brothers.com, for detailed information on obstetrics & gynecology books, visit our website www.jaypeebrothers.com, for detailed information on obstetrics & gynecology bo

Management of Menopause

Shaikh Zinnat Ara Nasreen

Forewords
Shahla Khatun
TA Chowdhury

Contents

1.	Introduction to Menopause	1
2.	How to Diagnose Menopause?	14
3.	Nutrition, Exercise and Lifestyle for Menopause Women	21
4.	Vasomotor Symptoms and Menopause	30
5.	Genitourinary Syndrome of Menopause	44
6.	Osteoporosis, Bone Health, and Menopause	61
7.	Cardiovascular Health and Menopause	81
8.	Brain, Cognition and Menopause	92
9.	Sexuality and Menopause	103
10.	Contraceptives in Perimenopause	110
11.	Skin Care and Menopause	119
12.	Mental Health and Menopause	131
13.	Premature Ovarian Insufficiency	140
14.	Metabolic Syndrome and Menopause	156
15.	Postmenopausal Bleeding	168
16.	Risk and Benefits of Menopausal Hormone Therapy	180
17.	Prescribing Hormone Replacement Therapy	190
Index		*209*

4 Vasomotor Symptoms and Menopause

CHAPTER

INTRODUCTION

Menopause is the permanent cessation of menstruation; ovaries stop producing estrogen; and may be associated with a wide range of symptoms. Menopause is a normal biological event that affects all women.

Life expectancy for women is increasing worldwide. Therefore, most women can expect to spend a significant portion of their lives in a postmenopausal state and may suffer from menopausal symptoms due to estrogen deficiency. The most common symptoms are vasomotor symptoms (VMS), which include hot flashes (also referred to as hot flushes) and night sweats. Beside VMS, women may suffer from vaginal dryness, sleep disturbances, and osteoporosis in addition to variety of other physical and psychological symptoms.[1] Hot flashes are one of the most common and distressing symptoms associated with menopause, occurring in >75% of postmenopausal women.[2]

Vasomotor symptoms encompass hot flashes, night sweats, feeling of cold, and palpitation. Again, VMS, or hot flashes and night sweats, are often considered the cardinal symptoms of menopause.

Hot flashes present as transient periods of intense heat in the upper body, arms, head, and face, often followed by flushing of the skin and profuse sweating all over the body. VMS can negatively affect the quality-of-life.[3] The prevalence of VMS is varying by geography, socioeconomic, and cultural context.[4] In the USA, over 60% of women have experienced VMS; the figure exceeds 60% in Europe and 50% in Australia. VMS are reported less frequently by Japanese and Chinese women but more frequently by African American women.[5]

Many to most women describe their symptoms as severe, but only approximately 20–30% of women seek medical attention for the treatment.[6-8] Women find VMS as more bothersome, even after accounting for the higher frequency of their VMS. It produces negative effects on their day-to-day activities and quality-of-life. The relationship between negative affect and VMS is not fully understood and may involve a complex interplay between physiologic and psychological factors. It is well-established that negative affect can influence symptom reporting, with a tendency toward elevated symptom reporting in the context of negative affect.[9]

JAYPEE BROTHERS

MECHANISM

The exact mechanism explaining the emergence of VMS is a mystery; however, evidence points toward a disturbance of the temperature regulating mechanism in the hypothalamus. The disturbances associated with estrogen deprivation render neurotransmitter within the central nervous system unable to maintain body temperature within the optimal range.[10] The thermoneutral zone is narrowed in women with hot flashes.[11] While premenopausal women initiate mechanisms to dissipate heat when the core body temperature increases by 0.4°C, this happens with much lower increase in temperature in menopausal women.[12]

The feeling of warmth results from inappropriate peripheral vasodilatation with increased digital and cutaneous blood flow. Perspiration results in rapid heat loss and a decrease in core body temperature below normal. Shivering may then occur as a normal mechanism to restore the core temperature to normal.[13] Estrogen (E2) administration restores the "thermoneutral zone" to normal and largely abolishes hot flashes. One hypothesis, now supported by increasing evidence, suggests that KNDy (kisspeptin, neurokinin B, and dynorphin) neurons mediate the luteinizing hormone (LH) and thermoregulatory changes.[14] High level of follicle-stimulating hormone (FSH) and low serum concentration of estrogen, testosterone, and progesterone[6] correlate with VMS. Though The Study of Women's Health Across the Nation (SWAN) fails to show any significant association between VMS and serum concentrations of estrogen, testosterone, dehydroepiandrosterone sulfate (DHEAS), sex-hormone binding globulin (SHBG) or with free testosterone index, most research indicating that E2 administration reduces VMS and widens the thermoneutral zone adds support to this treatment.[15] Recently, concern is raised for heart diseases in women suffering from VMS.

Vasomotor symptoms are shown to be associated with increased risk of cardiovascular disease,[16] and great bone loss.[17]

RISK FACTORS FOR VASOMOTOR SYMPTOMS

Obesity: Obese postmenopausal women have higher serum estrone concentrations than lean women due to increased peripheral conversion of androstenedione in adipose tissue[18,19] but paradoxically, these women are more likely to have hot flashes.[20,21] Weight loss may help reduce their hot flashes.[22] High BMI and weight gain have been documented as protective[5] and risk factors.[23] BMI did not associate significantly with psychosocial or sexual symptoms at either stage of menopause.[24]

Anxiety, depression, and perceived stress have been associated with increased VMS likelihood.[25] Negative mood has been associated with VMS.[26] VMS and mood appear to be related in numerous and potentially complex ways. However, interestingly many women with VMS do not experience mood disturbances or depression.

JAYPEE BROTHERS

Smoking and[20,21] reduced physical activity have not been related to VMS. Romani et al. reported significantly positive relation between physical activity and moderate or severe hot flashes but no relation between hot flash frequency and physical activity.[27] The effects of exercise on VMS are mixed;[28] however, increased physical activity may improve sleep and general well-being.

Socioeconomic factors: Obtaining less than a high school education and having difficulty paying for basics are associated with a higher frequency of hot flashes.[27] Low socioeconomic status has been consistently associated with VMS[28] dispelling the myth that menopausal symptoms are phenomena of the developed world.

Hormonal concentrations: Annual serum FSH levels, but not other hormones (estradiol, testosterone, DHEAS), when collectively modeled longitudinally, are associated with both the prevalence and frequency of VMS.[1]

Ethnic factors: African American women report more frequent hot flashes than Caucasian women, whereas Japanese and Chinese women report less frequent hot flashes.[5]

Genetic variants: Women who have variations in the gene that codes for tachykinin receptor 3 (*TACR3)* are more likely to experience hot flashes than women without those variations.[29]

The role of climate, environment, temperature, and altitude in the development of VMS has not been sufficiently explored. SWAN data found significant positive association between increasing seasonality and hot flashes.[30] The colligative group for research of the climacteric in Latin America found that women living at higher altitude had lower hot flashes, in contrast to UAE, where no association between season variability and hot flashes was found.

DURATION OF SYMPTOMS

It varies from woman to woman. There is no age limit at which menopausal symptoms cease. The best estimate of total VMS duration comes from the SWAN study,[31] which showed that the median total VMS duration was 7.4 years, with symptoms persisting for a median of 4.5 years after the final menstrual period. Women who were premenopausal or early perimenopausal when they first experienced VMS had the longest total duration (>11.8). Interestingly, at least 10% of women have bothersome VMS 10 years after their menopause has occurred, with as many as 16% of the 85 year olds continuing to experience VMS.[23]

PRESENTATION

Hot flashes typically begin as the sudden sensation of heat centered on the upper chest and face that rapidly becomes generalized. The sensation of heat

JAYPEE BROTHERS

often lasts from 2 to 4 minutes, is often associated with profuse perspiration and occasionally palpitations, and is sometimes followed by chills, shivering, and a feeling of anxiety. Hot flashes may range from an average of less than one each day to as many as one per hour during the day and night. Studies showed that hot flashes are associated with adverse health indicators such as increased cardiovascular risk and greater bone loss/increased bone turnover.[32,33] So history of any chest pain or bone pain needs to be evaluated thoroughly.

SLEEP DISTURBANCE

The optimum amount for a healthy adult is deemed to be around seven hours. Insufficient sleep has been shown to have later detrimental effects on things like our mental health, heart health, cognitive functions and even risk of osteoporosis. Further, too much sleep (more than 8 hours), can be associated with increased risk of cardiovascular disease though cause and effect are unclear; prolonged sleep may be a marker for underlying disease.

Vasomotor symptoms can disrupt sleep in peri- and postmenopausal women. Although VMS is not the only cause of sleep disturbance, it accounts for 27% of wakefulness during the night, the estimated prevalence of difficulty sleeping by studies was 32–40% in the early menopausal transition, increasing to 38–46% in the late transition.[34,35] There are many other issues that disturb sleep in menopause women including primary sleep disorders, anxiety, and depression.

HISTORY

Though symptoms of VMS are straightforward, it must include about the differential diagnosis of carcinoid syndrome, medications, hyperthyroidism, history of any infection, and mental disorder. Though symptoms are mainly hot flushes and night sweating, but we need to perform thorough general examination, breast examination, per abdominal examination, and vaginal examination.

INVESTIGATIONS

These are mainly done to exclude other causes of night sweat or hot flashes and eligibility for menopause hormone therapy (MHT) as one of the management options is MHT. Usually, complete blood count, postprandial sugar, thyroid hormone, liver function test, transvaginal sonography, and cervical smear are carried out. *All women* should be reviewed in terms of:

- Cardiovascular disease risk (blood pressure and lipids)
- Diabetes (fasting blood glucose)
- Urogenital health (consider local hormonal/nonhormonal therapy)
- Cancer screening—breast examination, PAP smear, and mammogram (recommended frequency varies between countries).

JAYPEE BROTHERS

MANAGEMENT

General Principle

It depends upon symptom severity, coexistent diseases, and personal choice. Lifestyle modification is one of the most important measures to alleviate VMS.

Lifestyle Modification

There are many lifestyle changes that can be implemented and should be encouraged to help women to alleviate the VMS associated with menopause. Many women have identified having triggering factors such as alcohol, spicy foods, and hot foods or drinks; simple avoidance of such substances may help to reduce their occurrence. If the patient is a smoker, smoking cessation should strongly be encouraged; other suggestions include lifestyle changes that will help lower or help prevent an increased core body temperature.

Cooling effects can be obtained by followings behavioral measures—women with mild flashes (hot flashes that do not interfere with usual activities) usually do not need pharmacotherapy. Instead, simple behavioral measures such as lowering room temperature, using fans, dressing in layers of clothing that can be easily shed, and avoiding triggers (such as spicy foods and stressful situations) can help to reduce the number of hot flashes. Women need to wear cotton light clothing, use bed fan, cold pack beneath pillow, and maintain low ambient temperature at home. Other potential options may include weight loss, cognitive behavioral therapy (CBT), vitamin E, and hypnosis.

Pharmacotherapy

Menopause hormone therapy is the choice of drug in most women with moderate to very severe hot flashes and having no contraindications. Most of the studies proved that MHT could improve hot flashes more effectively than any other interventions. Cochrane review of randomized controlled trials concluded that, for the treatment of VMS, MHT is highly efficacious, with reductions in both frequency and severity in the order of 75% (Alaster H Maclennan; Therapy versus Placebo for hot flushes: Cochrane Database Systemic Rev. 2004;(4):CD002978). Several core recommendations from different menopause societies and international menopause society suggest that—"MHT is the most effective treatment for VMS associated with menopause at any age, but *benefits are more likely to outweigh risks* for symptomatic women before the age of 60 years or within 10 years after menopause".

Women having uterus should use combined MHT, i.e., estrogen with progestin, while those who have undergone hysterectomy can receive estrogen only without progesterone. Progestins are used to prevent endometrial

JAYPEE BROTHERS

hyperplasia and thereby endometrial carcinoma. Women with premature ovarian insufficiency should be treated with MHT at least until the age of natural menopause. Oral estrogen is associated with an increased risk of venous thromboembolism (VTE), although the absolute risk is small for women <60 years old. The risk appears to be lower/not at all with transdermal estrogen. Therefore, transdermal estrogen is preferred for women at increased risk of VTE, i.e., smokers and obese women. The regimen containing estrogen in women having uterus must use progestin to prevent endometrial hyperplasia or endometrial carcinoma. The following types of progestins regimens can be used:

- Oral micronized *progesterone* (200 mg/day for 12 days) reduces the risk of hyperplasia to the same degree as *medroxyprogesterone acetate* (2.5 mg/day continuously or 10 mg/day for 12 days).
- Lower doses of combined estrogen-progestin therapy [conjugated estrogen (0.3 or 0.45 mg/day) with *medroxyprogesterone acetate* (1.5 or 2.5 mg/day)] also appear to be endometrial protective, and so can be used.
- Levonorgestrel-releasing intrauterine systems (LNG-IUS) are contraceptive agents that have been used for endometrial protection by some peri- and postmenopausal women taking estrogen. The strategy is to avoid the potential excess risk of cardiovascular disease and breast cancer associated with systemic therapy.

Most uniform regimen recommended oral or transdermal estrogen in combination with micronized progesterone at 100 mg daily, or sequential use of 200 mg micronized progesterone 14 days a month can also be employed.

Thorough discussion of risks and benefits of MHT is mandatory to empower women to choose the right treatment. However, for women with a history of breast cancer, coronary heart disease (CHD), a previous VTE or stroke, or those at moderate or high risk for these complications, alternatives to hormone therapy should be discussed and suggested.[36]

Bazedoxifene/Conjugated Estrogen

An emerging class of drugs called tissue selective estrogen complexes (TSECs) involves the combination of a selective estrogen receptor modulator (SERM) and an estrogen.[37] Bazedoxifene, a SERM, combined with conjugated estrogens, is available in the United States and the European Union for the treatment of postmenopausal VMS and osteoporosis prevention,[38] but not yet available in Bangladesh. This combination of conjugated estrogen 0.45 mg/bazedoxifene 20 mg in women with moderate-to-severe hot flashes decreases hot flash frequency by approximately 75% (vs. 50% for placebo).[39] This regimen may avoid side effects of progesterone.

Combination of estrogen plus intrauterine levonorgestrel approach has been suggested as a means of giving estrogen without the systemic effects

JAYPEE BROTHERS

of a progestogen, while preventing uterine stimulation.[40] Also, it is very effective for having abnormal bleeding, and/or who need contraception at perimenopause age.

Side effects: Common side effects of estrogen include breast soreness, which can often be minimized by using lower doses. Some women experience mood symptoms and bloating with progestin therapy. Vaginal bleeding may occur in women who receive cyclic estrogen–progestin regimens and is common in the early months of a continuous estrogen–progestin regimen, but in most cases, it subsides along with the time. If it persists beyond 6 months, primary evaluation should be carried out.

If the evaluation of postmenopausal bleeding reveals benign causes, MHT can be continued. To avoid bleeding or spotting, switching to a continuous regimen of progestin of MHT solve the problem. However, for women who are newly menopausal, breakthrough bleeding can be anticipated. In that case, continuous progesterone is better. Both oral and vaginal continuous administration of micronized progesterone 100 mg capsules is well-tolerated for most of the women.

The most effective pharmacologic alternatives to estrogen include some of the antidepressants in the selective serotonin reuptake inhibitors (SSRI) and selective norepinephrine reuptake inhibitors (SNRI) classes.[41] Their efficacy has been demonstrated in individual placebo-controlled trials.[42] Although no head-to-head trials have been performed, indirect comparisons suggest that venlafaxine, desvenlafaxine, paroxetine, and citalopram have a similar modest benefit for hot flashes. One author of this topic suggests low-dose paroxetine (7.5 mg/day)[43] as the first choice of SSRI/SNRI, since this is the only agent that has received approval by the US Food and Drug Administration (FDA) for the treatment of hot flashes. Paroxetine preparations shown to be modestly effective for hot flashes include paroxetine mesylate (7.5 mg/day) and paroxetine hydrochloride [10 and 20 mg/day, and 12.5 mg and 25 mg/day (controlled release)].[44] Side effects are nausea, change in bowel habits, decreased libido, dry mouth, and weight gain (not common). Concomitant use of tamoxifen should be avoided in women taking paroxetine.

Effectiveness: FDA approved it to treat hot flashes. It tends to be effective in women who are also suffering with insomnia and vasomotor symptoms. Improvement in hot flashes has been shown in well-designed studies. While SSRIs or SNRIs are preferred as first-line therapy for most women, gabapentin may be a better option in some women, for example, women whose hot flashes are primarily at night and who are the breast cancer survivors.

Side effects: Fatigue, dizziness, nausea, disorientation, swelling, and weight gain.

JAYPEE BROTHERS

In a trial comparing venlafaxine and gabapentin, hot flash reduction was similar with both drugs, but patients preferred venlafaxine by a 2:1 ratio.[45]

Clonidine, a centrally active alpha-2 adrenergic agonist, was modestly more effective than placebo in a meta-analysis of 10 trials.[46]

Oxybutynin, an oral anticholinergic agent used primarily for overactive bladder, was more effective than placebo for relief of hot flashes in an observational study, a randomized clinical trial, and a preliminary report from a second clinical trial.[47]

The thermoregulatory center in the hypothalamus is innervated by KNDy neurons that are stimulated by neurokinin B (NKB) and inhibited by estrogen. After menopause, estrogen declines and NKB signaling is increased. It has been proposed that this results in unregulated KNDy neuron activation and VMS.[48] Antagonism of NKB signaling at its receptor [neurokinin 3 receptor (NK3R)] has been studied as an alternative to MHT for management of hot flashes, an approach that appears to be promising.

Tibolone

It reduces VMS when compared with placebo, has a beneficial effect on bone mineral density,[49] and may be more effective than estrogen/progestin therapy for treatment of sexual dysfunction in postmenopausal women.

However, tibolone has been associated with an increased risk of stroke and possibly breast cancer, and it is not recommended in routine use for hot flash management. Some women may have vaginal bleeding/endometrial hyperplasia—while vaginal bleeding with tibolone[14] and the rate of unscheduled bleeding is lower than that for MHT. If tibolone is chosen, it should be administered in women who have passed 1 year of menopause.

Breast Cancer Survivors

Women with breast cancer have more problems with hot flashes than other women for a number of reasons. Aromatase inhibitors may also cause hot flashes, but they tend to be less frequent and less severe.[50]

Though there is no evidence for an increased risk of breast cancer recurrence in women taking strong inhibitors of *CYP2D6* (paroxetine) with tamoxifen, most studies suggest other agents such as citalopram or venlafaxine in this setting.

Cognitive Behavioral Therapy

Cognitive behavioral therapy appears to be a modestly effective intervention for menopause-associated insomnia[51] but less so for hot flashes.[52] A major limitation of CBT is the need for frequent in-person visits.

Hypnosis appears to reduce perceived hot flashes in breast cancer survivors and may have additional benefits such as reduced anxiety and depression and improves sleep.

JAYPEE BROTHERS

Mind–Body-based Therapies

Small number of studies of mind-body-based therapies (stress management, relaxation, deep breathing techniques, and guided imagery) had mixed results in two meta-analyses.[53]

Mindfulness training: A randomized trial of mindfulness-based stress reduction (MBSR) reported a decrease in menopausal hot flashes. Though mindfulness training was not shown to be very effective in reducing the hot flash intensity scores (based upon frequency and severity) when compared with no treatment.[54]

Black Cohosh

Among the alternative therapies available for management of hot flashes, black cohosh (*Actaea racemosa* or *Cimicifuga racemosa*) is one of the most widely used.[55] Black cohosh is a popular herbal supplement that is widely used for the management of the VMS associated with menopause. A 2012 Cochrane review of 16 controlled trials did not show any significant improvement of hot flashes. Position statement of North American menopause society. failed to demonstrate a clinical benefit associated with the herbal supplement.[52]

Acupuncture

Acupuncture is among the most frequently used complementary therapies for hot flashes; however, results thus far are conflicting.[56] In a systematic review and meta-analysis, acupuncture was less effective than MHT (three trials), no different from sham acupuncture (eight studies), but statistically more effective than no therapy (four trials).[57]

Flaxseed

Flaxseed is very popular for many years, but it has not been shown to be more effective than placebo for hot flashes.[58]

Exercise

An increasing amount of research is being undertaken on the effect of exercise on hot flashes. However, there is currently no evidence from randomized controlled trials that show that exercise is an effective treatment for hot flashes. But MHT is superior to any treatment for hot flashes. Clinical trials, systematic reviews, and a meta-analysis have not found a significant beneficial effect of exercise on hot flashes.[59,60] Hormone therapy was more effective than exercise in one trial.[61]

Evening primrose oil, Dong quai (*Angelica sinensis*) is a Chinese herb, Ginseng (*Panax ginseng*), and Wild Yam (*Dioscorea villosa*) a natural progesterone are being used to treat vasomotor symptoms and hot flashes.

JAYPEE BROTHERS

However, a double-blind, placebo-controlled, cross-over study found no significant difference in menopausal symptoms between these treatment and placebo groups. Isoflavones can be found in soybeans, chickpeas, lentils, and other legumes. Lignans can be found in flaxseed, whole grains, and some fruits and vegetables. Although these foods may be healthy, they have not been proven to be effective in alleviating menopausal symptoms.

Yoga

The symptom assessment was made using the Greene Climacteric Scale and it was reported that there was a decrease in VMS in the group involved in the yoga program.[62]

Stellate Ganglion Block

The positive effect of stellate ganglion block on hot flashes was first reported in a case report by Lipov and colleagues. In trial of 40 patients randomized to 3 months of stellate ganglion blocks or pregabalin therapy, both therapies were effective, but the reduction in hot flashes was greater with stellate ganglion blocks.[63] It is not popular and more studies yet to be required to recommend.

KEY MESSAGE

- Vasomotor symptoms or "hot flashes" are the most common complaint during the menopausal transition and beyond, occurring in up to 80% of women.
- Frequent VMS can be disabling, affecting a woman's social life, psychological health, sense of well-being, and ability to work. Women with hot flushes are more likely to experience disturbed sleep, depressive symptoms, and significant reductions in quality-of-life as compared to asymptomatic women.
- The most effective therapy for relieving VMS and reducing their impact on quality-of-life is MHT. However, postmenopausal women with mild hot flashes usually do not seek or require pharmacologic intervention. Simple lifestyle changes and behavioral therapy such as keeping the core body temperature cool are often adequate to manage symptoms.
- Menopause hormone therapies, including estrogens and progestogens, are the most well-known effective agents in relieving hot flashes.
- Nonhormonal prescription drugs, including certain antidepressant agents, SNRI, SSRI, gabapentin, and clonidine, may afford some relief from hot flashes. These alternatives can be considered when hormone therapy is contraindicated or not desired.
- A woman should know all the options with the risks and benefits to alleviate her symptoms so that she is able to improve her quality-of-life and prevent the long-term complications.

JAYPEE BROTHERS

REFERENCES

1. Woods NF, Mitchell ES. Symptoms during the perimenopause: Prevalence, severity, trajectory, and significance in women's lives. Am J Med. 2005;118:14-24.
2. Couzi R, Helzlsouer K, Fetting J. Prevalence of menopausal symptoms among women with a history of breast cancer and attitudes toward estrogen replacement therapy. J Clin Oncol. 1995;13(11):2737-44.
3. Williams RE, Levine KB, Kalilani L, Lewis J, Clark RV. Menopause-specific questionnaire assessment in US population –based study shows negative impact on health-related quality of life. Maturitas. 2009;62(2):153-9.
4. Islam MR, Gartoulla P, Bell RJ, Fradkin P, Davis SR. Prevalence of menopausal symptoms in Asian midlife women: a systematic review. Climacteric. 2015;18(2): 157-76.
5. Gold EB, Colvin A, Avis N, Bromberger J, Greendale GA, Powell L, et al. Longitudinal analysis of the association between vasomotor symptoms and race/ethnicity across the menopausal transition: study of women's health across the nation. Am J Public Health. 2006;96(7):1226-35.
6. Randolph JF Jr, Sowers M, Bondarenko I, Gold EB, Greendale GA, Bromberger JT, et al. The relationship of longitudinal change in reproductive hormones and vasomotor symptoms during the menopausal transition. J Clin Endocrinol Metab. 2005;90(11):6106-12.
7. Soules MR, Sherman S, Parrott E, Rebar R, Santoro N, Utian W, et al. Executive summary: Stages of Reproductive Aging Workshop (STRAW). Fertil Steril. 2001;76(5):874-8.
8. Kronenberg F. Hot flashes: epidemiology and physiology. Ann NY Acad Sci. 1990; 592:52-86.
9. Pennebaker J. The psychology of physical symptoms. New York: Springer-Verlag; 1982.
10. Archer DF, Sturdee DW, Baber R, de Villiers TJ, Pines A, Freedman RR, et al. Menopausal hot flushes and night sweats: where are we now? Climacteric. 2011;14(5):515-28.
11. Freedman RR. Hot flashes: behavioral treatments, mechanisms, and relation to sleep. Am J Med. 2005;118(Suppl 12B):124-30.
12. Freedman RR. Physiology of hot flashes. Am J Hum Biol. 2001;13(4):453-64.
13. Casper RF, Yen SS. Neuroendocrinology of menopausal flushes: an hypothesis of flush mechanism. Clin Endocrinol (Oxf). 1985;22(3):293-312.
14. Rance NE, Dacks PA, Mittelman-Smith MA, Romanovsky AA, Krajewski-Hall SJ. Modulation of body temperature and LH secretion by hypothalamic KNDy (kisspeptin, neurokinin B and dynorphin) neurons: a novel hypothesis on the mechanism of hot flushes. Front Neuroendocrinol 2013;34(3):211-27.
15. Freedman RR, Blacker CM. Estrogen raises the sweating threshold in postmenopausal women with hot flashes. Fertil Steril. 2002;77(3):487-90.
16. Crandall CJ, Zheng Y, Crawfold, SL, Thurston RC, Gold EB, Johnston JM, et al. Presence of vasomotor symptoms is associated with lower bone mineral density: A longitudinal analysis. Menopause. 2009;16(2):239-46.
17. Whiteman MK, Starpoll CA, Benedict LC, Borgest C, Flaws JA. Risk factors for hot flashes in midlife women. J Womens Health. 2003;12(5):459-72.
18. Grodin JM, Siiteri PK, MacDonald PC. Source of estrogen production in postmenopausal women. J Clin Endocrinol Metab. 1973;36(2):207-14.
19. MacDonald PC, Edman CD, Hemsell DL, Porter JC, Siiteri PK. Effect of obesity on conversion of plasma androstenedione to estrone in postmenopausal women with and without endometrial cancer. Am J Obstet Gynecol. 1978;130(4):448-55.
20. Gold EB, Sternfeld B, Kelsey JL, Brown C, Mouton C, Reame N, et al. Relation of demographic and lifestyle factors to symptoms in a multi-racial/ethnic population of women 40-55 years of age. Am J Epidemiol. 2000;152(5):463-73.

JAYPEE BROTHERS

21. Whiteman MK, Staropoli CA, Langenberg PW, McCarter RJ, Kjerulff KH, Flaws JA. Smoking, body mass, and hot flashes in midlife women. Obstet Gynecol. 2003;101(2):264-72.
22. Huang AJ, Subak LL, Wing R, West DS, Hernandez AL, Macer J, et al. An intensive behavioral weight loss intervention and hot flushes in women. Arch Intern Med. 2010;170(13):1161-7.
23. Thurston RC, Sower MR, Strendfeld B, Gold EB, Bromberger J, Chang Y, et al. Gains in body fat and vasomotor symptoms reporting over the menopausal transition; the study of women's Health across the nation. Am J Epidemiol. 2009;170(6):766-74.
24. Koo S, Ahn Y, Lim JY, Cho J, Park HY. Obesity associates with vasomotor symptoms in postmenopause but with physical symptoms in perimenopause: a cross-sectional study. BMC Women's Health. 2017; (17):126.
25. David PS, Kling JM, Vegunta S, Faubion SS, Kapoor E, Mara KC, et al. Vasomotor symptoms in women over 60: results from the Data Registry on Experiences of Aging, Menopause, and Sexuality (DREAMS). Menopause. 2018;25(10):1105-9.
26. Borkoles E, Reynolds N, Ski CF, Stojanovska L, Thompson DR, Polman RC. Relationship between type D personality, physical activity behavior and climacteric symptoms. BMC Women's Health. 2015;15:1.
27. Romani WA, Gallicchio L, Flaws JA. The physical association between physical activity and hot flash severity, frequency, and duration in mid-life women. Am J Hum Biol. 2009;21(1):127-9.
28. Smith RL, Flaws JA, Gallichio L. Does quitting smoking decrease the risk of midlife hot flashes? A longitudinal analysis. Maturitus. 2015:82:123-7.
29. Crandall CJ, Manson JE, Hohensee C, Horvath S, Wactawski-Wende J, LeBlanc ES, et al. Association of genetic variation in the tachykinin receptor 3 locus with hot flashes and night sweats in the Women's Health Initiative Study. Menopause. 2017;24(3):252-61.
30. Seivert LL, Flanagan EK. Geographical distribution of hot flash frequencies: considering climatic influences. Am J Phys Anthropol. 2005;128(2):437-43.
31. Avis NE, Crawford SL, Greendale G, Bromberger JT, Everson-Rose SA, Gold EB, et al. Duration of menopausal vasomotor symptoms over the menopause transition. JAMA Intern Med. 2015;175(4):531-9.
32. Thurston RC, Sutton-Tyrrell K, Everson-Rose SA, Hess R, Matthews KA. Hot flashes and subclinical cardiovascular disease: findings from the Study of Women's Health Across the Nation Heart Study. Circulation. 2008;118(12):1234-40.
33. Crandall CJ, Tseng CH, Crawford SL, Thurston RC, Gold EB, Johnston JM, et al. Association of menopausal vasomotor symptoms with increased bone turnover during the menopausal transition. J Bone Miner Res. 2011;26(4):840-9.
34. Dennerstein L, Dudley EC, Hopper JL, Guthrie JR, Burger HG. A prospective population-based study of menopausal symptoms. Obstet Gynecol. 2000;96(3): 351-8.
35. Kravitz HM, Janssen I, Santoro N, Bromberger JT, Schocken M, Everson-Rose SA, et al. Relationship of day-to-day reproductive hormone levels to sleep in midlife women. Arch Intern Med. 2005;165(20):2370-6.
36. Stuenkel CA, Davis SR, Gompel A, Lumsden MA, Murad MH, Pinkerton JV, et al. Treatment of symptoms of the menopause: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015;100(11):3975-4011.
37. Pinkerton JV, Harvey JA, Pan K, Thompson JR, Ryan KA, Chines AA, et al. Breast effects of bazedoxifene-conjugated estrogens: a randomized controlled trial. Obstet Gynecol. 2013;121(5):959-68.
38. Lobo RA, Pinkerton JV, Gass ML, Dorin MH, Ronkin S, Pickar JH. Evaluation of bazedoxifene/conjugated estrogens for the treatment of menopausal symptoms and effects on metabolic parameters and overall safety profile. Fertil Steril. 2009; 92(3):1025-38.

JAYPEE BROTHERS

For detailed information on obstetrics & gynecology books, visit our website www.jaypeebrothers.com, for detailed information on obstetrics & gynecology books, visit our website

Management of Menopause

The "Management of Menopause" book utilizes the biopsychosocial approach to inform Physician, Specialists, Practitioners, Residents and trainee about the latest that science has to offer for the evaluation and treatments of Menopause problems especially the utilization of the armamentarium of assessment methods and treatment interventions in order to restore menopause health and enhance the Quality-of-life of women with menopause and beyond.

Salient Features

- This book has highlighted "Lifestyle modification" as the key of healthy aging, describing in details about the optimum diet and role of exercise for menopause women.
- Some women might need hormone therapy for severe symptoms but there are concerns about the safety of hormone therapy regarding thromboembolism or breast cancer on the contrary withholding hormone from symptomatic women might pose a risk, particularly with regard to cardiovascular disease and osteoporosis.
- This book tried to shade light upon this challenge and bridge the gap between risk perception and hormone therapy prescription with evidence-based clear advice on menopause hormone therapy.
- There are plenty of references which might clarify many issues of menopause and hormone therapy.



Shaikh Zinnat Ara Nasreen MBBS MPH FCPS MRCOG FRCOG FIAOG is the Gold Medalist, Professor and Head, Department of Obstetrics and Gynecology, ZH Sikder Women's Medical College and Hospital, Dhaka, Bangladesh. She had nearly 20 years of experience to work with menopause women. She is a dedicated worker in Bangladesh Menopause Society since 16 years. She is researching the different aspects of menopause health with view to improve the quality-of-life of women.

She graduated from Dhaka Medical College in 1984 with distinction and honours marks. She was awarded Gold Medal for achieving record marks in Medicine. She obtained FCPS in obstetrics and gynecology from BCPS and MRCOG from Royal College of London in 2000. Later she obtained FRCOG and did her MPH and the thesis was on menopause health. She received number of award from country for working toward women health. She is a regular speaker in national and international conferences. She had more than 50 publications including both national and international journals. She wrote chapters in books of other author from home and abroad. She is the reviewer of many journals and member of executive board of international journal. She is Editor-in-Chief of JZHSWMCH.

Prof Zinnat Nasree is working as Professor and Head of Obstetrics and Gynecology in ZHSWMCH. She is the member of International Menopause Society (IMS), Secretary General of BMS. She is chairing website of SAFOM, Co-Chair of Maternal and Fetal Committee of SAFOG, member of ISSM and executive board of SASSM. She is Organizing Secretary of OGSB, BPS and honorary Secretary General of RCOG Bangladesh representative. She is the member Secretary of CPD committee of BCPS and she is also a kind Rotarian.

Printed in India

Available at all medical bookstores
or buy online at www.jaypeebrothers.com

JAYPEE BROTHERS
Medical Publishers (P) Ltd.
EMCA House, 23/23-B, Ansari Road,
Daryaganj, New Delhi - 110 002, INDIA
www.jaypeebrothers.com

Join us on facebook.com/JaypeeMedicalPublishers

Shelving Recommendation
OBSTETRICS & GYNECOLOGY