

2g. Phases of Menstrual cycle, Importance of HPO axis in menstrual regulation

Phases of the Menstrual Cycle (overview = 28-day reference; normal 21-35)

[Menstrual Cycle 3D Model](#)

1) Menstrual Phase (Days ~1-5)

- **Endometrium:** Shedding of the functional layer; spiral arteries constrict → ischemia → bleeding (≈ 30-80 mL).
- **Ovary:** Multiple **antral follicles** present but none dominant yet.
- **Hormones:** **Low E2 & P4** → loss of negative feedback → slight **FSH rise** to recruit a follicular cohort.
- **Cervical mucus:** Thick, scant, opaque.
- **Symptoms/markers:** Low basal body temp (BBT), cramps due to prostaglandins (PGF2α).

2) Follicular (Proliferative) Phase (Days ~1-13)

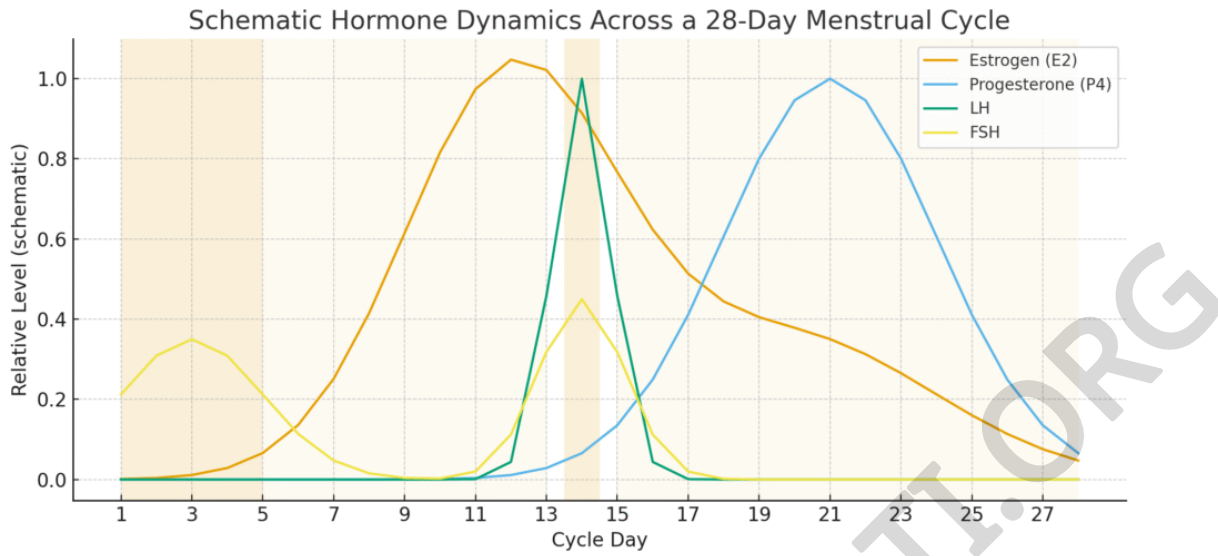
- **Endometrium:** Estrogen-driven **proliferation**; glands straight/tubular, stroma dense; thickness ↑.
- **Ovary:** FSH recruits follicles → **granulosa** proliferate; **aromatase** converts theca-androgens to **estradiol (E2)**; one **dominant follicle** emerges by ~day 7.
- **Hormones:** Gradual **E2 rise**; **FSH** trends down (E2 + inhibin B feedback). GnRH pulse frequency increases.
- **Cervical mucus:** Volume ↑, clearer and stretchier (spinnbarkeit), ↑ ferning.
- **Clinical notes:** Short cycles = shorter follicular phase; AMH reflects follicle pool (not cycle dynamics).

3) Ovulatory Window (≈ Day 14; fertile window -5 to +1 days)

- **Trigger:** Sustained high **E2** (>200 pg/mL for ~48 h) flips feedback **positive** at the hypothalamus/pituitary → **mid-cycle LH surge** (plus small FSH surge).
- **Events:** **Ovulation** ~34-36 h after LH surge onset (≈ 10-12 h after LH peak). Cumulus expansion; follicle rupture releases **metaphase-II oocyte**.
- **Endometrium:** Late-proliferative; receptive changes begin.
- **Cervical mucus:** Maximal stretch/clarity → peak fertility.
- **Markers:** Brief BBT nadir just before ovulation, then rise after.

4) Luteal (Secretory) Phase (Days ~15-28)

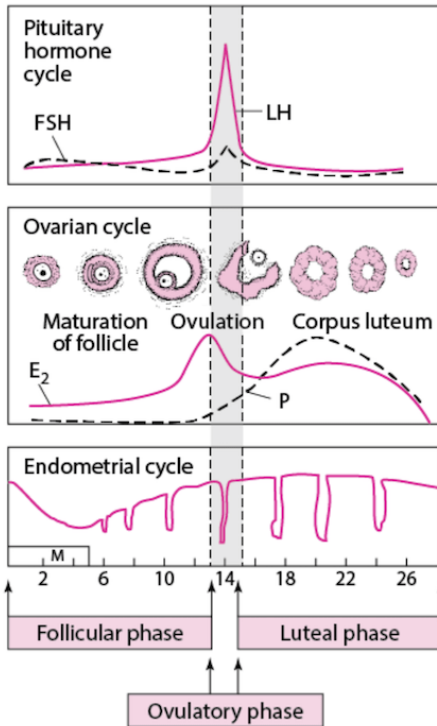
- **Ovary:** **Corpus luteum (CL)** forms → secretes **progesterone** (and E2, inhibin A).
- **Endometrium:** **Secretory transformation**—saw-tooth glands with glycogen, stromal edema, then predecidual change; peak receptivity ~**days 20-24** (implantation window).
- **Hormones:** **Progesterone dominates** → stabilizes endometrium, thick cervical mucus plug, thermogenic (BBT ↑ ~0.3-0.5 °C).
- **If no implantation:** CL regresses ~day 26-28 → **P4/E2 fall** → prostaglandins ↑, spiral artery spasm → **menses** (cycle restarts).
- **If implantation:** hCG rescues CL until placental takeover (≈ week 8-10 gestation).



The HPO Axis in Menstrual Regulation

Core circuitry

- **Hypothalamus:** Pulsatile **GnRH** (every 60–90 min follicular; slower in luteal) is essential; **kisspeptin** neurons (KISS1) are the key upstream regulators integrating energy/stress signals (leptin, insulin, cortisol).
- **Pituitary:** GnRH pulses drive **FSH** and **LH** synthesis & release.
- **Ovary:**
 - **Follicle phase:** FSH → granulosa proliferation, aromatase → **E2**; LH → theca androgen production.
 - **Ovulation:** High E2 → **positive feedback** → **LH surge**.
 - **Luteal:** LH maintains CL → **progesterone** (± E2, inhibin A).



Normal Menstrual Cycle

This figure shows the idealized cyclic changes in pituitary gonadotropins, estradiol (E₂), progesterone (P), and uterine endometrium during the normal menstrual cycle.

Feedback loops

- **Negative feedback (most of cycle):** E₂, P₄, inhibin **suppress** GnRH/FSH/LH (phase-dependent).
- **Positive feedback (pre-ovulatory only):** Sustained high E₂ → **LH surge**.
- **Inhibins/Activins:**
 - **Inhibin B** (granulosa, follicular phase) ↓ FSH after cohort selection.
 - **Inhibin A** (luteal phase) contributes to FSH suppression.
 - **Activins** locally ↑ FSH synthesis.

What HPO achieves

1. **Single-dominant follicle selection** (FSH “window”)
2. **Timed ovulation** via LH surge
3. **Endometrial synchronization** with ovarian hormones (receptive window)
4. **Cycle reset** via CL regression when conception doesn't occur

Practical clinical correlates (high-yield)

- **Hypothalamic amenorrhea:** ↓ GnRH from energy deficit/stress → low FSH/LH; thin endometrium; anovulation.
- **PCOS:** Relative ↑ LH:FSH, hyperandrogenism, arrested folliculogenesis → oligo/anovulation; E₂ often unopposed → thick endometrium.
- **Hyperprolactinemia:** Prolactin inhibits GnRH → luteal defects/amenorrhea.
- **Thyroid disorders:** Alter SHBG and GnRH—cycle irregularities.
- **Luteal phase defect:** Inadequate P₄ → short luteal phase/implantation issues.
- **Perimenopause:** Follicle pool ↓ → **FSH rises**, cycles irregular.



Quick comparison table

Feature	Menstrual	Follicular/Proliferative	Ovulatory	Luteal/Secretory
Ovarian event	Cohort present	Dominant follicle selection & growth	Follicle rupture	Corpus luteum active
Endometrium	Shedding	Proliferation (E2)	Transition	Secretory (P4)
Key hormones	Low E2/P4, FSH ↑	E2 ↑, FSH ↓ (Inhibin B)	LH surge	P4 high , E2 moderate
Cervical mucus	Thick/scant	Thin/stretchy	Max fertility	Thick plug
BBT	Low	Low	Nadir → rise	Elevated