Objective 1. Define the term hormone and describe the general functions of the endocrine system.

*Aims: Tortora, p. 642 or Wiley Plus – Chapter 18, Chapter Opener (Screen 4)*

**The Endocrine System**

- The endocrine system consists of the pituitary, thyroid, parathyroid, adrenal, and pineal glands.
- The are other organs and tissues that secrete hormones but they are not exclusively endocrine glands.
  - Hypothalamus, thymus, pancreas, ovaries, testes, kidneys, stomach, liver, small intestine, skin, heart, and placenta.

For the purpose of regulating homeostasis, the body is continually receiving, interpreting, and responding to stimuli. The two main systems of the body that are responsible for this task are the nervous and endocrine systems. Through the use of mediator molecules, homeostatic mechanisms are strictly controlled. In the nervous system, these molecules are referred to as neurotransmitters; in the endocrine system, they are hormones.

A hormone is a mediator molecule secreted from one part of the body that circulates via the body fluids to cells in another part of the body. Initially, the hormones are secreted into the interstitial fluid, then typically the bloodstream, thereby having access to the entire body. A specific cell will respond to the hormone due the presence of peripheral or intracellular receptors. Because these cells are the specific targets of the hormones, they are referred to as “target cells”.

![Diagram of the Endocrine System](image_url)
Objective 1 (continued). Define the term hormone and describe the general functions of the endocrine system.

**Hormones**

- The nervous and endocrine systems coordinate all of the body systems.
- Hormones are mediator molecules that are released in one part of the body to influence activity somewhere else.
  - Endocrine cell to interstitial fluid to the bloodstream
- The study of endocrine glands and hormones is called endocrinology.

The endocrine system is made up of primary and secondary endocrine organs that, together with the nervous system, coordinate vital body functions in an effort to maintain homeostasis. Hormones function to regulate the chemical composition and volume of the blood, metabolism and energy balance, contraction of smooth and cardiac muscle fibers, glandular secretion, growth and development, reproduction, sleep-wake cycles, and some immune functions.

Hormones are very powerful molecules. To illustrate this, a patient’s blood protein level is measured in g/dl, glucose in mg/dl, but hormones are often measured in μg/dl, ng/dl, and even pg/dl. So, hormones are not present in large amounts, but their effects are quite dramatic.

**Endocrine System Functions**

- Control of composition and volume of the internal environment
- Regulate metabolism and energy balance
- Contraction of smooth and cardiac muscle fibers
- Influence glandular secretions
- Regulation of sleep-wake cycles
- Emergency control during physical and mental stress (trauma, starvation, hemorrhage, etc.)
- Integration of growth and development
- Reproductive control
Objective 2. Compare and contrast the control mechanisms of the nervous and endocrine systems: mediator molecules, site of mediator action, target cells, time to onset of action and duration.

Assignment: Tortora, p. 643 or Wiley Plus 18.1 – Comparison of Control by the Nervous and Endocrine Systems

Molecules can be both neurotransmitters and hormones; it just depends on how they are used. Neurotransmitters are released from neurons to act locally in response to a nerve impulse. They bind to receptors in a postsynaptic membrane near their site of release. Neurotransmitters act very quickly and have a short duration. Their effectors are usually glandular cells, various types of muscle cells, and other neurons.

Hormones on the other hand can be delivered to cells throughout the body, and bind to receptors in or on the target cell. In contrast to neurotransmitters, hormones take anywhere from seconds to hours to days to work, and their duration tends to be much longer.
Objective 3. Describe the processes that increase or decrease the number of receptors on the cell membrane.

Hormone receptors are simply cellular proteins. Like any other protein, they can be synthesized, broken down, and synthesized again.

Target cells can dictate the number of receptors available to bind hormone. If a cell wants to increase its responsiveness to a hormone, it can increase the number of receptors. This is referred to as up-regulation. The opposite is true if a cell wants to decrease its response to excessive hormone. The cell can decrease the number of receptors, a process called down-regulation.

**Hormone Receptors**

- Hormone receptors are simply cellular proteins.
- Target cells can dictate the number of receptors available to bind hormone.
  - Up-regulation
    - Increased responsiveness by increasing receptor numbers
  - Down-regulation
    - Decreased responsiveness by decreasing receptor numbers
Objective 4. Compare the action of circulating versus local hormones, including the paracrines and autocrines.

Because most hormones are secreted into the interstitial fluid and then into the blood, thereby giving them access to the entire body, they are referred to as **circulating hormones**. There is a small group of hormones that act locally, causing changes in nearby cells. If these local hormones act on neighboring cells, they are called **paracrines**. There are also cells that have receptors for their own hormones, so they can stimulate themselves. These local-acting hormones are called **autocrines**.
**Objective 5.** List the major chemical classes of hormones of the body and describe how each is carried in the blood.

<table>
<thead>
<tr>
<th>Lipid-Soluble Hormones</th>
<th>Water-Soluble Hormones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid Hormones</td>
<td>Amine Hormones</td>
</tr>
<tr>
<td>Thyroid Hormones</td>
<td>Peptide and Protein Hormones</td>
</tr>
<tr>
<td>Nitric Oxide</td>
<td>Eicosanoid Hormones</td>
</tr>
</tbody>
</table>

Hormones can be classified in a number of ways. One of the main classifications separates different types of hormones based on their solubility in water or lipids. This is very important to keep in mind when determining how the hormone will act on a target cell. In Module 4, it was presented that a substance can more easily move into a cell if it is: small, neutrally-charged, or lipid soluble. Therefore, lipid-soluble hormones can diffuse into a cell and bind directly to intracellular receptors. On the other hand, water-soluble hormones must stimulate a cellular change by a more complex mechanism. They must bind to membrane receptors and initiate a change in the cell indirectly. So, this isn’t only a solubility classification; it is also a functional classification.

Solubility also dictates how hormones will be carried in the blood. The blood is approximately 55% plasma, and the plasma is 92% water. In this watery environment, water-soluble hormones can circulate as “free” hormones; they aren’t attached to any other molecules.

In the blood, lipid-soluble hormones must be bound to transport proteins. By binding to these proteins, the water solubility of these hormones is increased. The transport proteins also keep the smaller lipid-soluble hormones from getting filtered in the kidney and lost in the urine. Where most of the water-soluble hormones are free in the blood, only 0.1-10% of lipid-soluble hormones are free.
Objective 6. Relate the mechanism of hormone action to the biochemical nature of the hormone.

Assignment: Tortora, pp. 646-649, or Wiley Plus – 18.3 Hormone Activity (Table 18.2) & 18.4 Mechanisms of Hormone Action

The action of the lipid-soluble hormones is the easiest to understand. Again, because they are lipid soluble, they can diffuse through the lipid bilayer of the cell membrane. This gives them the opportunity to bind directly to intracellular receptors.

1. The hormone diffuses into the cell.

2. If the cell is a target cell for that hormone, the hormone can bind to a receptor and create a receptor-hormone complex within the cytosol or nucleus.

3. This complex can alter the gene expression of the cell by turning the genes encoded by the cell’s DNA on or off. So, depending on the type of receptor the hormone binds to, it can be excitatory or inhibitory in that cell. The end result is the alteration of the cell’s activity.
Objective 6 (continued). Relate the mechanism of hormone action to the biochemical nature of the hormone.

**Water-Soluble Hormone Action**

- The hormone (1st messenger) attaches to receptors on the plasma membrane of the target cell.
- Receptor-hormone complex activates a G protein
- G protein activates adenylate cyclase
- Adenylate cyclase converts ATP to cyclic AMP (cAMP) (2nd messenger) in the cytoplasm
- cAMP activates enzymes (protein kinases) which bring about the desired effect within the cell.
  - 2nd messengers can act as activators, inhibitors, or cofactors
- Ca++ is also a common 2nd messenger.

The action of water-soluble hormones is much more complex. Because of their limited lipid solubility, they can’t freely enter the cell. Here is an analogy that may help. What if a student has a friend that is registered for a particular history class and they are trying to get a message to them? (All right, it would be easy to text message, but in this case it isn’t allowed.)
Objective 6 (continued). Relate the mechanism of hormone action to the biochemical nature of the hormone.

The student with the message isn’t allowed to enter the classroom to deliver the message directly because the professor would get very upset. Their only option is to get another student who is close to the door to relay the message to their friend. In this scenario, the first student is the first messenger, and the second student is the second messenger. The message was delivered, it just wasn’t easy.

Here are the steps required for a water-soluble soluble hormone to initiate a cellular change.

1. **Hormone (first messenger)** binds to a receptor on the cell membrane. By forming a receptor-hormone complex a membrane protein called a G protein is activated. The activation of the G protein will then activate the enzyme adenylate cyclase.

2. Adenylate cyclase converts ATP into cyclic adenosine monophosphate (cAMP). **cAMP is the second messenger.**

3. cAMP will activate one or more protein kinases. Remember, kinases phosphorylate (add a phosphate to) other molecules.

4. In this case, the phosphorylated molecules are proteins. Through phosphorylation, some proteins are activated and some are deactivated. There are many different type of kinases, so the effects can be numerous.

5. To limit the duration of the response, unless new hormone binds to the receptors, an enzyme called **phosphodiesterase inactivates cAMP.**

   cAMP is one of a number of second messengers. Other second messengers include calcium (Ca++) ions and cyclic guanosine monophosphate (cGMP).
Objective 7. Describe the roles of negative and positive feedback in controlling hormone release.

Hormone secretion is signaled and regulated by a number of different mechanisms: signals from the nervous system, chemical fluctuations in the blood, and the secretion of other hormones. So, increased hormone release can result from a signal from the nervous system, the increase or decrease of a particular chemical in the blood, or due to the release of hormone from another organ.

Most hormone systems work via negative feedback. For these systems to function correctly, there must be receptors for the stimulus, an interpretation (control) center, and an initiated response. For example, receptors in the pancreas detect changes in the blood glucose level. If the blood glucose level is high, the pancreas secretes insulin. The increased level of insulin results in the increased production of glucose transporters, thereby facilitating the uptake of glucose into cells. The increased uptake of glucose into the body’s cells decreases the blood glucose level.

Hormone Feedback

- Hormone secretion is regulated by signals from the nervous system, chemical changes in the blood, and levels of other hormones.
- Most hormone systems work by negative feedback, few by positive feedback.
  - Negative feedback
    - The hormone output reverses a particular stimulus
  - Positive feedback
    - The hormone output encourages and reinforces the stimulus

Assignment: Tortora, p. 650 or Wiley Plus – 18.6 Hypothalamus and Pituitary Gland
Objective 8. Describe the factors that influence the responsiveness of a target cell to a hormone.

The ability of a target cell to respond to a hormone depends on a number of factors: the hormone concentration, the abundance of target-cell receptors, and the influences of other hormones. A target cell can react more energetically if there is a high level of hormone or the cell has up-regulated.

Hormones can also interact with each other. In some cases, to get the desired effect, two different hormones must both be present. This is referred to as a permissive effect. If two hormones dictate similar actions and they work together to create an even more powerful result; this is a synergistic effect.

Because most hormones work as part of a negative-feedback system, there are other hormones that oppose their actions. If a one hormone opposes the action of another, this is termed as an antagonistic effect.

Here is a summary that may help.
1) Two hormones required for a desired action - permissive effect
2) Two hormones present to create a stronger response - synergistic effect
3) Two hormones opposing each other - antagonistic effect

Target Cell Responsiveness

- Responsiveness depends on...
  - The concentration of the hormone
  - Number of receptors available to bind hormone
  - Influences of other hormones
    - Permissive effect
      - Action of one hormone requires the presence of another
    - Synergistic effect
      - The effect of two hormones acting together is greater than one acting alone
    - Antagonistic effect
      - One hormone opposes the action of another
Objective 9. Describe the anatomical and physiological relationships between the pituitary (which includes the adenohypophysis and the neurohypophysis) and the hypothalamus.

The pituitary gland was formerly referred to as the hypophysis. The origin of the term is Greek, referring to its position and growth under the brain. The pituitary is also commonly referenced as the master gland, but it also has a master, the hypothalamus. The hypothalamus is the connection between the nervous and endocrine systems.

The pituitary is a pea-shaped gland. It is anatomically and functionally connected to the hypothalamus by the infundibulum, a funnel-shaped stalk.

The pituitary has two lobes that are named based on their position and functional relationship to the hypothalamus. The anterior lobe of the pituitary, also called the adenohypophysis, is about 75% of the total pituitary weight. The second lobe is the posterior pituitary or neurohypophysis.

The terms adeno- and neuro- are very important to understand their relationships with the hypothalamus. “Adeno-” means “gland”, so the relationship of the hypothalamus and anterior pituitary is a gland-to-gland relationship. The hypothalamus produces hormones that will circulate through a vascular connection with the anterior pituitary stimulating the release of another group of hormones from the anterior pituitary.
Objective 9 (continued). Describe the anatomical and physiological relationships between the pituitary (which includes the adenohypophysis and the neurohypophysis) and the hypothalamus.

### Relationship to the Hypothalamus

<table>
<thead>
<tr>
<th>Anatomy</th>
<th>Physiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenohypophysis</td>
<td>anterior</td>
</tr>
<tr>
<td>Neurohypophysis</td>
<td>posterior</td>
</tr>
</tbody>
</table>
Objective 10. Define the terms releasing hormone, inhibiting hormone, and tropic hormone.

To understand the control of the hormones to and from the pituitary, it is important to learn some terminologies. To encourage the release of hormones from the pituitary, the hypothalamus secretes a number of releasing hormones. If “releasing” is in the name of the hormone, it comes from the hypothalamus.

### Hormones

- **Releasing hormones**
  - Hormones from the hypothalamus that stimulate the “release” of hormones from the adenohypophysis.

- **Inhibiting hormones**
  - Hormones from the hypothalamus that inhibit the release of hormones from the adenohypophysis.

- **Tropic hormones**
  - Hormones from the adenohypophysis that act on other endocrine glands

If the hypothalamus needs to suppress the action of the pituitary, it secretes specific inhibiting hormones. Again, this illustrates the negative-feedback responses of the endocrine system.

If a hormone is a **tropic hormone**, it is released from one endocrine gland and targets another. The term tropic (pronounced “troh-pick”, with a long ō) may also be used in the name of the specific cells that secrete it. Thyrotrophs, corticotrophs, gonadotrophs, are all cells of the anterior pituitary that secrete a particular hormone that targets another gland.
Objective 11. List the seven hormones of the adenohypophysis, their target organs, their principal actions, and the correlating releasing-hormone from the hypothalamus.

Assignment: Tortora, pp.650-655 or Wiley Plus – 18.6 Hypothalamus and Pituitary Gland

### Anterior Pituitary Hormones

<table>
<thead>
<tr>
<th>Hypothalamic Hormone</th>
<th>Anterior Pituitary</th>
<th>Major Function/Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth hormone-releasing hormone (GHRH)</td>
<td>Human growth hormone (hGH)</td>
<td>Stimulates growth of body cells</td>
</tr>
<tr>
<td>Thyrotropin-releasing hormone (TRH)</td>
<td>Thyroid stimulating hormone (TSH)</td>
<td>Stimulates thyroid gland</td>
</tr>
<tr>
<td>Corticotropin-releasing hormone (CRH)</td>
<td>Adrenocorticotropic hormone (ACTH)</td>
<td>Stimulates cortex of adrenal gland</td>
</tr>
</tbody>
</table>

### Anterior Pituitary Hormones

<table>
<thead>
<tr>
<th>Hypothalamic Hormone</th>
<th>Anterior Pituitary</th>
<th>Major Function/Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonadotropic-releasing hormone (GnRH)</td>
<td>Follicle stimulating hormone (FSH)</td>
<td>Ova/sperm development and production</td>
</tr>
<tr>
<td>Gonadotropic-releasing hormone (GnRH)</td>
<td>Lutenizing hormone (LH)</td>
<td>Maturation of uterine lining, testosterone production, and ovulation</td>
</tr>
</tbody>
</table>

### Anterior Pituitary Hormones

<table>
<thead>
<tr>
<th>Hypothalamic Hormone</th>
<th>Anterior Pituitary</th>
<th>Major Function/Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolactin-releasing hormone (PRH)</td>
<td>Prolactin (PRL)</td>
<td>Lactation of mammary glands</td>
</tr>
<tr>
<td>Corticotropin-releasing hormone (CRH)</td>
<td>Melanocyte-stimulating hormone (MSH)</td>
<td>Darkens melanocytes</td>
</tr>
</tbody>
</table>
Disorders of the endocrine system involve two main problems, having too much or too little. A patient's symptoms will always imply an over-production (hypersecretion) or under-production (hyposecretion), but there are a number of possibilities that can cause these symptoms.

<table>
<thead>
<tr>
<th>Hyposecretion</th>
<th>Hypersecretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Too little hormone production</td>
<td>Excessive hormone production</td>
</tr>
<tr>
<td>Decreased hormone receptors</td>
<td>Tumors of endocrine origin - causing excess hormone release. Benign or malignant.</td>
</tr>
<tr>
<td>Second-messenger system defects</td>
<td>Absence of normal feedback mechanisms.</td>
</tr>
<tr>
<td>Lack of hormone precursors</td>
<td></td>
</tr>
<tr>
<td>Degraded hormones</td>
<td></td>
</tr>
<tr>
<td>Poor blood flow (ischemia)</td>
<td></td>
</tr>
</tbody>
</table>
Objective 13. Predict the effects and provide examples of hyper- and hyposecretion disorders of human growth hormone (hGH) from the anterior pituitary.

Deficiency or excess of human growth hormone (hGH) from the adenohypophysis has widespread effects on the body because the majority of cells have hGH receptors. The severity of the symptoms relates to the age of the patient.

Endocrine Disorders of hGH Secretion

**Pituitary dwarfism**
- Caused by insufficient hGH release during an individual’s growth phase.
  - Growth plates close before patient reaches mature height
  - Patient manifests proportional growth changes

**Giantism**
- Occurs as a result of excess hGH during an individual’s growth phase.
  - The main cause is a pituitary adenoma.

**Pituitary dwarfism** is caused by hyposecretion of hGH during childhood. Without hGH, the epiphyseal plates will close before the child achieves a normal adult height. The deficient growth of tissue will affect all of the body systems; however, the child will have normal body proportions.

**Giantism** is caused by hypersecretion of hGH during childhood. Overall body proportions will remain the consistent, but the patient will be very tall. The main cause of giantism is a tumor of the anterior pituitary. Detection and treatment techniques have made giantism fairly rare. The *Guinness Book of World Records* lists a number of individuals who suffered from giantism.
Objective 13 (continued). Predict the effects and provide examples of hyper- and hyposecretion disorders of human growth hormone (hGH) from the anterior pituitary.

**Acromegaly** is a disorder caused by excessive hGH secretion; the problem occurs during adulthood after a person is done growing. After epiphyseal plate closure, one ceases to grow linearly, but tissues don’t cease to grow. Under the influence of hGH, bones can become thicker and denser and tissues of the eyelids, tongue, nose, lips, and skin can enlarge. The enlargement of these tissues can cause circulatory, nerve, and skin problems.

### Endocrine Disorders of hGH Secretion

- **Acromegaly**
  - Occurs as a result of excess hGH during adulthood.
    - Enlargement and elongation of the bones of the face, jaw, cheeks, and hands
    - The long bones of the extremities are unaffected because the growth plates are already closed
    - Commonly causes arthritis and carpal tunnel syndrome due to excess tissue growth
Objective 14. Identify the source of the hormones secreted by the neurohypophysis, their target organs, and principal actions.

As referenced previously, the hormones from the posterior pituitary are synthesized in the hypothalamus, secreted down special neurosecretory neurons to be stored and later released from the posterior pituitary.

The hypothalamic nuclei that produce the posterior pituitary hormones are the paraventricular and supraoptic nuclei. The axons from these nuclei form the hypothalamohypophyseal tract. (For the exam, students must be able to spell the name of the tract. OK, they don’t, but it would be a great fill-in-the-blank test question.) The tract ends near capillaries of the posterior pituitary. When stimulated, the hormones are released into the bloodstream.

The paraventricular nuclear cells and supraoptic nuclear cells produce oxytocin and antidiuretic hormone (ADH). ADH is also called vasopressin.

Oxytocin has two target tissues during and after the delivery of a baby, the uterus and the breasts. Through positive feedback, oxytocin stimulates uterine contractions to help with the delivery of the infant. It also stimulates milk release (“let down”) from the breasts in response to the sucking mechanism of the baby.

The function of oxytocin in men and non-pregnant women is not clearly understood. There are theories that it promotes feelings of sexual pleasure during and after intercourse and encourages emotional bonding between the mating pair. So, some call it the “love” hormone.

Hormones from the Neurohypophysis

- Oxytocin (OT) and antidiuretic hormone (ADH) are produced by the cell bodies of the neurosecretory cells in the hypothalamus.
- The hormones are transported down the cells’ axons to the neurohypophysis.
- The hormones are then secreted in response to nerve impulses from the hypothalamus through the neurosecretory neurons.

Hormones from the Neurohypophysis

- Oxytocin targets smooth muscle in the uterus and breasts. In the uterus, oxytocin stimulates uterine contractions, and in response to the sucking from an infant, oxytocin stimulates “milk letdown” in the breasts.
- ADH causes arterioles to constrict thereby increasing blood pressure, and ADH targets the collecting ducts in the kidney and sweat glands in the skin to minimize water loss.
Objective 14 (continued) Identify the source of the hormones secreted by the neurohypophysis, their target organs, and principal actions.

The name antidiuretic hormone tells us that it is a hormone that opposes urine formation. ADH is a hormone that decreases the amount of urine the body produces. In the hypothalamus, there are osmoreceptors that monitor blood osmotic pressure. The blood osmotic pressure relates to the concentration of the blood. When the osmotic pressure is high, the blood concentration is high. If the osmotic pressure is low, the concentration is low. If the blood osmotic pressure rises, in an effort to maintain fluid equilibrium, the body will try to increase the reabsorption of water and decrease the amount lost in the urine.

**ADH acts on three specific target tissues**: kidneys, sudoriferous (sweat) glands, and the smooth muscle cells of blood vessels. ADH specifically influences the collecting tubules (ducts) in the kidneys to increase water reabsorption and limit the amount of water excreted as urine. As water reabsorption is increased, there is a resulting increase in the blood volume and thus the blood pressure. ADH also increases the blood pressure by constricting the smooth muscle cells of arterioles.
Objective 15. Predict the effects and provide examples of hyper- and hyposecretion of antidiuretic hormone (ADH).

The most common condition related to ADH is diabetes insipidus. Don’t confuse diabetes insipidus with diabetes mellitus. Diabetes mellitus will be discussed shortly. Diabetes means to overflow or siphon; it relates to the development of polyuria (too much urine production). Insipidus means tasteless, so putting these two terms together would be ”the production of too much tasteless urine”.

How does this happen? A patient with physiologic diabetes insipidus can have one of two types, neurogenic or nephrogenic. This essentially means that they don’t secrete enough ADH (neurogenic) or they don’t respond to the ADH they make (nephrogenic). Either form will have the same effect. With limited amounts of ADH, the patient will not reabsorb water, therefore they will secrete large volumes of very dilute urine. Now, clinical laboratorians don’t taste urine, that was centuries ago, but if they did, it is very dilute, so essentially tasteless. This can increase urine production from 1-2 liters/day (normal) to as much as 20 liters/day.

### Diabetes Insipidus

- **Two Physiological Types**
  - Neurogenic
    - Insufficient production or secretion of ADH
  - Nephrogenic
    - Diminished renal response to the ADH that is produced

- The normal urine output of 1-1.5 liters increases to >2.5 to as much as 12 liters of very dilute urine per day.
Objective 16. Describe the anatomical location and general structure of the thyroid gland.

The thyroid gland is easy to find, it is located just inferior to the larynx, specifically the thyroid cartilage (Adam’s apple). The thyroid gland is butterfly-shaped and consists of two lobes, the left and right. The tissue connection between the two lobes is called the isthmus. Microscopically, the thyroid is made up of small spherical sacs called thyroid follicles. The follicles make up the largest portion of the gland’s mass.

The Thyroid Gland

- The thyroid gland has two lateral lobes and is located inferior to the larynx (voice box).
- To locate, think thyroid cartilage (Adam’s apple)
- The bridge-like connection between the two lobes lies anterior to the trachea and is called the isthmus.
- The thyroid stores a 100-day supply of its secretory products.
- Sacs called thyroid follicles make up most of the thyroid gland, and they secrete two hormones.
  - Thyroxine (tetraiodothyronine) (T₄)
  - Triiodothyronine (T₃)
Objective 17. Identify the general structure of a thyroid follicle and describe the process of thyroid hormone (T3 and T4) synthesis, secretion, transport, and control.

Thyroid Function

- Thyroglobulin (TGB) is a protein synthesized inside the thyroid’s follicular cells.
- TGB consists of ~5,000 amino acids, >100 of which are the amino acid tyrosine.
- To synthesize the thyroid hormones, TGB is released into the lumen of the thyroid follicles.
- Within the TGB molecule, one or two iodine atoms attach to each tyrosine molecule.

The main functional unit of the thyroid gland is the thyroid follicle. Each follicle consists of a central, internal space called the lumen, surrounded by a wall of cells called follicular cells. These cells change shape slightly from squamo-cuboidal to cuboido-columnar when stimulated to produce thyroid hormone. Squamo-cuboidal and cuboido-columnar are not true anatomical terms, they simply describe the size and shape of resting and non-resting follicular cells. A connective tissue basement surrounds the layer of follicular cells.

There is a scattered group of cells surrounding each follicle. They are called parafollicular cells or C cells. The hormone secreted by these cells is discussed in a later objective.

A thyroid follicle secretes two hormones, thyroxin (tetraiodothyronine, T4) and triiodothyronine, T3. The prefix of each term describes the number of iodine molecules they contain, tetra- meaning four (T4) and tri- meaning three (T3).

Production of thyroid hormone can be somewhat complex. First, one must understand how to stimulate the thyroid gland. Low T3 and T4 levels or a low metabolic rate stimulates the hypothalamus to secrete thyrotropin-releasing hormone (TRH), which results in the anterior pituitary producing thyroid-stimulating hormone (TSH). TSH binds to TSH receptors in the follicular cells and activates a number of processes required to synthesize T3 and T4 (see required steps for T3 and T4 synthesis).

Thyroid Hormone Secretion

- The hypothalamus secretes thyrotropin-releasing hormone (TRH)
- As a response, the adenohypophysis (anterior pituitary) secretes thyroid stimulating hormone (TSH).
- TSH in turn stimulates the thyroid to secrete T3 and T4.
- Most of the T4 released is converted to the more potent T3.
Objective 17 (continued). Identify the general structure of a thyroid follicle and describe the process of thyroid hormone (T₃ and T₄) synthesis, secretion, transport, and control.
Objective 17 (continued). Identify the general structure of a thyroid follicle and describe the process of thyroid hormone (T3 and T4) synthesis, secretion, transport, and control.

<table>
<thead>
<tr>
<th>Required steps for T3 and T4 synthesis</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iodide trapping</td>
<td>Iodine circulates in the blood as iodide (I(^-)). Iodide is actively transported into the follicular cells. Because of this process, the thyroid gland contains most of the iodide in the body.</td>
</tr>
<tr>
<td>Synthesis of thyroglobulin (TGB)</td>
<td>TGB is a glycoprotein produced by follicular cells. It contains large numbers of the amino acid tyrosine. Tyrosine is the site on the TGB molecule that will bind with iodine.</td>
</tr>
<tr>
<td>Oxidation of iodide</td>
<td>Before iodide can bind to tyrosine, it must be oxidized and combine with another iodide to form and iodine molecule (I(_2)).</td>
</tr>
<tr>
<td>Iodination of tyrosine</td>
<td>The side chain of tyrosine may pick up one (T(_1)) or two (T(_2)) iodine molecules.</td>
</tr>
<tr>
<td>Coupling of T(_1) and T(_2) to make T(_3) and T(_4)</td>
<td>As one of the last steps, two tyrosine molecules are joined to form either T(_3) (T(_1) + T(_2)) or T(_4) (T(_2) + T(_2)).</td>
</tr>
<tr>
<td>Pinocytosis and digestion of colloid</td>
<td>Once synthesized, the iodine-containing TGB reenters the follicular cells and digestive enzymes break down the molecule, releasing the formed T(_3) and T(_4).</td>
</tr>
<tr>
<td>Secretion of thyroid hormones</td>
<td>T(_3) and T(_4) are lipid soluble, so they freely pass the cell membrane into the interstitial fluid and into the blood.</td>
</tr>
<tr>
<td>Transport of T(_3) and T(_4) in the blood</td>
<td>Once in the blood stream, 99% of the secreted hormone binds to transport proteins, mainly thyroxine-binding globulin (TBG), not to be confused with</td>
</tr>
</tbody>
</table>
Objective 18. List and describe the actions of T3 and T4.

Most of the synthesized thyroid hormone is T4, but T3 is more physiologically potent. However, once secreted, most of the T4 is converted to T3 by enzymatic removal of an iodine. Most body cells have receptors for T3 and T4, so the hormones’ actions are quite broad. It should be noted that the thyroid gland is the only gland to store a large supply of its products (approximately 100 days worth).

<table>
<thead>
<tr>
<th>Thyroid Hormone Actions</th>
<th>The basal metabolic rate is the rate of oxygen consumption while awake, at rest, and fasting. When the need for ATP increases, the use of all nutrients increases.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increases the basal metabolic rate</td>
<td></td>
</tr>
<tr>
<td>Stimulates the synthesis of additional sodium-potassium (Na⁺/K⁺) pumps</td>
<td>This major action has a cascade of effects. With the increase in Na⁺/K⁺ pumps, the demand for ATP is greater. As ATP is produced, calories are used, and more heat is produced (exothermic). This is how thyroid hormones help a person regulate their normal body temperature.</td>
</tr>
<tr>
<td>Increases protein synthesis</td>
<td>Encourages growth.</td>
</tr>
<tr>
<td>Increases fatty acid and glucose catabolism</td>
<td>Fatty acids and glucose are used to synthesize ATP.</td>
</tr>
<tr>
<td>Decreases blood cholesterol</td>
<td>Reduces blood cholesterol by increasing cholesterol excretion.</td>
</tr>
<tr>
<td>Increases the effects or epinephrine and norepinephrine</td>
<td>Enhances the sympathetic nervous response (heart rate, force of heart contraction, and blood pressure).</td>
</tr>
<tr>
<td>Accelerates body growth, especially during fetal life and adolescence</td>
<td>Work synergistically with human growth hormone and insulin to develop the skeletal and nervous systems.</td>
</tr>
</tbody>
</table>
Objective 19. Predict the effects and provide examples of hyper- and hyposecretion disorders of the thyroid hormones.

A goiter is simply an enlargement of the thyroid, and it can be found in patients with hypothyroidism, hyperthyroidism, and euthyroidism, which means normal thyroid function. It is important for the physician to determine why the thyroid is enlarged.

In many countries, a goiter is due to iodine deficiency. The thyroid is making every effort to make thyroid hormone, but there isn’t any iodine. In the US, there isn’t a big problem; most of the available salt is “iodized”. With the amount of salt consumed in the American diet, iodine deficiency is rare.

<table>
<thead>
<tr>
<th>Thyroid Dysfunction</th>
<th>Hypothyroidism</th>
<th>Hyperthyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low basal metabolic rate</td>
<td>Low basal metabolic rate</td>
<td>High basal metabolic rate</td>
</tr>
<tr>
<td>Cold intolerant</td>
<td>Heat intolerant</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>Diarrhea</td>
<td></td>
</tr>
<tr>
<td>Decreased respiratory rate</td>
<td>Increased respiratory rate</td>
<td></td>
</tr>
<tr>
<td>Low heart rate (bradycardia)</td>
<td>High heart rate (tachycardia)</td>
<td></td>
</tr>
<tr>
<td>Weight gain</td>
<td>Weight loss</td>
<td></td>
</tr>
<tr>
<td>Lethargic</td>
<td>Anxious</td>
<td></td>
</tr>
</tbody>
</table>

Congenital hypothyroidism and myxedema are both hypothyroid disorders. Congenital hypothyroidism occurs in childhood; myxedema in adulthood.

Congenital hypothyroidism was formerly called cretinism. In the dictionary, a cretin is defined as an “idiot”. This definitely isn’t a politically-correct term, so it is now referred to as congenital hypothyroidism. In addition to the common symptoms of hypothyroidism, the patient demonstrates a low growth rate and mental retardation, due to the synergistic relationship between the thyroid hormones and human growth hormone. This decreases the development of the nervous and skeletal systems.
Objective 19 (*continued*). Predict the effects and provide examples of hyper- and hyposecretion disorders of the thyroid hormones.

**Hypothyroidism**

<table>
<thead>
<tr>
<th>Congenital Hypothyroidism</th>
<th>Myxedema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insufficient thyroid hormone during growth</td>
<td>Insufficient thyroxin during adulthood</td>
</tr>
<tr>
<td>Causes common symptoms of hypothyroidism, as well as mental retardation and dwarfism.</td>
<td>Causes dry brittle hair, dry skin due to decreased perspiration, edema, lethargy, low BMR, temperature, and heart rate</td>
</tr>
<tr>
<td>Decreased synergistic effect with hGH</td>
<td>Patients gain weight easily.</td>
</tr>
<tr>
<td>Formerly referred to as “cretinism”</td>
<td>Patients are not mentally retarded, but they do show some diminished intelligence.</td>
</tr>
</tbody>
</table>

**Myxedema** has similar symptoms to congenital hypothyroidism, without the CNS and skeletal abnormalities. By the time the patient develops the disease, the nervous system has developed and they are done growing. However, it is common for the patient to be mentally lethargic but not exhibit mental retardation. The abnormal edema in myxedema is related to deposition of excess connective tissue, resulting in the accumulation of water in the tissues.

**Graves disease** is the most common form of hyperthyroidism. It is an autoimmune disease that results in the production of antibodies against TSH receptors. Most often, autoimmune antibodies result in the destruction of cells. These antibodies act like TSH, so they stimulate thyroid hormone production. This is why a patient with Graves disease will demonstrate the symptoms of hyperthyroidism. A peculiar trait demonstrated by Graves disease is called exophthalmos. This condition causes protrusion or bulging of the eyes. It is due to abnormal fluid accumulation in the periorbital connective tissue and the extrinsic eye muscles.
Objective 20. Identify the cellular origin, physiological effect and regulation of calcitonin (thyrocalcitonin).

Thyrocalcitonin, more commonly just referred to as calcitonin, is produced by the parafollicular cells of the thyroid, also called C cells. The name is actually quite intuitive, thyro- meaning relating to the thyroid, and calcitonin, referring to the fact that its action is to regulate calcium levels. (If the name sounds familiar, that’s because you’ve already heard about calcitonin in the Skeletal System Module’s Objective 9.)

Calcitonin decreases calcium levels by inhibiting the action of osteoclasts. Calcitonin also increases the uptake of calcium and phosphates into the bone matrix, therefore decreasing blood calcium levels.
Objective 21. Identify the location, structure, and function of the parathyroid glands

The parathyroid glands are small masses of partially-embedded endocrine tissue, located on the posterior aspect of the thyroid gland. Typically, there are four parathyroid glands, two on each lobe of the thyroid, one superior and one inferior. The parathyroid glands contain chief (principal) cells, which produce and secrete parathyroid hormone (PTH).

Assignment: Tortora, pp. 662-664 or Wiley Plus – 18.8 Parathyroid Glands

Parathyroid Glands

- The parathyroid glands are small, round masses of tissue attached to the posterior surface of the lateral lobes of the thyroid.
- There are usually two parathyroid glands attached to each lobe of the thyroid, one superior and one inferior.
Objective 22. Describe the role of parathyroid hormone (PTH) in the regulation of calcium (Ca^{2+}), magnesium (Mg^{2+}), phosphate (HPO_4^{2-}) and calcitriol (active form of vitamin D).

Parathyroid hormone controls the levels of calcium (Ca^{2+}), magnesium (Mg^{2+}), and phosphate (HPO_4^{2-}) ions in the blood. The action of PTH is to increase the number and activity of osteoclasts. This causes an increase in bone reabsorption and releases more ions into the blood.

In the blood, the total amount of calcium and phosphate must be held constant, so if the level of calcium goes up, phosphate must go down, and visa versa. Here is an illustration that may help. If a person decides to carry no more than $100 in their wallet, it doesn’t matter if it’s five $20’s, ten $10’s, or 100 $1’s; they still only have $100. If they increase the number of one denomination, in order to maintain the $100, they have to decrease one of the others.

PTH regulates these ions by activating osteoclasts, decreasing calcium loss in the urine, increasing calcium and magnesium absorption in the intestines by increasing the amount of calcitriol (vitamin D), and increasing phosphate loss in the urine. Comparing their actions, parathyroid hormone and calcitonin are antagonists. The goal of PTH is to increase blood calcium levels. Calcitonin wants to lower them. This is how the body maintains normal calcium, phosphate, and magnesium homeostasis.
Objective 23. Describe the location, structure, and function of the adrenal glands.

Adrenal Glands

- There are two adrenal glands, one superior to each kidney.
- Each adrenal gland consists of two regions, the adrenal cortex and the adrenal medulla.
- The cortex is peripherally located and makes up 80-90% of the total weight of the gland.

Individuals have a pair of adrenal glands and each one is anatomically superior to one of the kidneys. Each adrenal gland has two distinct regions, the outer adrenal cortex and inner medulla. The cortex comprises 80 to 90% of the gland’s mass.

The adrenal glands are very important to human physiology. They produce steroid hormones that regulate glucose and electrolyte levels. Without sufficient production of these hormones, a person would die within days.

The adrenal medulla is the innermost region of the adrenal glands. The medullae are basically modified sympathetic ganglia of the autonomic nervous system that never formed post sympathetic neurons. Rather than secreting chemicals as neurotransmitters, they are released as hormones. The chromaffin cells of the medulla are controlled by sympathetic preganglionic neurons from the CNS. This is why the medullary response is very fast.

The adrenal medullae secrete two hormones, epinephrine and norepinephrine, also known as adrenaline and noradrenaline. The majority of the hormone secreted is epinephrine, about 80%. These hormones are intended to duplicate and prolong a flight-or-flight response from the sympathetic nervous system.
Objective 23 (continued). Describe the location, structure, and function of the adrenal glands.
Objective 24. Identify the functional zones of the adrenal cortex and list the types of hormones secreted from each, based on their function.

Assignment: Tortora, pp. 665-666 or Wiley Plus – 18.9 Adrenal Glands

The adrenal cortex consists of three functional zones and produces the “cortical” hormones. These zones, from superficial to deep, are the zona glomerulosa, zona fasciculata, and the zona reticularis. Cells in each of these zones produce and secrete different types of hormones; mineralocorticoids, glucocorticoids, and gonadocorticoids. The names of the different types of hormones provide information about their origin (cortex) and action.

**Adrenal Cortex**

- The adrenal cortex has three functional zones.
  - Zona glomerulosa
    - Produces and secretes the mineralocorticoids
  - Zona fasciculata
    - Produces and secretes the glucocorticoids
  - Zona reticularis
    - Produces and secretes the gonadocorticoids
  - CRH stimulates the release of ACTH, which in turn stimulates the release of the “cortical” hormones.

The **zona glomerulosa** secretes the **mineralocorticoids**, which function to regulate mineral homeostasis. **Aldosterone** is the main mineralocorticoid.

The **zona fasciculata** secretes the **glucocorticoids**. The primary glucocorticoid is **cortisol**, and it functions to regulate glucose availability and metabolism.

The **zona reticularis** secretes small amounts of the **gonadocorticoids**. These are weak androgens, which are simply masculinizing steroid hormones.

**Adrenal Medulla**

- The adrenal medulla secretions are very similar to the effects of the sympathetic nervous system
- Medulla
  - Secretes epinephrine and some norepinephrine
  - Innervated by sympathetic preganglionics
  - Acts similar to a sympathetic postganglionic
  - The secretions of the medulla duplicate and prolong the sympathetic response.
Objective 25. Relate the control and effects of the main mineralocorticoid, aldosterone to its role in the renin-angiotensin-aldosterone system (RAAS).

Assignments: Tortora, pp. 666-667 or Wiley Plus – 18.9 Adrenal Glands

Aldosterone is the main mineralocorticoid. Its main functions are to increase Na⁺ and water reabsorption, K⁺ excretion, and act as a vasoconstrictor. The **renin-angiotensin-aldosterone system (RAAS)** controls the secretion of aldosterone.

The RAAS can seem very complicated at first. The main stimuli that initiate the RAAS are: low blood sodium, low blood volume, or dehydration. All three of these stimuli result in a person having low blood pressure. This is where it all begins:

1) The low pressure stimulates a specific group of cells (juxtaglomerular cells) in the kidneys to secrete the enzyme **renin**.

2) Renin circulates in the blood and converts **angiotensinogen** (a plasma protein produced by the liver) into angiotensin I.

3) **Angiotensin I** continues to circulate in the blood and comes into contact with an enzyme in the lungs called **angiotensin-converting enzyme (ACE)**.

4) ACE converts angiotensin I to **angiotensin II**.

5) Angiotensin II has two main actions to increase blood pressure:
   a) stimulate the contraction of smooth muscle in the walls of arterioles,
   b) stimulate the release of **aldosterone** from the adrenal cortex.

5) Aldosterone circulates to the kidneys.

6) Aldosterone increases the reabsorption of Na⁺ and water, so less is lost in the urine, and stimulates the kidneys to excrete K⁺ and H⁺. The increased water reabsorption results in a blood volume and blood pressure increase.

**Adrenal Cortical Hormones**

- **Mineralocorticoids**
  - Mineralocorticoids help control water and electrolyte (Na⁺ and K⁺) balance.
  - **Aldosterone** plays the largest role of the mineralocorticoids.
    - Conserves Na⁺ and H₂O through reabsorption in the kidneys
    - Promotes the excretion of H⁺ and K⁺ into the urine.

**Aldosterone**

- The most important mechanism for control of aldosterone is the renin-angiotensin-aldosterone system (RAAS).
- This pathway is stimulated by one or more of the following:
  - Decrease in blood volume
  - Dehydration
  - Na⁺ deficiency
  - Hemorrhage
- All stimuli result in a decrease in blood pressure.
Objective 25 (continued). Relate the control and effects of the main mineralocorticoid, aldosterone to its role in the renin-angiotensin-aldosterone system (RAAS).

Release of Aldosterone

- The low blood pressure stimulates juxtaglomerular cells in the kidneys to secrete the enzyme renin.
- Renin converts the plasma protein angiotensinogen, produced in the liver into angiotensin I.
- As angiotensin I circulates to the lungs, an enzyme called angiotensin-converting enzyme (ACE) converts angiotensin I to angiotensin II.
- Angiotensin II has two effects:
  - Stimulates the adrenal cortex to secrete aldosterone
  - Vasoconstrictor

Renin-Angiotensin-Aldosterone System (RAAS)
Objective 26. Describe the control and effect of the main glucocorticoid, cortisol.

Cortisol (hydrocortisone) is the main glucocorticoid; it contributes >90% of the glucocorticoid activity. Other glucocorticoids are corticosterone and cortisone.

The glucocorticoids regulate glucose metabolism, suppress the immune system, and also facilitate resistance to stress, not necessarily psychological stress. Here is one way to help remember glucocorticoid function. **Cortisol is a person’s anti-hypoglycemic hormone.** This means cortisol will does whatever it can to keep a person’s glucose level up. If there isn’t enough available glucose, it will get it from somewhere else, protein and lipids. This is called gluconeogenesis.

### Effects of Glucocorticoids

1. Protein breakdown, mainly in muscle fibers, to free up amino acids for ATP production or synthesis of other proteins
2. Stimulates liver cells to convert amino acids and lactic acid to glucose (gluconeogenesis)
3. Stimulates the breakdown of triglycerides to release fatty acids into the blood
4. Inhibit the activity of white blood cells that participate in inflammation (anti-inflammatory and immune suppressive effects)
5. Stress resistance

### Adrenal Cortical Hormones

- **Glucocorticoids**
  - **Cortisol** is the main player of the glucocorticoids.
  - Glucocorticoids:
    - Regulate metabolism
    - Promote the breakdown of proteins (typically muscle) and triglycerides from adipose tissue to form glucose (gluconeogenesis)
    - Inhibit activity of white blood cells; this has anti-inflammatory and immunosuppressive effects.
    - Resist stress (extremes)
Objective 27. Describe the control and effects of the androgens (gonadocorticoids) secreted from the adrenal cortex.

Small amounts of androgens are secreted from the zona reticularis of the adrenal cortex in both males and females. The androgens are weak masculinizing steroid hormones. After puberty, the levels of these hormones are almost insignificant due to the amount of testosterone and estrogen from the gonads. In females, the androgens contribute to their libido (sex drive), and they are also converted to estrogens. After menopause (cessation of ovarian estrogen), the small amount of converted estrogens are likely beneficial.

Gonadocorticoids (Androgens)

- Gonadocorticoids
  - Weak androgens (masculinizing steroid hormones from the adrenal cortex)
  - In males, androgens are converted to testosterone.
  - In females, the androgens are converted to testosterone and finally estrogen.
    - The relatively small amount of estrogen produced from the androgens is insignificant, but after menopause, the secretion of estrogen from the adrenal gland may prove beneficial.
    - The androgens contribute to the development of secondary sex characteristics in both sexes, and they promote the female libido (sex drive).
### Objective 28. Predict the effects and provide examples of hyper- and hyposcretion disorders of the adrenal cortex.

Assignment: Tortora, pp. 681-682 or Wiley Plus – 18.17 Aging and the Endocrine System (Disorders: Homeostatic Imbalances)

#### Disorders of the Adrenal Cortex

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Cause</th>
<th>Hormone</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cushing Disease/Syndrome</strong></td>
<td>Cortisol or ACTH-secreting tumor</td>
<td>Increased cortisol</td>
<td>High blood glucose, Immune suppression, Poor wound healing, Hypertension, Lipolysis causing redistribution of body fat (moon face, buffalo hump, pendulous abdomen)</td>
</tr>
<tr>
<td><strong>Addison Disease</strong></td>
<td>Autoimmune destruction of the adrenal cortex</td>
<td>Decreased cortisol, Decreased aldosterone</td>
<td>Low blood glucose, Low blood Na+, High blood K+, Low blood pressure</td>
</tr>
</tbody>
</table>

#### Cortical Hormone Disorders

- **Addison Disease**
  - *Hyposcretion* of cortisol and aldosterone
  - Most cases are caused by autoimmune destruction of the adrenal cortex or blockage of ACTH binding.
  - Results in:
    - Low blood glucose
    - Na⁺ loss and K⁺ retention
    - Dehydration
    - Hypotension (low blood pressure)

- **Cushing Disease/Syndrome**
  - *Excess* cortisol or an ACTH-secreting tumor, causing an excess of cortisol
  - Results in:
    - High blood glucose
    - Immune suppression and poor wound healing
    - Hypertension (high blood pressure)
    - Body fat redistribution
      - Spindly arms and legs, moon face, buffalo hump (fat pads on shoulders), a hanging abdomen
Objective 29. Relate the secretion of the catecholamines to the symptoms of pheochromocytomas.

Adrenal Medulla Disorders

- Pheochromocytoma
  - Usually caused by benign tumors of the cells in the medulla.
  - Increased secretion of epinephrine and norepinephrine
  - Causes a prolonged fight or flight response.
  - Causes hypertension, increased metabolism, decreased gastric mobility, nervousness, hyperglycemia, and glucosuria.

A pheochromocytoma is a benign tumor of the chromaffin cells of the adrenal medulla. The tumor results in the hypersecretion of epinephrine and norepinephrine. There are about 1000 cases diagnosed in the US each year. The patient exhibits symptoms that would indicate sympathetic nervous system hyperactivity: high heart rate, elevated blood pressure, anxiety, sweating, weight loss, and headaches.
Objective 30. Describe the location and structure of the pancreas.

The pancreas is located posterior to the stomach and near the curve of the duodenum. It consists of a head, a body, and a tail. The pancreas is both an endocrine and an exocrine organ. 99% of the pancreas is made up of clusters of cells called acini. The cells contained in the acini produce digestive enzymes that are secreted into the small intestine. The exocrine function will be discussed in more detail in the digestion module of this course.

Within the pancreas, among the acini, there are 1-2 million tiny clusters of cells called pancreatic islets, or islets of Langerhans.

Pancreas

- The pancreas is both an endocrine and an exocrine gland.
- The pancreas is located posterior and inferior to the stomach.
- 99% of the pancreatic cells are arranged in clusters called acini.
  - The acini provide for the exocrine function of the pancreas.
- Distributed among the acini are clusters of endocrine tissue called pancreatic islets or islets of Langerhans.
Objective 31. Describe the structure and cell types of a pancreatic islet.

**Assignment:** Tortora, p. 671 or Wiley Plus – 18.10 Pancreatic Islets

The pancreatic islets contain four different types of endocrine cells (alpha, beta, delta, and F cells), each secreting separate hormones. Glucagon functions to raise blood sugar. Insulin lowers blood sugar levels. Somatostatin inhibits the release of insulin and glucagon, and pancreatic polypeptide acts as an inhibitor of digestion. The focus of this module will be on glucagon and insulin.

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>% of Islet</th>
<th>Hormone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha</td>
<td>17%</td>
<td>glucagon</td>
</tr>
<tr>
<td>Beta</td>
<td>70%</td>
<td>insulin</td>
</tr>
<tr>
<td>Delta (D cell)</td>
<td>7%</td>
<td>somatostatin</td>
</tr>
<tr>
<td>F cells</td>
<td>6%</td>
<td>pancreatic polypeptide</td>
</tr>
</tbody>
</table>
Objective 32. Compare the roles of glucagon and insulin in the control of blood glucose levels.

Glucagon and insulin are antagonists.

Low blood glucose levels stimulate the alpha cells to secrete glucagon.

Glucagon activates multiple mechanisms to increase the blood sugar level, conversion of glycogen to glucose (glycogenolysis) and formation of glucose from lactic acid and amino acids (gluconeogenesis).

Release of their products causes a net increase in blood sugar.

Assignment: Tortora, pp. 671-673 or Wiley Plus – 18.10 Pancreatic Islets
Objective 32 continued. Compare the roles of glucagon and insulin in the control of blood glucose levels.

Insulin

- Insulin
  - Accelerates facilitated diffusion of glucose into cells
    - Increases the number of transport proteins
  - Speed conversion of glucose into glycogen
  - Increases uptake of amino acids by cells to increase protein synthesis
  - Speeds up synthesis of fatty acids
  - Decreases gluconeogenesis

If blood sugar levels are high, beta cells release insulin. Insulin acts on cells throughout the body in a number of different ways, all of which will result in a decrease in a person’s blood sugar.

1) Increased facilitated diffusion of glucose out of the blood and into the cells by increasing the number of glucose transporters.
2) Increased protein synthesis by increasing the uptake of amino acids into cells.
3) Increased fatty acid synthesis
4) Conversion of glucose to glycogen
5) Decreased gluconeogenesis
Objective 33. Predict the effects of hypoinsulinism and relate insulin production and use to diabetes mellitus.

A continuous supply of glucose is necessary to maintain the necessary production of ATP for a cell to survive. A normal fasting blood glucose level averages between 80-120 mg/dl. If a person limits their food intake for 24 hours, their blood glucose level is still between 80-120 mg/dl. If a person limits their food intake for one week, their blood glucose level is still between 80-120 mg/dl. This is simply to illustrate the fact that individuals must maintain a minimum amount of blood glucose to provide enough ATP to meet physiological demands.

The body will utilize many resources (gluconeogenesis) to maintain a normal blood glucose level.

The most common disorder affecting insulin production is diabetes mellitus. The disorder results in a person not producing enough insulin, or they don’t respond well to the minimal or moderate amount they do produce.

There are unique subsets of the disorder. Terms such as type I, adult-onset, insulin-dependent, type II, juvenile-onset, and non-insulin dependent are all descriptors of diabetes used in an effort to describe the various causes of the insulin deficiency. Even these terms have difficulty grouping all diabetes sufferers, so don’t be surprised to see these terminologies change in the future.
Objective 33 (continued). Predict the effects of hypoinsulinism and relate insulin production and use to diabetes mellitus.

Type I, juvenile-onset, and insulin-dependent all describe a form of diabetes mellitus that typically occurs in a younger population. It results in complete loss of beta cells. There is a known genetic component to the disorder, but the current theory also involves an environmental influence. It is postulated that an individual acquires an infectious disease, most likely a virus that changes the cell signature on the beta cells, and results in the autoimmune destruction of the cells. With the loss of beta cells, the patient doesn’t have insulin to help facilitate diffusion of glucose into the body’s cells.

Type II, adult-onset, and non-insulin-dependent all describe individuals that still produce some insulin, but they either don’t produce enough, effectively utilize what they do produce, or maybe both. Studies show that there is a greater genetic influence with type II than type I, but there are other environmental factors that come into play. For example, one of the leading causes of type II diabetes is obesity. Individuals who overeat are continually giving their pancreas a carbohydrate challenge. When food is consumed, nutrients are absorbed, and there is an increase in the blood sugar level. The pancreas must secrete insulin to assist with the transport of glucose out of the blood and into the cells. If this process is happening too much, the body may respond by down-regulating insulin receptors, so even though there is insulin present, the body isn’t responding in a normal fashion; more glucose stays in the blood stream. This is what is referred to as decreased insulin sensitivity. Eventually, the pancreas will decrease the overall insulin output. Most medical scientists would re-classify type 2 diabetes as a part of metabolic syndrome, a cluster of hyperlipidemia, obesity, hypertension and insulin resistance.
Objective 33 (continued). Predict the effects of hypoinsulinism and relate insulin production and use to diabetes mellitus.

Individuals with diabetes are at risk for severe life-threatening fluctuations in blood glucose. A patient’s blood glucose level can be critically low or critically high, but the patient will come into the emergency room with similar symptoms in both scenarios. The problem with both levels is that the cells aren’t getting any glucose to use for fuel. The patient with a critically low blood glucose level doesn’t have any glucose to feed their cells. The patient with a critically high level has plenty of glucose, but it is in the wrong place; it is in the blood, not the cells. So, a patient with a blood glucose level of 20 mg/dl and a patient with a level of 900 mg/dl are both starving their cells.

There are two acute complications for diabetes mellitus, diabetic coma and insulin shock. With diabetic coma, the patient’s glucose is critically high. This commonly occurs with hypoinsulinism; the patient doesn’t have or take enough insulin or medication to match their caloric (food) intake. Insulin shock refers to someone that takes too much insulin; it moves too much glucose into the cells, and doesn’t leave enough for later. This would be like someone spending their monthly paycheck on golf, now they don’t have enough to pay the electrical bill.

With a complete lack of insulin, type I diabetics can experience a condition called ketoacidosis. This is where a patient doesn’t have any available glucose due to a complete lack of insulin. They rely on fatty acid metabolism for their ATP production. The byproducts of fatty acid metabolism are organic acids called ketoacids. The overproduction of these acids causes the person’s pH to fall and it becomes very life-threatening. A person with type II diabetes produces enough insulin to not rely completely on fatty acid metabolism for ATP.

<table>
<thead>
<tr>
<th>Hyperinsulinism</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Most common in diabetic patients that take too much insulin compared to their caloric intake</td>
</tr>
<tr>
<td>• The low glucose causes an increased amount of epinephrine, glucagon, and hGH.</td>
</tr>
<tr>
<td>- Causes anxiety, sweating, tremors, increased heart rate, hunger, and weakness</td>
</tr>
<tr>
<td>• Brain cells are deprived of glucose, so mental disorientation, convulsions, and unconsciousness can occur</td>
</tr>
<tr>
<td>• Can result in “insulin shock”</td>
</tr>
<tr>
<td>- Shock due to insulin overdose</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diabetic Ketoacidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• If a patient doesn’t have any available insulin, they will utilize fatty acids for their energy source.</td>
</tr>
<tr>
<td>- The byproducts of fatty acid metabolism (beta-oxidation) are ketoacids, simply called ketones.</td>
</tr>
<tr>
<td>- Everyone produces ketones when they metabolize fatty acids, but unless there is a complete lack of insulin, never in excess.</td>
</tr>
<tr>
<td>- Causes an acidic shift in the patient’s pH</td>
</tr>
</tbody>
</table>

577
The gonads (ovaries in women, testes in men) are the organs responsible for gamete production. They have endocrine functions. In response to FSH and LH from the pituitary, the gonads produce various hormones. The ovaries produce estrogen and progesterone, and the testes produce testosterone.

### Gonadal Hormones

- The ovaries and the testes respond to FSH and LH secretion from the anterior pituitary
- **Ovaries**
  - Estrogen
    - Development and maintenance of female reproductive structures and sex characteristics
  - Progesterone
    - Prepares the uterine lining (endometrium) for implantation
- **Testes**
  - Testosterone
    - Sperm production
    - Development and maintenance of masculine sex characteristics

The general functions of these hormones are the development and maintenance of the secondary sex characteristics and fertility. The secondary sex characteristics are those that are present during and after puberty.

<table>
<thead>
<tr>
<th>Estrogens and Progesterone</th>
<th>Testosterone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulate the female reproductive cycle</td>
<td>Sperm production (spermatogenesis)</td>
</tr>
<tr>
<td>Maintain pregnancy</td>
<td>Hair growth patterns</td>
</tr>
<tr>
<td>Breast development and maturation</td>
<td>Increased skeletal and muscular growth</td>
</tr>
<tr>
<td>Widening of the hips</td>
<td>Voice changes</td>
</tr>
<tr>
<td>Adipose tissue deposition in the breasts and around the hips</td>
<td></td>
</tr>
</tbody>
</table>
Objective 35. Identify the physiological effect of melatonin secreted from the pineal gland.

Assignment: Tortora, pp. 673-674 or Wiley Plus – 18.12 Pineal Gland

The pineal gland is attached to the top of the third ventricle of the brain; it is part of the epithalamus. The pineal gland produces and secretes a hormone called melatonin. It is theorized that melatonin assists with the setting of the daily biological clock by promoting sleepiness. More melatonin is released during darkness than light.

Sleep/wake cycles are very evident when comparing different seasons of the year. What if the doorbell rings at 8PM during the dark winter months? People get mad because they are getting ready for bed. What if the same salesman drops by at 8PM in the summer months? People still get mad, but it’s because he interrupted dinner on the patio.
Objective 36. Describe the basic effect of thymosin secretion from the thymus gland.

Assignment: Tortora, p. 674 or Wiley Plus – 18.13 Thymus

The thymus gland is located in the mediastinum (behind the sternum and between the lungs). The thymus is important to our immune system, and is discussed in more detail in the blood module of this course.

Thymosin and other related hormones from the thymus gland encourage the maturation of T-lymphocytes.

T-lymphocytes are a specific type of white blood cell (WBC). The WBCs give a person their ability to fight disease.

---

**Thymus gland**

- The thymus gland secretes thymosin, which promotes the proliferation and maturation of T cells.
- T cells are a type of white blood cell (lymphocyte) that destroys microorganisms and foreign substances through direct cellular contact or by recruiting other white cells.
Objective 37. Define stressor, and describe the stress response or general adaptation syndrome.

A stressor is anything that causes a stress response. Maybe an easier way to understand it is, a stressor is anything that disrupts normal homeostasis. Examples include: chemicals, psychological stress, heat, cold, confinement, injury, hemorrhage, etc.

Stress can be helpful in some situations; it heightens responsiveness and helps increase concentration. This type of stress is called eustress (eu = good). Stress that has a negative effect is called distress, and it is always harmful.

In the 1930’s, Dr. Hans Selye, demonstrated that a variety of stressors would invoke a very similar response, regardless of the stressor type. These common effects, controlled mainly by the hypothalamus, were termed the stress response or the general adaptation syndrome (GAS).

The three stages of the stress response or GAS are

1. **fight-or-flight** response,
2. **resistance** reaction,
3. **exhaustion**.

---

**General Adaptation Syndrome (“The Stress Response”)**

- A stress response is the body’s response to emergency or stressful situations, real or imagined.
- A stressor is any stimulus that causes a stress response.
  - Distress is a harmful response to a stressor.
  - Eustress is a productive use of a stressor. Some levels of stress help individuals perform well and be productive.
- It is the goal of the stress response to maintain homeostasis.

---

Assignment: Tortora, pp. 675-678 or Wiley Plus – 18.15 The Stress Response
Objective 38. Identify and describe the three stages of the stress response.

The **flight-or-flight stage** of the stress response is initiated by the hypothalamus. The body is trying to quickly activate mechanisms to allow an immediate physical response. This is essentially a sympathetic nervous system response, quick, but short-lived.

<table>
<thead>
<tr>
<th>General Adaptation Syndrome (Stress Response)</th>
<th>General Adaptation Syndrome (Stress Response)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• There are three stages to a prolonged stress response:</td>
<td>• Flight-or-flight response</td>
</tr>
<tr>
<td>– Flight-or-flight response</td>
<td>– Stimulation of the adrenal medulla by the sympathetic nervous system. This response is initiated by neurons in the hypothalamus (HPA axis).</td>
</tr>
<tr>
<td>– Resistance reaction</td>
<td>• Provides large amounts of glucose and oxygen</td>
</tr>
<tr>
<td>– Exhaustion</td>
<td>• Mental alertness</td>
</tr>
<tr>
<td></td>
<td>• Increased blood flow to essential organs</td>
</tr>
</tbody>
</table>

The **resistance reaction** is also initiated by the hypothalamus, but in this case by secreting the releasing-hormones: corticotrophin-releasing hormone, growth hormone-releasing hormone, and thyrotropin-releasing hormone. This response results in longer-lasting effects. With the secretion of these releasing hormones, one can easily predict the results, activation of the adrenal cortex (cortisol and aldosterone), secretion of growth hormone, and activation of the thyroid gland. This stage allows the body to fight a stressor after the fight-or-flight stage has diminished.

<table>
<thead>
<tr>
<th>General Adaptation Syndrome (Stress Response)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Resistance Reaction</td>
</tr>
<tr>
<td>– With the source of this response being hormonal rather than neural, it allows the body to continue fighting a stressor long after the flight-or-flight response dissipates.</td>
</tr>
<tr>
<td>– Activation of the adrenal cortex (ACTH), liver (hGH), and thyroid (TSH) causes:</td>
</tr>
<tr>
<td>• Increased blood pressure, glycogen catabolism, protein catabolism, lipolysis, and Na⁺ and water retention.</td>
</tr>
<tr>
<td>• Decreased inflammation, wound healing, and immune response.</td>
</tr>
</tbody>
</table>
Objective 38 (continued). Identify and describe the three stages of the stress response.

In the **exhaustion stage**, the body’s resources have become so depleted, they can’t maintain a resistance reaction/response. The symptoms of the exhaustion phase relate to prolonged exposure to high levels of hormone. Excess cortisol causes immune suppression, poor wound healing, and muscle wasting. Prolonged high insulin secretion results in pancreatic beta-cell failure. This stage is likely the link to many chronic diseases from prolonged stressor exposure.

---

**General Adaptation Syndrome (Stress Response)**

- Exhaustion Reaction
  - The exhaustion phase is when the body’s resources become depleted and the resistance reaction cannot be maintained.
  - Prolonged exposure to the resistance response causes immune suppression, muscle wasting, ulceration of the GI tract, failure of pancreatic cells, and depletion of K⁺.
  - Common relationship with chronic diseases
  - Death is a potential severe consequence.

---

**The Stress Response**

Figure 18.20 Tortora - PAP 12/e
Copyright © John Wiley and Sons, Inc. All rights reserved.
Objective 39. Describe the effects of aging on the endocrine system.

**Assignment:** Tortora, pp. 678-679 or Wiley Plus – 18.18 Aging and the Endocrine System

### Aging and the Endocrine System

- Diminished production of:
  - hGH
  - Thyroid hormones
  - Cortical hormones
  - Calcitonin
- Increased secretion of:
  - PTH
  - FSH and LH
- Thymic atrophy

| Effects of Aging on the Endocrine System |
|-------------------------------|------------------|
| **Cause**                        | **Effect**            |
| Decrease in hGH                  | Muscle atrophy        |
|                                 | Decreased cell replacement |
| Decreased thyroid hormone        | Cold intolerant     |
|                                 | Slower metabolism (increased body fat) |
| Increased PTH (increased due to negative feedback) | Osteoporosis |
| Decreased cortisol and aldosterone | Glucose and electrolyte changes |
| Decreased thymosin due to atrophied thymus | Diminished T lymphocyte production |
| Decreased insulin levels         | Faster increase, slower decrease of blood glucose levels |