Hormone-Dependent Cancers

BCH 130 — Advanced Human Biochemistry · Dr. Radi

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By the end of this unit, you can…

- Explain how unopposed estrogen and estrogen-receptor signaling drive endometrial cancer (Type I estrogen-dependent vs Type II), and the role of PTEN/PI3K.
- Classify ovarian cancers (epithelial, stromal/sex-cord, germ cell) and their hormone/marker biology (CA-125, inhibin, AFP/hCG).
- Connect estrogen-receptor biology to endocrine therapy targets (SERMs, aromatase inhibitors) as applied to these reproductive cancers.
- Explain androgen-receptor signaling in prostate cancer and the biochemistry of androgen-deprivation therapy (GnRH agonists/antagonists, abiraterone/CYP17, enzalutamide) and castration resistance.

Today's route

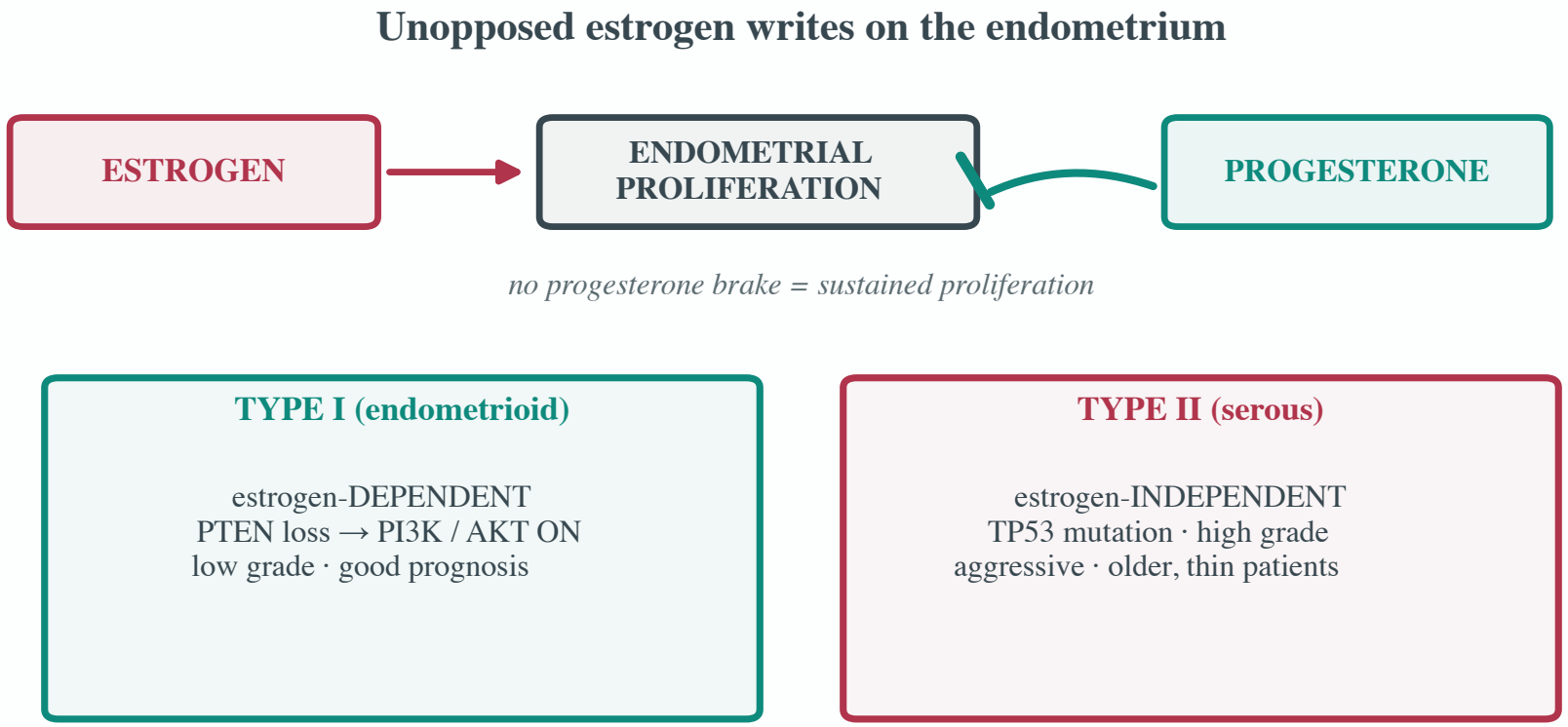
1. **Estrogen-Dependent Reproductive Cancers**
2. **Androgen-Dependent Cancer & Pituitary Adenomas**
3. **Thyroid & Adrenal Tumors + Cancer Cachexia**

1 · Estrogen-Dependent Reproductive Cancers

"When estrogen has nobody telling it to stop, tissues that answer to estrogen start growing without a plan. Let's follow that logic into endometrial and ovarian cancer — then turn the same receptor biology into treatment, with drugs that either cut estrogen off at its source or block its receptor."

Unopposed estrogen writes on the endometrium

Estrogen tells the endometrium to grow; progesterone is the brake that says stop. Take the brake away — **unopposed estrogen** — and proliferation never quits. That's **Type I** endometrial cancer: estrogen-driven, low-grade, losing **PTEN** so **PI3K/AKT** stays switched on. **Type II** is the ugly outlier — estrogen-independent, **TP53**-mutant, aggressive.



Ovarian cancer is three diseases

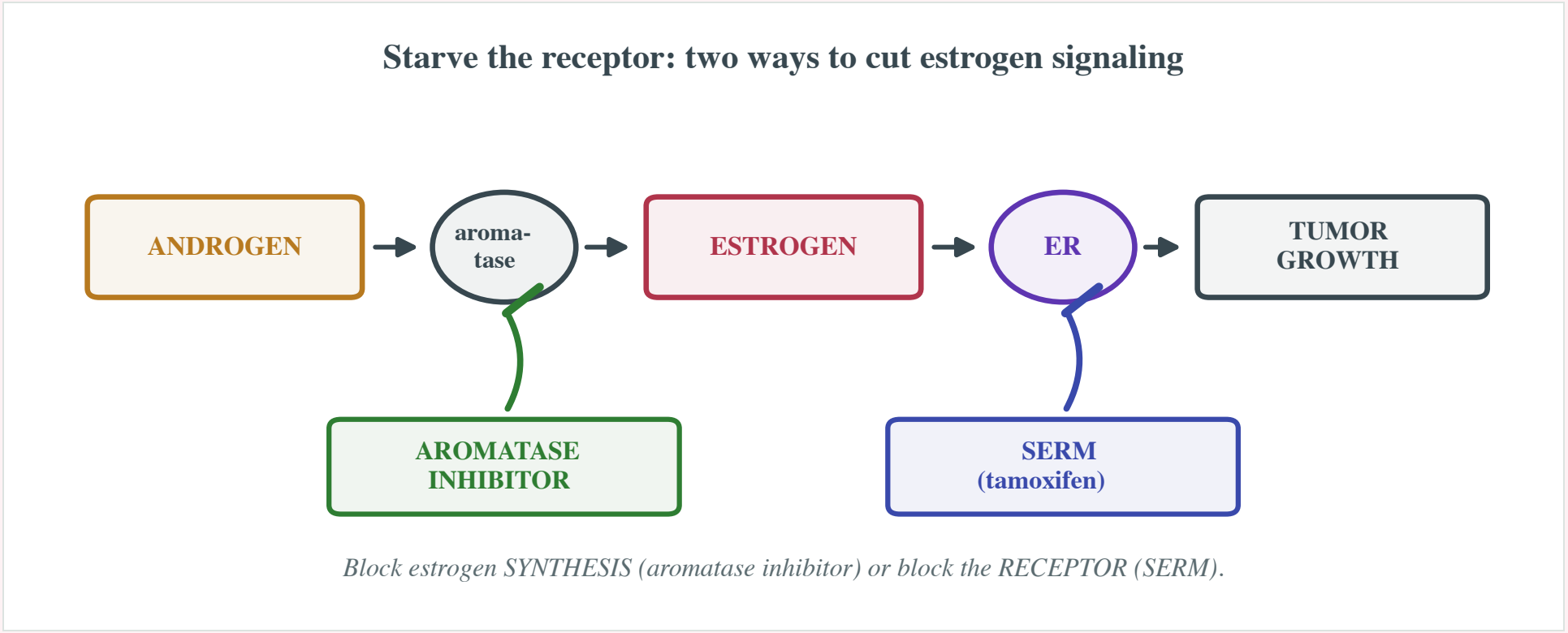
Ovarian cancer isn't one disease — it's three, sorted by the cell it came from, and each hands you a **marker**. **Epithelial** (the common one, older women) sheds **CA-125**. **Sex-cord/stromal** tumors from granulosa cells make **inhibin** — and often estrogen. **Germ-cell** tumors in young women spill **AFP** or **hCG**.

Three ovarian cancers — each with its own marker

The marker names the family — and tracks the tumor after you treat it.

If it grows on estrogen, cut the estrogen

If a tumor grows on estrogen, cut the estrogen — two clean targets. **Aromatase inhibitors** block the enzyme that builds estrogen from androgen, perfect after menopause when that's the main source left. Or hit the receptor: a **SERM** like **tamoxifen** parks on **ER** so estrogen can't. Same signal, two chokepoints.



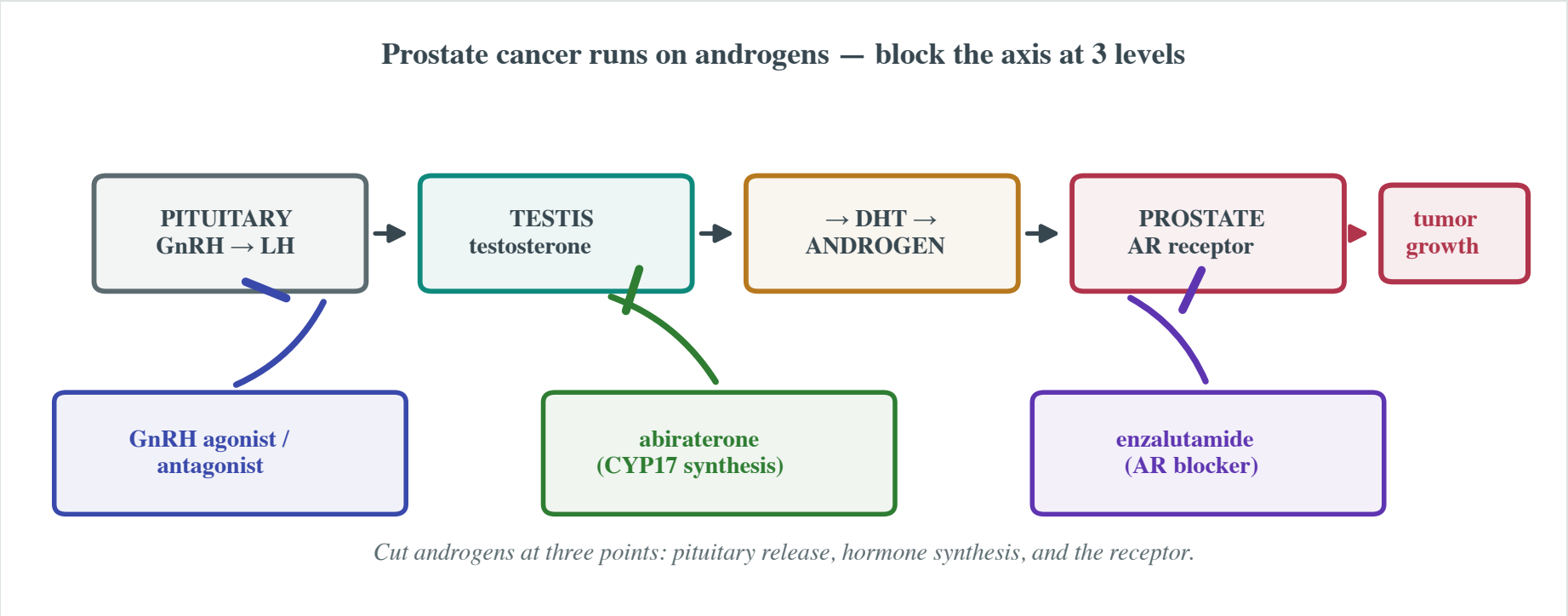
Block estrogen SYNTHESIS (aromatase inhibitor) or block the RECEPTOR (SERM).

2 · Androgen-Dependent Cancer & Pituitary Adenomas

"Prostate cancer lives on androgens, so we take them away — then watch it find clever ways around us. That same 'which hormone is too loud?' thinking cracks open the pituitary, where a tumor's secretion is its name tag, and a prolactinoma melts away with a pill instead of a scalpel."

Prostate cancer is addicted to androgens

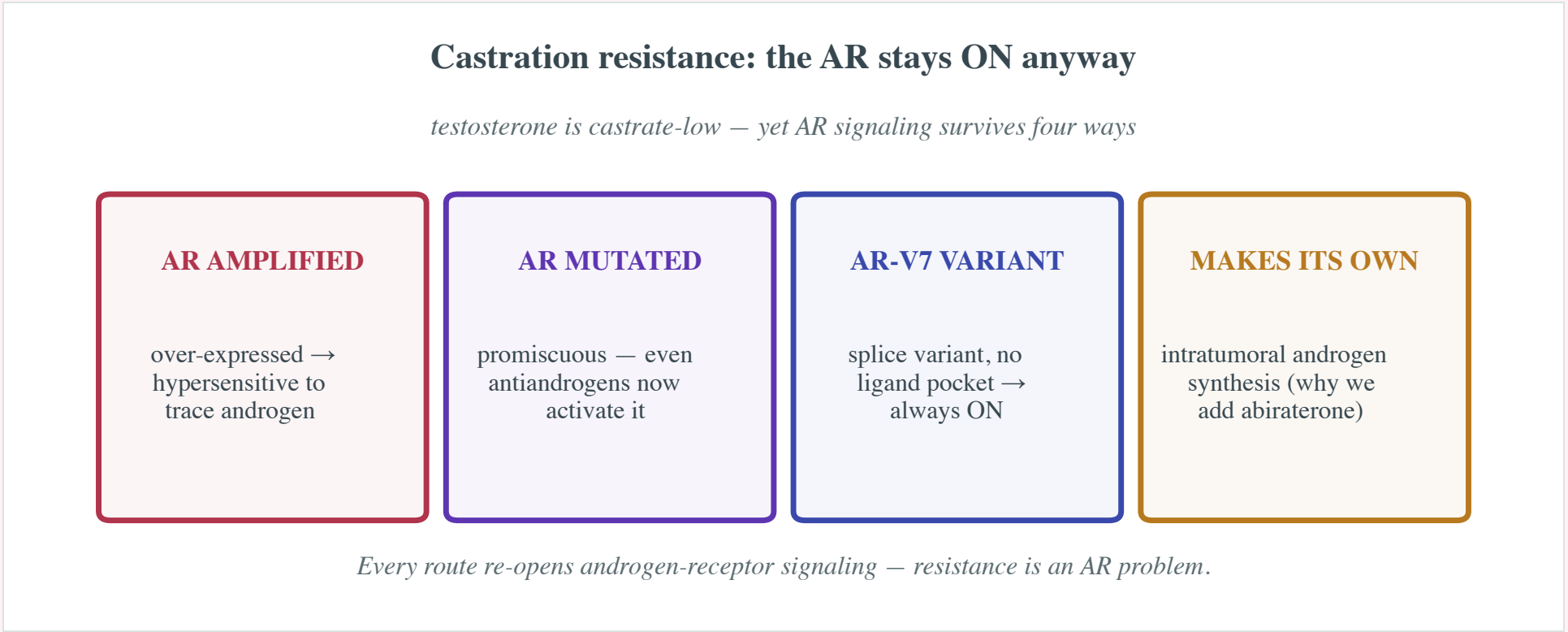
Prostate cancer is addicted to **androgens** — testosterone and DHT switch on the **androgen receptor**, and the tumor grows. So we starve it, at three levels. **GnRH agonists/antagonists** shut down pituitary LH, dropping testicular output. **Abiraterone** blocks **CYP17**, killing adrenal and tumor synthesis. **Enzalutamide** blocks the **receptor** itself.



Cut androgens at three points: pituitary release, hormone synthesis, and the receptor.

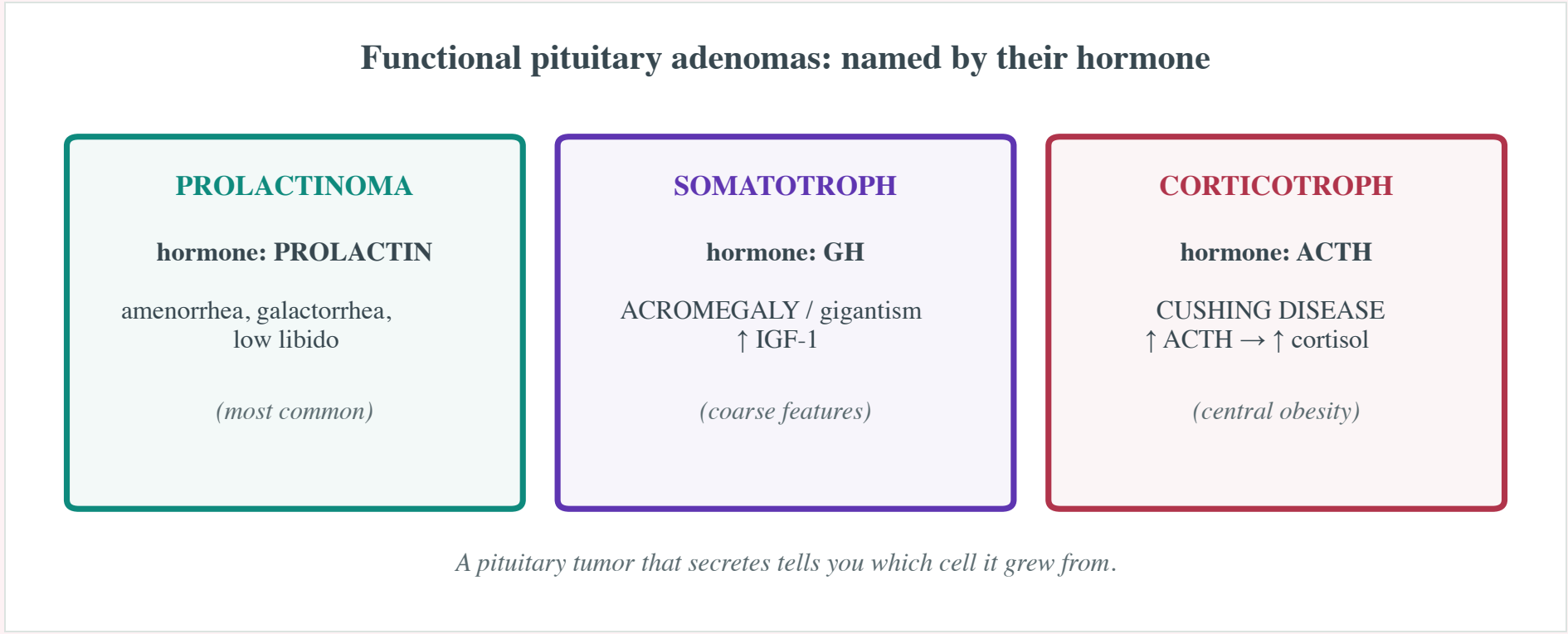
When castration stops working

Knock testosterone to castrate levels and the cancer often comes back anyway — **castration-resistant** prostate cancer. Every escape runs through the same receptor. The tumor **amplifies AR**, **mutates** it so even our blockers turn it on, splices an always-on **AR-V7**, or **makes its own androgens**. Resistance is an AR problem.



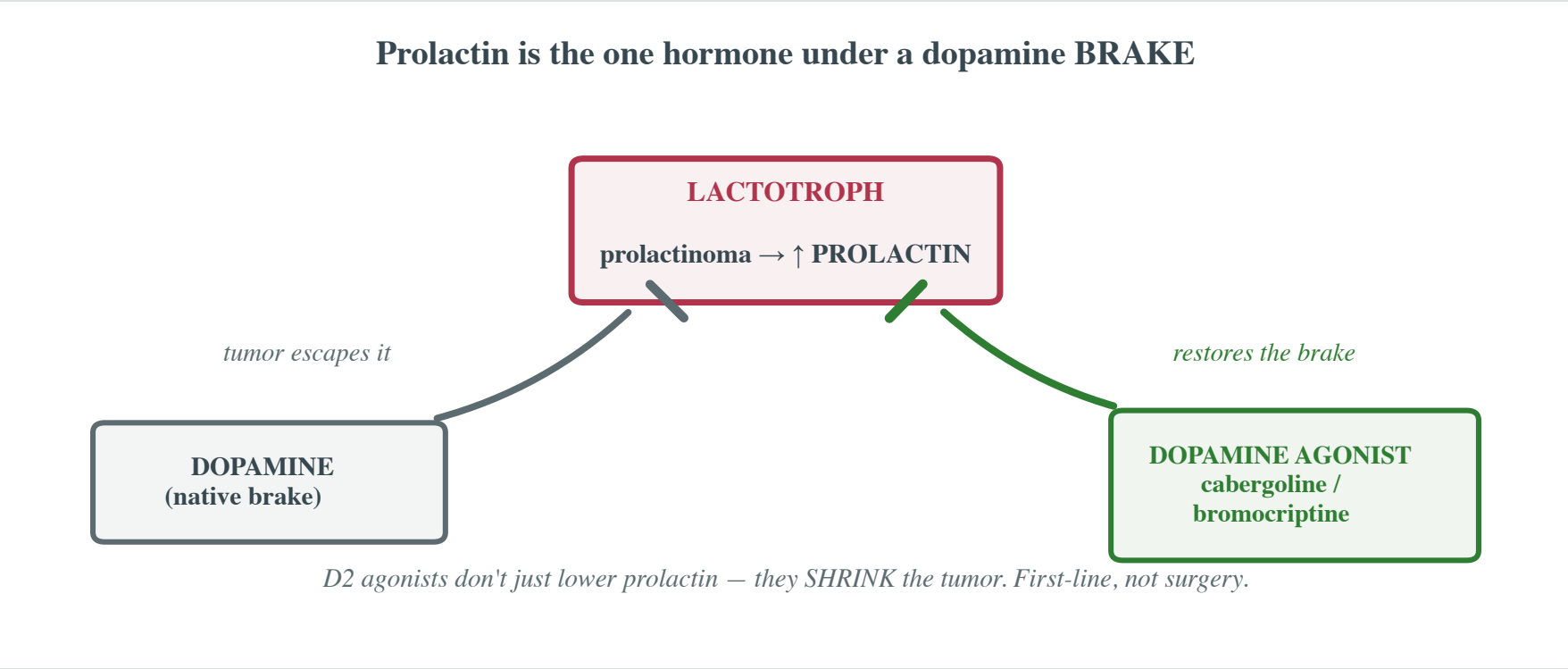
A pituitary tumor's secretion is its name

Switch glands. A **pituitary adenoma** that secretes tells you exactly which cell it grew from. Too much **prolactin**? A **prolactinoma** — amenorrhea and galactorrhea (most common). Too much **GH**? **Acromegaly**, with a rising **IGF-1**. Too much **ACTH**? **Cushing disease**, driving cortisol up. Name the hormone, name the tumor.



Prolactin's dopamine brake — and the pill that presses it

Prolactin is the pituitary's rebel — every other hormone gets a **go** signal, but prolactin lives under a constant **dopamine brake**. A prolactinoma just outgrows that brake. So the fix is elegant: a **dopamine agonist** — **cabergoline**, **bromocriptine** — presses the D2 receptor harder. It doesn't only lower prolactin; it **shrinks the tumor**. Drugs before surgery.

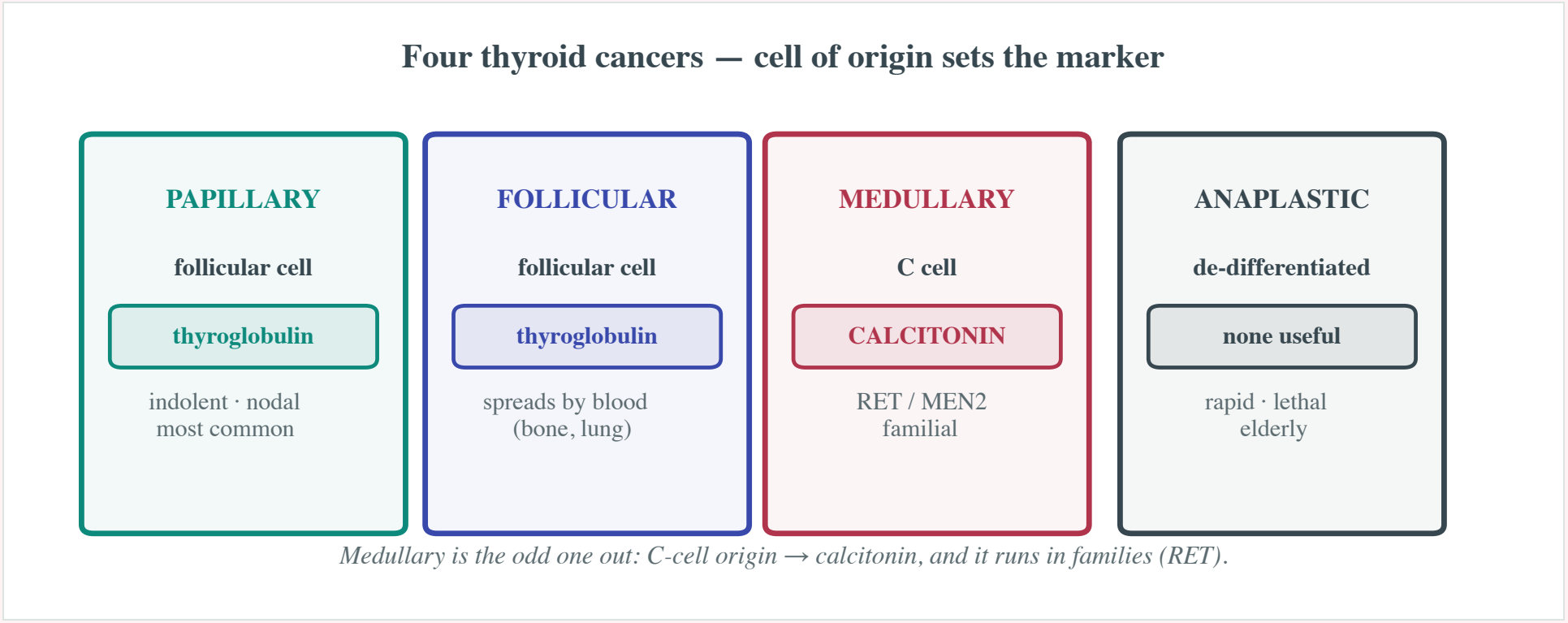


3 · Thyroid & Adrenal Tumors + Cancer Cachexia

"Two glands, one rule: let the tumor's product tell you what it is. Thyroid cancers sort by the cell they came from and the marker they shed; adrenal tumors sort by what they secrete. Then we close the whole cancer story with cachexia — why advanced cancer makes the body consume itself."

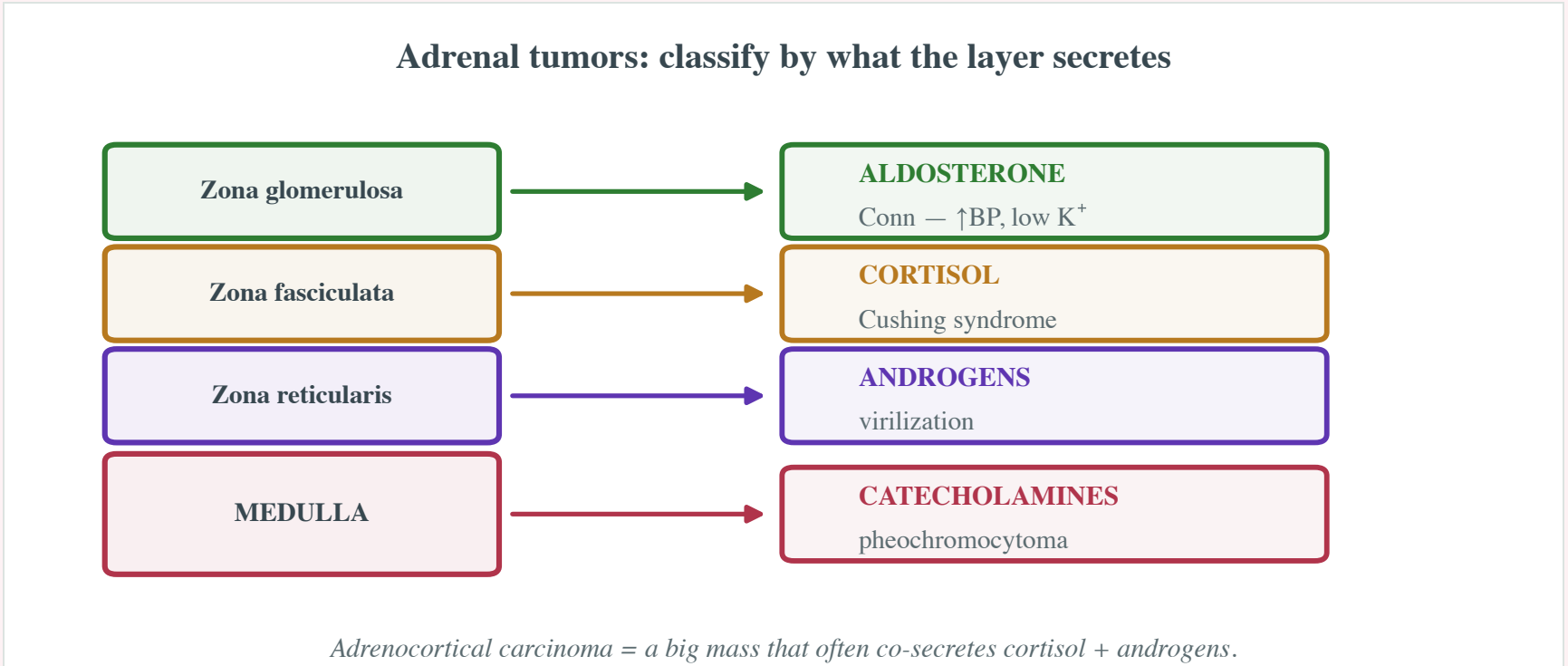
Thyroid cancer: cell of origin sets the marker

Four thyroid cancers, and the **cell of origin** predicts everything. **Papillary** and **follicular** come from follicular cells — both track with **thyroglobulin**; papillary is common and indolent, follicular spreads through blood. **Medullary** is the outlier: **C cells**, secreting **calcitonin**, driven by **RET** (think MEN2, familial). **Anaplastic** is de-differentiated and lethal.



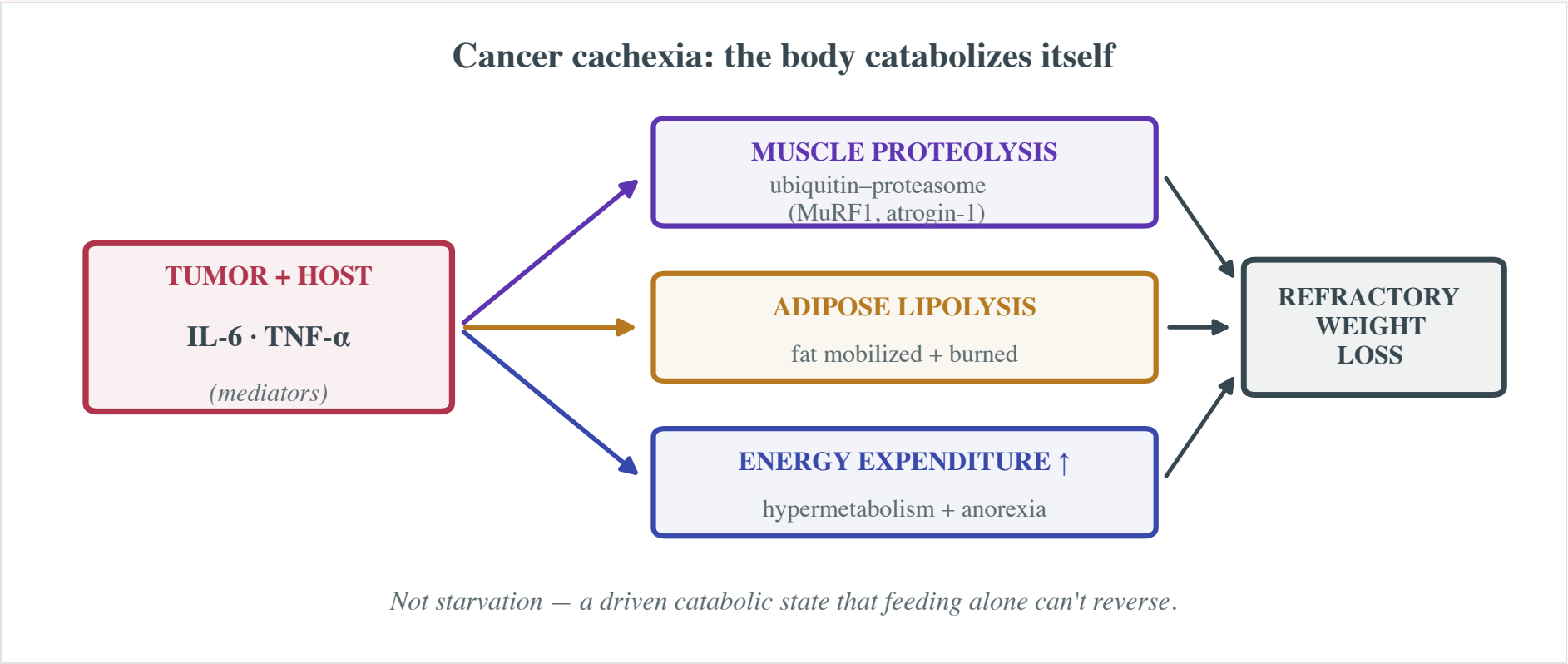
Adrenal tumors: ask what the layer secretes

The adrenal is layered, and each layer makes a tumor with its own signature. **Zona glomerulosa** → **aldosterone** → **Conn** (high blood pressure, low potassium). **Fasciculata** → **cortisol** → **Cushing**. **Reticularis** → **androgens** → virilization. And the **medulla** → **catecholamines** → **pheochromocytoma** (catch it on metanephrines). Ask what it secretes.



Cachexia: the body consumes itself

End on the whole-body cost. **Cachexia** is the wasting that kills many cancer patients — not simple starvation, but a **driven** catabolic state. Tumor and host pour out **IL-6** and **TNF-α**, which fire the **ubiquitin–proteasome** system to shred muscle, unleash **lipolysis**, and crank up **energy expenditure**. Feeding alone won't reverse it.



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