Reproduction

BCH 120 — Metabolic & Endocrine Biochemistry · Dr. Radi

By the end of this unit, you can…

- Explain sex-steroid synthesis (cholesterol → testosterone via StAR/LH; 5α-reductase → DHT; aromatase → estradiol) and the hypothalamic–pituitary–testis axis, testis structure, and kisspeptin
- Describe sex differentiation (SRY/AMH/testosterone; female default) and its disorders (CAH, 5α-reductase deficiency, androgen insensitivity), plus puberty and its timing disorders
- Explain ovarian estrogen synthesis (two-cell model), the hypothalamic–pituitary–ovarian axis with its estrogen positive-feedback LH surge, the menstrual cycle, and common disorders
- Describe pregnancy — hCG's rescue of the corpus luteum, the placenta's hormones (progesterone, hPL, relaxin, estrogen), miscarriage, and parturition (oxytocin positive feedback, prostaglandins, labor) and contraception
- Explain twins (mono- vs dizygotic), IVF, and lactation (prolactin/oxytocin, lactose synthesis, colostrum vs milk)

Today's route

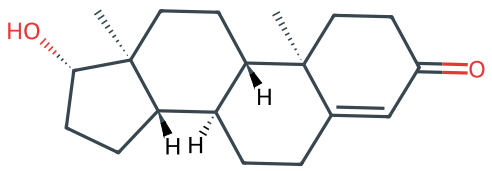
1. Sex Steroid Synthesis
2. The HPG Axis & the Testis
3. Sex Differentiation & Puberty
4. The Ovary, Estrogen & the HPO Axis
5. The Menstrual Cycle
6. Pregnancy, hCG & the Placenta
7. Parturition, Labor & Contraception
8. Twins, IVF & Lactation

1 · Sex Steroid Synthesis

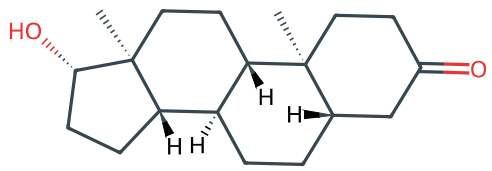
"The sex hormones — testosterone, DHT, estradiol — all come from the same cholesterol pathway you learned for the adrenal cortex. Three enzymes decide the outcome: StAR gates the whole thing, 5α-reductase sharpens the androgen, and aromatase turns androgens into estrogens."

Meet the sex steroids

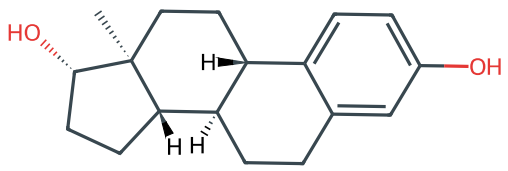
Here are the three you must know, and they're all **four-ring steroids** — cousins of cortisol from last unit. **Testosterone** is the main **androgen**. **DHT (dihydrotestosterone)** is testosterone with one extra reduction — and it's the **more potent** androgen (it binds the receptor harder and can't be aromatized away). **Estradiol** is the main **estrogen** — notice its **aromatic A-ring**, the tell-tale of an estrogen. Small edits to one skeleton, three very different signals.



Testosterone (androgen)



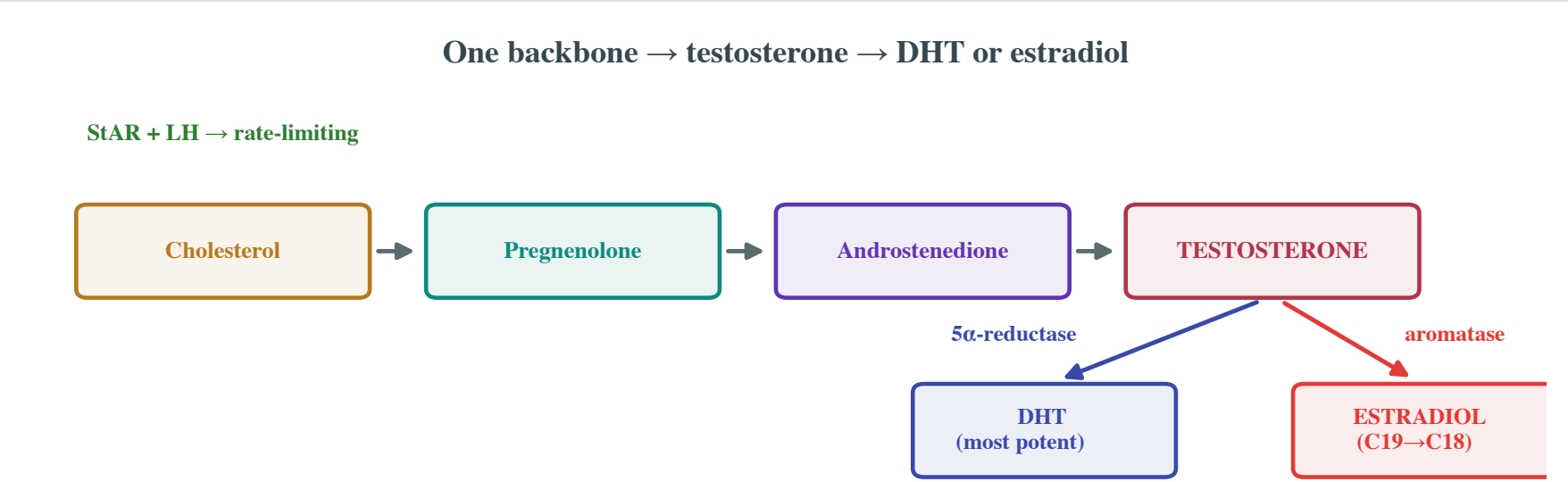
DHT (potent androgen)



Estradiol (estrogen)

One backbone, three fates

The synthesis is the **adrenal pathway again**: **cholesterol → pregnenolone → … → testosterone**, with the rate-limiting step being **StAR** ferrying cholesterol into the mitochondrion — driven here by **LH** (the same StAR that ACTH controls in the adrenal). Then testosterone branches. **5α-reductase** converts it to **DHT** — amplifying the androgen signal in target tissues. Or **aromatase** (a P450) converts the **C19 androgen into the C18 estrogen, estradiol**. One enzyme choice flips "male" to "female" signal.



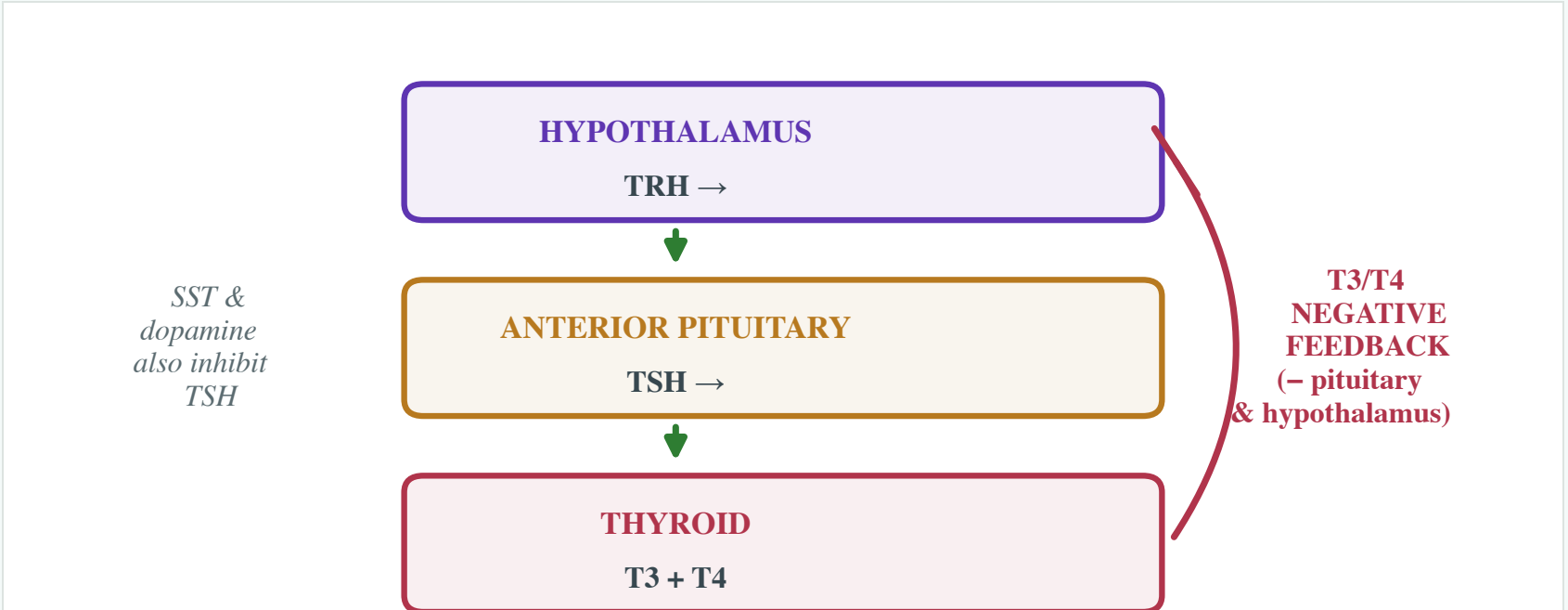
Same pathway as the adrenal — StAR ferries cholesterol in (LH-driven); aromatase turns androgens into estrogens.

2 · The HPG Axis & the Testis

"Male reproduction runs on the same three-tier axis as every gland in this course — hypothalamus, pituitary, testis — with a molecular gatekeeper (kisspeptin) that decides when puberty begins. And inside the testis, two cell types split the work."

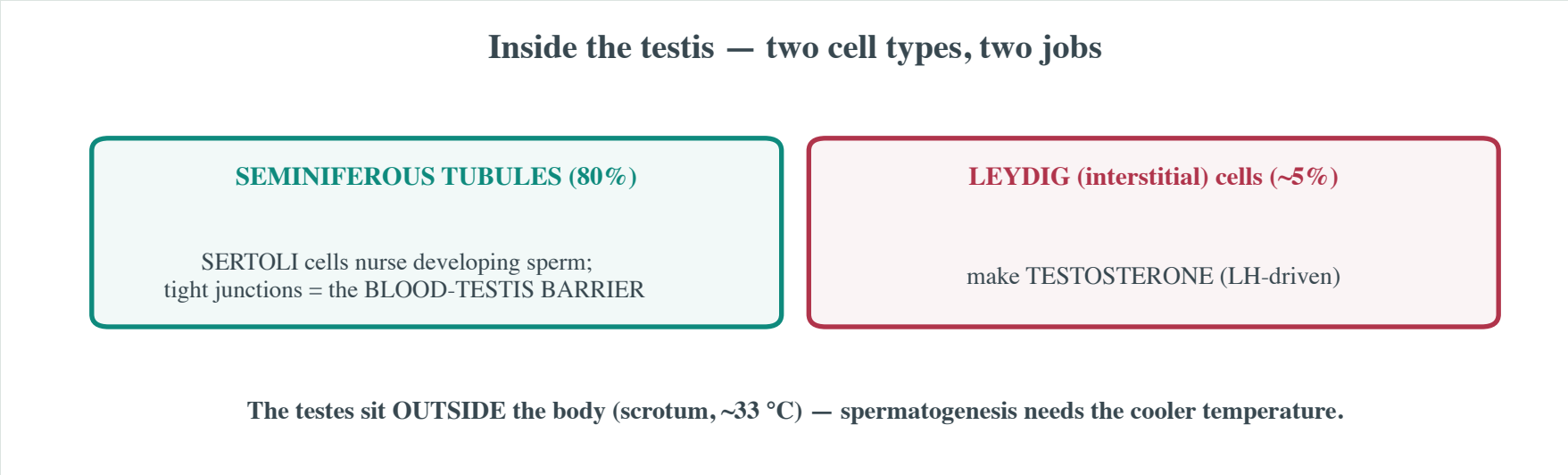
The hypothalamic–pituitary–testis axis

Same three-tier logic, one new gatekeeper. The **hypothalamus** releases **GnRH** — but only when **kisspeptin** (from KNDy neurons) gives the go-ahead, which is what flips on at **puberty**. GnRH drives the **pituitary** to release **LH and FSH**. **LH** hits **Leydig cells → testosterone**; **FSH** hits **Sertoli cells → sperm + inhibin B**. Then feedback: **testosterone inhibits GnRH/LH**, and **inhibin inhibits FSH**. All negative — so testosterone runs at a steady, **"tonic"** level (unlike the cyclic female).



Inside the testis

The testis divides its labor between two cell types. The **seminiferous tubules** (80% of the volume) house the **Sertoli cells**, which nurse developing sperm — and their tight junctions form the **blood-testis barrier**, walling sperm off from the immune system. Between the tubules sit the **Leydig cells**, which make **testosterone** on LH's command. One structural quirk worth knowing: the testes hang **outside the body** in the scrotum (**~33 °C**) because **spermatogenesis needs the cooler temperature** — undescended testes (**cryptorchidism**) impair it.

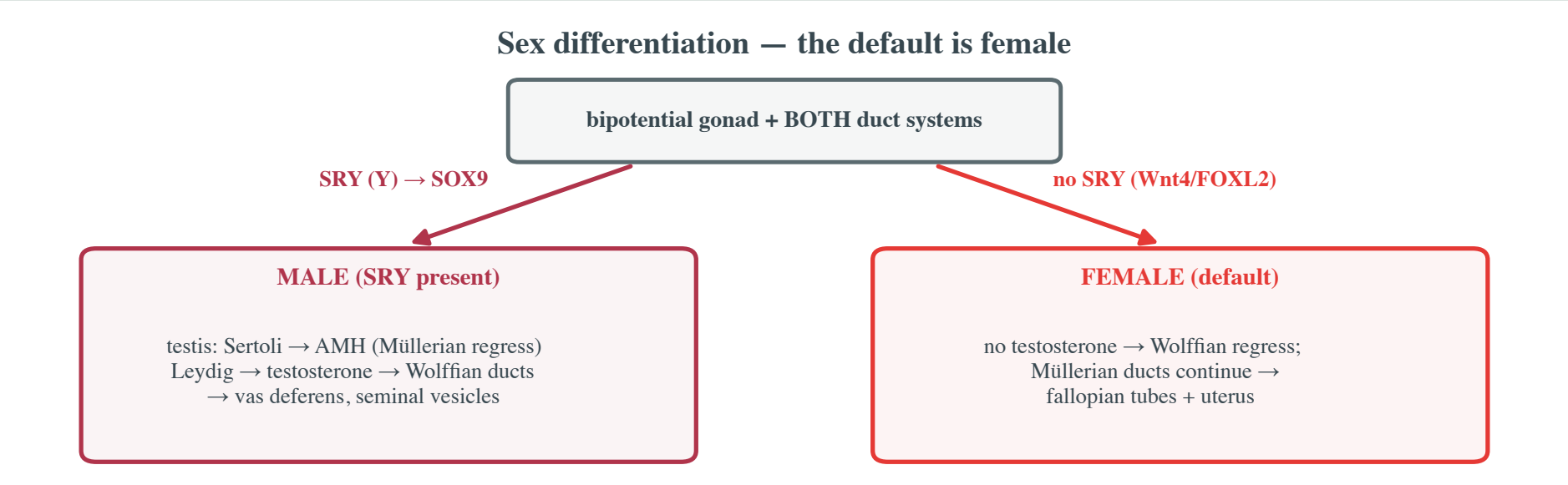


3 · Sex Differentiation & Puberty

"Every embryo starts the same — bipotential gonads and both duct systems — and the default path is female. One gene (SRY) and two hormones (AMH, testosterone) build the male. When they misfire, you get the disorders of sex development; and kisspeptin decides when puberty begins."

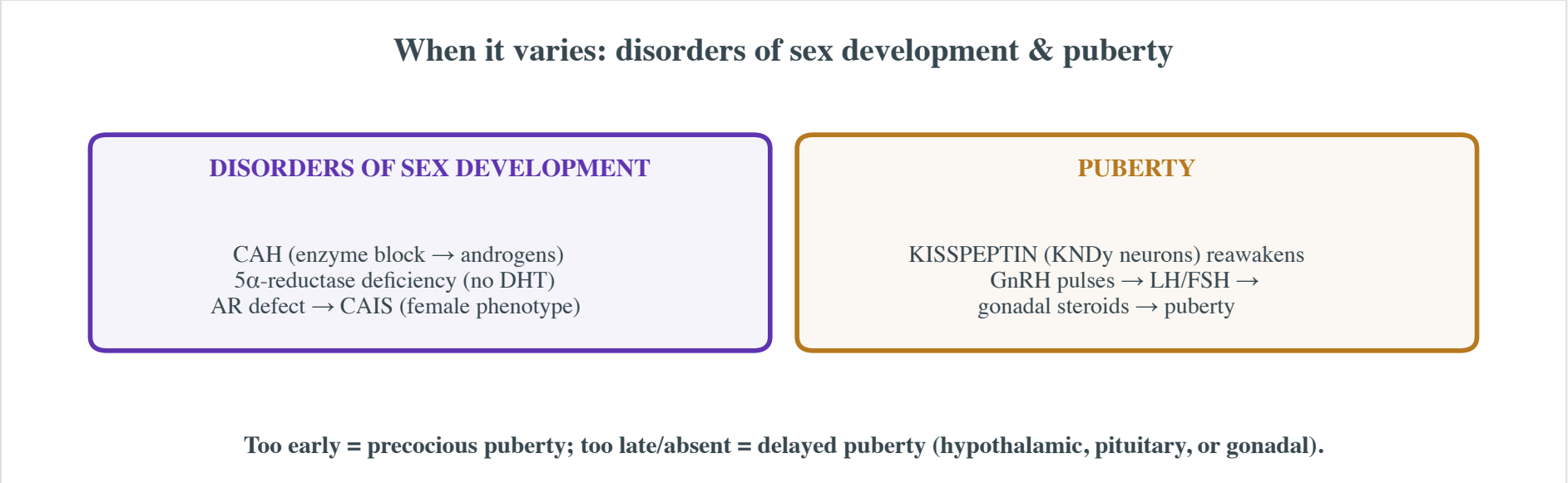
The default is female

Here's the elegant developmental logic. Every fetus begins with a **bipotential gonad** and **both** duct systems (Müllerian and Wolffian). The **male** path needs an active push: the **SRY gene** on the Y chromosome (via **SOX9**) turns the gonad into a **testis**, whose **Sertoli cells make AMH** (regressing the Müllerian ducts) and whose **Leydig cells make testosterone** (building the Wolffian ducts into the vas deferens). **Without SRY** — the **default** — the gonad becomes an **ovary**, Wolffian ducts regress, and the **Müllerian ducts** become the uterus and tubes. Female unless told otherwise.



When it varies — DSD and puberty

Break a step and you get a **disorder of sex development**. **CAH** (an enzyme block) shunts precursors into androgens, masculinizing a female fetus. **5α-reductase deficiency** (no DHT) leaves a male under-virilized at birth. An **androgen-receptor defect** gives **complete androgen insensitivity** — a genetic male with a **female phenotype** because tissues can't hear testosterone. And timing itself is controlled: **kisspeptin** reawakens GnRH pulses to start **puberty** — too early is **precocious**, too late is **delayed** puberty (a hypothalamic, pituitary, or gonadal fault).

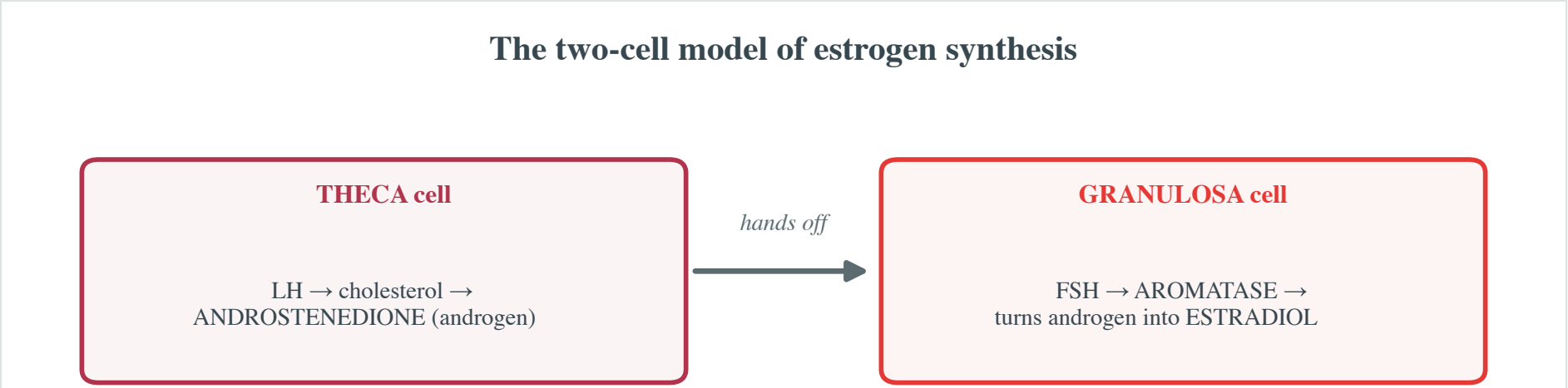


4 · The Ovary, Estrogen & the HPO Axis

"The ovary makes estrogen through a two-cell team that neither cell could run alone. And its axis has a twist found nowhere else in the body: estrogen's feedback flips from negative to positive to trigger ovulation."

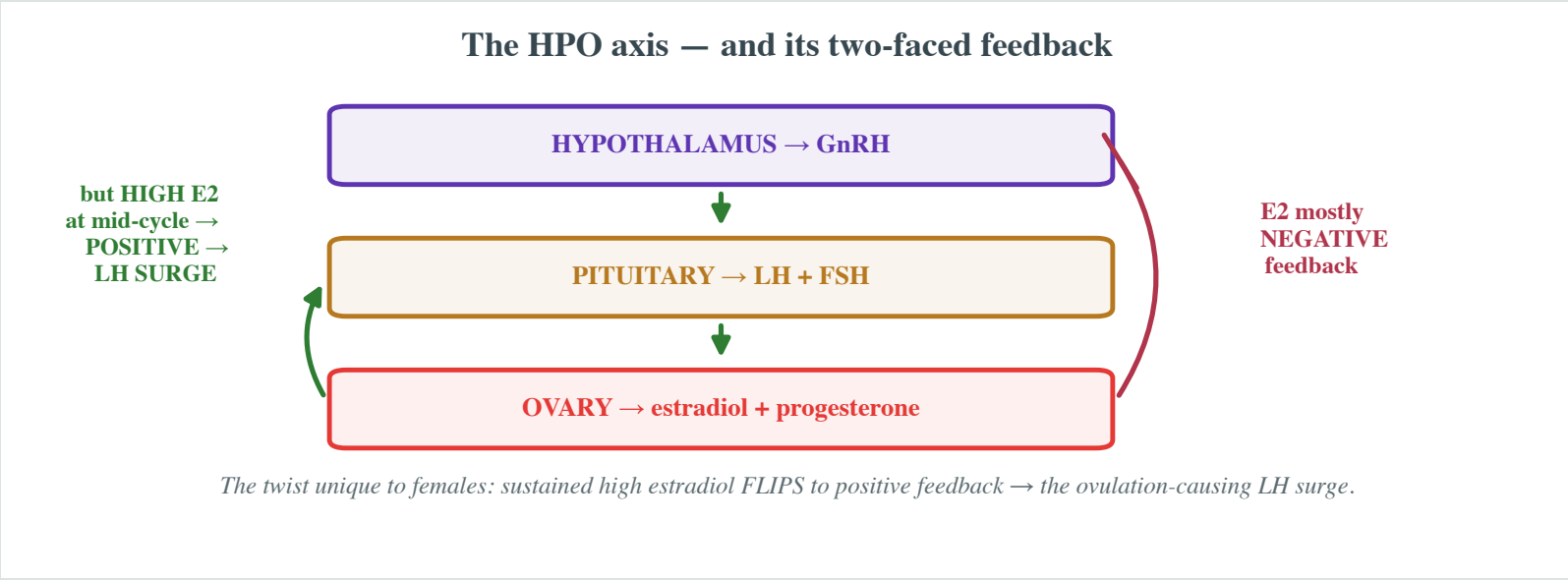
The two-cell model of estrogen

Estrogen synthesis in the ovarian follicle takes **two cells working together**. The **theca cell**, under **LH**, converts cholesterol to an **androgen (androstenedione)** — but it **can't** finish the job. It hands that androgen to the neighboring **granulosa cell**, which, under **FSH**, uses **aromatase** to turn it into **estradiol**. Neither cell can make estrogen alone: **theca makes the androgen, granulosa aromatizes it**. This division of labor is why both LH **and** FSH are needed to grow a follicle.



The HPO axis — feedback that flips

The **hypothalamic-pituitary-ovarian axis** starts like all the others: **GnRH → LH/FSH → ovarian estradiol + progesterone**, with estradiol normally feeding back **negatively**. But here's the twist that makes females **cyclic** rather than tonic: when a dominant follicle pumps out **sustained high estradiol** at mid-cycle, the feedback **flips to positive** — triggering a massive **LH surge** that causes **ovulation**. The follicle literally **times its own release** by how much estrogen it makes. No other axis in the body does this.

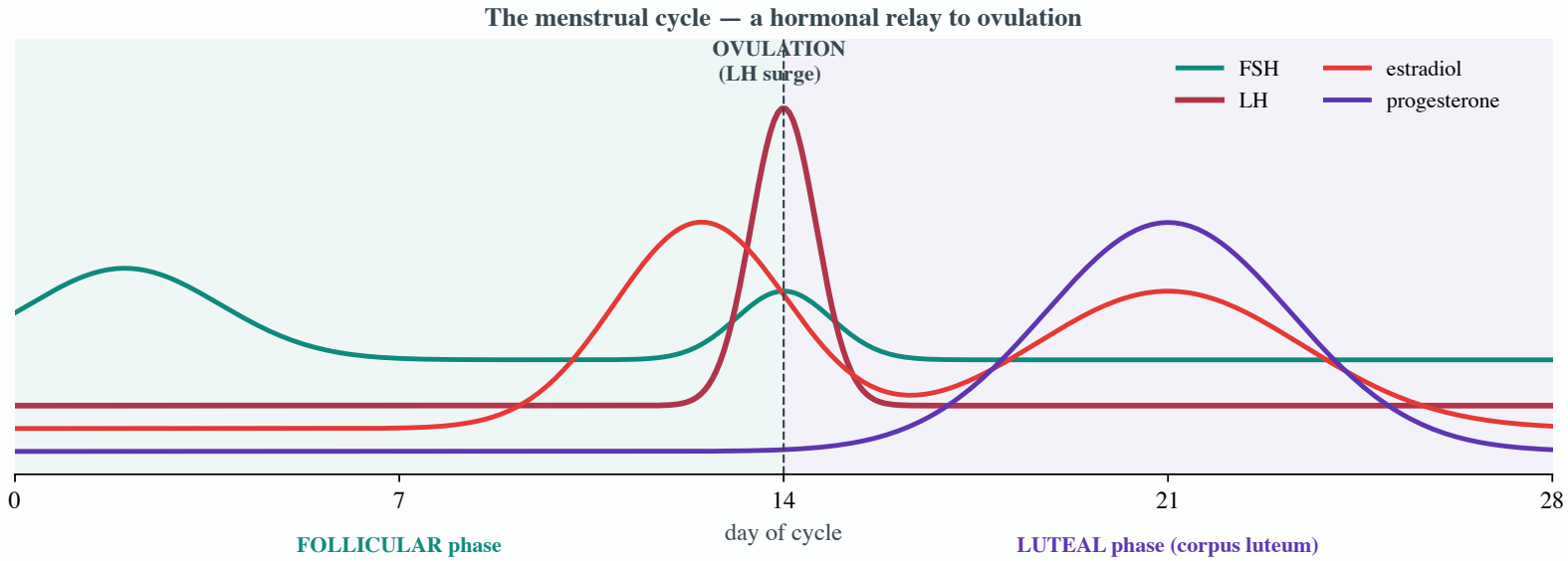


5 · The Menstrual Cycle

"The menstrual cycle is a monthly hormonal relay with one goal: release a mature egg and prepare the uterus for it. Learn the four hormone curves and the two phases, and the whole thing – including what goes wrong – falls into place."

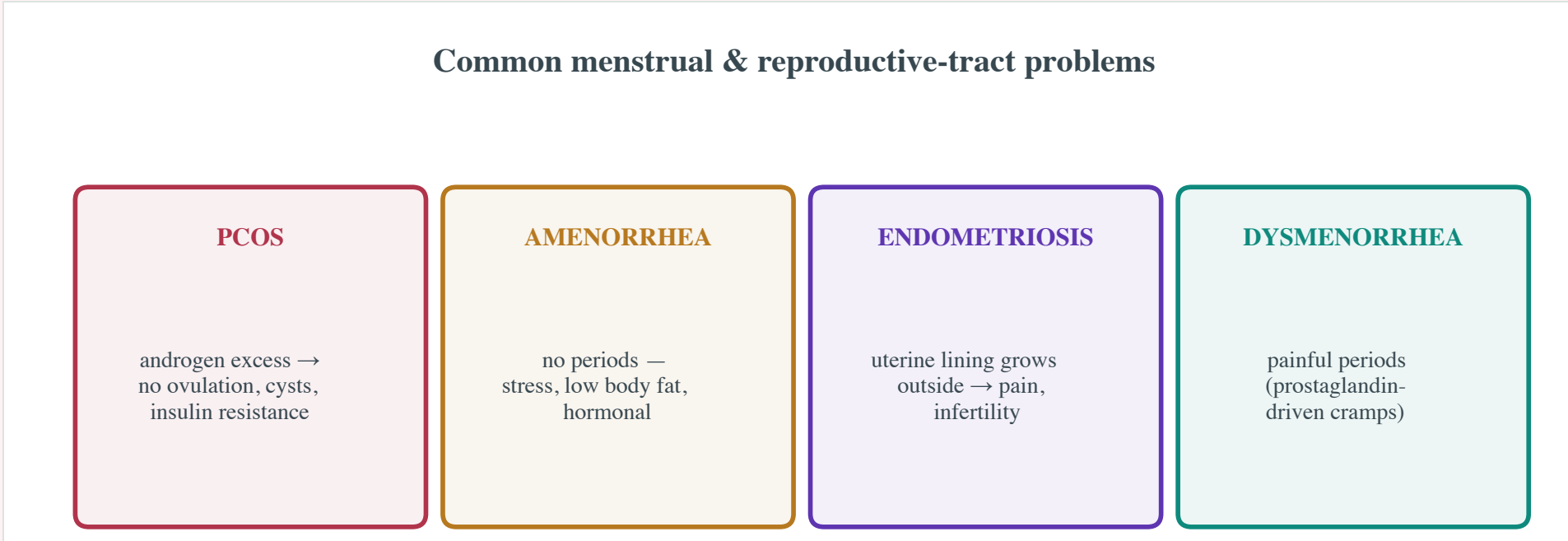
The cycle in four hormones

Read the ~28-day cycle as two phases split by ovulation. In the **follicular phase**, **FSH** grows a follicle, which makes rising **estradiol** (building the uterine lining). When estradiol peaks, its **positive feedback** fires the **mid-cycle LH surge** → **ovulation** (day ~14). In the **luteal phase**, the leftover follicle becomes the **corpus luteum**, pouring out **progesterone** to hold the lining ready. If no pregnancy, the corpus luteum dies, progesterone falls, and the lining sheds — **menstruation** — restarting the cycle.



When the cycle goes wrong

Because the cycle is a tightly timed hormone relay, a lot can perturb it. **PCOS** (polycystic ovary syndrome) — **androgen excess** blocks ovulation, causing cysts, irregular cycles, and **insulin resistance**. **Amenorrhea** — no periods at all, often from **stress or low body fat** shutting down GnRH. **Endometriosis** — uterine lining grows **outside** the uterus, causing pain and infertility. **Dysmenorrhea** — painful periods driven by **prostaglandin** cramps (which is why NSAIDs help). Common, and all traceable to the hormones you just mapped.

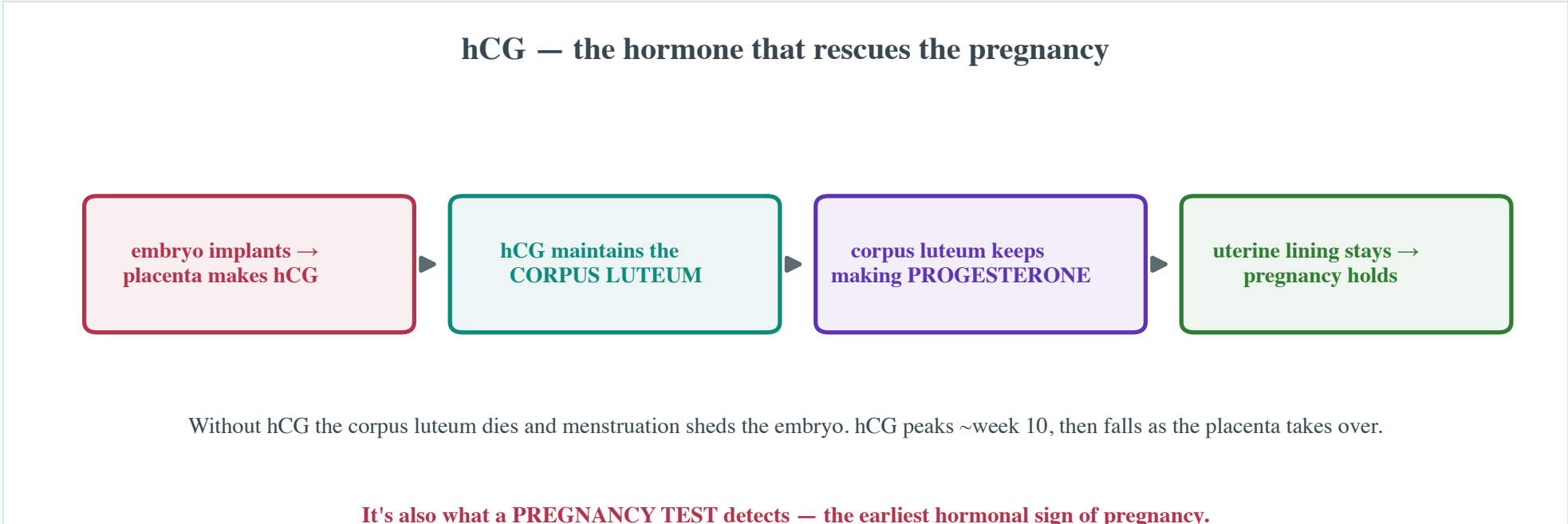


6 · Pregnancy, hCG & the Placenta

"Pregnancy hijacks the cycle to keep it from ending. A single hormone from the new embryo — hCG — rescues the corpus luteum so progesterone keeps flowing. Then the placenta takes over as a temporary endocrine organ running the whole show."

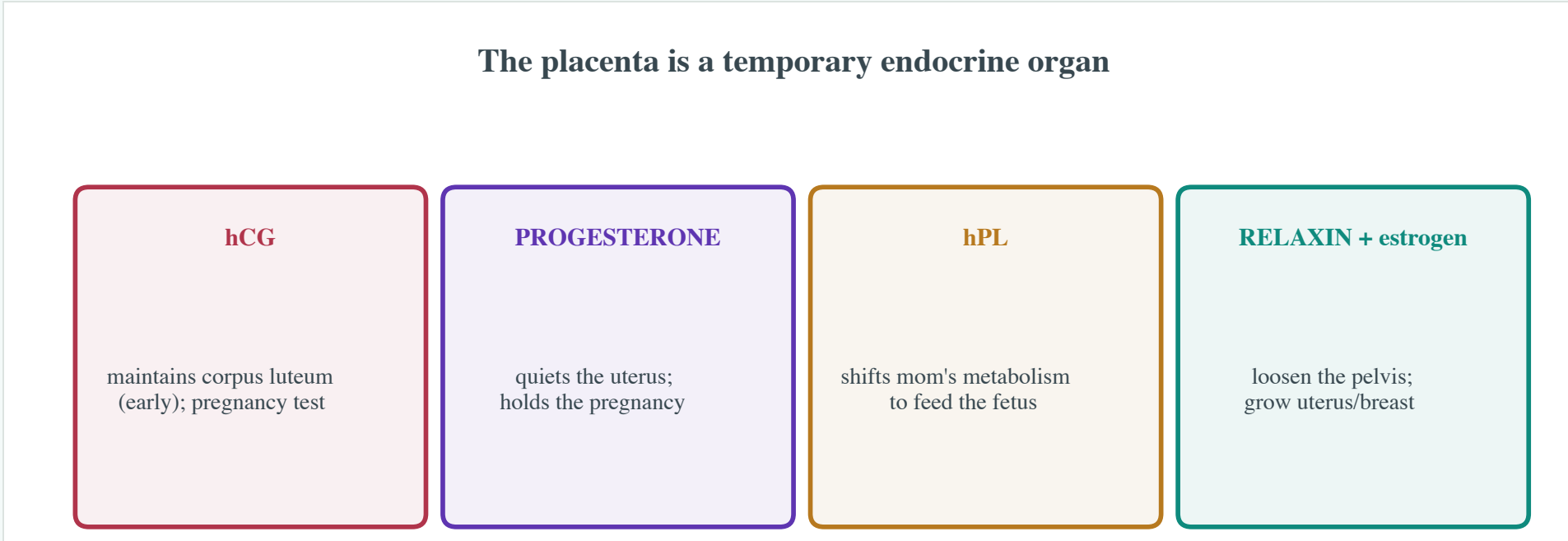
hCG rescues the pregnancy

Normally, if there's no pregnancy, the **corpus luteum dies**, progesterone falls, and the lining sheds. Pregnancy has to **prevent** that — and the trick is **hCG**. As soon as the embryo implants, its **placenta makes human chorionic gonadotropin (hCG)**, which acts like LH to **keep the corpus luteum alive**, so it **keeps making progesterone** and the uterine lining **holds**. hCG **peaks around week 10**, then fades as the placenta makes its own progesterone. And it's exactly what a **pregnancy test** detects — the earliest hormonal sign.



The placenta as an endocrine organ

Once established, the **placenta runs pregnancy hormonally**. **hCG** carries the early rescue. **Progesterone** keeps the uterus **quiet** (no contractions) and the pregnancy secure. **Human placental lactogen (hPL)** re-tunes the **mother's metabolism** to shunt fuel to the fetus (a bit like GH, and mildly diabetogenic). **Relaxin** and **estrogen** loosen the pelvis and grow the uterus and breasts for delivery and feeding. A whole temporary gland — and when it or the corpus luteum fails early, the result can be **miscarriage**.

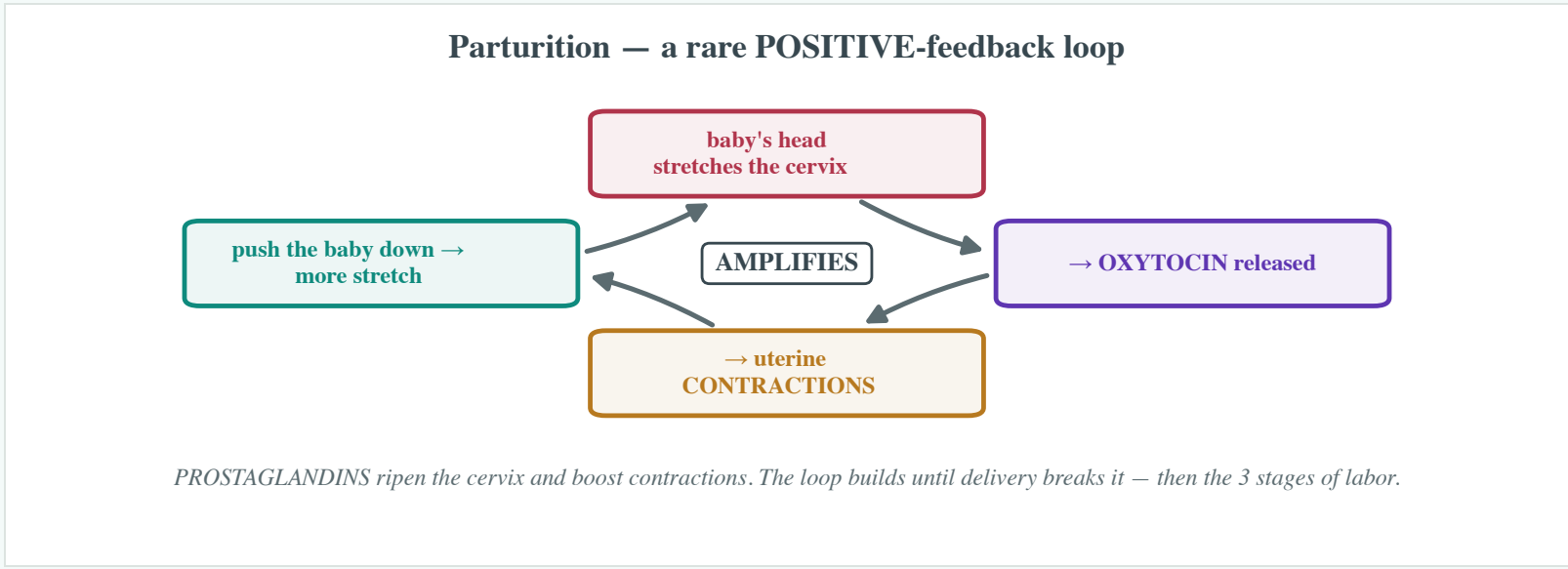


7 · Parturition, Labor & Contraception

"Birth is powered by one of the body's rare positive-feedback loops — the only place we celebrate a runaway cycle. And contraception works mostly by turning the female axis's own negative feedback against ovulation."

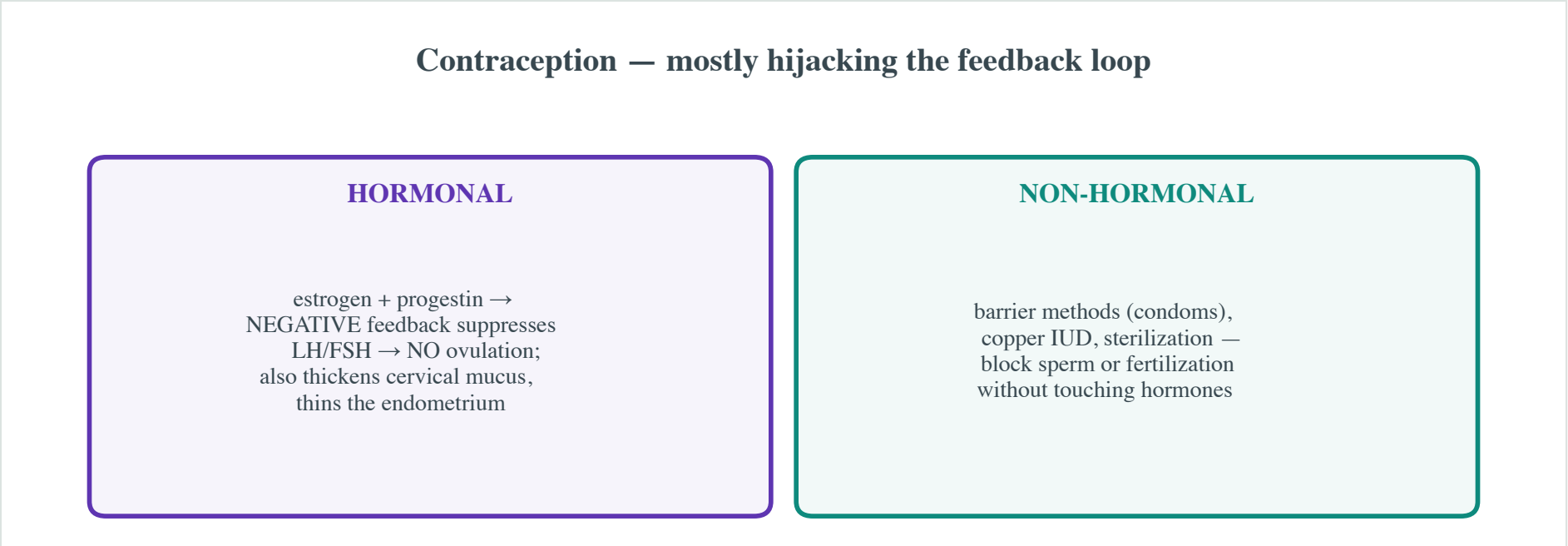
Birth: a rare positive-feedback loop

Almost every loop in this course is **negative** (self-limiting). Labor is the dramatic exception. As the baby's head **stretches the cervix**, the posterior pituitary releases **oxytocin**, which drives **uterine contractions**, which push the baby down and **stretch the cervix more** — releasing **still more oxytocin**. It **amplifies** instead of settling, building until delivery finally breaks the loop. **Prostaglandins** help by ripening the cervix and boosting contractions. The result is the three **stages of labor**: dilation, delivery of the baby, then delivery of the placenta.



Contraception — hijacking the feedback

Most contraception is just **clever endocrinology**. **Hormonal** methods give steady **estrogen + progestin**, which — through the **negative feedback** you learned — suppress **LH and FSH** so **no follicle matures and no ovulation happens**; as backup, they **thicken cervical mucus** and **thin the endometrium**. **Non-hormonal** methods work mechanically instead — **barrier methods** (condoms), the **copper IUD**, or **sterilization** — blocking sperm or fertilization without touching the hormone axis. Same goal, two very different levers.

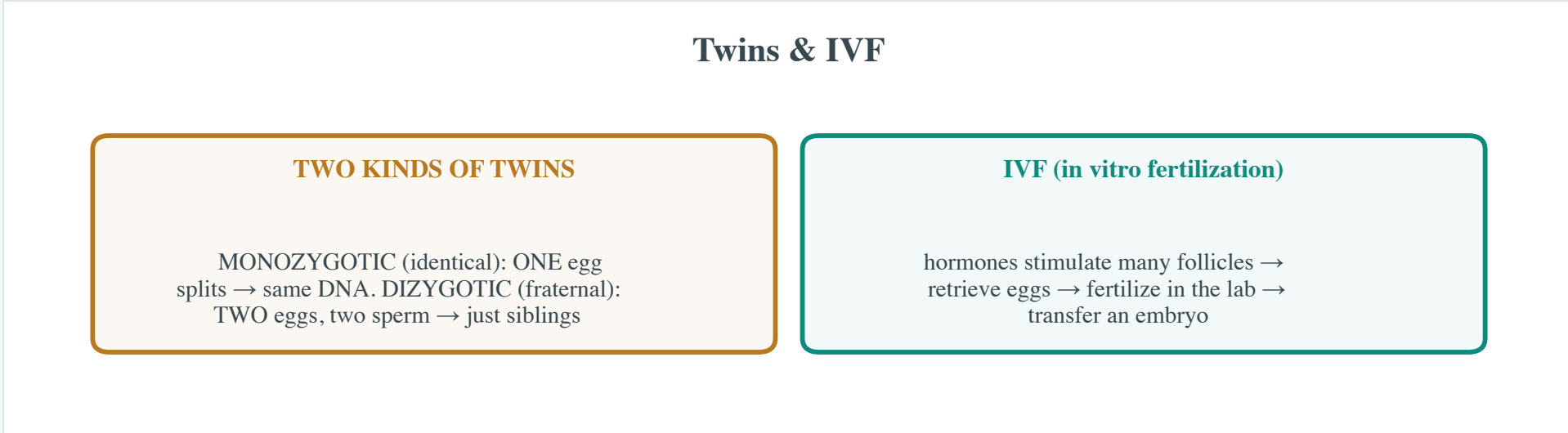


8 · Twins, IVF & Lactation

"Finish the course where life does: two babies from one egg (or two), a lab that borrows the whole HPO axis to make pregnancy happen, and the two-hormone system — prolactin and oxytocin — that feeds the newborn."

Twins and IVF

Two ways to get twins, and they're genetically opposite. **Monozygotic ("identical")** twins come from **one fertilized egg that splits** – same DNA. **Dizygotic ("fraternal")** twins come from **two eggs fertilized by two sperm** – just siblings who shared a womb. And when nature needs help, **IVF (in vitro fertilization)** borrows the whole axis on purpose: **high-dose FSH** forces **many follicles** to mature at once, an **LH-like trigger** finishes them, the **eggs are retrieved**, **fertilized in the lab**, and an **embryo is transferred** back. The endocrinology of the cycle, run deliberately.



IVF puts the whole HPO axis to work on purpose — high-dose FSH forces multiple follicles, then LH triggers maturation.

Lactation — the baby runs the supply

Feeding the newborn takes **two hormones**. **Prolactin** drives **milk synthesis** — including **lactose**, built by **lactose synthase** (galactosyltransferase + **α-lactalbumin**, the classic intro-biochem example). **Oxytocin** drives the **"let-down" reflex**, contracting the gland to **eject** milk. Both are triggered by **suckling**: nursing lifts the **dopamine brake** on prolactin **and** fires oxytocin, so the infant controls the supply. First comes **colostrum** — low in fat and volume but packed with protective **antibodies (IgA)** — then energy-dense **mature milk**; the baby's growth is then tracked on **percentile** charts against peers. And that's the endocrine journey, birth to first meal.

Can you…?

- □ explain sex-steroid synthesis (cholesterol → testosterone via StAR/LH; 5α-reductase → DHT; aromatase → estradiol) and the hypothalamic–pituitary–testis axis, testis structure, and kisspeptin?
- □ describe sex differentiation (SRY/AMH/testosterone; female default) and its disorders (CAH, 5α-reductase deficiency, androgen insensitivity), plus puberty and its timing disorders?
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- □ describe pregnancy — hCG's rescue of the corpus luteum, the placenta's hormones (progesterone, hPL, relaxin, estrogen), miscarriage, and parturition (oxytocin positive feedback, prostaglandins, labor) and contraception?
- □ explain twins (mono- vs dizygotic), IVF, and lactation (prolactin/oxytocin, lactose synthesis, colostrum vs milk)?

If any box stays empty, the practice site has a drill for it.

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