



Adrenal Hormones

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- **The adrenal produces various classes of hormones**, each of which aid in dealing with the stress faced by animals and people almost daily.
- At least two of these groups - glucocorticoids and mineralocorticoids - are necessary for life.

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Functional Anatomy

- An inner **medulla**, which is a source of the catecholamines: Adrenaline and nor-adrenaline.
- The chromaffin cell is the principal cell type.
- The medulla is richly innervated by preganglionic sympathetic fibers and is, in essence, an extension of the sympathetic nervous system.
- The medulla derives from ectoderm (neural crest)

- An outer **cortex**, which secretes several classes of steroid hormones (glucocorticoids and mineralocorticoids, plus a few others).
- The cortex has three concentric zones of cells that differ in the major steroid hormones they secrete.
- The cortex develops from mesoderm.

- **The adrenal cortex is a factory for steroid hormones.**
- 10-30 different steroids are synthesized and secreted from this tissue, but two classes are of particular importance:

| Steroid Class | Prototype | Physiological effect |
|-------------------|----------------------------------|-------------------------------------|
| Mineralocorticoid | Aldosterone | Na K & water Homeostasis |
| Glucocorticoid | Hydrocortisone Corticosterone | Glucose homeostasis and many others |

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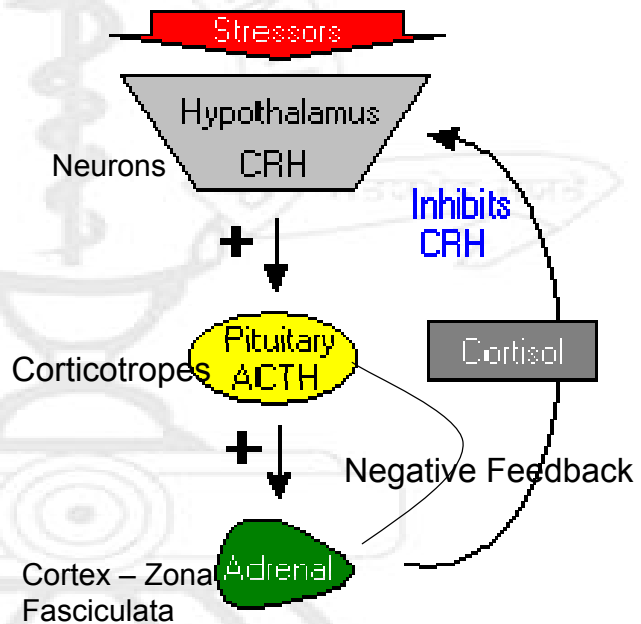
- Adrenal Cortex also produces sex steroids –
 - Androgens.
 - Dehydroepiandrosterone (DHEA)

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ACTH

- Synthesised and released under influence of ACTH-Ant. Pituitary
- Regulated by CRH from hypothalamus and by feedback levels of blood concentrations



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- Three modes of regulation of HPA axis
 - **Diurnal rhythm**
 - **Negative feedback** regulation
 - Increased production of steroids in response to **stress**.

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- ACTH influences the production of steroids in two ways:
 - **Acute phase**- occurs within seconds and reflects an increased availability of cholesterol substrate for production of steroids
 - **Chronic phase**- occurs over days and is because of increased transcription of steroidogenic enzymes.

ACTH

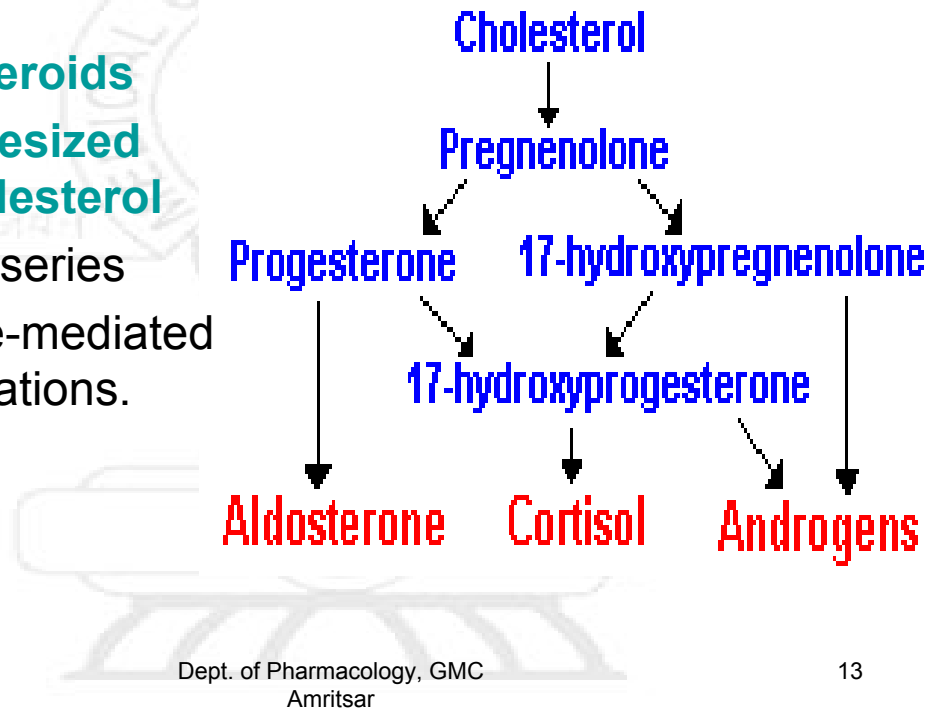
- Used previously as a therapeutic agent – with the belief that it causes less suppression of HPA axis.
- Less predictable
- Less convenient
- Stimulates mineralocorticoid and adrenal androgen secretion – Water retention and virilization.

- ACTH is used for testing integrity of HPA axis.
- 250 ug of cosyntropin (synthetic analog) leads to increased circulating cortisol levels.
 - Response absent in suppressed HPA axis.

ACTH-Actions

- increase in adrenal weight
- decrease in adrenal lipids
- decrease in adrenal cholesterol
- increase in protein synthesis (enzymes which hydroxylate steroids)
- increase in oxidative phosphorylation
- increase in rate of glycolysis

- **Adrenal corticosteroids are synthesized from cholesterol** through a series of enzyme-mediated transformations.



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Physiological Actions

- Numerous and widespread actions
- Carbohydrate, lipid and protein metabolism
- Fluid and electrolyte balance
- Normal functioning of CVS, Immune system, kidneys, skeletal muscle, nervous system
- Resistance to stress and noxious stimuli and environmental changes

- Permissive actions-permit and facilitate the actions of other hormones.
- Examples:
 - In absence of lipolytic hormones hydrocortisone shows no effect on lipolysis
 - Adrenaline and nor-adrenaline do not lead to lipolysis in the absence of glucocorticoids.

Mechanism of Action

- Not stored
- Rate synthesis = rate release
- Synthesized rhythmically
 - Controlled by irregular pulses of ACTH
 - Influenced by light
 - Major pulses early in morning and after meals

- GR is a nuclear receptor
- Inactive GR is found as a complex with other proteins HSP70 and HSP 90
- After ligand binding the GR dissociates and moves to the nucleus and combines with short DNA sequences-Glucocorticoid Responsive Elements
- These lead to gene transcription.
- Certain receptor independent mechanism also exist.

Carbohydrates & Protein MB

- Have a profound effect on carbohydrate and protein metabolism-evolved to protect glucose dependant tissue (brain and heart) from starvation
- Stimulate liver to form glucose from amino acids and glycerol
- In peripheral tissues decrease utilisation of glucose, increase protein breakdown and activate lipolysis thus forming amino acids and glycerol for gluconeogenesis.

Lipid Metabolism

- Redistribution of fat when there is excess activity of cortical steroids.
- Permissive facilitation of the effect of other agents eg: growth hormone, beta adrenergic receptor agonists