

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.

The above mechanism requires time to produce an effect, but other 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 cortisol 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)).

**CORTICOSTEROIDS**

Betamethasone **CELESTONE, DIPROLENE, LUXIQ**

Cortisone **CORTISONE ACETATE**

Dexamethasone **DECADRON**

Fludrocortisone **FLORINEF**

Hydrocortisone

Methylprednisolone **MEDROL**

Prednisolone **ORAPRED, PEDIAPRED**

Prednisone

Triamcinolone **KENALOG,**

**NASACORT,**

**ARISTOSPAN**

**2. Increase resistance to stress:**

- By raising plasma glucose levels, glucocorticoids provide the body with the energy it required to combat stress caused by e.g, 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 & antigens.

**c)** Decreasing the proinflammatory cytokines production and release.

**d)** Inhibition of phospholipase A2 (due to elevation of lipocortin). Thus decrease production of PGs and LTs that is believed to be central to the anti-inflammatory action.

**e)** Stabilizing mast cell & basophil membranes, decreasing histamine release.

**5. Effect on other systems:**

- On the endocrine system the elevated level of glucocorticoids cause feedback inhibition of corticotropin production, thus inhibiting further synthesis of both glucocorticoid & TSH.
- On the kidney an 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
<b>Short acting</b> (1-12 hours)	Hydrocortisone	1	1
	Cortisone	0.8	0.8
<b>Intermediate acting</b> (12-36 hours)	Prednisone	4	0.8
	Prednisolone	5	0.8
	Methylprednisolone	5	0.5
	Triamcinolone	5	0
<b>Long acting</b> (36-55 hours)	Betamethasone	35	0
	Dexamethasone	30	0
	<b>Mineralocorticoids</b>		
	Fludrocortisone	10	125
	Desoxycorticosterone	0	20