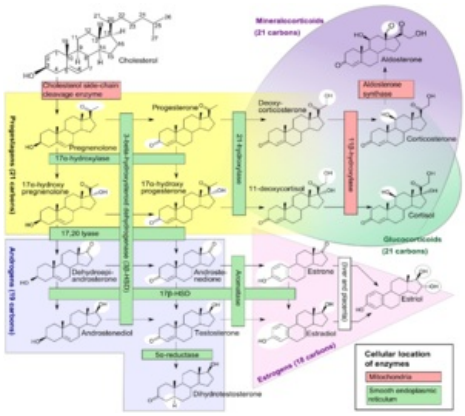
Glucocorticoids structure

This article has been translated from WikiSkripta; ready for the **editor's review**.

Glucocorticoids are steroid hormones. In the human body, they are produced mainly in the **zona fasciculata of the cortex' adrenal glands**. The most important of them is **cortisol**, or hydrocortisone, which has an essential function in metabolism. In the case of a large deficiency, the organism dies. The main function of glucocorticoids is the effect on the metabolism of carbohydrates, proteins and lipids.



Schematic of steroidogenesis.

Chemical Structure and Metabolism

The chemical basis of glucocorticoids, as well as other steroids, is a **sterane core'** (*cyclopentanoperhydrophenanthrene*) composed of 17 carbons. In the adrenal glands, it is formed from cholesterol, which is enzymatically converted into **pregnenolone**; this action affects ACTH, from the adenohypophysis. Cortisol and other steroids are gradually formed from pregnenolone.

Fate in the organism

Cortisol is released from the adrenal cells into the bloodplasma, where it is reversibly bound to plasma globulin - **transcortin**, plasma albumin and part is free in blood plasma and has a biological effect. Depending on the current needs of the organism, the ratio of bound and free hormone changes. Through the blood, glucocorticoids reach the whole organism, enter the cytoplasm of the target cells, where they act. Glucocorticoids can be absorbed from the skin and mucous membranes.

The formation of cortisol in the adrenal glands is influenced by the brain centers of the pituitary gland and the hypothalamus according to the classic formula: The hypothalamus produces the activating substance CRH, which acts on the pituitary gland → the pituitary gland produces ACTH, which acts on the adrenal glands → the adrenal glands begin to produce increased concentrations of cortisol. Cortisol then reverses the production of ACTH in the pituitary gland.

Effect and its mechanism

Glucocorticoids enable preferential energy utilization of proteins and fats. They have a catabolic effect in muscle, bone and adipose tissue, but in the liver they have an anabolic effect, increasing the synthesis of glucose and glycogen .

Effect on Scheme of Cortisol Synthesis

1. **intermediate metabolism**
2. **mesenchymal tissue**
3. **blood cells**
4. **muscles and bones**
5. **psychic**

Effect on intermediary metabolism

Mainly cortisol has an effect on the metabolism of carbohydrates, because it reduces the utilization of glucose in the periphery, so it has a hyperglycemic effect. It increases the formation of glycogen and its storage in the liver. It promotes gluconeogenesis from proteins, thereby also increasing glycemia. The main catabolic effect is the breakdown of proteins and the reduction of their formation. It causes a redistribution of lipids, increasing fat deposition in the abdomen, back and face at the expense of the limbs.

Effect on mesenchymal tissue

Glucocorticoids reduce the migration, proliferation and excretion of immunologically active substances, they have an anti-inflammatory effect. This effect is used in the treatment of inflammation, but without removing the cause. They also have an anti-allergic and immunosuppressant effect, as it suppresses immune reactions and shrinks lymph nodes.

Effect on blood cells

Cortisol decreases the number of lymphocytes, monocytes, eosinophils and other leukocytes, but increases the number of erythrocytes, which is probably caused by reduced phagocytosis.

Effect on muscles and bones

Because glucocorticoids have a catabolic effect mainly on protein metabolism, they slow down the formation and growth of bones and muscles. It is mainly caused by the degradation of proteins and their reduced production.

Psyche effect

Elevated glucose levels cause symptoms of euphoria and joy. However, administration of glucocorticoids in therapeutic doses can be complicated by the development of depression or other psychotic disorders.

Diseases associated with glucocorticoids and their use

Due to the multiple physiological effects of glucocorticoids in the body, side effects often occur. The intensity and occurrence of side effects depend on the dose, type of preparation and duration of use. The use of glucocorticoids for immunosuppression and antiphlogistic treatment can cause:

- **reduced response to infection or tissue damage**,
  - frequent bacterial, viral, fungal infections,
  - severe to fulminant course of infectious diseases,
  - activation of latent diseases,
  - wound healing complications,
- **reduced synthesis of hormones of the adrenal cortex**,
  - slowed or extinguished reaction of the organism to stress,
  - rebound phenomenon – acute cortical insufficiency occurs after discontinuation of long-term corticosteroids,
- **metabolic effects**,
  - iatrogenic Cushing's syndrome,
  - retarded growth in children,
  - tendency to hyperglycemia,
  - skin atrophy (especially at the site of administration),
  - muscle atrophy and muscle weakness,
  - osteoporosis,
  - risk of avascular necrosis of the femoral head,
  - increased risk of cataract occurrence,
  - increased intracranial pressure,
  - increased blood clotting,
  - menstrual disorders.

Usage

Covered the criterion for choosing a given glucocorticoid is its ratio between glucocorticoid and mineralocorticoid activity.

Substitution therapy

In case of insufficiency of the adrenal cortex, the smallest possible doses of glucocorticoids are used (30 mg of hydrocortisone/day - 2/3 of the dose in the morning, 1/3 of the dose in the evening) with a mineralocorticoid (0.05 - 0.3 mg of fludrocortisone/day). If the patient is exposed to stress and strain, these doses must be increased.

Anti-inflammatory and immunosuppressive therapy

Glucocorticoids have excellent *antiphlogistic and immunosuppressive effects*, they are mainly used for inflammations arising on an immunological basis. Synthetic glucocorticoids, which are more effective than hydrocortisone, are necessary. In non-endocrinological diseases, it suppresses the symptoms of the disease, but does not treat the cause itself, therefore the process can progress even while masking clinical manifestations. For this reason, it is necessary to consider whether the effect of use outweighs the possible risks. For life-threatening conditions, the use of large doses is necessary, otherwise we try to use the lowest possible doses.
We also use glucocorticoids in the long-term treatment of asthma bronchiale, allergic rhinitis and COPD caused by chronic bronchitis or emphysema.

Chemotherapy

Due to their immunosuppressive effect, glucocorticoids are also widely used in hematology. They are part of therapeutic protocols (drug combinations) to increase the chemotherapeutic effect. They are also used in the therapy of immune-related cytopenia (idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia).

Application Methods

- **Parenteral application** (intramuscular, intravenous) – does not necessarily mean a faster onset of action (intracellular influence of transcription takes about 8 hours from application).
- **Oral application**.
- **Local application** (including injection, aerosol, drops, creams and other external applications),
  - with short-term use, it has a minimal risk of systemic side effects,
  - for local use, the following are most often used: **betamethasone'**, **beclomethasone'**, **budesonide**, **fluticasone'**, **flunisolide'** (they have higher anti-inflammatory effect than when administered p.o.),

- with long-term local use, there is a high risk of local side effects (local atrophy, striae atrophicae distensae, purpura, telangiectasia, perioral dermatitis, steroid acne, hypertrichosis, pigmentation disorders, worsened wound healing, tachyphylaxis, rebound phenomenon (resurgence of the disease after sudden discontinuation of corticoids)).

Dosage

Different derivatives are characterized by the strength of their effect on the organism. In general, halogenated derivatives have a stronger anti-inflammatory effect (dexamethasone, betamethasone) than non-halogenated ones.

Cortisone

	Equivalent dose (mg)	**Anti-inflammatory effect**	**Mineralocorticoid effect**
Glucocorticoids			
Short acting (8 - 12 hours)			
Hydrocortisone (cortisol)	20	1	1
25	0.8		
Mid-term (12 - 36 hours)			
Prednisone	5	4	0.8
Prednisolone	5	4	0.8
Methylprednisolone	4	5	0
Triamcinolone	4	5	0
Long-term (36 - 72 hours)			
Dexamethasone	0.75	30	0
Betamethasone	0.6	30	0
Mineralocorticoids			
Aldosterone		0	500
Fludrocortisone		10 - 15	250

Links

Related Articles

- Cushing's Syndrome
- Synthesis of steroid hormones

External links

- Glucocorticoids (Czech Wikipedia)
- Glucocorticoid (English Wikipedia)

References

{Editorcheck}}

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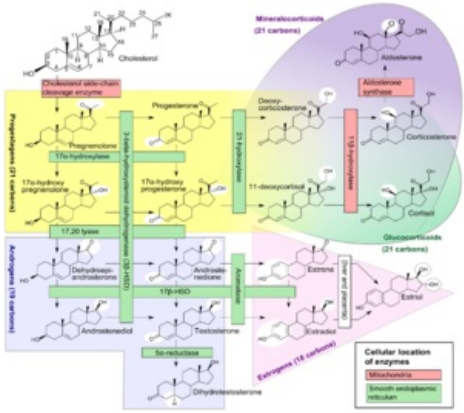

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Links

Related articles

Cushing's syndrome- Synthesis of steroid hormones

External links- Glucocorticoids (Czech Wikipedia)-Glucocorticoid (English Wikipedia)

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