BIOLOGICAL ACTION OF HORMONES

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ADRENAL CORTEX

produces steroid hormones:

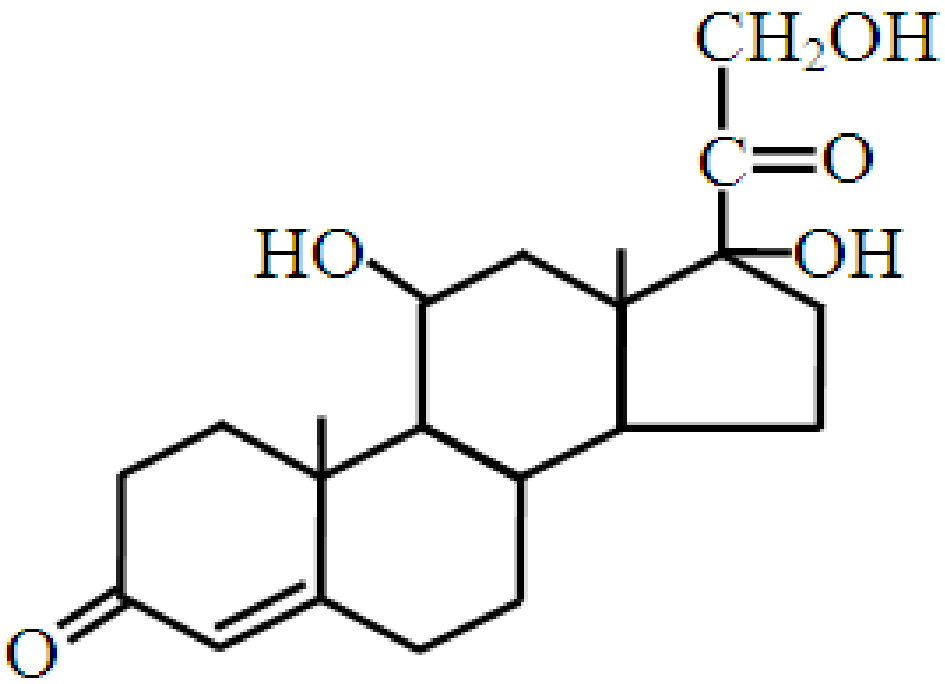
Glucocorticoids

Mineralocorticoids

Male and female sex hormones

- **Glucocorticoids (GCs): cortisol**, cortisone and corticosterone.

Structure of cortisol



- **Target-tissues** for GCs:

LIVER,

muscle,

adipose,

connective, and

lymphoid tissues.

- **In the liver**, GCs ↑ anabolic processes and ↑ transport of substrates into the cell (↑ **permeability** of membranes), and
- **in the other target-tissues** GCs ↑ catabolism and ↓ transport of substrates into the cell (↓ **permeability** of membranes).

Action of glucocorticoids

- 1) on **METABOLISM**
- 2) **SYSTEMIC** action

The effects of GCs on metabolism

- **GCs can influence:**

1) **Carbohydrate metabolism**
2) **Lipid metabolism**
3) **Protein and amino acid metabolism**

The effects of GCs on metabolism

1) Carbohydrate metabolism.

GCs ↓ **glycolysis** in all the target-tissues.

In the **liver**, GCs ↑ **gluconeogenesis** and synthesis of glycogen.

In the **other tissues**, GCs ↓ transport of glucose into the cell (↓ **permeability** of membranes).

The **excess of GCs** ↑ the blood glucose level and may cause **steroid diabetes**.

2) **Lipid metabolism.**

In the **liver**, GCs ↑ synthesis of fats (triacylglycerols), VLDL, and **ketone bodies**.

In the **adipose tissue** GCs ↑ **degradation** of triacylglycerols on the extremities but ↑ **deposition** of the triacylglycerols on the trunk and on the face.

The **excess of GCs** causes the **spider-like obesity**, and ↑ **[ketone bodies]** in the blood.

3) **Protein and amino acid metabolism.**

In the **liver**, GCs ↑ synthesis of protein and ↓ its degradation.

In the **other target-tissues**, GCs ↓ synthesis of protein, ↑ its degradation.

The excess of GCs leads to:

- muscle atrophy and weakness;
- bone fragility and fractures at minimal trauma; slow down of wounds' healing;
- ↑ susceptibility to infections.

Systemic effects of GCs:

1) ↑ **secretion of HCl in the stomach** (GCs ↓ synthesis of prostaglandins which ↓ secretion of HCl). The excess of GCs may cause stomach ulcers.

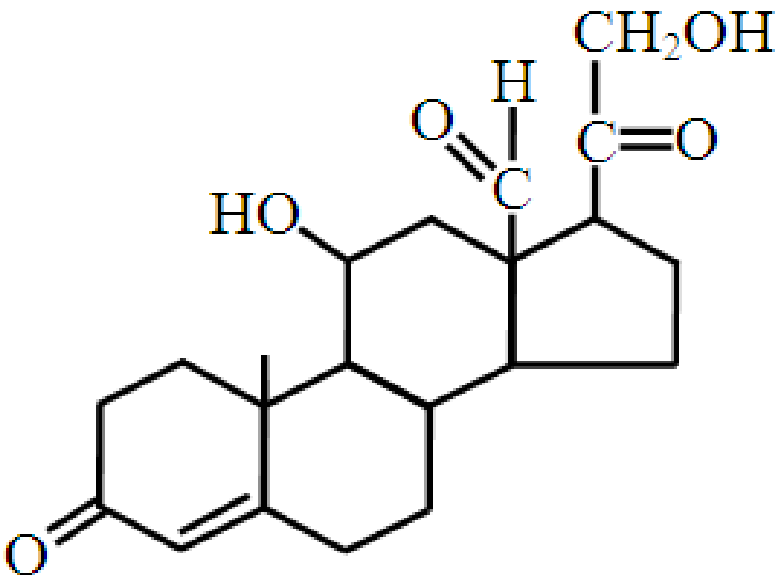
2) GCs **have anti-inflammatory effect** and may be used for treatment of inflammation. (GCs ↓ synthesis of prostaglandins – tissue inflammatory factors).

3) ↓ hypersensitivity of the organism, and may be used for treatment of allergy (e.g. anaphylactic shock).

Mineralocorticoids:

aldosterone and dehydroxycorticosterone regulate metabolism of **Na^+, K^+ and water** in the organism.

Structure of aldosterone



The target-tissue: epithelial cells of the distal renal tubules.

Aldosterone is called **sodium-retaining hormone** because in the kidney it ↑ reabsorption of Na^+ from the urine and ↑ [Na^+] in the blood.

Water follows the flow of Na^+ ⏩ ⏩ the ↑ of the circulating blood volume. The excess of aldosterone ⏩ ⏩ the ↑ BP.

Aldosterone ↑ excretion of K^+ into the urine. The excess of aldosterone leads to the ↓ of $[K^+]$ in the blood ⏩ ⏩ heartbeat impairments, heart failure, and heavy weakness.

Hypercorticoidism

3 types:

- 1) **Glucocorticoid excess** (hyperfunction of *zona fasciculata* of adrenal cortex) **Cushing's syndrome** (malignant adrenal cortex tumor) and **Cushing's disease** (benign enlargement of the adrenal glands).

- 2) **Mineralocorticoid excess** (hyperfunction of *zona arcuata*) - **Konn's disease.**
- 3) **Adrenal virilism**, or adrenogenital syndrome (**hyperproduction of male sex hormones** in *zona reticulata* of adrenal cortex).

In females, this leads to **virilism** (appearance of male signs);

in males, the ↑ of male signs;

in children – premature sex developing (maturation before puberty).

Hypocorticoidism (Addison's disease or bronze disease)

This is hypofunction of the adrenal cortex, ↓ both mineralocorticoids and glucocorticoids.

Symptoms: bronze pigmentation of the skin, weakness, hypoglycemia (hunger intolerance), subconscious preference of salt meals, the ↓ BP.

FEMALE SEX HORMONES

- **ESTROGENS**

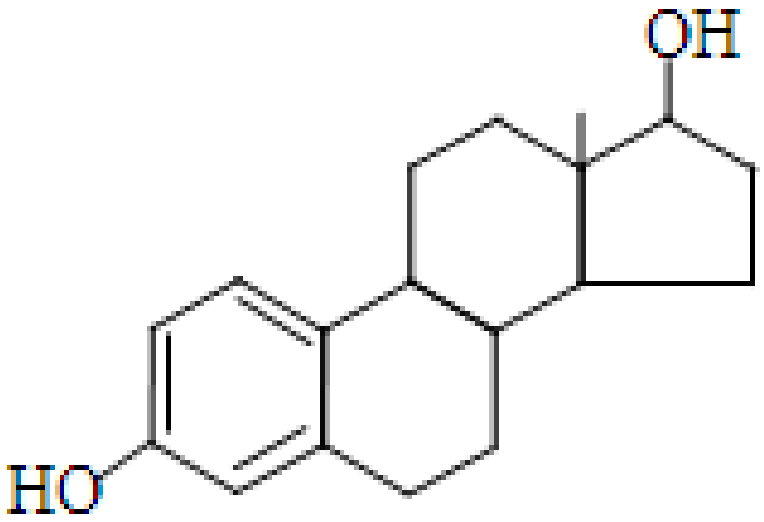
1) estradiol (is formed in ovaries),

2) estriol (in placenta),

3) estrone (in adrenal cortex),

- **PROGESTERON** (is formed by *corpus luteum* of ovaries).

Structure of estradiol



The target-tissues and effects:

- **sex organs –** development and functioning of sex organs;
- **non-sex organs:**

1) **CNS:** formation of sexual behaviour, instinct, and psychical status of a female.
2) **Bones, larynx:** formation of the female type of the skeleton, larynx and voice.

Estrogens ↑ ossification of epiphyses where the growth zone of the bone is located.

In a girl, lack of estrogens may cause tall height.

In women, **excess** of estrogens ↑ deposition of Ca in the bone cavities where the red bone marrow is located; therefore **anemia** may take place.

3) Skin – ↑ growth of hair on the female type, ↓ hair growth on the trunk and face, ↓ secretory activity of the sebaceous glands.

4) Adipose tissue – ↑ synthesis of triacylglycerols, promote formation of the typically female fat depositions.

5) Kidney – estrogens ↑ retaining of Na^+ in the organism, progesterone ↑ excretion of Na^+ into the urine. In pregnancy (much progesterone) the loss of Na^+ with the urine explains the subconscious preference of the salt food.

6) Liver. Estrogens ↑ synthesis of:

a) **blood clotting factors** (II, VII, IX, X) and **angiotensinogen**;

excess of estrogens may cause **thromboses** and **hypertension (↑BP).**

b) VLDL and HDL;

VLDL transfer triacylglycerols from the liver to adipose tissue, therefore, in female, muscles are always covered by the layer of subcutaneous adipose tissue.

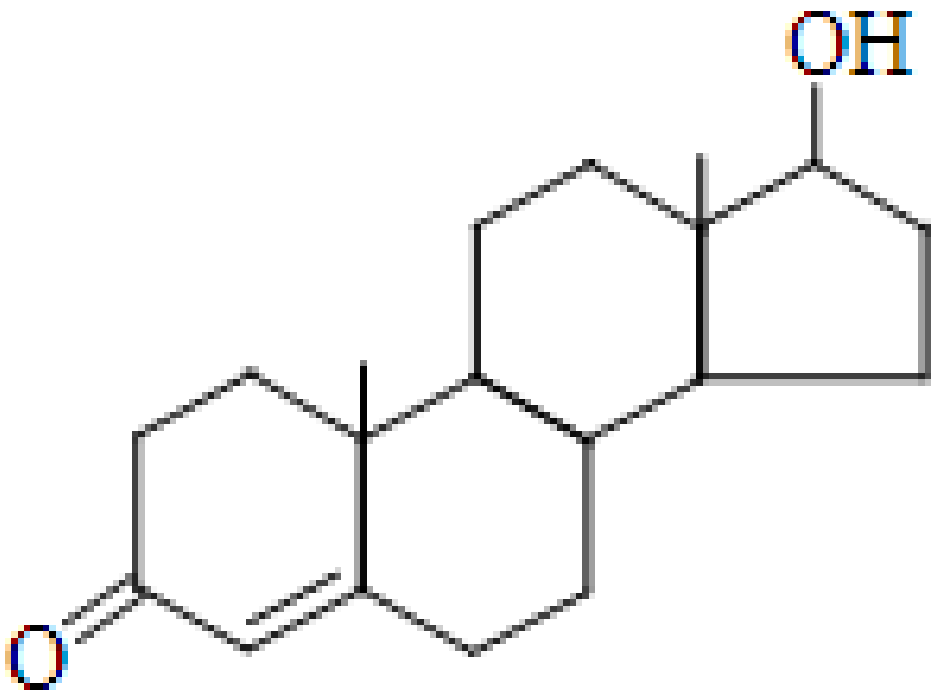
HDL remove cholesterol off the organism; therefore atherosclerosis and myocardial infarction (as consequences of the increased cholesterol level in the blood) are more often observed in men than in women.

MALE SEX HORMONES (androgens):

testosterone and **androsterone**.

They are formed in testes, adrenal cortex, prostate gland.

Structure of testosterone



The target-tissues and effects:

- **sex organs** – the hormones exert **androgenic effect** (development and functioning of sex organs).
- **non-sex organs:**

1) **CNS:** formation of sexual behaviour, instinct, and psychical status of a male. Excess of androgens may cause aggressiveness.

2) Bones, larynx: formation of the male type of the skeleton, larynx and voice.

Androgens ↑ ossification of epiphyses (the growth zone of the bone).

The **excess** of androgens may lead to the **short height**.

3) **Muscles –** ↑ synthesis of protein in the skeletal muscle, its mass and strength.

4) **Adipose tissue –** ↓ synthesis of triacylglycerols and ↑ their degradation; therefore in men the subcutaneous fat layer is thinner than in women.

5) Skin – ↑ growth of hair on the male type, stimulate hair growth on the trunk and face, pigmentation of the skin, secretory activity of the sebaceous glands. Excess of androgens may be a reason of baldness (the absence of hair on the head).

GROWTH HORMONE, its action

1) Anabolic effect. GH ↑ synthesis of nucleic acids and proteins in bones, cartilages, and soft tissues.

2) Diabetogenic effect. In the liver, GH ↑ gluconeogenesis. In the muscle and adipose tissue, GH ↓ **membrane permeability** for glucose to enter the cell. Excess of GH leads to the **insulinoresistancy** of peripheral tissues and results in **somatotropic diabetes**.

3) **Lipolytic effect.** In children, the adipose stores are absent because in the adipose tissue GH ↑ cleavage of triacylglycerols. Due to lipolytic effect and further utilization of fatty acids, in excess of GH, the ↑ amount of **ketone bodies** is produced in the liver and their concentration in the blood ↑.

Hypersecretion of GH

In childhood, this leads to **gigantism:** excessive height, the extremities are disproportionally long.

In adults, this results in **acromegaly:** intensive enlargement of individual parts of the skeleton bones (superciliary archs, cheekbones, jaw and chin), enlargement of the soft tissues of the face (lips, nose, tongue). Hands and feet are also abnormally large.

Hyposecretion of GH (dwarfism)

in childhood leads to the proportional underdevelopment of the skeleton and the whole body. Unlike in cretinism, no psychic abnormalities and no skeletal deformations.

ACTH: target tissues and effecs

1) adrenal cortex – ↑ synthesis and secretion of **glucocorticoids** and (to less extent) mineralocorticoids;
2) adipose tissue – ↑ cleavage of triacylglycerols;
3) liver – ↑cleavage of glycogen.

PROSTAGLANDINS AND OTHER EICOSANOIDS

This is a group of local, or tissue hormones, or hormone-like substances, because unlike “real” hormones that are synthesized in one type of organs but act in the other one, **eicosanoids are both formed and act at the same tissues**. These substances are called **eicosanoids** because they are produced from **eicosatetraenoic**, or arachidonic, acid.

Prostacyclins dilate arteries, ↓ aggregation of platelets.

Thromboxanes cause vasoconstriction and ↑ aggregation of platelet.

Leukotrienes take part in inflammation, allergic reactions, and immune response, attract leucocytes to the place of inflammation, constrict bronchi, and ↑ secretion of bronchial mucus.

Prostaglandins are synthesized in all cells excepting erythrocytes, and degraded very quickly – **in 20 minutes**.

Major classes of prostaglandins which have clinical importance:

- **Prostaglandins E**
- **Prostaglandins F**

Prostaglandins E:

1) ↓ cleavage of triacylglycerols and glycogen;
2) are the **tissue inflammatory factors**; ↑ permeability of vessels and cell membranes, dilate capillaries; they are **pyrogenic** agents, i.e. they ↑ the body t° ; therefore **aspirin** (as an **inhibitor of prostaglandin synthesis**) is used to ↓ t°.
3) cause **pulsating headache**, which may be revealed in 20 minutes by the administration of aspirin;

4) ↓ BP, therefore they are used in treatment of hypertension;

5) dilate bronchi, therefore may be used in treatment of bronchial asthma;

6) ↓ secretion of HCl in the stomach, therefore are used in the therapy of ulcers (aspirin and glucocorticoids ↓ synthesis of prostaglandins which ↓ HCl secretion; therefore the improper use of aspirin or the prolonged therapy with glucocorticoids may lead to ulcers in the stomach);

Prostaglandins F:

- stimulate peristalsis of the bowel;
- constrict bronchi;
- stimulate the smooth muscle of the uterus, therefore they are used for infant delivery.

THE USE OF HORMONES IN MEDICAL PRACTICE

1) Replacement therapy. Hormones are used in hypofunction of endocrine glands:

- vasopressin is used in diabetes insipidus;
- insulin – in diabetes mellitus;
- thyroxine – in hypofunction of thyroid gland (hypothyroidism);
- growth hormone – in hypophyseal dwarfism;
- glucocorticoids are used in hypocorticoidism;
- mineralocorticoids – in Addison's disease;
- estrogens – in hypofunction of ovaries;
- androgens – in hypofunction of testicles.

THE USE OF HORMONES IN MEDICAL PRACTICE

2) The use of mechanisms of hormonal action on biological processes and functions:

- oxitocin is used for the stimulation of labour;
- adrenalin – for the increase of the decreased blood pressure;
- glucocorticoids – are used as anti-inflammatory drugs, antiallergic drugs and immunosuppressors (tratment of autoimmune diseases, anaphylactic shock, allergy, in transplantation of organs to suppress the immune response);

THE USE OF HORMONES IN MEDICAL PRACTICE

- sex hormones – for the treatment of some hormone-dependent tumors (estrogens – for the treatment of prostate cancer, androgens – for the treatment of mammary gland cancer);
- prostaglandins E are used in arterial hypertension, bronchial asthma, gastric ulcer, prostaglandins F – for stimulation of the infant delivery.

THE USE OF HORMONES IN MEDICAL PRACTICE

3) The use of analogues of hormones:

- oral contraceptive pills are derivatives of female sex hormones;
- anabolic steroids (derivatives of male sex hormones) are used as therapeutic agents at small doses, in patients over 35, for the increase of body weight, stimulation of appetite, improvement of wounds healing during recovery period after heavy trauma, operations, myocardial infarction.