

UNIT XIV

GUYTON AND HALL *Textbook of* Medical Physiology

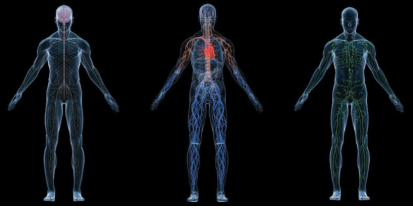
TWELFTH EDITION

Chapter 77:



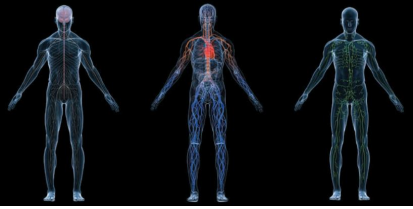
Adrenocortical Hormones

Slides by Thomas E. Lohmeier, PhD



Adrenal Glands

- Paired organs that cap the kidneys.
- Weight 5 gm each.
- Receive very high blood flow per unit weight, (5 ml/min/gm tissue relatively more than the RBF which is 4 ml/min/g).
- Each gland consists of an outer cortex and inner medulla.
- Adrenal medulla:
 - Derived from embryonic neural crest ectoderm (same tissue that produces the sympathetic ganglia).
 - Synthesizes and secretes:
 - Catecholamines (mainly Epi but some NE).



Secretion of Adrenocortical Hormones by Different Zones of the Adrenal Cortex

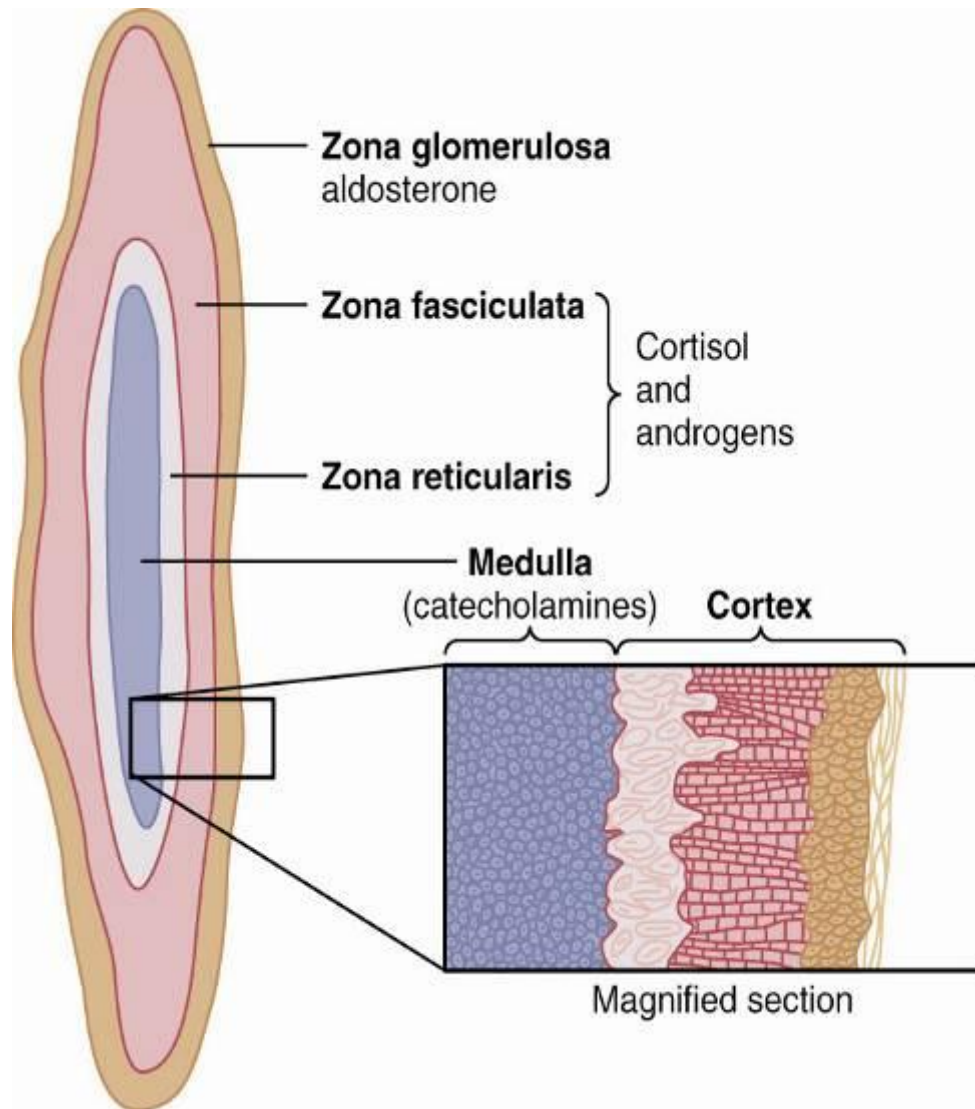
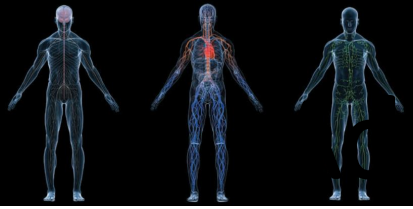
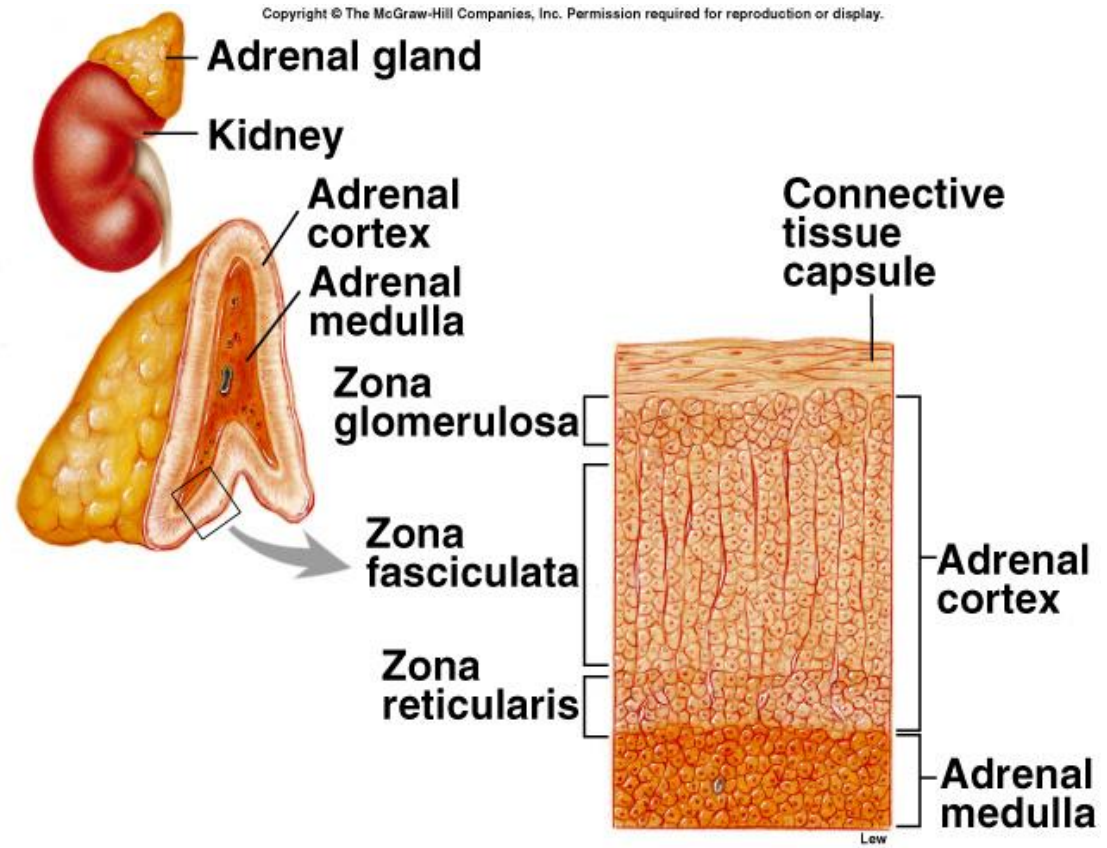


Figure 77-1



Adrenal Glands (continued)

- **Adrenal cortex:**
 - Does not receive neural innervation.
 - Must be stimulated hormonally (ACTH).
- **Consists of 3 zones:**
 - Zona glomerulosa.
 - Zona fasciculata.
 - Zona reticularis.
- **Secretes corticosteroids.**





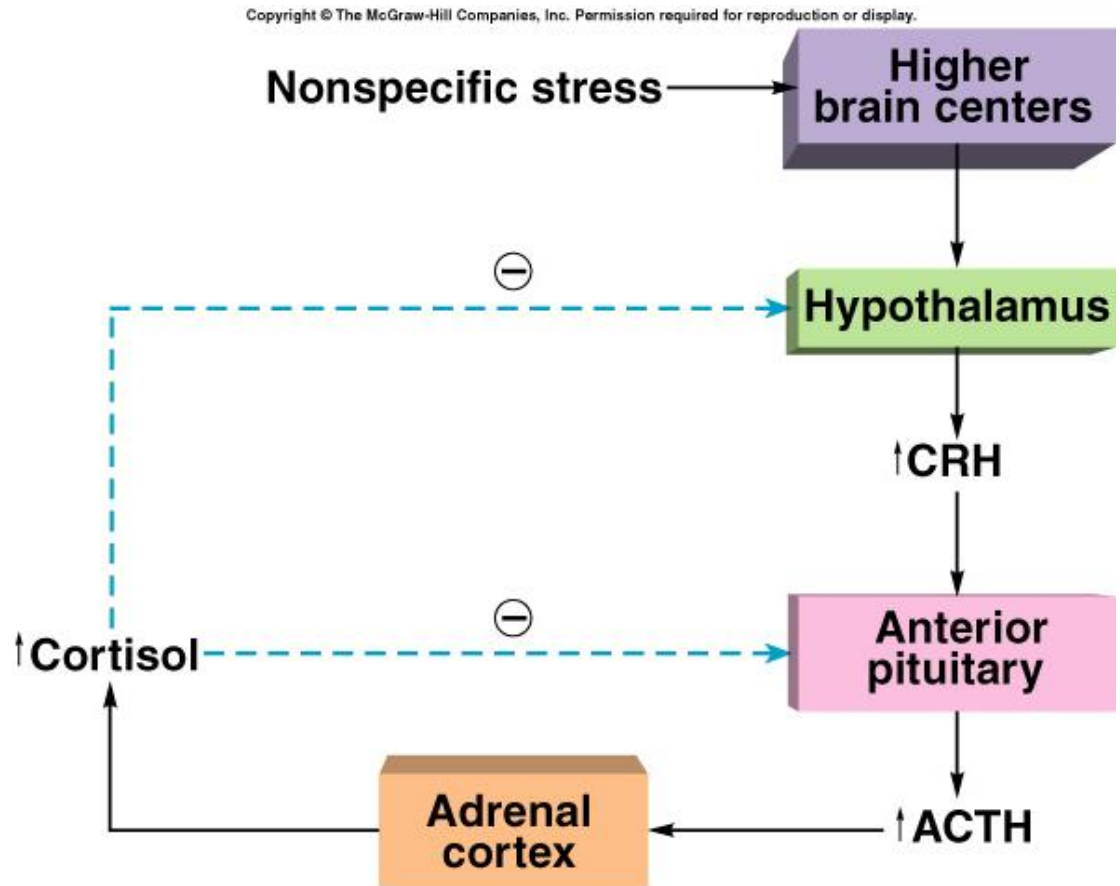
Functions of the Adrenal Cortex

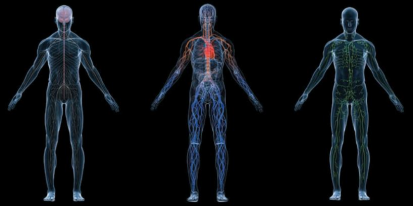
- Zona glomerulosa:
 - Mineralcorticoids (aldosterone):
 - Stimulate kidneys to reabsorb Na^+ and secrete K^+ .
- Zona fasciculata:
 - Glucocorticoids (cortisol):
 - Inhibit glucose utilization and stimulate gluconeogenesis. Aid in regulating the metabolic functions of the body and in controlling the inflammatory
 - Essential for survival in stress situations
- Zona reticularis (DHEA):
 - Sex steroids: Serve mainly as source of androgens for women



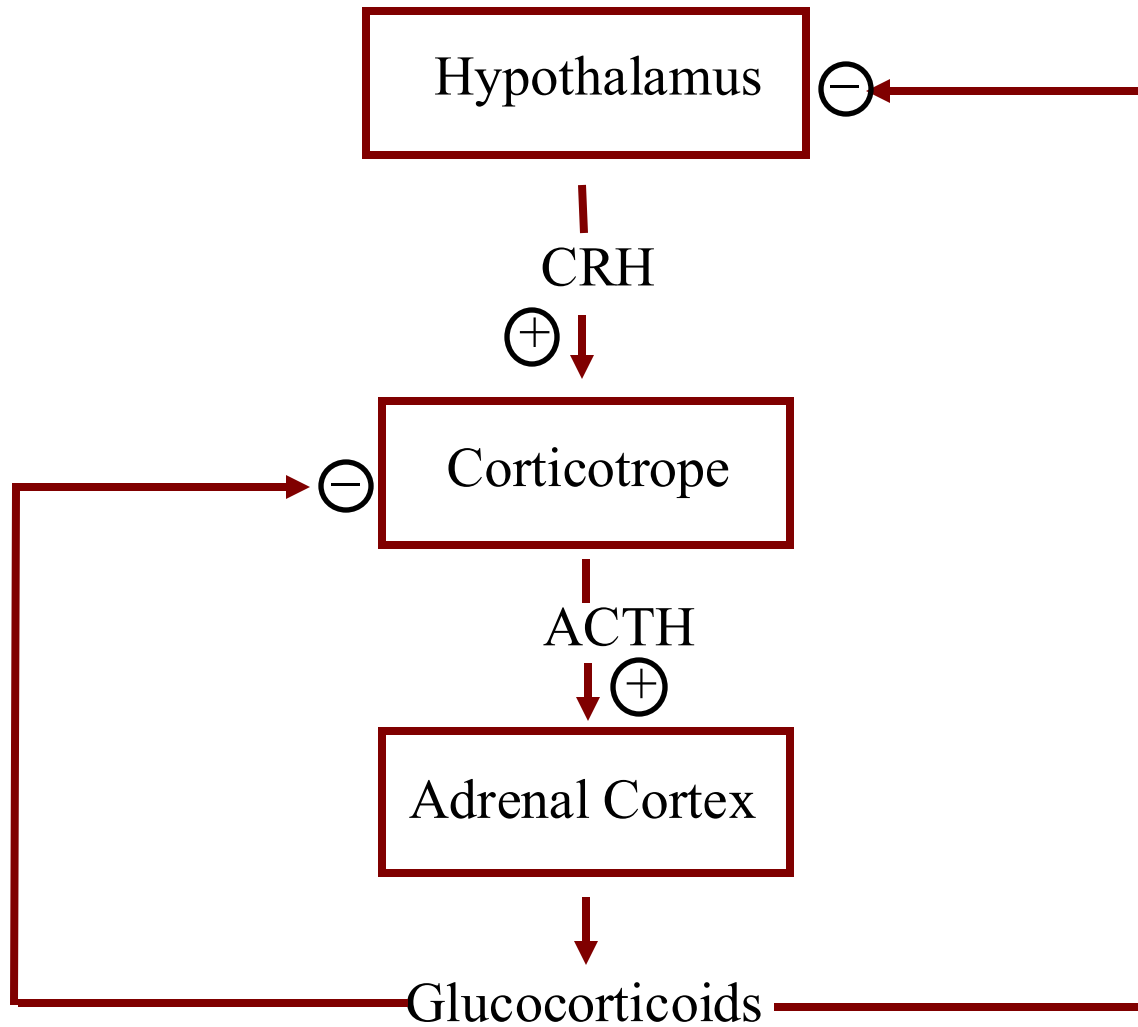
Stress and the Adrenal Gland

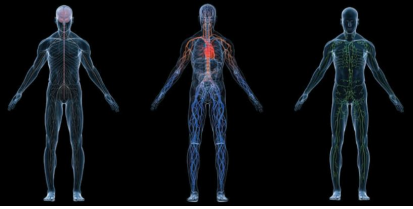
- Non-specific response to stress produces the general adaptation syndrome (GAS).
- Alarm phase:
 - Adrenal glands activated.
- Stage of resistance:
 - Stage of readjustment.
- Stage of exhaustion:
 - Sickness and/or death if readjustment is not complete.



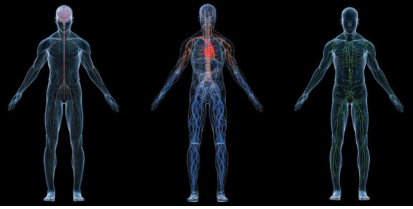


Hypothalamohypophyseal-Adrenal Axis

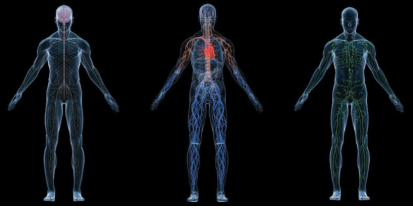




ACTH is a byproduct of POMC. Pro-opiomelanocortin (POMC) gives rise to ACTH and melanocyte-stimulating hormone (MSH). This association is clinically important for Addison disease. In Addison's disease, the increase in (MSH) leads to hyperpigmentation. ACTH receptors are in the adrenal cortex, in particular, the zona fasciculata and zona reticularis. The receptors are G protein-coupled receptors, thus stimulating adenylyl cyclase. cAMP is the secondary messenger system. The adrenal cortex secretes glucocorticoids from the zona fasciculata and androgens from the zona reticularis. Stress stimulates the release of ACTH. Pathophysiology associated with ACTH can be caused by 3 different mechanisms: the pituitary, adrenals, or ectopic secretion (lung tumors). The pituitary can be hypofunctioning or hyperfunctioning. The adrenal can also be hypofunctioning or hyperfunctioning. Diseases associated with the adrenals include Addison and Cushing.



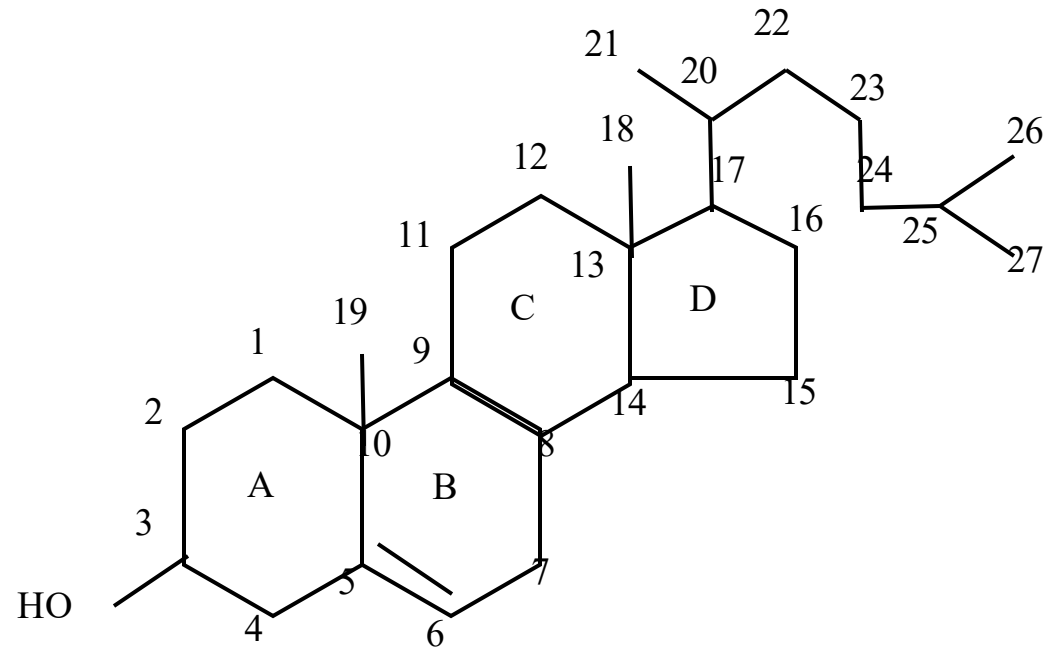
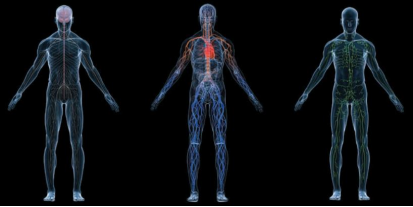
Cortisone and hydrocortisone are not the same. Cortisone is a **prodrug**, meaning it needs to be converted into hydrocortisone (also known as cortisol) in the **liver** before it can be active. Hydrocortisone is the active form and can be used topically, while cortisone is not as effective when applied to the skin.

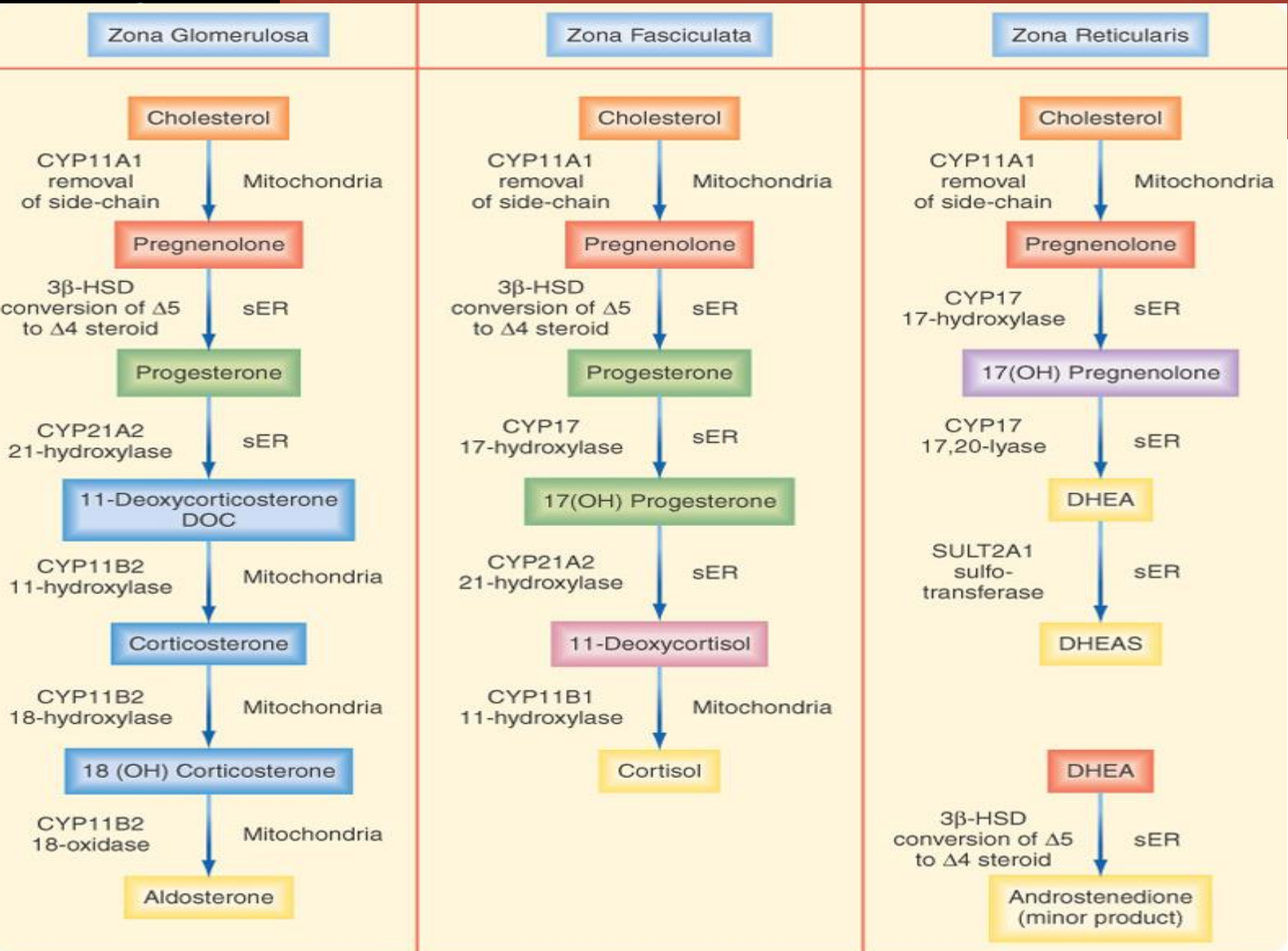


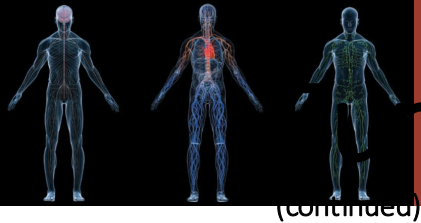
Gonane is a steroid nucleus, a fundamental structural component of many steroid compounds, including some hormones. It consists of four fused rings (three cyclohexanes and one cyclopentane) and has 17 carbon atoms. Gonane is the parent structure from which other steroids, like androstane and estrane, are derived.

Side chain cleavage enzyme (SCC) (also known as cholesterol **desmolase**) is a cytochrome P450 enzyme. This enzyme converts cholesterol to pregnenolone, is essential to steroidogenesis, and plays a crucial role in placental progesterone synthesis.

The word "glucocorticoid" is the combination of the (glucose + cortex + steroid) that refers to its role in glucose metabolism control, synthesis in the adrenal cortex, and its steroidal structure. The same principle applies to mineralocorticoid.

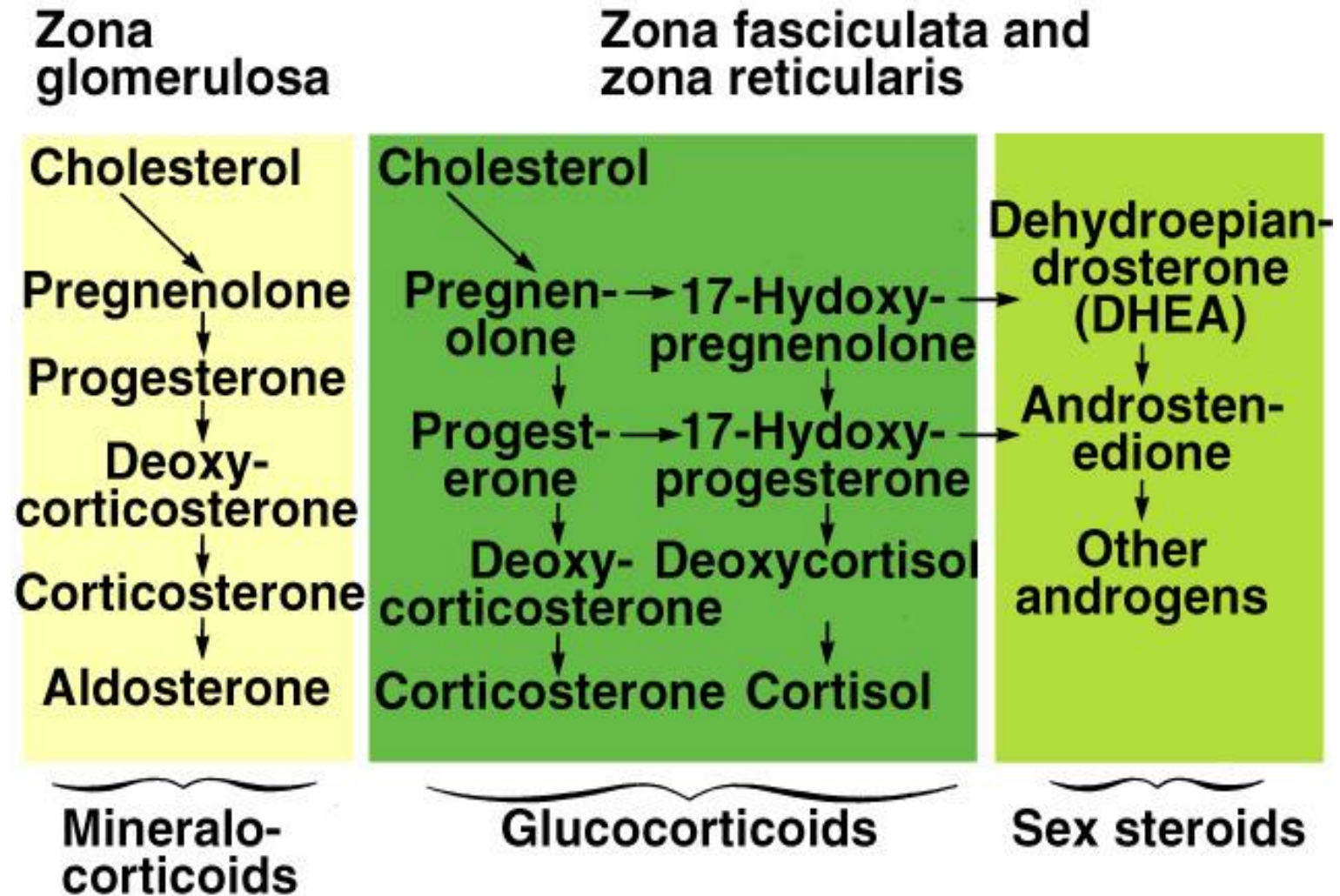






Functions of the Adrenal Cortex

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.





Actions of Cortisol

- Glucose metabolism
- Protein metabolism
- Fat metabolism
- Anti-inflammatory action
- Psychic effect
- Permissive effect



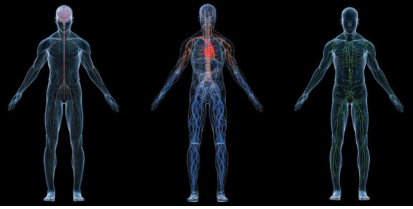
Common Enzyme Deficiencies

- 21-hydroxylase (accounting for >90% of cases)
- 11- β -hydroxylase deficiency 9%
- 17-hydroxylase deficiency 1%



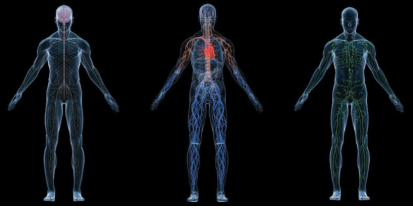
Stages of Adrenal Cortical Insufficiency

- **Primary adrenal cortical insufficiency** (Addison's disease)
 - ACTH levels are elevated because of lack of feedback inhibition
- **Secondary adrenal cortical insufficiency**
 - Occurs as a result of hypopituitarism or because pituitary gland has been surgically removed
- **Acute adrenal crisis**
 - Life-threatening situation occurs. Lack of cortisol can cause shock with 20% death rate.



Alterations of Adrenal Function

- ▶ Disorders of the adrenal cortex
 - ▶ Cushing disease
 - ▶ Excessive anterior pituitary secretion of ACTH
 - ▶ Cushing syndrome
 - ▶ Excessive level of cortisol, regardless of cause: exogenous or endogenous



Alterations of Adrenal Function

► Disorders of the adrenal cortex

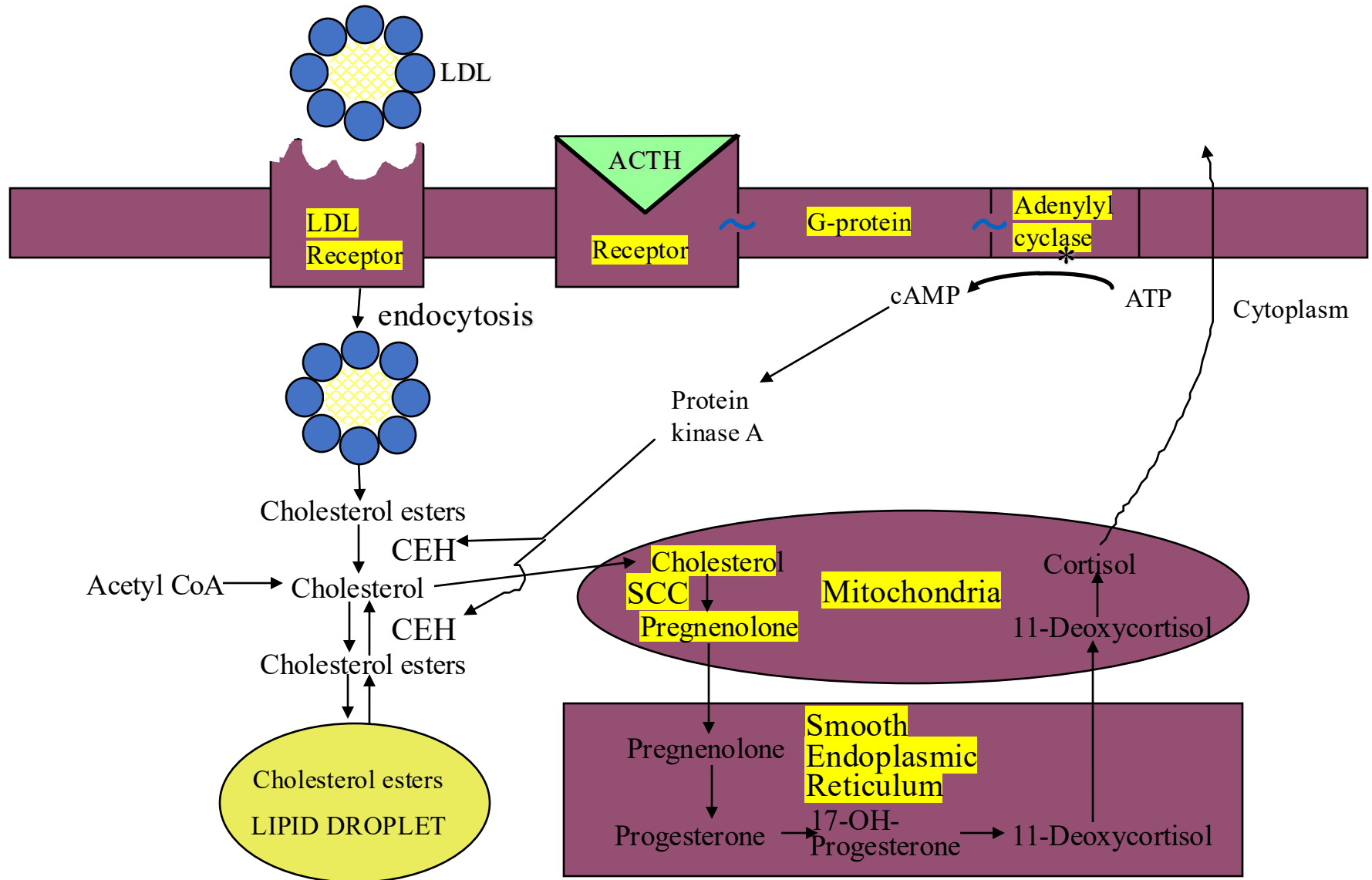
► Hyperaldosteronism

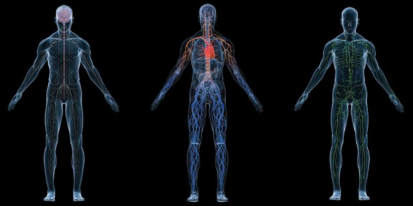
- Primary hyperaldosteronism (Conn disease)
- Secondary hyperaldosteronism: excess renin production due to various conditions, including renal artery stenosis, left heart failure, liver failure, cor pulmonale, pregnancy, renin-secreting tumor etc.



Steroid Hormone Synthesis and Secretion

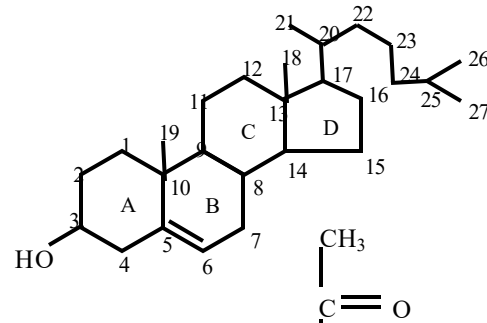
Cholesterol side chain cleavage



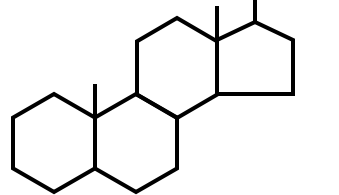


Basic Structure of Adrenocortical & Gonadal Steroids

Cholesterol
(27 carbons)

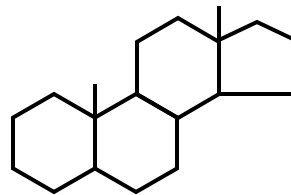


Pregnane derivatives
(21 carbons)



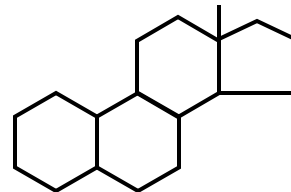
Progesterone
Corticoids

Androstane derivatives
(19 carbons)

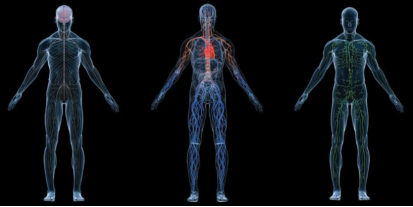


Androgens

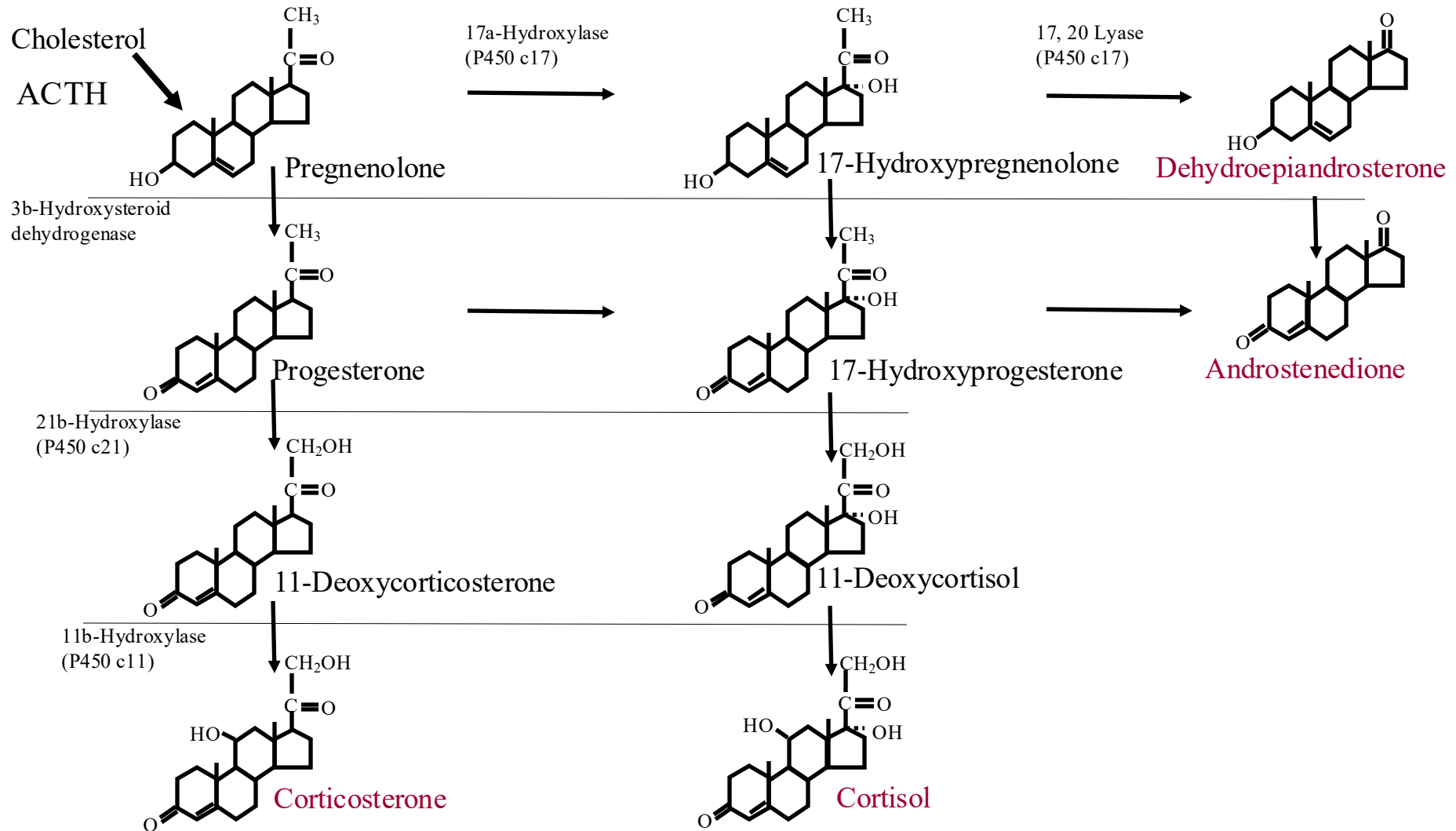
Estrane derivatives
(18 carbons)

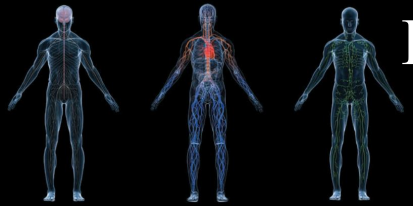


Estrogens

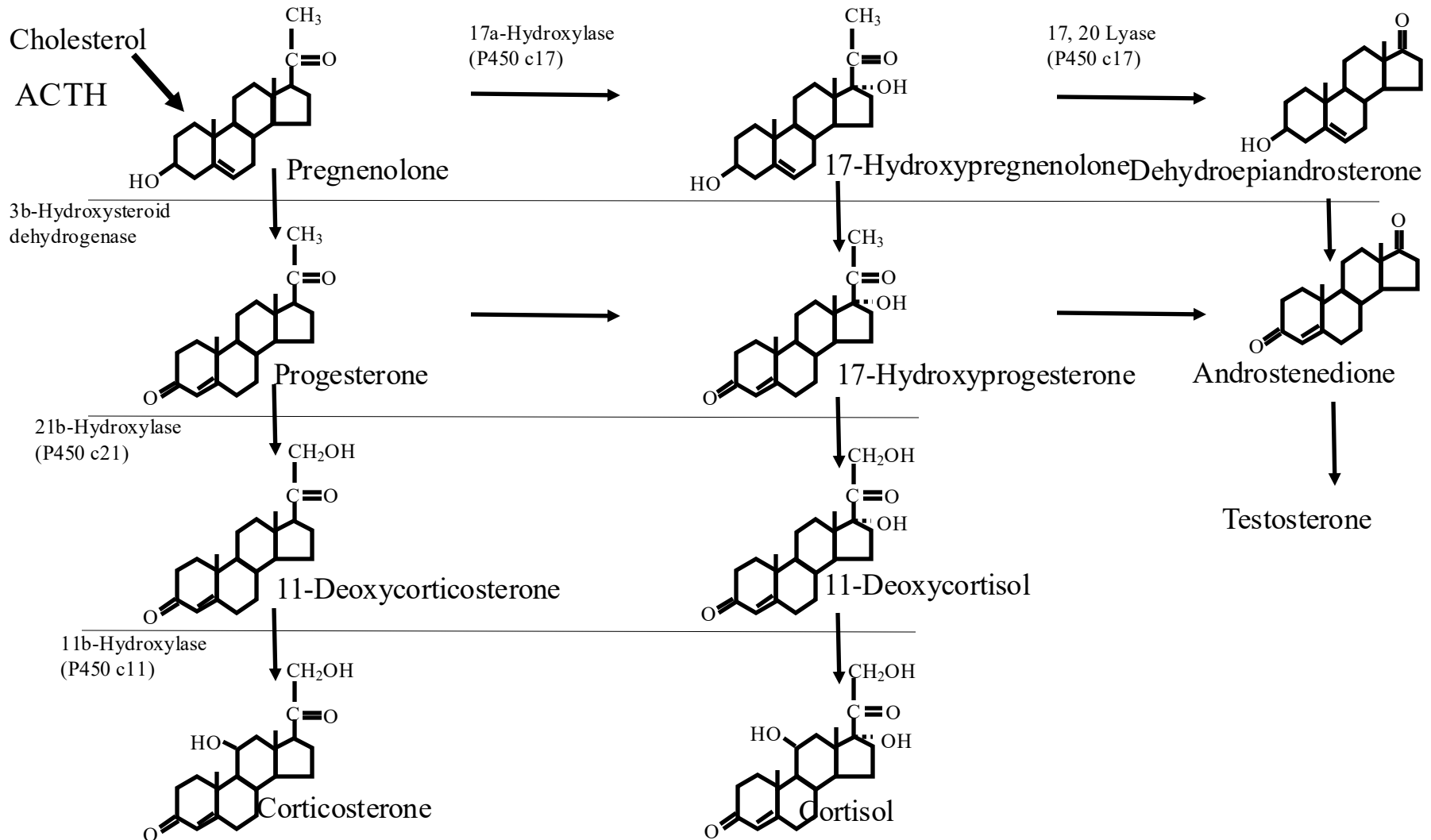


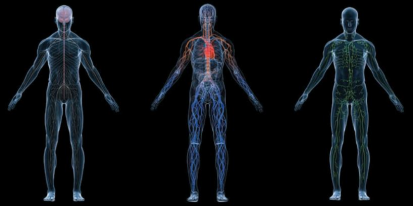
Hormone Biosynthesis in the Zona Fasciculata & Reticularis



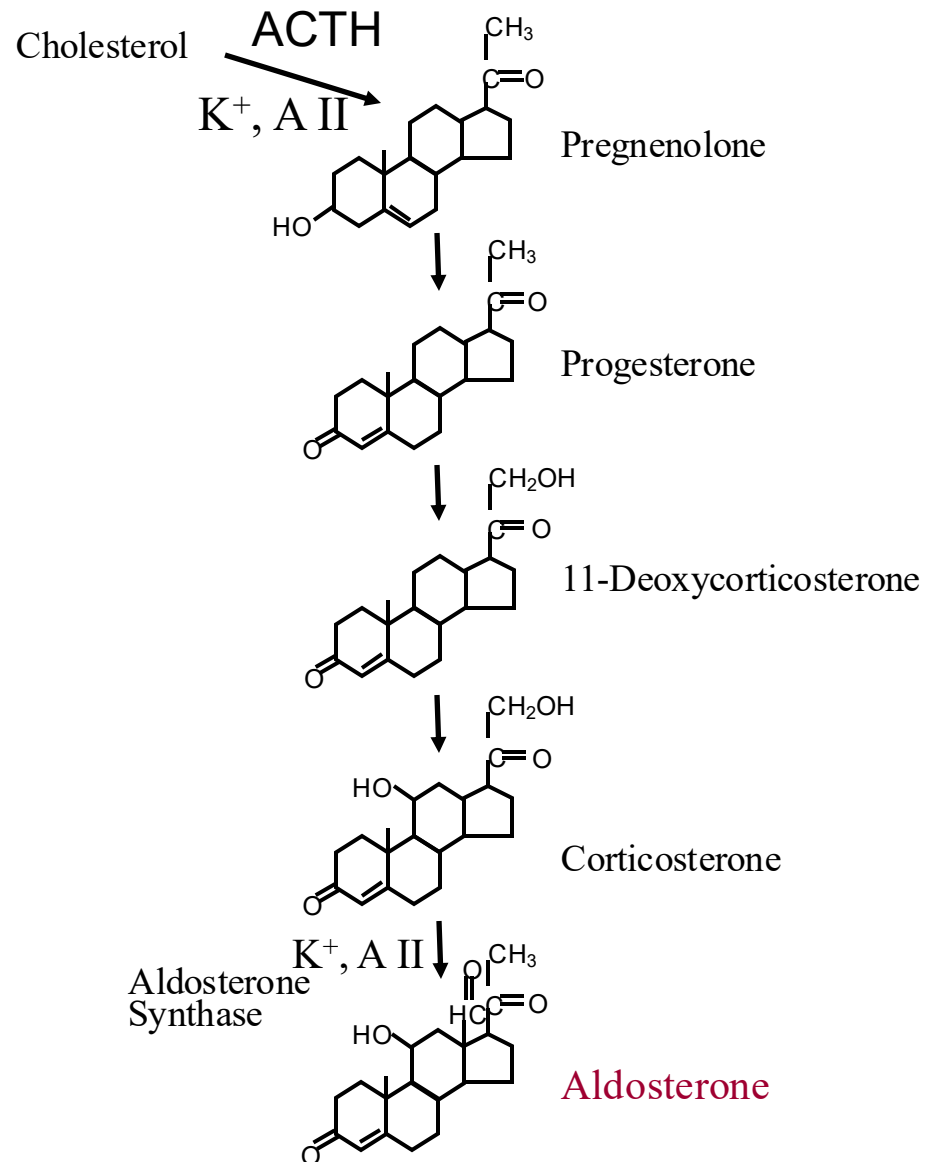


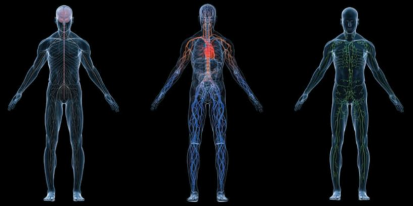
Hormone Biosynthesis in the Zona Fasciculata & Reticularis





Hormone Biosynthesis in the Zona Glomerulosa

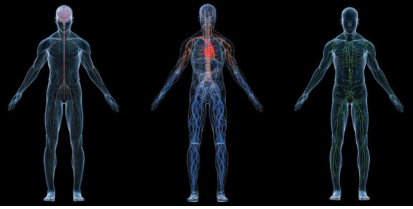




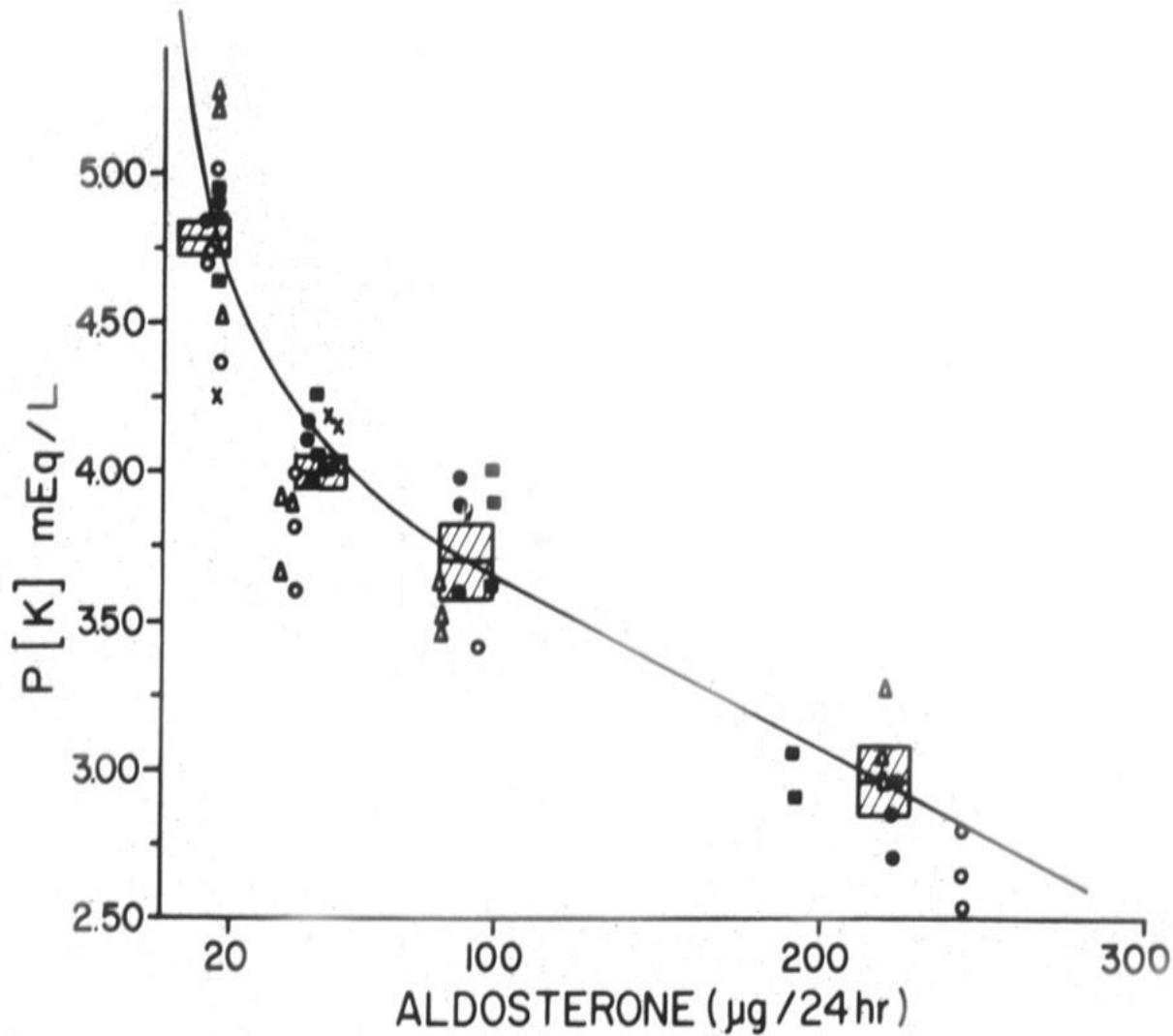
Corticosteroids & Their Relative Glucocorticoid & Mineralocorticoid Activities Compared to Cortisol

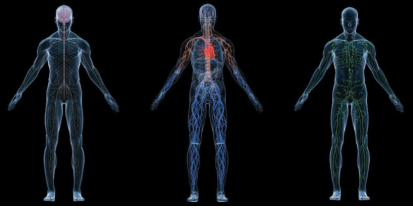
Steroids	Average Plasma Concentration (free and bound, µg/100 ml)	Average Amount Secreted (mg/24 hr)	Glucocorticoid Activity	Mineralocorticoid Activity
<i>Adrenal Steroids</i>				
Cortisol	12	15	1	1
Corticosterone	0.4	3	0.3	15.0
Aldosterone	0.006	0.15	0.3	3000
Deoxycorticosterone	0.006	0.2	0.2	100
Dehydropiandrosterone	175	20	—	—
<i>Synthetic Steroids</i>				
Cortisone	—	—	0.7	1.0
Prednisolone	—	—	4	0.8
Methylprednisone	—	—	5	—
Dexamethasone	—	—	30	—
9α-fluorocortisol	—	—	10	125

Table 77-1, Guyton & Hall

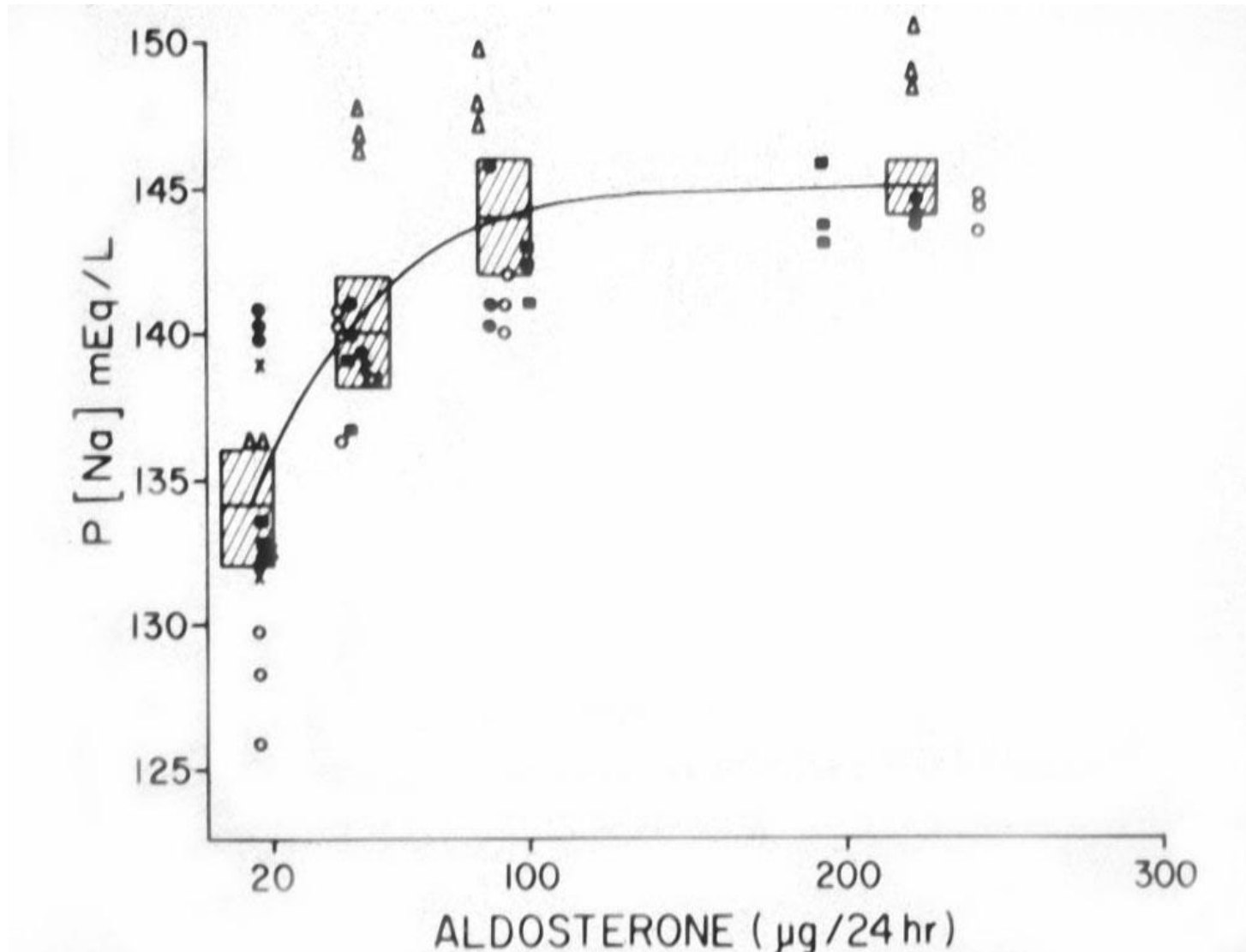


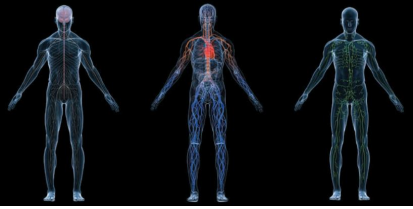
Aldosterone-Plasma [K] Relationships



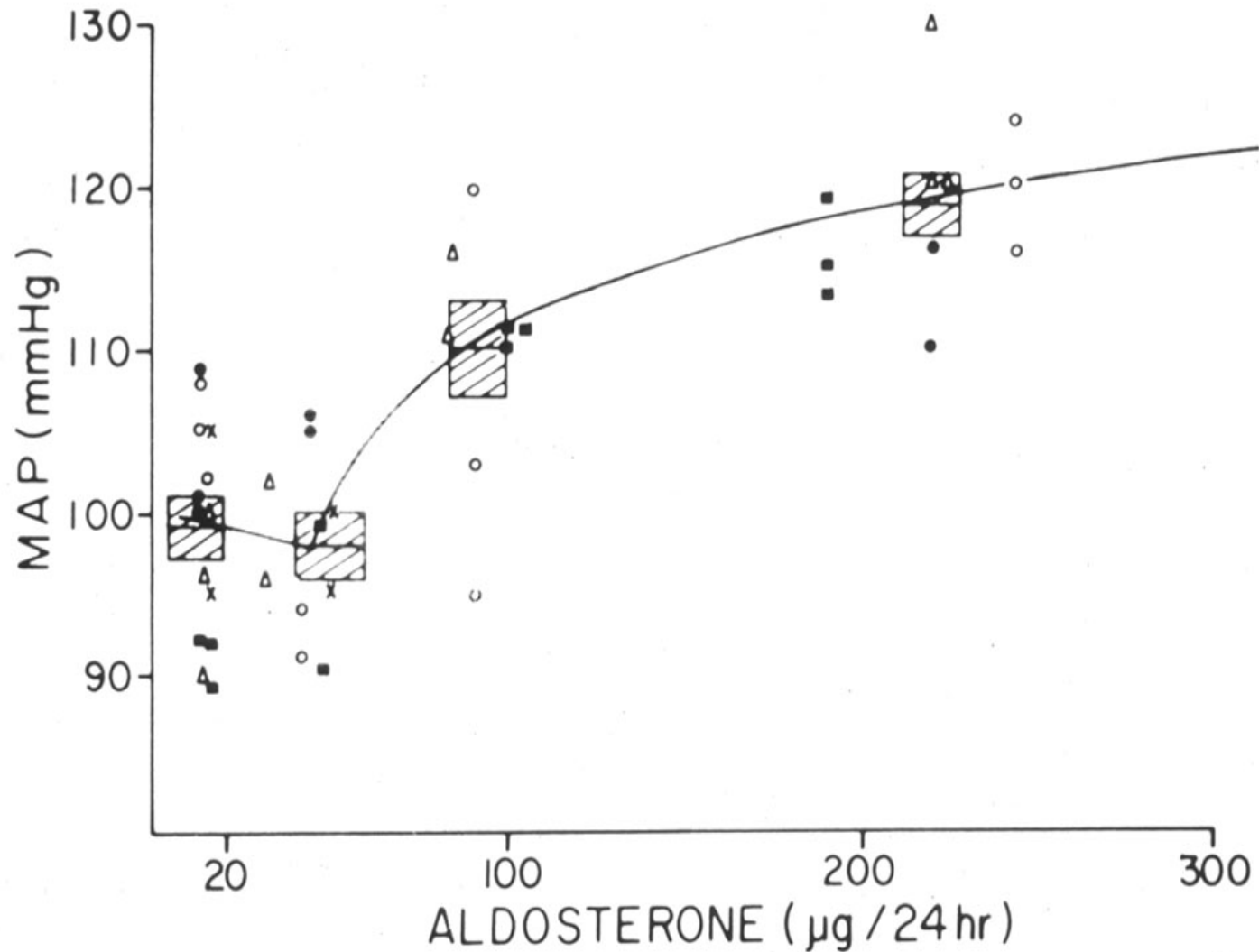


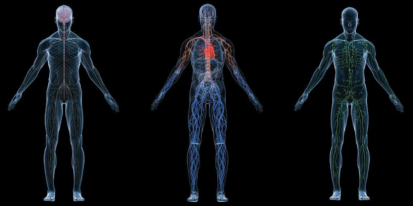
Aldosterone-Plasma [Na] Relationships





Aldosterone-MAP Relationships





Circulating Transport Proteins

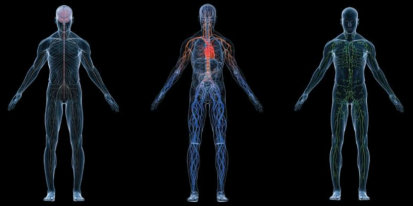
Transport Protein	Principle Hormone Transported
-------------------	-------------------------------

Specific

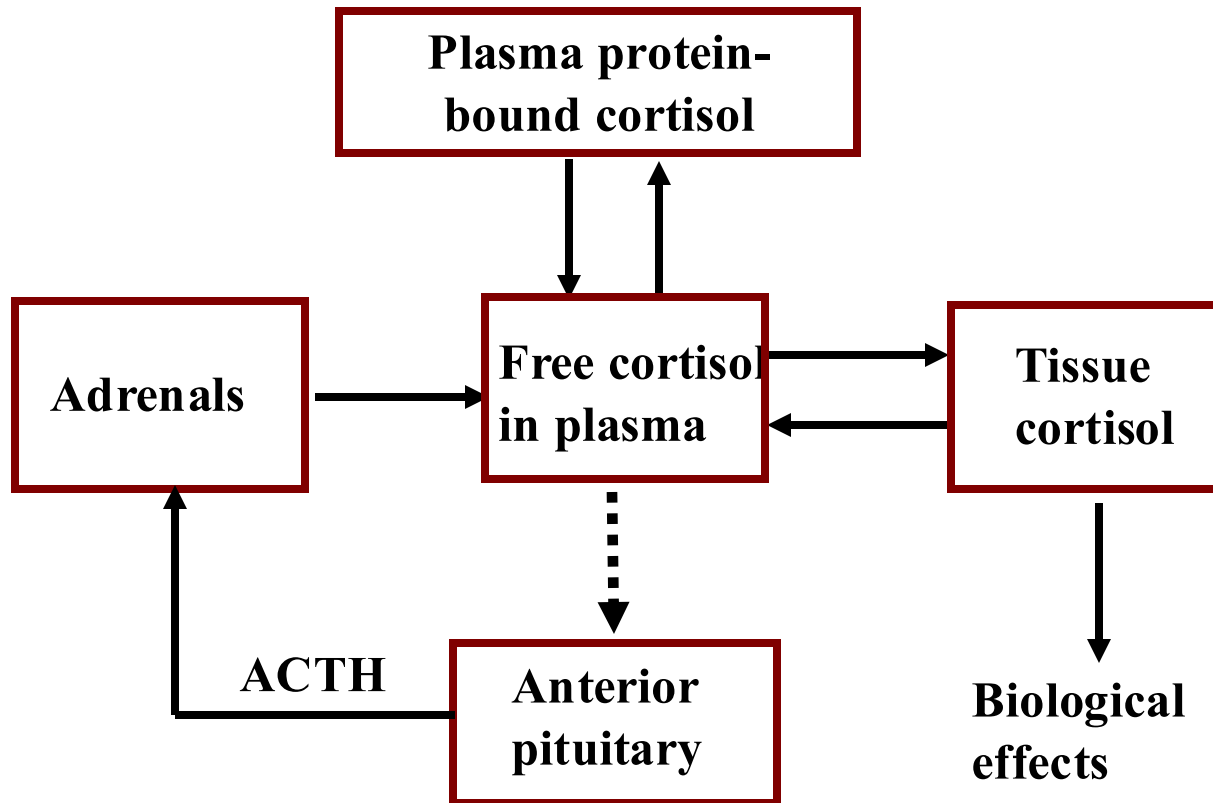
Corticosteroid binding globulin
(CBG, transcortin)

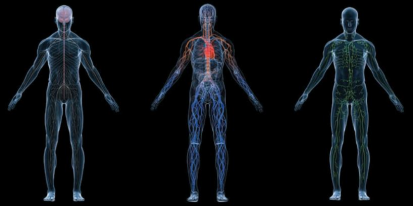
Nonspecific

Albumin

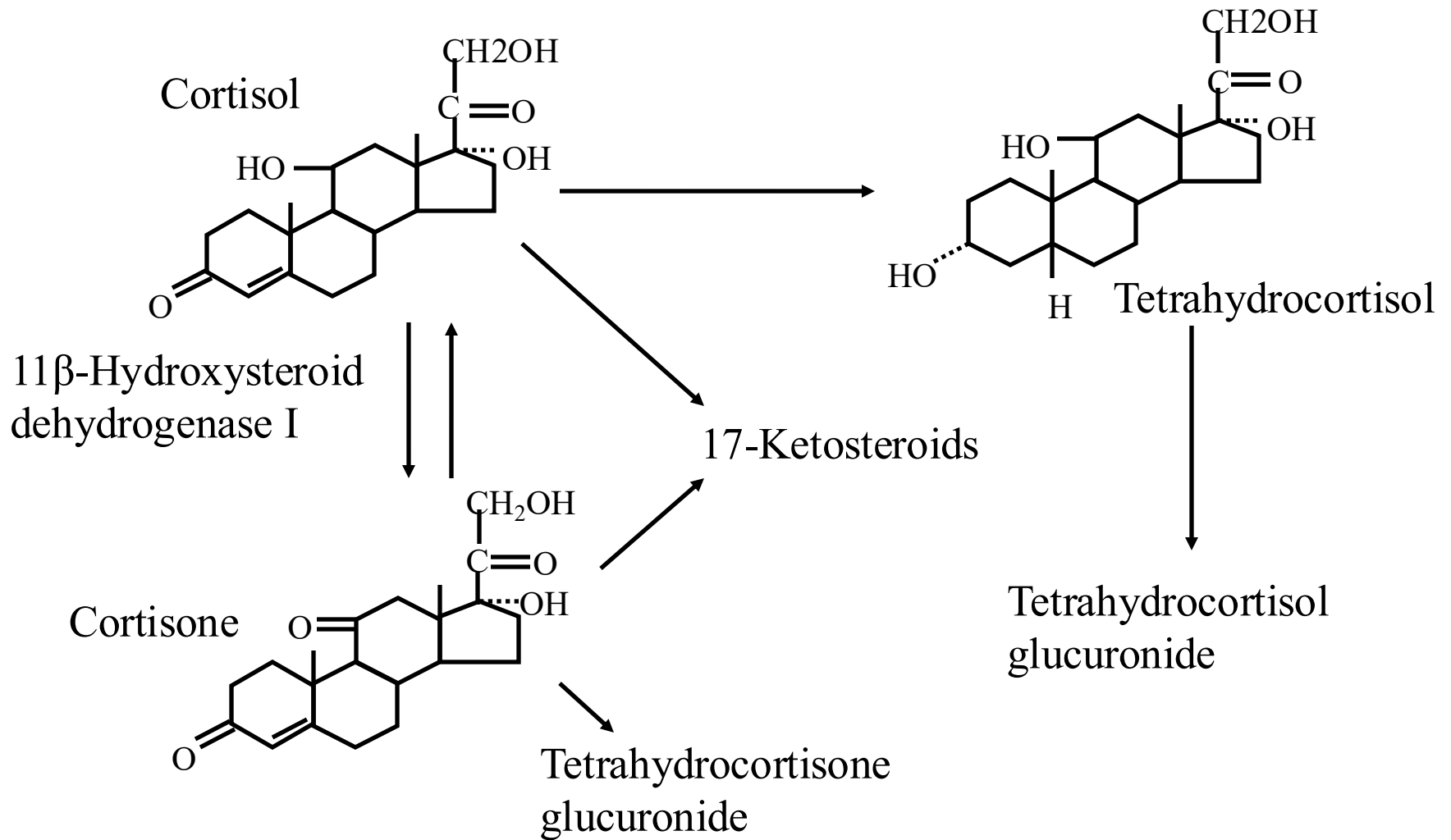


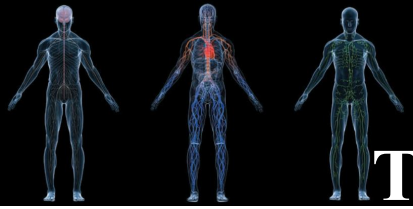
Interrelationships Between Free & Bound Cortisol



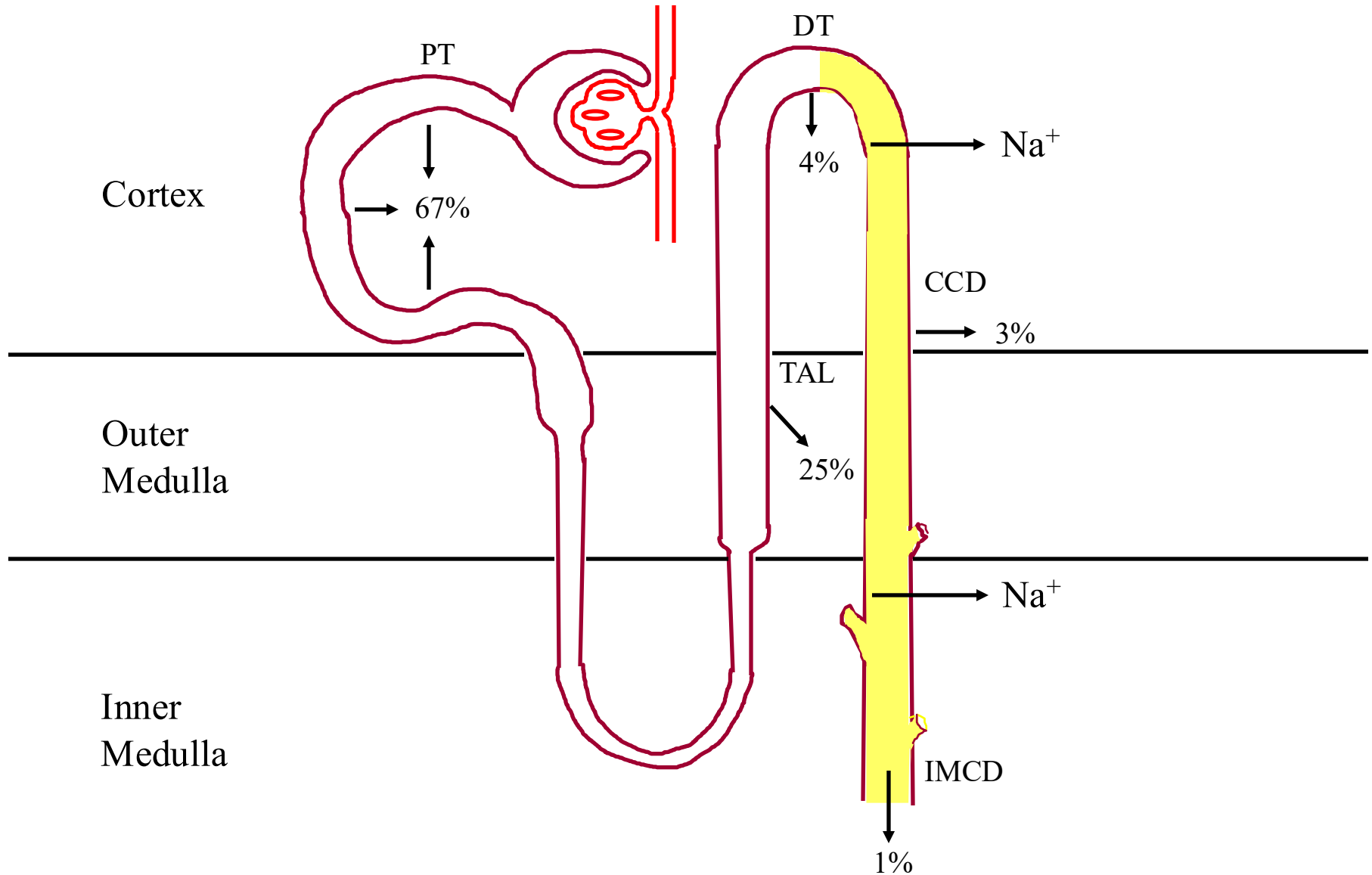


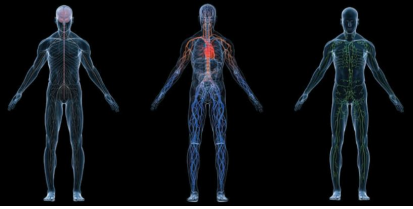
Hepatic Metabolism of Cortisol



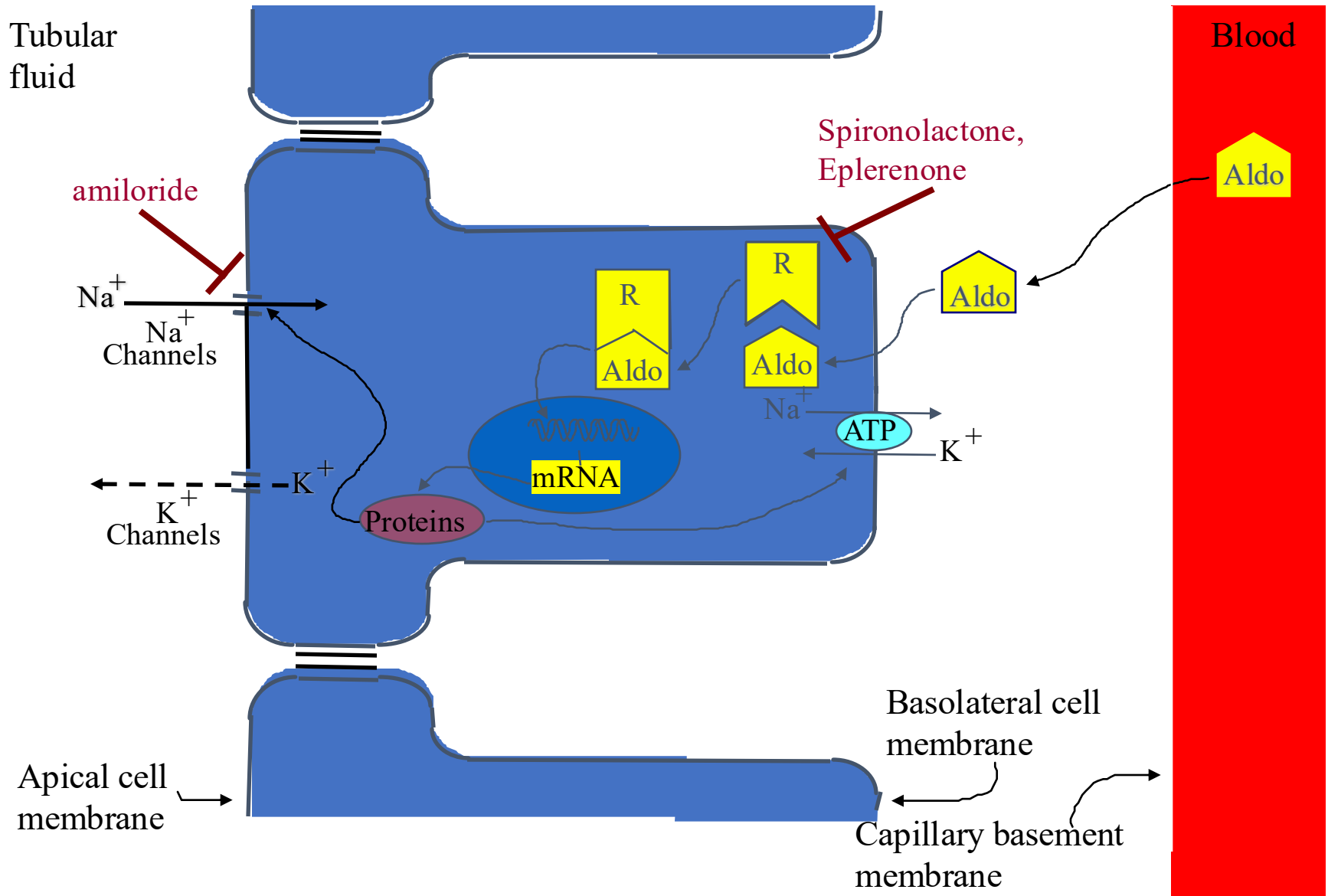


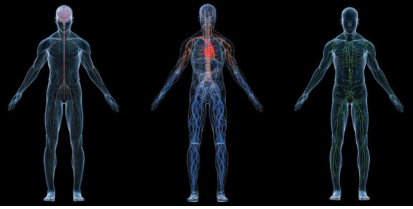
Tubular Effects of Aldosterone





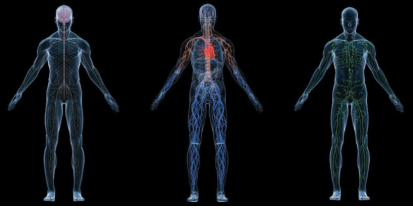
Cellular Actions of Aldosterone on Principal Cells of Collecting Tubules



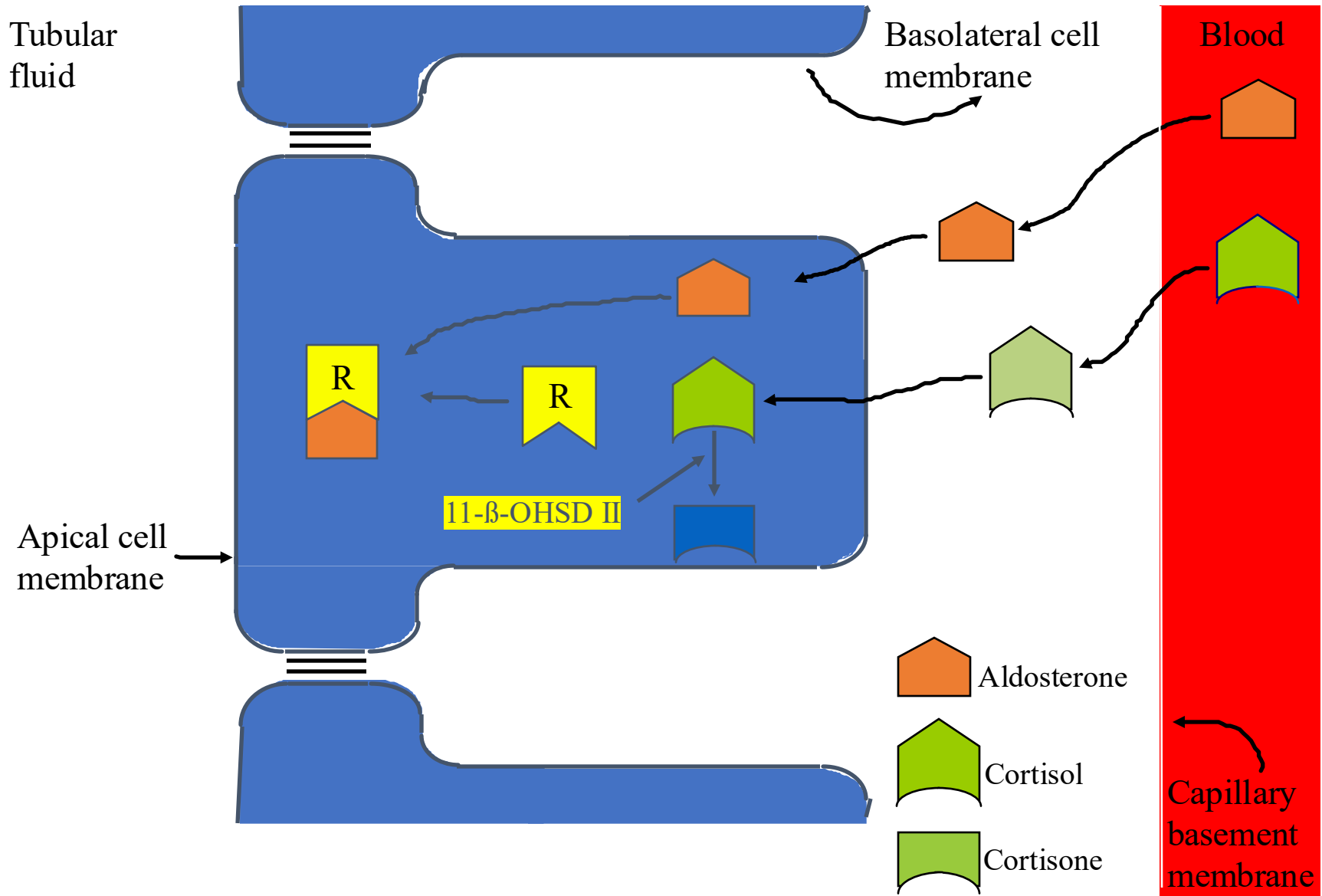


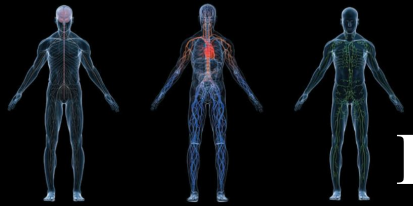
Pathophysiology of the Adrenal Cortex

- Cushing's syndrome
- Cushing's disease
- **Addison's disease**
- **Conn's syndrome**
- Apparent mineralocorticoid excess
- Congenital adrenal hyperplasia
 - 21 β - Hydroxylase deficiency
 - 11 β - Hydroxylase deficiency



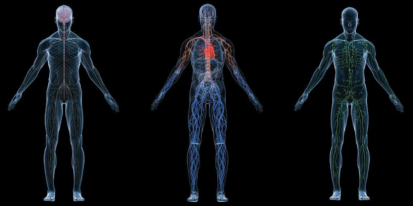
Mechanism for Aldosterone Specificity in Target Cells



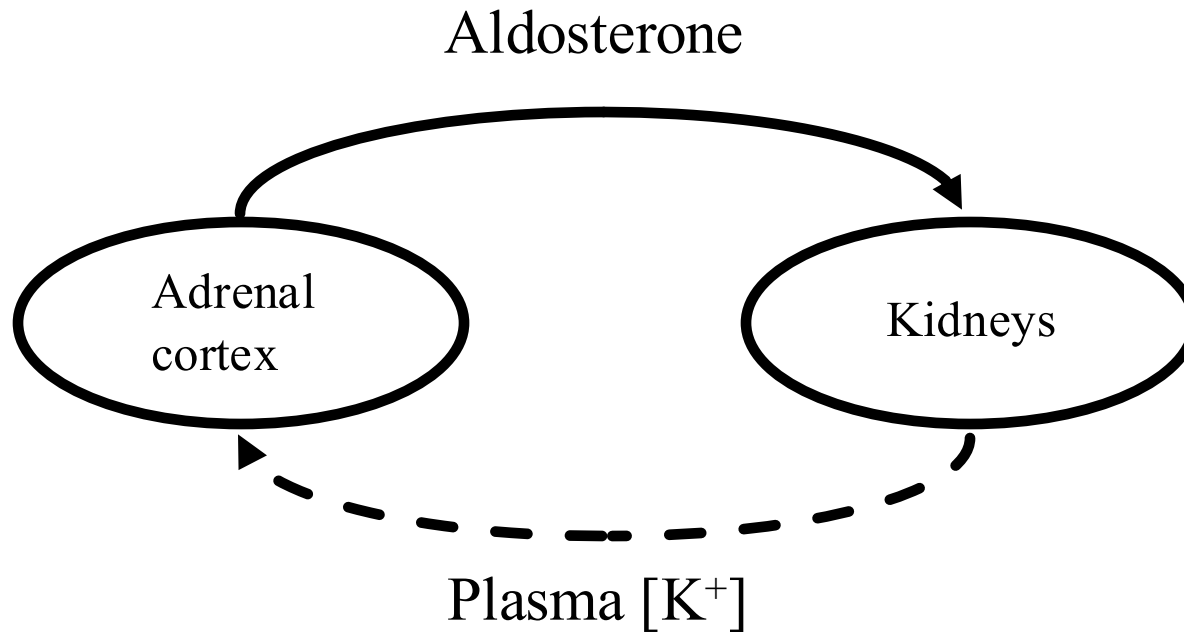


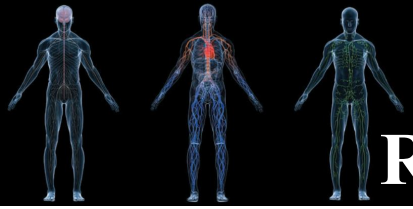
Regulation of Aldosterone Secretion

- **Plasma K**
- ANG II
- ACTH



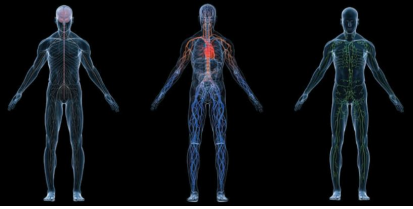
Aldosterone & Plasma [K] Regulation



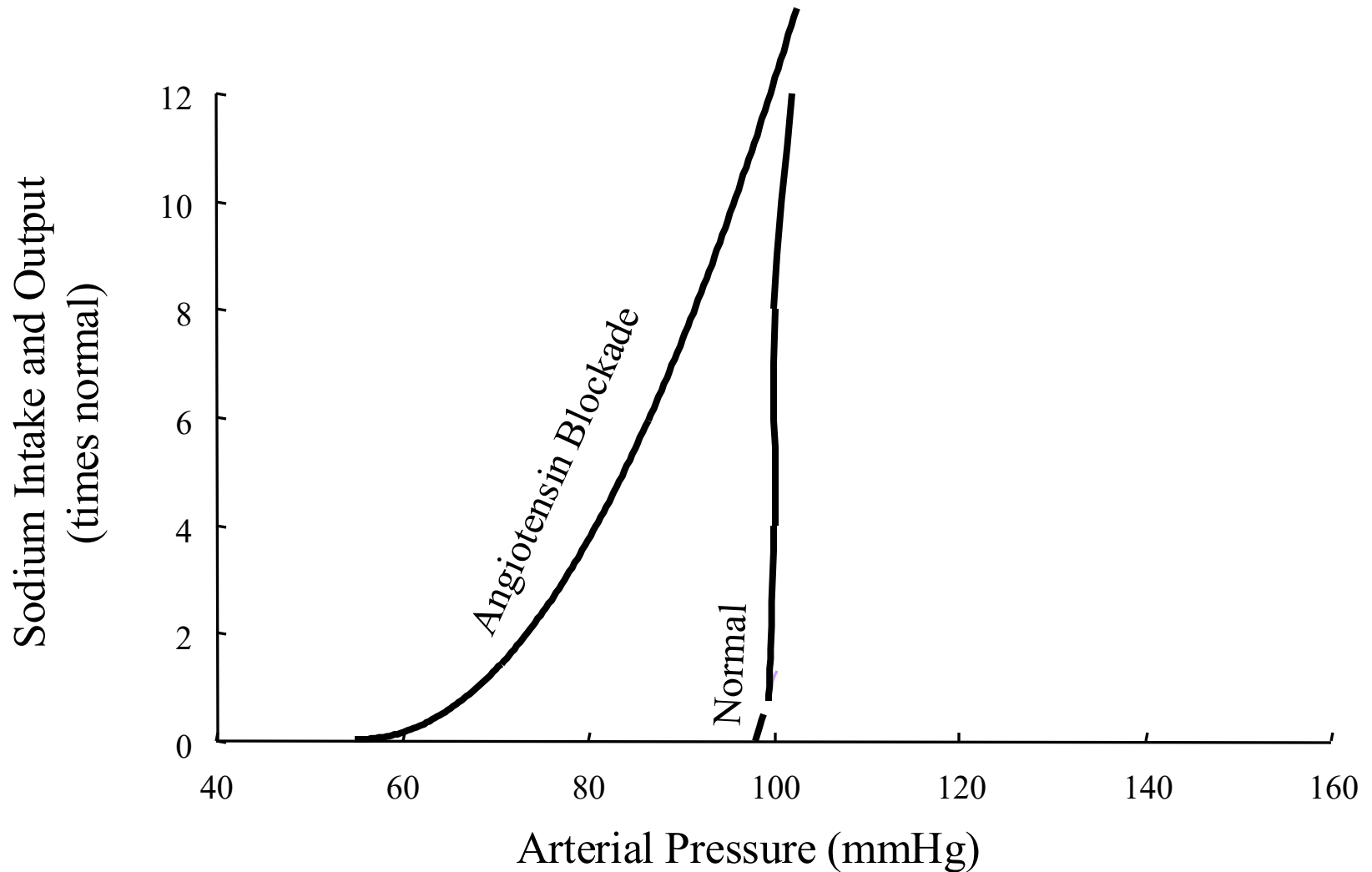


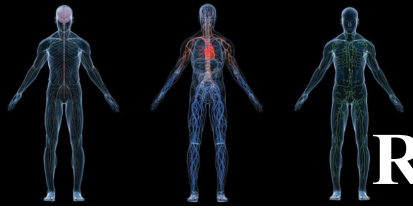
Regulation of Aldosterone Secretion

- Plasma K
- **ANG II**
- ACTH



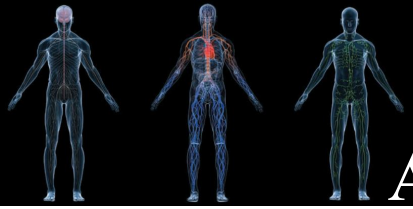
RAS & Regulation of Arterial Pressure





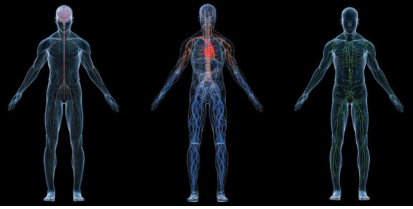
Regulation of Aldosterone Secretion

- Plasma K
- ANG II
- **ACTH**

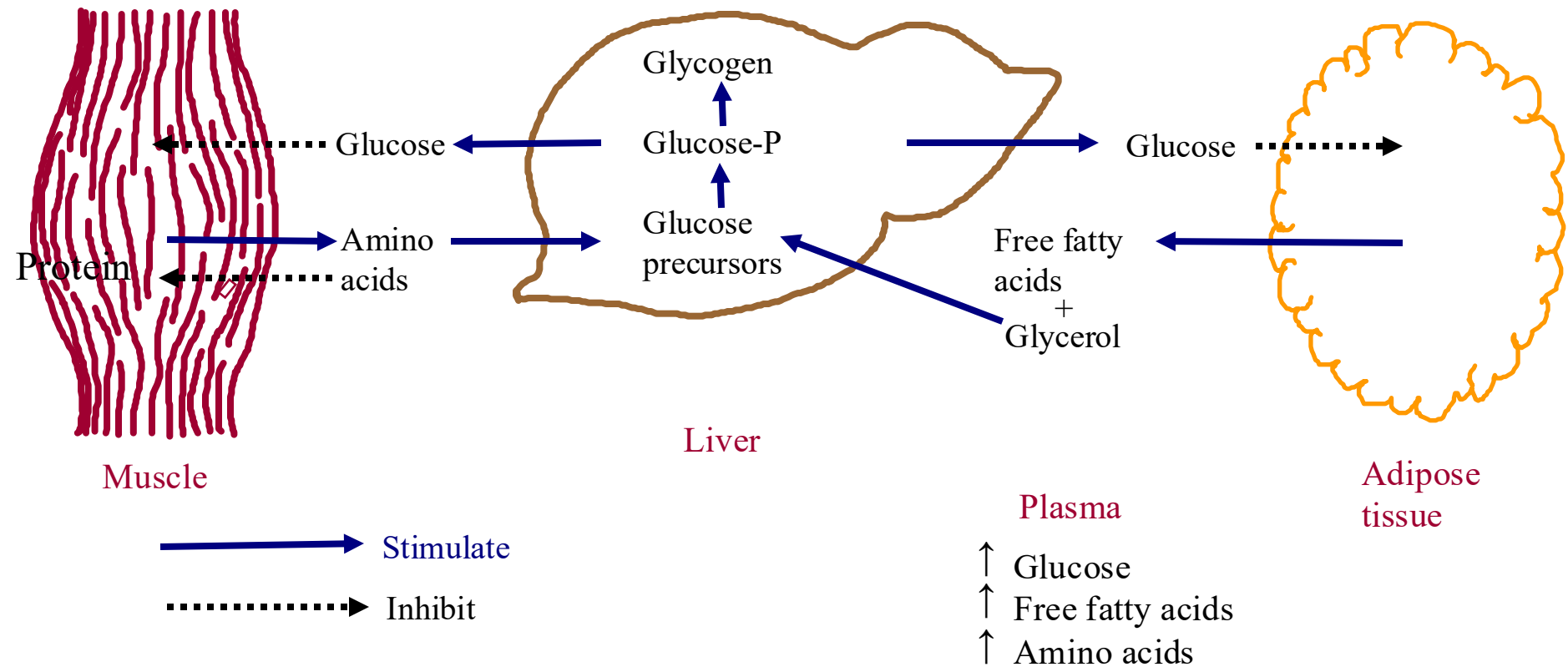


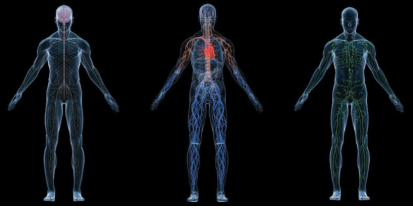
ACTH & Aldosterone Secretion

- Permissive effect
- Acute effect
- No chronic effect



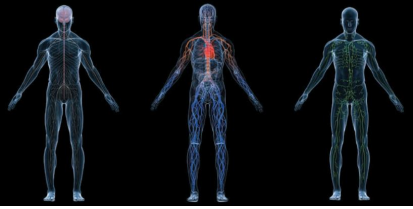
Metabolic Effects of Cortisol



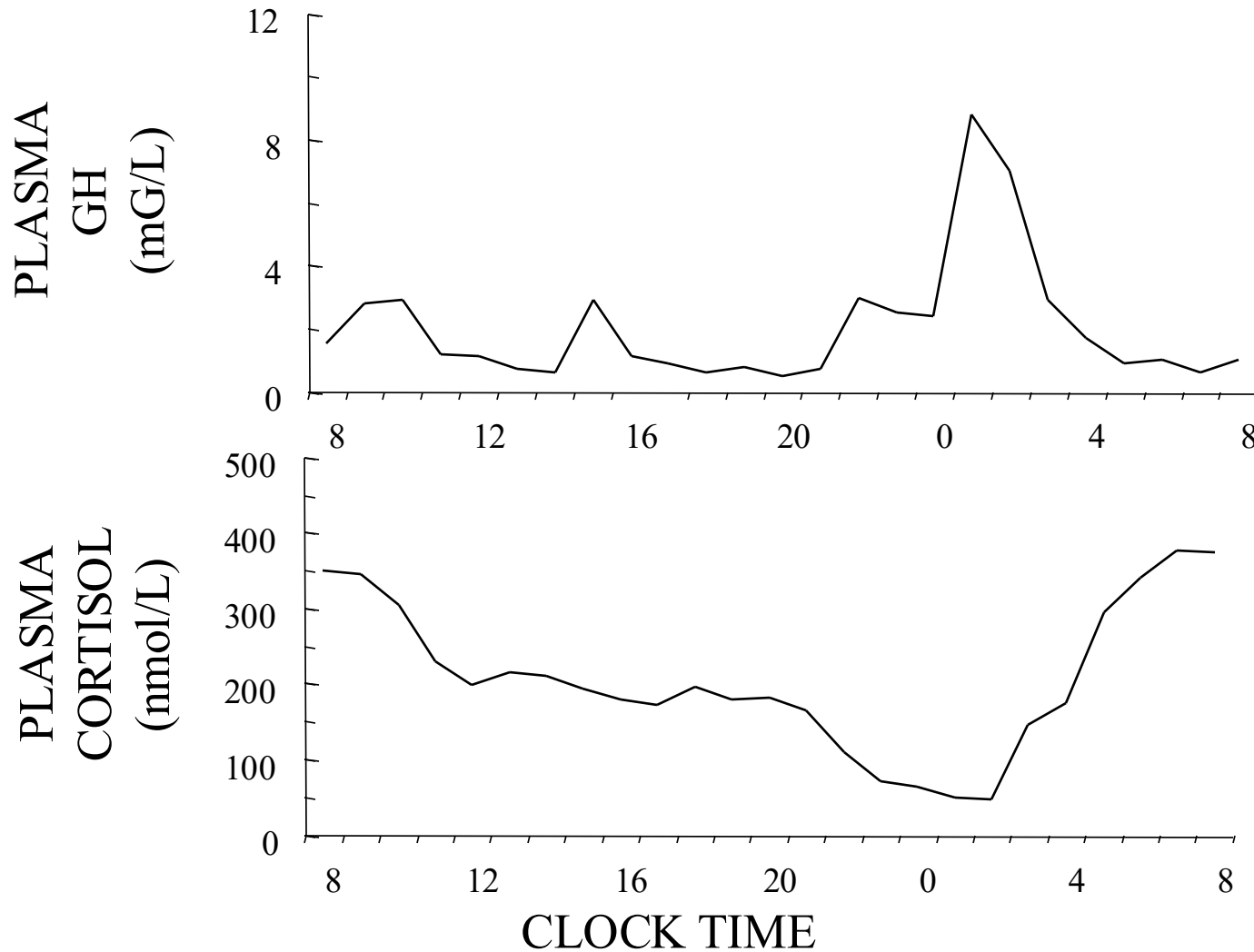


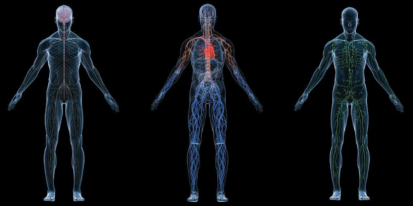
Regulation of Cortisol Secretion

- ACTH



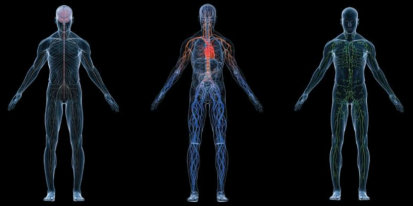
Hormone Secretion Profiles





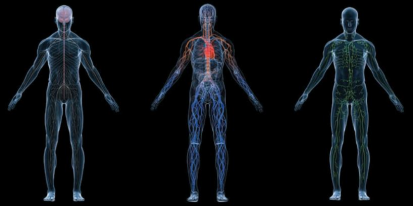
Pathophysiology of the Adrenal Cortex

- **Cushing's syndrome**
- **Cushing's disease**
- Addison's disease
- Conn's syndrome
- Apparent mineralocorticoid excess
- Congenital adrenal hyperplasia
 - 21 β - Hydroxylase deficiency
 - 11 β - Hydroxylase deficiency



Causes of Cushing's Syndrome

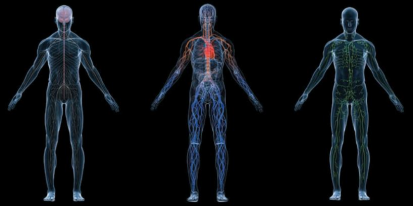
- Adrenal hyperplasia
 - ↑ Pituitary ACTH
hypothalamic dysfunction
pituitary tumors (Cushing's disease)
 - Nonpituitary tumors (ectopic)
ACTH
CRH
- Adrenal neoplasia
 - Adenoma
 - Carcinoma
- Iatrogenic: Most common



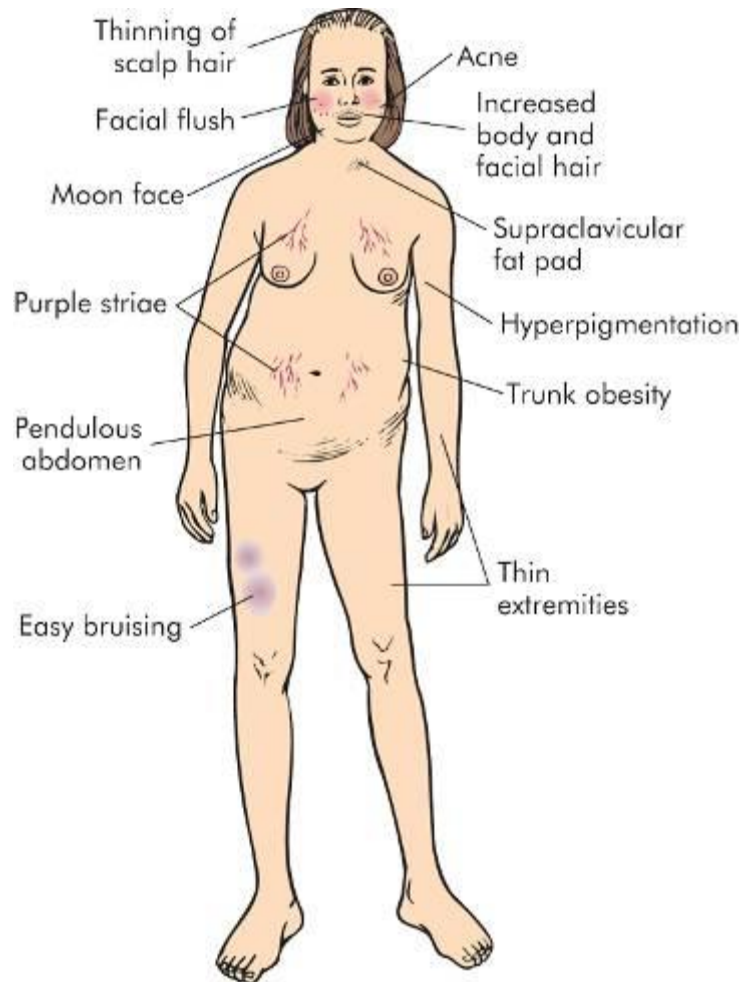
Signs & Symptoms in Cushing's Syndrome

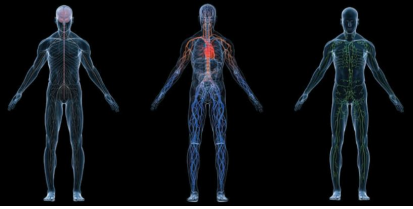
Sign or Symptom	Per Cent of Patients
Central Obesity*	97
Increased body weight	94
Fatigability & weakness	87
Hypertension	82
Hirsutism*	80
Amenorrhea*	77
Cutaneous striae*	67
Personality changes	66
Ecchymoses*	65
Proximal myopathy*	62
Edema	62

* More specific for Cushing's syndrome



Cushing Disease





Cushing Disease

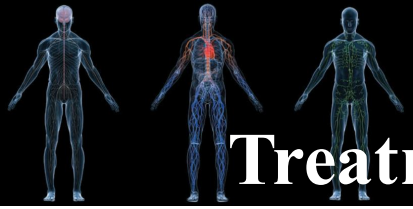


A



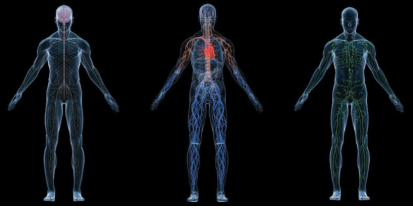
B

From Zitelli BJ, Davis HA: Atlas of pediatric physical diagnosis, ed 3. London, 1997; Gower.



Treatment of Cushing's Disease

- ↓ ACTH production
 - Hypophysectomy
 - Radiation
- ↓ Adrenocortical cortisol secretion
 - Bilateral adrenalectomy
 - Medical adrenalectomy (metyrapone, aminoglutethimide, ketoconazole)



Causes of Adrenal Insufficiency

- Primary adrenal insufficiency
 - Destruction of gland
 - Idiopathic atrophy - autoimmune
 - Infectious - tuberculous
 - Surgery
 - Hemorrhage
 - Metabolic
 - Congenital adrenal hyperplasia
- Secondary adrenal insufficiency
 - Hypothalamic-pituitary disease
 - Suppression of HPA - exogenous steroids

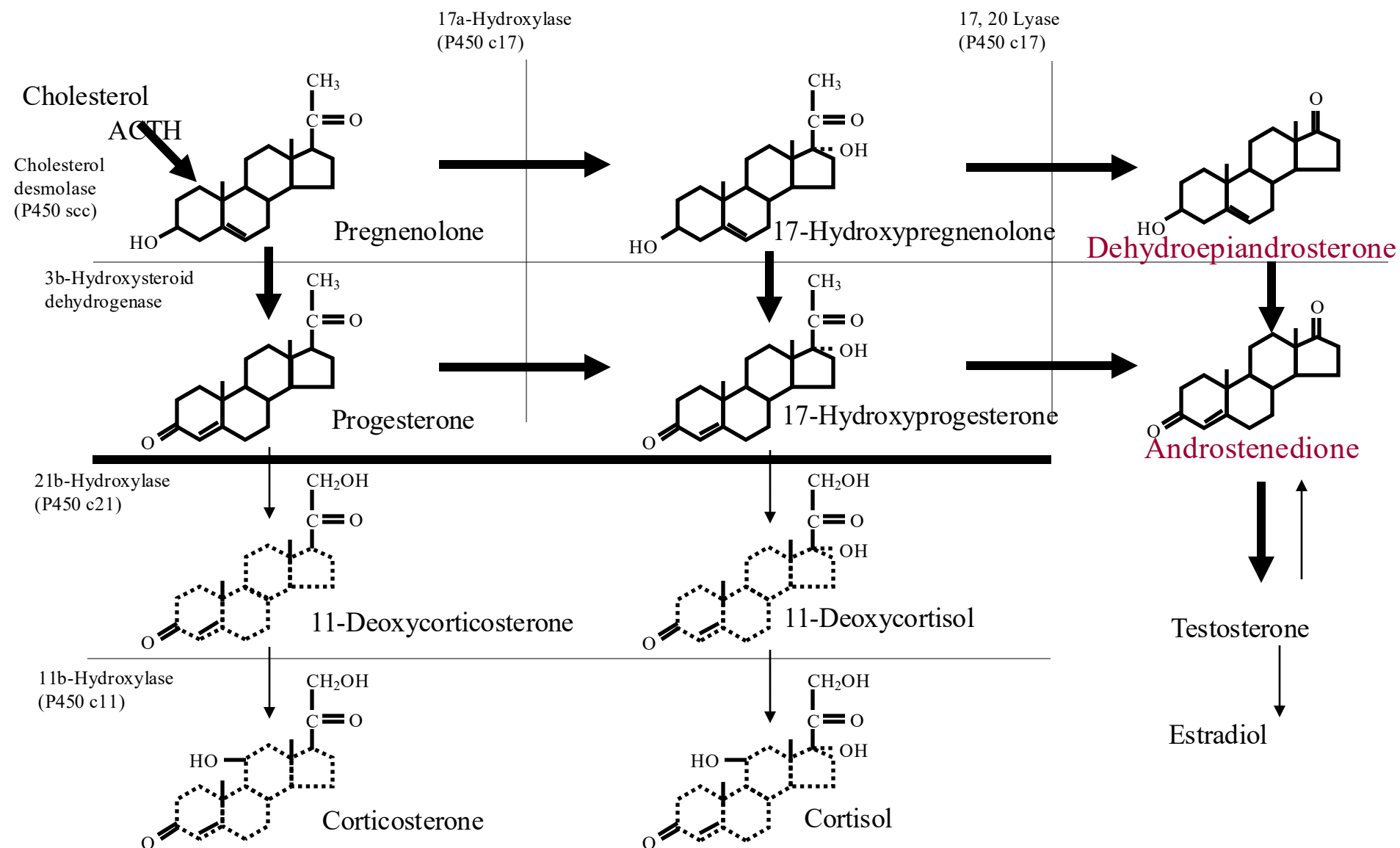


Signs & Symptoms in Adrenal insufficiency

Sign or Symptom	Per Cent of Patients
Weakness	99
Pigmentation of skin	98
Weight loss	97
Anorexia, nausea, & vomiting	90
Hypotension	87
Pigmentation of mucus membranes	82
Abdominal pain	34
Diarrhea	20
Syncope	16

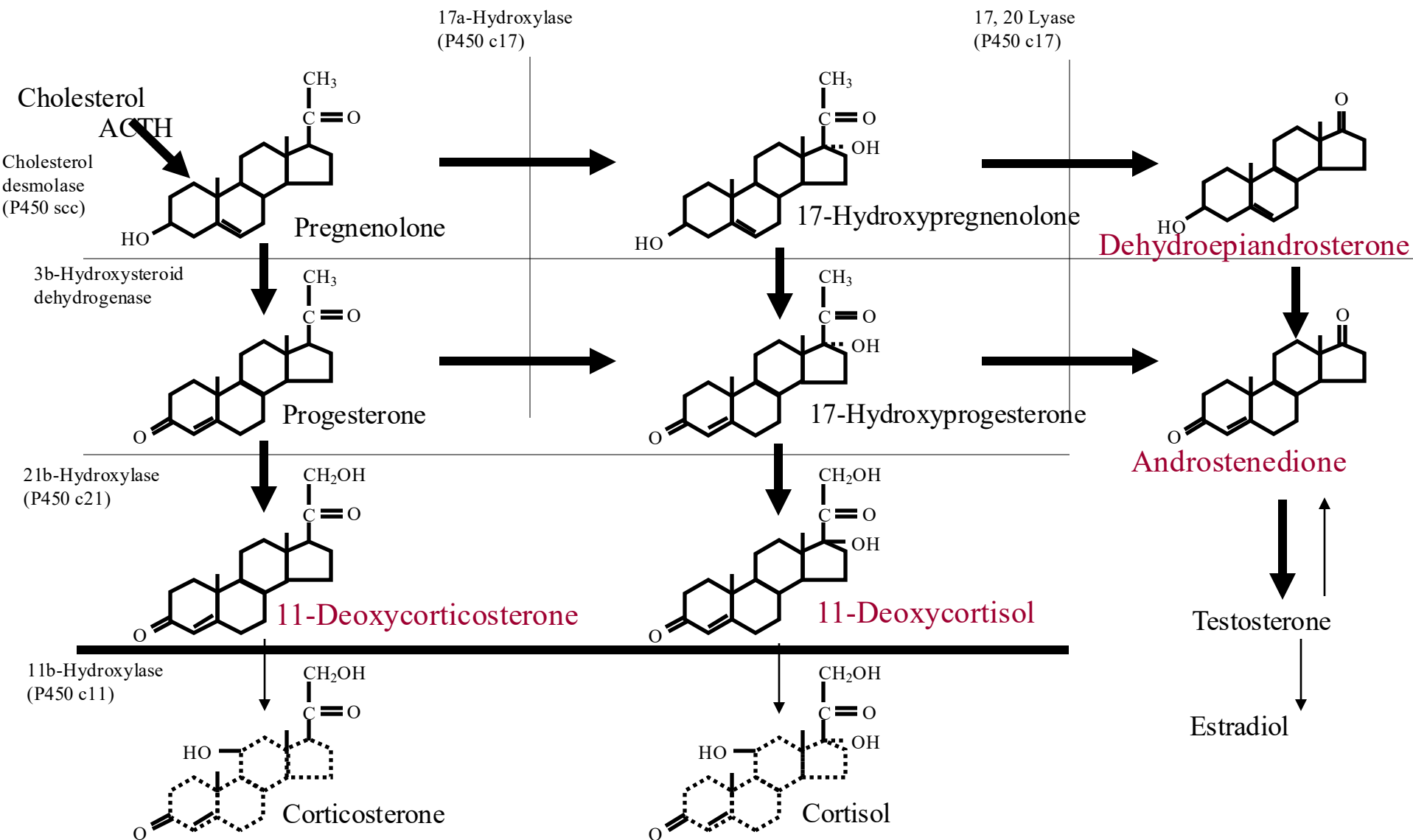


Congenital Adrenal Hyperplasia: 21 β -Hydroxylase Deficiency





Congenital Adrenal Hyperplasia: 11 β -Hydroxylase Deficiency





Thank you

