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MENOPAUSAL HORMONE THERAPHY – APPLICATION, RISKS AND BENEFITS IN CLINICAL PRACTICE

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ABSTRACT

Aim of the study: The aim of this review is to explore current evidence regarding physiological rationale, indications, contraindications and systemic use of MHT in clinical practice.
Materials and methods: Literature reviewed was conducted in medical databases such as PubMed, UpToDate and relevant subject literature published within last 30 years.
Results: Evidence indicates that early initiation (< 10 years after the onset of menopause) of combined estrogen-progestogen therapy significantly diminishes coronary events and prevents rapid bone loss, whereas later commencement increases ischaemic stroke and venous thrombo-embolism risk. Unopposed systemic oestrogen elevates endometrial-carcinoma incidence, and long-term systemic regimens may moderately increase breast-cancer risk. On the contrary, topical vaginal oestrogens reverse urogenital atrophy and lower recurrent urinary-tract infection rates with minimal systemic exposure.
Conclusion: MHT consistently alleviates vasomotor symptoms and improves quality of life, but does not constitute first-line therapy for established osteoporosis or primary cardiovascular prevention The therapeutic value of MHT is contingent upon timing, formulation, route and patient-specific comorbidities. When used for the shortest necessary duration and accompanied by careful surveillance, MHT offers substantial symptomatic benefit with acceptable safety in appropriately selected women.

KEYWORDS

Menopausal Hormone Therapy, Menopause, Oestrogen, Osteoporosis

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Introduction

Menopausal hormone therapy (MHT) remains an important form of treatment used for ameliorating estrogen-deficiency symptoms. However, its pleiotropic actions require a nuanced risk to benefit assessment.

Definition Of Menopause

Natural menopause is the irreversible cessation of ovarian hormonal function and is clinically diagnosed after 12 consecutive months of amenorrhea not due to a pathologic cause. It typically occurs between 45 and 55 years of age. Menstrual timing is established by a multifactorial interplay of environmental and genetic factors. Principal genetic determinants include age at menarche and family trends - chief of which are the mother's and grandmothers' menopausal age. Amongst environmental determinants, cigarette smoking has been consistently associated with an earlier menopausal age, accelerating it by approximately 1-2 years. Long-term consumption of hormonal contraceptives and alcohol consumption in excess have also been involved. Understanding variation in menopausal onset and progression is critical to predict associated health risks and optimize individualized care strategies among midlife women [1]. Cigarette smoking is particularly associated with the risk of vasomotor symptoms during the menopause [2]. Menopause may also be induced by surgical removal of the two ovaries or by medical treatments suppressing ovarian function, such as radiation therapy or chemotherapy [3]. The menopausal transition can typically be separated into two phases: (a)Premenopause: The years preceding the final menstrual period, often characterized by subtle hormonal fluctuations and the onset of early symptoms. (b)Postmenopause: Begins following 12 consecutive months of amenorrhea and continues through a woman's lifespan. It is defined by the sustained consequences of estrogen deficiency [1]. Clinical presentation and hormonal and metabolic alterations may begin with the premenopausal period as ovarian function gradually declines. It is important to note that the delineation of these phases is not strictly chronological but rather based on the progression of endocrine and physiological changes.

Pathophysiology

With advancing age, the female reproductive system undergoes progressive changes, particularly within the ovaries. Ovarian follicles progressively decrease in number, leading to a diminishing population of granulosa cells. The morphologic changes are linked to an impairment in the synthesis of ovarian hormones.

In premenopause, there is a profound reduction in the secretion of inhibin by the granulosa cells, leading to a compensatory rise in serum follicle-stimulating hormone (FSH) levels. There is a reduction in the level of estradiol typically around two years prior to the final menstrual period. The FSH levels rise even higher and plateau at high levels around two years after menopause. In the late reproductive phase, there is also minimal reduction in the circulating androgens, including testosterone and androstenedione [4].

At postmenopausal age, estradiol and estrone levels in the serum are reduced dramatically. Notably, estradiol levels fall below those of estrone, ranging between 10-25 pg/mL [1]. Peripheral aromatization of adrenal androgens is the primary source of estrone at this point. Serum levels of both gonadotropins from the pituitary - FSH and luteinizing hormone (LH) - remain elevated. SHBG levels also reduce, resulting in relative elevation of free (bioavailable) fraction of testosterone.

These endocrine changes are the cause of menstrual irregularities. The cycle initially shortens, with progressively longer intermenstrual periods, ultimately leading to cessation of menses.

Endocrine changes causing the menopausal transition underlie a broad range of clinical syndromes, which can significantly decrease quality of life. These are:

- Hot flushes
- Night sweats
- Irritability and anxiety
- Depressed mood
- Fatigue
- Disturbed sleep
- Decreased concentration and memory
- Decrease in cognitive function

These symptoms reflect the systemic impact of estrogen deficiency on thermoregulation, neuroendocrine transmission, and central nervous system function [7].

Hormonal Changes During Menopause and Their Systemic Clinical Implications

The hormonal alterations occurring during the menopausal transition give rise to a wide range of clinically significant symptoms. They include hot flashes, nocturnal sweats, irritability, nervousness, mood swings, fatigue, sleep disturbances, reduction in concentration and memory, and cognitive dysfunction [2].

Menopausal symptoms affect multiple organ systems, including the nervous, genitourinary, skeletal, cardiovascular systems, and the skin. Estrogen deficiency impacts central nervous system function, resulting in characteristic neuropsychiatric symptoms - such as anger, irritability, anxiety, restlessness, and impaired concentration - reported by up to 70% of women during menopause [4].

The most common menopausal symptom is the hot flashes. Their etiopathogenesis is multifactorial and primarily associated with hormonal alterations that influence the control of temperature. Hot flashes and night sweats occur in approximately 80% of menopausal women [4]. Hot flashes consist of sudden, subjective sensations of heat confined to the face, neck, and chest. They may be accompanied by flushing of the skin, sweating, chills, palpitations, and distress [6].

Up to 70% of women experience perimenopause and menopause psychological symptoms. Estrogen receptors are found in areas of the brain responsible for mood and cognition, and thus disturbances in these areas are likely to be felt during menopause. The conduction of serotonin and noradrenaline is also affected by estrogens, contributing even more to loss of emotional well-being during this period. These may be irritability, anxiety, depression, difficulty in concentrating, and decreased self-esteem or confidence. Sleep disorders such as sleep apnea, insomnia, and restless leg syndrome are also possible unrelated to night sweats [4].

Estrogen deficiency affects the skin negatively, expressed in terms of thinning and loss of elasticity. It is caused by defective collagen synthesis, and this can be explained because dermal fibroblasts contain estrogen receptors [1]. Women of menopausal age tend to complain of symptoms such as pruritus, hyperhidrosis, xerosis, eczema, and wound healing defect [7].

Within the genitourinary system, the decline in estrogen leads to thinning of endometrium and vaginal epithelium, decreased mucus production, and loss of tissue elasticity. All these effects lead to vaginal dryness, loss of wall tone, painful sexual intercourse, and increased susceptibility to local inflammation [4]. These

changes can be described as pruritus, burning, and irritation. About 27% to 60% of women develop moderate or severe vaginal dryness or dyspareunia symptoms. Urogenital atrophy is also involved in stress urinary incontinence, urgency incontinence, frequency, and nocturia [8].

Estrogens influence bone through multiple mechanisms; therefore, during menopause, when estrogen levels decline, bone structure becomes compromised, leading to the development of osteoporosis [10]. Postmenopausal osteoporosis is diagnosed in approximately 30-35% of white women [1].

Cardiovascular changes in menopause are defined by increases in total and LDL cholesterol, impaired vascular perfusion, reduced prostacyclin synthesis, diminished levels of nitric oxide, and elevated endothelin levels. These pathophysiological changes collectively contribute to a heightened cardiovascular risk in postmenopausal women [11].

Types Of Hormone Replacement Therapy

There are several types of hormone replacement therapy (HRT) used during menopause: estrogen-only therapy (administered orally or transdermally), combined estrogen-progestogen therapy (also oral or transdermal), and local vaginal estrogen therapy [9]. Estrogen-only therapy may be used exclusively in women who have undergone a hysterectomy [11].

Indications for estrogen-only or combined estrogen-progestogen therapy include moderate to severe vasomotor symptoms such as hot flashes and the prevention of osteoporosis in women who are at high risk of fractures and cannot take other osteoporosis medications [10].

Contraindications to these types of HRT are unexplained vaginal bleeding, liver disease, active or past venous thromboembolism, history or presence of malignancy that is estrogen dependent, suspected or diagnosed breast cancer, known disorders of blood clotting, and history of coronary heart disease, stroke, or transient ischemic attack (TIA). Relative contraindications are hypertriglyceridemia, gallbladder disease, and personal history of augmented risk of breast cancer [11].

Indications of local estrogen vaginal therapy are genitourinary menopausal symptoms (e.g., vaginal dryness, dyspareunia).

Contraindications for local estrogen vaginal therapy are unknown vaginal bleeding, known breast cancer, endometrial cancer, or other malignancies that are estrogen-dependent [11].

Risks and Benefits

Hormone-replacement therapy has a remarkably large effect on the function of many organs and tissues. To maintain clarity, the benefits and risks of menopausal hormone therapy (MHT) are given below under individual physiological systems.

Cardiovascular system

MHT therapy either increases or decreases the risk of coronary heart disease (CHD) depending on how old a woman is when therapy is initiated [12, 13]. A meta-analysis of randomized clinical trials in 23 centers with 39 049 participants indicates [14, 15] that combined estrogen-progestogen menopausal hormone therapy reduces cardiovascular risk in younger (50-59 years) but increases risk in women over 60 years. The greatest reduction in the incidence of coronary events is observed in those starting MHT in the first ten years of the onset of menopause [16]. MHT can raise the risk of stroke - particularly ischaemic stroke - during treatment [17]. In addition, strokes occurring in women on MHT are more likely to have serious neurological deficits resulting in disability or death [18, 19]. Another issue to be discussed is venous thrombosis risk. A 2017 Cochrane meta-analysis revealed an elevated rate of venous thrombosis with the use of MHT. The pathophysiologic mechanism is unclear; the principal hypothesis is one of increased resistance to activated protein C in women taking oral preparations. Protein C is an anticoagulant that inhibits factors Va and VIIIa and thus prevents thrombin formation (factor IIa) [20]. The risk is increased with oral rather than transdermal preparations [21].

Neoplastic diseases

MHT may be associated with increased risk of breast cancer. Evidence suggests [22] that women who have used MHT for five years or more are at higher risk of breast cancer, especially if unopposed, oral estrogen therapy is being administered. No risk augmentation has been found with local (topical) MHT. Endometrial carcinoma and hyperplasia must also be taken into account when MHT is administered. Because of the typical rise in risk of endometrial-cancer [23] with unopposed estrogen treatment, this regimen is limited to those

patients who have had a hysterectomy. Endometrial hyperplasia develops in 20-50 % of women taking estrogen-alone MHT by one year after initiation of treatment, based on research. With combined oestrogen-progestogen MHT the danger of endometrial-cancer is lessened and is similar to age-matched controls [24].

Urogenital system

Vaginal atrophy and mucosal dryness are frequent menopausal symptoms that cause discomfort, dyspareunia, micro-trauma and vulnerability to vaginal infection. Intravaginal local MHT - administered in the form of creams, gels or pessaries - is similarly a common prescription and usually leads to rapid relief of symptoms [25]. Local estrogen therapy also has a protective effect in women with recurrent urinary-tract infections (UTIs), by presumably restoring a normal vaginal microbiota. A surprisingly low incidence of UTI has been observed in such patients [26].

Vasomotor flashes and night sweats

Hot flushes and night sweats are among the most prevalent symptoms of menopause and can have a substantive impact on quality of life. Systemic MHT reduces the frequency of these events with benefit [27], thereby improving daily functioning.

Osteoporosis

Estrogens maintain an adequate bone-mineral density. Post-menopausal women are therefore at high risk for osteoporosis, and consequently low-energy fractures - most common being femoral neck and distal radius in patients above 60 years of age. In women receiving MHT, there has been a noted significant decrease in fracture incidence [28]. Where the bone density was lower before starting, therapeutic gain has ensued. MHT is not, however, prescribed as a form of treatment for already established osteoporosis [29].

Conclusionы

Menopausal hormone therapy (MHT) remains the best intervention for the quick relief of moderate-to-severe vasomotor symptoms and for the retardation of bone loss in the first few years after the menopause [27-29].

However, its systemic activity demands an individualized evaluation of benefit-to-risk ratio in each candidate [12-16]. Timing, formulation and route etiologically influence cardiovascular consequences. Starting combination estrogen-progestogen therapy within a decade of the last menstrual period and below 60 years of age is associated with reduced risk of coronary events, while delayed initiation may be associated with excess risk of ischaemic stroke and venous thrombo-embolism. Neoplastic risk is regimen-related and heterogeneous. Endometrial-cancer risk is raised by unopposed systemic estrogen and thus reserved for hysterectomised women [23, 24]. Long-term (> 5 years) systemic therapy will increasingly contribute to the risk of breast cancer [22].

Local oestrogen therapy provides targeted relief with minimal systemic exposure. Intravaginal formulations effectively reverse urogenital atrophy, diminish dyspareunia and lower recurrent urinary-tract infection rates while exerting negligible effects on distant organs [25, 26].

MHT should not be employed as initial treatment for confirmed osteoporosis or primary cardiovascular prevention. Although it increases bone-mineral density and fracture rate when begun close to the menopause, in preference other agents with more positive long-term safety profiles are employed in women with established osteoporosis or at high initial cardiovascular risk [28, 29] Shared decision-making, ongoing monitoring and the ideology of”lowest effective dose for the shortest required duration" facilitate safe MHT practice. Overall, therefore, MHT is not invariably harmless and never inherently dangerous; rather, its cumulative clinical utility will be a function of timing of initiation, preparation, route of administration, treatment duration and the woman's evolving risk profile.

Used within an evidence-based framework and accompanied by appropriate monitoring, MHT can genuinely enhance quality of life in women in midlife while offering reasonable safety margins [12-29].

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REFERENCES

1. Bręborowicz, G. (2020). Położnictwo i ginekologia. Warszawa: Wydawnictwo Lekarskie PZWL.
2. Avis, N. E., Crawford, S. L., & Green, R. (2018). Vasomotor symptoms across the menopause transition: differences among women. Obstet Gynecol Clin North Am, 45(4), 629–640.
3. World Health Organization (2024). Menopause fact sheet. Available at: https://www.who.int/news-room/fact-sheets/detail/menopause
4. Peacock K, Carlson K, Ketvertis KM. Menopause. [Updated 2023 Dec 21]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507826/
5. Yang JL, Hodara E, Sriprasert I, Shoupe D, Stanczyk FZ. Estrogen deficiency in the menopause and the role of hormone therapy: integrating the findings of basic science research with clinical trials. Menopause. 2024 Oct 1; 31(10):926-939. doi: 10.1097/GME.0000000000002407. Epub 2024 Jul 30. PMID: 39081162; PMCID: PMC12072814.
6. Freedman RR. Menopausal hot flashes: mechanisms, endocrinology, treatment. J Steroid Biochem Mol Biol. 2014 Jul; 142:115-20. doi: 10.1016/j.jsbmb.2013.08.010. Epub 2013 Sep 4. PMID: 24012626; PMCID: PMC4612529.
7. Kamp E, Ashraf M, Musbahi E, DeGiovanni C. Menopause, skin and common dermatoses. Part 2: skin disorders. Clin Exp Dermatol. 2022 Dec; 47(12):2117-2122. doi: 10.1111/ced.15308. Epub 2022 Oct 26. PMID: 35727900; PMCID: PMC10092853.
8. Santoro N, Epperson CN, Mathews SB. Menopausal Symptoms and Their Management. Endocrinol Metab Clin North Am. 2015 Sep; 44(3):497-515. doi: 10.1016/j.ecl.2015.05.001. PMID: 26316239; PMCID: PMC4890704.
9. Cho L, Kaunitz AM, Faubion SS, Hayes SN, Lau ES, Pristera N, Scott N, Shifren JL, Shufelt CL, Stuenkel CA, Lindley KJ; ACC CVD in Women Committee. Rethinking Menopausal Hormone Therapy: For Whom, What, When, and How Long? Circulation. 2023 Feb 14; 147(7):597-610. doi: 10.1161/CIRCULATIONAHA.122.061559. Epub 2023 Feb 13. PMID: 36780393; PMCID: PMC10708894.
10. Ji MX, Yu Q. Primary osteoporosis in postmenopausal women. Chronic Dis Transl Med. 2015 Mar 21; 1(1):9-13. doi: 10.1016/j.cdtm.2015.02.006. PMID: 29062981; PMCID: PMC5643776.
11. Mehta J, Kling JM, Manson JE. Risks, Benefits, and Treatment Modalities of Menopausal Hormone Therapy: Current Concepts. Front Endocrinol (Lausanne). 2021 Mar 26; 12:564781. doi: 10.3389/fendo.2021.564781. PMID: 33841322; PMCID: PMC8034540.
12. Giuseppe M C Rosano 1, Cristiana Vitale, Massimo Fini Ann Hormone replacement therapy and cardioprotection: what is good and what is bad for the cardiovascular system? N Y Acad Sci. 2006 Dec:1092:341-8. doi: 10.1196/annals.1365.031

13. Jacques E Rossouw 1, Ross L Prentice, JoAnn E Manson, Lieling Wu, David Barad, Vanessa M Barnabei, Marcia Ko, Andrea Z LaCroix, Karen L Margolis, Marcia L Stefanick Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause JAMA. 2007 Apr 4; 297(13):1465-77. doi: 10.1001/jama.297.13.1465.
14. Salpeter SR, Walsh JM, Greyber E, Salpeter EE Brief report: Coronary heart disease events associated with hormone therapy in younger and older women. A meta-analysis. J Gen Intern Med. 2006; 21(4):363.
15. Manson JE, Hsia J, Johnson KC, Rossouw JE, Assaf AR, Lasser NL, Trevisan M, Black HR, Heckbert SR, Detrano R, Strickland OL, Wong ND, Crouse JR, Stein E, Cushman M, Estrogen plus progestin and the risk of coronary heart disease. Women's Health Initiative Investigators N Engl J Med. 2003; 349(6):523
16. Boardman HM, Hartley L, Eisinga A, Main C, Roquéi Figuls M, Bonfill Cosp X, Gabriel Sanchez R, Knight B Hormone therapy for preventing cardiovascular disease in post-menopausal women. Cochrane Database Syst Rev. 2015;
17. Bushnell C, McCullough LD, Awad IA, Chireau MV, Fedder WN, Furie KL, Howard VJ, Lichtman JH, Lisabeth LD, Piña IL, Reeves MJ, Rexrode KM, Saposnik G, Singh V, Towfighi A, Vaccarino V, Walters MR, Guidelines for the prevention of stroke in women: a statement for healthcare professionals from the American Heart Association/American Stroke Association; .American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, Council for High Blood Pressure Research Stroke. 2014; 45(5):1545. Epub 2014 Feb 6.
18. Bath PM, Gray LJ Association between hormone replacement therapy and subsequent stroke: a meta-analysis BMJ. 2005; 330(7487):342. Epub 2005 Jan 7.
19. Marjoribanks J, Farquhar C, Roberts H, Lethaby A, Lee J Long-term hormone therapy for perimenopausal and postmenopausal women. Cochrane Database Syst Rev. 2017; 1(1):CD004143. Epub 2017 Jan 17.
20. Post MS, Rosing J, Van Der Mooren MJ, Zweegman S, Van Baal WM, Kenemans P, Stehouwer CD, Ageing Women' and the Institute for Cardiovascular Research-Vrije Universiteit (ICaR-VU) Br Increased resistance to activated protein C after short-term oral hormone replacement therapy in healthy post-menopausal women. J Haematol. 2002; 119(4):1017.
21. Canonico M, Oger E, Plu-Bureau G, Conard J, Meyer G, Lévesque H, Trillot N, Barrellier MT, Wahl D, Emmerich J, Scarabin PY, Estrogen and Thromboembolism Risk (ESTHER) Study Group Hormone therapy and venous thromboembolism among postmenopausal women: impact of the route of estrogen administration and progestogens: the ESTHER study. Circulation. 2007; 115(7):840.
22. Collaborative Group on Hormonal Factors in Breast Cancer Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. Lancet. 2019; 394(10204):1159. Epub 2019 Aug 29.
23. Beral V, Bull D, Reeves G, Million Women Study Collaborators Endometrial cancer and hormone-replacement therapy in the Million Women Study. Lancet. 2005; 365(9470):1543.
24. Anderson GL, Judd HL, Kaunitz AM, Barad DH, Beresford SA, Pettinger M, Liu J, McNeeley SG, Lopez AM, Women's Health Initiative Investigators Effects of estrogen plus progestin on gynecologic cancers and associated diagnostic procedures: the Women's Health Initiative randomized trial. JAMA. 2003; 290(13):1739.
25. Danan ER, Sowerby C, Ullman KE, Ensrud K, Forte ML, Zerzan N, Anthony M, Kalinowski C, Abdi HI, Friedman JK, Landsteiner A, Greer N, Nardos R, Fok C, Dahm P, Butler M, Wilt TJ, Diem S Ann Hormonal Treatments and Vaginal Moisturizers for Genitourinary Syndrome of Menopause: A Systematic Review.Intern Med. 2024; 177(10):1400. Epub 2024 Sep 10.
26. Cardozo L, Lose G, McClish D, Versi E, de Koning Gans H. A systematic review of estrogens for recurrent urinary tract infections: third report of the hormones and urogenital therapy (HUT) committee. Int Urogynecol J Pelvic Floor Dysfunct. 2001; 12(1):15-20. doi: 10.1007/s001920170088. PMID: 11294525.
27. MacLennan A, Lester S, Moore V Oral estrogen replacement therapy versus placebo for hot flushes: a systematic review.Climacteric. 2001; 4(1):58.
28. The Writing Group for the PEPI Effects of hormone therapy on bone mineral density: results from the postmenopausal estrogen/progestin interventions (PEPI) trial.JAMA. 1996; 276(17):1389.
29. Prince RL, Smith M, Dick IM, Price RI, Webb PG, Henderson NK, Harris MM Prevention of postmenopausal osteoporosis. A comparative study of exercise, calcium supplementation, and hormone-replacement therapy. N Engl J Med. 1991; 325(17):1189.