

The Menopausal Transition



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KEYWORDS

• Menopause • Perimenopause • Hormones

KEY POINTS

- Symptoms of menopause often begin 4 to 6 years before the cessation of menses and persist for years.
- Loss of ovarian hormones has widespread and often adverse effects on many organ systems.
- Therapy for menopausal symptoms must be individualized.

Menopause occurs when the ovaries have complete (or near-complete) follicular exhaustion, resulting in very low serum levels of estradiol and markedly increased follicle-stimulating hormone (FSH) levels. Common symptoms of menopause (**Box 1**) often begin during the perimenopausal transition at a median of 47 years or 4 to 6 years before menopause occurs. Because other medical disorders which occur frequently with aging exhibit some of the same symptoms as those of menopause, women may have difficulty distinguishing when they enter the menopausal transition. This is also true for women who have had irregular menses, an endometrial ablation or a hysterectomy. Symptoms continue for several years after menopause and some women continue to have vasomotor symptoms for even longer periods of time. Almost all women with an intact uterus experience menstrual irregularity in the menopausal transition years resulting from hormonal fluctuations before ovarian follicular depletion.

The largest longitudinal study of women's endocrine and clinical manifestations of menopausal transition comes from the Study of Women's Health Across the Nation (SWAN).¹ This research evaluated and followed more than 3000 women from diverse communities, aged 42 to 52 years, for 15 years. Scientific areas of study for SWAN included bone mineral density and body composition, cardiovascular measures and risk factors, and ovarian markers. Ovarian aging was assessed by serial assessment of FSH, luteinizing hormone, estradiol (E2), inhibin-B, and estrone (E1). Inhibins are peptides of the transforming growth factor family and are produced by granulosa cells of the ovarian follicle. Inhibin levels decline during menopause because of the negative

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Box 1

Frequent symptoms of menopause

Hot flashes (flushes)^a

Irregular menstrual bleeding

Insomnia

Mood changes (anxiety, depression)

Mastodynia

Headache

Vaginal dryness

^aMost frequent.

feedback of increasing FSH levels. Other hormonal assays included thyroid-stimulating hormone, dehydroepiandrosterone sulfate (DHEAS), sex hormone–binding globulin, and testosterone.

Results from these cohort studies assisted in defining a staging system now considered the gold standard for characterizing reproductive aging. This staging system, The Stages of Reproductive Aging Workshop (STRAW), in 2001 defined 7 stages of adult women’s lives broadly into 3 categories (reproductive, menopausal transition, and postmenopause) with subcategories in each defined by menstrual cycle data and endocrine studies (Table 1). In 2011, a review of significant advances in knowledge allowed recommendations for updating criteria and modifying the staging system. Although this system is important for research in maturing women’s health, it has applicability also to clinical care in the areas of fertility, contraception, and hormonal therapy.

THE LATE REPRODUCTIVE YEARS

Menstrual cycles are regular, but fertility begins to decline. While cycles are mainly ovulatory, luteal phase progesterone levels decline and the follicular phase becomes

Table 1 Staging of reproductive aging		
The Late Reproductive Years	Menopausal Transition (Perimenopause)	Menopause
Regular menses	Varying menstrual intervals	Vasomotor symptoms likely
Declining fertility	Rare fertility	Increased somatic aging
↓ Menstrual intervals	Onset of menopausal symptoms	↓ Estradiol
↓ Luteal phase progesterone	↓ Inhibin-B	↑ FSH
Shortened follicular phase	Variable or ↑ FSH	↓ AMH
Decreasing inhibin-B	↓ AMH	↓↓ Antral follicle count
Normal estradiol	↓ Antral follicle count	
Slightly ↑ FSH		
↓ AMH		
↓ Antral follicle count		

Abbreviation: AMH, antimüllerian hormone.

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