

# Endocrine

## I. Background

Hormones "send messages" to cells; they "tell" cells to do things, like make products to secrete or use certain nutrients from the blood. They represent long-distance communication, because a hormone released in one location can have effects on cells a long way away (ex, thyroid hormones from the thyroid gland affect all cells, including those in your big toe).

Cells can communicate in other ways, besides using hormones. These other ways represent local types of communication, though: between two cells, or between just a few cells:

- synaptic communication

- gap junctions

- paracrine communication- between cells within a tissue; cells can release chemicals that send messages to other cells in small amounts, so that local cells get the message, but generally not enough of those chemicals make it to the blood to have widespread effects. We call these types of chemicals "local hormones," and they include the prostaglandins (which are, incidentally, released by damaged cells and recognized by nociceptors).

## II. General Information about hormones

A. Where they come from, how they get around, how we get rid of them

1. Often produced in glands dedicated to hormone production (ex., thyroid gland) but not always (ex. kidneys). Cells that are specialized to produce hormones are considered endocrine tissue (specialized epithelia).
2. Hormones are released by endocrine cells into the interstitium. From there, the hormones diffuse into capillaries. Capillaries that serve endocrine tissue are highly permeable, and tend to be fenestrated. Fenestrated capillaries are porous, and allow even more exchange of solutes than do normal capillaries. The fenestra are pores within each cell that allow relatively large molecules like hormones to pass through.
3. Generally, they are eventually degraded by enzymes in a variety of places (ex, in tissues where they've been used, in the liver as they pass through). Some can be gotten rid of by other means as well, ex. cortisol, some of which is incorporated into saliva.

## B. Structure of hormones: 3 classes

### 1. Amino Acid Derivatives- related to single amino acids

tyrosine derivatives: E, NE, thyroid hormones (dopamine is also a tyrosine derivative)

tryptophan derivative: melatonin, serotonin

2. Peptide hormones- short peptide chains, these also include some glycoproteins (remember those?). I'd like you to know that the peptide hormones include both polypeptides and glycoproteins, but I won't ask you to know which hormones are glyco- or poly. Just generally know which are peptide hormones: all of them other than the Amino Acid Derivatives and the Lipids (so just memorize which are a.a. and lipids, then you'll automatically know the others!)

### 3. Lipid Derivatives

#### a. Steroid hormones: derived from cholesterol.

the sex hormones: androgens, estrogens, progestins

the adrenal cortex hormones: mineralocorticoids, glucocorticoids

calcitriol

#### b. Eicosanoids: derived from essential fatty acids. Most commonly used for paracrine communication; include the prostaglandins.

C. Regulation of hormone release: negative feedback. The release of hormone is always, ultimately, to end up opposing a particular stimulus. Some of the hormone systems and interactions are so complex, however, that it doesn't always seem particularly obvious (you'll see that when we get to hormone cycling in Reproduction). A nice, straightforward example is that of PTH.

## III. Hormone Action- what happens to a cell when a hormone arrives

### A. What hormones cause cells to do:

1. Turn genes on: remember that genes code for proteins, so "turning on" a gene will cause a protein to be made.

2. Activate or inactivate an existing enzyme or other protein in the cell

Overall, the effects of these actions can:

- a. Alter membrane permeability or solute absorption by opening or closing channels (#2), or causing them to be made (#1) (for example, calcitriol causes the production of  $\text{Ca}^{2+}$  channels in cells lining the small intestine, so that dietary  $\text{Ca}^{2+}$  may be absorbed; insulin causes the activation of glucose channels so that cells may take in glucose from the blood)
- b. Induce secretory activity; for example, by the production or activation of enzymes involved with making products for secretion
- c. Stimulate mitosis; for example, by the production or activation of enzymes involved with replication of organelles or DNA
- d. Alter metabolic activity; for example, by the production or activation of enzymes involved with ATP production
- e. Alter the rate of transcription or translation, ie, make particular proteins/enzymes faster or slower.

B. How hormones work; the biochemical events that end up causing a cell to change its activities.

- I. Amino Acid and Peptide hormones use 2nd messengers (with one exception, thyroid hormones, that act like steroid hormones).

These hormones are "greeted" by a receptor in the membrane of a target cell. For instance, Thyroid Stimulating Hormone from the adenohypophysis is recognized by cells of the thyroid gland. They have receptors for TSH in their membranes. When TSH reaches capillaries in the thyroid gland, it will bind to the receptors.

Using the most well-understood 2nd messenger, cyclicAMP (cAMP), as our example:

Binding of hormone to the receptors causes a cascade of chemical events within the cell. The ultimate goal is to activate protein kinases, enzymes that phosphorylate other chemicals (for example, kinases could phosphorylate enzymes that drive the production of thyroid hormones in thyroid cells). Why does this matter? Many proteins are activated or inactivated by the addition or removal of phosphate; so by adding phosphate to proteins, kinases can turn them "on" or

"off." For example, the enzymes in thyroid cells are present in the cell, but need Pi to function.

The substance that activates the kinases is the second messenger. A.a. and peptide hormones never make it into the cell; once they bind to receptor, their job is over. The cell takes over from there.

The Process:

First, be aware that there are 3 types of membrane proteins you need to know about: 1) the hormone receptor, which spans the membrane from the outside surface to the interior 2) the G-protein, which is bound to the receptor on the interior portion of the membrane and 3) Adenylate Cyclase, an enzyme that spans the membrane. Take a minute to draw a portion of the membrane with these 3 proteins. As you read each of the following steps, redraw the pictures, showing what's going on at each step.

Let's use a liver cell responding to epinephrine. One of the things that liver cells do in response to E is break down glycogen to release glucose to the blood (what other hormone has this effect?). When epinephrine binds to its receptor, the receptor changes shape and releases the G-protein.

The G-protein moves along the interior part of the cell membrane once it's released. It will bump into and bind an Adenylate Cyclase.

Adenylate Cyclase, upon being bumped and bound, will drive the reaction:  $ATP \rightarrow cAMP$ . That is, it will convert ATP to cAMP.

Again, cAMP is the 2nd messenger, whose job it is to activate kinases. So, cAMP cruises around the cytosol, activating kinases. Incidentally, there are enzymes ready to degrade cAMP almost as soon as it's made.

Now, we have a bunch of kinases running around really getting the job done: activating or inactivating proteins that will have the effect desired by the hormone. For example, in liver cells, one of the enzymes that gets activated by these kinases is responsible for chopping glucose units off of glycogen chains.

\*Study suggestion: Take a minute to go through a stepwise process of epinephrine release, starting with seeing a bear charging towards you, and ending with glucose being released from liver cells to fuel your muscles as you run away (rather than playing dead because, really, who's going to have the where-with-all to do that!). Don't skip the part about the hypothalamus directing the release of E. Draw E leaving the adrenal medullae, travelling through the blood, and hitting a receptor on a liver cell, and then draw the ensuing events in the cell, including the exodus of glucose.

Two other types of second messenger systems- know they exist, but we won't go into detail:

-  $\text{Ca}^{2+}$  can act as a second messenger

- G-protein activation can lead to a reduction of cAMP rather than an increase

2. Steroid hormones and thyroid hormones- these types of hormones enter the cell and activate genes.

They diffuse into their target cells. Once inside, they bind to receptors that are in the cytosol. The hormone-receptor complex then enters the nucleus, and binds to a second receptor that is associated with the DNA. This binding will activate a specific gene.

For example, thyroid hormones turn on genes that code for enzymes involved in the production of ATP.

Thyroid hormones (not the steroid hormones) affect metabolism in a second way: they bind to receptors attached to mitochondria within the cell, and increase ATP production directly at the mitochondria.

**IV. Regulation of hormones-** again, it is all ultimately negative feedback.

A. Some are regulated by relatively simple, direct negative feedback systems, for example: when blood glucose increases, insulin is released from the pancreas. Cells take glucose from the blood, so glucose levels start to drop. Falling blood glucose levels cause the pancreas to release less insulin.

Some other examples: PTH, calcitonin, calcitriol, aldosterone

B. Many hormones are regulated by hormones from the hypothalamus and pituitary gland. For instance, the hypothalamus monitors thyroid hormone levels in the blood. When they start to decline, the hypothalamus releases Thyroid Releasing Hormone to the adenohypophysis. In response, the adenohypophysis releases Thyroid Stimulating Hormone to general circulation. When TSH reaches the thyroid gland, it will start producing and releasing more thyroid hormones. The increased thyroid hormone in the blood will cause the hypothalamus to decrease its release of TRH.

The glands/organs and their hormones

**V. The hypothalamus and pituitary gland** (hypophysis)

## A. Anatomy

1. They are connected via the infundibulum
2. The pituitary rests in the sella turcica of the sphenoid bone
3. The pituitary has 2 functional areas:
  - a. Anterior (adenohypophysis)
  - b. Posterior (part of the neurohypophysis)
4. Neurons from the hypothalamus produce and release hormones, either directly or via blood, to the pituitary.
  - a. the adenohypophysis makes its own hormones; it contains endocrine cells. Hormones coming from the hypothalamus tell the adeno- which hormones to release.
  - b. the neurohypophysis does not make its own hormones. It contains lots of capillaries. Neurons of the hypothalamus travel through the infundibulum into the neurohypophysis, and release hormones directly onto the capillaries in the neurohypophysis.

## B. The Adenohypophysis

1. The hypophyseal portal system- the hypothalamus contains branched capillaries. These capillaries merge as they travel through the infundibulum. They enter the adenohypophysis, where they rebranch.

-From here on out I will abbreviate neurohypophysis and adenohypophysis as neuro- and adeno-.

The neurons of the hypothalamus release hormone onto the capillaries of the hypophyseal portal system. The hormones then travel in the blood, through the infundibulum, to the adeno-.

2. Releasing and Inhibiting hormones from the hypothalamus- the types of hormones that the hypothalamus sends to the adeno- are Releasing or Inhibiting. Releasing hormones cause the adeno- to release specific hormones; Inhibiting hormones cause the adeno- to stop releasing specific hormones. For example, the hypothalamus sends Thyroid Releasing Hormone through the hypophyseal portal system to the adeno-. Once it

gets there, cells of the adeno- will respond by sending Thyroid Stimulating Hormone to the blood. We will focus on Releasing Hormones, not Inhibiting Hormones.

3. I just said this in #2, but, in response to RH from the hypothalamus, the adeno- will send hormones into the blood. There are two different "types" of hormones from the adeno-hypophysis:

a. Stimulating Hormones- these target other glands/organs, and cause the release of specific hormones. SH do not have direct effects; instead, they direct the release of hormones that will have the ultimate, desired effect. For example, TSH will target the thyroid gland, and cause the release of thyroid hormones.

b. Hormones that have direct effects- a few of the hormones released by the pituitary produce the ultimate, desired effects. For example, Growth Hormone Releasing Hormone from the hypothalamus causes the pituitary to release Growth Hormone. GH will then (for ex.) cause adipose cells to breakdown triglycerides.

4. The Hormones of the Adeno-hypophysis: these will be presented in this order: Hormone, target cells, effect/s, name of RH from hypothalamus

a. Thyroid Stimulating Hormone- I've used this example so much that you probably know this, but: thyroid, increases the release of thyroid hormones, Thyroid RH

b. Adrenocorticotrophic Hormone (ACTH)- adrenal cortex, increases release of GlucoCorticoids, Corticotropin RH

c. Gonadotropins- there are two, both released in response to Gonadotropin RH (GnRH).

i) Follicle SH- has both Stimulating and Direct effects. Females: ovaries, increase estrogen production, aid development of follicles (nanny cells for the egg); males: testes, aid sperm development

ii) Leutinizing Hormone- females: ovaries, increase estrogens and progestins production; males: testes, increase adrogens production

d. Prolactin- Direct action. Mammary glands, support mammary development, stimulate milk production, Prolactin Releasing Factor

e. Growth Hormone (GH)- Direct action (also stimulating, in a way, but I won't focus on that). All cells, increase protein synthesis; Adipose, triglyceride breakdown; Liver, glycogen breakdown; Bone and Muscle, cell division; in response to GH-RH

f. Melanocyte Stimulating Hormone- Direct action, although its significance in humans is not established. Melanocytes, increase melanin production. Release is probably under hypothalamic control, but I haven't found the releasing factor from my sources, so it may not be known.

C. The neurohypophysis- again, neurons from the hypothalamus travel all the way into the posterior pituitary, and release 2 hormones directly into the blood. The hypophyseal portal system does not enter the neurohypophysis, and the neuro- does not make its own hormones.

1. AntiDiuretic Hormone (ADH)- kidneys, water retention, in response to increased blood electrolytes; inhibited by alcohol and caffeine

2. Oxytocin- gonads; females- induces muscle contractions related to labor and delivery, milk release, and moving sperm toward the egg; males- induces the release of semen into the urethra

## VI. The Thyroid Gland- produces thyroid hormones and calcitonin

### A. Structure-

1. Composed of hollow, fluid-filled spheres lined by simple cuboidal cells. These spheres are called follicles, this is where thyroid hormones are made.

2. In between the follicles are C-Cells (make calcitonin)

3. The fluid in the follicles is a colloid: viscous with proteins

### B. Follicles and thyroid hormones

1. Follicle cells make a precursor to the thyroid hormones. The precursor contains the amino acid tyrosine. This precursor is released into the colloid.

2. I<sup>-</sup> (iodide) from the blood is collected by follicle cells and incorporated into the precursor. This leads to the formation of the thyroid hormones.
3. The thyroid hormones are thyroxine (T<sub>4</sub>: has 4 I<sup>-</sup>) and Triiodothyronine (T<sub>3</sub>: has 3 I<sup>-</sup>)
4. They are released to the blood. Most released T-hormone is T<sub>4</sub>, which is less active/potent (T<sub>4</sub> can be converted to T<sub>3</sub> when needed). Most of the T<sub>3</sub> and T<sub>4</sub> released are bound to proteins. As such, neither is active. So, the blood contains a reserve of T-hormones: those that are bound to proteins, and T<sub>4</sub>. As T<sub>3</sub> is used by cells, T<sub>4</sub> is converted to T<sub>3</sub>, and both are released by the proteins. That is, as the blood concentration of T<sub>3</sub> drops, bound T-hormone dissociates from protein, and T<sub>4</sub> is converted to T<sub>3</sub>.

#### C. Functions/effects of T<sub>3</sub> (overall, increase metabolism)- targets ALL cells

1. Increase mitochondrial activity, by direct binding
2. Increase production of enzymes involved in all aspects of ATP production, by gene activation
3. Increase production of the Na<sup>+</sup>-K<sup>+</sup> pump, by gene activation

\*reference book to see how these effects affect specific areas of the body.

D. Goiter- with a lack of iodine in the diet, the precursors cannot be "finished," so the gland will not release them into the blood. The hypothalamus detects declining T-hormones, and directs the thyroid gland to release more. So the gland responds by making more precursor, but again, cannot finish or release the actual hormone. The follicles fill up, and the gland swells.

#### E. Calcitonin-produced by C-cells

-inhibits osteoclasts, increases Ca<sup>2+</sup> excretion by kidney; released in response to rising levels of blood Ca<sup>2+</sup>

-uncertain whether calcitonin is important in adults

**VII. Parathyroid Glands-** ParaThyroid Hormone (PTH)- The parathyroid glands are 4 small glands located on the posterior aspect of the Thyroid gland.

-stimulates osteoclasts, inhibits osteoblasts, stimulates calcitriol release by kidneys, encourages  $\text{Ca}^{2+}$  retention by kidneys; released in response to declining levels of blood  $\text{Ca}^{2+}$

## VIII. Adrenal Glands- Corticosteroids, androgens, E and NE

### A. Location, Anatomy & Structure

One gland sits atop each kidney

Composed of two functional areas: the cortex (outer portion) and the medulla (central portion).

The cortex, in turn, contains 3 functional areas, each of which secretes different hormones:

Zona Glomerulosa (outermost), Zona Fasciculata, Zona Reticularis

### B. The Adrenal cortex- **All hormones released by the cortex are steroid hormones.**

1. The Zona Glomerulosa- secretes mineralocorticoids, which affect blood electrolyte concentration. Aldosterone is the most abundant of the mineralocorticoids. Aldosterone increases  $\text{Na}^{+}$  retention and  $\text{K}^{+}$  excretion at the kidneys; it is released in response to declining  $\text{Na}^{+}$  or increasing  $\text{K}^{+}$  in the blood. It is also released as part of a general sympathetic stress response, which we will discuss later in the chapter.

2. Zona Fasciculata- secretes GlucoCorticoids (GC), which have many effects. One of the primary effects is to alter glucose metabolism, this is the derivative of their name.

GC are released constantly, and their "normal" release follows daily cycling. They are released in higher doses in response to stressful situations, both short-term and long-term. Their effects are extremely diverse and complex, but include:

stimulate gluconeogenesis (making glucose from other carbs and from amino acids) by liver cells,  
stimulate the breakdown of triglycerides and release of fatty acids by adipose,  
suppress immune response/inflammatory response.

3. Zona Reticularis- secretes androgens, but the significance of androgens from this area pales in comparison to that from the gonads.

C. The Adrenal Medulla- Composed of specialized neurons that secrete E and NE. Most hormone from the medulla is E. Both are released constantly; the amount released is adjusted by direct neural control by the hypothalamus. As hormones, they help to regulate metabolism, but they can also produce the effects seen by NE as a neurotransmitter (review from the ANS chapter).

Effects include: Breakdown of glycogen from liver and muscle cells, Breakdown of triglycerides and release of fatty acids from adipose, increased rate and force of heart beat and respiration; in addition to the other effects associated with sympathetic activation. Keep in mind that both are released constantly, so the degree of sympathetic effects seen depends on the amount released.

**IX. Pineal Gland-** releases melatonin, melatonin regulates sleep-wake cycles and serves as an antioxidant protecting brain cells; release is adjusted by day length. Remember that the hypothalamus receives information from the retina about light, and it sends that information on to the pineal gland.

**X. Other Systems** that have Endocrine function- we will discuss most of these in more detail as we get to these systems' chapters.

A. Intestines and stomach- variety of hormones, generally involved with digestion. For example, gastrin from the stomach causes the stomach to continue churning and producing juices when food is present.

B. Kidneys-

1. Calcitriol- The kidneys receive an inactive version of calcitriol. They will activate and release calcitriol in response to PTH. The production of calcitriol is complex, but the general overview is: Precursor in skin is converted to cholecalciferol and released to blood when struck by UV rays-> reaches the liver, which converts it to another precursor (here it can be stored) -> liver releases precursor to blood -> reaches kidneys, which convert precursor to calcitriol and release it to blood.

Calcitriol increases dietary  $Ca^{2+}$  absorption; released in response to PTH

2. Erythropoietin- increases Red Blood Cell production

3. Renin- this is actually an enzyme. It will begin the process of activating an inactive precursor to a hormone that will affect (raise) blood pressure and cause the release of mineralocorticoids from the adrenal cortex.

C. Heart- Atrial Natriuretic Peptide- affects (lowers) blood pressure

D. Thymus- Thymosins, support lymphocyte development (a type of immune cell)

E. Pancreas- Has two populations of glandular cells: Exocrine cells, that secrete enzymes into the small intestine through tubes; and Endocrine cells, that secrete hormones to the blood. Clusters of endocrine cells are found scattered throughout the exocrine cells. These clusters are called Islets of Langerhans. The Endocrine cells produce several hormones, including Insulin and Glucagon.

1. Insulin- Causes most body cells to increase uptake and metabolism of glucose in addition to increasing uptake of amino acids; muscle and liver cells to store glucose as glycogen; adipose cells to store fatty acids as triglycerides. Released in response to rising blood glucose levels.

2. Glucagon- Causes liver and muscle cells to break down glycogen; secondary role in encouraging breakdown of triglycerides and in gluconeogenesis. Released in response to declining blood glucose levels.

F. Gonads: testes and ovaries- Androgens (include testosterone), Estrogens and Progestins. Variety of complex effects; overall, promote the development and maintenance of secondary sexual characteristics, preparation for and support of pregnancy, childbirth and lactation in females.

\*Please read "Patterns of Hormonal Interaction," pg. 639 (Martini). I won't ask for definitions of the terms, but I'd like you to understand some of the various ways in which hormones can interact.

## **XI. The Stress Response**

This term refers to a general neuroendocrine response to a variety of stressors: fasting/starvation, illness, the threat (or reality) of physical harm, and exercise. Note that these are threats to physical well-being; they directly threaten homeostasis. The neuroendocrine response is designed to maintain homeostasis during these physical events.

So, what is the neuroendocrine response? Well, the events of the Stress Response are generally divided into three phases: the Alarm Phase, the Resistance Phase, and the Exhaustion Phase. As a brief introduction, the Alarm Phase is a general sympathetic activation; this phase is dominated by neural responses (the ANS) and it's quick. The

Resistance Phase is a longer term endocrine response. This can last for hours, days, weeks.... The Exhaustion Phase, well, this is what happens when the first two weren't able to restore homeostasis. It leads to death. So really, the exhaustion phase should NOT be a normal part of the stress response; the first two phases are designed to help you avoid the exhaustion phase.

Let's use the following example to see how it all works: you are a hunter-gatherer who has been eating greens, berries and tubers for weeks. Suddenly, you see a herd of buffalo in the distance (meat is an extremely dense source of calories and protein). Start the alarm phase, you are really excited! Gather a group of fellow hunters, grab your arrows and go! (Hopefully you've got some packs of dogs nearby who can help you)

**Alarm Phase:** the sympathetic division of the ANS steps up. Your heart will start racing, you will become more alert as blood is shunted to your brain, you will become stronger and have more endurance as blood is shunted to your muscles, you will start sweating more, your breathing rate and depth increases and your heart rate goes up. Sounds like you're getting ready to exercise, doesn't it?

Well, that's because general sympathetic activation is also called the "fight or flight response," and it's designed to help you exercise: fight a predator or competitor, run away from a predator or competitor, or in this case, track a herd of buffalo.

Now, the sympathetic division does something else that will help you exercise: starts the mobilization of stored energy. That means, it causes adipocytes to break down triglycerides and send fatty acids to the blood, and hepatocytes to break down glycogen and send glucose to the blood. Why does that help you exercise?

Of course, currently unnecessary functions like digestion and excretion will screech to almost a halt to conserve energy.

You already know all about the Alarm Phase, because you experienced it when the lion crashed through your window.

Okay, so you and your hunting party have started their journey. Unfortunately, the buffalo have a big head start on you, and you may actually end up tracking them for days with little or no food on the way. Luckily, during the alarm phase, hormones were being released that will get you through this long-term bout of exercise and fasting. You are now entering:

**The Resistance Phase:** this phase is dominated by endocrine responses, although the sympathetic division is still active. The primary goal of the resistance phase is to make sure that you maintain blood glucose, water and electrolyte levels. Electrolytes, by the way, are just minerals: Na<sup>+</sup>, Ca<sup>2+</sup>, etc.

Why is it important that you maintain blood glucose levels? Well, what does the brain eat? What DOESN'T the brain eat?

Your muscles are using up a lot of glucose and  $\text{Na}^+$  in their activity. Right now, you're in danger of starving your brain of both of these.

To maintain blood glucose, a number of events will occur. The liver will break down glycogen to release glucose to the blood. Body cells in general will start to switch to using fatty acids to make ATP. This allows glucose to be saved for the brain and for muscles when they need to perform fast strength contractions, like sprinting or wrestling a buffalo. Adipocytes will release fatty acids to make sure the body cells have access to fats. At some point, proteins will be digested to provide amino acids; those amino acids will travel to the liver where they will be converted to glucose. To conserve  $\text{Na}^+$  and water, the kidneys will work hard to retain them, rather than letting them go into the urine. Why retain  $\text{Na}^+$ ? In the natural world,  $\text{Na}^+$  is hard to come by. In fact, unless you live by the sea, meat is generally the best source.  $\text{K}^+$  is much easier to come by... it's abundant in plant foods, and the kidneys have no specific mechanism to conserve it. That'll be important later.

The primary hormone that kind of directs what's going on during this phase is cortisol, the major glucocorticoid. But, there are other hormones involved. Let's take a look at the major players:

**Glucagon:** induces glycogenolysis. This puts your stored glucose into circulation. Pretty soon, though, you're going to use up all that stored glucose.

**Cortisol:** does a number of things:

- stimulates lipolysis.
- stimulates protein hydrolysis
- stimulates gluconeogenesis
- enhances the effect of glucagon
- enhances the ability of E and NE to constrict blood vessels
- inhibits inflammation and certain other immune system functions (this MAY save energy and keep the immune response in check; but these are hypotheses)
- inhibits uptake of glucose by body cells (although, the lack of insulin at this point is also inhibitory to glucose uptake)

**Epinephrine:**

- stimulates lipolysis
- stimulates glycogenolysis
- stimulates gluconeogenesis

- increases blood pressure by inducing general vasoconstriction
- does all the things we associate with the sympathetic response

### **Growth Hormone:**

- stimulates gluconeogenesis
- stimulates lipolysis
- also stimulates amino acid uptake and protein synthesis by body cells, which is in opposition to cortisol. The relative amounts of these hormones dictate which events dominate, and exercise levels may also influence how much protein is broken down vs. built in muscles.

### **Aldosterone:**

- stimulates  $\text{Na}^+$  retention. Unfortunately, whenever  $\text{Na}^+$  is retained by the kidneys, it is exchanged for a  $\text{K}^+$ . So the retention of  $\text{Na}^+$  is coupled with the loss of  $\text{K}^+$ . In general, this shouldn't be a problem because you and your party can easily munch on some plant materials. But, if it continues for a long time, it could potentially throw your  $\text{K}^+$  levels way off and that could be a death knell.

### **ADH:**

- stimulates water retention at the kidneys.

Your party has been following the herd and munching on low-calorie (but  $\text{K}^+$  rich) plant foods for about a day. You've been able to drink some water, so you're not in too much danger of dehydration. But, in terms of calories you are definitely in a state of fasting. Your glycogen stores are long gone, and you've got some gluconeogenesis going on.

Suddenly, as you reach the crest of a hill, you see the herd down below. You and your fellows carefully plan your attack, and are able to take down a buffalo. Luckily you are still close enough to your camp, and strong enough, that together you can take the animal back to share with your family. Tonight, you'll have a big meal, your parasympathetic division will resume activity, and you can sleep well knowing that at least this time, you've avoided the exhaustion phase. Ahhhh....

But, what if you hadn't caught the buffalo? What if you'd gone too far in winter and couldn't find enough food to get you back? Then you'd have entered:

**The Exhaustion Phase:** Organ systems will fail. Contributing factors include:

- Exhaustion of lipid reserves
- Structural damage to organ systems because of protein loss
- Electrolyte imbalance, particularly  $\text{K}^+$  insufficiencies

A few extra thoughts: the nature and degree of the stress response, of course, depends on the nature and degree of the stressor. For example, when you go to the gym and work

out, your body undergoes physiological responses that are basically the stress response. Sympathetic activity steps up, the resistance hormones are secreted more. However, you don't have a sudden, extreme sympathetic activation like you would, well, if a lion crashed through your window. Okay, enough with the lion already, right?

Also, the degree to which the parasympathetic division tones down depends on the nature of the problem. It never "shuts off" completely.