Endocrine Test Review

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Question 1.

- Answer: B; Right adrenalectomy

Manage an adrenal incidentaloma:

- **Is it Benign vs. Malignant?**
  - Hounsfield units (HU)≤ 10 = benign
  - Size >4 cm likely malignant
  - CT contrast washout < 50% likely malignant

- **Is it Primary vs. Metastatic?**
  - Adrenal adenoma
  - Adrenocortical carcinoma
  - Pheochromocytoma
  - Metastasis
    - Lung
    - Renal cell
    - Melanoma
    - Colon
    - Lymphoma

- **Is it Functional vs. Not?**
  - **Cushing's**
    - 24 hour urine free cortisol
    - Dexamethasone suppression test
  - **Pheochromocytoma**
    - 24 hour urine metanephrines
    - Serum metanephrines
  - **Aldosterone producing (IF HTN)**
    - Aldosterone/Renin Ratio

- **Who Gets Surgery:**
  1. **HU> 10 + ≥ 4 cm**
  2. **Any HU or size that is functional (producing hormones)**
  3. **HU > 10 , < 4 cm + non-functional IF:**
     - **<50% washout**
     - **> 50% washout with growth in 6-12 months**

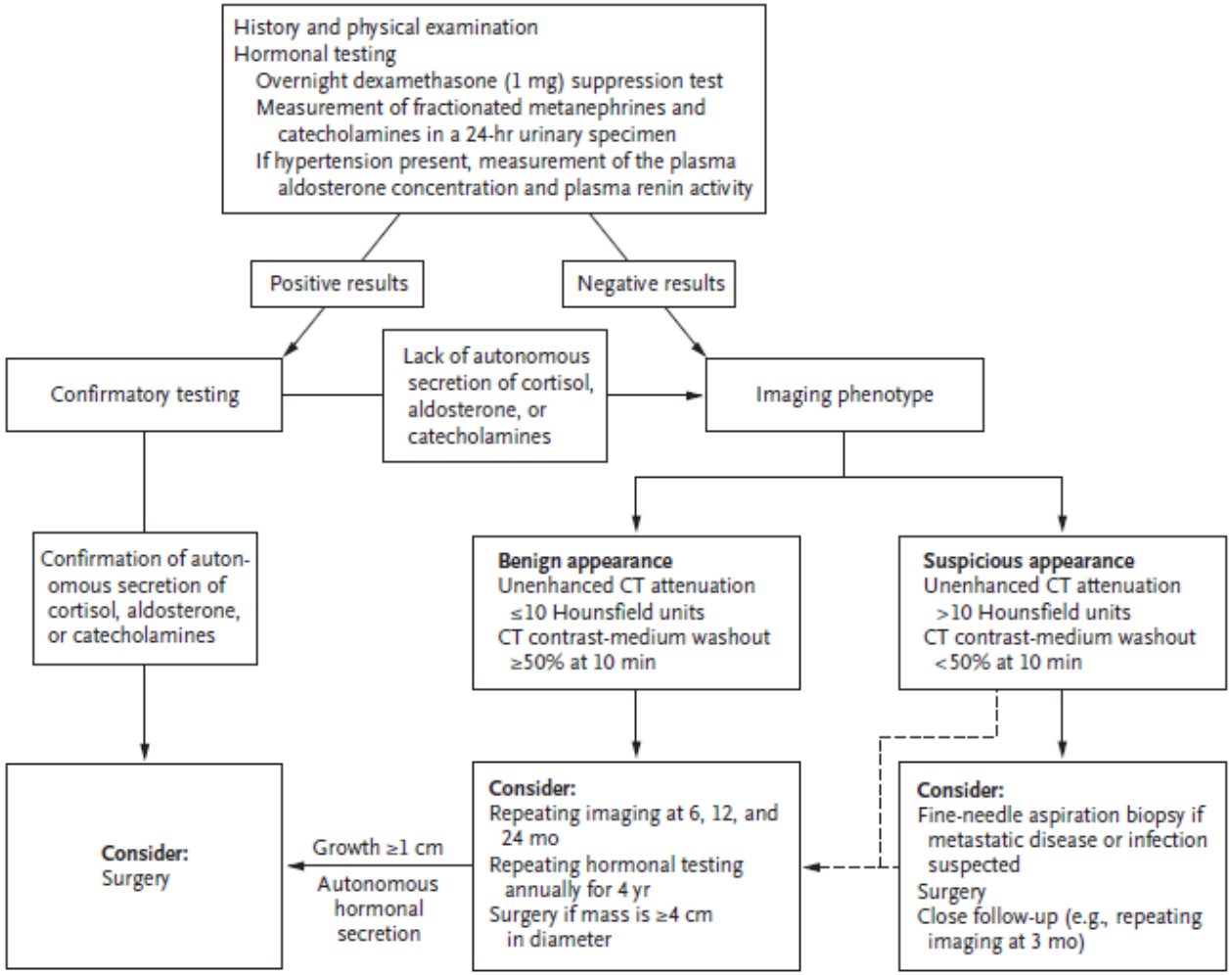


Figure 1. Algorithm for the Evaluation of Patients with an Adrenal Incidentaloma.

The algorithm should be individualized according to the clinical circumstance, the imaging phenotype of the mass, the patient's age, and the patient's preferences. Given the strong association between the imaging features and pheochromocytoma, some advocate treatment with α- and β-adrenergic blockade and tumor resection in patients with this imaging phenotype, even when the results of biochemical testing for pheochromocytoma are normal. The dashed line indicates that for some patients, on the basis of the physician's clinical judgment, serial imaging and hormonal testing may be an alternative approach.

Question 2.

- Answer: B; Levothyroxine therapy

Subclinical Hypothyroidism

- **Definition:**
- Increased TSH (usually <10)
- Normal Free T4

- **Differential:**
- Recovery from sick euthyroid
- Recovery from thyroiditis

- **Consequences:**
- Eventual overt hypothyroidism (up to ½ in 10 years)
- Increased risk CAD
- Dyslipidemia
- NAFLD

- **Who to treat?**
- All patients with TSH > 10
- Age < 70 *with symptoms* at TSH 4.5-10
- Anti-thyroid antibodies
- Goiter
- Pregnant women
- Women who wish to become pregnant

- **Goals of treatment:**
- Age < 70 TSH 0.5-2.5
- Age > 70 TSH 3-5

- **IF no treatment:**
- Repeat labs Q 6-12 months

Question 3.

- Answer: E; 24-hour urine free cortisol excretion

Diagnose Cushing syndrome as a secondary cause of DM (2-3%)

- **Hypercortisolism:**
  - Hyperglycemia
  - Hypertension
  - Hyperlipidemia
  - Central obesity
  - Menstrual irregularity

- **Metabolic syndrome:**
  - Glucose intolerance
  - Hypertension
  - Dyslipidemia
    - Increased TG, low HDL
  - Abdominal circumference
    - Men > 40 in, Women >35 in*
  - Polycystic ovarian syndrome

- **4 etiologies of excess cortisol:**

ACTH-*independent* (suppressed)

  - 1. Exogenous
  - 2. Adrenal gland overproduction

ACTH-*dependent* (elevated)

  - 3. ACTH overproduction from *pituitary*
  - 4. ACTH overproduction from *ectopic source* (neuroendocrine tumor)

Diagnosis of Hypercortisolism

Testing Options:

1. 24-hr urine free cortisol
2. Midnight serum cortisol
3. Nighttime salivary cortisol
4. Low-dose dexamethasone suppression test

Testing Inaccuracies:

False Negatives:

Inadequate urine collection

Renal Insufficiency (CrCl <30)

FalsePositives:

PseudoCushing's

Depression

Central obesity

Alcoholism

Question 4.

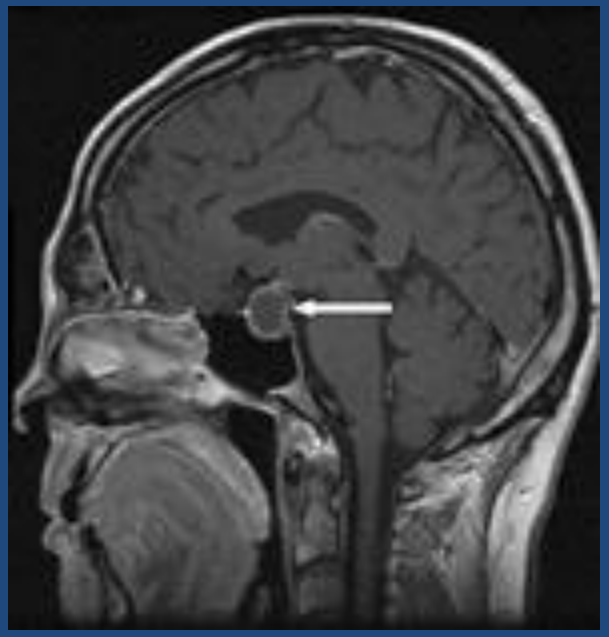
- Answer: C; Serum prolactin measurement

Evaluation of a Sellar mass: Size matters

Pituitary incidentaloma:

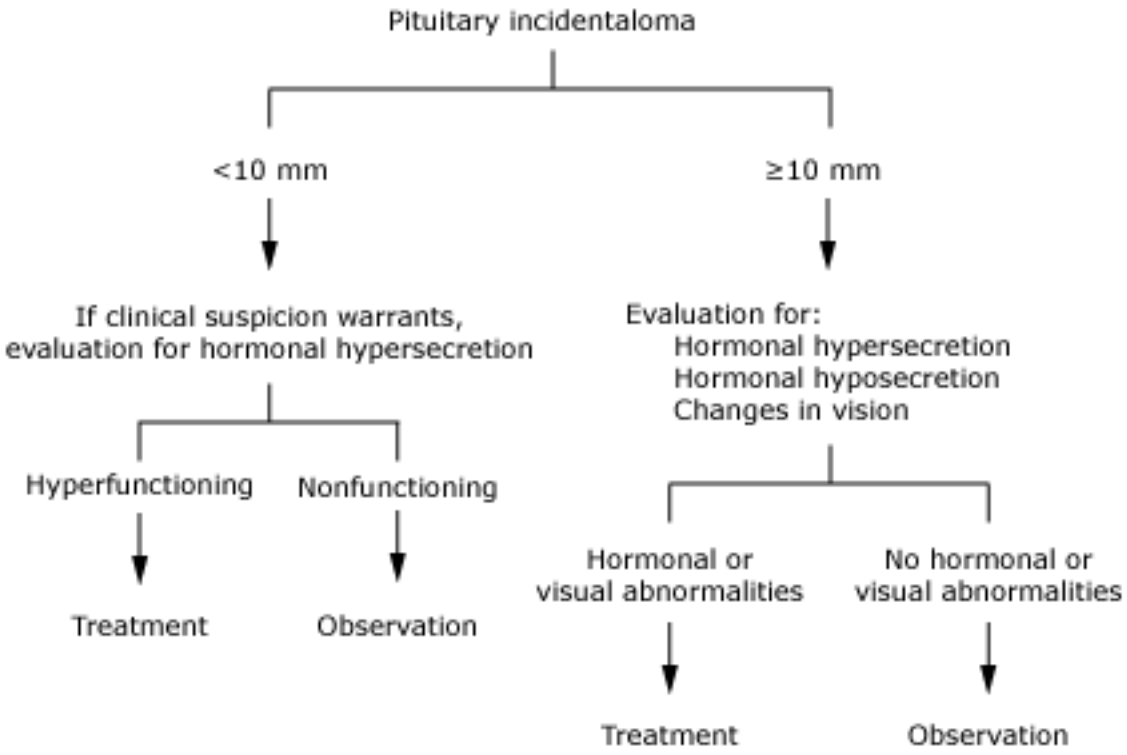
- Is it hyperfunctioning? *(microadenomas only need this w/u)*
  - IGF-1 level (acromegaly)
  - 24 hour urine free cortisol (Cushing's disease)
  - Prolactin level (Prolactinoma)
  - LH and FSH (Gonadotrophin)

- Is it causing hypopituitarism? *(macroadenomas need this in addition to hyperfunction w/u)*
  - 8 AM serum cortisol
  - Free T4 and TSH
  - Total testosterone
  - Estrodiol (E2) in premenopausal women with amenorrhea



- Is it causing compressive symptoms?
  - MRI
  - Visual field testing (bitemporal hemianopsia)

Approach to the patient with an incidental signal abnormality on MRI of the pituitary gland



Question 5.

- Answer: B; Lymphocytic hypophysitis

Diagnose Pituitary Insufficiency

- **Anterior Pituitary:**
  - TSH
  - ACTH
    - (↓)
  - LH
  - FSH
  - Prolactin
  - Growth hormone

- **Posterior Pituitary**
  - Oxytocin
  - Vasopressin (ADH)
    - Central DI (polyuria)

- **Diseases of the Pituitary causing hypopituitarism**
  - Pituitary masses
  - Surgery/Radiation
  - Infiltrative
  - Sarcoidosis
  - Hemachromatosis
  - Infarction/Apoplexy
  - Inflammatory
    - Lymphocytic hypophysitis
    - Granulomatous hypophysitis
    - Histiocytic hypophysitis

Lymphocytic hypophysitis

- Who gets this?
  - Pregnant or post-partum
  - Anti-CTLA-4 chemotherapy for melanoma, renal cell, prostate cancer
- Clinical presentation
  - Severe headache out of proportion to radiographic findings
  - Hypopituitarism with adrenal insufficiency most common
- Diagnosis
  - MRI reveals mass mimicking an adenoma
  - Enhancement with contrast diffusely in anterior pituitary
- Treatment
  - Replacement of the insufficient hormones, especially corticosteroids

Question 6.

- Answer: B; Increase the levothyroxine dosage by 30% now

Manage hypothyroidism during pregnancy

Hypothyroid: Risk to mom:

- Preeclampsia
- Gestational hypertension
- Increased risk of c-section
- Postpartum hemorrhage

Hypothyroid: Risk to baby:

- Placental abruption
- Low birth weight
- Preterm delivery
- Neuropsychological and cognitive impairment

Normal changes in TFTs in pregnancy:

- Increase thyroxine binding globulin
- Increased *Total* T3 and T4
- Decreased TSH due to elevated HCG
- Trimester specific normal values should be used

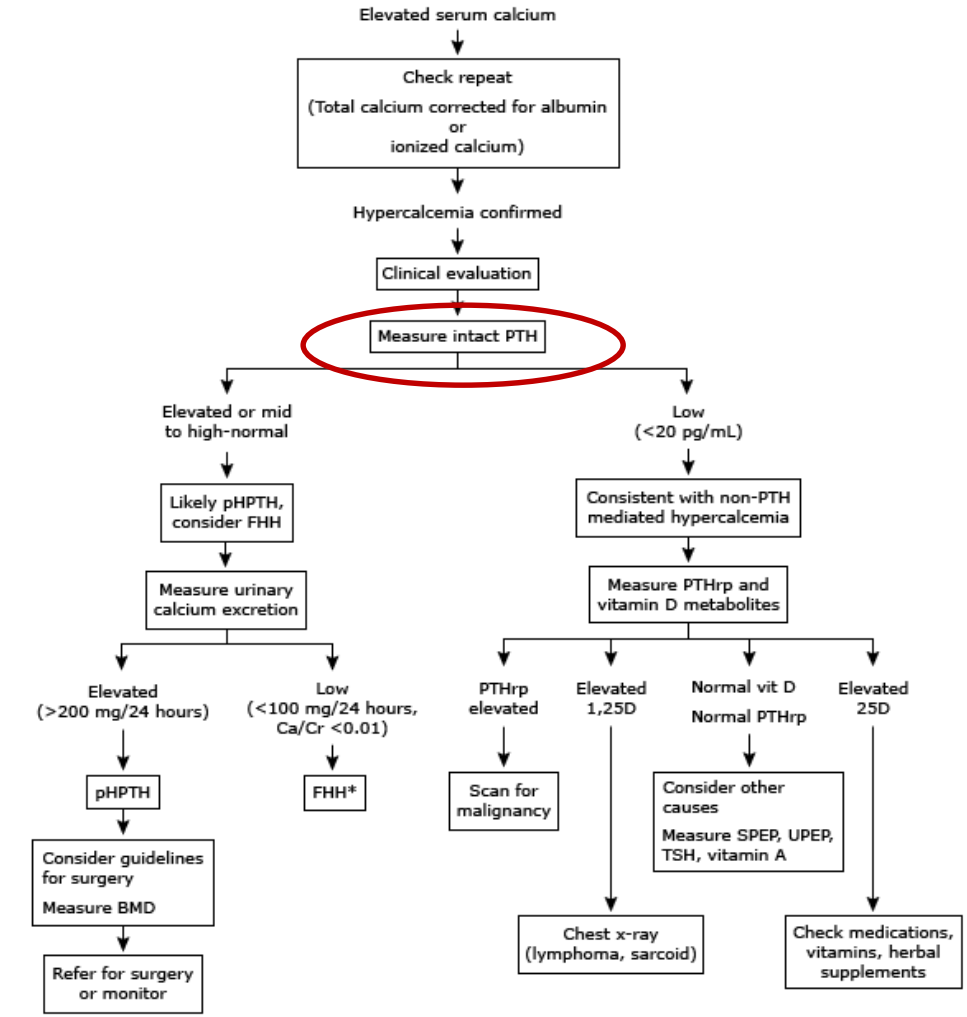
Who to treat and how:

- Overtly hypothyroid
- Subclinical hypothyroid with positive antibodies
- Increase dose by 30% when pregnancy confirmed and recheck TFTs q 4 weeks until normal and then q trimester

Question 7.

- Answer: B; Primary hyperparathyroidism

Diagnostic approach to hypercalcemia



PTH: parathyroid hormone; pHPTH: primary hyperparathyroidism; FHH: familial hypocalciuric hypercalcemia; PTHrp: parathyroid hormone-related peptide; 1,25D: 1,25-dihydroxyvitamin D; 25D: 25-hydroxyvitamin D; SPEP: serum protein electrophoresis; UPEP: urine protein electrophoresis; TSH: thyroid stimulating hormone.
* Further evaluation with measurement of 25-hydroxyvitamin D may be needed to differentiate FHH from primary hyperparathyroidism with concomitant vitamin D deficiency.

Question 8.

- Answer: B; Measurement of 25-hydroxyvitamin D level

Diagnose Vitamin D deficiency

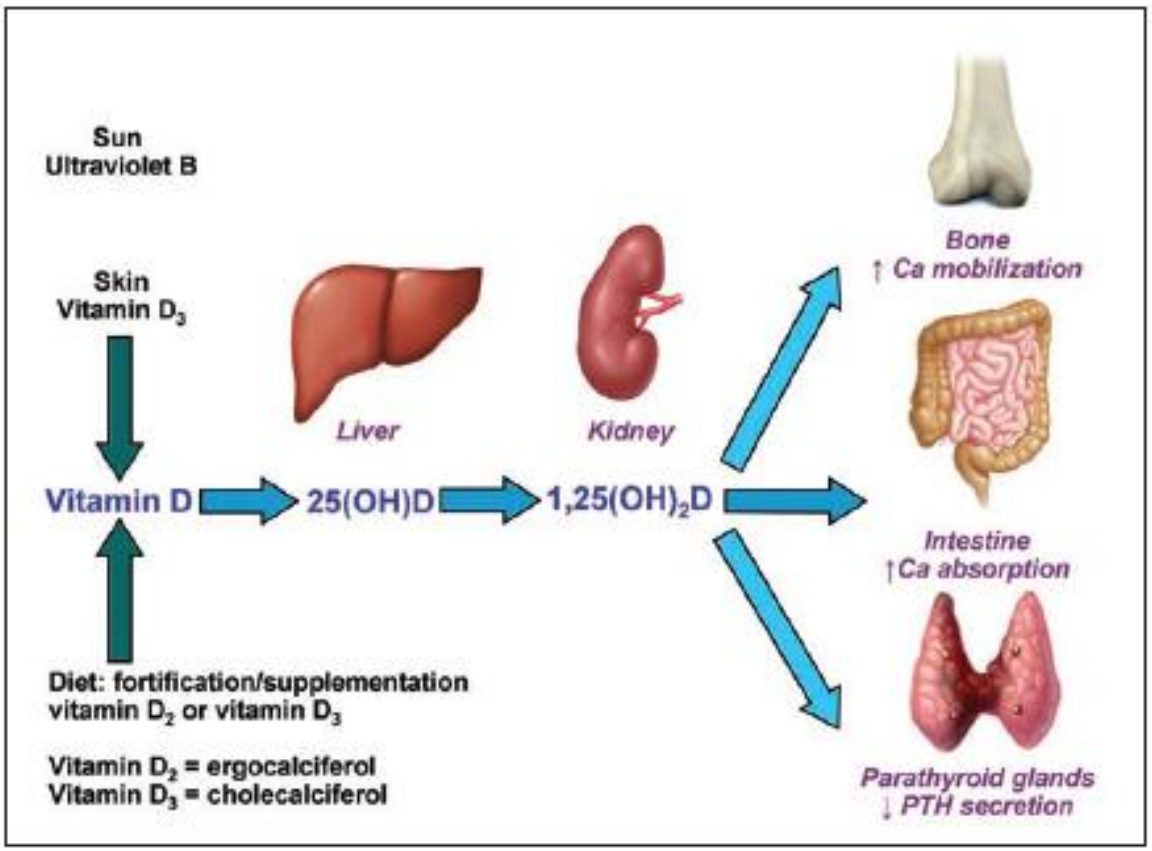


FIGURE. Vitamin D metabolism. Ca = calcium; $1,25(OH)_2D$ = 1,25-dihydroxyvitamin D; 25(OH)D = 25-hydroxyvitamin D; PTH = parathyroid hormone.

Vitamin D Insufficiency; Thatcher et al; Mayo Clinic Proceedings; January 2011;86 (1) 50-60

Diagnose Vitamin D deficiency

If most of the population is deficient, how is a normal value determined?

- Optimal level to suppress PTH
- Optimal level of 25-OH after which there is no increase in 1,25 OH
- Optimal level for maximal intestinal calcium absorption

25-OH vit D levels

- ≤ 10 ng/mL Deficient
- 11-20 ng/mL Insufficient
- >20 -80 ng/mL Optimal
- >80 ng/mL Toxic

Who should have 25-OH vitamin D levels checked?

- Bone pain/ Fibromyalgia?
- Elevated serum alkaline phosphatase from bone
- Low serum calcium
- Low serum phosphorus
- Osteomalacia or secondary osteoporosis in adults
- Advanced age
- Risk for falls

Question 9.

- Answer: B; Alpha blocker therapy

Treat pheochromocytoma prior to surgery

When to suspect a pheochromocytoma:

- Hyperadrenergic spells
- Resistant hypertension
- Pressor response during anesthesia or procedure
- Early onset HTN <20 yo
- Adrenal incidenaloma
- Familial predisposition (MEN2, VHL, NF-1)
- Idiopathic cardiomyopathy

Diagnosis:

- 24 hour urine metanephrines + creatinine in lower pre-test probability
- Serum free metanephrines in higher pretest probability
- Tricyclic antidepressants should be stopped 2 weeks prior
- CT or MRI of the adrenals
- MIBG scan to localize

Treatment:

NO beta-blockers until adequately alpha blocked with phenoxybenzamine

Surgical removal

Question 10.

- Answer: A; Hydrocortisone

Manage newly diagnosed adrenal insufficiency

Equivalent doses of steroids:

- Hydrocortisone 20
- Prednisone 5
- Methylprednisolone 4
- Dexamethasone 0.75

Physiologic doses:

- Hydrocortisone 25 mg q day divided into three doses
- Prednisone 5 mg q day divided into two doses
- Dexamethasone 0.75 q day in one dose or divided in two doses

Mild illness:

Double or Triple physiologic dose for 3 days

Pt needs injectable for home

Serious illness Trauma/Surgery:

100-200 mg IV hydrocortisone q day in 4 divided doses

Question 11.

- Answer: D; Postprandial hyperglycemia

Interpret hemoglobin A1c results

A1c% correlated to mean blood sugar:

- 6%- 135 mg/dL
- 7%- 170 mg/dL
- 8%- 205 mg/dL
- 9%- 240 mg/dL
- 10%- 275 mg/dL
- 11%- 310 mg/dL
- 12%- 345 mg/dL

- Falsely low A1c%:

Increased RBC turnover (hemolytic anemia, *treated* iron, B12, or folate deficiency)

- Falsely high A1c%:

Decreased RBC turnover (*untreated* iron, B12, or folate deficiency)

- Discrepancies in A1c% with measured sugars could be due to undetected highs (post-prandial) or undetected lows (overnight)

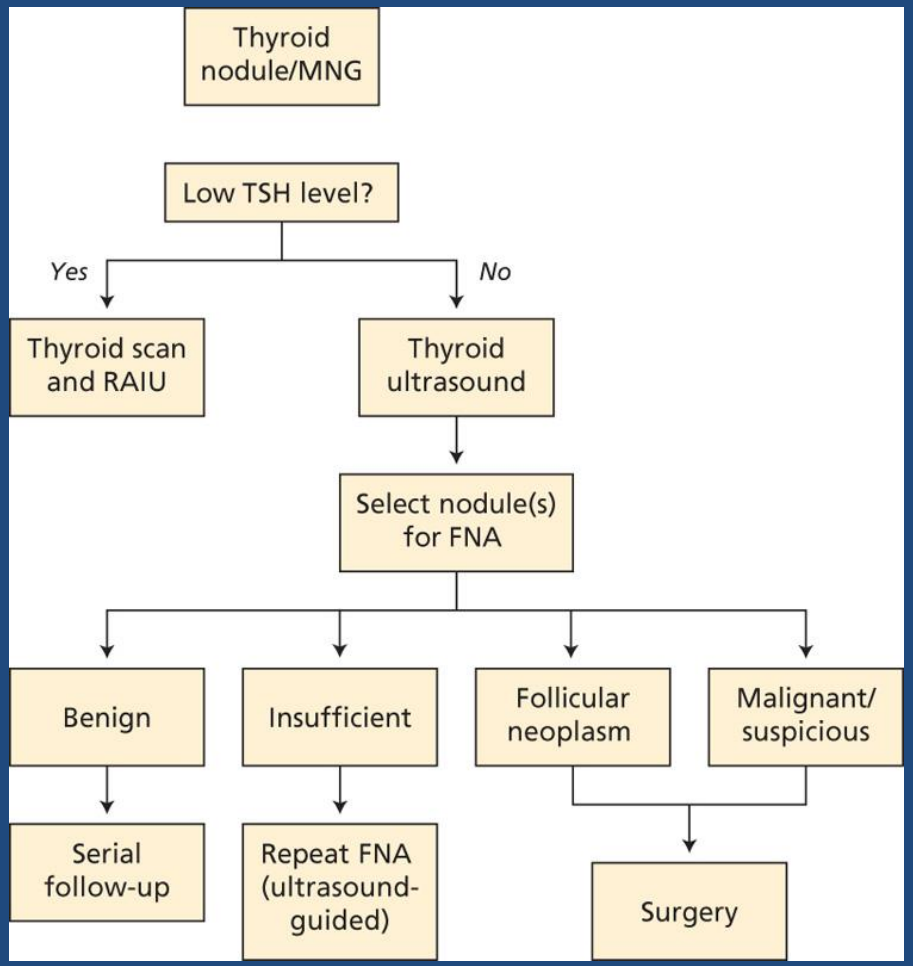
Question 12.

- Answer: D; Thyroid lobectomy

Manage a thyroid nodule: Start with a TSH!

Risks for thyroid cancer in a patient with a thyroid nodule:

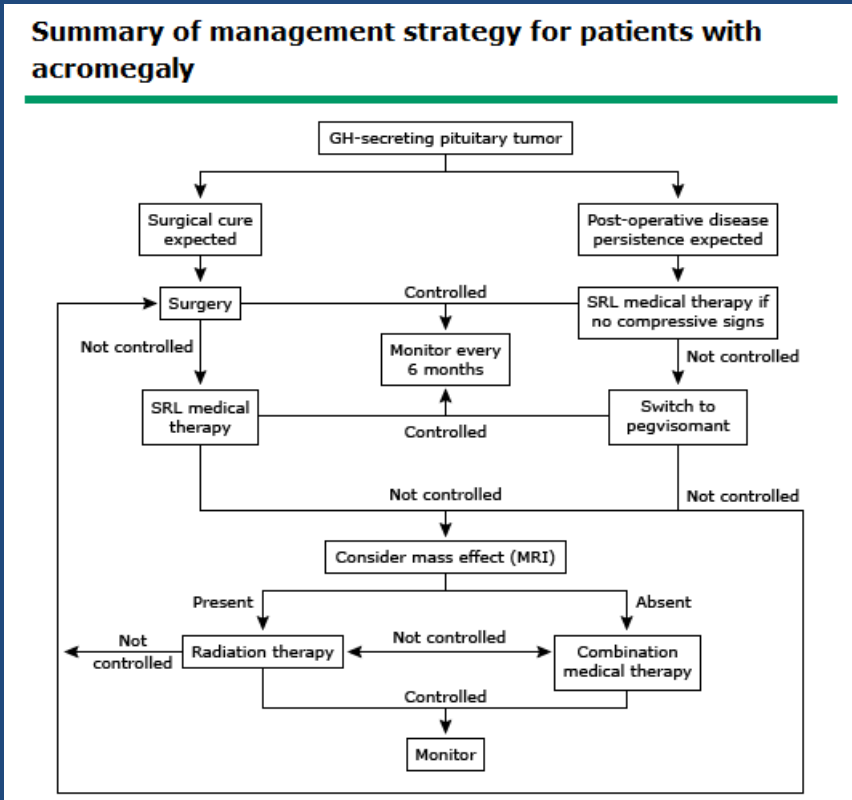
- Age < 20 or > 60
- Male
- Radiation
- Family hx (esp. medullary)
- Hoarseness
- Cervical adenopathy
- Worrisome ultrasound findings
  - Microcalcifications
  - Increased vascular flow



Question 13.

- Answer: B; Octreotide

Treatment of Acromegaly



Somatostatin receptor agonist:
Octreotide
Lanreotide

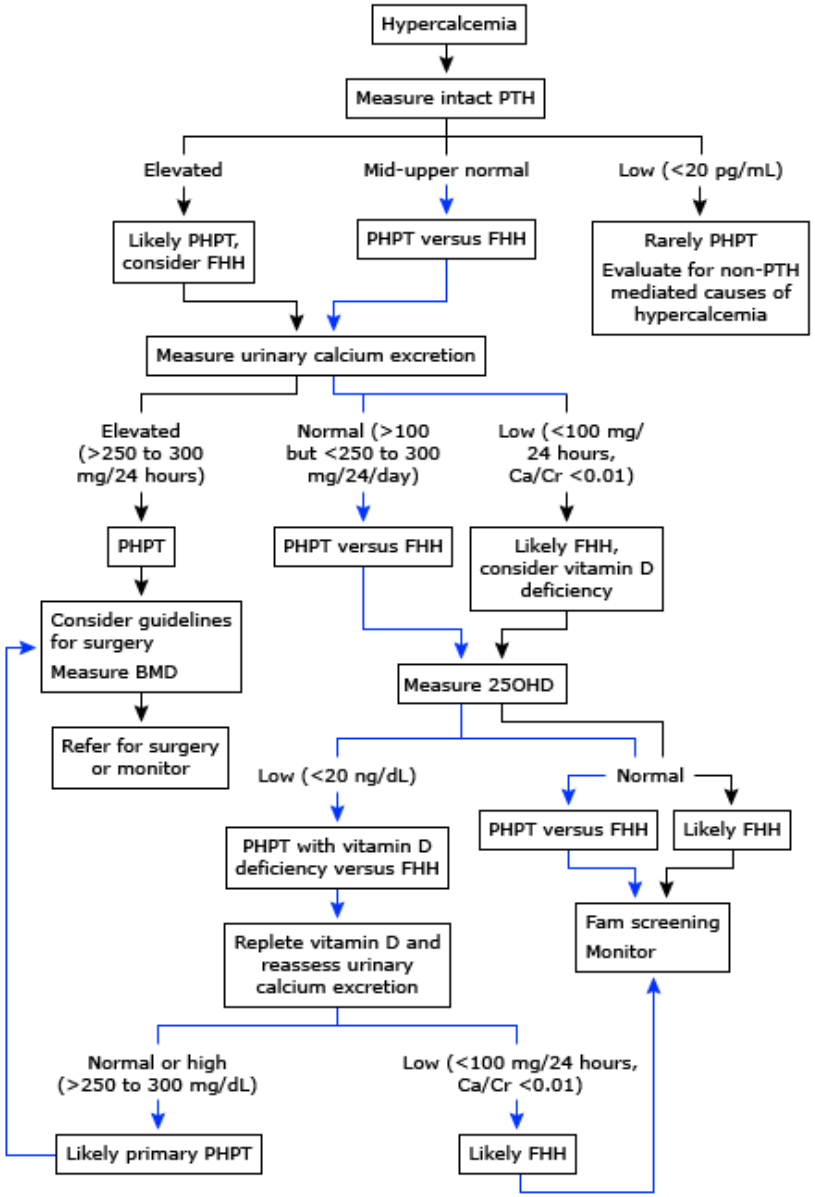
Dopamine antagonist:
Cabergoline

Growth hormone receptor antagonist:
Pegvisomant

Question 14.

- Answer: C; Measurement of the urine calcium and urine creatinine levels

Diagnosis of primary hyperparathyroidism



PHPT: primary hyperparathyroidism; FHH: familial hypocalciuric hypercalcemia.

Question 15.

- Answer: C; Estimate a 10-year ASCVD risk

Lipid Management for Primary Prevention of CAD

Table 1. Major Recommendations for the Treatment of Blood Cholesterol to Reduce ASCVD Risk in Adults*†

Healthy lifestyle habits should be encouraged for all persons.

The appropriate intensity of statin therapy should be initiated or continued:

1. Clinical ASCVD‡
   a. Persons aged ≤75 y with no safety concerns: high-intensity statin (class I, level A)
   b. Persons aged >75 y or with safety concerns: moderate-intensity statin (class I, level A)
2. Primary prevention: primary LDL-C level ≥190 mg/dL
   a. Rule out secondary causes of hypercholesterolemia
   b. Persons aged ≥21 y: high-intensity statin (class I, level B)
   c. Achieve ≥50% reduction in LDL-C level (class IIa, level B)
   d. May consider LDL-C–lowering nonstatin therapy to further reduce LDL-C levels (class IIb, level C)
3. Primary prevention: persons with diabetes aged 40–75 y with an LDL-C level of 70–189 mg/dL
   a. Moderate-intensity statin (class I, level A)
   b. Consider high-intensity statin when 10-y ASCVD risk is ≥7.5% (class IIa, level B)
4. Primary prevention: persons aged 40–75 y without diabetes with an LDL-C level of 70–189 mg/dL
   a. Estimate 10-y ASCVD risk (risk calculator based on Pooled Cohort Equations recommended)§ in those not receiving a statin; estimate risk every 4–6 y (class I, level B)
   b. To determine whether to initiate a statin, engage in clinician–patient discussion of potential for ASCVD risk reduction, adverse effects, drug–drug interactions, and patient preferences (class IIa, level C). Reemphasize healthy lifestyle habits and address other risk factors. If statin therapy is chosen:
      i. Persons with ≥7.5% 10-y ASCVD risk: moderate- or high-intensity statin (class I, level A)
      ii. Persons with 5% to <7.5% 10-y ASCVD risk: consider moderate-intensity statin (class IIa, level B)
      iii. Other factors may be considered‖: LDL-C level ≥160 mg/dL, family history of premature ASCVD, lifetime ASCVD risk, high-sensitivity C-reactive protein level of ≥2.0 mg/L, coronary artery calcification score ≥300 Agatston units, or ankle–brachial index <0.9 (class IIb, level C)
5. Primary prevention when LDL-C level is <190 mg/dL and person is aged <40 y or >75 y or has <5% 10-y ASCVD risk
   a. Statin therapy may be considered in selected persons‖ (class IIb, level C)
6. Statin initiation is not routinely recommended for persons with NYHA class II–IV heart failure or those who are receiving maintenance hemodialysis.

Question 16.

- Answer: B; Intravenous levothyroxine and hydrocortisone

Treat myxedema coma

Clinical features of myxedema coma
Decreased mental status
Hypothermia
Bradycardia
Hyponatremia
Hypoglycemia
Hypotension
Precipitating illness

Treatment of myxedema coma
Draw serum for T4, TSH, and cortisol.
Administer thyroxine 200 to 400 µg (0.2 to 0.4 mg) intravenously followed by daily doses of 50 to 100 µg, and triiodothyronine 5 to 20 µg intravenously followed by 2.5 to 10 µg every 8 hours.
Change to an equivalent oral dose of thyroxine when the patient can tolerate oral medications. (Oral dose = intravenous dose ÷ 0.75).
Supportive measures:
Mechanical ventilation
Fluids and vasopressor drugs to correct hypotension
Passive rewarming
Intravenous dextrose
Stress-doses glucocorticoids
Consider empirical antibiotic treatment
Monitor for arrhythmias and treat when indicated

Question 17.

- Answer: D; 24-hour radioactive iodine uptake test

Diagnose subacute thyroiditis as a cause of thyrotoxicosis

Thyrotoxicosis:

1. Grave's Disease
2. Toxic adenoma
3. Multinodular goiter
4. Thyroiditis
   - A. Lymphocytic (painless, postpartum)
   - B. Granulomatous (painful, subacute, de Quervain's)
   - C. Suppurative
   - D. Drug-induced (amiodarone)
5. Factitious
6. Struma ovarii
7. TSH-secreting pituitary
8. Hamburger thyrotoxicosis
9. Jod-basedow phenomenon

Radioactive Iodine Uptake (RAIU)

- **HIGH:**
- Graves
- Toxic adenoma
- Multinodular goiter
- TSH-secreting pituitary
- Jod-basedow phenomenon

- **LOW:**
- **Thyroiditis**
- **Factitious**
- **Struma ovarii**
- **Hamburger thyrotoxicosis**

Question 18.

- Answer: C; Parathyroidectomy

Know the indications for parathyroidectomy in primary hyperparathyroidism

TABLE 2. NIH Criteria for Parathyroidectomy

Markedly elevated serum calcium (1–1.6 mg/dL above normal, ie, >12 mg/dL
History of an episode of life-threatening hypercalcemia
Creatinine clearance reduced by 30% with age-matched normal subjects
Markedly elevated 24-hour urine calcium (>400 mg/d)
Nephrolithiasis
Age < 50
Osteitis fibrosa cystica
Substantially reduced bone mass as determined by direct measurement (eg, Bone mass > 2 SD below controls matched for age, gender, and ethnic group)
Neuromuscular symptoms: documented proximal weakness, atrophy, hyper-reflexia, and gait disturbance

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TABLE 2. NIH Criteria for Parathyroidectomy

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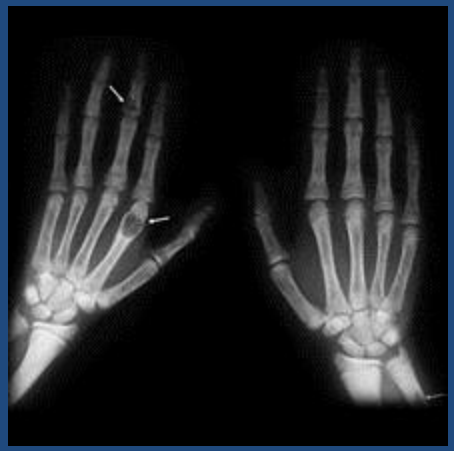
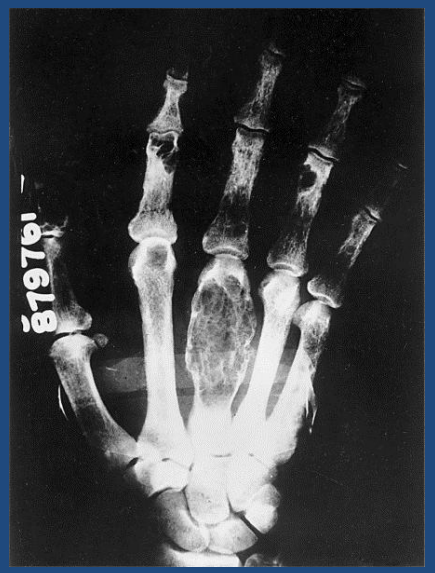
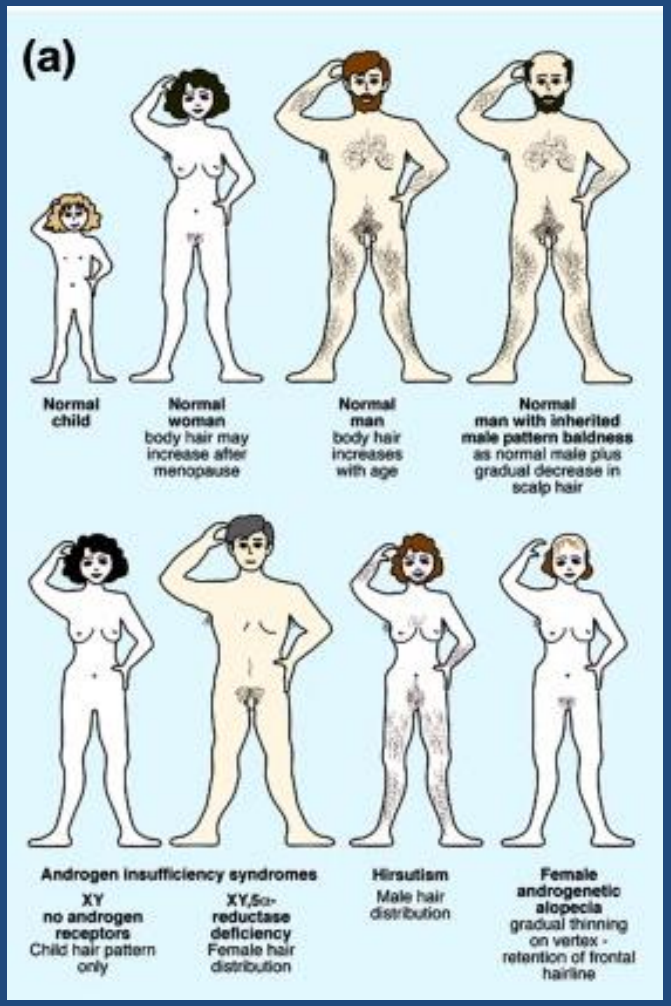




Question 19.

- Answer: C; Estrogen-progesterone oral contraceptive

Diagnose Polycystic Ovarian Syndrome as a cause of Hirsuitism



Proposed diagnostic criteria for polycystic ovary syndrome

NIH consensus criteria 1990[1] (All required)	Rotterdam criteria 2003*[2] (Two out of three required)	AES definition 2008[3] (All required)
Menstrual irregularity due to oligo- or anovulation	Oligo- or anovulation	Androgen excess (clinical and/or biochemical hyperandrogenism)
Evidence of hyperandrogenism	Clinical and/or biochemical signs of hyperandrogenism	Ovarian dysfunction – oligo-anovulation and/or polycystic ovaries on ultrasound
Exclusion of other disorders: NCCAH, androgen-secreting tumors	Polycystic ovaries (by ultrasound)	Exclusion of other androgen excess or ovulatory disorders

NIH: National Institutes of Health; AES: Androgen Excess Society; NCCAH: nonclassic congenital adrenal hyperplasia; PCOS: polycystic ovary syndrome.
* Rotterdam criteria based upon a 2003 concensus meeting held in Rotterdam (European Society of Human Reproduction and Embryology/American Society of Reproductive Medicine consensus workshop group).

First question to a hirsute woman is:

"Are you having regular periods?"

"YES": NO workup;

"NO": Procede with evaluation

HIRSUTE W/U	Normal	Cushing disease (central)	Adrenal cancer	Ovarian cancer (stromal)	Congenital Adrenal Hyperplasia	PCOS
Testosterone	N	N,+	N,+	+++	N,+	N,+
DHEA	N	N,+	+++	N, +	N,+	N,+
LH/FSH ratio	N	N	N	N	N	>3
Dex suppression	N	Low dose + High dose -	Low dose + High dose +	N	N	N
ACTH	N	+++	low	N	+++	N

Second question: Do you desire fertility?

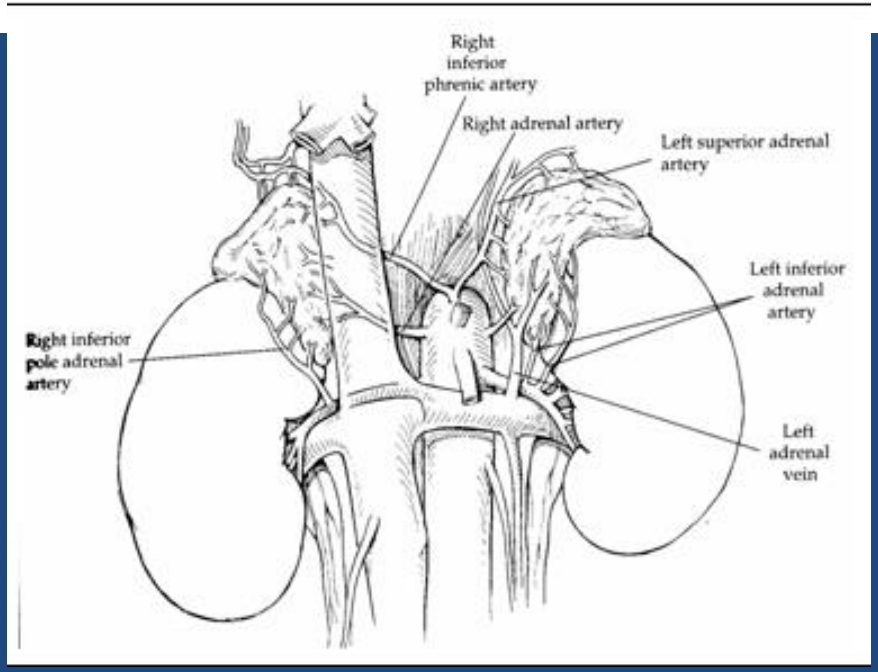
Question 20.

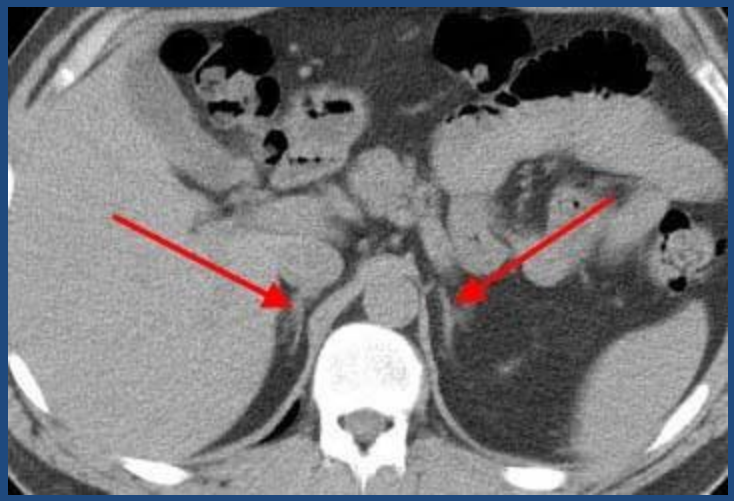
- Answer: A; Adrenal infarction and hemorrhage

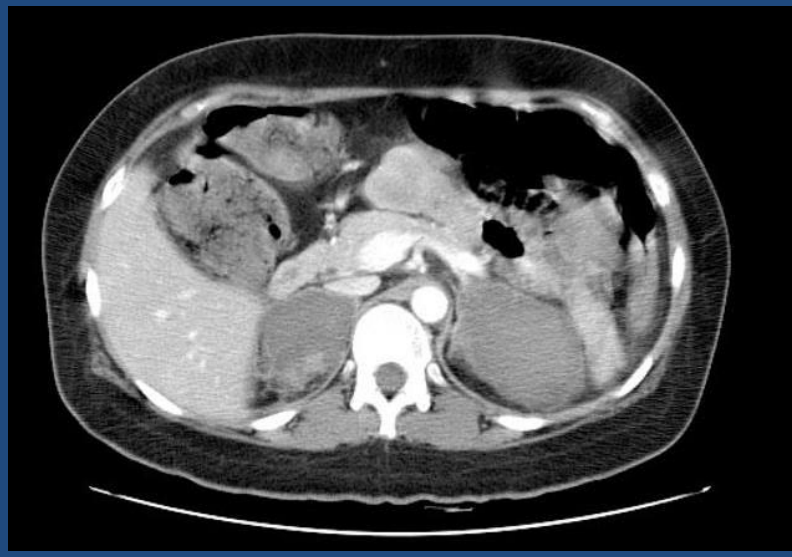
Understand the adrenal gland's potential for infarction and hemorrhage

ADRENAL HEMORRHAGE AND INFARCTION

The adrenal glands are prone to vascular damage because of the lack of a direct arterial supply. The adrenal cortex receives arterial supply from a subcapsular arteriolar plexus, rendering it vulnerable to infarction during systemic hypotension. An abrupt change in flow dynamics in the medullary sinusoids predisposes the gland to microvascular thrombosis and infarction. Necrotic areas are prone to hemorrhagic transformation during reperfusion. Anticoagulant use, thrombocytopaenia, and sepsis are the 3 most important risk factors associated with adrenal hemorrhage *(27–28)*.







The END of ENDOCRINE REVIEW