Mirror Lake, Mount Hood, OR. Photo by Kristin Childress

Adrenal Cases

School of Medicine
Endocrinology, Diabetes and Clinical Nutrition

Kristin Childress, MD, MPH

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Disclosures

I have no conflicts of interest to report.

OHSU CPD

Roadmap

Review of adrenal physiology

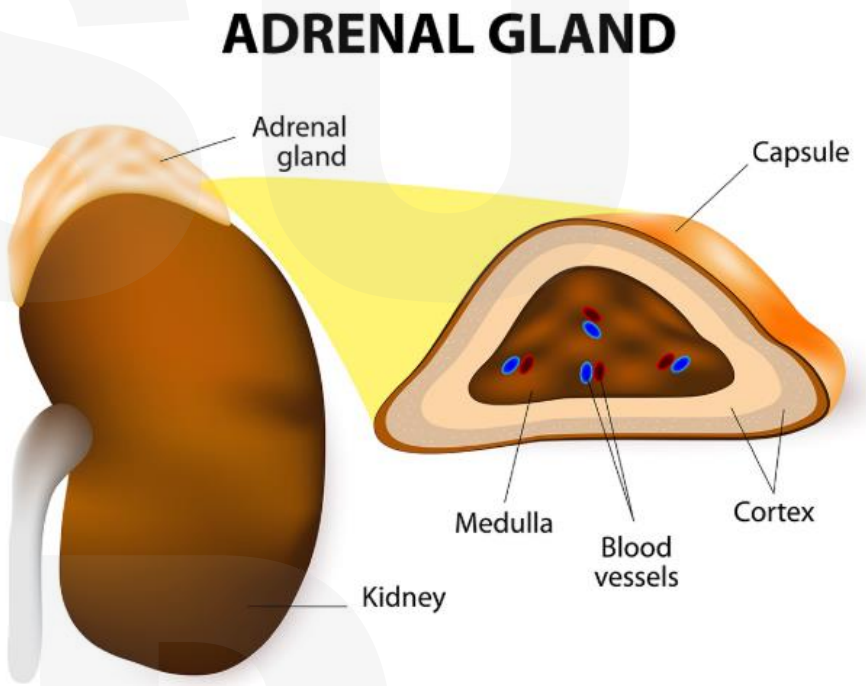
Adrenal insufficiency

Primary aldosteronism

Adrenal nodules

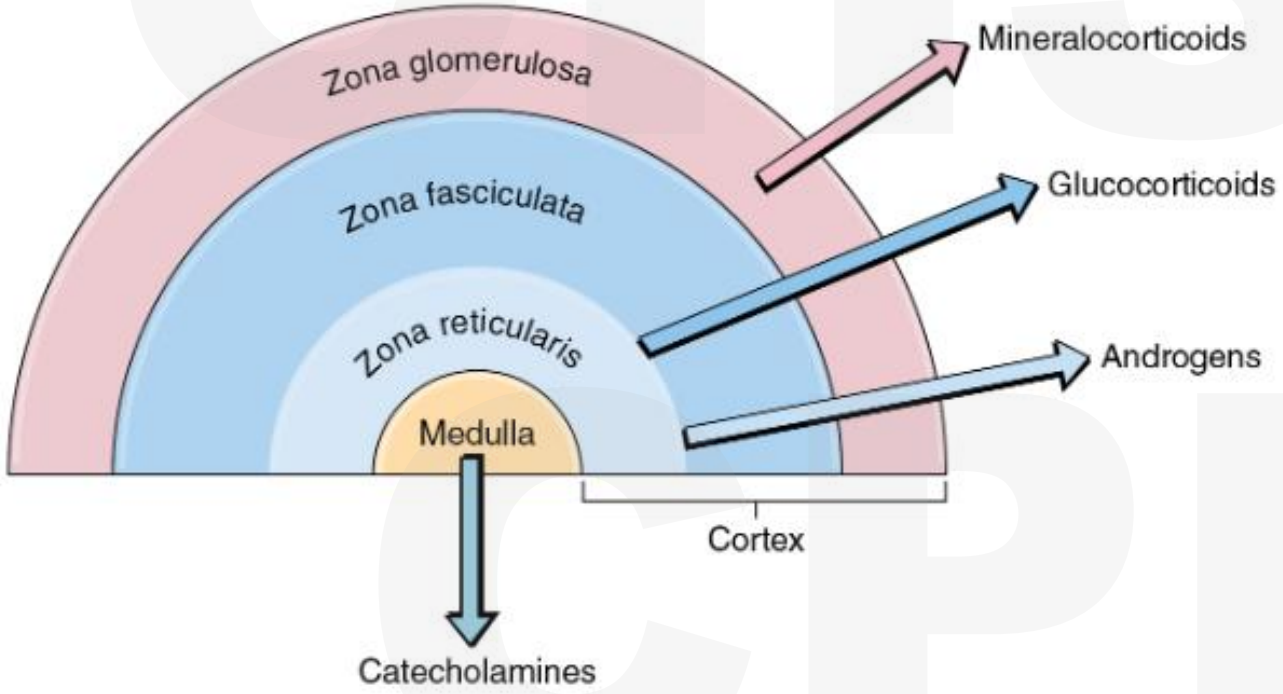
The Adrenal Gland

- Located in the retroperitoneal gland above each kidney.
- Two separate glands:
  - Adrenal Medulla
  - Adrenal Cortex
- Adrenal medulla secretes catecholamines.
- Adrenal cortex has 3 distinct layers and secretes adrenocortical steroid hormones.



https://www.hopkinsmedicine.org/health/conditions-and-diseases/adrenal-glands

The Adrenal Gland



Secretions of the adrenal medulla and adrenal cortex.

Linda S. Costanzo, PhD, CHAPTER 9, 399-464

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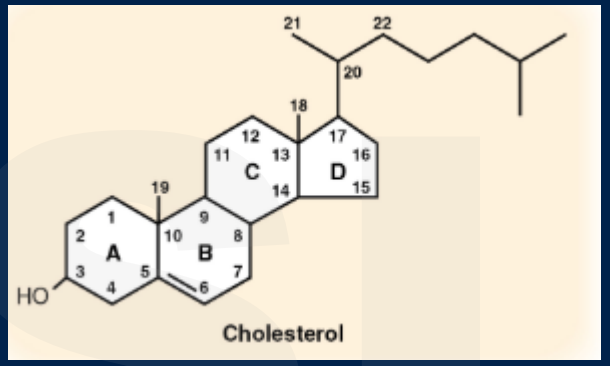
The Adrenal Cortex

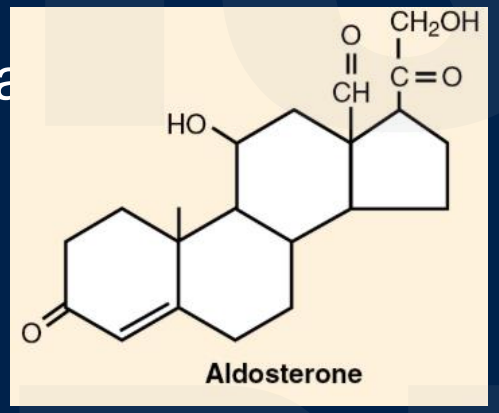
- The cortex produces steroid hormones.
- The precursor for all adrenocortica steroidogenesis is cholesterol.

Major Players:

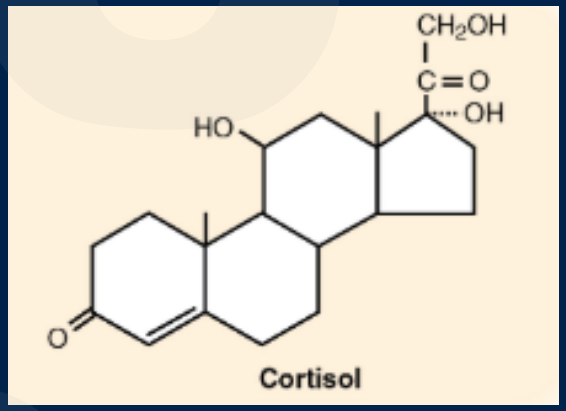
- Glucocorticoids: Cortisol
- Mineralocorticoids: Aldosterone
- Androgens: Dehydroepiandrosterone (DHEA)



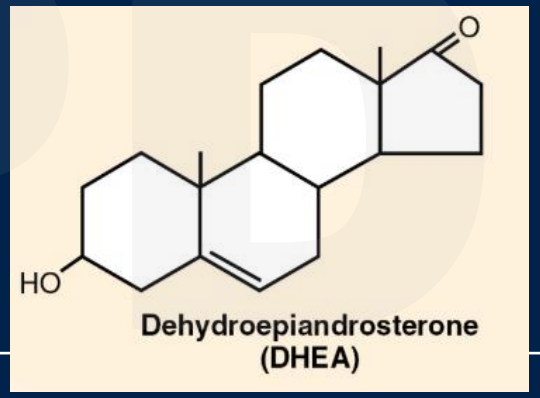
Cholesterol



Aldosterone



Cortisol



Dehydroepiandrosterone (DHEA)

Structures of adrenocortical steroids.

Linda S. Costanzo, PhD, CHAPTER 9, 399-464

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Actions of Adrenal Cortical Steroids

Actions of Adrenocortical Steroids

Actions of Glucocorticoids	Actions of Mineralocorticoids	Actions of Adrenal Androgens
Increase gluconeogenesis	Increase Na^+ reabsorption	Females: stimulate growth of pubic and axillary hair; stimulate libido
Increase proteolysis (catabolic)	Increase K^+ secretion	Males: same as testosterone
Increase lipolysis	Increase H^+ secretion	
Decrease glucose utilization		
Decrease insulin sensitivity		
Inhibit inflammatory response		
Suppress immune response		
Enhance vascular responsiveness to catecholamines		
Inhibit bone formation		
Increase GFR		
Decrease REM sleep		

GFR, Glomerular filtration rate; *REM*, rapid eye movement.

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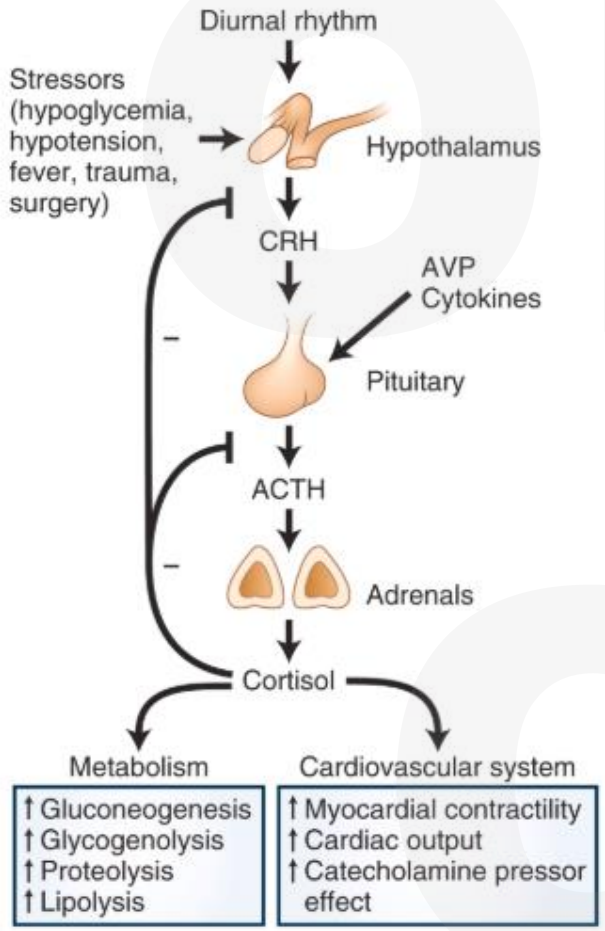
Adrenal Cortex Regulation

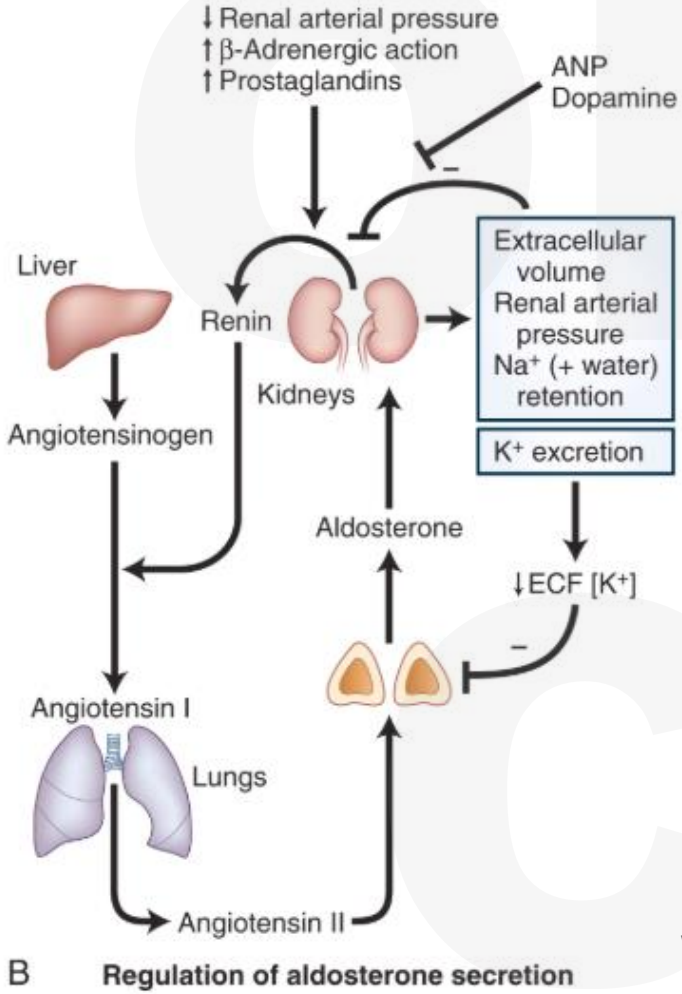


A **Regulation of cortisol secretion**

- Zona fasciculata and Zona reticularis are controlled by the HPA (hypothalamic-pituitary-adrenal) axis.
- Negative feedback loop.

Williams Endocriology
Richard J. Auchus; Christa E. Flück Pandey, 13, 471-533.e13

Adrenal Cortex Regulation



B **Regulation of aldosterone secretion**

- Zona glomerulosa is controlled separately via renin-angiotensin-aldosterone system (RAAS).

Williams Endocriology
Richard J. Auchus; Christa E. Flück Pandey, 13, 471-533.e13

Adrenal Medulla Regulation

- Under sympathetic nervous system control.
- Lower thoracic and lumbar preganglionic neurons innervate the cells of the adrenal medulla.
- Secretion of catecholamines, which increase HR, BP, myocardial contractility.

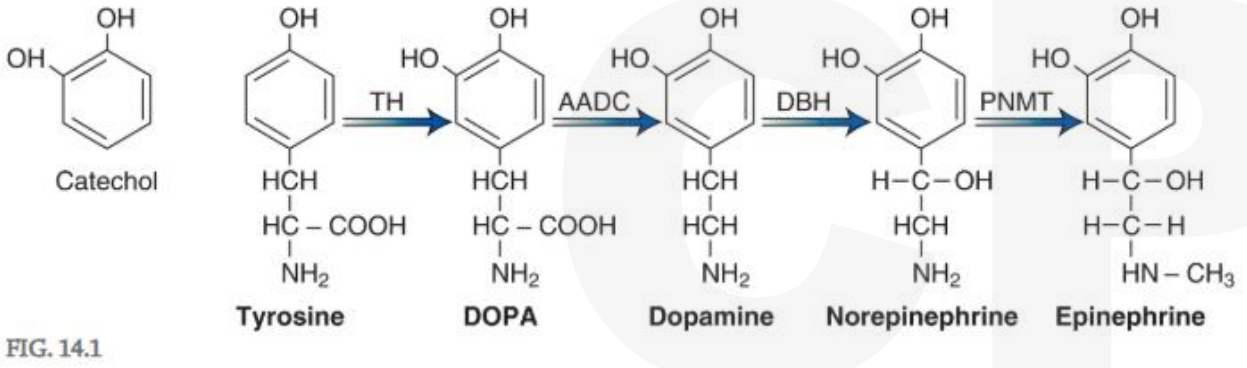


FIG. 14.1

Williams Endocrinology
William F. Young, 14, 534-564.e8

Case # 1

An 18 y/o man presents to the hospital with fatigue, poor oral intake, and vomiting. He had a recent hospital admission with hyponatremia, hypokalemia, and AKI thought to be due to a viral infection and dehydration. His PMHx is significant for asthma. Of note, he finished a prednisone taper for asthma a few days before his recent symptoms began.

Family history is significant for mother with DM1.

VS – tachycardic, mildly hypotensive.

Thin young man.

Tan skin.

Labs:

Na 123, K 7.0, Cr 1.01

Random cortisol 3.2

CIRSU CPD

Adrenal Insufficiency (AI)

- Glucocorticoid deficiency:
  Primary = adrenal disease. Low cortisol, high ACTH.
  Secondary (Central) = ACTH deficiency (pituitary). Low cortisol with low or normal ACTH.

- Mineralocorticoid deficiency accompanies primary disease due to adrenal gland destruction.

- Mineralocorticoid production remains intact in central AI due to regulation by RAAS, not HPA axis.

Adrenal Insufficiency

Primary Causes: Addison Disease

Autoimmune

- Sporadic
- Autoimmune polyendocrine syndrome type I (Addison disease, chronic mucocutaneous candidiasis, hypoparathyroidism, dental enamel hypoplasia, alopecia, primary gonadal failure—see Chapter 44)
- Autoimmune polyendocrine syndrome type II (Schmidt syndrome) (Addison disease, primary hypothyroidism, primary hypogonadism, insulin-dependent diabetes, pernicious anemia, vitiligo—see Chapter 44)

Infections

- Tuberculosis
- Fungal infections
- Cytomegalovirus

HIV

Metastatic tumor

Infiltrations

- Amyloidosis

HemochromatosisIntraadrenal hemorrhage (Waterhouse-Friderichsen syndrome) after meningococcal septicemia

Monogenetic Disorders

Congenital adrenal hypoplasia/developmental disorders

Adrenal Insufficiency

- No absolute guidelines for steroid type, dose, route, or duration to predict adrenal suppression.
- But adrenal atrophy should be anticipated in a patient who has taken hydrocortisone 30mg (prednisone 7.5mg) per day for longer than 3 weeks.

Secondary Causes: Central Hypoadrenalism

Exogenous glucocorticoid therapy

Hypopituitarism

Selective removal of ACTH-secreting pituitary adenoma

Pituitary tumors and pituitary surgery, craniopharyngiomas

Pituitary apoplexy

Granulomatous disease (tuberculosis, sarcoid, eosinophilic granuloma)

Secondary tumor deposits (breast, bronchus)

Postpartum pituitary infarction (Sheehan syndrome)

Pituitary irradiation (effect usually delayed for several years)

Isolated ACTH deficiency

Hospital Presentation: Adrenal Crisis

- No universally accepted definition, but adrenal crisis is considered severe, acute adrenal insufficiency.
- Life-threatening.
- Inadequate cortisol production due to primary or secondary causes.
- Consider with hypotension + hyponatremia +/- hypokalemia.
- Consider with refractory shock despite adequate fluids and vasopressor support.

Table 1. Symptoms, Signs, and Biochemical Characteristics of Adrenal Crisis.*

Symptoms
Gastrointestinal: anorexia, nausea, vomiting
Pain: abdominal, limb, back
Severe fatigue
Severe weakness
Postural dizziness, syncope
Confusion
Signs
Abdominal tenderness or guarding
Hyperpigmentation (only in primary adrenal insufficiency)†
Pyrexia
Hypotension: systolic pressure <100 mm Hg in adults or ≥20 mm Hg lower than usual in adults, acute hemodynamic disturbance according to age-related normative levels in children, delayed capillary refill or tachycardia in young children, circulatory collapse
Impaired consciousness: delirium, obtundation, coma
Biochemical abnormalities on routine blood tests
Hyponatremia
Hyperkalemia
Hypercalcemia
Hypoglycemia (more common in children than in adults)
Altered immune-cell populations: neutropenia, eosinophilia, lymphocytosis
Mild normocytic anemia

Hyperkalemia generally occurs in primary AI.

Rushworth RL, Torpy DJ, Falhammar H. Adrenal Crisis. N Engl J Med. 2019;381(9):852-861. doi:10.1056/NEJMra1807486

Adrenal Crisis: Precipitating Events

- Infections
- Injury
- Surgery
- Non-adherence to glucocorticoid replacement in someone with AI or withdrawal of exogenous steroid.
- Undiagnosed hyperthyroidism or initiating LT4 in someone with untreated AI.
- Immune checkpoint inhibitor therapy or TKI therapy.

Suspected Adrenal Crisis: Management

- **Do NOT delay treatment** by waiting for lab results.
- If possible, check random cortisol and ACTH **before** treating with glucocorticoids. Does not need to be an AM check.
- A random cortisol value < 18 mcg/dL in a hypotensive patient suggests AI.
- Some scenarios can alter corticosteroid binding globulin (CBG) leading to incorrect diagnosis.
- Critical illness can lead to variable cortisol and ACTH values due to abnormal CBG and reduced clearance of cortisol.

Suspected Adrenal Crisis: Management

Table 2. Management of Adrenal Crisis.

Treatment	Dose and Procedure
Adults	
Hydrocortisone*	Provide prompt administration at a dose of 100 mg intravenously (or intramuscularly if intravenous access is not feasible), followed by 200 mg every 24 hr, given as a continuous infusion or as intravenous (or intramuscular) boluses (50 mg) every 6 hr; if initial treatment is successful (usually after 24 hr), oral hydrocortisone at 2 to 3 times the usual dose can be given, with tapering down to the usual dose over the next 2 to 3 days†
Fluids	Provide intravenous administration of 1000 ml of normal saline (0.9% isotonic sodium chloride) in the first hour, with intravenous dextrose to 5% concentration in normal saline added if the patient has hypoglycemia; subsequently, administer crystalloid fluids according to standard resuscitation guidelines‡

Case # 2

A 41 y/o man with a hx of ADHD, anxiety, and BPH present with uncontrolled hypertension. The patient reports he developed hypertension sometime during the pandemic in approximately 2020 (age 37). He started losartan in 2021 and then needed amlodipine added after losartan maxed out. He was noted to have mildly low potassium in 2023, but labs had not been checked for a few years.

Pt's BP meds had been switched to losartan and eplerenone when he presented to endocrine clinic. He was not requiring potassium with this combination.

The primary care suspected primary aldosteronism and ordered a CT adrenal scan, which revealed a 9mm Right adrenal nodule.

Primary Aldosteronism (PA)

A unilateral or bilateral adrenal disorder resulting in excess adrenal production of aldosterone.

At least partially autonomous from the regulation of renin and angiotensin system.

Excess aldosterone causes:
- sodium retention-> volume expansion -> elevated BP
- hypokalemia (in more severe forms).

Why is primary aldosteronism important to identify and treat?

Patients with PA have higher health risks compared to primary HTN:

- Stroke
- CAD
- A-fib
- CHF
- Renal disease
- Mortality

When to consider this diagnosis

- Screening for PA is low.
- *Hot of the Press!!* New Endocrine Society Guidelines (July 2025) suggest screening for PA in all patients with hypertension.
- Definitely consider screening with the **traditional risk factors:**

  - Unexplained worsening or resistant HTN (3+ drugs)
  - Hypokalemia (spontaneous or diuretic-induced)
  - Adrenal nodule
  - family hx of early onset HTN or stroke (<40 years)

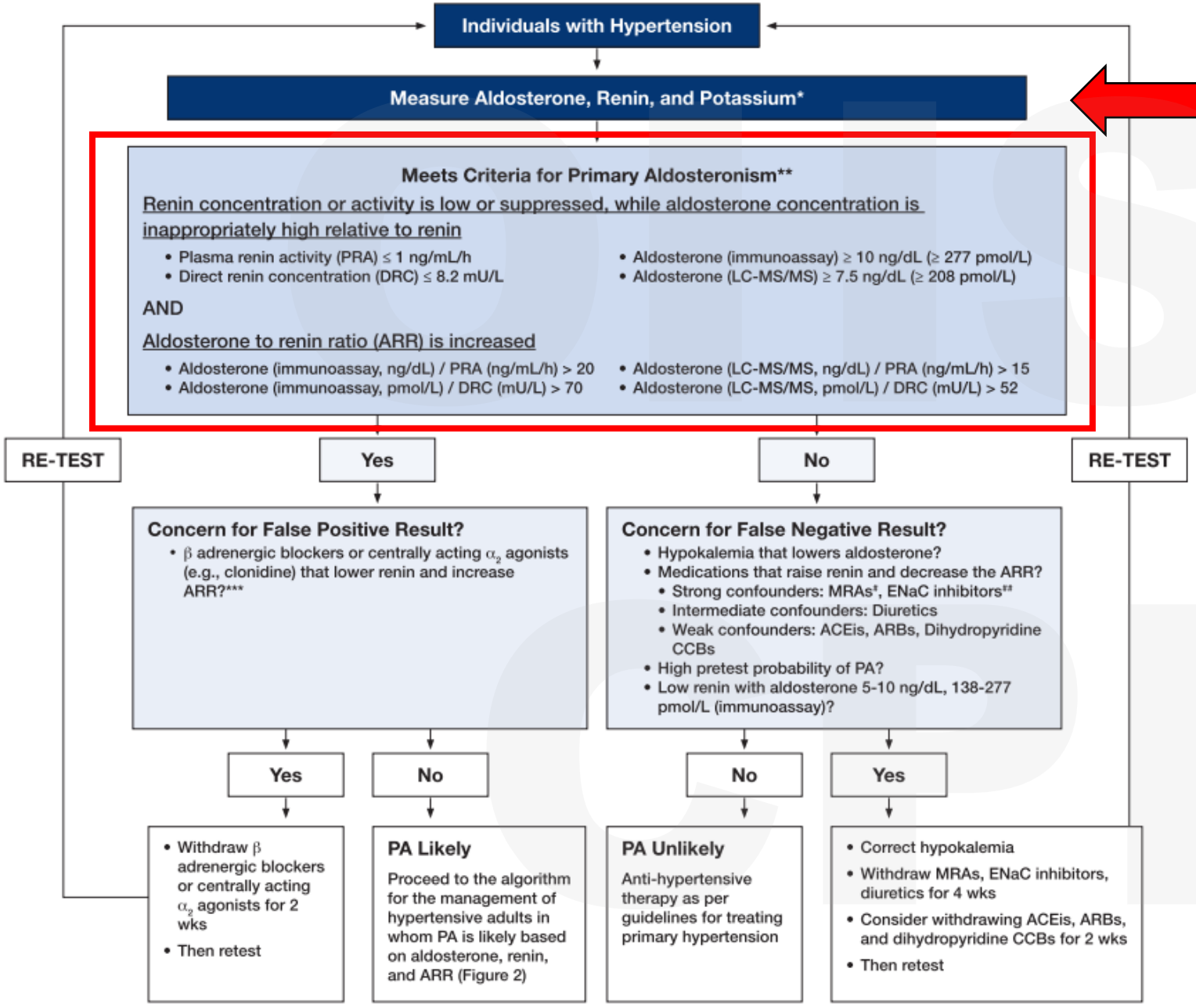


Figure 1. How to screen for PA in individuals with hypertension. This figure diagrams the process of screening for PA in individuals with hypertension.

PA Screening Algorithm

PA Treatment Algorithm

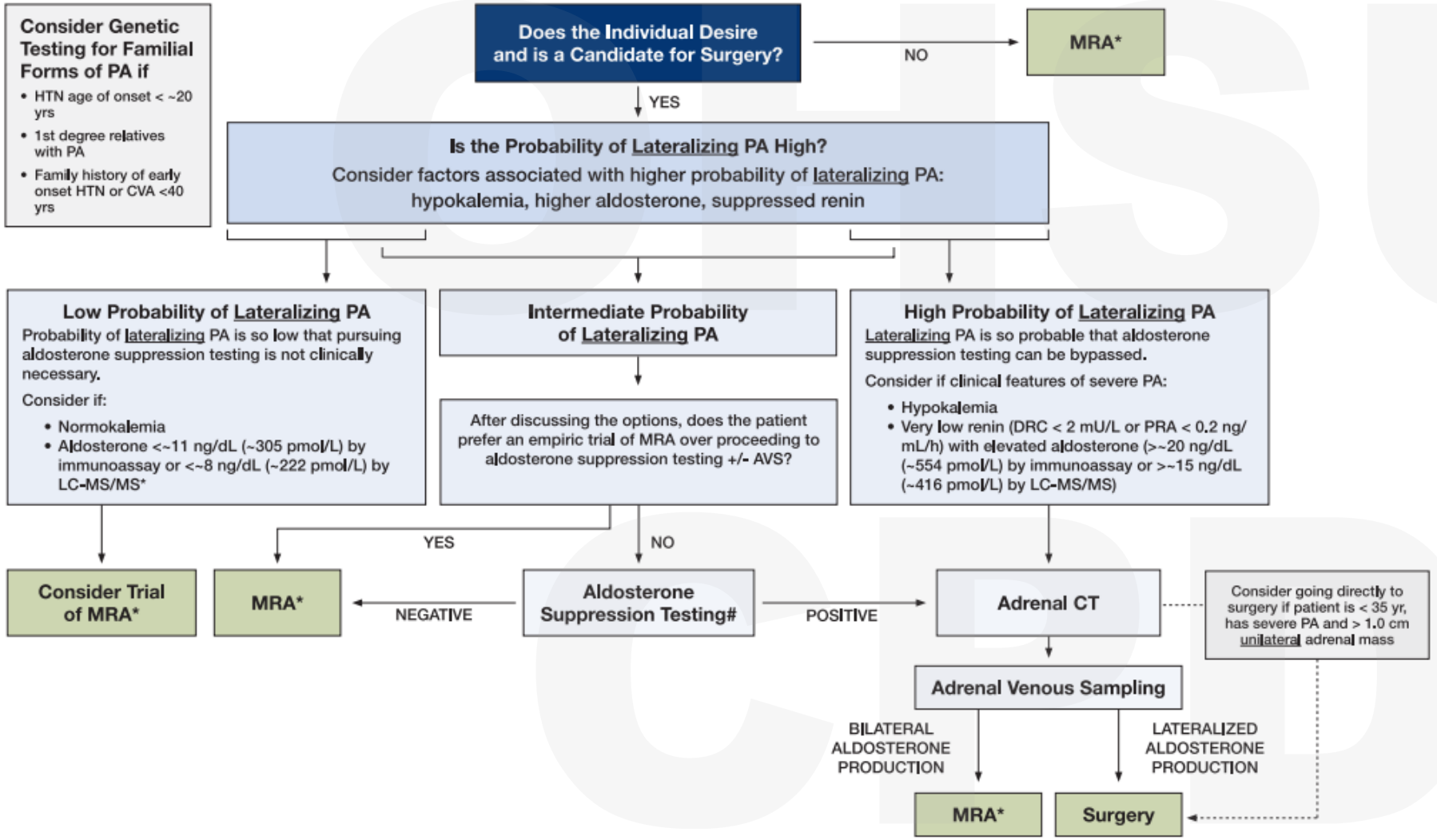


Figure 2. Algorithm for the management of adults with hypertension in whom PA is likely based on aldosterone, renin, and ARR. Patients who are likely

Key points for hospital management with suspicion of PA

- Correct potassium.
- Try to draw aldosterone and renin before 10AM.
- Do NOT draw aldo and renin if patient is taking or has taken MRA (spironolactone or eplerenone) or epithelial sodium channel inhibitors (amiloride, triamterene) within the last 4 weeks; these interfere with test results.
- If patient does not desire adrenalectomy evaluation or is poor surgical candidate, MRA can be started when PA is considered likely.

Case # 3

A 62 y/o woman presents with abdominal pain. She undergoes CT abdomen in the ER which shows an incidental right adrenal nodule, 2.5 cm.

She has a history of HTN, controlled with two medications, prediabetes, and obesity (BMI 35).

Adrenal Incidentalomas

- Often discovered on abdominal imaging done for other indications.
- Incidence is adrenal tumors increased 10 x over the past two decades, in step with the increasing number of abdominal CT and MRI studies performed.
- Important to evaluate for:
  - Malignancy
  - Hormone excess

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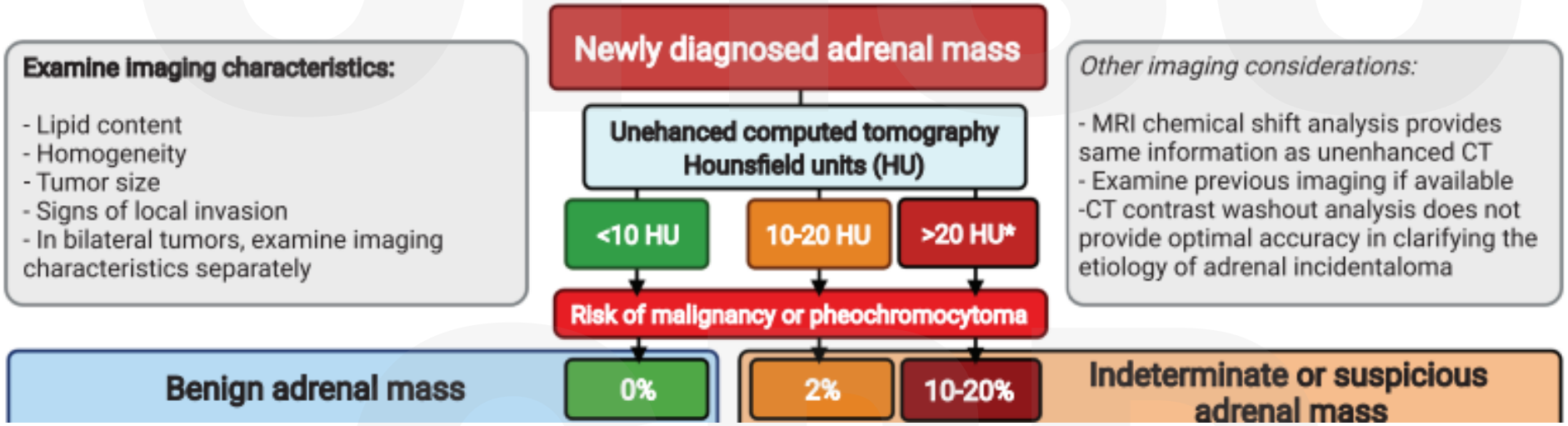
Adrenal Mass Classification

- Adenomas and nodular hyperplasia (85% of all adrenal tumors).
  - about 50-60% have hormonal excess, usually mild autonomous cortisol secretion.
- Other benign lesions (myelolipomas, cysts, hematomas).
- Adrenocortical carcinoma (0.3% of all tumors).
- Other malignancy (metastases, lymphoma).
- Pheochromocytoma (1.1%).

Adrenal Mass Evaluation



Adrenal Mass Evaluation when unenhanced HU < 10

- These tumors are benign.
- Do not need to check for catecholamine excess.
- Testing:
  - check for glucocorticoid excess in all patients: 1 mg dexamethasone suppression test (DST).
  - check for aldosterone excess if HTN and/or hypokalemia: AM aldosterone and renin.

1 mg Dexamethasone Suppression Test (DST)

Take 1 mg dexamethasone PO between 11 PM and midnight.

Draw cortisol and dexamethasone level before 9 AM the next day.

Normal cortisol < 1.8 mcg/dL

Adrenal Mass Evaluation when unenhanced HU > 10

- Concern for malignancy or pheo.
- Test for glucocorticoid and aldosterone excess.
- Test for catecholamine excess: 24 hour urine metanephrines provides less false positives than plasma.
- Test for DHEA-s with any evidence of androgenic symptoms in women.
- Think about primary adrenal insufficiency in patients with bilateral adrenal masses with elevated HU (malignancy, infection).
- Adrenal **biopsy is rarely needed.**
  - risk of needle track seeding of adrenocortical carcinoma.
  - risk of HTN, tachycardia with a pheo.

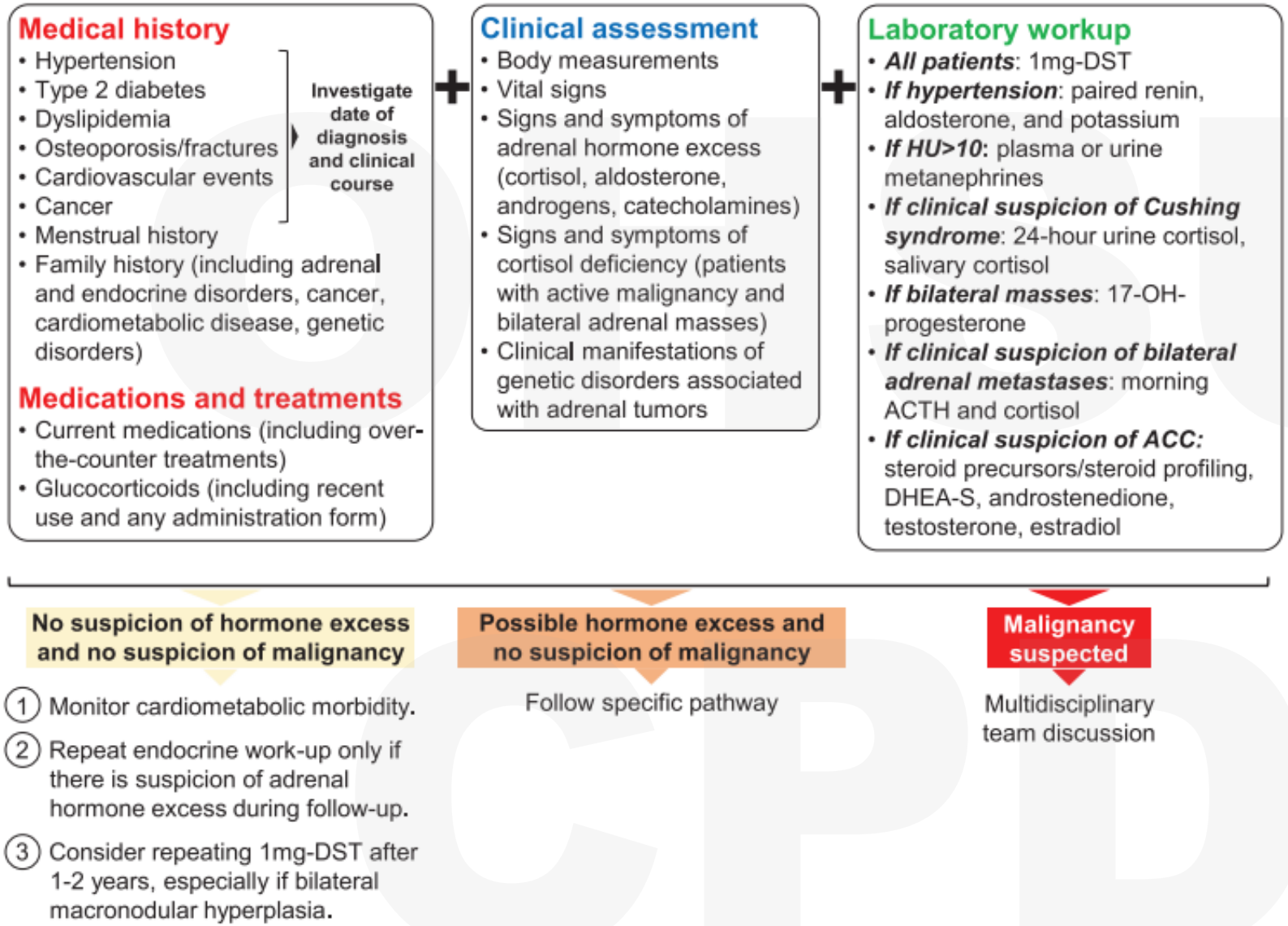


Figure 3. Adrenal incidentaloma evaluation: clinical and hormonal assessment. Abbreviations: 1-mg DST, 1-mg overnight dexamethasone suppression test; ACC, adrenocortical cancer; DHEA-S, dehydroepiandrosterone sulfate.

Management

- Resection of ACC, pheo, and hormonally functional tumors.
- ? Repeat imaging for masses < 4 cm, low HU, and no hormonal excess. Newer guidance says no.
- Masses with higher density, size > 3.5 cm, follow up imaging is still recommended.
- Repeat 1 mg DST, especially in those with cardiometaboic risk factors.

Questions?

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