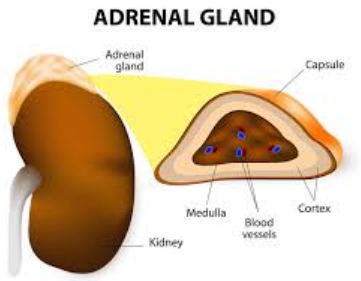
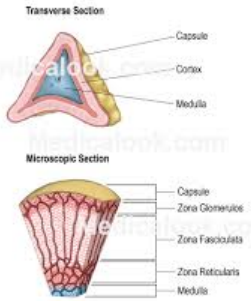
4- Adrenal gland

An adrenal (suprarenal) gland sits like a cap on the superior

pole of each kidney In adults, the adrenal is about 5 cm (2 in.) long, 3 cm (1.2 in.) wide, and weighs about 4 g; it weighs about twice this much at birth. Like the pituitary gland, the adrenal gland is formed by the merger of two fetal glands with different origins and functions. Its inner core, the **adrenal medulla,** is a small portion of the total gland. Surrounding it is a much thicker **adrenal cortex**.





The Adrenal Medulla

Like posterior pituitary ,It arises from the neural crest and is not fully formed until the age of three. It is actually a sympathetic ganglion consisting of modified neurons called **chromaffin cells,** that lack dendrites and axons. These cells are richly innervated by sympathetic preganglionic fibers , when the medulla stimulated by sympathetic nervous system neurons , its cells release two similar hormones , **epinephrine** also called **adrenaline** and **norepinephrine(noradrenaline**), into blood stream. Collectively , these hormones called are called catecholamine, About three-quarters of the output is epinephrine.

When you are (or feel) threatened physically or emotionally , the sympathetic nervous system brings about the " fight – or- flight" response to help you cope with stressful situation. one of the organ it stimulates is the adrenal medulla and pumps it is hormones into the blood stream to enhance and prolong the effects of the neurotransmitters of the sympathetic nervous system. Basically , the catecholamine

1.Increase heart rate.

2.Increase blood pressure.

3.Increase blood glucose levels(They stimulate

glycogenolysis (hydrolysis of glycogen to glucose) and

gluconeogenesis (the synthesis of glucose from non carbohydrate sources like glycerol and glucogenic amino

acids). In order to further ensure an adequate supply of glucose to the brain, epinephrine inhibits insulin secretion and thus, the uptake and use of glucose by the muscles and other insulin-dependent organs. Thus, epinephrine has a glucose-sparing effect, sparing it from needless consumption by organs that can use alternative fuels to ensure that the nervous system has an adequate supply.

4.Dilate the small passageways of the lungs.

These events results in more oxygen and glucose in the blood and a faster circulation in the blood to the body organs (most importantly , to the brain , muscles , and heart) , thus the body is better able to deal with short term stress.

The catecholamine of the adrenal medulla prepare the body to cope with a brief or short term stressful situation and cause so called **alarm stage** of the stress response. **Glucocorticoids** , by contrast , are produced by adrenal cortex and are important in body to cope with continuing or prolonged stress, such as dealing with the death of a family member or having a major operation. Glucocorticoids operate primarily during **resistant stage** of the stress response.

The medulla and cortex are not as functionally independent as once thought. The boundary between them is indistinct and some cells of the medulla extend into the cortex. When stress activates the sympathetic nervous system, these medullary cells secrete catecholamines that stimulate the cortex to secrete corticosterone.

Hormones of the adrenal gland

The adrenal cortex produces three major groups of steroid hormones , which are collectively called **corticosteroids**

1.mineralocorticoids

2.glucocorticoids

3.sex hormones

The **mineralocorticoids** mainly **aldosterone** are produced by the outermost adrenal cortex cell layer. As their name suggests , the mineralocorticoids are important in regulating the mineral(salt) content of the blood , particularly the concentrations of sodium and potassium ions. their target is the renal tubules that selectively reabsorb the minerals or allow them to be flushed out of the body in urine. When the level of the blood aldosterone rise , the kidney tubules cell reabsorb increasing amounts of sodium ions and secrete more potassium ions into the urine. When sodium reabsorbed , water follows. Thus mineralocorticoids regulate both water and electrolyte balance in body fluids ,The single most abundant cation in extracellular fluid is Na, and the amount of Na in the body largely determines the volume of the extracellular fluid—where Na goes, water follows. Changes in Na concentration lead to changes in blood volume and blood pressure. Moreover, the regulation of Na is coupled to the regulation of many other ions, including K, H, HCO_3^- (bicarbonate), and Cl^- (chloride). The extracellular concentration of K is also critical—it sets the resting membrane potential of all cells and determines how easily action potentials are generated in nerve and muscle. Not surprisingly, Na and K regulation are crucial to overall body homeostasis.

Their regulation is the primary job of **aldosterone**. The release of aldosterone is stimulated by

1-increase potassium(1 meq) **Plasma Concentrations of Potassium** Fluctuating blood levels of K directly influence the zona glomerulosa cells in the adrenal cortex. Increased K stimulates aldosterone release, whereas decreased K inhibits it.

2- decrease sodium ion(about 10 meq)

3-angiotensin II

4-**ACTH**(does not affect basal aldosterone , only in stressful conditions). **ACTH** Under normal circumstances, ACTH released by the anterior pituitary has little or no effect on aldosterone release. However, when a person is severely stressed, the hypothalamus secretes more corticotropin-releasing hormone (CRH), and the resulting rise in ACTH blood levels steps up the rate of aldosterone secretion to a small extent.

The resulting increase in blood volume and blood pressure helps deliver nutrients and respiratory gases during the stressful period.

Renin , an enzyme produced by the kidneys when blood pressure drops , also causes the release aldosterone by triggering a series of reactions that form **angiotensin II** , a potent stimulator of aldosterone release . a hormone release by the heart , **atrial natriuretic peptide(ANP)** , One of its major effects is to inhibit the renin-angiotensin aldosterone

mechanism. It blocks renin and aldosterone secretion

and inhibits other angiotensin-induced mechanisms that

enhance water and Na reabsorption. Consequently, ANP

overall influence is to decrease blood pressure by allowing Na

(and water) to flow out of the body in urine prevents aldosterone release , it is goal being to reduce blood volume and blood pressure.

The middle cortical layer mainly produces glucocorticoids , which include cortisone and cortisol. Glucocorticoids promote normal cell metabolism and help the body to resist **long term stress,** when blood levels of glucocorticoids are high , fats and even proteins are broken down by body cells and converted to glucose , which is released to the blood. For this reason , glucocorticoids are said to be **hyperglycemic hormones**. Glucocorticoids also seem to control the more unpleasant effects of inflammation by decreasing edema , and they reduce pain by inhibiting some pain causing molecules called **prostaglandins**, because their anti-inflammatory properties , glucocorticoids are often prescribed as a drug to suppress inflammation for patients with rheumatoid arthritis, glucocorticoids released from adrenal cortex in response to rising blood level of ACTH.

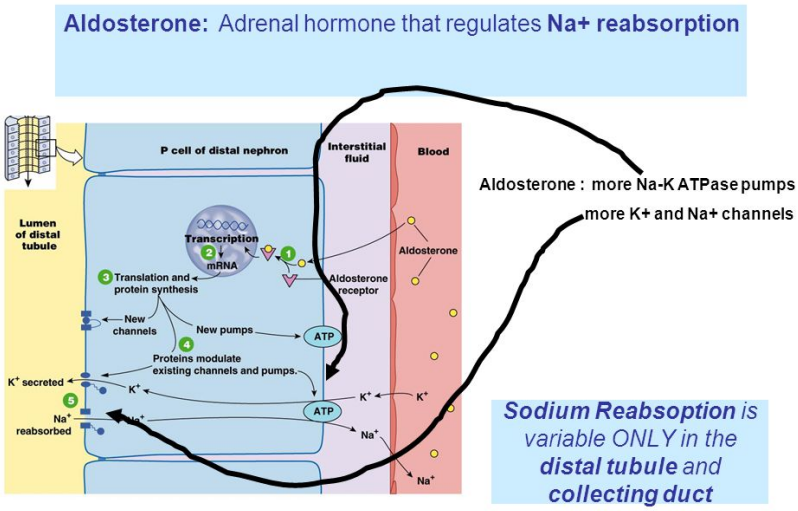
In both men and women , the adrenal cortex produces both male and female **sex hormones** throughout the life in small amounts. He bulk of the sex hormones produced by the cortex layer are **androgens** , but some **estrogens** are also formed.

the most potent mineralocorticoid. Aldosterone accounts for more than 95% of the mineralocorticoids produced. Aldosterone reduces excretion of Na from the body. Its

primary target is the distal parts of the kidney tubules, where it

stimulates Na reabsorption and water retention accompanied by elimination of K and, in some instances, alterations in the acid-base balance of the blood (by H excretion). Aldosterone also enhances Na reabsorption from perspiration, saliva, and gastric juice. Aldosterones regulatory effects are brief (lasting approximately20 minutes), allowing plasma electrolyte balance to be precisely controlled and continuously modified.

The mechanism of aldosterone activity involves the synthesis and activation of proteins required for Na transport such as Na-K ATPase, the pump that exchanges Na for K.



The Renin-Angiotensin-Aldosterone Mechanism The reninangiotensin-aldosterone mechanism influences both blood volume and blood pressure by regulating the release of aldosterone and therefore Na and water reabsorption

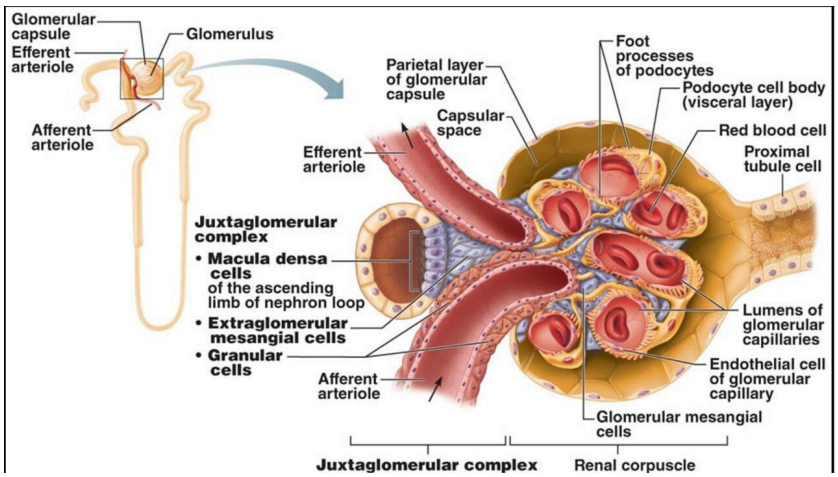
by the kidneys.

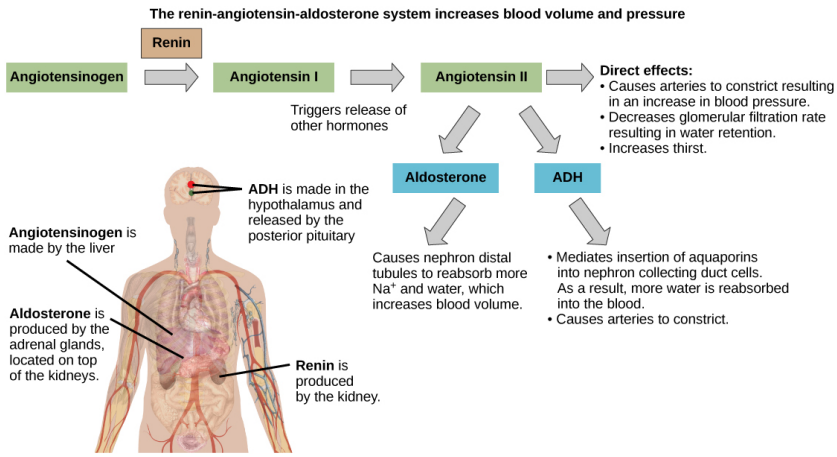
1. When blood pressure (or blood volume) falls, specialized cells of the **juxtaglomerular complex** in the kidneys are excited.

2. These cells respond by releasing **renin** into the blood.

3. Renin cleaves off part of the plasma protein **angiotensinogen**, triggering an enzymatic cascade that forms angiotensin II, which stimulates the glomerulosa cells to release aldosterone. However, the

renin-angiotensin-aldosterone mechanism does much more than trigger aldosterone release, and all of its effects ultimately raise blood pressure.





Homeostatic imbalance

Hypersecretion of aldosterone, a condition called **aldosteronism**, typically results from adrenal tumors.

Two major sets of problems result: (1) hypertension and edema due to excessive Na and water retention, and (2) accelerated excretion of potassium ions. If K loss is extreme, neurons become nonresponsive, leading to muscle weakness and eventually paralysis.

Glucocorticoids

Essential to life, the **glucocorticoids** influence the energy metabolism of most body cells and help us resist stressors. Under normal circumstances, they help the body adapt to intermittent food intake by keeping blood glucose levels fairly constant, and maintain blood pressure by increasing the action of vasoconstrictors. However, severe stress due to hemorrhage, infection, or physical or emotional trauma evokes a dramatically higher output of glucocorticoids, which helps the body negotiate the crisis.

Glucocorticoid hormones include **cortisol (hydrocortisone)**, **cortisone**, and **corticosterone**, but only cortisol is secreted in significant amounts in humans. As with all steroid hormones, glucocorticoids act on target cells by modifying gene activity.

Negative feedback regulates glucocorticoid secretion. Cortisol release is promoted by ACTH. ACTH release is triggered in turn by the hypothalamic releasing hormone CRH. Rising cortisol levels feed back to act on both the hypothalamus and the anterior pituitary, preventing CRH release and shutting off ACTH and cortisol secretion.

Cortisol secretory bursts, driven by patterns of eating and activity, occur in a definite pattern throughout the day and night Cortisol blood levels peak shortly before we rise in the morning. The lowest levels occur in the evening just before and shortly after we fall asleep. However, acute stress of any variety interrupts the normal cortisol rhythm as higher CNS centers override the(usually) inhibitory effects of elevated cortisol levels and trigger CRH release. The resulting increase in ACTH blood levels causes an outpouring of cortisol from the adrenal cortex.

Stress results in a dramatic rise in blood levels of glucose, fatty acids, and amino acids, all provoked by cortisol. Cortisols prime metabolic effect is to provoke **gluconeogenesis**, that is, the formation of glucose from fats and proteins. In order to save glucose for the brain, cortisol mobilizes fatty acids from adipose tissue and encourages their increased use for energy. Under cortisols influence, stored proteins are broken down to provide building blocks for repair or to make enzymes for metabolic processes.

Cortisol enhances the sympathetic nervous systems vasoconstrictive effects, and the rise in blood pressure and circulatory efficiency that results helps ensure that these nutrients are quickly

distributed to cells. Note that ideal amounts of glucocorticoids promote normal function,

but too much cortisol exerts significant anti-inflammatory

and anti-immune effects. Excessive levels of glucocorticoids

■ Depress cartilage and bone formation

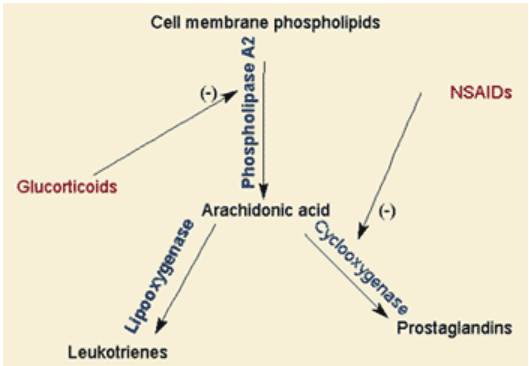
■ Inhibit inflammation by decreasing the release of inflammatory chemicals(prostaglandins, leukotriene's, interleukin2 , and lysosomes)

■ Depress the immune system(important in organ transplantation, but may increase risk of infectious diseases)

■ Disrupt normal cardiovascular, neural, and gastrointestinal

function.

Inhibit allergic reaction by (decrease the number of basophils and eosinophil and inhibit degranulation of mast cells so will inhibit release of allergic mediators and allergic reaction.



Glucocorticoid drugs can control symptoms of many chronic

inflammatory disorders, such as rheumatoid arthritis and allergic responses.

However, these potent drugs are a double-edged

sword because they also cause the undesirable effects of excessive levels of these hormones.

Homeostatic imbalance

The pathology of glucocorticoid excess, Cushing's syndrome,

may be caused by an ACTH-releasing pituitary tumor (in which

case it is called Cushing's disease); by an ACTH-releasing malignancy of the lungs, pancreas, or kidneys; or by a tumor of the adrenal cortex. However, it most often results from the clinical administration of glucocorticoid drugs.

The syndrome is characterized by persistent elevated blood

glucose levels (*steroid diabetes*), dramatic losses in muscle and

bone protein, and water and salt retention, leading to hypertension and edema.

The so-called *cushingoid signs*

include a swollen "moon" face, redistribution of fat to the abdomen and the posterior neck (causing a "buffalo hump"), easy bruising, and poor wound healing.

Because of enhanced antiinflammatory effects, infections may become overwhelmingly severe before producing recognizable symptoms.

Eventually, muscles weaken and spontaneous fractures force the person to become bedridden. The only treatment is to

remove the cause—be it surgically removing the tumor or discontinuing the drug.

Addison's disease, the major hyposecretory disorder of the

adrenal cortex, usually involves deficits in both glucocorticoids

and mineralocorticoids. Its victims tend to lose weight; plasma

glucose and sodium levels drop, and potassium levels rise. Severe dehydration and hypotension are common.

replacement therapy is the usual treatment. Corticosteroid

Gonadocorticoids (Adrenal Sex Hormones) Most

secreted by the adrenal cortex are weak gonadocorticoids

androgens, or male sex hormones, such as **androstenedione** and **dehydroepiandrosterone (DHEA).** Most are converted in tissue cells to more potent male hormones, such as *testosterone*, and some are converted to estrogens. The amount of gonadocorticoids produced by the

adrenal cortex is insignificant compared with the amounts made by the gonads during late puberty and adulthood.

The exact role of the adrenal sex hormones is still in question, but we know that they contribute to axillary and pubic hair development. In adult women adrenal androgens are thought estrogens produced after menopause when ovarian estrogens are no longer produced. Control of gonadocorticoid secretion is not completely understood. ACTH stimulates their release, but the gonadocorticoids do not appear to exert feedback inhibition on ACTH release.

Hormone imbalance

Since androgens predominate, hypersecretion of gonadocorticoids causes **adrenogenital syndrome** (masculinization). In adult males, elevated gonadocorticoid levels may not be noticeable since testicular testosterone has already produced masculinization, but in prepubertal males and in females, the results can be dramatic. In boys, the reproductive organs mature and secondary sex characteristics appear early, and the sex drive emerges with a vengeance. Females develop a beard and a masculine distribution of body hair, and the clitoris grows to resemble a small penis.

The adrenal medulla

spherical **medullary chromaffin cells** , which crowd around blood-filled capillaries and sinusoids, are modified postganglionic sympathetic neurons that synthesize the **catecholamines epinephrine** and **norepinephrine (NE)** via a molecular sequence from tyrosine to dopamine to NE to epinephrine. When a short-term stressor activates the body to fight-orflight status, the sympathetic nervous system is mobilized. Blood vessels constrict and the heart beats faster (together raising the blood pressure), and blood is diverted from temporarily nonessential organs to the heart and skeletal muscles.

endings weaving through the adrenal medulla signal for release of catecholamines, which reinforce and prolong the fight-or-flight response. Unequal amounts of the two hormones are stored and released.

Approximately 80% is epinephrine and 20% norepinephrine.

With a few exceptions, the two hormones exert the

same effects . Epinephrine is the more potent stimulator of metabolic activities, bronchial dilation, and increased blood flow to skeletal muscles and the heart, but norepinephrine has a greater influence on peripheral vasoconstriction and blood pressure.

Epinephrine is used clinically as a heart stimulant and to dilate the bronchioles during acute asthmatic attacks.

Unlike hormones from the adrenal cortex, which promote

long-lasting body responses to stressors, catecholamines cause

fairly brief responses. A deficiency in adrenal medulla hormones is not a problem these hormones merely intensify activities set into motion because by the sympathetic nervous system neurons. Unlike glucocorticoids and mineralocorticoids, adrenal catecholamines are not essential for life.

On the other hand, hypersecretion of catecholamines, sometimes arising from a medullary chromaffin cell tumor called a **pheochromocytoma** , produces symptoms of uncontrolled sympathetic nervous system activity —**hyperglycemia** (elevated blood glucose), increased metabolic rate, rapid heartbeat and palpitations, hypertension, intense nervousness, and sweating.

Tikrit university

College of medicine

Physiology department

Endocrine system

Year 3

By dr. Abdulhadi M. Jumaa Aljubori