ENDOCRINE REVIEW

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NEW NUMBER 11:

A 65-year-old woman comes to the office to establish care. Her medical history is notable for hypothyroidism due to Hashimoto thyroiditis treated with levothyroxine. She does not have any symptoms at this time. There is no history of head or neck radiation exposure.

On physical examination, vital signs are normal. The patient's thyroid gland is enlarged. The right lobe is larger than the left, and a mobile 2-cm nodule is palpable in the lower pole. There is no palpable cervical adenopathy.
Laboratory studies show a serum thyroid-stimulating hormone level of 2.0 µU/mL (2.0 mU/L).

Which of the following is the most appropriate diagnostic test to perform next?

A) CT scan of the neck
B) Fine-Needle Aspiration of the Nodule
C) Thyroid uptake an I131 Scan
D) Ultrasound the neck

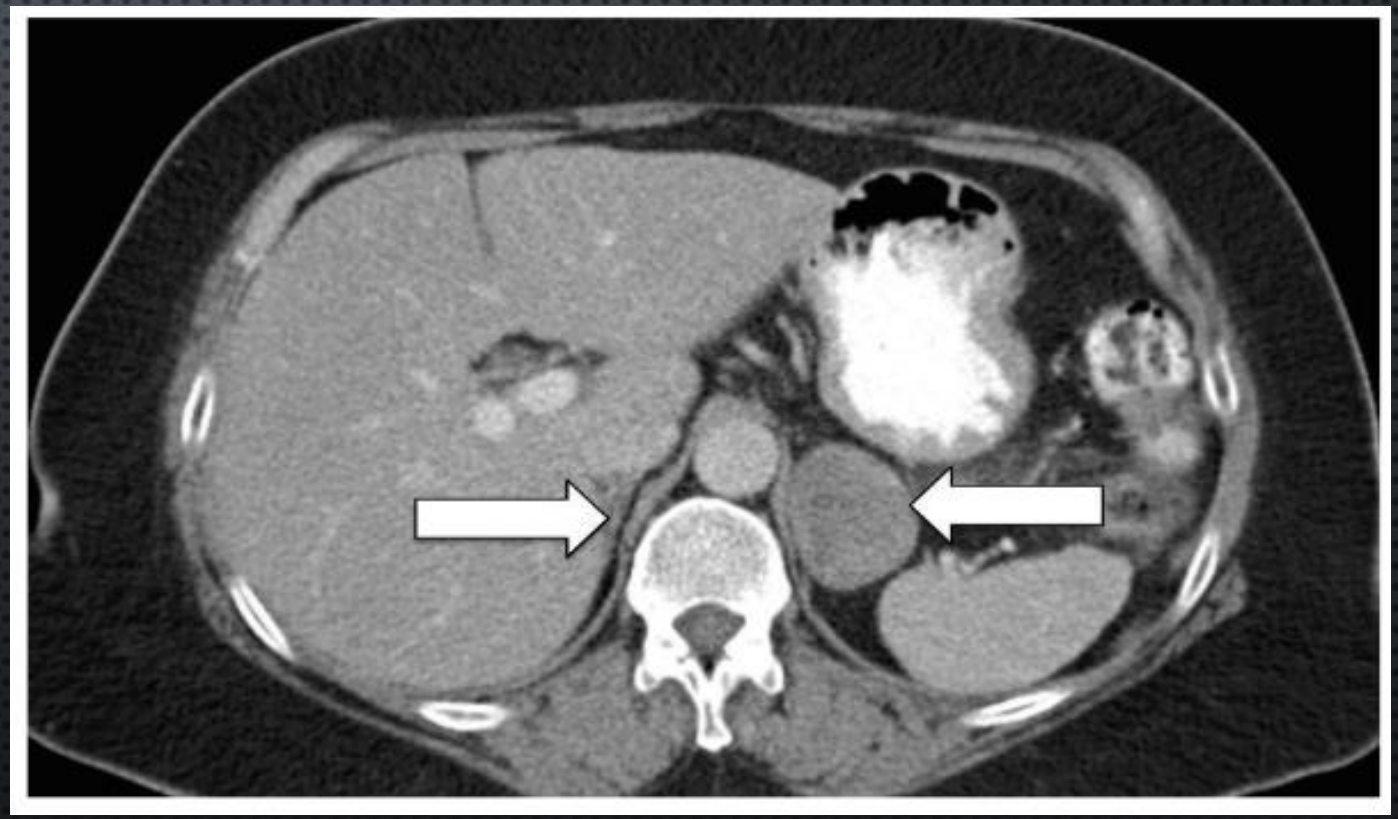


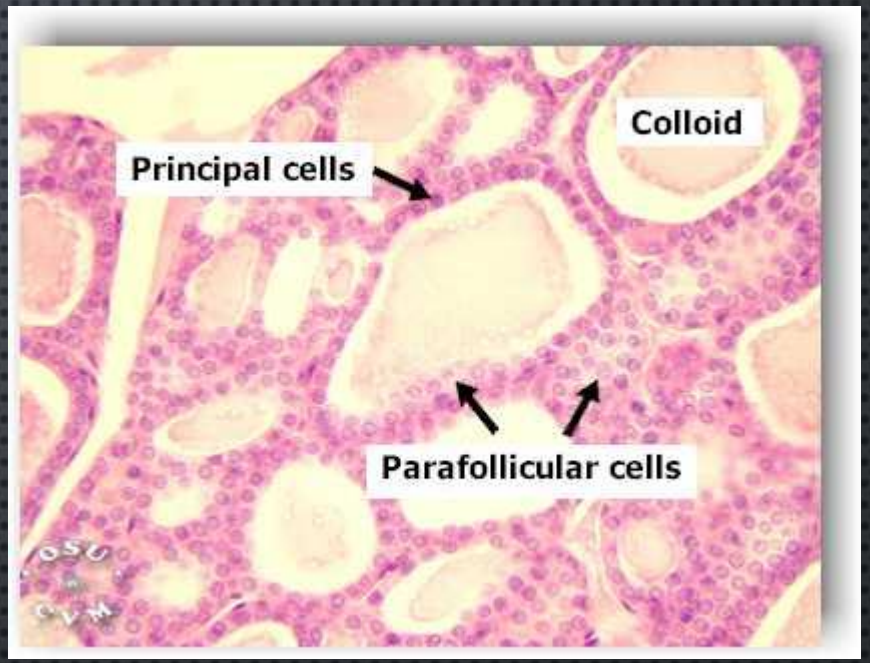
Image for question #20

#1 – (MKSAP 76)

- A 69-year-old woman is seen in the office following a left thyroid lobectomy and isthmusectomy 1 week ago for management of compressive symptoms related to a large left thyroid nodule. The preoperative thyroid/neck ultrasound showed the nodule without suspicious features and no abnormal cervical lymph nodes. The pathology report describes a 4.5-cm left adenomatous nodule in a background of multinodular hyperplasia. There is a single focus of papillary thyroid carcinoma measuring 0.5 cm in the greatest dimension. No lymphovascular or extrathyroidal invasion is noted. Surgical margins are negative.
- The patient is currently feeling well and reports complete resolution of her prior symptoms. Her medical history is otherwise unremarkable, and she takes no medications.
- On physical examination, vital signs are normal. There is a well-healed anterior neck scar. Laboratory studies show a serum thyroid-stimulating hormone (TSH) level of 1.8 mU/mL (1.8 mU/L).
- What is the most appropriate treatment?

D – NO ADDITIONAL TREATMENT

#1 – THYROID CANCERS



- Follicular Epithelial Derived – Differentiated:
  - Papillary: (85%) often to LN, rarely distant mets
  - Follicular: (15%) Lung and bone mets, rarely LN
- Follicular Epithelial Derived – Undifferentiated:
  - Anaplastic (3%) – rare, aggressive, usually large, mean survival 5 months
- Other thyroid cancers:
  - Medullary – from parafollicular cells that make calcitonin – MEN 2A and 2B
  - ~primary thyroid lymphoma – rapidly growing mass

#1 – MANAGEMENT … D CANCERS

- **STEP 1 = SURGERY**
- **TUMOR <1 CM WITHOUT EXTRATHYR… MY**
- ALL OTHERS = TOTAL THYROIDECTO…
- STEP 2 = RADIOIODINE THERAPY

ATA risk stratification system to estimate risk of persistent/recurrent disease

Low risk	Intermediate risk	High risk
Papillary thyroid cancer with all of the following present:	**Any of the following present:**	**Any of the following present:**
▪ No local or distant metastases	Microscopic invasion into the perithyroidal soft tissues	Macroscopic tumor invasion
▪ All macroscopic tumor has been resected	Cervical lymph node metastases or ^{131}I avid metastatic foci in the neck on the post-treatment scan done after thyroid remnant ablation	Incomplete tumor resection with gross residual disease
▪ No invasion of locoregional tissues	Tumor with aggressive histology or vascular invasion (aggressive histologies include tall cell, insular, columnar cell carcinoma, Hürthle cell carcinoma, follicular thyroid cancer, hobnail variant)	Distant metastases
▪ Tumor does not have aggressive histology (aggressive histologies include tall cell, insular, columnar cell carcinoma, Hürthle cell carcinoma, follicular thyroid cancer, hobnail variant)	Clinical N1 or >5 pathologic N1 with all involved lymph nodes <3 cm in largest dimension*	Postoperative serum thyroglobulin suggestive of distant metastases
▪ No vascular invasion	Multifocal papillary thyroid microcarcinoma with extrathyroidal extension and *BRAF* V600E mutated (if known)*	Pathologic N1 with any metastatic lymph node ≥3 cm in largest dimension*
▪ No ^{131}I uptake outside the thyroid bed on the post-treatment scan, if done		Follicular thyroid cancer with extensive vascular invasion (>4 foci of vascular invasion) *
▪ Clinical N0 or ≤5 pathologic N1 micrometastases (<0.2 cm in largest dimension)*		
Intrathyroidal, encapsulated follicular variant of papillary thyroid cancer*		
Intrathyroidal, well-differentiated follicular thyroid cancer with capsular invasion and no or minimal (<4 foci) vascular invasion*		
Intrathyroidal, papillary microcarcinoma, unifocal or multifocal, including *BRAF* V600E mutated (if known)*		

#1 – Management of Differentiated Thyroid Cancers

- Step 1 = surgery
- Tumor <1 cm without extrathyroidal extension and no lymph nodes = lobectomy
- All others = total thyroidectomy

- Step 2 = radioiodine therapy for high and maybe intermediate risk

- Step 3 = External beam radiotherapy (EBRT) can be used as adjuvant therapy for: older patients with gross extrathyroid extension at the time of surgery or selected younger patients with extensive disease and poor histologic features (poorly differentiated histology) whose disease is resected but in whom there is a high likelihood of residual microscopic disease.

#1 – MANAGEMENT OF DIFFERENTIATED THYROID CANCERS

- **AMERICAN THYROID ASSOCIATION (ATA) LOW RISK –**
  - THYROIDECTOMY + DETECTABLE SERUM THYROGLOBULIN (TG) LEVELS:

    TSH = 0.1 TO 0.5 MU/L.
  - LOBECTOMY OR UNDETECTABLE SERUM TG LEVELS: TSH = MID TO LOWER HALF OF THE REFERENCE RANGE (0.5 TO 2.0 MU/L)
- **●ATA INTERMEDIATE RISK –**0.1 TO 0.5 MU/L
- **●ATA INTERMEDIATE OR HIGH RISK –** <0.1 MU/L.

ATA risk stratification system to estimate risk of persistent/recurrent disease

Low risk	Intermediate risk	High risk
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▪ No local or distant metastases	Microscopic invasion into the perithyroidal soft tissues	Macroscopic tumor invasion
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▪ No vascular invasion	Multifocal papillary thyroid microcarcinoma with extrathyroidal extension and *BRAF* V600E mutated (if known)*	Pathologic N1 with any metastatic lymph node ≥3 cm in largest dimension*
▪ No ^{131}I uptake outside the thyroid bed on the post-treatment scan, if done		Follicular thyroid cancer with extensive vascular invasion (>4 foci of vascular invasion) *
▪ Clinical N0 or ≤5 pathologic N1 micrometastases (<0.2 cm in largest dimension)*		
Intrathyroidal, encapsulated follicular variant of papillary thyroid cancer*		
Intrathyroidal, well-differentiated follicular thyroid cancer with capsular invasion and no or minimal (<4 foci) vascular invasion*		
Intrathyroidal, papillary microcarcinoma, unifocal or multifocal, including *BRAF* V600E mutated (if known)*		

#2

- A 72-year-old woman is evaluated during a routine wellness examination. She is asymptomatic. Past medical history relevant for hypertension for the last 10 year. She is taking losartan.
- On physical examination, blood pressure is 142/92 mm Hg. Other vital signs and physical examination findings are normal. BMI is 29.
- Laboratory studies show a fasting plasma glucose level of 135 mg/dL (7.2 mmol/L) and a hemoglobin A 1c level of 5.4%.
- Which of the following is the most appropriate diagnostic test to perform next?

A – FASTING BLOOD GLUCOSE

Table 2.2—Criteria for the diagnosis of diabetes

FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*
OR
2-h PG ≥200 mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.*
OR
A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR
In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

*In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate test samples.

- The screening tests have different diagnostic sensitivities based on the detected glucose abnormality; thus, discordant results may occur. Additional factors, such as illness or stress, may affect the results of screening tests based on plasma glucose values.
- This patient has a fasting blood glucose value within the diagnostic range for diabetes with a hemoglobin A_{1C} value in the normal range. When there is a discrepancy in screening test results, the American Diabetes Association recommends repeating the abnormal test.

#3 – (MKSAP 65)

- A 45-year-old man is seen for follow-up evaluation for depression and to review the results of laboratory testing. He was seen 1 month ago for a 6-month history of depressed mood, difficulty sleeping, decreased appetite, 2.3-kg (5-lb) weight loss, and fatigue. Major depressive disorder was diagnosed, and escitalopram was prescribed. Today the patient reports a significant improvement in his mood, appetite, and the quality of his sleep since starting treatment.
- On physical examination, vital signs and physical examination are normal. Screening laboratory studies from 1 month ago show a thyroid-stimulating hormone (TSH) level of 7 mU/mL (7 mU/L) and a free thyroxine (T_4) level of 1.0 ng/dL (12.9 pmol/L).
- What is the most appropriate management?

E – REPEAT TSH IN 2 MONTH

Subclinical Thyroid

- The following five criteria define endogenous subclinical thyroid dysfunction:
  - TSH increased above, or decreased below designated limits
  - Normal free T4 concentration (and free T3 for hyperthyroidism)
  - The abnormality is not due to medication
  - There is no concurrent critical illness or pituitary dysfunction.
  - A sustained abnormality is demonstrated over 3-6 months

Indications for Treatment

- **Subclinical Hypothyroidism**
  - Woman in reproductive age
  - TSH >10 mU/L
  - Age < 65 with TSH 7-10 mU/L with symptoms
  - Anyone with TSH < 7 mU/L: Consider monitoring unless severely symptomatic
- **Overt or Central Hypothyroidism**
  - Symptomatic or asymptomatic
  - High TSH >10
  - Low Free T4
- If TSH is mildly elevated (<10), repeat TSH and T4 within a month

#3 – Subclinical Hypothyroidism

- Step 1 = rule out transient elevation in TSH! (or normal elevation… 10=normal for 80yo!)
- repeat TSH, T4, (and TPO antibodies if undecided about tx) in 2-3 months
- Definition: An early form of primary hypothyroidism affecting up to 10% of the population. 2-4% progress to overt hypothyroidism.

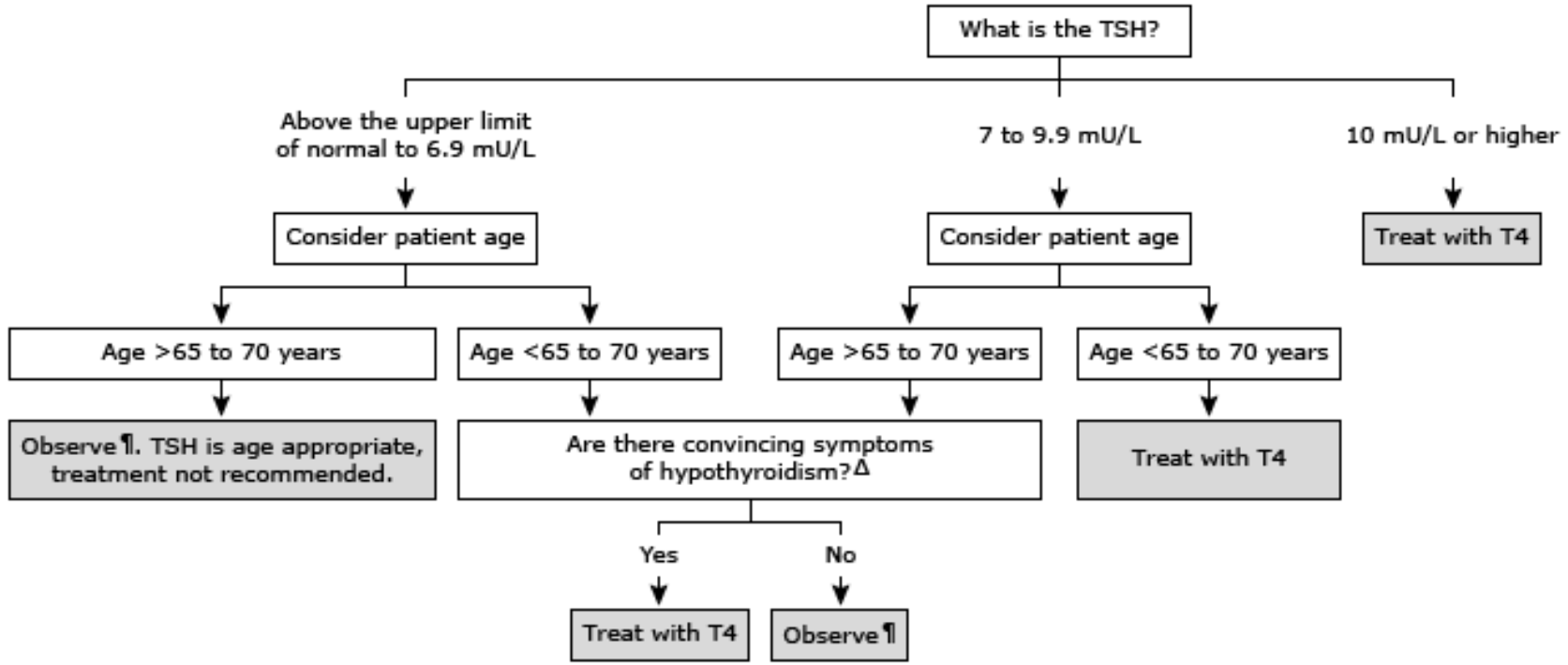
Ddx transient elevation TSH:

Acute illness – after ~24 hours

Indications to treat:

TSH>10
Age <65 and TSH 7-10 + symptomatic
Trying to get pregnant
Anti-TPO positive
~lipids abnl
~ ovulation dysfunction
~ osteoporosis

Indications for thyroid hormone replacement in nonpregnant adults with subclinical hypothyroidism*



What's New

Treatment of subclinical hy

The treatment of subclinical hypothyroidism is controversial. In a meta-analysis of 21 randomized trials (over 2000 nonpregnant adults with baseline thyroid-stimulating hormone [TSH] values ranging from 4.4 to 12.8 mIU/L), there were no differences in hypothyroid signs or symptoms or general quality of life between the levothyroxine (T4)-treated and placebo groups after a mean follow-up of eight months [1]. However, observational data show a benefit of T4 treatment in reducing ischemic heart disease events and overall mortality in younger individuals with subclinical hypothyroidism, and we suggest T4 treatment in most patients <65 years of age with a TSH ≥7.0 mIU/L (algorithm 1). (See "Subclinical hypothyroidism in nonpregnant adults", section on 'Hypothyroid signs and symptoms'.)

Still a moving target!

#4

- A 78-year-old man with type 2 diabetes mellitus is evaluated during a routine follow-up examination. He reports hypoglycemia occurring approximately twice per week mostly before dinner. It is worse if he plays golf in the afternoon. He has had three episodes in the last 3 months in which he required assistance from his wife. Medical history is significant for dyslipidemia, hypertension, and obesity. Medications are aspirin, atorvastatin, glyburide, lisinopril, and metformin.
- On physical examination, vital signs are normal. BMI is 32. The rest of the examination is normal.
- Laboratory studies show a hemoglobin A 1c level of 6.5% and an estimated glomerular filtration rate (eGFR) of 50 mL/min/1.73 m 2 .
- Which of the following is the most appropriate next best step in the management of this patient's hypoglycemia?

C – STOP GLYBURIDE THERAPY

- Hypoglycemia can become a rate-limiting step in achieving glycemic goals for many persons. Clinicians should consider de-intensifying pharmacologic therapy in patients with type 2 diabetes who achieve hemoglobin A_{1C} levels less than 6.5%; furthermore, benefits of targeting a specific hemoglobin A_{1C} target level in patients with a life expectancy less than 10 years due to advanced age should be considered carefully because the harms outweigh benefits in this population.
- Sulfonylureas stimulate insulin secretion regardless of glycemic status. Thus, they pose risk for hypoglycemia, especially drugs with long half-lives, such as glyburide, or in older persons. In light of this patient's age, kidney impairment, and frequency of hypoglycemia, glyburide should be stopped

Table 12.1—Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes (2)

Patient characteristics/ health status	Rationale	Reasonable A1C goal‡	Fasting or preprandial glucose	Bedtime glucose	Blood pressure	Lipids
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5% (58 mmol/mol)	90–130 mg/dL (5.0–7.2 mmol/L)	90–150 mg/dL (5.0–8.3 mmol/L)	<140/90 mmHg	Statin unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0% (64 mmol/mol)	90–150 mg/dL (5.0–8.3 mmol/L)	100–180 mg/dL (5.6–10.0 mmol/L)	<140/90 mmHg	Statin unless contraindicated or not tolerated
Very complex/poor health (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5%† (69 mmol/mol)	100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<150/90 mmHg	Consider likelihood of benefit with statin (secondary prevention more so than primary)

Recommendations

12.11 In older adults at increased risk of hypoglycemia, medication classes with low risk of hypoglycemia are preferred. **B**

12.12 Overtreatment of diabetes is common in older adults and should be avoided. **B**

12.13 Deintensification (or simplification) of complex regimens is recommended to reduce the risk of hypoglycemia, if it can be achieved within the individualized A1C target. **B**

#5 – (MKSAP 11)

- A 70-year-old man was admitted to the hospital 3 days ago with an ST-elevation myocardial infarction complicated by pulmonary edema and atrial fibrillation. He underwent emergency cardiac catheterization and left anterior descending (LAD) artery stent placement. Today the patient is feeling much better with complete resolution of his initial presenting symptoms.
- Medications are aspirin, atorvastatin, clopidogrel, lisinopril, metoprolol, and low-molecular-weight heparin.
- On physical examination, pulse rate is 92/min. Other vital signs are normal.
- Cardiac examination reveals new findings of an irregularly irregular rhythm and an S_4. His physical examination is otherwise normal.

Thyroid studies are shown.

What is the most likely diagnosis?

Laboratory studies obtained at the time of cardiac catheterization:		
Thyroid-stimulating hormone (TSH)	0.2 µU/mL (0.2 mU/L)	Low
Thyroxine (T_4), total	6.5 µg/dL (83.8 nmol/L)	Low normal
Thyroxine (T_4), free	1.0 ng/dL (12.9 pmol/L)	Low normal
Triiodothyronine (T_3), total	60 ng/dL (0.9 nmol/L)	Low

C – NONTHYROIDAL ILLNESS SYNDROME

#5 – NONTHYROIDAL ILLNESS SYNDROME

- **Definition:** nonthyroidal illness syndrome (euthyroid sick syndrome) is most often seen in critically ill hospitalized patients and is characterized by a **reduced** serum triiodothyronine (T_3) level, low or **low-normal** serum thyroxine (T_4) level, and **normal or low** (but detectable) serum thyroid-stimulating hormone (TSH) level.

- Mechanisms:
  - 1) changes in the peripheral uptake of thyroid hormones
  - 2) reduced levels of thyroid hormone–binding proteins
  - 3) alterations in the expression and activity of deiodinases

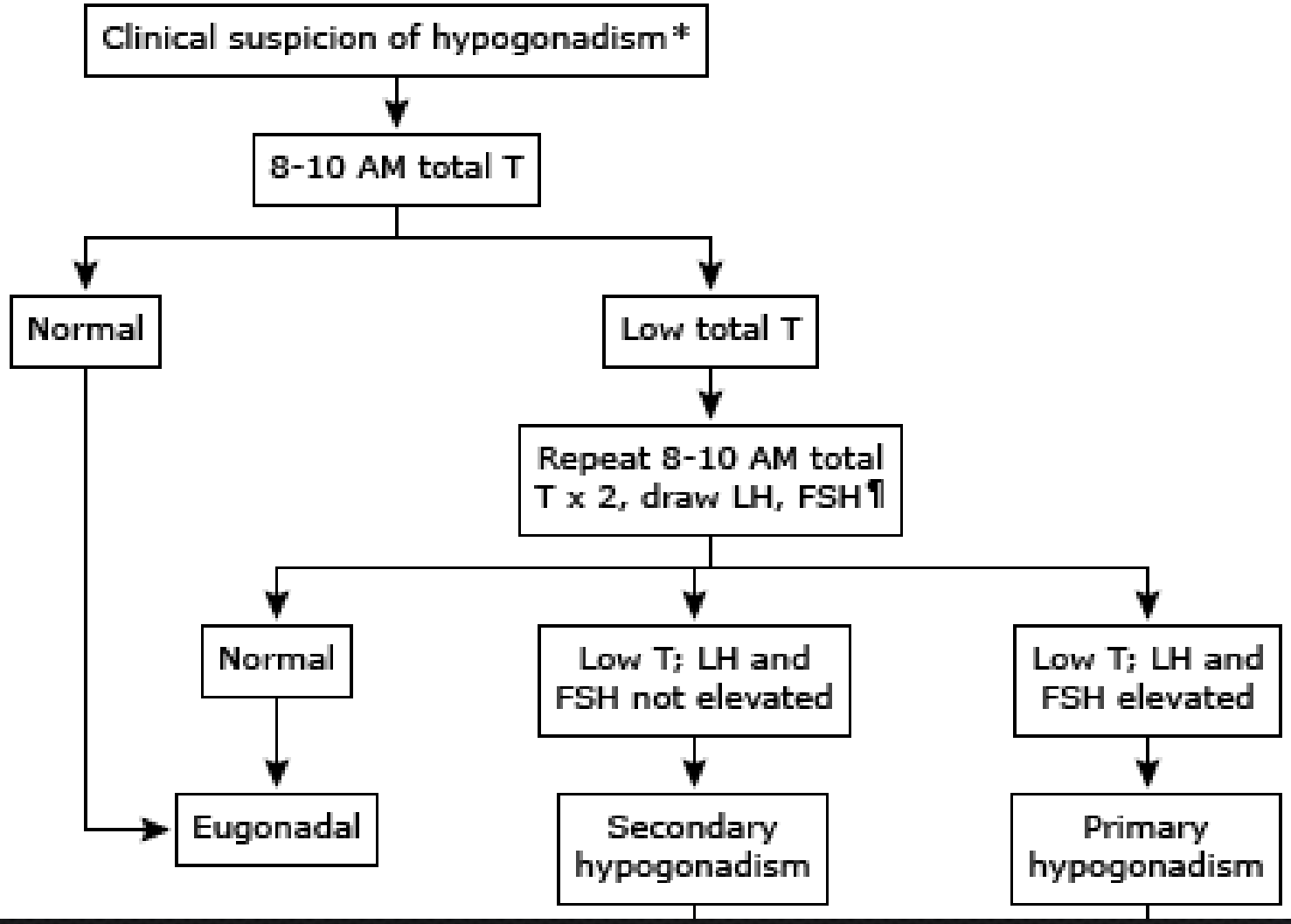
Very low serum T_4 levels are associated with poor overall outcome, but treatment with levothyroxine has unfortunately not shown improvement in mortality.

#6

- A 46-year-old man is evaluated for a 1-year history of low libido and excessive fatigue. He underwent normal puberty and has two teenaged children. The patient has a history of hypertension. He is taking chlorthalidone.
- On physical examination, temperature is 98.6, blood pressure is 125/72 mm Hg, respiratory rate is 16/min and pulse rate is 80/min. BMI is 42. No gynecomastia is present, and testicular volume is normal. A normal male distribution of body hair is noted.
- Results of laboratory studies show a serum follicle-stimulating hormone level of 5 mU/mL (5U/L), a serum luteinizing hormone level of 4 mU/mL (4 U/L), and an 8:00 AM serum total testosterone level of 210 ng/dL (7 nmol/L). Repeated serum total testosterone level of 200 ng/dl (6.9 nmol/L). The serum thyroid-stimulating hormone and prolactin levels are normal.
- Which of the following is the most appropriate next test?

A – FREE TESTOSTERONE LEVEL

Evaluation of the male with possible hypogonadism



- A free testosterone assessment, preferably one using equilibrium dialysis, is the most appropriate diagnostic test to determine whether this patient truly has hypogonadism. In patients with clinical features suggestive of androgen deficiency, a morning (ideally, 8:00 AM to 9:00 AM) serum total testosterone level should be measured as an initial diagnostic test. If low, the total testosterone level should be confirmed with a repeat morning measurement.
- Free and bioavailable testosterone measurements should **be reserved for patients with total testosterone levels in the low-normal range and for patients suspected of having alterations in sex hormone–binding globulin (SHBG) levels**. Total testosterone measurements may be unreliable in patients with increased SHBG levels (advanced age, liver disease) and decreased SHBG levels (obesity, diabetes/insulin resistance, glucocorticoid use), necessitating measurement of free and bioavailable testosterone in these patient populations

- In patients with obesity and low SHBG levels, the free testosterone level can be normal even when the total testosterone level appears decreased. If the free testosterone level is normal, then hypogonadism is excluded and another cause of this patient's erectile dysfunction, such as medication, should be explored.

#7 – (MKSAP 51)

- A 24-year-old woman is evaluated for 6 months of amenorrhea, weight gain, and depressed mood. Medical history is otherwise unremarkable, and she takes no medications.
- On physical examination, blood pressure is 134/86 mm Hg and pulse rate is 82/min. BMI is 31. Other vital signs are normal. The patient has facial plethora. Skin examination reveals multiple ecchymoses. There are wide pigmented striae on the abdomen as well as a dorsocervical fat pad.

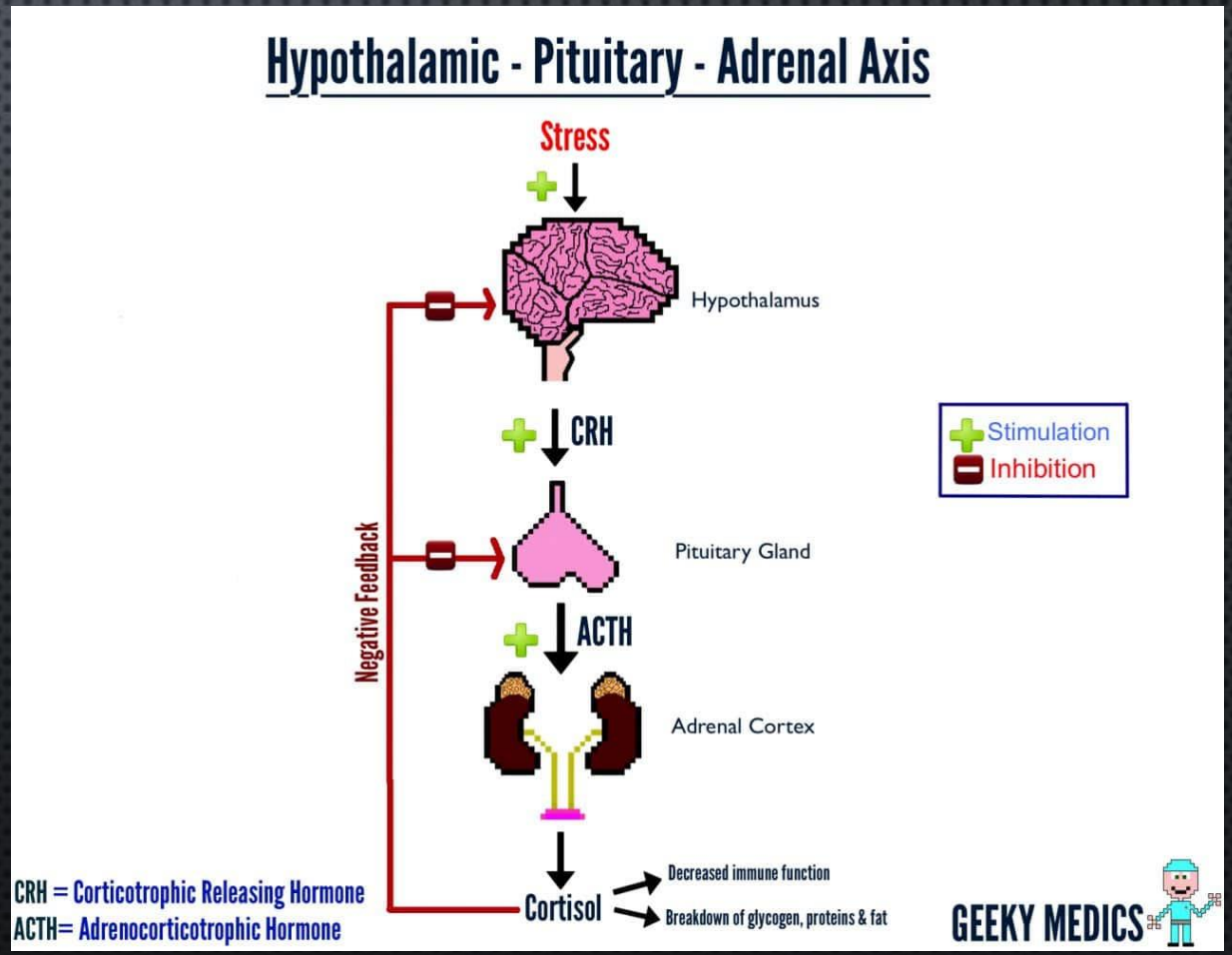
Laboratory studies:	
Cortisol, free, urine	
Initial measurement	120 µg/24 h (330.7 nmol/24 h)
Repeat measurement	240 µg/24 h (661.3 nmol/24 h)
Cortisol after 1 mg dexamethasone test	6.0 µg/dL (165.6 nmol/L)

- Which of the following is the most appropriate diagnostic test to perform next?

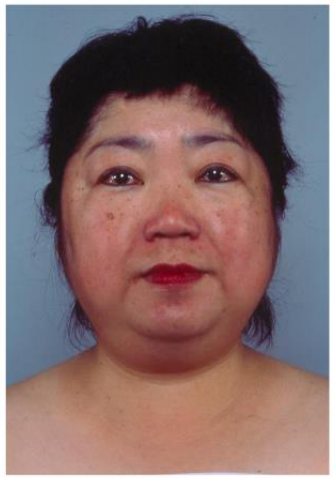
A – ADRENOCORTICOTROPIN HORMONE (ACTH) LEVEL

#7 – CUSHING

- CUSHING SYNDROME = HYPERCORTISOLISM FROM ANY CAUSE, EXOGENOUS OR ENDOGENOUS, ACTH-DEPENDENT OR NOT
- CUSHING DISEASE IS THE TERM USED TO INDICATE EXCESS CORTISOL PRODUCTION DUE TO AN ACTH-SECRETING PITUITARY ADENOMA
- THE MOST COMMON CAUSE OF SYNDROME = DISEASE



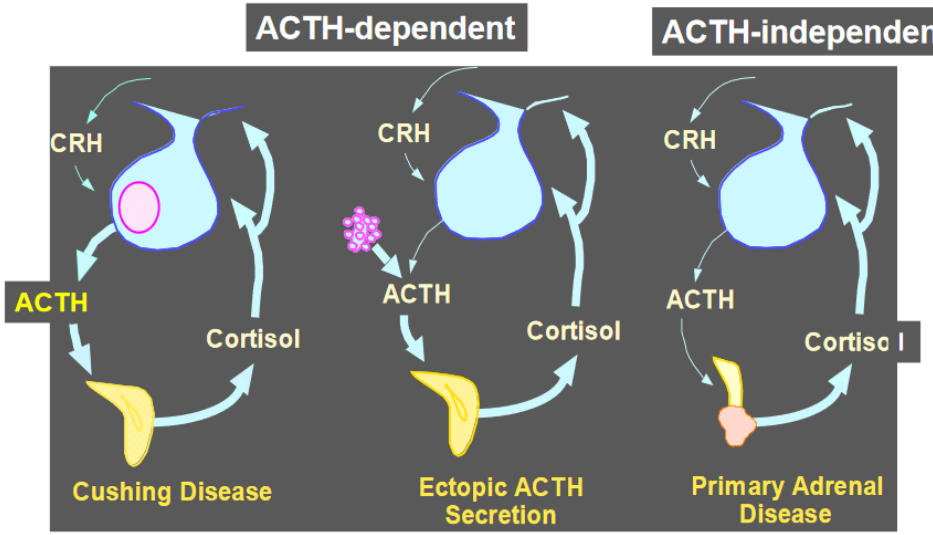
Cushing's Syndrome – too much cortisol



- Harvey Cushing first described a patient with hypercortisolemia in 1932
- Observed signs/symptoms:
  - Weight gain
  - Muscle weakness
  - Irregular menstrual cycles
  - Headache and vision changes
  - Large round face
  - Striae
  - Insomnia
  - Inability to concentrate
  - Fits of irritability alternating with periods of depression

From Dr. Correa's lecture:

Differential Diagnosis of Cushing's Syndrome



Diagnostic stepwise approach

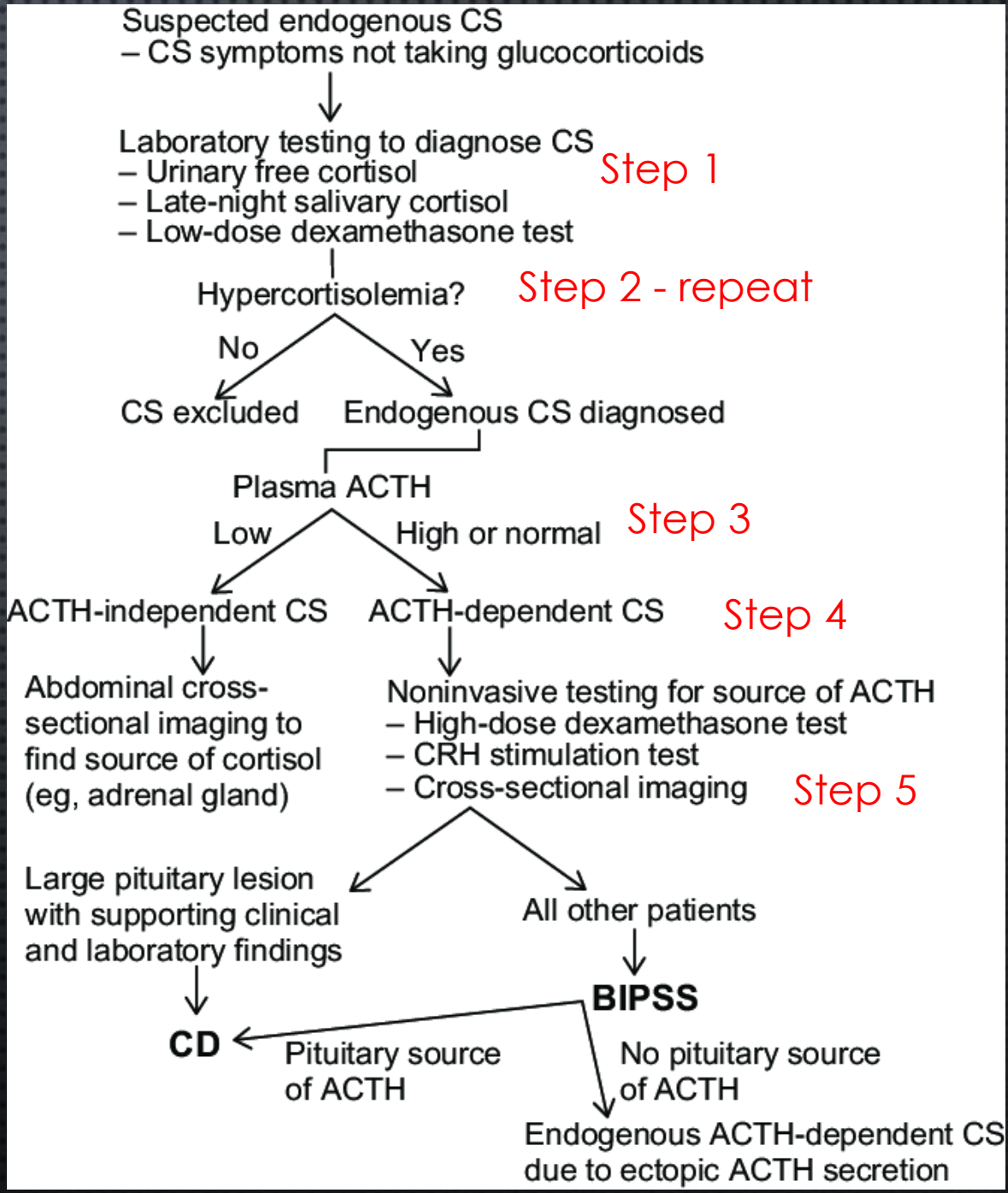
- Screening and confirmation - Does the patient have Cushing's syndrome? (clinical suspicion plays a big role in interpretation of the result)
- Subtype evaluation – is the Cushing's syndrome ACTH-dependent (pituitary or ectopic source) or ACTH-independent (adrenal adenoma)?
- Localization – where is the source of ACTH secretion in ACTH-dependent disease (pituitary or ectopic)?

Hypercortisolism

- ACTH dependent Cushing's syndrome:
  - Pituitary adenoma
  - Ectopic ACTH production (often in the lung)
- ACTH independent Cushing's syndrome:
  - Adrenal adenoma
  - Adrenal cancer
  - Adrenal hyperplasia
- Other causes of hypercortisolism:
  - Depression
  - Alcoholism
  - Obesity, and stressful situation

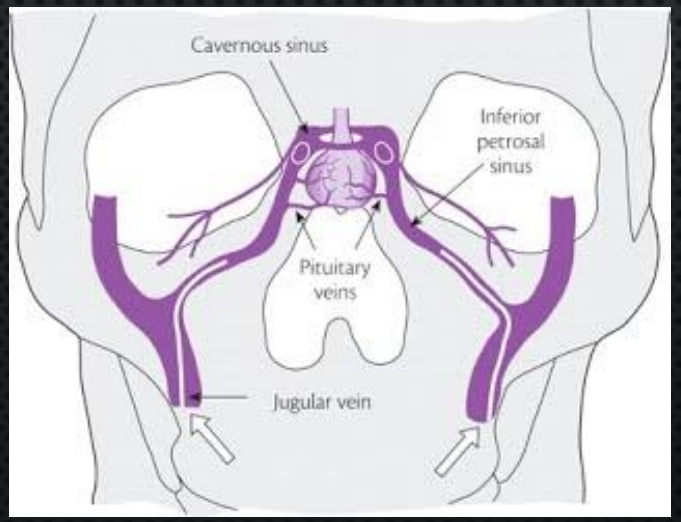
#7 – CUSHING

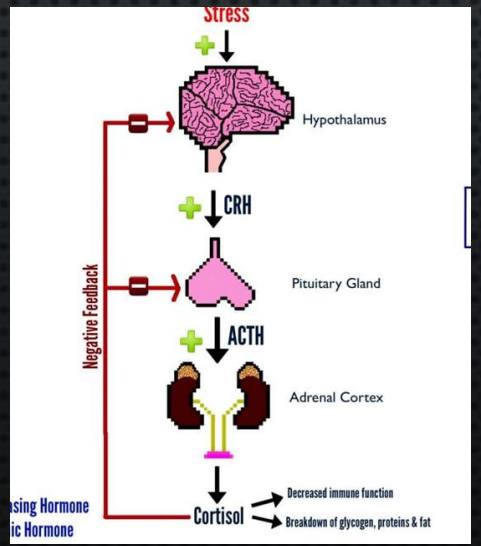
- STEP 1 – THINK IT'S HIGH? PROVE IT! (TRY TO SUPPRESS IT!)
- STEP 2 – CONFIRM IT A SECOND TIME
- STEP 3 – SEE IF IT'S ACTH-DEPENDENT
  - -IF NOT, SOURCE IS LIKELY ADRENAL ADENOMA
- STEP 4 – IF ACTH-DEPENDENT, GET AN MRI OF BRAIN TO PROVE CUSHING DISEASE
- STEP 5 - IF NO PITUITARY TUMOR (OR A TUMOR LESS THAN 6 MM), 8MG DEX SUPPRESSION TEST. A PITUITARY SOURCE OF ACTH WILL RESPOND TO NEGATIVE FEEDBACK FROM HIGH DOSES OF DEX, SUPPRESSING AM CORTISOL BY >50% (ECTOPIC SOURCE OF ACTH WILL NOT)
- BUT…

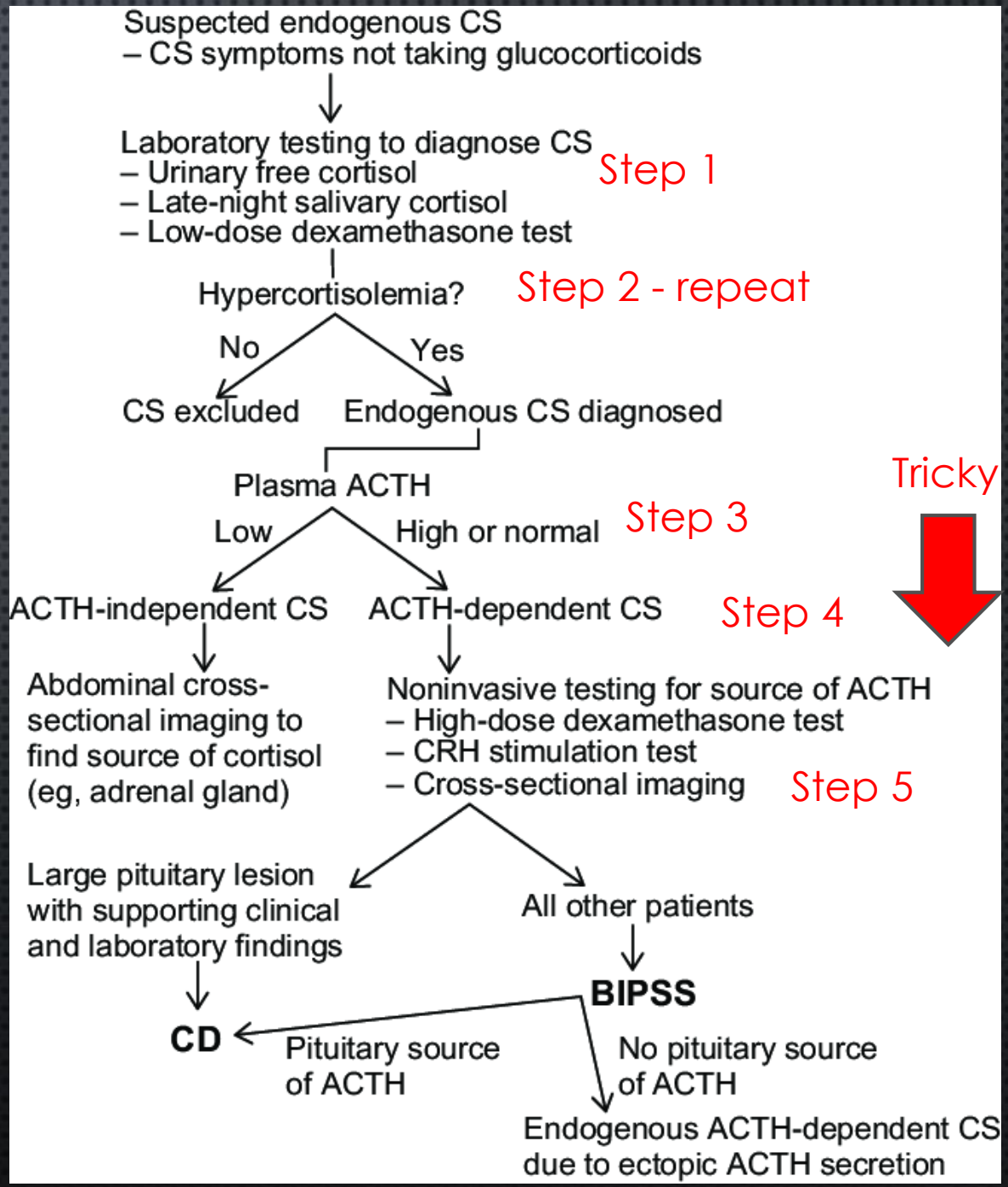


#7 – CUSHING

- BUT 8MG SUPPRESSION TEST IS ONLY 88%/57% SENSITIVITY/SPECIFICITY FOR CUSHING DISEASE, SO INFERIOR PETROSAL SINUS SAMPLING (IPSS) IS OFTEN RECOMMENDED BEFORE PITUITARY SURGERY
- IN IPSS, ACTH LEVELS IN THE PETROSAL SINUS ARE COMPARED WITH THOSE IN THE PERIPHERY AFTER THE ADMINISTRATION OF CORTICOTROPIN-RELEASING HORMONE (CRH). A CENTRAL TO PERIPHERAL GRADIENT GREATER THAN 2.0 BEFORE CRH OR GREATER THAN 3.0 AFTER CRH IS DIAGNOSTIC OF CUSHING DISEASE.







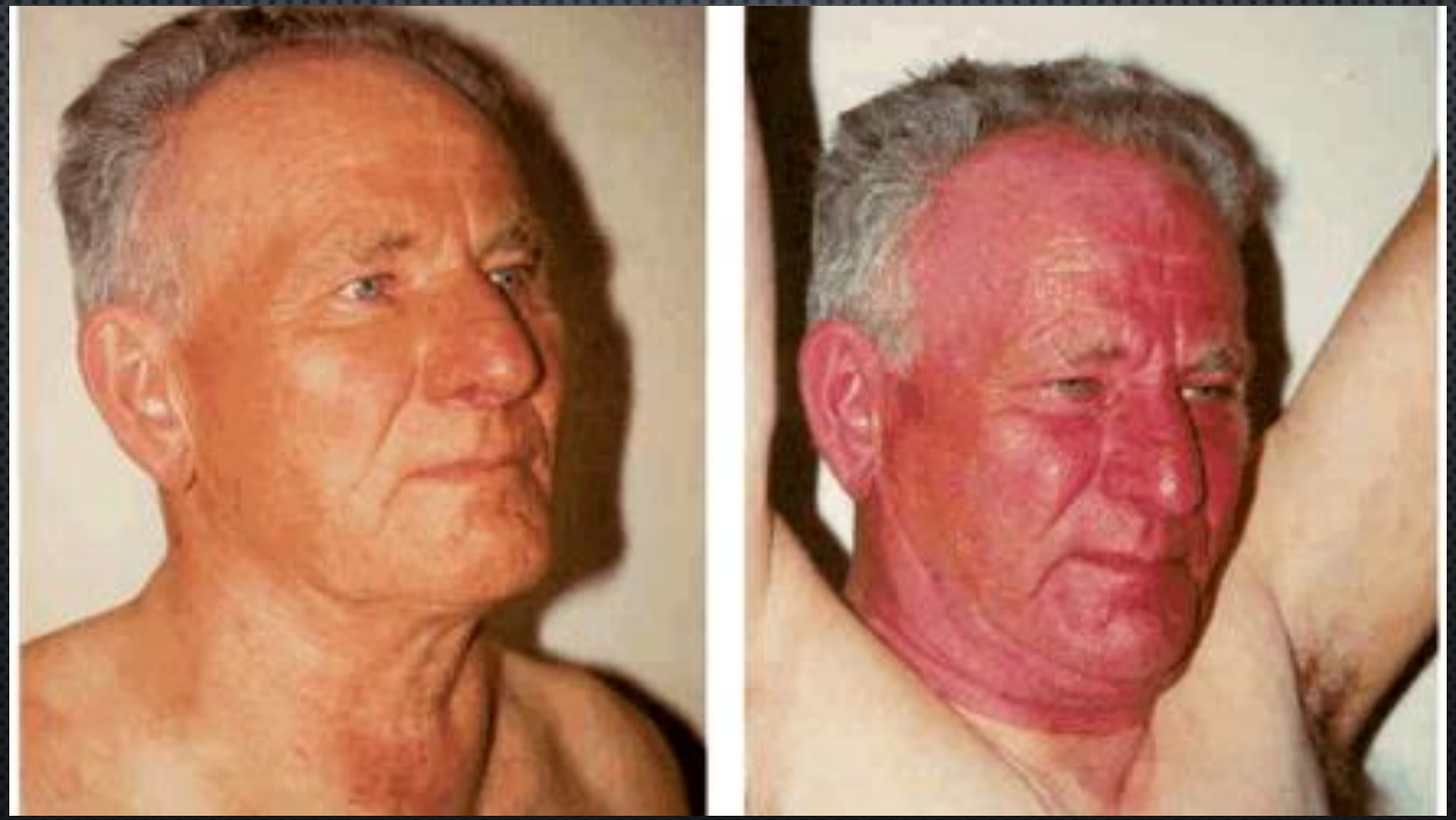
#8

- A 71-year-old woman is evaluated for a 3-month history of occasional hoarseness and intermittent difficulty swallowing. The patient has a 10-year history of a multinodular goiter. Results of previous fine-needle aspiration biopsies, including one performed 6 months ago, have been negative for cancer. She is otherwise healthy and takes no medication.
- On physical examination, vital signs are normal. The patient's face becomes flushed when she raises her arms above her head. Examination of the neck shows an enlarged thyroid gland that contains several firm nodules. The gland moves easily with swallowing. All other physical examination findings are normal, with no evidence of thyrotoxicosis.
- Results of laboratory studies show a serum thyroid-stimulating hormone level of 3.0 mU/mL (3.0 mU/L) and free thyroxine (T 4) level of 1.6 ng/dL (21 pmol/L).
- Radioactive iodine uptake is 28%. A thyroid scan shows multiple patchy areas of either increased or decreased uptake. A CT scan without contrast shows a large multinodular goiter, with substernal extension and extrinsic moderate compression of the trachea on the right, and a patent airway.
- Which of the following is the most appropriate treatment?

D – THYROIDECTOMY

- In iodine-sufficient areas of the world, multinodular goiter is an idiopathic condition characterized by both solid and partially cystic thyroid nodules.
- It is more common in older persons. Over time, the goiter generally grows and may require treatment.
- Fine-needle aspiration biopsy is used to exclude cancer in this generally benign condition and has excluded it in this patient.
- However, goiter growth can lead to impingement on the trachea, esophagus, or recurrent laryngeal nerve, and can result in dyspnea, stridor, chronic cough, a sensation of fullness or pressure, dysphagia, or hoarseness.
  - No evidence of the effectiveness of external-beam radiation therapy for benign thyroid disease has been shown, which makes the therapy inappropriate in this patient.
  - The previous practice of giving patients levothyroxine to shrink thyroid nodules has been abandoned because of its inefficacy and the morbidities associated with iatrogenic thyrotoxicosis.

Possible venous obstruction should be assessed by having the patient raise the arms above the head. The findings of jugular venous distension, facial plethora, and flushing indicate possible thoracic outlet obstruction with reduced venous return (Pemberton sign).



#9 – (MKSAP 66)

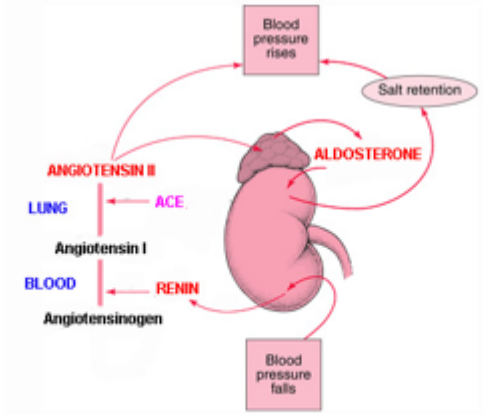
- A 52-year-old man is evaluated for difficult-to-control hypertension. Biochemical evaluation confirms a diagnosis of primary aldosteronism. Medications are amlodipine, losartan, and metoprolol.
- On physical examination, blood pressure is 149/98 mm Hg and pulse rate is 75/min. The remainder of the vital signs and physical examination are unremarkable.
- CT scan shows a 0.8-cm right adrenal mass with a density of 13 Hounsfield units.
- Which of the following is the most appropriate management?

A – ADRENAL VEIN SAMPLING

#9 – PRIMARY HYPERALDOSTERONISM

- STEP 1 = BIOCHEMICALLY CONFIRM HYPERALDO
- STEP 2 = CT (NOT MRI) TO LOOK FOR ADRENAL HYPERPLASIA AND NODULES
- STEP 3 = CONFIRM THE MASS IS SECRETING (DETERMINE THE SOURCE OF ALDOSTERONE SECRETION WHEN IMAGING IS UNREVEALING AND TO CONFIRM LATERALIZATION WHEN IMAGING DEMONSTRATES AN ADRENAL ADENOMA, SUCH AS IN THIS CASE)

	Renin	Aldo	Ddx
Primary	↓	↑	adrenal adenoma/carcinoma, adrenal hyperplasia syndromes
Secondary	↑	↑	RAS, low effective circulating volume
Mimics	↓	↓	AME, licorice ingestion, Liddle's syndrome



Adrenal vein sampling is especially important in older patients because of a higher frequency of nonfunctioning adrenal incidentalomas. Patients with an aldosterone-secreting adenoma are usually offered adrenalectomy, whereas those with primary aldosteronism due to bilateral adrenal hyperplasia are treated medically. Omission of adrenal vein sampling can lead to misdiagnosis in approximately 25% of cases!

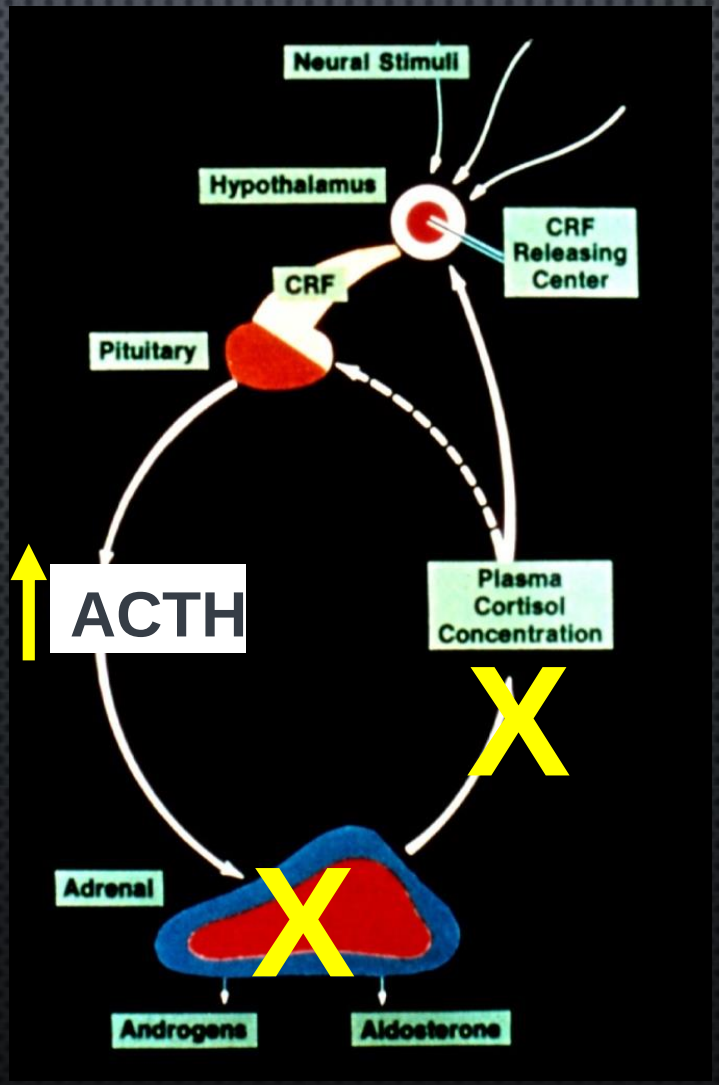
#10

- A 30-year-old man is evaluated after the diagnosis of PRIMARY ADRENAL INSUFFICIENCY one week prior. Other than a 6-month history of weight loss and fatigue, his medical history is unremarkable. His medications are daily hydrocortisone and fludrocortisone, both started recently.
- Vital signs and the remainder of the physical examination are normal. Laboratory studies obtained the week prior, before the initiation of hydrocortisone and fludrocortisone, showed a morning cortisol level of 2.6 mg/dL (71.8 nmol/L),a simultaneous adrenocorticotropin hormone level of 459 pg/mL (101 pmol/L) and a plasma renin of 26 ng/ml/hr (26 mg/L/hour) normal level 2.9 - 24 ng/mL/hour (2.9 - 24 mg/L/hour)

- Which of the following is the most appropriate next test?

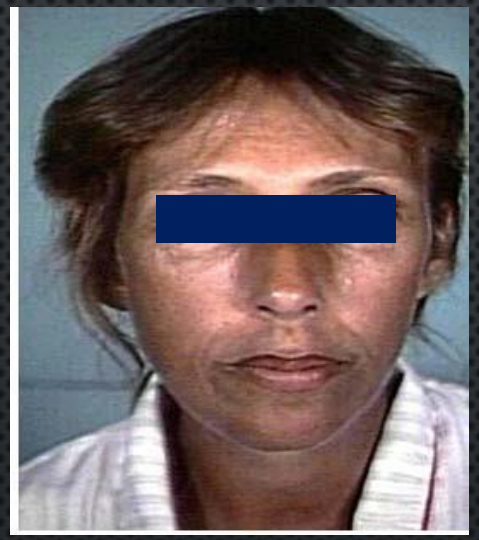
C: 21-HYDROXYLASE ANTIBODY MEASUREMENT

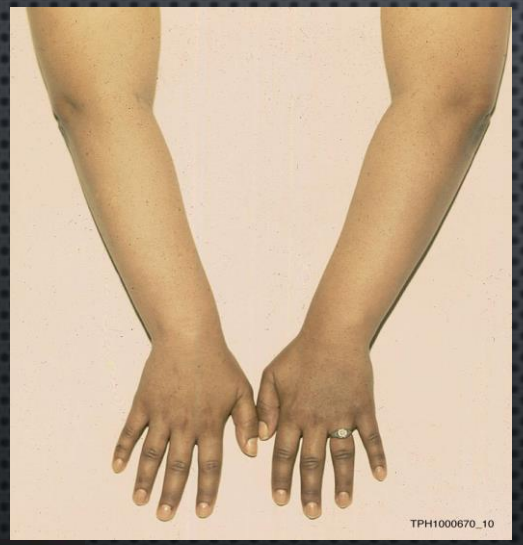
PRIMARY ADRENAL INSUFFICIENCY

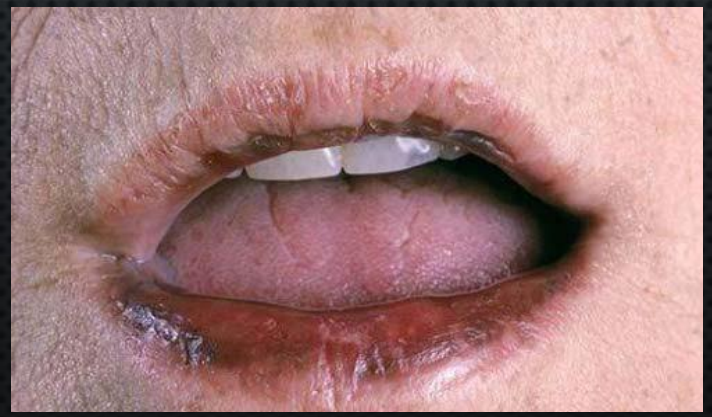


Note: the autoimmune process destroy all layers of the adrenal cortex

- Cause of PAI
  - Autoimmune disease (Addison's disease)
    - 50% of patients have another autoimmune disorder (thyroid disease, vitiligo, type 1 diabetes mellitus, pernicious anemia)







- Fatigue
- Skin darker (stimulation of ACTH production)
- Decreased appetite and nausea
- Dizzy
- Felt like she had the flu

FINDING THE ETIOLOGY AI IS IMPORTANT!

- Primary AI is rare! So etiology should be pursued due to additional consequences of the diagnosis
  - Children look for genetic causes
  - 21- hydroxylase Ab
  - Young men Adrenal X- linked leukodystrophy

21 HYDROXYLASE ANTIBODY

- Cause of autoimmune Addison's disease
- Should be checked in all cases of primary AI
- Sensitivity 90% Sensitivity 100% but immunofluorescence technique is less sensitive
- Young male with primary AI and antibody negative check very long chain fatty acids for Adrenal X-linked leukodystrophy

#11 – (MKSAP 67)

- A 65-year-old woman comes to the office to establish care. Her medical history is notable for hypothyroidism due to Hashimoto thyroiditis treated with levothyroxine. She does not have any symptoms at this time. There is no history of head or neck radiation exposure.
- On physical examination, vital signs are normal. The patient's thyroid gland is enlarged. The right lobe is larger than the left, and a mobile 2-cm nodule is palpable in the lower pole. There is no palpable cervical adenopathy.
- Laboratory studies show a serum thyroid-stimulating hormone level of 2.0 mU/mL (2.0 mU/L).
- Which of the following is the most appropriate diagnostic test to perform next?

D – ULTRASOUND OF THE NECK

11 - Thyroid Nodule

Need to:
1) confirm presence of a nodule,
2) determine that biopsy is indicated
3) ensure that there are no additional nonpalpable nodules that warrant FNAB
4) assess the cervical lymph nodes.

15% of palpable nodules not seen on US and 15% have another nodule!!

The TAKE-HOME

- Inspection, palpation, percussion, auscultation, and *insonation* (JAMA 2018): ULTRASOUND
- TSH prior to any FNA: hyperthyroidism no FNA
- Please select expert ultrasound centers

  Please select expert thyroid physicians & surgeons

  "do not stick needle into anything if it does not change what you're going to do"
- All thyroid disorders on neck US need LN screen
- Bethesda Cytology System & Molecular Markers
- Take the lead: SUSME

"Code words" in US reports that suggest high suspicion of malignancy

Microcalcifications

Coarse/peripheral calcifications (eggshell gaps)

Indistinct borders/local invasion/infiltrating or irregular margins

Lymphadenopathy (LN screen vs LN mapping)

Taller than wide

Markedly hypoechoic

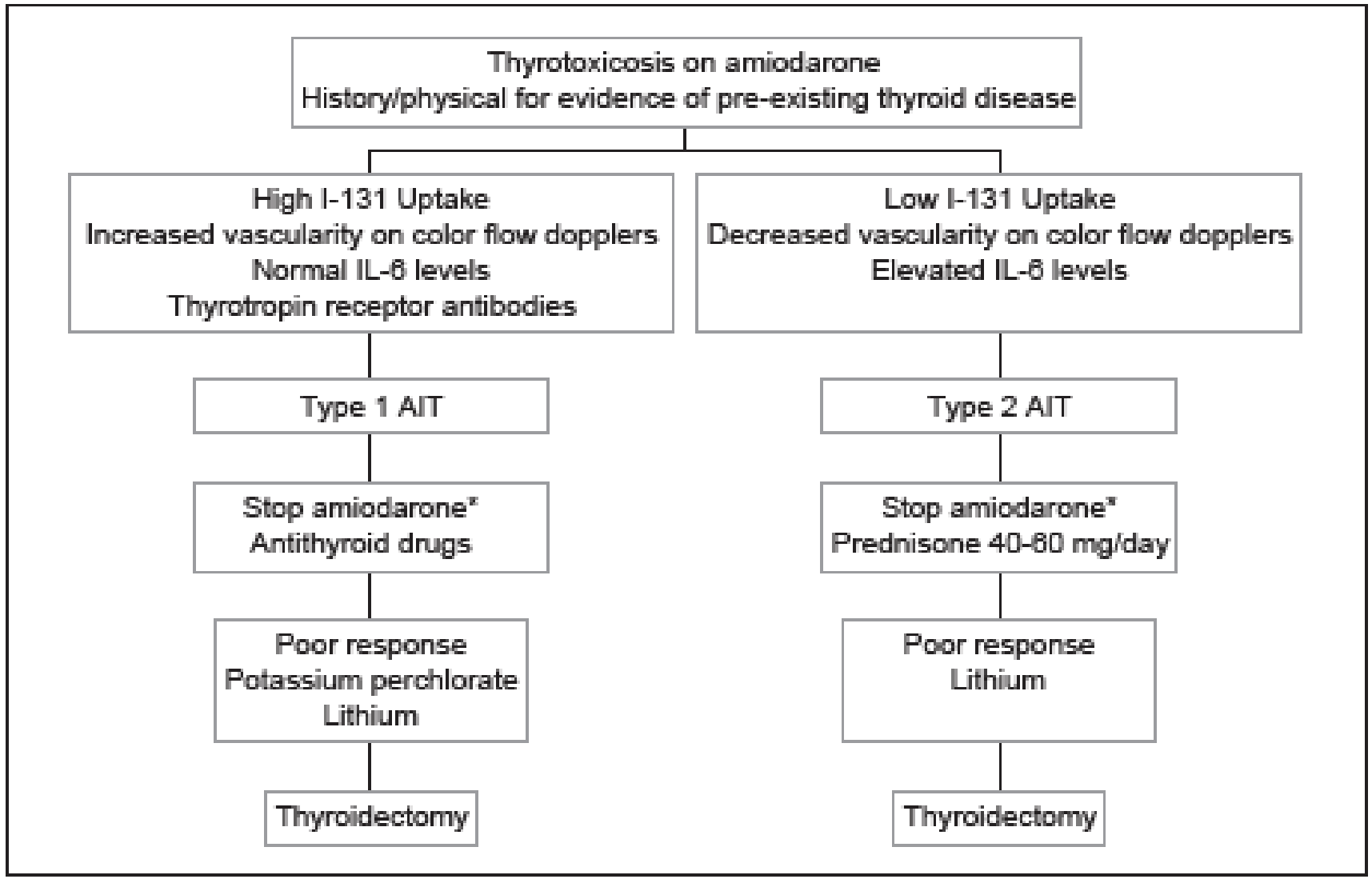
Intranodular hypervascularity

#12

- A 71-year-old man is evaluated in the office for thyrotoxicosis. His medical history is significant for heart failure and atrial fibrillation. For the past 2 years his medications have been metoprolol, lisinopril, amiodarone, and rivaroxaban.
- On physical examination, the patient is afebrile, blood pressure is 150/80 mm Hg, pulse rate is 116/min, and respiration rate is 24/min. Bilateral lid lag is noted and there is a fine tremor of his outstretched hands. Deep tendon reflexes are brisk. Examination of the thyroid gland and the remainder of the physical examination are normal.
- Laboratory showed a TSH of 0.001 miliinternational unit/L and a free T4 of 2.7 ng/dl. TSH receptor antibodies and Thyroid stimulating immunoglobulin are undetectable.
- On thyroid ultrasound, the thyroid lobes and isthmus are normal in size. No thyroid nodules are seen. The background thyroid parenchyma shows no demonstrable vascularity on color flow Doppler.
- Which of the following is the most likely diagnosis?

D – AMIODARONE-INDUCED THYROTOXICOSIS

- Thyrotoxicosis affects 5% of patients taking amiodarone and can occur at any time during or up to 9 months after treatment.
- Type 1 (hyperthyroidism) amiodarone-induced thyrotoxicosis occurs in patients with underlying multinodular goiter or latent Graves disease and is associated with increased vascularity on color flow Doppler ultrasonography.
- Type 2 (destructive thyroiditis) usually affects patients without thyroid disease and is not associated with increased vascularity on color flow Doppler
- amiodarone-induced thyrotoxicosis should be the initial diagnostic consideration in a patient on long-term amiodarone therapy.


Thyrotoxicosis on amiodarone
History/physical for evidence of pre-existing thyroid disease
High I-131 Uptake
Increased vascularity on color flow dopplers
Normal IL-6 levels
Thyrotropin receptor antibodies
Low I-131 Uptake
Decreased vascularity on color flow dopplers
Elevated IL-6 levels
Type 1 AIT
Type 2 AIT
Stop amiodarone*
Antithyroid drugs
Stop amiodarone*
Prednisone 40-60 mg/day
Poor response
Potassium perchlorate
Lithium
Poor response
Lithium
Thyroidectomy
Thyroidectomy

#13 – (MKSAP 24)

- A 42-year-old woman is evaluated prior to surgery following a diagnosis of pheochromocytoma. Her symptoms are palpitations, hypertension, and sweating for 8 months' duration. Medications are lisinopril and hydralazine.
- On physical examination, blood pressure is 155/98 mm Hg. Other vital signs and the remainder of the examination are normal.
- Which of the following is the most appropriate next step in management?

E – START PHENOXYBENZAMINE

Pheochromocytoma

- TRIAD: Palpitation, headache, diaphoresis
- only in <50%
- Syndromes:
  - MEN 1
  - Von Hippel-Lindau
  - Neurofibromatosis type II
- Diagnosis: CT scan w/ contrast
- Who to test:
  - Typical triad
  - All adrenal masses
  - Hypertension on 3+ drugs
  - Idiopathic cardiomyopathy
  - Hypertension during anesthesia
  - Paragangliomas
  - Syndromes (listed)
  - Family history
- Treat - Surgical resection

#13: PHEO-CHROMO-CYTOMA

	α_1 receptor	α_2 receptor	β_1 receptor	β_2 receptor
Norepinephrine	Smooth muscle, hypothalamus	Nerve endings, stomach, hypothalamus	Heart, fat cells, kidneys, brain (posterior lobe of pituitary gland)	No interaction
Epinephrine	Smooth muscle	No interaction	Heart, fat cells, kidneys	Lungs, arterioles, stomach, liver or pancreas, uterus, skeletal muscle
End effect	Vasoconstriction, elevated blood pressure, mydriasis, decreased ability to defecate and/or urinate	Vasodilatation, lowers blood pressure, constipation	Increases heart rate, increases cardiac output and force of contraction, increased conduction, lipolysis, release of renin, release of antidiuretic hormone	Relaxation of smooth muscle (vasodilatation, bronchodilatation, constipation), increased glucose production and insulin release, contraction of skeletal muscle

- Phenoxybenzamine
  - Irreversible, nonspecific alpha blocker (mostly1)
  - Start 10-14 days prior
  - Titrate to goal BP 130/80 (seating) and SBP >90 when standing
  - Side effect: postural hypotension (Rx: HIGH SODIUM DIET)
  - Start beta-blocker second, treats reflex tachycardia (NEVER START BETA-BLOCKER FIRST – we need Beta2 to oppose alpha1!)
- Metyrosine
  - Catecholamine synthesis inhibitor
  - Given if tumor is very large or metanephrines are significantly high
  - Significant side effects
- Alpha-1 blockers (selective)
  - Prazosin, terazosin, doxazosin
  - Cheaper and fewer side effects than phenoxybenzamine

#14

- An 18-year-old woman is evaluated after the diagnosis of autoimmune hypoparathyroidism 1 month ago. She is now asymptomatic. Calcium citrate and calcitriol were initiated at the time of diagnosis.
- The physical examination, including vital signs, is normal.
- At the time of diagnosis, laboratory studies showed a low serum parathyroid hormone level, hypocalcemia, and a normal serum creatinine level.
- In addition to serum calcium, phosphate, and magnesium, which of the following should be measured today?

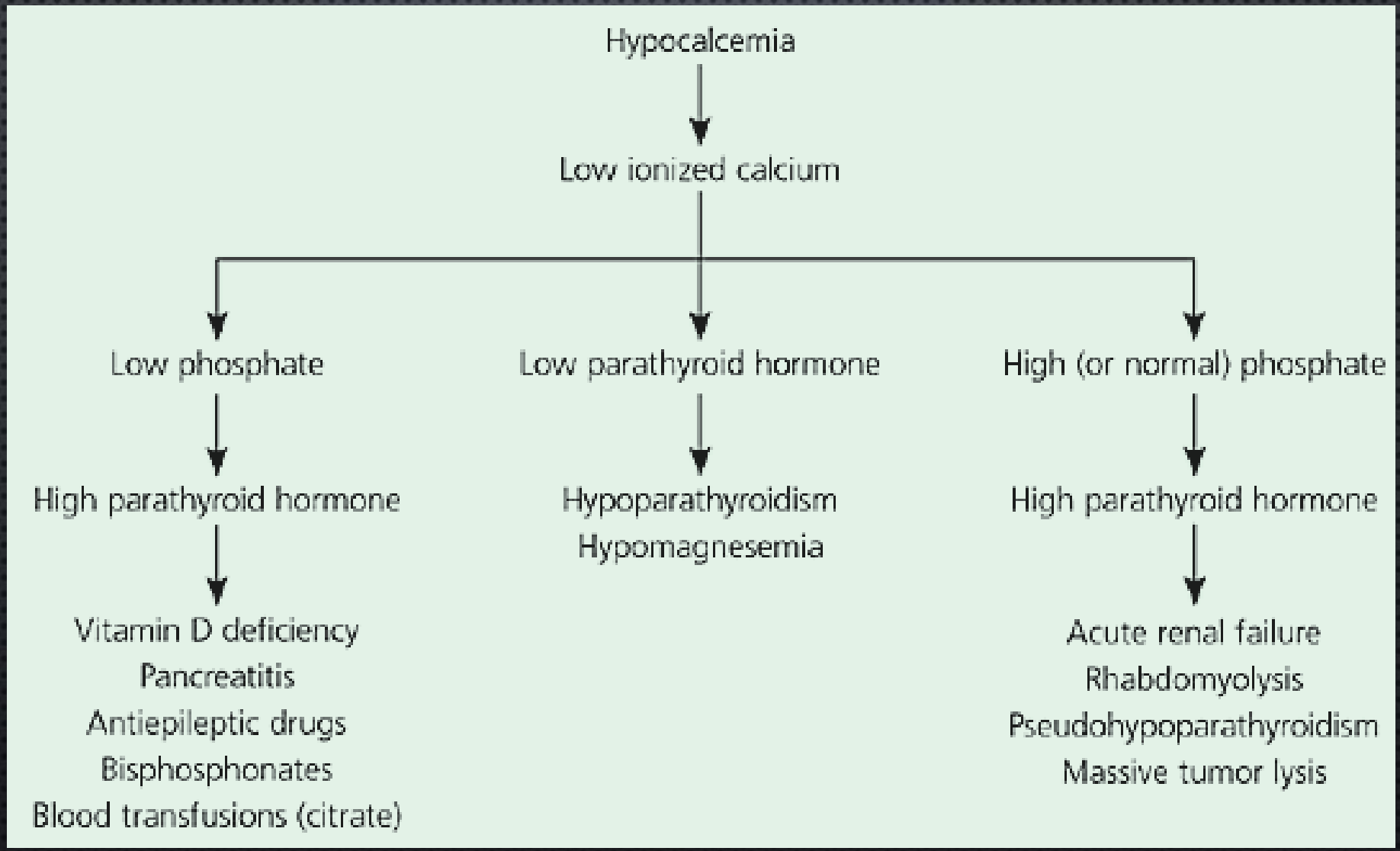
B – 24-HOUR URINE CALCIUM

- In chronic hypoparathyroidism, goals of therapy are to eliminate symptoms while avoiding complications of therapy; monitoring of urine calcium excretion is mandatory because hypercalciuria often limits therapy. Without parathyroid hormone (PTH), urinary calcium excretion is higher than normal for any given serum calcium level. Complications of prolonged hypercalciuria include nephrolithiasis and impaired glomerular filtration rate. Serum calcium, magnesium, creatinine, and urine calcium levels should be assessed on a regular basis. The goal calcium levels should be low-normal without hypercalciuria
- Thiazide diuretics reduce urine calcium excretion and thus may permit sufficient calcium and vitamin D therapy to achieve goal calcium levels.

Laboratory evaluation hypocalcemia

	PTH	Corrected serum calcium	Phos	Mag	25OHD	1,25 (OH) 2D	Creatinine
Hypoparathyroidism	Low	Low	Elevated	Normal	Normal	Normal or low	Normal
Activating mutation calcium sensing receptor	Normal or low	Low	Elevated	Normal	Normal	Normal	Normal
Hypomagnesemia	Normal or low	Low	Normal	Low	Normal	Normal	Normal
PTH resistance (pseudohypoparathyroidism)	Elevated	Low	Elevated	Normal	Normal	Normal	Normal
Vitamin D deficiency	Elevated	Low or normal	Low or normal	Normal	Low	Normal or high	Normal
Chronic kidney disease	Elevated	Low	Elevated	Elevated or normal	Normal or low*	Low	Elevated

* In individuals with concurrent nutritional deficiency.


Hypocalcemia
Low ionized calcium
Low phosphate
Low parathyroid hormone
High (or normal) phosphate
High parathyroid hormone
Hypoparathyroidism
Hypomagnesemia
High parathyroid hormone
Vitamin D deficiency
Pancreatitis
Antiepileptic drugs
Bisphosphonates
Blood transfusions (citrate)
Acute renal failure
Rhabdomyolysis
Pseudohypoparathyroidism
Massive tumor lysis

#15 – (MKSAP 25)

- A 60-year-old man is evaluated during a routine office visit. He was diagnosed with type 2 diabetes mellitus 6 years ago. Medical history is significant for coronary artery disease, hypertension, hyperlipidemia, and biliary pancreatitis. Medications are lisinopril, metoprolol, metformin, aspirin, and atorvastatin.
- On physical examination, other than a blood pressure of 152/91 mm Hg, the vital signs are normal. BMI is 27. The remainder of the examination is normal.
- Laboratory studies show a hemoglobin A_{1C} level of 8.2%.
- Which of the following is the most appropriate treatment for this patient?

A – EMPAGLIFLOZIN

Metformin	1.0 to 2.0	Weight neutral
Additional therapy[¶]		
Insulin (usually with a single daily injection of intermediate- or long-acting insulin initially)	1.5 to 3.5	No dose limit, rapidly effective, improved lipid profile
Sulfonylurea (shorter-acting agents preferred)	1.0 to 2.0	Rapidly effective
GLP-1 receptor agonist (daily to weekly injections)	0.5 to 1.0	Weight loss, reduced cardiovascular mortality (liraglutide, semaglutide) in patients with established CVD
Thiazolidinedione	0.5 to 1.4	Improved lipid profile (pioglitazone), potential decrease in MI (pioglitazone)
Glinide	0.5 to 1.5[Δ]	Rapidly effective
SGLT2 inhibitor	0.5 to 0.7	Weight loss, reduction in systolic blood pressure, reduced cardiovascular mortality in patients with established CVD
DPP-4 inhibitor	0.5 to 0.8	Weight neutral
Alpha-glucosidase inhibitor	0.5 to 0.8	Weight neutral
Pramlintide	0.5 to 1.0	Weight loss

Decrease hepatic gluconeogesnsis, decrease insulin resistance, decrease weight, TGAs/chol

Increase release insulin from beta cells (glipizide)

Decrease hepatic gluconeogenesis, slow gastric emptying, early satiety [incretin mimetic] (exenatide Trulicity)

Bind PPAR gamma receptors = increase glucose transport, decrease insulin resistance, lipids (pioglitazone)

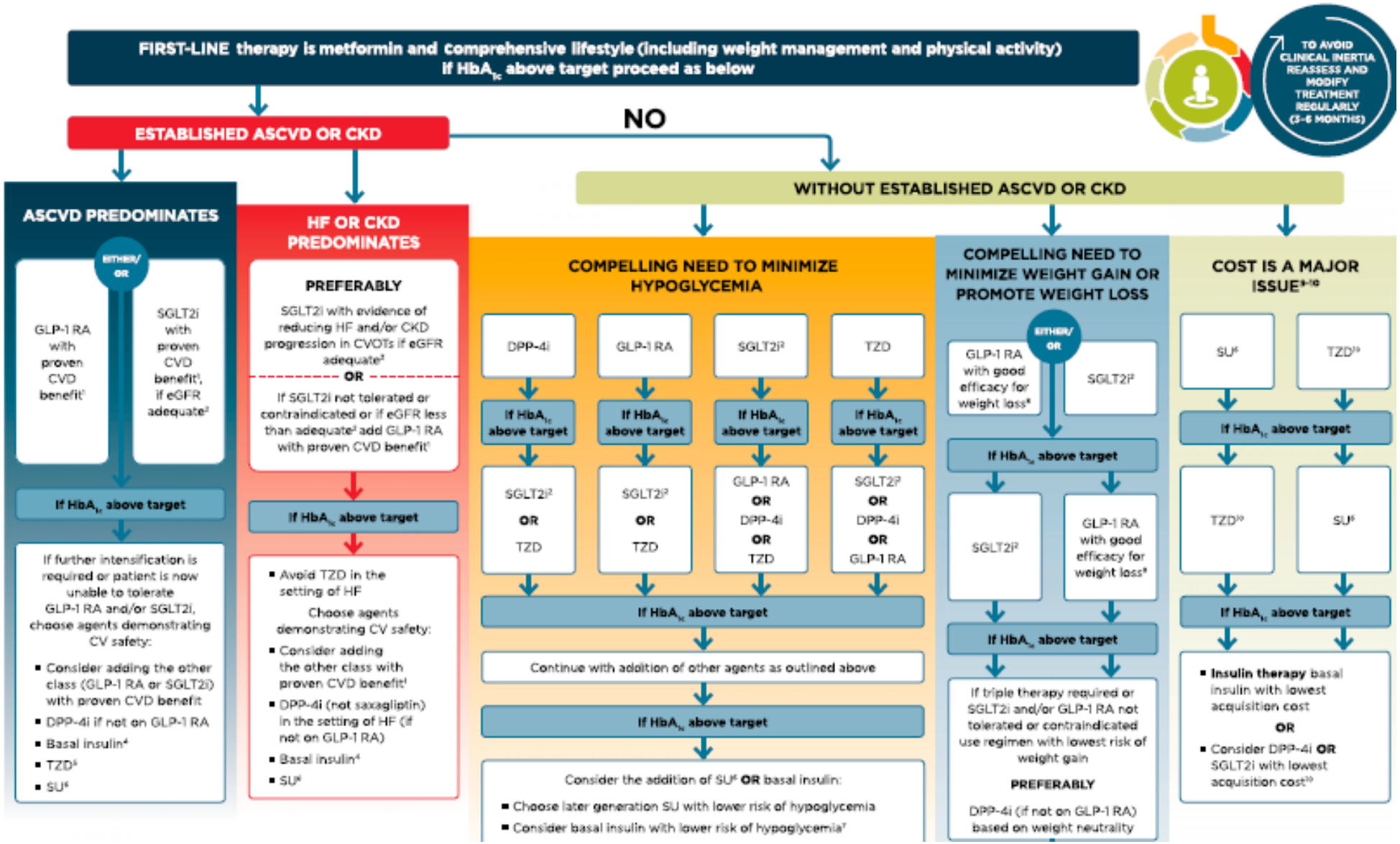
Increases release from beta cells (repaglinide = Prandin)

Blocks resorption of glucose by the kidney thereby increasing excretion of glucose in the urine (canagliflozin Invokana, empagliflozin Jardiance)

Mimetic = decrease gastric emptying, weight loss, early satiety, decreased hepatic gluconeogenesis (sitagliptin Januvia)

Inhibits breakdown of carbs and decreases absorption of glucose (acarbose)

Complements insulin, no hypoglycemia, slows gastric emptying (amylin analogue)


FIRST-LINE therapy is metformin and comprehensive lifestyle (including weight management and physical activity)
If HbA1c above target proceed as below
TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)
ESTABLISHED ASCVD OR CKD
NO
WITHOUT ESTABLISHED ASCVD OR CKD
ASCVD PREDOMINATES
EITHER/ OR
GLP-1 RA with proven CVD benefit[1]
SGLT2i with proven CVD benefit[1], if eGFR adequate[2]
If HbA1c above target
If further intensification is required or patient is now unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety:
Consider adding the other class (GLP-1 RA or SGLT2i) with proven CVD benefit
DPP-4i if not on GLP-1 RA
Basal insulin[4]
TZD[5]
SU[6]
HF OR CKD PREDOMINATES
PREFERABLY
SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate[2]
OR
If SGLT2i not tolerated or contraindicated or if eGFR less than adequate[2] add GLP-1 RA with proven CVD benefit[1]
If HbA1c above target
Avoid TZD in the setting of HF
Choose agents demonstrating CV safety:
Consider adding the other class with proven CVD benefit[1]
DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA)
Basal insulin[4]
SU[6]
COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA
DPP-4i
GLP-1 RA
SGLT2i[2]
TZD
If HbA1c above target
SGLT2i[2] OR TZD
GLP-1 RA OR DPP-4i OR TZD
SGLT2i[2] OR DPP-4i OR GLP-1 RA
If HbA1c above target
Continue with addition of other agents as outlined above
If HbA1c above target
Consider the addition of SU[6] OR basal insulin:
Choose later generation SU with lower risk of hypoglycemia
Consider basal insulin with lower risk of hypoglycemia[7]
COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS
EITHER/ OR
GLP-1 RA with good efficacy for weight loss[8]
SGLT2i[2]
If HbA1c above target
SGLT2i[2]
GLP-1 RA with good efficacy for weight loss[8]
If HbA1c above target
If triple therapy required or SGLT2i and/or GLP-1 RA not tolerated or contraindicated use regimen with lowest risk of weight gain
PREFERABLY
DPP-4i (if not on GLP-1 RA) based on weight neutrality
COST IS A MAJOR ISSUE[9-10]
SU[6]
TZD[10]
If HbA1c above target
TZD[10]
SU[6]
If HbA1c above target
Insulin therapy basal insulin with lowest acquisition cost
OR
Consider DPP-4i OR SGLT2i with lowest acquisition cost[10]

#16 – (MKSAP 72)

- A 66-year-old man recently diagnosed with type 2 diabetes mellitus is evaluated in the emergency department for nausea, vomiting, and fatigue. He was diagnosed with type 2 diabetes 18 months ago. In the past month metformin was discontinued due to severe diarrhea, and glipizide and empagliflozin were initiated. In addition to type 2 diabetes, medical history is significant for coronary artery disease, hypertension, and dyslipidemia. Medications are aspirin, lisinopril, metoprolol, atorvastatin, glipizide, and empagliflozin.
- On physical examination, temperature is normal, blood pressure is 90/60 mm Hg, pulse rate is 120/min, and respiration rate is 22/min. Dry mucous membranes are noted. There is diffuse abdominal tenderness to palpation without guarding. Other than tachycardia, the remainder of the examination is normal.

Laboratory studies:	
Sodium	133 mEq/L (133 mmol/L)
Bicarbonate	10 mEq/L (10 mmol/L)
Glucose	150 mg/dL (8.3 mmol/L)
Anion gap	17 mEq/L (17 mmol/L)
β-hydroxybutyrate	Elevated

- Which of the following is most likely responsible for the patient's findings?

C – EMPAGLIFLOZIN

Sulfonylurea (shorter-acting agents preferred)	1.0 to 2.0	Weight gain, hypoglycemia (especially with glibenclamide or chlorpropamide)
GLP-1 receptor agonist (daily to weekly injections)	0.5 to 1.0	Requires injection, frequent GI side effects, long-term safety not established, expensive
Thiazolidinedione	0.5 to 1.4	Fluid retention, HF, weight gain, bone fractures, potential increase in MI (rosiglitazone) and bladder cancer (pioglitazone)
Glinide	0.5 to 1.5$^{\Delta}$	Weight gain, 3 times/day dosing, hypoglycemia
SGLT2 inhibitor	0.5 to 0.7	Vulvovaginal candidiasis, urinary tract infections, bone fractures, lower limb amputations, acute kidney injury, DKA, long-term safety not established
DPP-4 inhibitor	0.5 to 0.8	Long-term safety not established, expensive, possible increased risk of HF with saxagliptin
Alpha-glucosidase inhibitor	0.5 to 0.8	Frequent GI side effects, 3 times/day dosing
Pramlintide	0.5 to 1.0	3 injections daily, frequent GI side effects, long-term safety not established, expensive

Pancreatitis, MEN2/medullary thyroid cancer

Sodium-glucose cotransporter 2 (SGLT2) inhibitors (canagliflozin, dapagliflozin, and empagliflozin) improve glycemia by increasing excretion of glucose by the kidney. SGLT2 is expressed in the proximal tubule and mediates reabsorption of approximately 90% of the filtered glucose load. SGLT2 inhibitors promote excretion of glucose by the kidneys and thereby modestly lower elevated blood glucose levels in patients with type 2 diabetes. Euglycemic diabetic ketoacidosis has been reported in patients with type 2 diabetes taking SGLT2 inhibitors. Because of this, the FDA issued a Drug Safety Communication that warns of an increased risk of

diabetic ketoacidosis with uncharacteristically mild to moderate glucose elevations (euglycemic diabetic ketoacidosis) associated with the use of all the approved SGLT2 inhibitors. SGLT2 inhibitors should be discontinued in patients who develop acidosis on these agents.

#17

- A 28-year-old woman is evaluated during the first trimester of her pregnancy. Medical history is significant for type 1 diabetes mellitus diagnosed at 14 years of age. She has no known complications of diabetes. Her last dilated comprehensive eye examination was performed during preconception counseling 7 months ago and was normal. Recent evaluations of kidney function and lipids were normal, as was foot examination. Medications are insulin lispro delivered through continuous subcutaneous insulin infusion and levothyroxine.
- The physical examination, including vital signs, is normal.
- Laboratory studies reveal that hemoglobin A 1c level is currently 6.7%, improved from 9%, 3 months ago.
- When should the next dilated eye examination be performed?

A – NOW

- The 2019 American Diabetes Association Standards of Care recommended that women with preexisting type 1 or type 2 diabetes who are planning pregnancy or who have become pregnant should be counseled on the risk for development and/or progression of diabetic retinopathy.
- Dilated eye examinations should occur ideally before pregnancy or in the first trimester, and then patients should be monitored every trimester and for 1 year postpartum, as indicated by the degree of retinopathy and as recommended by the eye specialist.

Recommendations

14.4 Women with preexisting type 1 or type 2 diabetes who are planning pregnancy or who have become pregnant should be counseled on the risk of development and/or progression of diabetic retinopathy. Dilated eye examinations should occur ideally before pregnancy or in the first trimester, and then patients should be monitored every trimester and for 1-year postpartum as indicated by the degree of retinopathy and as recommended by the eye care provider. B

Recommendation

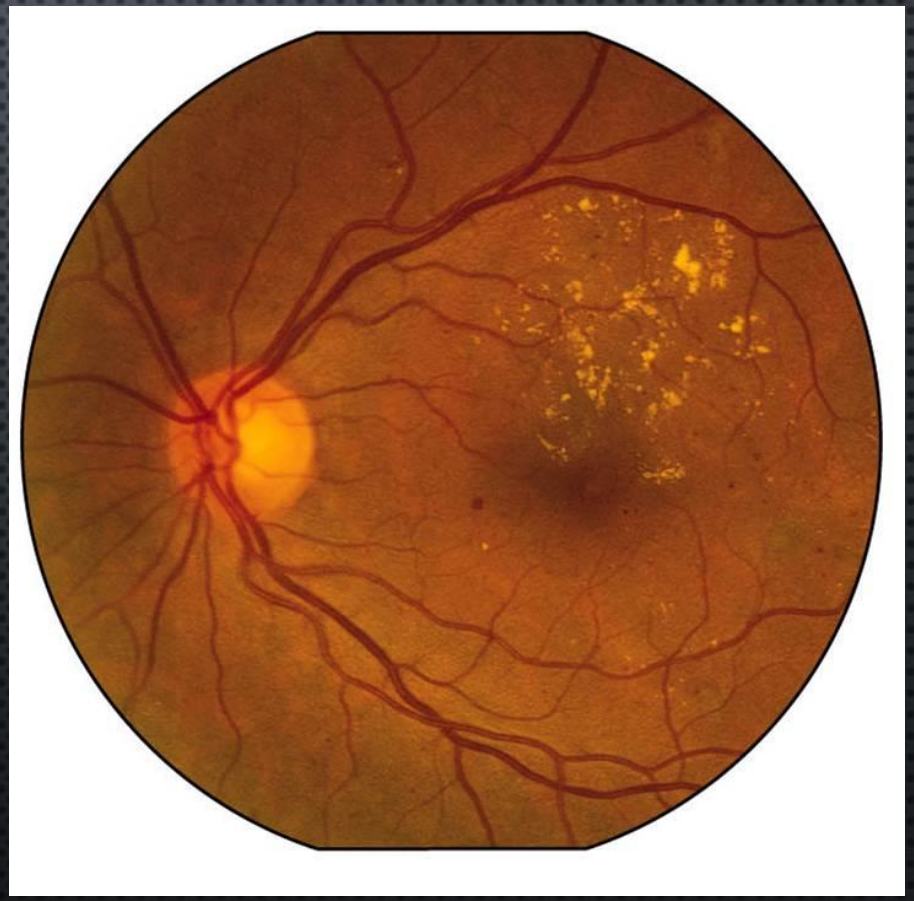
14.12 Women with type 1 or type 2 diabetes should be prescribed low-dose aspirin 60–150 mg/day (usual dose 81 mg/day) from the end of the first trimester until the baby is born in order to lower the risk of preeclampsia. A

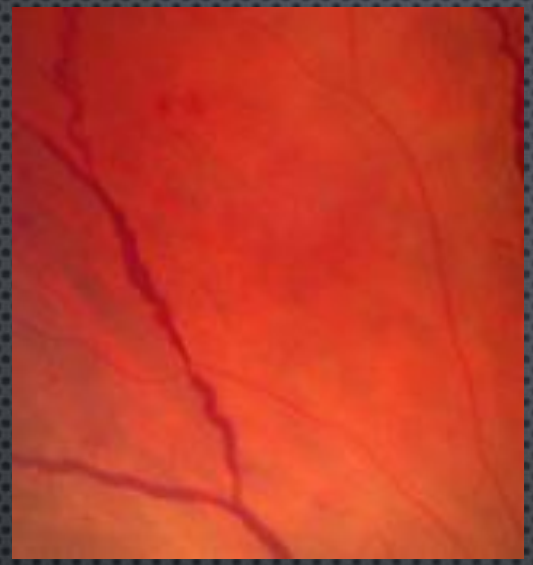
Screening for diabetic retinopathy

- Type 1 DM: within 5 years after DM diagnosis, then yearly
- Type 2 DM: at time of DM diagnosis then yearly
- Pregnancy in pre-existing diabetes: Prior to conception and during first trimester

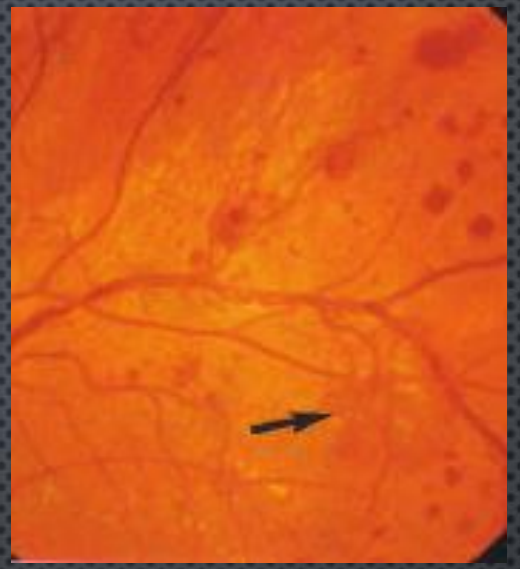
Diabetic Retinopathy

- Most common cause of blindness in adults 20-74 years old
- Accounts for at least 12,000 new cases in US each year
- Visual loss may be secondary to macular edema, hemorrhage from new vessels, retinal detachment, or neovascular glaucoma

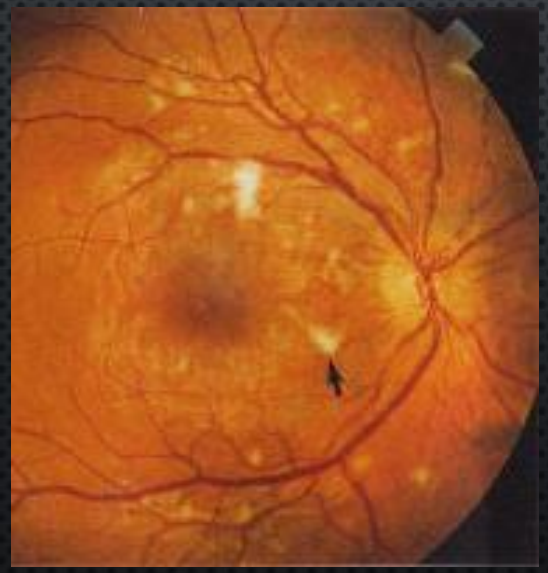




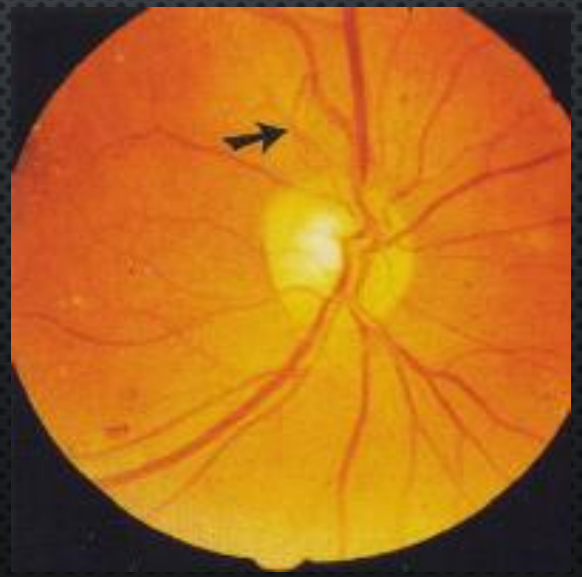
Venous beading



Hemorrhages



Cotton-wool spots



Neovascularization

CLINICAL MANIFESTATIONS, DR

	Nonproliferative	Proliferative	Macular Edema
Symptoms	None, or blurred vision and glare	None, or reduced vision or floaters	None, or blurred vision
Signs	**Mild** - Microaneurysms **Moderate** - More than just microaneurysms Severe ->20 intraretinal hemorrhages - Venous beading - Prominent IRMA - No signs of PDR	Retinal venous dilation Neovascularization of optic disc, retina, and/or iris Vitreous/pre-retinal hemorrhage	**Mild** - Retinal thickening, hard exudates distant from center of macula **Moderate** - retinal thickening, hard exudates approaching center of macula **Severe** -retinal thickening, hard exudates involving center of macula

IRMA = intraretinal microvascular abnormalities

#18

- A 32-year-old woman is evaluated after a recent diagnosis of hyperprolactinemia, discovered during investigation of amenorrhea of 4 month's duration. She has a history of type 1 diabetes mellitus, hypertension, dyslipidemia, and gastroparesis, for which she takes long-term metoclopramide. Her other medications include basal and prandial insulin, atorvastatin, and losartan.
- Laboratory studies obtained last week show a serum prolactin level of 90 ng/mL (90 mg/L). Thyroid function tests are normal and a urine pregnancy test is negative.
- Which of the following is the most appropriate next step?

D – STOP METOCLOPRAMIDE

- The most common cause of hyperprolactinemia is physiologic: prolactin is released during pregnancy and postpartum to cause lactation.
- Another common cause of hyperprolactinemia is primary hypothyroidism.
- Nonfunctioning pituitary adenomas can also cause hyperprolactinemia by compressing the pituitary stalk and decreasing dopamine inhibition of prolactin secretion. Medications are a common cause of hyperprolactinemia.
- drugs such as metoclopramide, risperidone, and phenothiazines can lead to High prolactin).
  - Confirming that the hyperprolactinemia is related to medication can be challenging. When the prolactin level is only mildly elevated (<100 ng/mL [1-- mg/L]), it may be reasonable to assume that hyperprolactinemia is a medication side effect.
    - the offending medication should be withheld for 3 days if possible to determine whether prolactin levels return to normal.

Neuroendocrine Pharmacology

Prolactin Inhibitory Factor – Dopamine

- Prolactin is under tonic *INHIBITORY* control and predominant inhibitor is dopamine
- D2 receptors are coupled to G-proteins and increase intracellular C-AMP
- Growth hormone secreting tumors may also express D2 receptors

Treatment:

- First line of treatment is Dopamine agonists (may have dramatic effects on prolactin secreting tumors)
- Cabergoline (weekly) or bromocriptine (twice daily)
- Microadenomas respond dramatically; often with resumption of menses and restoration of fertility
- +/- surgical resection

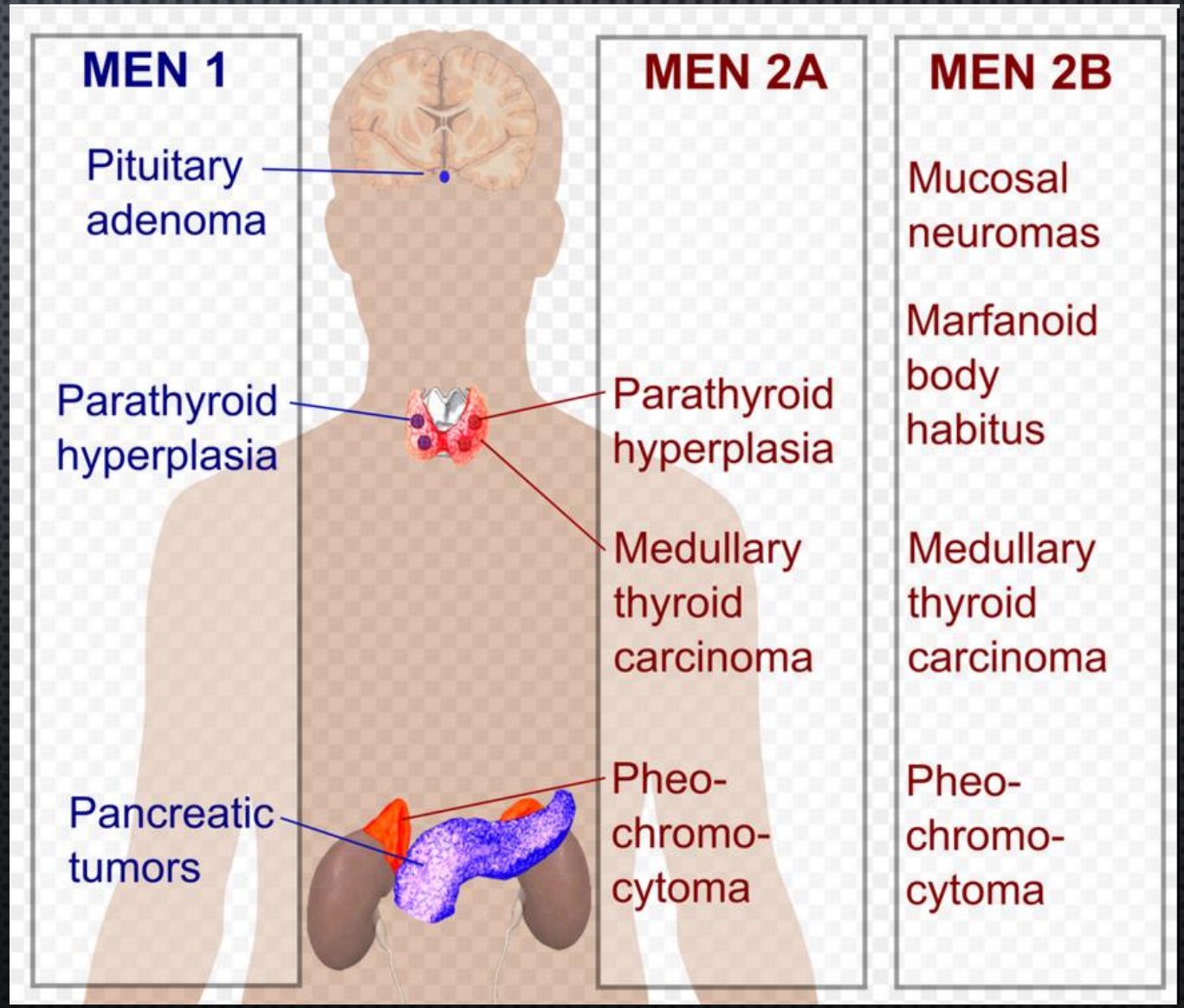
#19 – (MKSAP 30)

- A 21-year-old woman is seen in the office following parathyroidectomy for hyperparathyroidism. The pathology of three resected enlarged parathyroid glands showed hyperplasia. Her medical history is significant for oligomenorrhea. Family history is notable for hypercalcemia and kidney stones in her father, who died at age 49 from pancreatic cancer, and a pituitary tumor in her sister at age 16.
- Her vital signs are normal. Skin findings include dermatofibroma. Her physical examination is normal with the exception of the surgical scar on her neck.
- Which of the following is the most likely diagnosis?

B – MULTIPLE ENDOCRINE NEOPLASIA TYPE 1 (MEN1)

#19 – MEN1

- Primary hyperparathyroidism in adolescents and young adults may be the first sign of multiple endocrine neoplasia syndrome (MEN) 1 & 2
- If family history reveals primary hyperparathyroidism, pituitary tumor, Zollinger-Ellison syndrome, early death from pancreatic neoplasm, pheochromocytoma, or medullary thyroid cancer, MEN is more likely and screening should be considered
- In contrast to sporadic primary hyperparathyroidism, MEN syndromes have recurrence of hyperparathyroidism due to ongoing hyperplasia in the remaining parathyroid tissue after parathyroidectomy
- MEN1 is associated with mutation of the tumor suppressor *MEN1* gene, and MEN2A is associated with mutation of the *RET* gene



#20

- A 54-year-old man has had difficult-to-control hypertension for 3 years. He has gained 33 lb (15kg) in the last 3 years and diabetes mellitus was diagnosed 1 year ago. His medications include metformin, amlodipine, valsartan, and hydrochlorothiazide.
- On physical examination, his BMI is 35 kg/m2 and blood pressure is 148/92 mm Hg. He has scattered 1- to 2-cm bruises on his extremities. He has no dorsocervical fat pad, striae, or proximal muscle strength weakness.
- Laboratory test results:

Sodium = 139 mEq/L (136-142 mEq/L)

Potassium = 3.5 mEq/L (3.5-5.0 mEq/L)

Serum aldosterone = 14 ng/dL (4-21 ng/dL)

renin activity = 0.6 ng/mL per h (0.6-4.3 ng/mL per h)

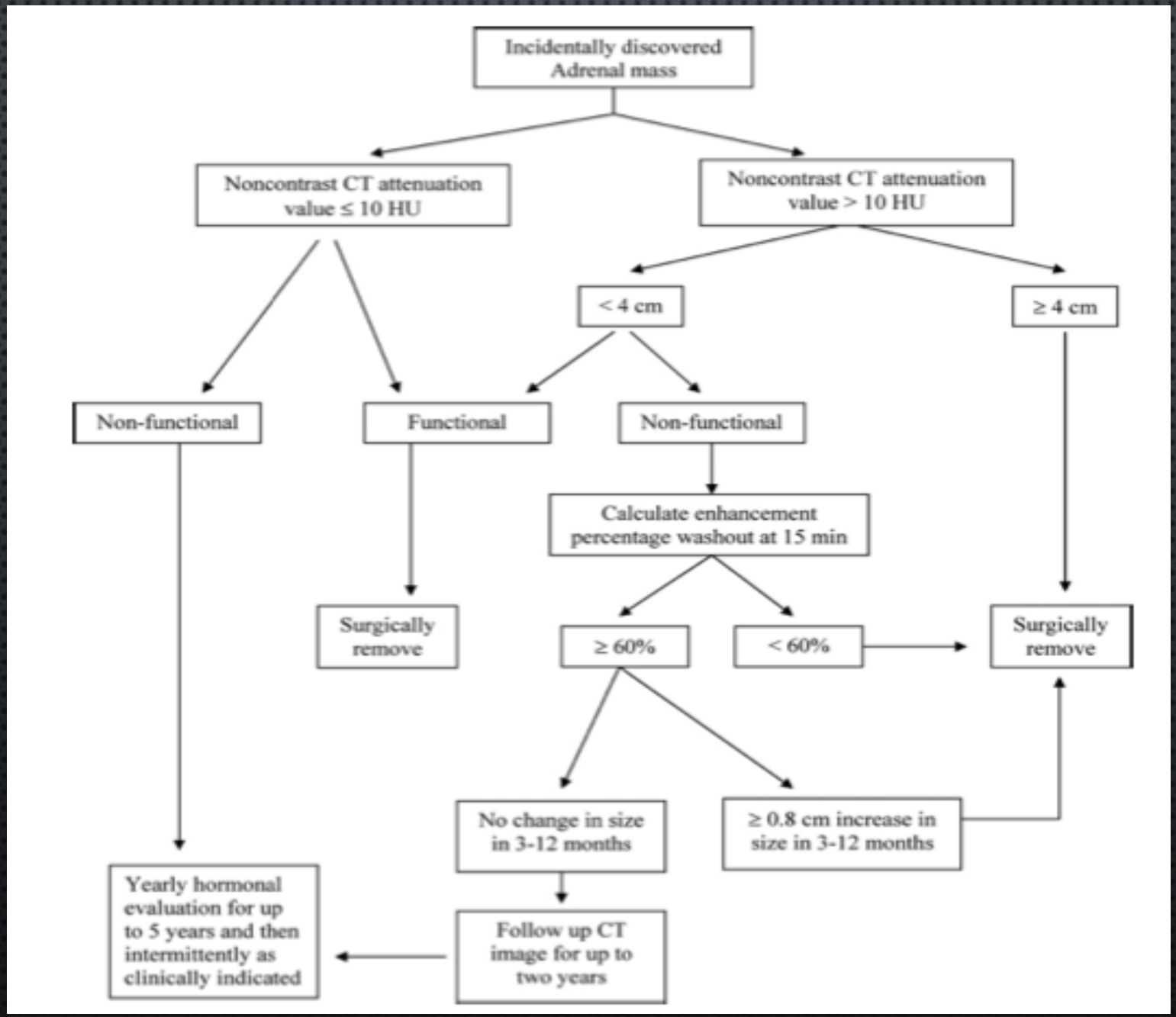
Fasting glucose = 165 mg/dL (70-99 mg/dL)

- Abdominal CT with contrast demonstrates a 3.8-cm left adrenal mass and an atrophic right adrenal gland (see image, arrows).

- Which of the following is the best next step in this patient's management?

B – MEASURE PLASMA METANEPHRINES AND PERFORM A 1-MG OVERNIGHT DEXAMETHASONE SUPPRESSION TEST

Diagnosis	Features	Biochemical Tests
Pheochromocytoma	High blood pressure, catechol symptoms	Urine-free and plasma-free metanephrines
Primary aldosteronism	High blood pressure, low K^+, low PRA*	Plasma aldosterone-to-renin ratio
Adrenocortical carcinoma	Virilization or feminization	Urine 17-ketosteroids
Cushing or "silent" Cushing syndrome	Cushing symptoms or normal examination results	Overnight 1-mg dexamethasone test


Incidentally discovered Adrenal mass
Noncontrast CT attenuation value ≤ 10 HU
Noncontrast CT attenuation value > 10 HU
< 4 cm
≥ 4 cm
Non-functional
Functional
Non-functional
Calculate enhancement percentage washout at 15 min
Surgically remove
≥ 60%
< 60%
Surgically remove
No change in size in 3-12 months
≥ 0.8 cm increase in size in 3-12 months
Yearly hormonal evaluation for up to 5 years and then intermittently as clinically indicated
Follow up CT image for up to two years

FINDING	Benign adenoma	ACC	Pheochromocytoma	Metastases
Size	Usually <4cm	Usually >4cm	Variable	Variable
Growth rate	Stable or <0.8cm/year	Significant growth (>1cm/year)	Slow growth	Significant growth (>1cm/year)
Shape & margins	Round or oval with well-defined margins	Irregular shape and margins. Invasion to surrounding tissues	Variable	Variable
Composition	Homogenous	Heterogeneous (hemorrhage, necrosis)	Heterogeneous (necrosis)	Heterogeneous (hemorrhage, necrosis)
CT Unenhanced attenuation	≤10 HU (or >10 HU for lipid-poor adenomas)	>10 HU	>10 HU	>10 HU
CT Percent Washout (PW)	APW >60% RPW>40%	APW<60%, RPW<40%	APW<60% RPW<40%	APW<60%, RPW<40%
MRI - CSI (out-of phase)	Signal loss (except in lipid-poor adenomas)	No change in signal intensity	No change in signal intensity	No change in signal intensity
FDG uptake (PET)	Low (some can have low to moderate uptake)	High	Low (malignant pheochromocytomas show high uptake)	High
NP-59 uptake	Present	Absent (except in some secreting tumors)	Absent	Absent

ACC: Adrenocortical carcinoma; HU: Hounsfield Units; APW: Absolute PW; RPW: Relative PW; CSI: Chemical-shift Imaging; FDG: fluoro-deoxyglucose; NP-59: 131I-6-b-iodomethyl-norcholesterol

Happy Thanksgiving!!!