GI Hormone Disorders

BCH 130 — Advanced Human Biochemistry · Dr. Radi

By the end of this unit, you can…

- Diagram the gut-brain appetite axis
- Explain leptin resistance and the defended-set-point model of why obesity resists dietary weight loss.
- Justify obesity pharmacotherapy and bariatric surgery mechanistically (GLP-1 / GIP agonists, incretin remodeling).
- Match functional GI/pancreatic neuroendocrine tumors to their hormone and syndrome

Today's route

1. **Obesity & the Gut-Brain Appetite Axis**
2. **Neuroendocrine Tumors**

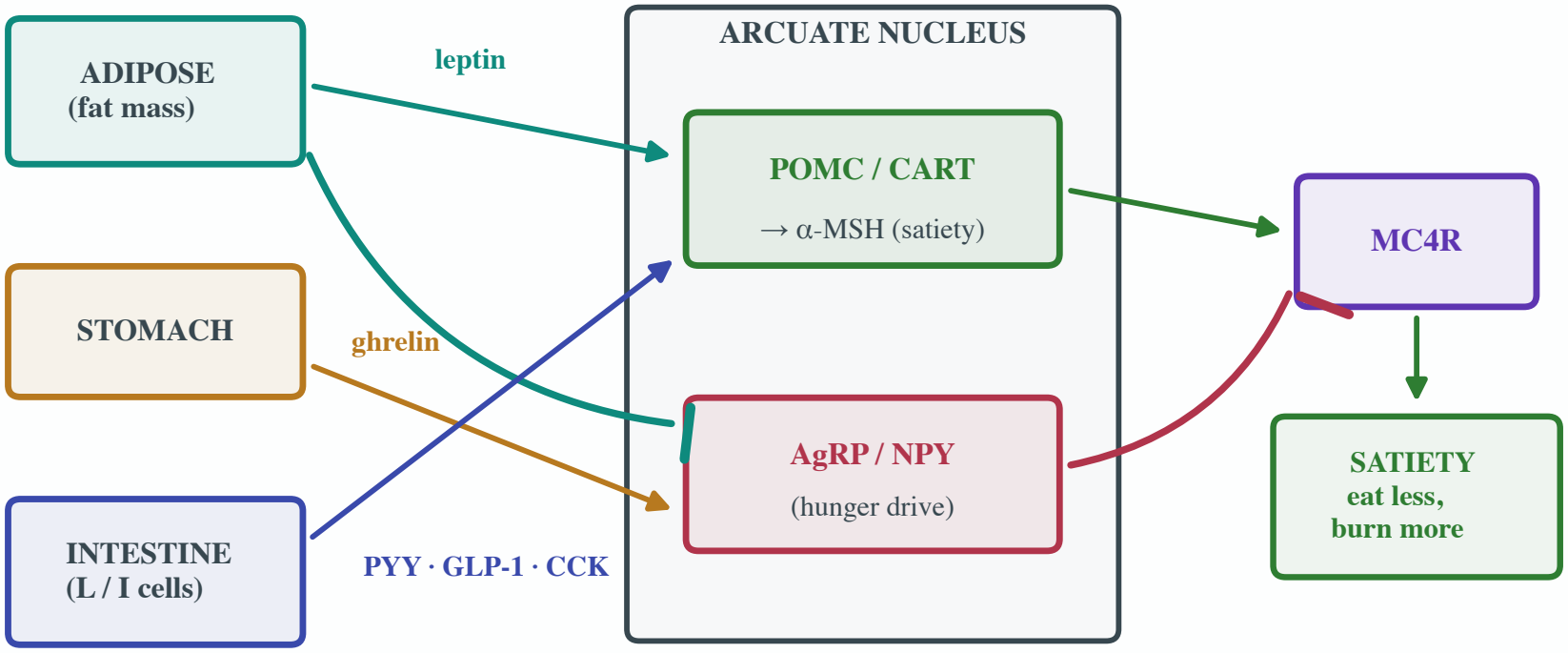
1 · Obesity & the Gut-Brain Appetite Axis

"Appetite isn't willpower — it's biochemistry! A whole cast of gut and fat hormones reports to one hub in your hypothalamus, and obesity is what happens when that hub stops listening. Let's meet the signals, see why diets rebound, and turn the whole axis into a treatment."

One hub hears every hormone

Hunger runs on hormones — a conversation between gut, fat, and brain. **Leptin** (from fat) and the post-meal crew — **PYY, GLP-1, CCK** — push hypothalamic **POMC** toward **satiety**. **Ghrelin**, from an empty stomach, is the lone hunger voice, firing up **AgRP**. Both report to one integrator: **MC4R**.

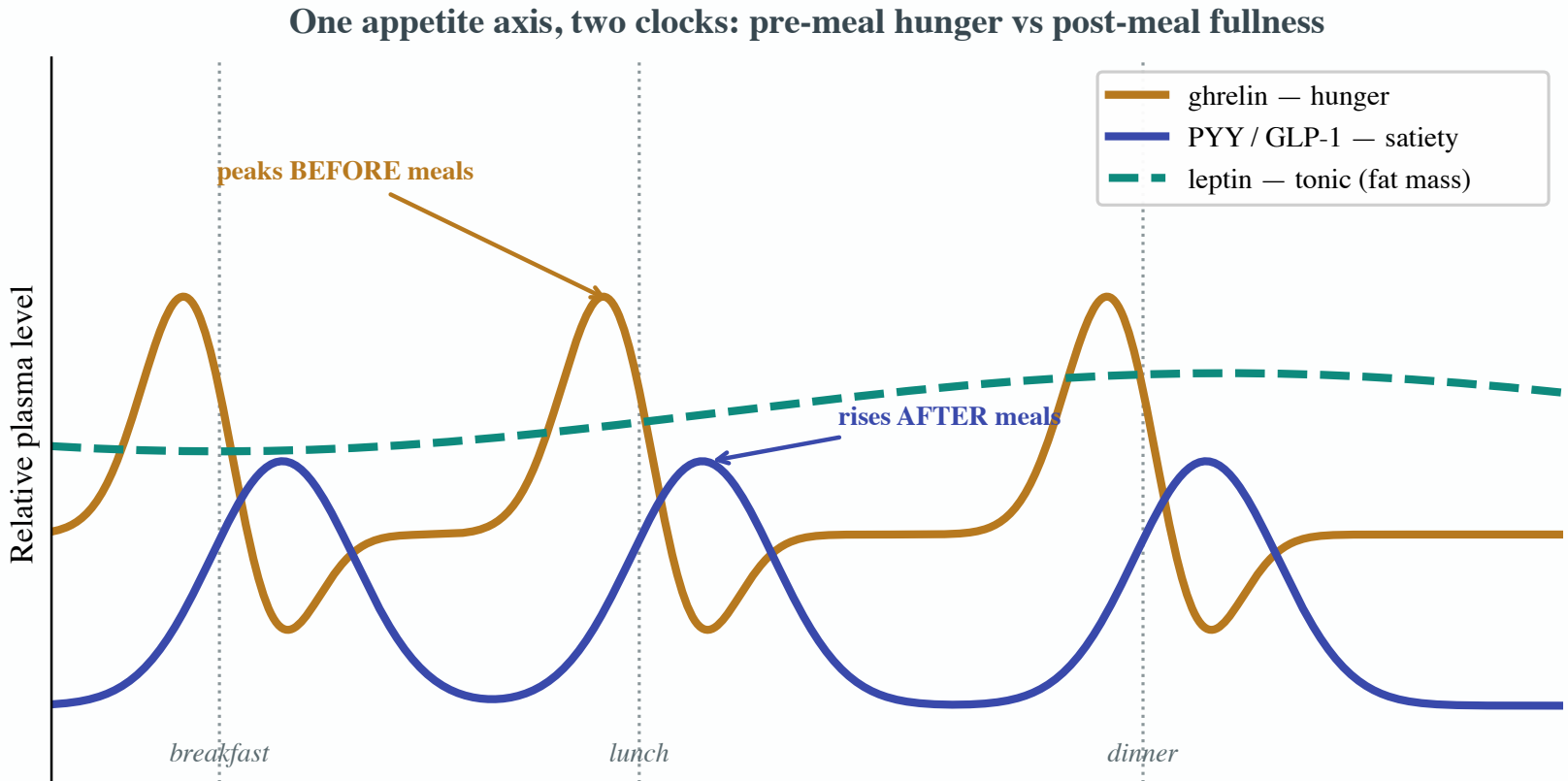
The gut-brain appetite axis: hormones meet the melanocortin hub



Leptin & gut satiety signals push POMC; ghrelin pushes AgRP — MC4R reads the balance.

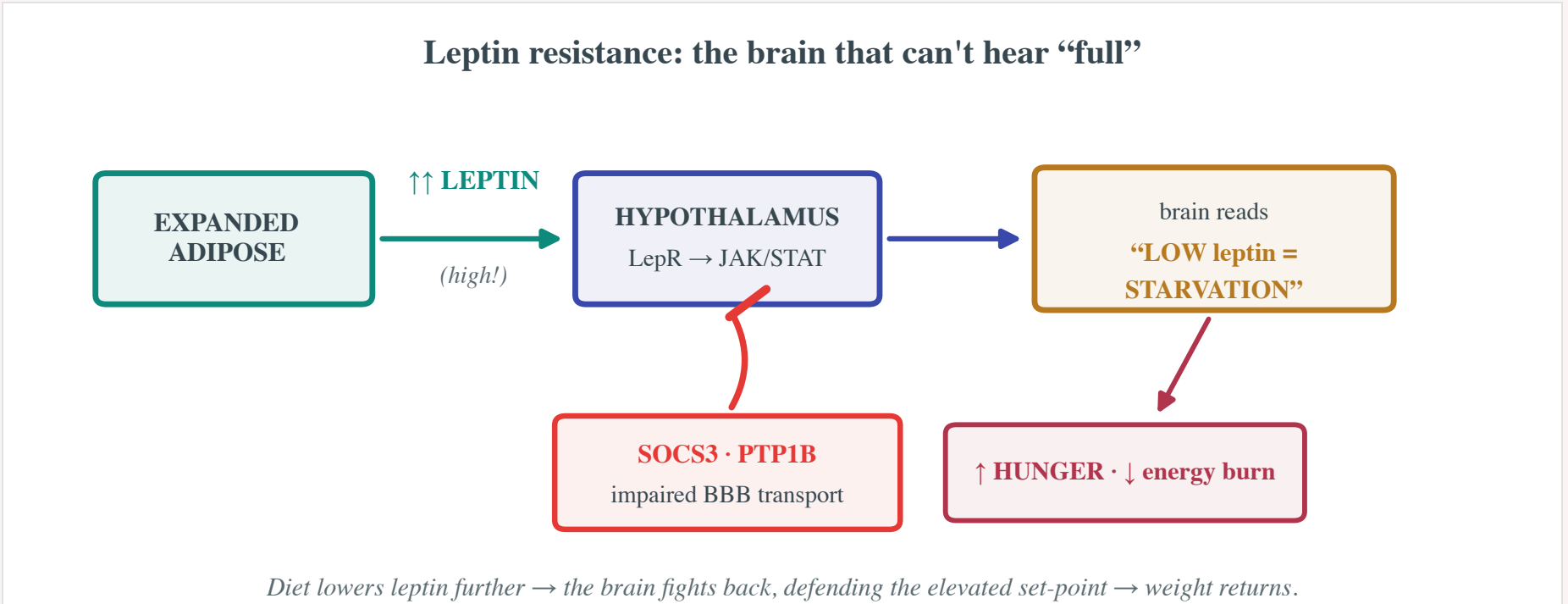
Two clocks, one axis

Watch the timing — it tells you each hormone's job. **Ghrelin** climbs **before** every meal, the biochemical growl that says "feed me," then crashes once you eat. **PYY and GLP-1** do the opposite, rising **after** a meal to call it quits. And **leptin**? Nearly flat — a slow, tonic readout of how much fat you're carrying.



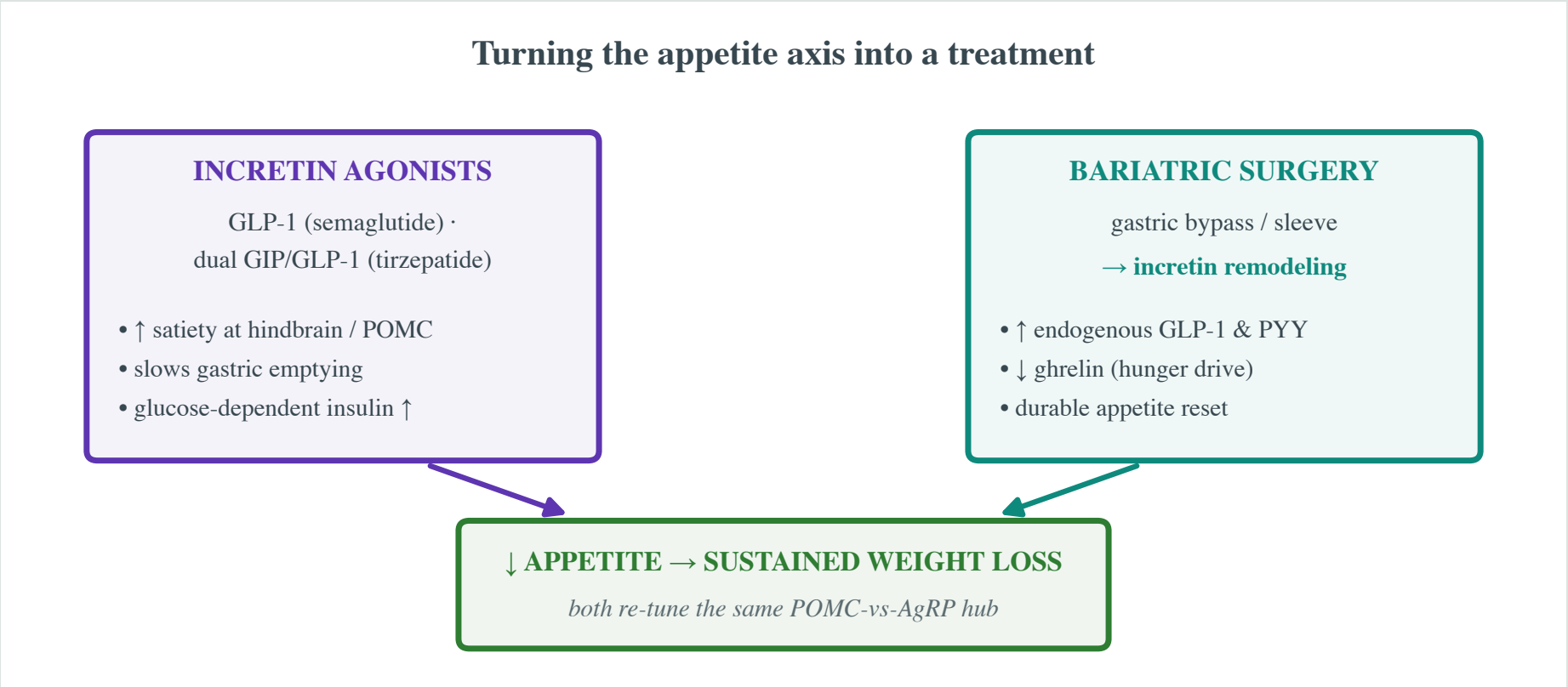
Why the diet always wins

Here's the cruel twist of obesity. More fat means **more leptin** — yet the brain stops hearing it. **SOCS3, PTP1B**, and poor transport across the blood-brain barrier jam the LepR signal, so the hypothalamus reads **starvation** despite plenty. Diet down and leptin drops further, and biology fights back — more hunger, slower metabolism — **defending the set-point**.



Prescribing the axis

Now the payoff: the best obesity therapies don't fight the axis, they **work through it**. **GLP-1 agonists** (semaglutide) and **dual GIP/GLP-1** drugs (tirzepatide) amplify satiety and slow the stomach. **Bariatric surgery** rewires the gut so it pours out more GLP-1 and PYY and less ghrelin — an **incretin remodel** that resets appetite for good.



2 · Neuroendocrine Tumors

"A neuroendocrine tumor is a hormone gland gone rogue — it picks one signal and screams it. The beautiful part for us: each hormone writes its own unmistakable syndrome. Learn the pairings, meet carcinoid's tryptophan heist, spot the inherited clusters, and you can diagnose from the labs alone."

One hormone, one syndrome

Each functional NET over-secretes a single hormone, and that hormone **is** the diagnosis. **Gastrinoma** floods gastrin → **Zollinger-Ellison** ulcers. **Insulinoma** → fasting hypoglycemia with high C-peptide. **VIPoma** → the watery-diarrhea **WDHA** syndrome. **Glucagonoma** → a migratory rash and hyperglycemia. **Somatostatinoma** → diabetes, gallstones, steatorrhea.

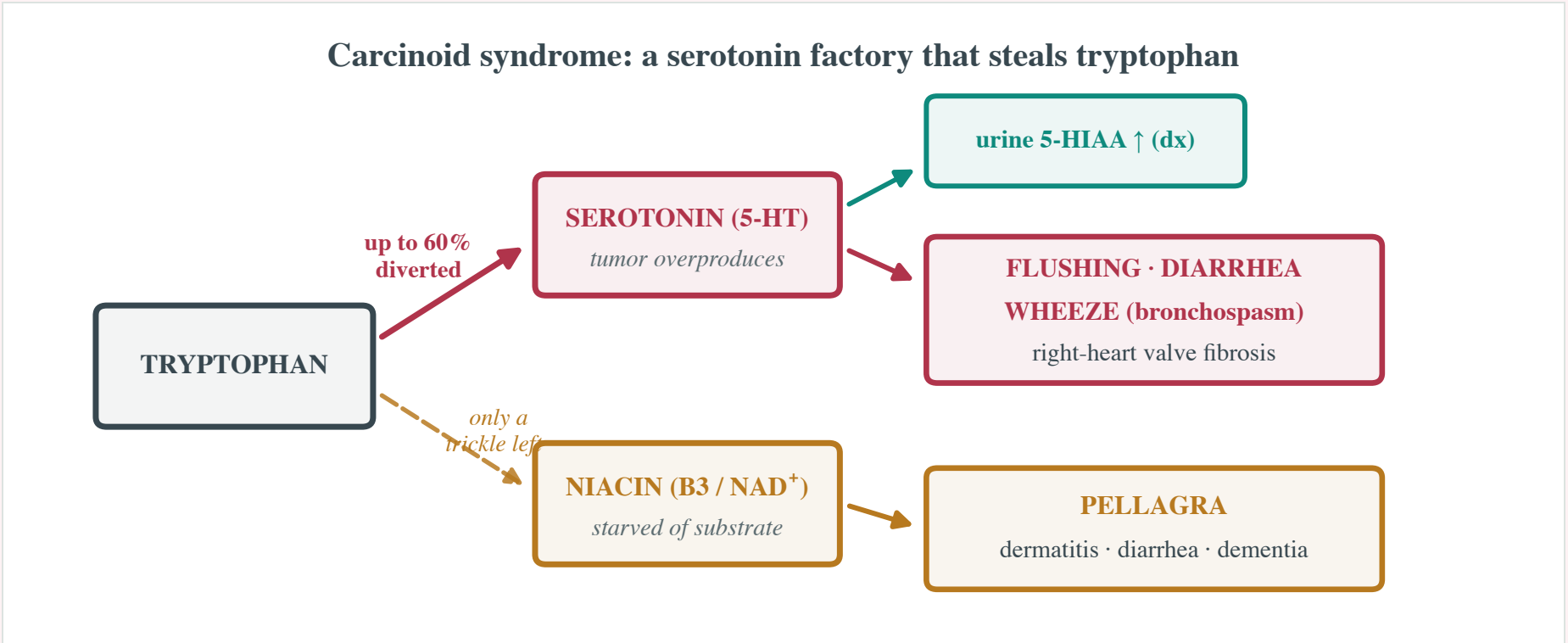
Functional GI / pancreatic NETs: match the hormone to the syndrome

TUMOR	HORMONE		SYNDROME / CLUE
GASTRINOMA	gastrin	→	Zollinger-Ellison: refractory ulcers + diarrhea
INSULINOMA	insulin	→	fasting hypoglycemia (Whipple); ↑ insulin + C-peptide
VIPoma	VIP	→	WDHA: watery diarrhea, hypokalemia, achlorhydria
GLUCAGONOMA	glucagon	→	necrolytic migratory rash, hyperglycemia, weight loss
SOMATOSTATINOMA	somatostatin	→	diabetes, gallstones, steatorrhea

One cell type, one hormone, one recognizable syndrome — that pairing is the whole game.

Carcinoid steals your tryptophan

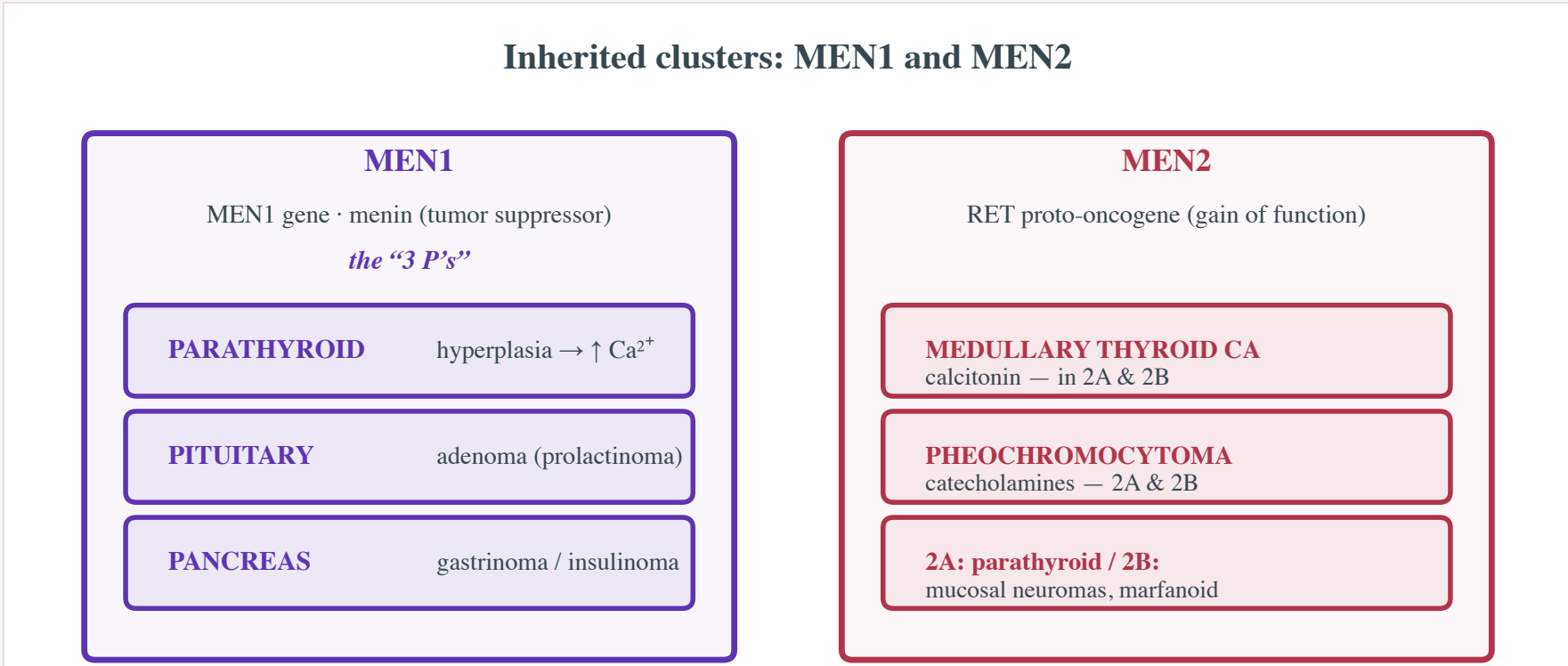
Carcinoid tumors pump out **serotonin**, giving the classic triad — **flushing, diarrhea, wheezing** — plus right-sided valve fibrosis (symptoms need to bypass the liver first). We catch it by **urinary 5-HIAA**. And the sneaky part: the tumor diverts so much **tryptophan** into serotonin that little is left for **niacin** — so patients can slide into **pellagra**.



Serotonin symptoms need bypass of the liver (mets / lung primary); the steal drains niacin → pellagra.

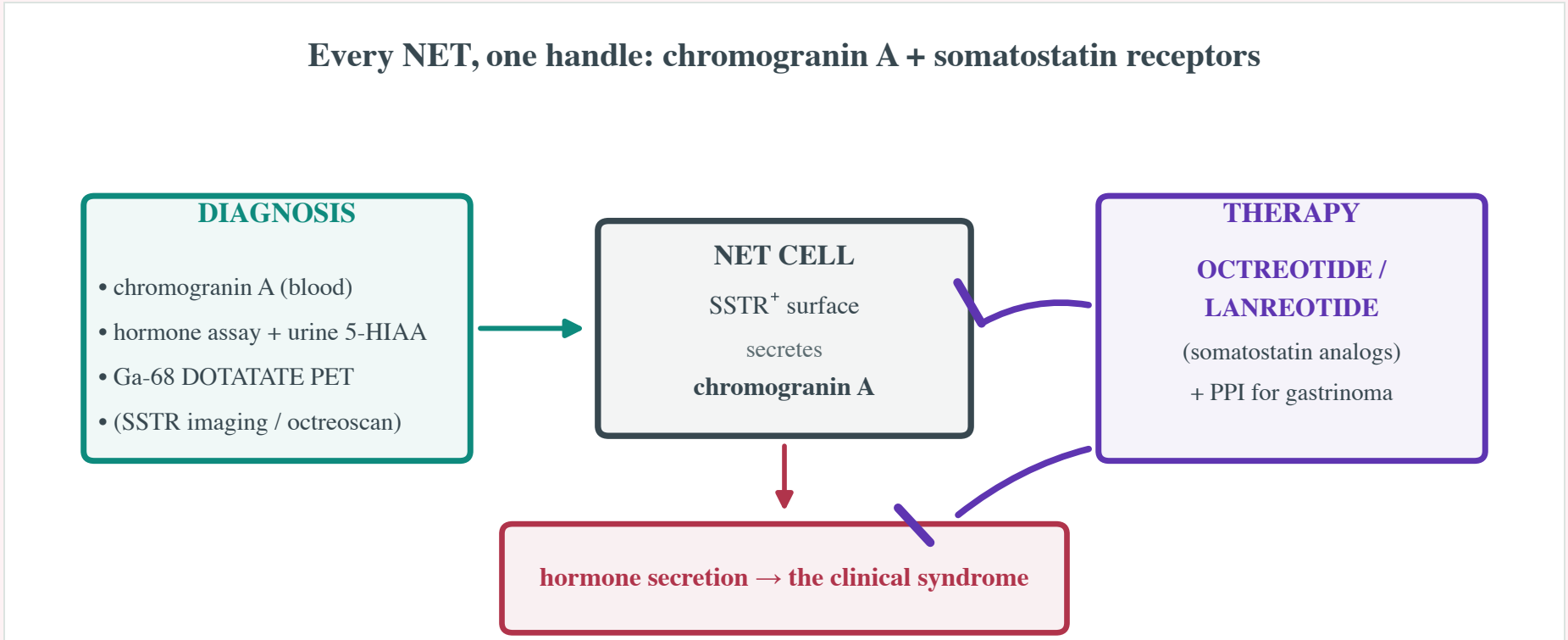
When it runs in the family

Sometimes these tumors travel in inherited packs. **MEN1** (mutated **menin**) is the **"3 P's"** – **p**arathyroid, **p**ituitary, and **p**ancreatic islet tumors. **MEN2** (an activated **RET** oncogene) always brings **medullary thyroid carcinoma**, with **pheochromocytoma** in about half. Spot one germline case and you screen the whole family.



The universal handle

However exotic the hormone, every NET shares two features you can grab. They spill **chromogranin A** into the blood (a pan-NET marker) and stud their surface with **somatostatin receptors**. That second one is a gift: **Ga-68 DOTATATE PET** lights them up for imaging, and **octreotide** binds the same receptor to switch the secretion — and the syndrome — right off.



Somatostatin analogs bind SSTR to switch OFF secretion — and slow tumor growth.

Can you…?

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