Adrenal Disorders: Mini Board Simulation

Internal Medicine Board Review

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OBJECTIVES

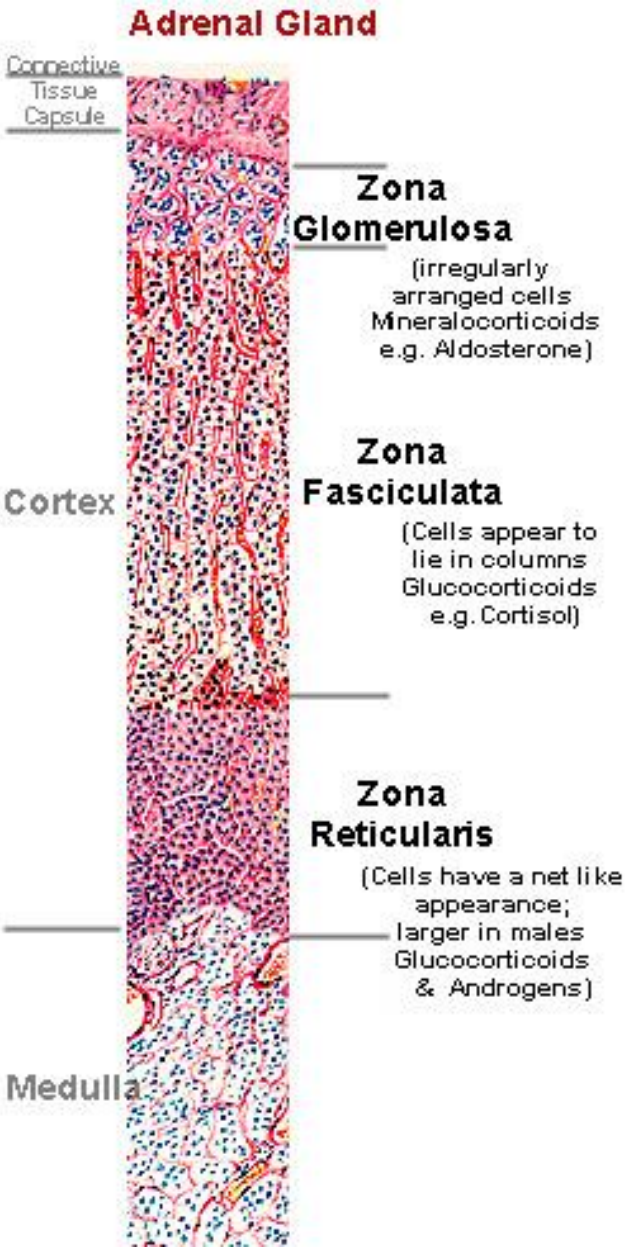
- Identify adrenal pathology and important evaluations to discriminate between several disease states with similar clinical presentation

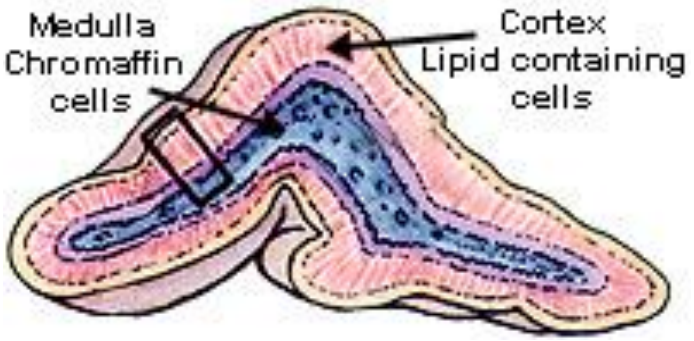
- Approach to adrenal incidentalomas

Aldosterone

Cortisol

Cortisol & Androgens



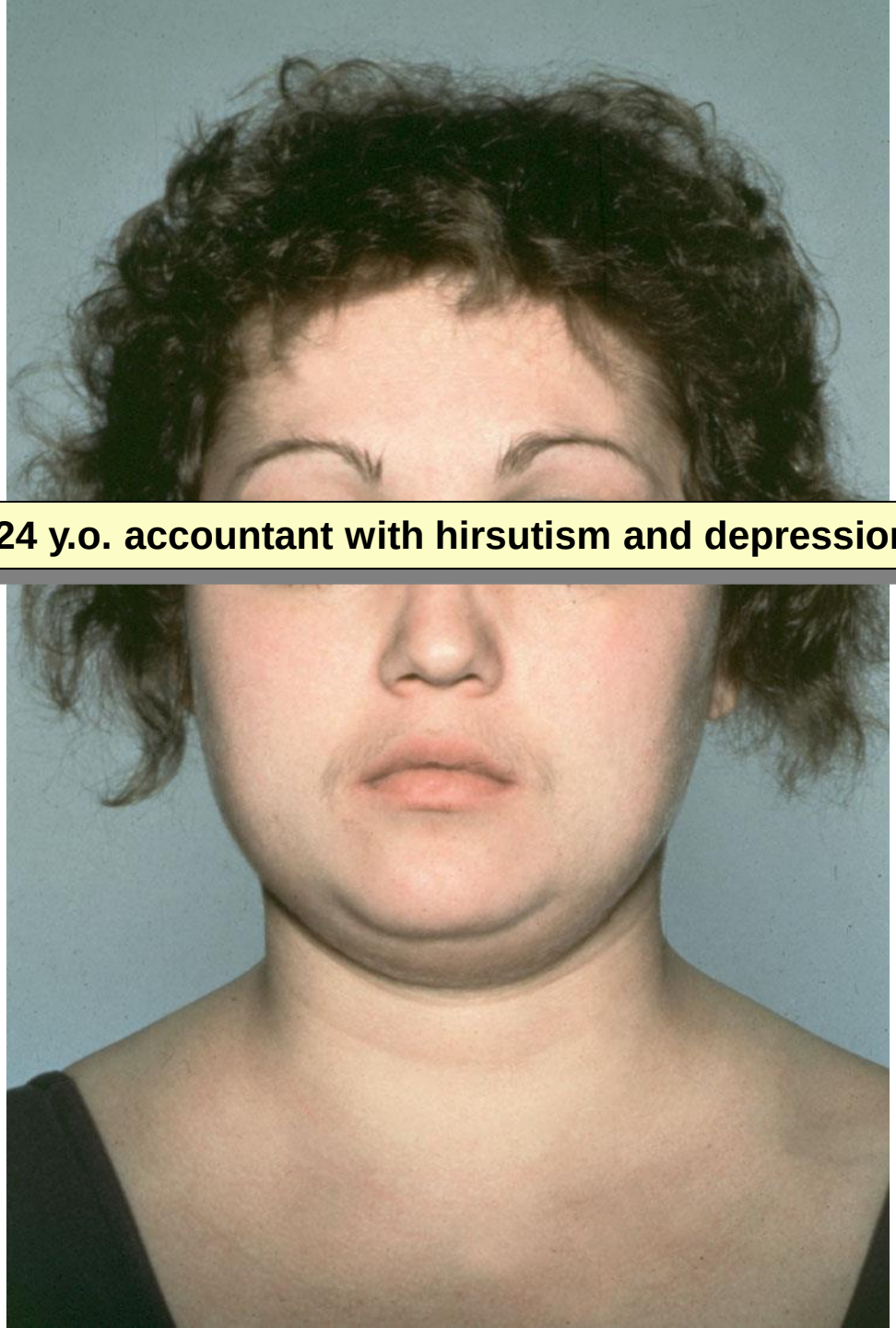


Catecholamines

McGill Univeristy

Adrenal Topics

- A. Screening for Cushing Syndrome
- B. Evaluation of Hyperaldosteronism
- C. Adrenal Insufficiency
- D. Pheochromocytoma
- E. Adrenal Incidentaloma



24 y.o. accountant with hirsutism and depression


Photo 1 year before

1. 24 yr old woman with hirsutism and amenorrhea is suspected of having Cushing's syndrome. Her PCP checks an AM serum cortisol which is 30 ug/dL. What test should you do next?

- A) Late night salivary cortisol
- B) 24 hour urine for free cortisol
- C) 1 mg overnight dexamethasone test
- D) Check 4 PM cortisol to look for loss of diurnal variation
- E) a, b and c are all acceptable next steps

Differential Diagnosis

- Pituitary Cushing
- Adrenal Cushing
- Psuedo Cushing

2 What is the most economical test to distinguish adrenal Cushing from the other possibilities?

A. Late night salivary cortisol

B. ACTH

C. Free Cortisol

D. CT of adrenals

E. MRI of the pituitary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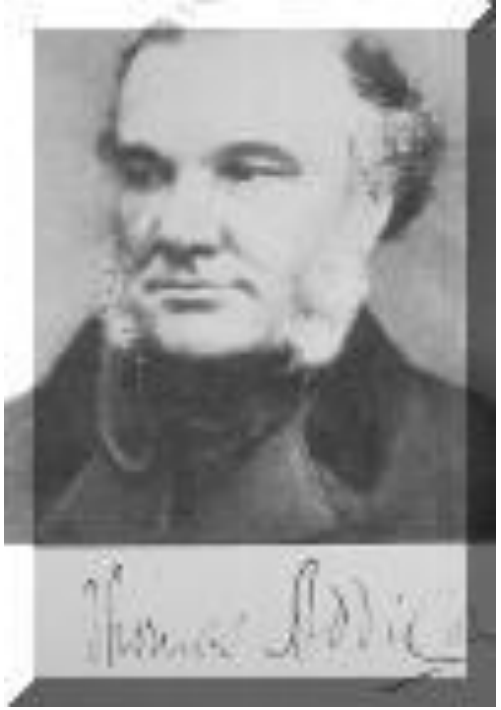
3. What is she at risk for now?

a. Permanent adrenal insufficiency
b. Secondary adrenal insufficiency
c. Adrenergic insufficiency
d. No real risk

4.

Six months after surgery she remains on hydrocortisone 15 mg q am and 5 mg at 4 pm but would like to get off this. The best evidence that she could would be to do this is to hold the replacement hydrocortisone and check:

A. 8 am cortisol
B. 8 am ACTH
C. Cortrosyn stimulation
D. 24 hr urine for free cortisol



Adrenal Insufficiency

Adrenal Insufficiency

- Hypotension
- Hyperpigmentation
- Weight loss
- Hyperkalemia, metabolic acidosis
- Moderate eosinophilia, mild hypochromic anemia, mild hypercalcemia

5.

A teenager presents with hypotension and increased skin pigmentation. His father apparently died of a neurological disorder at age 42. What diagnostic tests would be least helpful?

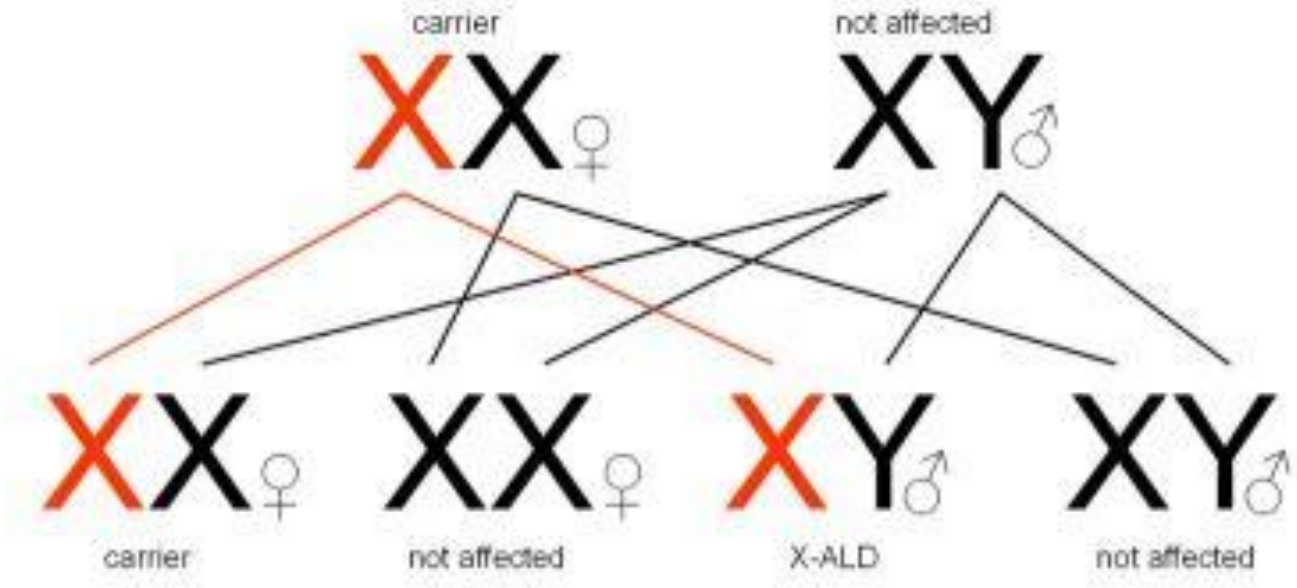
A) 1 hour ACTH stimulation test

B) ACTH levels

C) Anti-adrenal antibody levels

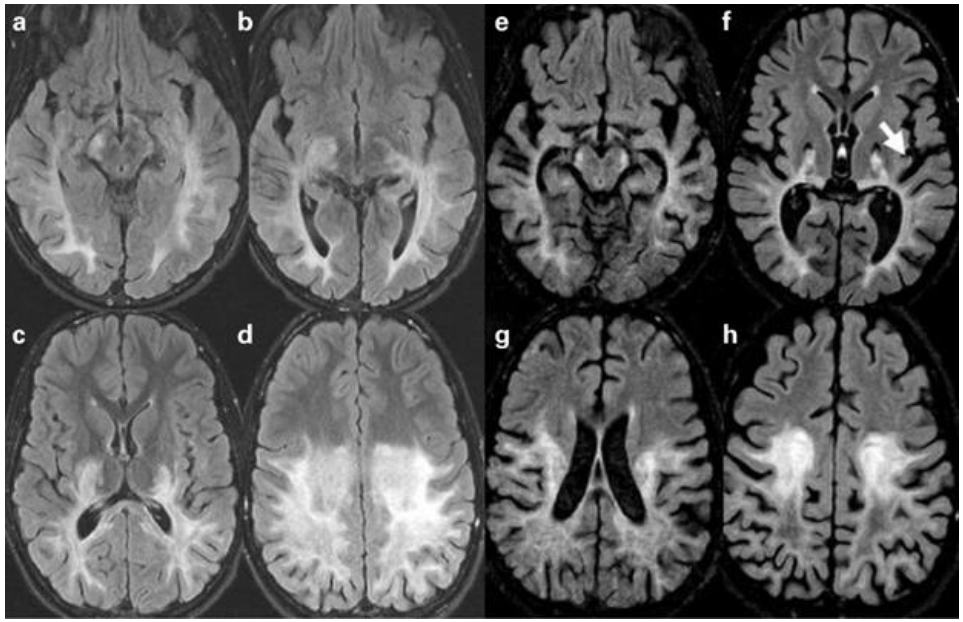
D) Very long-chain fatty acid levels in plasma

Adrenoleukodystrophy-X linked



X **X-ALD X-chromosome**
X **normal X-chromosome**
Y **y-chromosome**

Adrenoleukodystrophy



Adrenal Insufficiency: Etiology

- Autoimmune endocrine disease
- Metastatic cancer
- Anticoagulation
- Meningococcemia
- HIV
- Tuberculosis or Fungal infection
- Certain Drugs

5.
Which of these drugs increases catabolism of cortisol?

A) Aminoglutethimide

B) Etomidate, Suramin

C) Ketoconazole

D) Rifampin

E) Metyrapone

F) Megestrol acetate

Ten S, New M, McLaren N. Addison's disease 2001 JCEM 86: 2909-2922

Testing Adrenal Reserve

- Cosyntropin (250 ug IV or IM Stim Test)
  - prednisone, hydrocortisone, prednisolone all may interfere with cortisol assay
  - dexamethasone does not interfere
- Insulin induced hypoglycemia
  - typically performed in pituitary evaluation

Management of suspected adrenal crisis

- IV Normal Saline
- Draw ACTH, BMP, cortisol levels and treat
- Begin Solucortef 100 mg IV q 6h
- Treat underlying infection or precipitating cause

6.

29 y.o. male with type 1 DM presents with brittle diabetes. He also has asthma treated with inhaled steroids. He has patches of vitiligo. He is found to have K=5.8 with Cr= 1.2 mg/dl. Which of these is least compatible with his situation?

- A) Primary adrenal insufficiency
- B) Isolated primary hypoaldosteronism
- C) Hyporeninemic hypoaldosteronism
- D) Licorice ingestion

Isolated Hypoaldosteronism: Clinical Scenarios

- High renin
  - **adrenal insufficiency**
  - **critically ill patient**
  - **heparin**
  - **ACE inhibitors**
- Low renin
  - **Renal insufficiency**

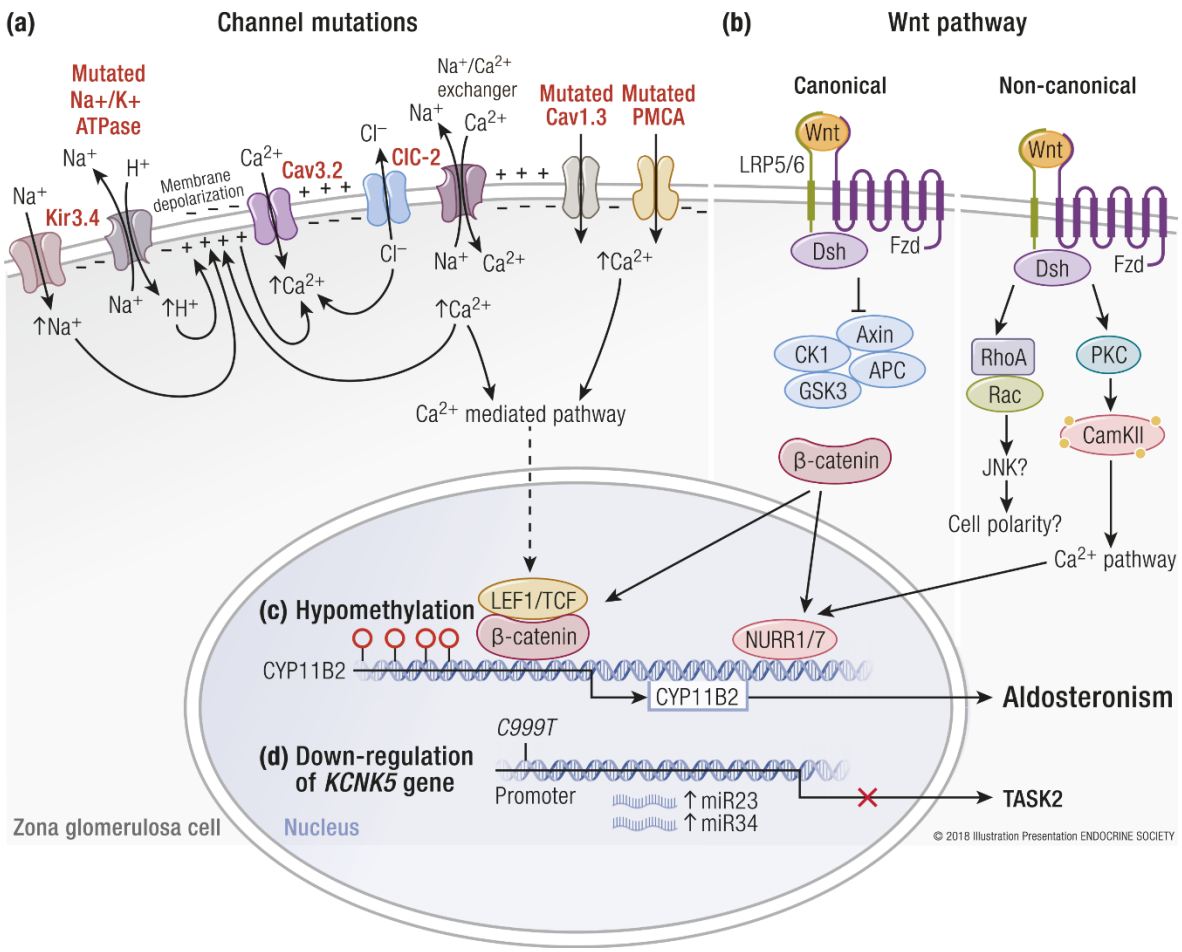
    DM, pyelonephritis or gout
  - **NSAIDs, Beta Blockers**
  - **Autonomic insufficiency**
  - **HIV-AIDS**

Primary Hyperaldosteronism

- APA (aldosterone producing adenoma)
- Primary bilateral adrenal hyperplasia
- Dexamethasone suppressible hyperaldosteronism
- Adrenocortical Carcinoma (Very Rarely)

Bilateral Hyperplasia of the Glomerulosa

- About 50% of primary aldosteronism
- Unilateral adrenalectomy does not correct the BP so this should to be treated medically
- Treatment:
  - MRA: Spironolactone, Eplerenone
  - ENaC blockers: Amiloride, Triamterene
  - NS MRA: Finerenone can be tried



From: The Biology of Normal Zona Glomerulosa and Aldosterone-Producing Adenoma: Pathological Implications

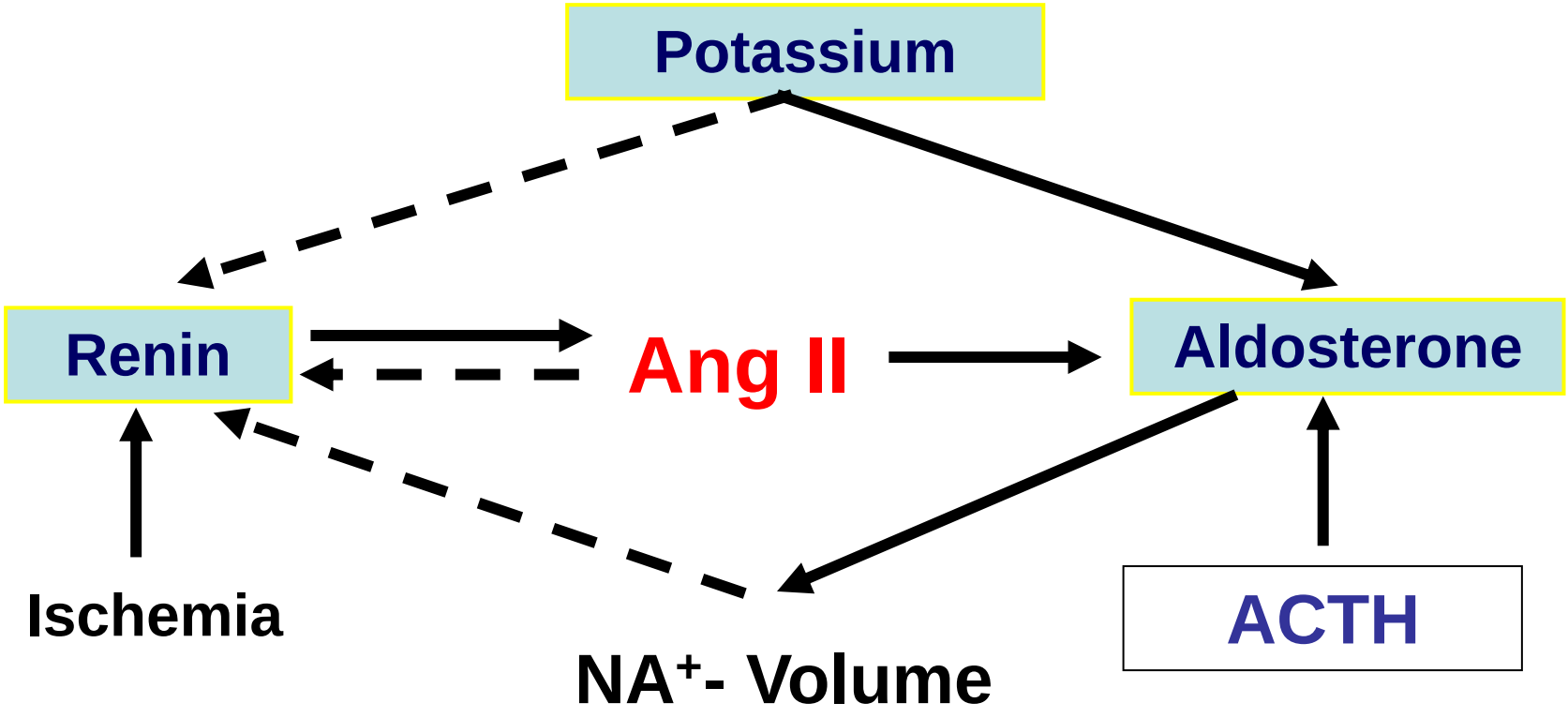
Endocr Rev. 2018;39(6):1029-1056. doi:10.1210/er.2018-00060

7.

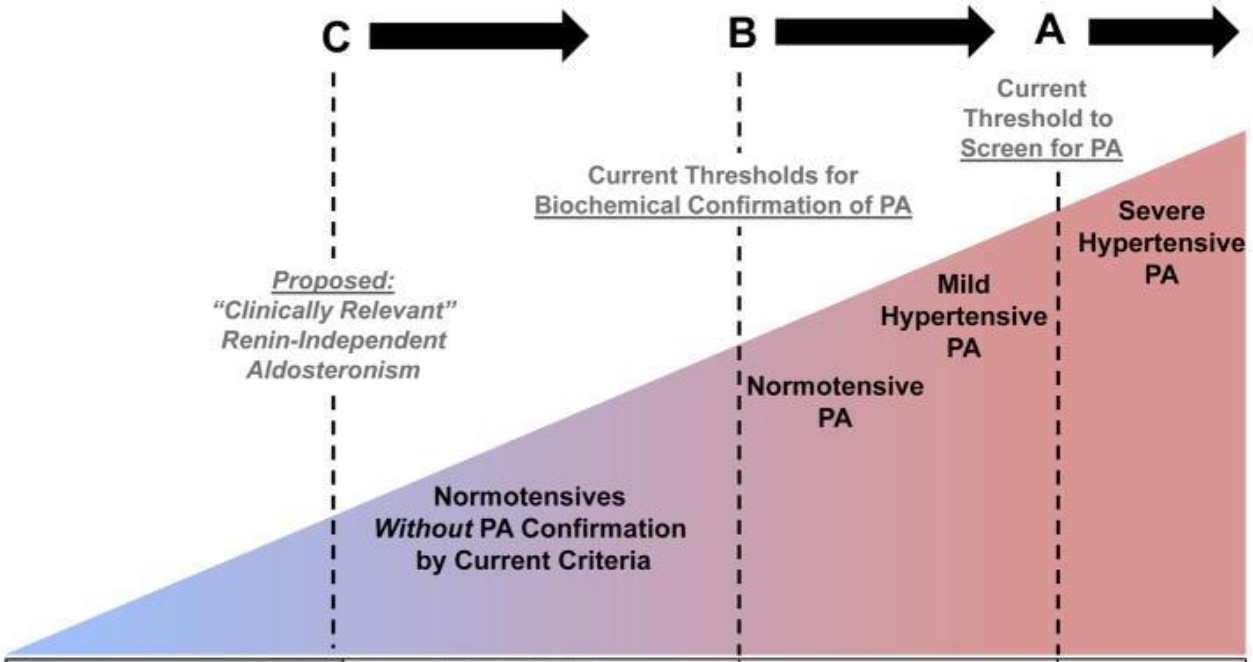
Patient presents with hypertension and hypokalemia. To work up for primary hyperaldosteronism it is important:

- A) Have the patient on diuretic therapy
- B) Have the patient restrict sodium.
- C) Restore potassium to at least 3.5
- D) Have a therapeutic trial of spironolactone

Major Determinants of Renin and Aldosterone Production



Spectrum of Primary Aldosteronism



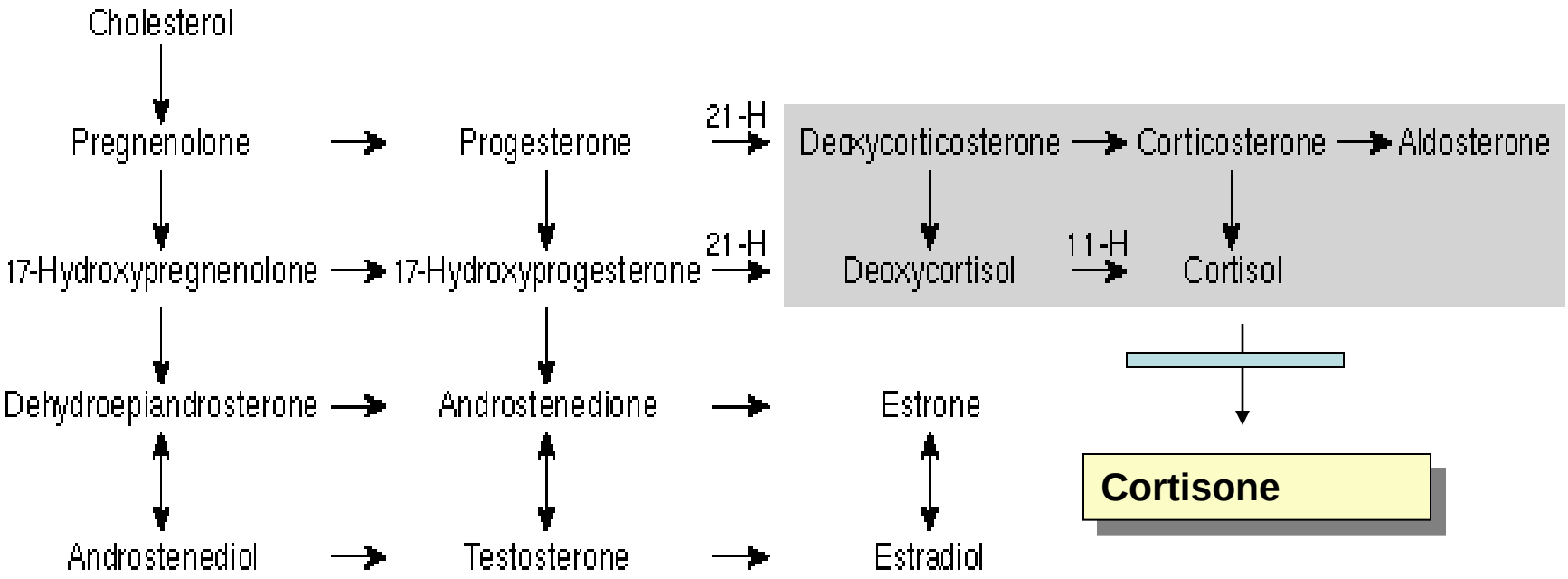
DISEASE	Subclinical Primary Aldosteronism: "Syndrome of Renin-Independent Aldosteronism"	Unrecognized Yet Biochemically Overt PA	Overt PA
Obvious Clinical Syndrome of Excessive MR Activation?	NO	NO	YES
Biochemical Confirmation of PA Using *Current* Thresholds?	NO	YES	YES
Histopathology	*Aldosterone Producing Cell Clusters (APCCs)*		*APA/BAH*

Jenifer M. Brown, et al. Ann Intern Med. 167(9):630-641

Dexamethasone-suppressible Hyperaldosteronism

- Fairly rare, familial, autosomal dominant
- Caused by a Chimeric gene of 5’ region of 11-beta OHase and coding region of aldosterone synthase on Chr. 8
- Zonal fasciculata produces aldosterone under ACTH control
- Higher amounts of 18-OH-cortisol and 18-oxocortisol are seen.

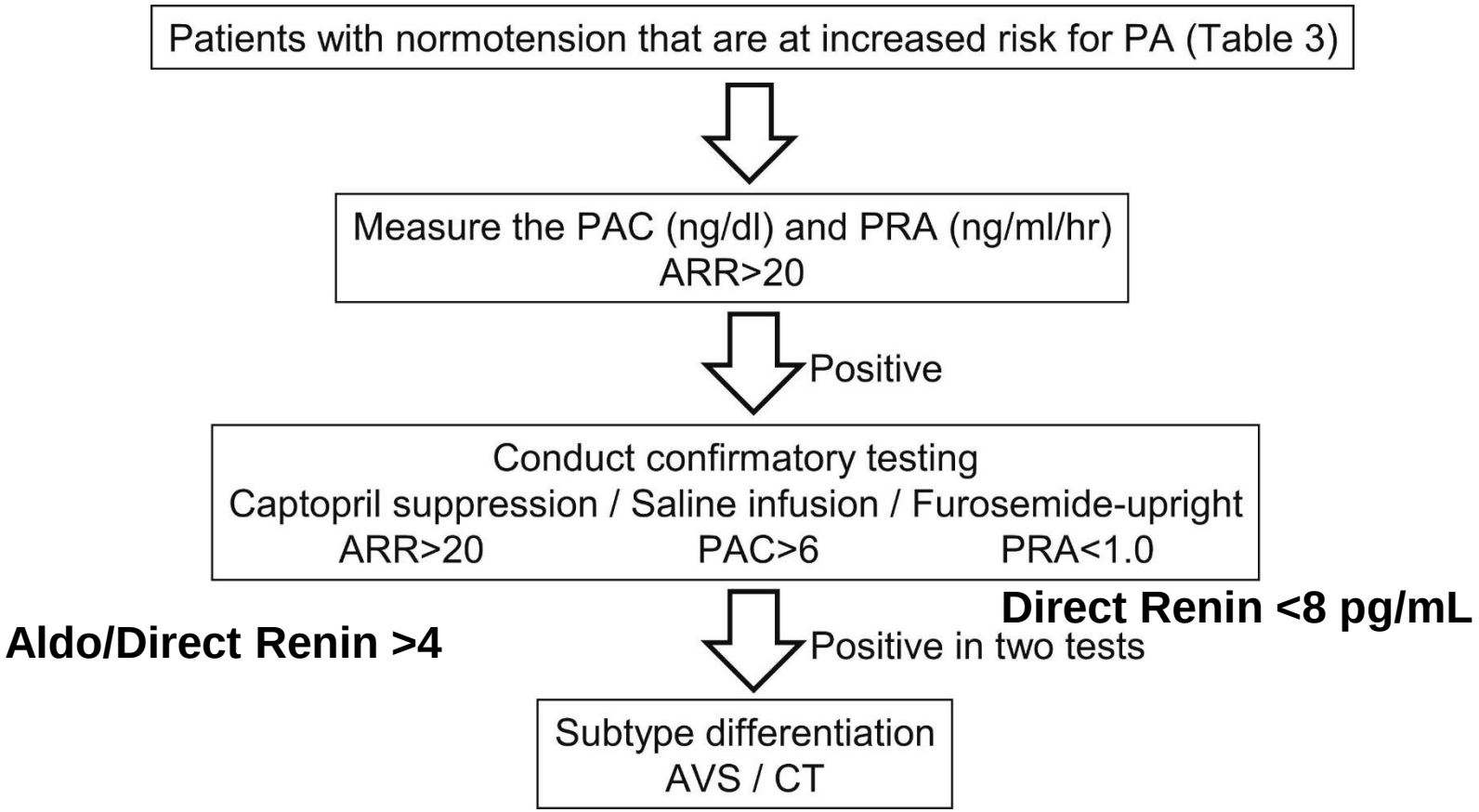
Licorice Excess: 11 β HSD2 inhibition



Liddle's Syndrome

- Familial condition with defect in the regulation of sodium transport in the distal nephron leading to increased sodium reabsorption leading to HTN
- Clinically resembles primary aldosteronism
- Low aldosterone and low renin levels
- Hypertension and hypokalemia

Renin Independent Aldosteronism



Ito Y, Takeda R, Takeda Y. Best Pract Res Clin Endocrinol Metab. 2012 26(4):485-95.

8.

AGW is suspected to have pheochromocytoma. Which of these would you order initially (i.e. best sensitivity and specificity)?

- A) 24 hr urine for VMA
- B) 24 hr urine for metanephrines
- C) 24 hr urine for free catecholamines
- D) A and B
- E) B and C
- F) Peripheral chromogranin A levels

Clinical Conditions that May Activate the SNS & Increase Circulating Catecholamines and Their Metabolites

- CHF, Class III – IV
- Acute Stroke/MI
- Hypothyroidism
- Hypoglycemia
- Clonidine/ β-adrenergic blocker withdrawal
- Peripheral vasodilators (hydralazine/minoxidil/ non-dihydropyridine CCB)
- Acute hypotension
- Salt/water depletion
- Alcohol withdrawal

Medications That Can Cause False-Positive Elevations of Plasma and Urinary Catecholamines or Metanephrines

Medications	Catecholamines NE	Catecholamines E	Metanephrines NMN	Metanephrines MN
Tricyclic antidepressants	+++	—	+++	—
Phenoxybenzamine	+++	—	+++	—
Labetalol*	+++	—	+++	—
Monoamine oxidase inhibitors	—	—	+++	+++
Sympathomimetics	++	++	++	++
Caffeine	++	++	?	
Levodopa, Carbidopa	++	—	?	
Cocaine	++	++	?	
Acetaminophen*			++	
Buspirone*				+++

* cause biochemical interference

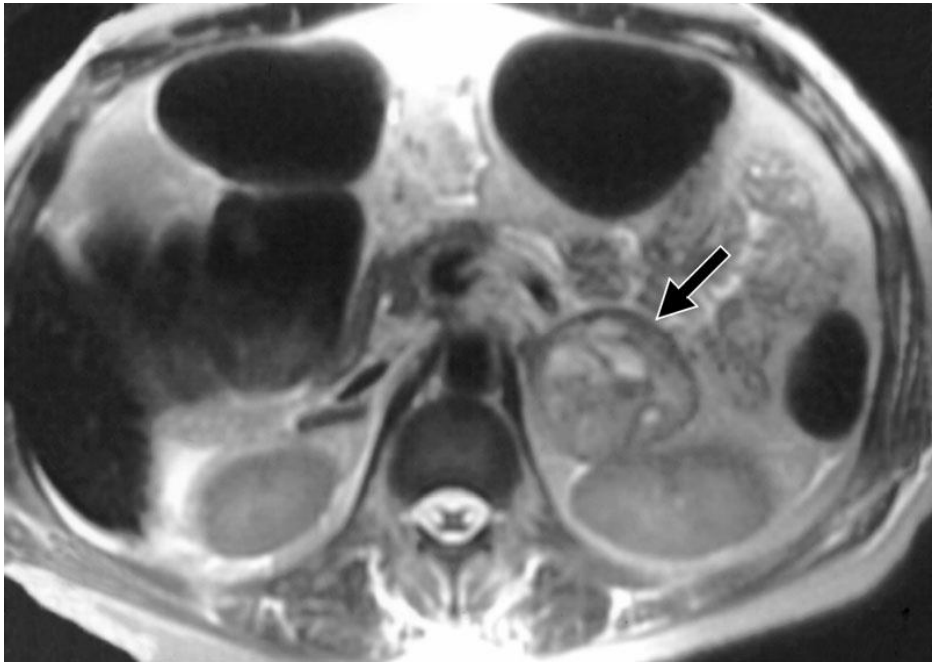
Suspect Pheochromocytoma

- Episodes of headache, palpitations and diaphoresis classic but not necessary
- Postural hypotension
- Labile hypertension
- Pallor; anxiety; tremor
- Weight loss; hyperglycemia
- Nausea, vomiting, constipation

Pheochromocytoma

- Hypertension, palpitations, sweating, orthostatic hypotension
- Emergencies:
  - Sodium nitroprusside
  - Calcium channel blocker
  - Alpha blockers

Large left adrenal on contrast CT



T2-weighted left adrenal

AmershamHealth

9

A 45 yr-old lecturer (JS) preparing for the IM Board Review complains of episodes of pallor, diaphoresis and palpitations. His BP is 150/95 mm Hg and Heart rate: 102/min but the rest of physical examination is normal.

Laboratory Studies

freeT3 2.6 pg/ml ; freeT4 = 1.5 µg/dL (NORMAL)

Plasma E	**55 pg/ml**	**(10-200 pg/ml)**
Plasma NE	**1368 pg/ml**	**(80-520 pg/ml)**
Urinary metanephrines:	**360µg/24h**	**(52-341 ug/24h)**
U normetanephrines:	**1256 µg/24 h**	**(88-444 ug/24h)**

10.

Which of the following studies would be next step in establishing the cause of the patient's symptoms?

A. CT/MRI

B. Glucagon stimulation

C. Quantitative urinary 5-HIAA

D. Clonidine Suppression Test

E. MIBG

11 Preparation for Resection

The best preparation for removal of pheo is

a. Phenoxybenzamine
b. Clonidine
c. Doxazosin
d. Labetolol
e. Calcium channel blockers
f. a or c are equally effective

Incidentalomas: What to ask?

- Functioning or nonfunctioning
- Benign or malignant
- Size may not be important if HU less than 10

12. 40 yo man found to have a left adrenal mass that is 1.8 cm and 8 HU after CT done to evaluate a renal stone. BP is normal and BMP is normal. Which test is absolutely not indicated?

A. 1 mg dex suppression for cortisol

B. Aldosterone and renin levels check

C. Late night salivary cortisol

D. CT guided FNA

Adrenal Incidentaloma: Also think about

- Myelolipomas, cysts, non-functioning adenomas
- Pseudoadrenal mass from nearby organs
- Metastatic disease
- Adrenal carcinoma

Adrenal Incidentolomas

- Cumulative risk of enlargement is 23% and hyperfunction is 10% in 10 years
- Increasing size on serial CTs also an indication for surgery.

Barzon L. Scaroni C. et al. JCEM 84:520-526; 1999

Kloos RT, Gross MD, et al. Endo. Rev. 16:460-484;1995

Adrenal metastases

- Variable in size
- Inhomogeneous
- Irregular margins
- Often bilateral
- Contrast enhancing
- Intermediate intensity on T2 weighted MRI

Answers to Adrenal Session

- 1- E
- 2 - B
- 3 - A
- 4 - A
- 5 - D
- 6 - D
- 7 - C
- 8 - E
- 9 - E
- 10 - A
- 11 - F
- 12 - D

Cleveland Clinic

Every life deserves world class care.