ADRENAL GLAND

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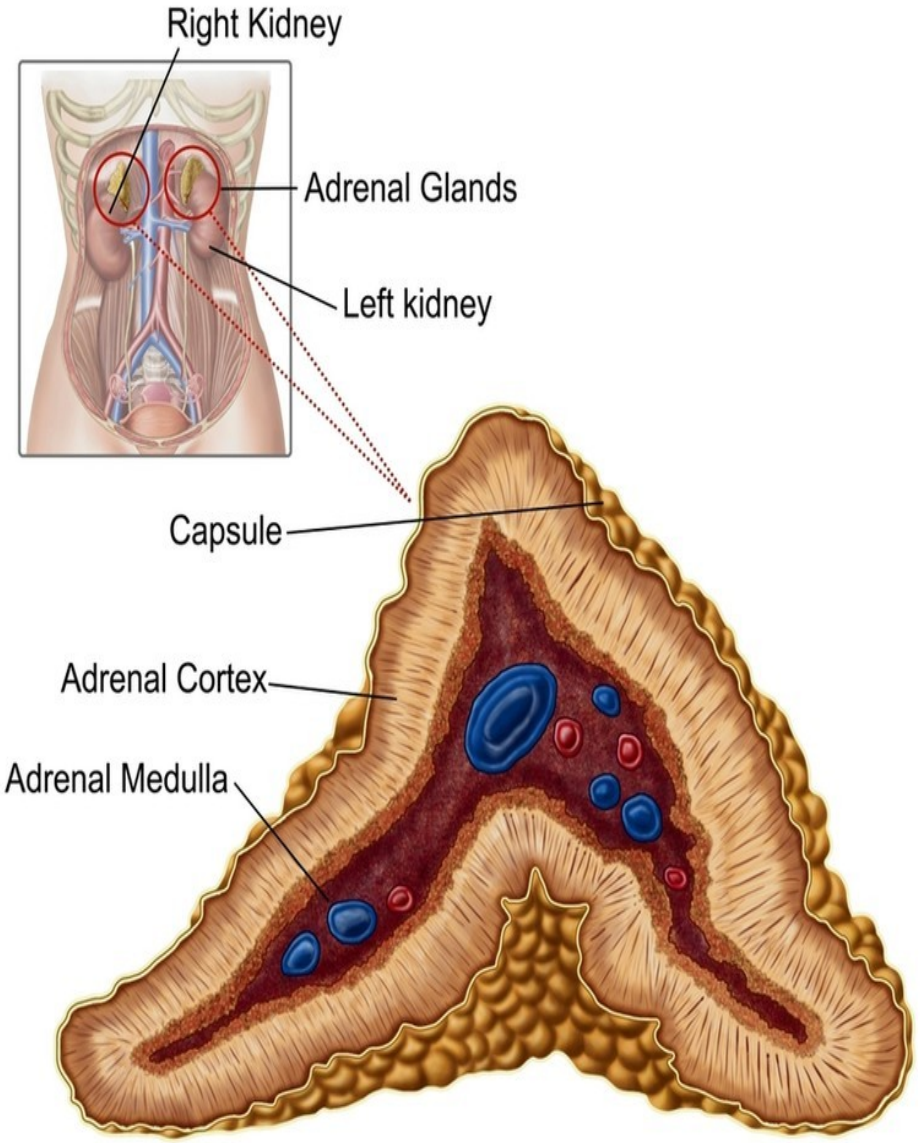
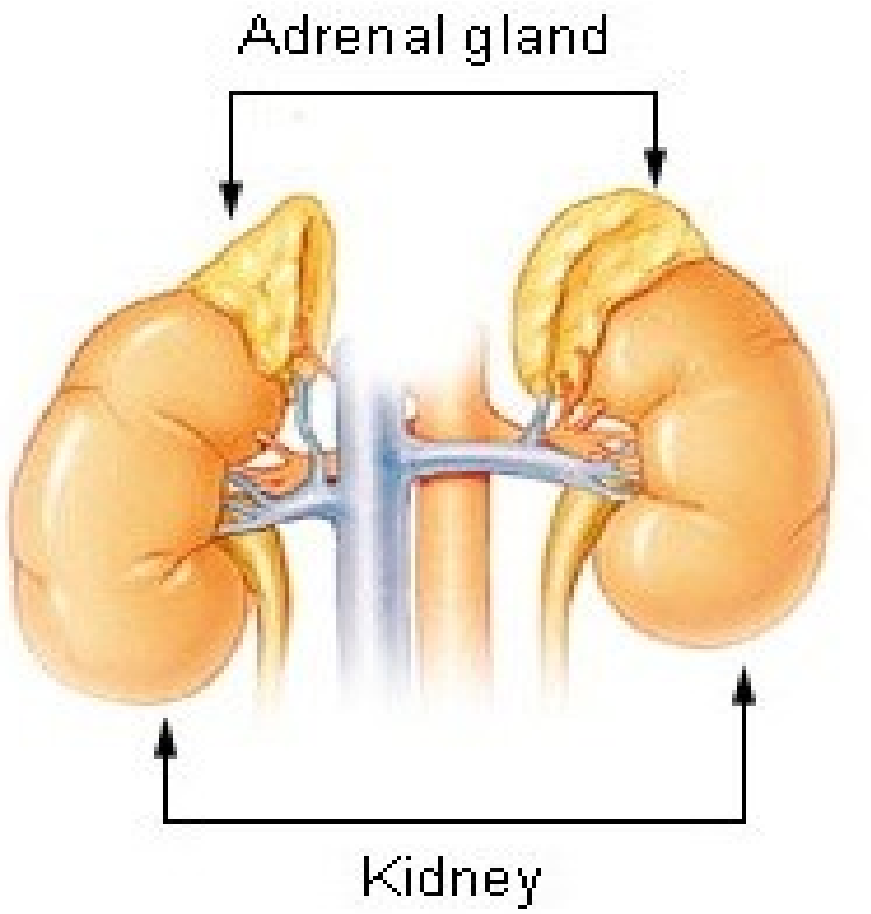
INTRODUCTION

- Adrenal glands are called the 'life-saving glands' or 'essential endocrine glands'.
- It is because the absence of adrenocortical hormones causes death within 3 to 15 days.
- Absence of adrenomedullary hormones, drastically decreases the resistance to mental and physical stress.



FUNCTIONAL ANATOMY OF ADRENAL GLANDS

- There are two parts of adrenal glands.
- It is situated on the upper pole of each kidney.
- Because of the situation, adrenal gland are otherwise called suprarenal gland.
- Each gland weighs about 4 g



PARTS OF ADRENAL GLAND

- Adrenal gland is made of two distinct parts:

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

- These two parts are different from each other in development, structure and functions.

- Adrenal medulla develops from the neural crest, which gives origin to sympathetic nervous system. So, its secretions and functions resemble that of sympathetic nervous system.

- Adrenal cortex develops from the mesonephros, which give rise to the renal tissues. It secretes entirely a different group of hormones known as corticosteroids.

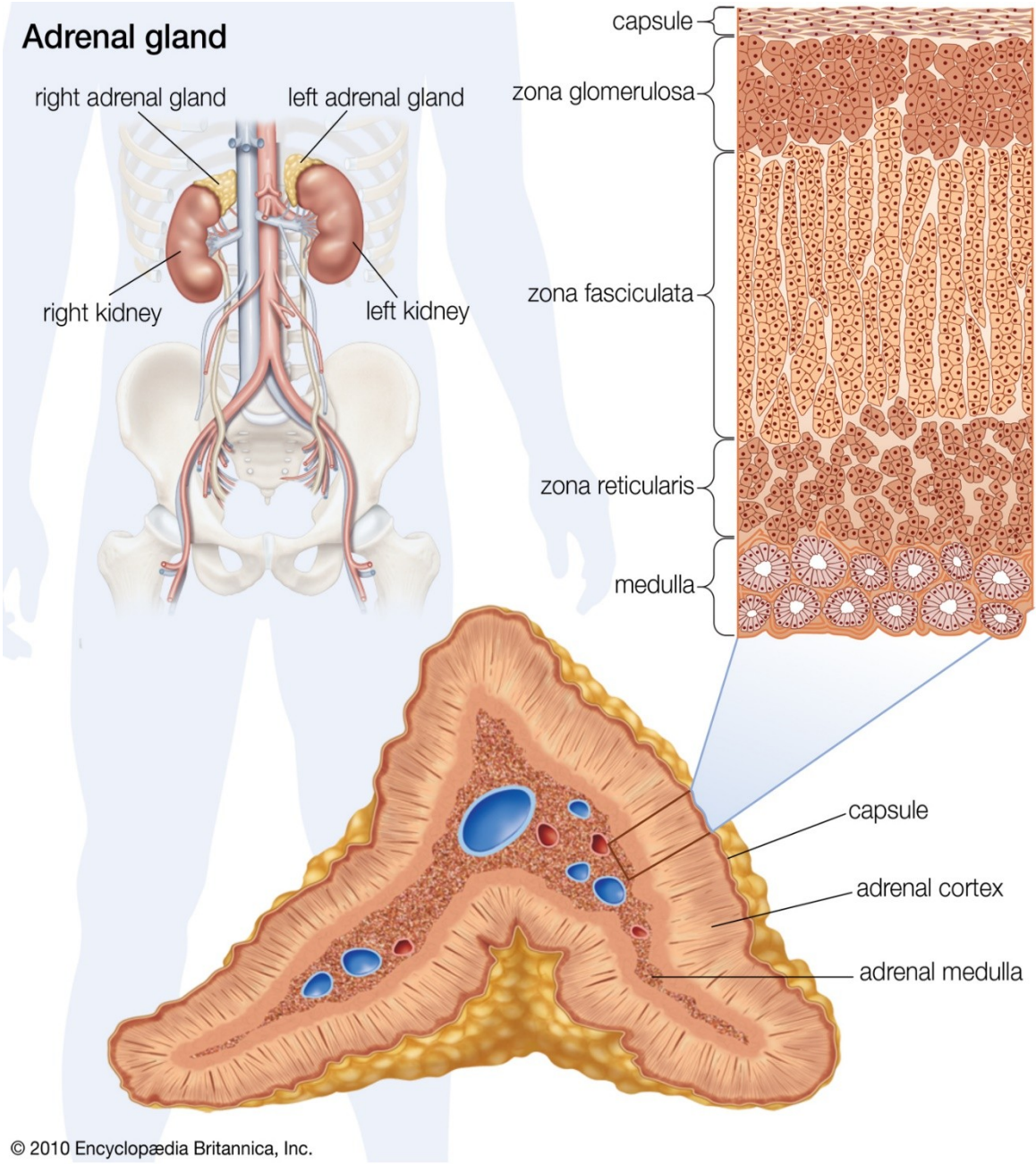
1. ADRENAL CORTEX

HISTOLOGY

- 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 OF ADRENOCORTICAL HORMONES

- Adrenocortical hormones are steroid in nature and are synthesized mainly from cholesterol.
- Small quantity of cholesterol is also synthesized within the cortical cells from acetylcoenzyme A (acetyl-CoA).

TRANSPORT OF ADRENOCORTICAL HORMONES

1. Mineralocorticoids

- These 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.

2. Glucocorticoids

- These are transported by a special plasma protein known as glucocorticoids-binding globulin or transcortin.

3. Sex Hormones

- These are transported by another special plasma protein known as sex hormone-binding globulin.

I. MINERALOCORTICOIDS

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

1. Aldosterone
2. 11-deoxycorticosterone

SOURCE OF SECRETION

- Mineralocorticoids are secreted by zona glomerulosa of adrenal cortex.

CHEMISTRY AND HALF-LIFE

- Mineralocorticoids are C21 steroids having 21 carbon atoms. Half-life of mineralocorticoids is 20 minutes.

FUNCTIONS OF MINERALOCORTICOIDS

- Ninety percent of mineralocorticoid activity is provided by aldosterone.
- Life-saving Hormone Aldosterone is very essential for life and it maintains the osmolarity and volume of ECF.
- It is usually called life-saving hormone because, its absence causes death within 3 days to 2 weeks.
- Aldosterone has three important functions.

It increases:

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

Actions of aldosterone are:

1. On Sodium Ions

- Aldosterone acts on the distal convoluted tubule and the collecting duct and increases the reabsorption of sodium.
- During hyposecretion of aldosterone, the loss of sodium through urine increases 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, it result's in the increase of ECF volume.

3. On Blood Pressure

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

4. On Potassium Ions

- Aldosterone increases the potassium excretion through the renal tubules.
- Hyposecreation of aldosterone leads the potassium ion concentration in ECF increases resulting in hyperkalemia.
- Which leads serious cardiac toxicity, with weak contractions and development of arrhythmia. In very severe conditions, it may cause cardiac death.
- Hypersecreation of aldosterone leads to hypokalemia and muscular weakness.

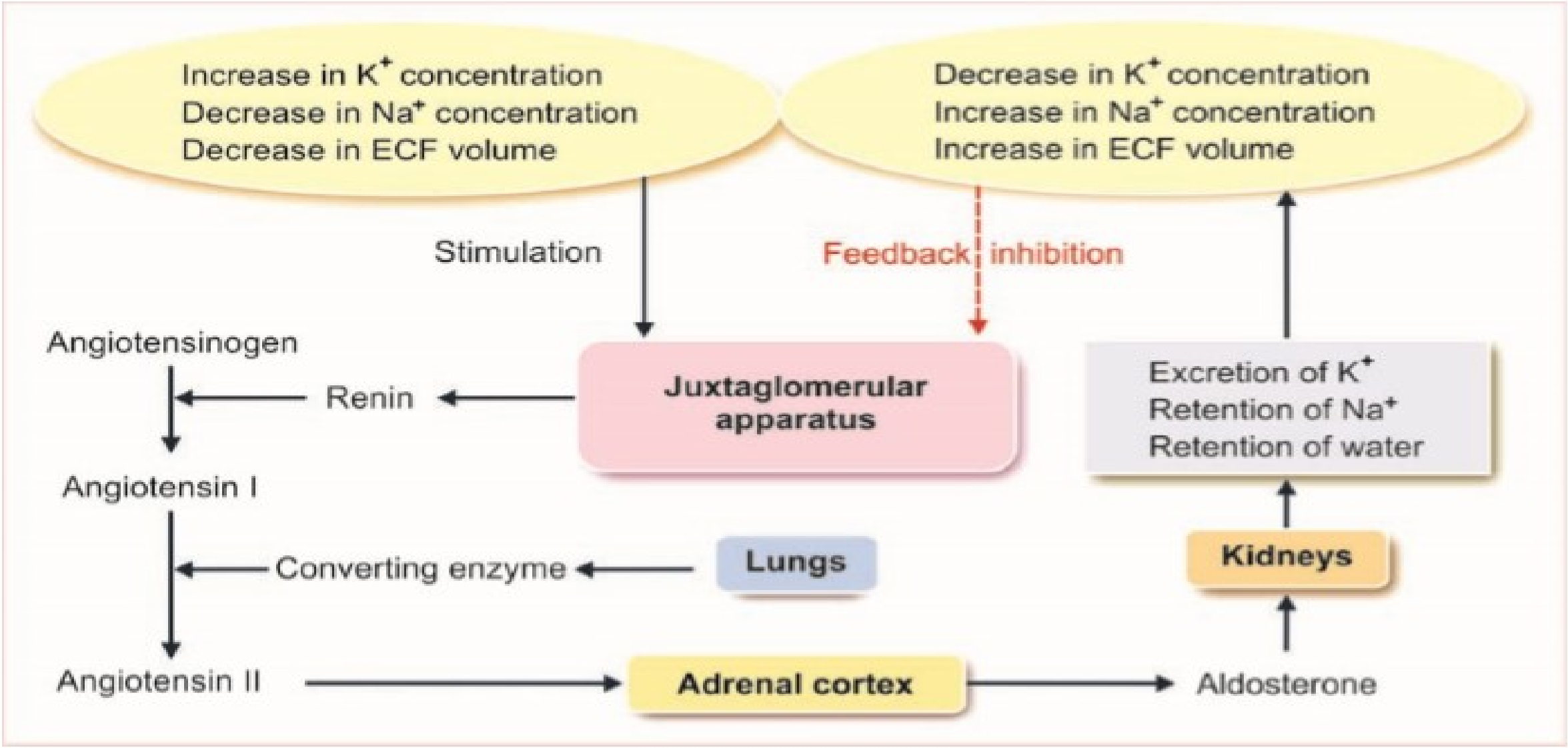
5. On Sweat Glands and Salivary Glands

- Aldosterone has almost the similar effect on sweat glands and salivary glands as it shows on renal tubules.
- 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.

6. 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.

Regulation of Aldosterone Secretion



II. GLUCOCORTICOIDS

- Glucocorticoids act mainly on glucose metabolism.
- Glucocorticoids are:

1. Cortisol
2. Corticosterone
3. Cortisone

SOURCE OF SECRETION

- Glucocorticoids are secreted mainly by zona fasciculata of adrenal cortex.

CHEMISTRY AND HALF-LIFE

- Glucocorticoids are C21 steroids having 21 carbon atoms. Half-life of cortisol is 70 to 90 minutes and that of corticosterone is 50 minutes. Half-life of cortisone is not known.

DAILY OUTPUT AND PLASMA LEVEL

- Daily output and plasma level of glucocorticoids are given in Table.

Hormone	Daily output (µg)	Plasma level (µg/dL)
Cortisol	10.0	13.9
Corticosterone	3.0	0.4

FUNCTIONS OF GLUCOCORTICOIDS

- Cortisol or hydrocortisone is more potent and it has 95% of glucocorticoid activity.
- Corticosterone is less potent, showing only 4% of glucocorticoid activity and rest of 1% activity is shown by Cortisone.

LIFE-PROTECTING HORMONE

- Like aldosterone, cortisol is also essential for life.
- Aldosterone is a life-saving hormone, whereas cortisol is a life-protecting hormone
- Cortisol helps to withstand the stress and trauma in life.
- Glucocorticoids have metabolic effects on carbohydrates, proteins, fats and water.
- Removal of adrenal glands causes disturbances of metabolism.
- Exposure to even mild harmful stress after adrenalectomy, leads to collapse and death.

Actions of Glucocorticoids are:

1. 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 muscles. These amino acids comes into circulation than enter in liver and get converted into glucose.

ii. By inhibiting the uptake and utilization of glucose by peripheral cells:

- This action is called antiinsulin action of glucocorticoids.
- Hypersecretion of glucocorticoids increases the blood glucose level, resulting in hyperglycemia, glucosuria and adrenal diabetes.
- Hyposecretion of these hormones causes hypoglycemia and fasting during adrenal insufficiency will be fatal. It decreases blood glucose level to a great extent, resulting in death.

2. 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. Uptake of amino acids by hepatic cells from blood.
iv. In hepatic cells, the amino acids are used for the synthesis of proteins and carbohydrates (gluconeogenesis).

- In hypersecretion of glucocorticoids, there is excess catabolism of proteins, resulting in muscular wasting and negative nitrogen balance.

3. 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.
iv. It leads to the formation of a large amount of ketone bodies. It is called ketogenic effect of glucocorticoids.

- Hypersecretion of glucocorticoids causes an abnormal type of obesity by increasing the deposition of fat in certain areas such as abdomen, chest, face and buttocks.

4. On Water Metabolism

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

5. On Bones

- Glucocorticoids stimulate the bone resorption (osteoclastic activity) and inhibit bone formation and mineralization.
- Hypersecretion of glucocorticoids, osteoporosis occurs.

6. On Muscles

- Glucocorticoids increase the catabolism of proteins in muscle.
- Hypersecretion causes muscular weakness due to loss of protein.

7. On Blood Cells

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

8. On Central Nervous System

- Glucocorticoids are essential for normal functioning of nervous system.
- Hyposecretion of these hormones causes personality changes like irritability and lack of concentration along with Sensitivity to olfactory and taste stimuli.

9. On Resistance to Stress

- Exposure to any type of stress, either physical or mental, increases the secretion of adrenocorticotropic hormone (ACTH), which in turn increases glucocorticoid secretion.
- Glucocorticoids enhance the resistance to the body against stress by the following ways:

i. Immediate release and transport of amino acids from tissues to liver cells.
ii. Release of fatty acids from cells for the production of more energy during stress.
iii. Prevention of severity of other changes in the body caused by stress.

10. Anti-inflammatory Effects

- Inflammation is defined as a localized protective response induced by injury or destruction of tissues.
- In that condition Glucocorticoids acts as:

i. Inhibiting the release of chemical substances from damaged tissues and thereby preventing vasodilatation and erythema in the affected area.
ii. Causing vasoconstriction, This also prevents rushing of blood to the injured area.
iii. Decreasing the permeability of capillaries and preventing loss of fluid from plasma into the affected tissue.
iv. Inhibiting the migration of leukocytes into the affected area.
v. Suppressing T cells and other leukocytes, so that there is reduction in the reactions of tissues which enhance the inflammatory process.

MODE OF ACTION

- Glucocorticoids bind with receptors to form hormonereceptor complex, which activates DNA to form mRNA. mRNA causes synthesis of enzymes, which alter the cell function.

REGULATION OF SECRETION

- Glucocorticoid secretion regulates by Anterior pituitary and Hypothalamus.

i. Role of Anterior Pituitary

- Anterior pituitary controls the activities of adrenal cortex by secreting ACTH.
- ACTH is mainly concerned with the regulation of cortisol secretion.
- ACTH is necessary for the structural integrity and secretory activity of adrenal cortex.

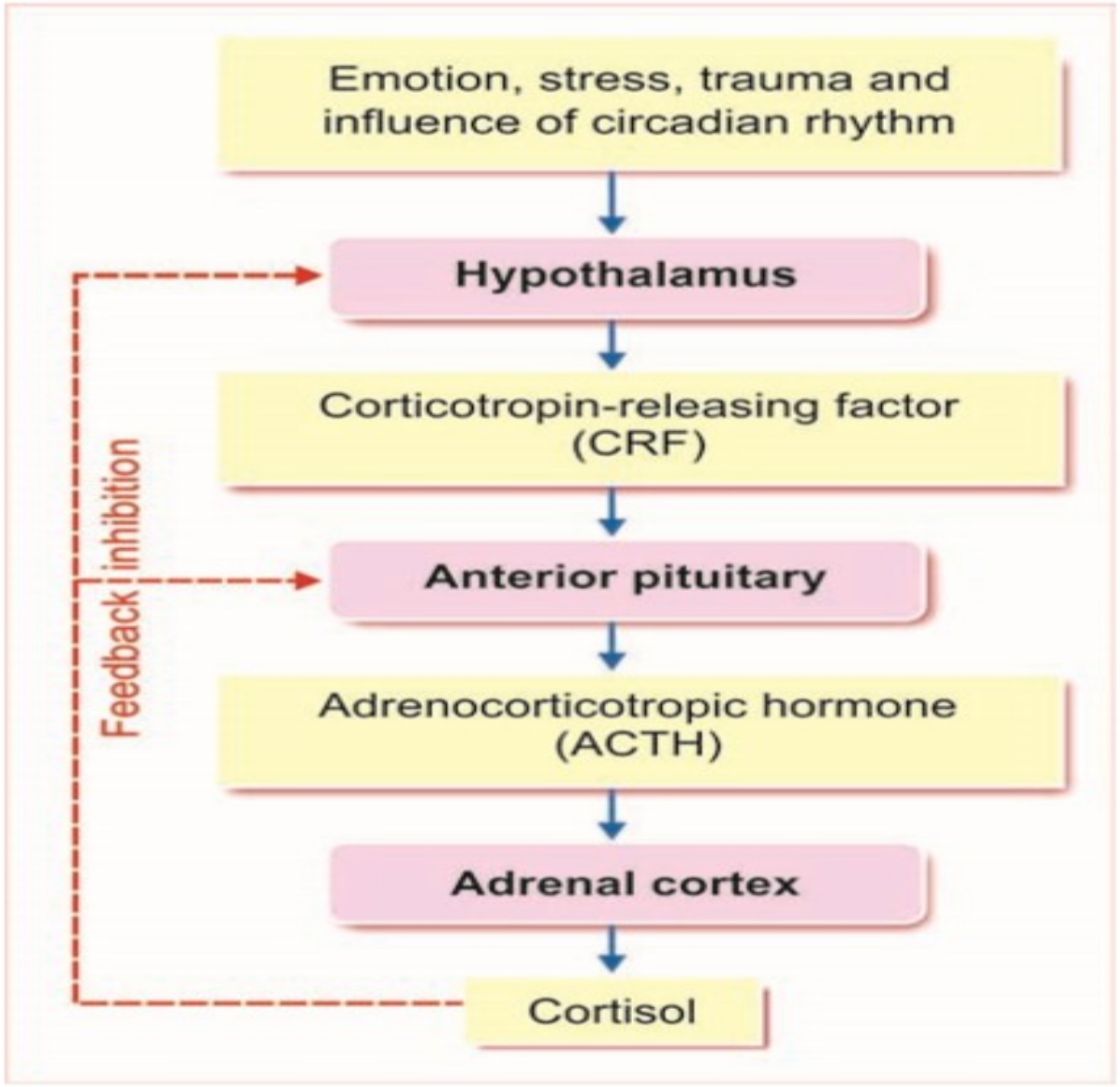
- ACTH Convers cholesterol into pregnenolone, which is the precursor of glucocorticoids. Thus, it is responsible for the synthesis of glucocorticoids.
- Release and prolongation of glucocorticoid action on various cells.

ii. Role of Hypothalamus

- Hypothalamus also plays an important role in the regulation of cortisol secretion.
- It acts by controlling the ACTH secretion through corticotropin-releasing factor (CRF).
- CRF secretion is induced by several factors such as emotion, stress, trauma and circadian rhythm.

iii. Feedback Control

- Cortisol regulates its own secretion through negative feedback control by inhibiting the release of CRF from hypothalamus and ACTH from anterior pituitary



REGULATION OF SECRETION

III. ADRENAL SEX HORMONES

- Adrenal sex hormones are secreted mainly by zona reticularis.
- Adrenal cortex secretes mainly the male sex hormones, which are called androgens.
- Small quantity of estrogen and progesterone are also secreted by adrenal cortex.
- Androgens are:

1. Dehydroepiandrosterone
2. Androstenedione
3. Testosterone

Actions of Androgens:

- Dehydroepiandrosterone is the most active adrenal androgen.
- Androgens, in general, are responsible for masculine features of the body.
- Normally, the adrenal androgens have insignificant physiological effects, because of the low amount of secretion both in males and females.
- The adrenal androgens also exert mild effects in the female, not only before puberty but also throughout life. the growth of the pubic and axillary hair in the female results from the action of these hormones.
- Hypersecretion of adrenal androgens causes no any any special effect in male because, large quantity of androgens are produced by testes also.
- But in females, the androgens produce masculine features.

APPLIED PHYSIOLOGY

HYPERACTIVITY OF ADRENAL CORTEX

- Hypersecretion of adrenocortical hormones leads to the following conditions:

1. Cushing syndrome
2. Hyperaldosteronism
3. Adrenogenital syndrome

1. CUSHING SYNDROME

- Cushing syndrome is a disorder characterized by obesity.

Causes

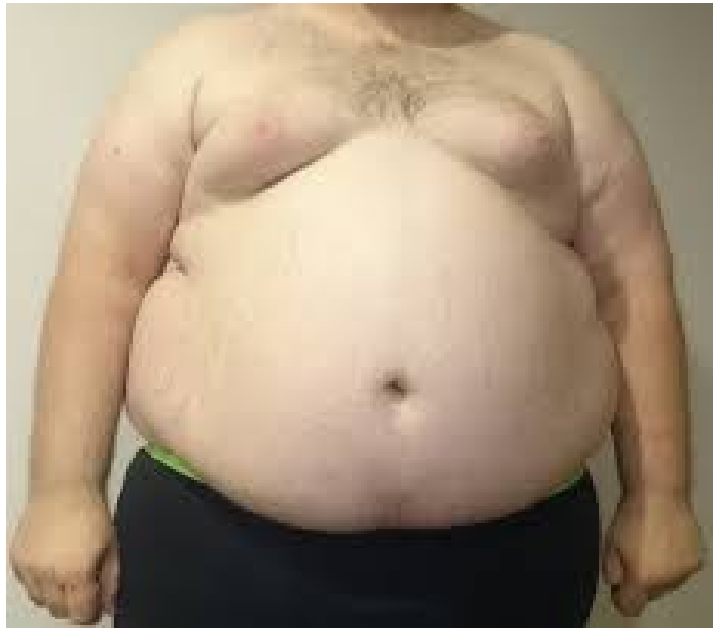
- Cushing syndrome is due to the hypersecretion of glucocorticoids, particularly cortisol.
- It may be either due to pituitary origin or adrenal origin.
- If it is due to pituitary origin, it is known as Cushing disease.
- If it is due to adrenal origin it is called Cushing syndrome.

Signs and Symptoms

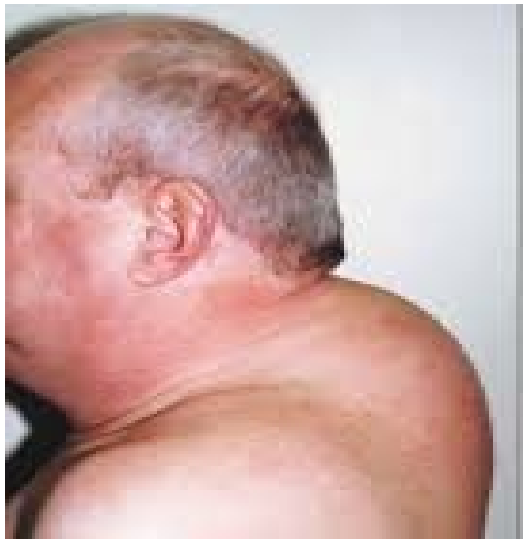
i. Characteristic feature of this disease is the disproportionate distribution of body fat, resulting in some abnormal features:

a. Moon face: The edematous facial appearance due to fat accumulation and retention of water and salt.

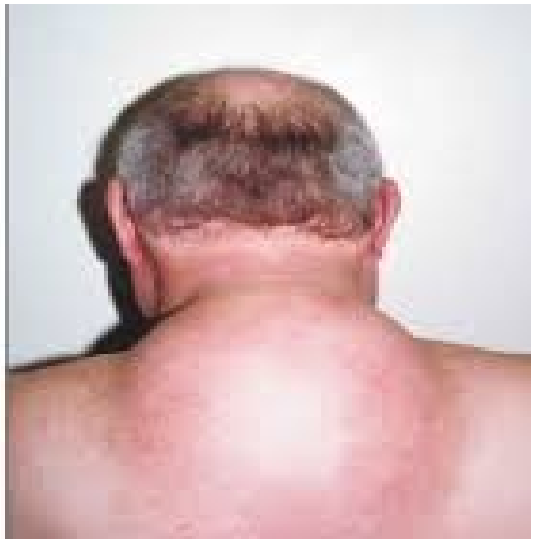
b. Torso: Fat accumulation in the chest and abdomen. Arms and legs are very slim in proportion to torso (torso means trunk of the body).



c. Buffalo hump: Due to fat deposit on the back of neck and shoulder.

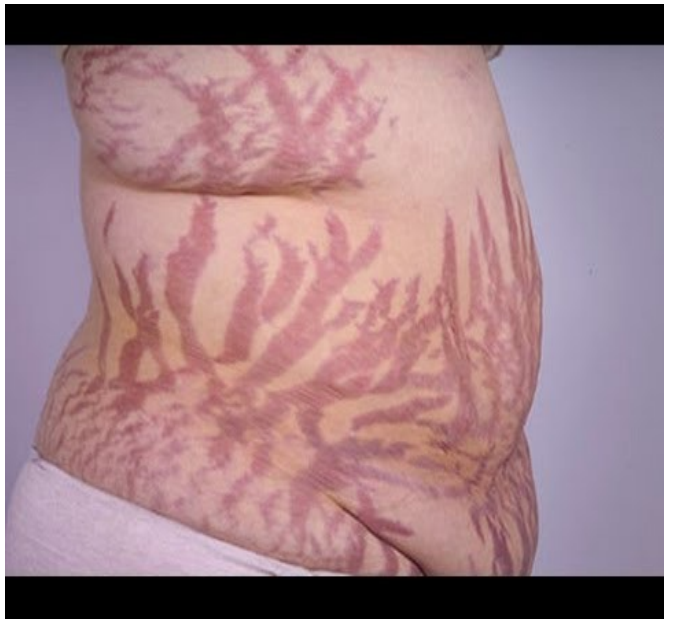


d. Pot belly: Due to fat accumulation in upper abdomen.



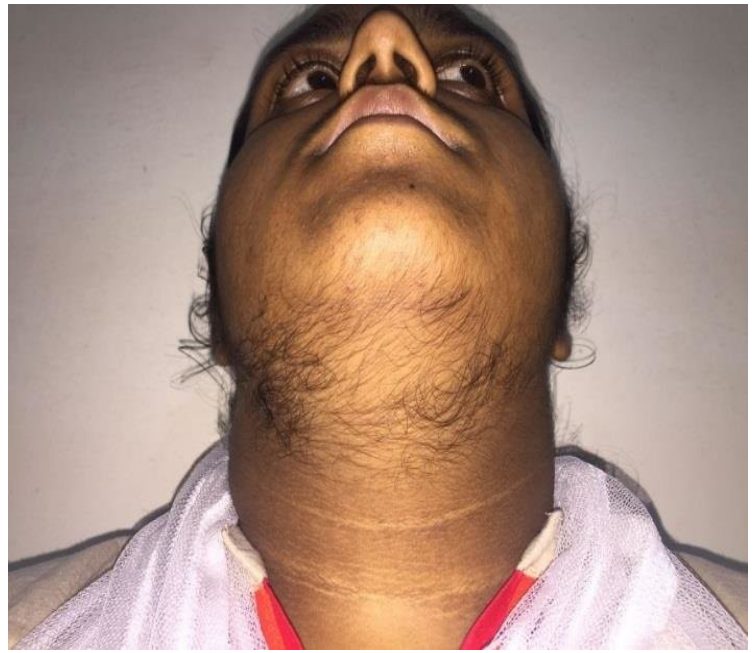
ii. Purple striae: Reddish purple stripes on abdomen due to three reasons:

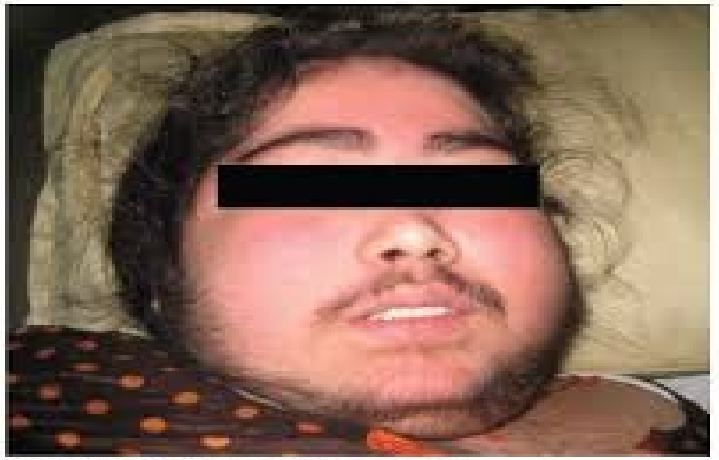
a. Stretching of abdominal wall by excess subcutaneous fat.
b. Rupture of subdermal tissues due to stretching.
c. Deficiency of collagen fibers due to protein depletion.



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

v. Aconthosis: Skin disease characterized by darkened skin patches in certain areas such as axilla, neck and groin.
vi. Facial plethora: Facial redness.
vii. Hirsutism: Heavy growth of body and facial hair.
viii. Weakening of muscles because of protein depletion.
ix. Hyperglycemia: Due to gluconeogenesis (from proteins) and inhibition of peripheral utilization of glucose which leads to glucosuria and adrenal diabetes.





2. HYPERALDOSTERONISM

- Increased secretion of aldosterone is called hyperaldosteronism.

Causes and Types

Depending upon the causes, hyperaldosteronism is classified into two types:

a) Primary hyperaldosteronism

- It was otherwise known as Conn syndrome.
- It develops due to tumor in zona glomerulosa of adrenal cortex. In primary hyperaldosteronism, edema does not occurs.

b) Secondary hyperaldosteronism.

- It is 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.
iv. The kidneys fail to produce concen trated urine. It leads to polyuria and polydipsia.

3. ADRENOGENITAL SYNDROME

- Secretion of abnormal quantities of adrenal androgens develops adrenogenital syndrome.
- Testosterone is responsible for the androgenic activity in adrenogenital syndrome.

Causes

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

Symptoms

- Adrenogenital syndrome is characterized by the tendency for the development of secondary sexual character of opposite sex.

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.

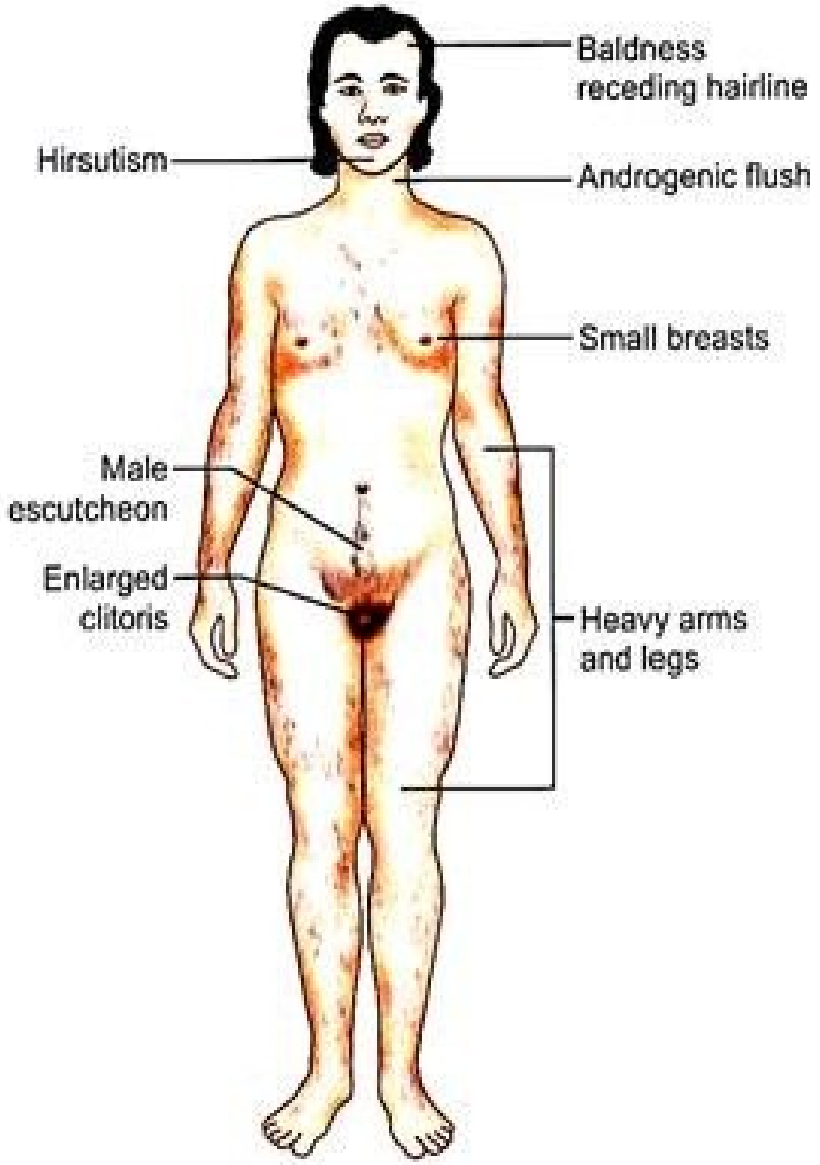


Fig. 6.27: Features of adrenogenital syndrome in a female

Symptoms 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.

1. 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 CRF

Causes for Primary Addison Disease

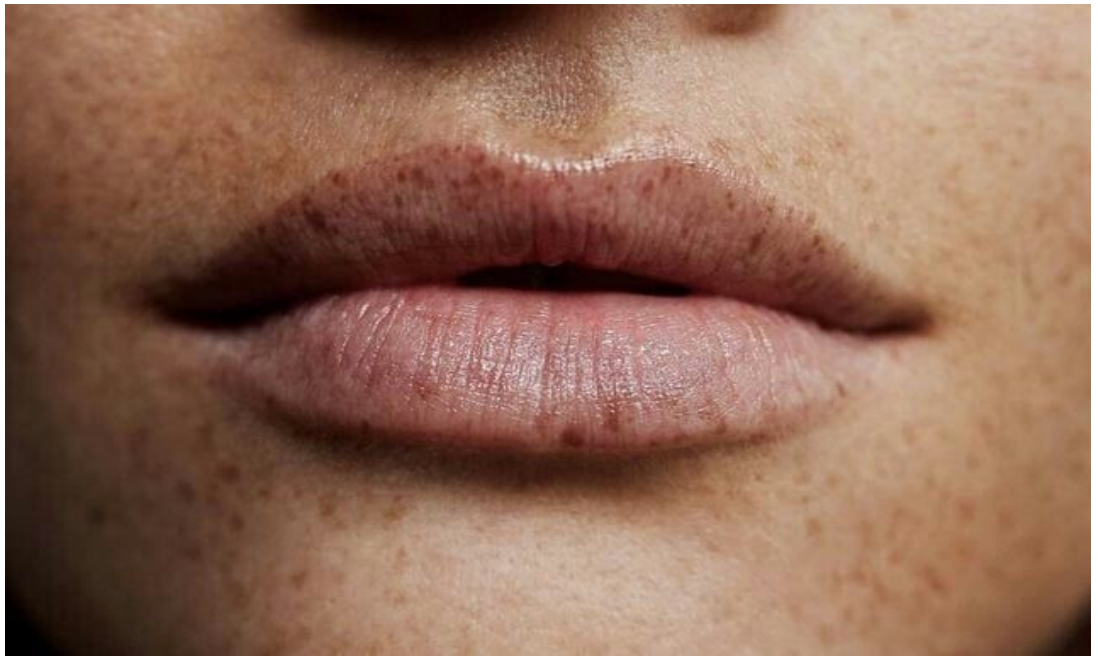
i. Atrophy of adrenal cortex due to autoimmune diseases
ii. Destruction of the gland because of tuberculosis
iii. Destruction of hormone-secreting cells in adrenal cortex by malignant tissues
iv. Adrenalectomy and failure to take hormone therapy.

Signs and Symptoms

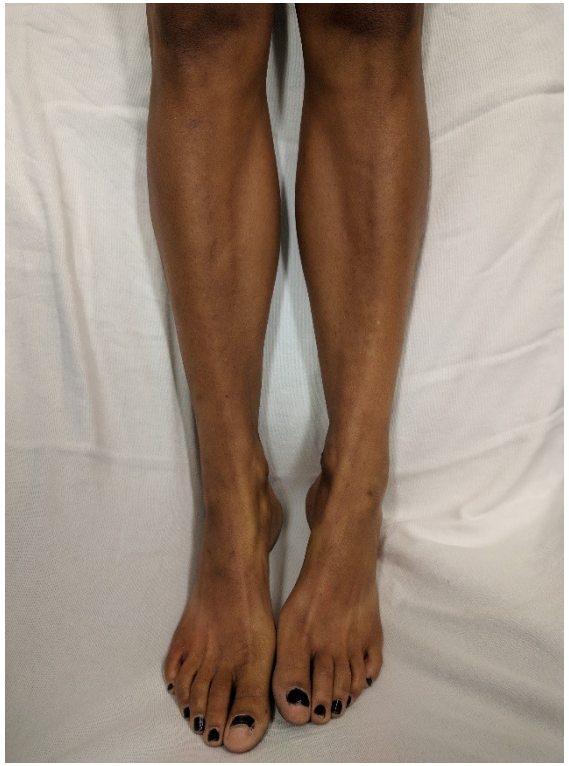
- Signs and symptoms develops due to deficiency of both cortisol and aldosterone.

Common signs and symptom are:

i. Pigmentation of skin and mucous membrane due to excess ACTH secretion, induced by cortisol deficiency.
ii. Muscular weakness
iii. Hypoglycemia
iv. Dehydration and Hypotension due to loss of sodium.



v. Decreased cardiac output leading to decrease in size of the heart.
vi. Nausea, vomiting and diarrhea.
vii. Inability to withstand any stress, resulting in Addisonian crisis.



2. CONGENITAL ADRENAL HYPERPLASIA

- Congenital adrenal hyperplasia is a congenital disorder, characterized by increase in size of adrenal cortex.
- Size increases due to abnormal increase in the number of steroid-secreting cortical cells.

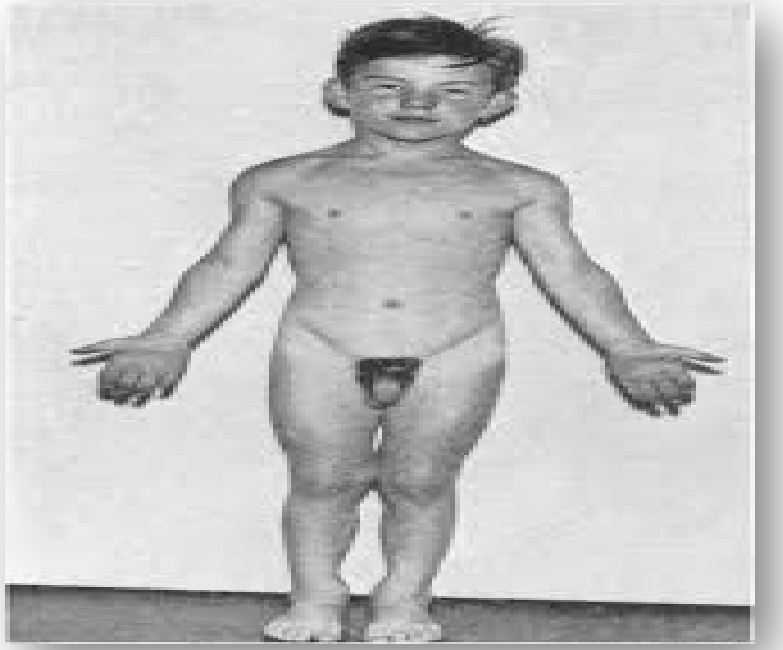
Causes

- Even though the size of the gland increases, cortisol secretion decreases.
- It is because of the congenital deficiency of the 21-hydroxylase enzyme necessary for the synthesis of cortisol.
- Lack of this enzyme reduces the synthesis of cortisol, resulting increase ACTH secretion.
- ACTH stimulates the adrenal cortex causing hyperplasia.
- Therefore, due to the constant simulation of adrenal cortex by ACTH, the secretion of androgens increases.
- It results in sexual abnormalities such as virilism.

Symptoms

i. In boys

- Adrenal hyperplasia produces a condition known as macrogenitosomia praecox.
- Precocious sexual development with enlarged penis even at the age of 4 years.



ii. In girls

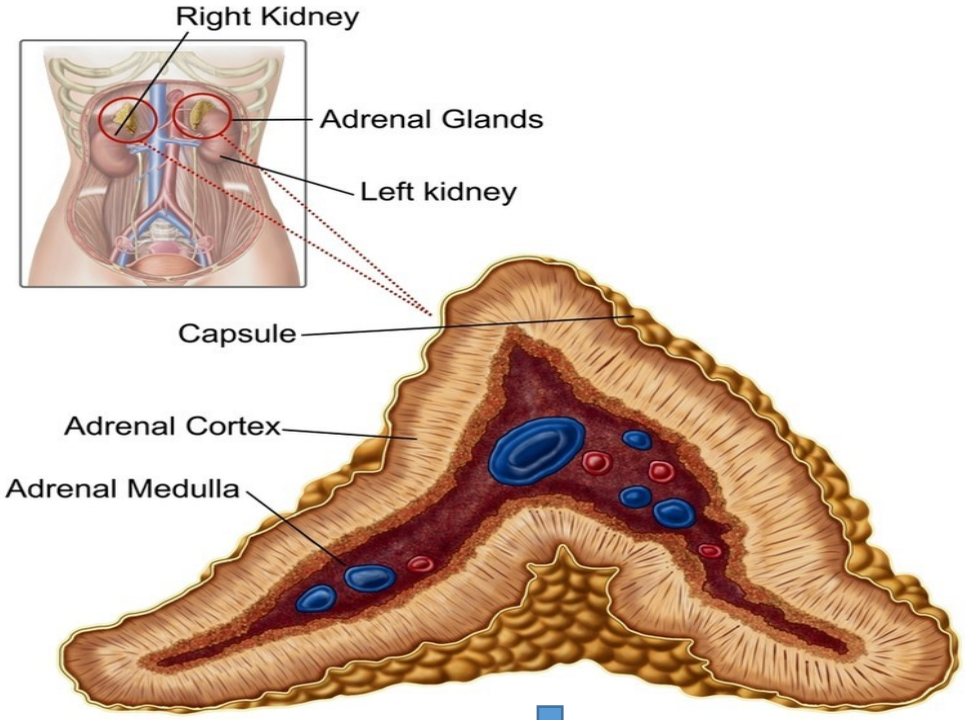
- Adrenal hyperplasia produces masculinization. It is otherwise called virilism.
- In some cases of genetic disorders, the female child is born with external genitalia of male type. This condition is called pseudohermaphroditism.

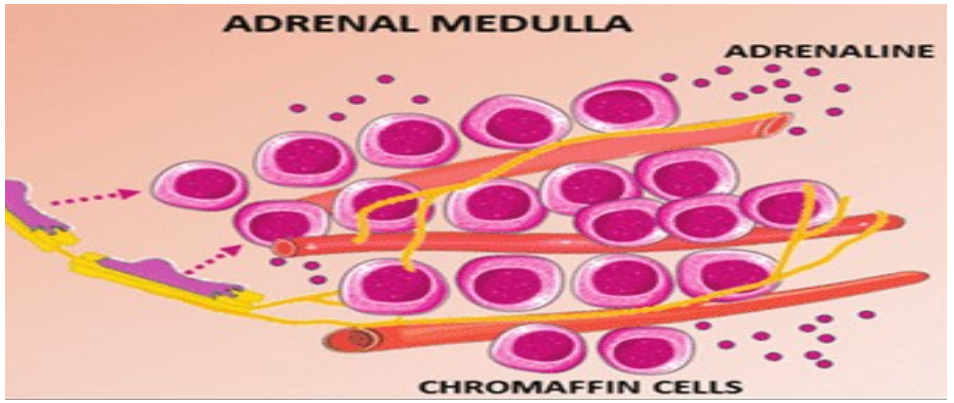
2. ADRENAL MEDULLA

HISTOLOGY

- It is made up of chromaffin cells. These cells also called pheochrome cells or chromophil cells.
- Adrenal medulla is formed by two types of chromaffin cells:

1. Adrenaline-secreting cells (90%)
2. Noradrenaline-secreting cells (10%)





HORMONES OF ADRENAL MEDULLA

- Adrenal medullary hormones are the amines derived from catechol so these hormones are called catecholamines.
- Based on their functions, catecholamines are classified into three groups:

1. Adrenaline or epinephrine
2. Noradrenaline or norepinephrine
3. Dopamine.

PLASMA LEVEL OF CATECHOLAMINES

1. Adrenaline : 3 µg/dL
2. Noradrenaline : 30 µg/dL
3. Dopamine : 3.5 µg/d

HALF-LIFE OF CATECHOLAMINES

- Half-life of catecholamines is about 2 minutes.

SYNTHESIS OF CATECHOLAMINES

- Catecholamines are synthesized from the amino acid tyrosine in the chromaffin cells of adrenal medulla.
- These hormones are formed from phenylalanine also. But phenylalanine has to be converted into tyrosine.

METABOLISM OF CATECHOLAMINES

- Eighty five percent of noradrenaline is taken up by the sympathetic adrenergic neurons.
- Remaining 15% of noradrenaline and adrenaline are degraded.

ACTIONS OF ADRENALINE AND NORADRENALINE

- Adrenaline and noradrenaline stimulate the nervous system.
- Adrenaline has significant effects on metabolic functions and both adrenaline and noradrenaline have significant effects on cardiovascular system.

ACTIONS

- Circulating adrenaline and noradrenaline have similar effect of sympathetic stimulation.
- Effects of adrenaline and noradrenaline on various target organs depend upon the type of receptors present in the cells of the organs.
- Adrenaline acts through both alpha and beta receptors equally. Noradrenaline acts mainly through alpha receptors and occasionally through beta receptors.

1. On Metabolism (via Alpha and Beta Receptors)

- Adrenaline influences the metabolic functions more than noradrenaline.
- Adrenaline increases oxygen consumption and carbon dioxide removal. It increases basal metabolic rate. So, it is said to be a calorigenic hormone.
- Adrenaline increases the blood glucose level by increasing the glycogenolysis in liver and muscle.
- Adrenaline causes mobilization of free fatty acids from adipose tissues.

2. On Blood (via Beta Receptors)

- Adrenaline decreases blood coagulation time.
- It increases RBC count in blood by contracting smooth muscles of splenic capsule and releasing RBCs from spleen into circulation.

3. On Heart (via Beta Receptors)

- Adrenaline has stronger effects on heart than noradrenaline.
- It increases:

i. Heart rate
ii. Force of contraction
iii. Excitability of heart muscles
iv. Conductivity in heart muscles

4. On Respiration (via Beta-2 Receptors)

- Adrenaline increases rate and force of respiration.
- Adrenaline injection produces apnea, which is known as adrenaline apnea. It also causes bronchodilation.

5. On Blood Pressure (via Alpha and Beta Receptors)

- Adrenaline increases systolic blood pressure by increasing the force of contraction of the heart But, it decreases diastolic blood pressure by reducing the total peripheral resistance.
- Noradrenaline increases diastolic pressure due to general vasoconstrictor effect and It also increases the systolic blood pressure to a slight extent by its actions on heart.

6. On Central Nervous System (via Beta Receptors)

- Adrenaline increases the activity of brain. Adrenaline secretion increases during 'fight or flight reactions' after exposure to stress.

ACTIONS OF DOPAMINE

- Dopamine is secreted by adrenal medulla.
- In brain, this hormone acts as a neurotransmitter.
- Injected dopamine produces the following effects:
  1. Vasoconstriction by releasing norepinephrine
  2. Vasodilatation in mesentery
  3. Increase in heart rate via beta receptors
  4. Increase in systolic blood pressure
- Dopamine does not affect diastolic blood pressure.
- Deficiency of dopamine in basal ganglia produces nervous disorder called parkinsonism.

APPLIED PHYSIOLOGY

PHEOCHROMOCYTOMA

- Pheochromocytoma is a condition characterized by hypersecretion of catecholamines.

Cause

- Pheochromocytoma is caused by tumor of chromophil cells in adrenal medulla.
- It is also caused rarely by tumor of sympathetic ganglia (extra-adrenal pheochromocytoma).

Signs and Symptoms

- Characteristic feature of pheochromocytoma is hypertension.
- This type of hypertension is known as endocrine or secondary hypertension.

Other features:

1. Anxiety
2. Chest pain
3. Fever
4. Headache
5. Hyperglycemia
6. Nausea and vomiting
7. Palpitation
8. Polyuria and glucosuria
9. Sweating and flushing
10. Weight loss.

THANK YOU