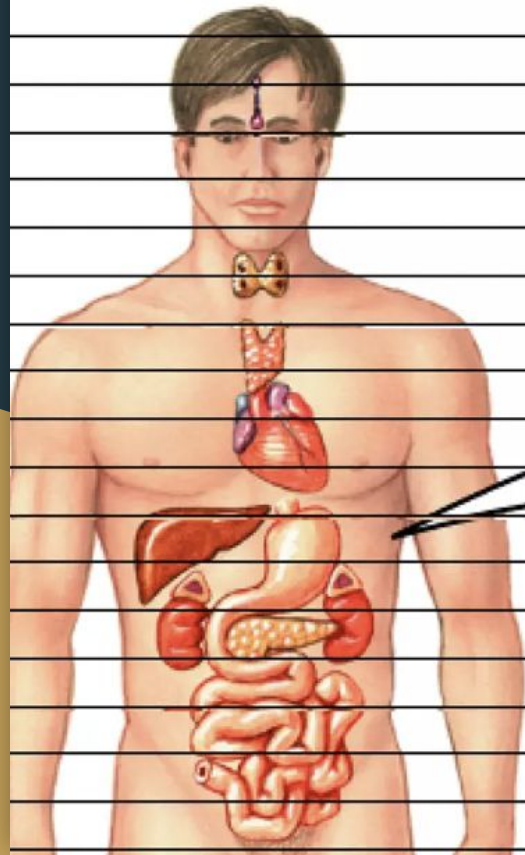




Adrenal hormones

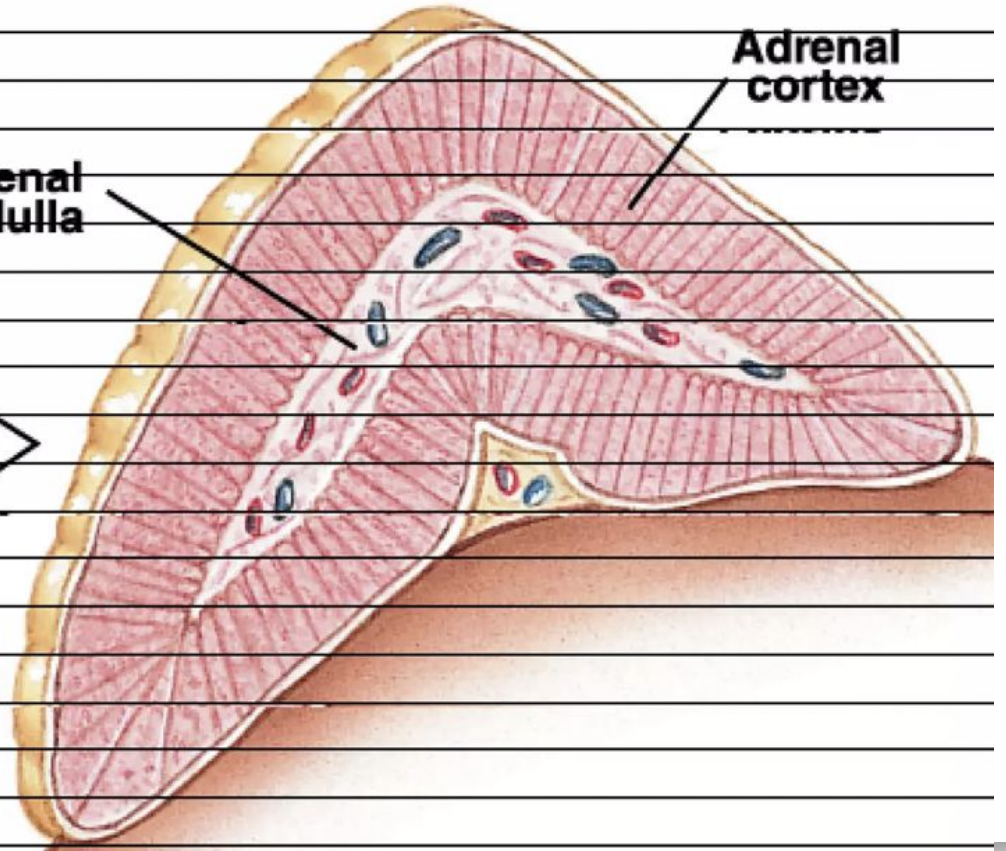
Adrenal glands

- Small, triangular glands loosely attached to the kidneys
- Divided into two morphologically distinct regions
 - adrenal cortex (outer)
 - adrenal medulla (inner)



Adrenal medulla

Adrenal cortex



PARTS OF ADRENAL GLAND

Adrenal gland is made of two distinct parts: hormones from cortex are Regulated by ACTH

1. Adrenal cortex: Outer portion, constituting 80% of the gland
2. Adrenal medulla: Central portion, constituting 20% of the gland.

Adrenal cortex is formed by three layers of structure. Each layer is distinct from one another.

1. Outer zona glomerulosa
2. Middle zona fasciculata
3. Inner zona reticularis.

HORMONES OF ADRENAL CORTEX

Adrenocortical hormones are steroids in nature, hence the name 'corticosteroids'. Based on their functions, corticosteroids are classified into three groups:

1. Mineralocorticoids
2. Glucocorticoids
3. Sex hormones.

SYNTHESIS, TRANSPORT AND FATE OF ADRENOCORTICAL HORMONES

SYNTHESIS

- All adrenocortical hormones are steroid in nature (lipophilic) and are synthesized mainly from cholesterol .
- Mineralocorticoids are transported in blood by binding with plasma proteins, especially globulins. The binding is loose and 50% of these hormones are present in free form.
- Glucocorticoids are transported by a special plasma protein known as **glucocorticoids-binding globulin or transcortin**.
- Corticosteroids are degraded mainly in the liver and conjugated in excreted Some in bile and feces and mainly in the urine.

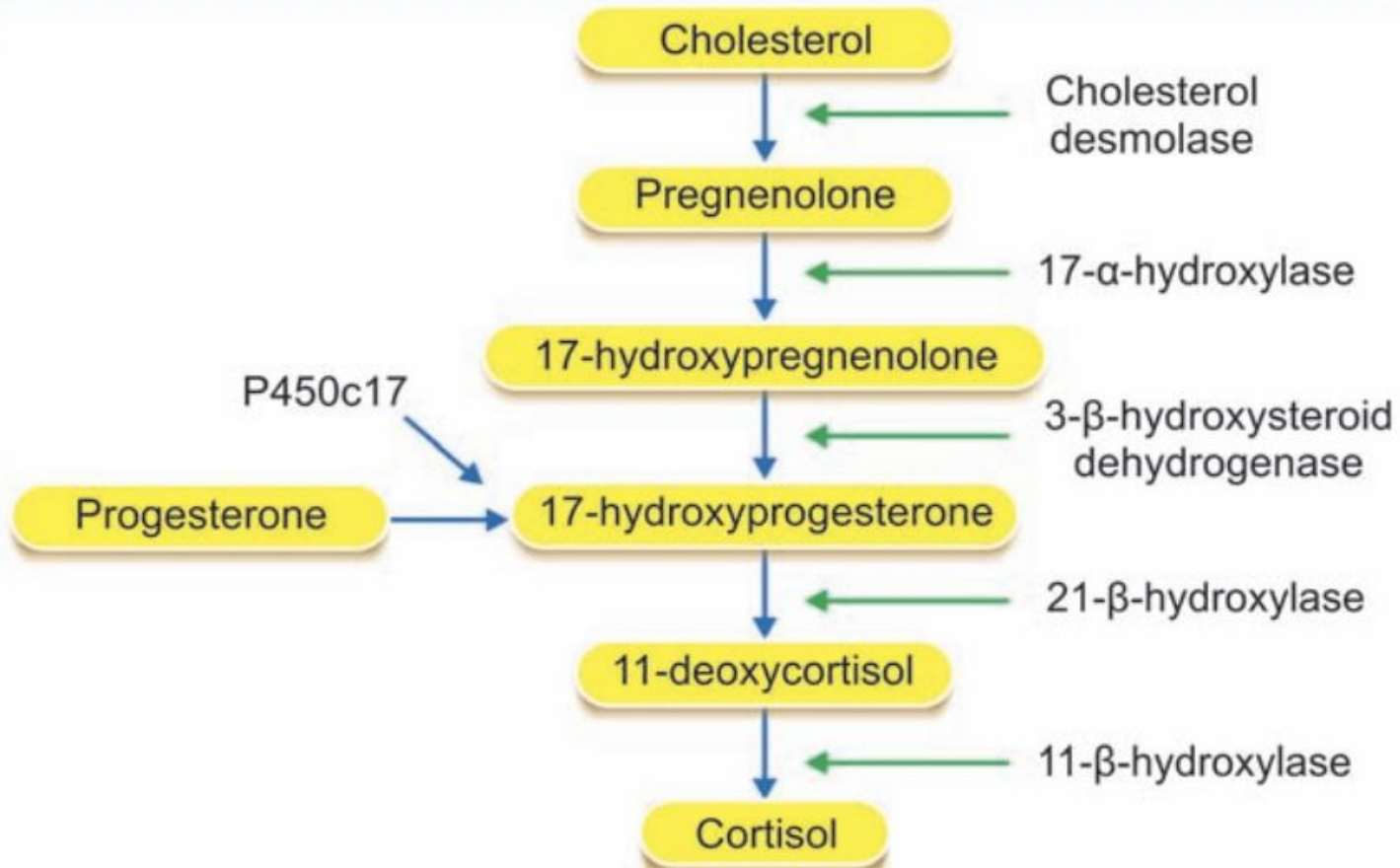


FIGURE 70.6: Synthesis of cortisol

MINERALOCORTICIDS

Mineralocorticoids are the corticosteroids that act on the minerals (electrolytes), particularly sodium and potassium.

Mineralocorticoids are:

1. Aldosterone
2. 11-deoxycorticosterone.

Mineralocorticoids are secreted by zona glomerulosa of adrenal cortex.

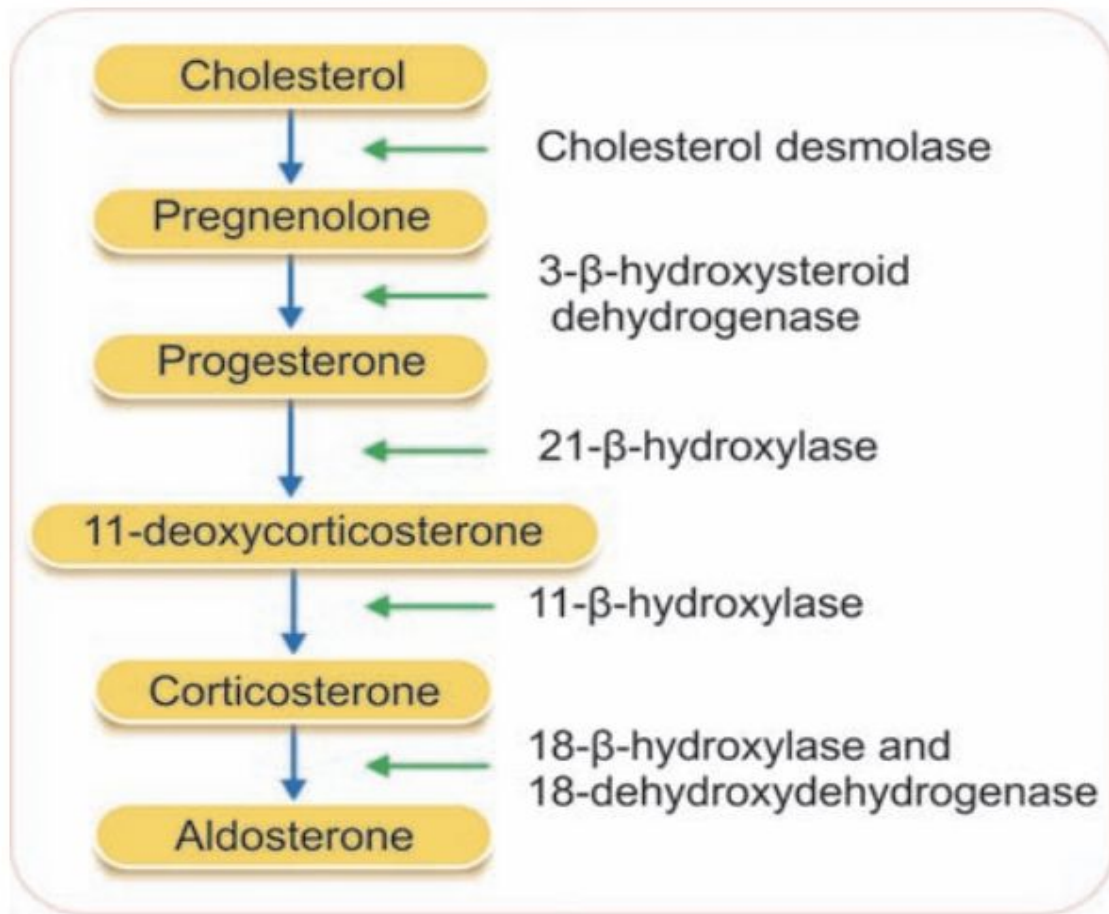


FIGURE 70.2: Synthesis of aldosterone

Aldosterone functions - 3 functions

It increases:

1. Reabsorption of sodium from renal tubules
2. Excretion of potassium through renal tubules
3. Secretion of hydrogen into renal tubules.

1. **On Sodium Ions**

Aldosterone acts on the distal convoluted tubule and the collecting duct and increases the reabsorption of sodium.

During hypersecretion of aldosterone, the loss of sodium through urine is only few milligram per day. But during hyposecretion of aldosterone, the loss of sodium through urine increases (hypernatruria) up to about 20 g/day. It proves the importance of aldosterone in regulation of sodium ion concentration and osmolality in the body.

2. **On Extracellular Fluid Volume**

When sodium ions are reabsorbed from the renal tubules, simultaneously water is also reabsorbed. Water reabsorption is almost equal to sodium reabsorption; so the net result is the increase in ECF volume. Even though aldosterone increases the sodium reabsorption from renal tubules, the concentration of sodium in the body does not increase very much because water is also reabsorbed simultaneously. But still, there is a possibility for mild increase in concentration of sodium in blood (mild hypernatremia). It induces thirst, leading to intake of water which again increases the ECF volume and blood volume.

3. **On Blood Pressure**

Increase in ECF volume and the blood volume finally leads to increase in blood pressure.

On Potassium Ions

Aldosterone increases the potassium excretion through the renal tubules. When aldosterone is deficient, the potassium ion concentration in ECF increases leading to hyperkalemia. Hyperkalemia results in serious cardiac toxicity, with weak contractions of heart and development of arrhythmia. In very severe conditions, it may cause cardiac death. When aldosterone secretion increases, it leads to hypokalemia and muscular weakness.

5. On Hydrogen Ion Concentration

While increasing the sodium reabsorption from renal tubules, aldosterone causes tubular secretion of hydrogen ions. It obviously reduces the hydrogen ion concentration in the ECF. In normal conditions, aldosterone is essential to maintain acid-base balance in the body. In hypersecretion, it causes alkalosis and in hyposecretion, it causes acidosis.

On Sweat Glands and Salivary Glands

Sodium is reabsorbed from sweat glands under the influence of aldosterone, thus the loss of sodium from the body is prevented.

Same effect is shown on saliva

also. Thus, aldosterone helps in the conservation of sodium in the body.

On Intestine

Aldosterone increases sodium absorption from the intestine, especially from colon and prevents loss of sodium through feces.

Aldosterone deficiency leads to diarrhea, with loss of sodium and water.

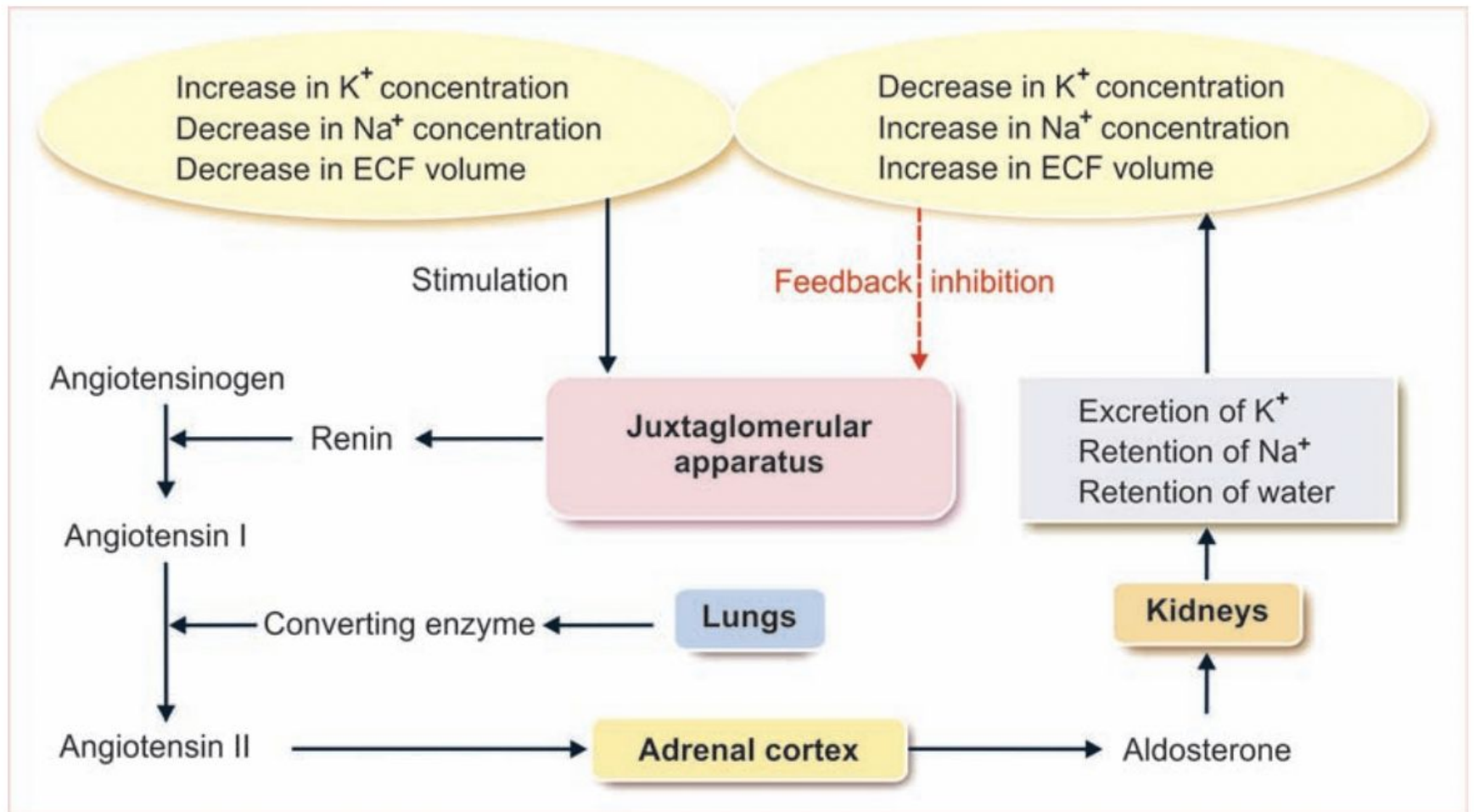


FIGURE 70-5 Regulation of aldosterone secretion

Aldosterone secretion is regulated by four important factors which are given below in the order of their potency:

1. Increase in potassium ion (K^+) concentration in ECF
2. Decrease in sodium ion (Na^+) concentration in ECF
3. Decrease in ECF volume
4. Adrenocorticotrophic hormone (ACTH).

Increase in the concentration of potassium ions acts directly on the zona glomerulosa and increases the secretion of aldosterone.

Decrease in sodium ion concentration and ECF volume stimulates aldosterone secretion through renin-angiotensin mechanism.

Renin secreted from juxtaglomerular apparatus of kidney acts on angiotensinogen in the plasma and converts it into angiotensin I, which is converted into angiotensin II by converting enzyme (ACE) secreted by lungs. Angiotensin II acts on the zona glomerulosa to secrete more aldosterone. Aldosterone in turn, increases the retention of sodium and water and excretion of potassium. This leads to increase in the sodium ion concentration and ECF volume. Now, the increased sodium ion concentration and the ECF volume inhibit the juxtaglomerular apparatus and stop the release of renin. So, angiotensin II is not formed and release of aldosterone from adrenal cortex is stopped. Adrenocorticotrophic hormone mainly stimulates the secretion of glucocorticoids.

GLUCOCORTICIDS

Glucocorticoids act mainly on glucose metabolism.

Glucocorticoids are:

1. Cortisol
2. Corticosterone
3. Cortisone.

Glucocorticoids

Regulate blood glucose level

Stimulate gluconeogenesis

Enhance synthesis of amino acids which are substrate for gluconeogenesis

Promote protein and nucleic acid metabolism

Regulated by ACTH

Acts as anti-inflammatory agents

Functions of glucocorticoids

On Carbohydrate Metabolism

Glucocorticoids increase the blood glucose level by two ways:

- i. By promoting gluconeogenesis in liver from amino acids: Glucocorticoids enhance the breakdown of proteins in extrahepatic cells, particularly the muscle. It is followed by release of amino acids into circulation. From blood, amino acids enter the liver and get converted into glucose (**gluconeogenesis**)
- ii. By inhibiting the uptake and utilization of glucose by peripheral cells: This action is called anti-insulin action of glucocorticoids. Hypersecretion of glucocorticoids increases the blood glucose level, resulting in hyperglycemia, glucosuria and adrenal diabetes. Hyposecretion leads to hypoglycemia.

On Protein Metabolism

Glucocorticoids promote the catabolism of proteins, leading to:

- i. Decrease in cellular proteins
- ii. Increase in plasma level of amino acids
- iii. Increase in protein content in liver.

Glucocorticoids cause catabolism of proteins by the following methods:

- i. By releasing amino acids from body cells (except liver cells), into the blood
- ii. By increasing the uptake of amino acids by hepatic cells from blood. In hepatic cells, the amino acids are used for the synthesis of proteins and carbohydrates (gluconeogenesis).

Thus, glucocorticoids cause mobilization of proteins from tissues other than liver. In hypersecretion of glucocorticoids, there is excess catabolism of proteins, resulting in muscular wasting and negative nitrogen balance.

On Fat Metabolism

Glucocorticoids cause mobilization and redistribution of fats. Actions on fats are:

- i. Mobilization of fatty acids from adipose tissue
- ii. Increasing the concentration of fatty acids in blood
- iii. Increasing the utilization of fat for energy.

On Water Metabolism

Glucocorticoids play an important role in the maintenance of water balance, by accelerating excretion of water. The adrenal insufficiency causes water retention and water intoxication after intake of large quantity of water.

On Mineral Metabolism

Glucocorticoids increase the excretion of potassium.

On Bone

Glucocorticoids stimulate the bone resorption (osteoclastic activity) and inhibit bone formation and mineralization (osteoblastic activity). So, in hypersecretion of glucocorticoids, osteoporosis occurs.

On Muscles

Glucocorticoids increase the catabolism of proteins in muscle.

On Blood Cells

Glucocorticoids decrease the number of circulating eosinophils, basophils and lymphocytes. These hormones increase the number of circulating neutrophils, RBCs and platelets.

On Vascular Response

Presence of glucocorticoids is essential for the constrictor action of adrenaline and noradrenaline.

On Central Nervous System

Glucocorticoids are essential for normal functioning of nervous system.

Permissive Action of Glucocorticoids

Permissive action of glucocorticoids refers to execution of actions of some hormones only in the presence of glucocorticoids.

Examples:

- i. Calorigenic effect of glucagon
- ii. Lipolytic effect of catecholamines
- iii. Vascular effects of catecholamines
- iv. Bronchodilator effect of catecholamines.

Anti-inflammatory Effects

Glucocorticoids prevent the inflammatory reactions. Even if inflammation has already started, the glucocorticoids cause an early resolution of inflammation and rapid healing.

ADRENAL SEX HORMONES

Adrenal sex hormones are secreted mainly by zona reticularis. Adrenal cortex secretes mainly the male sex hormones, which are called androgens.

Androgens secreted by adrenal cortex:

1. Dehydroepiandrosterone
2. Androstenedione
3. Testosterone.

Dehydroepiandrosterone is the most active adrenal androgen. Androgens, in general, are responsible for masculine features of the body. But in normal conditions, the adrenal androgens have insignificant physiological effects, because of the low amount of secretion both in males and females.

In congenital hyperplasia of adrenal cortex or tumor of zona reticularis, an excess quantity of androgens is secreted. In males, it does not produce any special effect because, large quantity of androgens are produced by testes also. But in females, the androgens produce masculine features.

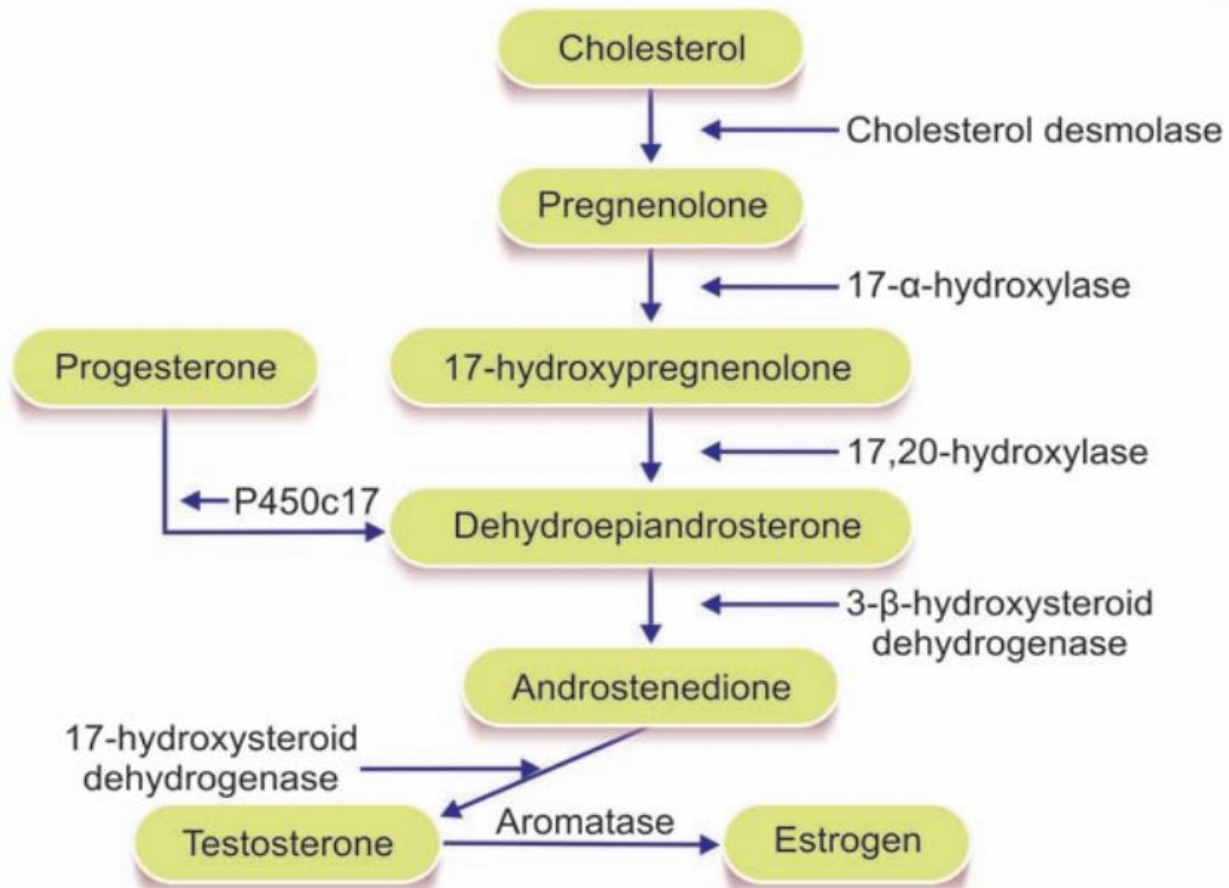


FIGURE 70.8: Synthesis of adrenal sex hormones

HYPERACTIVITY OF ADRENAL CORTEX

Hypersecretion of adrenocortical hormones leads to the following conditions:

1. Cushing syndrome
2. Hyperaldosteronism
3. Adrenogenital syndrome.

CUSHING SYNDROME

A disorder characterized by obesity.

Causes

Cushing syndrome is due to the hypersecretion of glucocorticoids, particularly cortisol. It may be either due to pituitary origin or adrenal origin. If it is due to pituitary origin, it is known as Cushing disease. If it is due to adrenal origin it is called Cushing syndrome.

Pituitary Origin - (ACTH-dependent Cushing syndrome)

Increased secretion of ACTH from pituitary due to tumors, causes hyperplasia of adrenal cortex, leading to hypersecretion of glucocorticoid.

Adrenal Origin- (ACTH-independent Cushing syndrome) In this ACTH secretion is normal.

Cortisol secretion is increased.

Cortisol secretion is increased by:

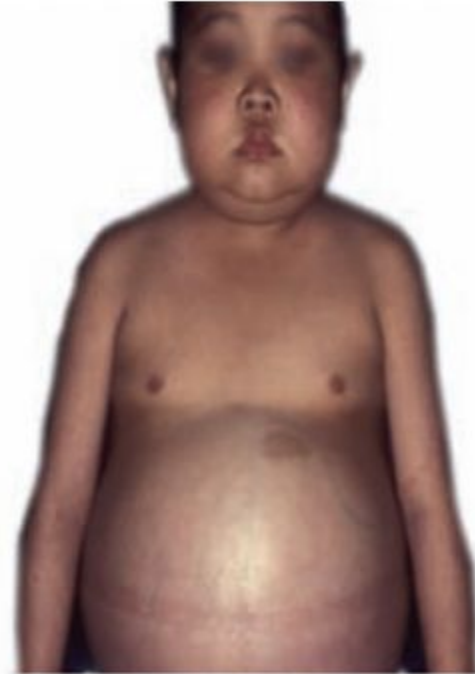
- i. Tumor in zona fasciculata of adrenal cortex
- ii. Carcinoma of adrenal cortex

Signs and Symptoms

- i. Characteristic feature of this disease is the disproportionate distribution of body fat, resulting in some abnormal features:
 - a. **Moon face:** The edematous facial appearance due to fat accumulation and retention of water and salt
 - b. **Torso:** Fat accumulation in the chest and abdomen. Arms and legs are very slim in proportion to torso (torso means trunk of the body)
 - c. **Buffalo hump:** Due to fat deposit on the back of neck and shoulder
 - d. **Pot belly:** Due to fat accumulation in upper abdomen
- ii. **Purple striae:** Reddish purple stripes on abdomen due to three reasons:
 - a. Stretching of abdominal wall by excess subcutaneous fat



Pot belly with
purple striae



Fat deposition in upper
abdomen, thorax and face
(moon face) with thin hands

FIGURE 70.9: Cushing syndrome

iii Thinning of extremities

iv. Thinning of skin and subcutaneous tissues due to protein depletion caused by increased catabolism of proteins

v. Acanthosis: Skin disease characterized by darkened skin patches in certain areas such as axilla, neck and groin

vi. Pigmentation of skin, especially in ACTH- dependent type due to hypersecretion of ACTH which has got melanocyte-stimulating effect

vii. Facial plethora: Facial redness

viii. Hirsutism: Heavy growth of body and facial hair

ix. Weakening of muscles because of protein depletion.

X. Bone resorption and osteoporosis due to protein depletion.

Bone becomes susceptible to easy fracture

xi. Hyperglycemia due to gluconeogenesis (from proteins) and inhibition of peripheral utilization of glucose. Hyperglycemia leads to glucosuria and adrenal diabetes

xii. Hypertension by the mineralocorticoid effects of glucocorticoids – retention of sodium and water results in increase in ECF volume and blood volume, leading to hypertension

xiii. Immunosuppression resulting in susceptibility for infection

xiv. Poor wound healing.

HYPERALDOSTERONISM

Primary Hyperaldosteronism

Primary hyperaldosteronism is otherwise known as Conn syndrome. It develops due to tumor in zona glomerulosa of adrenal cortex. In primary hyperaldosteronism, edema does not occur because of escape phenomenon.

Secondary Hyperaldosteronism

Secondary hyperaldosteronism occurs due to extra adrenal causes such as:

- i. Congestive cardiac failure
- ii. Nephrosis
- iii. Toxemia of pregnancy
- iv. Cirrhosis of liver.

Signs and Symptoms

- i. Increase in ECF volume and blood volume
- ii. Hypertension due to increase in ECF volume and blood volume
- iii. Severe depletion of potassium, which causes renal damage. The kidneys fail to produce concentrated urine. It leads to polyuria and polydipsia Muscular weakness due to potassium depletion.

ADRENOGENITAL SYNDROME

Secretion of abnormal quantities of adrenal androgens develops adrenogenital syndrome.

Causes: Adrenogenital syndrome is due to the tumor of zona reticularis in adrenal cortex.

Symptoms in females

Increased secretion of androgens causes development of male secondary sexual characters. The condition is called adrenal virilism.

Symptoms are:

- i. Masculinization due to increased muscular growth
- ii. Deepening of voice
- iii. Amenorrhea
- iv. Enlargement of clitoris
- v. Male type of hair growth.

Symptoms in males

Sometimes, the tumor of estrogen secreting cells produces more than normal quantity of estrogens in males. It produces some symptoms such as:

- i. Feminization
- ii. Gynecomastia (enlargement of breast)
- iii. Atrophy of testis
- iv. Loss of interest in women.

HYPOACTIVITY OF ADRENAL CORTEX

Hyposecretion of adrenocortical hormones leads to the following conditions:

1. Addison disease or chronic adrenal insufficiency
2. Congenital adrenal hyperplasia.

ADDISON DISEASE OR CHRONIC ADRENAL INSUFFICIENCY

Addison disease is the failure of adrenal cortex to secrete corticosteroids.

Types of Addison Disease

- i. Primary Addison disease due to adrenal cause
- ii. Secondary Addison disease due to failure of anterior pituitary to secrete ACTH
- iii. Tertiary Addison disease due failure of hypothalamus to secrete corticotropin-releasing factor (CRF).

Causes for Primary Addison Disease

- i. Atrophy of adrenal cortex due to autoimmune diseases
- ii. Destruction of the gland because of tuberculosis
- iii. Destruction of hormone-secreting cells in adrenal cortex by malignant tissues
- iv. Congenital failure to secrete cortisol

Signs and Symptoms

- i. Pigmentation of skin and mucous membrane due to excess ACTH secretion, induced by cortisol deficiency. ACTH causes pigmentation by its melanocyte-stimulating action
- ii. Muscular weakness
- iii. Dehydration with loss of sodium
- iv. Hypotension
- v. Decreased cardiac output and decreased workload of the heart, leading to decrease in size of the heart
- vi. Hypoglycemia
- vii. Nausea, vomiting and diarrhea. Prolonged vomiting and diarrhea cause dehydration and loss of body weight
- viii. Susceptibility to any type of infection
- ix. Inability to withstand any stress, resulting in Addisonian crisis .

Adrenal crisis is a common symptom of Addison disease, characterized by sudden collapse associated with an increase in need for large quantities of glucocorticoids.

CONGENITAL ADRENAL HYPERPLASIA

Congenital adrenal hyperplasia is a congenital disorder, characterized by increase in size of adrenal cortex. Even though the size of the gland increases, cortisol secretion decreases.

Symptoms

In boys - Adrenal hyperplasia produces a condition known as macrogenitosomia praecox (Fig. 70.10).

Features of macrogenitosomia praecox: ii. Precocious body growth, causing stocky appearance called infant Hercules

ii. Precocious sexual development with enlarge penis even at the age of 4 years.

In girls - In girls, adrenal hyperplasia produces masculinization. It is otherwise called virilism. The female child is born with external genitalia of male type. This condition is called pseudohermaphroditism.

Thank you





Steroid hormones

Steroid hormones are produced from gonads and adrenal cortex.

Steroid hormones synthesised from cholesterol in smooth endoplasmic reticulum and from mitochondria of endocrine cells. Steroid hormones are lipid soluble and their receptor sites are present in the cytoplasm of target cells. These hormones are not stored in vesicles, as soon as produced diffused into blood stream. They bind carrier protein and travel in blood. On reaching the target cell only the hormone enters the cell.





