5.5.7

Adrenal Hormones

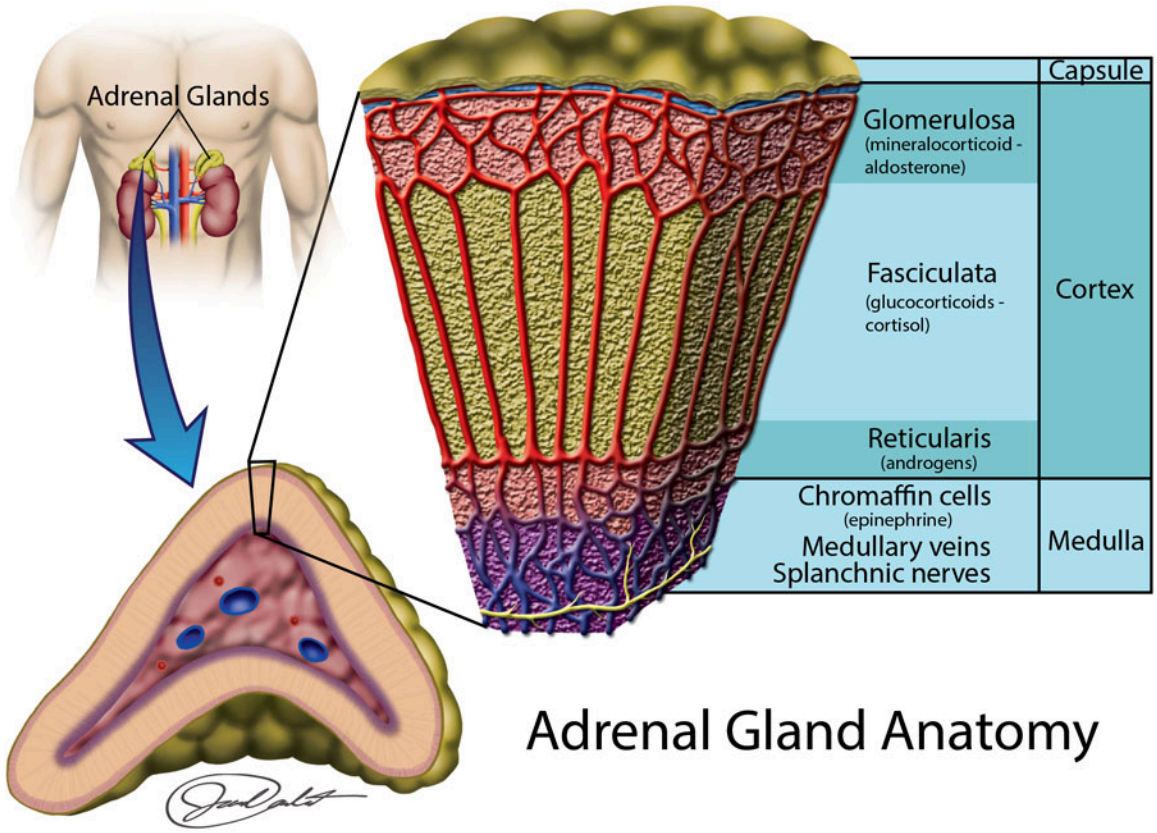


Image by BYU-Idaho Spring 2015

Image by BYU-I Student Jared C. 2015

The adrenal glands are paired organs that sit atop either kidney. The adrenal gland is composed of two distinct structures, an outer **cortex** and an inner **medulla**, both of which produce hormones. The cortex secretes a variety of steroid hormones, including cortisol, aldosterone and androgens. The medulla produces primarily epinephrine (80%) and norepinephrine (20%) and embryologically is an extension of the sympathetic nervous system.

The adrenal cortex produces various hormones, all of which are derived from cholesterol. Collectively these hormones are referred to as adrenal steroids. The adrenal cortex can be subdivided into three zones or layers. Starting from the outside and moving in, these zones are called the **zona glomerulosa**, the **zona fasciculata**, and the **zona reticularis**. The zona glomerulosa produces a number of hormones that are collectively known as **mineralocorticoids**, the most common is **aldosterone**. The production of aldosterone is controlled by angiotensin II and/or extracellular potassium. The zona fasciculata produces the **glucocorticoids**. The most common glucocorticoid in humans is **cortisol.** The zona

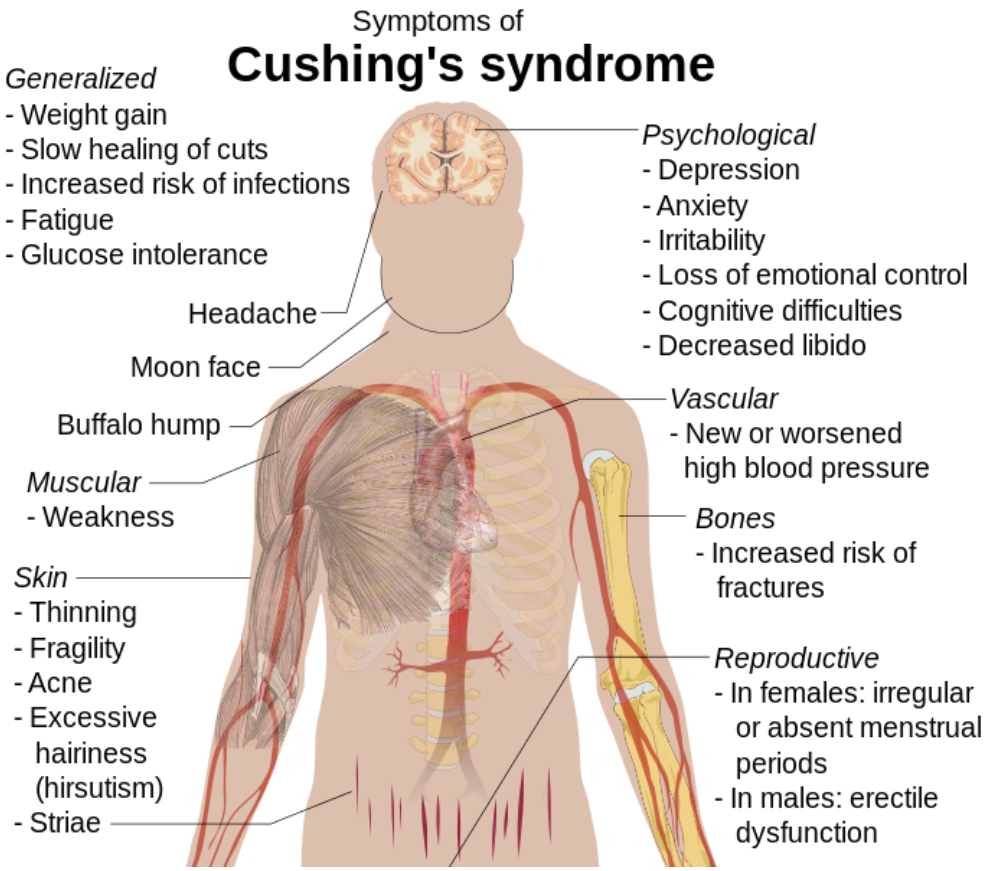
reticularis produces androgens such as DHEA and androstenedione, which contribute to the male secondary sex characteristics. (androgens will be discussed in the unit on reproduction).

Cortisol plays a role in mobilization or breakdown of carbohydrates (hence the name glucocorticoid), fats, and proteins. Cortisol production is stimulated by adrenocorticotropic hormone (ACTH) from the anterior pituitary gland. Like growth hormone, it is secreted in a circadian pattern with highest levels occurring in the early morning. Other factors that stimulate cortisol secretion include hypoglycemia and stress. The control of cortisol release by adrenocorticotropic hormone is through a pathway called the hypothalamic-pituitary-adrenal pathway and is categorized as a classical negative feedback pathway. The pathway begins with the release of CRH from the hypothalamus in response to physiological stress or hypoglycemia. CRH enters the pituitary portal system and induces the release of ACTH which acts to increase the synthesis and release of cortisol by cells in the zona fasciculata of the adrenal cortex. Cortisol diffuses out of the cell and is immediately bound by the carrier protein corticosteroid-binding globulin. Cortisol interacts with cytoplasmic receptors on target tissue. Cortisol acts in a negative feedback fashion to decrease ACTH secretion. Cortisol is anabolic in the liver and catabolic towards other tissues. The effects of cortisol are listed below:

1. **Gluconeogenesis**: cortisol stimulates glucose production by the liver from other sources such as amino acids or glycerol. Some of this glucose is released into the blood and some of it is stored as glycogen.
2. **Protein catabolism**: cortisol stimulates the breakdown of protein to amino acids in skeletal muscle, mainly to provide amino acids for glucose production by the liver.
3. **Lipid catabolism**: Cortisol stimulates the breakdown of fat into glycerol and fatty acids. Fatty acids will be used as energy and glycerol as a substrate for the liver. Sounds like a good weight loss idea? Actually, probably not, as cortisol favors the breakdown of fat from arms and legs but deposits fat in the torso.
4. **Immuno-suppressant**: Cortisol suppresses inflammation by decreasing antibody production, decreasing white blood cell migration and decreasing pro-inflammatory signaling from immune cells. Hence the logic behind a cortisol injection into an inflamed joint.
5. **Brain function**: Cortisol can cause mood changes and memory alterations. As may be evident, cortisol is a hormone that is essential for life; however, abnormal levels can cause problems. Excessive cortisol production results in hypercortisolism whereas low levels of cortisol results in hypocortisolism.

Hypercortisolism

Excessive cortisol release can result from a tumor in the adrenal cortex which would result in excessive cortisol secretion. It could result from a tumor in the pituitary gland that would produce excessive amounts of ACTH or a tumor in the hypothalamus that would produce excessive amounts of CRH. In either event the adrenal gland would secrete excessive amounts of cortisol (**Cushing's syndrome**). The most common cause of Cushing's syndrome is the over-administration of glucocorticoids prescribed to treat some other condition such as an autoimmune disorder like rheumatoid arthritis or as an immunosuppressant after organ transplant. Looking at the actions of cortisol you might be able to predict what excessive cortisol might do: hyperglycemia (too much glucose), muscle breakdown, fat breakdown and re-deposition in the face and trunk, depression and learning difficulties.



Symptoms of Cushing's (Hypercortisolism)

By Mikael Häggström (Own work) [CC0], via Wikimedia Commons Link: https://commons.wikimedia.org/wiki/File%3ACushing's_syndrome_(vector_image).svg

Hypocortisolism

Loss of cortisol production is usually accompanied by a total loss in the function of all the layers of the adrenal cortex. The condition is known as **Addison' disease** and although rare is usually due to an autoimmune disease that destroys the adrenal cortex. Patients usually suffer from problems not necessarily associated with cortisol like **hyperkalemia** (excess potassium) or **hyponatremia** (low sodium) due to the loss of aldosterone. However, other symptoms associated with loss of cortisol may also be present. These include: fatigue, muscle weakness, fever, and difficulty standing up, diarrhea, sweating, mood changes and muscle pains. The adrenal insufficiency can also result in increased ACTH production since the normal negative feedback control is lost. The excess ACTH is associated with increased skin pigmentation due to the cross reactivity of ACTH with receptors for melanocyte stimulating hormone.

Clical Pearl: Black Licorice and glycyrrhizin

The hormone cortisol has been shown to cross react with the aldosterone receptor (meaning that it can do the same thing as aldosterone) but only at very high blood concentrations. At normal concentrations, it does not act as an agonist on the aldosterone receptor because of the enzyme 11 beta hydroxysteroid dehydrogenase, which is found in the kidneys, can convert cortisol to an inactive form called cortisone. However, when cortisol levels are very high the enzyme becomes quickly overwhelmed and a portion of the existing cortisol will activate aldosterone receptors. In addition, the chemical glycyrrhizin, found in black licorice, has been shown to inhibit 11 beta hydroxysteroid dehydrogenase. Thus, individuals that consume large amounts of black licorice can substantially increase their cortisol levels, and depending on the amount consumed, can even induce Cushing's like symptoms. Moreover, it should be noted that measuring blood cortisol levels is only part of the picture because it leaves out the metabolites. Having low cortisol could mean that the adrenal gland is producing less or it could mean that enzymes like 11 beta hydroxysteroid, or the reductase enzymes are working too much. For example, diseases like inflammation, hypothyroidism, leptin resistance, and obesity tend to cause 11 beta hydroxysteroid to convert cortisone back to cortisol, increasing blood levels of cortisol. Conversely, diseases like hyperthyroidism, PCOS, or supplements like progesterone and prednisone tend to cause 11 beta hydroxysteroid to convert cortisol to cortisone, reducing blood levels of cortisol.