

Menopause & Andropause

BCH 130 – Advanced Human Biochemistry · Dr. Radi

By the end of this unit, you can...

- Explain the endocrinology of the menopausal transition
- Connect estrogen withdrawal to vasomotor symptoms and the biochemistry of hot flashes (KNDy neurons / thermoregulatory setpoint).
- Trace the systemic consequences of chronic estrogen loss
- Explain hormone-replacement therapy – estrogen +/- progestin, routes, benefits/risks – as targeted replacement of the deficient hormone.

Today's route



1. **The Menopausal Transition**
2. **Menopause – Systemic Effects & HRT**
3. **Andropause & Male Reproductive Aging**

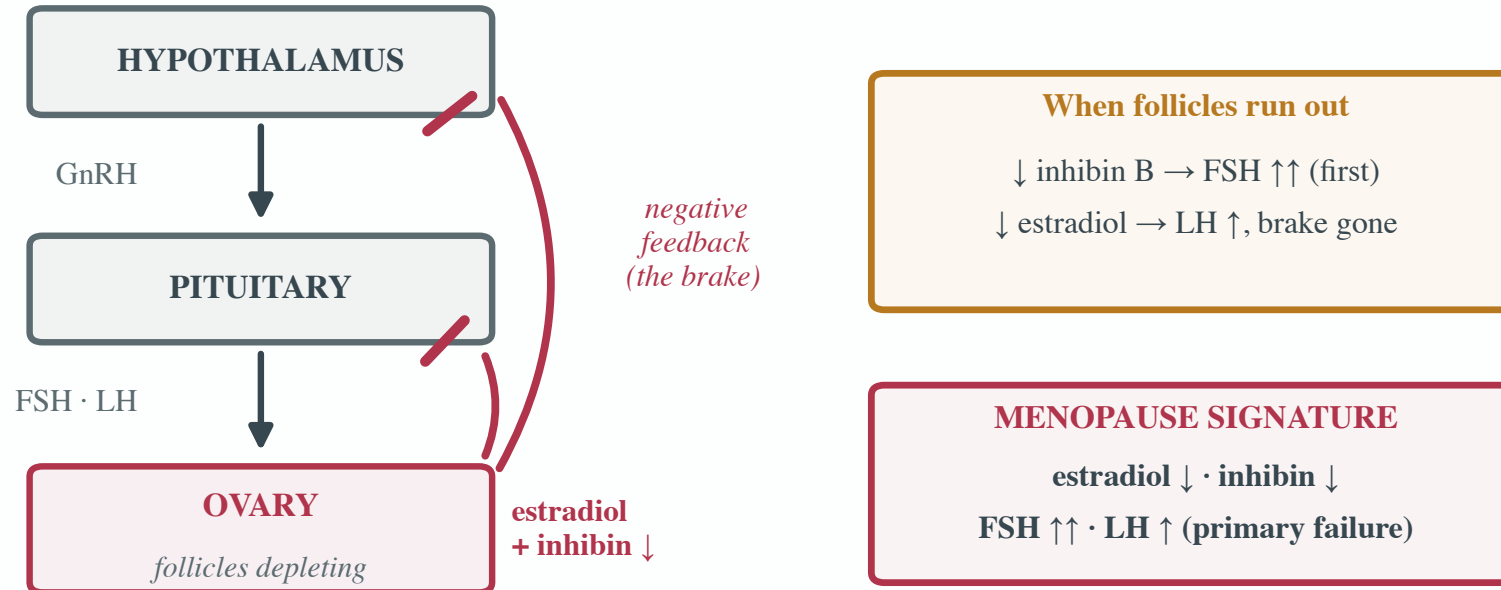
1 • The Menopausal Transition

"Menopause isn't a hormone running low – it's a gland running OUT. Watch the HPG axis lose its ovarian brakes: follicles deplete, inhibin and estradiol fall, and FSH and LH climb. Then we'll trace that estrogen withdrawal all the way up to the hot flash."

The ovarian brakes come off

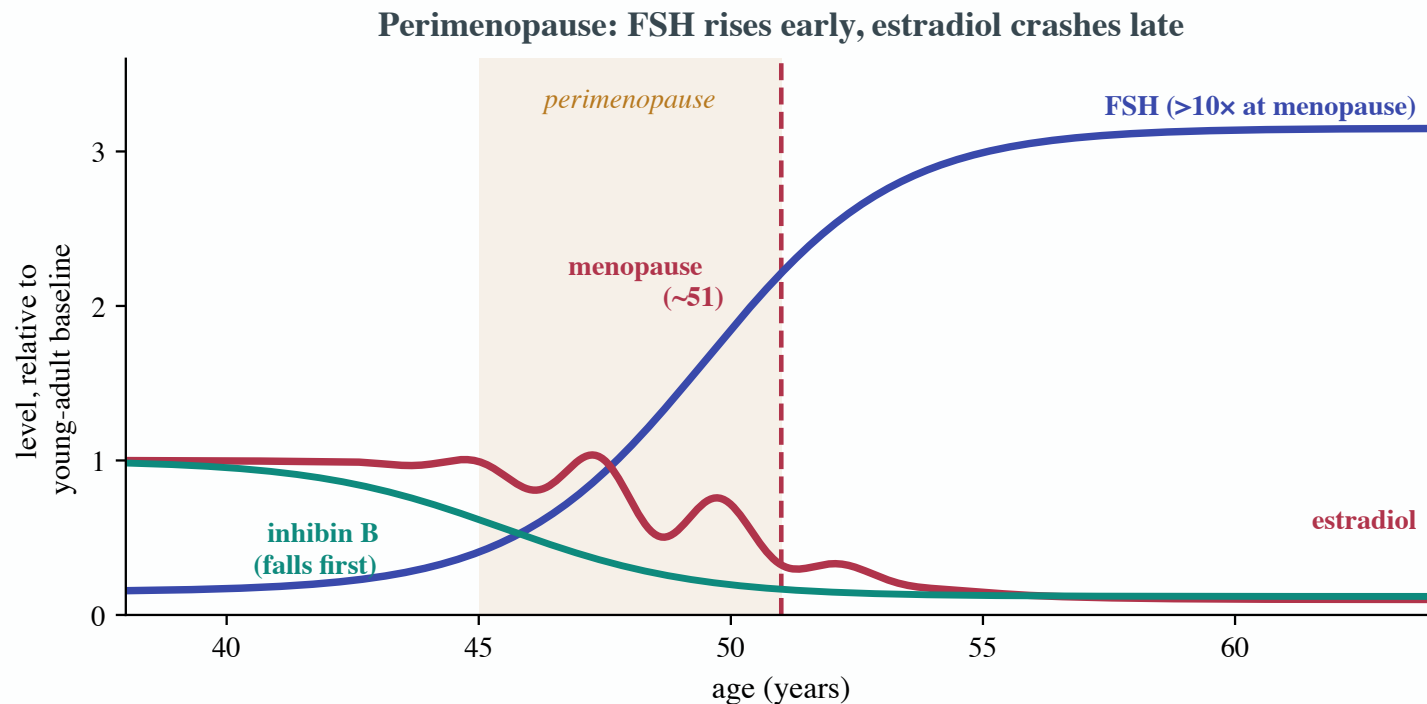
You've met the HPG axis – now watch it lose its **off switch**. A woman is born with every follicle she'll ever have, and the pool runs down. As it empties, granulosa cells make less **inhibin B** and **estradiol** – the very hormones that restrained the pituitary. Brakes gone, **FSH and LH** climb.

Follicles run out → the ovarian brakes come off



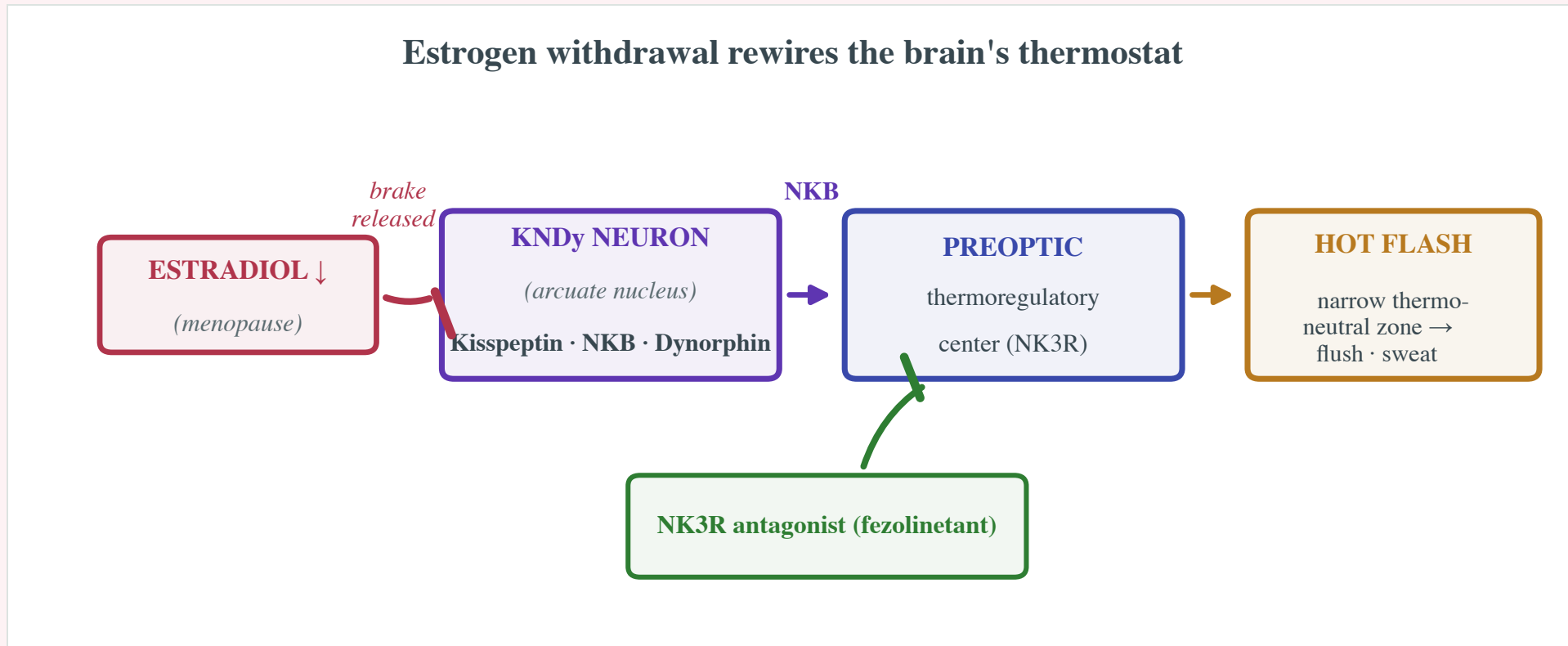
FSH rises first

Here's the tell: the hormones don't all move together. **Inhibin B falls first**, so its brake on the pituitary lifts early and **FSH creeps up years before periods stop**. Estradiol lurches through the erratic **perimenopause**, then crashes at the final period – **high FSH, low estradiol** is the fingerprint.



Where hot flashes come from

So why the **hot flashes**? In the hypothalamus sit **KNDy neurons**, normally kept quiet by estradiol. Withdraw the estrogen and they **hypertrophy and fire**, flooding the preoptic **thermostat** with neurokinin B. The thermoneutral zone narrows to a sliver – a trivial warmth triggers a full **flush**. Blocking **NK3R** (fezolinetant) calms it.

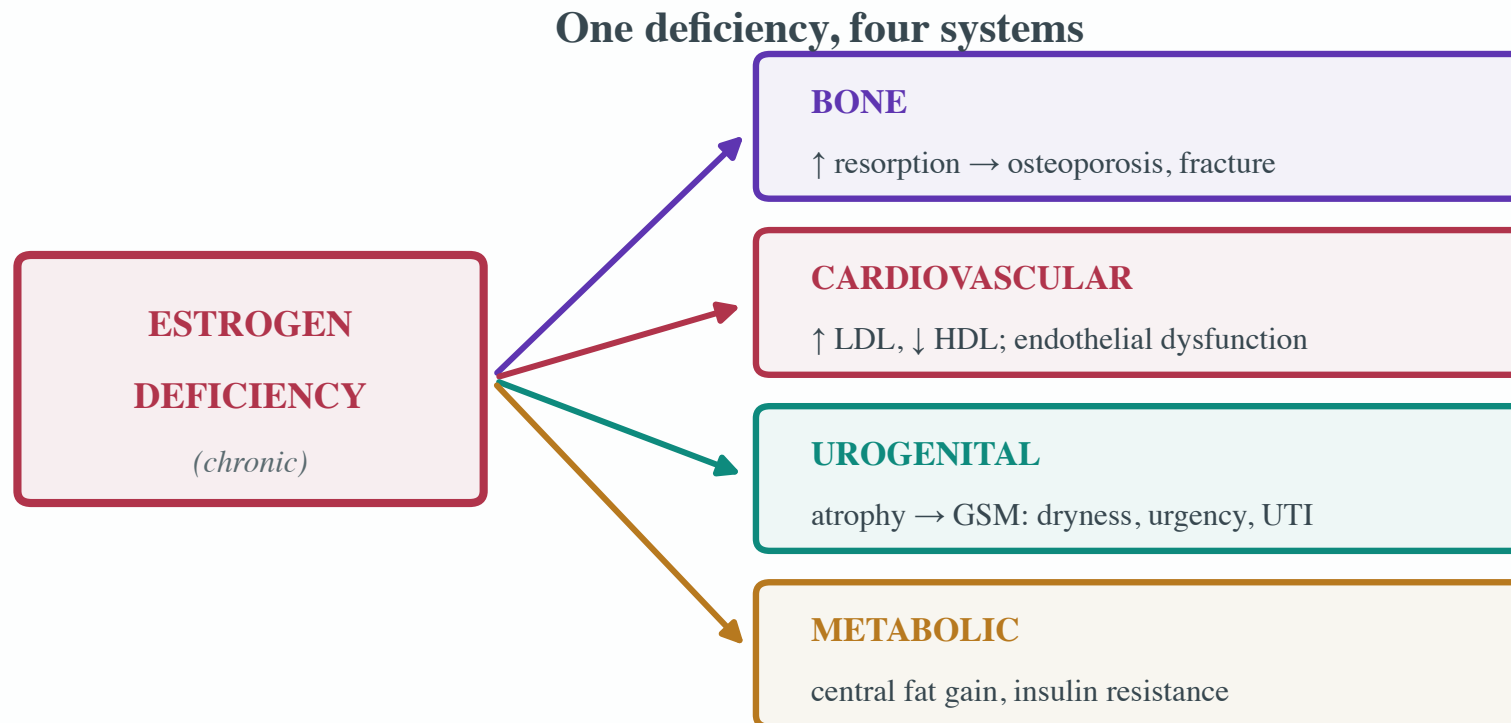


2 · Menopause – Systemic Effects & HRT

"Estrogen was quietly protecting four systems at once – bone, heart, urogenital tract, and metabolism. Take it away for good and each one drifts. Then the fix that follows straight from the mechanism: replace the deficient hormone, and know exactly when to add a progestin."

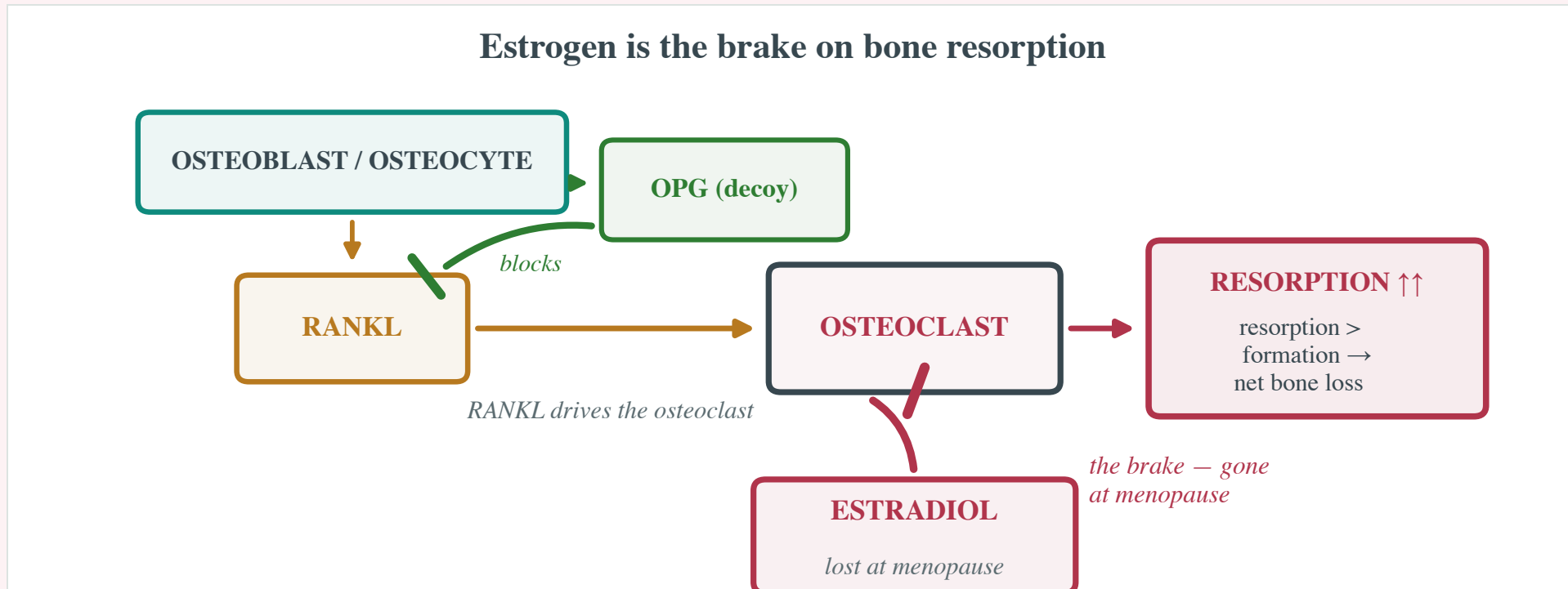
One deficiency, four systems

Menopause isn't just symptoms – it's **decades of estrogen withdrawal**, and estrogen was quietly protecting four systems at once. **Bone** loses its brake on resorption. The **cardiovascular** profile turns (LDL up, HDL down). **Urogenital** tissues thin and atrophy. And **metabolism** shifts toward belly fat and insulin resistance. One deficiency, four fronts.



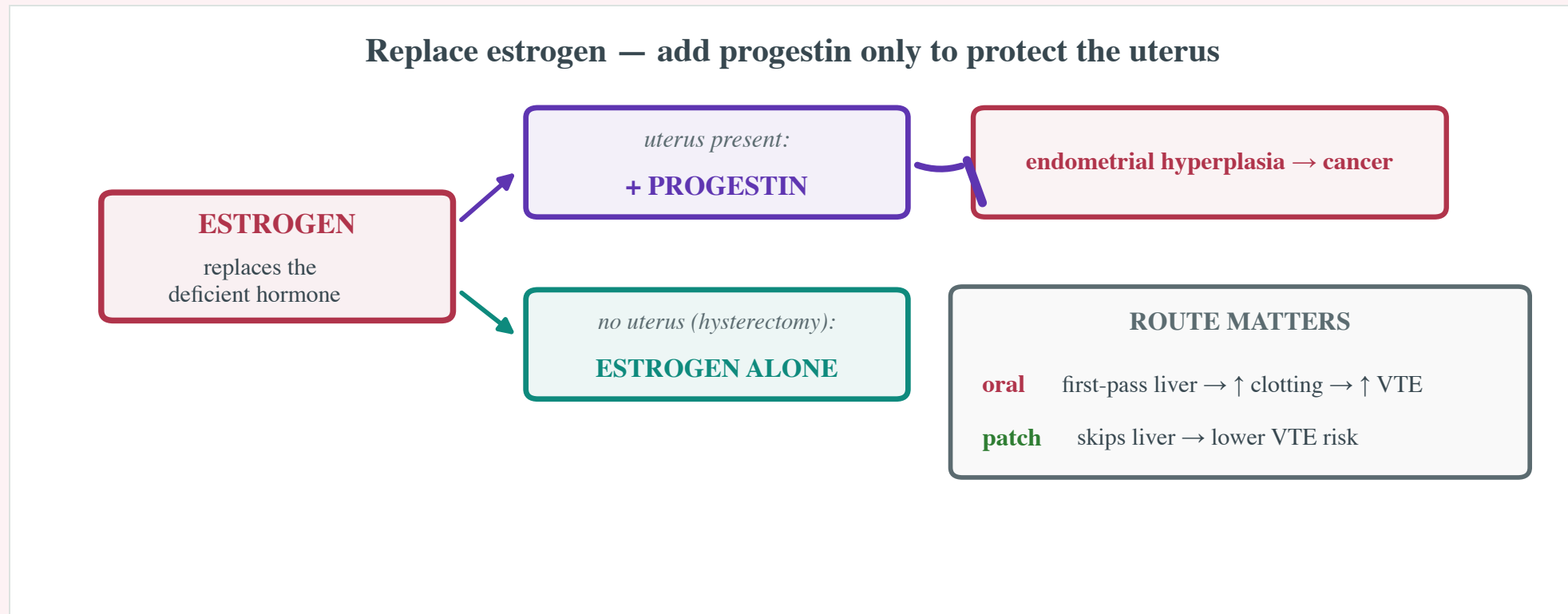
Estrogen was the brake on bone

Zoom in on **bone**, where the loss runs fastest – up to **20% in the first years**. Estradiol is the **brake** on the osteoclast: it lowers **RANKL**, raises the decoy **OPG**, and shortens the osteoclast's life. Pull estrogen out and the osteoclast is unleashed – **resorption outruns formation**, and bone thins toward osteoporosis.



Replace the missing hormone

The fix is logical: **replace the missing hormone**. **Estrogen** melts hot flashes, protects bone, and restores urogenital tissue. But unopposed estrogen overgrows the **endometrium** – so with a uterus, **add a progestin** to guard it. Route matters: **oral** raises clot risk (first-pass liver); the **patch** avoids it. Best started **near menopause**.

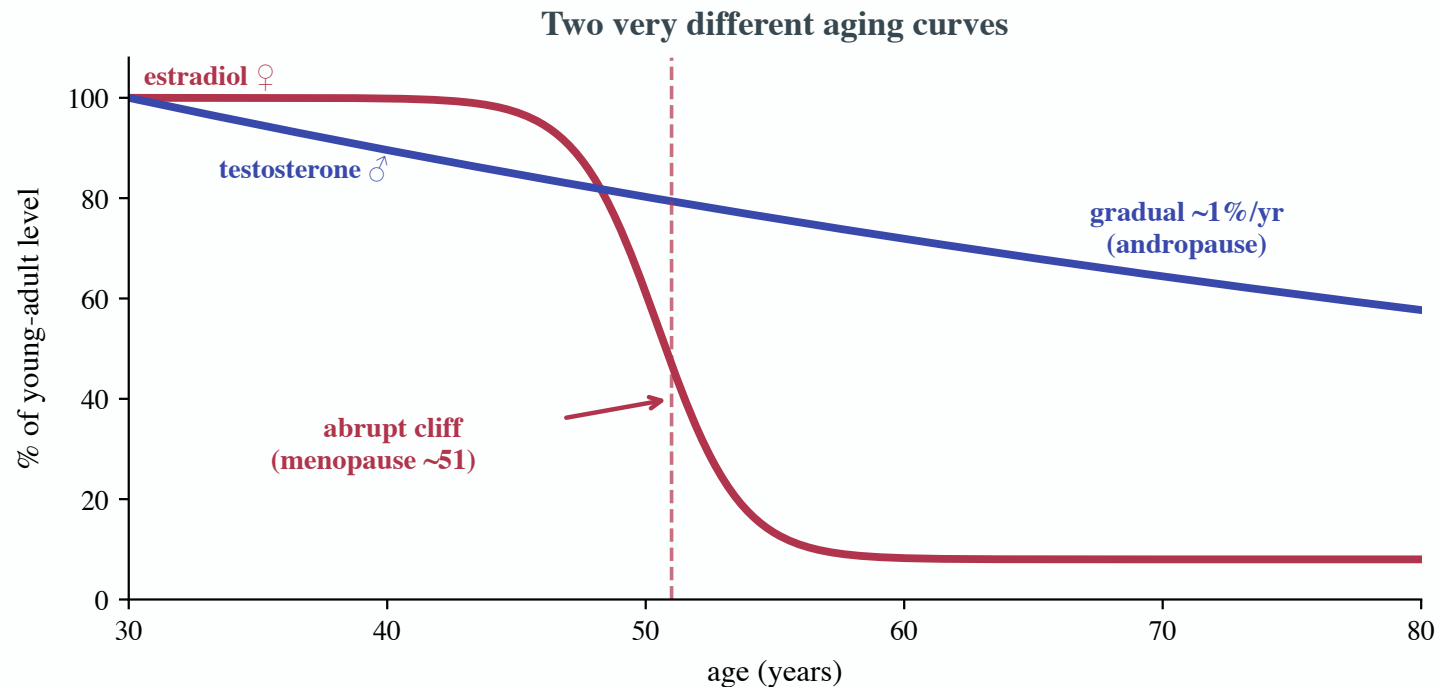


3 · Andropause & Male Reproductive Aging

"Do men have a menopause? Not really – and the difference is the whole point. Where the ovary fails like a cliff, the testis drifts down a gentle slope. We'll watch total testosterone, free testosterone, and SHBG pull apart with age, then weigh testosterone-replacement therapy honestly."

A cliff versus a slope

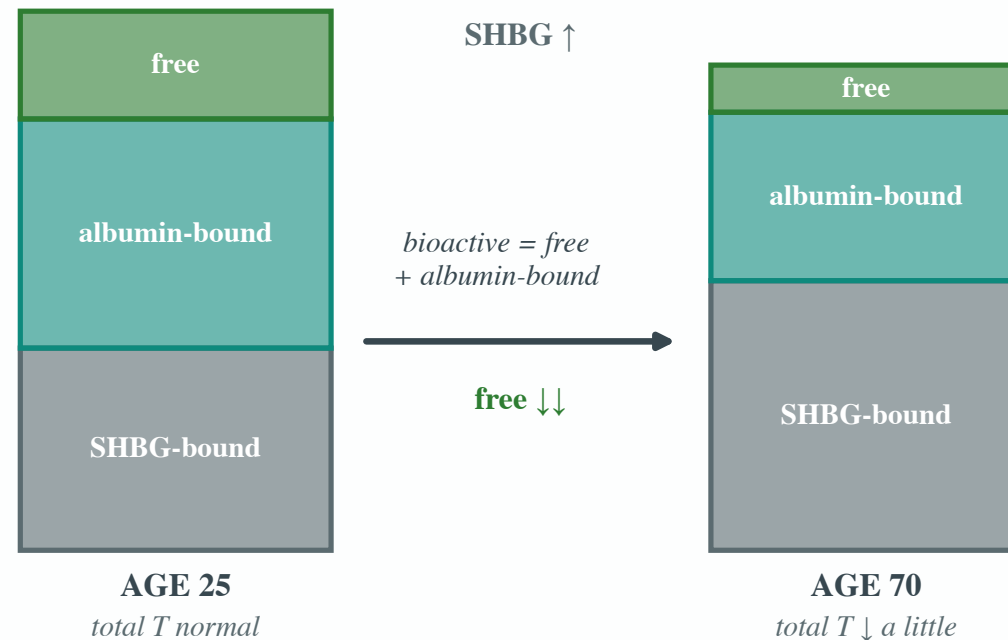
Do men have a "menopause"? Not really – and this graph is why. The ovary fails like a **cliff**: estradiol plummets over a couple of years around 51. Testosterone instead drifts down a gentle **slope**, roughly **1% per year** from your thirties. Gradual, partial, and never complete – men stay fertile for decades.



The free-testosterone squeeze

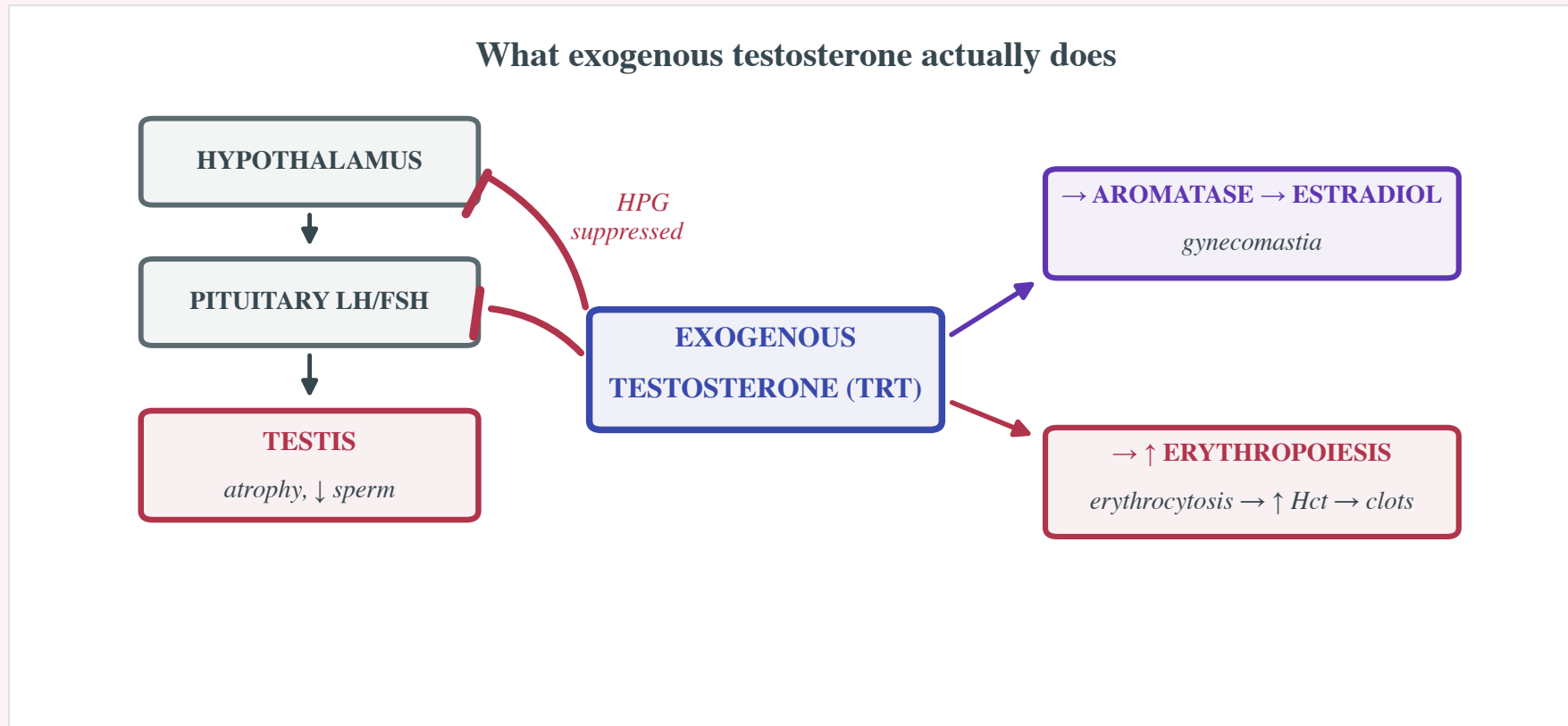
Here's the subtlety. As men age, **total testosterone** only dips a little – but **SHBG rises**, gripping more of it tightly. Since only **free and albumin-bound T** is usable, the **bioactive fraction shrinks far more than the total does**. So read **free testosterone**, not just total, or you'll miss it.

Rising SHBG squeezes out free testosterone



Testosterone therapy, honestly

If a man has **real symptoms plus low morning testosterone**, replacement helps – but know the biochemistry. Exogenous T **feeds back and shuts down the HPG axis**, so LH and FSH fall and the **testes shrink and sperm dries up**. Some **aromatizes to estradiol** (gynecomastia), and it **revs erythropoiesis** – watch the **hematocrit** for clot risk.



Can you...?

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- ☐ trace the systemic consequences of chronic estrogen loss?
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If any box stays empty, the practice site has a drill for it.

