Introduction to menopause

Menopause is the moment when a woman has had no menstrual periods (amenorrhea) for 12 consecutive months. If this cessation of periods results from the spontaneous halt of ovarian hormone production and is not the result of other physical or pathological conditions or treatments, it's termed *natural menopause*. The average age of menopause in Canada is 51 years and this has been constant throughout the last few centuries.[1] *Induced menopause* is caused by medical or surgical intervention, such as radiation or chemotherapy treatment, or ovary removal during hysterectomy (oophorectomy). *Premature menopause* refers to menopause before age 40, and *early menopause* refers to menopause before age 45.[2]

Perimenopause is a time that begins with an alteration in menstrual cycle length and ends 12 months after the final menstrual period. The *menopause transition* is a term preferred by the Stages of Reproductive Aging Workshop (STRAW) as more appropriate to describe this phase. The North American Menopause Society (NAMS) uses the terms perimenopause and menopausal transition interchangeably.

During a woman's reproductive years, estrogen (primarily as estradiol) and progesterone levels rise and fall with her cycles, as the follicle-stimulating hormone (FSH) promotes follicle development and ovum release. By menopause, a woman's ovaries have no follicles left that respond to FSH.[3] The lack of follicular stimulation and development signals the end of the regular menstrual cycle and the monthly fluctuations of both estradiol and progesterone concentrations.[3] Without follicular development and the designation of a graafian (dominant) follicle, estradiol concentrations remain low and ovulation does not occur, so progesterone concentrations also remain low.[3] As a result, endometrial proliferation occurs rarely and there are no secretory changes. The pituitary gland increases the production and release of both FSH and luteinizing hormone (LH) in an attempt to entice the ovary to initiate follicular development.[3] Because the ovary cannot respond, FSH and LH concentrations remain elevated, while estradiol and progesterone concentrations remain low.[3] Testosterone, however, continues to be produced by the ovaries after menopause.

Cessation of menses, along with the increase in FSH and LH and decrease in estradiol and progesterone, occurs gradually over several months to years.[3] In perimenopause, ovary response to FSH and LH slows, taking longer for follicular development and endometrial proliferation to occur, but unlike in menopause, the follicles in the ovary are still able to respond and ovulation does still occur.[3] These physiologic changes affect normal hormone balance and can result in fluctuating estrogen levels that contribute to symptoms.

The postmenopausal female continues to produce a form of estrogen in the adipose tissue as a result of the conversion of androstenedione (from the adrenal gland) to estrone.[3] The amount

TABLE 1 Menopause terminology[2]

Early menopause	Natural or induced menopause that occurs well before the average age of natural menopause (51 years), at or under age 45.
Early postmenopause	The time period within 5 years after the final menstrual period (FMP), resulting from natural or induced menopause.
EPT	Combined estrogen-progestin therapy.
ET	Estrogen therapy.
FMP	Final menstrual period.
HT	Hormone therapy (encompassing both ET and EPT).
Induced menopause	Permanent cessation of menstruation after bilateral oophorectomy (i.e., surgical menopause) or iatrogenic ablation of ovarian function (e.g., by chemotherapy or pelvic radiation therapy).
Local therapy	Vaginal ET administration that does not result in clinically significant systemic absorption.
Natural/spontaneous menopause	The FMP, confirmed after 12 consecutive months of amenorrhea with no obvious pathologic cause.
Perimenopause/ menopause transition	Span of time when menstrual cycle and endocrine changes occur a few years before and 12 months after an FMP resulting from natural menopause.
Premature menopause	Menopause reached at or under age 40, whether natural or induced.
Premature ovarian insufficiency	Loss of ovarian function before age 40, leading to permanent or transient amenorrhea (often described as premature ovarian insufficiency or premature menopause).
Systemic therapy	HT administration that results in absorption in the blood high enough to provide clinically significant effects; in this supplement, the terms ET, EPT, HT and progestin are presented as systemic therapy unless stated otherwise.

Adapted with permission from: Estrogen and progestogen use in postmenopausal women: 2010 position statement of The North American Menopause Society. *Menopause* 2010;17(2):242-55.

TABLE 2 Absolute contraindications to estrogen and progestin therapy

Estrogen therapy	• Undiagnosed vaginal bleeding • Active liver disease • Active thromboembolic disease

The risk of recurrence of breast cancer or thrombosis following estrogen therapy is unknown. Caution is recommended in women with cardiovascular disease. For all women, the risk versus the benefit must be taken into consideration when prescribing estrogen therapy.

Progestin therapy	• Undiagnosed vaginal bleeding • Known or suspected carcinoma of the breast • Pregnancy

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TABLE 3 Selected estrogen product doses[4]

Product	Low dose	Standard dose	High dose
Conjugated estrogen (oral)			
Premarin, CES	0.3 mg	0.625 mg	0.9 mg or 1.25 mg
17β-estradiol (oral)			
Estrace	0.5 mg	1 mg–2 mg	N/A
17β-estradiol (transdermal patches)			
Climara	0.025 mg/day	0.05 mg/day	0.075 mg/day 0.1 mg/day
Estradot	25 mcg/day	37.5 mcg/day 50 mcg/day	75 mcg/day 100 mcg/day
Oesclim	25 mcg/day	50 mcg/day	N/A
17β-estradiol (topical gel)			
Estrogel	N/A	1 actuation	2 actuations 4 actuations

of estrone produced depends on the amount of adipose tissue present. Estrone has a weaker effect on the endometrium than estradiol; therefore, proliferation of endometrial tissue is rare, except in women who are obese.

Vasomotor symptoms, commonly known as hot flashes and night sweats, are the most common presenting complaint of menopausal women. Bothersome hot flashes often commence about 2 years before the final menstrual period, with maximum symptoms occurring within the first 2 years after the last period. The frequency of hot flashes gradually decreases over 6 years;[1,7] however, some women experience hot flashes many years after menopause.

Other associated complaints of menopause, including vaginal symptoms such as dryness, itching, vaginitis and dyspareunia, generally persist or worsen with aging due to low estrogen levels. Women tend to complain of vaginal symptoms a few years after the last menstrual period. Unlike hot flashes, vaginal atrophy does not improve over time. Some women notice decreasing libido and an alteration in sexual function with the onset of menopause. There is a gradual decline in testosterone production from the ovaries, associated with normal aging; however, sexual function changes are multifaceted.

Sleep disturbances and mood changes have also been reported in the menopausal transition and may continue into early menopause. Stress incontinence, skin changes, memory and decreased concentration may also occur. Perimenopausal women can also suffer from premenstrual symptoms (bloating, water retention) and increase in headaches or migraines. Even though there is a decline in fertility with perimenopause, pregnancy is a possibility and contraception should be continued. ■

Estrogen through a woman's life

The predominant estrogen prior to menopause is estradiol (E2), but this shifts to estrone (E1) after menopause, as estrone is converted from androstenedione in adipose tissue.[5] Estriol (E3) is the predominant estrogen in pregnancy, as it is produced by the placenta.[6]

Adapted with permission from the following sources:
- Brown TER. Menopause and perimenopause. In: Repchinsky C, editor. *Patient self-care.* 2nd ed. Ottawa (ON): Canadian Pharmacists Association; 2010. p. 811-7.
- Cullimore AJ. Menopause. eTherapeutics [database]. April 2007. Available: www.etherapeutics.ca (accessed Sept. 13, 2010).

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7. Kronenberg F. Hot flashes: epidemiology and physiology. *Ann N Y Acad Sci* 1990;592:52-86.

Weblinks

- Canadian Menopause Society: www. sigmamenopause.com
- North American Menopause Society: www.menopause.org
- Society of Obstetricians and Gynaecologists of Canada: www.menopauseandu.ca