



Brigham and Women's Hospital

Founding Member, Mass General Brigham

Endocrinology: Additional Clinical Pearls and Take-Home Messages

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- Clinical focus: Diabetes, Endocrine Disease in Pregnancy
- Research focus: barriers to diabetes care, transition of care, system improvement and development of innovative models of diabetes care

DISCLOSURES

Research funding: Dexcom

Topics

- Diabetes
- Thyroid
- Pituitary
- Adrenal
- Hypoglycemia

A 63-year-old male with longstanding history of DM type 2 now complicated by retinopathy, albuminuria (>300 mg/d) and neuropathy. PMHx also notable for CAD, OSA, MASH, class II obesity

Current diabetes regimen:

Metformin 1000 mg BID

Glimepiride 4 mg daily

Glargine 40 units daily

HbA1c is 8.5%

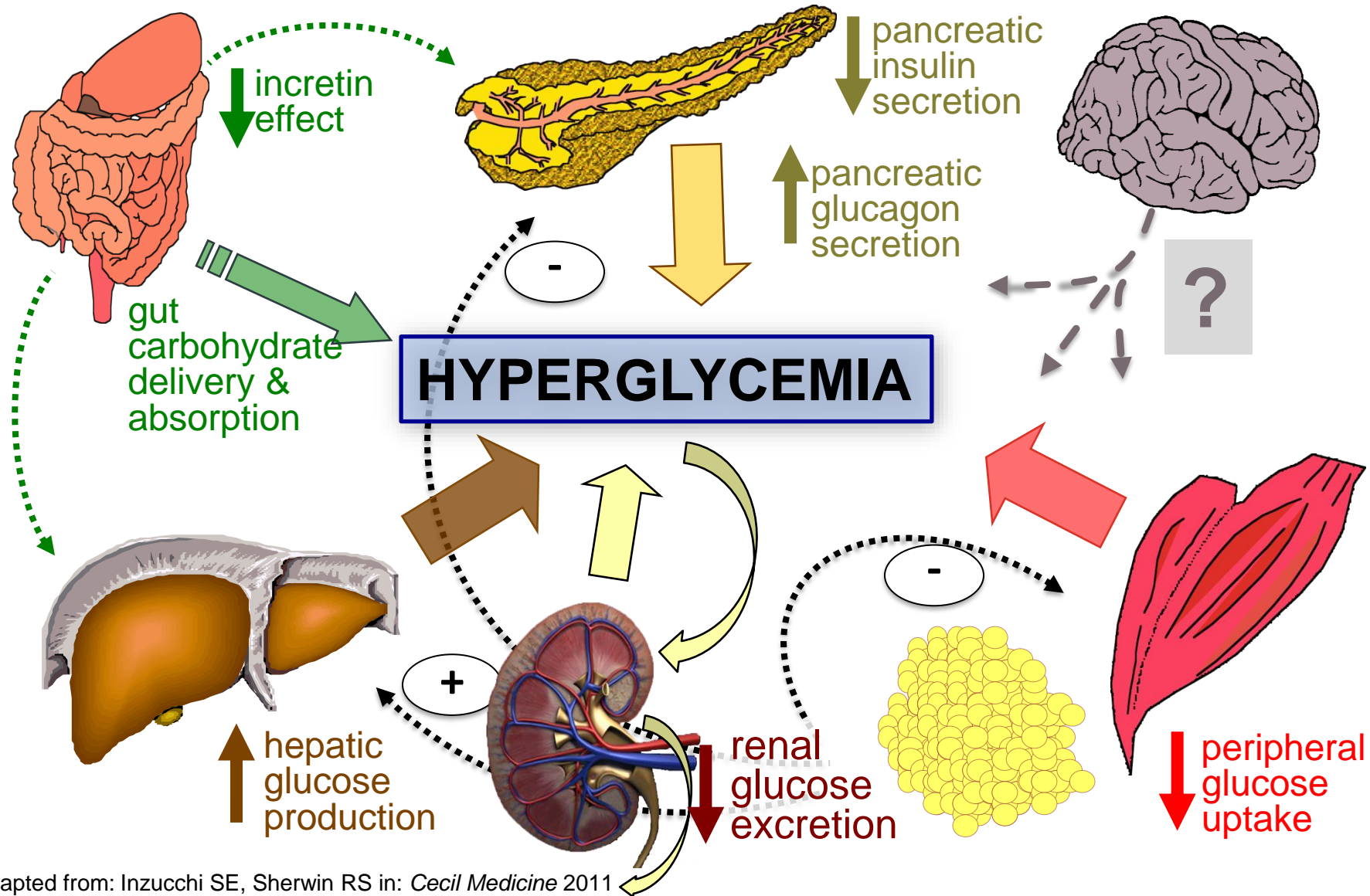
Which of the following treatments would you add to diabetes regimen?

- A. GLP1-receptor agonist
- B. SGLT2-inhibitor
- C. DPP4-inhibitor
- D. TZD
- E. Rapid acting insulin with largest meal

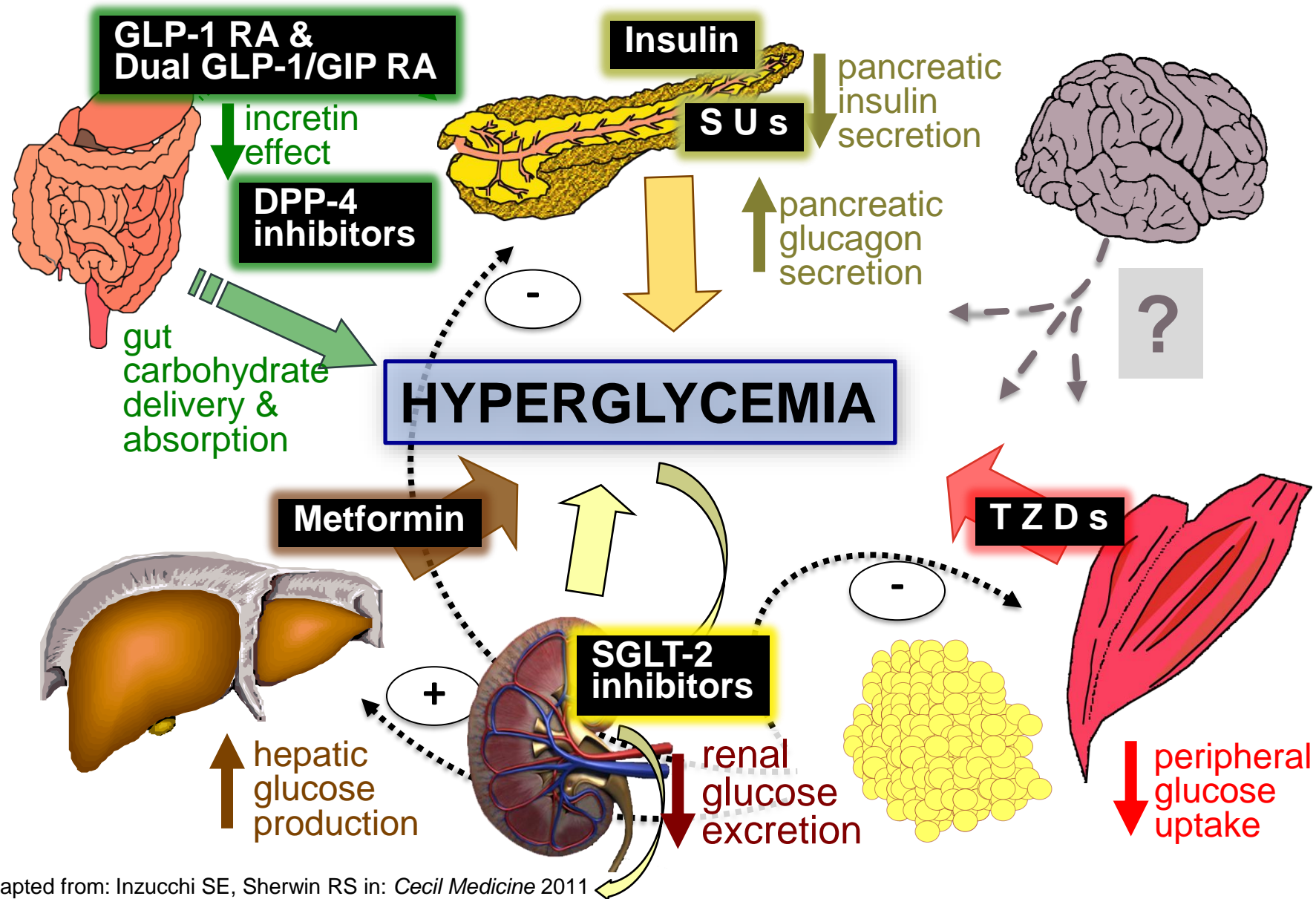
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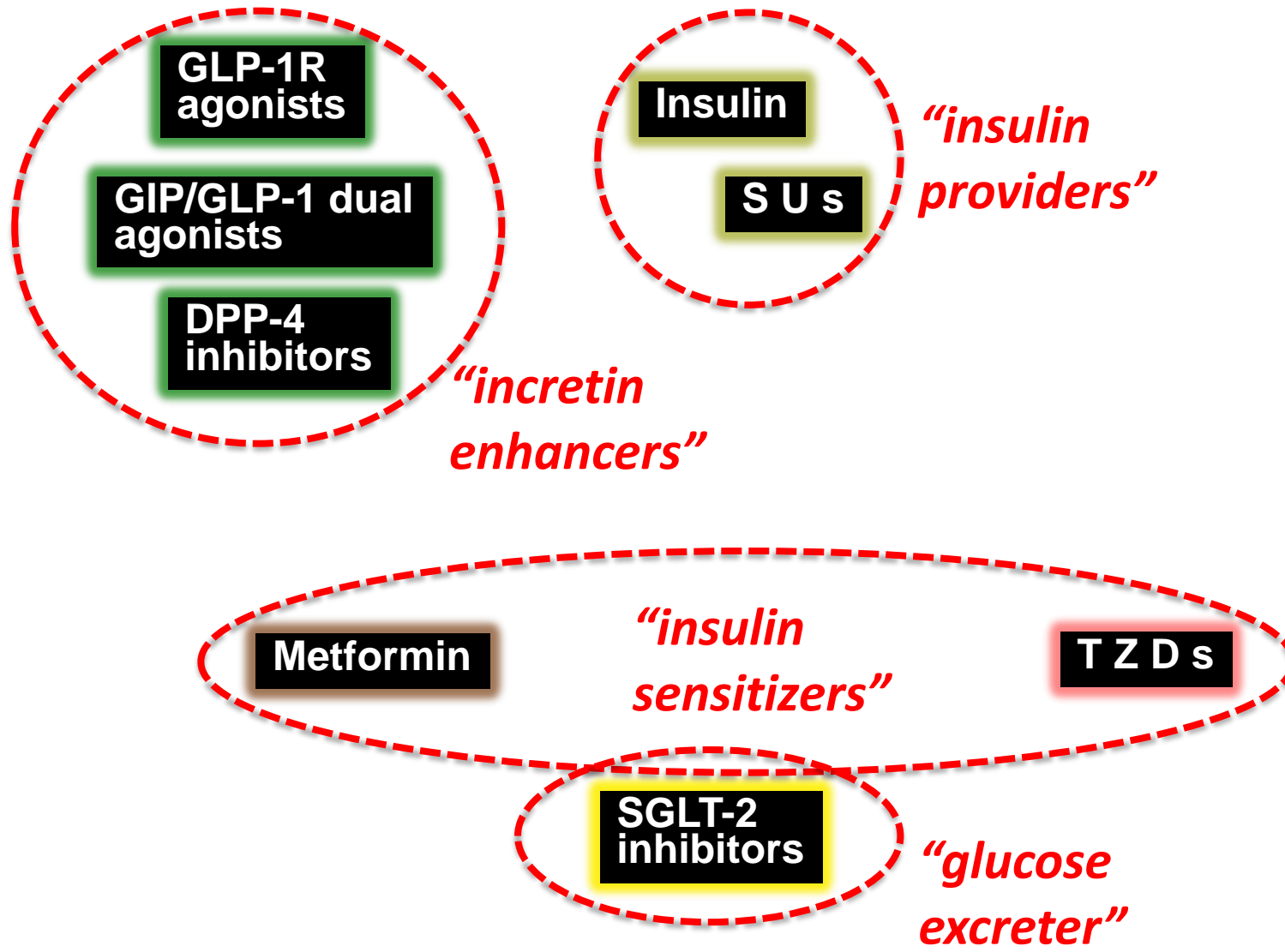
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Multiple Complex Pathophysiological Abnormalities in T2DM










Major Pathophysiologically-Based Therapies for T2DM





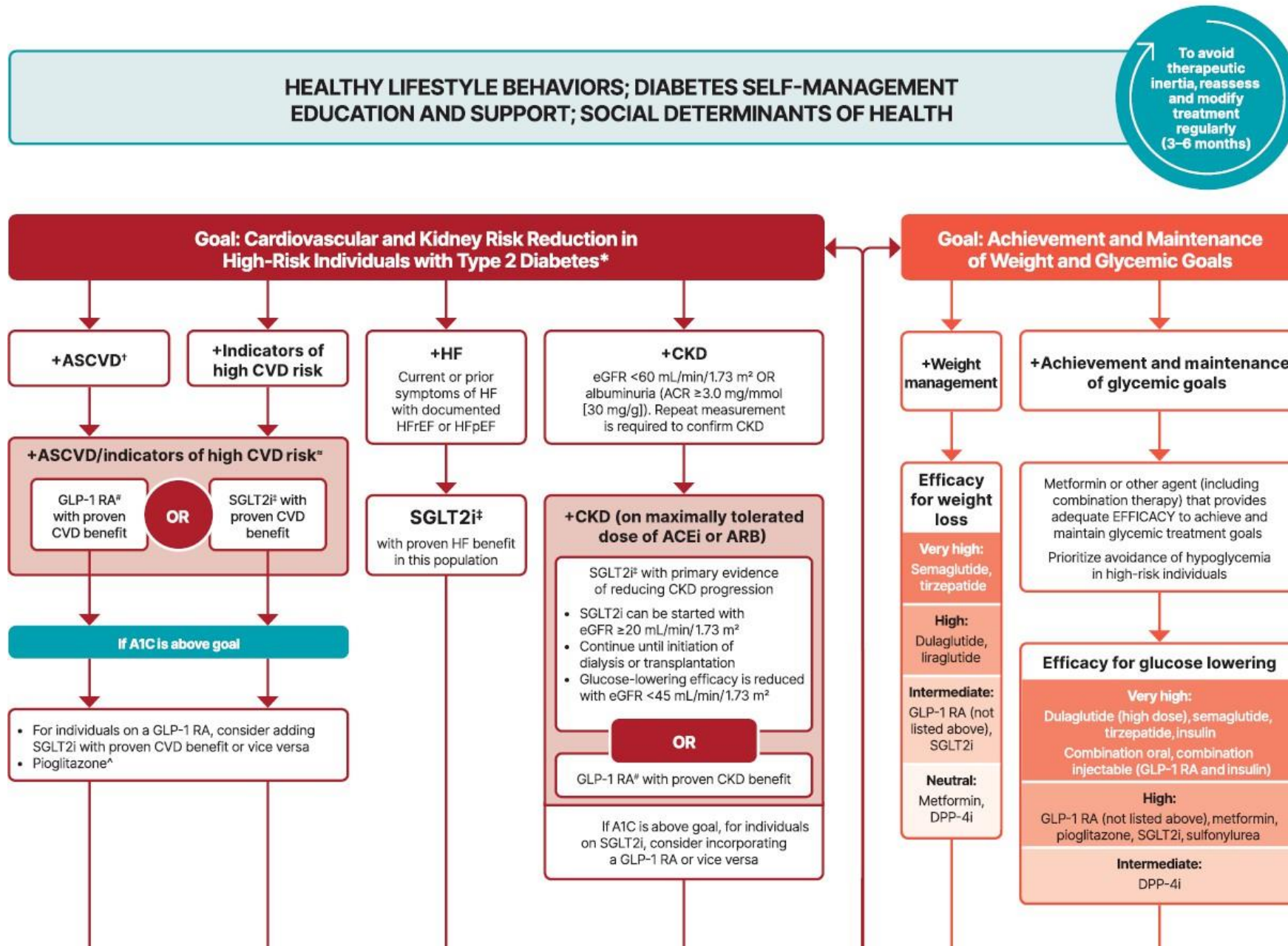
Glucose Lowering Drugs Classes

Classes	Generic Names	↓ A1c	Side effects
Insulin 	Degludec, Glargine, Detemir, NPH, Regular, Lispro, Aspart, Glulisine	No limit	<u>Hypoglycemia</u> , weight gain, Injections
SU's 	Glyburide, Glipizide, Glimepiride	1-1.5%	<u>Hypoglycemia</u> , weight gain
Metformin 	Metformin	1-1.5%	<u>GI</u> , B-12 deficiency, lactic acidosis
TZD's 	Pioglitazone	1-1.5%	<u>CHF</u> , Weight gain, edema, bone fx's, ?bladder ca
DPP-4 i's 	Sitagliptin, Saxagliptin, Alogliptin, Linagliptin	0.5-1%	Urticaria, arthralgias (rare) pancreatitis
Incretin RA's  	GLP-1: Exenatide, Liraglutide, Dulaglutide, Semaglutide GLP-1/GIP dRA: Tirzepatide	1-1.5%	<u>GI</u> , gallbladder, ?pancreatitis
SGLT2-i's	Canagliflozin, Dapagliflozin, Empagliflozin	0.5-1%	<u>GU infections</u> , Polyuria, euDKA, ?fractures

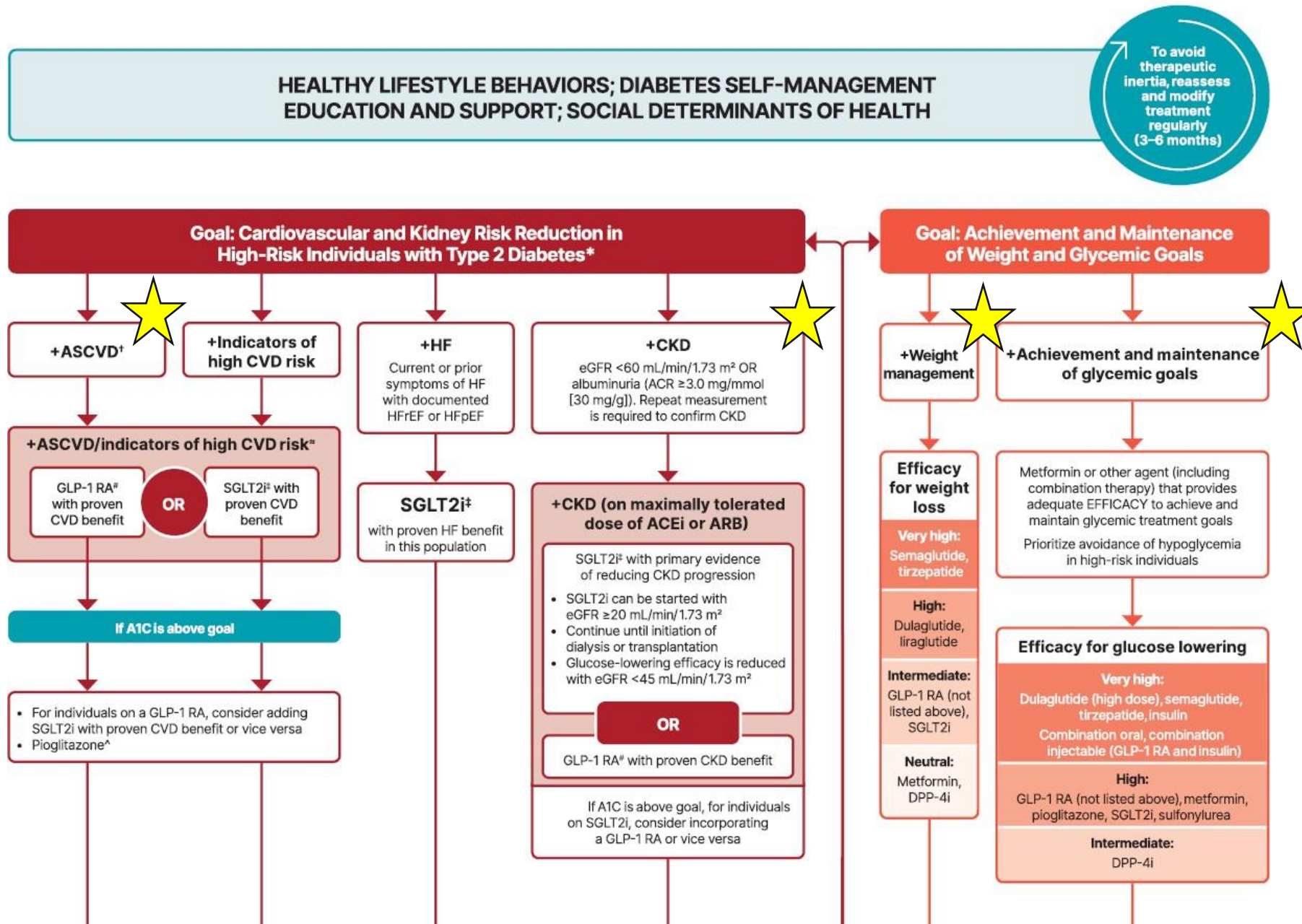
Putting it all Together for the Individual



Use of Glucose-Lowering Medications in the Management of Type 2 Diabetes



Use of Glucose-Lowering Medications in the Management of Type 2 Diabetes



A 55-year-old female with longstanding DM type 2 and no known diabetes-related complications

Current diabetes regimen:

metformin 1000 mg BID

glipizide 10 mg BID

dulaglutide 4.5 mg weekly

SMBG are consistently 180 –220 mg/dL fasting and post-prandial levels 230 – 300 mg/dL

HbA1c is 10.2% and amenable to insulin

Weight is 220 lbs (100 kg)

Which of the following regimens would you recommend?

- A. Start glargine 10 units/day (0.1 unit/kg) and increase by 2-3 units every 3 days to reach FPG target
- B. Start glargine 25 units/day (0.25 units/kg) and increase by 2-3 units every 3 days to reach FPG target
- C. Start glargine 10 units/day + prandial insulin 4 units before largest meal of the day
- D. Start glargine 10 units/day + prandial insulin 4 units before every meal

Which of the following regimens would you recommend?

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Initiating insulin

Add basal insulin

Initial dose 10 units or 0.1-0.2 units/kg
Titrate based on self-monitored fasting plasma glucose*

If above HbA1c goal

Add mealtime insulin at main meal of the day

Start with 4 units or 10% of basal dose
Titrate based on self-monitored post-prandial glucose

If above HbA1c goal

Add mealtime insulin at other meals

If using pre-mixed insulin, dose up to twice daily

Taper
off SU
in most
cases
to
reduce
risk of
hypo

A 40-year-old woman presenting for annual exam. She feels well and is without complaints. On exam, her pulse is 84 and regular. She appears euthyroid without lid lag or exophthalmos. On neck exam, she has a smooth, mobile, rubbery nodule measuring ~2.5 cm. There is no lymphadenopathy, stridor, or other worrisome signs or symptoms.

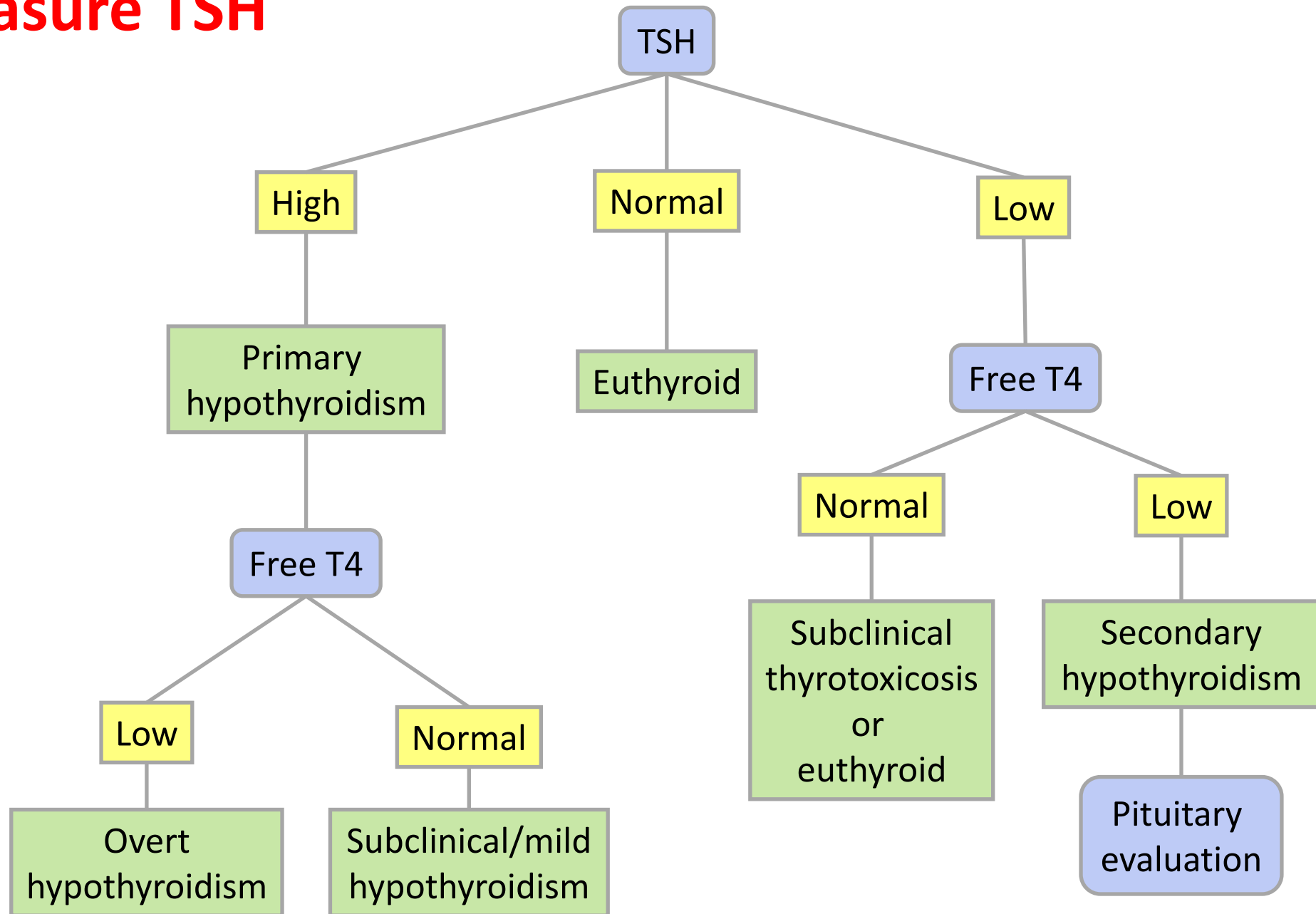
What would be your best next step?

- A. Order a thyroid ultrasound
- B. Order a TSH level
- C. Order a thyroid ultrasound and TSH level
- D. Send immediately to the Thyroid Clinic for a fine needle aspiration of the nodule

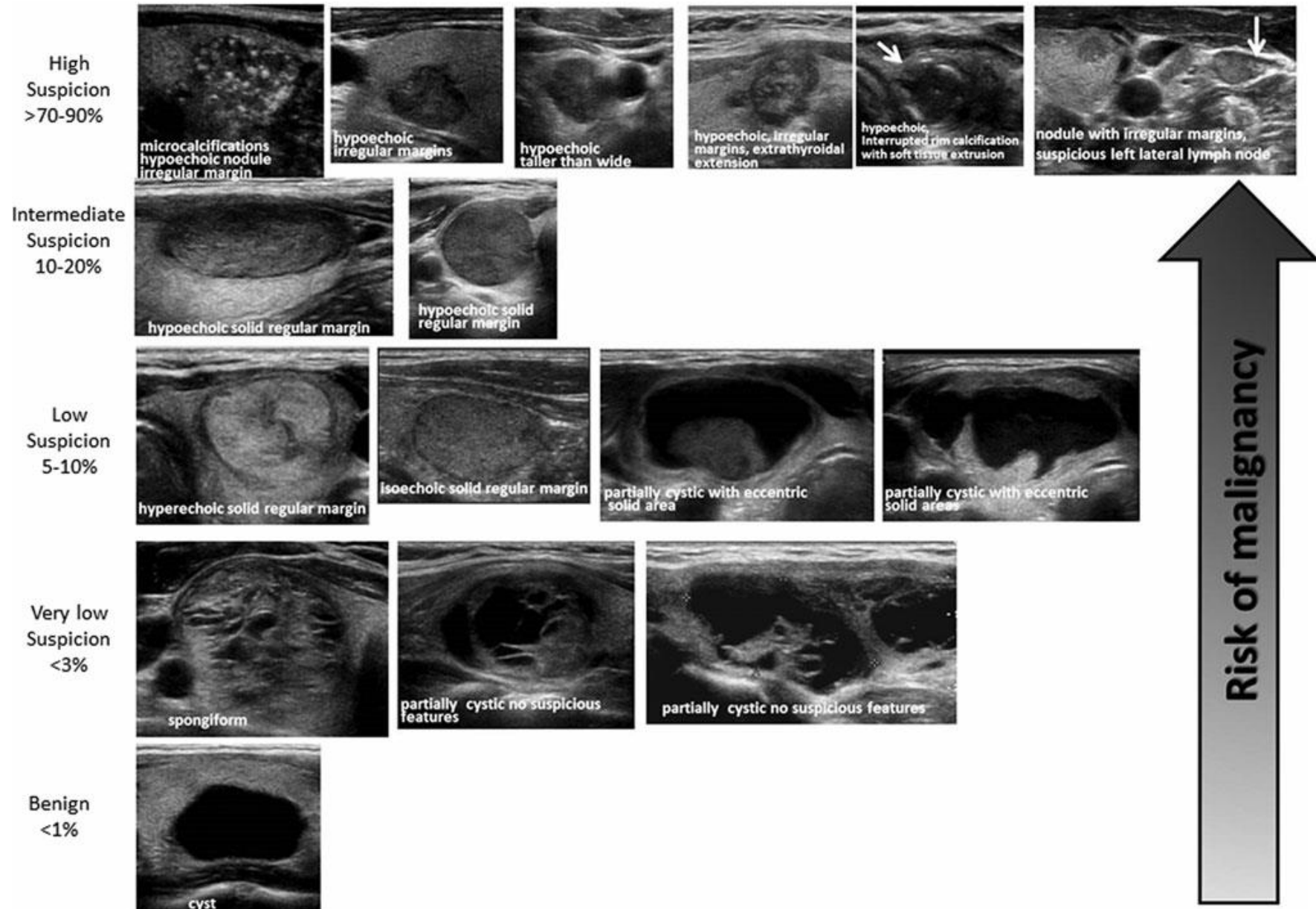
What would be your best next step?

- A. Order a thyroid ultrasound
- B. Order a TSH level
- C. Order a thyroid ultrasound and TSH level**
- D. Send immediately for a fine needle aspiration (FNA) of the nodule

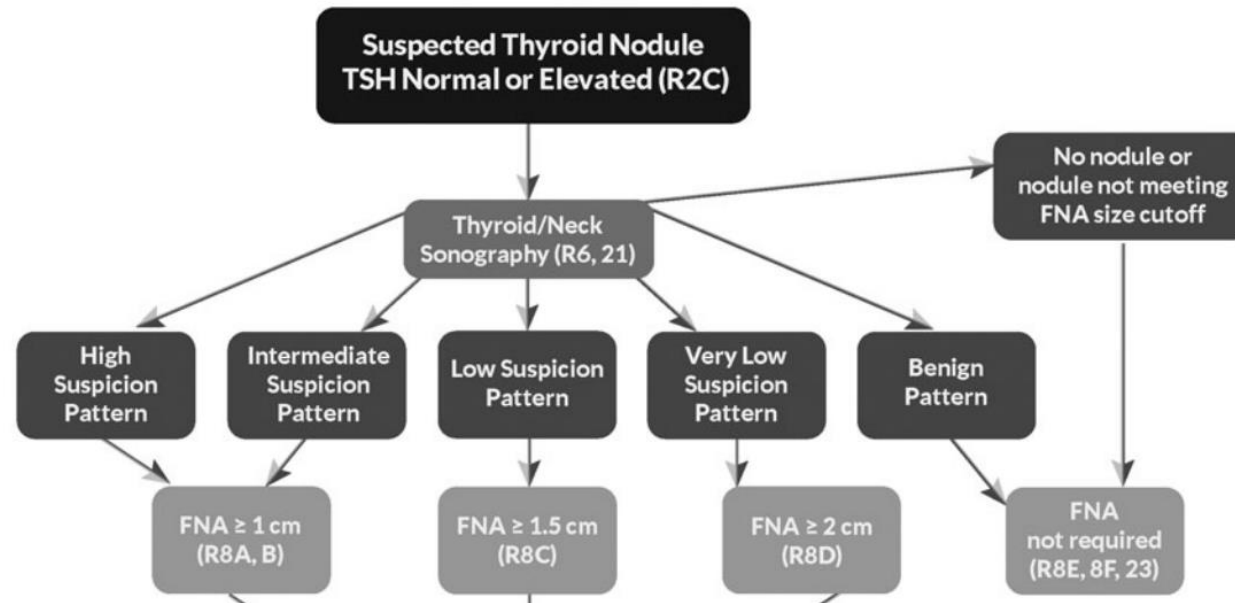
Measure TSH



Thyroid Ultrasound: Radiologic Features

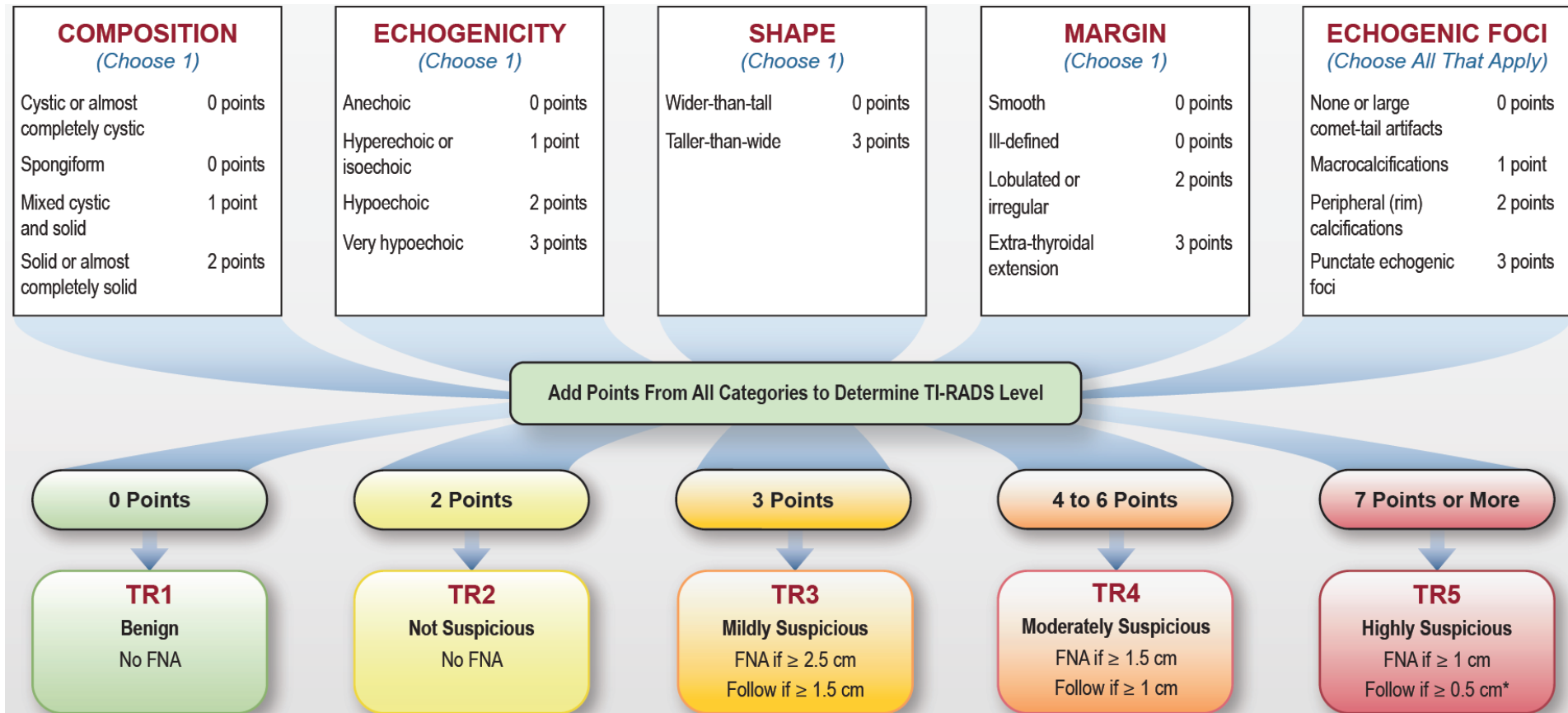


Thyroid Nodules: ATA FNA Criteria



- ≥ 1.0 cm: nodules with suspicious features
- ≥ 1.5 cm: isoechoic and hyperechoic nodules
- ≥ 2.0 cm: spongiform nodules

ACR Thyroid Imaging Reporting and Data System (TI-RADS)



Thyroid Nodules: TI-RADS FNA Thresholds

- TI-RADS 1 or 2: Not required
- TI-RADS 3: ≥ 2.5 cm
- TI-RADS 4: ≥ 1.5 cm
- TI-RADS 5: ≥ 1.0 cm
- Previously biopsied benign thyroid nodules that have enlarged do not need to be re-sampled*

30-year-old woman (G1P1) presents with excess fatigue and inability to breastfeed **2 weeks** after a difficult labor and delivery. Her traumatic delivery resulted in extensive **blood loss** and **hypotension**, requiring pressors and transfusion of 2 units PRBCs.

Meds: prenatal MVI with extra iron

On exam, she appears pale and weak, BP 90/60; visual fields and cranial nerve exams are normal; **no galactorrhea** with nipple pressure, bilaterally.

- Labs reveal: Na 130 mEq/L, K 3.6, TSH 0.1, free T4 0.8 (0.8 – 1.6), prolactin < assay, AM cortisol 1.8 ug/dL

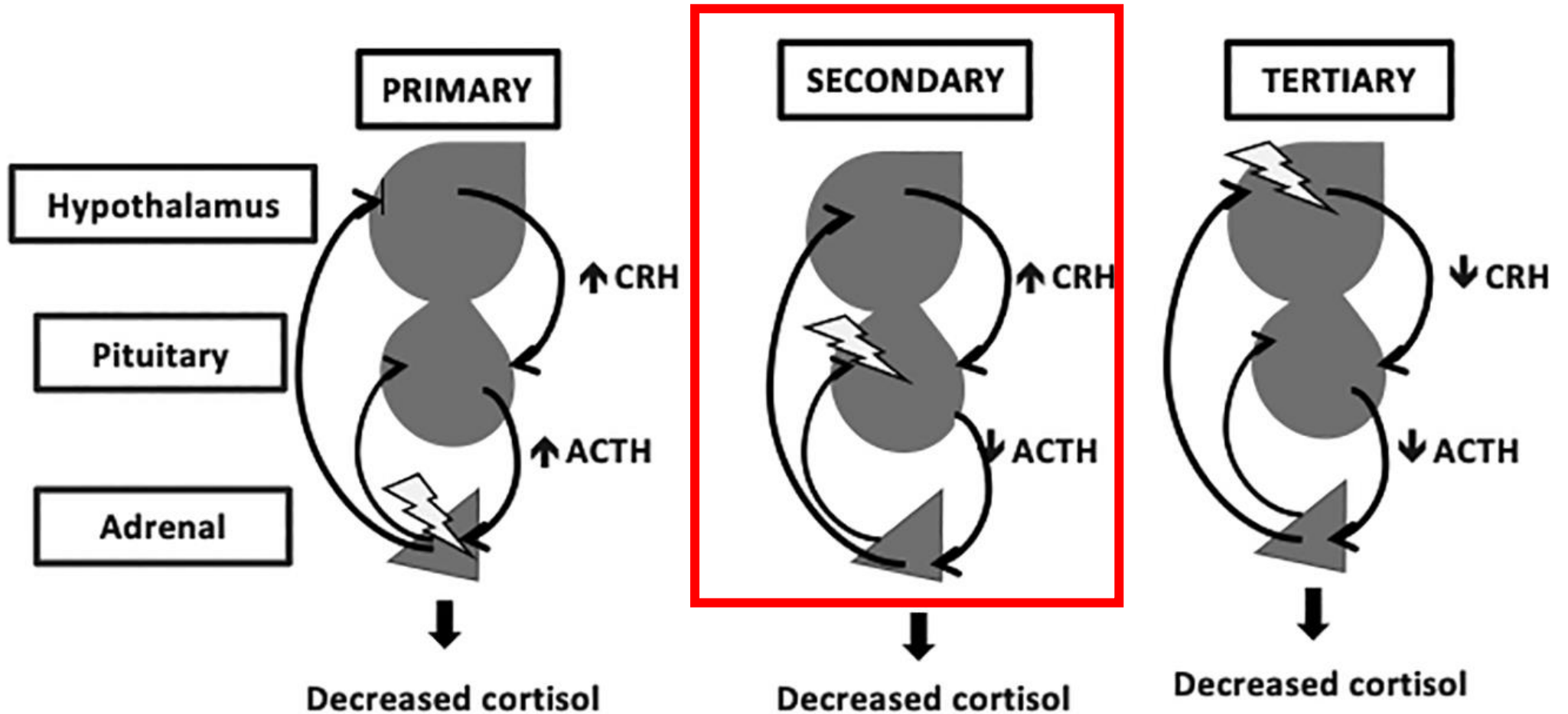
What is the most likely etiology of her adrenal insufficiency?

- A. Primary adrenal insufficiency (adrenal)
- B. Secondary adrenal insufficiency (pituitary)
- C. Tertiary adrenal insufficiency (hypothalamus)

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Adrenal Insufficiency Categories



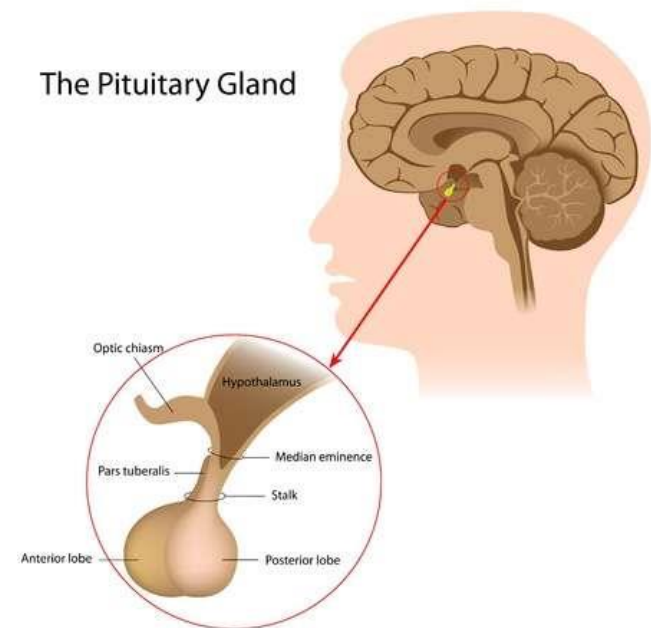
Causes of Secondary Adrenal Insufficiency

- **Pituitary Causes**

- Pituitary mass (adenoma or metastatic lesion)
- Pituitary infiltration (iron, granulomatous, etc.)
- Pituitary infection
- Pituitary infarction/hemorrhage
- Pituitary trauma (e.g. MVA)

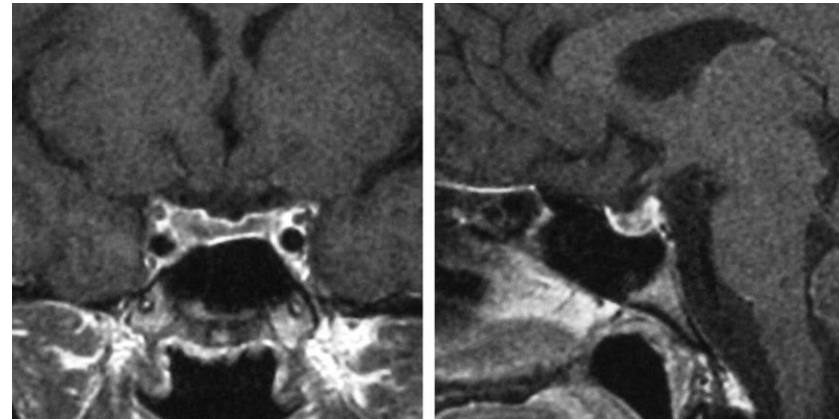
- **Medications**

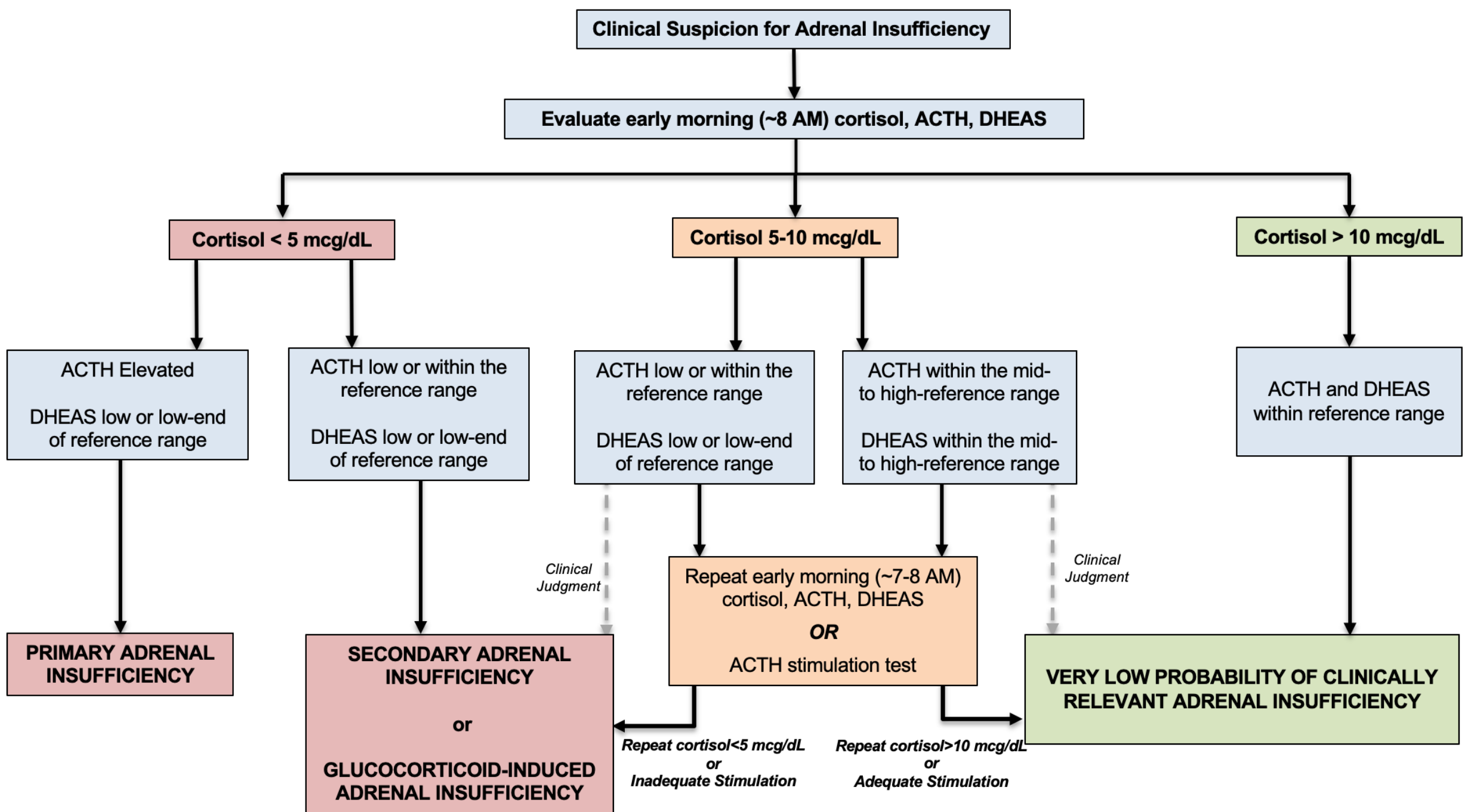
- Glucocorticoids
- Opioids



Secondary Adrenal Insufficiency Due to Postpartum Pituitary Necrosis (Sheehan's Syndrome)

- **Hemorrhagic shock** during delivery or postpartum causes arterial spasm in the blood supply to the enlarged anterior pituitary → acute infarction and necrosis of the anterior pituitary (Sheehan's Syndrome).
- **Loss of anterior pituitary hormones** (TSH, LH, FSH, GH, prolactin, and ACTH) → classic symptoms of fatigue, weakness, dizziness, hypotension, amenorrhea, inability to lactate
- **Mineralocorticoids remain intact** so **less likely** to present with “crisis”, salt craving, etc. but “crisis” may occur.





73-year-old male undergoing evaluation for hematuria is found to have 1.6 cm right adrenal adenoma (10 HU).

PMHx is notable for DM type 2, HTN, hyperlipidemia, atrial fibrillation, CVA

Medications: metformin 1000 mg daily, dulaglutide 1.5 mg weekly, atorvastatin 40 mg daily, apixaban 5 mg BID, HCTZ 25 mg daily, atenolol 50 mg daily, potassium chloride 20 mEq daily

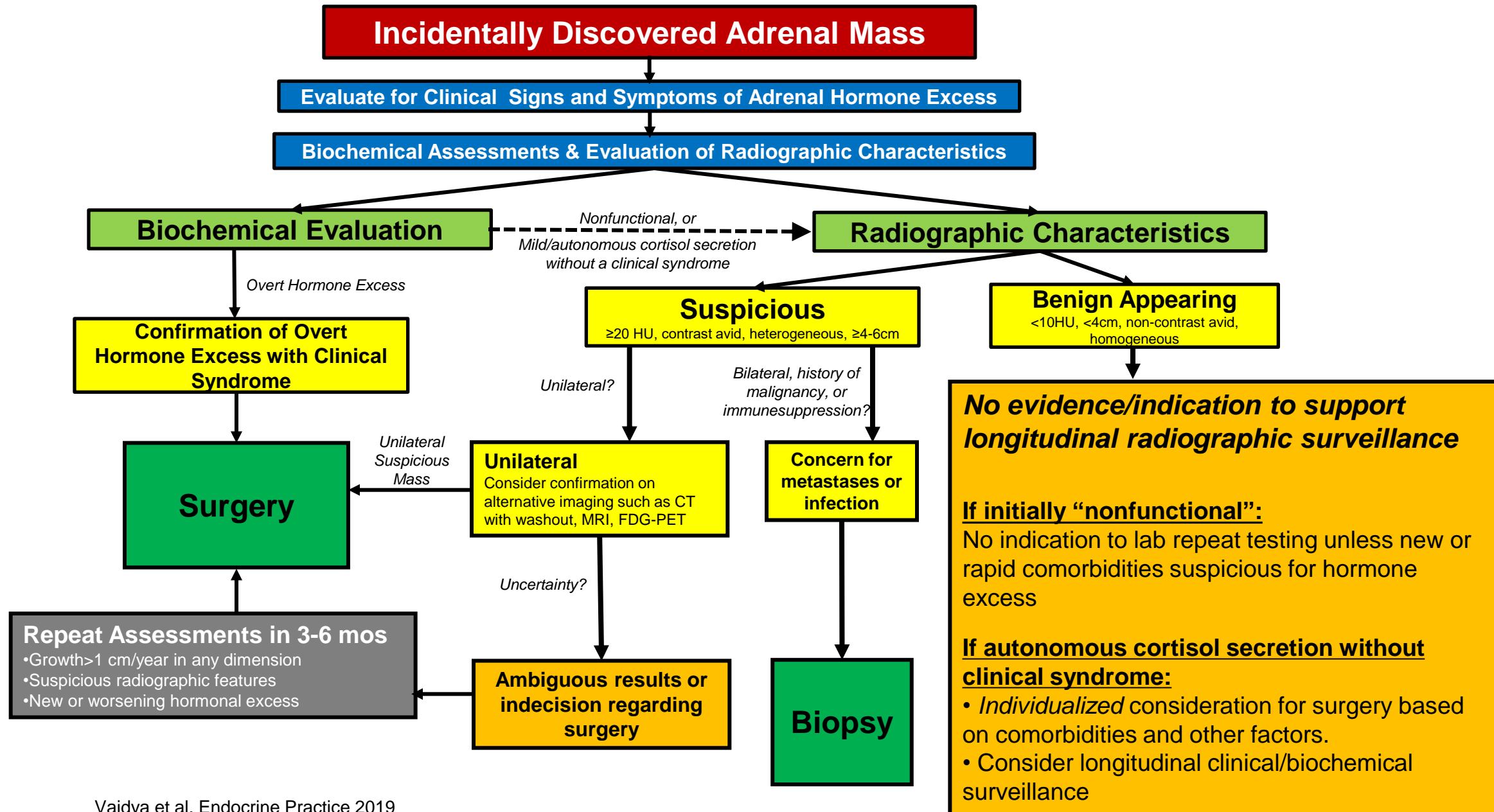
What is the next best step in evaluation?

- A. Plasma renin and aldosterone
- B. Plasma metanephrines
- C. Dexamethasone suppression testing
- D. all of the above

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Approach to the Incidentally Discovered Adrenal Mass



35-year-old pharmacist is brought to the ED following a seizure at work. He has no history of IFG/IGT and is not taking any medications.

- At time of EMS arrival glucose < 50 mg/dL and improved with dextrose.
- He is admitted and while in the hospital, becomes unresponsive with repeat FS <50 mg/dL
- Biochemical evaluation at the time of low FS and prior to dextrose confirms glucose 32 mg/dL, insulin 15 μ IU/mL, c-peptide 4.2 ng/mL, hypoglycemia panel screen: negative.

Which of the following is the most likely diagnosis?

- A. Insulinoma
- B. Surreptitious use of exogenous insulin
- C. Sulfonylurea ingestion
- D. Metformin overdose
- E. Adrenal insufficiency

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Evaluation of Hypoglycemia

Confirm consistent with Whipple's triad and assess the following:
when patient is **symptomatic** and **the glucose is LOW:**

- ✓ Glucose
- ✓ Insulin
- ✓ Pro-insulin
- ✓ C-peptide
- ✓ Serum ketones
- ✓ Hypoglycemia panel screen (sulfonylurea and meglitinide)
- ✓ Cortisol/ACTH

Note: biochemical evaluation to be completed when BG LOW and PRIOR to treatment

TABLE 3. Patterns of findings during fasting or after a mixed meal in normal individuals with no symptoms or signs despite relatively low plasma glucose concentrations (*i.e.* Whipple's triad not documented) and in individuals with hyperinsulinemic (or IGF-mediated) hypoglycemia or hypoglycemia caused by other mechanisms

Symptoms, signs, or both	Glucose (mg/dl)	Insulin (μ U/ml)	C-peptide (nmol/liter)	Proinsulin (pmol/liter)	β -Hydroxybutyrate (mmol/liter)	Glucose increase after glucagon (mg/dl)	Circulating oral hypoglycemic agent	Antibody to insulin	Diagnostic interpretation
No	<55	<3	<0.2	<5	>2.7	<25	No	No	Normal
Yes	<55	\gg 3	<0.2	<5	\leq 2.7	>25	No	Neg (Pos)	Exogenous insulin
Yes	<55	\geq 3	\geq 0.2	\geq 5	\leq 2.7	>25	No	Neg	Insulinoma, NIPHS, PGBH
Yes	<55	\geq 3	\geq 0.2	\geq 5	\leq 2.7	>25	Yes	Neg	Oral hypoglycemic agent
Yes	<55	\gg 3	\gg 0.2 ^a	\gg 5 ^a	\leq 2.7	>25	No	Pos	Insulin autoimmune
Yes	<55	<3	<0.2	<5	\leq 2.7	>25	No	Neg	IGF ^b
Yes	<55	<3	<0.2	<5	>2.7	<25	No	Neg	Not insulin (or IGF)-mediated

Neg, Negative; Pos, positive; PGBH, post gastric bypass hypoglycemia.

^a Free C-peptide and proinsulin concentrations are low.

^b Increased pro-IGF-II, free IGF-II, IGF-II/IGF-I ratio.

When Glucose is Low (<55 mg/dL)....

- **INSULIN HIGH**

- **C-peptide high**

- Hypoglycemia panel negative → insulinoma
 - Hypoglycemia panel positive → drug effect (SU/MEG)

- **C-peptide low** → surreptitious insulin use

- **INSULIN LOW**

- Liver, heart, or kidney failure; sepsis, ETOH, Cortisol or GH deficiency, nonpancreatic tumors, inborn errors of metabolism

THANK YOU!



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