RUTGERS WOMEN'S BRAIN HEALTH INITIATIVE

Estrogen

One of the two principal female sex hormones: where it comes from, what it does, how it changes across life, and the disorders it drives

Class	Main Source	Receptors	Crosses Blood-Brain Barrier?
Steroid (from cholesterol)	**Ovaries; fat (post menopause); placenta (pregnancy)**	**ER-alpha, ER-beta, GPER**	**Yes, also made in the brain (neurosteroid)**

What it is

A group of steroid sex hormones present in both sexes but far higher in females; its levels change dramatically across female life stages (puberty, menstrual cycles, pregnancy, menopause), while male levels stay modest. Major forms: estradiol (E2, most potent, dominant in the reproductive years), estriol (E3, rises markedly in pregnancy), and estrone (E1, the main form after menopause). [3]

How and where it is made

All estrogens are made from androgens by the enzyme aromatase (CYP19A1). Estradiol comes mainly from the ovaries in the reproductive years; the placenta makes large amounts of estriol in pregnancy [6]; after menopause, estrone is made mostly in adipose (fat) tissue. In males, small amounts come from the testes and peripheral conversion of androgens. Estrogen is also made locally in the brain. [3][8]

What it does

Drives female secondary sexual development and regulates the menstrual cycle, and acts well beyond reproduction: maintaining bone density, cardiovascular and metabolic health, skin collagen and genitourinary tissues, modulating immunity, and exerting neuroprotective and mood-stabilizing effects in the brain. The small amounts in males support sexual health, sperm maturation, and bone density. [3][4]

When it fluctuates

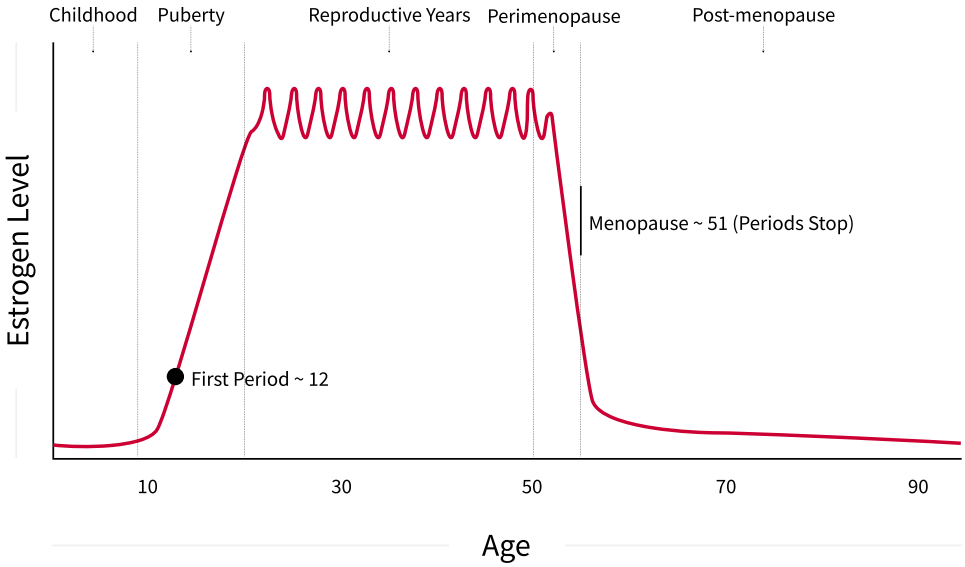
Across the menstrual cycle, estrogen rises through the follicular phase to a sharp mid-cycle peak that triggers the luteinizing hormone surge and ovulation; a smaller secondary rise follows in the luteal phase before it falls to bring on the next period. [1]

Receptors, function & brain

Signals through intracellular nuclear receptors ER-alpha (ESR1) and ER-beta (ESR2) and cell-surface receptors; the estrogen-nuclear-receptor complex binds DNA to control gene expression, while surface receptors alter calcium via G-protein signaling. [4] Estradiol crosses the blood-brain barrier [9], helps maintain its integrity [5], and is neuroprotective. [7]

In disease

Most breast cancers are estrogen-receptor-positive and grow in response to estrogen, so drugs that block it (tamoxifen) or its production (aromatase inhibitors) are central treatments. Unopposed estrogen raises endometrial cancer risk and fuels endometriosis and fibroids, while menopausal estrogen loss accelerates bone loss and coincides with rising cardiovascular risk. [3] Oral (less so transdermal) estrogen can raise venous thromboembolism [10] and gallbladder-disease risk. [11]

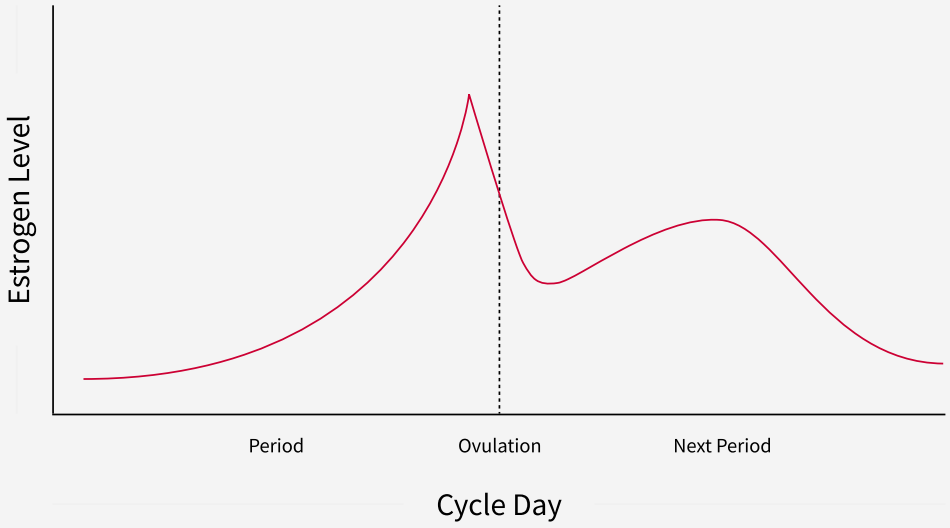


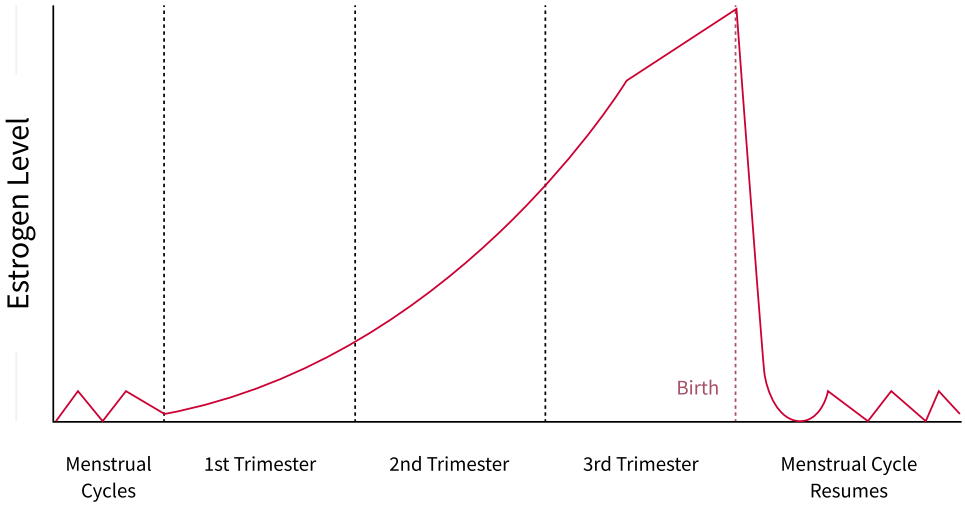
Estrogen across the lifespan

Very low in childhood, it climbs at puberty to establish monthly cycles, oscillates through the reproductive years, surges markedly in pregnancy (not shown here), swings erratically in perimenopause, then settles low after menopause near age 51 [6]. Shape from Stricker 2006 [1] and Frederiksen 2020 [2].

Estrogen across one menstrual cycle.

It rises through the follicular (first) half to a sharp peak that triggers ovulation near day 13, dips, then has a smaller second rise in the luteal half before falling to bring on the next period. The profile approximates Stricker 2006 [1]. Larger swings drive premenstrual symptoms and the erratic highs and lows of perimenopause. [3]





Menstrual cycles, then pregnancy and birth, then menstrual cycles resume

Estrogen during pregnancy

When pregnancy begins, the monthly cycle pauses and estrogen rises to roughly 100 times its usual level, reaching a maximum near birth. Afterward it drops sharply and the monthly cycle resumes. These are among the largest hormone changes the human body undergoes.

Estrogen's role in disease and disorders Implicated in:

(grouped by dominant association)

Excess Estrogen

- ER+ breast cancer
- Endometriosis
- Ovarian cancer (subset)
- Endometrial hyperplasia & cancer
- Uterine fibroids

Fluctuations In Estrogen Level

- PMS/PMDD
- Menopausal transition symptoms
- Menstrual migraine
- Catamenial seizures*
- Postpartum depression

Estrogen Deficiency

- Osteoporosis & fracture risk
- Cardiovascular disease
- Menopausal cognitive changes (brain fog, memory slips)
- Mood & sleep vulnerability
- Genitourinary syndrome of menopause
- Premature ovarian insufficiency
- Dementia risk
- Central obesity/insulin resistance

Other Modulatory Roles of Estrogen

- Autoimmune/neuroinflammatory (MS)
- Gallbladder disease (oral estrogen)
- VTE risk (oral estrogen)
- PCOS (imbalance + anovulation)

*In women with catamenial epilepsy, the estrogen-to-progesterone ratio can influence seizure patterns. Estrogen does not cause epilepsy itself. [12] Design mockup to illustrate layout and content. Figures use representative values consistent with the cited reference ranges; both panels are stylized, units-free overviews for quick reading. Not medical advice.

References

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