Eicosanoids in Disease & Pregnancy Endocrinology

BCH 130 — Advanced Human Biochemistry · Dr. Radi

By the end of this unit, you can…

- Review eicosanoid biosynthesis (arachidonate → COX/LOX → prostaglandins, thromboxane, leukotrienes) as the basis for their disease roles.
- Connect eicosanoids to disease
- Explain the pharmacology by target
- Explain the endocrinology of pregnancy (hCG, the placenta as an endocrine organ, insulin resistance of pregnancy) as the backdrop for its disorders.

Today's route

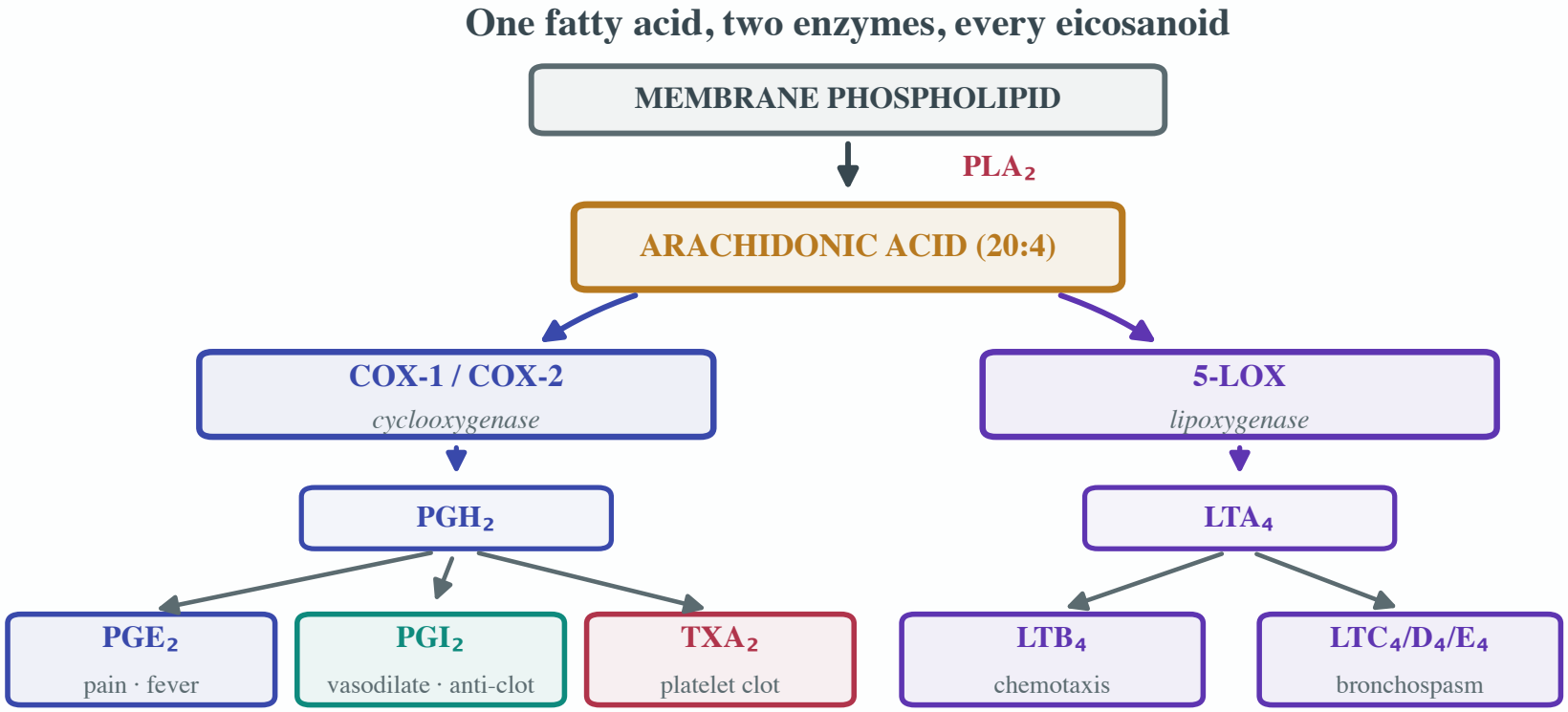
1. **Eicosanoids in Disease**
2. **Pregnancy Endocrine Disorders**

1 · Eicosanoids in Disease

"You met the eicosanoids in BCH 120 — now watch them cause disease. One fatty acid, two enzymes, and suddenly you can explain pain, fever, clots, asthma, and half the drugs in the pharmacy. This is where the biosynthesis pays off."

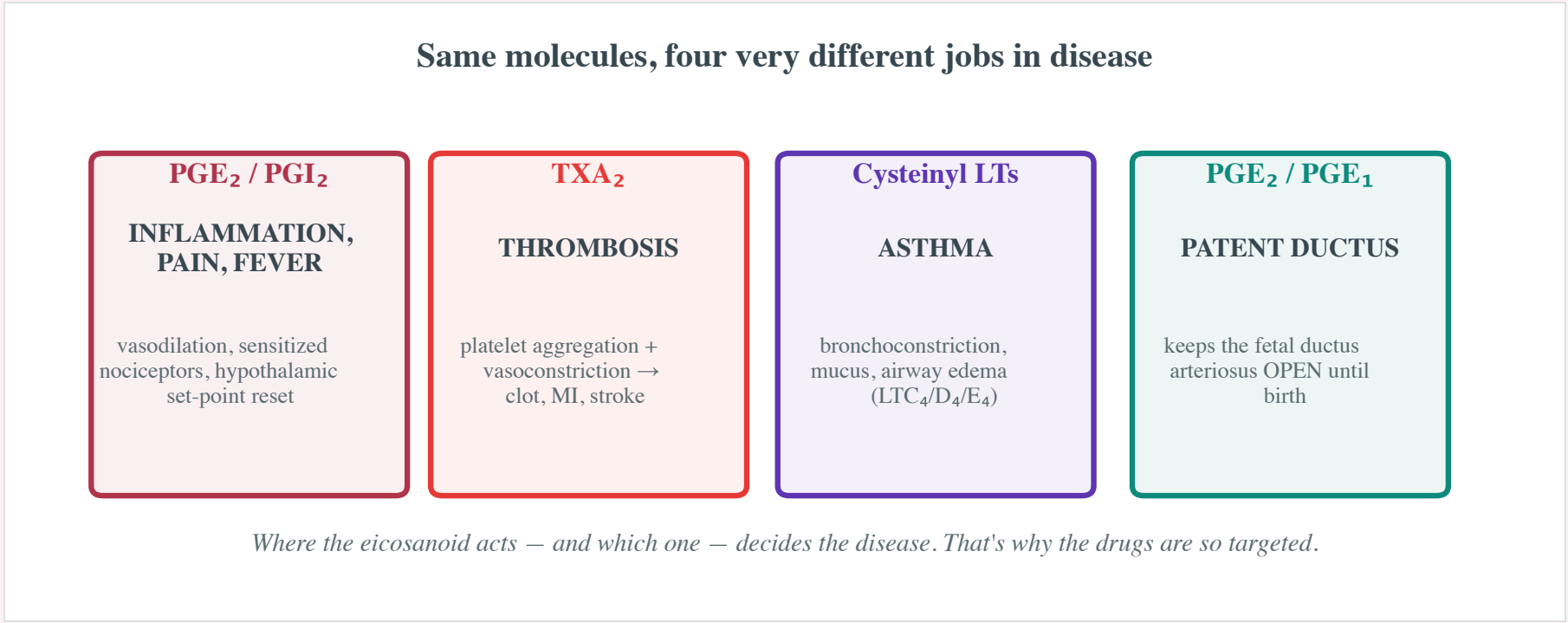
The branch point that runs the pharmacy

Quick refresher, because everything today hangs on it. **Phospholipase A_2** frees **arachidonic acid** from the membrane, and then it forks. Down the **COX** arm come the **prostaglandins** and **thromboxane**; down the **5-LOX** arm come the **leukotrienes**. Same starting fatty acid — completely different jobs. Memorize **this** fork and every drug we meet today explains itself.



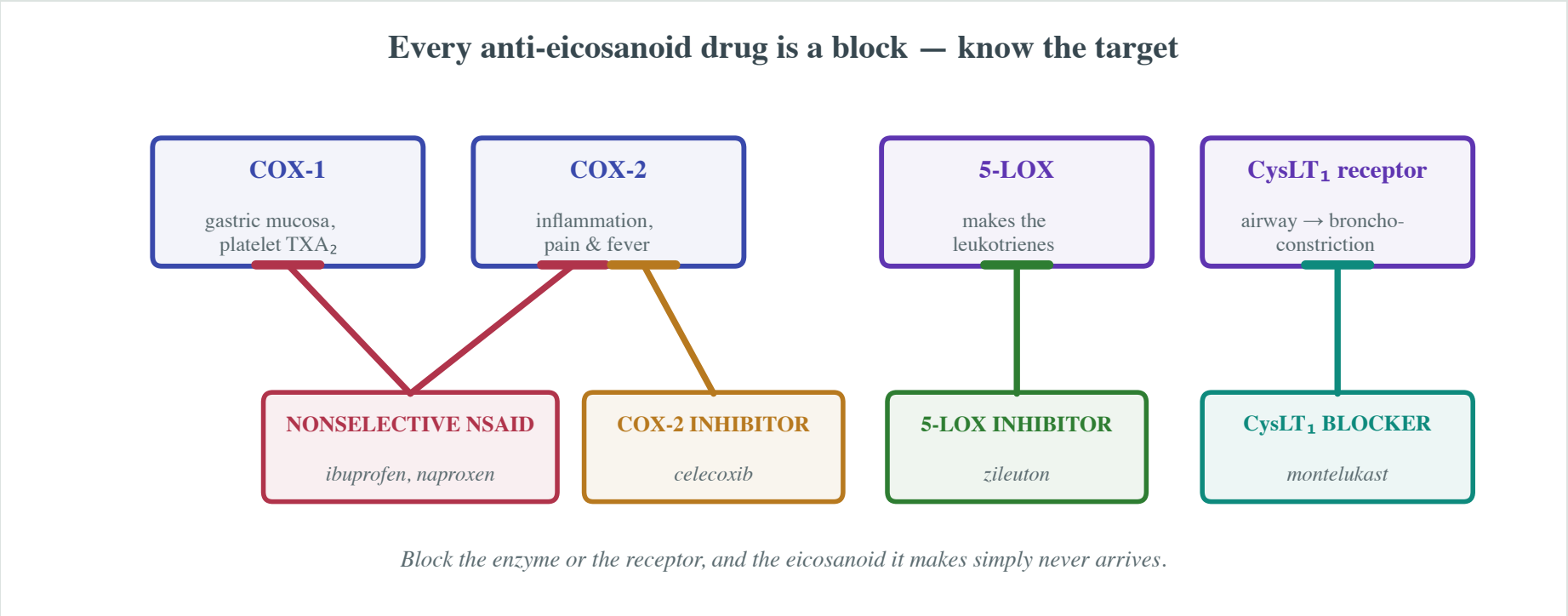
One family, four diseases

Here's why we care. **PGE_2** dilates vessels, sensitizes pain nerves, and resets the hypothalamic thermostat — **inflammation, pain, and fever**. **TXA_2** aggregates platelets → **thrombosis**. **Cysteinyl leukotrienes** clamp the airways → **asthma**. And **PGE_2** holds the fetal **ductus arteriosus** open. Same chemistry, four very different bedside stories.



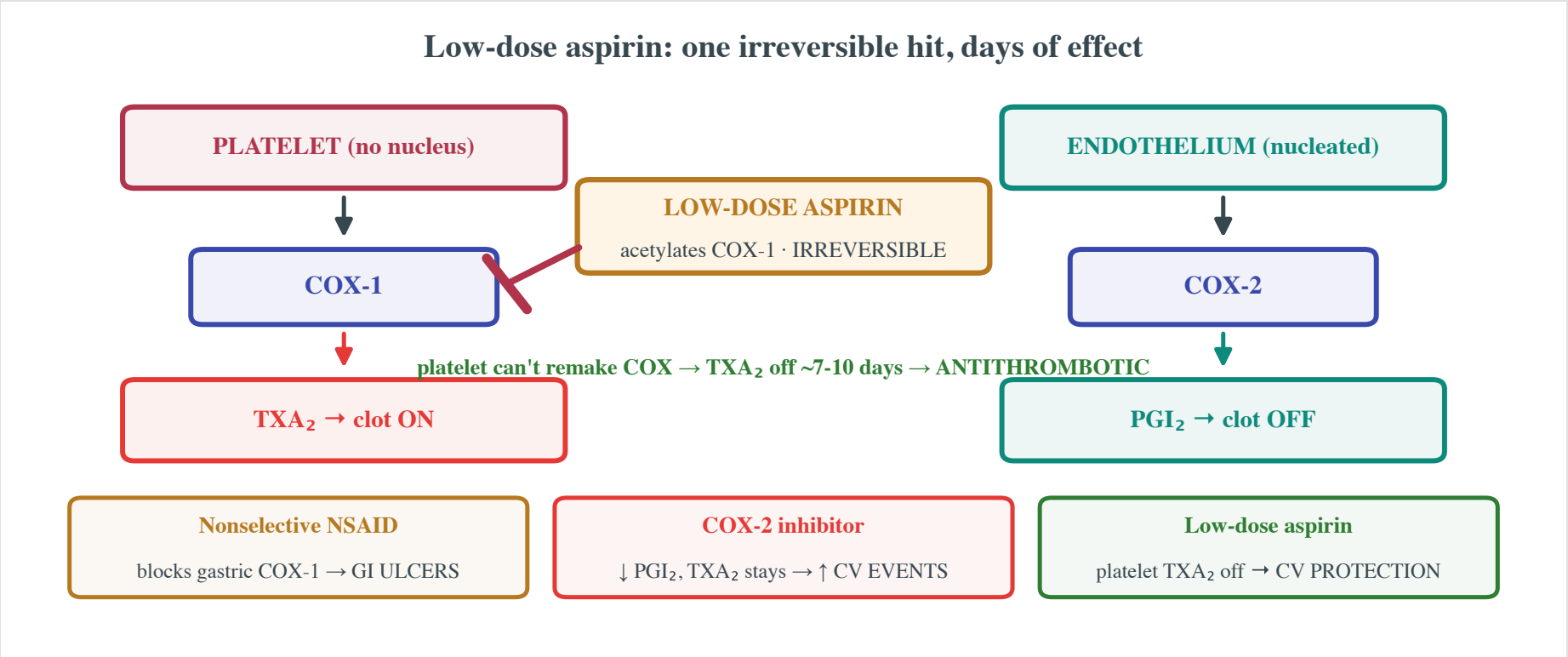
Every drug is a block — name the target

Now the payoff. Anti-eicosanoid drugs just **block** one step, and the mediator downstream never shows up. **Nonselective NSAIDs** (ibuprofen) bar **both COX-1 and COX-2**. **Coxibs** (celecoxib) hit **COX-2** only. **Zileuton** blocks **5-LOX**; **montelukast** blocks the **CysLT$_1$ receptor** in asthma. Know the target, predict the effect.



Aspirin's clever, cruel trade-off

Aspirin is different — it **irreversibly acetylates COX-1**. A **platelet has no nucleus**, so it **can't** make new enzyme: one low dose silences its **TXA_2 for the platelet's whole life** → **antithrombotic**. The trade-off? Nonselective NSAIDs strip gastric prostaglandins → **ulcers**; coxibs drop protective **PGI_2** → **more cardiovascular events**.

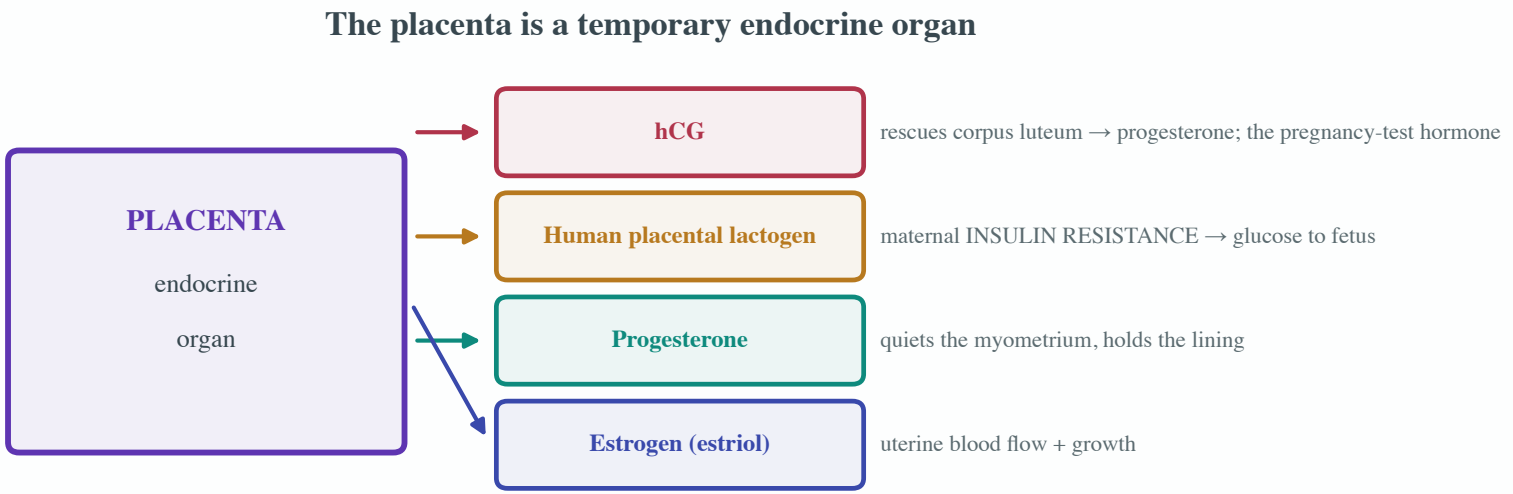


2 · Pregnancy Endocrine Disorders

"Pregnancy grows a brand-new endocrine organ from scratch — the placenta — and it rewires the mother's metabolism on purpose. Understand that reprogramming and the disorders make perfect sense: gestational diabetes, pre-eclampsia, thyroid trouble, and the hCG-driven tumors."

The placenta is an endocrine organ

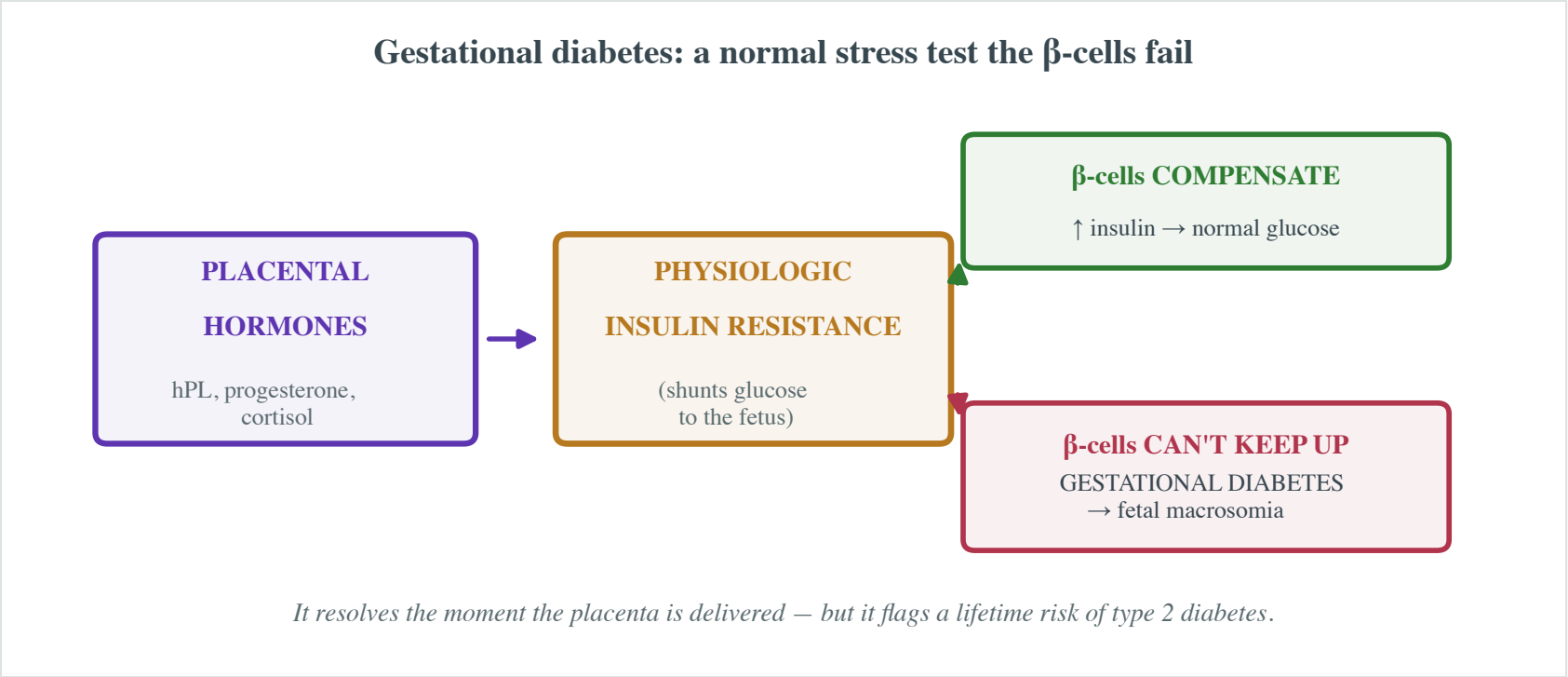
Think of pregnancy as growing a **temporary endocrine gland**. **hCG** is the opening act — it rescues the corpus luteum so **progesterone** keeps flowing, and it's the hormone your pregnancy test detects. Then the placenta takes over, pouring out **progesterone**, **estrogen**, and **human placental lactogen (hPL)**. That last one is the troublemaker: it deliberately makes mom **insulin-resistant**.



By ~week 8-10 the placenta takes over from the corpus luteum — and quietly reprograms maternal metabolism.

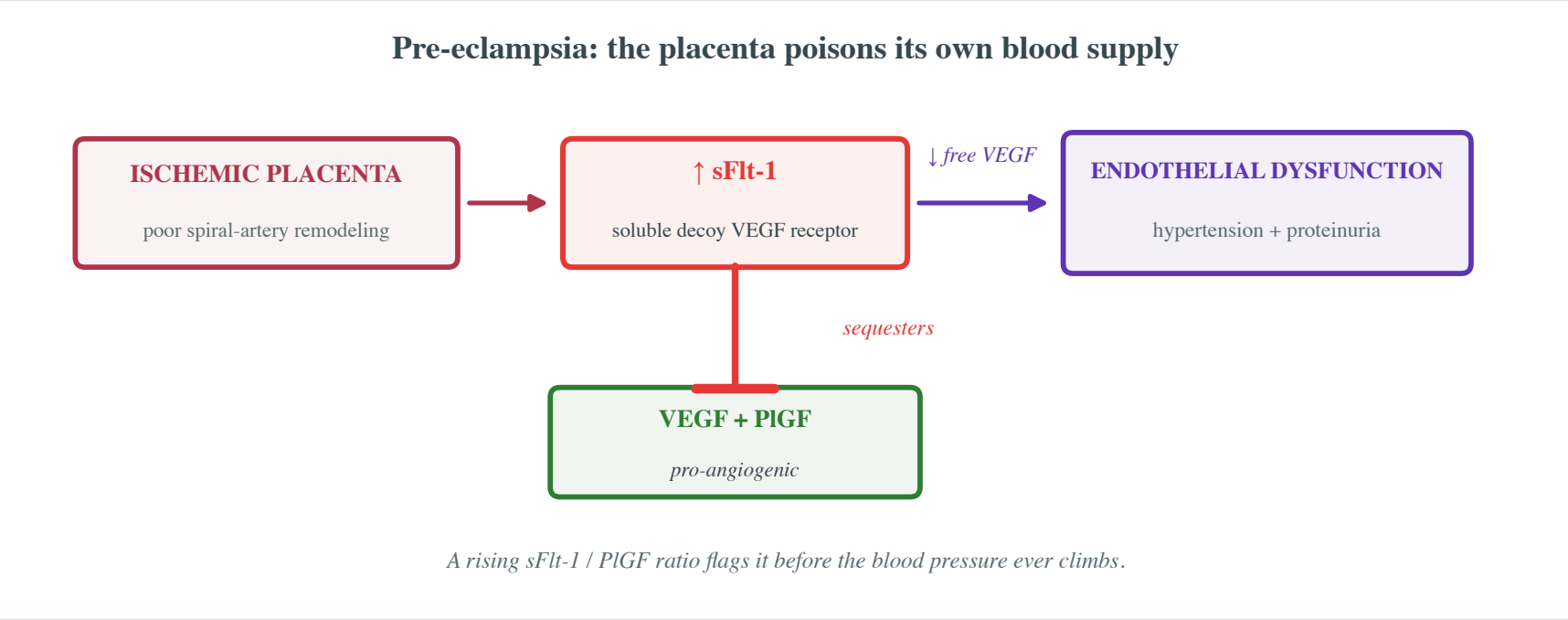
Gestational diabetes: a stress test she fails

Why make mom insulin-resistant? To **shunt glucose to the fetus**. hPL, progesterone, and cortisol drive up resistance, and the β-cells are **supposed** to answer with more insulin. **Gestational diabetes** is when the **β-cells can't keep up** → hyperglycemia → a **big baby**. It clears at delivery but flags lifelong type 2 diabetes risk.



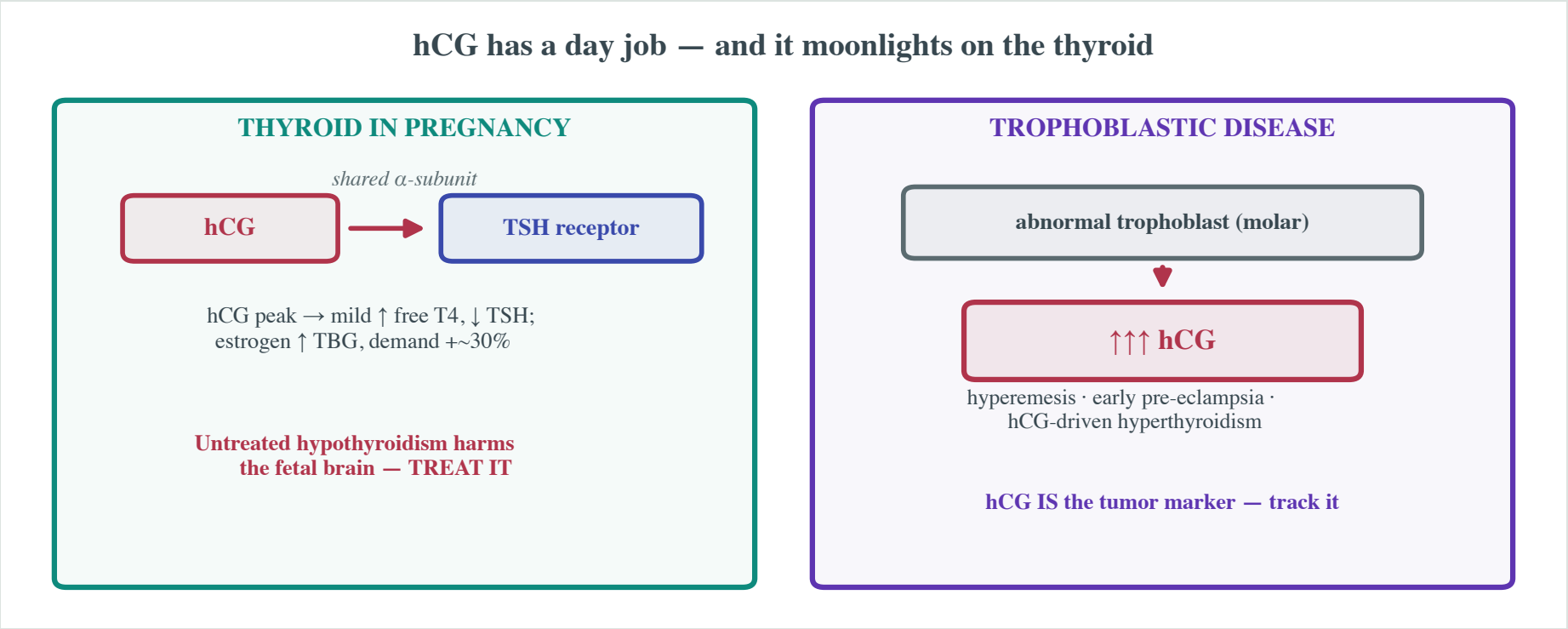
Pre-eclampsia: an anti-angiogenic storm

Pre-eclampsia is a **placental** disease, not a blood-pressure disease. A poorly-perfused, **ischemic placenta** dumps **sFlt-1** — a **soluble decoy VEGF receptor** — into mom's blood. It **sequesters VEGF and PlGF**, so the vessels she needs go unmaintained → **endothelial dysfunction, hypertension, and proteinuria**. That **sFlt-1/PlGF ratio** climbs **before** the pressure does — a biochemical early warning.



When hCG moonlights on the thyroid

Two more, both about **hCG**. It shares an **α-subunit with TSH**, so it weakly stimulates the **TSH receptor** — early pregnancy brings a mild, physiologic **↑ free T4, ↓ TSH**. Untreated hypothyroidism threatens the fetal brain. And in **gestational trophoblastic disease**, abnormal trophoblast makes **hCG go wild**.



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