

MENOPAUSE

Menopause is the time at which a woman permanently stops menstruating, usually between 45 and 55 years of age, and is diagnosed after 12 months of [amenorrhea](#). It is preceded by the [climacteric period](#), sometimes referred to as [perimenopause](#) or [menopausal transition](#), which is the transition period in a woman's life from the time of full sexual maturity to the onset of menopause. The physical manifestations are caused by hormonal changes (primarily a drop in progesterone and estrogen levels) that occur during the [climacteric period](#). Clinical features leading up to menopause include irregular [menses](#), autonomic symptoms (e.g., hot flashes), mental symptoms (e.g., mood swings), and atrophic features (e.g., reduced breast size, [vaginal atrophy](#)). [Menopausal transition](#) is a natural phase of the aging process in females, and as such does not usually warrant treatment. However, treatment is warranted in the case of severe symptoms or early onset menopause. The choice of treatment is decided on a case-by-case basis and includes conservative methods, [hormone replacement therapy](#), and non-hormonal therapy.

Menopause occurring before the age of 40 is considered premature. A common cause of [premature menopause](#) is [ovarian insufficiency](#). The diagnosis is confirmed by increased [FSH](#) levels occurring after more than three months of [amenorrhea](#) in a woman under the age of 40. Treatment involves [hormone replacement therapy](#).

Pathophysiology

↓ Ovarian function → ↓ estrogen and progesterone levels → loss of negative feedback to the gonadotropic [hormones](#) → ↑ [GnRH](#) levels → ↑ levels of [FSH](#) and [LH](#) in blood ([hypergonadotropic hypogonadism](#)) → [anovulatory cycles](#) become more and more frequent → progressive follicular depletion → ovarian function eventually stops permanently

In menopausal women, estrogens are mainly produced by peripheral aromatase conversion of adrenal androgens in adipose tissue. Therefore onset of menopause might be delayed and symptoms might be milder in [obese](#) women.

Definition

Perimenopause ([menopausal transition](#), MT): The time period from the first instance of climacteric symptoms caused by fluctuating hormonal levels to multiple years after menopause. (The duration can vary greatly in different women. However, the average length of [perimenopause](#) is 4 years.)

1. Premenopause

- The time period from the first occurrence of climacteric irregular **menstruation** cycles to the last menstrual period
 - Onset: usually **45–55 years** of age
 - Characterized by increasingly infrequent **menstruation**
2. **Menopause**
- Time at which **menstruation** ceases permanently
 - Confirmed after **12 months** of **amenorrhea**
 - The average age at menopause is ~ **49–52 years**.
3. **Postmenopause**: the time period beginning 12 months after the last menstrual period

Clinical features

The onset and intensity of symptoms is dependent on the phase of **menopausal transition**.

- Irregular **menses** (which gradually decrease in frequency) → complete **amenorrhea**
- **Autonomic symptoms**
- Increased **sweating**, **hot flashes**, and **heat intolerance**
- Vertigo
- **Headache**
- **Mental symptoms**
- Impaired sleep (**insomnia** and/or night sweats)
- Depressed mood or **mood swings**
- Anxiety/irritability
- Loss of libido
- **Atrophic features**
- Breast tenderness and reduced breast size
- **Vulvovaginal atrophy**
- Atrophy of the vulva, cervix, vagina (thin, pale, smooth epithelial layer, associated with vaginal dryness, pruritus, and **dyspareunia**; see **atrophic vaginitis** for details)
- May present with features that mimic a **urinary tract infection** (i.e., dysuria, urinary frequency and urgency)
- Weight gain and bloating

The onset and duration of these symptoms is widely variable. Symptoms may begin up to 6 years before the menopause and continue for a number of years after the last menstrual period!

Subtypes and variants

- Surgical menopause: due to removal of ovaries (commonly after hysterectomy with bilateral salpingo-oophorectomy)

References:^[8]

Diagnostics

Diagnosis is usually clinical. However, certain laboratory tests may help confirm the onset/presence of [perimenopause](#).

- ↓ Estrogen and ↓ progesterone
- [FSH](#) levels can fluctuate widely in [perimenopause](#).
- [Testosterone](#) and [prolactin](#) levels are within normal ranges.
- Lipid profile: ↑ total cholesterol, ↓ HDL

All [postmenopausal](#) women above the age of 65 should be screened for [osteoporosis](#) (i.e., using the [DEXA](#) scan to measure bone mineral density).

[Hyperthyroidism](#) and menopause present similarly. For this reason, serum [TSH](#) should be checked in all suspected [perimenopausal](#) cases with heat intolerance and disturbed sleep to determine the cause!

Treatment

Indications

- Treatment is not warranted for all women approaching or undergoing menopause, as it is a normal aging process. Treatment may be considered in the following cases:
- Symptoms are severe enough to infringe significantly on functional capacity, and hence affect quality of life.
- In [premature menopause](#)
- [Surgical menopause](#) (e.g., post-oophorectomy)

Lifestyle modifications and local medical therapy

- For hot flashes: avoidance of triggers (e.g., bright lights, predictable emotional triggers); environmental temperature regulation (e.g., using fans)
- For atrophic vaginal symptoms: **vaginal estrogen creams**, rings, or tablets (estrogen therapy may reduce the incidence of [UTIs](#) and features of [overactive bladder](#))

- For impaired sleep and/or hot flashes: exercise, acupuncture, and relaxation techniques
- Prevention of [osteoporosis](#)
- Smoking cessation, adequate [vitamin D](#) intake and regular weight-bearing exercise
- For more details, see “treatment” of [osteoporosis](#).

Hormone replacement therapy ([HRT](#))

[HRT](#) is usually employed for the short-term treatment of menopausal symptoms.

- **Types**
- Estrogen therapy: for women who have had a hysterectomy
- Estrogen plus progestin therapy: **for women with a [uterus](#)**
- **Routes:** oral, transdermal
- **Risks**
- Cancer
- **Unopposed estrogen** can result in [endometrial hyperplasia](#) → increased risk of [endometrial cancer](#)
- Estrogen plus progestin therapy → increased risk of [breast cancer](#)
- Cardiovascular disease: [coronary heart disease](#), [deep vein thrombosis](#), [pulmonary embolism](#), [stroke](#)
- Gallbladder disease
- [Stress urinary incontinence](#)
- **Contraindications**
- Undiagnosed vaginal bleeding
- [Pregnancy](#)
- [Breast cancer](#)/[endometrial cancer](#)
- Chronic liver disease
- [Hyperlipidemia](#)
- Recent [DVT](#)/[stroke](#)
- [Coronary artery disease](#)

Non-hormonal therapy

Non-hormonal therapy is used to treat menopausal vasomotor symptoms in women who do not want to use hormonal medications or who have contraindications for [HRT](#).

- Selective estrogen receptor modulators: [tamoxifen](#), ospemifene , and [raloxifene](#)
- [Paroxetine](#): for vasomotor symptoms (i.e., hot flashes)
- [Clonidine](#) and/or [gabapentin](#)

Premature menopause (**menopause precox**)

- **Definition:** cessation of periods **before the age of 40**
- **Etiology**
- Idiopathic
- Can be surgically induced by bilateral oophorectomy (removal of ovaries)
- Primary (or premature) **ovarian insufficiency**

Early menopause is often associated with smoking!

Ovarian insufficiency

- **Definition:** cessation of **menses** due to primary ovarian failure (failure of the ovary to function adequately, both as an endocrine gland and a reproductive organ) before age 40.
- **Etiology**
- Primary ovarian insufficiency (**POI**): idiopathic primary disorder in the ovary
- This condition is sometimes referred to as **premature menopause**, but the terms are not synonymous.
- Secondary **ovarian insufficiency**: **ovarian insufficiency** caused by an underlying disorder
- Functional disorder affecting the reproductive system (e.g., ovarian **endometriosis**, **polycystic ovary syndrome**, cancer of the reproductive organs)
- Genetic syndromes with hypoplastic ovaries, e.g., **Turner syndrome**, **Swyer syndrome**, **androgen insensitivity syndrome**, **adrenogenital syndrome**
- Autoimmune diseases (autoimmune **lymphocytic** oophoritis, **Hashimoto's thyroiditis**)
- Infections: **measles**, **mumps**, **tuberculosis** of the genital tract
- Smoking
- Post-oophorectomy
- **Radiation** and/or **chemotherapy**
- Prolonged **GnRH** (**gonadotropin-releasing hormone**) therapy
- Induction of multiple ovulation in **infertility**
- Other conditions: **Addison's disease**, **type I diabetes mellitus**, and **pernicious anemia**
- Hypothalamo-pituitary causes
- **Pathophysiology:** impaired follicular development → ↓ estrogen levels → loss of feedback inhibition of estrogen on **FSH** and **LH** → ↑ **FSH** and **LH** (usually **FSH** > **LH**)
- **Clinical features:** climacteric features followed by cessation of **menstruation**
- **Diagnostics**
- Confirmed by ↑ **FSH** after > **3 months** of **amenorrhea** in a woman under age 40
- Further tests to determine the underlying disorder in secondary **ovarian insufficiency**
- **Treatment**

- [Hormone replacement therapy](#), as detailed above
- [In vitro fertilization](#) for [infertility](#) (for women who wish to bear children)
- Treatment of underlying disorder if present