



EMAS position statement: Menopause for medical students



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Discussions with patients about the menopause are becoming more complex because of women's increasing longevity, the wide range of therapeutic options, the controversies regarding menopausal hormone therapy (MHT) and the increasing use of alternative and complementary therapies. The aim of this document is to provide guidance in bullet-point style on the essential issues that medical students need to know about the stages of reproductive aging, menopause terminology, menopause and postmenopausal health [1].

- The menopause, or the cessation of the menstrual cycle, is the result of ovarian aging and is a natural event experienced by most women in their late 40s or early 50s. With increasing longevity the menopause can now be considered to be a midlife event. Thus managing postmenopausal health is a key issue for all health professionals, not just gynecologists.
- While for most women the menopause is a natural process, it can be induced by medical intervention such as bilateral oophorectomy or iatrogenic ablation of ovarian function by chemotherapy, radiotherapy or treatment with gonadotrophin-releasing hormone analogs and occur earlier (see premature/early menopause). In the absence of surgery, induced menopause may be permanent or temporary.
- Ovarian insufficiency leads to estrogen deficiency and potentially debilitating menopausal symptoms such as hot flushes, night sweats and vaginal dryness (urogenital atrophy). Although hot flushes and night sweats usually are present for less than five

years, some women will continue to flush beyond the age of 60 years. Self reported menopausal symptoms vary considerably between races and ethnic groups. The chronic conditions affecting postmenopausal health are osteoporosis, cardiovascular disease, dementia and cognitive decline. Again risk of chronic disease depends on ethnic group, medical history, diet and lifestyle.

- Measurement of follicle-stimulating hormone (FSH) is helpful only if the diagnosis is in doubt, such as in women with suspected premature ovarian failure and the levels are reported in the menopausal range (>25 IU/l). In menstruating women, measurement of FSH should be performed at the beginning of the follicular phase (days 2–5 of the cycle) to avoid ovulation-induced elevations of FSH. Measurement of thyroid stimulating hormone (TSH) and prolactin are also helpful in investigating menstrual irregularity [2]. Levels of FSH do not predict when the last menstrual period will occur and are not a guide to fertility status, as increased levels can occur in the presence of ovulatory cycles. Estimates of the levels of luteinizing hormone, estradiol, progesterone and testosterone are of no value in the diagnosis of ovarian failure, but may provide information about other menstrual cycle disorders.
- Assessment should include detailing symptoms and their impact on quality of life, menstrual history including the type of menopause (natural or iatrogenic) and contraception. Family or personal history should include that of breast, ovarian, endometrial and colon cancer; venous thromboembolism, migraine, and risk factors for osteoporosis, heart disease and stroke. The women's preference about treatment must be recorded. Physical examination should include recording of weight, height, waist-hip ratio and blood pressure. Whether breast or pelvic examination, mammography or transvaginal ultrasound should

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be undertaken initially and then at regular intervals is a controversial area with practice varying worldwide [3]. Women should be encouraged to participate in national screening programs for cervical and breast cancer. Patients at risk of osteoporosis are identified opportunistically using a case finding strategy. FRAX can be used for people aged between 40 and 90 years, either with or without measuring bone mineral density [4].

- There is increasing evidence that life-style factors, such as nutrition, physical activity, smoking and alcohol consumption have a profound effect on health and menopause symptoms. Women gain on average 10 kilos from 40 to 60 years independently of menopause. Thus women should be encouraged to stop smoking, to have a balanced healthy diet rich in fiber, fruit and vegetables and to exercise regularly, aiming to prevent the midlife increase in body weight and to preserve their muscle mass [5–7].
- Menopausal hormone therapy (MHT) can either be systemic or topical. Systemic MHT consists of estrogen-only preparations for hysterectomized women. Women with an intact uterus should receive in addition a progestogen for at least 10 days per month to prevent endometrial hyperplasia [8]. The estrogen dose is inversely related to the age of the woman: younger women need higher doses, while older women need lower doses. Both estrogens and progestogens can be given orally or transdermally; in addition the progestogen levonorgestrel can be delivered directly into the uterus. Estrogen is administered continuously. The progestogen can be administered either continuously or intermittently, usually, every 10–14 days per month. Continuous administration results in amenorrhea, while intermittent administration leads to withdrawal bleeding.
- Tibolone is a synthetic steroid with estrogenic progestogenic and weak androgenic activity indicated for the management of menopausal symptoms and urogenital atrophy in postmenopausal women. It does not require the addition of a progestogen in women with an intact uterus.
- Topical low dose vaginal estrogens are given for symptoms associated with urogenital atrophy and do not require the addition of a progestogen, as systemic absorption is low [9]. MHT is the most effective treatment for menopausal symptoms and reduces the risk of osteoporotic fracture.
- Benefits of MHT are more likely to outweigh risks for symptomatic women before the age of 60 years or within 10 years after menopause. Transdermal estrogen delivery is associated with a lower risk of venous thromboembolism than oral therapy. The risk of breast cancer in women over 50 years associated with MHT is primarily associated with the addition of a progestogen to estrogen therapy and related to the duration of use. The risk of breast cancer attributable to MHT is small and decreases after treatment is stopped. Safety data do not support the use of MHT in women with a history of breast or other estrogen-sensitive cancer.
- Non estrogen based treatments can be used for vasomotor symptoms and those associated with urogenital atrophy [10]. They are used in women who do not wish to take estrogens either through choice or because of concerns about comorbidities such as personal or family history of breast cancer or venous thromboembolism. They tend to be less effective than systemic or topical estrogens. A variety of agents can be used for hot flushes which include clonidine, paroxetine, fluoxetine, citalopram, venlafaxine, desvenlafaxine, gabapentin and pregabalin. Many lubricants and vaginal moisturizers are available. Lubricants are usually used to relieve vaginal dryness during intercourse and moisturizers provide symptom relief from vaginal dryness.
- Non estrogen based treatments for osteoporosis include bisphosphonates (alendronate, risedronate, ibandronic acid, zoledronic acid), denosumab, Selective Estrogen Receptor Modulators (SERMs: raloxifene and bazedoxifene) and parathormone analogs

(teriparatide and intact recombinant PTH) [11]. Women at risk for an osteoporotic fracture who receive MHT for the management of menopausal symptoms do not require additional treatment for osteoporosis. Asymptomatic women at high risk for fracture, however, should receive non-estrogen based treatment for osteoporosis. The choice of the drug depends on the medical history of the patient and the efficacy and safety profile of the particular treatment [12].

- New preparations for menopause management will become available such as ospemifene for urogenital atrophy and bazedoxifene combined with estrogen for menopausal symptoms and osteoporosis [13].
- Alternative and complementary therapies are popular in that they are perceived as 'natural' and safe. However evidence from randomized trials that they improve menopausal symptoms or reduce the risk of osteoporotic fracture is poor. There are concerns about herb-drug interactions and adverse effects. The use of bio-identical hormone therapy is unregulated, under-researched and therefore not recommended [8].
- Premature ovarian insufficiency (POI) is the exhaustion of ovarian follicles resulting in amenorrhea before the age of 40. Early menopause refers to menopause before the age of 45 [14]. Ovulation may occur intermittently after diagnosis of POI, possibly resulting in menstrual bleeding and pregnancy and thus fertility and contraception need to be discussed. Untreated it increases the risk of osteoporosis, cardiovascular disease, dementia, cognitive decline and Parkinsonism. The treatment of choice is MHT until the average age of the natural menopause (i.e. late 40s early 50s). In women under age 50 MHT use is not associated with an increased risk of breast cancer compared to that found in normally menstruating women. Few data are available on the efficacy of alternatives such as bisphosphonates in women with POI or early menopause and the long-term effects on the skeleton of any offspring are unknown.

Contributors

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Competing interests

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