

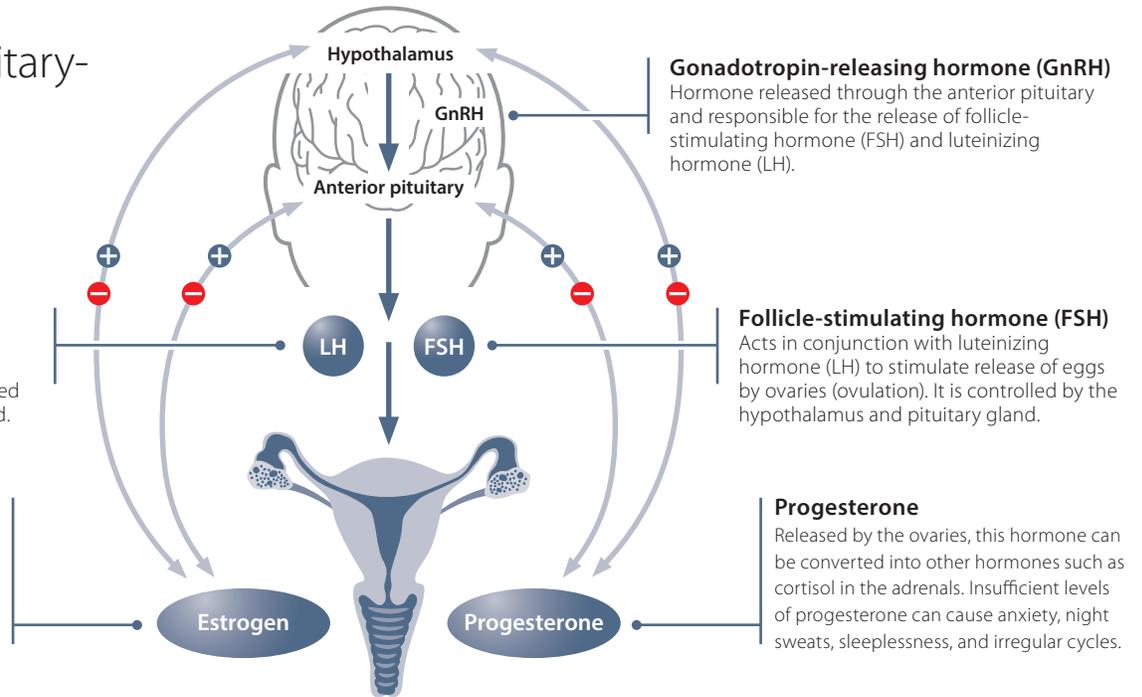
Hormone Function and Estrogen Dysregulation

Estrogen affects the growth, differentiation, and function of numerous tissues throughout the female body—not just those involved in reproduction. This hormone plays an important role in bone health, protects the cardiovascular system, and influences behavior and mood. While appropriate levels of estrogens are essential for good health, several studies conclude inappropriate, and increased, exposure to estrogen leads to elevated risk for several types of cancers including those affecting breast, ovaries and thyroid. Furthermore, disproportionate estrogen exposure can play a role in other female-related health problems including polycystic ovarian syndrome (PCOS), premenstrual syndrome (PMS),

endometriosis, and fibrocystic or painful breasts (mastalgia).

Various lifestyle and environmental factors can influence estrogen production, metabolism, and balance. These include poor diet, obesity, excess alcohol consumption, high insulin levels, medications such as those used for hormone replacement therapy, contraceptive pills and over exposure to chemicals used in pesticides and other industrial compounds. Estrogen levels have also been found to be affected downstream by agricultural hormones found in animal products that are subsequently consumed by humans. Genetics can also play an important role in determining estrogen levels.

Hypothalamic-pituitary-gonadal (HPG) axis



Luteinizing hormone (LH)
Works with follicle-stimulating hormone (FSH) to stimulate the release of the egg from the ovary (ovulation). LH is controlled by the hypothalamus and pituitary gland.

Estrogen
A hormone that plays a role in many aspects of a woman's health throughout her lifespan including libido, mood, joint health, and cognition. It is used to treat breast tenderness, breast cysts, some cancers, fibroids, endometriosis, hot flashes, and other symptoms in women who are experiencing, or have experienced, menopause.

Gonadotropin-releasing hormone (GnRH)
Hormone released through the anterior pituitary and responsible for the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH).

Follicle-stimulating hormone (FSH)
Acts in conjunction with luteinizing hormone (LH) to stimulate release of eggs by ovaries (ovulation). It is controlled by the hypothalamus and pituitary gland.

Progesterone
Released by the ovaries, this hormone can be converted into other hormones such as cortisol in the adrenals. Insufficient levels of progesterone can cause anxiety, night sweats, sleeplessness, and irregular cycles.

Hormone feedback control

Estrogen and progesterone exert feedback control on the hypothalamus and anterior pituitary gland, helping control the release of GnRH, LH, and FSH.

Hormone	Reference Range		Notes
Estradiol (E2) • Follicular phase • Midcycle • Luteal phase • Postmenopause	LOW 19 pg/mL 64 pg/mL 56 pg/mL ≤ 31 pg/mL	HIGH 144 pg/mL 357 pg/mL 214 pg/mL	• E2 tested to assess HRT given during menopause • E2 is useful in determining ovarian function
Sex hormone-binding globulin (SHBG) 18 – 55 years > 55 years	17 nmol/L 14 nmol/L	124 nmol/L 73 nmol/L	Raised in pregnancy, hyperthyroidism
Progesterone • Follicular phase • Luteal phase • Postmenopause • Pregnancy	< 1.0 ng/mL 2.6 ng/mL < 0.5 ng/mL 4.1 ng/mL	21.5 ng/mL 302 ng/mL	• Day 21 progesterone > 9.5 ng/mL indicates ovulation • Progesterone rises during luteal phase of menses and increases from weeks 9-32 of pregnancy
Free testosterone	15 ng/dL	70 ng/dL	Used for assessing virilization
Insulin	1.4 µIU/mL	14.0 µIU/mL	PCOS, T2D
• FSH Follicular phase • Mid Cycle • Luteal phase • Postmenopause	2.5 mIU/mL 3.1 mIU/mL 1.5 mIU/mL 23 mIU/mL	10.2 mIU/mL 17.7 mIU/mL 9.1 mIU/mL 116.3 mIU/mL	Menstrual irregularities, infertility, perimenopause

Hormone test considerations

- Estrogen dysregulation occurs when estradiol and progesterone levels are in an unbalanced or inappropriate ratio outside of normal reference ranges.
- Labs to consider are urine, blood, and saliva.
- Genomic testing may be added for a more comprehensive evaluation.

Causes



Perimenopause

Women experiencing perimenopause may show higher levels of estrogen relative to progesterone during the initial phase.



High cortisol levels

High levels of cortisol can block progesterone receptors, leading to an imbalanced estrogen to progesterone ratio.



Xenoestrogens

Synthetic chemicals can mimic effects of estrogen and are also known as endocrine disruptors. These include BPA, phthalates, parabens, and other industrial chemicals.



Obesity & weight gain

Fat cells produce more estrogen, while obesity lowers sex hormone-binding globulin (SHBG), leading to the increase of free estrogen in the blood.



Diet & alcohol

A diet high in conventionally raised red meat and refined carbohydrates may lead to increased levels of estrogen. Excess consumption of alcohol can also raise estrogen levels.



Nutritional deficiencies

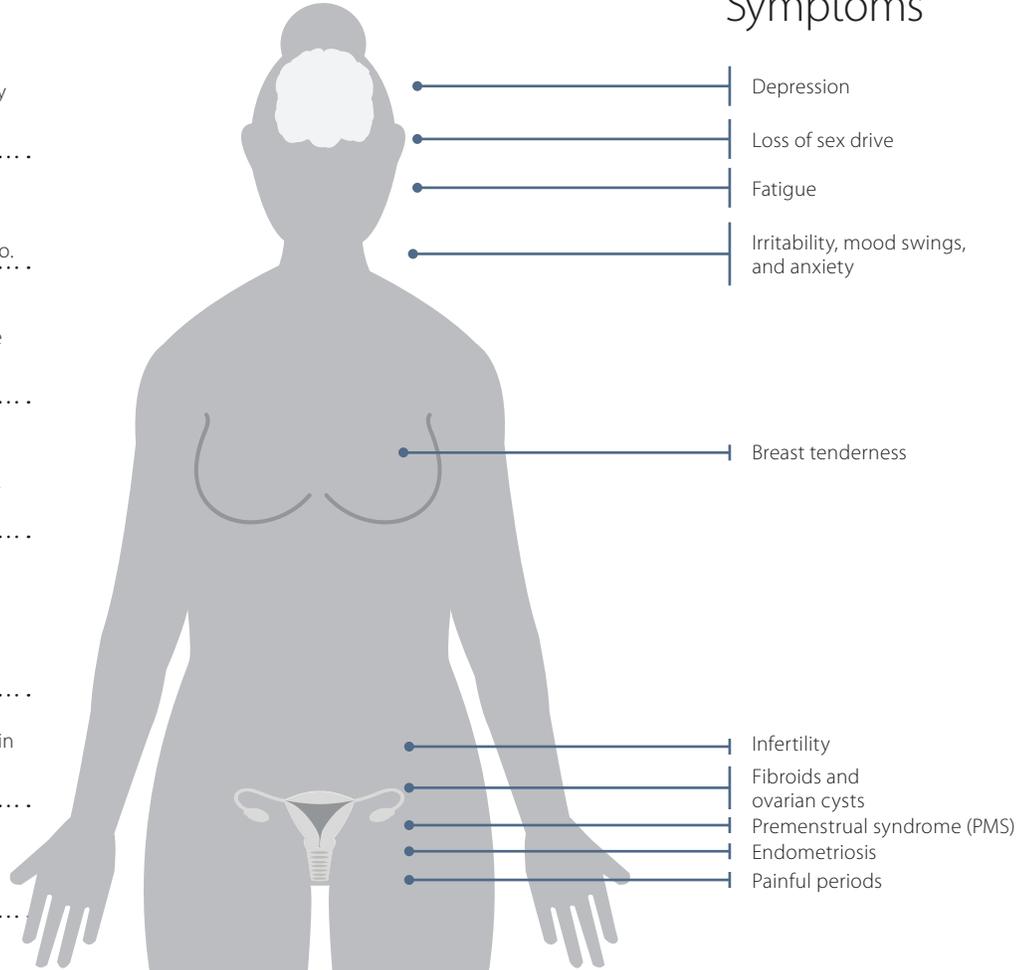
Specific deficiencies of magnesium, vitamin B₁₂, folate, zinc, and copper can lead to increased levels of estrogen.



Heavy metals

Heavy metals including mercury act as xenoestrogens by binding to estrogen receptors.

Symptoms



References:

- Seifert-Klauss V et al. *Zentralbl Gynakol*. 2005;127(3):132-139.
 Kalleinen N et al. *J Clin Endocrinol Metab*. 2008;93(5):1655-1661.
 Peretz J et al. *Toxicol Sci*. 2011;119(1):209-217.
 Lovekamp-Swan T et al. *Environ Health Perspect*. 2003;111(2):139-145.
 Freeman EW et al. *Menopause*. 2010;17(4):718-726.
 Key TJ et al. *Br J Cancer*. 1988;57:205-212.
 Miller PE et al. *Nutr Cancer*. 2010;62(4):413-424.
 Dorgan J et al. *J Natl Cancer Inst*. 2001;93:710-715.
 Mahabir S et al. *Nutr J*. 2004;3(11).
 Muneyyirci-Delale O et al. *Fertil Steril*. 1998;69(5):958-962.
 Muneyyirci-Delale O et al. *Fertil Steril*. 1999;71(5):869-872.
 Zhang X et al. *Biomaterials*. 2007;28(1):143-150.
 Bolton JL et al. *Chem Res Toxicol*. 1998;11:1113-1127.
 Colditz GA. *J Natl Cancer Inst*. 1998;90(11):814-823.
 Thomas HV et al. *Cancer Causes Control*. 1997;8(6):922-928.
 Rose PG. *New Eng J Med*. 1996;335(9):640-649.
 Hankinson SE et al. *J Natl Cancer Inst*. 1998;90(17):1292-1299.
 Zanetta GM et al. *Gynecol Oncol*. 2000;79(1):18-22.
 Kuiper GG et al. *Endocrinology*. 1998;139(10):4252-4263.
 Kaaks R. *Cancer Causes Control*. 1996;7:605-625.
 Snedeker SM et al. *Prog Clin Biol Res*. 1996;394:211-253.
 Fan S et al. *Cancer Res*. 2000;60(20):5635-5639.
 Steingraber S. *Living Downstream*. Reading, MA: Addison-Wesley; 1997.
 Endocrine Self-Assessment Program. Laboratory Reference Ranges. <https://education.endocrine.org/system/files/ESAP%202015%20Laboratory%20Reference%20Ranges.pdf>. Accessed September 28, 2018.
 Quest Diagnostics. <https://www.questdiagnostics.com/home.html>. Accessed September 27, 2018.
 BioHealth Laboratory. Female and Male Hormones. <https://www.biohealthlab.com/test-menu/female-and-male-hormones/>. Accessed September 28, 2018.
 Precision Analytical, Inc. Dutch Testing. <https://dutchtest.com/>. Accessed September 28, 2018.

DISCLAIMER: The information provided in this literature is for educational purposes only and is intended for use by licensed healthcare practitioners. This content is not to be used as a substitute for professional medical advice, diagnosis, or treatment.

Always consult with the testing laboratory for collection and pre-collection guidelines. General recommendations tend to be:

- If using a topical or sublingual product, it is recommended to stop hormones for 48-72 hours prior to saliva or urine collection to avoid contamination or falsely elevated readings.
- For premenopausal and perimenopausal women treated with progesterone augmentation, labs need to be collected on days 19-22 of the menstrual cycle, ideally five days prior to expected menses.
- If taking oral hormones (DHEA, micronized progesterone, thyroid, etc.), allow 24 hours to pass from the last dosage before performing saliva collections.
- In postmenopausal women, samples can be collected any time. However, the rules for collection vary depending on the type of hormones being used and laboratory specifications.
- For baseline testing with oral progesterone or transdermal estradiol, stop use seven days prior to testing.

