Menopause

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LEARNING OBJECTIVES

- Definition of menopause
- Physiological menopause
- Non-physiological menopause
Definition

- The menopause is defined as the woman’s final menstrual period.
- The accepted confirmation of this is made retrospectively after 1 year of amenorrhea.
- The cause of the menopause is cessation of regular ovarian function.
The stages of the menopause

1. **Perimenopause**: The 3-5 year period before menopause when your estrogen and hormone levels begin to drop is called **climacteric phase**. You typically enter into perimenopause in your late 40's and could begin to experience irregular menstrual cycles and symptoms. There is still a chance that you could get pregnant during this time and if you want to avoid this, a form of birth control is recommended until one year after your last period.

2. **The menopause**: The final menstrual period (no more eggs)

3. **Postmenopause**: Starts when you have had no periods for 12 months
When does the menopause happen?

- The menopause can start at any time from late 30s to late 50s. For most women it happens between age 45 and 55.
- A natural menopause between the ages of 40 and 45 is called an early menopause.
- A natural menopause before the age of 40 is considered a premature menopause which is mostly idiopathic, but can also occur after radiation therapy or surgical oophorectomy.
Endocrine changes

- Hormonal control of the menstrual cycle and hormonal disorders, reproductive function is maintained by a subtle interplay of the hypothalamic production of gonadotrophin-releasing hormone (GnRH), the pituitary hormones luteinizing hormone (LH) and follicle-stimulating hormone (FSH), the ovarian peptide hormone inhibin B and the steroid hormones oestrogen, progesterone and testosterone. These hormones not only change during the menstrual cycle but also throughout a woman’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 decline 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 ovaries, peripheral adipose tissue and the adrenal glands, with the ovaries producing approximately 30–50% of total circulating levels. A decline in ovarian testosterone and other androgens accompanies the process of ageing in women.
Laboratory markers of menopause include the following:

- An increase in serum follicle-stimulating hormone (FSH) and decreases in estradiol and inhibin are the major endocrine changes that occur during the transition to menopause.
- FSH levels are higher than luteinizing hormone (LH) levels, and both rise to even higher values than those seen in the surge during the menstrual cycle.
- The FSH rise precedes the LH rise; FSH is the diagnostic marker for ovarian failure, while LH is not necessary to make the diagnosis.
- No specific changes in thyroid function related to menopause have been found.
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<td>Progressive decrease in pulsatility</td>
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<tr>
<td>LH &amp; FSH</td>
<td>Increased</td>
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<td>Inhibin</td>
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<td>Testosterone</td>
<td>Progressive decline</td>
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<td>Sustained low levels</td>
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FSH, follicle-stimulating hormone; GnRH, gonadotrophin-releasing hormone; LH, luteinizing hormone.
Diagnosis

The diagnosis of menopause is a largely clinical diagnosis that is made according to symptoms experienced, mostly due to lack of estrogen.

- Irregular periods
- Hot flushes
- Heart palpitations
- Increased vaginal pH and increased vaginal infections
- Night sweats
- Decreased libido (sex drive)
- Decreased risk of CVS diseases
- Vaginal dryness or discomfort during sexual intercourse
- Osteoporosis
- Psychological: Mood swings, Irritability, Increasing anxiety, Insomnia, Poor sleep pattern, Difficulty concentrating, Forgetfulness

# An elevated serum FSH in association with a low serum oestradiol may be suggestive of menopause.
The special circumstance of diagnosis of menopause in a woman who has undergone hysterectomy can be difficult due to the lack of signaling from the bleeding that accompanies the menstrual cycle. However, in these circumstances the use of symptoms of the menopause as biological indicators is usually enough to make a confident diagnosis.

- Hysterectomy (uterus removed)—symptoms appear gradually
- Oophorectomy (ovaries removed)—symptoms appear immediately
Non-physiological menopause

- Premature ovarian insufficiency
- Iatrogenic menopause – medical treatments and menopause after cancer treatment
- Iatrogenic menopause – surgical menopause
Premature ovarian insufficiency

- If menopause occurs before the age of 40 years it is defined as premature ovarian insufficiency (POI), also sometimes called premature ovarian failure (POF).
- It is thought to occur in approximately 1% of women under 40 years and 0.1% under 30 years. It is a distressing diagnosis for a woman to receive, especially if it occurs prior to the completion of her family.
- While no cause is found in most cases of primary POI, a suspected case should be investigated where possible for causes that are associated with issues that require separate treatment.

**Primary**
1. Chromosome anomalies (e.g. Turner’s, fragile X)
2. Autoimmune disease (e.g. hypothyroidism, Addison’s, myasthenia gravis)
3. Enzyme deficiencies (e.g. galactosaemia, 17a-hydroxylase deficiency)

**Secondary**
1. Chemotherapy or radiotherapy
2. Infections (e.g. tuberculosis, mumps, malaria, varicella)
Iatrogenic menopause – medical treatments

- If GnRH is given in a constant high dose, it desensitizes the GnRH receptor and reduces LH and FSH release. Drugs that are GnRH agonists (e.g. buserelin and goserelin) can be used as treatments for endometriosis and other gynaecological problems. Although they mimic the GnRH hormone, when administered continuously they will down-regulate the pituitary and consequently decrease LH and FSH secretion. This will induce a temporary menopause with a relatively rapid onset, which can be managed with the introduction of hormone therapies and other drugs to relieve some of the unwanted menopausal symptoms – known as add-back therapy.
Iatrogenic menopause – surgical menopause

- Women may be placed into surgical menopause aiming to permanently treat benign gynaecological conditions such as menstrual disorders, fibroids and endometriosis. Bilateral salpingo-oophorectomy (BSO) may also be performed prophylactically for women at high risk of inherited malignancies such as breast and ovarian cancer, with BRCA 1 and 2 gene mutation screening. Good clinical practice in these women should ensure that before making the irreversible decision to have a BSO for these diseases they consider the correct time in their life for the procedure and that they are given plans for how they can manage the sudden hormone deficits that they will have to endure.