CHAPTER 7: ENDOCRINE SYSTEM

At the end of this chapter, student will be able to:

a) Name the endocrine glands and the hormones secreted by each.
b) Explain how a negative feedback mechanism works.
c) Explain how the hypothalamus is involved in the secretion of hormones from the posterior pituitary gland and anterior pituitary gland.
d) State the functions of oxytocin and antidiuretic hormone, and explain the stimulus for secretion of each.
e) State the functions of the hormones of the anterior pituitary gland, and state the stimulus for secretion of each.

7.1. INTRODUCTION TO ENDOCRINE SYSTEM

The endocrine system, along with the nervous system, functions in the regulation of body activities. The nervous system acts through electrical impulses and neurotransmitters to cause muscle contraction and glandular secretion. The effect is of short duration, measured in seconds, and localized. The endocrine system acts through chemical messengers called hormones that influence growth, development, and metabolic activities. The action of the endocrine system is measured in minutes, hours, or weeks and is more generalized than the action of the nervous system. The growth and repair of tissues, the utilization of food to produce energy, responses to stress, the maintenance of the proper levels and pH of body fluids, and the continuance of the human species all depend on hormones.

Regulatory functions of endocrine system.

- Metabolism and tissue maturation: E.S regulates the rate of metabolism and influences of tissus, such as those of nervous system.
- Iron regulation: regulate blood pH, as well as Na, K, and Ca concentration in the blood.
- Water balance: by controlling the solute concentration of blood.
- Immune system regulation: controls the production of immune cells.

- Heart rate and blood pressure regulation
- Control of blood glucose level and other nutrients in the blood.
- Control of reproductive functions in males and females.
- Uterine contractions and milk release.

Categories of endocrine system.

There are two major categories of glands in the body - exocrine and endocrine.

❖ ***Exocrine Glands***

Exocrine glands have ducts that carry their secretory product to a surface. These glands include the sweat, sebaceous, and mammary glands and, the glands that secrete digestive enzymes.

❖ ***Endocrine Glands***

Endocrine glands secrete their products (hormones) into the interstitial fluid surrounding the secretory cells rather than into ducts. From the interstitial fluid, hormones diffuse into blood capillaries and blood carries them to target cells throughout the body. Because most hormones are required in very small amounts, circulating levels typically are low.

The endocrine glands include the pituitary, thyroid, parathyroid, adrenal, and pineal glands. In addition, several organs and tissues are not exclusively classified as endocrine glands but contain cells that secrete hormones. These include the hypothalamus, thymus, pancreas, ovaries, testes, kidneys, stomach, liver, small intestine, skin, heart, adipose tissue, and placenta. Taken together, all endocrine glands and hormone-secreting cells constitute the **endocrine system.**

7.2. CHARACTERISTICS OF HORMONES

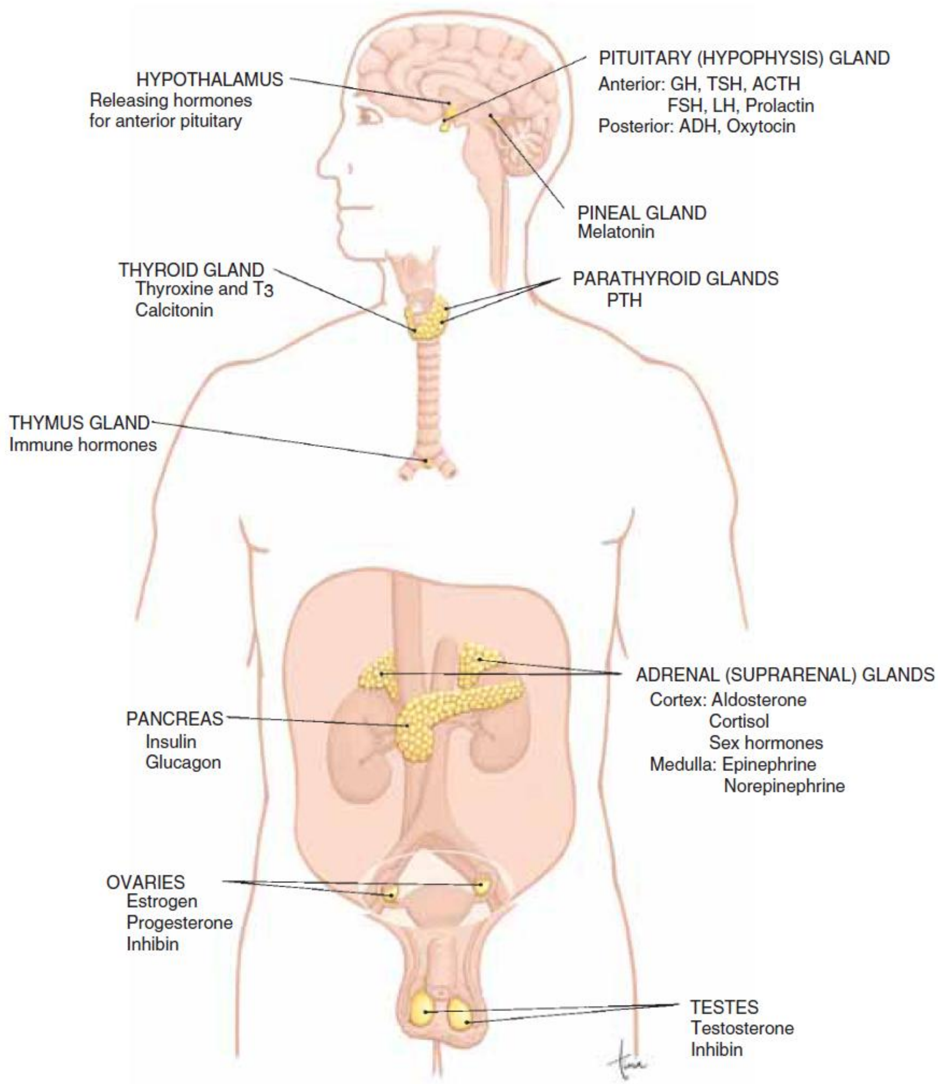
Chemical Nature of Hormones: Chemically, hormones may be classified as either proteins or steroids. All of the hormones in the human body, except the sex hormones and those from the adrenal cortex, are proteins or protein derivatives.

7.3. MECHANISM OF HORMONE

Hormones are carried by the blood throughout the entire body, yet they affect only certain cells. The specific cells that respond to a given hormone have receptor sites for that hormone. This is sort of a lock and key mechanism. If the key fits the lock, then the door will open. If a hormone fits the receptor site, then there will be an effect. If a hormone and a receptor site do not match, then there is no reaction.

All the cells that have receptor sites for a given hormone make up the target tissue for that hormone. In some cases, the target tissue is localized in a single gland or organ. In other cases, the target tissue is diffuse and scattered throughout the body so that many areas are affected. Hormones bring about their characteristic effects on target cells by modifying cellular activity.

Protein hormones react with receptors on the surface of the cell, and the sequence of events that results in hormone action is relatively rapid. Steroid hormones typically react with receptor sites inside a cell. Because this method of action actually involves synthesis of proteins, it is relatively slow.



<u>Figure</u>: Locations of many endocrine glands. Testes for males and ovaries for females (gonads).

7.4. CONTROL OF HORMONE ACTION

Hormones are very potent substances, which mean that very small amounts of a hormone may have profound effects on metabolic processes. Because of their potency, hormone secretion must be regulated within very narrow limits in order to maintain homeostasis in the body.

Many hormones are controlled by some form of a negative feedback mechanism. In this type of system, a gland is sensitive to the concentration of a substance that it regulates.

A negative feedback system causes a reversal of increases and decreases in body conditions in order to maintain a state of stability or homeostasis. Some endocrine glands secrete hormones in response to other hormones. The hormones that cause secretion of other hormones are called tropic hormones. A hormone from gland A causes gland B to secrete its hormone. A third method of regulating hormone secretion is by direct nervous stimulation. A nerve stimulus causes gland A to secrete its hormone.

7.5 CHEMISTRY OF HORMONES

With respect to their chemical structure, hormones may be classified into three groups: amines, proteins, and steroids.

1. **Amines**: these simple hormones are structural variations of the amino acid tyrosine. This group includes thyroxine from the thyroid gland and epinephrine and norepinephrine from the adrenal medulla.

2. **Proteins**: these hormones are chains of amino acids. Insulin from the pancreas, growth hormone from the anterior pituitary gland, and calcitonin from the thyroid gland are all proteins. Short chains of amino acids may be called **peptides**. Antidiuretic hormone and oxytocin, synthesized by the hypothalamus, are peptide hormones.

3. **Steroids**: cholesterol is the precursor for the steroid hormones, which include cortisol and aldosterone from the adrenal cortex, estrogen and progesterone from the ovaries, and testosterone from the testes.

7.6 REGULATION OF HORMONE SECRETION

Hormones are secreted by endocrine glands when there is a need for them, that is, for their effects on their target organs. The cells of endocrine glands respond to changes in the blood or perhaps to other hormones in the blood. These stimuli are the information they use to increase or decrease secretion of their own hormones. When a hormone brings about its effects, the stimulus is reversed, and secretion of the hormone decreases until the stimulus reoccurs. Let us use insulin as a different example here.

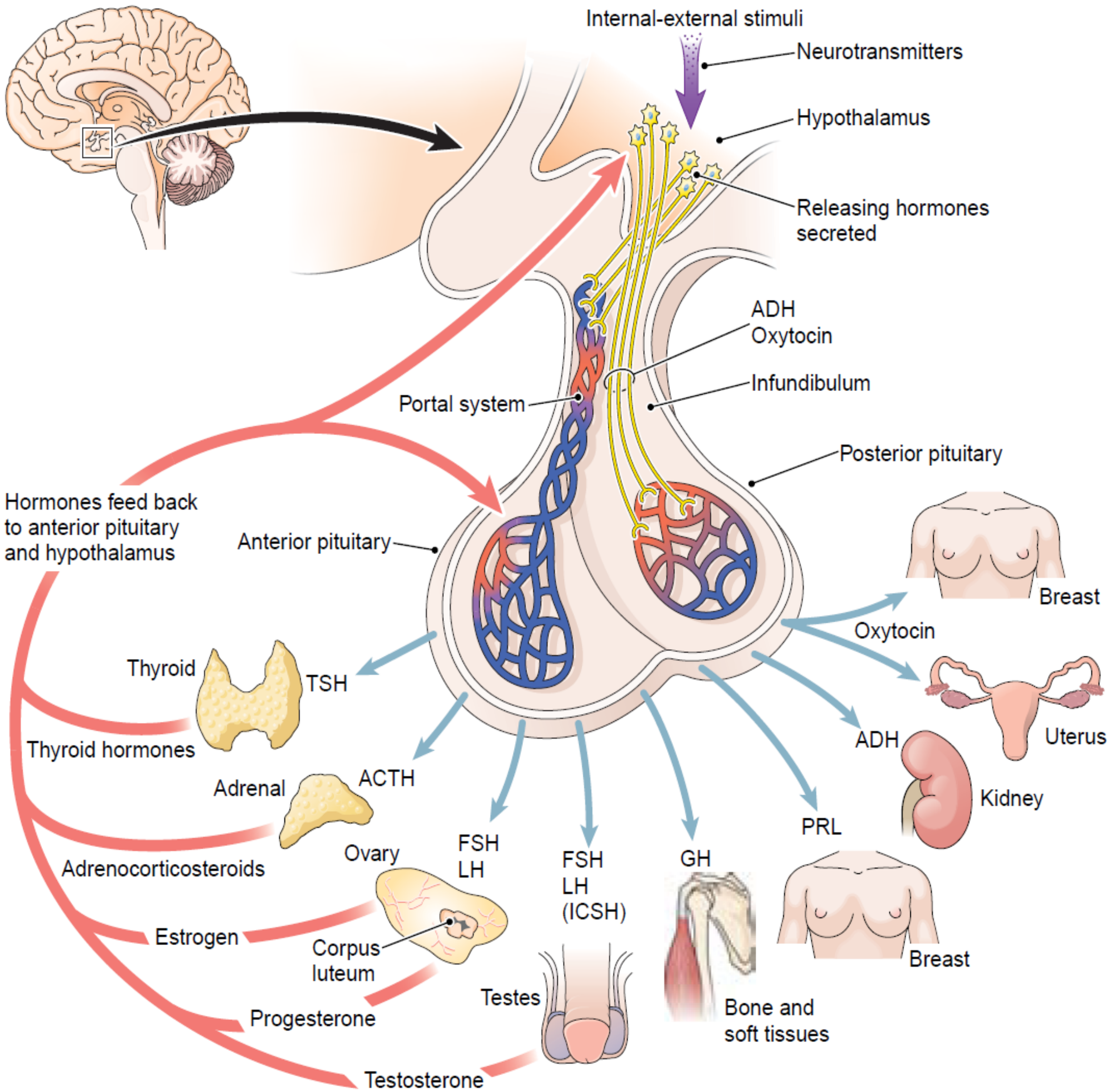
Insulin is secreted by the pancreas when the blood glucose level is high; that is, hyperglycemia is the stimulus for secretion of insulin. Once circulating in the blood, insulin enables cells to remove glucose from the blood so that it can be used for energy production and enables the liver to store glucose as glycogen. As a result of these actions of insulin, the blood glucose level decreases, reversing the stimulus for secretion of insulin. Insulin secretion then decreases until the blood glucose level increases again.

In any hormonal **negative feedback mechanism**, information about the effects of the hormone is "fed back" to the gland, which then decreases its secretion of the hormone. This is why the mechanism is called "negative": The effects of the hormone reverse the stimulus and decrease the secretion of the hormone. The secretion of many other hormones is regulated in a similar way. The hormones of the anterior pituitary gland are secreted in response to **releasing hormones** (also called releasing factors) secreted by the hypothalamus.
For example, is secreted in response to growth hormone–releasing hormone (GHRH) from the hypothalamus. As growth hormone exerts its effects, the secretion of GHRH decreases, which in turn decreases the secretion of growth hormone. This is another type of negative feedback mechanism. Some hormones function as an **antagonistic pair** to regulate a particular aspect of blood chemistry; these mechanisms will also be covered.

7.7 PITUITARY GLAND

The pituitary gland or hypophysis is a small gland about 1 centimeter in diameter or the size of a pea. It is nearly surrounded by bone as it rests in the sella turcica, a depression in the sphenoid bone. The gland is connected to the hypothalamus of the brain by a slender stalk called the infundibulum.

There are two distinct regions in the gland: the anterior lobe (adenohypophysis) and the posterior lobe (neurohypophysis). The activity of the adenohypophysis is controlled by releasing hormones from the hypothalamus. The neurohypophysis is controlled by nerve stimulation.



<u>Figure</u>: The hypothalamus, pituitary gland, and target tissues. Arrows indicate the hormones' target issues and feedback pathways.

7.7.1 POSTERIOR PITUITARY GLAND

The two hormones of the **posterior pituitary gland** are actually produced by the hypothalamus and simply stored in the posterior pituitary until needed. Their release is stimulated by nerve impulses from the hypothalamus**.**

a) Antidiuretic Hormone

Antidiuretic hormone (**ADH**, also called **vasopressin**) increases the reabsorption of water by kidney tubules, which decreases the amount of urine formed. The water is reabsorbed into the blood, so as urinary output is decreased, blood volume is increased, which helps maintain normal blood pressure. ADH also decreases sweating, but the amount of water conserved is much less than that conserved by the kidneys. The stimulus for secretion of ADH is decreased water content of the body. If too much water is lost through sweating or diarrhea, for example, **osmoreceptors** in the hypothalamus detect the increased "saltiness" of body fluids. The hypothalamus then transmits impulses to the posterior pituitary to increase the secretion of ADH and decrease the loss of more water in urine. Any type of dehydration stimulates the secretion of ADH to conserve body water. In the case of severe hemorrhage, ADH is released in large amounts and will also cause vasoconstriction, especially in arterioles, which will help to raise or at least maintain blood pressure. This function gives ADH its other name, **vasopressin**.

Ingestion of alcohol inhibits the secretion of ADH and increases urinary output. If alcohol intake is excessive and fluid is not replaced, a person will feel thirsty and dizzy the next morning. The thirst is due to the loss of body water, and the dizziness is the result of low blood pressure.

b) Oxytocin

Oxytocin stimulates contraction of the uterus at the end of pregnancy and stimulates release of milk from the mammary glands. As labor begins, the cervix of the uterus is stretched, which generates sensory impulses to the hypothalamus, which in turn stimulates the posterior pituitary to release oxytocin. Oxytocin then causes strong contractions of the smooth muscle (myometrium) of the uterus to bring about delivery of the baby and the placenta. The secretion of oxytocin is one of the few positive feedback mechanisms within the body, and the external brake or shutoff of the feedback cycle is delivery of the baby and the placenta.

It has been discovered that the placenta itself secretes oxytocin at the end of gestation and in an amount far higher than that from the posterior pituitary gland. Research is continuing to determine the exact mechanism and precise role of the placenta in labor. When a baby is breast-fed, the sucking of the baby stimulates sensory impulses from the mother's nipple to the hypothalamus.

Nerve impulses from the hypothalamus to the posterior pituitary cause the release of oxytocin, which stimulates contraction of the smooth muscle cells around the mammary ducts. This release of milk is sometimes called the “milk let-down” reflex. Both ADH and oxytocin are peptide hormones with similar structure, having nine amino acids each.And both have been found to influence aspects of behavior such as nurturing and trustfulness. Certain brain cells have receptors for vasopressin, and they seem to be involved in creating the bonds that sustain family life. Trust is part of many social encounters such as friendship, school, sports and games, and buying and selling, as well as family life. These two small hormones seem to have some influence on us mentally as well as physically.

7.7.2 ANTERIOR PITUITARY GLAND

The hormones of the **anterior pituitary gland** regulate many body functions. They are in turn regulated by **releasing hormones** from the hypothalamus. These releasing hormones are secreted into capillaries in the hypothalamus and pass through the **hypophyseal portal** veins to another capillary network in the anterior pituitary gland. Here, the releasing hormones are absorbed and stimulate secretion of the anterior pituitary hormones. This pathway permits the releasing hormones to rapidly stimulate the anterior pituitary, without having to pass through general circulation.

a) Growth Hormone

Growth hormone (**GH**) is also called **somatotropin**, and it does indeed promote growth. GH stimulates cells to produce insulin-like growth factors (IGFs), intermediary molecules that bring about the functions of GH. Growth hormone increases the transport of amino acids into cells, and increases the rate of protein synthesis. Amino acids cannot be stored in the body, so when they are available, they must beused in protein synthesis. Excess amino acids are changed to carbohydrates or fat, for energy storage.

Growth hormone ensures that amino acids will be used for whatever protein synthesis is necessary, before the amino acids can be changed to carbohydrates. Growth hormone also stimulates cell division in those tissues capable of mitosis.

These functions contribute to the growth of the body during childhood, especially growth of bones and muscles. You may now be wondering if GH is secreted in adults, and the answer is yes. The use of amino acids for the synthesis of proteins is still necessary. Even if the body is not growing in height, some tissues will require new proteins for repair or replacement. GH also stimulates the release of fat from adipose tissue and the use of fats for energy production. This is important any time we go for extended periods without eating, no matter what our ages. The secretion of GH is regulated by two releasing hormones from the hypothalamus. Growth hormone– releasing hormone (GHRH), which increases the secretion of GH, is produced during hypoglycemia and during exercise. Another stimulus for GHRH is a high blood level of amino acids; the GH then secreted will ensure the conversion of these amino acids into protein.

Somatostatin may also be called growth hormone inhibiting hormone (GHIH), and, as its name tells us, it decreases the secretion of GH. Somatostatin is produced during hyperglycemia.

b) Thyroid-Stimulating Hormone

Thyroid-stimulating hormone (**TSH**) is also called thyrotropin, and its target organ is the thyroid gland.TSH stimulates the normal growth of the thyroid and the secretion of thyroxine (T4) and triiodothyronine (T3). The secretion of TSH is stimulated by thyrotropinreleasing hormone (TRH) from the hypothalamus. When metabolic rate (energy production) decreases, TRH is produced.

c) Adrenocorticotropic Hormone

Adrenocorticotropic hormone (**ACTH**) stimulates the secretion of cortisol and other hormones by the adrenal cortex. Secretion of ACTH is increased by corticotropin-releasing hormone (CRH) from the hypothalamus. CRH is produced in any type of physiological stress situation such as injury, disease, exercise, or hypoglycemia (being hungry is stressful).

d) Prolactin

Prolactin, as its name suggests, is responsible for lactation. More precisely, prolactin initiates and maintains milk production by the mammary glands. The regulation of secretion of prolactin is complex, involving both prolactin-releasing hormone (PRH) and prolactin-inhibiting hormone (PIH) from the hypothalamus.The mammary glands must first be acted upon by other hormones such as estrogen and progesterone which are secreted in large amounts by the placenta during pregnancy. Then, after delivery of the baby, prolactin secretion increases and milk is produced. If the mother continues to breast-feed, prolactin levels remain high.

e) Follicle-Stimulating Hormone

Follicle-stimulating hormone (**FSH**) is one of the gonadotropic hormones; that is, it has its effects on the gonads: the ovaries or testes. FSH is named for one of its functions in women. Within the ovaries are ovarian follicles that contain potential ova (egg cells). FSH stimulates the growth of ovarian follicles; that is, it initiates egg development in cycles of approximately 28 days. FSH also stimulates secretion of estrogen by the follicle cells. In men, FSH initiates sperm production within the testes. The secretion of FSH is stimulated by the hypothalamus, which produces **gonadotropin-releasing hormone** (**GnRH**). FSH secretion is decreased by inhibin, a hormone produced by the ovaries or testes.

f) Luteinizing Hormone

Luteinizing hormone **(LH)** is another gonadotropic hormone. In women, LH is responsible for ovulation, the release of a mature ovum from an ovarian follicle. LH then stimulates that follicle to develop into the corpus luteum, which secretes progesterone, also under the influence of LH. In men, LH stimulates the interstitial cells of the testes to secrete testosterone. (LH is also called ICSH, interstitial cell stimulating hormone.) Secretion of LH is also regulated by GnRH from the hypothalamus.

7.8 THYROID GLAND

The **thyroid gland** is located on the front and sides of the trachea just below the larynx. Its two lobes are connected by a middle piece called the isthmus. The structural units of the thyroid gland are thyroid follicles, which produce **thyroxine** (**T4**) and **triiodothyronine** (**T3**). Iodine is necessary for the synthesis of these hormones; thyroxine contains four atoms of iodine, and

T3 contains three atoms of iodine.The third hormone produced by the thyroid gland is **calcitonin**, which is secreted by parafollicular cells. Its function is very different from those of thyroxine and T3.

7.8.1 THYROXINE AND T3

Thyroxine (T4) and T3 have the same functions: regulation of energy production and protein synthesis, which contribute to growth of the body and to normal body functioning throughout life. Thyroxine and T3 increase cell respiration of all food types (carbohydrates, fats, and excess amino acids) and thereby increase energy and heat production. They also increase the rate of protein synthesis within cells. Normal production of thyroxine and T3 is essential for physical growth, normal mental development, and maturation of the reproductive system.

These hormones are the most important day-to-day regulators of metabolic rate; their activity is reflected in the functioning of the brain, muscles, heart, and virtually all other organs. Although thyroxine and T3 are not vital hormones, in that they are not crucial to survival, their absence greatly diminishes physical and mental growth and abilities. Secretion of thyroxine and T3 is stimulated by **thyroid-stimulating hormone** (**TSH**) from the anterior pituitary gland.

When the metabolic rate (energy production) decreases, this change is detected by the hypothalamus, which secretes thyrotropin releasing hormone (TRH). TRH stimulates the anterior pituitary to secrete TSH, which stimulates the thyroid to release thyroxine and T3, which raise the metabolic rate by increasing energy production. This negative feedback mechanism then shuts off TRH from the hypothalamus until the metabolic rate decreases again.

7.8.2 CALCITONIN

Calcitonin decreases the reabsorption of calcium and phosphate from the bones to the blood, thereby lowering blood levels of these minerals. This function of calcitonin helps maintain normal blood levels of calcium and phosphate and also helps maintain a stable, strong bone matrix. It is believed that calcitonin exerts its most important effects during childhood, when bones are growing. The stimulus for secretion of calcitonin is **hypercalcemia**, that is, a high blood calcium level. When blood calcium is high, calcitonin ensures that no more calcium will be removed from bones until there is a real need for more calcium in the blood.

7.9 PARATHYROID GLANDS

There are four **parathyroid glands**: two on the back of each lobe of the thyroid gland.The hormone they produce is called parathyroid hormone.

PARATHYROID HORMONE

Parathyroid hormone (**PTH**) is an antagonist to calcitonin and is important for the maintenance of normal blood levels of calcium and phosphate. The target organs of PTH are the bones, small intestine, and kidneys. PTH increases the reabsorption of calcium and phosphate from bones to the blood, thereby raising their blood levels. Absorption of calcium and phosphate from food in the small intestine, which also requires vitamin D, is increased by PTH. This too raises the blood levels of these minerals. In the kidneys, PTH stimulates the activation of vitamin D and increases the reabsorption of calcium and the excretion of phosphate (more than is obtained from bones). Therefore, the overall effect of PTH is to raise the blood calcium level and lower the blood phosphate level. Secretion of PTH is stimulated by **hypocalcemia**, a low blood calcium level, and inhibited by hypercalcemia.

Together, these hormones maintain blood calcium within a normal range. Calcium in the blood is essential for the process of blood clotting and for normal activity of neurons and muscle cells. As you might expect, a sustained hypersecretion of PTH, such as is caused by a parathyroid tumor, would remove calcium from bones and weaken them. It has been found, however, that an intermittent, brief excess of PTH, such as can occur by injection, will stimulate the formation of more bone matrix, rather than matrix reabsorption. This may seem very strange, the opposite of what we would expect—but it shows how much we have yet to learn about the body. PTH is being investigated as a possible way to help prevent osteoporosis.

7.10 PANCREAS

The **pancreas** is located in the upper left quadrant of the abdominal cavity, extending from the curve of the duodenum to the spleen. The pancreas is both an exocrine (digestive) gland as well as an endocrine gland. The hormone-producing cells of the pancreas are called **islets of Langerhans**; they contain **alpha cells** that produce glucagon and **beta cells** that produce insulin.

7.10.1 GLUCAGON

Glucagon stimulates the liver to change glycogen to glucose (this process is called **glycogenolysis**, which literally means "glycogen breakdown") and to increase the use of fats and excess amino acids for energy production. The process of **gluconeogenesis** (literally, "making new glucose") is the conversion of excess amino acids into simple carbohydrates that may enter the reactions of cell respiration. The overall effect of glucagon, therefore, is to raise the blood glucose level and to make all types of food available for energy production. The secretion of glucagon is stimulated by **hypoglycemia**, a low blood glucose level. Such a state may occur between meals or during physiological stress situations such as exercise.

7.10.2 INSULIN

Insulin increases the transport of glucose from the blood into cells by increasing the permeability of cell membranes to glucose. (Brain, liver, and kidney cells, however, are not dependent on insulin for glucose intake.) Once inside cells, glucose is used in cell respiration to produce energy, the liver and skeletal muscles also change glucose to glycogen (**glycogenesis**, which means "glycogen production") to be stored for later use. Insulin is also important in the metabolism of other food types; it enables cells to take in fatty acids and amino acids to use in the synthesis of lipids and proteins (*not* energy production). Without insulin, blood levels of lipids tend to rise and cells accumulate excess fatty acids.

With respect to blood glucose, insulin decreases its level by promoting the use of glucose for energy production. Insulin is a vital hormone; we cannot survive for very long without it. A deficiency of insulin or in its functioning is called **diabetes mellitus**. Secretion of insulin is stimulated by **hyperglycemia**, a high blood glucose level. This state occurs after eating, especially of meals high in carbohydrates. As glucose is absorbed from the small intestine into the blood, insulin is secreted to enable cells to use the glucose for immediate energy.

At the same time, any excess glucose will be stored in the liver and muscles as glycogen. These produce the hormone somatostatin, which is identical to growth hormone–inhibiting hormone from the hypothalamus. Pancreatic somatostatin acts locally to inhibit the secretion of insulin and glucagon, and it seems to slow the absorption of the end products of digestion in the small intestine.

7.11 ADRENAL GLANDS

The two **adrenal glands** are located one on top of each kidney, which gives them their other name of **suprarenal glands**. Each adrenal gland consists of two parts: an inner adrenal medulla and an outer adrenal cortex. The hormones produced by each part have very different functions.

7.11.1 ADRENAL MEDULLA

The cells of the **adrenal medulla** secrete epinephrine and norepinephrine, which collectively are called **catecholamines** and are **sympathomimetic**. The secretion of both hormones is stimulated by sympathetic impulses from the hypothalamus, and their functions duplicate and prolong those of the sympathetic division of the autonomic nervous system (*mimetic* means "to mimic").

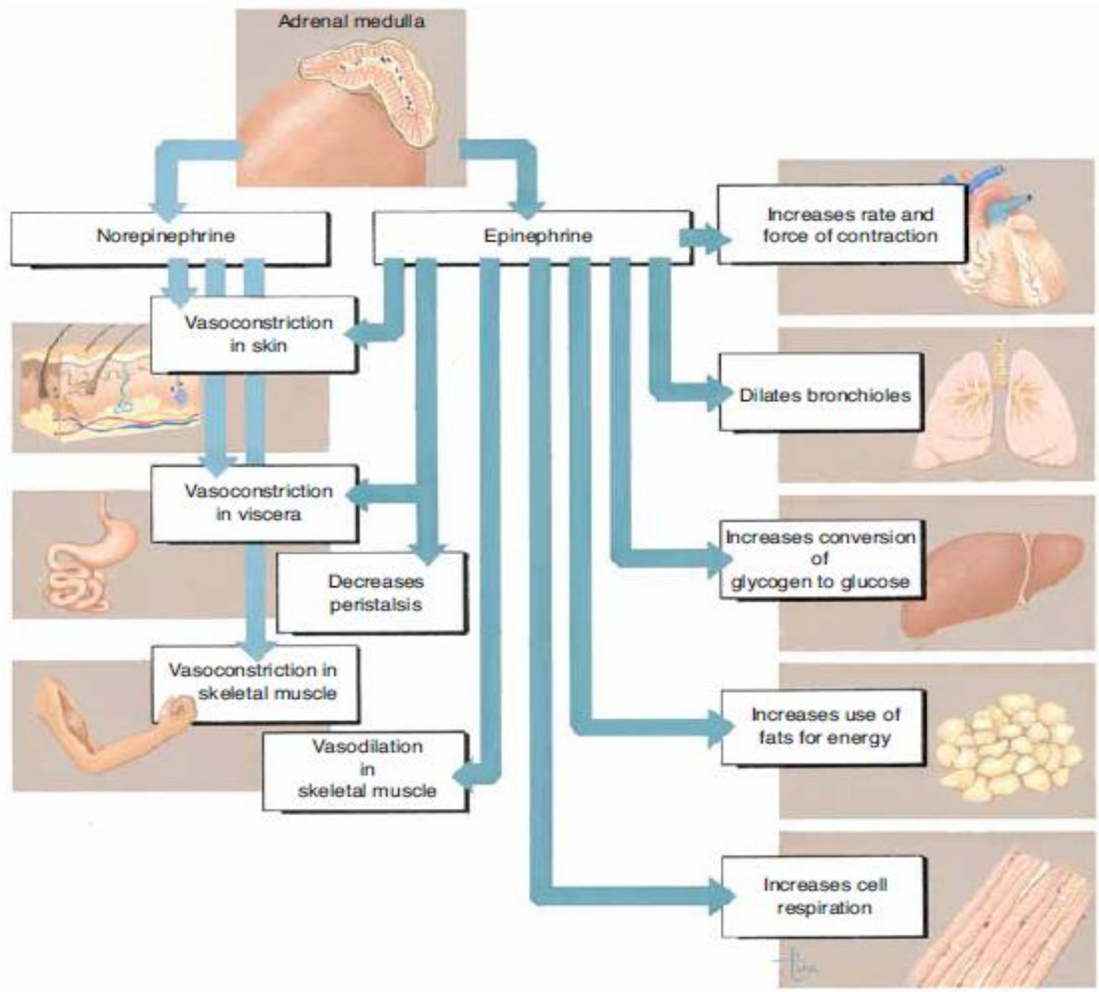


Figure: Functions of epinephrine and norepinephrine.

- ***Epinephrine and Norepinephrine***

Epinephrine (Adrenalin) and norepinephrine (noradrenalin) are both secreted in stress situations and help prepare the body for "fight or flight." **Norepinephrine** is secreted in small amounts, and its most significant function is to cause vasoconstriction in the skin, viscera, and skeletal muscles (that is, throughout the body), which raises blood pressure. **Epinephrine**, secreted in larger amounts, increases the heart rate and force of contraction and stimulates vasoconstriction in skin and viscera and vasodilation in skeletal muscles.

It also dilates the bronchioles, decreases peristalsis, stimulates the liver to change glycogen to glucose, increases the use of fats for energy, and increases the rate of cell respiration. Many of these effects do indeed seem to be an echo of sympathetic responses, don't they? Responding to stress is so important that the body acts redundantly (that is, exceeds what is necessary, or repeats itself) and has both a nervous mechanism and a hormonal mechanism. Epinephrine is actually more effective than sympathetic stimulation, however, because the hormone increases energy production and cardiac output to a greater extent.

7.11.2 ADRENAL CORTEX

The **adrenal cortex** secretes three types of steroid hormones: mineralocorticoids, glucocorticoids, and sex hormones. The sex hormones, "female" estrogens and "male" androgens (similar to testosterone), are produced in very small amounts, and their importance is not known with certainty. They may contribute to rapid body growth during early puberty. They may also be important in supplying estrogen to women after menopause and to men throughout life. The functions of the other adrenal cortical hormones are well known, however, and these are considered vital hormones.

- ***Aldosterone***

Aldosterone is the most abundant of the **mineralocorticoids**. The target organs of aldosterone are the kidneys, but there are important secondary effects as well. Aldosterone increases the reabsorption of sodium and the excretion of potassium by the kidney tubules. Sodium ions (Na^-) are returned to the blood, and potassium ions (K^-) are excreted in urine.

As Na^{-} ions are reabsorbed, hydrogen ions (H^{-}) may be excreted in exchange. This is one mechanism to prevent the accumulation of excess H^{-} ions, which would cause acidosis of body fluids. Also, as Na^{-} ions are reabsorbed, negative ions such as chloride (Cl^{-}) and bicarbonate (HCO3–) follow the Na^{-} ions back to the blood, and water follows by osmosis. This indirect effect of aldosterone, the reabsorption of water by the kidneys, is very important to maintain normal blood volume and blood pressure.

In summary, then, aldosterone maintains normal blood levels of sodium and potassium, and contributes to the maintenance of normal blood pH, blood volume, and blood pressure. A number of factors stimulate the secretion of aldosterone. These are a deficiency of sodium, loss of blood or dehydration that lowers blood pressure, or an elevated blood level of potassium. Low blood pressure or blood volume activates the **renin-angiotensin mechanism** of the kidneys.

- ***Cortisol***

Cortisol is among the group of hormones called **glucocorticoids**, and it is responsible for most of the actions of this group. Cortisol increases the use of fats and excess amino acids (gluconeogenesis) for energy and decreases the use of glucose. This is called the glucose sparing effect, and it is important because it conserves glucose for use by the brain. Cortisol is secreted in any type of physiological stress situation: disease, physical injury, hemorrhage, fear or anger, exercise, and hunger. Although most body cells easily use fatty acids and excess amino acids in cell respiration, brain cells do not, so they must have glucose. By enabling other cells to use the alternative energy sources, cortisol ensures that whatever glucose is present will be available to the brain. Cortisol also has an **anti-inflammatory effect**.

During inflammation, **histamine** from damaged tissues makes capillaries more permeable, and the lysosomes of damaged cells release their enzymes, which help break down damaged tissue but may also cause destruction of nearby healthy tissue. Cortisol blocks the effects of histamine and stabilizes lysosomal membranes, preventing excessive tissue destruction. Inflammation is a beneficial process up to a point, and is an essential first step if tissue repair is to take place. It may, however, become a vicious cycle of damage, inflammation, more damage, more inflammation, and so on—a positive feedback mechanism.

Normal cortisol secretion seems to be the brake, to limit the inflammation process to what is useful for tissue repair, and to prevent excessive tissue destruction. Too much cortisol, however, decreases the immune response, leaving the body susceptible to infection and significantly slowing the healing of damaged tissue.

The direct stimulus for cortisol secretion is **ACTH** from the anterior pituitary gland, which in turn is stimulated by corticotropin releasing hormone (CRH) from the hypothalamus. CRH is produced in the physiological stress situations mentioned earlier. Although we often think of epinephrine as a hormone important in stress, cortisol is also important.

7.12 OVARIES

The **ovaries** are located in the pelvic cavity, one on each side of the uterus. The hormones produced by the ovaries are the steroids estrogen and progesterone, and the protein inhibin.

7.12.1 ESTROGEN

Estrogen is secreted by the follicle cells of the ovary; secretion is stimulated by **FSH** from the anterior pituitary gland. Estrogen promotes the maturation of the ovum in the ovarian follicle and stimulates the growth of blood vessels in the endometrium (lining) of the uterus in preparation for a possible fertilized egg. The **secondary sex characteristics** in women also develop in response to estrogen. These include growth of the duct system of the mammary glands, growth of the uterus, and the deposition of fat subcutaneously in the hips and thighs.

The closure of the epiphyseal discs in long bones is brought about by estrogen, and growth in height stops. Estrogen is also believed to lower blood levels of cholesterol and triglycerides. For women before the age of menopause this is beneficial in that it decreases the risk of atherosclerosis and coronary artery disease. Research suggests that estrogen no longer be considered only a “female” hormone. Estrogen seems to have effects on many organs, including the brain, the heart, and blood vessels. In the brain, testosterone from the testes or the adrenal cortex can be converted to estrogen, which may be important for memory, especially for older people.

Estrogen seems to have non-reproductive functions in both men and women, although we cannot yet be as specific as we can be with the reproductive functions in women.

7.12.2 PROGESTERONE

When a mature ovarian follicle releases an ovum, the follicle becomes the **corpus luteum** and begins to secrete **progesterone** in addition to estrogen. This is stimulated by **LH** from the anterior pituitary gland. Progesterone promotes the storage of glycogen and the further growth of blood vessels in the endometrium, which thus becomes a potential placenta. The secretory cells of the mammary glands also develop under the influence of progesterone. Both progesterone and estrogen are secreted by the placenta during pregnancy.

7.12.3 INHIBIN

The corpus luteum secretes another hormone, called inhibin. **Inhibin** helps decrease the secretion of FSH by the anterior pituitary gland, and GnRH by the hypothalamus.

7.13 TESTES

The **testes** are located in the scrotum, a sac of skin between the upper thighs. Two hormones, testosterone and inhibin, are secreted by the testes.

A. TESTOSTERONE

Testosterone is a steroid hormone secreted by the interstitial cells of the testes; the stimulus for secretion is LH from the anterior pituitary gland. Testosterone promotes maturation of sperm in the seminiferous tubules of the testes; this process begins at puberty and continues throughout life. At puberty, testosterone stimulates development of the male **secondary sex characteristics**. These include growth of all the reproductive organs, growth of facial and body hair, growth of the larynx and deepening of the voice, and growth (protein synthesis) of the skeletal muscles. Testosterone also brings about closure of the epiphyses of the long bones.

B. INHIBIN

The hormone **inhibin** is secreted by the sustentacular cells of the testes; the stimulus for secretion is increased testosterone. The function of inhibin is to decrease the secretion of FSH by the anterior pituitary gland. The interaction of inhibin, testosterone, and the anterior pituitary hormones maintains spermatogenesis at a constant rate.

7.14 OTHER HORMONES

Melatonin is a hormone produced by the **pineal gland**, which is located at the back of the third ventricle of the brain. The secretion of melatonin is greatest during darkness and decreases when light enters the eye and the retina signals the hypothalamus. A recent discovery is that the retina also produces melatonin, which seems to indicate that the eyes and pineal gland work with the biological clock of the hypothalamus. In other mammals, melatonin helps regulate seasonal reproductive cycles. For people, melatonin definitely stimulates the onset of sleep and increases its duration. Other claims, such as that melatonin strengthens the immune system or prevents cellular damage and aging, are without evidence as yet. There are other organs that produce hormones that have only one or a few target organs. For example, the stomach and duodenum produce hormones that regulate aspects of digestion and appetite. Adipose tissue produces the appetite-suppressing hormone leptin. The thymus gland produces hormones necessary for the normal functioning of the immune system, and the kidneys produce a hormone that stimulates red blood cell production.

PROSTAGLANDINS

Prostaglandins (**PGs**) are made by virtually all cells from the phospholipids of their cell membranes. They differ from other hormones in that they do not circulate in the blood to target organs, but rather exert their effects locally, where they are produced. There are many types of prostaglandins, designated by the letters A through I, as in PGA, PGB, and so on. Prostaglandins have many functions, and some of them are listed here.

Prostaglandins are known to be involved in inflammation, pain mechanisms, blood clotting, vasoconstriction and vasodilation, contraction of the uterus, reproduction, secretion of digestive glands, and nutrient metabolism. Current research is directed at determining the normal functioning of prostaglandins in the hope that many of them may eventually be used clinically. One familiar example may illustrate the widespread activity of prostaglandins. For minor pain such as a headache, many people take aspirin. Aspirin inhibits the synthesis of prostaglandins involved in pain mechanisms and usually relieves the pain. Some people, however, such as those with rheumatoid arthritis, may take large amounts of aspirin to diminish pain and inflammation.

These people may bruise easily because blood clotting has been impaired. This too is an effect of aspirin, which blocks the synthesis of prostaglandins necessary for blood clotting.

GLAND	HORMONE	PRINCIPAL FUNCTIONS
Anterior pituitary	GH (growth hormone)	Promotes growth of all body tissues
	TSH (thyroid-stimulating hormone)	Stimulates thyroid gland to produce thyroid hormones
	ACTH (adrenocorticotropic hormone)	Stimulates adrenal cortex to produce cortical hormones; aids in protecting body in stress situations (injury, pain)
	PRL (prolactin)	Stimulates secretion of milk by mammary glands
	FSH (follicle-stimulating hormone)	Stimulates growth and hormone activity of ovarian follicles; stimulates growth of testes; promotes development of sperm cells
	LH (luteinizing hormone); ICSH (interstitial cell-stimulating hormone) in males	Causes development of corpus luteum at site of ruptured ovarian follicle in female; stimulates secretion of testosterone in male
Posterior pituitary	ADH (antidiuretic hormone)	Promotes reabsorption of water in kidney tubules; at high concentration stimulates constriction of blood vessels
	Oxytocin	Causes contraction of uterine muscle; causes ejection of milk from mammary glands
Thyroid	Thyroxine (T_4) and triiodothyronine(T_3)	Increases metabolic rate, influencing both physical and mental activities; required for normal growth
	Calcitonin	Decreases calcium level in blood
Parathyroids	Parathyroid hormone (PTH)	Regulates exchange of calcium between blood and bones; increases calcium level in blood
Adrenal medulla	Epinephrine and norephinephrine	Increases blood pressure and heart rate; activates cells influenced by sympathetic nervous system plus many not affected by sympathetic nerves
Adrenal cortex	Cortisol (95% of glucocorticoids)	Aids in metabolism of carbohydrates, proteins, and fats; active during stress
	Aldosterone (95% of mineralocorticoids)	Aids in regulating electrolytes and water balance
	Sex hormones	May influence secondary sexual characteristics
Pancreatic islets	Insulin	Needed for transport of glucose into cells; required for cellular metabolism of foods, especially glucose; decreases blood sugar levels
	Glucagon	Stimulates liver to release glucose, thereby increasing blood sugar levels
Testes	Testosterone	Stimulates growth and development of sexual organs (testes, penis) plus development of secondary sexual characteristics, such as hair growth on body and face and deepening of voice; stimulates maturation of sperm cells
Ovaries	Estrogens (*e.g.*, estradiol)	Stimulates growth of primary sexual organs (uterus, tubes) and development of secondary sexual organs, such as breasts, plus changes in pelvis to ovoid, broader shape
	Progesterone	Stimulates development of secretory parts of mammary glands; prepares uterine lining for implantation of fertilized ovum; aids in maintaining pregnancy
Thymus	Thymosin	Promotes growth of T cells active in immunity
Pineal	Melatonin	Regulates mood, sexual development, and daily cycles in response to the amount of light in the environment

Table: Summary of Endocrine Glands and Their Hormones

Disorders Associated with Endocrine Dysfunction

Hormone	Effects of hypersecretion	Effects of hyposecretion
Growth hormone	Gigantism (children), acromegaly (adults)	Dwarfism (children)
Antidiuretic hormone	Syndrome of inappropriate antidiuretic hormone (SIADH)	Diabetes insipidus
Aldosterone	Aldosteronism	Addison disease
Cortisol	Cushing syndrome	Addison disease
Thyroid hormone	Graves disease, thyrotoxicosis	Infantile hypothyroidism (cretinism) in children; myxedema in adults
Insulin	Hypoglycemia	Diabetes mellitus
Parathyroid hormone	Bone degeneration	Tetany (muscle spasms)

7.15 MECHANISMS OF HORMONE ACTION

Exactly how hormones exert their effects on their target organs involves a number of complex processes, which will be presented simply here. A hormone must first bond to a **receptor** for it on or in the target cell. Cells respond to certain hormones and not to others because of the presence of specific receptors, which are proteins. These receptor proteins may be part of the cell membrane or within the cytoplasm or nucleus of the target cells. A hormone will affect only those cells that have its specific receptors. Liver cells, for example, have cell membrane receptors for insulin, glucagon, growth hormone, and epinephrine; bone cells have receptors for growth hormone, PTH, and calcitonin. Cells of the ovaries and testes do not have receptors for PTH and calcitonin, but do have receptors for FSH and LH, which bone cells and liver cells do not have. Once a hormone has bonded to a receptor on or in its target cell, other reactions will take place.

A. THE TWO-MESSENGER MECHANISM PROTEIN HORMONES

The two-messenger mechanism of hormone action involves "messengers" that make something happen, that is, stimulate specific reactions. **Protein hormones** usually bond to receptors of the cell membrane, and the hormone is called the first messenger. The hormone–receptor bonding activates the enzyme adenyl cyclase on the inner surface of the cell membrane. Adenyl cyclase synthesizes a substance called cyclic adenosine monophosphate (**cyclic AMP** or **cAMP**) from

ATP, and cyclic AMP is the second messenger. Cyclic AMP activates specific enzymes within the cell, which bring about the cell's characteristic response to the hormone.

These responses include a change in the permeability of the cell membrane to a specific substance, an increase in protein synthesis, activation of other enzymes, or the secretion of a cellular product. In summary, a cell's response to a hormone is determined by the enzymes within the cell, that is, the reactions of which the cell is capable. These reactions are brought about by the first messenger, the hormone, which stimulates the formation of the second messenger, cyclic AMP. Cyclic AMP then activates the cell's enzymes to elicit a response to the hormone.

B. ACTION OF STEROID HORMONES

Steroid hormones are soluble in the lipids of the cell membrane and diffuse easily into a target cell. Once inside the cell, the steroid hormone combines with a protein receptor in the cytoplasm, and this steroidprotein complex enters the nucleus of the cell. Within the nucleus, the steroid-protein complex activates specific genes, which begin the process of **protein synthesis**.

AGING AND THE ENDOCRINE SYSTEM

Most of the endocrine glands decrease their secretions with age, but normal aging usually does not lead to serious hormone deficiencies. There are decreases in adrenol cortical hormones, for example, but the levels are usually sufficient to maintain homeostasis of water, electrolytes, and nutrients. The decreased secretion of growth hormone leads to a decrease in muscle mass and an increase in fat storage. A lower basal metabolic rate is common in elderly people as the thyroid slows its secretion of thyroxine. Unless specific pathologies develop, however, the endocrine system usually continues to function adequately in old age.

- **Applications to the nursing care**

1. DISORDERS OF GROWTH HORMONE

A deficiency or excess of growth hormone (GH) during childhood will have marked effects on the growth of a child. Hyposecretion of GH results in **pituitary dwarfism**, in which the person may attain a final height of only 3 to 4 feet but will have normal body proportions.

GH can now be produced using genetic engineering and may be used to stimulate growth in children with this disorder. GH will not increase growth of children with the genetic potential for short stature. Reports that GH will reverse the effects of aging are simply not true.

Hypersecretion of GH results in **giantism** (or gigantism), in which the long bones grow excessively and the person may attain a height of 8 feet. Most very tall people, such as basketball players, do *not* have this condition; they are tall as a result of their genetic makeup and good nutrition. In an adult, hypersecretion of GH is caused by a pituitary tumor, and results in **acromegaly**. The long bones cannot grow because the epiphyseal discs are closed, but the growth of other bones is stimulated. The jaw and other facial bones become disproportionately large, as do the bones of the hands and feet.

The skin becomes thicker, and the tongue also grows and may protrude. Other consequences include compression of nerves by abnormally growing bones and growth of the articular cartilages, which then erode and bring on arthritis. Treatment of acromegaly requires surgical removal of the tumor or its destruction by radiation.

2. DISORDERS OF THYROXINE

Iodine is an essential component of thyroxine (and T3), and a dietary deficiency of iodine causes **goiter**. In an attempt to produce more thyroxine, the thyroid cells become enlarged, and hence the thyroid gland enlarges and becomes visible on the front of the neck. The use of iodized salt has made goiter a rare condition in many parts of the world. Hyposecretion of thyroxine in a newborn has devastating effects on the growth of the child. Without thyroxine, physical growth is diminished, as is mental development.

This condition is called **cretinism**, characterized by severe physical and mental retardation. If the thyroxine deficiency is detected shortly after birth, the child may be treated with thyroid hormones to promote normal development. Hyposecretion of thyroxine in an adult is called **myxedema**. Without thyroxine, the metabolic rate (energy production) decreases, resulting in lethargy, muscular weakness, slow heart rate, a feeling of cold, weight gain, and a characteristic puffiness of the face. The administration of thyroid hormones will return the metabolic rate to normal. **Graves' disease** is an autoimmune disorder that causes hypersecretion of thyroxine. The autoantibodies seem to bind to TSH receptors on the thyroid cells and stimulate secretion of excess thyroxine.

The symptoms are those that would be expected when the metabolic rate is abnormally elevated: weight loss accompanied by increased appetite, increased sweating, fast heart rate, feeling of warmth, and fatigue. Also present may be goiter and exophthalmos, which is protrusion of the eyes. Treatment is aimed at decreasing the secretion of thyroxine by the thyroid, and medications or radioactive iodine may be used to accomplish this.

3. DISORDERS OF THE ADRENAL CORTEX

Addison's disease is the result of hyposecretion of the adrenol cortical hormones. Most cases are idiopathic, that is, of unknown cause; atrophy of the adrenal cortex decreases both cortisol and aldosterone secretion. Deficiency of cortisol is characterized by hypoglycemia, decreased gluconeogenesis, and depletion of glycogen in the liver. Consequences are muscle weakness and the inability to resist physiological stress.

Aldosterone deficiency leads to retention of potassium and excretion of sodium and water in urine. The result is severe dehydration, low blood volume, and low blood pressure.

Without treatment, circulatory shock and death will follow. Treatment involves administration of hydrocortisone; in high doses this will also compensate for the aldosterone deficiency.

Cushing's syndrome is the result of hypersecretion of the adrenal cortex, primarily cortisol. The cause may be a pituitary tumor that increases ACTH secretion or a tumor of the adrenal cortex itself. Excessive cortisol promotes fat deposition in the trunk of the body, while the extremities remain thin. The skin becomes thin and fragile, and healing after injury is slow. The bones also become fragile because osteoporosis is accelerated.

Also characteristic of this syndrome is the rounded appearance of the face. Treatment is aimed at removal of the cause of the hypersecretion, whether it is a pituitary or adrenal tumor. Cushing's syndrome may also be seen in people who receive corticosteroids for medical reasons. Transplant recipients or people with rheumatoid arthritis or severe asthma who must take corticosteroids may exhibit any of the above symptoms. In such cases, the disadvantages of this medication must be weighed against the benefits provided.

4. DIABETES MELLITUS

There are two types of **diabetes mellitus**: Type 1 (insulin-dependent diabetes) and its onset is usually in childhood (juvenile onset). Type 2 (non–insulin-dependent diabetes), and its onset is usually later in life (maturity onset).

Type 1 diabetes is characterized by destruction of the beta cells of the islets of Langerhans and a complete lack of insulin; onset is usually abrupt. Destruction of the beta cells is an autoimmune response, perhaps triggered by a virus. There may be a genetic predisposition, because certain HLA *(Human Leukocyte Antigens)* types are found more frequently in type 1 diabetics than in other children. Insulin by injection (inhaled insulin is undergoing clinical trials) is essential to control type 1 diabetes. Research is continuing on the use of immunosuppressant medications to try to preserve some beta cells (if diagnosis is early), and also on the transplantation of stem cells to replace lost beta cells.

In **type 2** diabetes, insulin is produced but cannot exert its effects on cells because of a loss of insulin receptors on cell membranes. Onset of type 2 diabetes is usually gradual, and risk factors include a family history of diabetes and being overweight. Control may not require insulin, but rather medications that enable insulin to react with the remaining membrane receptors.

For those with a family history of diabetes, a low-fat diet and regular exercise reduce the risk of developing the disease. The commitment to exercise must be lifelong but is well worth the effort, because diabetes is very destructive.

Without insulin (or its effects) blood glucose level remains high, and glucose is lost in urine. Since more water is lost as well, symptoms include greater urinary output (*polyuria*) and thirst (*polydipsia*). The long-term effects of hyperglycemia produce distinctive vascular changes. The capillary walls thicken, and exchange of gases and nutrients diminishes. The most damaging effects are seen in the skin (especially of the feet), the retina (diabetic *retinopathy*), and the kidneys. Poorly controlled diabetes may lead to dry gangrene, blindness, and severe kidney damage. Atherosclerosis is common, because faulty triglyceride metabolism is linked to faulty glucose metabolism. Neuropathy (damage to nerves) leads to impaired cutaneous sensation and difficulty with fine movements, such as buttoning a shirt.

It is now possible for diabetics to prevent much of this tissue damage by precise monitoring of the blood glucose level and more frequent administration of insulin. Insulin pumps are able to more closely mimic the natural secretion of insulin.

A very serious potential problem for the type 1 diabetic is **ketoacidosis**. When glucose cannot be used for energy, the body turns to fats and proteins, which are converted by the liver to ketones. Ketones are organic acids (acetone, acetoacetic acid) that can be used in cell respiration, but cells are not able to utilize them rapidly so ketones accumulate in the blood. Ketones are acids, and lower the pH of the blood as they accumulate. The kidneys excrete excess ketones, but in doing so excrete more water as well, which leads to dehydration and worsens the acidosis. Without administration of insulin to permit the use of glucose, and IV fluids to restore blood volume to normal, ketoacidosis will progress to coma and death.