CHAPTER 13a

The Endocrine System: Being Hormonal

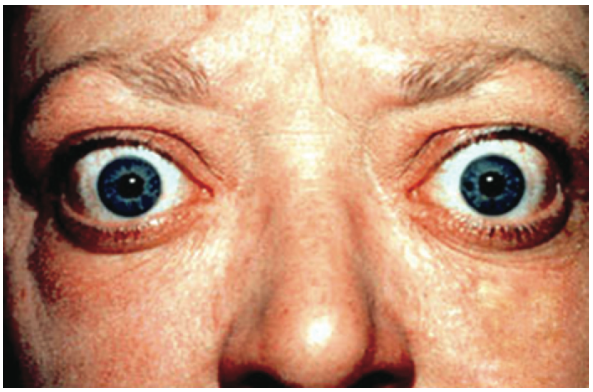
LEARNING OBJECTIVES

By the end of this class you should be able to:

- List the different types of hormones and explain their roles in maintaining homeostasis
- Explain how hormones work
- Explain how hormone production is regulated
- Describe the role of different glands in the endocrine system
- Explain how the different glands work together to maintain homeostasis
- Explain the regulation of blood glucose and diabetes
- Provide a list of endocrine disorders

Introduction

You may never have thought of it this way, but when you send a text message to two friends to meet you at the dining hall at six, you're sending digital signals that (you hope) will affect their behavior—even though they are some distance away. Similarly, certain cells send chemical signals to other cells in the body that influence their behavior. This long-distance intercellular communication, coordination, and control is critical for homeostasis, and it is the fundamental function of the endocrine system. The endocrine system controls body processes through the production, secretion, and regulation of hormones, which serve as chemical "messengers" functioning in cellular and organ activity and, ultimately, maintaining the body's homeostasis. The endocrine system coordinates with the nervous system to control the functions of the other organ systems. The endocrine system plays a role in growth, metabolism, and sexual development. In humans, common endocrine system diseases include thyroid disease and diabetes mellitus.



Hyperthyroidism. Exophtalmos, protruding eyes, can be a symptom of an overactive thyroid gland, a diseases referred to as Grave's disease or hyperthyroidism (credit: CNX OpenStax CC BY 4.0).

How Hormones Control Us

The endocrine system produces hormones that function to control and regulate many different body processes. Hormones are released into body fluids, usually blood, which carries them to their target cells where they elicit a response. The cells that secrete hormones are often located in specific organs, called **endocrine glands**, and the cells, tissues, and organs that secrete hormones make up the endocrine system. Examples of endocrine organs include the pancreas, which produces the hormones insulin and glucagon to regulate blood-glucose levels, the adrenal glands, which produce hormones such as epinephrine and norepinephrine that regulate responses to stress, and the thyroid gland, which produces thyroid hormones that regulate metabolic rates. The endocrine glands differ from the **exocrine glands**. Exocrine glands secrete chemicals through ducts that lead outside the gland (not to the blood). For example, sweat produced by sweat glands is released into ducts that carry sweat to the surface of the skin. The pancreas has both endocrine and exocrine functions because besides releasing hormones into the blood. It also produces digestive juices, which are carried by ducts into the small intestine.

How Hormones Work

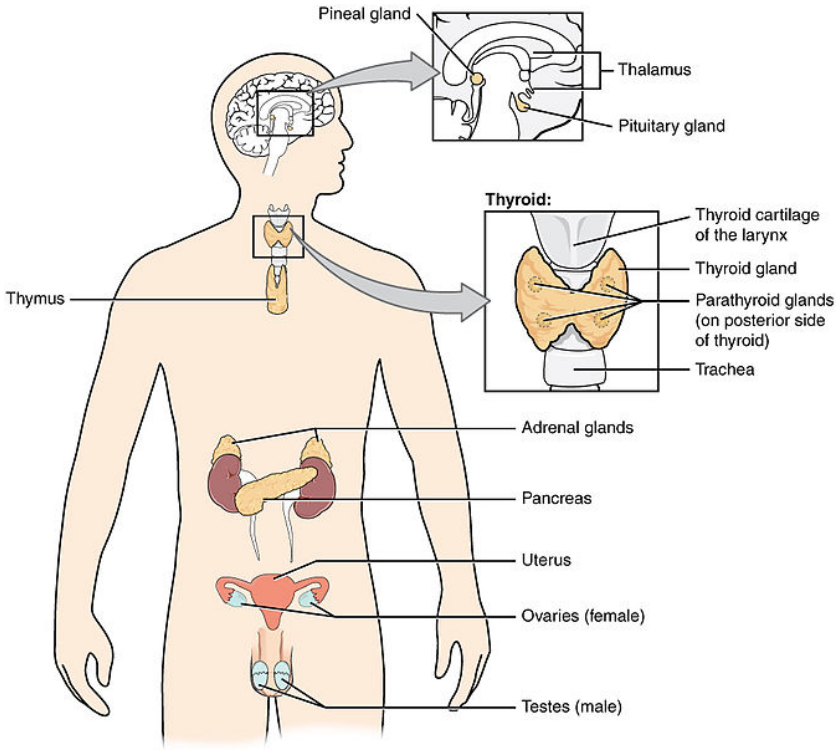
Hormones cause changes in target cells by binding to specific cell-surface or **intracellular hormone receptors**, molecules embedded in the cell membrane or floating in the cytoplasm with a binding site that matches a binding site on the hormone molecule. In this way, even though hormones circulate throughout the body and come into contact with many different cell types, they only affect cells that possess the necessary receptors. Receptors for a specific hormone may be found on or in many different cells or may be limited to a small number of specialized cells. For example, thyroid hormones act on many different tissue types, stimulating metabolic activity throughout the body. Cells can have many receptors for the same hormone but often also possess receptors for different types of hormones. The number of receptors that respond to a hormone determines the cell's sensitivity to that hormone, and the resulting cellular response. Additionally, the number of receptors available to respond to a hormone can change over time, resulting in increased or decreased cell sensitivity. In **up-regulation**, the number of receptors increases in response to rising hormone levels, making the cell more sensitive to the hormone and allowing for more cellular activity. An example of upregulation in pregnancy is hormones that cause cells in the uterus to become more sensitive to oxytocin which causes contractions during childbirth labor. When the number of receptors decreases in response to rising hormone levels, called **down-regulation**, cellular activity is reduced. Thus, the cells are less reactive to the hormone. This is observed, for example, in overweight people who have constant high levels of insulin. This cause receptor sites on the liver cells to downregulate and not respond as much to insulin a phenomenon called insulin resistance.

Regulation of Hormone Secretion

To prevent abnormal hormone levels and a potential disease state, hormone levels must be tightly controlled. The body maintains this control by balancing hormone production and degradation. Hormone production and release are primarily controlled by negative feedback, as described in the discussion on homeostasis. In this way, the concentration of hormones in blood is maintained within a narrow range. For example, the anterior pituitary signals the thyroid to release thyroid hormones. Increasing levels of these hormones in the blood then give feedback to the hypothalamus and anterior pituitary to inhibit further signaling to the thyroid gland.

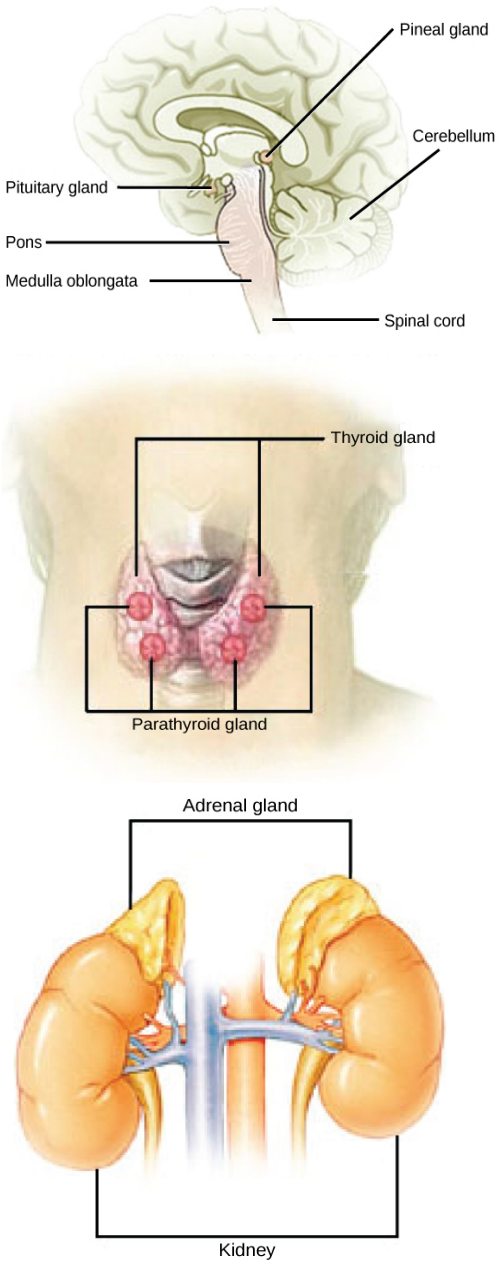
Endocrine Glands

The endocrine glands secrete hormones into the surrounding interstitial fluid; those hormones then diffuse into blood and are carried to various organs and tissues within the body. The endocrine glands include the pituitary, thyroid, parathyroid, adrenal glands, gonads, pineal gland, and pancreas.



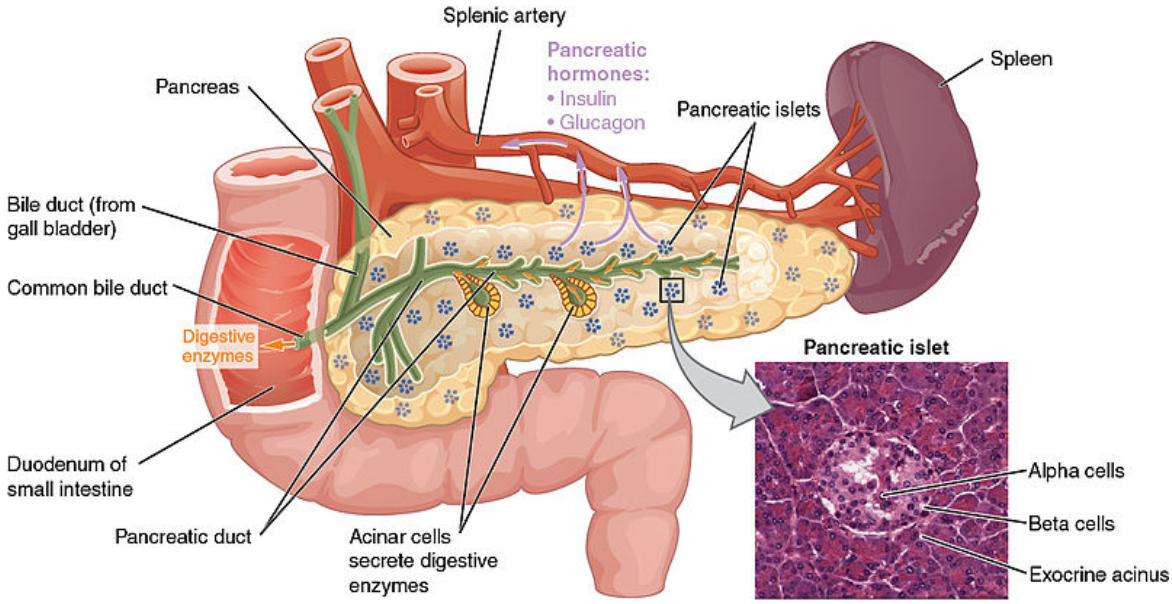
Endocrine System. Endocrine glands and cells are located throughout the body and play an important role in homeostasis (credit: OpenStax College CC BY 4.0).

- The **pituitary gland**, sometimes called the hypophysis, is located at the base of the brain. It is attached to the hypothalamus. The posterior lobe stores and releases oxytocin and antidiuretic hormone produced by the hypothalamus. The anterior lobe responds to hormones produced by the hypothalamus by producing its own hormones, most of which regulate other hormone-producing glands.The anterior pituitary produces six hormones: growth hormone, prolactin, thyroid-stimulating hormone, adrenocorticotropic hormone, follicle-stimulating hormone, and luteinizing hormone. Growth hormone stimulates cellular activities like protein synthesis that promote growth. Prolactin stimulates the production of milk by the mammary glands. The other hormones produced by the anterior pituitary regulate the production of hormones by other endocrine tissues. The posterior pituitary is significantly different in structure from the anterior pituitary. It is a part of the brain, extending down from the hypothalamus, and contains mostly nerve fibers that extend from the hypothalamus to the posterior pituitary.
- The **thyroid gland** is located in the neck, just below the larynx and in front of the trachea. It is a butterfly-shaped gland with two lobes that are connected. The thyroid follicle cells synthesize the hormone thyroxine, which is also known as T_4 because it contains four atoms of iodine, and triiodothyronine, also known as T_3 because it contains three atoms of iodine. T_3 and T_4 are released by the thyroid in response to thyroid-stimulating hormone produced by the anterior pituitary, and both T_3 and T_4 have the effect of stimulating metabolic activity in the body and increasing energy use. A third hormone, calcitonin, is also produced by the thyroid. Calcitonin is released in response to rising calcium ion concentrations in the blood and has the effect of reducing those levels.
- Most people have four **parathyroid glands**; however, the number can vary from two to six. These glands are located on the posterior surface of the thyroid gland. The parathyroid glands produce parathyroid hormone. Parathyroid hormone increases blood calcium concentrations when calcium ion levels fall below normal.
- The **adrenal glands** are located on top of each kidney. The adrenal glands consist of an outer adrenal cortex and an inner adrenal medulla. These regions secrete different hormones. The adrenal cortex produces mineralocorticoids, glucocorticoids, and androgens. The main mineralocorticoid is aldosterone, which regulates the concentration of ions in urine, sweat, and saliva. Aldosterone release from the adrenal cortex is stimulated by a decrease in blood concentrations of sodium ions, blood volume, or blood pressure, or by an increase in blood potassium levels. The glucocorticoids maintain proper blood-glucose levels between meals. They also control a response to stress by increasing glucose synthesis from fats and proteins and interact with epinephrine to cause vasoconstriction. Androgens are sex hormones that are produced in small amounts by the adrenal cortex. They do not normally affect sexual characteristics and may supplement sex hormones released from the gonads. The adrenal medulla contains two types of secretory cells: one that produces epinephrine (adrenaline) and another that produces norepinephrine (noradrenaline). Epinephrine and norepinephrine cause immediate, short-term changes in response to stressors, inducing the so-called fight-or-flight response. The responses include increased heart rate, breathing rate, cardiac muscle contractions, and blood-glucose levels. They also accelerate the breakdown of glucose in skeletal muscles and stored fats in adipose tissue, and redirect blood flow toward skeletal muscles and away from skin and viscera. The release of epinephrine and norepinephrine is stimulated by neural impulses from the sympathetic nervous system that originate from the hypothalamus.



Endocrine Glands. Top: The pituitary gland sits at the base of the brain, just above the brain stem. Middle: The parathyroid glands are located on the posterior of the thyroid gland; Bottom: the adrenal glands are on top of the kidneys (credit: OpenStax College CC BY 4.0).

- The **pancreas** is an elongate organ located between the stomach and the proximal portion of the small intestine. It contains both exocrine cells that excrete digestive enzymes and endocrine cells that release hormones. It is sometimes referred to as a heterocrine gland because it has both endocrine and exocrine functions. The endocrine cells of the pancreas form clusters called pancreatic islets or the islets of Langerhans. The pancreatic islets contain two primary cell types: alpha cells, which produce the hormone **glucagon**, and beta cells, which produce the hormone **insulin**. These hormones regulate blood glucose levels. As blood glucose levels decline, alpha cells release glucagon to raise the blood glucose levels by increasing rates of glycogen breakdown and glucose release by the liver. When blood glucose levels rise, such as after a meal, beta cells release insulin to lower blood glucose levels by increasing the rate of glucose uptake in most body cells, and by increasing glycogen synthesis in skeletal muscles and the liver. Together, glucagon and insulin regulate blood glucose levels.



The Pancreas. The pancreatic exocrine function involves the acinar cells secreting digestive enzymes that are transported into the small intestine by the pancreatic duct. Its endocrine function involves the secretion of insulin (produced by beta cells) and glucagon (produced by alpha cells) within the pancreatic islets. These two hormones regulate the rate of glucose metabolism in the body. The micrograph reveals pancreatic islets. LM × 760 (credit: OpenStax College CC BY 4.0).

- The **gonads**—the male testes and female ovaries—produce steroid hormones. The testes produce androgens, testosterone being the most prominent, which allow for the development of secondary sex characteristics and the production of sperm cells. The ovaries produce estrogen and progesterone, which cause secondary sex characteristics, regulate production of eggs, control pregnancy, and prepare the body for childbirth.

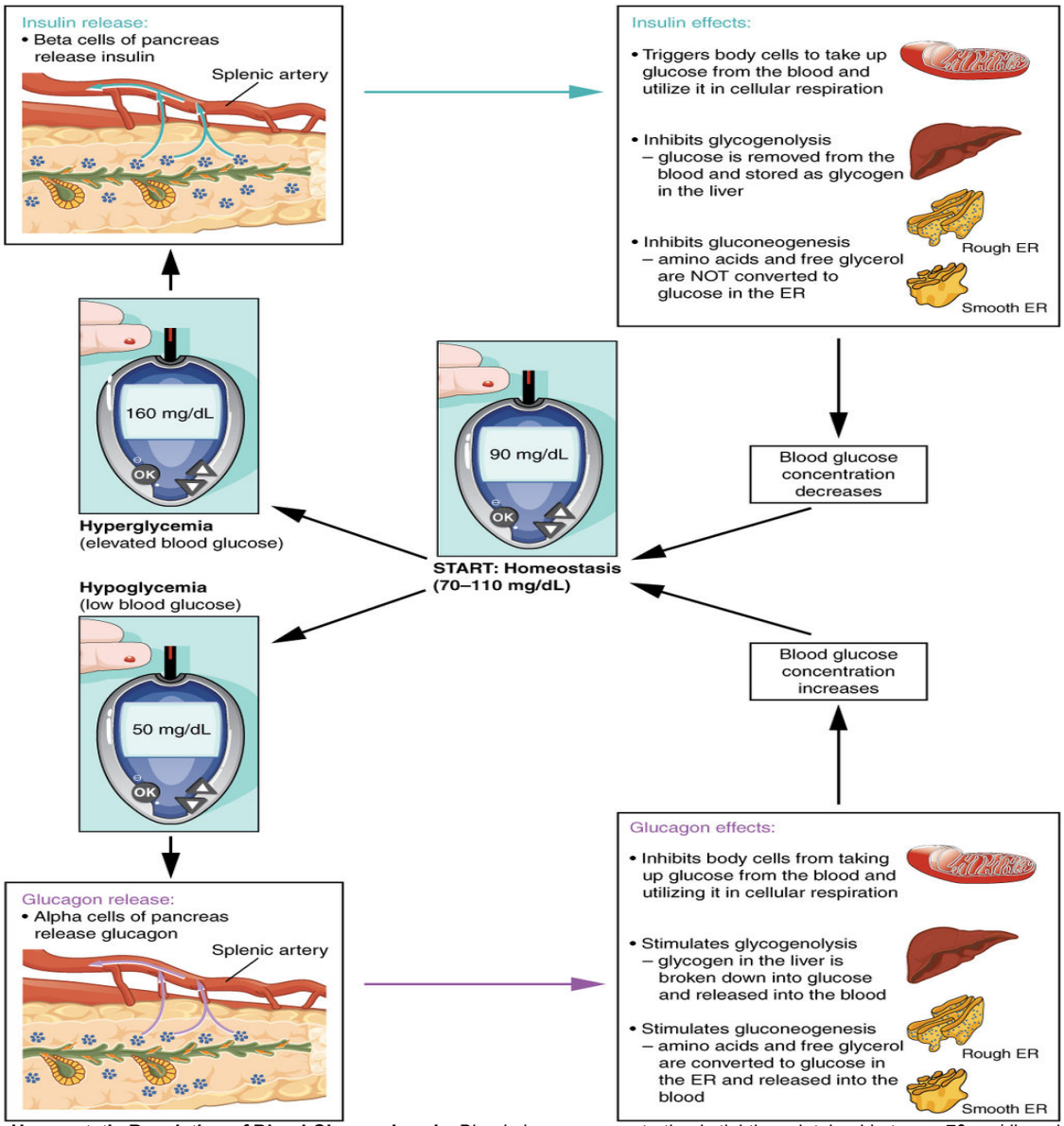
There are several organs whose primary functions are non-endocrine but that also possess endocrine functions. These include the heart, kidneys, intestines, thymus, and adipose tissue.

- The heart has endocrine cells in the walls of the atria that release a hormone in response to increased blood volume. It causes a reduction in blood volume and blood pressure, and reduces the concentration of Na^+ in the blood.
- The gastrointestinal tract produces several hormones that aid in digestion. The endocrine cells are located in the mucosa of the GI tract throughout the stomach and small intestine. They trigger the release of gastric juices, which help to break down and digest food in the GI tract.
- The kidneys also possess endocrine function. Two of these hormones regulate ion concentrations and blood volume or pressure. Erythropoietin (EPO) is released by kidneys in response to low oxygen levels. EPO triggers the formation of red blood cells in the bone marrow. EPO has been used by athletes to improve performance. But EPO doping has its risks, since it thickens the blood and increases strain on the heart; it also increases the risk of blood clots and therefore heart attacks and stroke.
- The thymus is found behind the sternum. The thymus produces hormones referred to as thymosins, which contribute to the development of the immune response in infants. Adipose tissue, or fat tissue, produces the hormone leptin in response to food intake. Leptin produces a feeling of satiety after eating, reducing the urge for further eating.

Diabetes and Regulation of Blood Glucose Levels by Insulin and Glucagon

Regulation of Blood Glucose

Cells of the body require nutrients in order to function, and these nutrients are obtained through feeding. In order to manage nutrient intake, storing excess intake and utilizing reserves when necessary, the body uses hormones to moderate energy stores. Insulin is produced by the beta cells of the pancreas, which are stimulated to release insulin as blood glucose levels rise (for example, after a meal is consumed). Insulin lowers blood glucose levels by enhancing the rate of glucose uptake and utilization by target cells, which use glucose for ATP production. It also stimulates the liver to convert glucose to glycogen, which is then stored by cells for later use. Insulin also increases glucose transport into certain cells, such as muscle cells and the liver. This results from an insulin-mediated increase in the number of glucose transporter proteins in cell membranes, which remove glucose from circulation by facilitated diffusion. As insulin binds to its target cell via insulin receptors and signal transduction, it triggers the cell to incorporate glucose transport proteins into its membrane. This allows glucose to enter the cell, where it can be used as an energy source. However, this does not occur in all cells: some cells, including those in the kidneys and brain, can access glucose without the use of insulin. Insulin also stimulates the conversion of glucose to fat in adipocytes and the synthesis of proteins. These actions mediated by insulin cause blood glucose concentrations to fall, called a hypoglycemic "low sugar" effect, which inhibits further insulin release from beta cells through a negative feedback loop.



Homeostatic Regulation of Blood Glucose Levels. Blood glucose concentration is tightly maintained between 70 mg/dL and 110 mg/dL. If blood glucose concentration rises above this range, insulin is released, which stimulates body cells to remove glucose from the blood. If blood glucose concentration drops below this range, glucagon is released, which stimulates body cells to release glucose into the blood (credit: OpenStax College CC BY 4.0).

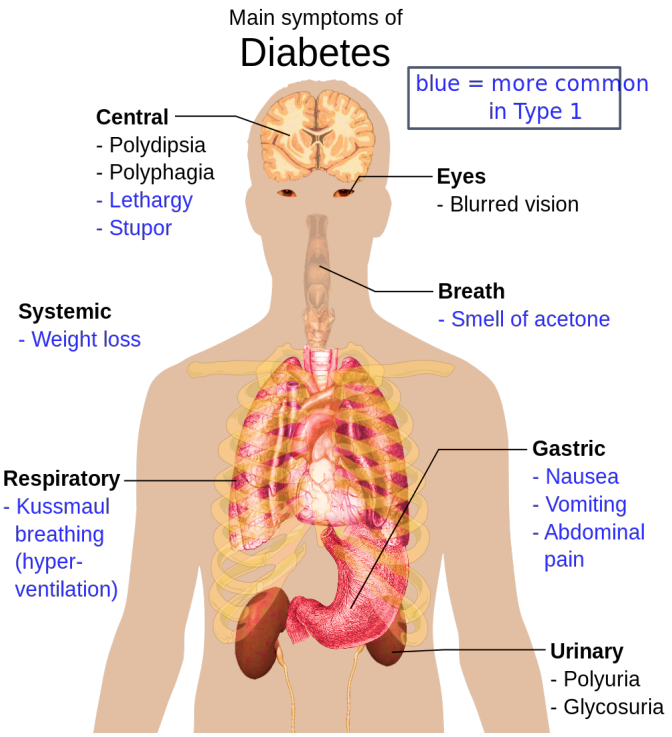
Diabetes Mellitus

Dysfunction of insulin production and secretion, as well as the target cells' responsiveness to insulin, can lead to a condition called diabetes mellitus. As of 2015, 30.3 million people in the United States, or 9.4 percent of the population, had diabetes. More than 1 in 4 of them didn't know they had the disease. Diabetes affects 1 in 4 people over the age of 65.

There are two main forms of diabetes mellitus:

- **Type 1 diabetes** is an autoimmune disease affecting the beta cells of the pancreas. Certain genes are recognized to increase susceptibility. The beta cells of people with type 1 diabetes do not produce insulin; thus, synthetic insulin must be administered by injection or infusion. This form of diabetes accounts for less than five percent of all diabetes cases.

-**Type 2 diabetes** accounts for approximately 95 percent of all cases. It is acquired, and lifestyle factors such as poor diet, inactivity, and the presence of pre-diabetes greatly increase a person's risk. About 80 to 90 percent of people with type 2 diabetes are overweight or obese. In type 2 diabetes, cells become resistant to the effects of insulin. In response, the pancreas increases its insulin secretion, but over time, the beta cells become exhausted. In many cases, type 2 diabetes can be reversed by moderate weight loss, regular physical activity, and consumption of a healthy diet; however, if blood glucose levels cannot be controlled, the diabetic will eventually require insulin.



Overview of the most significant possible symptoms of diabetes (credit: Mikael Haggstrom, Public Domain).

Scientists believe **gestational diabetes**, a type of diabetes that develops during pregnancy, is caused by the hormonal changes of pregnancy along with genetic and lifestyle factors. As with type 2 diabetes, extra weight is linked to gestational diabetes. Women who are overweight or obese may already have insulin resistance when they become pregnant. Gaining too much weight during pregnancy may also be a factor.

Two of the early manifestations of diabetes are excessive urination and excessive thirst. They demonstrate how the out-of-control levels of glucose in the blood affect kidney function. The kidneys are responsible for filtering glucose from the blood. Excessive blood glucose draws water into the urine, and as a result the person eliminates an abnormally large quantity of sweet urine. The use of body water to dilute the urine leaves the body dehydrated, and so the person is unusually and continually thirsty. The person may also experience persistent hunger because the body cells are unable to access the glucose in the bloodstream. Over time, persistently high levels of glucose in the blood injure tissues throughout the body, especially those of the blood vessels and nerves. Inflammation and injury of the lining of arteries lead to atherosclerosis and an increased risk of heart attack and stroke. Damage to the microscopic blood vessels of the kidney impairs kidney function and can lead to kidney failure. Damage to blood vessels that serve the eyes can lead to blindness. Blood vessel damage also reduces circulation to the limbs, whereas nerve damage leads to a loss of sensation, called neuropathy, particularly in the hands and feet. Together, these changes increase the risk of injury, infection, and tissue death (necrosis), contributing to a high rate of toe, foot, and lower leg amputations in people with diabetes. Uncontrolled diabetes can also lead to a dangerous form of metabolic acidosis called ketoacidosis. Deprived of glucose, cells increasingly rely on fat stores for fuel. However, in a glucose-deficient state, the liver is forced to use an alternative lipid metabolism pathway that results in the increased production of ketone bodies (or ketones), which are acidic. The build-up of ketones in the blood causes ketoacidosis, which—if left untreated—may lead to a life-threatening "diabetic coma." Together, these complications make diabetes the seventh leading cause of death in the United States.

Diabetes is diagnosed when lab tests reveal that blood glucose levels are higher than normal, a condition called hyperglycemia. The treatment of diabetes depends on the type, the severity of the condition, and the ability of the patient to make lifestyle changes. As noted earlier, moderate weight loss, regular physical activity, and consumption of a healthful diet can reduce blood glucose levels. Some patients with type 2 diabetes may be unable to control their disease with these lifestyle changes, and will require medication. Historically, the first-line treatment of type 2 diabetes was insulin. Research advances have resulted in alternative options, including medications that enhance pancreatic function.

Activity 1. Endocrine Glands and Hormones

1.1 - Complete the table below with the information in the text above. Add rows as you deem fit.

Endocrine Gland	Associated Hormone(s)	Effect
Pituitary gland		
Thyroid		
Parathyroid glands		
Adrenal gland		
Pancreas		

1.2 - Reading the text above, identify organs that have other functions than endocrine ones, and were discussed in previous chapters. List their non-endocrine functions as well as their endocrine ones. Present the information in a table.

Activity 2. Endocrine System Vocabulary (Wordsearch)

Complete the table below with the information in the text above. Add rows as you deem fit.

S	Q	N	X	O	W	N	J	O	C	F	M	G	C	M	E
R	D	P	I	P	X	Q	I	O	Z	E	T	I	A	S	N
P	I	I	G	L	A	Y	R	L	L	Z	J	W	L	I	I
K	A	G	O	O	A	T	T	A	U	F	X	S	C	D	R
I	B	R	U	R	I	N	T	O	G	S	U	N	I	I	C
D	E	C	A	S	E	O	E	B	C	M	N	B	T	O	O
N	T	J	O	T	N	T	N	R	A	I	D	I	O	R	D
E	E	L	P	I	H	E	S	L	D	N	N	C	N	Y	N
Y	S	J	N	I	G	Y	A	O	V	A	K	U	I	H	E
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X	S	C	R	P	T	E	R	O	G	I	B	K	I	O	I
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E	S	M	P	I	F	H	A	L	O	D	I	R	P	Y	J
E	U	Y	G	L	U	C	A	G	O	N	X	J	O	H	X
X	H	T	E	S	T	O	S	T	E	R	O	N	E	C	U
S	A	E	R	C	N	A	P	M	E	D	U	L	L	A	H

1. Gland in the brain that is the control center for all regulatory activities of the body
2. Condition in which levels of thyroid hormones in the blood are very low
3. Helps regulate when you sleep at night and when you wake in the morning
4. Master gland, makes hormones that control several other endocrine glands
5. Hormone that reproductive glands produce for females
6. Two hormones produced by the pancreas
7. Gland produces hormones that control the rate at which cells produce energy
8. 4 tiny glands that function together that release hormones that regulates calcium levels:
9. General name given to hormones banned in most sports organizations
10. The inner part of the Adrenal gland:
11. Hormone that reproductive glands produce for males:
12. Gland that produces melatonin: _____ body.
13. Causes milk production in nursing mothers and contractions during childbirth:
14. Increases blood pressure and heart rate when the body experiences stress:
15. Helps regulate calcium in the bones:
16. Adrenal glands are located above this major organ:
17. Disease caused by a failure of the body to produce insulin:
18. Produced in the adrenal cortex, keeps blood glucose levels stable:
19. Contains cells called the Islets of Langerhans:
20. Collection of glands that secret chemicals that maintain homeostasis: _____ system

Review Questions

1. What is a hormone?
2. Why are some organs responsive to hormones and others are not?
3. Explain what happens during upregulation and downregulation.
4. What is the difference between an endocrine and an exocrine gland? Provide examples.
5. Can an organ belong to the endocrine system and to another organ system? Provide examples.
6. Describe the body's response to insulin and glucagon.
7. What is are the different forms of diabetes? What are their respective causes?
8. How is diabetes diagnosed.
9. What are possible symptoms and consequences of diabetes?
10. How is diabetes managed/treated?

With text modified from OpenStax Biology 2e, Anatomy and Physiology, Concepts of Biology and National Institute of Health / National Institute of Diabetes and Digestive and Kidney Disease (NIH/NIDDK)