NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health.

StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-.

Menopause

Authors

Kimberly Peacock[1]; Karen Carlson[2]; Kari M. Ketvertis[3].

Affiliations

[1] FIrelands Regional Medical Center
[2] University of Nebraska Medical Center and Nebraska Medicine
[3] Firelands Regional Medical Center

Last Update: December 21, 2023.

Continuing Education Activity

Menopause is a normal condition involving the permanent end of menstrual cycles due to the cessation of the production of reproductive hormones from the ovaries for at least 12 consecutive months. It is a diagnosis that is made retrospectively. Menopause occurs in all menstruating females due to nonpathologic estrogen deficiency. Many women experience symptoms for several years before menopause, which is marked by the final menstrual period. Most women experience vasomotor symptoms, but menopause can affect many different organ systems. This activity reviews the presentation, evaluation, and management of menopause and stresses the role of an interprofessional team approach to evaluating, treating, and improving care for women.

Clinicians will explore the various symptoms women may experience in the years leading up to menopause and will gain comprehensive insights into the normal condition of menopause. Participants will acquire a heightened appreciation for the complexities of menopausal care, ensuring they are well-equipped to navigate the challenges and provide evidence-based, patient-centered solutions in clinical practice.

Objectives:

- Assess the etiology of menopause.
- Identify the most common symptoms of menopause.
- Select the available treatment and management options for bothersome symptoms of menopause.
- Implement interprofessional team strategies for improving coordination and communication to advance menopause management.

Access free multiple choice questions on this topic.

Introduction

Menopause is the natural and permanent cessation of menses resulting from estrogen deficiency that is not associated with a pathologic process. The name menopause comes from the Greek words *pausis,* which means pause, and *men,* which means month. Amenorrhea lasting for twelve months marks the end of a woman's reproductive, childbearing time.[1] This occurs between the ages of 45 and 56 years in most women. The median age of natural menopause is 51 years in the United States.[2] Most women experience vasomotor symptoms, but menopause can affect many other organ systems, such as urogenital, psychogenic, and cardiovascular. This review presents hormonal and nonhormonal treatments, as well as complications of menopause. As women live longer, they spend roughly 40%of their lives in the postmenopausal years, which equates to more than 30 years for most women.[2]

Etiology

As women grow older, their ovarian follicles diminish in number due to atresia and ovulation.[1] There is a decline in granulosa cells of the ovary, which were the leading producers of estradiol and inhibin B.[3] Antimullerian hormone (AMH) levels, another hormone secreted by the ovary's granulosa cells, also decrease. With the lack of inhibition on

gonadotropins from estrogen and inhibin A and B, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) production increases.[4] This decline in estrogen levels also disrupts the hypothalamic-pituitary-ovarian axis. As a result, a failure of endometrial development occurs, which may cause irregular menstrual cycles until menses eventually stop completely.

Frequently, the initial menstrual symptom in the perimenopausal timeframe is a shortened follicular phase. This causes more frequent menses. Next, the menstrual cycle length usually increases. Cycles may become anovulatory and cause perimenopausal abnormal uterine bleeding. Eventually, menses stop.[1] Since testosterone levels do not change significantly early in menopause, there is a relative increase in the ratio of testosterone to estrogen, which can lead to symptoms of excess androgens.[5]

Menopause may occur due to surgical procedures such as bilateral oophorectomy. Menopause can also be caused by treatment for certain conditions, like endometriosis, cancer chemotherapy, especially with alkylating agents, radiation, chronic illnesses, like HIV-AIDS, or other therapies with antiestrogenic agents.[6] This article will focus on natural menopause.

Epidemiology

In the United States, approximately 1.3 million women become menopausal each year. Menopause typically begins between the ages of 45 and 56 years.[7] However, about 5% of women experience early natural menopause, occurring between the ages of 40 and 45 years. Additionally, 1% of women experience primary ovarian insufficiency with complete cessation of menses before the age of 40 years due to permanent ovarian failure.[8]

Black and Hispanic women have more frequent rates of premature and early menopause than white women. The incidence of premature menopause in black and Hispanic women is 1.4% versus 1% for white women. Similarly, the incidence of early menopause in black and Hispanic women is 3.7% to 4.1% compared to 2.9% for white women. However, when confounding factors are considered, race does not seem to contribute to the differences in the timing of menopause for an individual patient. Yet, it may be a contributor when looking at the population level.[8] [9] Additionally, Black women consistently have more bothersome issues with vasomotor symptoms of menopause than other racial groups. Eighty percent of Black women experience vasomotor symptoms, and the median duration is 10.1 years. Of White women, 65% experience vasomotor symptoms with a median duration of 6.5 years.[9]

Pathophysiology

Menopause is a normal physiologic process in aging women in which the number of primary ovarian follicles quickly diminishes, such that there are inadequate amounts to respond to the effects of FSH. In turn, there is no LH surge, and ovulation does not occur, resulting in the decline of estrogen production and the cessation of menstruation. LH and FSH go uninhibited and remain at high levels years after the onset of menopause. Small amounts of estrogen may still be produced via conversion from testosterone released by the adrenal glands, such that symptoms other than the discontinuation of periods may be negligible in some individuals.[10]

Although more than 80% of women experience menopausal symptoms, there is much variation in women's personal experiences of menopausal changes. Many factors can play into the physiologic processes of menopause. These include diet, smoking, ethnicity, medical problems, exercise, socioeconomic background, body mass index, and overall gynecologic health.[5]

Histopathology

Although menopause affects various tissues at a microscopic level, the focus here will be mainly on the gynecologic manifestations of the condition.

Ovaries

The maximum and finite number of follicles in the ovary occurs in neonatal life. One million follicles are present at birth. At puberty, 250,000 to 400,000 follicles remain. In menopause, follicles age, and structures within the ovaries change. Ovarian aging involves not only a decrease in the number of follicles but also a decrease in the quality of

oocytes. Changes are noted in the telomere, mitochondria, and other components of the ovary. Mechanisms involved in ovarian aging are still not thoroughly understood on a cellular level.[11]

Urogenital

There is a significant change in the vulva and vagina during menopause due to decreasing levels of estrogen. Inflammation of the mucosal surfaces occurs with resultant erythema and friability. An increase in vaginal pH and parabasal cells is noted. There is a narrowing of the introitus, labial thinning, and decreased depth and width of the vagina.[12]

History and Physical

The history and physical examination findings associated with menopause should focus on symptoms related to estrogen deficiency.

Vasomotor Symptoms

Vasomotor symptoms are the most common symptoms seen during the menopausal transition years. Approximately 75% and up to 80% of women experience vasomotor symptoms, varying in severity. These symptoms may include hot flashes, night sweats, palpitations, and migraines. Hot flashes occur day and night at unpredictable intervals, often lasting approximately 3 to 4 minutes each. A hot flash starts with a sensation of flushing that spreads to the upper body due to central nervous system changes specific to thermoregulation. Hot flashes can impact the daily quality of life as well as the sleep of some women. Vasomotor symptoms last on average for 1 to 6 years but can last up to 15 years in 10% to 15% of postmenopausal women.[5] They may be worsened by alcohol, smoking, obesity, physical inactivity, and emotional stress.

Migraines may change in intensity and severity with menopause. Migraines are neurovascular headaches that may be triggered by fluctuating estrogen levels. During early menopause, the fluctuating levels of estrogen that are seen may worsen migraines. After menopause, most women experience improvement in their migraines. However, few may have worsening migraines. Migraines with aura have an associated increased risk of stroke, especially with concomitant smoking or the use of oral contraceptives.[13] Other types of headaches, such as cluster and tension headaches, may also increase with a change in hormone levels.

Genitourinary Symptoms

Approximately 50% to 75% of women experience genitourinary syndrome of menopause. The vaginal mucosa thins, and there is reduced elasticity of the vagina. These changes can cause vaginal dryness, burning, pruritus, and irritation. Urinary symptoms of frequency and urgency are common, as there are estrogen receptors on the bladder and urethra. Urethral atrophy may result in frequency, urgency, and dysuria.[5]

The low estrogen effects of menopause may also cause recurrent urinary tract infections due to increased bacterial colonization of the vagina with bladder pathogens from the increase in vaginal pH in menopause.[12] Urinary incontinence, however, is not related to estrogen level declines or menopause. Rather, being overweight, diabetic, and increasing age are factors associated with more frequent urinary incontinence episodes. A decline in sexual function may begin almost 2 years before the final menstrual period, and this decline is smaller in black women as compared to white and Japanese women.[12]

Psychogenic Symptoms

Up to 70% of women experience psychogenic symptoms associated with perimenopause and menopause.[14] These symptoms may include anger/irritability, anxiety/tension, depression, loss of concentration, and loss of self-esteem/confidence. Sleep apnea, insomnia, and restless leg syndrome may cause further sleep disturbances that are not explained purely by night sweats. Because there are estrogen receptors in a variety of regions of the brain in areas that regulate mood and cognition, it is not surprising that a decrease in levels of estrogen affects mood. In addition, estrogen has mediating effects on serotonin and noradrenaline transmission, both of which may benefit mood.[14] Alternatively, some mood changes may be attributed to changes in personal life and social circumstances rather than hormonal changes.[5] The risk of depressive symptoms and a higher level of depressive symptom severity are noted in perimenopause as compared to premenopausal women. Vasomotor symptoms and a

variety of other potential reasons that have not yet been well-delineated may be associated with this increase in depression seen especially in perimenopausal but also in menopausal women.[15]

Physical Examination

- Blood pressure: Elevated blood pressure may be noted resulting from arterial vasoconstriction.
- Weight and height: Weight gain may be noted, as many women report some degree of weight gain during menopause. The North American Menopause Society stated women gained an average of 5 pounds (2 kg) over the menopause transitional period. Additionally, a decrease in height may be noted, associated with osteoporosis.
- Breast and vagina: Breasts increase in fatty deposition and show involution after menopause. Vaginal changes may include dryness and urogenital atrophy.
- Arthralgias and sarcopenia (gradual loss of muscle mass, function, and strength) may occur.

Sleep

Menopausal women generally report more sleep difficulties than premenopausal women, regardless of hormone replacement therapy (HRT) use or the presence of vasomotor symptoms. Sleep disturbances include trouble falling asleep, waking up earlier than planned, and especially waking up several times during the night. Black and white women experience the latter sleep problem more frequently than other racial and ethnic groups, with Hispanic women having the least problems with sleep.[16]

Cognitive Performance

There may be a temporary decrease in some aspects of cognitive performance, specifically an absence of learning, during the perimenopausal timeframe, which resolves in the postmenopausal years. However, age-related cognitive decline is more related to age than to the time since the start of menopause.[16]

Sexual Function

Estrogen plays an essential role in female sexual function.[17] Sexual desire and function may decrease, and pain with sexual intercourse may increase related to the menopausal transition.[16]

Bone

Healthy normal bone is constantly remodeled via a 5-step process, which involves osteoclast resorption and osteoblast production. During menopause, estrogen deficiency increases osteoclastic activity such that there is an imbalance of osteoclastic and osteoblastic activity. This results in more bone being reabsorbed and overall bone loss. Bone mineral density loss likely begins several years before menopause starts.[16]

Evaluation

Generally, no laboratory tests are required for the diagnosis of menopause. The diagnosis is made clinically based on the patient's age and symptoms.[1] Symptoms may precede changes in laboratory values. In some clinical situations, like women who are amenorrheic due to previous hysterectomy, endometrial ablation, or women with anovulation, measuring hormone levels, particularly follicle-stimulating hormone (FSH) and estradiol levels, can help diagnose menopause. The use of serum antimullerian hormone (AMH) levels for predicting the age of menopause is controversial, and more studies are needed, especially as they relate to comparing AMH levels of different ethnicities. AMH levels may be a marker for functional ovarian reserve, however, there is a variable decline in AMH levels among women. Therefore, AMH levels may require additional variables to accurately predict a woman's age at menopause.[18]

An elevated serum FSH (>30 mIU/mL) is an objective indicator of menopause. It is important to remember that pelvic surgeries may elevate FSH levels transiently, so to assess menopausal status, FSH should not be drawn until at least 3 months postop.[6] Estradiol levels of <20 pg/mL are suggestive of menopause.[9] However, the FSH levels of women aged 40 to 50 years vary significantly and do not stabilize until 3 to 6 years after menopause.[19] Levels of Inhibin B and AMH are not routinely measured to help with diagnosing menopause, as discussed above.

Due to the significant variation in hormone levels, measurements of FSH and estradiol are not routinely indicated to diagnose menopause.[7] Estradiol levels during perimenopause are known to average about 20% to 30% higher than premenopausal levels. Other laboratory evaluations that may be helpful to rule out causes for amenorrhea other than menopause include human chorionic gonadotropin, thyroid stimulating hormone, and prolactin. Of note, medications like estrogens, androgens, and hormonal contraceptives may alter FSH lab results. Hormonal testing should be done at least 2 weeks after discontinuing hormonal medications.[1]

Treatment / Management

According to the 2022 North American Menopause Society Position Statement, menopause treatment and management revolve around minimizing disruptive symptoms and preventing long-term complications. The overall timing hypothesis for the use of HRT in menopause suggests that the most favorable use of HRT is when it is started within 10 years of the final menstrual period and before the age of 60 to reduce the increased incidence of stroke, systemic embolism, and transient ischemic attack. Initiation of hormone therapy beyond 10 years after the final menstrual period or at an age older than 60 years comes with a less favorable risk-to-benefit ratio. There are no standard recommendations for the age of stopping HRT because women may experience vasomotor symptoms for many years. Thus, therapy may be continued on an individual basis and at the lowest dose that controls symptoms.

Systemic Hormonal Treatment

Hormonal therapy is primarily indicated to treat moderate to severe vasomotor symptoms of menopause.[7] It is the most beneficial treatment for bothersome vasomotor symptoms. Systemic hormonal treatment can be given in various forms (tablets, sprays, gels, vaginal rings, or patches), in different modalities (continuous versus cyclic), and is available as estrogen alone, estrogen-progestin combination, estrogen-bazedoxifene, and progestin alone. The use of unopposed estrogen should be avoided in women with a uterus. A progesterone to prevent endometrial hyperplasia and cancer should be added in these patients. The use of estrogen alone in women with an intact uterus will increase the incidence of endometrial hyperplasia to about 30% in 1 year. Bazedoxifene, a selective estrogen receptor modulator, may be used to reduce the risk of endometrial hyperplasia and cancer as an alternative to progesterone.[7]

Systemic hormonal therapy significantly decreases the severity and frequency of hot flashes and improves urogenital atrophy and sleep disturbances. It is also useful in preventing osteoporosis and associated fractures. However, hormone therapy should only be used for the shortest duration of time and at its lowest effective dose, as estrogen therapy alone increases the relative risk of deep venous thromboembolism and stroke. Combination HRT also may increase the risk of breast cancer. However, the absolute increased risk in women in early menopause is minimal.[7]

It is unclear if systemic HRT influences the risk of coronary heart disease, as more studies need to be done in this area. Estrogen plus progesterone therapy increases the risk of breast cancer, stroke, pulmonary embolism, and deep vein thrombosis but not coronary heart disease. Estrogen is contraindicated in those with a history of breast cancer, endometrial cancer, deep vein thrombosis, pulmonary embolism, liver disease, and unexplained vaginal bleeding. Although they are sometimes used off-label, levonorgestrel-containing intrauterine devices are not FDA-approved for protecting the endometrium.[7]

Systemic HRT's effects on cardiovascular disease in postmenopausal women vary based on when the treatment is started. Beginning HRT within 10 years of the final menstrual period has been shown to decrease cardiovascular disease and all-cause mortality. However, the use of hormones is not recommended solely for preventing heart disease.[20]

Transdermal estrogen has fewer adverse effects on coagulation and inflammatory markers than oral estrogen, possibly avoiding the increase in venous thromboembolism risk. Migraine with aura is, therefore, not a contraindication for the use of transdermal estrogen replacement therapy.[13] More robust evidence currently exists for transdermal estrogen as a beneficial treatment for mood changes in the perimenopausal timeframe.[14]

The Federal Drug Administration (FDA) does not approve of compounded preparations of bioidentical hormones, because they are not monitored for quality and not evaluated for safety or efficacy. These preparations should be avoided, as controlled studies have not been done with them.[7]

According to the United States Preventative Services Task Force statement from November 2022, systemic HRT should not be used for the primary prevention of chronic conditions in postmenopausal persons.[7] This conclusion was made with moderate certainty, as no benefit to systemic hormonal therapy in preventing chronic conditions has been found. Indications for systemic HRT in menopausal women are limited to treating menopausal symptoms. The data analyzed to come to this conclusion came from the Women's Health Initiative trials, as these were the only studies with enough participants to assess the prevention of various chronic conditions.[2]

Local Estrogen Treatment

Women who are not on systemic hormonal therapy almost inevitably develop the genitourinary syndrome of menopause. Even women taking systemic hormone replacement may need additional local estrogen therapy for the relief of urogenital symptoms. Recurrent urinary tract infections are not reduced with systemic HRT alone, and local estrogen therapy reduces this risk by acidifying the vagina and allowing lactobacillus to dominate the flora.[12] For atrophic vaginitis, localized estrogen therapy via vaginal rings, creams, or tablets has been shown to enhance blood flow and reverse vaginal atrophy. Many women who are unable to take systemic hormonal replacement therapy are still candidates for local estrogen therapy without the need for progesterone. These local therapies show improvements in vulvovaginal health that are fully achieved after 2 to 3 months of use.[12]

Intravaginal dehydroepiandrosterone is also used to treat local symptoms of menopause. This therapy can help dyspareunia and vaginal dryness and improve the vaginal pH and maturation index of the vagina.

Oral ospemifene is approved for use in the treatment of dyspareunia due to menopause. Once daily oral dosing improves vulvovaginal symptoms similar to local estrogen therapy but is not approved for use with breast cancer and may increase venous thromboembolism risks.[12]

Minimally ablative fractional carbon dioxide laser therapy of the vagina causes skin resurfacing but remains a controversial and costly approach with unknown long-term effects on the vagina. More studies must be performed before wide use of laser therapy is recommended.[12]

Selective Estrogen Receptor Modulators

Selective estrogen receptor modulators (SERMS), such as raloxifene, tamoxifen, bazedoxifene, and ospemifene, have varying mechanisms of action, each having a unique response in different tissue types.[21] SERMs may act on 1 tissue type as an estrogen agonist and on another tissue type as an antagonist. As noted above, ospemifene is approved for the treatment of the genitourinary syndrome of menopause.[21] Thus, SERMs are commonly used as versatile compounds for treating and preventing various medical conditions, some of which may be beneficial for use in menopausal women.

Nonhormonal Treatment

Selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and gabapentin can be used for the treatment of vasomotor menopausal symptoms. SSRIs and SNRIs, like paroxetine, escitalopram, and venlafaxine, are antidepressants that treat vasomotor symptoms. Paroxetine, in particular, is the only FDA-approved drug for this indication, and symptoms diminish within a week of initiating treatment. Paroxetine and fluoxetine, however, should not be used concurrently with tamoxifen due to inhibitory effects on the CYP2D6 enzyme.[22][23]

While not FDA-approved for the treatment of vasomotor symptoms, gabapentin has been shown to reduce hot flashes in menopausal women. High doses of gabapentin (900 mg/d to 2400 mg/d) reduce hot flashes as much as estrogen and at least up to 2 hot flashes per day. Clonidine may be modestly effective in mild hot flashes, but it is less effective than SSRIs/SNRIs and gabapentin and is generally not recommended.[22]

Neurokinin B, acting through the neurokinin 3 receptors (NK3R) in the infundibular nucleus of the hypothalamus, has been recently implicated in the cause of hot flashes of menopause. The NK3R antagonists are showing encouraging treatment results and safety as nonhormonal therapy for vasomotor symptoms of menopause. Initial studies suggest that they may be more effective than SNRIs.[23] Fezolinetant is now FDA-approved as an NK3R antagonist that is used for moderate to severe vasomotor symptoms. It is used as a single dose at 45 mg per day that does not need

titration. Headache is the most common adverse effect. Oxybutynin 2.5 mg or 5 mg twice daily up to 15 mg extended-release daily may improve vasomotor symptoms of menopause in a dose-dependent fashion.[22]

Osteoporosis-Specific Treatment

The FDA has approved systemic HRT to prevent but not treat osteoporosis. However, women with osteoporosis and vasomotor symptoms that are not bothersome should not be prescribed HRT.[7] For menopausal women experiencing osteoporosis alone, bisphosphonates, denosumab, and calcium and vitamin D supplementation can be utilized. Bisphosphonates inhibit osteoclast action and resorption of bone. They have been shown to be safe and efficacious in treating osteoporosis. However, there may be a risk of developing adynamic bone at high doses and over a prolonged period. For this reason, periodic discontinuation of this drug class is recommended, as bone density is retained for quite a few years.

Denosumab is a monoclonal antibody to the receptor activator of the nuclear factor kappa-B ligand, otherwise known as RANKL. It inhibits the osteoclasts and their activity, such that bone resorption decreases and bone density increases. In turn, it reduces the risk of fractures in menopausal women with osteoporosis. It is given as a subcutaneous injection on a biannual basis.[24]

Nonprescription Remedies

There is limited evidence to support dietary modifications in improving vasomotor symptoms of menopause.[22] Complementary and alternative treatments include phytoestrogens, vitamin E, and omega-3 fatty acids. Vitamin E, milk thistle, and omega-3 fatty acids have been used to treat the vasomotor symptoms of menopause. They are generally safe; however, studies have shown they are no better than placebo. Relaxation therapy, cannabinoids, wild yam, dong quai, evening primrose oil, ginseng, chaste berry, phytoestrogens, exercise, black cohosh, chiropractic, and acupuncture have not been shown to alleviate vasomotor symptoms.[7]

Lifestyle practices such as wearing breathable clothing, using fans or cold packs under pillows, lowering the room temperature, and using a forehead cooling device are feasible but have not shown benefit in clinical trials. The same applies to exercise, yoga, and avoiding triggers like hot liquids and certain foods. Weight loss, hypnosis, and cognitive behavioral therapy may, however, improve some women's vasomotor symptoms.[22]

Differential Diagnosis

If typical menopausal symptoms occur at 45 years of age or older, a diagnosis of menopause can be made clinically without testing. In younger women, it is necessary to exclude other diagnoses that cause secondary amenorrhea. The most common cause of secondary amenorrhea is pregnancy, and it should be ruled out first.[25]

Anatomic defects: Some causes of amenorrhea in women less than 45 years of age include anatomic defects, such as Asherman’s syndrome, the scarring of the uterine cavity that usually occurs after dilation and curettage (D&C). In addition, chronic endometritis from infections, specifically tuberculosis, can cause intrauterine scarring.[26]

Hypothalamic-pituitary-gonadal axis dysfunction: Amenorrhea may result from a dysfunction in the hypothalamic-pituitary-gonadal axis. Etiologies of cessation of menses in this category include obesity, anorexia, bulimia, chronic illnesses (kidney disease and inflammatory bowel disease), certain medications, excessive exercise, poor nutrition, stress, and malignancy.[25] Celiac disease, adrenal disorders, chemotherapy or radiation, Sheehan syndrome (necrosis of the anterior pituitary), and pituitary adenoma should also be considered. Ovarian dysfunction from ovarian tumors, polycystic ovarian syndrome, and premature ovarian insufficiency may be included in the differential diagnosis of the absence of menses in women younger than 45 years.[25]

Staging

During the Stages of Reproductive Aging Workshop (STRAW) in 2011, the STRAW + 10 staging system was established by 41 scientists who convened and proposed modifications to the original STRAW staging.[6] Since then, this system has become the gold standard in the staging of menopause. The STRAW + 10 criteria apply to most women and have advanced the understanding of women's health.[27] The principal criteria rely on the menstrual cycle (with supportive criteria being lab work) and divide the female reproductive cycle into 3 general categories:

reproductive, menopause transition, and postmenopause. Menopause is considered point 0. There are 10 stages to the STRAW criteria. Five stages come before the final menstrual cycle, and 2 come after.[27]

Reproductive Stage (stages -5, -4, -3b and -3a)

During the reproductive stage, which begins with menarche, the menstrual cycle is regular. There may be variability earlier on following menarche, as well as slight changes to flow (lighter or heavier) and duration (shorter or longer) before entering the next stage. Supportive lab work may be done during the late reproductive stage and typically conveys low to variable levels of FSH when blood is drawn between days 2 and 5 of the menstrual cycle. The late reproductive stage of -3 is subdivided into stages -3b and -3a. These 2 stages vary in the menstrual cycle characteristics and levels of FSH.[27]

Menopausal Transition Stage (stages -2 and -1)

The menopausal transition stage is when perimenopause primarily occurs. This stage is subdivided into the early (-2) and late (-1) menopausal transition. Earlier in this stage, the menstrual cycle undergoes variability in duration, such that the length of time between menstruation differs by 7 or more days each cycle. As this stage progresses, women typically experience amenorrhea for a period of 60 or more days. Once this occurs, women are in the late menopausal transition stage (-1), which takes place for 1 to 3 years before the final menstrual period occurs. Supportive lab work may show a variable elevated FSH level earlier in the menopausal transition stage and an elevated FSH >25 IU/L in the late menopausal transition phase. The FSH >25 IU/L is due to the decline of estrogen production.[27] In the late menopausal stage of -1, women may likely begin to experience vasomotor symptoms.[27]

Postmenopause Stage (stages +1a, +1b, +1c, and stage +2)

The postmenopause stages begin when menstruation has ceased. Perimenopause continues until there has been no menstruation for 1 year. Early postmenopause, or stage +1, is subdivided into stages +1a, +1b, and +1c. Stage +1a includes the 12 months after the final menstrual period. Stage +1b is the year prior to stage +1c. Stage +1c marks the stabilization of high FSH and low estradiol levels. Then, early postmenopause continues for another year. Supportive lab work conveys that this interval of time is characterized by an elevated FSH level >40 IU/L, in which women are more likely to experience vasomotor symptoms. As the postmenopause stage progresses, lab work indicates that FSH levels stabilize and antral follicle count is very low. After 3 to 6 years, women enter into late postmenopause, stage 2, in which they may experience more symptoms of urogenital atrophy. Stage +2 continues until the end of life.[27]

Prognosis

Menopause, by definition, is the point in time 12 months after the final menstrual period occurs. However, the menopausal transition and postmenopausal stages may last several years. Vasomotor symptoms from menopause usually last more than 7 years and may continue beyond 10 years past the final menstrual period in some women.[7] If untreated, vasomotor symptoms will eventually dissipate after approximately 7.4 years. However, 10% to 20% of women have intolerable hot flashes.[23] Additional information has been gathered from 1 of the largest and longest studies, the SWAN study, which started in 1996. This study looked at over 3000 women at multiple locations in the United States as they went through menopause. Interviews and questionnaires were collected from various ethnic and racial groups to help understand the menopausal transition and midlife aging.

For those women with moderate to severe vasomotor symptoms, HRT may be utilized. Additional medications can be used, depending on specific symptoms that are bothersome. Therefore, with treatment, the prognosis of menopausal symptoms is very good.

Complications

Long-term complications related to menopause are associated with decreased estrogen levels. Cardiovascular disease and osteoporosis are the most concerning of complications.

Cardiovascular Disease

During menopause, the decline in estrogen causes an increased risk for cardiovascular disease in women. Several changes underlie this increased risk, including negative changes in the lipid profile, impaired arterial endothelial

function, and activation of the renin-angiotensin system.[20] Coronary heart disease rates are 2 to 3 times higher in those who have reached menopause than those of the same age who have not. For this reason, menopausal and postmenopausal women are encouraged to maintain a healthy diet and exercise to mitigate any possible risk factors.

Osteoporosis

More than 250,000 menopausal and postmenopausal women are affected by osteoporosis. The characteristic bone loss or decreased bone density in osteoporosis is due to estrogen deficiency in these women. At the age of 40, women begin to lose bone at a rate of 0.3% to 0.5% per year. During menopause, women experience an increased rate of bone loss of 3% to 5% per year for 5 to 7 years. In the Women's Health Initiative study, HRT was chosen to decrease osteoporotic fractures. This study and various others have shown that hormone therapy is protective against menopausal bone loss. However, there are risks associated with the long-term use of hormone therapy. For this reason, several other approaches to decreasing the risk of osteoporosis and related injuries are encouraged. Among these approaches are smoking cessation, physical activity, calcium supplementation, and nonhormonal treatments such as bisphosphonates and denosumab, which are antiresorptive medications. Anabolic medications, like teriparatide and romosozumab, are the second class of medical therapies available for the treatment of osteoporosis in postmenopausal women.[28]

Deterrence and Patient Education

Key educational facts to keep in mind about menopause are as follows:

- Patients should be encouraged to stop smoking, especially if considering starting HRT.
- Women should aim to do 150 minutes of cardiovascular exercise per week and 2 to 3 days of weight-bearing exercise.
- Women should eat a healthy diet to maintain a healthy weight.
- Women should feel comfortable speaking to healthcare providers if they are having painful intercourse.
- Contraception is recommended until menopause or age 50 to 55, as the specific age at which reproductive capacity ends is unknown. HRT is not a reliable method of contraception.[19]
- If bothersome menopausal symptoms are present, discussion with a medical provider is encouraged because many treatment options are available.
- Compounded bioidentical hormone therapy is not recommended for use due to a lack of data regarding efficacy and safety, as well as unsubstantiated marketing claims.[29]

Enhancing Healthcare Team Outcomes

Although menopause is a physiological condition and not a disease, it can have significant associated morbidity. The symptoms of menopause, particularly vasomotor symptoms, are at times poorly tolerated and lead to poor quality of life. Most menopausal women are seen in clinical practice by advanced care practitioners, gynecologists, primary care physicians, or internists. Enhancing patient-centered care, outcomes, patient safety, and team performance related to menopause requires a collaborative and multidisciplinary approach.

Healthcare professionals, including nurses and pharmacists, should educate patients on the stages and expectations of menopause and the perimenopausal years. Women who struggle to tolerate symptoms of menopause should be offered individualized treatment based on their symptoms, desires, and risk factors. Hormonal agents should only be used to treat vasomotor symptoms for the shortest period of time needed and at the lowest dose for symptom relief. HRT is not recommended to prevent chronic diseases; therefore, additional skills, strategies, and care coordination of health professionals are necessary to utilize other methods of chronic disease prevention for women.

Nurses can play various roles, including emphasizing patient education and preventative measures. Dieticians can help educate patients about maintaining a healthy diet and healthy weight. Women should be encouraged to exercise

regularly, discontinue smoking, and be offered systemic or local estrogen therapy if symptoms indicate a need. Since perimenopause can also result in mood changes, a mental health care provider may be recommended to enhance patient outcomes. Clinicians should be aware of the various body systems that can be affected by menopause and be alert to available strategies to minimize complications that occur after menopause. The pharmacist may help in communication by teaching and urging women not to take untested, unregulated compounded hormones and products and to seek guidance from reliable clinicians.

A successful approach to menopause care involves honing specialized skills, implementing strategic practices, sharing responsibilities, fostering effective interprofessional communication, and ensuring seamless care coordination. By collectively leveraging the strengths of diverse healthcare professionals, patient-centered care for menopausal individuals can be optimized, leading to improved outcomes and enhanced overall team performance.

Review Questions

- Access free multiple choice questions on this topic.
- Click here for a simplified version.
- Comment on this article.

References

1. McNeil MA, Merriam SB. Menopause. Ann Intern Med. 2021 Jul;174(7):ITC97-ITC112. [PubMed: 34251902]
2. US Preventive Services Task Force. Mangione CM, Barry MJ, Nicholson WK, Cabana M, Caughey AB, Chelmow D, Coker TR, Davis EM, Donahue KE, Jaén CR, Kubik M, Li L, Ogedegbe G, Pbert L, Ruiz JM, Stevermer J, Wong JB. Hormone Therapy for the Primary Prevention of Chronic Conditions in Postmenopausal Persons: US Preventive Services Task Force Recommendation Statement. JAMA. 2022 Nov 01;328(17):1740-1746. [PubMed: 36318127]
3. Hall JE. Endocrinology of the Menopause. Endocrinol Metab Clin North Am. 2015 Sep;44(3):485-96. [PMC free article: PMC6983294] [PubMed: 26316238]
4. Tanbo TG, Fedorcsak PZ. Can time to menopause be predicted? Acta Obstet Gynecol Scand. 2021 Nov;100(11):1961-1968. [PubMed: 34546564]
5. Talaulikar V. Menopause transition: Physiology and symptoms. Best Pract Res Clin Obstet Gynaecol. 2022 May;81:3-7. [PubMed: 35382992]
6. Harlow SD, Gass M, Hall JE, Lobo R, Maki P, Rebar RW, Sherman S, Sluss PM, de Villiers TJ., STRAW+10 Collaborative Group. Executive summary of the Stages of Reproductive Aging Workshop +10: addressing the unfinished agenda of staging reproductive aging. Climacteric. 2012 Apr;15(2):105-14. [PMC free article: PMC3580996] [PubMed: 22338612]
7. Crandall CJ, Mehta JM, Manson JE. Management of Menopausal Symptoms: A Review. JAMA. 2023 Feb 07;329(5):405-420. [PubMed: 36749328]
8. Burkard T, Moser M, Rauch M, Jick SS, Meier CR. Utilization pattern of hormone therapy in UK general practice between 1996 and 2015: a descriptive study. Menopause. 2019 Jul;26(7):741-749. [PubMed: 30889086]
9. Williams M, Richard-Davis G, Weickert V, Christensen L, Ward E, Schrager S. A review of African American women's experiences in menopause. Menopause. 2022 Nov 01;29(11):1331-1337. [PubMed: 36126249]
10. Polo-Kantola P, Rantala MJ. Menopause, a curse or an opportunity? An evolutionary biological view. Acta Obstet Gynecol Scand. 2019 Jun;98(6):687-688. [PubMed: 31087567]
11. Wang X, Wang L, Xiang W. Mechanisms of ovarian aging in women: a review. J Ovarian Res. 2023 Apr 06;16(1):67. [PMC free article: PMC10080932] [PubMed: 37024976]
12. Shifren JL. Genitourinary Syndrome of Menopause. Clin Obstet Gynecol. 2018 Sep;61(3):508-516. [PubMed: 29787390]
13. Khandelwal S, Meeta M, Tanvir T. Menopause hormone therapy, migraines, and thromboembolism. Best Pract Res Clin Obstet Gynaecol. 2022 May;81:31-44. [PubMed: 34974967]
14. Soares CN. Depression and Menopause: An Update on Current Knowledge and Clinical Management for this Critical Window. Med Clin North Am. 2019 Jul;103(4):651-667. [PubMed: 31078198]
15.

de Kruif M, Spijker AT, Molendijk ML. Depression during the perimenopause: A meta-analysis. J Affect Disord. 2016 Dec;206:174-180. [PubMed: 27475888]

16. El Khoudary SR, Greendale G, Crawford SL, Avis NE, Brooks MM, Thurston RC, Karvonen-Gutierrez C, Waetjen LE, Matthews K. The menopause transition and women's health at midlife: a progress report from the Study of Women's Health Across the Nation (SWAN). Menopause. 2019 Oct;26(10):1213-1227. [PMC free article: PMC6784846] [PubMed: 31568098]
17. Lee JH, Lee JE, Harsh V, Clayton AH. Pharmacotherapy for Sexual Dysfunction in Women. Curr Psychiatry Rep. 2022 Feb;24(2):99-109. [PubMed: 35102537]
18. Moolhuijsen LME, Visser JA. Anti-Müllerian Hormone and Ovarian Reserve: Update on Assessing Ovarian Function. J Clin Endocrinol Metab. 2020 Nov 01;105(11):3361-73. [PMC free article: PMC7486884] [PubMed: 32770239]
19. Voedisch AJ, Ariel D. Perimenopausal contraception. Curr Opin Obstet Gynecol. 2020 Dec;32(6):399-407. [PubMed: 33002952]
20. Davis SR, Baber RJ. Treating menopause - MHT and beyond. Nat Rev Endocrinol. 2022 Aug;18(8):490-502. [PubMed: 35624141]
21. Liu JH. Selective estrogen receptor modulators (SERMS): keys to understanding their function. Menopause. 2020 Oct;27(10):1171-1176. [PubMed: 32576800]
22. “The 2023 Nonhormone Therapy Position Statement of The North American Menopause Society” Advisory Panel. The 2023 nonhormone therapy position statement of The North American Menopause Society. Menopause. 2023 Jun 01;30(6):573-590. [PubMed: 37252752]
23. Menown SJ, Tello JA. Neurokinin 3 Receptor Antagonists Compared With Serotonin Norepinephrine Reuptake Inhibitors for Non-Hormonal Treatment of Menopausal Hot Flushes: A Systematic Qualitative Review. Adv Ther. 2021 Oct;38(10):5025-5045. [PMC free article: PMC8478773] [PubMed: 34514552]
24. Reid IR, Billington EO. Drug therapy for osteoporosis in older adults. Lancet. 2022 Mar 12;399(10329):1080-1092. [PubMed: 35279261]
25. Stuenkel CA, Gompel A, Davis SR, Pinkerton JV, Lumsden MA, Santen RJ. Approach to the Patient With New-Onset Secondary Amenorrhea: Is This Primary Ovarian Insufficiency? J Clin Endocrinol Metab. 2022 Feb 17;107(3):825-835. [PubMed: 34693971]
26. Singh N, Sethi A. Endometritis - Diagnosis,Treatment and its impact on fertility - A Scoping Review. JBRA Assist Reprod. 2022 Aug 04;26(3):538-546. [PMC free article: PMC9355436] [PubMed: 35621273]
27. Ambikairajah A, Walsh E, Cherbuin N. A review of menopause nomenclature. Reprod Health. 2022 Jan 31;19(1):29. [PMC free article: PMC8805414] [PubMed: 35101087]
28. Wu D, Cline-Smith A, Shashkova E, Perla A, Katyal A, Aurora R. T-Cell Mediated Inflammation in Postmenopausal Osteoporosis. Front Immunol. 2021;12:687551. [PMC free article: PMC8278518] [PubMed: 34276675]
29. Stuenkel CA, Manson JE. Compounded Bioidentical Hormone Therapy: The National Academies Weigh In. JAMA Intern Med. 2021 Mar 01;181(3):370-371. [PubMed: 33315055]

Disclosure: Kimberly Peacock declares no relevant financial relationships with ineligible companies.

Disclosure: Karen Carlson declares no relevant financial relationships with ineligible companies.

Disclosure: Kari Ketvertis declares no relevant financial relationships with ineligible companies.

Bookshelf ID: NBK507826 PMID: 29939603