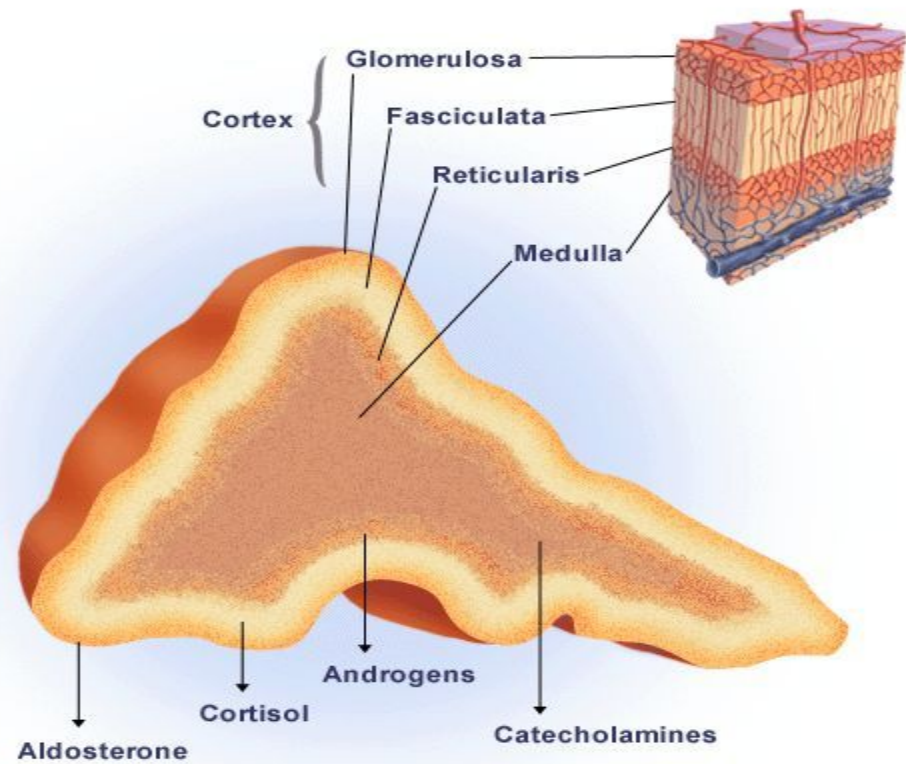
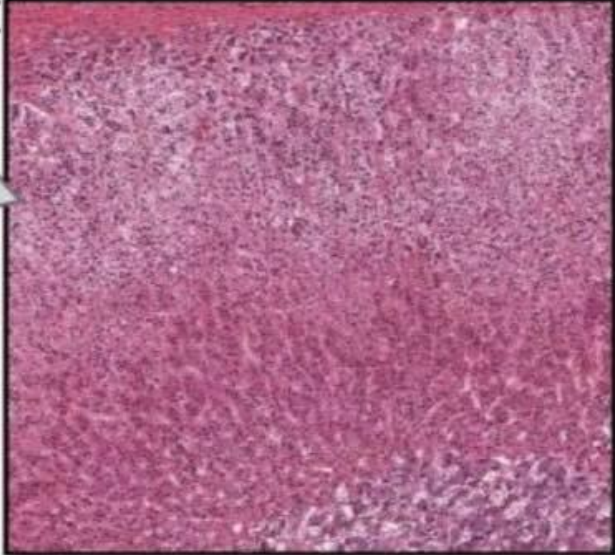




PATHOLOGY LAB- ADRENAL GLAND

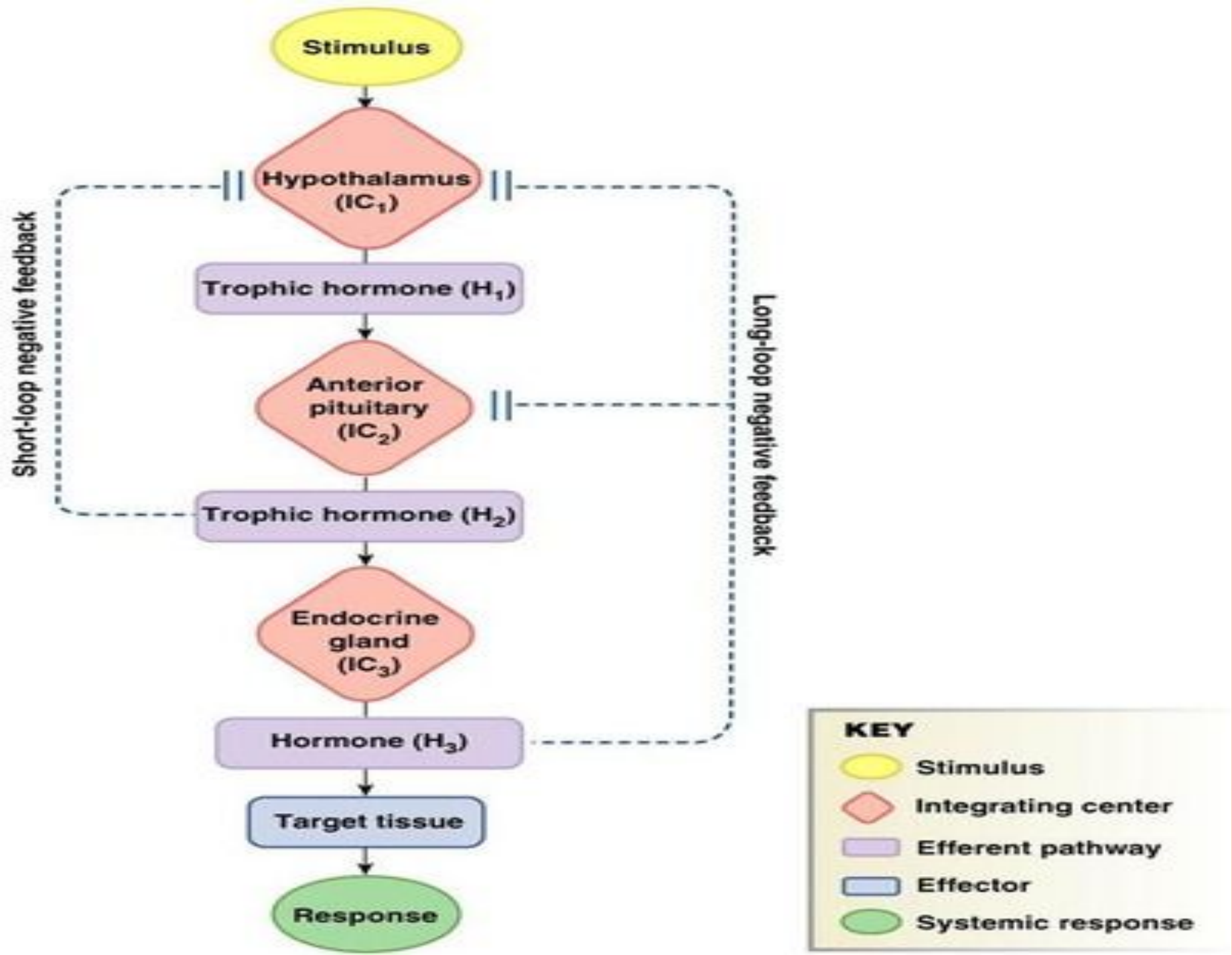
Rola Alwaheidi , MD

Zones of the Adrenal Glands



A microscopic image of the adrenal cortex, showing the three distinct zones: the outermost zona glomerulosa (stained dark purple), the middle zona fasciculata (stained a lighter purple), and the innermost zona reticularis (stained a darker purple). The adrenal medulla is visible at the bottom of the image.

	Tissue area	Hormones released	Examples
	Zona glomerulosa (adrenal cortex)	Mineralcorticoids (regulate mineral balance)	Aldosterone
	Zona fasciculata (adrenal cortex)	Glucocorticoids (regulate glucose metabolism)	Cortisol Corticosterone Cortisone
	Zona reticularis (adrenal cortex)	Androgens (stimulate masculinization)	Dehydroepian-drosterone
	Adrenal medulla	Stress hormones (stimulate sympathetic ANS)	Epinephrine Norepinephrine



PRIMARY HYPERALDOSTERONISM

- Primary hyperaldosteronism is caused by autonomous overproduction of aldosterone in the zona glomerulosa of one or both adrenal glands
- Most commonly due to the following conditions:
 - Bilateral idiopathic hyperplasia of the adrenal glands (~ 60%)
 - Often manifests with only mild symptoms and normokalemia.
 - Aldosterone-producing adrenal adenoma or **aldosteronoma** (**Conn Syndrome**) (~ 30%)
 - Usually manifests with marked hypokalemia and more severe symptoms than idiopathic hyperplasia of the adrenal glands



LESS COMMON CAUSES INCLUDE:

- Unilateral hyperplasia of one adrenal gland
- Aldosterone-secreting carcinomas of the adrenal cortex
- Familial hyperaldosteronism (e.g., FH-I)
- Ectopic aldosterone production
 - Autonomous aldosterone production that occurs outside the adrenal gland (e.g., aldosterone-producing tumors in the kidneys or ovaries)



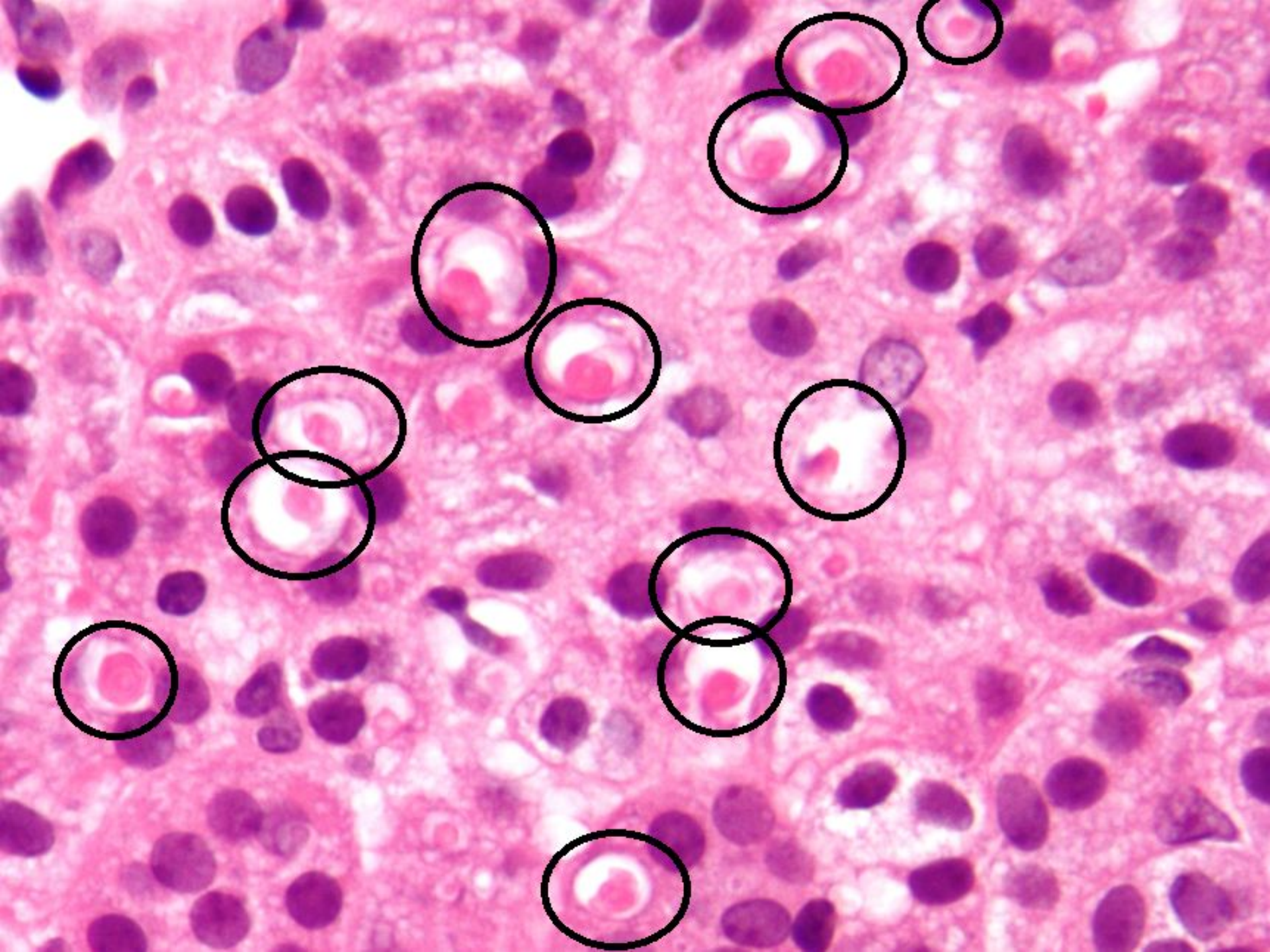
MORPHOLOGY OF ADRENAL GLAND

- They do not suppress ACTH secretion, so the adjacent adrenal cortex and that of the contralateral gland are not atrophic
- Bright yellow **on cut section**
- **Microscopically** are composed of lipid-laden cortical cells resembling **fasciculata** cells

spironolactone bodies

- A characteristic feature of aldosterone producing adenoma treated by spironolactone
- Eosinophilic, laminated cytoplasmic inclusions
- IHC positive for aldosterone





SECONDARY HYPERALDOSTERONISM

Etiology

- Renal artery stenosis (e.g., due to atherosclerosis, fibromuscular dysplasia)
- Renin-secreting tumor
- Chronic kidney disease
- Advanced CHF
- Fibromuscular dysplasia
- Liver cirrhosis
- Diuretics
- Laxative abuse
- **Diagnostics:** ↑ PAC and ↑ PRA (Stimulation of aldosterone release caused by increased renin levels)



PATHOPHYSIOLOGY

Autonomous aldosterone secretion and hypertension

- Physiological aldosterone secretion is regulated by the renin-angiotensin-aldosterone system (RAAS) and occurs in response to the detection of low blood pressure in the kidneys
- $\uparrow$ Aldosterone $\rightarrow$ $\uparrow$ open Na^+ channels in principal cells of luminal membrane at the cortical collecting ducts of the kidneys $\rightarrow$ $\uparrow$ Na^+ reabsorption and retention $\rightarrow$ water retention $\rightarrow$ hypertension



ALDOSTERONE ESCAPE

- Definition: Evasion of the Na^+ -retaining effects of inappropriately elevated aldosterone levels in conditions such as primary hyperaldosteronism or congestive heart failure
- Mechanism: sodium and water retention → volume expansion → secretion of atrial natriuretic peptide (ANP) and pressure natriuresis → compensatory diuresis → “escape” from edema formation and hypernatremia



HYPOKALEMIA AND METABOLIC ALKALOSIS

- $\uparrow$ Na^+ reabsorption $\rightarrow$ electronegative lumen $\rightarrow$ electrical gradient through open K^+ channels $\rightarrow \uparrow$ K^+ secretion $\rightarrow$ hypokalemia
- Hypokalemia $\rightarrow$ metabolic alkalosis via two mechanisms (both of which decrease extracellular H^+ , thereby increasing extracellular pH):
 - Efflux of K^+ from intracellular to extracellular space in exchange for H^+
 - $\uparrow$ H^+ secretion in the kidney in order to enable $\uparrow$ K^+ reabsorption



CLINICAL FEATURES

□ Hypertension

- Sustained systolic blood pressure > 150 mm Hg or diastolic > 100 mm Hg over three measurements on three different days
- Systolic blood pressure > 140 mm Hg or diastolic > 90 mmHg AND resistant to three-drug therapy with an adrenergic inhibitor, a vasodilator, and a diuretic



▣ Features of hypokalemia

Fatigue

Muscle weakness, cramping

Headaches

Paresthesia in severe cases due to metabolic alkalosis

Polyuria and polydipsia

Palpitations

Constipation

Absence of significant edema (due to aldosterone escape)



- Hypokalemia is part of the classical picture of primary hyperaldosteronism. However, normokalemia may actually be much more common than was previously thought and does not rule out the diagnosis.
- Primary hyperaldosteronism is characterized by hypokalemia and drug-resistant hypertension.



DIAGNOSIS

- • Plasma aldosterone concentration (PAC)
- • Plasma renin activity (PRA)
- • $\downarrow$ PRA and $\uparrow$ PAC = Primary aldosteronism
- • $\uparrow$ PRA and $\uparrow$ PAC = Secondary aldosteronism
 - Renal artery stenosis, CHF, low volume
- ❖ The aldosterone-to-renin ratio (ARR) is used to screen for primary hyperaldosteronism and differentiate it from other causes of elevated aldosterone (e.g., secondary hyperaldosteronism).
- ❖ Patients with primary hyperaldosteronism have elevated aldosterone levels (PAC) that cause decreased renin activity (PRA), resulting in an elevated ARR. [$(\uparrow \text{PAC} / \downarrow \text{PRA}) = \uparrow\uparrow \text{ARR}$]



- ❑ • Abdominal imaging for adrenal nodules/tumors
- ❑ • Adrenal vein sampling
 - Differentiates unilateral vs. bilateral disease
 - Measure PAC and PRA in each vein



TREATMENT

- Unilateral disease or adrenal carcinoma: surgery preferred
- Bilateral disease: medical management preferred



MEDICAL MANAGEMENT

- **First-line: aldosterone receptor antagonists**
- **Spironolactone** (preferred)- Side effects are dose-dependent and may include **gynecomastia** and decreased libido.
- **Eplerenone** - In contrast to spironolactone, eplerenone does not block androgen or progesterone receptors, which decreases certain side effects (e.g., gynecomastia and decreased libido); however, eplerenone is only half as potent at blocking the mineralocorticoid receptor and is less effective at lowering blood pressure.



CUSHING SYNDROME

□ Etiology:

1) Exogenous (**iatrogenic**) Cushing syndrome

Prolonged glucocorticoid therapy →

hypercortisolism → decreased ACTH → bilateral adrenal atrophy

❖ Most common cause of hypercortisolism



2) Endogenous Cushing syndrome

Types	Primary hypercortisolism (<u>A</u> <u>CTH</u> -independent Cushing syndrome)	Secondary hypercortisolism	
		<u>Pituitary ACTH</u> production (Cushing disease)	Ectopic ACTH production
Relative frequency ^[3]	• 5–10%	• ~ 75%	• ~ 15%
Sex	• ♂ < ♀ (1:4)	• ♂ < ♀ (1:4)	• ♂ = ♀



Causes

- Autonomous overproduction of cortisol by the adrenal gland
→ ACTH suppression → atrophy of the contralateral adrenal gland
 - **Adrenal adenomas**
 - Adrenal carcinoma
 - Macronodular adrenal hyperplasia

- Pituitary adenomas → ACTH secretion
→ bilateral adrenal gland hyperplasia

- Paraneoplastic syndrome → ↑ ACTH secretion → bilateral adrenal gland hyperplasia
- Carcinomas include:
 - Small cell lung cancer
 - Renal cell carcinoma
 - Pancreatic or bronchial carcinoid tumors
 - Pheochromocytoma
 - Medullary thyroid carcinoma



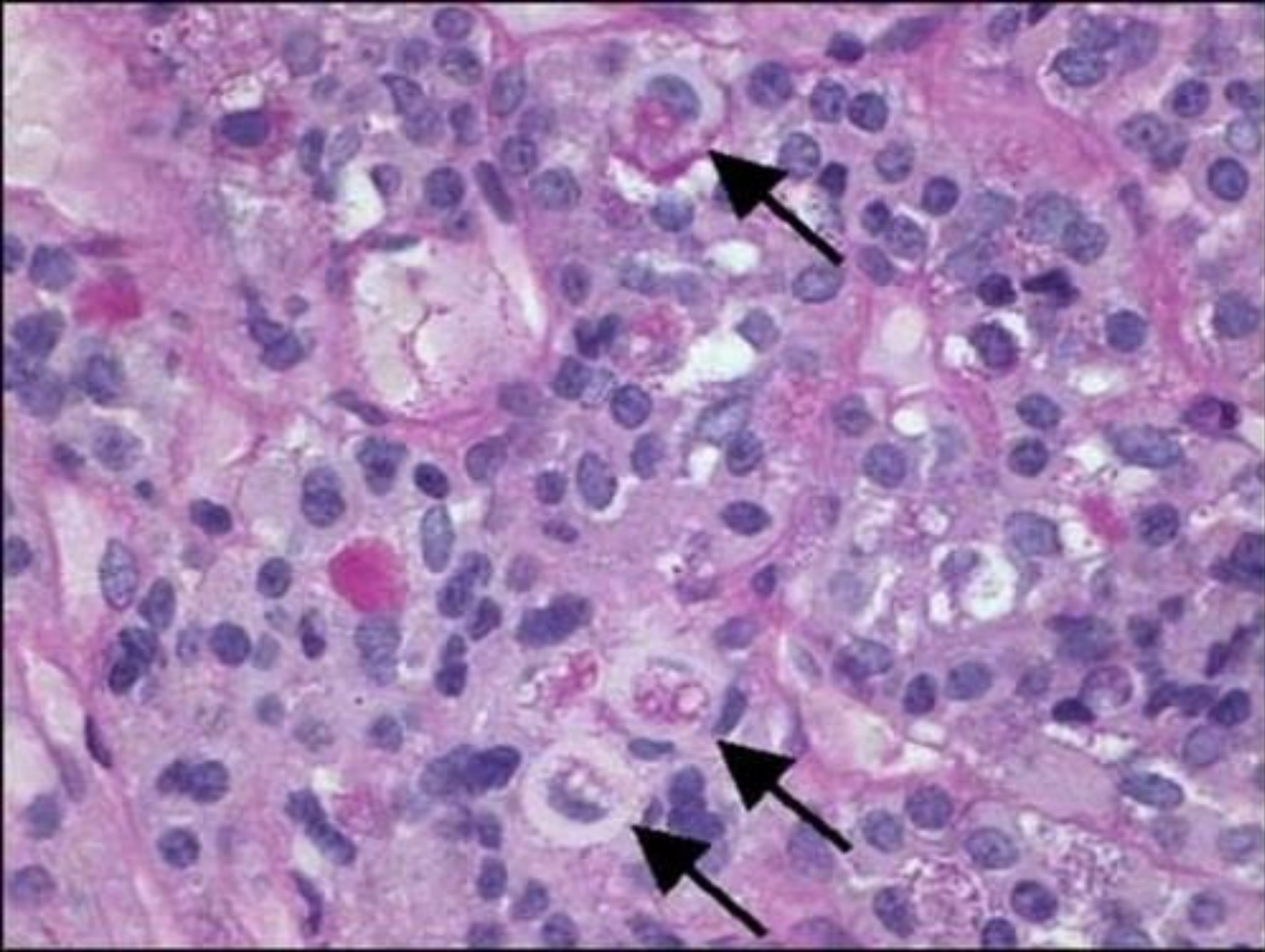
- While the term “Cushing syndrome” can be applied to any cause of hypercortisolism, “Cushing disease” refers specifically to secondary hypercortisolism that results from excessive production of ACTH by pituitary adenomas.
- Secondary hypercortisolism is also called ACTH-dependent Cushing syndrome because hypercortisolism is the result of increased ACTH levels.



MORPHOLOGY

- The pituitary in Cushing syndrome shows changes regardless of the cause.
- ❖ **Crooke hyaline change:**
 - Result from high levels of glucocorticoids
 - The accumulation of homogeneous, glassy material (intermediate keratin filaments) in ACTH producing cells





MORPHOLOGY OF ADRENAL GLAND

The cause	Finding
Exogenous glucocorticoids Most common	Bilateral cortical atrophy Zona glomerulosa is of normal thickness
Pituitary cushing Ectopic ACTH	Diffuse hyperplasia 60-70% Nodular hyperplasia
Adrenocortical neoplasms Adenoma carcinoma	Similar to non-functional tumors The adjacent adrenal cortex & that of contralateral adrenal are atrophic due to suppression of endogenous ACTH by high cortisol



CLINICAL FEATURES

Skin

- Thin, easily bruisable skin with ecchymoses
- Stretch marks (classically purple abdominal striae)
- Hirsutism
- Acne
- If secondary hypercortisolism: often hyperpigmentation (darkening of the skin due to an overproduction of melanin), Caused by excessive ACTH production because melanocyte-stimulating hormone (MSH) is cleaved from the same precursor as ACTH called proopiomelanocortin (POMC)
- Not a feature of primary hypercortisolism
- Delayed wound healing



□ Musculoskeletal

- Osteopenia, osteoporosis, pathological fractures, avascular necrosis of the femoral head
- Muscle atrophy/weakness

□ Neuropsychological

- Anxiety, irritability
- Lethargy, fatigue
- Sleep disturbance
- Memory deficits
- Depression
- Psychosis



□ Endocrine and metabolic

- Insulin resistance → hyperglycemia (see “Diabetes mellitus”) → mild polyuria in the case of severe hyperglycemia
 - Dyslipidemia
 - Weight gain characterized by central obesity, **moon facies**, and a **dorsocervical fat pad**
 - ♂: Decreased libido
 - ♀: Decreased libido, virilization, and/or irregular menstrual cycles (e.g., amenorrhea)
 - Growth delay (in children)
-
- Secondary hypertension (~ 90% of cases)
 - Increased susceptibility to infections (due to immunosuppression)
 - Peptic ulcer disease



DIAGNOSIS

- ❑ Measuring plasma cortisol difficult
 - Circadian rhythm → high levels in AM
 - Most cortisol bound to CBG • CBG levels can affect serum measurement
- ❑ 24-hour urine free cortisol
 - Integrates cortisol level over time
- ❑ Salivary cortisol
 - No cortisol binding globulin in saliva
 - Free cortisol level measured at night (should be low)



- Low dose testing (1mg)
- Used to establish diagnosis of Cushing's syndrome
- Serum ACTH level
- • High dose dexamethasone test (8mg)
 - Differentiate causes of high ACTH Cushing's syndrome
 - Will suppress cortisol in pituitary adenomas (↑ set point)
 - Will not suppress cortisol from ACTH tumors



TREATMENT

□ Surgery

- Removal of adenoma (adrenal gland, pituitary)
- Removal of lung tumor

□ • Ketoconazole

- Antifungal
- Potent inhibitor of 17,20 lyase (Also potent inhibitor androgen synthesis)
- ↓ androstenedione/testosterone

Key side effect: gynecomastia

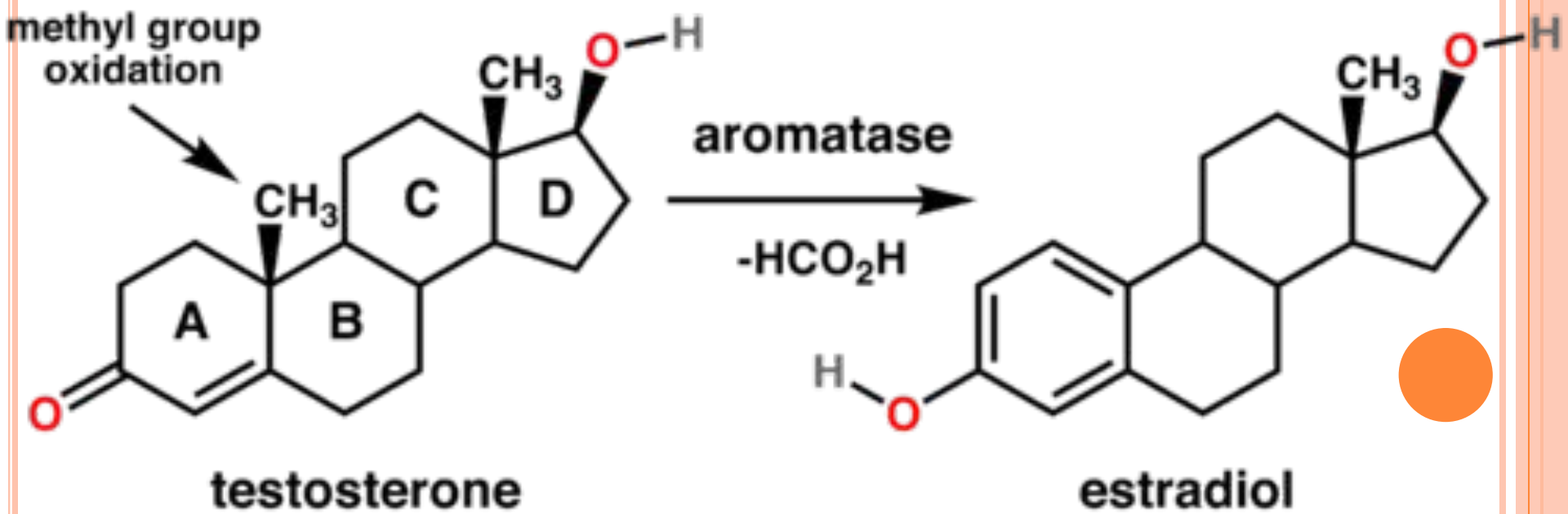
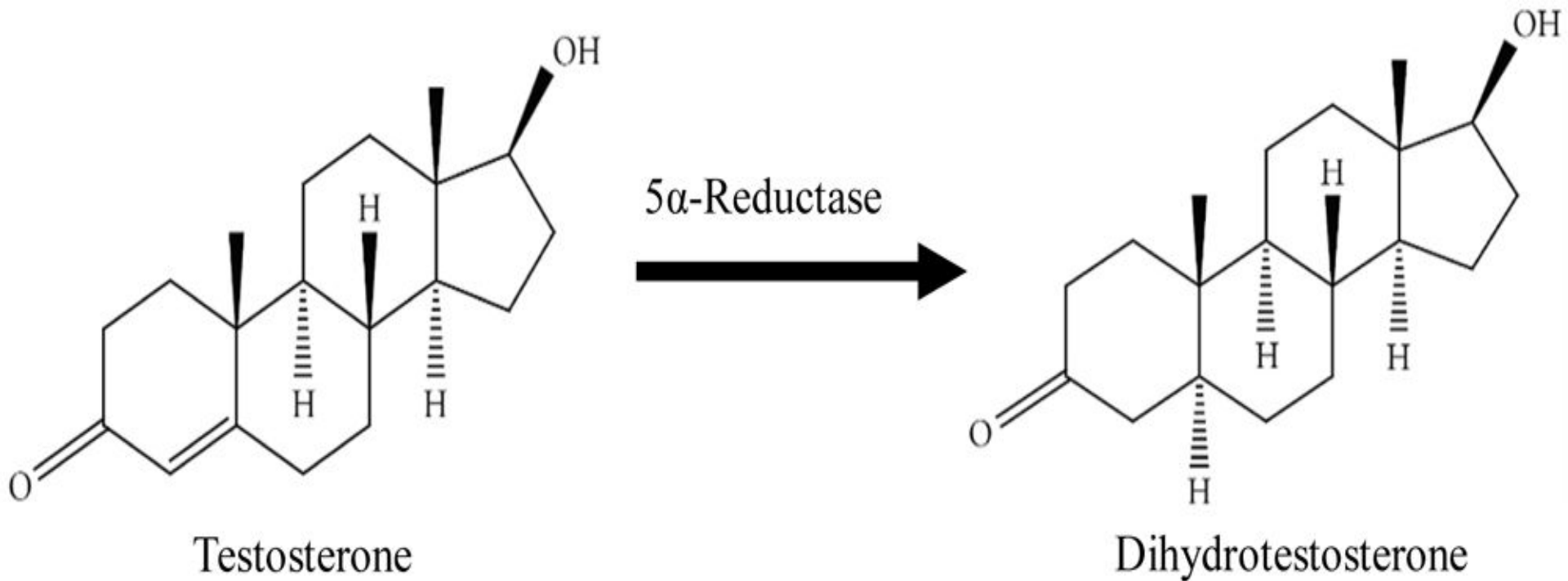
- Also inhibits 17-alpha hydroxylase, desmolase
- Blocks cortisol synthesis
- Can be used to treat Cushing's syndrome



ANDROGENS- PHYSIOLOGY TO BE REMEMBERED

- ❑ Adrenal androgen synthesis
- ❑ Although the majority of testosterone is produced by the Leydig cells in the testicles, the adrenal cortex contributes to androgen production as well.
- ❑ A stimulus triggers the secretion of CRH, leading to increased secretion of ACTH by the pituitary gland.
- ❑ ACTH stimulates the conversion of cholesterol into pregnenolone in the adrenal cortex.
- ❑ Enzymatic pathways trigger DHEA and androstenedione production in the zona reticularis.
- ❑ Androstenedione is converted into testosterone, which is then transformed into dihydrotestosterone via 5 α -reductase.
- ❑ Aromatase converts testosterone into estradiol and andros tenedione, which is then transformed into estrone.





PATHOPHYSIOLOGY

- CAH is caused by **autosomal recessive** defects in enzymes that are responsible for the **production of cortisol**.
- There are three subtypes of CAH:
 - **21 β -hydroxylase** (~ 95% of CAH)
 - **11 β -hydroxylase** (~ 5% of CAH)
 - **17 α -hydroxylase** (rare)
- **Low levels of cortisol** → lack of negative feedback to the **pituitary** → increased **ACTH** → **adrenal hyperplasia** and increased synthesis of **adrenal precursor steroids**

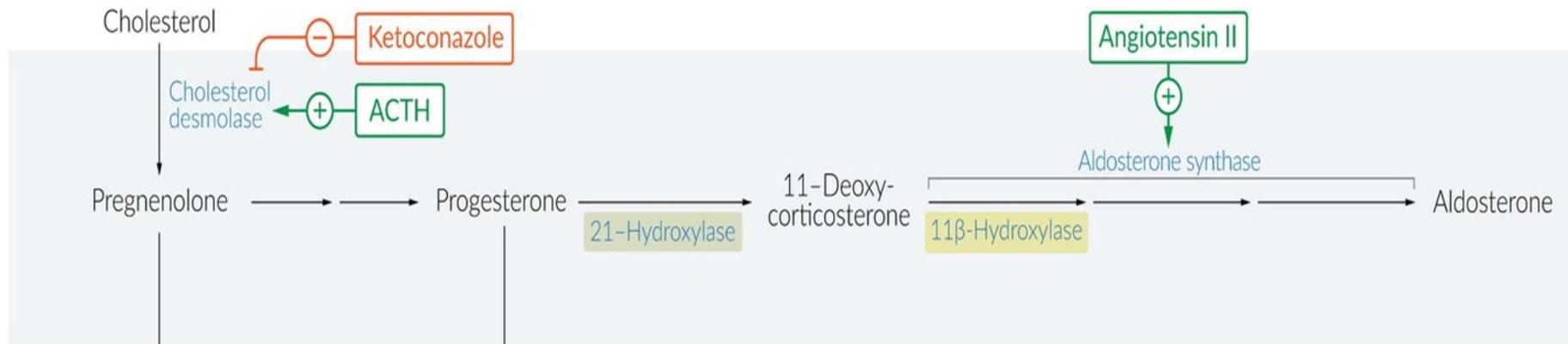


DEPENDING ON WHICH ENZYME IS AFFECTED, THE FOLLOWING ENDOCRINE CHANGES ARE SEEN:

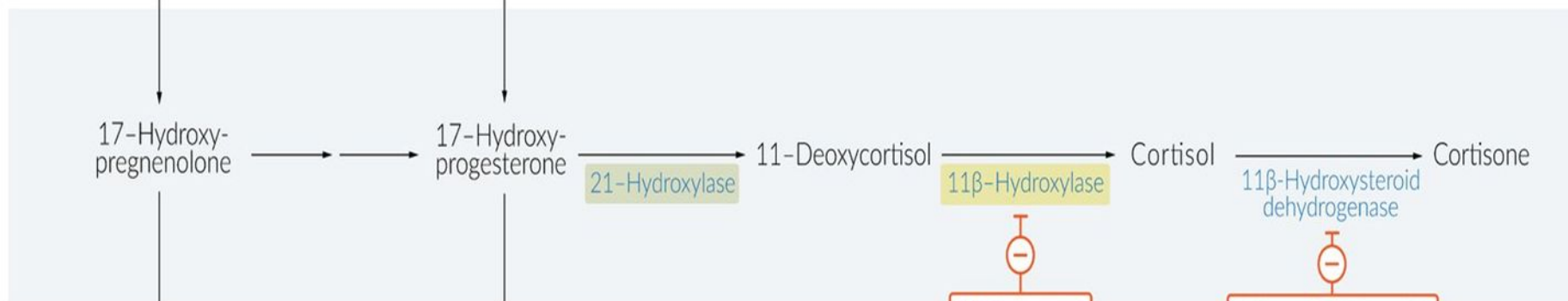
Enzyme deficiency	<u>Cortisol</u>	<u>Aldosterone</u>	<u>11-Deoxycorticosterone (DOC)</u>	<u>Androgens</u>
<u>21β-hydroxylase</u>			•↓	
<u>11β-hydroxylase</u>	•↓	•↓		•↑
<u>17α-hydroxylase</u>			•↑	•↓



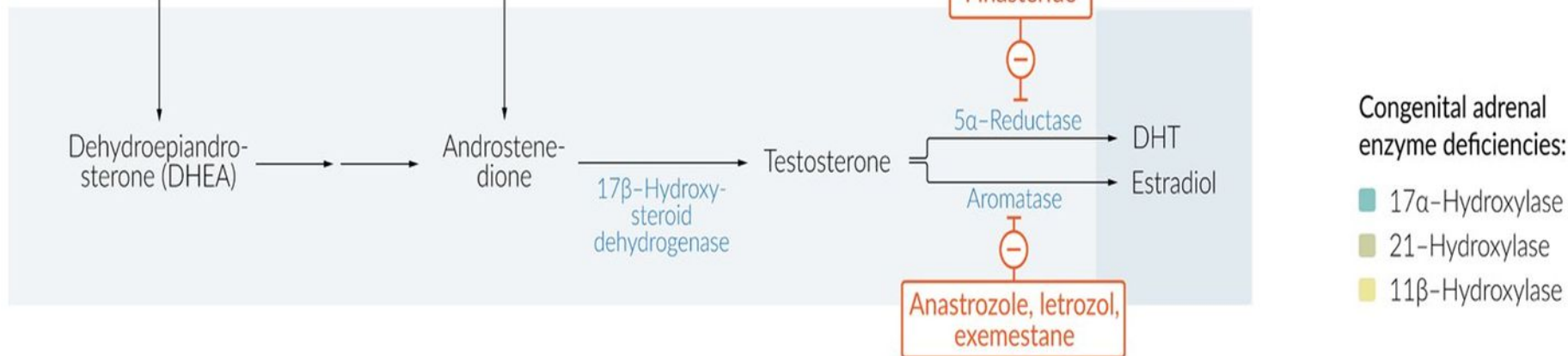
Mineralcorticoids



Glucocorticoids



Androgens



Congenital adrenal enzyme deficiencies:

- 17α-Hydroxylase
- 21-Hydroxylase
- 11β-Hydroxylase

- ↓ Cortisol--- ↑ACTH ----Adrenal Hyperplasia----
- ↑ Non-cortisol hormone synthesis

Low Cortisol Signs/Symptoms

- Hypoglycemia
- Nausea/vomiting



Aldosterone Signs/Symptoms

• Deficiency

Na loss → water loss

Hypovolemia → shock

Hyperkalemia

↑ renin

• Excess

Na retention

Hypertension

Hypokalemia

↓ renin



Androgens Signs/Symptoms

- Depend on chromosomal sex of child (XX/XY)

Excess androgens

- • Female (XX): Ambiguous genitalia
- • Male (XY): Precocious (early) puberty

Androgen deficiency

- • Female (XX): Normal genitalia
- • Male (XY): Female or ambiguous genitalia



□ Ambiguous Genitalia

- Females (XX) with excess androgen exposure
- Males (XY) with deficient androgen exposure

□ ACTH Effects

- High ACTH can cause skin hyperpigmentation
- Melanocyte stimulating hormone (MSH)

Common precursor protein in pituitary with ACTH

- ↑ melanin synthesis



MORPHOLOGY

- In all cases of CAH, the adrenals are bilaterally hyperplastic, sometimes increasing to 10 to 15 times their normal weight because of the sustained elevation in ACTH. The adrenal cortex is thickened and nodular, and on cut section the widened cortex appears brown because of lipid depletion. The proliferating cells are mostly compact, eosinophilic, lipid-depleted cells intermixed with lipid-laden clear cells. Hyperplasia of corticotroph (ACTH-producing) cells is present in the anterior pituitary in most persons with CAH.



21-A HYDROXYLASE DEFICIENCY

- Classic cause of CAH (90% of CAH)
- Low cortisol symptoms
- Low mineralocorticoid symptoms
- Excess androgen symptoms
 - Girls (XX): ambiguous genitalia
 - Boys (XY): precocious puberty (early onset)
- Variable symptoms based on enzyme levels
 - Classic form: 0 to 2% normal enzyme activity
 - Non-classic forms: 20-50% normal enzyme activity



- Infants with 21 β -hydroxylase deficiency can present with shock within the first few weeks of life because of severe dehydration due to an adrenal crisis and salt-wasting due to hypoaldosteronism.



11-B HYDROXYLASE DEFICIENCY

- Similar to 21- α hydroxylase deficiency
 - Low cortisol symptoms
 - Girls: ambiguous genitalia
 - Boys: precocious puberty
- One exception: $\uparrow$ mineralocorticoid activity
 - $\uparrow$ 11-deoxycorticosterone (weak mineralocorticoid)
 - Hypertension
 - Hypokalemia



17- α HYDROXYLASE DEFICIENCY

- Low cortisol
- Excess mineralocorticoids: HTN, $\downarrow$ K⁺
- Low androgens

Males (XY):

- Female or ambiguous external genitalia
- Absent uterus/fallopian tubes (Sertoli cells $\rightarrow$ MIH)
- Undescended testes



□ Females (XX):

- Normal at birth
- Primary amenorrhea at puberty
- Theca cells lack of androgens → ↓ estradiol

Often diagnosed at puberty

CAH SCREENING

- Measure level of 17-Hydroxyprogesterone
 - Elevated level in 21- α hydroxylase deficiency (most common)



CAH TREATMENT

- Glucocorticoid replacement therapy is indicated in all forms of CAH.

Lifelong daily regimen

- Replenishes cortisol
 - Lowers ACTH
 - Stops overproduction of other hormones
- **21 β -hydroxylase deficiency**

Lifelong fludrocortisone therapy (aldosterone substitution)

- **11 β -hydroxylase deficiency/17 α -hydroxylase deficiency**

Spironolactone to block mineralocorticoid receptors



ADRENAL INSUFFICIENCY

- Adrenal insufficiency is a failure of the adrenal glands to produce adequate amounts of adrenocortical hormones. It can be primary, secondary, or tertiary.



PRIMARY ADRENAL INSUFFICIENCY (ADDISON DISEASE)

- Primary adrenal insufficiency can be caused by abrupt destruction of the adrenal gland (acute adrenal insufficiency; e.g., due to massive adrenal hemorrhage) or by its gradual progressive destruction or atrophy (chronic adrenal insufficiency; e.g., due to autoimmune conditions, infection).



- Autoimmune adrenalitis MCC in US
 - Antibody and cell-mediated disorder
 - Antibodies to 21-hydroxylase commonly seen
 - Atrophy of adrenal gland
 - Loss of cortex
 - Medulla is spared
- • Infections
 - Tuberculosis MCC worldwide
 - Fungal (histoplasmosis, cryptococcus)
 - CMV
- • Rare: tumor metastasis especially lung
- Trauma



WATERHOUSE-FRIDERICHSEN SYNDROME

- Rare cause of acute adrenal insufficiency
 - Caused by acute hemorrhage into adrenal glands
 - Associated with meningococemia
- • Clinical scenario
 - Patient with bacterial meningitis
 - Acute onset of shock



SECONDARY ADRENAL INSUFFICIENCY

- Secondary adrenal insufficiency is caused by conditions that **decrease** ACTH production (impaired hypothalamic-pituitary-adrenal axis).
- Sudden discontinuation of chronic glucocorticoid therapy or stress (e.g., infection, trauma, surgery) during prolonged glucocorticoid therapy
 - Prolonged iatrogenic suppression of the hypothalamic-pituitary-adrenal axis
 - Impaired endogenous cortisol production in addition to discontinuation of steroid treatment, decrease in dosage, or increase in requirement (e.g., stress)
→ acute glucocorticoid deficiency
- Hypopituitarism: ↓ ACTH → ↓ endogenous cortisol



TERTIARY ADRENAL INSUFFICIENCY

- Tertiary adrenal insufficiency is caused by conditions that **decrease** CRH production.
- The most common cause is **sudden discontinuation of chronic glucocorticoid therapy**.
- Rarer causes include hypothalamic dysfunction (e.g., due to trauma, mass, hemorrhage, or anorexia): $\downarrow \text{CRH} \rightarrow \downarrow \text{ACTH} \rightarrow \downarrow \text{cortisol}$ release
- The hyperpigmentation of primary Addison disease is lacking because MSH levels are low



PATHOPHYSIOLOGY

▣ Primary adrenal insufficiency (Addison disease)

Damage to the adrenal gland leads to the deficiency in all three hormones produced by the adrenal cortex: androgen, cortisol, and aldosterone.

- ▣ Symptoms usually do not appear before > 90% of the adrenal cortices have been destroyed.



□ Hypoandrogenism

- Loss of libido
 - Impaired spermatogenesis (in men)
- Occurs more commonly in women because men usually produce sufficient androgen in the testes.



□ Hypocortisolism leads to:

- ↑ ACTH → ↑ production of POMC (in order to increase ACTH production) → ↑ melanocyte-stimulating hormone (MSH) → hyperpigmentation of the skin (bronze skin) ^[11]
- ↑ ADH level → retention of free water → dilutional hyponatremia
- ↓ Expression of enzymes involved in gluconeogenesis → ↓ rate of gluconeogenesis → hypoglycemia
- Lack of potentiation of catecholamines action → hypotension

□ Hypoaldosteronism → hypotension (hypotonic hyponatremia and volume contraction), hyperkalemia, metabolic acidosis



- Secondary adrenal insufficiency
- ↓ ACTH → **hypoandrogenism** and hypocortisolism
- Aldosterone synthesis is not affected (mineralocorticoid production is controlled by RAAS and angiotensin II, not by ACTH).
- Tertiary adrenal insufficiency
- ↓ CRH → ↓ ACTH → **hypoandrogenism** and hypocortisolism
- Aldosterone synthesis is not affected.

So no hyperkalemia, no skin changes in both 2ry and 3ry adrenal insufficiency



CLINICAL FEATURES

- • Loss of cortisol
 - Weakness, fatigue
 - Weight loss
 - Postural hypotension
 - Nausea, abdominal pain, diarrhea
 - Hypoglycemia
- • Loss of aldosterone
 - Potassium retention → hyperkalemia
 - H⁺ retention → acidosis
 - Sodium loss in urine → hypovolemia



- Stresses such as infections, trauma, or surgery may precipitate an acute adrenal crisis
- Adrenal Crisis
 - Acute adrenal insufficiency
 - Abrupt loss of cortisol and aldosterone
 - Main manifestation is shock
 - Hypoglycemia
 - Other symptoms: nausea, vomiting, fatigue, confusion



MORPHOLOGY

Cause	Morphology
secondary hypoaldrenalism	Bilateral atrophic glands Microscopic: Atrophic cortex & intact medulla
Autoimmune adrenalitis	Irregularly atrophic glands Microscopic: Atrophic cortex Lymphocytic infiltrate
TB & fungal infection	Granulomatous inflammation
Metastatic carcinoma	Effacement of the normal gland by the metastatic tumor



□ Diagnostic Tests

- 8 AM serum cortisol
- Levels should be highest at this time
- Low level indicates disease

□ • Serum ACTH

- High ACTH with low cortisol = primary disease
- Low ACTH with low cortisol = secondary disease



TREATMENT

- ▣ **Primary adrenal insufficiency**: replacement for hypocortisolism, hypoaldosteronism, and hypoandrogenism
 - Glucocorticoids
 - Mineralocorticoids
 - Androgens (as needed)
- ▣ **Secondary/tertiary adrenal insufficiency**: replacement for hypocortisolism and hypoandrogenism
 - Glucocorticoids
 - Androgens (as needed)



PHEOCHROMOCYTOMA

- Catecholamine-secreting tumor
- Secrete epinephrine, norepinephrine, dopamine
- Chromaffin cells of adrenal medulla
- Derivatives of neural crest

▣ **Incidence**

- Most common tumor of the adrenal medulla in adults
- Present in up to 1% of all hypertensive patients

▣ **Age: 3rd–5th** decades of life



ETIOLOGY

- The majority of pheochromocytomas are benign, unilateral, catecholamine-producing tumors, that rarely produce other hormones such as EPO.
- Tumors arise from chromaffin cells, which are derived from the neural crest.
- Localization ^[4]
 - ~ 90% adrenal medulla (physiologically activated by acetylcholine)
 - ~ 10% extra-adrenal in the sympathetic ganglia
 - ~ 10% at multiple locations
- 25% of pheochromocytomas are hereditary



CLINICAL PRESENTATION

- Classically episodic symptoms
- Hypertension
- Headaches
- Palpitations
- Sweating
- Pallor (pale skin)



Pheochromocytoma

- 10% extraadrenal
- 10% bilateral
- 10% familial
- 10% children
- 10% malignant
- 10% assoc with MEN
- 10% present with a stroke

DIAGNOSIS

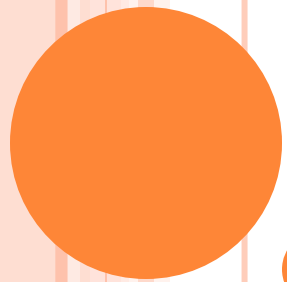
- • Serum catecholamine levels not routinely used
 - Levels fluctuate
- • Breakdown products of catecholamines measured
 - Usually via 24 hour urine collection
- • Metanephrines often measured for diagnosis
 - Metanephrines and normetanephrine
 - 24hour urine collection or plasma



TREATMENT

- • Definitive therapy: Surgery
- Pre-operative management:
- Phenoxybenzamine (irreversible α blocker)
- Non-selective beta blockers (propranolol)





THANK YOU