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## The menopause transition and women's health at midlife

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### Abstract

The menopause is a physiological event involving ovarian failure as a result of a loss of ovarian follicular activity, which leads to estrogen deficiency, resulting in permanent cessation of menstruation and loss of reproductive function. Women undergoing the menopause are seen in a range of healthcare settings. It is important that all nurses, particularly those practising in primary care and women's health, have an understanding of the symptoms, treatment and long-term implications of the menopause on women's health and quality of life. This article outlines the symptoms of the menopause and the available treatments for these, including hormone replacement therapy, non-hormonal treatments and alternative therapies, and discusses how nurses can assist women undergoing the menopause to improve their health and quality of life during this often challenging time.

**Keywords:** Menopause, Estrogen, MHT-Menopausal hormone therapy and HRT-hormonal replacement therapy.

### Introduction

The menopause transition is experienced by 1.5 million women each year and often involves troublesome symptoms, including vasomotor symptoms, vaginal dryness, decreased libido, insomnia, fatigue, and joint pain in one population-based assessment of 386 Australian women, 86% consulted a clinician at least once to discuss menopausal symptoms. Several symptoms bear an obvious relationship to the changing hormonal milieu associated with menopause, and most women make direct linkages between menopause and the common symptoms of hot flashes, vaginal dryness, and disrupted sleep (with or without associated night sweats). In addition, during menopause, women may develop depressive symptoms and cognitive difficulties, which are more subtly and inconsistently linked to hormones. Depression and cognitive impairment can be burdensome for women and also compound the burden of medical illness for the aging female population. As postmenopausal women are already at risk for osteoporosis and cardiovascular disease, it is important to address potentially changeable psychiatric issues that may make medical issues more difficult to treat. An understanding of the risk factors, clinical presentation, and management of these common menopausal symptoms allows for improved patient care and health outcomes for older female patients.

### Epidemiology

Population-based, epidemiologic studies of menopausal women have recently been conducted and are yielding reliable and consistent information about the incidence, prevalence, and severity of several menopausal symptoms. However, the field is relatively new, and it is likely that there are subsets of women who are more or less vulnerable to particular symptoms or sets of symptoms. In 2005, a state-of-the-science conference on menopausal symptoms was convened, with a worldwide panel of expert evaluators who were tasked with determining which among the large set of midlife symptoms are most likely to be due to menopause. Symptoms were evaluated for their proximity to menopause, apart from the aging process, and the likelihood that estrogen is effective in relieving symptoms. Based on this evidence review, 3 symptoms emerged as having good evidence for linkage to menopause: vasomotor symptoms, vaginal dryness/dyspareunia, and difficulty sleeping/insomnia. After this conference and based on 3 seminal studies adverse mood/depression was added to the list.

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Adequate longitudinal studies on cognitive function during the menopause were not yet available but have also become subsequently widely reported.

### **Vasomotor symptoms**

Vasomotor symptoms afflict most women during the menopausal transition, although their severity, frequency, and duration vary widely between women. Hot flashes are reported by up to 85% of menopausal women. Hot flashes are present in as many as 55% of women even before the onset of the menstrual irregularity that defines entry into the menopausal transition<sup>[9]</sup> and their incidence and severity increases as women traverse the menopause, peaking in the late transition and tapering off within the next several years. The average duration of hot flashes is about 5.2 years, based on an analysis of the Melbourne Women's Health Project, a longitudinal study that included 438 women. However, symptoms of lesser intensity may be present for a longer period. Approximately 25% of women continue to have hot flashes up to 5 or more years after menopause. A meta-analysis of 35,445 women taken from 10 different studies confirmed a 4-year duration of hot flashes, with the most bothersome symptoms beginning about 1 year before the final menstrual period and declining thereafter.

The exact cause of the hot flash has not been elucidated. The most accessible theory purports that there is a resetting and narrowing of the thermoregulatory system in association with fluctuations in or loss of estrogen production. In the past, hot flashes were thought to be related solely to a withdrawal of estrogen; however, there is no acute change in serum estradiol during a hot flash.

### **Vulvovaginal atrophy**

Urogenital tissues are exquisitely sensitive to estrogen, and the fluctuations in estrogen that occur during the menopausal transition, followed by sustained low levels after menopause, can render these tissues fragile and cause distressing symptoms. Multiple population- and community-based studies confirm that about 27% to 60% of women report moderate to severe symptoms of vaginal dryness or dyspareunia in association with menopause in addition to vaginal atrophy, narrowing and shortening of the vagina and uterine prolapse can also occur, leading to high rates of dyspareunia. Furthermore, the urinary tract contains estrogen receptors in the urethra and bladder, and as the loss of estrogen becomes evident, patients may experience UI. Unlike vasomotor symptoms, vulvovaginal atrophy does not improve over time without treatment.

Menopausal hormone therapy (MHT) is an effective treatment of vaginal atrophy and dryness. For this purpose, systemic or vaginal estrogen can be used, although locally applied estrogen is recommended and can be administered in very low doses. These low doses are believed to be safe for the uterus, even without concomitant use of a progestin. Data are currently insufficient to define the minimum effective dose, but vaginal rings, creams, and tablets have all been tested and demonstrated to reduce vaginal symptoms.

### **Sleep disturbances and insomnia**

Sleep quality generally deteriorates with aging, and menopause seems to add an additional, acute layer of complexity to this gradual process. Women report more trouble sleeping as they enter into the menopausal transition,

and sleep has been shown to be worse around the time of menses, both by self-report as well as by actigraphy. Actigraphy studies indicate that as much as 25 minutes of sleep per night can be lost when a woman is premenstrual in her late reproductive years. Women report sleep difficulties approximately twice as much as do men. Further compromise in sleep quality is associated with the hormonal changes associated with the menopausal transition and with aging, apart from hormones. Over time, reports of sleep difficulties increase in women such that by the postmenopause more than 50% of women report sleep disturbance. Women seem to experience more detrimental effects on sleep in association with aging, when compared with men. The nature of the sleep disturbance can help guide the clinician to appropriate treatment. Women who report nighttime awakening in association with night sweats are candidates for hormone therapy. However, the clinical history is not often so simple. Women with mood disorders, particularly anxiety and depression, may experience difficulty falling asleep and/or early awakening. Women aged 40 years and older also frequently report difficulty staying asleep. Lower socio-economic status (SES), white race, and low marital happiness are social factors that have all been associated with worse sleep. Disorders such as sleep apnea and restless leg syndrome need to be considered. The clinical consequences of a poor night's sleep include daytime fatigue and sleepiness, which can be subjectively measured and form the basis for a referral for a sleep study. Displays a clinically useful scale that can help the clinician estimate the daytime impact of the sleep complaint.

### **Adverse mood**

One-fifth of the US population will have an episode of depression in their lifetime, and women are twice as likely to be affected. Although depression is more likely to occur in young adults, with peak onset in the fourth decade of life, there is evidence that the perimenopause represents another period of vulnerability for women. Several large prospective cohort studies have shown an increased risk of depressed mood during the menopause transition and an approximately 3-fold risk for the development of a major depressive episode during perimenopause compared with premenopause. Other independent risk factors for the development of depressed mood during the menopause transition include poor sleep, stressful or negative life events, lack of employment, higher body mass index, smoking, younger age, and race (African Americans twice as likely to have depressive symptoms). In addition, there is evidence that hormonal changes occurring during menopause play a role, as evidenced by increased risk for depression in association with variability in estradiol levels, increasing FSH levels, surgical menopause, the presence of hot flashes, and a history of premenstrual syndrome. There may also be significant environmental stressors present at the time that a woman reaches menopause. During midlife, a woman may be faced with changes in her marriage and family structure, with children no longer living in the home. She may experience changes in her career path, possibly returning to work or retiring. She may be taking on new responsibilities as a caregiver to her parents or in-laws, a well-known risk factor for depression. Although these factors do not likely cause depression on their own, they can certainly contribute and should be considered.

## Menopause and cognition

Many women complain of changes in their cognitive function during the menopause transition, with the majority reporting worsening of memory. Verbal memory (word list learning and recall), which women generally excel at when compared with men, is often the type of complaint noted. Women may notice difficulty remembering names and other verbally told information. In addition, they may report other cognitive challenges, with more trouble organizing and planning or possibly with concentration. In one study of 205 menopausal women, 72% reported some subjective memory impairment. Symptoms were more likely to be associated with perceived stress or depressive symptoms than perimenopausal stage, but overall, cognitive symptoms were more prevalent early in the menopause transition. Aside from being bothersome, these symptoms raise women's concerns regarding their risk for dementia; however, it remains unclear whether these symptoms correspond to an increased risk for more serious chronic issues.

## Summary

The menopausal transition and postmenopausal years are associated with significant symptoms. Vasomotor symptoms and adverse mood often demonstrate improvement after a woman is postmenopausal, whereas sleep complaints, vaginal dryness/dyspareunia, and cognitive complaints tend to persist or worsen in association with aging. There is evidence that the changing hormone milieu, with significant changes in estrogen levels, can affect the brain systems involved in mood and cognition. Patients often present to their primary care provider with these symptoms first, and endocrinologists are in a position to identify more serious issues, provide education, begin treatment, and make appropriate referrals to when necessary. A better understanding of the nature of the risk for these common symptoms in menopausal women will aid in prevention, detection, and treatment.

## The menopause: how nurses can help

About a quarter of the women going through the menopause will have severe symptoms. They may also notice emotional changes, such as mood swings, anxiety and depression. Untreated menopausal symptoms usually settle within two to three years, but they can persist for a decade. However, declining oestrogen levels also increase bone resorption, particularly in the hips, wrists and spine, which can lead to osteoporotic fractures in later life. Another consequence of the menopause is an increased risk of cardiovascular disease. Oestrogen protects the heart, so when levels fall the risk of coronary disease and stroke increases.

## How HRT works

HRT, which combines oestrogen replacement therapy with synthetic progesterone, replaces the hormones that a woman's body stops producing during the menopause. As such it is the only treatment to relieve the symptoms of the menopause and provide long-term protection against osteoporosis cardiovascular disease. Oestrogen replacement therapy alone would effectively achieve these aims, but it stimulates the growth of the endometrium, which increases the risk of endometrial cancer. To prevent this, women must also take a course of synthetic progesterone, known as progestogen. The progestogen component of HRT creates

an artificial bleed that is similar to a period. It can be taken on a monthly or quarterly basis or as continuous combined therapy. Postmenopausal women could be offered a continuous combined low-dose oestrogen-progestogen preparation. Because of the low dose, this does not encourage the growth of the endometrium.

A synthetic, period-free HRT is available which improves libido and enhances mood.

Women who have had a hysterectomy are not at risk of endometrial cancer so they can safely take unopposed oestrogens.

## Treatment methods

HRT can be administered in several ways, depending on personal preference and the possible side-effects. These methods include:

1. Oral therapy.
2. Transdermal HRT.
3. Oestrogen implants.
4. Vaginal creams, pessaries and rings.

**1. Oral therapy:** There are many different brands of oestrogen tablets. Some are fixed-dose regimens while others mimic the menstrual cycle by changing the dose throughout the 28-day course. Women with a uterus also need to take a course of progestogen tablets for about 12 days each month. The tablets are easy to take and their effects can be reversed quickly, but they can cause side-effects. Altering the dosage often alleviates the side-effects, but if they persist some women may need to switch to a different form of HRT.

**2. Transdermal HRT:** There are two forms of transdermal HRT: skin patches and oestrogen gels. Both are absorbed through the skin directly into the bloodstream. This bypasses the liver, giving them an advantage over oral treatment.

Rapid absorption provides fast and effective symptomatic relief. And women using transdermal HRT require lower doses to achieve natural physiological levels than those using oral HRT, which should limit the side-effects. A wide variety of HRT patches are available. Some contain oestrogen alone while others are made up of a combination of oestrogen and progestogen. Most have to be changed twice a week, but some seven-day systems are available. They are usually well tolerated but can cause skin irritation. Some women also find them unsightly. There are two oestrogen gels. One comes in a pump-action canister, making it easy to adjust the dose, and the other comes in sachets. Oestrogen gels are spread onto the arm, shoulder or inner thigh daily. They are alcohol-based, so they are not greasy or messy, and seldom cause skin irritation. Women who have had a hysterectomy can use unopposed oestrogen gels. All others need to take progestogen tablets or patches as well.

**3. Oestrogen implants:** Implants are small pellets of oestrogen inserted into the fat under the skin. They last six months and their main advantage is that women do not need to remember to take tablets or change patches. They are difficult to remove if they are not suitable, which means that many women have to wait until they dissolve. They can also remain in the system for some time. Women with a uterus need additional progestogen.

**4. Vaginal creams, pessaries and rings:** These are local therapies that can be useful to women who are affected only by genital symptoms, such as a dry vagina. If vaginal dryness is a continuing problem they must be accompanied by a cyclical progestogen because systemic absorption can stimulate the growth of the endometrium.

#### Indications for treatment

Oestrogen deficiency is by far the most important cause of long-term complications during and after the menopause. Oestrogen replacement therapy is therefore the only treatment that addresses the cause of the problem rather than providing only symptomatic relief.

HRT should always be considered for:

1. An early menopause;
2. Those who have had a hysterectomy, even if the ovaries remain;
3. Any woman who requests or shows an interest in HRT;
4. Menopausal women with a high risk of osteoporosis or coronary heart disease, which includes smokers, stabilised hypertension or a family history of Alzheimer's disease;
5. Long-term users of corticosteroids or thyroid replacement drugs as both could lead to a loss of bone density.

#### Contraindications

HRT is contraindicated in women with:

1. Acute-phase myocardial infarction, pulmonary embolism or deep-vein thrombosis;
2. Endometrial or breast cancer;
3. A pregnancy;
4. An undiagnosed breast mass;
5. Uninvestigated abnormal vaginal bleeding;
6. Severe liver disease with abnormal liver function tests, although if the symptoms of the menopause are severe a non-oral route should be considered.

Many of the contraindications described in prescribed data sheets are based on those for high-dose combined oral contraceptives and are not applicable to hormone replacement therapies. The following are no longer considered to be contraindications for oestrogen replacement therapy:

1. Controlled hypertension;
2. Angina or previous myocardial infarction;
3. A family history of ischaemic heart disease;
4. Varicose veins;
5. Previous superficial thrombophlebitis;
6. Heavy smoking;
7. Obesity;
8. Migraine;
9. Otosclerosis;
10. Malignant melanoma;
11. A previous abnormal cervical smear;
12. Previous cervical cancer;
13. Previous ovarian cancer;
14. Benign breast disease.

#### Duration of treatment

It is never too late to start HRT, but most specialists recommend that women begin treatment at or shortly before the menopause to gain maximum protection against

osteoporosis and cardiovascular disease. It is generally accepted that women seeking only symptomatic relief should take it for two to three years, while those who want long-term protection against osteoporosis and heart disease should continue for at least five, and preferably 10, years.

#### Conclusion

Postmenopausal women who have been counselled on the risks and benefits of HRT and the options available to them are more likely to have realistic expectations of the treatment and therefore to persevere with it. Nurses have a vital role to play in helping women to cope during and after the menopause, offering individual assessment, education and support. All those involved in counselling such women must ensure that they know where to get up-to-date information and where to direct clients who are in need of further information.

Nurses should explain all aspects of the menopause to each woman and ensure that she is aware of all the available options. This will enable women to make informed decisions on appropriate treatment and encourage them to be active rather than passive recipients of care.

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