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Menopause Period, Endocrine Changes and its Menifestations in Various Symptoms

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Annotation. The menopause is literally defined as a woman's or person's final menstrual period and so the accepted confirmation of this can only be made retrospectively after 1 year of amenorrhoea. The cause of the menopause is cessation of regular ovarian function with the corresponding decline in oestrogen levels. This is usually a gradual process over several years and there is great heterogeneity in the experiences of women as they go through the menopausal transition

Keywords: menopause, perimenopause, climacteric, early menopause, postmenopause.

Introduction

The average age of the menopause worldwide has not changed for decades, remaining at a median age of between 51 and 52 years, with 95% of women attaining menopause between the ages of 45 and 55 years. Menopause occurring outside these ages is relatively uncommon. Premature menopause (POI) is discussed later. Several different descriptive phrases exist:

Menopause: the last menstrual period.

Perimenopause: from the onset of ovarian dysfunction until 1 year after the last period and the diagnosis of menopause is made. It is usually characterised by irregular menstruation and the onset of menopausal symptoms. Typically starts after the age of 45 but can occur earlier.

Climacteric: another term for the perimenopause.

Postmenopause: all women who have had 1 year or more since their last period are deemed postmenopausal.

The ‘change’: a colloquial description of the perimenopause and postmenopause.

Premature menopause: a menopause that occurs before the age of 40. The correct term is premature ovarian insufficien (POI).

Early menopause: a menopause that occurs after the age of 40 but before the age of 45.

Endocrine changes in menopause. The current understanding is that the menopause occurs at the time of the depletion of oocytes from the ovary and is irreversible. Unsurprisingly, the endocrinology is not as simple as the ovaries just running out of eggs and losing the capacity to produce hormones at a particular age. Reproductive function is maintained by a subtle interplay between the hypothalamic production of gonadotrophin releasing hormone (GnRH), the anterior pituitary hormones luteinizing hormone (LH) and follicle-stimulating hormone (FSH), the ovarian peptide hormone inhibin B and the steroid hormones oestrogen and progesterone. These hormones change not only during the menstrual cycle but also throughout an individual’s reproductive life, with their production changing at differing times and rates according to the age of the woman. Inhibin B is produced by follicles within the ovary, so, as the number of follicles declines, the production of inhibin decreases. In the perimenopausal years, small declines in inhibin drive an overall increase in the pulsatility of GnRH secretion and overall serum FSH and LH levels, which results in an increased drive to the remaining follicles in an attempt to maintain follicle production and oestrogen levels. Androgenic hormone production comes from the ovaries, peripheral adipose tissue

and the adrenal glands, with the ovaries producing approximately 30–50% of total circulating levels. Although these hormones play no role in the control of ovulation, a decline in ovarian testosterone and other androgens accompanies the process of ageing in women. This is shown by the fact that overall androgen concentrations in a woman in their 20s are approximately double those of a woman of 40 years, and then slowly decline throughout life thereafter. Recent research has suggested that levels may start to rise again after 70 years of age, but the significance this is not yet clear.

Diagnosis of menopause: the diagnosis of menopause is largely a clinical diagnosis based on menstrual irregularities and amenorrhoea together with oestrogen deficiency symptoms, such as vasomotor symptoms. The use of ser endocrine tests such as hormone levels are of little value in the perimenopausal years, as they are unpredictable due to the hormonal variations that frequently occur in association with episodic and irregular ovulatory cycles at this time of life. An elevated serum FSH in association with a low serum oestradiol may be suggestive of the menopause, but as this combination of levels can occur during a normal menstrual cycle, this test can be misleading. Two raised FSH levels (>30 IU) at least 6 weeks apart are required to make a diagnosis. In all women in whom a diagnosis of menopause is being considered, the possibility of pregnancy should also be considered. The diagnosis of menopause in a hysterectomized individual can be more difficult due the lack of signalling from the bleeding that accompanies the menstrual cycle. However, in these circumstances, the use of other symptoms of the menopause as biological indicators is usually enough to make a confide diagnosis.

Symptoms of menopause: the hormonal changes that occur during and immediately after the menopause can lead to profound changes in a variety of different systems. Not only does the timing of when each system is affected vary dramatically between individuals, but also the degree of how the changes influence each individual is remarkably unpredictable. The reasons for these variations are not clearly understood, but there is some evidence that genetic influences play a par While most effects of the menopause have longterm implications, the effects of menopause are commonly categorized as having an early onset or an onset in the medium to long term.

Vasomotor symptoms: some of the earliest changes during the menopause are the onset of vasomotor symptoms that typically appear during the perimenopausal years. The colloquial term applied to vasomotor symptoms is a 'hot flus and these usually coexist with night sweats, that is, when hot flush occur during sleep. The exact aetiology of vasomotor symptoms is unknown, but they may be due to loss of the modulating effect of oestrogen on serotonergic receptors within the thermoregulatory centre in the brain, resulting in exaggerated peripheral vasodilatory responses to minor atmospheric changes in temperature. Hot flushes occur in up to 80% of women and may continue for up 7 years, sometimes longer. Many women manage these symptoms without the need for specific treatment but, for some, these flushes ca extremely debilitating. Night sweats lead to sleep disturbance, which causes tiredness, exhaustion, poor performance during the day and impaired quality of life. There is also the suggestion that severe vasomotor symptoms are a marker for cardiovascular disease. While hot flushes tend to appear unpredictably, triggers inclu alcohol, spicy foods, caffeine and smoking. Individuals with a high body mass index (BMI) tend to get worse vasomotor symptoms.

Psychological symptoms: while there is little evidence to support a direct effect of the menopause as a cause for depression, menopause is associated with low mood, irritability, lack of energy, tiredness and impaired quality of life. Alongside vasomotor symptoms, these symptoms can be very debilitating for some women. While these symptoms may be attributed to hormonal changes, it is important to consider other influences mood such as relationship and family changes, financial issues, previo history of depression and anxiety, and the woman's or person's attitude to ageing.

Cognitive function: many women complain of change in memory, concentration and global cognitive function around the time of the menopause, which is often described as ‘brain fog’. Some of these changes can be explained by the impact of vasomotor symptoms and other symptoms on patterns of sleep, but a

direct effect of oestrogen deprivation on brain function cannot be excluded.

Endometrial effects: changes in menstrual bleeding herald the onset of the menopause and occur early during the menopausal transition. The initial scanty vaginal bleeding is due to the reduction in oestrogenic endometrial stimulation with failing ovarian function, ultimately resulting in periods completely stopping when the endometrium is no longer stimulated. Episodic and infrequent ovulation leads to unpredictable progestogen levels, which causes inadequate endometrial shedding with irregular, prolonged and sometimes heavy bleeding.

Bone health and osteoporosis: one of the best understood areas of long-term postreproductive health is the changes to bone that occur on loss of oestrogenic support of skeletal metabolism. The skeleton is maintained by a constant process of remodelling, with bone being laid down by osteoblasts and resorbed by osteoclasts. The balance of the rates of resorption versus deposition is affected by many different factors, one of which is oestrogen. An important consideration is the attainment of peak bone mass. Bone density naturally increases during childhood, reaching a peak between 20 and 30 years of age. Males generally achieve a greater peak bone density than females. After peak bone mass attainment in women, there is a gradual decline until the menopause, then an accelerated phase of bone loss until 60 years of age, followed by a further steady decline until death, which leads to increasing fragility of the trabecular bone. After the age of 60 in women, the likelihood of osteoporotic fractures of the wrist, hip and spine increases. Osteoporosis is defined as a skeletal disorder characterized compromised bone strength predisposing to an increased risk of fracture. It is more frequent in women than men, with an approximate ratio of 4:1. Osteoporosis is a major health problem that will only worsen as the population ages. Identifying those most at risk and determining targeted prevention strategies is required. Again, the menopause is an ideal time to assess this.

Cardiovascular system: approximately 30% of all deaths occur as a result of ischaemic heart disease and stroke. This makes cardiovascular disease (CVD) a condition that significantly burdens the global health system. While CVD relatively uncommon before the menopause, this changes rapidly after the menopause and CVD becomes the leading cause of death among women over 60 years of age. During the menopausal transition, there are several changes in the female physiology brought about by the loss of oestrogen that can influence individual risk of CVD. These include changes in t distribution in fat from more gynaecoid (fat on breasts and hips) to android (abdominal fat deposition); changes in serum lipid levels that include increases in triglycerides, total cholesterol and low-density lipoprotein cholesterol and a reduction in high-density lipoprotein cholesterol; and changes in blood vessel dynamics. Oestrogen has a supportive effedt on the vessel wall that favours vasodilatation and prevents atherogenesis and these effects are reduced after the menopause. Thus, while the management of CVD is not usually within the realms of the gynaecologist, it is important to recognize that, because many women seek the help of a gynaecologist during their life, and particularly around the menopause, there may be opportunities for the identificati of, and improvement in, modifiable risk factors for CVD.

All in all, the menopause is a natural event, and many women have mild symptoms or no symptoms requiring intervention. The menopause is viewed differently in different cultures, and an empathy of the widely different experiences and symptoms around the menopause is important. Raising awareness of the long-term implications discussed previously, such as osteoporosis and CVD, should be part of good preventative medicine, even in those without significant symptoms.

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