Adrenal glands

Anatomy:

The adrenal gland or the suprarenal glands are associated with the superior pole of each kidney. They consist of an :

1. Outer cortex (yellow in color)
2. Inner medulla (red in color)

The right gland is shaped like a pyramid, where as the left gland is semi lunar in shape and larger in size.

Anatomical relations:

Right suprarenal gland:

Anterior: part of the right lobe of the liver and inferior vena cava.

Posterior: the diaphragm.

Left suprarenal gland:

Anterior: part of the stomach, pancreas, and sometimes the spleen.

Posterior: the diaphragm.

The suprarenal glands are surrounded by perinephric fat and enclosed in the renal fascia, though a thin septum separates the gland from the kidney.

Perinephric fat (perirenal fat): immediately outside the renal capsule there is an accumulation of extra peritoneal fat which completely surrounds the kidney. Enclosing the perinephric fat is a membranous condensation of extra peritoneal fascia (the renal fascia) which surrounds the adrenal glands as well.

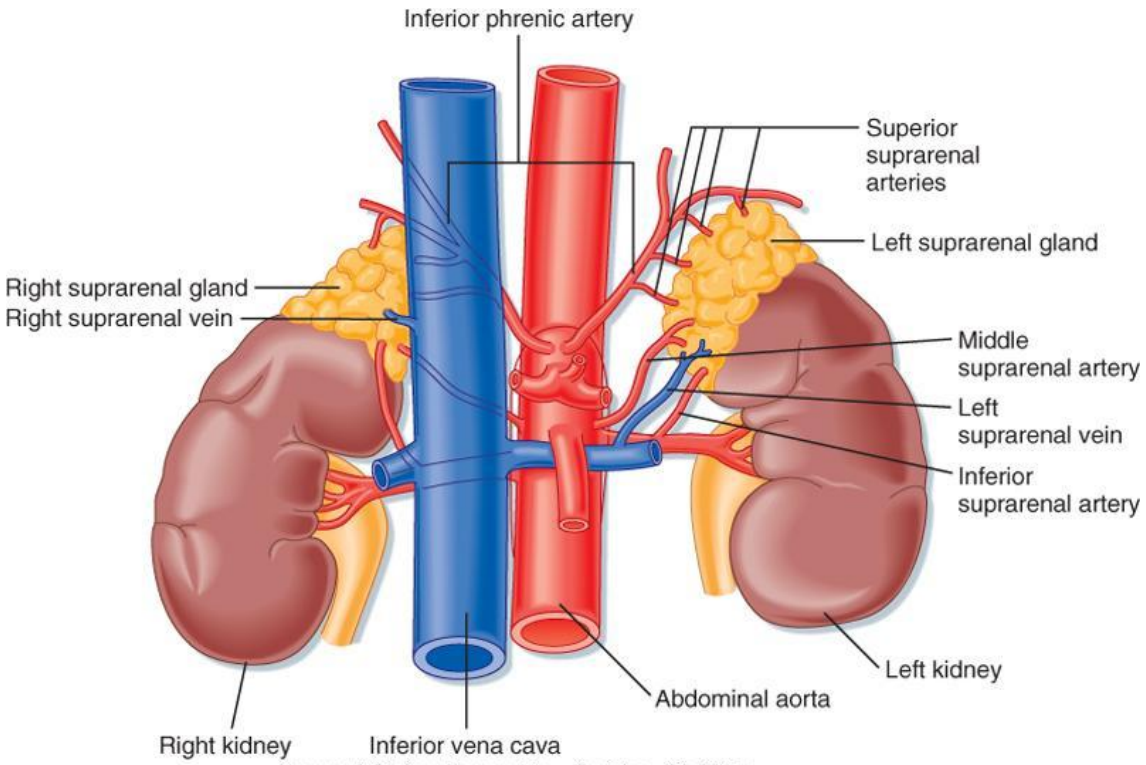
Blood supply:3 arteries and 1 vein

Arteries:

1. Superior supra renal artery ⟶ inferior phrenic artery ⟶ abdominal aorta.
2. Middle supra renal artery ⟶ abdominal aorta.
3. Inferior supra renal artery ⟶ renal artery ⟶ abdominal aorta.

Vein: supra renal vein leaving the hilum of each gland, the right suprarenal vein is short and empties directly to inferior vena cava but the left supra renal vein empties to the left renal vein which empties to inferior vena cava.

The arteries penetrate the cortex and divide into cortical arterioles and medullar arterioles, the cortical arteriole form capillaries ad those capillaries unite with the medullar arterioles and then penetrate the medulla of the adrenal gland so that the medulla is receiving arterial blood(medullar arterioles) and venous blood(venous ends of cortical capillaries). In the medulla a network of capillaries is formed and those capillaries will collect to form the supra renal vein which will leave the gland.



Histology:

The gland is composed of :

- Covering of dense connective tissue (capsule). The capsule sends thin trabeculae into the gland parenchyma.
- Stroma: reticular fibers supporting the secretory cells
  Microvasculature
- Parenchyma: secretory cells of the cortex and medulla.

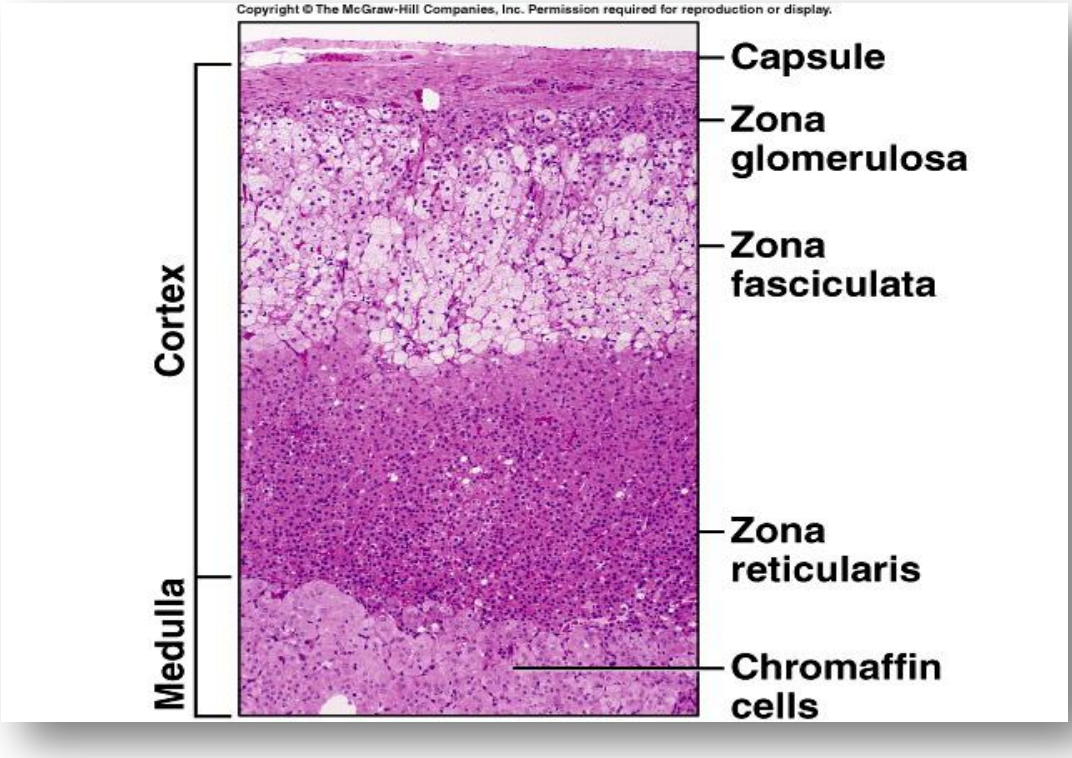
Adrenal cortex:

- Adrenocortical hormones are steroids derived from cholesterol
- The synthesis of the adrenocortical hormones is located in the mitochondria and the smooth endoplasmic reticulum.
- Cells of the adrenal cortex have characteristics of steroid secreting cells:
  1. Acidophilic cytoplasm rich in lipid droplets.
  2. Central nuclei
  3. Profuse smooth SER rich in enzymes for cholesterol synthesis and conversion of steroid prohormone into active steroid hormones.
  4. Highly active mitochondria which also contain enzymes needed in hormone synthesis.
- The adrenal cortex has three distinct layers:
  1. The zona glomerulosa (15% of the adrenal cortex): just underneath the capsule secreting Mineralocorticoids.th cells are pyramidal in shape.
  2. The zona fasiculata (75 % of the adrenal cortex): the middle and widest layer of the adrenal cortex and secretes glucocorticoids and small amounts of adrenal androgens. The cells are polyhedral in shape and surrounded by fenestrated capillaries.
  3. The zona reticularis: the deep layer of the cortex secretes adrenal androgens and small amounts of glucocorticoids. The cells are small and are heavily stained than those of the other zones

because they contain fewer lipid droplets and more lipofuscin pigment.

The adrenal medulla:

- Composed of large, pale staining polyhedral cells (chromaffin cells) supported by a stroma of reticular fiber network with few parasympathetic ganglia cells.
- Chromaffin cells are considered modified sympathetic postganglionic neurons which has the ability to secrete catecholamines (epinephrine and norepinephrine)
- Note that epinephrine is only synthesized in the adrenal medulla.



Embryology: adrenal cortex (mesoderm)/ adrenal medulla(neural crest)

Physiology:

General information:

- Steroid hormones once synthesized are not stored in granules like protein or undergo exocytosis ; they diffuse freely from the cell membrane.
- Adrenocortical hormones are bound to plasma proteins in the blood which reflexes:
    1. Serves as a reservoir to lessen rapid fluctuation in free hormone concentration
    2. Serves to insure a relatively uniform distribution of the adrenal hormones to the tissues.

First: Mineralocorticoids (aldosterone)

Principle of Aldosterone: stimulates the reabsorbtion of Na+, Cl- , and water

Stimulates the secretion of K+.

Site of action:

- renal tubular epithelial cells(kidney)
- Sweat glands
- Salivary glands.
- Intestinal epithelial cells

In renal tubular epithelial cells:

1. Aldosterone deficiency ⟶ [K+] INCREASES in the extra cellular fluid , Na+& Cl- DECREASES in the body⟶ ***water*** is lost ⟶ total extracellular fluid volume decreases as well as blood volume⟶ diminished cardiac output &circulatory shock .
   So lack of aldosterone causes: HYPERKALEMIA (K+ excess)
   And ***CARDIAC TOXICITY.***

2. Aldosterone excess → INCREASES Na+ reabsorbtion & INCREASES K+ → WATER IS ABSORBED → INCREASE of extra cellular fluid volume → INCREASE in arterial pressure → STIMULATES THE KIDNEY to INCREASE the excretion of both salt and water so the elevated blood pressure returns the renal output of salt and water back to normal despite the excess aldosterone.

Note: this return to normal of salt and water excretion by the kidney as a result of high blood pressure is called ***aldosterone escape***.

So excess aldosterone causes: HYPOKALEMIA (K+ deficiency) , muscle weakness because excess aldosterone not only causes loss of potassium ions from the extracellular fluid into the urine but also stimulates the transport of potassium from the extracellular fluid into most cells of the body, which will cause alterations in the electrical excitability of the nerve and muscle fiber membrane. Also, excess aldosterone causes alkalosis because it doesn't only stimulate the excretion of potassium in exchange for sodium reabsorbtion but also causes secretion of hydrogen ions in exchange for sodium.

Remember: hydrogen ions are responsible for regulating the acidity in the body.

In sweat glands, salivary glands, and intestinal epithelial cells:

Aldosterone stimulates sodium and potassium transport in the same way as it does in the renal cells (sodium reabsorbtion and potassium excretion). In the sweat glands this effect is important to conserve body salt and fluid in hot environment. In salivary glands, the effect is important to conserve salt when excessive amounts of saliva are lost. In the intestine, this effect

prevents the loss of sodium in the stool which will prevent the loss of water, if there was a lack of aldosterone diarrhea will develop.

Regulation of aldosterone secretion:

1. **Potassium ion concentration, for example:**
   [K+]↑ ⟶ high increase in ALDOSTERONE↑
2. **Angiotensin 2 concentration, for example:**
   [Angiotensin 2]↑ ⟶ high increase in ALDOSTERONE↑
   Angiotensin 2 is secreted in response to diminished blood flow to the kidneys or to sodium loss.
   Angiotensin2 is secreted in response to renin which is secreted by the kidney.
3. **Sodium concentration, increased sodium concentration in the extra cellular fluid <u>slightly</u> decreases aldosterone secretion.**
4. **ACTH is necessary for aldosterone secretion but has a slight role in regulating the amount of secretion.**

Cellular mechanism of aldosterone action:

i. **Aldosterone diffuses readily to the interior of the cell (renal tubular epithelial /intestinal/sweat/salivary cells).**
ii. **In the cytoplasm, aldosterone binds its receptor(MR= mineralocorticoid receptor).**
iii. **Aldosterone receptor complex diffuses into the nucleus and stimulate DNA transcription to mRNA.**
iv. **mRNA diffuses back to the cytoplasm where it is translated to proteins. The protein formed are 2 types:**
   - **Enzymes: Na+_K+ ATPase which serves as the principle part of the pump for sodium and potassium exchange.**
   - **Membrane transport proteins: epithelial sodium channel (ENaC) which allows rapid diffusion of sodium into the cell from the lumen.**

Note : aldosterone has a slow effect because its action is dependent on DNA transcription and translation which takes time.

<u>Second: Glucocorticoids (cortisol):</u>

Cortisol & carbohydrate:

Cortisol is glucagon friend in the liver so it stimulate:

1. Gluconeogenesis either directly by increasing the enzymes required to convert amino acids into glucose in the liver cells and mobilization of amino acids from the extra hepatic tissue and thus high amino acid concentration in the plasma. Or indirectly by having a permissive effect on glucagon.
   This action is responsible for replenishing glycogen stores in the liver
2. Decrasing glucose usage in cells.

The elevated blood glucose level stimulates insulin secretion which wont be effective in lowering blood glucose level in the presence of cortisol. with time diabetes will develop (adrenal diabetes) .

Cortisol & proteins:

Reduction in cellular protein and increasing liver and plasma protein: by increased amino acid transport from the extra hepatic tissues and not other tissues in the body and by enhancing enzymes required for protein synthesis in the liver.
Remember that plasma proteins are synthesized in the liver.

Cortisol and fat:

Stimulates Lipolysis

Note: ***despite*** the fact that cortisol causes a moderate degree of fatty acid mobilization (Lipolysis) from adipose tissue. Many people with excess cortisol secretion develop a peculiar type of obesity, with excess deposition of fat in the head and chest regions of the body, giving a buffalo-like torso and a rounded “moon face”.

Cortisol and (stress & inflammation)

Cortisol resists stress and inflammation by several mechanisms such as suppressing the immune system and decreasing lymphocyte production.

Regulation of cortisol secretion:

Cortisol secretion is regulated by adrenocortico tropic hormone (ACTH) which regulates androgen secretion as well.

ACTH secretion is regulated by:

1. corticotrophin releasing factor (CRF) from the hypothalamus. CRF is highly secreted in response to physiological stimuli.
2. Cortisol by negative feedback mechanism. so excess cortisol has inhibitory effect on the hypothalamus(decrease CRF secretion) and the anterior pituitary (decrease ACTH secretion)
3. ADH

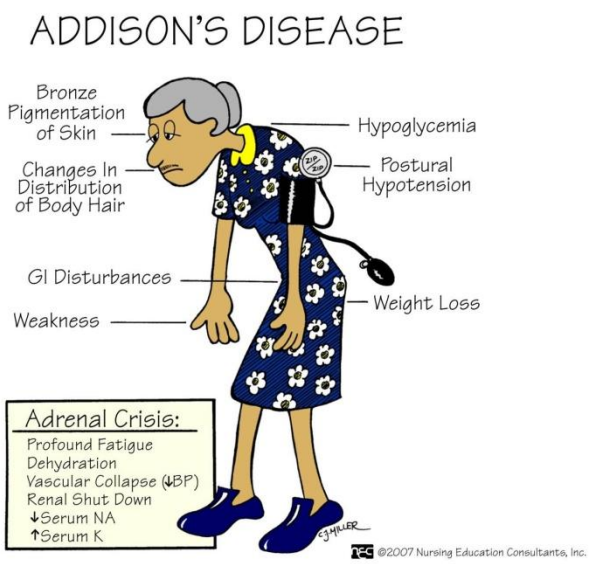
Third: androgens: several moderately active male sex hormones are secreted especially during fetal life. Some of those androgens once secreted are converted to testosterone in the extra adrenal tissues
The effect of androgen are mainly enhancing male sexual characteristics (growth of the pubic and axillary hair ,increasing libido) in both males and famales.

Note that the adrenal gland is the only source of testosterone in females where as in males testosterone is also synthesized in the testis.
NOTE: androgen secretion is dependent on ACTH secretion

<u>Pathological problems of the adrenal cortex & its relation to physiology:</u>

1. Hypoadrenalism (adrenal insufficiency) _Addison disease:
   Inability of the adrenal cortex to produce sufficient amounts of Adrenocortical hormones. The disease is caused by:
   i) Primary adrenal insufficiency which is in 80% of the cases is caused by an autoimmune problem against the cortex. In 20% of the cases it is caused by tuberculoses or by cancer invasion.
   ii) Secondary adrenal insufficiency: by impaired function of the pituitary gland which fails to secrete ACTH or the hypothalamus to secrete CRH.
   Note: Addison disease is sometimes recognized as primary not secondary adrenal insufficiency.

Physiology of primary adrenal insufficiency(direct relation to the cortex):
[ALDOSTERONE]↓ &[CORTISOL]↓ &[androgen and sex hormones]↓
Low aldosterone: hypotension /mild acidosis/decrease in cardiac output
Low cortisol: hypoglycemia/ melanin pigmentation because when cortisol is deficient the pituitary will try to elevate its concentration by secreting higher amounts of ACTH. ACTH and MSH are derived from the same precursor so a high secretion of ACTH means a high secretion of MSH which will cause skin pigmentation.
Note that ACTH has some MSH activity and can by its self cause skin pigmentation.



Low androgens : changes in distribution of body hair and sexual desire.

2. Hyperadrenalism_ Cushing's syndrome:
   Hyper secretion by the Adrenocortical causes Hyperadrenalism. The causes are:
   I. Abnormal function of the hypothalamus which causes excessive secretion of CRH which indirectly stimulates Adrenocortical hormones secretion.
   II. Adenomas of the anterior pituitary that secrete high amounts of ACTH and thus stimulates the secretion of Adrenocortical hormones. (Cushing ***disease***)
   III. Ectopic secretion of ACTH by a tumor elsewhere in the body.
   IV. Adenomas of the adrenal cortex. (Cushing ***syndrome***).

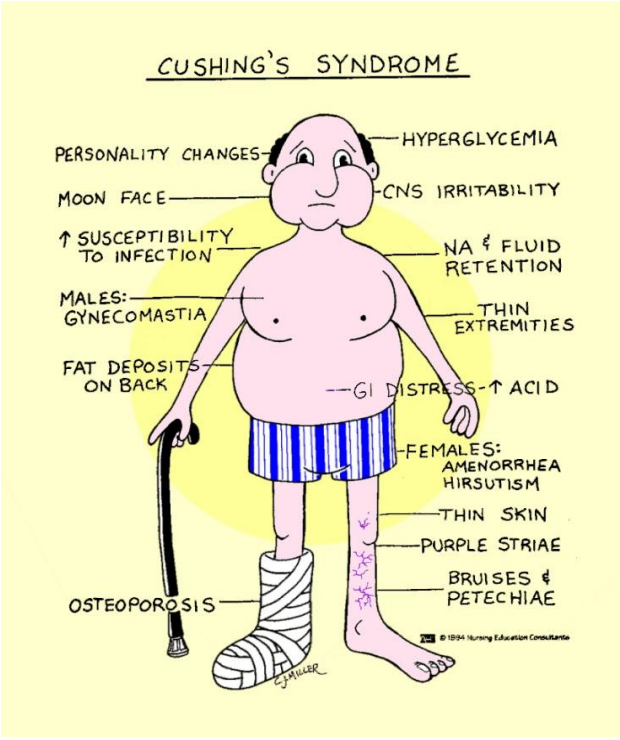
Cushing syndrome:

Many of the abnormalities caused by this syndrome are related to the excess secretion of cortisol but some important effects are caused by excessive secretion of androgens.

High cortisol causes: obesity (moon face) and buffalo like torso/hyperglycemia/muscle weakness duo to protein degradation in the body except the liver and this also causes osteoporosis and tearing of the collagen fibers in the connective tissue (purple striae)

High androgens causes: excess growth of facial hair

High aldosterone causes: hypertension.



Primary aldosteronism_ Conn's Syndrome:
Caused by a tumor in the zona glomerulosa which secretes high amounts of aldosterone or sometimes by a hyperplasia in the adrenal cortex with a resultant secretion of aldosterone.
The effect are similar to those caused by excess aldosterone in Cushing syndrome.

Adrenogenital Syndrome:
Caused by an Adrenocortical tumor which secretes high amounts of androgens.
The effect in males: rapid growth of a beard, a much deeper voice, baldness if he has the genetic trait for badness, masculine distribution of hair on the body, rapid development of male sexual organs.
The effect in females: rapid growth of a beard, a much deeper voice, baldness if he has the genetic trait for badness, masculine distribution of hair on the body, growth of clitoris to resemble a penis.

The End

Done by : Russole Emad