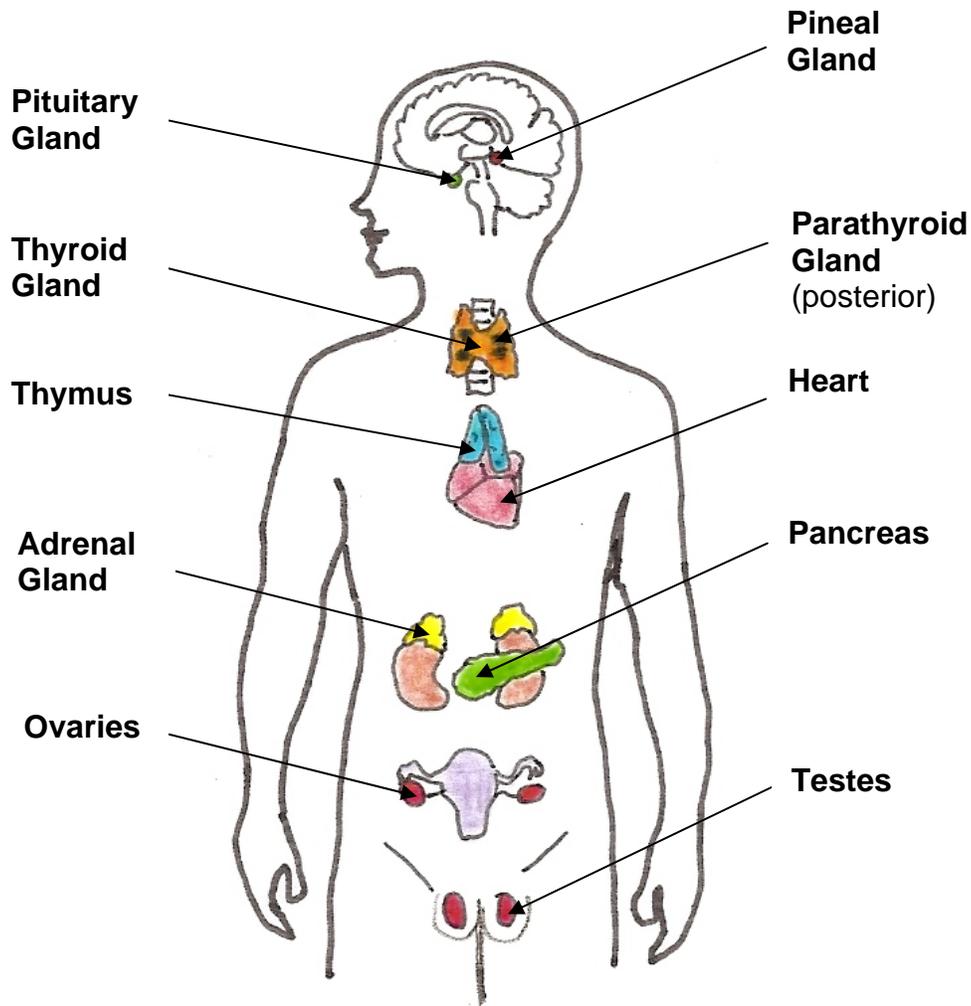
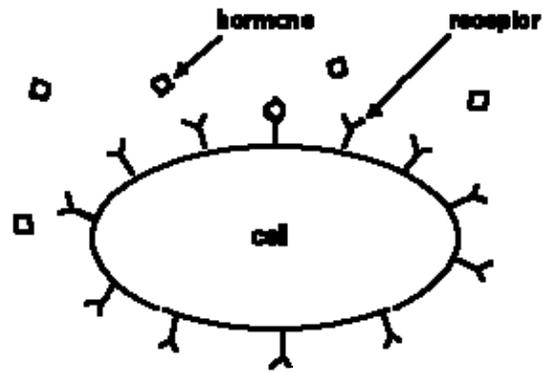


# The Endocrine System

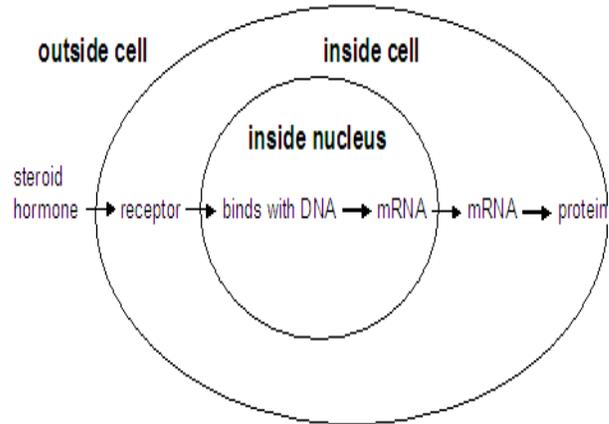


In the body, the endocrine system is composed of a variety of different glands. The term ‘endocrine’ loosely means “secreting within”. Endocrine glands send chemical signal molecules around the body to communicate information. Together with the nervous system, it is considered one of the two ‘long distance control systems’ of the body.

The way the endocrine system works is by releasing chemical messengers called **hormones** into the blood stream which are then transported throughout the body. Hormones act on specific *target* cells that have receptors for the specific signal molecule. As such, a hormone can only affect a tissue that has receptors for it. When the hormones bind to the receptors on or within the target cell, it produces a response in the target cell. Hormones can act within seconds (epinephrine or adrenaline), over a few hours (insulin, glucagon), maybe weeks (estrogen, testosterone) or can have an effect over years (human growth hormone).



**Figure 1.** The cells in the body have receptors on the external surface of the plasma membrane. Hormones circulating in the blood can bind to these receptors and change the activity of the cell.



**Figure 2.** Cells also have internal receptors. Hormones that are lipid soluble, such as steroids and thyroxine, can slip through the plasma membrane and bind to these internal receptors whereby they influence DNA transcription and change the activity of the cell.

**Exercise 1.** Identify the endocrine organ shown above as described by each of the statements below:

1. \_\_\_\_\_ located in the throat; bi-lobed gland connected by an isthmus.
2. \_\_\_\_\_ found sitting on top of the kidneys.
3. \_\_\_\_\_ connected to the hypothalamus, it has a front and back portion.
4. \_\_\_\_\_ paired glands suspended in the scrotum outside of the body.
5. \_\_\_\_\_ small structures sitting on the posterior surface of the thyroid gland.
6. \_\_\_\_\_ found in the pelvic cavity of females, concerned with ova and estrogen.
7. \_\_\_\_\_ sits in the upper thorax overlying the heart.
8. \_\_\_\_\_ found in the center of the brain and shaped like a tiny pine cone.
9. \_\_\_\_\_ a mixed gland, located close to the stomach and small intestine.
10. \_\_\_\_\_ although not a primary endocrine gland, it releases hormones.

Here is a simple comparison between the **Nervous** and **Endocrine** systems.

**The Nervous System** conducts signals throughout the body with neurons. Neurotransmitters are the chemical messengers released from neurons and they travel across a narrow synaptic cleft and bind to receptors on the target cell. Communication is very fast, typically measured in milliseconds, it is brief and it is usually highly specific in terms of location.

**The Endocrine System**, in contrast, conducts signals throughout the body via glands. Hormones are the chemical messengers released by these glands and they travel through the blood stream to target cells that have receptors for those hormones. Communication can happen within seconds but is considered slow compared to the nervous system. Its signals often linger for a longer time and are usually more broad in terms of effects on various tissues.

**Exercise 2.** Answer the questions below regarding the endocrine system.

1. Define hormone:

2. Can you think of a hormone that may take months to have its effects? \_\_\_\_\_.

3. Can you think of a hormone that only takes seconds to have its effects? \_\_\_\_\_.

4. Define target tissue:

5. If hormones travel where ever blood goes, why don't all cells respond to all hormones?

**There are basically two general classes of hormones, classified by their chemical structure.**

1. **Steroid and Thyroid Hormones**: Since these are chemically hydrophobic (or lipophilic), which means they are not soluble in water but soluble in lipids, they readily pass through the plasma membrane and enter the cytoplasm of the cells in the target tissue. They can also enter the nucleus and bind to chromatin 'receptors' associated with DNA. They have their effects by activating transcription of the DNA, basically reading a gene, making mRNA and generating various proteins. Steroid hormones often act more slowly than peptide hormones because of the time required to produce new proteins as opposed to activating proteins that are already present. Examples are: Prostaglandins, the sex hormones thyroxin and calcitonin.
2. **Peptide Hormones**: Peptide hormones are composed of a short chain of amino acids and the catecholamines are derived from amino acids, especially tyrosine. They are water soluble (hydrophilic or lipophobic) and cannot slip into the cell but instead bind to a receptor on the outer surface of the cell. In a typical pathway the resulting complex activates an a G protein, which then switches on an enzyme that catalyzes the synthesis of cyclic AMP (cAMP) from ATP and then cAMP activates other enzymes that are inactive inside the cell. In this case, the hormone is the first messenger and cyclic AMP is a second messenger. Examples are: Insulin, glucagon, epinephrine, and the pituitary hormones.

**Hormone interactions:**

**a) Antagonistic** – one hormone having the opposite effect of another. (e.g., insulin and glucagon on blood glucose levels).

**b) Synergistic** – two or more hormones act together to have a greater effect than the sum of them separately. (e.g., testosterone and FSH on sperm production).

**c) Permissive** – one hormone enhances the effect of another hormone secreted later. (e.g., estrogen and progesterone in the uterine cycle)

After a few questions let's take a look at the fascinating world of these endocrine glands and their signals.

**Exercise 3.** Answer the questions below regarding the endocrine system.

1. Chemically, hormones belong to two molecular groups: 1) \_\_\_\_\_ and 2) \_\_\_\_\_.
2. The \_\_\_\_\_ hormones often change DNA transcription in the nucleus.
3. The \_\_\_\_\_ hormones are not lipid soluble and so must bind to the plasma membrane.
4. What do all hormones have in common?
5. If one hormone has an opposing action to another, this interaction is termed \_\_\_\_\_.

**The Pineal Gland**

The name of the pineal gland refers to its resemblance to a tiny pine cone. This gland is located deep within the center of the brain in humans and is stimulated by signals from the optic nerve of the eyes. It releases several chemical messengers, including **Melatonin** and **Dimethyltryptamine (DMT)**.

**1. Melatonin**

When **melatonin** is secreted into the blood stream by the pineal gland it helps regulate the circadian rhythms of the body. The amount of melatonin released depends on the level of light in your surroundings; as light levels decrease, more melatonin is released and this signals the onset of sleepiness; as light levels increase, less melatonin is released and we become more alert and awake. In relation to this, some people are adversely affected by the short days and long nights during the winter and experience what's called 'seasonal affective disorder' (SAD). This is a situation in which too much melatonin is produced and can cause depression, sleepiness, lethargy and weight gain.

Melatonin also affects reproductive functions by depressing the activity of the gonads when there is less daylight. As such, animal studies show that melatonin levels have been connected to seasonal mating behavior. This makes sense as levels of daylight change with the seasons and this is connected to changes in sex hormone levels. An interesting aspect to this is the presence of photoreceptors on the pineal gland, even though in most animals (including humans) the pineal gland is not directly exposed to light.

The pineal gland also contains a small amount of calcium ( $\text{Ca}^{2+}$ ) hydroxyapatite (a calcium-phosphorus salt) that is also contained in bone tissue. As it turns out, Sodium Fluoride – which is now added to most municipal water supplies - is attracted to  $\text{Ca}^{2+}$  hydroxyapatite like a magnet and this can cause the pineal gland to become ‘calcified’ with sodium fluoride. If melatonin levels are suppressed by this calcification, this can shorten the time to puberty. Recent studies show a dramatic decrease in the age for the onset of menstruation for girls in developed countries, including the United States. Whereas more than 20 years ago the onset of puberty for girls was from about 12 to 14 years of age, now in some areas it is as early as 7 to 9 years of age. Although this situation is likely to have many aspects to it, there are many deleterious consequences as a result of these changes in human development.

## 2. Dimethyltryptamine (DMT)

Dimethyltryptamine or DMT is one of the most powerful hallucinogens of the tryptamine family! Not only do humans make DMT themselves in their pineal glands, i.e., we have our own endogenous supply, but it is also ubiquitous in many plants. DMT is believed to be released during birth and also during near-death experiences. It is also thought to play a role in facilitating the visual aspects of dreaming during sleep, spiritual visions and experiences in deep meditations. As such, it can be viewed as an important element of exploring your own consciousness. Structurally it is very similar to the neurotransmitter serotonin (5-HT), which is also similar to melatonin (also released by the pineal gland). Ayahuasca (pronounced: i-a-waz-ka) is a drink containing DMT that is commonly used in South American Shamanic practices for those who wish to explore their own consciousness. It is created by using plants that contain DMT mixed with other plants containing monoamine oxidase (MAO) inhibitors. Consuming this drink is one way to receive the active DMT orally without it being enzymatically degraded by MAO inhibitors in the stomach. In Shamanic traditional settings, ayahuasca is considered a *medicine* and not a ‘recreational drug’; it is used for spiritual, emotional, physical and mental healing.

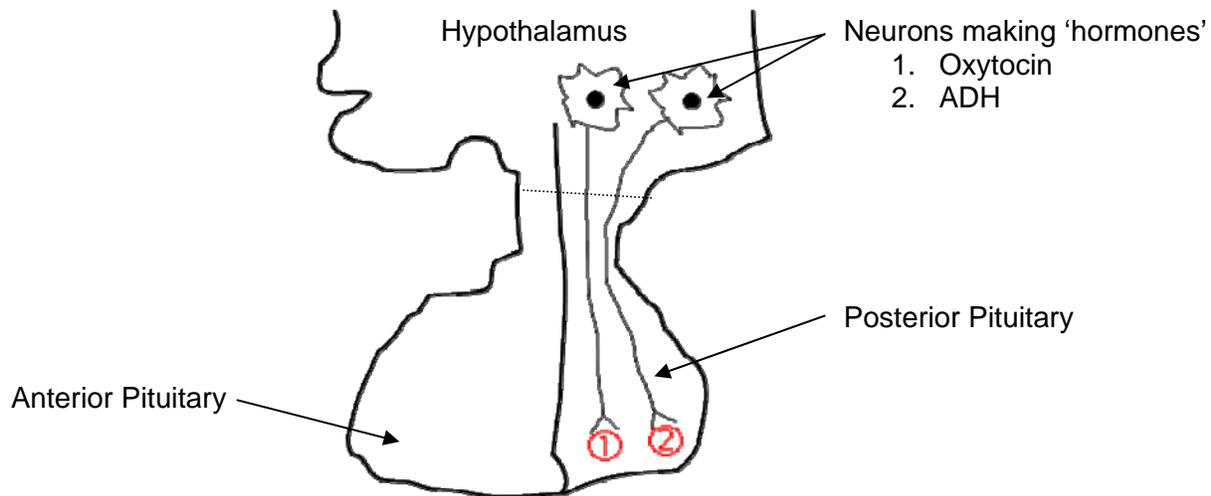
In many cultures the pineal gland is thought of as the spiritual ‘third eye’, meaning it has a role in connecting us to the rest of the universe and is related to intuition and extra sensory perception. In some animals, the pineal gland is closer to the skin and directly stimulated by light; indeed, some lizards even have a literal third eye. It is fascinating that this tiny pine cone-shaped structure in the middle of our brain can release many powerful chemicals that can act as an ‘eye’ in a variety of ways. As noted previously, sodium fluoride (added to tap water and found in dental products and much more) has been shown to have no significant effect on preventing cavities but has been shown to calcify the pineal gland, thus restricting its function! There are also numerous studies that show children who drink fluoridated water have lower IQ’s than those who drink un-fluoridated water. Many consider sodium fluoride a toxin that should be actively avoided. Look up the topic yourself if you want to examine the facts that are currently known regarding the usefulness and safety concerns of water fluoridation.

## The Pituitary Gland

The pituitary gland is also located in the brain and is actually connected to and closely associated with the *hypothalamus*. Essentially the pituitary gland is really two separate glands and both are under the control of the hypothalamus. The two distinct regions in the gland are; the **anterior pituitary** (also called the *adenohypophysis*); and the **posterior pituitary** (also called the *neurohypophysis*). The activity of the adenohypophysis is controlled by releasing hormones from the hypothalamus. The neurohypophysis is controlled by nervous stimulation, namely by the hypothalamus.

## Posterior Pituitary (Neurohypophysis)

The name **neurohypophysis** denotes that it's really nervous tissue, not glandular tissue. As shown in the sketch below, the posterior pituitary contains axons of neurons that extend from the hypothalamus. The two hormones Oxytocin (OT) and Antidiuretic Hormone (ADH) are stored in and released from axonal endings in the posterior lobe of the pituitary.



**1. Oxytocin** – an important action of this hormone is to stimulate the smooth muscle of the uterine walls called myometrium. This causes the significant contractions of the uterus during child birth or ‘labor’. This hormone also stimulates the release of milk from the mammary glands by causing surrounding cells to contract. After birth, stimulation of the breast by the infant feeding stimulates the posterior pituitary to produce additional oxytocin.

### Positive Feedback Loop in Homeostasis:

The release of oxytocin during child birth is one of the best examples of a positive feedback loop in human physiology. The basic details are as follows: As the birthing time approaches, the baby’s head pushes against the cervix and increases pressure on the cervix. Stretch sensitive receptors detect this and send incoming signals to the posterior pituitary. This triggers the release of oxytocin from the posterior pituitary into the blood stream which binds to receptors on the myometrium and causes the body of uterus to contract, pushing the baby’s head against the cervix, increasing the pressure, which triggers more oxytocin release, etc., so the cycle continues to become amplified until it is broken! (=birth occurs).

### ***Oxytocin: The Love and Bonding Hormone***

Recently the role of oxytocin in human bonding has been revealed more clearly such that it is considered by some to be the ‘love’ or ‘bonding’ hormone. Oxytocin is very important in the bonding between a mother and her infant, specifically with regard to physical touch and olfaction. Human touch and expressions of love are essential to health. A lack of stimulus and touch very early on causes excess cortisol release (also related to elevated stress) which can create a toxic brain environment and damage certain neural structures. Research in neuroscience shows that the easiest and quickest way to induce depression and alienation in an infant or child is not to touch it, hold it, or carry it on your body. It has also been proposed that a lack of touch damages not only individuals, but our whole society. Ultimately, human sensory deprivation can result in behavioral abnormalities such as depression, violence, substance abuse, and an impaired immunological functioning in mother deprived infants.

Oxytocin is also associated with the act of closeness and touching between adult humans, where this hormone helps to create an emotional bond. For example, a study shows that even the simple act of sharing a meal with another person increases your levels of oxytocin. Additionally, for adults during sexual intercourse both females and males release high levels of oxytocin.

There is also a literal connection of touch and bonding to another organ, namely the heart. A researcher in 1992 described the dual role of the heart cells: Not only do heart cells contract and expand rhythmically to pump blood, but they also communicate with each other. If you isolated a single heart cell (myocardocyte) from others around it, it loses its rhythmicity and begins to fibrillate and die. If, however, another isolated heart cell is placed in close proximity to it, they synchronize and beat in unison and do not die. Perhaps this is why most mothers instinctively place their new born babies on their left breast, keeping their hearts in close proximity so they may synchronize and connect better.

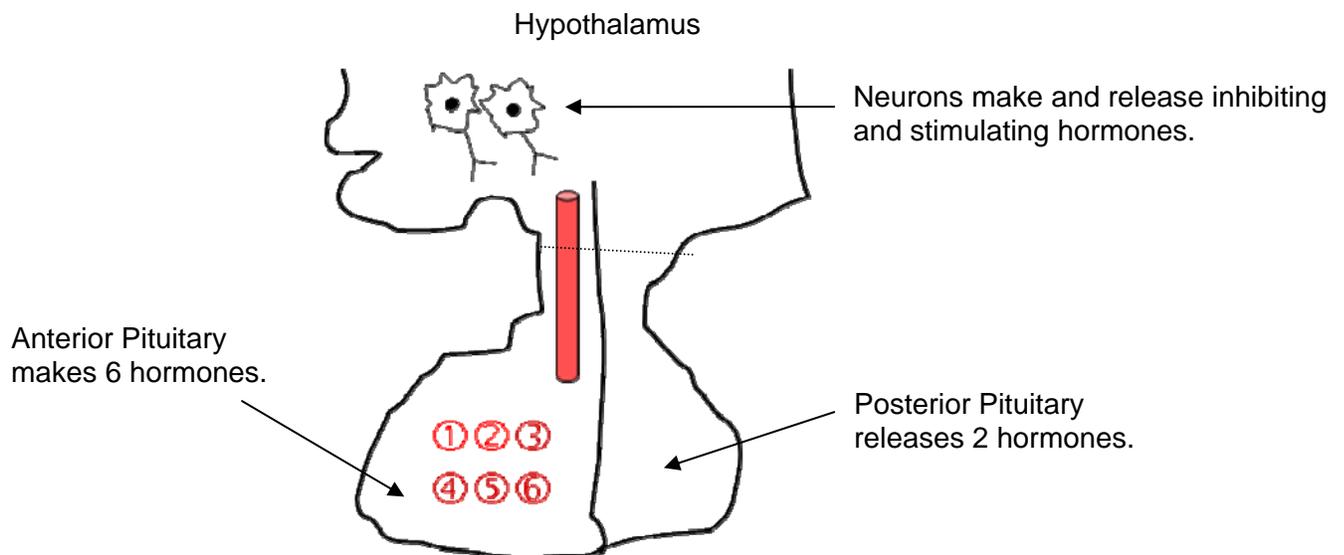
**2. Antidiuretic Hormone (ADH)** – this hormone is also known as **Vasopressin** and is released in response to the body's need to conserve water. Osmoreceptors detect changes in the 'concentration' of blood in the nephron of the kidney and in the hypothalamus. If the osmolarity of the blood is too high (over 308 mOsM) it is considered too concentrated or hypertonic, that is, there is not enough water in the body.

The receptors that detect this change then send signals to the hypothalamus and the neurons sitting in the hypothalamus trigger the release of ADH from the posterior pituitary. The ADH travels in the blood stream to the collecting duct of the nephron in the kidney and act to insert water pores there. This results in more water being retained by the body, hence less water in the urine and the urine becomes more concentrated as water is conserved.

In the disease diabetes insipidus, there is a decrease in ADH release which results in an excessive amount of urination (polyuria) leading to dehydration. The urine is very dilute and for health care workers in the past who had to "test" a patient's urine, it was reported to be 'tasteless or insipid'. Alcohol inhibits the release of ADH and can cause polyuria and dehydration. As the alternate name vasopressin implies (vaso = vessel, pressin = pressure), this hormone also acts as a vasoconstrictor for blood vessels and can elevate blood pressure. If a person were experiencing cardiovascular shock, the actions of conserving water, together with increasing blood pressure is a very effective way for the body to re-establish adequate blood pressure and maintain homeostasis.

### **Anterior Pituitary (Adenohypophysis)**

The name **adenohypophysis** denotes that it is glandular tissue (adeno = gland). The hypothalamus produces hormones (hypothalamic-releasing hormones) that travel in blood vessels to the anterior pituitary, stimulating it to produce other hormones. The anterior pituitary produces 6 different hormones. Each one is produced in response to a specific hypothalamic-releasing hormone.



1. Growth Hormone, often denote human growth hormone (hGH)
2. Thyroid Stimulating Hormone (TSH)
3. Adrenocorticotropic Hormone (ACTH)
4. Follicle-stimulating Hormone (FSH)
5. Lutinizing Hormone (LH)
6. Prolactin (PRL)

Brief Summary of the 6 hormones from the Anterior Pituitary:

1. hGH – is the primary hormone that regulates overall body growth, and is also important in general metabolism. Severe hGH deficiency during growth phases leads to dwarfism. Over-secretion of hGH in children leads to gigantism. Sever over-secretion of hGH in adults’ leads to acromegaly, a genetic disorder in which hGH is over-produced throughout a person’s lifetime.
2. TSH – stimulates secretion of thyroid hormone such as thyroxine from the thyroid gland and stimulates the growth of the thyroid. Important regulator of metabolic activity in the body.
3. ACTH – stimulates cortisol secretion from the adrenal cortex (often called the ‘stress hormone’, but in appropriate levels, cortisol is your friend!). Also promotes growth of adrenal cortex.
4. FSH – **a)** in females: stimulates growth and maturation of the ovarian follicles, and promotes estrogen secretion. **b)** in males: it is required for sperm production (together with ICSH).
5. LH – **a)** in females: responsible for ovulation and for luteinization. Regulates estrogen and progesterone **b)** in males: stimulates interstitial cells (in testes) to secrete testosterone, and therefore in males it’s typically called interstitial cell stimulating hormone (ICSH).
6. PRL – produced in high quantities after childbirth, it enhances breast development and stimulates mammary gland development for the production of milk. It is also involved in the metabolism of fats and carbohydrates.

### Negative Feedback Loop Inhibition

Almost all hormone secretions by glands that are under the control of the hypothalamus are controlled by a negative feedback loop. When the hormone levels are high, they inhibit the hypothalamus and anterior pituitary, resulting in a decline in their levels.

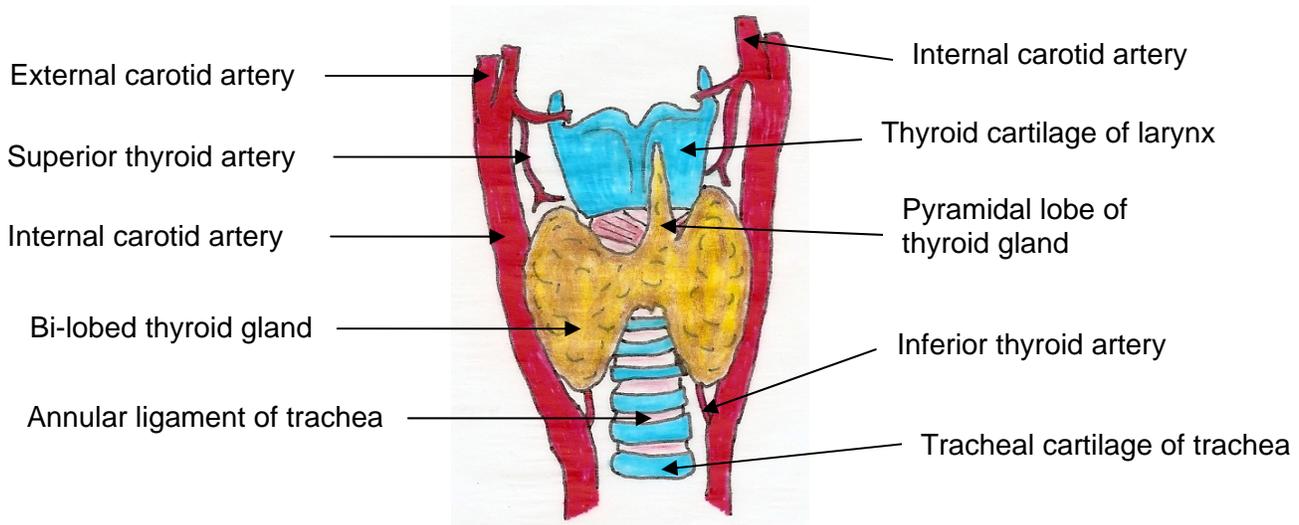
**Exercise 4.** Complete the information that is missing below regarding the endocrine system.

**Table 1.** Fill in the information about the hormone, gland or action that is compatible.

Hormone	Secreted by	Actions
Luteinizing Hormone (LH)		
	Posterior Pituitary	
		Stimulates cortisol release.
Melatonin		
		Stimulates follicular growth in females; required for sperm production in males.
	Pancreas	
Cortisol		
		Stimulates release of T <sub>3</sub> and T <sub>4</sub> and helps regulate metabolic rate.

### **The Thyroid Gland**

The thyroid is a butterfly-shaped gland in the neck, sitting just under the thyroid cartilage of the larynx and just over the top portion of the trachea. Normally it should weigh less than an ounce (about 30 g). During development in utero, the thyroid gland originates in the back of the tongue and migrates to the front of the neck. In rare instances it sometimes fails to migrate properly and stays very high in the neck much closer to the tongue; other times it may migrate too far and end up in the chest. Thyroid hormones, including **Thyroxine** and **Calcitonin**, regulate metabolic rate, growth, and development throughout the body. This gland is composed of follicles which can be seen in histological slides, these structures produce the hormone precursor thyroglobulin.



**The Thyroid Gland**

### 1. Thyroxine

The thyroid produces **thyroxine** (also called  $T_4$  because it contains 4 iodine atoms) and triiodothyronine (also called  $T_3$  because it contains 3 iodine atoms). Both  $T_4$  and  $T_3$  have similar effects on target cells, but the thyroid gland predominately makes  $T_4$  and in most target tissues the  $T_4$  is converted to  $T_3$ . These thyroid hormones are regulated by a negative feedback mechanism interaction with the hypothalamus and anterior pituitary gland. Basically this means that when there are sufficient thyroid hormones levels in the body, this inhibit the further production of them by the thyroid gland and inhibits stimulation of the thyroid by the hypothalamus. If the body lacks iodine (which you can only get from your diet), it cannot produce adequate amounts of the  $T_4$  hormone for the appropriate conversion to  $T_3$  to take place. When there are lower than normal thyroxine levels in the blood, this results in an excessive amount of thyroid stimulating hormone (TSH) being produced by the anterior pituitary. Due to the constant stimulation of the thyroid gland it enlarges and as a consequence a goiter results - yet it still can't make more  $T_3$ . A good dietary source of iodine is ocean fish and seaweeds like kelp.

Thyroxine is an important regulator of a person's Basal Metabolic Rate (BMR), that's like the idling speed of your body at rest and it is an indication of how much energy you require to sit and do nothing! This rate varies for everyone. Interestingly, during the cold months of winter the thyroid gland releases more thyroxine in an attempt body rev up your body and make you warmer. One of the ways thyroxine does this is to signal your cells to make more  $Na^+/K^+$  pumps. These pumps are active transporters in all cells and use a lot of ATP to continuously pump  $Na^+$  out and  $K^+$  into your cells. As ATP is broken down (hydrolyzed) it releases heat energy (second law of thermodynamics) making you warmer. Thank you thyroid gland!

**Hypothyroidism** occurs when the thyroid produce too little thyroxin. In adults this results in lethargy and weight gain. In infants, it causes cretinism, which is characterized by dwarfism, mental retardation, and lack of sexual maturity. **Hyperthyroidism** is when too much  $T_3$  and  $T_4$  are released; this increases heart rate and blood pressure, and causes weight loss.

### 2. Calcitonin

The thyroid gland also secretes the calcium ( $Ca^{2+}$ ) regulating hormone calcitonin. When  $Ca^{2+}$  levels in the blood are elevated, calcitonin is released to stimulate bone cells to deposit calcium into bone tissue. Bone is a dynamic tissue and functions as a storage site for important minerals such as  $Ca^{2+}$  and phosphorus.

Bone cells called osteoblasts (literally meaning ‘bone makers’) are the cells stimulated by calcitonin to make more bone matrix and thus decrease the  $\text{Ca}^{2+}$  levels in the blood. Please note, the actions of calcitonin are *antagonistic* or opposite to those of the parathyroid hormone.

### The Parathyroid Gland

There are actually 4 small parathyroid glands that are embedded on the posterior surface of the thyroid gland. They secrete **parathyroid hormone** (PTH), which helps to control blood calcium ( $\text{Ca}^{2+}$ ) levels in the body. When  $\text{Ca}^{2+}$  levels in the blood are too low, parathyroid hormone is released in order to elevate blood  $\text{Ca}^{2+}$  levels, and bone is the  $\text{Ca}^{2+}$  source that is tapped into. A type of bone cell called osteoclasts (literally meaning ‘bone destroyers’) are stimulated to dissolve the bone matrix and thus release free  $\text{Ca}^{2+}$  from bone into the blood stream. The regulation of  $\text{Ca}^{2+}$  in body fluids is extremely important, not only for bones and teeth, but also for nerve functioning, muscle contractions, blood clotting and glandular secretion. If we don't have enough calcium available for these functions, the body will take too much from the bones and cause them to decrease in mass and they may more easily fracture (e.g. osteoporosis). Too much calcium can cause kidney stones and weakening of muscle tone.

### The Thymus

The thymus is part of the immune system as well as being an endocrine gland. Sitting comfortably above anterior aspect of the heart directly behind the sternum (breastbone), it has two lobes that join in front of the trachea. Each lobe is made of lymphoid tissue, consisting of tightly packed white blood cells and fat. Its function is to transform lymphocytes (a type of white blood cells) into T-cells. In fact, the name *T-cell* denotes that they develop and mature in the Thymus! The T-cells are then transported to various lymphoid glands and tissues where they play an important part in fighting infections and disease and also guard against abnormal cell growth, as in cancer, and any foreign tissues that gets into our bodies. **Thymosine** is a polypeptide hormone present in the thymus that increases the activity of T-lymphocytes. Swelling of lymph glands and fever are signals that immune cells are multiplying to fight off invaders of the body.

Early in life the thymus enlarges significantly until puberty. Based on cadaver studies, medical institutions contend that the thymus gland atrophies (gets smaller) into adulthood and turns into adipose and fibrous tissue as we age, a process called involution. However, many other studies show that a healthy thymus should remain large and robust throughout life. A key to a happy and healthy thymus is adequate vitamins, minerals, exercise, eating un-processed (organic) whole foods and avoiding unhealthy refined foods and toxins. But this is a remedy for most things. Additionally, avoid horrific anti-nutrients such as unfermented soy, high fructose corn syrup, neurotoxins such as aspartame and Splenda, MSG, trans-fats, artificial colors and artificial flavors. Please note: Coconut oil, which is very beneficial for your body, is a saturated fat, not a trans-fat. Despite the well promoted notion that ‘saturated fats are bad and cause heart disease’ this is *not true* but widely believed; what a shame. Break the shackles of bad-information, do some research for yourself and find out the facts.

### The Heart

The heart is an amazing pump for the cardiovascular system, but it is also a secondary endocrine gland because it produces several hormones, one of which is **atrial natriuretic peptide** (ANP) or factor (ANF). ANP is a 28-amino acid peptide synthesized and released by atrial myocytes in response to atrial distension (elevated blood volume). It is a powerful vasodilator which acts to lower blood pressure. It also functions to increase sodium excretion (**natriuresis**) and increase fluid excretion (**diuresis**) from the body. ANP inhibits renin secretion from the kidneys, thereby inhibiting the renin-angiotensin-aldosterone system that acts to conserve water. Thus its release is primarily triggered in response to high blood pressure.

**Exercise 5.** Based on the information provided about these endocrine glands and their function, for each hormone in column A, select the appropriate endocrine gland that makes it from column B. The various endocrine glands in column B may be used more than once.

**Column A**

- |                  |                   |                                |
|------------------|-------------------|--------------------------------|
| ___ 1. LH        | ___ 6. $T_4/T_3$  | ___ 11. Calcitonin             |
| ___ 2. oxytocin  | ___ 7. FSH        | ___ 12. Vasopressin            |
| ___ 3. DMT       | ___ 8. thyroxine  | ___ 13. hGH                    |
| ___ 4. prolactin | ___ 9. TSH        | ___ 14. ANP                    |
| ___ 5. PTH       | ___ 10. melatonin | ___ 15. T-cell differentiation |

**Column B**

- |                       |                    |
|-----------------------|--------------------|
| A. Parathyroid glands | E. Adenohypophysis |
| B. Pineal gland       | F. Thyroid gland   |
| C. Neurohypophysis    | G. Pineal gland    |
| D. Thymus             | H. Heart           |

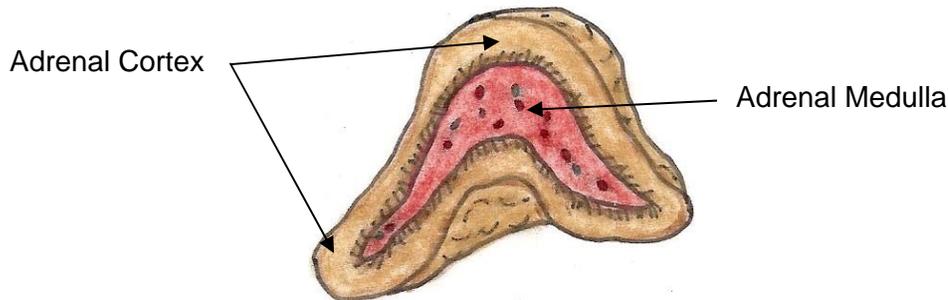
**Exercise 6. Multiple Choice Questions – select the best answer.**

- Somatotrophs, gonadotrophs, and corticotrophs are associated with the  
**a) thyroid gland   b) adenohypophysis   c) parathyroid glands   d) adrenal glands   e) neurohypophysis**
- The posterior pituitary gland is not truly considered an endocrine gland because it  
**a) has a rich blood supply   b) is not located near the brain   c) has no real blood supply   d) contains ducts   e) does not synthesize hormones**
- The endocrine gland that is probably malfunctioning if a person has a high metabolic rate is the  
**a) thymus gland   b) thyroid gland   c) pineal gland   d) posterior pituitary gland   e) pancreas**
- The antagonistic hormones that regulate blood calcium level are  
**a) h growth hormone-thyroid stimulating hormone (TSH)   b) insulin-glucagon   c) aldosterone-cortisone   d) calcitonin (CT)-parathyroid hormone (PTH)   e) estrogen-progesterone**
- The endocrine gland that significantly contributes to setting the body's biological clock is the  
**a) pineal gland   b) thymus gland   c) thyroid gland   d) adrenal gland   e) pancreas**
- The thymus can be considered an endocrine gland because  
**a) it is in the thoracic cavity   b) it makes ANP   c) it is where T cells differentiate   d) it is connected to all other glands by the lymphatic system   e) it makes thyroxine**
- Calcitonin stimulates which type of cell?  
**a) all bones cells   b) osteoblasts   c) osteoclasts   d) beta cells   e) osteocytes**
- For the *adrenocorticotropic* hormone, cortico means \_\_\_\_\_ and tropic means \_\_\_\_\_.  
**a) middle and top   b) inner(medulla) and growth   c) outer(cortex) and growth   d) outer(cortex) and shrink   e) inner(medulla) and growth**

## The Adrenal Gland

The adrenal glands sit on top of each kidney and hence are sometimes referred to as the *suprarenal* glands. This gland has two distinct anatomical and physiological portions that function as separate glands; the outer adrenal cortex and the inner adrenal medulla. Both the adrenal cortex and medulla are influenced by the anterior pituitary as directed by the hypothalamus. The adrenal cortex is regulated by negative feedback involving ACTH and the medulla is regulated by nerve impulses from the hypothalamus.

### The Adrenal Gland



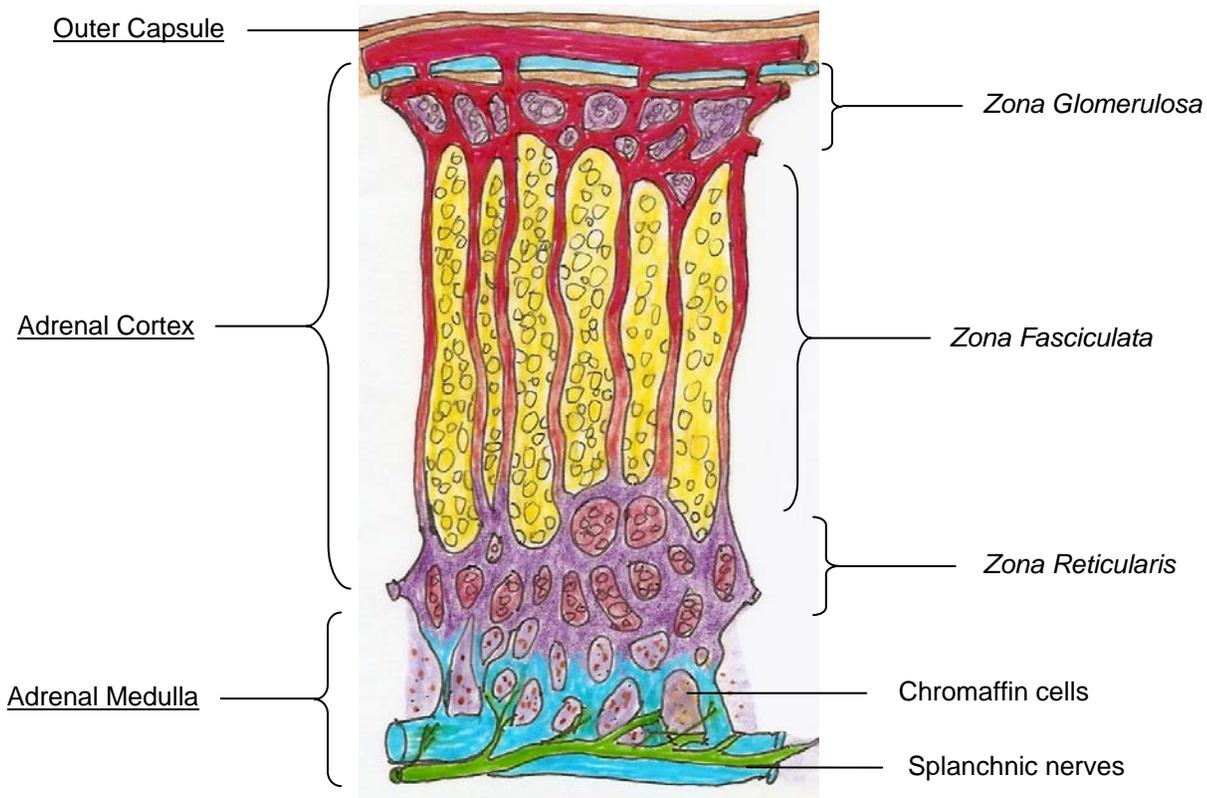
### A. Adrenal Cortex

The adrenal cortex is divided into 3 different regions and each region produces a different type of hormone. All of the cortical hormones are steroids. This means they are all derived from **cholesterol!**

The 3 Zones release 3 Types of Hormones from the Adrenal Cortex:

- 1) **Zona Glomerulosa** – thin outermost portion, the **Mineralocorticoids** are made here, including *Aldosterone*.
- 2) **Zona Fasciculata** – the thick, middle portion – the **Glucocorticoids** are made here, including *Cortisol*.
- 3) **Zona Reticularis** – the inner, thin portion – the **Sex Steroids** are made here, including *Androgens*.

### Zones of the Adrenal Cortex and Medulla



The hormone **aldosterone** is released when the body is trying to conserve water by helping the kidneys to retain sodium. This helps maintain blood pressure and salt balance. Increased sodium levels contribute to the retention of water and thus increased blood volume. In the absence of aldosterone, sodium is excreted and the lower sodium levels result in decreased blood volume and lower blood pressure.

The hormone **cortisol** has many vital roles in the body and it is also released in significant amounts in response to stress. Cortisol raises the level of glucose in the blood by stimulating the liver to produce glucose from stored non-carbohydrate sources such as proteins and lipids and to release it into the blood. Cortisol acts as a natural anti-inflammatory agent by inhibiting the immune system and thereby reduces swelling. It promotes gluconeogenesis – which means the body produces glucose from proteins and lipids in order to spare the use of glucose by most cells to ensure that cells like neurons, which can *only* use glucose, have enough in times of glucose scarcity. Gluconeogenesis can involve enhanced lipolysis and breakdown of skeletal muscle proteins. Cortisol is also needed for NE to have its vasoconstrictive effects. Many drugs are derived from cortisol to treat inflammation.

The steroid sex hormones **gonadocorticoids** androgens hormones (male) and estrogens (female) are secreted in minimal amounts in both sexes by the adrenal cortex, but their effect is usually masked by the hormones from the testes and ovaries.

## B. Adrenal Medulla

The adrenal medulla is composed of modified neural tissue and secretes two catecholamine hormones **epinephrine** (E) and **norepinephrine** (NE), which used to be called adrenaline and noradrenalin respectively. A variety of stressful conditions can stimulate the fight-or-flight response of the sympathetic division of the autonomic nervous system and trigger the adrenal medulla to release E (80%) and NE (20%) which act in concert with the sympathetic division. *Chromaffin cells* in the adrenal medulla are modified post-synaptic sympathetic neurons that receive sympathetic input and release E and NE into circulation. Hence they are called neuroendocrine cells. The effects on the body are a faster heart rate, increased blood pressure and dilated airways to facilitate greater oxygen flow to the lungs. In addition, blood glucose levels are increased to make energy more available. Predominantly, the secretion of E and NE is controlled by the hypothalamus via sympathetic nerves and not by pituitary hormones.

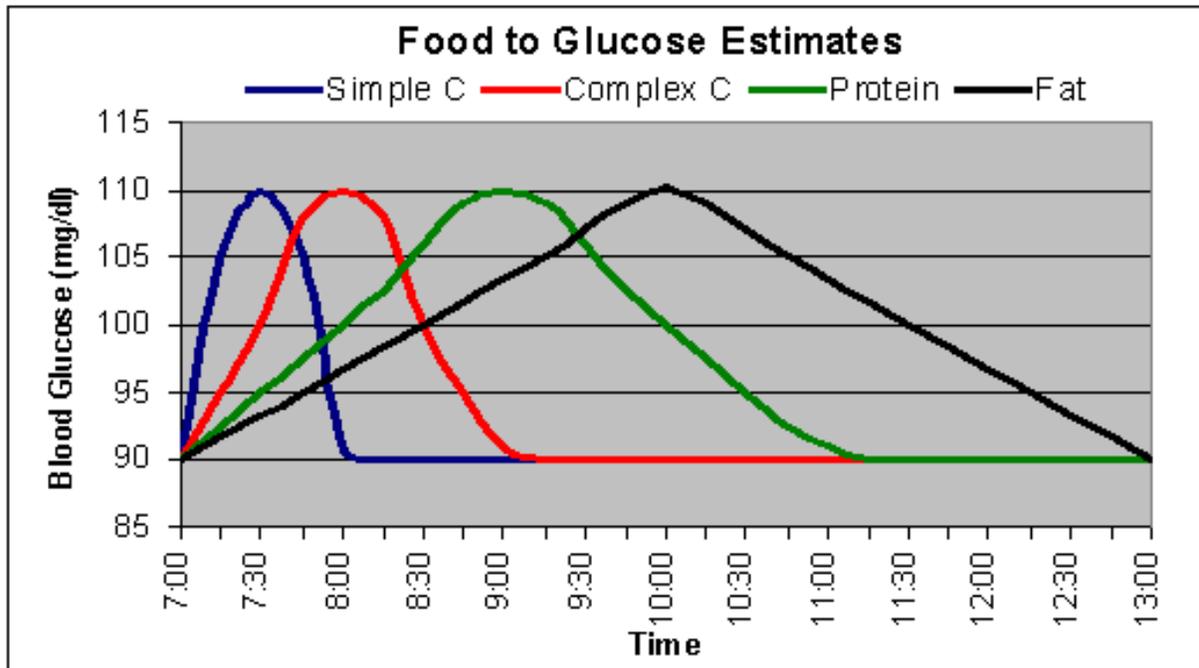
## The Pancreas

The pancreas is both an exocrine and an endocrine gland and is nestled behind the stomach where its head is in close proximity to the duodenum of the small intestine. The exocrine portion makes ‘pancreatic juices’ (in the pancreatic acini) which are digestive enzymes used in the digestive system to break down and absorb nutrients. The exocrine portion of this gland is contained in the pancreatic islets or islets of Langerhans and makes 2 hormones that regulate blood glucose levels: **Insulin** and **Glucagon**.

### 1. Insulin

The role of insulin is to lower elevated blood glucose levels after a meal. When your blood glucose concentrations are elevated, the beta ( $\beta$ ) cells in the pancreatic islets (or islets of Langerhans) secrete insulin. Insulin signals target cells to insert glucose transporters into their plasma membranes, this way they can take up the excess glucose circulating in the blood. Thus, insulin promotes the removal of glucose from the blood so it can be stored as glycogen in the liver and skeletal muscle. It also promotes other anabolic activities such as the storage of adipose (fats) in adipocytes (fat cells) as well as other anabolic activities. If the pancreas fails to produce enough insulin (type I) or the body becomes desensitized to insulin (type II), the result is a serious disease called diabetes mellitus. Interestingly, the neurons in the brain and spinal cord do not require insulin in order to use glucose. In addition, skeletal muscle when contracting during exercising use insulin independent glucose transporters, thus exercise lowers blood glucose without requiring insulin.

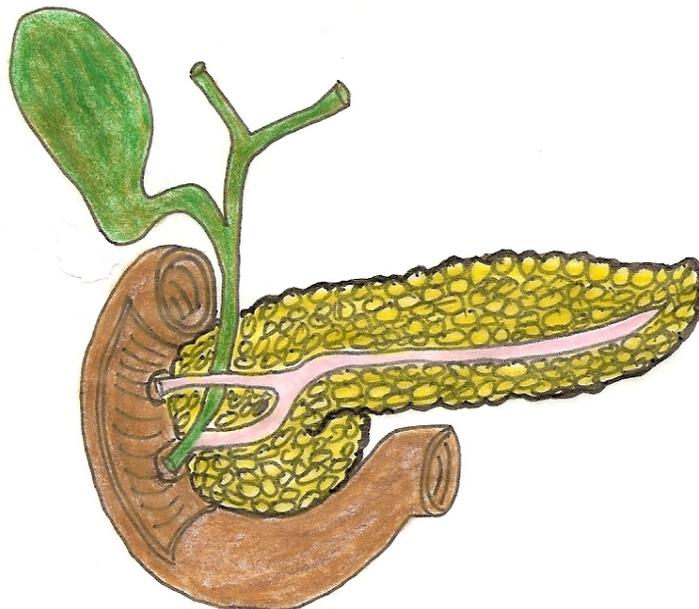
## What does the Glycemic Index represent?



**Figure 3.** The glycemic index is a measure of how different foods affect blood glucose levels. Above are examples of changes in blood glucose after a meal of simple and complex carbohydrates (C), proteins and fats (lipids). Notice the variation in the peak and span of glucose levels in the blood between the three basic food groups of carbs, proteins and fats.

## 2. Glucagon

The alpha ( $\alpha$ ) cells in the pancreatic islets secrete glucagon in response to low concentrations of glucose in the blood, so its actions are *antagonistic* or the opposite of insulin. It is normally secreted between meals to maintain stable concentration of glucose in the blood. Glucagon causes the liver to hydrolyze its glycogen stores into glucose and release it into the blood stream, thereby increasing blood glucose levels. It also causes fats and proteins to be converted into glucose, a process called *gluconeogenesis*, as well as other catabolic activities.



**The Pancreas, Gallbladder and Duodenum**

**Diabetes Mellitus** is a disease in which glucose cannot be sufficiently metabolized by the body, such that a person has high blood glucose but cannot use this glucose that is in the blood. The term for elevated glucose levels in the blood is *hyperglycemia* (emia = blood) and glucose in the urine is called *glucosuria* (uria = urine). In this situation, cells can starve because glucose is not being metabolized, even though there is an excess of glucose in the blood.

**Type I Diabetes Mellitus** - is also called "juvenile-onset diabetes" or "insulin-dependent diabetes" because the symptoms usually appear during childhood and insulin injections are used to treat it. It is caused by an autoimmune disorder in which the immune cells of the body attack the beta cells of the pancreas until they are destroyed. Initially the pancreas is unable to make enough insulin to cope with normal elevations in blood glucose, until gradually it cannot make any insulin at all. As a consequence, the body cannot utilize the glucose floating around in the blood, so blood glucose levels remain high, a state which is called hyperglycemia. The body then gets rid of excess glucose in the urine and this is called glucosuria and causes dehydration. In addition, this excess blood glucose attaches non-enzymatically to plasma proteins in the blood and results in *Advanced Glycated End-products* (AGE's) which wreak havoc on the body. Because type I is caused by a lack of insulin, it can be treated with insulin injections after a meal to enable cells to utilize the glucose ingested.

**Type II Diabetes Mellitus** – is also call "non-insulin-dependent diabetes" and is much more common than type I, accounting for about 90% of cases. This is caused by life-style choices. The main culprit is a poor diet; it is basically created by consuming excessive amounts of refined carbohydrates (especially sugars) over a long period of time. This includes simple carbohydrates like breads and cereals, as well as candy and soda. When glucose levels are chronically elevated in the blood, insulin levels must also be very high in order to utilize this excess sugar. Thus your pancreas must produce massive amounts of insulin, a situation which is deleterious for many reasons. A major consequence is that insulin receptors on the target cells of the body experience a huge down-regulation due to too much insulin. This ultimately brings about a *desensitization* of the body to insulin. The result is elevated blood glucose while many cells in the body starve because they cannot use this glucose! In addition, your pancreas must make more and more insulin since the cells have lost their sensitivity to it – this causes the pancreas to become exhausted. As in type I, the same symptoms arise such as, hyperglycemia, glucosuria, dehydration and AGE's. Diabetes mellitus can lead to blindness and such poor circulation as to cause tissue necrosis (death), often resulting in procedures such as below the knee amputations (BKA's).

Type II used to be called “adult onset” diabetes mellitus, as it was generally found that this form of diabetes became noticeable in middle age. However, now that every school yard is replete with soda and vending machines in addition to highly refined carbohydrate lunches, *young children* are presenting with type II diabetes mellitus! This should be viewed as astonishing and urgent positive action should be taken. Instead the bulk of our society is encouraged to believe that we should be interested to hear that a pill has been developed to address this issue, such as the potentially dangerous ‘Avandia’. Naturally no pill can cure this disease, which is completely reversible; a pill can only mask the *symptoms* as the body is thrown even further out of balance.

Diabetes mellitus II is easily treated by changing to a whole food diet and getting regular exercise. As it turns out, contraction of skeletal muscle uses glucose without the need for insulin! This is one reason why exercise is such a good activity for your body. Treatments that involve a medication designed to stimulate more insulin production is analogous to being moved from a low cliff to a very high cliff before you are pushed off it. I encourage you to investigate the simple and monumental relationship between the quality of the food you eat and its impact on the health of your body.

**Exercise 7.** Fill in the table below with relevant information about Type I and Type II Diabetes Mellitus.

**Table 2.** The Characteristic of Type I and Type II Diabetes Mellitus.

Characteristic	Type I Diabetes	Type II Diabetes
Age of onset		
Are the onset of symptoms fast or slow?		
Percentage of diabetics with this type of diabetes:		
Fasting blood glucose levels		
Natural insulin levels		
Beta cells of pancreatic islets		
Pancreatic islet cell antibodies		
Risk factors for getting disease		
Typical treatments		
List 3 symptoms:	1) 2) 3)	1) 2) 3)

*Go to the website (<http://faculty.sdmiramar.edu/faculty/sdccc/mcmahon>) and select urinalysis tests under the physiology mini labs.*

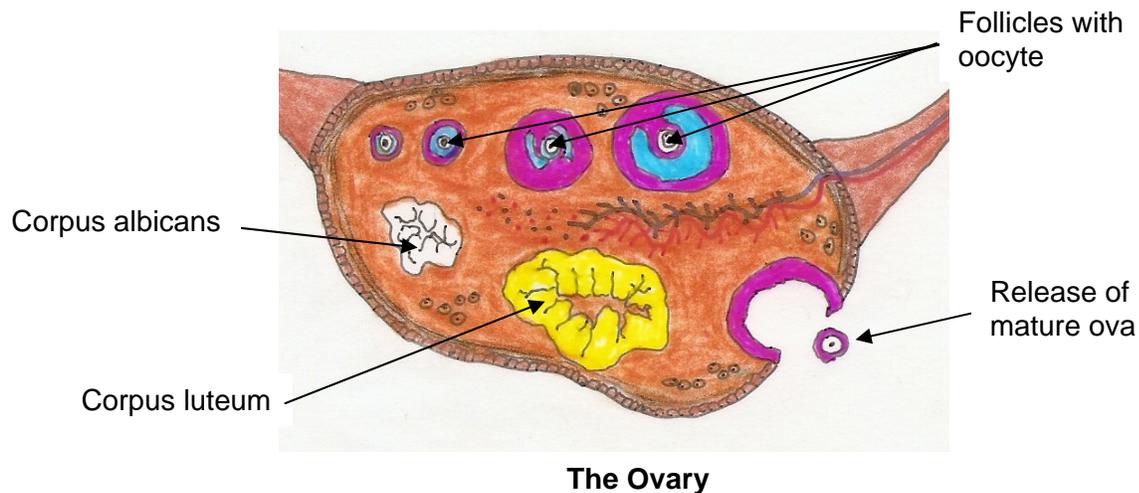
### The Female and Male Gonads

Gonads are the primary reproductive organ in humans; in female they are the ovaries and in males they are the testes. The gonads produce gametes or the *sex cells* for reproduction; in females the ovaries make egg cells (or oocytes) and in males the testes make sperm cells. The gonads also produce the sex hormones; in females the ovaries make **estrogen** and **progesterone** and in males the testes make **testosterone**.

Sex hormones are responsible for the development of secondary sex characteristics, which develop at puberty. Some secondary sex characteristics in females are development of the breasts and broadening of the pelvis. Some examples of secondary sex characteristics in males are deepening of the voice (due to a large larynx), growth of facial hair, and muscle development. During puberty, both sexes have increased activity of sweat glands and sebaceous glands (oil glands in the skin), and growth of pubic and axillary (armpit) hair.

## Ovaries

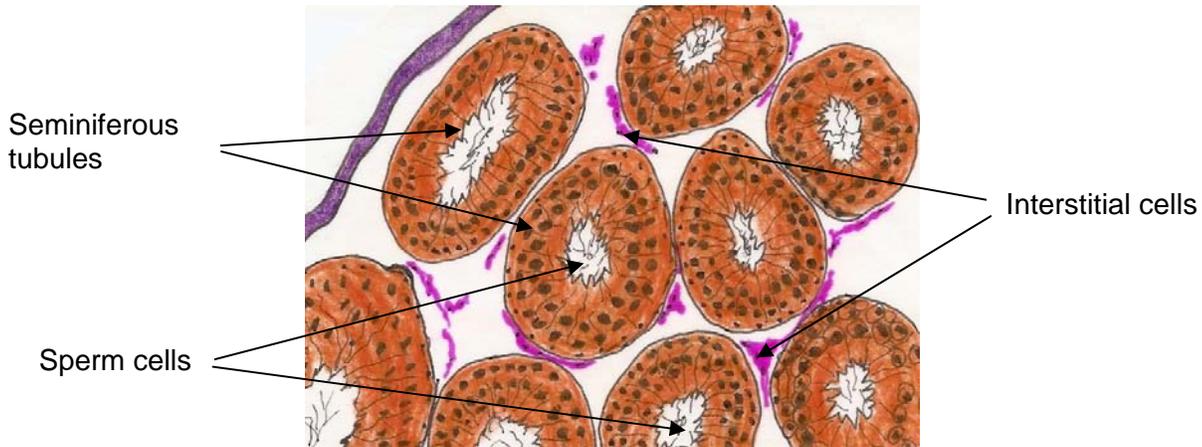
Flanking either side of the uterus, the oval-shaped ovaries release an egg or "ova," each month and release the female sex hormones **estrogen** and **progesterone**. The ovarian cycle is dictated by the release of LH and FSH from the anterior pituitary gland. The ovary in turn dictates the uterine cycle which involves changes in progesterone and estrogen levels that are responsible for the sloughing off of the inner endometrial layer of the uterus every month during the female menstrual cycle. A female is born with about 60,000 cells that all have the potential to develop into mature reproductive cells. These cells are housed in follicles that go through various stages of development within the ovary. Roughly only about 400 of these will ever fully develop during the woman's lifetime. The estrogen and progesterone made by ovarian structures, such as the corpus luteum, are responsible for regulating the uterine cycle and for the obvious secondary sexual characteristics of females, such as growth of mammary glands, widening of pelvis, and distribution of fat and muscle mass.



## Testes

The testis are enclosed in the scrotum, which is a sac sitting outside of the abdominal cavity of the body. The adequate production sperm requires a temperature that is two to three degrees F below body temperature, therefore they are stored 'outside' of the body. Two different types of muscle (dartos of the scrotum and cremaster of the spermatic cord) regulate the temperature of the testes. Sperm cells are made in the seminiferous tubules of the testes. A typical male may produce as many as 12 trillion sperm cells in his lifetime and a typical ejaculation releases from 50 to 100 million sperm/ml. If a man's sperm count is less than 20 million/ml, this is considered infertile. The development of sperm takes over 70 days to mature and its maturity is overseen by a complex interaction of hormones.

Androgens are male sex hormones and the principal androgen is **testosterone**, which is secreted by the interstitial cells of the testes. These cells used to be called 'cells of Leydig' so sometimes the term interstitial cells of Leydig is used. A small amount of testosterone is also produced by the adrenal cortex. Production of testosterone begins during fetal development, continues for a short time after birth, nearly ceases during childhood, and then resumes at puberty. Testosterone is responsible for the obvious secondary male sexual characteristics such as growth and distribution of body hair, skeletal and muscular growth, and enlargement of larynx creating a low pitch voice.



**The Seminiferous Tubules of the Testes**

**Exercise 8.** For each hormone in column A, select the appropriate endocrine gland that makes it from column B. The various endocrine glands in column B may be used more than once.

**Column A**

- \_\_\_ 1. ACTH
- \_\_\_ 2. ADH
- \_\_\_ 3. aldosterone
- \_\_\_ 4. calcitonin
- \_\_\_ 5. cortisol
- \_\_\_ 6. epinephrine

- \_\_\_ 7. estrogens
- \_\_\_ 8. testosterone
- \_\_\_ 9. glucagon
- \_\_\_ 10. insulin
- \_\_\_ 11. progesterone
- \_\_\_ 12. glucocorticoids

**Column B**

- A. Adrenal cortex
- B. Adrenal medulla
- C. Testes

- D. Hypothalamus
- E. Ovaries
- F. Pancreas

**Multiple Choice Questions**

1. The endocrine gland in the peripheral body that develops from the sympathetic nervous system is the  
**a) adrenal medulla b) pancreas c) thyroid gland d) anterior pituitary gland e) adrenal cortex**
2. The hormone that aids in sodium conservation and potassium excretion is  
**a) hydrocortisone b) CT c) ADH d) aldosterone e) calcitonin**
3. Which of these hormones produce effects that mimic those of the sympathetic nervous system?  
**a) insulin b) oxytocin (OT) c) epinephrine d) testosterone e) h growth hormone**
4. Which hormone lowers blood glucose level?  
**a) epinephrine b) melatonin c) insulin d) cortisol e) glucagon**
5. Which hormone(s) elevate blood glucose levels?  
**a) epinephrine b) glucagon c) insulin d) cortisol e) a, b and d**
6. Which hormone assumes a role in the development and discharge of a secondary oocyte?  
**a) hGH b) TSH c) LH d) PRL e) ACTH**

7. If the thyroid gland is over stimulated with \_\_\_\_\_, typically a goiter will result.  
 a) hGH b) TSH c) LH d) PRL e) ACTH
8. Which of the following produce testosterone?  
 a) adrenal medulla b) interstitial cells of Leydig c) adrenal cortex d) anterior pituitary gland e) b and c
9. Typically a female is born with about \_\_\_\_\_ potential egg cells and only releases about \_\_\_\_\_.  
 a) 60; 40 b) 60,000; 40,000 c) 1,000; 500 d) 100,000; 500,000 e) 60,000; 400
10. According to the Glycemic Index shown in **Figure 3**, which type of food produces the most gradual rise and decline of blood glucose?  
 a) fats b) simple carbohydrates c) proteins d) complex carbohydrates e) complex proteins

**Exercise 9.** For the following disorders of the endocrine system, suggest which hormone is either over or under-produced and what cells, tissues or glands are responsible.

a) If too much bones growth occurs after the growth plates have fused together, then bones can no longer grow in length but instead widen & thicken. This happens when \_\_\_\_\_ is released in \_\_\_\_\_ amounts. In adults this disorder is called \_\_\_\_\_.

b) Cells cannot absorb glucose due to lack of the hormone \_\_\_\_\_. It results in low energy levels, hyperglycemia, glycosuria, polyuria and excessive thirst. The endocrine structure is the \_\_\_\_\_.

c) Results in increased metabolic rate, elevated heart rate, weight loss, sweating, high BP, and protruding eyeballs. This is due to \_\_\_\_\_ amounts of the hormone \_\_\_\_\_ released from the \_\_\_\_\_ gland and the common name for this disease is \_\_\_\_\_.

d) A disease that occurs as the result of too much cortisol in the blood for an extended period of time. Cortisol is released from the zona \_\_\_\_\_ of the \_\_\_\_\_. The hormone that signals the release of cortisol is \_\_\_\_\_ from the \_\_\_\_\_. The common name for this disease is \_\_\_\_\_. It results in high blood pressure, hyperglycemia and loss of muscle mass.

e) If too little of the hormone \_\_\_\_\_ is released or if its actions are blocked by alcohol, then it will result in large volumes of dilute urine being voided from the body, this is called \_\_\_\_\_.

f) This disease is often referred to as primary adrenal insufficiency because an insufficient amount of these general hormones \_\_\_\_\_ and \_\_\_\_\_ are released, despite the presence of an adequate amount of \_\_\_\_\_. It results in low blood pressure, hypoglycemia and fatigue.