Reproductive Endocrine Disorders

BCH 130 — Advanced Human Biochemistry · Dr. Radi

By the end of this unit, you can…

- Explain PCOS pathophysiology: LH-driven ovarian hyperandrogenism amplified by insulin resistance, and the Rotterdam…
- Connect PCOS to anovulation, metabolic risk, and its management (insulin sensitizers, anti-androgens, ovulation induction).
- Describe endometriosis as estrogen-dependent ectopic endometrial tissue with local aromatase expression and progesterone resistance.
- Justify hormonal therapy (progestins, GnRH analogs, aromatase inhibitors) by the estrogen-dependence of the lesions.

Today's route

1. **Polycystic Ovary Syndrome**
2. **Endometriosis**
3. **Sex Determination & Its Disorders**

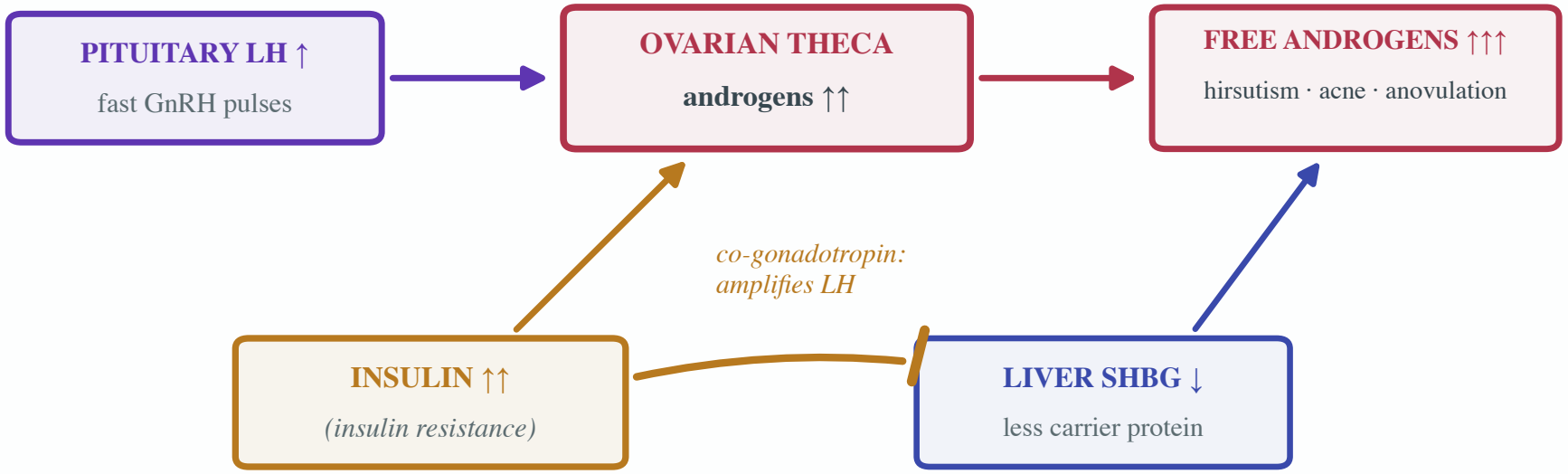
1 · Polycystic Ovary Syndrome

"PCOS is the most common endocrine disorder in women of reproductive age — and it's a beautiful crossroads of reproductive AND metabolic biochemistry. Let's build it from the molecule up: too much LH, an ovary making too many androgens, and insulin resistance pouring gasoline on the fire."

Two hits pile androgens onto the ovary

Here's the engine. Rapid **GnRH pulses** push the pituitary to favor **LH over FSH**, and LH drives the **theca cell** to crank out **androgens**. Now the twist that makes PCOS **metabolic**: **insulin resistance** means insulin runs sky-high — and insulin is a **co-gonadotropin**, amplifying LH at the theca **and** dropping liver **SHBG** so even more androgen runs free.

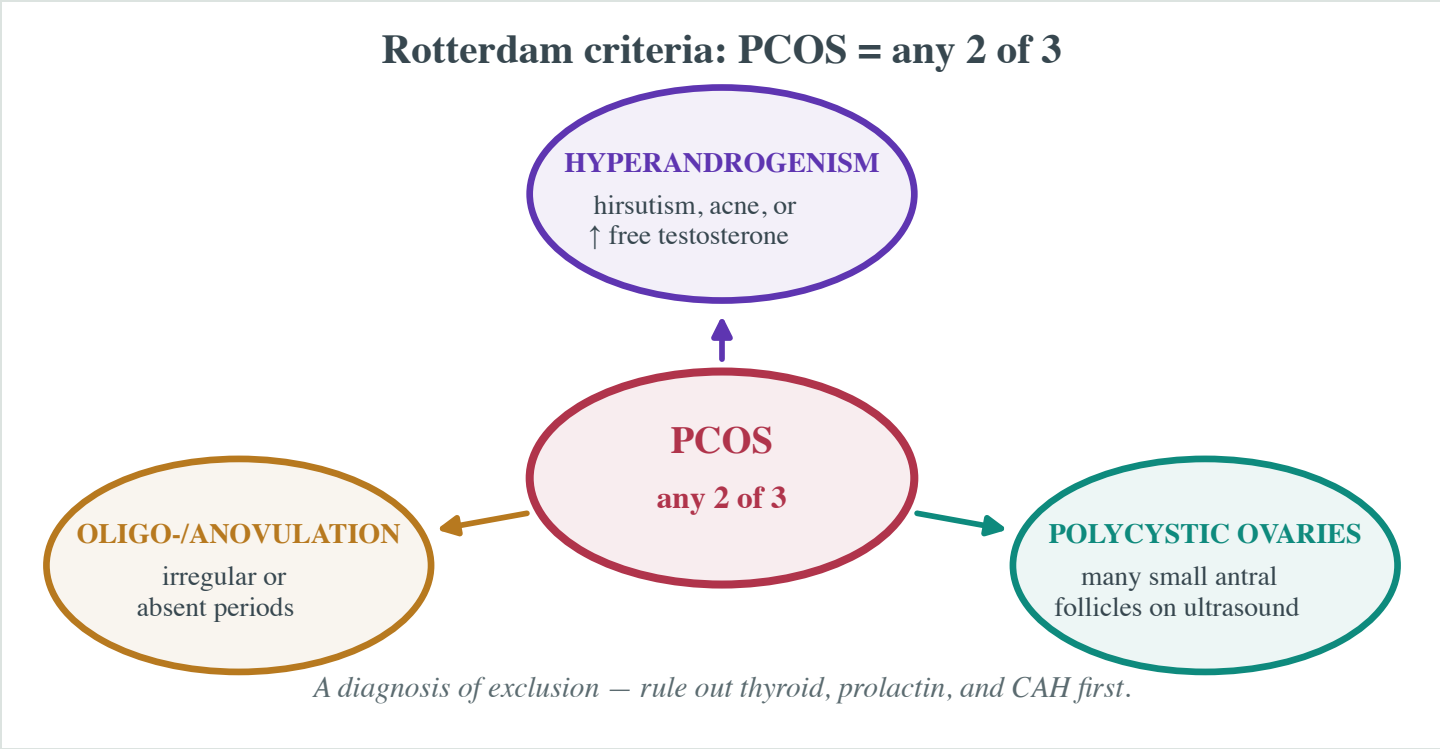
PCOS: LH drives it, insulin resistance amplifies it



LH makes the androgens; insulin amplifies LH at the theca AND drops SHBG, so even more runs free.

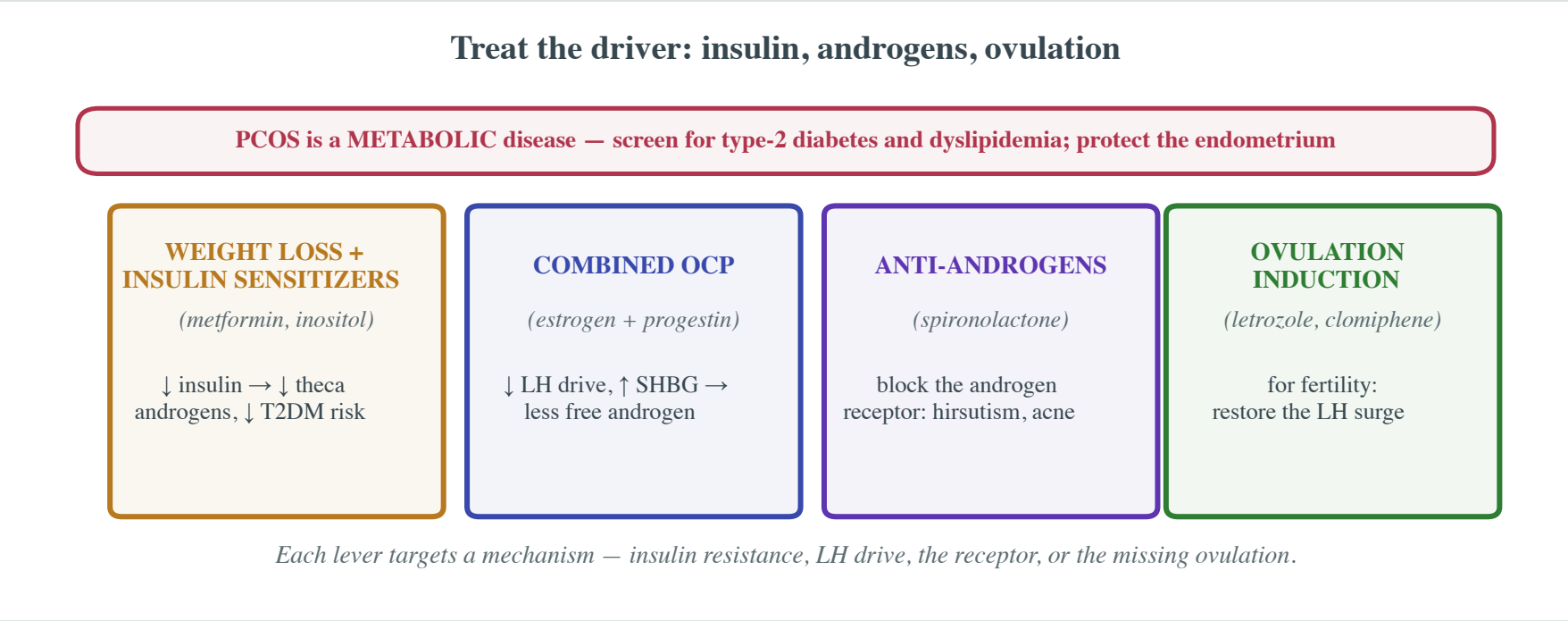
Rotterdam: any two of three

How do we name it? **Rotterdam criteria** — any **2 of 3**: **hyperandrogenism** (hirsutism, acne, high free testosterone), **oligo-/anovulation**, and **polycystic ovaries** on ultrasound. Those "cysts" are really **antral follicles arrested** mid-development — no FSH surge, so no follicle is ever chosen to ovulate.



Treat the driver, not just the symptom

PCOS is a **metabolic** disease, so we treat mechanisms. **Insulin sensitizers** (metformin) and weight loss attack the insulin driver. A **combined OCP** quiets LH and raises SHBG; **anti-androgens** block the receptor for hirsutism. For fertility, **ovulation induction** with **letrozole** restores the surge. And screen everyone for diabetes!



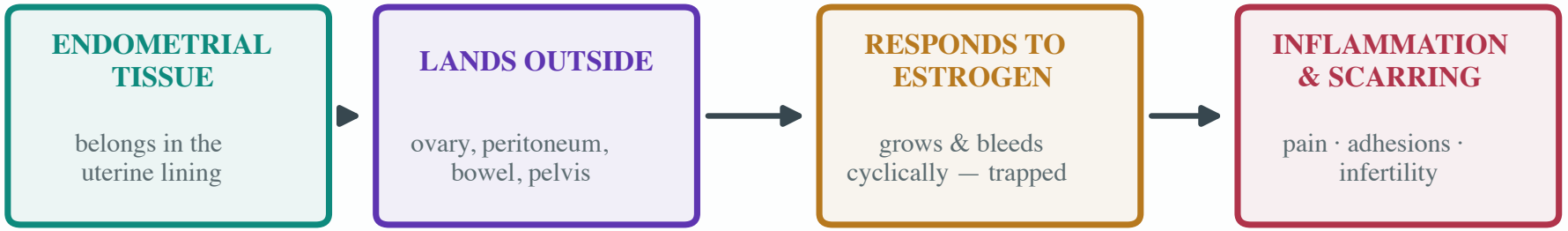
2 · Endometriosis

"Endometriosis is deceptively simple to state — endometrial tissue growing where it doesn't belong — and fiendishly biochemical underneath. The lesion makes its OWN estrogen and ignores the hormone that's supposed to shut it down. Get that, and every drug we use makes perfect sense."

Right tissue, wrong place

Endometriosis is functioning **endometrial tissue** growing **outside the uterus** — on the ovary, peritoneum, bowel, anywhere in the pelvis. It's still hormone-responsive, so it **grows and bleeds cyclically** wherever it landed. Trapped blood means **inflammation, adhesions, and scarring** — the source of the crushing **pain and infertility**. And every implant runs on one fuel: **estrogen**.

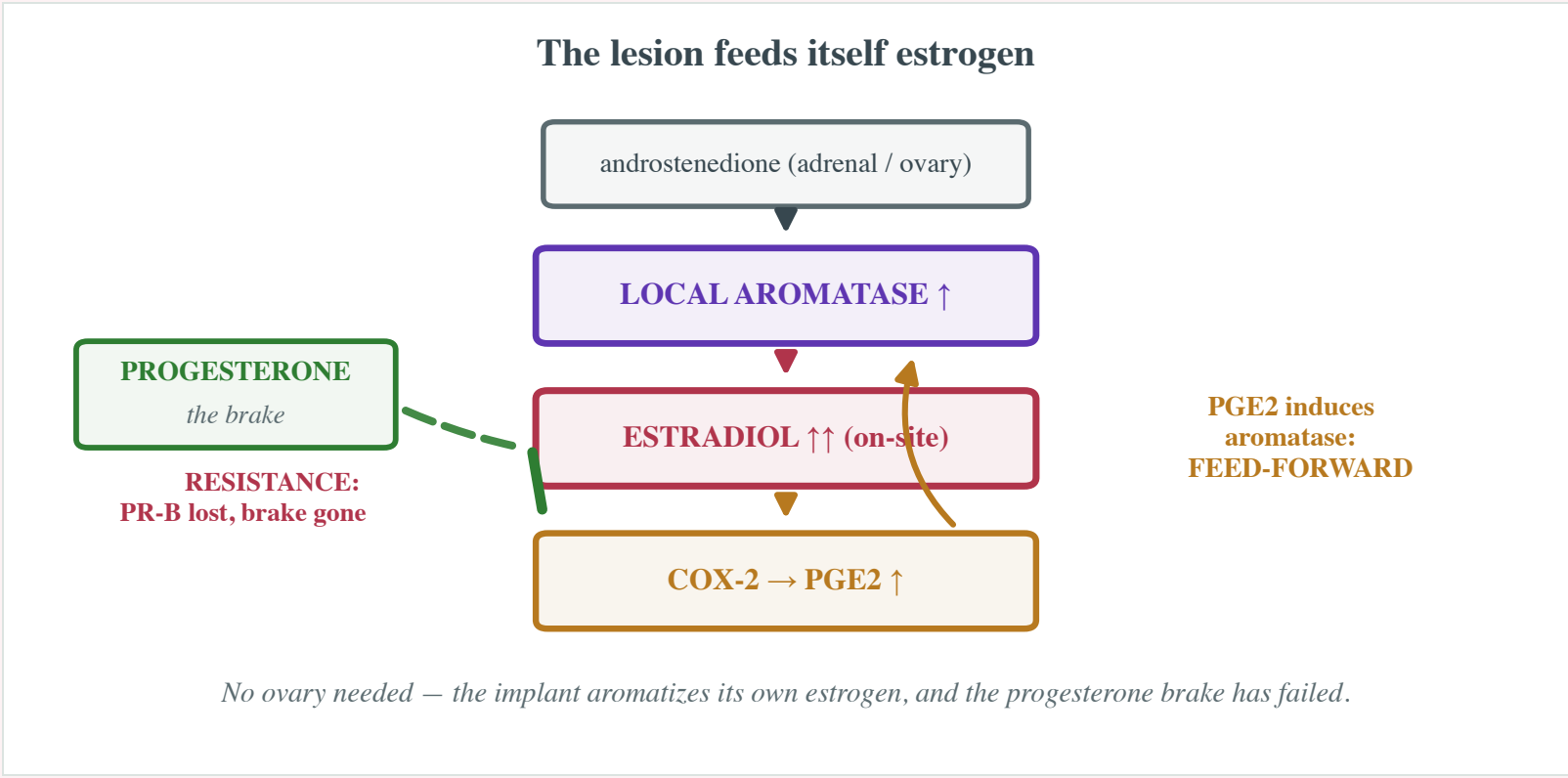
Endometrium in exile: right tissue, wrong place



Estrogen is the fuel for every ectopic implant — which is exactly where therapy strikes.

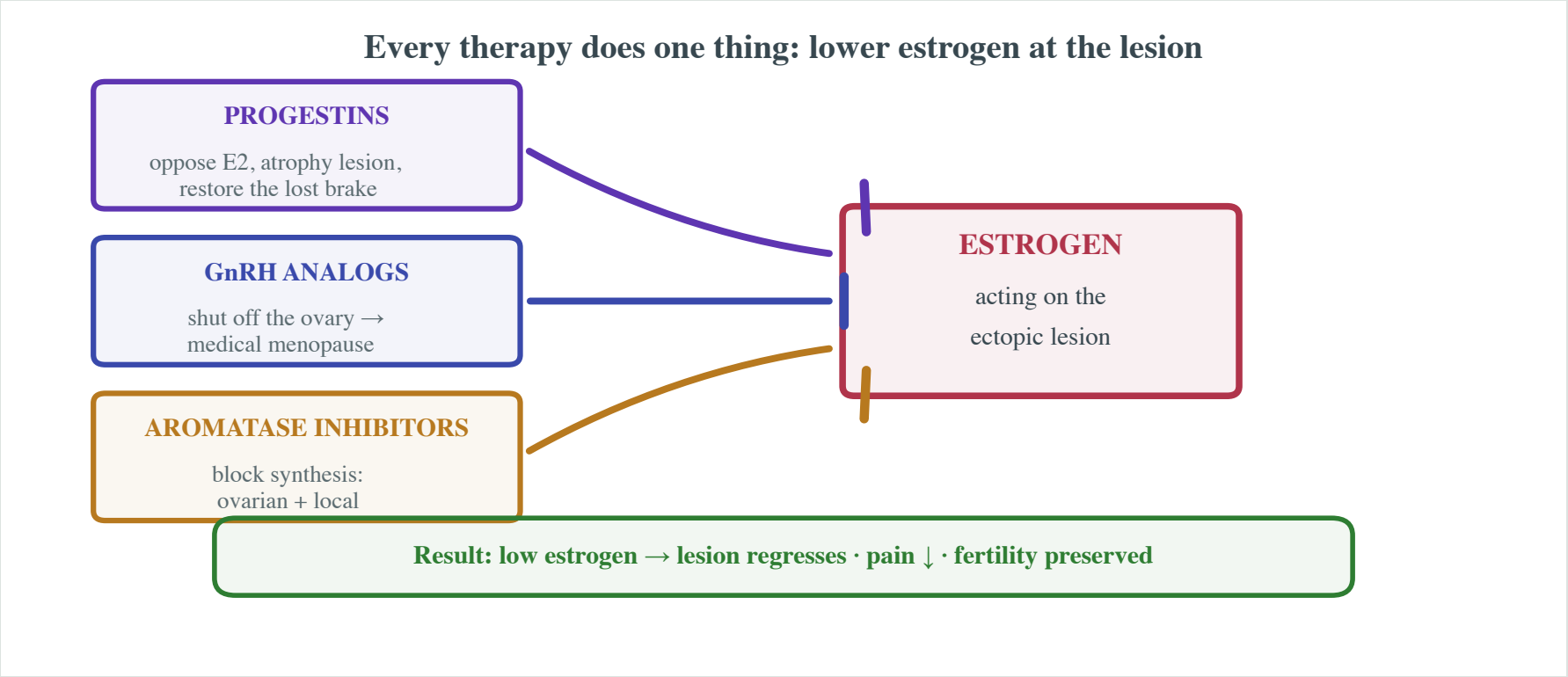
The lesion feeds itself estrogen

Here's what makes it relentless. The lesion expresses **local aromatase** — making **estradiol on-site**, no ovary required. That estrogen drives **COX-2 → PGE2**, and PGE2 **induces more aromatase**: a vicious **feed-forward loop**. Worse, the lesion is **progesterone-resistant** (PR-B lost) — the hormone that should brake estrogen can't.



Every drug lowers estrogen

See the lesions as estrogen-dependent and therapy is obvious — **starve them of estrogen**. **Progestins** oppose estrogen and atrophy the tissue. **GnRH analogs** shut the ovary down — a reversible medical menopause. **Aromatase inhibitors** block estrogen **synthesis**, hitting both ovarian and that sneaky **local** source.

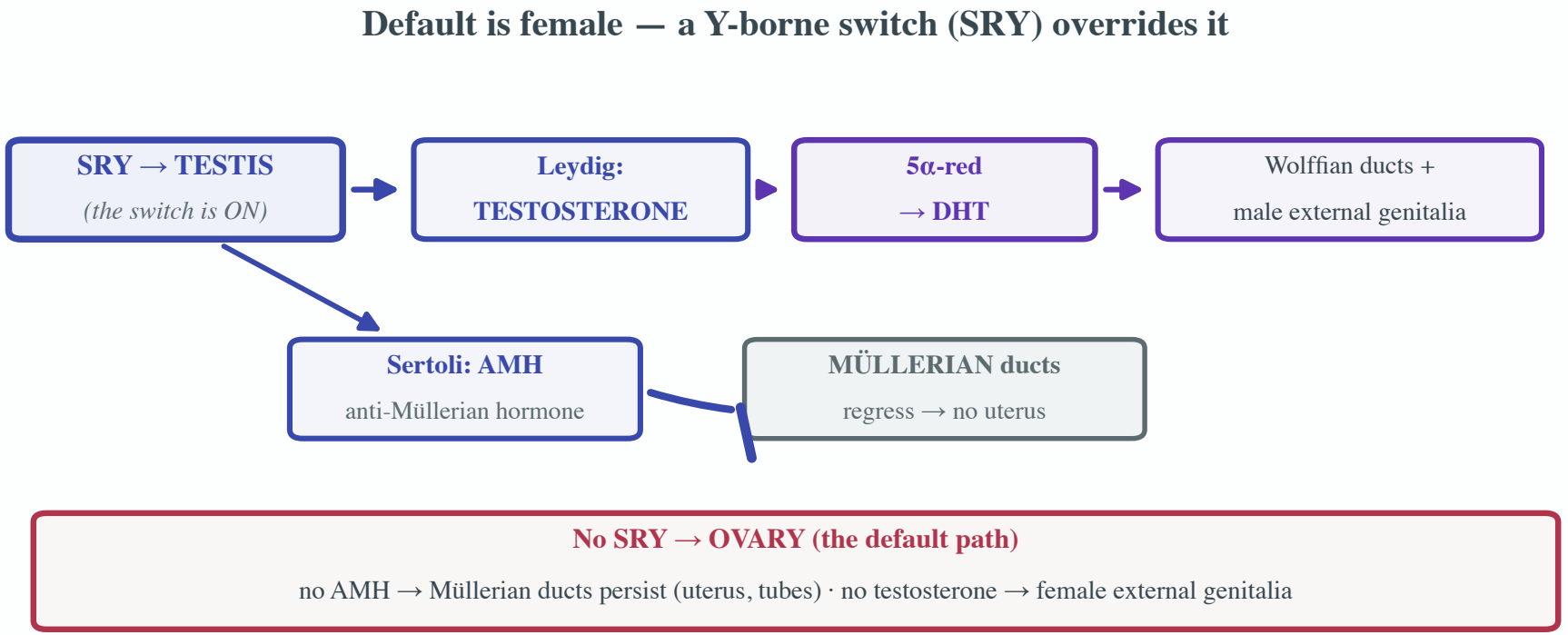


3 · Sex Determination & Its Disorders

"To understand what goes wrong, you first need the normal blueprint — and it's gorgeous biochemistry. One gene flips the switch, two hormones from the testis build the male body plan, and the default is female. Learn the three signals, and every disorder is just a broken step in that sequence."

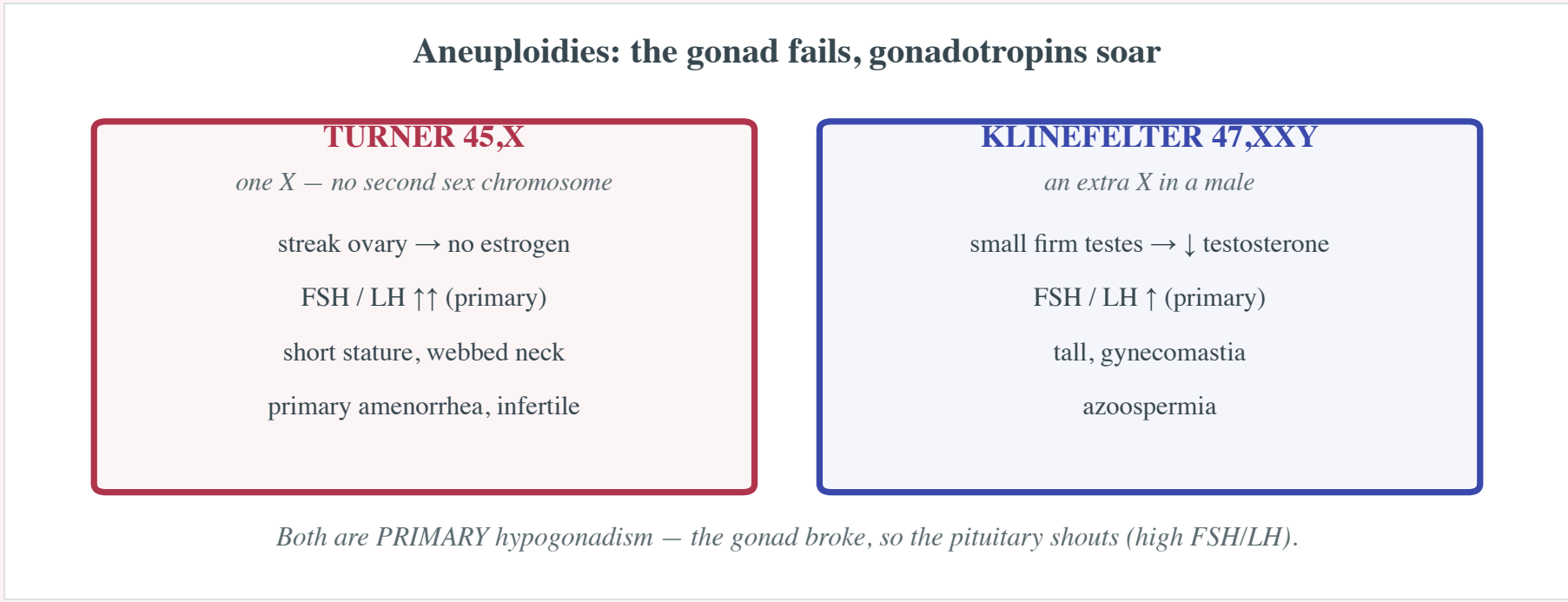
The blueprint: SRY, AMH, and DHT

The default body plan is **female**. A single Y-borne gene, **SRY**, flips the bipotential gonad into a **testis** — and the testis makes two things. **Sertoli cells** secrete **AMH**, which **removes** the Müllerian ducts. **Leydig cells** make **testosterone**, which builds the Wolffian ducts and — after **5α-reductase** converts it to **DHT** — the external male genitalia. No SRY, no testis: ovary, uterus, female.



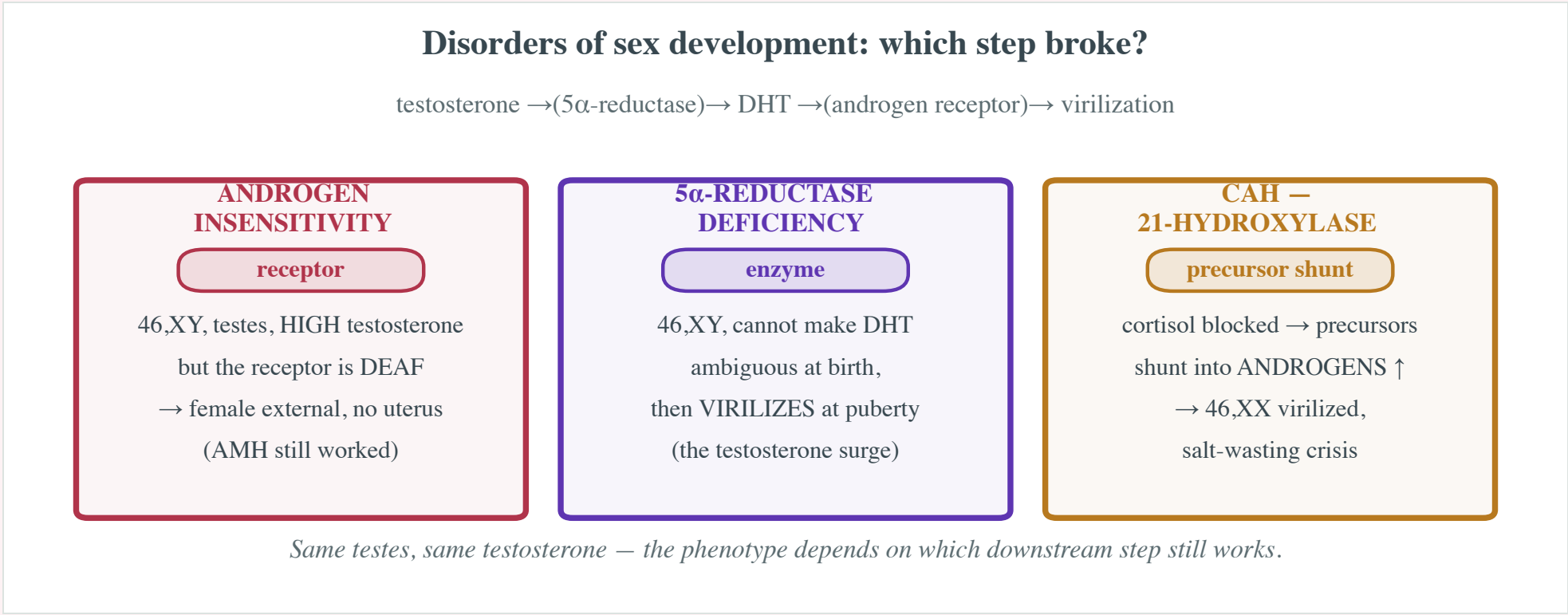
When a whole chromosome is off

Start with the **aneuploidies**. **Turner (45,X)** has a single X — a **streak** gonad, so no estrogen and **primary amenorrhea**; the short stature (SHOX loss) and webbed neck (fetal lymphedema) come from the missing X itself. **Klinefelter (47,XXY)** has an extra X — small firm testes, low testosterone, tall stature, gynecomastia. Both are **primary hypogonadism**: the gonad failed, so **FSH and LH climb**.



When one step in the pathway breaks

Now watch the **same** testes and testosterone give three different bodies — depending on which step fails. **Androgen insensitivity**: the **receptor is deaf**, so a 46,XY body goes female. **5α-reductase deficiency**: no **DHT**, so ambiguous at birth, then virilizing at puberty. **CAH (21-hydroxylase)**: blocked cortisol shunts precursors into **androgens**, virilizing a 46,XX child.



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