is not always permanent and is often associated with other health problems, such as autoimmune and genetic disorders. Temporary menopause can occur at any age when normal ovarian function is lost and then resumes. This condition can be idiopathic, related to a disease entity, or induced by medications.

Women who experience induced or premature menopause have early loss of fertility and often experience more severe symptoms. They are at greater risk for developing cardiovascular disease (CVD) and osteoporosis (Gallagher, 2007; Lobo, 2007), and may also face significant health problems related to underlying disease processes.

Diagnosing Menopause

Menopause is actually a retrospective diagnosis because it is based on the clinical absence of menses for 12 consecutive months. Serial FSH testing that revealed levels sustained at less than 40 mIU/mL was used in the past to determine menopause status. However, because FSH levels can return to normal and estrogen levels can unexpectedly rise high enough to trigger the LH surge needed for ovulation, serum FSH testing is no longer recommended for determining perimenopausal or menopausal status (Bastian, Smith, & Nanda, 2003; NAMS, 2007, 2008). Similarly, perimenopause is most accurately identified based on a variety of factors, including age and symptoms such as hot flashes, irregular menses, and vaginal dryness. Due to the potential for unexpected ovulation, women who are perimenopausal need to continue to use a reliable form of birth control (see Chapter 12 for information about contraception). Perimenopausal women experience a high rate of unintended pregnancies with as many as 40% to 50% of pregnancies in these women reported as unintended (Finer & Henshaw, 2006; Sherman, Harvey, & Noell, 2005).

Differential Diagnoses

Other health problems can mimic the symptoms of menopause and must also be considered when a woman presents with perimenopausal and menopausal symptoms (NAMS, 2007). These diagnoses may include diabetes, hypertension, arrhythmias, thyroid disorders (hypothyroid or hyperthyroid), anemia, depression, tumors, or carcinoma. A sample list of differential diagnoses is provided in **Table 13-3**. Medications, alcohol, or drug use can also cause many symptoms similar to perimenopause and menopause.

Each woman presenting with menopausal symptoms must be carefully evaluated with a thorough history, a physical examination, and selective laboratory testing (such as a complete blood count, fasting glucose, and serum thyroid-stimulating hormone level) to accurately identify the cause of her symptoms. Often a woman has several diagnoses to contend with at once, such as hypertension, diabetes, and menopause. Controlling her diabetes and hypertension may also reduce her menopausal symptoms enough so that they no longer are bothersome for her.

TABLE 13-3 Sample of Differential Diagnoses That Have Symptoms Similar to Perimenopause and Menopause

Diagnosis	Symptoms Similar to Perimenopause/Menopause
Anemia	Fatigue Cognitive changes
Anovulation	Amenorrhea
Pregnancy	Irregular bleeding
Arrhythmias	Fatigue Palpitations
Arthritis	Joint aches/pain
Depression	Fatigue Moodiness Anxiety Sleep disturbances, insomnia
Diabetes	Fatigue Hot flashes/heat intolerance
Hypertension	Headaches
Hyperthyroidism	Sleep disturbance, insomnia Nervousness, irritability Heat intolerance
Hypothyroidism	Fatigue Dry skin Cognitive problems
Infections (viral illnesses, HIV, influenza, fever, tuberculosis, sexually transmitted infections)	Vasomotor symptoms Dyspareunia Cystitis symptoms Vaginitis
Pregnancy	Menstrual changes
Spontaneous abortion	Menorrhagia
Uterine fibroids	
Uterine polyps	
Endometriosis	
Adenomyosis	
Ovarian cysts	

TABLE 13-3 Sample of Differential Diagnoses That Have Symptoms Similar to Perimenopause and Menopause *(Continued)*

Ovarian tumors	
Vulvar dystrophy	Vaginal atrophy Dyspareunia

Presentation and Variation of the Menopause Experience

The experience of menopause is unique and personal. Some women have severe symptoms that disrupt all aspects of their lives, whereas others find menopause to be almost a "non-event" and report no bothersome symptoms. Most symptoms that do occur are related to reduced levels of estrogen and progesterone. Two types of estrogen receptors have been identified (alpha and beta), which are located in the cognitive and vasomotor centers of the brain, eyes, skin, heart, vascular system, gastrointestinal tract, breast tissue, urogenital tract, and bone. Progesterone receptors have been identified in the hypothalamus, pituitary, and vasomotor areas of the brain, as well as in the heart, vascular tissues, lung, breast, pancreas, reproductive organs, and bones. As hormone levels rise and fall, symptoms may develop. An individual woman's symptom experience may be related to her body size as adipose tissues store and convert androstenedione to estrogen (Speroff et al., 1999). Additionally, women with greater abdominal adiposity are more likely to experience hot flashes than their slimmer counterparts (Thurston et al., 2008).

Both the type (Table 13-2) and severity of menopausal symptoms can vary. Symptoms usually begin in the perimenopausal period and may gradually increase in severity. Postmenopausal women typically experience more symptoms with greater severity than do perimenopausal women (Avis et al., 2001). The symptoms women report most frequently are vasomotor in nature, including hot flashes, or hot flushes, and sweats. Hot flashes are most frequent in the first five to seven years following menopause but can last for many more years in some women (Kronenberg, 1990).

Hot flashes are experienced as an intense heat sensation and may or may not be followed by sweating, which can be profuse. They are characterized by a measurable increase in skin temperature and conductance that is followed by a decrease in core body temperature. Hot flushes are similar to hot flashes but include a flushing over the face and upper chest, most likely due to peripheral vascular dilatation. Vasomotor symptoms that occur during the night are termed night sweats. Hot flashes occur concurrently with a surge in LH levels. Although the relationship between LH secretion and body temperature change is not well understood, the same mechanisms that trigger the hypothalamic event that causes the temperature increase also stimulates GnRH secretion and causes LH elevation. Some women experience a prodrome prior to a hot flash. Many women feel cold following a hot flash owing to the reduction in core temperature; this effect is exacerbated if sweating is also present. Postmenopausal women are more sensitive to core temperature changes because their

thermoneutral zone—the range of internally recognized normal core body temperature—narrows (Freedman & Blacker, 2002). Thus, when core temperature rises, they feel overly hot; conversely, when it falls, they feel overly chilled.

Sleep disruptions are also common among menopausal women. Some of these sleep changes are related to normal aging, such as reduced time in sleep stages three (early deep sleep) and four (deep sleep and relaxation), more periods of brief arousal, and an overall decreased need for sleep—an average of five to seven hours for adults (Blackman, 2000). Hot flashes and sweats can further interrupt sleep (Baker, Simpson, & Dawson, 1997; Kronenberg, 1990; NAMS, 2007). Sleep loss, in turn, causes daytime fatigue and has been associated with irritability; emotional lability; stress; depression; headache; poor functioning at home, work, or school; and difficulty concentrating, reasoning, and remembering (NIH, 2007).

Urogenital changes leading to atrophy affect all women and may cause vaginal dryness and dyspareunia, and can predispose women to urinary incontinence. The risk of urinary incontinence increases with age, but this condition is never considered normal. Lower estrogen levels are associated with urethral atrophy, which can increase the likelihood of developing incontinence further.

Many normal changes of aging can also affect sexual function in women, such as longer time to achieve vaginal lubrication and production of fewer vaginal secretions overall; reduced vaginal elasticity, pigment, rugation, and number of superficial epithelial cells, leading to increased petechiae and bleeding following minor trauma (including sexual activity); reduced lactobacilli populations, which increase pH and the risk of infection; and atrophy of adipose and collagen tissue in the vulva. Women may also experience lowered libido, lessened sexual activity, problems with their partner's sexual performance, or relationship problems that make them less interested in sex (Dennerstein, Dudley, & Burger, 2001). Whatever the causes of dyspareunia or sexual dysfunction may be, this subject is often difficult for women to broach with their clinicians. It is important for clinicians to ask women about sexual function and satisfaction, and remain open to the fact that sexual expression can take many forms (see Chapters 11 and 17).

Cultural or racial background may have an effect on menopausal symptoms. The SWAN study indicated that while Caucasian and Hispanic women reported the greatest number of psychosomatic symptoms, such as moodiness, headaches, and palpitations (Avis et al., 2001), the severity of vasomotor symptoms (hot flashes, sweats) was highest among African American women, followed by Hispanic, Caucasian, Chinese, and Japanese women (Gold et al., 2000). Vaginal dryness was more common among African American and Hispanic women, and Hispanic women were more likely to report urine leakage, forgetfulness, and heart pounding or racing than Caucasian women. Caucasian women were more likely to experience difficulty sleeping than women of other races (Gold et al.). In the WHI study, Hispanic women were more likely to have experienced urogenital symptoms such as dryness, irritation, discharge, and itching (Pastore, Carter, Hulka, & Wells, 2004). Additionally, some symptoms may be more bothersome for certain women. For example, African American women have described a high degree of discomfort attributable to vaginal and body odor, sleep changes and night sweats, weight gain, moodiness, "rage," and irritability (Alexander

et al., 2003). Asian women have reported more severe problems with joint pain and stiffness, especially in the neck, shoulders, and back (Gold et al.).

A woman's expectations for menopause may also affect her experience. Expectations can range from no expectations, to positive or negative expectations, to uncertainty (Woods & Mitchell, 2008). Similarly, a woman's response to menopause can affect her experience. Many women view menopause as a natural life transition and may not be interested in any treatment options besides lifestyle changes. Others see it as a disruption of their lives and a sign of aging that they want to minimize as much as possible. Many women identify menopause as a time for reflection and reevaluation of their lives and health (Alexander et al., 2003; Woods & Mitchell).

Midlife Health Issues

Health risks change for women at midlife, partly due to the changed hormonal milieu and partly due to other normal aging processes. In particular, women are at greater risk for developing heart disease, osteoporosis, and diabetes. Weight management is also a significant issue. See Chapter 8 for a full discussion of routine health screening for midlife women.

Overweight and Obesity

As women age, weight management often becomes a struggle. Although women tend to associate increased weight with menopause, it is not related specifically to hormonal changes but rather is a natural part of aging. Women gain an average of five pounds at midlife (NAMS, 2007). This increase is partly due to the normal slowing in metabolism that occurs with age, and partly due to a decrease in activity that often accompanies midlife. Maintaining one's weight through midlife usually requires both a reduction in caloric intake and an increase in activity.

Not only does weight increase at midlife, but the distribution of body fat also changes. Adipose tissue tends to accumulate at the hips and thighs in younger women (the "pear" shaped body). As women age, adipose tissue is redistributed and begins to accumulate at the waist (the "apple" shaped body). Abdominal adiposity and weight gain at midlife are significant issues. This concern relates not only to the potentially negative body-image concerns for women, but also to the fact that both obesity—defined as a body mass index (BMI) greater than 30 kg/ m^2 and a waist circumference larger than 35 in.—are individually associated with a greater risk for developing insulin resistance that can lead to CVD and diabetes (American Diabetes Association [ADA], 2004a). In addition, obesity is associated with osteoarthritis, cholecystic disease, and urinary incontinence, as well as with cancers such as breast, endometrial, and colorectal (American Obesity Association, 2002; Centers for Disease Control and Prevention, 2003). Furthermore, having a BMI greater than 27 kg/m^2 was associated with a greater frequency of hot flashes, night sweats, and soreness or stiffness in the back, shoulders, and neck in the SWAN study (Gold et al., 2000).

Cardiovascular Disease

The number one cause of mortality for both women and men in the United States is CVD. Approximately 500,000 women die from CVD each year in the United States. This number is higher than that from the next seven causes of mortality in women combined and exceeds the CVD mortality rate in men (American Heart Association [AHA], 2002, 2004). Notably, heart disease disproportionately affects women of color. After the age of 50 years, more than 50% of all deaths among women are attributed to some type of CVD. CVD includes hypertension, valvular heart disease, coronary artery disease, or coronary heart disease (leading to angina or myocardial infarction), stroke, arrhythmias, congestive heart failure, and congenital heart defects.

Women are at a significantly increased risk for developing heart disease following menopause (AHA, 2004; NAMS, 2007, 2008). Some of this increased risk is due to changes in cholesterol levels that are found in postmenopausal women. Low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL) levels increase, and LDL oxidation is enhanced. Additionally, high-density lipoprotein (HDL) levels may decrease somewhat. However, the HDL changes are far less significant than the LDL changes. Other changes, such as the reduced elasticity in the vascular system and associated hypertension, may be related to decreased levels of estrogen and progestin. Moreover, production of some precoagulation factors (e.g., fibrinogen, factor VII) and some fibrinolytic factors (e.g., plasminogen, antithrombin III) increase, and may interact with hormonal and vascular changes to further increase risk. General risk factors for CVD include cigarette smoking, a sedentary lifestyle, stress, obesity, preexisting hypertension, abnormal serum lipids, and diabetes mellitus. Women who experience premature menopause may have an even greater risk, especially if they smoke (Lobo, 2007; NAMS, 2007).

Diabetes Mellitus

The likelihood of developing type 2 diabetes mellitus increases with age and disproportionately affects women of minority racial and ethnic groups, such as Native Americans, Hispanics or Latinas, African Americans, Asian Americans, and Pacific Islanders. General risk factors for developing diabetes include being overweight or obese (BMI greater than 25), having abdominal adiposity (waist circumference over 35 inches in women), a sedentary lifestyle, insulin resistance, a history of gestational diabetes or polycystic ovary syndrome, and a family history of diabetes. Hypertension and dyslipidemia also predispose an individual to developing diabetes. Individuals with impaired fasting glucose levels (100–125 mg/dL) or impaired glucose tolerance (2-hour post 75-gm glucose load of 140–199 mg/dL) are identified as having pre-diabetes, and 30% to 40% of them will develop type 2 diabetes within five years (ADA, 2004b; Mayer-Davis, D'Antonio, & Tudor-Locke, 2003). In addition to significantly increasing the risk for CVD and cerebrovascular disease, diabetes increases the risk for developing infections, foot ulcers, peripheral vascular disease, peripheral neuropathy, nephropathy, and retinopathy (ADA, 2004a; Franz, 2003). The American Association of

Clinical Endocrinologists (AACE, 2008) recommends aggressive treatment for both women and men with pre-diabetes (elevated fasting blood sugars in the 100–125 mg/dL range).

Managing diabetes is more difficult for women during perimenopause due to fluctuations in hormone concentrations. Insulin resistance increases with reduced levels of estrogen, causing higher serum glucose levels. Progesterone changes have a converse effect on glucose, causing lower levels due to the increase in insulin sensitivity that accompanies falling progesterone concentrations. After menopause, glucose levels tend to be lower because insulin sensitivity increases and insulin use becomes more efficient as estrogen and progesterone concentrations stabilize (Gaspar, Gotta, & van den Brule, 1995; Godsland, 1996; Porth & Kunert, 2002). At the same, other midlife changes, such as weight gain and slowed metabolism, affect glucose levels; thus numerous adjustments in medications and regimens are often necessary to maintain adequate glucose control.

Cancer

In 2004, the leading cause of mortality from cancer among women in the United States was lung and bronchus cancer (25%), followed by breast (15%), and colon (10%) cancers (American Cancer Society [ACS], 2004). These same three types of cancer were expected to be the most often diagnosed forms among women in 2008 (National Cancer Institute [NCI], 2008). Mortality from cancer has decreased overall among women, with the exception of lung cancer, for which mortality is leveling off.

The risk for developing cancer increases as women age. A woman's risk for developing breast cancer is approximately 1 out of 30 at the age of 50, then increases gradually to approximately 1 out of 9 for a woman who lives into her 80s. The lifetime risk for a woman to develop breast cancer is about 1 in 7 (ACS, 2004; NCI, 2003, 2008). Chapter 8 provides cancer screening recommendations, and Chapter 16 offers further information on breast cancer.

Osteoporosis

Osteoporosis is a disorder of the skeletal system characterized by reduced bone strength that increases the risk for fracture (Hodgson & Watts, 2003). Bone strength incorporates factors of both bone density and bone quality. Bone density is the volume of bone, whereas bone quality refers to the rate of turnover, bone architecture, mineralization, and accumulated damage.

There are two types of osteoporosis: primary and secondary (Dawson-Hughes, Lindsay, et al., 2008). Secondary osteoporosis occurs in response to medication (e.g., corticosteroids, anticonvulsants, or methotrexate) or other disease processes (e.g., hyperthyroidism, chronic liver disease, or gastrointestinal diseases, such as malabsorption) that interfere with the normal process of bone formation and can affect women or men at any age. Primary osteoporosis is associated with aging and affects women much more significantly than men. Adults achieve peak bone mass in their late 20s to mid-30s, after which time the rates of bone resorption and formation become relatively stable. However, as women age, their bone

resorption rate slowly begins to exceed that of bone formation, resulting in a slow decline of bone mass. Because of the loss of estrogen, the rate of bone loss in the first year after menopause is especially rapid, between 1% and 5%, but then slows to approximately 1% per year. In contrast, bone mass is lost in men at a rate of 0.2% to 0.5% per year. **Table 13-4** lists risk factors for osteoporosis. Screening recommendations can be found in Chapter 8.

The gold standard for diagnosing osteopenia or osteoporosis is bone mineral density (BMD) measurement by dual-energy x-ray absorptiometry (DEXA or DXA)—a technique that is used to evaluate central BMD at the spine and hip. Although DXA can also be used to evaluate the wrist BMD, central testing is much more predictive of overall BMD and fracture risk. Quantitative computed tomography (CT) scan can be used to perform spine measurements and is particularly useful for testing individuals with arthritis, as it is less likely to reflect osteocytes. BMD results are reported as *T*-scores and *Z*-scores. The *T*-score identifies the number of standard deviations the patient's BMD is above or below that for a young adult and a gender-matched norm. Osteopenia is present when the *T*-score is –1.0 to –2.5. Osteoporosis is present when the *T*-score is –2.5 or less. Severe or established osteoporosis is present when the *T*-score is –2.5 or less and fragility fractures are present. The *Z*-score provides a

TABLE 13-4 Risk Factors for Osteoporosis

Potentially Modifiable Risk Factors	Nonmodifiable Risk Factors
Body weight < 127 pounds	Advanced age
BMI < 22–24	Female gender
Amenorrhea (due to eating disorder or excessive exercise)	Race (Caucasian and Asian women at greatest risk, followed by Hispanic and African American women)
Nulliparity	Personal history of fracture during adulthood
Low estrogen levels (e.g., menopause)	Family history of osteoporosis
Lifestyle factors (e.g., cigarette smoking, excessive alcohol or caffeine intake, sedentary activity level, or inadequate calcium/vitamin D intake)	First-degree relative with a history of fracture
Medications (e.g., thyroid hormone, corticosteroids, anticonvulsants, aluminum-containing antacids, lithium, methotrexate, gonadotropin-releasing hormone, cholesteramine, heparin, warfarin)	
Chronic diseases (e.g., endocrine disorders, gastrointestinal disorders, connective tissue diseases, bone disorders, chronic liver disease, cystic fibrosis, seizure disorders, hematologic malignancies, prolonged immobility, eating disorders, chronic renal failure, or frailty)	

Sources: Dawson-Hughes, Lindsay, et al., 2008; Hodgson & Watts, 2003.

comparison in BMD for the patient to an age-matched mean and is used for diagnosis only in children (Dawson-Hughes, Lindsay, et al., 2008).

Women with osteoporosis are at increased risk for fracture. Interestingly, fracture rates are even higher among women with osteopenia (Dawson-Hughes, Lindsay, et al., 2008). Although osteoporosis and osteopenia by themselves are painless and not functionally problematic, the risk for fractures puts a patient at significant risk. Following a hip fracture, there is a 10% to 20% increase in mortality. Among survivors, 30% to 40% sustain some degree of permanent disability and 24% to 50% never return to independent living (Dawson-Hughes, Tosteson, et al., 2008; Hodgson & Watts, 2003).

Prevention is a key factor in osteoporosis management. For perimenopausal and postmenopausal women, prevention strategies focus on the following considerations:

1. Adequate intake of calcium
   - 1000 mg/day for premenopausal women and postmenopausal women on HT
   - 1200 mg/day for perimenopausal or premenopausal women older than 50 years
   - 1500 mg/day for postmenopausal women not taking HT and women older than 65 years
2. Adequate intake of vitamin D (400–800 international units/day),
3. Weight bearing and resistance exercise
4. Fall prevention
5. Avoiding tobacco
6. Moderating alcohol intake (Dawson-Hughes, Tosteson, et al., 2008; Hodgson & Watts, 2003; NIH, 1994)

Exercise is site specific and needs to be continued to maintain bone strength, and medication management is recommended for women with *T*-scores of –2.5 or lower, and for those with hip or vertebral fractures (Dawson-Hughes, Lindsay, et al., 2008). For women with *T*-scores in the osteopenic range (–1.0 to –2.5), medication is recommended if they also have fractures or are at high risk for fracture (e.g., are immobilized, are taking glucocorticoids, are at high risk for falls).

For other women with *T*-scores in the osteopenic range, use of the World Health Organization's (WHO's) Fracture Risk Assessment Tool (FRAX) is recommended to identify those who would realize a cost-effective benefit from initiating medication therapy (Dawson-Hughes, Tosteson, et al., 2008; Tosteson et al., 2008; WHO, 2007). The FRAX tool is accessible online (http://www.shef.ac.uk/FRAX/) and is applicable for women who have not previously been treated with medications. Information is entered for 11 different risk factors plus the hip raw BMD value (in g/cm^2) to calculate the 10-year probability for a hip fracture and the 10-year probability for any type of major osteoporotic fracture. If the rates for hip fracture probability are greater than 3% or the rate for any major osteoporotic fracture is greater than 20%, medication therapy is recommended (Dawson-Hughes, Lindsay, et al.).

The treatment decision must be weighed against the clinical presentation, with the clinician recognizing the limitations of FRAX. "The FRAX provides an estimated fracture risk in a given individual but does not identify the level of fracture risk at which treatment should be

started ('intervention threshold')." (Lane & Silverman, 2008). Many of the variables entered are dichotomous ("yes/no") and do not capture the increased risk present with a higher level on a continuous variable scale (e.g., use of higher doses of corticosteroid increases risk for fracture). Additionally, the *T*-score used in the FRAX calculations is not the same as that obtained with DXA testing. A conversion program is available on the National Osteoporosis Foundation (NOF) website that can be downloaded to the clinician's computer for use, however. The converted *T*-score should then be entered into the FRAX program.

Repeat BMD testing for osteoporosis is recommended every 2 years after treatment is initiated, to monitor the effects of therapy (Dawson-Hughes, Lindsay, et al., 2008). **Table 13-5** summarizes the available pharmacologic treatment options for osteoporosis in postmenopausal women. Combination therapy, initiated by an osteoporosis specialist, is also possible; usually a bisphosphonate (alendronate or risedronate) is combined with another class (e.g., estrogen or raloxifene).

Thyroid Disease and Depression

Thyroid disease and depression are other health issues that must be considered at midlife. Thyroid disease affects women more than men, and its incidence increases with age (Baskin, 2002). Symptoms of hyperthyroidism or hypothyroidism can mimic perimenopause and menopause symptoms.

The risk of depression also increases during midlife both due to symptoms caused by hormonal fluctuations and midlife stresses such as financial concerns, employment issues, relationship problems, family changes, or health issues of self or family members (NAMS, 2007). Depression rates are approximately three times as high in perimenopausal women as they are in premenopausal women (Cohen, 2004). These problems and other differential diagnoses (Table 13-3) must be considered when a woman presents with menopausal symptoms.

Lifestyle Approaches for Symptom Management

Several lifestyle alterations can be implemented to reduce menopausal symptoms. Some of these interventions also afford additional health benefits such as reducing risk for CVD or osteoporosis. Lifestyle management may encompass dietary changes, exercise, vitamins or supplements, vaginal lubricants and moisturizers, changes in clothing, smoking cessation, stress management techniques, sleep aids, and activities to enhance memory function.

Dietary Changes

Several dietary substances have been linked with more frequent or more severe hot flashes. They include sugar (especially refined), caffeine (including hot and cold beverages and other foods, such as chocolate, that contain caffeine), spicy foods, and alcohol (Alexander et al., 2003; NAMS, 2007). Avoidance or moderate intake of these substances should be recommended.

TABLE 13-5 Pharmacologic Treatment Options for Osteoporosis in Postmenopausal Women*

Medication	FDA Approved for	Considerations
Alendronate (Fosamax)	Prevention—5 mg orally daily or 35 mg orally weekly	Use with caution if the patient has upper gastrointestinal disease, owing to its clinical association with dysphagia, esophagitis, and ulceration
	Treatment—10 mg orally daily or 70 mg orally weekly	Take first thing in the morning on an empty stomach with an 8-oz glass of water, remain upright, and take no other food or drink for at least 30 minutes
Risedronate (Actonel)	Prevention or treatment—5 mg orally daily or 35 mg orally weekly	Take 2 hours before antacids/ calcium
Calcitonin (Miacalcin)	Treatment—200 international units intranasal spray daily or 100 international units IM or SC every other day	Usually administered as nasal spray Has an analgesic effect on osteoporotic fractures
Estrogen (i.e., Premarin, Estratab, Menest, Alora, Climara, Estraderm, Menostar, Vivelle, Vivelle Dot, Estrace, Femhrt,* Activella,† Ortho-prefest,† Prempro,† others)	Prevention—Doses and routes vary‡	Also effective in alleviating most symptoms of menopause Comes in several forms, including pills, patch, ring, and cream
Raloxifene (Evista)	Prevention or treatment—60 mg orally daily	May cause hot flashes Not recommended if the patient is taking ET or EPT
Teriparitide (Forteo)	Treatment—20 mcg subcutaneously daily	Reserved for use after failure of first-line agents

*See prescribing reference for full information on doses, side effects, contraindications, and cautions.
†Also contain progesterone compounds.
‡Lowest effective dose should be used.The FDA recommends considering nonestrogen osteoporotic agents when ET/EPT use is solely for the purpose of osteoporosis prevention.

Source: North American Menopause Society (NAMS). (2009). Government approved postmenopausal osteoporosis drugs in the United States and Canada. Retrieved from http://www.menopause.org/otcharts.pdf

Increased water intake is also recommended because of the augmented insensible loss of fluids through sweating. Water intake, especially cold water, has been reported to help with reducing symptoms such as skin dryness, and it reduces the discomfort associated with hot flashes and sweating (Alexander et al., 2003; NAMS, 2004). The usual water intake of six to eight glasses per day should be recommended. However, for women who experience

urinary incontinence, water consumption may need to be restricted for social occasions when there is no easy access to a bathroom, or limited to the morning for women who experience nocturia.

Exercise

Lower levels of physical activity have been linked with a higher frequency of menopausal symptoms, especially forgetfulness, difficulty sleeping, heart pounding or racing, and stiffness or soreness (Gold et al., 2000). Similarly, higher levels of physical activity have been associated with reduced severity of menopausal symptoms such as vasomotor symptoms, depression, and forgetfulness (Alexander, Ruff, & Udemezue, n.d.; NAMS, 2004). In addition to mediating menopause symptoms, exercise reduces cardiovascular and osteoporosis risks, improves sleep, and assists with maintaining a healthy weight, relieving stress, reducing moodiness, and improving mental function.

Vitamins and Supplements

Several vitamins and supplements may be useful for minimizing menopausal symptoms and improving overall health. For example, calcium (1200–1500 mg/day) and vitamin D (400–800 IU/day) are needed for postmenopausal women to maintain bone strength (NIH, 1994).

Vitamin E in doses up to 800 IU/day has shown to produce either small improvements or no changes in hot flashes in clinical trials (Barton et al., 1998; Blatt, Weisbader, & Kupperman, 1953). A meta-analysis indicated that vitamin E did not provide a reduction in overall mortality, cerebrovascular accident, or cardiovascular death (Vivekananthan, Penn, Sapp, Hsu, & Topol, 2003). In the same meta-analysis, beta-carotene was shown to have a slightly increased risk for all-cause mortality. Vitamin E has, however, been linked with a reduced risk for developing Alzheimer's disease (Klatte, Scharre, Nagaraja, Davis, & Beversdorf, 2003; Onofrj et al., 2002; Thomas, Iacono, Bonanni, D'Andreamatteo, & Onofrj, 2001).

The B vitamins are known to reduce homocysteine levels; high levels are associated with cerebrovascular accident, CVD, Alzheimer's disease, and osteoporotic fracture. For reduction of homocysteine and to partly compensate for the lack of fruits and vegetables usually found in the U.S. diet, daily supplementation with a multivitamin containing the B vitamins (folate, B_6, and B_{12}) is recommended (Fairfield & Fletcher, 2002; Fletcher & Fairfield, 2002; McLean et al., 2004; van Meurs et al., 2004). Formulations that include iron should be avoided unless there is a documented need for iron supplementation, as excess iron can have negative effects on the cardiovascular system or liver over time.

Vaginal Lubricants and Moisturizers

Vaginal lubricants can be used to relieve vaginal dryness and dyspareunia caused by reduced vaginal secretions. Several nonhormonal water-based preparations are available as over-the-counter products (e.g., K-Y Personal Lubricant, Astroglide, Lubrin, Moist Again) and can be used for daily comfort for vaginal dryness and during sexual activity. Longer-acting

vaginal moisturizers (e.g., Replens, K-Y Long-Lasting Vaginal Moisturizer) may be more appropriate for some women. The moisturizers replenish and maintain fluids in the vaginal epithelial cells and provide longer relief. Moisturizers may be particularly beneficial for women who experience daily discomfort and can reduce vaginitis by supporting a normal pH (Nachtigall, 1994).

Women must be cautioned against using any oil-based products, such as petroleum jelly (Vaseline), as these preparations can injure vaginal tissue and are not easily removed. Vitamin E oil, when applied topically to the vaginal walls, is an exception to this caution. It can provide relief for vaginal dryness without interfering with condom or diaphragm function, and it rarely irritates tissues. Other products that contain oils or fragrances should also be discouraged as they often cause vaginitis or irritation. Douching is not effective for moisturizing and will remove normal flora, thereby increasing the risk for infection (NAMS, 2007; Willhite, 2001).

Clothing and Environment

Wearing layered clothes, breathable fabrics such as cotton or linen, or moisture-wicking fabrics, such as those worn by runners, is recommended to reduce discomfort with hot flashes and sweats (Alexander et al., 2004; NAMS, 2007). Avoiding turtlenecks, fabrics that do not allow circulation or absorb sweat (e.g., polyester and silk), and extra layers (e.g., slips and full-length stockings) is also recommended. Keeping the room temperature cool, having an open window or using a fan to circulate air, and ingesting cold foods or beverages can reduce core body temperature and are also helpful in reducing the symptoms of menopause (NAMS, 2004, 2007).

Smoking Cessation

Smoking is associated with increased morbidity and mortality, especially related to CVD and cancers; earlier age at menopause; increased rate of bone loss; and increased prevalence of all menopausal symptoms except vaginal dryness (Gold et al., 2000, 2001; NAMS, 2007). Various smoking cessation programs are available, but the most successful program is ultimately the one that is of interest to a specific woman. She needs to be both interested in quitting and motivated to quit. Support from a clinician and use of medications or patches can significantly improve cessation rates (ACS, 2007).

Stress Management

Stress has been reported to increase menopause symptoms (Alexander et al., 2003). Additionally, stress is associated with poor sleep and can increase depression or moodiness. At midlife, women may face multiple stressors such as health changes for themselves or family members, financial concerns, loss of a parent, children leaving home, or relationship struggles with a partner, child, or parent.

Managing stress must be individualized, as each woman may find different tactics helpful. Some suggestions include regular exercise, meditation, relaxation techniques such as deep breathing, yoga, tai-chi, taking a bath, reading, having a massage, seeking support from

friends, or activities related to spirituality or religion. Few studies have evaluated the effects of such techniques on menopausal symptoms; however, reports indicate that avoiding and effectively managing stress are associated with less intense and fewer hot flashes (Alexander et al., 2003). While studies have not shown that progressive muscle relaxation and biofeedback control produce any significant change in hot flashes, paced respiration has been linked with a significant reduction in hot flashes (Freedman & Woodward, 1992; Freedman, Woodward, Brown, Javaid, & Pandy, 1995; Irvin, Domar, Clark, Zuttermeister, & Freidman, 1996). Many women find that yoga breathing—a variation of paced respiration—can enhance relaxation and reduce hot flashes. Yoga breathing consists of a deep inhalation for the count of four, holding the breath for a count of seven, and slowly exhaling over a count of eight.

Sleep

Evaluating the cause of sleep disruptions is important for developing a plan of management. If sleep disruption is related to hot flashes or other menopausal symptoms, control of those symptoms will usually restore normal sleep patterns. Light blankets, cotton sleepwear or moisture-wicking pajamas, and a well-ventilated room are recommended for reducing nocturnal hot flashes. However, if sleep disruption is unrelated to hot flashes, a more generalized approach is needed.

Developing good sleep hygiene is especially important for perimenopausal and menopausal women. Sleep hygiene refers to actions that cue the mind that it is time for sleep and allow the part of the brain that controls the body during sleep to take over. Developing regular routines prior to bedtime, such as brushing the teeth or changing into sleepwear, and doing something relaxing, such as paced respirations, progressive relaxation, guided imagery, taking a warm bath, reading a relaxing book, or drinking a warm beverage without caffeine, can help cue the mind that it is time to sleep. Similarly, activities that tend to stimulate the mind should be avoided just before bed, such as watching television, reading a fast-paced or stimulating book, doing work, or exercise. The bedroom should be reserved for sleep and sexual activities. This is especially important for individuals who have difficulty falling asleep, as doing work or watching television in bed can have a stimulating effect. Establishing regular times for sleep and waking is also important for developing good sleep patterns, as this consistency will help in developing normal daily routines.

Lifestyle changes that can help restore sleep patterns include avoiding use of stimulants, such as caffeine, alcohol, or nicotine, and engaging in exercise. The effects of caffeine can last as long as 20 hours in some individuals, so total elimination is preferable (Landolt, Werth, Borbely, & Dijk, 1995). Although alcohol initially can have a sedative effect, it can cause interruptions in normal sleep patterns after falling asleep, including fragmented sleep and rebound awakening (Landolt, Rioth, Dijk, & Borbely, 1996). Similarly, nicotine can cause increased sleep latency and reduces overall sleep duration. Exercise can enhance sleep quality, reduce sleep latency, and increase the amount of time spent in deep sleep. However, timing for exercise is important, as engaging in exercise right before bedtime will increase sleep latency.

For those with short sleep duration, sleep-restriction therapy can be tried (Morin et al., 1999). First the current average duration of sleep is identified, along with a needed and consistent time for awakening. The woman is instructed to go to bed four hours prior to the determined time for wakening, and to get up at the predetermined wake time. She needs to stay awake except for the determined sleep time (no napping). After she is sleeping more than 95% of this time for several nights consistently, the time to go to bed is moved to one half hour earlier. This pattern is continued until the desired sleep time is achieved.

It is also important to educate women that they require less sleep as they age. Few postmenopausal women need 8 hours of sleep per night; rather, 6 to 7 hours is the norm.

Mental Function

A slow decline in mental function is expected with aging. However, some women experience bothersome cognitive changes that develop as menopausal symptoms occur. Poor mental functioning is often associated with lack of sleep or high levels of stress, but cognitive impairment can also be related to a myriad of medical problems. Thus the first step in evaluating mental function is to complete a comprehensive assessment to identify potential causes of the cognitive problems.

For women who are experiencing reduced cognitive function that is unrelated to other organic problems, several simple memory aids may be of use. Noting appointments and dates of importance in a calendar, or writing lists to use for completing tasks, work activities, or shopping can help reduce stress associated with forgetting these items. Participating in activities that keep the mind engaged, such as intellectually stimulating work, puzzles, or other activities, can also help to maintain cognitive function.

Pharmacologic Options for Menopause Symptom Management

NAMS (2007, 2008) recommends lifestyle changes alone or in combination with nonprescription remedies for women with mild vasomotor symptoms; however, prescription systemic hormone products remain the standard for women with moderate to severe symptoms. The U.S. Food and Drug Administration (FDA) defines moderate to severe hot flashes as 7 to 8 episodes per day or at least 60 episodes per week. It is important to note that hot flashes will eventually resolve over time without medication in most women.

The Cochrane Group conducted a meta-analysis of 21 randomized, double-blind, placebo-controlled clinical trials that enrolled 2511 women. The researchers reported that systemic ET/EPT reduced hot flash severity and frequency significantly more than placebos. Some antidepressant, antihypertensive, and anticonvulsant agents have also been shown to reduce vasomotor symptoms (NAMS, 2004). **Table 13-6** lists currently recommended estrogen and estrogen/progestogen products. Note that in their review of efficacy of various preparations, the NAMS researchers concluded that there is no evidence to claim that one product is superior to another in terms of ability to yield symptom relief. **Table 13-7** lists nonhormonal prescription options and **Table 13-8** lists vaginal preparations.

TABLE 13-6 Hormone Therapy Options*

Type	Product Name (Manufacturer)	Active Ingredient	Dosage
Estrogens, oral	Cenestin (Duramed)	Conjugated estrogens	0.3 mg, 0.625 mg, 0.9 mg, or 1.25 mg once daily
	Estrace (Warner Chilcott)	Micronized estradiol	0.5 mg, 1 mg, or 2 mg once daily
	Estratab (Solvay)	Esterified estrogens	0.3 mg, 0.625 mg, or 2.5 mg once daily
	Menest (Monarch)	Esterified estrogens	0.3 mg, 0.625 mg, 1.25 mg, or 2.5 mg once daily
	Ogen (Pharmacia)	Estropipate	0.625 mg, 1.25 mg, or 2.5 mg once daily
	Ortho-est (Women First)	Estropipate	0.625 mg or 1.25 mg once daily
	Premarin (Wyeth)	Conjugated equine estrogens (CEE)	0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg, or 2.5 mg once daily
Estrogens, transdermal	Climara (Berlex)	Estradiol	0.025 mg, 0.0375 mg, 0.05 mg, 0.60 mg, 0.075 mg, or 0.1 mg once weekly
	Esclim (Women First), Vivelle, Vivelle-Dot (Novartis)	Estradiol	0.025 mg, 0.0375 mg, 0.05 mg, 0.075 mg, or 0.1 mg twice weekly
	Alora (Watson)	Estradiol	0.025 mg, 0.05 mg, 0.075 mg, or 0.1 mg twice weekly
	Estrogel (Solvay)	Estradiol	1.25 gm applied once daily to arm from shoulder to wrists
	Estraderm (Novartis)	Estradiol	0.05 mg or 0.1 mg twice weekly
	Estrasorb Cream (Novavax)	Estradiol	4.35 mg (one pouch) rubbed into each thigh every morning (total 8.7 mg daily)

Progestogens	Provera (Pharmacia)	Medroxyprogesterone acetate (MPA)	2.5 mg, 5 mg, or 10 mg continuously or on set cycle schedule
	Prometrium (Solvay)	Micronized progesterone	100 mg or 200 mg continuously or on set cycle schedule
	Aygestin (Barr)	Norethindrone acetate	5 mg or 10 mg continuously or on set cycle schedule
	Amen (Carnick), Cycrin (Wyeth-Ayerst)	MPA	2.5 mg, 5 mg, or 10 mg continuously or on set cycle schedule
Combination estrogen + progestogen, oral preparations	Prempro (Wyeth)	CEE + MPA	0.3 mg + 1.5 mg once daily 0.45 mg + 1.5 mg once daily 0.625 mg + 2.5 mg once daily, or 0.625 mg + 5 mg once daily continuously
	Premphase (Wyeth)	CEE (14 tabs), then CEE + MPA (14 tabs)	0.625 mg, then 0.625 mg + 5 mg once daily sequentially
	Femhrt (Warner Chilcott)	Norethindrone acetate + ethinyl estradiol	1 mg + 5 mcg once daily, continuously
	Prefest (Monarch)	Estradiol 3 tabs then estradiol + norgestimate 3 tabs	1 mg, then 1 mg + 0.9 mg, once daily sequentially
	Activella (Novo Nordisk)	Estradiol + norethindrone acetate	1 mg + 0.5 mg once daily
Combination estrogen + progestogen transdermals	Climara Pro (Berlex)	Estradiol + levonorgestrel	0.045 mg + 0.015 mg once weekly
	Combipatch (Novartis)	Estradiol + norethindrone acetate	0.05 mg + 0.14 mg per day 0.05 mg + 0.25 mg per day twice weekly

*See prescribing reference for full information on doses, side effects, contraindications, and cautions.

TABLE 13-7 Nonhormonal Pharmacologic Options for Vasomotor Symptoms*

Category	Drug	Dosage	Comments	Side Effects	Contraindications
Antidepressants	Venlafaxine (Effexor)	37.5–75 mg/day; uptitrate when starting therapy	Response is immediate	Nausea, vomiting, mouth dryness, decreased appetite	Concomitant use of MAO inhibitors; taper when discontinuing
	Fluoxetine (Prozac)	20 mg/day; uptitrate when starting therapy	Response is immediate	Asthenia, sweating, nausea, somnolence, anorgasmia, decreased libido	Concomitant use of MAO inhibitors or thioridazine; caution with warfarin; taper when discontinuing
	Paroxetine (Paxil)	12.5–25 mg/day; uptitrate when starting therapy	Response is immediate	See fluoxetine	See fluoxetine; taper when discontinuing
Anticonvulsants	Gabapentin (Neurontin)	Initial dose 300 mg/day, increasing to 300 mg three times per day at 3–4 day intervals		Somnolence, dizziness, ataxia, fatigue	Avoid antacids within 2 hours of use

Antihypertensives	Clonidine (Catapres)	0.05–0.1 mg twice daily	Available as a patch, less effective than antidepressants or gabapentin	Dry mouth, drowsiness, dizziness, weakness, constipation, rash, myalgia, urticaria, insomnia, nausea, agitation, orthostatic hypotension, impotence, arrhythmias	Taper when discontinuing
Antihypertensives	Methyldopa (Aldomet) and belladonna, ergotamine, and phenobarbitol (Bellergal)		NAMS does not recommend due to toxicity		
Breast cancer agents	Megestrol (Megace)	20 mg daily (divided doses)		Intestinal disturbance, weight gain, chest pain, edema, hypertension, hyperglycemia, rash, fever, insomnia, urinary frequency, asthenia, decreased libido, dyspepsia	Caution in diabetes, history of thromboembolic disease

*See prescribing reference for full information on doses, side effects, contraindications, and cautions.

Sources: Grady, 2002; NAMS, 2004.

TABLE 13-8 Vaginal Hormone Products*

Type	Product Name (Manufacturer)	Active Ingredient	Dose
Estrogen			
Vaginal hormone creams	Estrace (Warner Chilcott)	Micronized 17-betaestradiol	2–4 gm daily for 1–4 weeks, then 1 gm daily 1–3 times per week for 1–3 weeks. Maintenance: 1 gm 1–3 times a week, cyclically (3 weeks on, 1 week off). Taper dosage or discontinue at 3–6 month intervals
	Premarin (Wyeth)	Conjugated equine estrogen	0.5–2 g intravaginally daily cyclically (3 weeks on, 1 week off). Reevaluate periodically. Tapering is frequently appropriate but not specified in product information
Vaginal tablets	Vagifem (Novo Nordisk)	Estradiol hemihydrate	25 mcg once daily for two weeks then twice weekly
Ring	Estring (Pharmacia)	Micronized 17-betaestradiol	7.5 mcg/24 hours once every 90 days
	Femring (Warner Chilcott)	Estradiol acetate	0.05 mg/day or 0.1 mg/day once every 3 months
Progestogen			
Gel	Crinone (Serono)	Progesterone	4% gel–45 mg, 1 applicator every other day, give 6 doses; increase to 8% if no response
IUD	Mirena (Berlex)	Evonorgestrel	20 mcg daily

*See prescribing reference for full information on doses, side effects, contraindications, and cautions.

There is no FDA-approved therapy for treating hot flashes in women who are at high risk for, or who have been diagnosed with, breast cancer. Nonhormonal agents may provide hot flash relief for women who have had breast cancer. Herbal alternatives to HT should be used with caution because they can have estrogen-like activity.

Therapy Considerations

Prior to prescribing HT, it is imperative that clinicians and their patients review any cautions or contraindications to hormone use (**Table 13-9**). The clinician must engage the patient in the decision-making process and weigh the risks, benefits, and scientific uncertainty with each woman to individualize her treatment options. The risk of breast cancer increases after three to five years of EPT. As mentioned earlier, HT should not be used for protection against CVD, although some data indicate that beginning HT use in early menopause may have a cardioprotective effect. Recent data do not support decreased risk of dementia (NAMS, 2008) and the data to support EPT as preventive measure for colorectal cancer are insufficient to recommend its use for this purpose (NAMS).

Women considering using HT should have the recommended screening tests for health promotion and disease prevention in addition to a complete history and physical examination (see Chapter 8 for screening recommendations). Special attention should be paid to any personal or family history of health problems that would contraindicate ET or EPT use. If the woman is considered an appropriate candidate for this therapy, the clinician explains the various protocols for administering HT: ET alone (for women without an intact uterus), EPT continuously or sequentially, local ET, or estrogen–androgen therapy.

TABLE 13-9 Contraindications to HT and Adverse Effects

Absolute Contraindications to Estrogen Use	**Adverse Effects of ET**
Known or suspected cancer of the breast Known or suspected estrogen-dependent neoplasia History of uterine or ovarian cancer History of coronary heart disease or stroke History of biliary tract disorder Undiagnosed, abnormal genital bleeding History of or active thrombophlebitis or thromboembolic disorders	Uterine bleeding Breast tenderness Nausea Abdominal bloating Fluid retention in extremities Headache Dizziness Hair loss
Absolute Contraindications to Progestogen Use	**Adverse Effects of EPT**
Active thrombophlebitis or thromboembolic disorders Liver dysfunction or disease Known or suspected cancer of the breast Undiagnosed abnormal vaginal bleeding Pregnancy	Mood changes Possible increased uterine bleeding than if taking ET alone

HT Protocols and Formulations

Estrogen Therapy ET has been prescribed exclusively for women who have had a hysterectomy because the evidence reported in 1975 suggested that unopposed estrogen increases risk for endometrial hyperplasia and cancer. Side effects of ET are listed Table **13-10**.

Estrogen–Progestogen Therapy Combination estrogen and progestogen therapy can be taken either sequentially (CS-EPT) or continuously (CC-EPT). In the sequential regimen, an estrogen is taken daily with the addition of a progestogen in a cyclic fashion, usually on days 1 to 12 of the month. One side effect often noted with this therapy is that most women will have a withdrawal bleed monthly. To avoid this consequence, the continuous regimen was developed in which the estrogen and progestogen are taken on a daily basis. Another option includes pulsed combination therapy, wherein the progestogen is taken for two days, followed by a day off, in a repeating pattern. The original idea was to reduce potential side effects from the progestogen; however, breakthrough bleeding is usually more problematic with this regimen. A less frequently used regimen is the cyclic regimen, where estrogen is taken daily for the first 21 days of the cycle and then progestogen is added for days 12 to 21. A withdrawal bleed usually occurs between days 22 and 28, during which neither estrogen nor progestogen is taken. However, menopausal symptoms usually rebound when the estrogen is not taken; therefore, few women opt for the cyclic regimen.

TABLE 13-10 Management of HT Side Effects

Side Effect	Strategy
Fluid retention	Decrease salt intake; maintain adequate water intake; exercise; recommend an herbal diuretic or mild prescription diuretic
Bloating	Change to low-dose transdermal estrogen; lower the progestogen dose to a level that still protects the uterus; change the progestogen or try micronized progesterone
Breast tenderness	Lower the estrogen dose; change the estrogen; decrease salt intake; change the progestogen; decrease caffeine and chocolate consumption
Headaches	Change to transdermal estrogen; lower the estrogen and/or progestogen dose; change to a CC-EPT regimen; ensure adequate water intake; decrease salt, caffeine, and alcohol use
Mood changes	Lower the progestogen dose; change to a CC-EPT regimen; ensure adequate water intake; restrict salt, caffeine, and alcohol consumption
Nausea	Take hormones with meals; change the estrogen; change to transdermal estrogen; lower the estrogen or progestogen dose

Source: Adapted with permission from North American Menopause Society. (2002). *Menopause core curriculum study guide* (2nd ed.). Cleveland, OH: Author.

Estrogens A variety of estrogen compounds exist: estrogens that are bioidentical and transformed into human estrogens, such as 17-beta estradiol, estriol, and estrone; synthetic estrogen analogs, such as ethinyl estradiol; and nonhuman estrogens, such as CEE. CEE is the most widely used estrogen and has been the product used in the majority of clinical trials, including the WHI and HERS.

Estrogens differ in target tissue response and in dose equivalency. They can be administered either systemically or locally. Systemic preparations are available as oral tablets or transdermal patches. Local preparations are available as creams, tablets, or rings. The vaginal ring containing 0.5 mg or 0.1 mg/day of estradiol acetate over three months is the only local treatment that has proved effective in treating hot flashes (NAMS, 2004). Local treatment with estrogen theoretically avoids systemic absorption; however, in a review of the studies on vaginal preparations, Crandall (2002) found that the ring has slightly more systemic absorption. Women who want to avoid systemic effects, such as breast cancer survivors, should probably use a different preparation until more evidence is available.

Progestogens Progestogens are hormones that possess progestational properties. The most commonly prescribed progestogen has been MPA, but others are being used with more regularity, such as micronized progesterone (which is bioidentical), norgestimate, and norethindrone acetate. Side effects of adding progestogens to estrogens are listed in Table 13-9.

Estrogen–Androgen Therapy Therapy combining androgens and estrogens has been theorized to improve loss of libido in postmenopausal women; however, there is not enough scientific evidence from randomized clinical trials to say with certainty that testosterone plus estrogen is more effective than estrogen alone. One older study of 40 women showed no significant differences in levels of self-reported sexual enjoyment and desire (Dow, Hart, & Forrest, 1982). Another crossover study from the same era compared estrogen alone, estrogen plus testosterone, testosterone, and placebo. These researchers found that women reported significantly improved levels of sexual desire, arousal, and fantasies while taking testosterone and estrogen plus testosterone (Sherwin, Gelfand, & Brender, 1985). Additional clinical trials are currently being conducted. Known side effects of androgens include alopecia, acne, deepening of the voice, and hirsutism. As of this writing, there are no androgen therapies approved by the Food and Drug Administration (FDA) for use in women. See Chapter 17 for additional information on use of androgen preparations in women with decreased sexual desire.

Plan of Care and Patient Education

NAMS recommends initiating ET and EPT at lower than standard doses, such as 0.3 mg CEE, 0.25 to 0.5 mg 17-beta estradiol patch, or the equivalent. Studies have shown that these dosages provide adequate vasomotor relief, although the level of endometrial protection afforded by these regimens has not been evaluated in long-term clinical trials. Vasomotor symptoms usually begin to resolve in two to six weeks after initiating HT.

Patients should be offered anticipatory guidance about management of side effects, should they occur. Research evidence has absolved HT from contributing to weight gain; however, fluid retention may make women feel as if they are gaining weight. Table 13-10 lists possible side effects and strategies.

Patients should return for a follow-up visit with the clinician in six to eight weeks to evaluate their progress; if the initial dose of ET/EPT does not provide adequate symptom relief, it can be increased or taken on a daily divided dose schedule. The decision to continue or discontinue HT should be revisited at least annually. Some women will have symptoms for a short time, such as a few months to a year. Others remain symptomatic for years and may need to continue HT as long as five years (Wysocki et al., 2003).

When the patient seeks to discontinue therapy, HT should be tapered to avoid rebound symptoms. While no census guidelines for weaning patients have been established, NAMS (2008) advises gradually decreasing the dose or gradually lengthening the time between doses.

Complementary and Alternative Medicine Options for Menopause Symptom Management

The use of complementary and alternative medicine (CAM) is on the rise in the United States (Eisenberg et al., 1993; Eisenberg et al., 1998; Kessler et al., 2001), especially among women (Upchurch & Chyu, 2005). Visits to alternative providers now exceed visits to primary care clinicians, and most patients who use CAM do not report this usage to their primary care clinicians. Furthermore, women are the largest group of CAM users, and the use of CAM to manage menopause symptoms is growing (Bair et al., 2005; Brett & Keenan, 2007; Daley et al., 2006; Newton, Buist, Keenan, Anderson, & LaCroix, 2002). It is imperative for clinicians to ask patients about the use of CAM and to become knowledgeable about the CAM therapies that women are using.

Natural Versus Bioidentical Hormones

Many women seek "natural" hormones, believing that they are less likely to cause harmful side effects than manufactured hormones (Alexander, 2006). The term "natural" actually refers to any product with principal components that originate from plant, animal, or mineral sources. Thus this definition encompasses pharmaceutically manufactured hormones, which are also derived from animal, plant, or mineral substances. "Natural" hormones are not necessarily identical to the hormones produced by a woman's body.

Several hormones available that are "bioidentical" to the hormones produced in women's bodies, however. Frequently women requesting "natural hormones" are actually seeking "bioidentical" formulations (Alexander, 2006). Bioidentical hormones are available through prescription from both usual and compounding pharmacies. Several forms of estrogen are available in bioidentical formulations such as estrone, estriol, and 17-beta estradiol. Bioidentical progesterone is also available in micronized form.

Many women prefer to get estrogens through compounding pharmacies. Two commonly available preparations that contain bioidentical estrogens are Bi-est and Tri-est. Bi-est contains 2 mg estriol (80%) and 0.5 mg estradiol (20%); Tri-est contains 2 mg estriol (80%), 0.25 mg estrone (10%), and 0.25 mg estradiol (10%). These products are advertised as containing 80% estriol, which is correct. However, they contain significant amounts of estradiol and, therefore, may require progesterone for endometrial protection (Gaudet, 2004). Estriol also can be compounded as a vaginal cream.

The FDA (2008) has recently taken action against compounding pharmacies to stop unwarranted and misleading claims in advertisements that their products are safer than the estrogen products produced by traditional pharmaceutical companies. In reality, all estrogens carry a similar safety and risk profile.

Herbals

Although many women seek relief of menopausal symptoms, especially hot flashes, from herbal preparations, few studies exist to offer information regarding their efficacy or safety. Because these products are generally identified as diet supplements, rather than as medications, they are not regulated by the FDA in the same way as prescription medications and other over-the-counter products. Federal regulations for these products do exist, but they are poorly enforced. This lax supervision raises questions regarding the purity, contents, and consistency from package to package or tablet to tablet. Various preparations of the same herbal product may contain dramatically different amounts of active ingredients (e.g., extract versus tincture), and many products consist of mixtures of many different herbs in a single preparation, making dosing difficult. Furthermore, little is known regarding the interactions between various herbal products and prescription medications or other herbal products.

Despite these concerns, herbal products are widely used for menopausal symptom relief. Several of them are commonly used in combination products or in Chinese herb mixtures. **Table 13-11** provides information about some of these preparations.

Isoflavones

Isoflavones are compounds derived from plants that have both estrogenic and nonestrogenic properties. They are present in foods, such as soy and red clover, as well as in commercial preparations. Isoflavones are often referred to as phytoestrogens because of their ability to bind weakly with estrogen receptors, especially the beta receptors, and have been extensively studied for reducing hot flashes. Several recent placebo-controlled trials show little or no statistically significant differences in hot flash reduction in treatment versus control groups (Lewis et al., 2006; Nikander et al., 2003; Penotti et al., 2003; Tice et al., 2003). Nelson and colleagues (2006) analyzed 17 studies evaluating the effectiveness of soy for menopause-related hot flashes; in the 11 soy extract trials considered, 4 showed some improvement or mixed results, while mixed results or no differences were found in 6 studies of red clover.

TABLE 13-11 Herbals Commonly Used for Menopausal Symptom Relief*

Product	Usual Dosage†	Purpose in Menopause	Comments
Black cohosh (*Cimicifuga racemosa*)	20 mg twice daily (proprietary standardized extract)	Vasomotor symptoms	Multiple products and formulations available Research evidence suggests beneficial effect on menopausal symptoms, benefit similar to estrogen for hot flash relief Safety for use > 6 months not established Product labels frequently recommend much higher doses Can potentiate antihypertensives Wide variations in product ingredients, extraction processes, and purity Side effects rare, usually intestinal upset, headache, dizziness, hypotension, or painful extremities; more common with higher doses
Chastetree berry (*Vitex agnus castus*)	Effective dose unknown, hard to find standardized extract	Menstrual irregularity	More popular in Europe than the US; approved in Germany for PMS, mastalgia, and menopause symptoms Often found in combination products Research focuses on PMS symptoms, no data on relief of menopause symptoms Side effects rare, usually headache, intestinal upset
Dong quai (*Angelica sinensis*)	2 capsules two to three times per day; usually in combination products	Gynecologic conditions	Widely used in Asia Research found no benefit for menopause symptoms Often in Chinese herb combination products (*Chinese Materia Medica* advises against giving it alone) A "heating" herb, can cause a red face, hot flashes, sweating, irritability, or insomnia Contains coumarin derivatives, contraindicated in those taking warfarin Can cause photosensitivity, hypotension
Evening primrose oil (*Oenothera biennis*)	3–4 gm daily in divided doses	Hot flashes Mastalgia	Data show no benefit in treatment versus controls Potentiates risk for seizure if taken with seizure disorder, phenothiazines, and other medications that lower the seizure threshold Side effects include diarrhea and nausea

Ginkgo (*Ginkgo biloba*)	40–80 mg of standardized extract three times daily	Memory changes	Insufficient research on safety and efficacy Memory changes often related to sleep disturbances, menopausal sleep disturbances frequently related to vasomotor symptoms or other life stressors Side effects include gastrointestinal distress, hypotension; chronic use had been linked with subarachnoid hemorrhage, subdural hematoma, and increased bleeding times
Ginseng (*Panax ginseng*)	1–2 gm root daily in divided doses	General "tonic" Improved mood, fatigue	Heavily adulterated Research showed no benefit on menopausal symptoms; showed benefits on well-being, general health, and depression Can cause uterine bleeding, mastalgia Contraindicated with breast cancer, and with monoamine oxidase inhibitors, stimulants, or anticoagulants; may potentiate digoxin and others (multiple drug interactions) Side effects include rash, nervousness, insomnia, hypertension
Kava (*Piper methysticum*)	150–300 mg of root extract daily in divided doses	Irritability Insomnia	Banned in several countries due to hepatotoxicity, thus not recommended Contraindicated with depression Side effects include gastrointestinal discomfort, impaired reflexes and motor function, weight loss, hepatotoxicity, rash
Licorice root (*Glycyrrhiza glabra*)	5–15 mg of root equivalent daily in divided doses	Menopause-related symptoms	Found in many Chinese herb mixtures No data supporting relief of hot flashes High doses can lead to primary aldosteronism cardiac arrhythmias, cardiac arrest Contraindicated if hepatic or renal disease, diabetes, hypertension, arrhythmia, hypokalemia, hypertonis, pregnancy, or on diuretics
Passion flower (*Passiflora incarnata*)	3–10 grains daily in divided doses	Sedative	Research shows mixed results in sleep improvement Menopausal sleep disturbances frequently related to vasomotor symptoms or other life stressors

(*continues*)

TABLE 13-11 Herbals Commonly Used for Menopausal Symptom Relief* *(Continued)*

Product	Usual Dosage†	Purpose in Menopause	Comments
St. John's wort (*Hypericum perforatum*)	300 mg three times daily (standardized extract)	Vasomotor symptoms Irritability Depression	No data supporting vasomotor relief Research findings support use for depression, there are no clinical trials for menopause Often combined with black cohosh for menopause symptom treatment Interferes with metabolism of many medications that are metabolized in the liver (C 450) (e.g., estrogen, digoxin, theophylline), reduces international normalized ratio (INR) levels, not to be used concomitantly with antidepressants, monoamine oxidase inhibitors, or immunosuppressants Side effects include photosensitivity, rash, constipation, cramping, dry mouth, fatigue, dizziness, restlessness, insomnia
Valerian root (*Valeriana officinalis*)	300–600 mg aqueous extract 1/2–1 hour before bed (insomnia); 150–300 mg aqueous extract each morning and 300–400 mg each evening (anxiety)	Sedative Antianxiety	Used for insomnia in intermittent dosing, for anxiety with chronic dosing Research showed improvement in sleep and depression/mood scales Side effects include headache, uneasiness, excitability, arrhythmias, morning sedation, gastrointestinal upset, cardiac function disorders (with long-term use)
Wild yam (*Dioscorea villosa*)	Unknown	Menopausal symptoms	Products claim that creams are converted to progesterone; however, the human body cannot convert topical or ingested wild yam into progesterone Research showed no benefit on menopausal symptoms

*See prescribing reference for full information on doses, side effects, contraindications, and cautions.
†Dosages vary and differ according to form (e.g., tincture, liquid extract, drops, essential oil, standardized extract).

Sources: Decker & Myers, 2001; Gaudet, 2004; Low Dog, 2004; NAMS, 2004.

Despite these disappointing findings, soy is a healthy food that the FDA has allowed to be identified as reducing the risk of heart disease. There is no evidence that soy predisposes women to breast cancer, and it can be used by breast cancer survivors. Some data suggest that use of soy for 5 years or more could cause endometrial overgrowth (Unfer et al., 2004). Women who choose to add soy to their diets need to be educated to use the soy to replace something else, rather than adding extra calories through soy nuts, shakes, or cereals.

Other classes of phytoestrogens include flavonoids, lignans, and coumestrans. These classes have much lower hormonal affinity and are generally not thought to be useful for menopausal symptom management. They are found in some foods and food products and carry some of the cardioprotective properties of isoflavones. Lignans are found in flaxseed oil, whole grains, and some fruits and vegetables. Flavonoids are found in oils, spices, wine, tea, and some vegetables. Coumestrans are found in alfalfa sprouts, red beans, split peas, spinach, and some species of clover; these phytoestrogens can interfere with bleeding profiles and may have interactions with warfarin.

Progesterone Creams

Several different progesterone creams are available over-the-counter. FDA regulations are not currently enforced for these products, again raising concerns about their purity and content. Progesterone creams include products such as PhytoGest, Pro-Gest, Endocreme, and Pro-Dermex, and the stated progesterone content varies from less than 2 mg to 700 mg. These creams can also be prescribed using compounding pharmacies.

Although some women taking systemic estrogens may want to use progesterone creams for endometrial protection to avoid systemic progesterone effects, there are no data that support the use of progesterone creams for endometrial protection. At least one randomized, controlled study identified improvement in vasomotor symptoms for women using transdermal progesterone cream as compared with controls (Leonetti, Longo, & Anasti, 1999). Topical progesterone creams may be a promising option if future research supports these findings.

Acupuncture

Research findings evaluating acupuncture for the relief of menopause-related hot flashes have been contradictory. One small study of 24 women identified no differences in subjects treated with electroacupuncture versus controls (Wyon, Lindgren, Lundberg, & Hammar, 1995). In contrast, a more recent study ($N = 17$) identified significant reductions in hot flashes and sleep disturbances in women treated over a six-week period with acupuncture at menopause symptom-specific sites as compared with controls who were treated with a general tonic acupuncture (Cohen, Rousseau, & Carey, 2003). Some other studies comparing effects of acupuncture to sham or placebo have demonstrated a reduction in severity, but not frequency, of hot flashes (Huang, Nir, Chen, Schnyer, & Manber, 2006; Nir, Huang, Schnyer, Chen, & Manber, 2007), while others showed no differences (Deng et al., 2007; Vincent et

al., 2007). Acupuncture may prove to provide some benefit but further research is needed to clarify its usefulness.

Conclusion

Menopause is a marker in the lives of middle-aged women. While a normal developmental stage, it gives women the opportunity to evaluate their health and risks for diseases of aging, thereby instituting lifestyle changes that prevent disease and promote health. Although many women will transition through perimenopause to postmenopause without incident, many will also experience mild to severe vasomotor symptoms. Treatments for these problems can decrease symptoms and improve women's quality of life. As the numbers of postmenopausal women increase, clinicians are in a prime position to counsel their patients about healthy aging.

References

Administration on Aging. (2008). *A profile of older Americans: 2008*. Washington, DC: Author. Retrieved from http://www.aoa.gov/AoARoot/Aging_Statistics/Profile/2008/docs/2008profile.pdf

Alexander, I. M. (2006). Bioidentical hormones for menopause therapy: Separating the myths from the reality. *Women's Health Care: A Practical Journal for Nurse Practitioners, 5*(1), 7–17.

Alexander, I. M., Ruff, C., Rousseau, M. E., White, K., Motter, S., McKie, C., et al. (2003). Menopause symptoms and management strategies identified by black women [Abstract]. *Menopause, 10*(6), 601.

Alexander, I. M., Ruff, C., Rousseau, M. E., White, K., Motter, S., McKie, C., et al. (2004, April). *Experiences and perceptions of menopause and midlife health among black women*. Paper presented at the meeting of the Eastern Nursing Research Society 16th Annual Scientific Sessions, Quincy, MA.

Alexander, I. M., Ruff, C. C., & Udemezue, C. (n.d.). *Correlation between lifestyle behaviors and severity of menopausal symptoms in black women. [Unpublished data.] P20 pilot study in the Yale-Howard Center for reducing health disparities through self- and family-management* (Grant No. 1P20NR08349-01). Bethesda, MD: National Institute of Nursing Research.

American Association of Clinical Endocrinologists (AACE). (2008). Diabetes experts recommend one-two punch for treating patients with pre-diabetes. Retrieved from http://media.aace.com/article_display.cfm?article_id=4828

American Cancer Society (ACS). (2004). Cancer statistics 2004. Retrieved http://www.cancer.org/docroot/STT/stt_0_2004.asp.

American Cancer Society (ACS). (2007). Guide to quitting smoking. Retrieved from http://www.cancer.org/docroot/PED/content/PED_10_13X_Guide_for_Quitting_Smoking.asp

American Diabetes Association (ADA). (2004a). Position statement: Diagnosis and classification of diabetes mellitus. *Diabetes Care, 27*(suppl 1), S5–S10.

American Diabetes Association (ADA). (2004b). Position statement: Screening for type 2 diabetes. *Diabetes Care, 27*(suppl. 1), S11–S14.

American Heart Association (AHA). (2002). *Heart disease and stroke statistics: 2003 update*. Dallas, TX: Author.

American Heart Association (AHA). (2004). Women and cardiovascular disease. Retrieved from http://www.americanheart.org

American Obesity Association. (2002). Obesity fact sheets (Updated March 24, 2004). Retrieved from http://www.obesity.org

Anderson, G. L., Limacher, M., Assaf, A. R., Bassford, T., Beresford, S. A., Black, H., et al. (2004). Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: The Women's Health Initiative randomized controlled trial. *Journal of the American Medical Association, 291*(14), 1701–1712.

Arnold, E. (2005). A voice of their own: Women moving into their fifties. *Health Care for Women International, 26*(8), 630–657

Avis, N. E., Stellato, R., Crawford, S., Bromberger, J., Ganz, P., Cain, V., et al. (2001). Is there a menopausal syndrome? Menopausal status and symptoms across racial/ethnic groups. *Social Science and Medicine, 52*(3), 345–356.

Bair, Y. A., Gold, E. B., Azari, R. A., Greendale, G., Sternfeld, B., Harkey, M. R., et al. (2005). Use of conventional and complementary health care during the transition to menopause: Longitudinal results from the Study of Women's Health Across the Nation (SWAN). *Menopause, 12*(1), 31–39.

Baker, A., Simpson, S., & Dawson, D. (1997). Sleep disruption and mood changes associated with menopause. *Journal of Psychosomatic Research, 43*(4), 359–369.

Ballard, K. D., Kuh, D. J., & Wadsworth, M. E. J. (2001). The role of the menopause in women's experiences of the "change of life." *Sociology of Health and Illness, 23*(4), 397–424.

Barton, D. L., Loprinzi, C. L., Quella, S. K., Sloan, J. A., Veeder, M. H., Egner, J. R., et al. (1998). Prospective evaluation of vitamin E for hot flashes in breast cancer survivors. *Journal of Clinical Oncology, 16*(2), 495–500.

Baskin, H. J. (2002). American Association of Clinical Endocrinologists' medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. *Endocrine Practice, 8*(6), 457–469.

Bastian, L. A., Smith, C. M., & Nanda, K. (2003). Is this woman perimenopausal? *Journal of the American Medical Association, 289*(7), 895–902.

Blackman, M. R. (2000). Age-related alterations in sleep quality and neuroendocrine function: Interrelationships and implications. *Journal of the American Medical Association, 284*(7), 879–881.

Blatt, M. H. G., Weisbader, H., & Kupperman, H. S. (1953). Vitamin E and the climacteric syndrome. *Archives of Internal Medicine, 91*, 792–796.

Brett, K. M., & Keenan, N. L. (2007). Complementary and alternative medicine use among midlife women for reasons including menopause in the United States: 2002. *Menopause, 14*(2), 300–307.

Bromberger, J. T., Matthews, K. A., Kuller, L. H., Wing, R. R., Meilahn, E. N., & Plantinga, P. (1997). Prospective study of the determinants of age at menopause. *American Journal of Epidemiology, 145*(2), 124–133.

Busch, H., Barth-Olofsson, A. S., Rosenhagen, S., & Collins, A. (2003). Menopause transition and psychological development. *Menopause, 10*(2), 179–187.

Centers for Disease Control and Prevention. (2003). Nutrition and physical activity: Overweight and obesity. (Updated December 8, 2003.) Retrieved May 7, 2004, from www.cdc.gov

Cohen, L. (2004, April). *Depression rates in perimenopausal and premenopausal women: A longitudinal study*. Paper presented at the meeting of the American Psychiatric Association, New York.

Cohen, S. M., Rousseau, M. E., & Carey, B. (2003). Can acupuncture ease the symptoms of menopause? *Holistic Nursing Practice, 17*(6), 295–299.

Collins, P. H. (1990). *Black feminist thought: Knowledge, consciousness, and the politics of empowerment*. Boston: Unwin Hyman.

Cooper, G. S., Sandler, D. P., & Bohlig, M. (1999). Active and passive smoking and the occurrence of natural menopause. *Epidemiology, 10*(6), 771–773.

Cramer, G., Xu, H., & Harlow, B. L. (1995). Family history as a predictor of early menopause. *Fertility and Sterility, 64*, 740–745.

Crandall, C. (2002). Vaginal estrogen preparations: A review of safety and efficacy for vaginal atrophy. *Journal of Women's Health, 11*(10), 857–877.

Daley, A., MacArthur, C., McManus, R., Stokes-Lampard, H., Wilson, S., Roalfe, A., et al. (2006). Factors associated with the use of complementary medicine and non-pharmacological interventions in symptomatic menopausal women. *Climacteric, 9*(5), 336–346.

Davis, R., & Huber, K. (2004). Class, ethnicity, age, physical status, and sexual orientation: Implications for health and healthcare. In M. Condon (Ed.), *Women's health* (pp. 21–40). Upper Saddle River, NJ: Prentice Hall.

Dawson-Hughes, B., Lindsay, R., Khosla, S., Melton, L. J., Tosteson, A. N., Favus, M., et al. (2008). *Clinician's guide to prevention and treatment of osteoporosis* (Vol. 2008). Washington, DC: National Osteoporosis Foundation.

Dawson-Hughes, B., Tosteson, A. N., Melton, L. J. 3rd, Baim, S., Favus, M. J., Khosla, S., et al. (2008). Implications of absolute fracture risk assessment for osteoporosis practice guidelines in the USA. *Osteoporosis International, 19*(4), 449–458.

de Bruin, J. P., Bovenhuis, H., van Noord, P. A. H., Pearson, P. L., van Arendonk, J. A. M., te Velde, E. R., et al. (2001). The role of genetic factors in age at natural menopause. *Human Reproduction, 16*(9), 2014–2018.

Decker, G. M., & Myers, J. (2001). Commonly used herbs: Implications for clinical practice [insert]. *Clinical Journal of Oncology Nursing, 5*(2), 13p.

Deng, G., Vickers, A., Yeung, S., D'Andrea, G. M., Xiao, H., Heerdt, A. S., et al. (2007). Randomized, controlled trial of acupuncture for the treatment of hot flashes in breast cancer patients. *Journal of Clinical Oncology, 25*(35), 5584–5590.

Dennerstein, L., Dudley, E., & Burger, H. (2001). Are changes in sexual functioning during midlife due to aging or menopause? *Fertility & Sterility, 76*(3), 456–460.

Dow, M. G., Hart, D. M., & Forrest, C. A. (1982). Hormonal treatments of sexual unresponsiveness in postmenopausal women: A comparative study. *British Journal of Obstetrics and Gynaecology, 90*, 361–366.

Dvornyk, V., Long, J. R., Liu, P. Y., Zhao, L. J., Shen, H., Recker, R. R., et al. (2006). Predictive factors for age at menopause in Caucasian females. *Maturitas, 54*(1), 19–26.

Eisenberg, D. M., Davis, R. B., Ettner, S. L., Appel, S., Wilkey, S., Van Rompay, M., et al. (1998). Trends in alternative medicine use in the United States, 1990–1997: Results of a follow-up national survey. *Journal of the American Medical Association, 280*(18), 1569–1575.

Eisenberg, D. M., Kessler, R. C., Foster, C., Norlock, F. E., Calkins, D. R., & Delbanco, T. L. (1993). Unconventional medicine in the United States: Prevalence, costs, and patterns of use. *New England Journal of Medicine, 328*(4), 246–252.

Fairfield, K. M., & Fletcher, R. H. (2002). Vitamins for chronic disease prevention in adults: Scientific review. *Journal of the American Medical Association, 287*(23), 3116–3126.

Finer, L. B., & Henshaw, S. K. (2006). Disparities in rates of unintended pregnancy in the United States, 1994 and 2001. *Perspectives on Sexual and Reproductive Health, 38*(2), 90–96.

Fletcher, R. H., & Fairfield, K. M. (2002). Vitamins for chronic disease prevention in adults: Clinical applications. *Journal of the American Medical Association, 287*(23), 3127–3129.

Fogel, C. I., & Woods, N. F. (Eds.). (2008). *Women's health care in advanced practice nursing*. New York: Springer.

Food and Drug Administration (FDA). (2008). FDA takes action against compounded menopause hormone therapy drugs. Retrieved from http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm116832.htm

Franz, M. J. (Ed.). (2003). *A CORE curriculum for diabetes education: Diabetes and complications* (5th ed.). Chicago: American Association of Diabetes Educators.

Freedman, R. R., & Blacker, C. M. (2002). Estrogen raises the sweating threshold in postmenopausal women with hot flashes. *Fertility and Sterility, 77*(3), 487–490.

Freedman, R. R., & Woodward, S. (1992). Behavioral treatment of menopausal hot flashes: Evaluation by ambulatory monitoring. *American Journal of Obstetrics and Gynecology, 167*, 436–439.

Freedman, R. R., Woodward, S., Brown, B., Javaid, J. I., & Pandy, G. N. (1995). Biochemical and thermoregulatory effects of treatment for menopausal hot flashes. *Menopause, 2*, 211–218.

Gallagher, J. C. (2007). Effect of early menopause on bone mineral density and fractures. *Menopause, 14*(3 Pt 2), 567–571.

Garcia, C. R., Sammel, M. D., Freeman, E. W., Lin, H., Langan, E., Kapoor, S., et al. (2005). Defining menopause status: Creation of a new definition to identify the early changes of the menopausal transition. *Menopause, 12*(2), 128–135.

Gaspar, U. J., Gotta, J. M., & van den Brule, F. A. (1995). Post menopausal changes of lipid and glucose metabolism: A review of the main aspects. *Maturitas, 21*, 171–178.

Gaudet, T. W. (2004). CAM approaches to menopause management: Overview of the options. *Menopause Management: Women's Health Through Midlife & Beyond, 13*(suppl 1), 48–50.

Gilligan, C. (1982). *In a different voice: Psychological theory and women's development*. Cambridge, MA: Harvard University Press.

Godsland, I. F. (1996). The influence of female sex steroids on glucose metabolism and insulin action. *Journal of Internal Medicine, 738*(suppl), 1–60.

Gold, E. B., Bromberger, J., Crawford, S., Samuels, S., Greendale, G. A., Harlow, S. D., et al. (2001). Factors associated with age at natural menopause in a multiethnic sample of midlife women. *American Journal of Epidemiology, 153*(9), 865–874.

Gold, E. B., Sternfeld, B., Kelsey, J. L., Brown, C., Mouton, C., Reame, N., et al. (2000). Relation of demographic and lifestyle factors to symptoms in a multi-racial/ethnic population of women 40–55 years of age. *American Journal of Epidemiology, 152*(5), 463–473.

Grady, D. (2002). A 60-year-old woman trying to discontinue hormone replacement therapy. *Journal of the American Medical Association, 287*(16), 2130–2137.

Greendale, G. A., Lee, N. P., & Arriola, E. R. (1999). The menopause. *Lancet, 353*(9152), 571–580.

Grodstein, F., Manson, J. E., & Stampfer, M. J. (2006). Hormone therapy and coronary heart disease: The role of time since menopause and age at hormone initiation. *Journal of Women's Health (Larchmont), 15*(1), 35–44.

Harlow, S. D., Cain, K., Crawford, S., Dennerstein, L., Little, R., Mitchell, E. S., et al. (2006). Evaluation of four proposed bleeding criteria for the onset of late menopausal transition. *Journal of Clinical Endocrinology and Metabolism, 91*(9), 3432–3438.

Hefler, L. A., Grimm, C., Bentz, E. K., Reinthaller, A., Heinze, G., & Tempfer, C. B. (2006). A model for predicting age at menopause in white women. *Fertility and Sterility, 85*(2), 451–454.

Hodgson, S. F., & Watts, S. F. (2003). American Association of Clinical Endocrinologists medical guidelines for clinical practice for the prevention and treatment of postmenopausal osteoporosis: 2001 edition with selected updates for 2003. *Endocrine Practice, 9*(6), 544–564.

Huang, M. I., Nir, Y., Chen, B., Schnyer, R., & Manber, R. (2006). A randomized controlled pilot study of acupuncture for postmenopausal hot flashes: Effect on nocturnal hot flashes and sleep quality. *Fertility and Sterility, 86*(3), 700–710.

Huber, A., Grimm, C., Huber, J. C., Schneeberger, C., Leodolter, S., Reinthaller, A., et al. (2006). A common polymorphism within the steroid 5-alpha-reductase type 2 gene and timing of menopause in Caucasian women. *European Journal of Obstetrics, Gynecology, and Reproductive Biology, 125*(2), 221–225.

Irvin, J. H., Domar, A. D., Clark, C., Zuttermeister, P. C., & Freidman, R. (1996). The effects of relaxation response training on menopausal symptoms. *Journal of Psychosomatic Obstetrics and Gynaecology, 17*, 202–207.

Jacobs Institute on Women's Health. (2003). Expert panel on menopause counseling. Retrieved from http://www.jiwh.org/menodownload.htm

Jordan, J. V., Kaplan, A. G., Miller, J. B., Stiver, I. P., & Surrey, J. L. (1991). *Women's growth in connection*. New York: Guilford Press.

Kessler, R. C., Davis, R. B., Foster, D. F., Van Rompay, M. I., Walters, E. E., Wilkey, S. A., et al. (2001). Long-term trends in the use of complementary and alternative medical therapies in the United States. *Annals of Internal Medicine, 135*(4), 262–268.

Klatte, E. T., Scharre, D. W., Nagaraja, H. N., Davis, R. A., & Beversdorf, D. Q. (2003). Combination therapy of donepezil and vitamin E in Alzheimer disease. *Alzheimer Disease & Associated Disorders, 17*(2), 113–116.

Kronenberg, F. (1990). Hot flashes: Epidemiology and physiology. *Annals of the New York Academy of Sciences, 592*, 52–86, 123–133.

Landolt, H. P., Rioth, C., Dijk, D. J., & Borbely, A. A. (1996). Late-afternoon ethanol intake affects nocturnal sleep and the sleep EEG in middle-aged men. *Journal of Clinical Psychopharmacology, 16*, 428–436.

Landolt, H. P., Werth, E., Borbely, A. A., & Dijk, D. J. (1995). Caffeine intake (200 mg) in the morning affects human sleep and EEG spectra at night. *Brain Research, 675*, 67–74.

Lane, N., & Silverman, S. (2008). Hotline: New NOF guidelines and the WHO Fracture Assessment Tool or FRAX. Retrieved from http://www.rheumatology.org/publications/hotline/03_18_flax.asp

Leonetti, H. B., Longo, S., & Anasti, J. N. (1999). Transdermal progesterone cream for vasomotor symptoms and postmenopausal bone loss. *Obstetrics & Gynecology, 94*(2), 225–228.

Lewis, J. E., Nickell, L. A., Thompson, L. U., Szalai, J. P., Kiss, A., & Hilditch, J. R. (2006). A randomized controlled trial of the effect of dietary soy and flaxseed muffins on quality of life and hot flashes during menopause. *Menopause, 13*(4), 631–642.

Liu, J. (2004). Use of conjugated estrogens after the Women's Health Initiative. *The Female Patient, 29*, 8–13.

Lobo, R. A. (2007). Surgical menopause and cardiovascular risks. *Menopause, 14*(3 Pt 2), 562–566.

Low Dog, T. (2004). CAM approaches to menopause management: The role for botanicals in menopause. *Menopause Management: Women's Health Through Midlife & Beyond, 13*(suppl 1), 51–53.

MacPherson, K. I. (1981). Menopause as disease: The social construction of a metaphor. *Advances in Nursing Science, 3*, 95–113.

Mayer-Davis, E. J., D'Antonio, A., & Tudor-Locke, C. (2003). Lifestyle for diabetes prevention. In M. J. Franz (Ed.), *A core curriculum for diabetes education: Diabetes in the life cycle and research* (5th ed., pp. 1–30). Chicago: American Association of Diabetes Educators.

McKinlay, S. M. (1996). The normal menopause transition: An overview. *Maturitas, 23*(2), 137–145.

McLean, R. R., Jacques, P. F., Selhub, J., Tucker, K. L., Samelson, E. J., Broe, K. E., et al. (2004). Homocysteine as a predictive factor for hip fracture in older persons. *New England Journal of Medicine, 350*(20), 2042–2049.

Morin, C. M., Hauri, P. J., Espie, C. A., Speilman, A. J., Buysse, D. J., & Bootzin, R. R. (1999). Nonpharmacologic treatment of chronic insomnia: An American Academy of Sleep Medicine review. *Sleep, 22*, 1134–1156.

Nachtigall, L. E. (1994). Comparative study: Replens versus local estrogen in menopausal women. *Fertility & Sterility, 61*, 178–180.

National Cancer Institute (NCI). (2003). Probability of developing or dying of cancer. Retrieved from http://srab.cancer.gov/devcan

National Cancer Institute (NCI). (2008). Cancer facts and figures, 2008. Retrieved September 26, 2009, from http://www.cancer.org/downloads/STT/2008CAFFfinalsecured.pdf

National Institutes of Health (NIH). (1994). Optimal calcium intake: NIH consensus statement. Retrieved from http://text.nlm.nih.gov/nih/cdc/www/ 97txt .html

National Institutes of Health (NIH). (2004). NIH asks participants in Women's Health Initiative Estrogen-Alone Study to stop study pills, begin follow-up phase. Retrieved from http://www.nhlbi.nih.gov/new/press/04-03-02.htm

National Institutes of Health (NIH). (2007). National Center on Sleep Disorder Research and Office of Prevention, Education, and Control. Retrieved from www.nhlbi.nih.gov/health/prof/sleep/pslp_pat.htm

National Women's Health Network. (2000). *Taking hormones and women's health: Choices, risks, and benefits*. Washington, DC: Author.

Nelson, H. D., Vesco, K. K., Haney, E., Fu, R., Nedrow, A., Miller, J., et al. (2006). Nonhormonal therapies for menopausal hot flashes: systematic review and meta-analysis. *Journal of the American Medical Association, 295*(17), 2057–2071.

Newton, K. M., Buist, D. S., Keenan, N. L., Anderson, L. A., & LaCroix, A. Z. (2002). Use of alternative therapies for menopause symptoms: Results of a population-based survey. *Obstetrics and Gynecology, 100*(1), 18–25.

Newton, K. M., Buist, D. S., Yu, O., Hartsfield, C. L., Andrade, S. E., Wei, F., et al. (2008). Hormone therapy initiation after the Women's Health Initiative. *Menopause, 15*(3), 487–493.

Nikander, E., Kilkkinen, A., Metsa-Heikkila, M., Adlercreutz, H., Pietinen, P., Tiitinen, A., et al. (2003). A randomized placebo-controlled crossover trial with phytoestrogens in treatment of menopause in breast cancer patients. *Obstetrics & Gynecology, 101*(6), 1213–1220.

Nir, Y., Huang, M. I., Schnyer, R., Chen, B., & Manber, R. (2007). Acupuncture for postmenopausal hot flashes. *Maturitas, 56*(4), 383–395.

North American Menopause Society (NAMS). (2003). Estrogen and progestogen use in peri- and postmenopausal women: September 2003 position statement of the North American Menopause Society. *Menopause, 10*(6), 497–506.

North American Menopause Society (NAMS). (2004). Treatment of menopause-associated vasomotor symptoms: Position statement of the North American Menopause Society. *Menopause, 11*(1), 11–33.

North American Menopause Society (NAMS). (2007). *Menopause practice: A clinician's guide* (3rd ed.). Cleveland, OH: Author.

North American Menopause Society (NAMS). (2008). Estrogen and progestogen use in postmenopausal women: July, 2008 position statement of the North American Menopause Society. *Menopause: The Journal of the North American Menopause Society, 15*(4), 584–603.

••North American Menopause Society (NAMS). (2009). Government approved postmenopausal osteoporosis drugs in the United States and Canada. Retrieved September 26, 2009, from http://www.menopause.org/otcharts.pdf

Onofrj, M., Thomas, A., Luciano, A. L., Iacono, D., Di Rollo, A., D'Andreamatteo, G., et al. (2002). Donepezil versus vitamin E in Alzheimer's disease: Part 2: Mild versus moderate–severe Alzheimer's disease. *Clinical Neuropharmacology, 25*(4), 207–215.

Palmer, J. R., Rosenberg, L., Wise, L. A., Horton, N. J., & Adams-Campbell, L. L. (2003). Onset of natural menopause in African American women. *American Journal of Public Health, 93*(2), 299–306.

Pastore, L. M., Carter, R. A., Hulka, B. S., & Wells, E. (2004). Self-reported urogenital symptoms in postmenopausal women: Women's Health Initiative. *Maturitas, 49*(4), 292–303.

I cannot find this in any tables or in the chapter. Will check with Francie because she may want it to replace some of the NAMS 2004 sources cited in the table.

Penotti, M., Fabio, E., Modena, A. B., Rinaldi, M., Omodei, U., & Vigano, P. (2003). Effect of soy-derived isoflavones on hot flushes, endometrial thickness, and the pulsatility index of the uterine and cerebral arteries. *Fertility & Sterility, 79*(5), 1112–1117.

Porth, C. M., & Kunert, M. P. (Eds.). (2002). *Pathophysiology concepts of altered health states* (6th ed.). Philadelphia: Lippincott Williams & Wilkins.

Quinn, A. A. (1991). A theoretical model of the perimenopausal process. *Journal of Nurse-Midwifery, 36*(1), 25–29.

Rossouw, J. E., Anderson, G. L., Prentice, R. L., LaCroix, A. Z., Jackson, R. D., Beresford, S. A. A., et al. (2002). Risks and benefits of estrogen plus progestin in healthy postmenopausal women: Principal results from the Women's Health Initiative Randomized Controlled Trial. *Journal of the American Medical Association, 288*(3), 321–333.

Salpeter, S. R., Walsh, J. M. E., Greyber, E., Ormiston, T. M., & Salpeter, E. E. (2004). Mortality associated with hormone replacement therapy in younger and older women. *Journal of General Internal Medicine, 19*(7), 791–804.

Sampselle, C. M., Harris, V. H., Harlow, S. D., & Sowers, M. (2002). Midlife development and menopause in African American and Caucasian women. *Health Care for Women International, 23*(4), 351–363.

Santoro, N., Brockwell, S., Johnston, J., Crawford, S. L., Gold, E. B., Harlow, S. D., et al. (2007). Helping midlife women predict the onset of the final menses: SWAN, the Study of Women's Health Across the Nation. *Menopause, 14*(3 Pt 1), 415–424.

Santoro, N., Lasley, B., McConnell, D., Allsworth, J., Crawford, S., Gold, E. B., et al. (2004). Body size and ethnicity are associated with menstrual cycle alterations in women in the early menopausal transition: The Study of Women's Health Across the Nation (SWAN) Daily Hormone Study. *Journal of Clinical Endocrinology & Metabolism, 89*(6), 2622–2631.

Sheehy, G. (1976). *Passages: Predictable crises of adult life*. New York: Dutton.

Sheehy, G. (1995). *New passages: Mapping your life across time*. New York: Random House.

Sherman, C. A., Harvey, S. M., & Noell, J. (2005). "Are they still having sex?" STI's and unintended pregnancy among mid-life women. *Journal of Women and Aging, 17*(3), 41–55.

Sherwin, B. B., Gelfand, M. M., & Brender, W. (1985). Androgen enhances sexual motivation in females: A prospective crossover study of sex steroid administration in the surgical menopause. *Psychosomatic Medicine, 47*, 339–351.

Soules, M. R., Sherman, S., Parrott, E., Rebar, R., Santoro, N., Utian, W., et al. (2001). Executive summary: Stages of Reproductive Aging Workshop (STRAW). *Fertility & Sterility, 76*(5), 874–878.

Speroff, L., Glass, R. H., & Kase, N. G. (1999). *Clinical gynecologic endocrinology and infertility* (6th ed.). Philadelphia: Lippincott Williams & Wilkins.

Thomas, A., Iacono, D., Bonanni, L., D'Andreamatteo, G., & Onofrj, M. (2001). Donepezil, rivastigmine, and vitamin E in Alzheimer disease: A combined P300 event-related potentials/neuropsychologic evaluation over 6 months. *Clinical Neuropharmacology, 24*(1), 31–42.

Thurston, R. C., Sowers, M. R., Sutton-Tyrrell, K., Everson-Rose, S. A., Lewis, T. T., Edmundowicz, D., et al. (2008). Abdominal adiposity and hot flashes among midlife women. *Menopause, 15*(3), 429–434.

Tice, J. A., Ettinger, B., Ensrud, K., Wallace, R., Blackwell, T., & Cummings, S. R. (2003). Phytoestrogen supplements for the treatment of hot flashes: The Isoflavone Clover Extract (ICE) Study: A randomized controlled trial. *Journal of the American Medical Association, 290*(2), 207–214.

Tosteson, A. N., Melton, L. J. 3rd, Dawson-Hughes, B., Baim, S., Favus, M. J., Khosla, S., et al. (2008). Cost-effective osteoporosis treatment thresholds: The United States perspective. *Osteoporosis International*. Retrieved from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18292976

Unfer, V., Casini, M. L., Costabile, L., Mignosa, M., Gerli, S., & Di Renzo, G. C. (2004). Endometrial effects of long-term treatment with phytoestrogens: A randomized, double-blind, placebo-controlled study. *Fertility and Sterility, 82*(1), 145–148, quiz 265.

Upchurch, D. M., & Chyu, L. (2005). Use of complementary and alternative medicine among American women. *Women's Health Issues, 15*(1), 5–13.

U.S. Department of Health, Education, and Welfare, National Institute on Aging. (1979). *Summary of conclusions of the NIH Conference on Estrogen Use and Postmenopausal Women*. Washington, DC: Author.

U.S. Preventive Services Task Force (USPSTF). (1996). *Guide to preventive services*. Rockville, MD: Agency for Healthcare Research and Quality.

Utian, W. H. (1987). Overview on menopause. *American Journal of Obstetrics and Gynecology, 156*, 1280–1283.

Utian, W. (1999a). The International Menopause Society: Menopause-related terminology definitions. *Climacteric, 2*, 284–286.

Utian, W. H. (1999b). An historical perspective of natural and surgical menopause. *Menopause, 6*(2), 83–86.

Utian, W. H. (2001). Semantics, menopause-related terminology, and the STRAW reproductive aging staging system. *Menopause, 8*(6), 398–401.

van Disseldorp, J., Faddy, M. J., Themmen, A. P., de Jong, F. H., Peeters, P. H., van der Schouw, Y. T., et al. (2008). Relationship of serum anti-Mullerian hormone concentration to age of menopause. *Journal of Clinical Endocrinology and Metabolism, 93*(6), 2129–2134.

van Meurs, J. B. J., Dhonukshe-Rutten, R. A. M., Pluijm, S. M. F., van der Klift, M., de Jonge, R., Lindemans, J., et al. (2004). Homocysteine levels and the risk of osteoporotic fracture. *New England Journal of Medicine, 350*(20), 2033–2041.

van Noord, P. A., Dubas, J. S., Dorland, M., Boersma, H., & te Velde, E. (1997). Age at natural menopause in a population-based screening cohort: The role of menarche, fecundity, and lifestyle factors. *Fertility & Sterility, 68*(1), 95–102.

Van Voorhis, B. J., Santoro, N., Harlow, S., Crawford, S. L., & Randolph, J. (2008). The relationship of bleeding patterns to daily reproductive hormones in women approaching menopause. *Obstetrics and Gynecology, 112*(1), 101–108.

Vincent, A., Barton, D. L., Mandrekar, J. N., Cha, S. S., Zais, T., Wahner-Roedler, D. L., et al. (2007). Acupuncture for hot flashes: A randomized, sham-controlled clinical study. *Menopause, 14*(1), 45–52.

Vivekananthan, D. P., Penn, M. S., Sapp, S. K., Hsu, A., & Topol, E. J. (2003). Use of antioxidant vitamins for the prevention of cardiovascular disease: Meta-analysis of randomized trials. *Lancet, 361*(9374), 2017–2023.

Weiss, N. S., Ure, C. L., Ballard, J. H., William, A. R., & Daling, J. R. (1980). Decreased risk of fractures of the hip and lower forearm with postmenopausal use of estrogen. *New England Journal of Medicine, 303*, 1195–1198.

Willhite, L. A. (2001). Urogenital atrophy: Prevention and treatment. *Pharmacotherapy, 21*, 464–480.

Wilmoth, M. C. (1996). The middle years: Women, sexuality, and the self. *Journal of Obstetric, Gynecologic, and Neonatal Nursing, 25*(7), 615–621.

Wilson, R. (1966). *Feminine forever*. New York: Evans.

••Woods, N. F., & Mitchell, E. S. (2008). Mid-life women's health. In C.I. Fogel, & N. F. Woods (Eds.), *Women's health care in advanced practice nursing* (pp. 121–148). New York: Springer.

World Health Organization (WHO). (2007). WHO FRAX Technical Report. Retrieved June 6, 2008, from http://www.shef.ac.uk/FRAX/

Wyon, Y., Lindgren, R., Lundberg, T., & Hammar, M. (1995). Effects of acupuncture on climacteric vasomotor symptoms, quality of life, and urinary excretion of neuropeptides among postmenopausal women. *Menopause, 2*, 3–12.

Wysocki, S., Alexander, I., Schnare, S. M., Moore, A., & Freeman, S. B. (2003). Individualized care for menopausal women: Counseling women about hormone therapy. *Women's Health Care: A Practical Journal for Nurse Practitioners, 2*(12), 8–16.

Francie did you want this ref to replace the citation for Woods & Mitchell on pages 19 & 20?