Adrenal Glands and its hormones

There are 2 adrenal glands that lie anteriorly to kidneys. Each is embedded in a capsule of fat. Each adrenal gland is composed of 2 endocrine organs, one surrounding the other. There are 2 parts actually: an adrenal cortex and an adrenal medulla.

The adrenal medulla is the inner portion and it secretes epinephrine and norepinephrine when stimulated to do so by the sympathetic nervous system. These two hormones are called catecholamines and are involved in the “fight or flight” mechanism of the nervous system.

The adrenal cortex is the outer portion and secretes a variety of steroid hormones called corticosteroids (precursor is cholesterol).

Anatomy of the Adrenal Glands

About 80% of the adrenal gland is composed of the cortex which has three layers or zones:

1) Zona glomerulosa – the outermost region or layer
2) Zona fasciculata – the middle and largest portion
3) Zona reticularis – the innermost layer.

All three layers secrete corticosteroids of which cholesterol is the common precursor. On the basis of their primary actions, the adrenal steroids can be divided into 3 categories:

a) mineralocorticoids – aldosterone, which influences mineral or electrolyte balance; from z. glomerulosa
b) glucocorticoids – cortisol, which plays a role in glucose metabolism and proteins and lipids as well; from z. fasciculata
c) sex hormones – identical to those produced by the gonads (male – testes; female – ovaries); from z. reticularis

Mineralocorticoids from the zona glomerulosa

Aldosterone is the primary one and its most important effect is its action on electrolyte balance. Its primary site of action is the distal tubules of the kidney nephron where it promotes Na⁺ retention into the blood and enhances K⁺ elimination into the urine filtrate.

If Na⁺ is retained, H₂O is osmotically attracted to Na⁺ and therefore is retained as well. This increase in water in the blood causes an increased blood volume. This is important in the longterm regulation of blood pressure.

Without mineralocorticoids, death will occur due to large loss of plasma volume that would be lead to circulatory shock. Other hormone deficiencies won’t cause death directly such as this but problems associated could lead to premature death.

Regulation of Aldosterone release or secretion

Aldosterone is released due to:
1) Activation of the renin-angiotensin system in the kidneys and related to a decrease in Na⁺ and decrease in BP.
2) Direct stimulation of the adrenal cortex by increase in blood K⁺ concentration

This zone is relatively independent of the anterior pituitary hormone influence of ACTH. It may have a weak effect in releasing aldosterone but in general it does not.
Glucocorticoids from the zona fasciculata and its metabolic effects

The main glucocorticoid is cortisol from the zona fasciculata and it has an important role in carbohydrate, fat, and protein metabolism.

Overall, cortisol's main effect is to increase concentration of blood glucose at the expense of fat and proteins. Let’s view cortisol release with respect to CHO metabolism:

1) **Gluconeogenesis** - this is the conversion of nonCHO precursors (aa) into CHO within the liver, primarily. Between meals or during periods of fasting, when no new nutrients are being absorbed into the blood, the liver delivers glycogen to become glucose to maintain normal blood glucose levels for the brain. However, if glycogen is depleted, then new glucose is made upon the stimulus of cortisol and turned into glycogen to be used as needed. This is essential because the brain can only function on glucose and cannot store glucose as glycogen. All done in order to maintain normal blood glucose levels.

Cortisol effects on CHO metabolism, cont.

2) Decrease utilization of glucose by cells everywhere else in the body except the brain. Cortisol can cause other cells not to take up glucose so more available to the brain but cannot decrease uptake by the brain, has no influence on the cells of brain.

Summary on CHOs: cortisol increases gluconeogenesis and decreases other cells’ uptake of glucose, so cortisol has caused a diabetogenic effect or increases blood glucose. Occasionally, this could be great enough or 50% above normal that it is called an Adrenal diabetes. Would only weakly respond if given insulin.

Cortisol effects with respect to Protein metabolism

1) Cortisol stimulates protein degradation in all cells except liver cells. In other words, specifically it decreases protein synthesis (anabolism) and increases protein catabolism (break down to amino acids). So, by breaking down a portion of muscle proteins into their amino acid components, cortisol increases the concentration of blood amino acids. Now these amino acids are available for gluconeogenesis at the liver. In the presence of large amounts of cortisol, the muscles could become so weak that a person couldn’t rise from a squatting position.

2) Cortisol promotes formation of proteins (anabolism) by the liver which is opposite to the rest of the body proteins. The liver makes plasma proteins so these would be increased as well.

Summary on protein metabolism: ↓ muscle proteins, ↑ liver proteins.

Cortisol on Lipid Metabolism

1) Cortisol increases lipolysis or increased fatty acids in the blood from adipose tissue. These fatty acids can then be used for energy source instead of glucose thereby conserving glucose for the brain.

So in times of starvation, cortisol shifts the cells from utilizing glucose for energy to using fats for energy and thereby conserving glucose for the brain only. It requires several hours to become fully developed.

Cortisol presence allows for permissiveness

Cortisol presence permits catecholamines to induce vasoconstriction. If not, a person lacking cortisol, may go into circulatory shock (decrease in blood volume or blood pressure) in a stressful situation that needs widespread vasoconstriction.

Cortisol and Stress.

Stress is defined as the generalized nonspecific response to the body to any factor that overwhelms, or threatens to overwhelm the body’s compensatory abilities to maintain homeostasis. The stressor is the agent inducing the response while stress is the state induced by the stressor.

Types of stimuli that can induce a stress response:

1) **Physical** - trauma, surgery, intense heat or cold, restraining the person
2) **Chemical** - ↓O₂ supply, acid-base imbalance
3) **Physiological** – heavy exercise, pain, hemorrhagic shock
4) **Psychological or emotional** – anxiety (exams), fear, sorrow
5) **Social** – personal conflicts, changes in lifestyle

Any of these stresses can cause an immediate and marked increase in ACTH from the anterior pituitary thereby causing an increase in cortisol from the adrenal cortex. Why cortisol is released in stress is unknown but consider the example of a primitive human or animal faced with life threatening situation where eating is not a plausible event at that time.

Result is increase blood glucose for the brain, increase free fatty acids for energy and increase amino acids for liver proteins.
Anti-inflammatory and Immunosuppressive Effect of cortisol

If higher than normal physiological concentrations of cortisol or synthetic glucocorticoids are administered, not only will the metabolic effects be increased but there are several important actions that can be seen:

1) Anti-inflammatory - Synthetic glucocorticoids are being administered to inhibit all steps in inflammation that are actually very destructive, such as in rheumatoid arthritis. They act to decrease inflammation and swelling and stabilize capillary membranes. They don’t affect the underlying disease process but merely suppress the body’s response to the disease.

2) Immunosuppression – Corticosteroids are also given to inhibit the effects of the immune system by knocking out of commission the white blood cells responsible for antibody production and destruction of foreign cells. Useful in allergic disorders and preventing organ transplant rejection.

Reasons why therapeutic use should be limited:
1) Persons using have limited ability to resist infections
2) Other undesirable effects can occur with the good ones such as: Gastric ulcers
3) Blood pressure
4) Atherosclerosis
5) Menstrual irregularities

Overuse and increased amounts of corticosteroids should be avoided and should only be used sparingly.

Regulation of Cortisol release

Two factors that can also influence the negative feedback are diurnal variation in cortisol and stress.

1) Cortisol levels are highest in the morning and lowest at night. This is primarily related to the sleep-wake cycle. They will be reversed in one who works nightly and sleeps daily. This information is particularly important to know: 1) when blood sample is taken; 2) the sleep cycle of person being sampled or swing shifts; and 3) the effect of surgery time of day in helping the individual handle the stress.

2) Stress can greatly affect levels of cortisol in the blood. It can override, for example the hypothalamic-pituitary axis of negative feedback. The magnitude of the increase of blood cortisol is proportional to the intensity of the stressful stimulation. More stress – more cortisol. Less stress – less cortisol.

Negative feedback from cortisol to hypothalamus/anterior pituitary

Pathologies associated with Adrenal cortex hormone secretion

A) Oversecretion of Adrenal Cortex Hormones

1) Hyperaldosteronism – Conn’s syndrome – hypersecreting adrenal tumor of zona glomerulosa; ↑ aldosterone with no negative feedback. High Na+ and H2O retention (hyponatremia) and low plasma K+ (hypokalemia) which leads to ↑ BP

2) Hyperaldosteronism – produced by any condition that causes a chronic reduction in arterial blood flow to the kidneys, thereby excessively activating the renin-angiotensin system. Ex. Is atherosclerotic narrowing of the renal arteries. Similar results as in #1 above.

3) Cushing’s Disease – Oversecretion of cortisol, so see exaggerated effects of cortisol which includes glucose excess (hyperglycemia) and protein shortage. The excess glucose is deposited as fat so see “moonface”, “buffalo hump” (fat above the shoulder blades), spindly legs, fat in facial area or strange redistribution of fat. Diabeticogenic effect. Glycosuria occurs and the condition is called an adrenal diabetes. Could be due to a) oversecretion of CRH or ACTH causing overstimulation of the adrenal cortex; or, b) adrenal tumors that uncontrollably secrete cortisol independent of ACTH; or, c) ACTH-secreting tumors located in places other than the pituitary, most commonly the lung.

Pathologies, cont.

4) Adrenal Androgen Hypersecretion – excess adrenal androgen secretion could either be a virilizing adenoma in females with too much testosterone produced. Will give the female overdeveloped male characteristics such as hirsutism, deepening voice and more muscular arms and legs. In males, it may show up as a feminizing adenoma with too much estrogen but is very rare. This would give males more female characteristics such as breasts that are more developed. If androgens occur in prepubertal boys, it may cause premature secondary sex characteristics such as deep voice, beard, enlarged penis and a sex drive. This is not a true puberty. There will be no sperm production or other gonadal activity because the testes are still not functioning. If it occurs in adult males, no effect will be seen. Inherited condition.
B) Insufficiency of Adrenal Cortex Hormones

1) Primary adrenal insufficiency – called Addison’s Disease – Hyposecretion of cortisol but all hormones of the cortex are undersecreting. Most commonly due to idiopathic atrophy of the adrenal gland. Could be an antibody (autoimmune) that is attacking the adrenal cortex. Hypoglycemia, cortisol ↓ as well as aldosterone ↓, ACTH ↑ (darkens skin due to ↑ MSH as well from the same precursor and cell), lethargy, poor response to stress, mimics depression and misdiagnosed at times. Will see hyperkalemia and hyponatremia with hypotension and if aldosterone low enough, can be very life-threatening.

↑ CRH → ↑ ACTH → ↓ (atrophied adrenal gland) cortisol, aldosterone.

1) Secondary adrenal insufficiency – This may be due to a pituitary or hypothalamic abnormality with only a decrease in cortisol. ACTH does not cause the release of ald.

No ACTH → ↓ cortisol only