

Adrenocorticosteroids (1)

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The adrenal medulla secretes epinephrine, whereas the adrenal cortex secretes two types of corticosteroids (glucocorticoids & mineralocorticoids) & adrenal androgens.

Adrenal cortex has three zones that produce various steroids hormones from cholesterol as follows:

1. Outer zona (glomerulosa) produces mineralocorticoids (eg. aldosterone). Production of aldosterone is regulated primarily by the renin-angiotensin system.
 2. Middle zona (fasciculata) synthesizes glucocorticoids (eg. cortisol).
 3. Inner zona (reticularis) secretes adrenal androgens (eg. dehydroepiandrosterone).
- Secretion of both glucocorticoids & adrenal androgens &, to a lesser extent mineralocorticoids is under the control of ACTH (corticotropin).
 - Glucocorticoids serve as feedback inhibitors of ACTH and CRH secretion.

Corticosteroids:

- Their receptors are intracytoplasmic.
- Glucocorticoid receptors are widely distributed throughout the body, whereas mineralocorticoid receptors are confined mainly to excretory organs (eg. kidney, colon, and salivary and sweat glands).
- Both types of receptors are found in the brain.
- Receptor-hormone complex translocates into the nucleus, and acts as a transcription factor to turn genes on (if complexed with co-activators) or off (if complexed with co-repressors), depending on the tissue.

This mechanism requires time to produce an effect, but other

CORTICOSTEROIDS

Betamethasone **CELESTONE,**
DIPROLENE,
LUXIQ

Cortisone **CORTISONE ACETATE**

Dexamethasone **DECADRON**

Fludrocortisone **FLORINEF**

Hydrocortisone

Methylprednisolone **MEDROL**

Prednisolone **ORAPRED,**

PEDIAPRED

Prednisone

Triamcinolone **KENALOG,**

NASACORT,

ARISTOSPAN

INHIBITORS OF

ADRENOCORTICOID

BIOSYNTHESIS OR FUNCTION

Eplerenone **INSPIRA**

Ketoconazole **NIZORAL**

Spirolactone **ALDACTONE**

glucocorticoid effects, such as their interaction with catecholamines to mediate bronchial relaxation or lipolysis are immediate.

A. Glucocorticoids

Cortisol is the principal human glucocorticoid. Its production is diurnal, with a peak early in the morning followed by a decline and then a secondary, smaller peak in the late afternoon. Stress and levels of the circulating steroid influence secretion. Glucocorticoids effects include:

1. Promote normal intermediary metabolism: by

- Favor gluconeogenesis through increasing amino acid uptake by the liver and kidney also they elevate the activities of gluconeogenic enzymes.
- Stimulate protein catabolism (except in the liver) and lipolysis, thereby providing building blocks and energy needed for glucose synthesis (**note:** glucocorticoid insufficiency may result in hypoglycemia (eg. during stressful periods or fasting)).

2. Increase resistance to stress:

- By raising plasma glucose levels, glucocorticoids provide the body with the energy it required to combat stress caused by, eg. trauma, fright, infection, bleeding, or debilitating disease.
- Glucocorticoids enhance the vasoconstrictor action of adrenergic stimuli on small vessels result in a modest rise in BP.

3. Alter blood cell levels in plasma:

- Glucocorticoids redistribute eosinophils, basophils, monocytes and lymphocytes from the circulation to lymphoid tissue.
- Increase blood levels of Hb, erythrocytes, platelets & polymorphonuclear leukocytes.

4. Anti-inflammatory action:

- Glucocorticoids cause dramatic reduction in the inflammatory & immunologic responses which is thought to be through:
 - a) Lowering the circulating lymphocytes.
 - b) Inhibiting the response of leukocytes and macrophages to mitogens and antigens.
 - c) Decreasing the proinflammatory cytokines production and release.

- d) Inhibition of phospholipase A2 (due to elevation of lipocortin). The decreased production of PGs and LTs is believed to be central to the anti-inflammatory action.
- e) Stabilizing mast cell and basophil membranes, decreasing histamine release.

5. Affect other systems:

- Elevated level of glucocorticoids cause feedback inhibition of corticotropin production, thus inhibiting further synthesis of both glucocorticoid and TSH.
- Adequate cortisol levels are essential for normal glomerular filtration.
- Effects of corticosteroids on other systems are mostly associated with the adverse effects of the hormones.

B. Mineralocorticoids:

- They control fluid status and concentration of electrolytes (Na & K).
- Aldosterone causes reabsorption of sodium, bicarbonate and water. While decreasing potassium reabsorption. Aldosterone also enhances sodium reabsorption in GI mucosa, sweat & salivary glands.

Note: Elevated aldosterone levels may cause alkalosis & hypokalemia, sodium & water retention increasing blood volume and BP.

- Hyperaldosteronism is treated with **spironolactone** (aldosterone antagonist).

Uses of corticosteroids:

Several semisynthetic derivatives of the glucocorticoids are available, they vary in their anti-inflammatory potency, mineralocorticoid activity & duration of action as follows:

Duration of action	Glucocorticoids	Anti-inflammatory effect	Salt-retaining effect
Short acting (1-12 hours)	Hydrocortisone	1	1
	Cortisone	0.8	0.8
Intermediate acting (12-36 hours)	Prednisone	4	0.8
	Prednisolone	5	0.8
	Methylprednisolone	5	0.5
	Triamcinolone	5	0
Long acting (36-55 hours)	Betamethasone	35	0
	Dexamethasone	30	0
	Mineralocorticoids		
	Fludrocortisone	10	125
	Desoxycorticosterone	0	20