

Endocrine Flags in Primary Care: *When It's Not Just Fatigue*

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DALHOUSIE
UNIVERSITY



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Disclosures



I. None relevant to today's topic

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OTHER:	Assistant Professor in Medicine (Dalhousie)

I will be using AI-generated images (not content)
Off-label recommendations will be clearly indicated

Objectives

At the conclusion of this activity, participants will be able to

- I. Explore the presentation of endocrine causes of fatigue in adults and an *approach to initial workup [Medical Expert]
 - Focus: recognize red flags 
 - II. Identify some nuances and possible pitfalls in endocrine interpretation [Medical Expert, Scholar] and investigation
 - III. List the criteria for involving endocrinology (and what to include in the referral) [Medical Expert, Communicator]
- No Slides incl. for your reference

*Patient Oriented

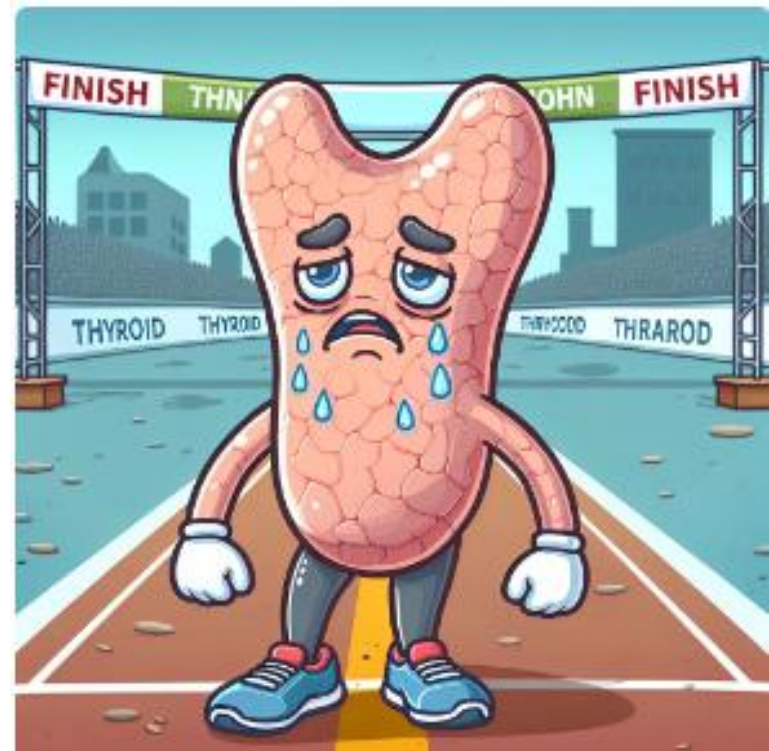


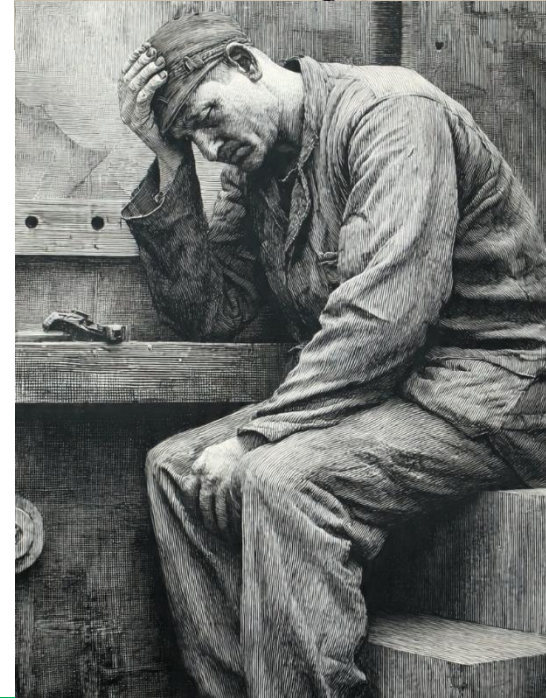
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“I can’t explain it, but I’m
so *tired* lately...”

I. Fatigue: Definition

What do patients describe?

"Fatigued"	"Running on empty"	"Wiped"
"Tired"	"Low battery"	"Faint"
"Exhausted"	"Brain fog"	"Overtired"
"Beat"	"Overwhelmed"	"Sapped"
"Lethargic"	"Tuckered out"	"Pooped"
"Weak"	"Worn out/down"	"Weary"
"Drained"	"Burned out"	"Spent"
"Listless"	"Bedraggled"	"Fagged out"
"Unwell"	"No/low energy"	"Zonked"
"Run down"	"Haggard"	"Done in"
"Zapped"	"Sleepy"	"Dead"



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I. Fatigue: Definition

Fatigue:

- Difficulty/inability to initiate activity
- Reduced capacity to maintain activity
- Difficulty with concentration, memory, emotional stability

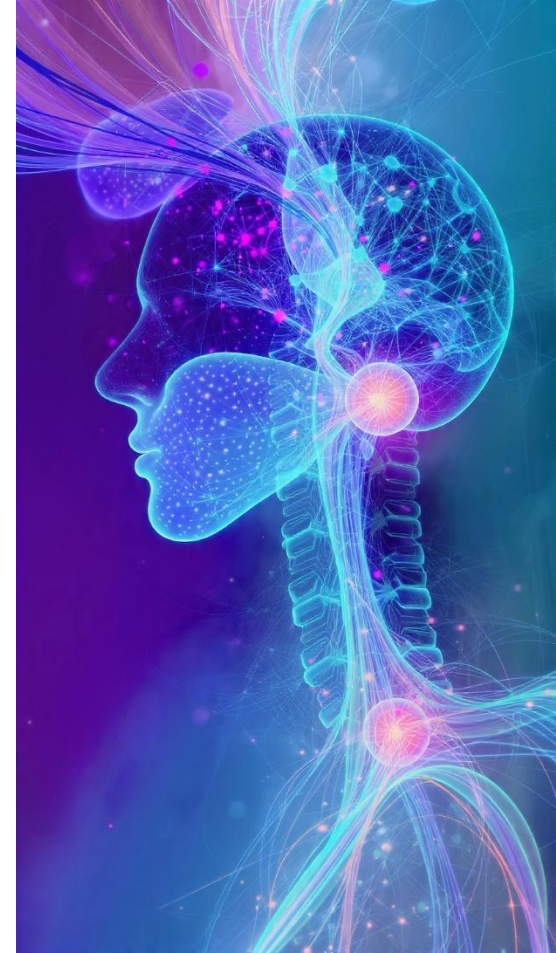


Related, but different terms:

- Somnolence, malaise, lethargy, dyspnea, weakness (myasthenia), abulia, apathy

I. Fatigue: Etiology

- Many things cause fatigue
- Few serious conditions cause fatigue in isolation
- Many endocrine abnormalities can cause fatigue, but do so with other symptom(s)
- Our job is to uncover serious symptoms i.e. “red flags” (localized findings)



I. Fatigue: Etiology

- Some entities that do NOT exist:
 - “Endocrine Fatigue”
 - “Adrenal Fatigue”
- Patients inappropriately take supplements that claim to treat symptoms of these non-conditions

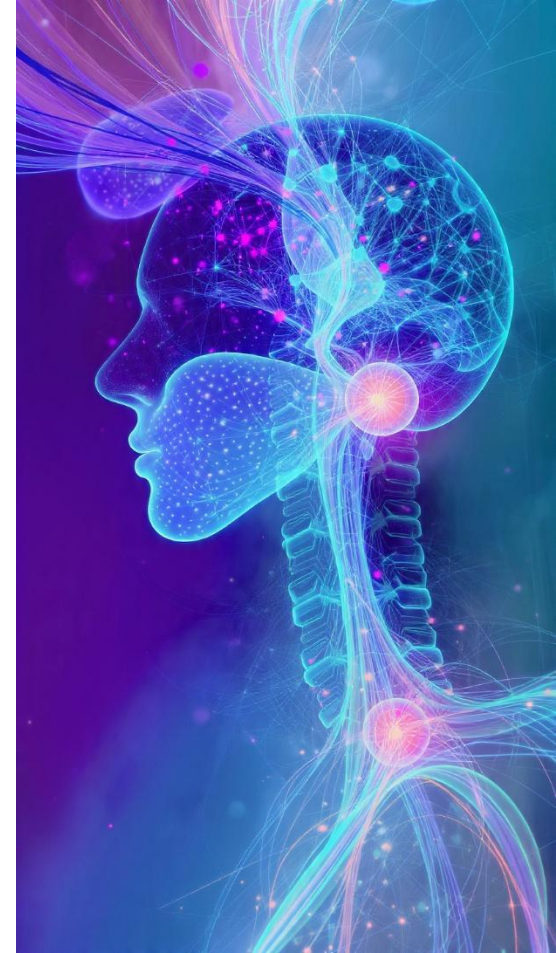


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I. Fatigue: Etiology

Aging

1. Iron deficiency ~25%
2. Depression/anxiety ~10-15%
3. Obstructive sleep apnea ~15-30%
4. Hypothyroidism ~5-10%
5. Vitamin B12 deficiency ~5-20%
6. Diabetes mellitus ~10%
7. Vitamin D deficiency ~10-40%
8. Chronic infection/
post-viral ~10-30%
9. Heart disease ~5-10%
10. Fibromyalgia/
myalgic encephalomyelitis/
chronic fatigue syndrome ~2-5%



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“Could it be my *hormones*?”

I. Fatigue: Endo DDx – Anything?

Common

- Diabetes mellitus
- Hypothyroidism
- Menopause
- Metabolic syndrome
 - Insulin resistance
 - Polycystic ovarian syndrome
- Obesity

Less common

- Adrenal insufficiency
- Hyperaldosteronism
- Hyperparathyroidism ($\uparrow$ Ca)
- Hyperthyroidism
- Hypogonadism
- Hyponatremia
- *Vitamin D deficiency

Others

- | | | |
|-----------------------------|----------------------|---|
| • Carcinoid syndrome | • Hypercortisolism | • Hypoparathyroidism ($\downarrow$ Ca) |
| • Diabetes insipidus | • Hyperprolactinemia | • Hypopituitarism |
| • Growth hormone deficiency | • Hypoglycemia | • Pheochromocytoma |

I. Fatigue: Endo DDx – Flags

Common

- Diabetes mellitus 
- Hypothyroidism
- Menopause
- Metabolic syndrome
 - Insulin resistance
 - Polycystic ovarian syndrome
- Obesity

Less common

- Adrenal insufficiency 
- Hyperaldosteronism 
- Hyperparathyroidism (↑Ca) 
- Hyperthyroidism 
- Hypogonadism
- Hyponatremia
- *Vitamin D deficiency

Others

- | | | |
|--|--|--|
| • Carcinoid syndrome  | • Hypercortisolism  | • Hypoparathyroidism (↓Ca) |
| • Diabetes insipidus | • Hyperprolactinemia | • Hypopituitarism  |
| • Growth hormone deficiency | • Hypoglycemia  | • Pheochromocytoma  |

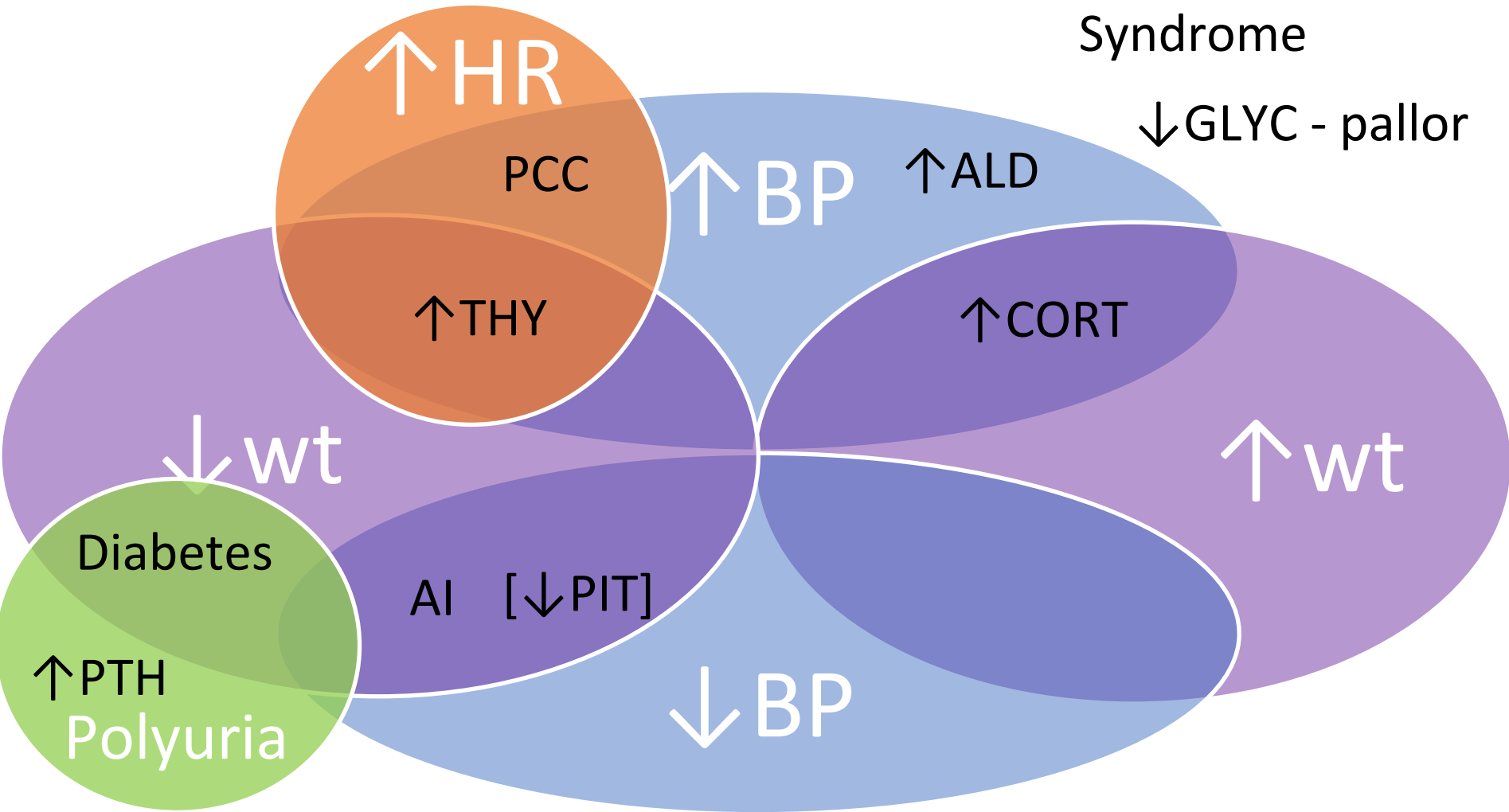
Cause	Key Symptom(s)	Key Sign(s)	Screening Test(s)	Other Test(s)
AI	Anorexia, abdominal pain, nausea/vomiting *salt craving	↓BP, ↓wt *orthostasis, *↑pigmentation	8AM cortisol	↓Na, *↑K , ACTH (ACTH stimulation)
Carcinoid	Flushing , diarrhea, bronchospasm	Murmur, telangiectasia	Urine 5-HIAA	(Nuclear imaging)
Diabetes	Polyuria/dipsia , visual changes	↓wt	A1C, glucose (fasting, random), 75g OGTT	GAD antibodies, insulin/C-peptide
↑ALD	↑BP	↑BP (resistant)	30min seated aldosterone/renin	↓K , ↑Na (Saline suppression)
↑CORT	Bruising, proximal weakness , facial plethora , central obesity	↑BP , thin skin, purple striae , ↑wt , dorsocervical/facial	1mg DST 24h urine free cortisol	Late night salivary cortisol, ACTH , ↓DHEAS
↑PTH	Polyuria/dipsia , nephrolithiasis , fracture	None	Albumin, cCa, ↓PO4	PTH , 25-vitamin D 24h urine Ca/Cr
↑THY	Heat intolerance , diarrhea, diaphoresis, palpitations	↑HR , ↑BP , ↓wt tremor, ocular symptoms , goitre	TSH	Thyroid receptor antibody
↓GLYC	*Whipple's triad	Pallor	Fasting glucose	Insulin, C-peptide
↓PIT	Headache (+/- AI)	↓peripheral vision	Prolactin, free T4 , FSH, LH, 8 AM cortisol	Insulin-like growth factor-1, seller MRI
PCC	Triad (headache, diaphoresis, palpitations)	↑BP , ↑HR , orthostasis	24h urine fractionated metanephrines /catecholamines	Serum metanephrines /catecholamines (Abdominal imaging)

AI = adrenal insufficiency; ACTH = adrenocorticotrophic hormone; 5-HIAA = 5-hydroxyindoleacetic acid; OGTT = oral glucose tolerance test; GAD = glutamic acid decarboxylase; ↑ALD = hyperaldosteronism; ↑CORT = hypercortisolism; DST = dexamethasone suppression test; DHEAS = dehydroepiandrosterone sulfate; cCa = corrected calcium; ↑PTH = hyperparathyroidism; ↑THY = hyperthyroidism; PCC = pheochromocytoma; TSH = thyroid-stimulating hormone; ↓GLYC = hypoglycemia; ↓PIT = hypopituitarism; FSH = follicle-stimulating hormone; LH = luteinizing hormone;

I. Fatigue: Endo Differential

Carcinoid - flushing
Syndrome

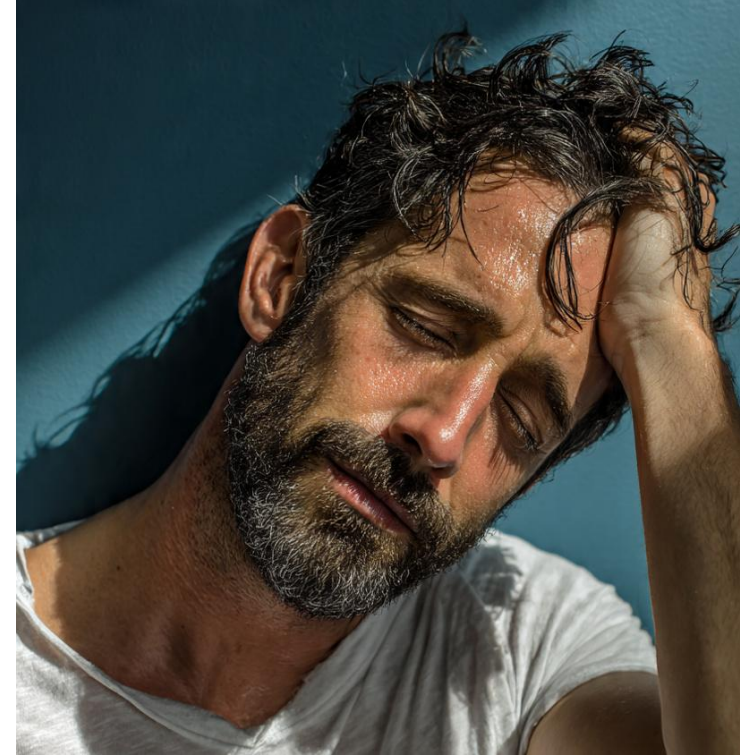
↓GLYC - pallor



“But I haven’t been on a
cruise...”

Case 1: AD 38M

- 3mo of fatigue, thirsty, ↓wt, anorexia, eating ++chips (salt craving), “like on a cruise”
- PHx: none
- Meds: none
- Exam: ↓wt, ↓BP, HR N, orthostatic drop, tanned, vitiligo
- Labs: K 5.2 ↑, Na 124 ↓



“No cruise!”

Next steps?

1. Adrenal Insufficiency: Etiology

Cortisol underproduction
(i.e. hypocortisolism)

1. Primary: adrenal injury

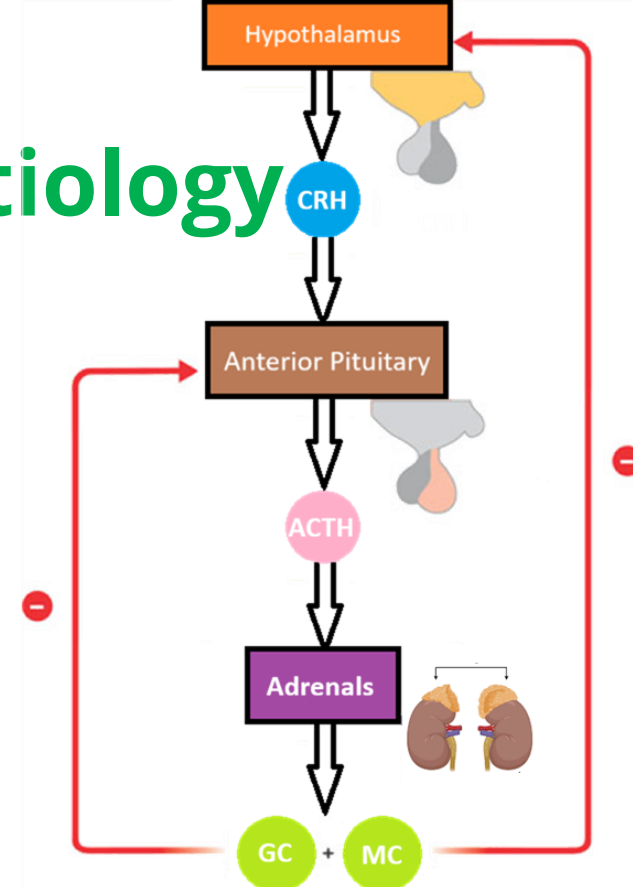
- Addison's: $\uparrow$ ACTH, $\uparrow$ CRH
+/- $\uparrow$ K, $\downarrow$ Na, $\downarrow$ glucose

2. Secondary: pituitary injury

- See Hypopituitarism
 - * $\downarrow$ ACTH, $\uparrow$ CRH +/- $\downarrow$ Na

3. [Tertiary: hypothalamic injury]

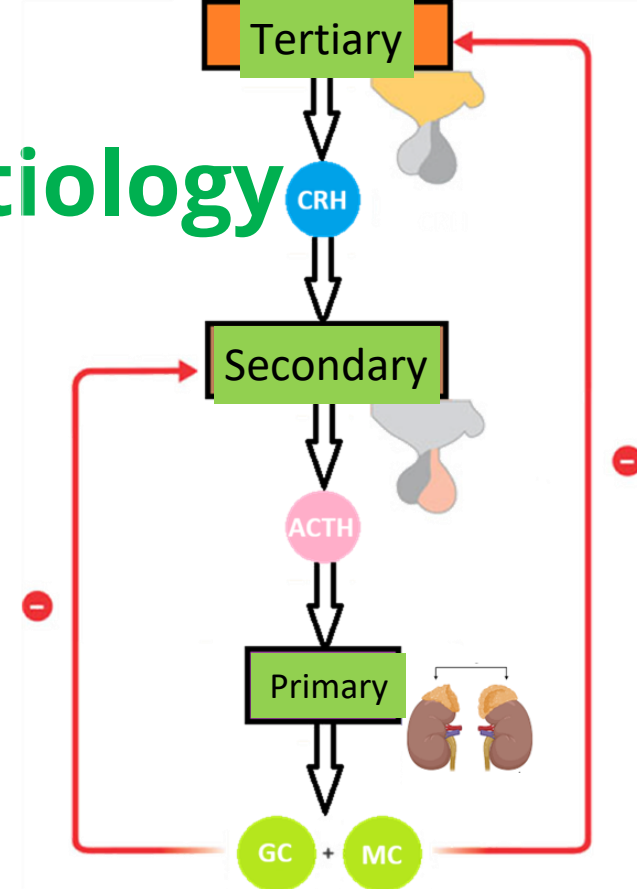
- Chronic GCs, opioids
 - $\downarrow$ ACTH, $\downarrow$ CRH, +/- $\downarrow$ Na



1. Adrenal Insufficiency: Etiology

Cortisol underproduction
(i.e. hypocortisolism)

1. Primary: adrenal injury
 - Addison's: $\uparrow$ ACTH, $\uparrow$ CRH
+/- $\uparrow$ K, $\downarrow$ Na, $\downarrow$ glucose
2. Secondary: pituitary injury
 - See Hypopituitarism
 - * $\downarrow$ ACTH, $\uparrow$ CRH +/- $\downarrow$ Na
3. [Tertiary: hypothalamic injury]
 - Chronic GCs, opioids
 - $\downarrow$ ACTH, $\downarrow$ CRH, +/- $\downarrow$ Na



1. Adrenal Insufficiency: Approach

1. Symptoms? Signs?

- Anorexia, abdominal pain, nausea/vomiting, diarrhea, weakness, unintentional weight loss, hypotension, myalgia, arthralgia, oligo/amenorrhea, ↓Na
- Primary: orthostasis, hyperpigmentation, salt craving, ↑K, ↓glucose

2. Offending agents?

- Biotin, medications (steroids, opioids, immunotherapy, etomidate, antifungals, metyrapone, phenytoin, mitotane, barbiturates, megestrol, rifampin, anticoagulants, anticonvulsants, antiretrovirals)

3. Screening (after minimizing interference from 2.)

- AM cortisol, ACTH, electrolytes, fasting glucose
- hCG (♀ child-bearing)



1. Adrenal Insufficiency: Nuance

- Screening: 8AM cortisol + ACTH
 - Random cortisol NOT helpful
 - >350-500 = normal (depends on assay)
 - <50: clearly adrenal insufficiency
 - 50-350: confirmation needed
 - No GCs for 48h (dexamethasone for 7d)
- Confirmation: ACTH stimulation (GIM/Endo)
 - Cosyntropin 250mcg IV, then cortisol at time = 30 min and 60 min
 - >350-500 = normal (depends on assay)

*Pearl: screen
8AM cortisol

*Pearl: hold
GCs before
screening

1. Adrenal Insufficiency: Treatment

1. Primary: glucocorticoid + mineralocorticoid

- Hydrocortisone 10mg PO qAM + 5mg qPM + fludrocortisone 0.05mg PO qAM
- Crisis: hydrocortisone injection kit

2. Secondary: glucocorticoid only

- Hydrocortisone 10mg PO qAM + 5mg qPM

1. Adrenal Insufficiency: Summary

Symptoms?

- ↓wt
- ↓BP
- Anorexia
- *Salt craving
- *↑pigmentation
- *Orthostasis



Screen

- No biotin x 7d
- Offending agent?

8AM cortisol,
ACTH,
electrolytes,
fasting glucose
(**hCG**)



Confirm

- GIM/Endo

ACTH
Stimulation



Treat

Hydrocortisone
10mg PO qAM
+
5mg PO qPM

“I keep *gaining* weight”

Case 2: CS 43F

- 6mo of fatigue, ↑wt (50 pounds, mostly stomach/face), oligomenorrhea, hirsutism
- PHx: none
- Meds: none
- Exam: ↑wt (face/nape), ↑BP, HR N, facial plethora, proximal weakness, wide violaceous striae
- Labs: K N, Na N, fasting glucose 7.5 ↑, random cortisol 502

Next steps?



“Weight gain”

2. Hypercortisolism: Etiology

Cortisol overproduction

1. Primary: adrenal source

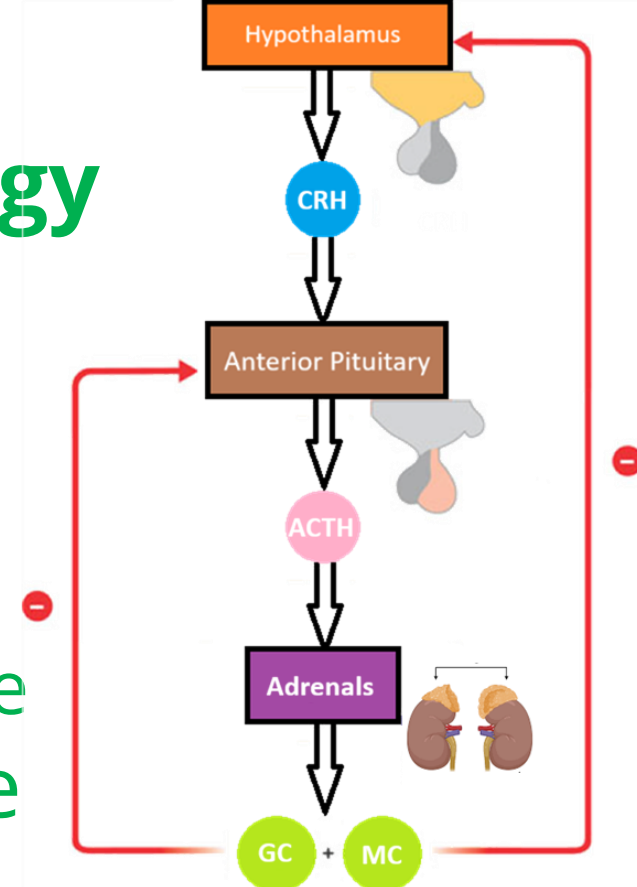
- Adenoma
 - $\downarrow$ ACTH, $\downarrow$ CRH +/- $\uparrow$ glucose

2. Secondary: pituitary source

- Cushing disease
 - * $\uparrow$ ACTH, $\downarrow$ CRH +/- $\uparrow$ glucose

3. Other source

- E.g. exogenous



2. Hypercortisolism: Etiology

Cortisol overproduction

1. Primary: adrenal source

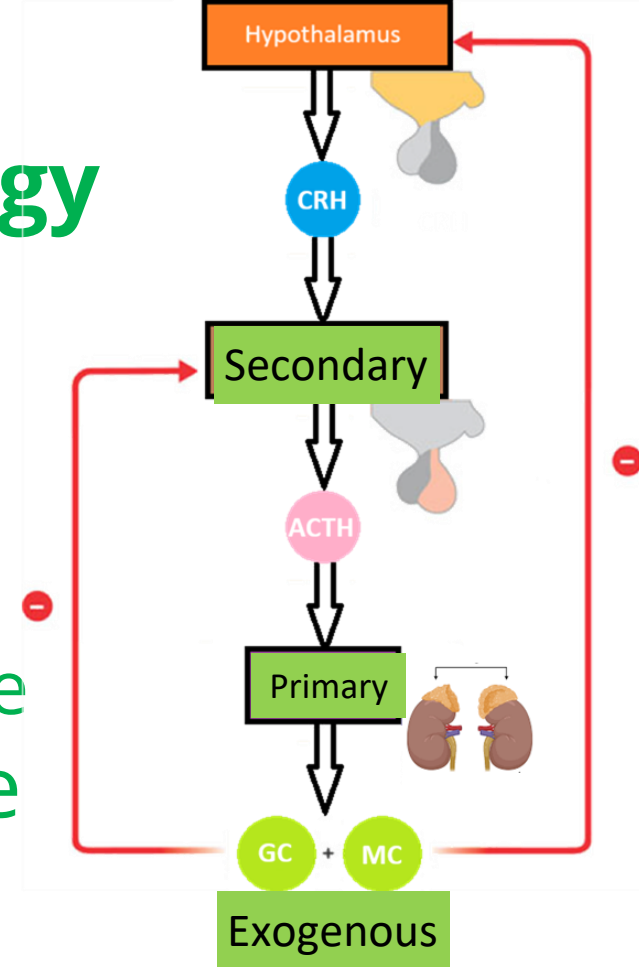
- Adenoma
 - $\downarrow$ ACTH, $\downarrow$ CRH +/- $\uparrow$ glucose

2. Secondary: pituitary source

- Cushing disease
 - * $\uparrow$ ACTH, $\downarrow$ CRH +/- $\uparrow$ glucose

3. Other source

- E.g. exogenous



2. Hypercortisolism: Approach

1. Symptoms? Signs?

- Fatigue, violaceous striae, facial plethora, easy bruising, proximal myopathy, unintentional weight gain (central, dorsocervical fat pad, facial fullness), fragility fracture, depression, hypertension, thin skin, peripheral edema, cognitive changes
- Hyperandrogenism: oligo/amenorrhea, hirsutism, acne, deepening voice, androgenic alopecia, clitoromegaly

2. Offending agents?

- Biotin, medications (steroids, estrogen, anticonvulsants, rifampin, pioglitazone, antifungals, antiretrovirals, fluoxetine, diltiazem, mitotane, fenofibrate)

3. Screening (after minimizing interference from 2.)

- 1mg DST, ACTH, DHEAS, A1C, fasting glucose/lipids
- hCG (♀ child-bearing), 24h UFC (estrogen)



³Nieman et al. 2016

DST = dexamethasone suppression test; ACTH = adrenocorticotrophic hormone; DHEAS = dehydroepiandrosterone sulfate

hCG = beta-human chorionic gonadotropin; UFC = urine free cortisol

2. Hypercortisolism: Nuance

- Screening: 1mg DST 11PM + 8AM cortisol
 - Random cortisol NOT helpful
 - 8AM cortisol: <50 = normal
 - No other GCs for 48h
 - Estrogen use: false positives
- Confirmation:
 - 24h urine free cortisol (esp. estrogen)
 - 8mg DST 11PM + 8AM cortisol
 - 12AM salivary cortisol

*Pearl: screen
1mg DST (not
random
cortisol)

*Pearl: screen
24h UFC with
estrogen

2. Hypercortisolism: Treatment

1. Surgery preferred
2. Medications 2nd-line

2. Hypercortisolism: Summary

Symptoms?

- ↑wt
- Purple striae
- Facial plethora
- Prox. weakness
- Dorsocervical/ facial fullness
- Thin skin



Screen

- No biotin x 7d
- Offending agent?



Confirm

- 2nd test



Treat

1mg DST,
ACTH, A1C,
glucose, lipids,
DHEAS
(**hCG**)

24h UFC
12AM salivary
cortisol
8mg DST

Surgery

“Why am I *peeing* so much?
– I’m NOT pregnant!”

Case 3: DM 29F

- 6wk fatigue, polyuria, polydipsia, intermittent blurry vision
- PHx: hypothyroidism
- Meds: levothyroxine 50mcg
- Exam: ↓wt, BP N, HR N, mild dehydration, otherwise normal
- TSH N, hCG N, fasting glucose 7.4↑



Next steps?

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3. Diabetes: Etiology

1. Insulin deficiency

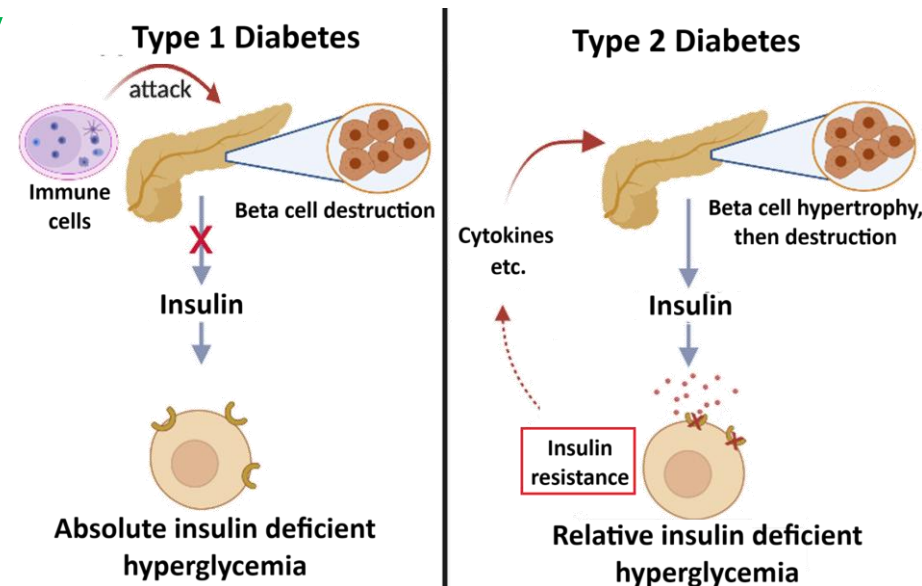
- “Type 1” diabetes
 - Pancreatic antibodies (GAD)

2. Insulin resistance

- Type 2 diabetes
 - Other comorbidities

3. Others

- LADA, monogenic, meds



⁴Inzucchi et al. 2026; ⁵Punthakee et al. 2018

GAD = glutamic acid decarboxylase; LADA = latent autoimmune diabetes of adulthood

3. Diabetes: Etiology

1. Insulin deficiency

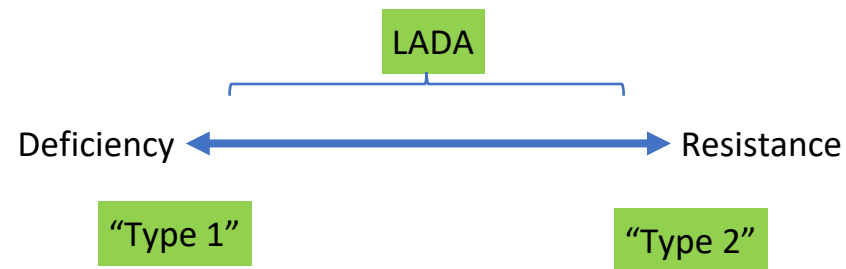
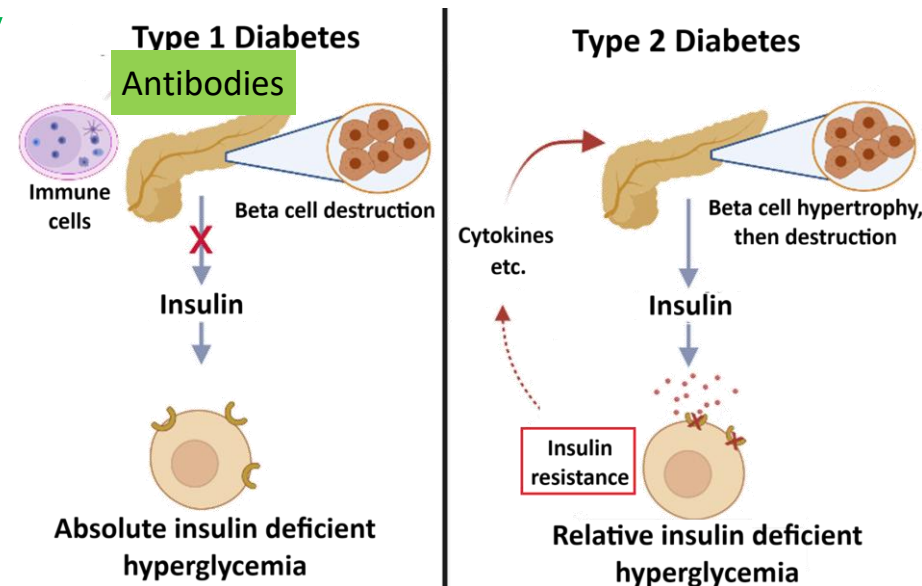
- “Type 1” diabetes
 - Pancreatic antibodies (GAD)

2. Insulin resistance

- Type 2 diabetes
 - Other comorbidities

3. Others

- LADA, monogenic, meds



3. Diabetes: Approach

1. Symptoms? Signs?

- Polyuria, polydipsia, nocturia, visual changes, unintentional weight loss, oligo/amenorrhea, dehydration, hypertension, obesity, metabolic syndrome, microvascular complications
- Type 1: autoimmune, age <30, low BMI, DKA

2. Offending agents?

- Medications (steroids, levothyroxine, beta-agonists, thiazides, atypical antipsychotics, phenytoin, protease inhibitors, etc.)

3. Screening

- A1C, fasting glucose/lipids, urine ACR
- *Antibodies: GAD-65
- hCG (♀ child-bearing)

⁴Inzucchi et al. 2026; ⁵Punthakee et al. 2018

BMI = body mass index; DKA = diabetic ketoacidosis; ACR = albumin creatinine ratio;

GAD = glutamic acid decarboxylase; hCG = beta-human chorionic gonadotropin

3. Diabetes: Nuance

*Pearl: screen
8AM cortisol

- Screen: A1C ≥ 6.5 , fasting glucose ≥ 126 , random glucose ≥ 200
- Confirm: 75g OGTT ≥ 200
- Autoimmune? (see Diabetes Canada)
 - Antibodies: [GAD-65](#)
- Insulin needed? (*Asymptomatic)
 - Labs: fasting insulin, [C-peptide](#) level (<300)

3. Diabetes: Treatment

1. Lifestyle

- Referral to diabetes centre to review diagnosis/treatment

2. Metformin

- Next “salient” feature
 - Obesity, CKD, CAD, CHF...

3. Insulin

- If symptomatic hyperglycemia
- If fasting C-peptide <300)

*Pearl:
symptomatic
↑glucose
requires
insulin

3. Diabetes: Summary

Symptoms?

- ↓wt
- Polyuria
- Polydipsia
- Visual changes
- Complications



Screen

- Metabolic
- *Autoimmune



Confirm

- 2nd test



Treat

A1C, fasting
glucose/lipids,
ACR *GAD 65
(**hCG**)

75g OGTT
*Fasting insulin
C-peptide

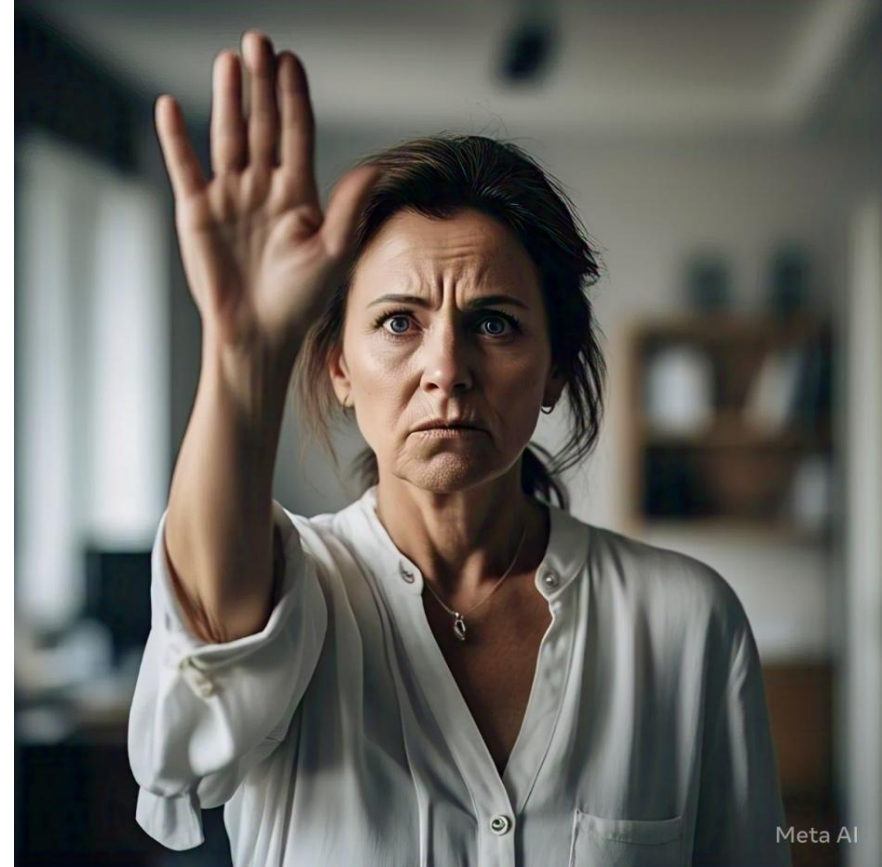
Metformin +/-
non-insulin
vs.
*Insulin

“Why am I shaking
after I eat?”

Case 4: RH 57F

- 3mo of fatigue, “feeling off” after eating large meals
- PHx: prediabetes, GERD
- Meds: sucralfate
- Exam: wt stable, BP N, HR N, pale, otherwise normal
- Labs: ferritin N, fasting glucose 6.5 ↑, A1C 6.2 ↑

Next steps?



“Shaky meals”

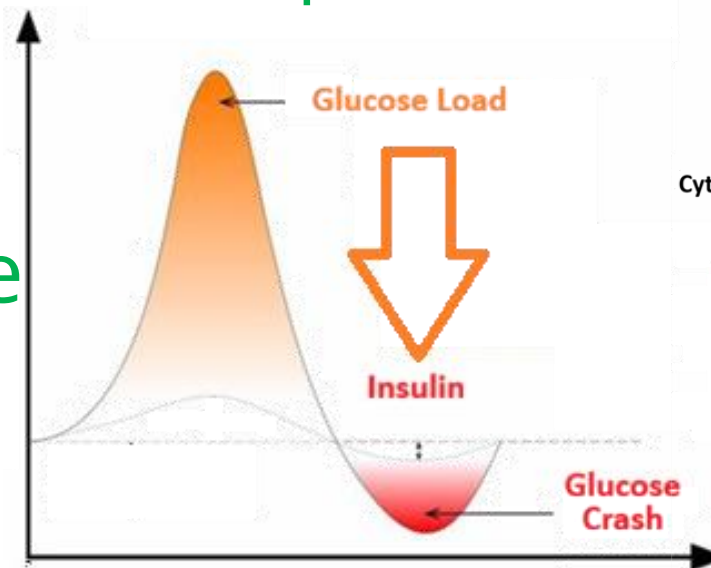
4. Hypoglycemia: Etiology

1. Insulin overproduction

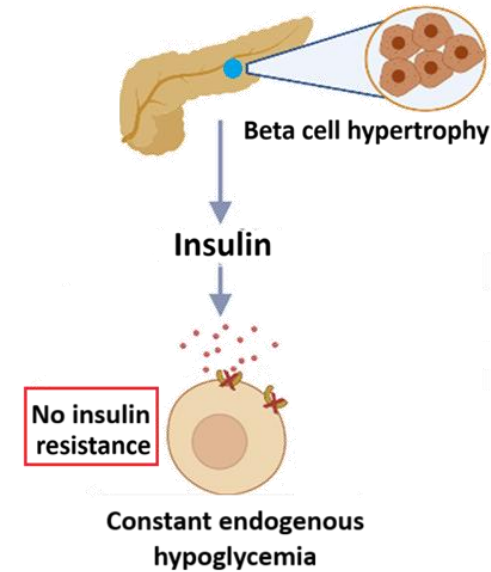
- Fasting: insulinoma
- Postprandial: prediabetes ("reactive": loss of 1st-phase)

2. Others

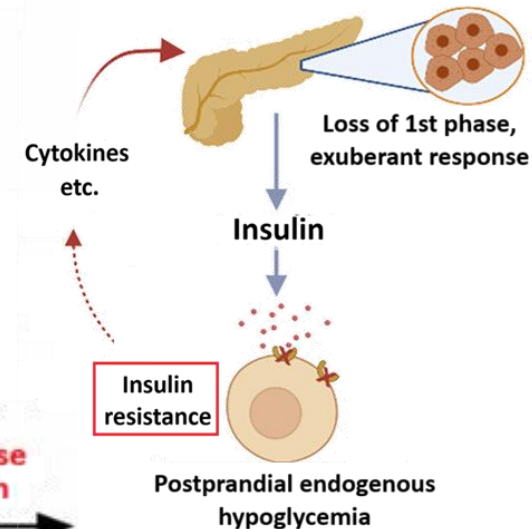
- AI
- Liver disease
- CKD
- Alcohol



Insulinoma



"Reactive" Hypoglycemia



4. Hypoglycemia: Approach

1. Symptoms? Signs?

- Tremor, palpitations, anxiety, diaphoresis, pallor, hunger, paresthesia, weakness, reduced LoC, dizziness, weight gain, timing (fasting vs. postprandial), *adrenal insufficiency, *diabetes, *liver disease
- Whipple's triad: 1. Symptoms 2. Documented ↓glucose 3. Improvement with normalized glucose

2. Offending agents?

- Biotin, medications (pentamidine, quinine, indomethacin, glucagon, lithium, ACEi, ARB, beta-agonists, levofloxacin, mifepristone, septria, heparin, 6-mercaptopurine, sucralfate)

3. Screening (after minimizing interference from 2.)

- *Fasting glucose, insulin, C-peptide, ketones
- Other causes: 8AM cortisol, liver/renal function



4. Hypoglycemia: Nuance

- Screening: replicate situation
 - Fasting: insulin, C-peptide, BHB
 - Postprandial: mixed meal (GIM/Endo)
- Confirmation:
 - Continuous glucose monitor
 - 72h fast (GIM/Endo): rarely needed



*Pearl: use
CGM trial to
document
↓glucose

4. Hypoglycemia: Treatment

1. Lifestyle factors

- Referral to [diabetes centre](#) to review prevention/treatment
 - Postprandial: smaller, frequent, lower carb, higher-protein meals

2. Medications 2nd-line (off-label)

3. *Insulinoma: surgery preferred

4. Hypoglycemia: Summary

Symptoms?

- Whipple's triad



Screen

- Fasting
- Postprandial



Confirm

- Diabetes centre



Treat

Glucose,
insulin,
C-peptide,
ketones, 8AM
cortisol, liver,
renal

CGM

Lifestyle
vs.
Surgery

“Could my *thyroid* be off?”

Case 5: GD 73M

- New diagnosis of atrial fibrillation and heart failure
- 3mo history of fatigue, dry eyes, tremor, “sweatiness”
- PHx: GERD, allergies, gout
- Meds: rabeprazole, cetirizine, allopurinol

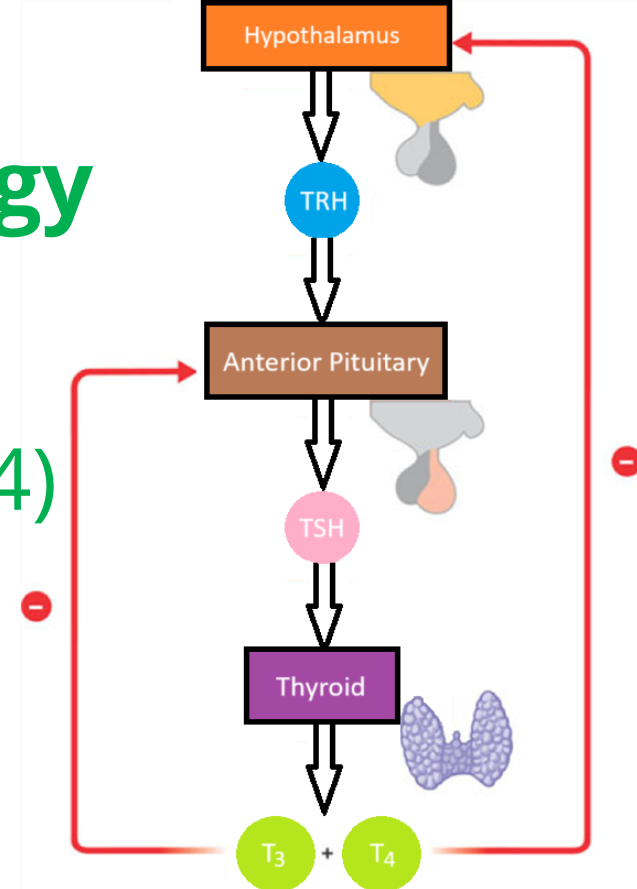


- Exam: ↓wt, ↑BP, ↑HR, heart failure, goitre, proptosis
- TSH undetectable ↓, free T4 28.4

Next steps?

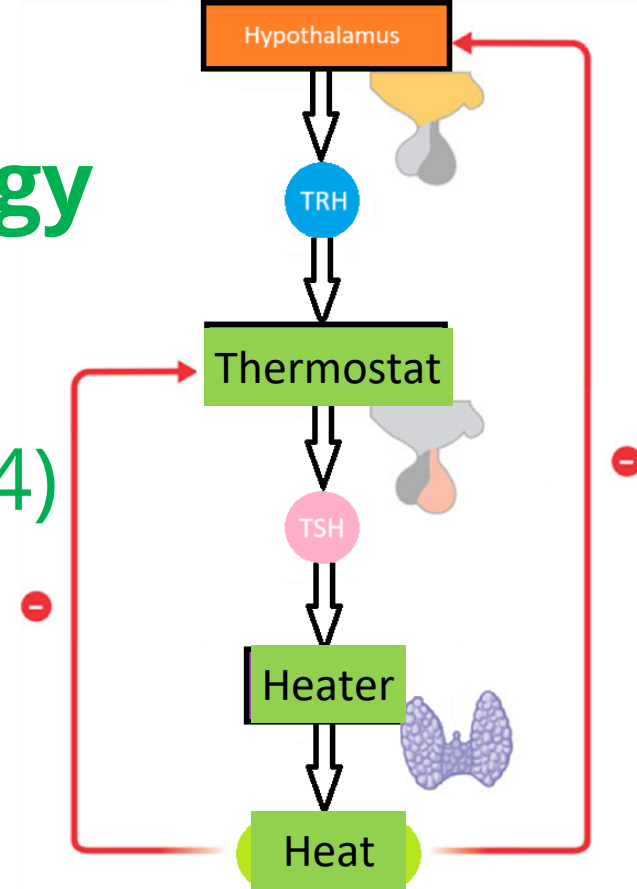
5. Hyperthyroidism: Etiology

1. Overproduction of thyroid hormones (free T3 > free T4)
 - Graves' disease: thyroid receptor antibody
 - Toxic nodule(s)
2. Release of stored thyroid hormones (free T4 > free T3)
 - Thyroiditis: TPO antibody
3. [Extrathyroidal source]



5. Hyperthyroidism: Etiology

1. Overproduction of thyroid hormones (free T3 > free T4)
 - Graves' disease: thyroid receptor antibody
 - Toxic nodule(s)
2. Release of stored thyroid hormones (free T4 > free T3)
 - Thyroiditis: TPO antibody
3. [Extrathyroidal source]



5. Hyperthyroidism: Approach

1. Symptoms?

- Palpitations, tremor, diaphoresis, heat intolerance, diarrhea, polyphagia, unintentional weight loss, worsened anxiety, cognitive changes, congestive heart failure, weakness, oligo/amenorrhea, goitre
- Ocular manifestations: proptosis, chemosis, blepharitis, diplopia

2. Offending agents?

- Biotin, iodine, medications (steroids, levothyroxine, liothyronine, lithium, amiodarone, immunotherapy, cytokines, TKIs)

3. Screening (after minimizing interference from 2.)

- Thyroid function studies: TSH, fT4, fT3
- Antibodies: TPO, thyroid receptor antibodies (or thyroid-stimulating immunoglobulin)
- CBC, CRP, ALT, bilirubin, hCG (♀ child-bearing)

4. Imaging: uptake (quantity) and scan (quality)→GIM/Endo

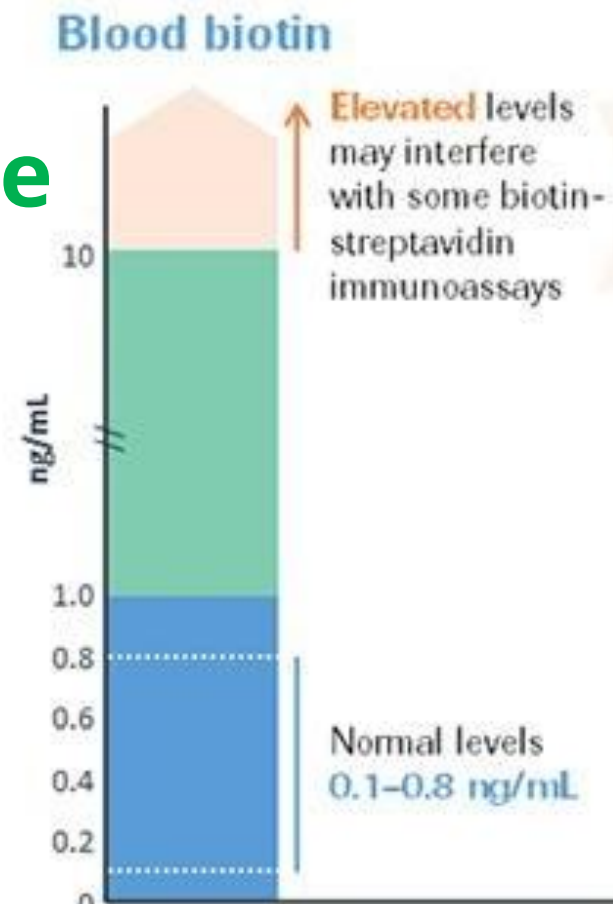


⁷Ross et al. 2025

TSH = thyroid-stimulating hormone; fT4 = free thyroxine; fT3 = free triiodothyronine; TPO = thyroid peroxidase antibody; CBC = complete blood count; CRP = C reactive protein; ALT = alanine aminotransferase; hCG = human chorionic gonadotropin; GIM/Endo = general internal medicine/endocrinology; TKIs = tyrosine kinase inhibitors

5. Hyperthyroidism: Nuance

- Vitamin B7 (water-soluble)
 - Many names: vitamin H, coenzyme R, factor S, factor W, vitamin Ba, protective factor X
- Biotin-streptavidin is one of nature's strongest non-covalent interactions
 - In vitro diagnostic tests take advantage of by immobilizing biotinylated capture antibodies
- Up to 85% of common immunochemistry analyzers used biotin-streptavidin immunoassays
- Immunoassay manufacturers and FDA have issued safety warnings about biotin interference
 - Reported levels of 1.0-1200ng/mL



5. Hyperthyroidism: Nuance

- Falsely low immunometric assays (e.g. TSH) ↓
- Falsely high competitive-binding assays (e.g. fT4, fT3, TRAB, TPO) ↑

Hormones

Test	Potential impact
Parathyroid Hormone (LAB108)	False decrease
Follicle Stimulating Hormone (LAB86)	
Luteinizing Hormone (LAB88)	
Adrenocorticotrophic Hormone (LAB511)	
Prolactin (LAB531)	
Growth Hormone (LAB525)	
Insulin (LAB7389)	
C-Peptide (LAB521)	
Insulin-Like Growth Factor 1 (LAB8787)	
Anti-Mullerian Hormone (LAB7364)	
Cortisol (LAB61)	False increase
Estradiol (LAB523)	
Testosterone (LAB124)	
Progesterone (LAB529)	
Dehydroepiandrosterone Sulfate (LAB524)	

Nutritional Markers

Test	Potential impact
Ferritin (LAB68)	False decrease
Vitamin D, 25-Hydroxy (LAB535)	False increase
Vitamin B12 (LAB67)	
Vitamin B12, Reflexive (LAB882)	
Folate (LAB69)	

Other Proteins

Test	Potential impact
Immunoglobulin E (LAB74)	False decrease
Myoglobin (LAB105)	
Sex Hormone Binding Globulin (LAB4945)	

Pregnancy-Related Markers

Test	Potential impact
Pregnancy Screen, Qualitative (LAB1166)	False decrease
HCG – Pregnancy (LAB1148)	
HCG – Tumor Marker or Pregnancy (LAB142)	

Assays at The Moncton Hospital lab should
not be susceptible to biotin interference



5. Hyperthyroidism: Nuance

Multivitamin



30-60
mcg/day

No recommended daily intake (RDI) exists,
as deficiencies are rare

Hair & nail supplement



5,000-10,000
mcg/day

More than 125 times the suggested intake

Experimental therapeutic
regimen



>10,000
mcg/day

Doctor-directed for specific patient
populations

1 ASK your patients
to report everything they
are taking, including
prescription and OTC
medicines, vitamins and
supplements, prior to a
blood draw.

2 UNDERSTAND
that many patients are not
aware that they are taking
high dose biotin because it
is packaged as a
supplement for hair, skin
and nail beauty.

3 INFORM your
patients about how to
prepare for blood work.
If they take high dose
biotin, they will need to
wait before a blood
draw.

49 *Pearl: when in doubt, hold biotin for 7d

5. Hyperthyroidism: Treatment

- Symptoms: tremor, palpitations
 - Beta blockade: propranolol vs. other
- Subacute: pain
 - NSAIDs (naproxen 250-500 mg twice daily)
 - GCs (prednisone 20-40mg)
- Persistent, overt ↑THY: antithyroid medication
 - Methimazole: 10mg PO twice daily
 - (*Propylthiouracil: preferred during 1st trimester)

5. Hyperthyroidism: Summary

Symptoms?

- Palpitations or tremor?
- Neck pain or swelling?



Repeat labs

- 6-8wk
- No biotin x 7d
- Offending agent?



Abnormal exam?

- Goitre
- Nodule



Treatment

Persistent,
overt
hyperthyroidism

*Subclinical
hyperthyroidism

Beta blockade if
palpitations or
heart rate >90

NSAIDs
(+/- GCs)

fT4, fT3
TRAB, TPO
CBC, ALT,
bilirubin, CRP
(**hCG**)

Thyroid
ultrasound

Methimazole
10 PO daily

“Why can’t we control my
blood pressure?”

Case 6: HA 52M

- 15yr of hypertension ("never controlled"), 6mo of fatigue
- PHx: hypertension
- Meds: telmisartan 80mg, amlodipine 10mg, metoprolol 25mg BID, spironolactone 12.5mg
- Exam: wt stable, ↑BP, HR N, otherwise normal
- Labs: K 3.2 ↓, Na N



"BP control?"

Next steps?

6. Hyperaldosteronism: Etiology⁸RAAS

Aldosterone overproduction

1. Primary: adrenal source

- Adenoma

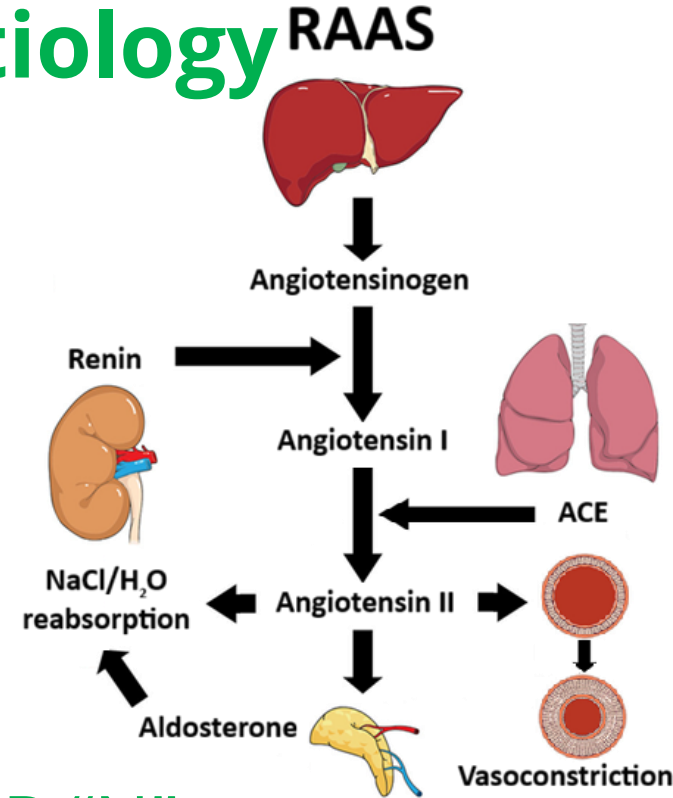
- ↓renin, ↑aldosterone, ↑ARR

2. Secondary: ↑BP vs. BP N

- ↑renin, ↑ aldosterone, ARR “N”

3. Pseudohyperaldosteronism

- ↓ renin, ↓aldosterone, ARR “N”



6. Hyperaldosteronism: Etiology⁸RAAS

Aldosterone overproduction

1. Primary: adrenal source

- Adenoma

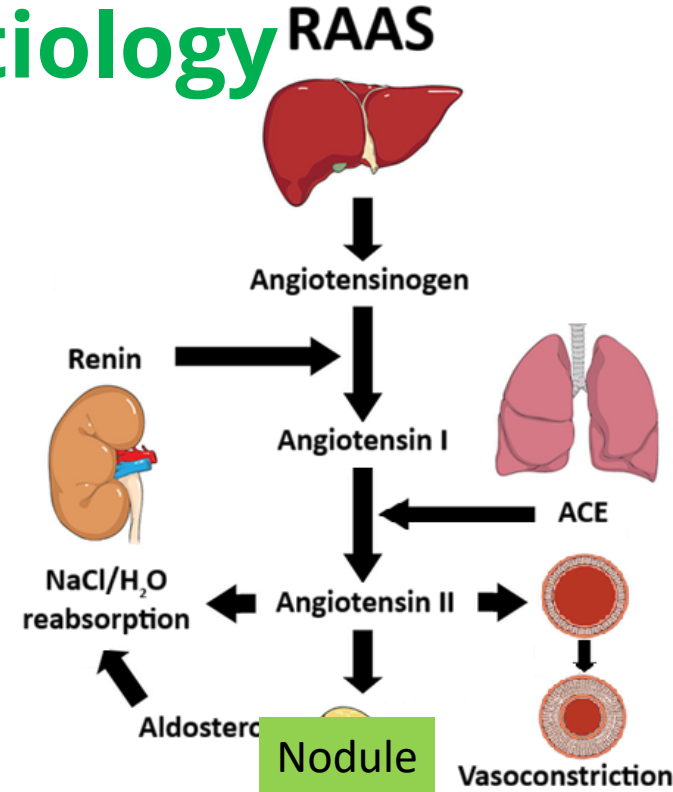
- ↓renin, ↑aldosterone, ↑ARR

2. Secondary: ↑BP vs. BP N

- ↑renin, ↑ aldosterone, ARR “N”

3. Pseudohyperaldosteronism

- ↓ renin, ↓aldosterone, ARR “N”



6. Hyperaldosteronism: Approach

1. Symptoms? Signs?

- ↑BP (resistant), ↓K (+/- diuretic use)

2. Offending agents?

- Biotin, black licorice, medications (antifungals),
 - ↑BP: steroids, OCPs, NSAIDs, sympathomimetics, calcineurin inhibitors, antidepressants, atypical antipsychotics, TKIs, chemotherapy, MAOis
 - ↓K: insulin, beta-agonists, thiazides, loop diuretics, B12/folic acid, GSF, combined antipsychotics, laxatives, abiraterone
- Spironolactone

3. Screening (after minimizing interference from 2.)

- Seated 30 min aldosterone renin ratio, electrolytes



6. Hyperaldosteronism: Nuance

- Screening: aldosterone renin ratio
 - Seated 30 min
 - False positives/negatives
 - No spironolactone!
- Confirmation (GIM/Endo):
 - Oral salt load
 - Saline suppression
- [Localization: adrenal venous sampling]

*Pearl: no spironolactone before ARR

6. Hyperaldosteronism: Treatment

1. Surgery preferred
2. Aldosterone-blocker 2nd-line
 - E.g. spironolactone

6. Hyperaldosteronism: Summary

Symptoms?

- ↑BP (resistant)
- ↓K



Screen

- No biotin x 7d
- Offending agent?
- 6wk no spiro



Confirm

- GIM/Endo



Treat

Seated 30 min
aldosterone
renin ratio,
electrolytes
(**hCG**)

Saline
suppression

Surgery
vs.
Aldosterone
blockade

“I can feel it in my *bones*”

Case 7: PH 69F

- 6mo of fatigue, polyuria, kidney stones, bony pain
- PHx: breast cancer, fibromyalgia
- Meds: letrozole
- Exam: wt stable, BP N, HR N, normal
- Labs: Ca 2.75 ↑, Cr 110, eGFR 52 ↓

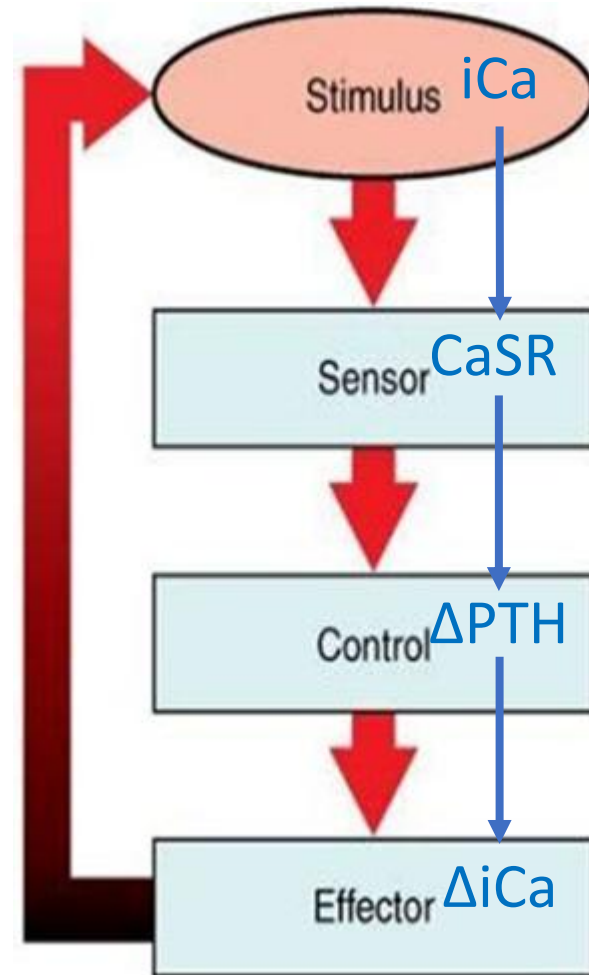


“Bone ache”

Next steps?

7. Hyperparathyroidism: Etiology

1. Primary: parathyroid source
 - Adenoma
 - $\uparrow$ cCa, * $\uparrow$ PTH, $\downarrow$ PO₄
2. Secondary: appropriate
 - $\downarrow$ Vitamin D, celiac, CKD
 - cCa N (or $\downarrow$), $\uparrow$ PTH
3. Tertiary: parathyroid source
 - Advanced CKD
 - $\uparrow$ cCa, $\uparrow$ PTH



7. Hyperparathyroidism: Approach

1. Symptoms? Signs?

- Bone pain, anorexia, nausea/vomiting, constipation, lethargy, weakness, polyuria, polydipsia, depression, arthralgia, cognitive changes, nephrolithiasis, fragility fracture

2. Offending agents?

- Biotin, medications (calcium, thiazides, lithium, teriparatide, vitamin A, theophylline, tamoxifen, TPN)

3. Screening (after minimizing interference from 2.)

- Calcium, albumin, magnesium, PO₄, PTH, hCG (♀ child-bearing)
- Complications: BMD (distal radius), abdominal imaging, 24h urine calcium/creatinine



7. Hyperparathyroidism: Nuance

- Screening: cCa (Ca + ALB), PTH
 - Correct up or down
 - ↓PO4 (PTH – “Phosphate Trashing Hormone”)
- Complications:
 - Serum Ca/Cr + 24h urine Ca/Cr
 - BMD (incl. “distal radius”)
 - Imaging (nephrocalcinosis/lithiasis)

Corrected Ca (cCa): ↑ serum [Ca] by 0.2 mmol/L for every ↓ of 10 g/L (below 40 g/L) in serum [ALB]
(or ↑ 0.02 for every ↓ 1 g/L)

***Pearl: use corrected Ca**

Corrected Ca (cCa): ↓ serum [Ca] by 0.2 mmol/L for every ↑ of 10 g/L (above 40 g/L) in serum [ALB]
(or ↓ 0.02 for every ↑ 1 g/L)

7. Hyperparathyroidism: Treatment

1. Surgery preferred

- Symptomatic
- Asymptomatic
 - <50 y, osteoporosis/fragility fracture, [Ca] >0.25 ULN, 24h uCa >10 ♂ (>6.5 ♀), CrCl <60, nephrolithiasis/calcinosis

2. Medications 2nd-line

- Osteoporosis/penia: bisphosphonates
- Very ↑Ca: cinacalcet

7. Hyperparathyroidism: Summary

Symptoms?

- Polyuria
- Polydipsia
- Nephrolithiasis
- Fragility fracture



Screen

- No biotin x 7d
- Offending agent?



Confirm

- Complications



Treat

Calcium,
albumin
(corrected),
PTH, PO4
(**hCG**)

24h urine
calcium/
creatinine, BMD,
Imaging

Surgery
vs.
Medications

“Clumsy me, *bumping*
into things”

Case 8: PA 61M

- 6mo of fatigue, headaches, “brain fog”, erectile dysfunction, reduced libido, minor MVC
- PHx: depression, obesity
- Meds: bupropion, citalopram
- Exam: wt stable, BP N, ↓HR, ↓reflexes visual field deficit, dry skin, no orthostasis
- Labs: TSH N, total testosterone 5.5 ↓



“Clumsy”

Next steps?

8. Hypopituitarism: Etiology

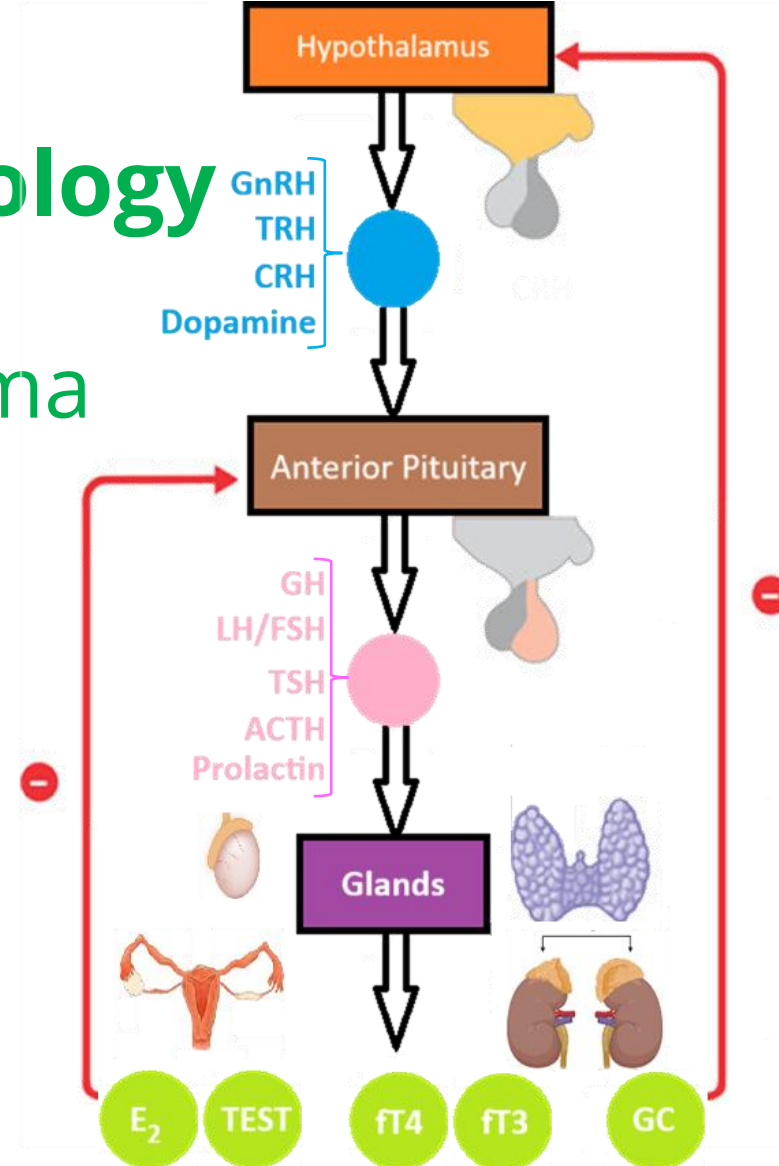
1. Nonfunctioning adenoma

- Most common

2. Functioning adenoma

- Prolactinoma most common
- Cushing's disease next
- Rare: GnRHoma, TSHoma

3. Non-pituitary mass



¹⁰Snyder et al. 2026

GnRH = gonadotropin-releasing hormone; TRH = thyrotropin-releasing hormone; CRH = corticotropin-releasing hormone
GH = growth hormone; LH = luteinizing hormone; FSH = follicle-stimulating hormone; ACTH = adrenocorticotrophic hormone;
E₂ = estradiol; TEST = testosterone; fT4 = free thyroxine; fT3 = free triiodothyronine; GC = glucocorticoids

8. Hypopituitarism: Etiology

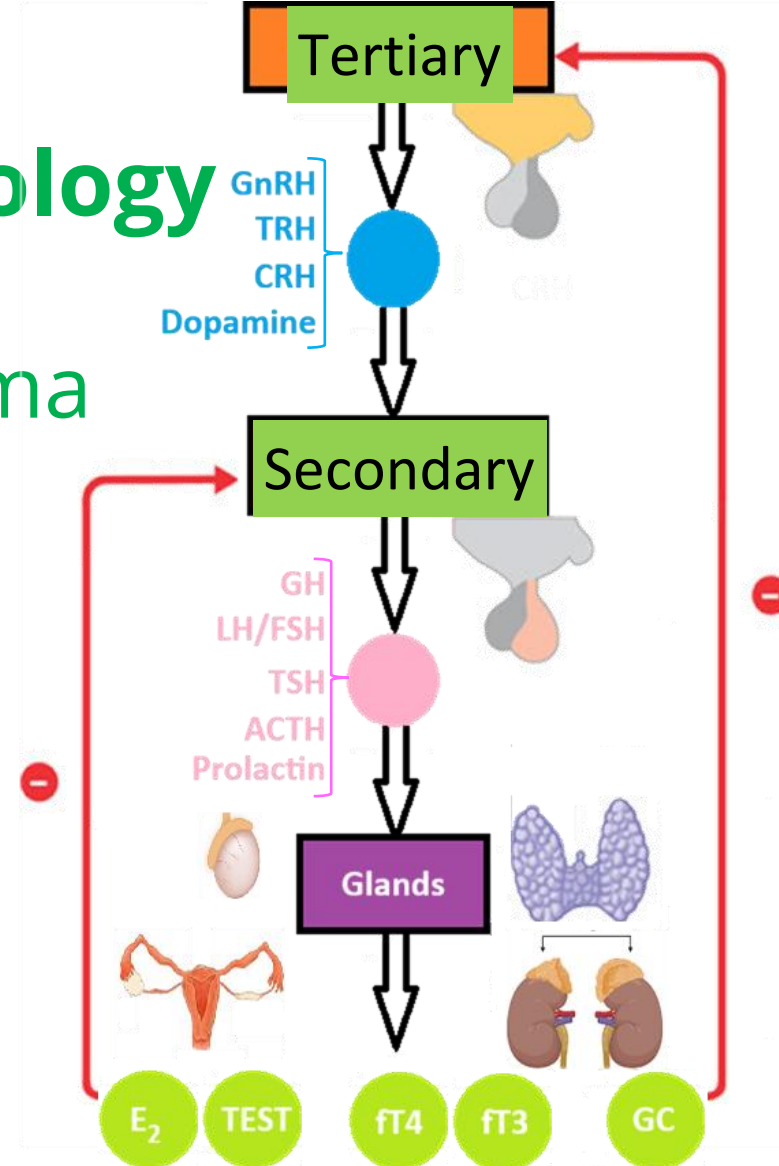
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E₂ = estradiol; TEST = testosterone; fT₄ = free thyroxine; fT₃ = free triiodothyronine; GC = glucocorticoids

8. Hypopituitarism: Approach

1. Symptoms? Signs?

- Galactorrhea, polyuria, polydipsia, skin tags, changes to ring/shoe/gat size, *hypothyroidism, *adrenal insufficiency, *hypogonadism
- Mass effect: new/persistent headache, peripheral vision changes

2. Offending agents?

- Biotin, cannabis, medications (steroids, opioids, immunotherapy, chemotherapy, radiation)

3. Screening (after minimizing interference from 2.)

- Prolactin, FSH, LH, E2/testosterone, fT4, 8AM cortisol, insulin-like growth factor-1, creatinine, eGFR, hCG (♀ child-bearing)

4. Imaging: sellar MRI (NOT CT head)



¹⁰Snyder et al. 2026

LH = luteinizing hormone; FSH = follicle-stimulating hormone;
E2 = estradiol; fT4 = free thyroxine; hCG = beta-human chorionic gonadotropin;

8. Hypopituitarism: Nuance

*Pearl: fT4 to screen for central hypothyroidism

- Can present as hyperfunctioning, hypofunctioning, or both
- Screen for other deficiencies

- 
- | | | |
|-------------------------------|-----------|------------------------|
| • (<u>G</u> o): | GH | IGF-1 |
| • (<u>L</u> ook <u>E</u> or) | LH/FSH | E2/testosterone |
| • (<u>T</u> he) | TSH | TSH <u>AND</u> fT4 |
| • (<u>A</u> denoma) | ACTH | 8AM cortisol |
| • (<u>P</u> lease) | Prolactin | 8AM, fasting prolactin |

*Pearl: order of
↓pituitary affected

¹⁰Snyder et al. 2026

GH = growth hormone; IGF-1 = insulin-like growth factor-1; LH = luteinizing hormone; FSH = follicle-stimulating hormone; E2 = estradiol; fT4 = free thyroxine; ACTH = adrenocorticotrophic hormone

8. Hypopituitarism: Nuance

*Pearl: exclude
physiologic
↑PRL

- (Go): GH – IGF-1
 - Do NOT order GH
- (Look For): LH/FSH – fasting, 8AM testosterone
 - Need low level x 2 to diagnose hypogonadism
- (The): TSH – free T4 (write “exception”)
 - TSH can be inappropriately N despite ↓fT4
- (Adenoma): ACTH – 8AM cortisol (i.e. Case 1)
- (Please): prolactin – fasting, no sexual/physical activity for 48h, no biotin/marijuana for 7d
 - Minimize physiologic causes of ↑PRL

¹⁰Snyder et al. 2026

GH = growth hormone; IGF-1 = insulin-like growth factor-1; LH = luteinizing hormone; FSH = follicle-stimulating hormone; T4 = thyroxine; ACTH = adrenocorticotrophic hormone

8. Hypopituitarism: Treatment

1. Surgery preferred

2. Medications 2nd-line

- *Prolactinoma: 1st-line
 - Dopamine agonists

8. Hypopituitarism: Summary

Symptoms?

- Galactorrhea
- Visual field changes
- *Other axes



Screen

- No biotin/
cannabis x
7d
- Offending
agent?

Prolactin, FSH,
LH, E2/test,
fT4, 8AM
cortisol, IGF-1,
creatinine,
eGFR (**hCG**)



Confirm

- GIM/Endo

Sellar MRI



Treat

Surgery
vs.
*Medication

“I’m *anxious* all of a sudden”

Case 9: PCC 27F

- 3mo of fatigue, anxiety, palpitations, headache, diaphoresis
- PHx: none
- Meds: ashwanganda
- Exam: wt stable, BP N, HR N, normal
- 2nd visit: pallor, ↑BP, ↑HR, orthostasis, diaphoretic
- Labs: TSH N, 8AM cortisol 410, ferritin N



“New anxiety”

Next steps?

9. Pheochromocytoma: Etiology

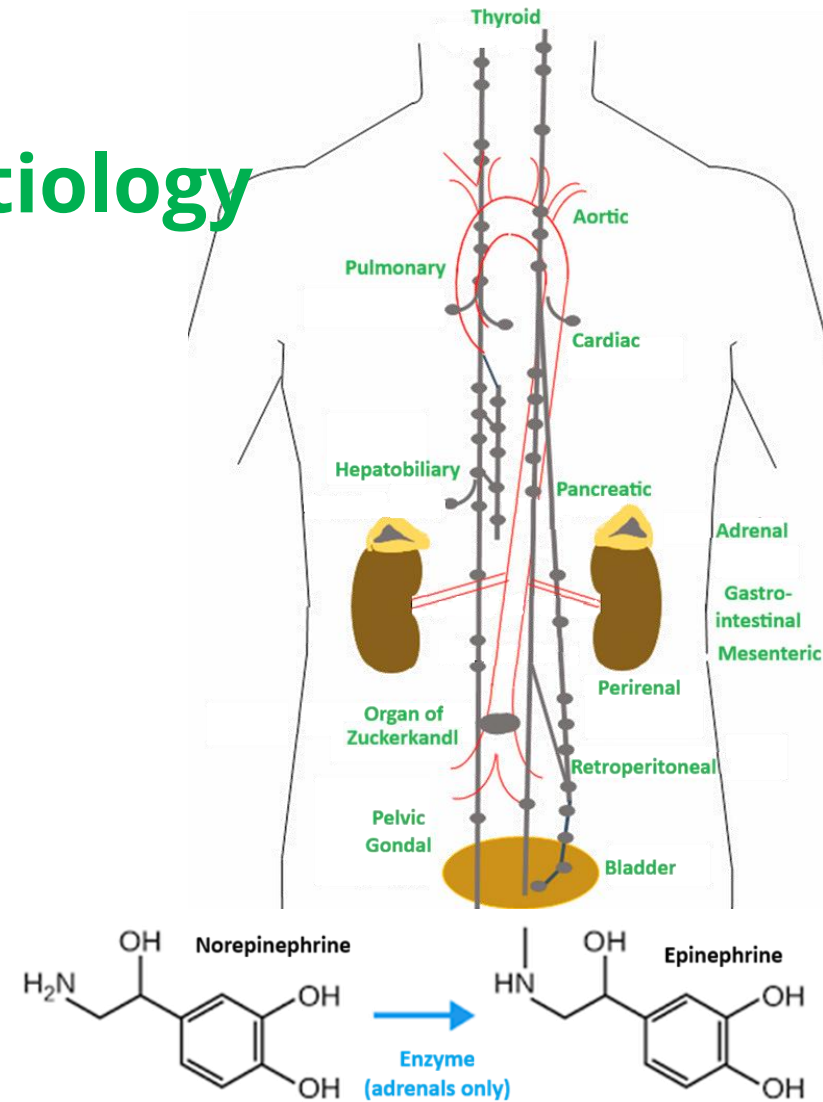
1. Pheochromocytoma:

- Adrenal
 - ↑epinephrine,
↑norepinephrine

2. Paraganglioma:

- Sympathetic chain
 - Epinephrine N,
↑norepinephrine

3. Other



9. Pheochromocytoma: Etiology

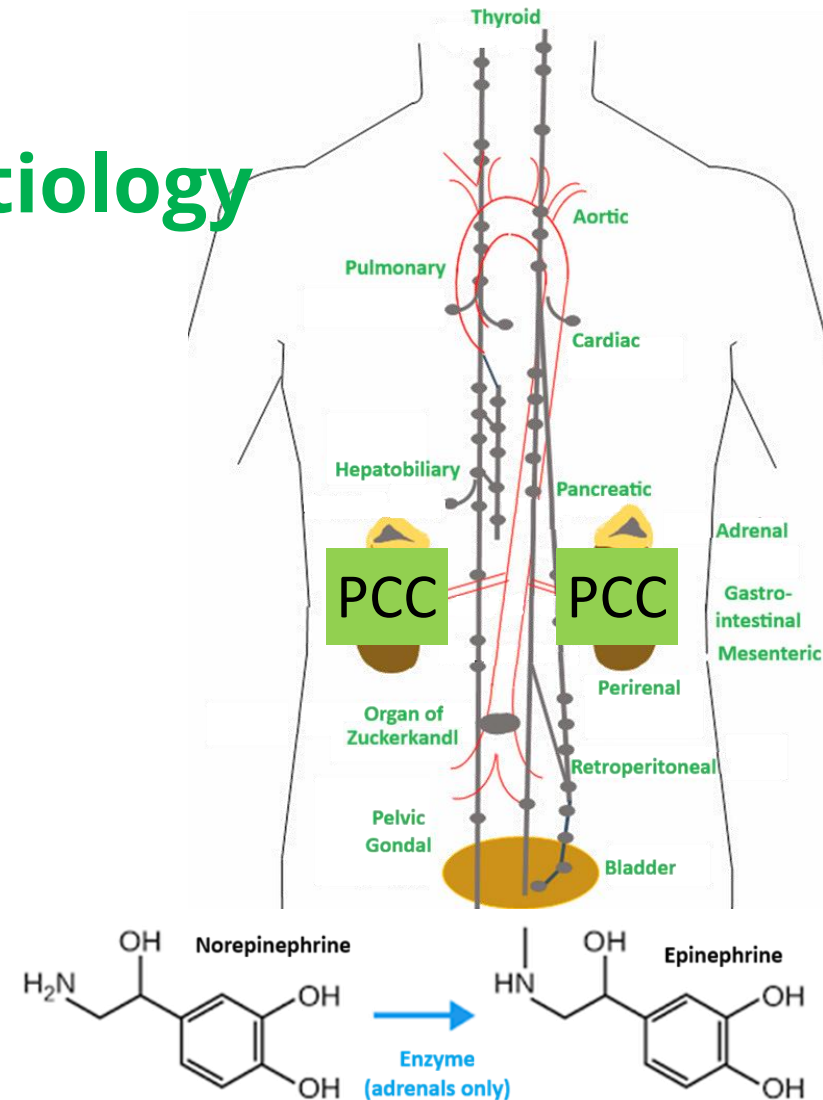
1. Pheochromocytoma:

- Adrenal
 - ↑epinephrine,
↑norepinephrine

2. Paraganglioma:

- Sympathetic chain
 - Epinephrine N,
↑norepinephrine

3. Other



9. Pheochromocytoma: Approach

1. Symptoms? Signs?

- Episodic **triad** (headache, palpitations, diaphoresis), tremor, diaphoresis, pallor, weakness, anxiety, orthostasis, presyncope, visual changes, polyuria, polydipsia, cognitive changes, *hypertension

2. Offending agents?

- [Biotin](#), [ashwaganda](#), medications – palpitations (anticholinergics, vasodilators, sympathomimetics), diaphoresis (antidepressants, cholinergics, aromatase/ADT, beta blockers, CCBs, triptans, interferon, opioids, donepezil, niacin)

3. Screening (after minimizing interference from 2.)

- 24h urine catecholamines, fractionated metanephrines, creatinine
- Other: TSH, FSH/LH/E2, [hCG](#) (♀ child-bearing)

4. Imaging: [unenhanced](#) abdominal CT reporting “Hounsfield units”



¹¹Young et al. 2026

ADT = androgen deprivation therapy; CCBs = calcium channel blockers; E2 = estradiol
hCG = human chorionic gonadotropin;

9. Pheochromocytoma: Nuance

- Screening: 24h urine catecholamines + fractionated metanephrines
 - False positives
- [Localization: abdominal imaging +/- others]
 - If HU < 10, then it's not a pheo...

9. Pheochromocytoma: Treatment

1. Surgery preferred
2. Medications required beforehand
 - Alpha blockade, then beta blockade

9. Pheochromocytoma: Summary

Symptoms?

- Triad
- ↑BP



Screen

- No biotin x 7d
- Offending agent?



Confirm

- GIM/Endo



Treat

24h urine
catecholamines
fractionated
metanephrines,
creatinine,
(hCG)

Unenhanced
abdominal CT

Medication
(alpha→beta),
then
Surgery

“I feel like I’m *blushing* all
the time”

Case 10: CS 82M

- 6mo of fatigue, “flushing”, diarrhea, wheezing
- PHx: hypertension, dyslipidemia, type 2 diabetes, obesity
- Meds: metformin 1000mg BID, semaglutide 1.0 mg, ramipril 10mg, spironolactone 25mg, rosuvastatin 10mg
- Exam: wt stable, BP N, HR N, facial plethora, new systolic ejection murmur, chest telangiectasia
- Labs: TSH N, liver tests N, testosterone N

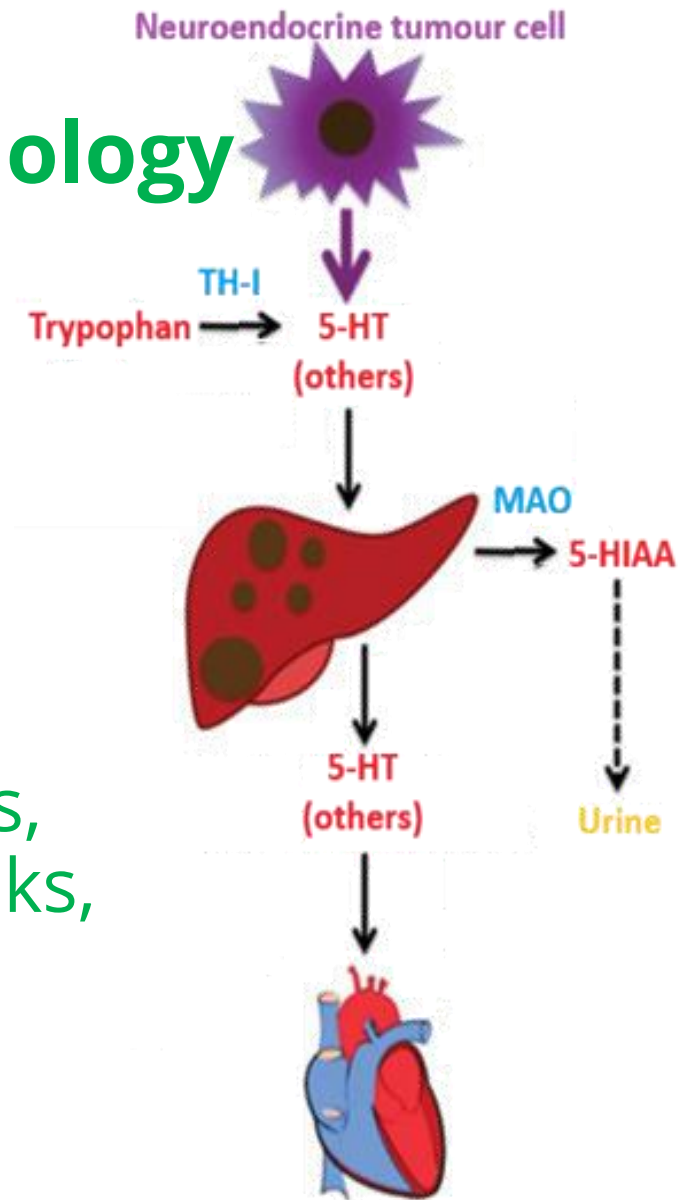


“Blushing”

Next steps?

10. Carcinoid Syndrome: Etiology

- Neuroendocrine tumor
 - Serotonin excess
 - ↑5-HIAA (urine)
- Flushing:
 - Menopause, emotional stress, anaphylaxis, alcohol/hot drinks, POTS, liver disease, *↑THY, medications



10. Carcinoid Syndrome: Approach

1. Symptoms? Signs?

- Flushing, diarrhea, abdominal pain, telangiectasia, bronchoconstriction, cyanosis, pellagra, heart murmur

2. Offending agents?

- Biotin, tryptophan foods, medications (acetaminophen, phenobarbital, ephedrine, methamphetamine, nicotine, phentolamine, caffeine, fluorouracil, mesalamine)

3. Screening (after minimizing interference from 2.)

- Urine 5-HIAA
- Other: TSH, FSH/LH/E2, hCG (♀ child-bearing), Echocardiogram (if new murmur)



10. Carcinoid Syndrome: Nuance

- Screening: urinary 5-HIAA
 - NOT serotonin, serum 5-HIAA
 - False positives:
 - Tryptophan foods, caffeine, nicotine, OTC medications
 - Restrict diet for 3d before testing
- [Localization: imaging]

*Pearl: exclude
exogenous
causes of
↑5-HIAA

10. Carcinoid Syndrome: Treatment

1. Surgery preferred

2. Medications 2nd-line

10. Carcinoid Syndrome: Summary

Symptoms?

- Flushing
- Diarrhea
- Telangiectasia
- Murmur



Screen

- No biotin x 7d
- Offending agent/food?



Confirm

- GIM/Endo



Treat

Urine 5-HIAA,
TSH,
FSH/LH/E2,
+/- Echo
(**hCG**)

Various
imaging
modalities

Surgery
vs.
Medications

III. When to Call Endocrinology



- Red flag + abnormal workup
- If you need help ordering the right test
- If you need help interpreting the test
- When something does not make sense...
 - Referral checklists included below
- Common causes of fatigue: referral NOT required: ↓THY, type 2 diabetes, ↓ vitamin D

“I want to see a specialist”

III. Checklist Template

- ☐ Clear clinical question
- ☐ Symptoms of issue
- ☐ Supplements containing [biotin](#)
- ☐ Updated medication list, including drug allergies, medications tried for this issue
- ☐ Labs (7d [no biotin](#)):
- ☐ Imaging:

Take Away Points

- When faced with fatigue, identify red flags
- Initial workup for fatigue should be guided by symptoms/findings
 - Not all testing is useful
- Be mindful of common nuances of endocrine testing
 - Try to eliminate interferences before screening
- Refer to Endocrinology for less common causes (if red flag AND abnormal result)

**Questions?
Thoughts?**

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III. Adrenal Insufficiency Checklist

- ☐ Clear clinical question
- ☐ Symptoms of adrenal insufficiency
- ☐ Supplements containing [biotin](#)
- ☐ Updated medication list, including drug allergies, medications tried for this issue
- ☐ Labs (7d [no biotin](#), 48h no GCs): 8 AM cortisol, ACTH, electrolytes, fasting glucose, creatinine, eGFR, ALT, bilirubin, albumin, TSH, free T4, FSH, LH, E2/total testosterone, 21-hydroxylase antibodies, hCG (if ♀)

III. Hypercortisolism Checklist

- ☐ Clear clinical question
- ☐ Symptoms of cortisol excess
- ☐ Supplements containing [biotin](#)
- ☐ Updated medication list, including drug allergies, medications tried for this issue
- ☐ Labs (7d [no biotin](#), 48h no GCs): 8AM cortisol (following 1mg dexamethasone at 11PM evening before), ACTH, 24h urine free cortisol/creatinine, A1C, fasting glucose/lipids, creatinine, eGFR, ALT, TSH, 25-vitamin D, vitamin B12, urate, hCG (if ♀)

III. Diabetes Checklist

- ☐ Clear clinical question
- ☐ Symptoms of hyperglycemia
- ☐ Supplements containing [biotin](#)
- ☐ Updated medication list, including drug allergies, medications tried for this issue
- ☐ Refer to diabetes centre for review
- ☐ Dilated eye exam (if type 2 diabetes)
- ☐ Labs (7d [no biotin](#)): A1C, fasting glucose/lipids, creatinine, eGFR, urine ACR, ALT (if type 2 diabetes), TSH (if type 1 diabetes), hCG (if ♀), +/- GAD

III. Hypoglycemia Checklist

- ☐ Clear clinical question
- ☐ Whipple's triad?
- ☐ Supplements containing [biotin](#)
- ☐ Updated medication list, including drug allergies, medications tried for this issue
- ☐ Refer to diabetes centre for 2wk CGM trial
- ☐ Labs (7d [no biotin](#)): *fasting glucose, insulin, C-peptide, BHB, TSH, creatinine, eGFR, ALT, bilirubin, INR, 8 AM cortisol

III. Hyperthyroidism Checklist

- ☐ Clear clinical question
- ☐ Symptoms of hyperthyroidism
- ☐ Supplements containing [biotin](#), iodine
- ☐ Updated medication list, including drug allergies, medications tried for this issue
- ☐ Labs (7d [no biotin](#)): TSH, free T4, free T3, antibodies ([thyroid receptor antibody](#) AND anti-TPO), CBC, ALT, bilirubin, CRP, hCG (if ♀)
- ☐ Thyroid ultrasound (only if [abnormal](#) exam)

III. Hyperaldosteronism Checklist

- ☐ Clear clinical question
- ☐ Resistant hypertension or hypokalemia
- ☐ Supplements containing [biotin](#), sodium, potassium, black licorice
- ☐ Updated medication list, including drug allergies, medications tried for this issue
- ☐ Labs (7d [no biotin](#)), 6wk no spironolactone): seated 30 min aldosterone renin ratio, electrolytes, creatinine, eGFR, hCG (if ♀)

III. Hypercalcemia Checklist

- ☐ Clear clinical question
- ☐ Symptoms of hypercalcemia
- ☐ Supplements containing [biotin](#), calcium, vitamin D
- ☐ Updated medication list, including drug allergies, medications tried for this issue
- ☐ Labs (7d [no biotin](#)): calcium, albumin, PTH, magnesium, phosphate, creatinine, eGFR, ALP, 25-vitamin D collected concurrently with 24h urine calcium and creatinine, hCG (if ♀)
- ☐ BMD: include distal radius

III. Pituitary Mass Checklist

- ☐ Clear clinical question
- ☐ Symptoms of hormone excess/deficiency or mass effect
- ☐ Supplements containing [biotin](#)
- ☐ Updated medication list, including drug allergies, medications tried for this issue
- ☐ Labs (fasting, 7d [no biotin](#)/cannabis, 48h no physical/sexual activity): prolactin, FSH, LH, E2/testosterone, free T4, 8AM cortisol, insulin-like growth factor-1, creatinine, eGFR, hCG (if ♀)
- ☐ Sellar MRI: esp. if 2 abnormal axes

III. Pheochromocytoma Checklist

- ☐ Clear clinical question
- ☐ Symptoms of catecholamine excess
- ☐ Supplements containing [biotin](#)
- ☐ Updated medication list, including drug allergies, medications tried for this issue
- ☐ Labs (7d [no biotin](#)): TSH, creatinine, eGFR, 24h urine (catecholamines/fractionated metanephrines, creatinine), hCG (if ♀)
- ☐ Abdominal CT (unenhanced)

III. Carcinoid Checklist

- ☐ Clear clinical question
- ☐ Symptoms of carcinoid syndrome
- ☐ Supplements containing [biotin](#)
- ☐ Updated medication list, including drug allergies, medications tried for this issue
- ☐ Labs (7d [no biotin](#), 3d foods): urine 5-HIAA, TSH, FSH/LH/E2, hCG (if ♀)
- ☐ Echocardiogram (if new murmur)