Adrenal & Fluid-Balance Disorders

BCH 130 — Advanced Human Biochemistry · Dr. Radi

By the end of this unit, you can…

- Walk the renin-angiotensin-aldosterone system and diagnose primary aldosteronism (Conn) via the aldosterone-to-renin ratio.
- Distinguish endocrine causes of secondary hypertension (primary aldosteronism, renovascular, Cushing, pheochromocytoma) and their labs.
- Explain RAAS-blocking pharmacology: ACE inhibitors, ARBs, mineralocorticoid-receptor antagonists, and direct renin inhibitors.
- Explain vasopressin (ADH) physiology — osmoreceptor control, V2/aquaporin-2 — and the biochemistry of water reabsorption.

Today's route

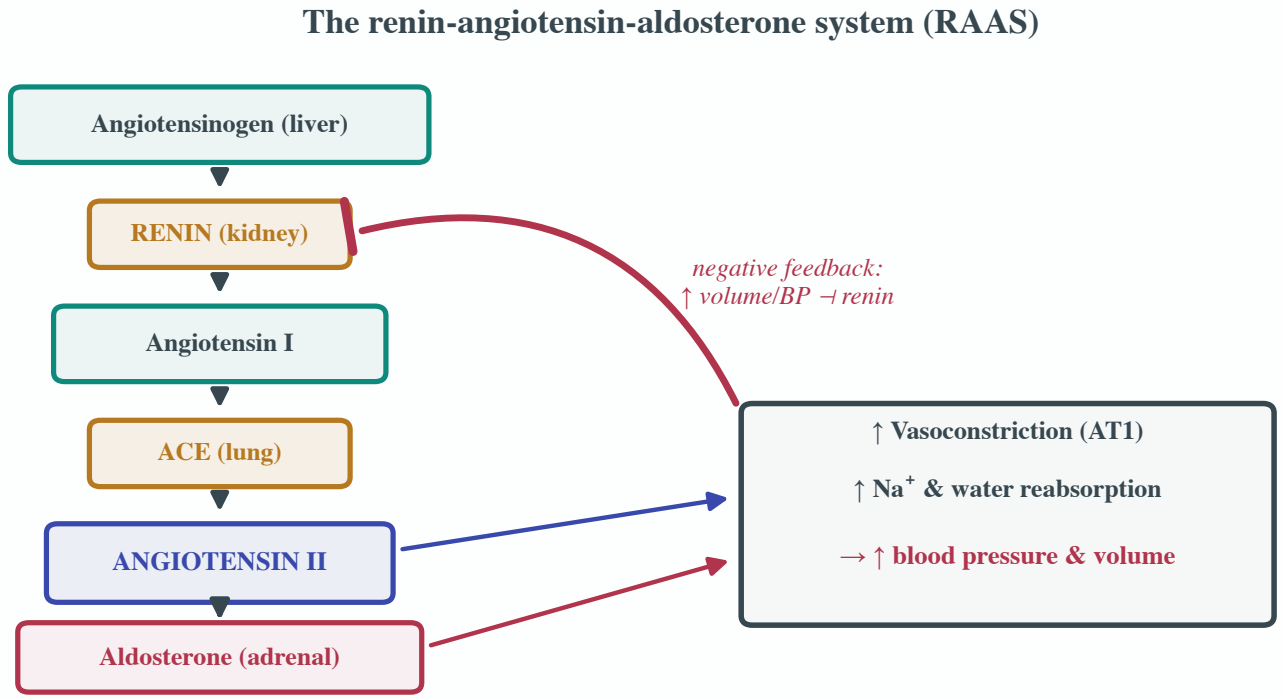
1. **RAAS Disorders & Secondary Hypertension**
2. **Vasopressin & Water-Balance Disorders**
3. **Catecholamine Excess & the Adrenal Medulla**

1 · RAAS Disorders & Secondary Hypertension

"Most high blood pressure is 'essential' — no single cause. But a slice of it is endocrine, and that slice is CURABLE if you name the hormone. Today we walk the renin-angiotensin-aldosterone system, catch primary aldosteronism with one ratio, and block the pathway at four different points."

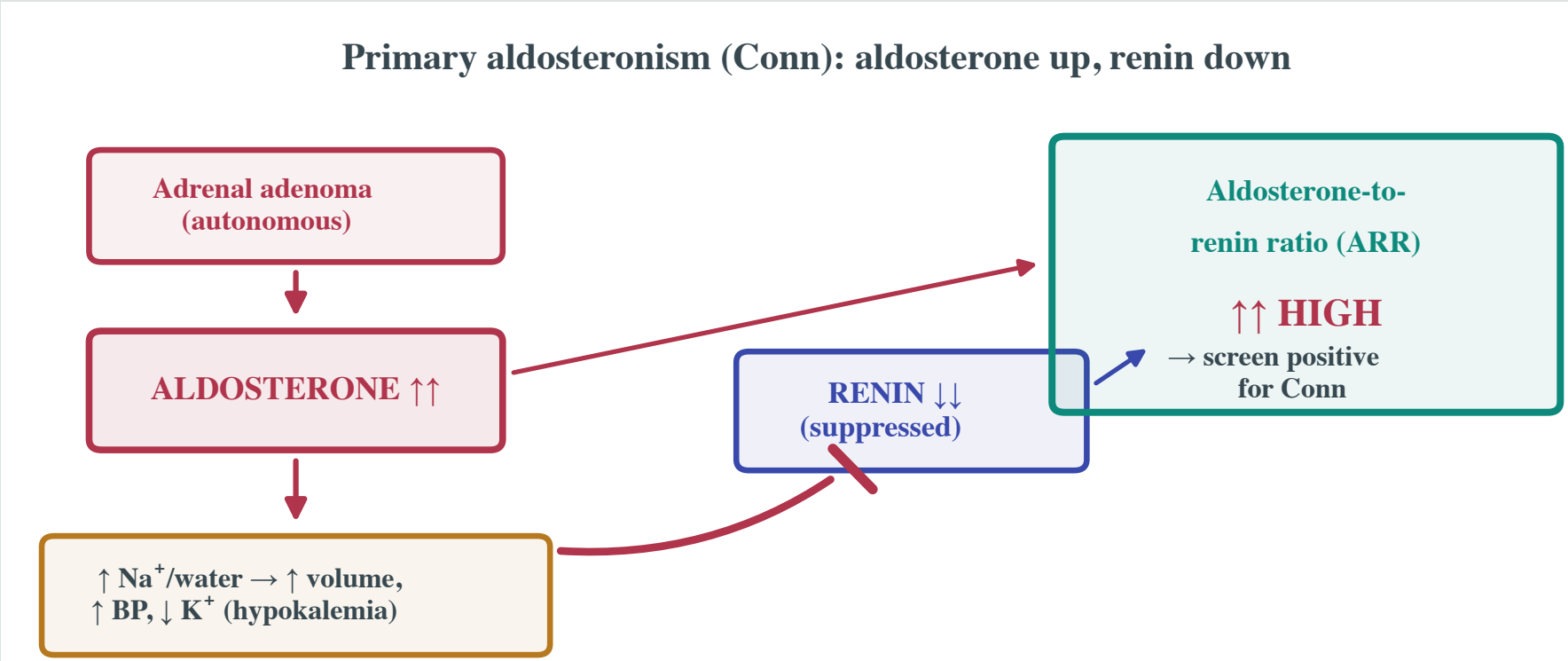
The RAAS, one enzyme at a time

The body's blood-pressure thermostat. Low renal pressure releases **renin**, which clips **angiotensinogen** to **angiotensin I**; **ACE** (lung) makes **angiotensin II** — a vasoconstrictor that drives adrenal **aldosterone** (holds Na^+ and water). Pressure and volume climb — and that climb feeds **back** to shut renin off.



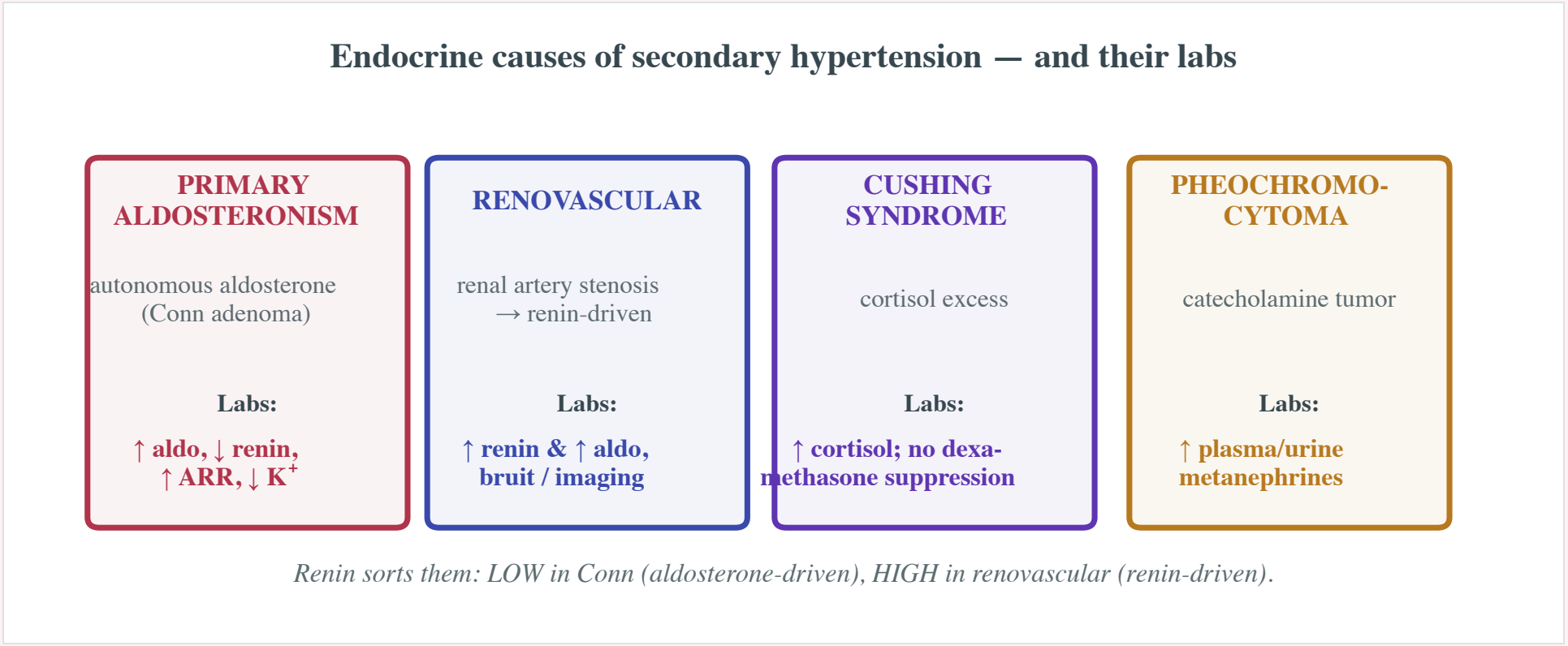
One ratio catches Conn

The most under-diagnosed **curable** hypertension. In **Conn**, an adrenal adenoma makes aldosterone **autonomously** – volume climbs, potassium drops, and the high volume **suppresses renin to the floor**. High aldosterone **with** low renin is the tell: the **aldosterone-to-renin ratio (ARR)** shoots up. Screen positive → hunt the adenoma.



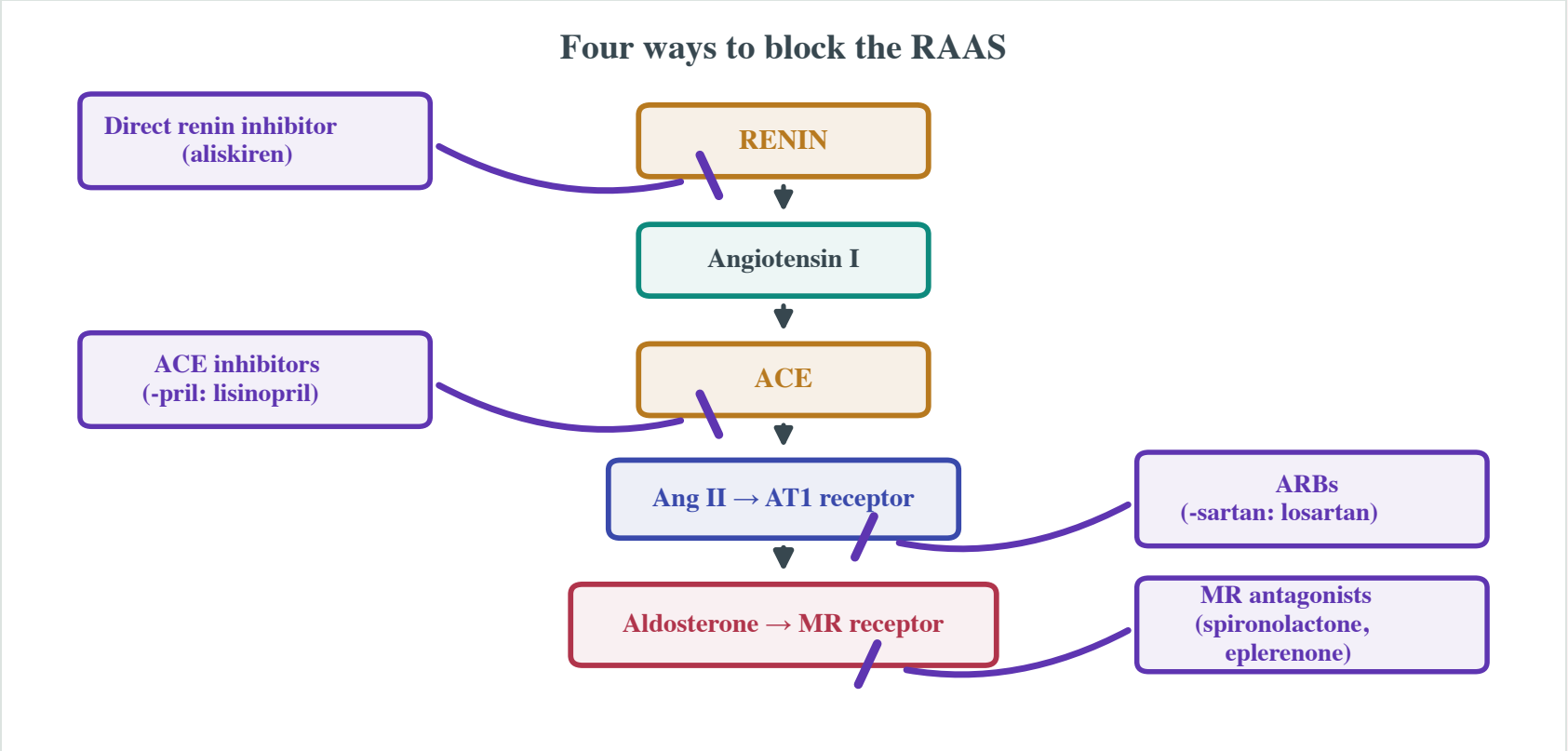
Four endocrine causes — sorted by lab

When hypertension is young, severe, or drug-resistant, think **endocrine** — and the **labs** sort the four culprits. **Renin** is the first fork: **low** in Conn (aldosterone-driven), **high** in **renovascular** disease. **Cushing** shows cortisol that won't suppress with dexamethasone; **pheochromocytoma** shows sky-high metanephrines.



Block it in four places

Now the payoff — every RAAS drug is a **⊣ on the cascade**. **Direct renin inhibitors** (aliskiren) cap the top. **ACE inhibitors** (**-prils**) stop angiotensin II forming. **ARBs** (**-sartans**) block its **AT1 receptor**. **MR antagonists** (spironolactone, eplerenone) block aldosterone itself. One pathway, four levers.

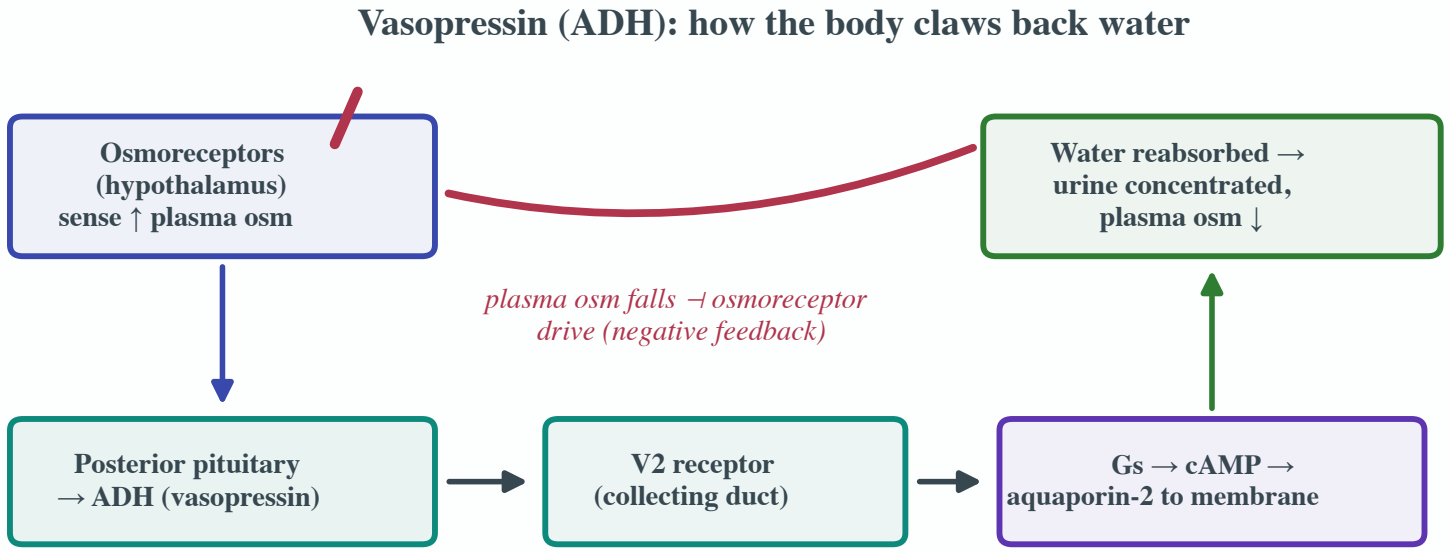


2 · Vasopressin & Water-Balance Disorders

"Aldosterone handled the salt; now meet the hormone that handles the WATER. Vasopressin (ADH) lets the kidney reclaim free water on demand — and when it's too loud, too quiet, or ignored, the serum sodium tells you exactly which. Learn to read osmolality and the diagnosis falls out."

How the body claws back water

When plasma turns too **concentrated**, hypothalamic **osmoreceptors** fire and the posterior pituitary releases **ADH**. ADH hits the **V2 receptor** → Gs → cAMP → and the cell inserts **aquaporin-2** into its apical membrane. Water flows back, urine concentrates, plasma osmolality falls — quieting the osmoreceptors. Fast and self-correcting.



Serum vs urine: three diseases

Break it three ways and the **osmolality pair** names each. **SIADH** = too much ADH → water trapped → **dilute** serum ($Na^+ < 135$), wrongly **concentrated** urine. Both **DI** types lose water (dilute urine, **concentrated** serum): **central DI** makes no ADH; **nephrogenic DI** makes plenty but the kidney ignores it.

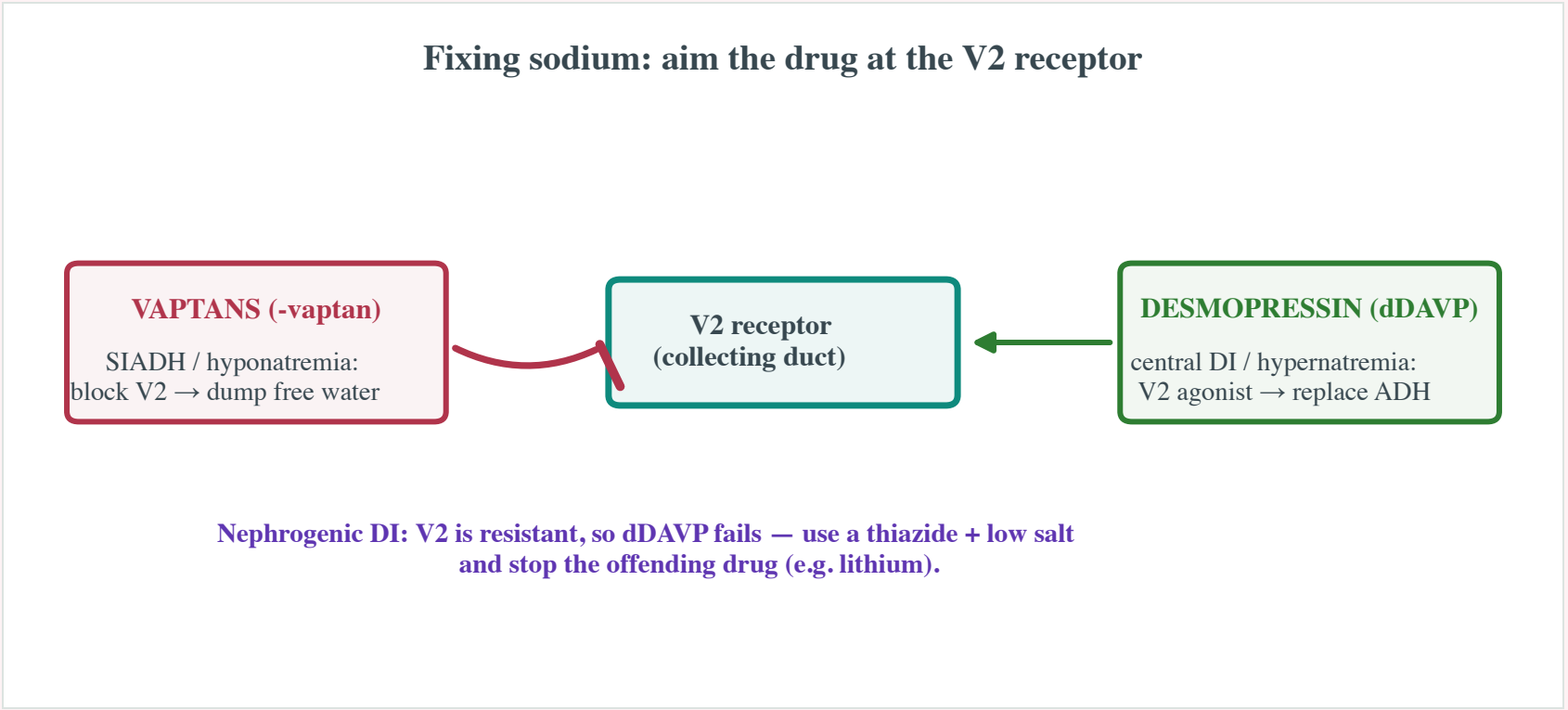
Too much water or too little: read serum vs urine osmolality

	SIADH	CENTRAL DI	NEPHROGENIC DI
Defect	too much ADH	no ADH made	kidney resistant (V2 / AQP2)
ADH level	HIGH	LOW	normal / HIGH
Serum osm (Na^+)	LOW ($Na^+ < 135$)	HIGH ($Na^+ > 145$)	HIGH ($Na^+ > 145$)
Urine osm	HIGH (concentrated)	LOW (dilute)	LOW (dilute)
Responds to dDAVP?	n/a	yes ✓ (corrects)	no ✗

SIADH = water trapped (serum dilute, urine concentrated). DI = water lost (serum concentrated, urine dilute).

Same receptor, opposite drug

Management is beautifully logical — aim at **V2**. For **SIADH** (hyponatremia), fluid-restrict and add a **vaptan** that **blocks** V2, dumping free water. For **central DI** (hypernatremia), give **desmopressin** — a V2 **agonist** replacing the missing ADH. **Nephrogenic DI** resists V2, so desmopressin fails: use a thiazide + low salt, stop the offender.

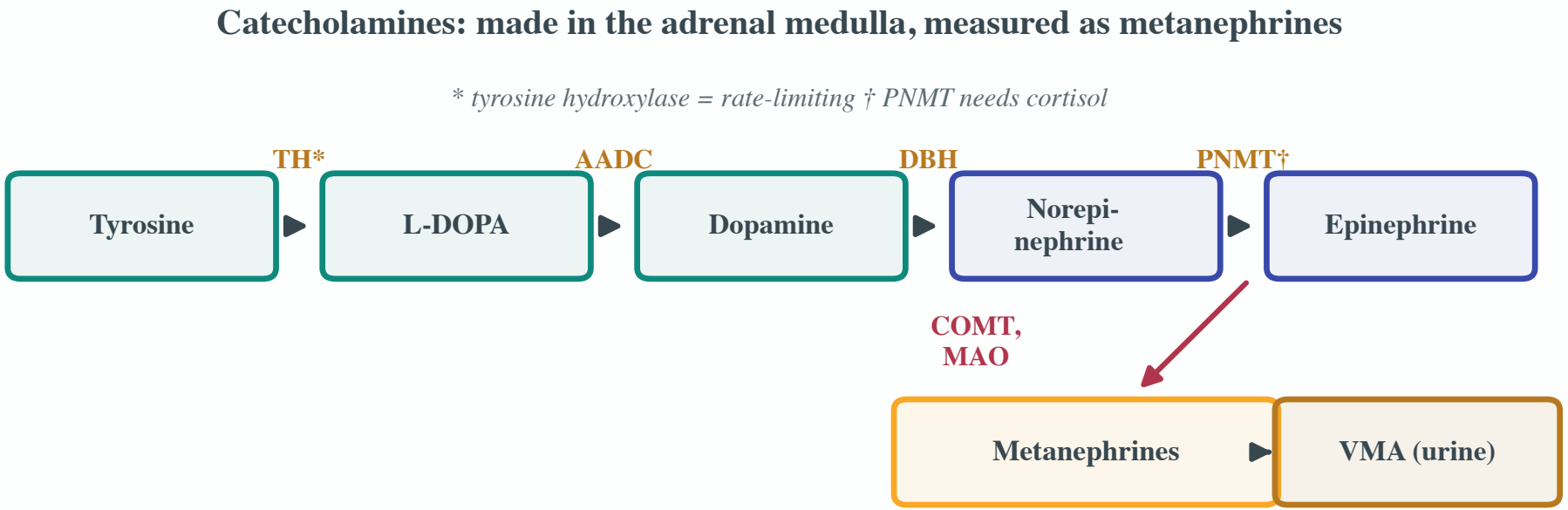


3 · Catecholamine Excess & the Adrenal Medulla

"The adrenal cortex made steroids; the adrenal MEDULLA makes catecholamines. Follow tyrosine all the way to epinephrine, see how it's broken down into the metanephrines we measure — and meet pheochromocytoma, the tumor that comes in spells and can kill you if you block the wrong receptor first."

Tyrosine to epinephrine — and back down

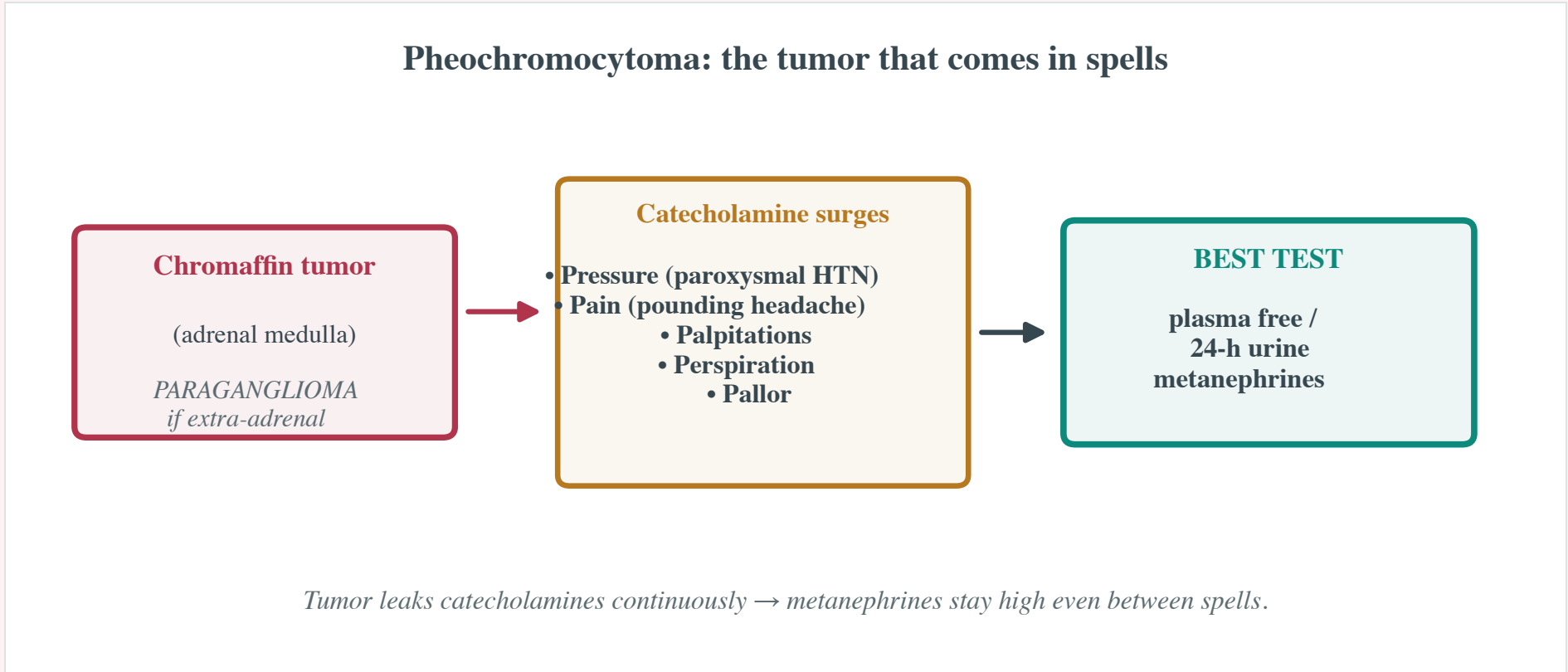
One amino acid builds them all. **Tyrosine** → (tyrosine hydroxylase, **rate-limiting**) → L-DOPA → dopamine → **norepinephrine** → (PNMT, needs cortisol) → **epinephrine**, stored in chromaffin granules. Breakdown matters too: **COMT and MAO** convert them to **metanephrines** and finally **VMA** — the stable products we measure.



Stored in chromaffin granules; broken down continuously → plasma/urine metanephrines are the fingerprint we test for.

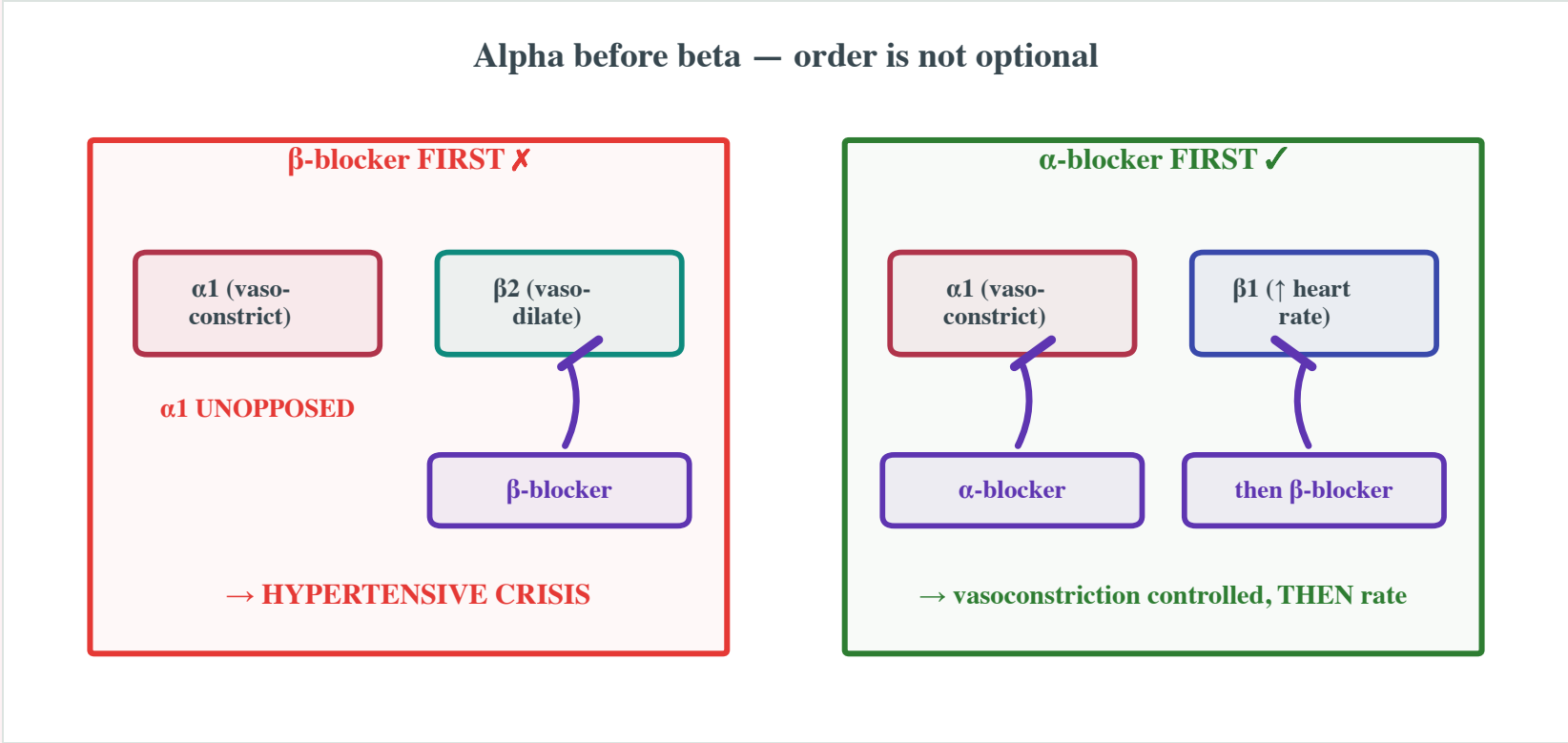
The tumor that comes in spells

Pheochromocytoma is a chromaffin-cell tumor of the adrenal medulla (**paraganglioma** if extra-adrenal). It fires catecholamines in **paroxysms** — the **P's**: **P**ressure (episodic HTN), **P**ain (headache), **P**alpitations, **P**erspiration, **P**allor. It leaks **continuously**, so **plasma free or 24-h urine metanephrines** stay high even between spells — the best test.



Alpha before beta – always

The one on every exam and every ward. Catecholamines drive **α1** (vasoconstriction) **and β2** (vasodilation). Block **β first** and you strip the dilating brake – leaving **α1 unopposed**, vessels clamp, **hypertensive crisis**. So the order is fixed: **α-blocker first** (phenoxybenzamine, doxazosin), **then** the β-blocker for rate.



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