

# Menopausal Disorders

## Summary

A change in demographics with increased ageing of population and decreased mortality in the elderly resulted in increased life expectancy. Thus, the average women can now expect to spend nearly one-third of her life in postmenopausal state.

Oestrogen deficiency causes vasomotor symptoms such as hot flushes and night sweats, mood disorders and urogenital atrophy. Another important aspect of menopause is sexual dysfunction which affects the quality of life of postmenopausal women. Long term sequelae of ovarian failure include cardiovascular disease, osteoporosis and Alzheimer's disease.

## Key points

- Vasomotor symptoms occur in approximately 50-75% of women.
- Lower genital tract symptoms and urological symptoms are common in menopause.
- Sexual desire and sexual activity declines with increasing age especially in women.
- Oestrogen deficiency associated with menopause, influences the risk of postmenopausal women to Alzheimer's disease.
- The risk of cardiovascular disease increases after menopause.
- Oestrogen deficiency increases the risk of osteoporosis.

## Introduction

The word menopause literally means the cessation of menstrual cycles. It is derived from the Greek 'meno-' (month) and 'pauis' (a pause, a cessation). Natural menopause is recognised after 12 consecutive months of amenorrhoea, for which there is no other pathological or physiological cause.

Menopause results from loss of ovarian follicular activity. The ovaries fail to respond to gonadotrophin stimulation and this leads to an increase in the plasma levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH). The cessation of ovarian function leads to lack of oestrogen.

Oestrogen deficiency causes vasomotor symptoms such as hot flushes and night sweats, mood disorders and urogenital atrophy. Another important aspect of menopause is sexual dysfunction which affects the quality of life of postmenopausal women. Long term sequelae of ovarian failure include cardiovascular disease, osteoporosis and Alzheimer's disease.

Menopausal symptoms exhibit cultural differences. Japanese and Chinese women tend to have less menopausal symptoms than North American women<sup>1,2</sup>. It was also shown that women who exercise regularly suffer less menopausal symptoms<sup>3</sup>.

The median age of menopause is 51 years. It tends to occur earlier in smokers<sup>4</sup> and in women with Down's syndrome<sup>5</sup>. A change in demographics with increased ageing of population and decreased mortality in the elderly resulted in increased life expectancy. Thus, the average women can now expect to spend nearly one-third of her life in postmenopausal state. Postmenopausal women account for over 20% of UK population. Thus a good understanding of menopause and the related disorders is of extreme importance at this day and age.

### **Vasomotor symptoms**

Vasomotor symptoms include hot flushes and night sweats. They occur in approximately 50-75% of women and tend to be more severe after surgical menopause. These vasomotor symptoms can occur at any time, often disturbing sleep. This in turn can lead to insomnia, irritability, exhaustion and lack of concentration.

A hot flush often starts in the head or neck and then involves the whole body. This is usually followed by intense sweating and then by shivering. There is a rise in skin temperature of about 1<sup>0</sup>C<sup>6</sup>.

The underlying cause of these vasomotor symptoms may be impairment of the sympathetic nervous control of skin blood flow<sup>7</sup>. Serotonin and its receptors have also been implicated<sup>8</sup>.

### **Mood disorders**

Mood disorders associated with menopause include depression, anxiety, irritability and mood swings. A long standing history of depression increases the risk of mood disorders at menopause<sup>9,10</sup>. Life changes that occur at the time of the menopause, such as the loss of fertility and lack of femininity, contribute to depression.

However general population studies have shown that most women going through the menopause do not experience severe psychological problems<sup>11,12</sup>.

### **Urogenital symptoms**

Both the female genital tract and the lower urinary system develop from the primitive urogenital sinus. Both are very sensitive to oestrogen, with oestrogen receptors present in lower genital tract and throughout the urinary tract, except from the bladder dome. Thus it is not surprising that both lower genital tract symptoms and urological symptoms occur concurrently in menopause.

Lower genital tract symptoms include vaginal dryness and superficial dyspareunia. Vaginal atrophy also predisposes to recurrent bacterial vaginosis. Urological symptoms include dysuria, nocturia, urgency, urinary frequency, stress incontinence and recurrent urinary tract infections. About 50% of postmenopausal women suffer from at least one of these symptoms<sup>13, 14</sup>.

### **Sexual Dysfunction**

Sexual desire and sexual activity declines with increasing age especially in women. Female Sexual dysfunction includes decreased sexual desire, decreased sexual arousal, dyspareunia and inability to achieve orgasm. This often leads to personal distress and decreased quality of life.

The underlying causes are multifactorial. Change in sex hormones may be implicated however other factors such as relationship with partner, mood disorders, decreased self esteem and the presence of a disease can be more important<sup>15</sup>. Other physiological factors which influence the sexual life of menopausal women include vaginal dryness, dyspareunia and urinary incontinence.

### **Dementia and Alzheimer's disease**

Women suffer from Alzheimer's disease between 1.5 to 3 times more than men. The prevalence of this disease increases considerably and doubles every 5 years after the age of 65 years. The oestrogen deficiency associated with menopause, influences the risk of postmenopausal women to Alzheimer's disease.

Throughout life time oestrogen is important for the proper function of the brain, as indicated by the widespread presence of oestrogen aromatase and oestrogen receptors (ER $\alpha$  and ER $\beta$ ) in the brain<sup>16, 17</sup>. Oestrogen is a primary regulator of brain neurogenesis and cell number, synaptogenesis, synaptolysis, multiple cognitive and autonomic functions, vascular function, immune responses and defense measures against brain lesions and dystrophy<sup>18</sup>. The brain is constantly being exposed to internal and external toxins. These trigger inflammatory responses by the brain's immune and vascular systems. Oestrogen is important in regulating these inflammatory responses by keeping them local and thus avoiding damage to nearby neurons. In oestrogen deficiency, the immune and vascular responses are less controlled and this can lead to brain dysfunction and diseases. Lack of oestrogen may also slow down the reparative functions of the brain vessel endothelium and failure of vascular clearance<sup>19</sup>.

### **Cardiovascular Disease**

The risk of cardiovascular disease increases after menopause. Postmenopausal women are about 2-4 times more at risk of ischaemic heart disease than premenopausal women. Cardiovascular disease (such as myocardial infarction and stroke) is the leading cause of death in women after menopause. In addition to the increasing risk for cardiovascular disease with ageing, menopause itself produces a significant superimposed risk<sup>20</sup>.

Menopause results in metabolic changes that contribute to increased risk for cardiovascular disease. Women have higher high-density lipoprotein (HDL) and lower low-density lipoprotein (LDL) compared to men. After the menopause, the HDL:LDL ratio in women becomes closer to the male ratio. Triglycerides also increase after menopause. There is also a decrease in insulin secretion by the pancreas and decrease in circulating insulin elimination. Insulin resistance gradually increases after the menopause. Moreover there is usually an increase in weight in postmenopausal women especially around the abdomen. The incidence of essential hypertension and diabetes mellitus type 2 is also increased. All these changes lead to an increased risk of cardiovascular diseases<sup>21, 21, 23</sup>.

Oestrogen deficiency also appears to have a more direct effect on the vessel walls. It affects arterial tone and lack of it increases blood flow resistance. It also influences nitric oxide metabolism and modifies thromboxane and prostaglandin synthesis. Thus lack of oestrogen means that these mechanisms are disrupted and this can lead to adverse changes on the cardiovascular system.

### **Osteoporosis**

Osteoporosis has been defined by the WHO as a 'disease characterised by low bone mass and micro-architectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk'<sup>24</sup>. One in three postmenopausal women has osteoporosis. The incidence of osteoporosis show ethnic variation with Caucasian women having a higher fracture rate than Afro-Caribbean women.

Bone mass reaches a peak in women in the third decade. Oestrogen exerts its protective effect on the skeleton through the oestrogen sensitive calcitropic hormones (parathyroid hormone and 1, 25 (OH)2D) and oestrogen sensitive cytokines<sup>25,26</sup>. Moreover calcium absorption from the gut and its re-absorption by the kidneys is partially oestrogen-dependent<sup>27</sup>. At the time of menopause, oestrogen deficiency lead to an accelerated period of bone loss, lasting about 6-10 years. Then bone loss continues at a slower rate. The bone loss is secondary to an increase in bone turnover with bone resorption being more increased than bone formation.

Postmenopausal bone loss mostly affects cancellous bone found in vertebral bodies and at the end of long bones. Osteoporosis leads to Colles wrist fractures, hip fractures and vertebral fractures. These fractures lead to significant morbidity. Moreover hip fractures are also associated with increased mortality rates<sup>28</sup>.

Predisposing factors for osteoporosis include family history of osteoporosis, low body mass index, premature ovarian failure, endocrine diseases (e.g. hyperthyroidism, Cushing's syndrome), corticosteroids, smoking, alcohol, low calcium intake, immobilisation and rheumatoid arthritis.

### **Conclusion**

Oestrogen deficiency results in physical and psychological disorders such as vasomotor symptoms, sexual dysfunction and urogenital symptoms which have a profound impact on the quality of life of postmenopausal women.

Menopause is also associated with other diseases that cause significant morbidity and mortality such as cardiovascular disease, Alzheimer's disease and osteoporosis.

More than one third of women are in menopause and most of them experience at least one of the symptoms/diseases related to oestrogen deficiency. Thus it is of great importance to be aware of menopausal disorders and understand and offer the appropriate treatment to women going through such changes in their life.

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