HISTOLOGY AND PHYSIOLOGY OF ADRENAL GLAND

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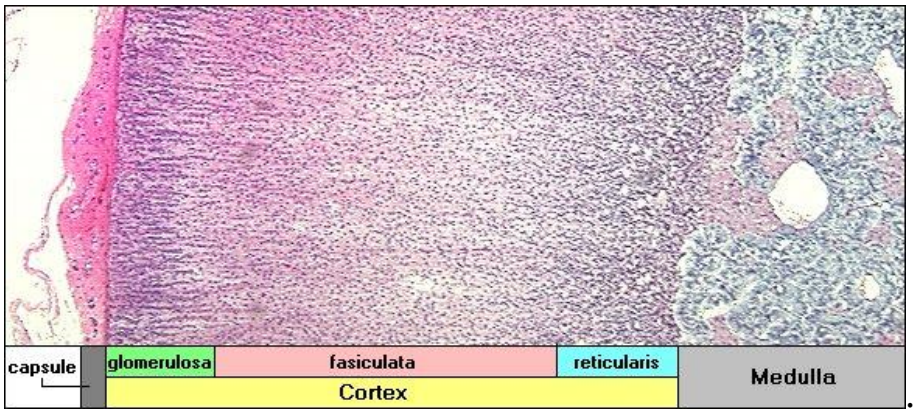
The adrenal glands are wedges of glandular and neuroendocrine tissue adhering to the top of the kidneys by a fibrous capsule. The adrenal glands have a rich blood supply and experience one of the highest rates of blood flow in the body.

The adrenal gland is encased in a connective tissue capsule that extends septae into the substance of the gland. The organ is richly vascularized and capsular blood vessels, nerves and lymphatics penetrate along with the connective tissue septae.

The most distinctive feature of the adrenal is its partitioning into cortex and medulla. The medulla is fairly homogeneous, but even when viewed a low power, three concentric zones can be distinguished in the cortex:

- zona glomerulosa - thin, outermost zone
- zona fasiculata - thick, middle zone
- zona reticularis - thin, inner zone

The three cortical zones and part of the medulla are evident in the section of rabbit adrenal gland seen below.



T.S of Adrenal gland

Based on embryologic origin and type of hormones produced, the cortex and medulla are best though of as separate endocrine organs. The medulla produces catecholamines and the cortex produces several steroid hormones, as depicted in the table below. There is some overlap in hormones synthesized by the zonae fasiculata and reticularis (i.e. cells in the fasiculata produce a small amount of androgens and cells in the reticularis secrete some cortisol).

Zona Glomerulosa: Outer Layer

- Cells of the Zona Glomerulosa are separated into small oval-shaped clusters by the fibrous capsule which invests the entire adrenal gland. These structures are reminiscent of glomeruli which gives this zone its namesake. Cells of this zone synthesize mineralocorticoids which were originally so named because they were shown to affect blood mineral levels. The physiologically most important mineralocorticoid is aldosterone.

Zona Fasciculata: Middle Layer

- The Zona Fasciculata is the thickest layer and its cells are arranged in long cords or "Fascicula", giving this zone its namesake. Cells of this zone synthesizes Glucocorticoids which were originally so named because they were shown to affect blood glucose levels. Physiologically most important glucocorticoid is cortisol.

Zona Reticularis: Inner Layer

- Cells of the Zona Reticularis are arranged in an inter-connecting network of cords giving the impression of a reticulum and thus the zone's namesake. Cells of this zone synthesizes "Adrenal Androgens": Named as such because they are androgens that are derived from the adrenal cortex and not from the gonads. The physiologically most important adrenal androgens are DHEA and androstenedione.

Adrenal Cortex

The function of the cortex is to produce adrenocorticoid hormones. The three zones each make a specific type of hormone:

The Zona Glomerulosa secretes mineralocorticoids,

The Zona Fasciculata secretes glucocorticoids,

The Zona Reticularis secretes sex steroids or androgens.

The hormones are formed from the esterified cholesterol that is stored in intracellular lipid droplets. Below is the steps of how the adrenocorticoid hormones are made from cholesterol.

1) The P450scc enzyme converts cholesterol to pregnenolone by the removal of a side chain. This is regulated by ACTH and is the rate determining step of adrenocorticoid hormone production. This occurs in the mitochondria.

2) Hydroxylation reactions occur in the mitochondria and endoplasmic reticulum converting pregnenolone into specific hormones. The location within the cortex determines the hormones produced.

Mineralocorticoids

These hormones regulate the metabolism of inorganic ions, such as sodium, potassium and chloride. Several hormones are produced but the most important is aldosterone. Aldosterone is formed in the zona glomerulosa by the conversion of pregnenolone to cortisol and then to corticosterone, before finally becoming aldosterone. It circulates by binding to album and cortisol-binding globulin. It's plasma half-life is 20 minutes. It is eventually inactivated in the liver, where it binds to glucuronic acid and is excreted in bile and urine.

Regulation and action

It's main regulators of synthesis and secretion are; Renin and extracellular concentrations of potassium ions. Its main action is upon renal regulation and electrolyte and fluid balance. These are fully explained within the renin-angiotensin and aldosterone system pages.

Glucocorticoids

These hormones are important in regulating glucose metabolism; the most important of them is cortisol. This is formed within the zona fasciculata by the conversion of pregnenolone directly to cortisol. It is transported by cortisol-binding globulin and has a half-life of 90 minutes.

Action

These are essential hormones and have multiple effects around the body. Cortisol has a permissive action, i.e. without cortisol certain chemical reactions within cells are unable to occur, for example the production of epinephrine and glucagon. Cortisol is a stress hormone, in times of stress it is released and enhances the effect of norepinephrine on blood pressure. It is also essential for the day to day maintenance of normal blood pressure and will also stimulate gluconeogenesis and inhibit certain tissues utilization of glucose. Cortisol stimulates the degradation of fats and proteins and inhibits DNA synthesis in some tissues. This along with degradation of protein, results in a growth-inhibiting effect in times of stress. It can also have anti-inflammatory effects. It inhibits the formation of prostaglandins and cytokines and reduces the ability of white blood cells being transported to an injured area. It helps keep in check inflammatory processes that could potentially cause tissue damage. Cortisol is also immunosuppressive, by reducing the lymphocyte numbers in circulation and reducing antibody production.

Androgens

These hormones function as male sex hormones. The most important of these is testosterone. This is produced by the conversion of pregnenolone to dehydroepiandrosterone, then to androstenedione and finally to testosterone. This occurs in the zona reticularis. They bind in the blood to sex hormone-binding globulin (SHBG) and albumin. Most adrenal androgens have little physiological action until they are converted to testosterone. They have little importance within the male, however, in women adrenal androgens, which are converted to oestrogen in adipose tissue, is the most important source of oestrogen after the menopause.

Adrenal Medulla

The adrenal medulla converts the amino acid to catecholamines. This group of hormones contains epinephrine and norepinephrine. All of the bodies circulating epinephrine is produced by the adrenal medulla, where as norepinephrine comes from both the medulla and postganglionic sympathetic neurons.

Synthesis, secretion and metabolism

Tyrosine is firstly converted to dihydroxyphenylalanine by tyrosine hydroxylase. This is the rate-limiting step. Dihydroxyphenylalanine is then converted into dopamine, then into norepinephrine and finally into epinephrine. They are stored in secretory vesicles and are released by exocytosis. They are metabolised in the liver and kidney and their half-lives are only 1-3 minutes. Some unmetabolised catecholamines are excreted in the urine.

Regulation of synthesis and secretion

They are released in response to stress by the firing of preganglionic sympathetic nerve fibres in the adrenal medulla. This causes release of acetylcholine, thus depolarizing the cell membrane. An action potential is generated and an influx of calcium ions results in the exocytosis of the catecholamine vesicles.

Adrenergic Receptors

The catecholamines bind to two types of receptor proteins in cell membranes to elicit a response; these are alpha and beta receptors. The following is a table of where the receptors are located in the body and their effects when stimulated.