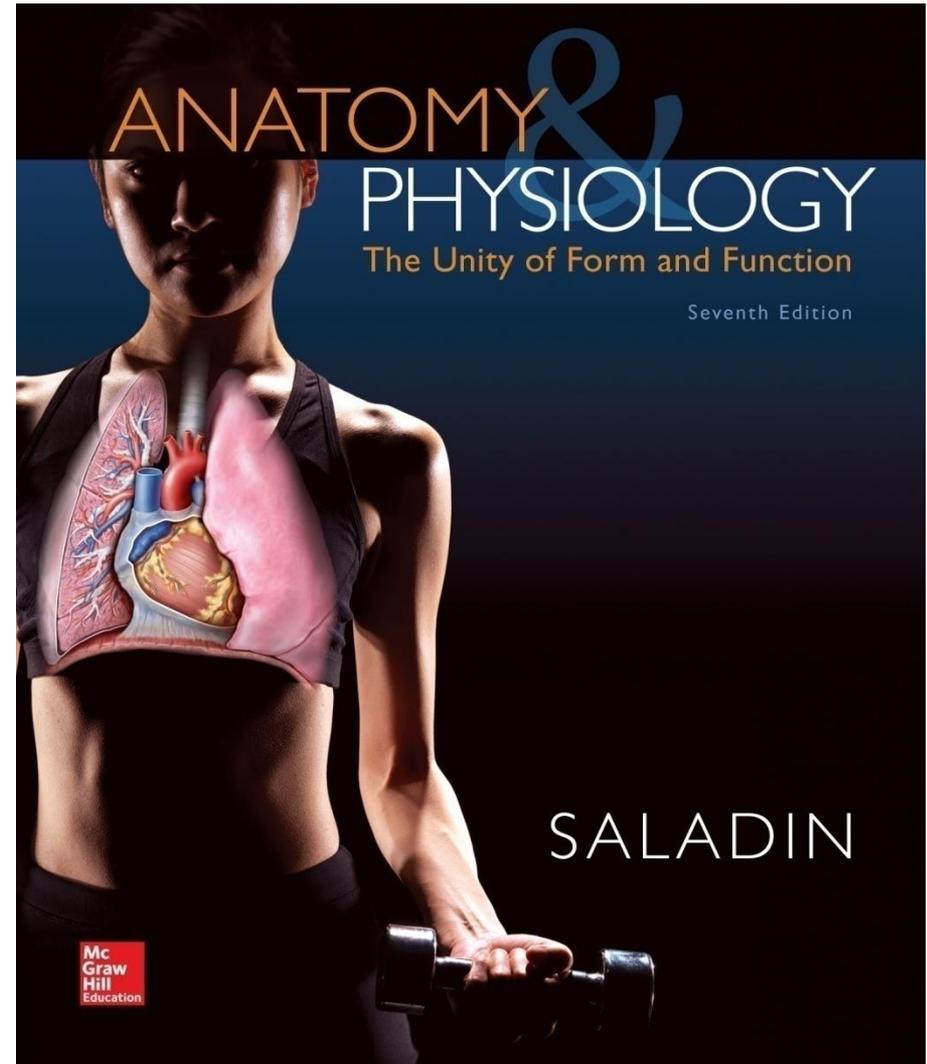


Chapter 17

Lecture Outline

See separate PowerPoint slides for all figures and tables pre-inserted into PowerPoint without notes.



Introduction

- **In humans, the endocrine and nervous systems specialize in communication and coordination**
- **The endocrine system uses hormones; the nervous system uses neurotransmitters**
- **This chapter will cover the endocrine system, including:**
 - The basics regarding glands, hormones, and their effects
 - The details regarding hormone chemistry, production, transportation, and mechanism of action
 - The endocrine system and stress
 - Paracrine secretions
 - Endocrine dysfunctions

Overview of the Endocrine System

- **Expected Learning Outcomes**
 - Define *hormone* and *endocrine system*.
 - Name several organs of the endocrine system.
 - Contrast endocrine with exocrine glands.
 - Recognize the standard abbreviations for many hormones.
 - Compare and contrast the nervous and endocrine systems.

Overview of the Endocrine System

- **The body has four principal mechanisms of communication between cells**
 - **Gap junctions**
 - Pores in cell membrane allow signaling molecules, nutrients, and electrolytes to move from cell to cell
 - **Neurotransmitters**
 - Released from neurons to travel across synaptic cleft to second cell
 - **Paracrines**
 - Secreted into tissue fluids to affect nearby cells
 - **Hormones**
 - Chemical messengers that travel in the bloodstream to other tissues and organs

Overview of the Endocrine System

- **Endocrine system**—glands, tissues, and cells that secrete hormones
- **Endocrinology**—the study of this system and the diagnosis and treatment of its disorders
- **Endocrine glands**—organs that are traditional sources of hormones
- **Hormones**—chemical messengers that are transported by the bloodstream and stimulate physiological responses in cells of another tissue or organ, often a considerable distance away

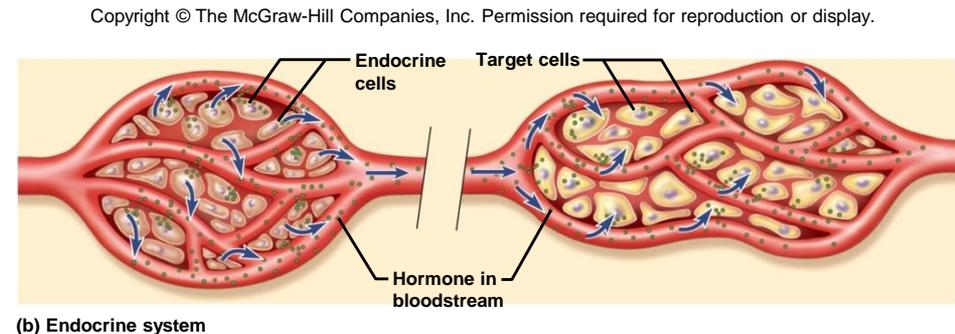


Figure 17.2b

Overview of the Endocrine System

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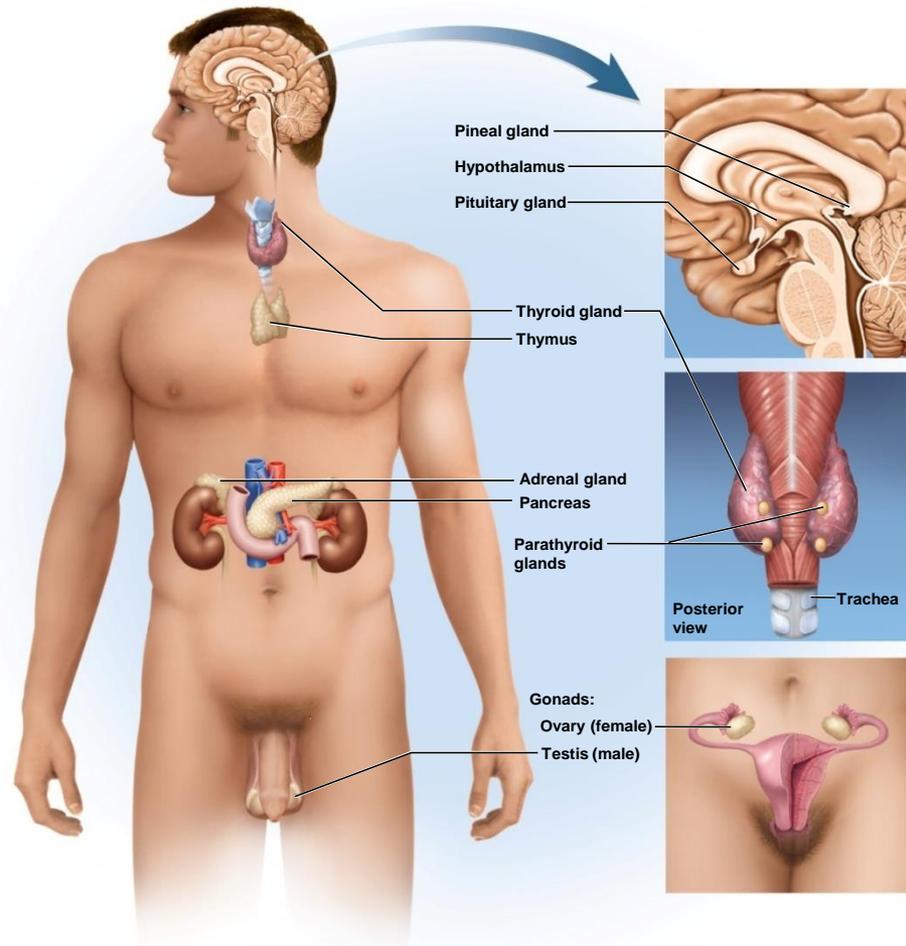


Figure 17.1

Comparison of Endocrine and Exocrine Glands

- **Exocrine glands**
 - Have ducts; carry secretion to an epithelial surface or the mucosa of the digestive tract: “external secretions”
 - Extracellular effects (food digestion)
- **Endocrine glands**
 - No ducts
 - Contain dense, fenestrated capillary networks which allow easy uptake of hormones into bloodstream
 - “Internal secretions”
 - Intracellular effects such as altering target cell metabolism
- **Liver cells defy rigid classification—releases hormones, releases bile into ducts, releases albumin and blood-clotting factors into blood (not hormones)**

Comparison of the Nervous and Endocrine Systems

- **Both systems serve for internal communication**
- **Speed and persistence of response**
 - Nervous: reacts quickly (ms timescale), stops quickly
 - Endocrine: reacts slowly (seconds or days), effect may continue for days or longer
- **Adaptation to long-term stimuli**
 - Nervous: response declines (adapts quickly)
 - Endocrine: response persists (adapts slowly)
- **Area of effect**
 - Nervous: targeted and specific (one organ)
 - Endocrine: general, widespread effects (many organs)

Comparison of the Nervous and Endocrine Systems

- **Several chemicals function as both hormones and neurotransmitters**
 - Norepinephrine, dopamine, and antidiuretic hormone
- **Both systems can have similar effects on target cells**
 - Norepinephrine and glucagon both cause glycogen hydrolysis in liver
- **The two systems can regulate each other**
 - Neurotransmitters can affect glands, and hormones can affect neurons
- **Neuroendocrine cells share characteristics with both systems**
 - Neuron-like cells that secrete oxytocin into blood

Comparison of the Nervous and Endocrine Systems

- **Target organs or cells**—those organs or cells that have receptors for a hormone and can respond to it
 - Some target cells possess enzymes that convert a circulating hormone to its more active form

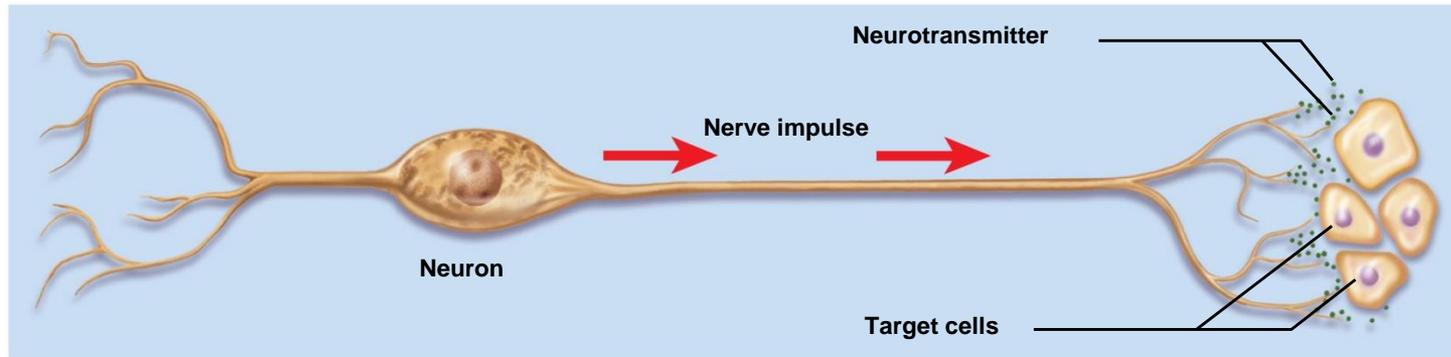
Comparison of the Nervous and Endocrine Systems

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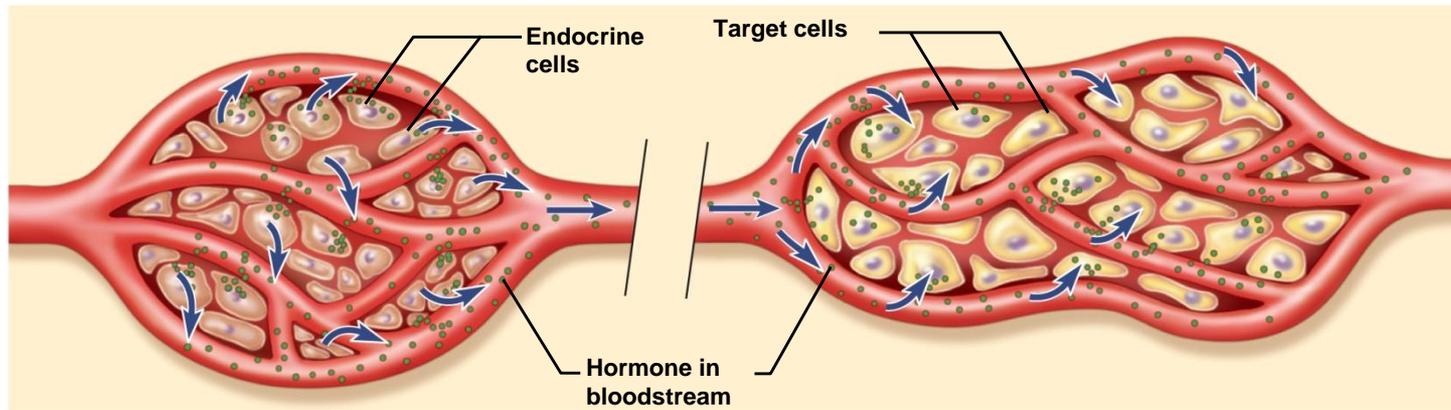
TABLE 17.1		Comparison of the Nervous and Endocrine Systems	
Nervous System		Endocrine System	
Communicates by means of electrical impulses and neurotransmitters		Communicates by means of hormones	
Releases neurotransmitters at synapses at specific target cells		Releases hormones into bloodstream for general distribution throughout body	
Usually has relatively local, specific effects		Sometimes has very general, widespread effects	
Reacts quickly to stimuli, usually within 1–10 ms		Reacts more slowly to stimuli, often taking seconds to days	
Stops quickly when stimulus stops		May continue responding long after stimulus stops	
Adapts relatively quickly to continual stimulation		Adapts relatively slowly; may respond for days to weeks	

Communication by the Nervous and Endocrine Systems

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(a) Nervous system



(b) Endocrine system

Figure 17.2a,b

The Hypothalamus and Pituitary Gland

- **Expected Learning Outcomes**

- Describe the anatomical relationships between the hypothalamus and pituitary gland.
- Distinguish between the anterior and posterior lobes of the pituitary.
- List the hormones produced by the hypothalamus and each lobe of the pituitary, and identify the functions of each hormone.
- Explain how the pituitary is controlled by the hypothalamus and its target organs.
- Describe the effects of growth hormone.

Anatomy

- **The hypothalamus is shaped like a flattened funnel**
- **Forms floor and walls of third ventricle of brain**
- **Regulates primitive functions from water balance and thermoregulation to sex drive and childbirth**
- **Many of its functions carried out by pituitary gland**

Anatomy

- The pituitary gland is suspended from hypothalamus by a stalk—**infundibulum**
- **Location and size**
 - Housed in **sella turcica of sphenoid bone**
 - Size and shape of kidney bean
- **Composed of two structures with independent origins and separate functions**
 - **Adenohypophysis** (anterior pituitary)
 - **Neurohypophysis** (posterior pituitary)

Embryonic Development

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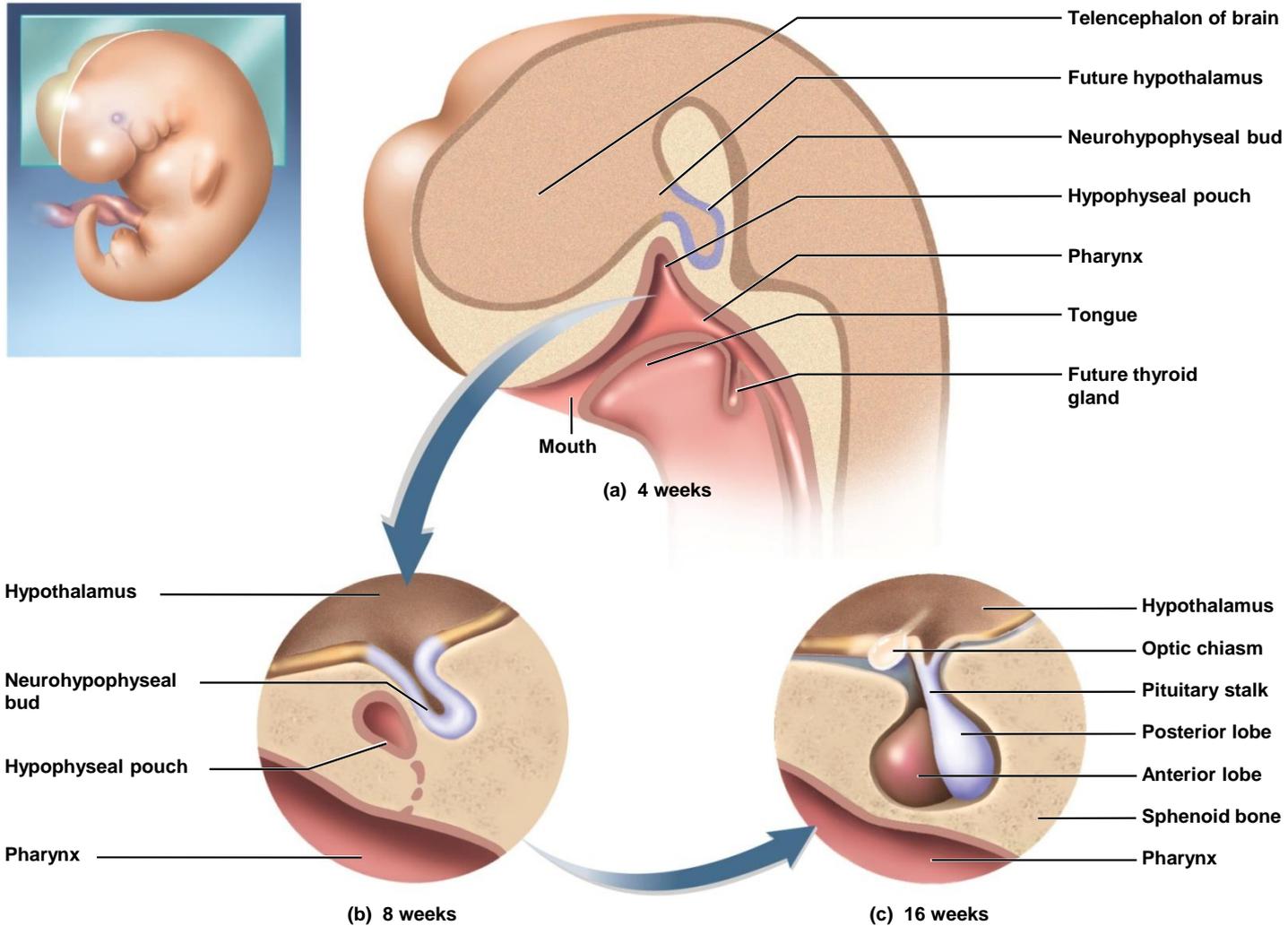


Figure 17.3a–c

Anatomy

- **Adenohypophysis (anterior lobe)** constitutes anterior three-quarters of pituitary
 - Linked to hypothalamus by **hypophyseal portal system**
 - Primary capillaries in hypothalamus connected to secondary capillaries in adenohypophysis by portal venules
 - Hypothalamic hormones regulate adenohypophysis cells

Anatomy

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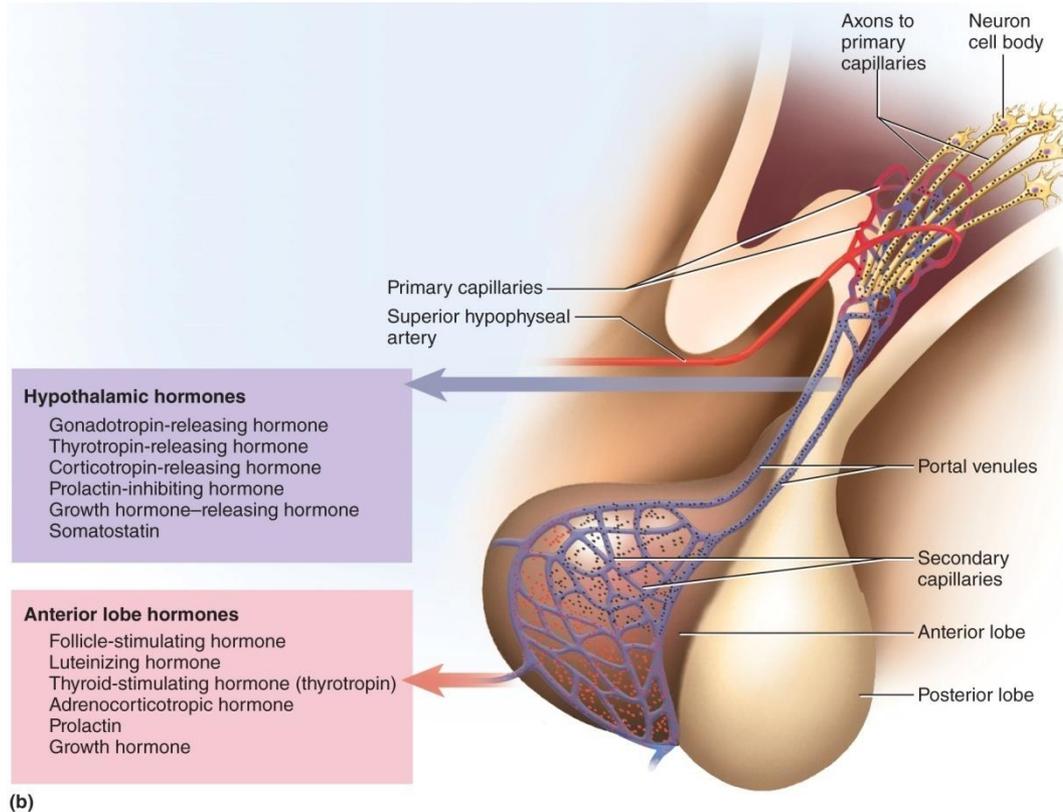


Figure 17.4b

- **Hypothalamic-releasing and -inhibiting hormones travel in hypophyseal portal system from hypothalamus to anterior pituitary**
- **Different hormones are secreted by anterior pituitary**

Anatomy

- **Neurohypophysis (posterior lobe)** constitutes the posterior one-quarter of the pituitary
 - Nerve tissue, not a true gland
 - Nerve cell bodies in hypothalamus pass down the stalk as **hypothalamo–hypophyseal tract** and end in posterior lobe
 - Hypothalamic neurons secrete hormones that are stored in neurohypophysis until released into blood

Hypothalamic Hormones

- **Eight hormones produced in hypothalamus**
 - Six regulate the anterior pituitary
 - Two are released into capillaries in the posterior pituitary
- **Six releasing and inhibiting hormones** stimulate or inhibit the anterior pituitary
 - TRH, CRH, GnRH, and GHRH are releasing hormones that promote anterior pituitary secretion of TSH, PRL, ACTH, FSH, LH, and GH
 - PIH inhibits secretion of prolactin, and somatostatin inhibits secretion growth hormone and thyroid-stimulating hormone by the anterior pituitary

Hypothalamic Hormones

- **Two** other hypothalamic hormones are **oxytocin (OT)** and **antidiuretic hormone (ADH)**
 - Both stored and released by posterior pituitary
 - **Paraventricular nuclei** of hypothalamus produce OT
 - **Supraoptic nuclei** produce ADH
 - Posterior pituitary does not synthesize them

Hypothalamic Hormones

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TABLE 17.3

Hypothalamic Releasing and Inhibiting Hormones That Regulate the Anterior Pituitary

Hormone	Principal Effects
Thyrotropin-releasing hormone (TRH)	Promotes secretion of thyroid-stimulating hormone (TSH) and prolactin (PRL)
Corticotropin-releasing hormone (CRH)	Promotes secretion of adrenocorticotrophic hormone (ACTH)
Gonadotropin-releasing hormone (GnRH)	Promotes secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
Growth hormone–releasing hormone (GHRH)	Promotes secretion of growth hormone (GH)
Prolactin-inhibiting hormone (PIH)	Inhibits secretion of prolactin (PRL)
Somatostatin	Inhibits secretion of growth hormone (GH) and thyroid-stimulating hormone (TSH)

Histology of Pituitary Gland

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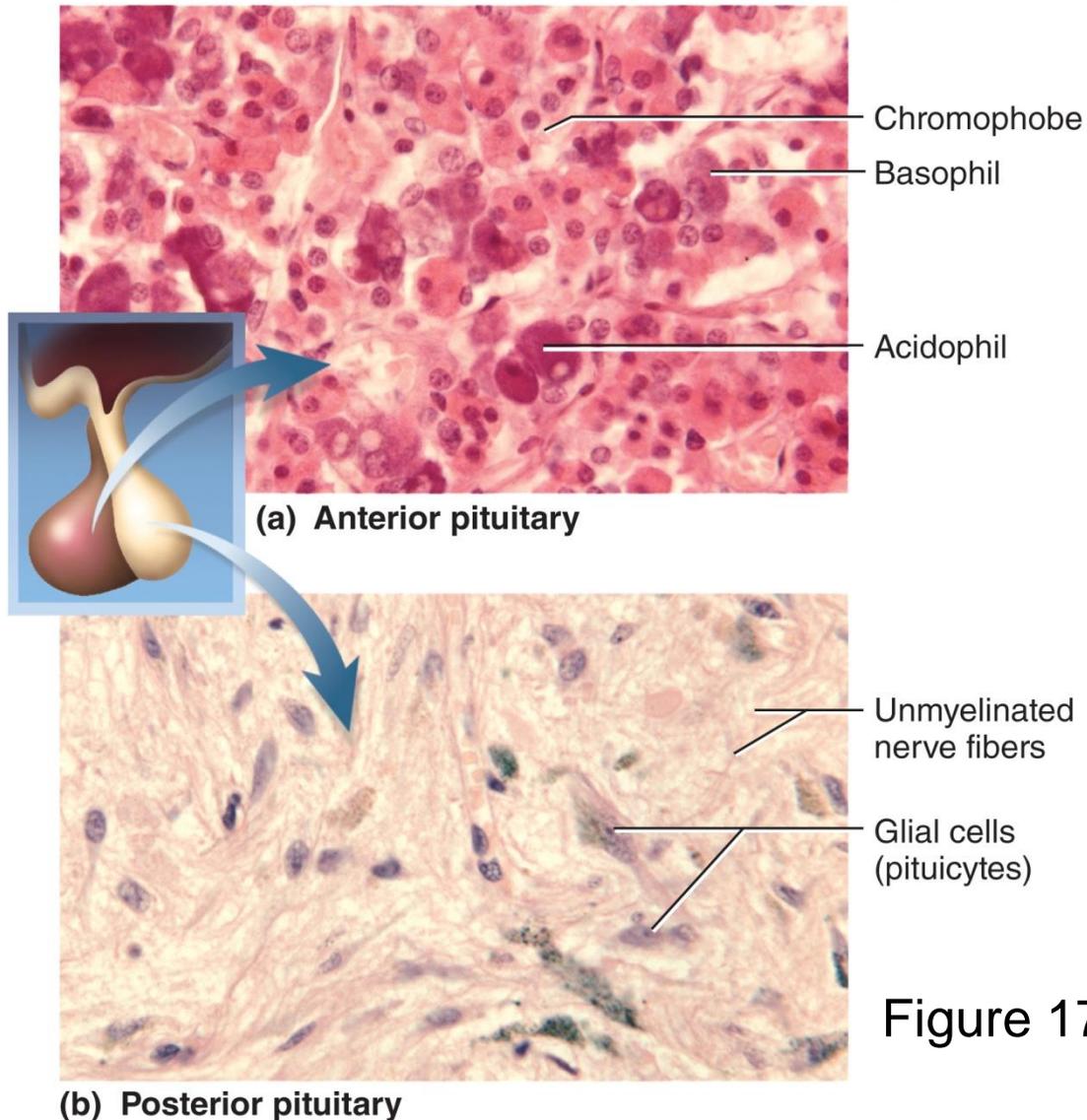


Figure 17.5a,b

a: ©Dr. John D. Cunningham/Visuals Unlimited; b: ©Science VU/Visuals Unlimited

Anterior Pituitary Hormones

- Anterior lobe of the pituitary synthesizes and secretes **six principal hormones**
- **Two gonadotropin hormones** that target gonads
 - **Follicle-stimulating hormone (FSH)**
 - Stimulates secretion of ovarian sex hormones, development of ovarian follicles, and sperm production
 - **Luteinizing hormone (LH)**
 - Stimulates ovulation, stimulates corpus luteum to secrete progesterone, stimulates testes to secrete testosterone
- **Thyroid-stimulating hormone (TSH)**
 - Stimulates secretion of thyroid hormone

Anterior Pituitary Hormones

(Continued)

- **Adrenocorticotrophic hormone (ACTH)**
 - Stimulates adrenal cortex to secrete glucocorticoids
- **Prolactin (PRL)**
 - After birth, stimulates mammary glands to synthesize milk
- **Growth hormone (GH)**
 - Stimulates mitosis and cellular differentiation

Hypothalamo–Pituitary–Target Organ Relationships

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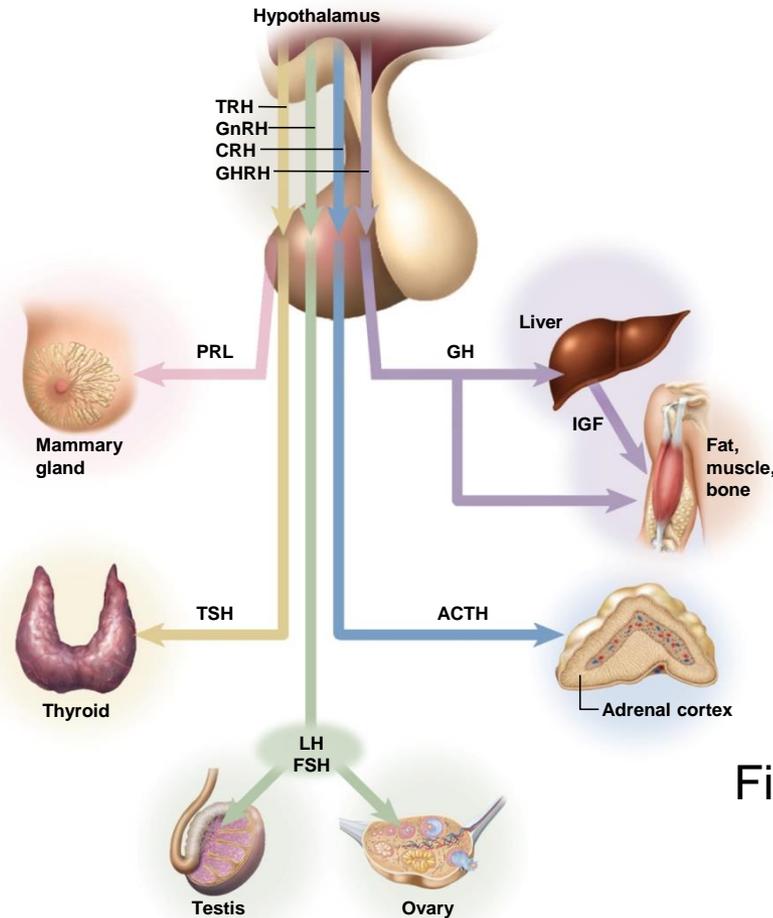


Figure 17.6

- Principle hormones and target organs

Posterior Pituitary Hormones

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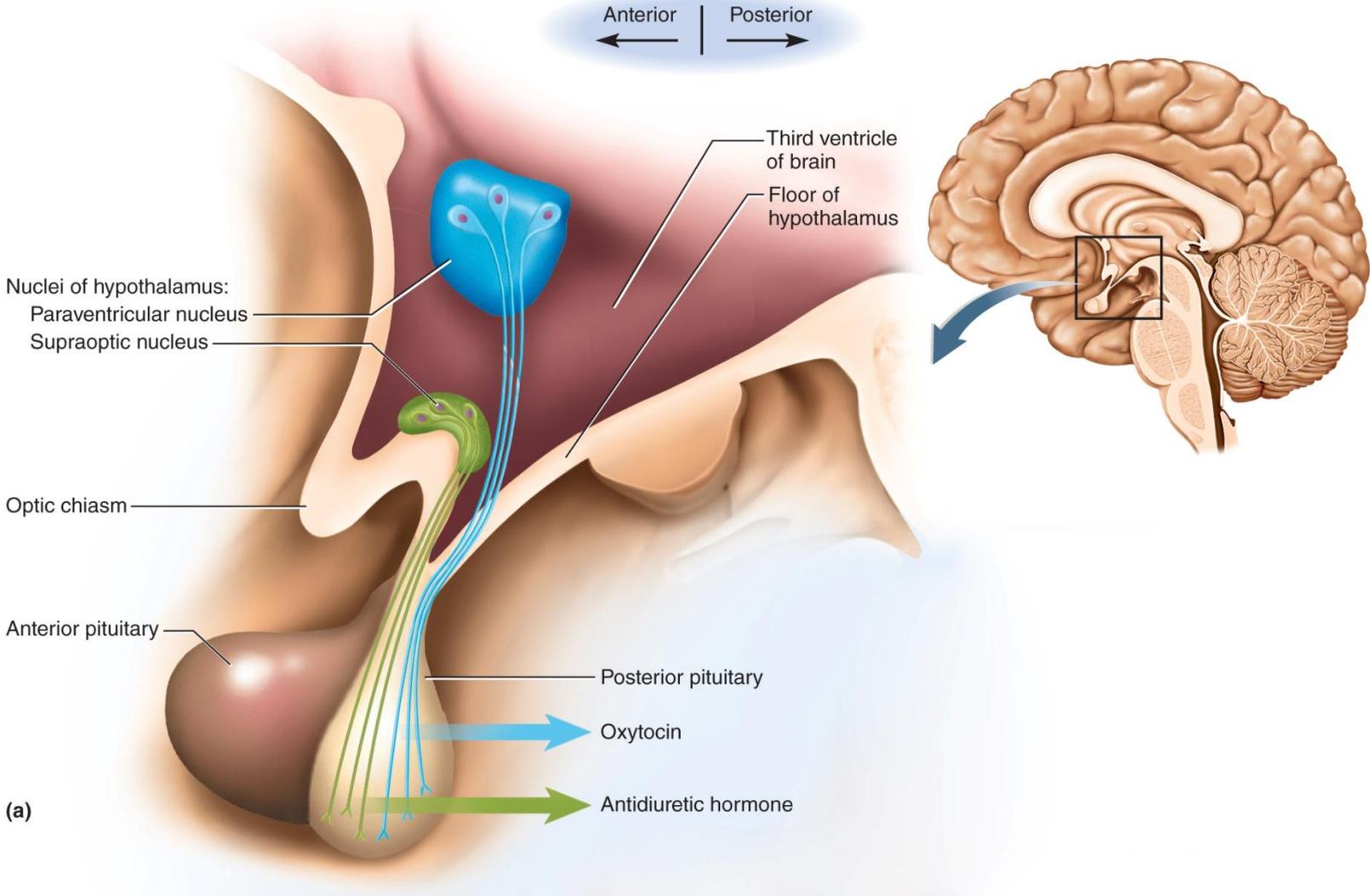


Figure 17.4a

Posterior Pituitary Hormones

- **Two hormones are produced in hypothalamus and transported to the posterior lobe of pituitary**
 - Hormone released when hypothalamic neurons are stimulated
- **ADH (antidiuretic hormone)**
 - Increases water retention, thus reducing urine volume, and preventing dehydration
 - Also called vasopressin because it can cause vasoconstriction

Posterior Pituitary Hormones

- **Oxytocin (OT)**

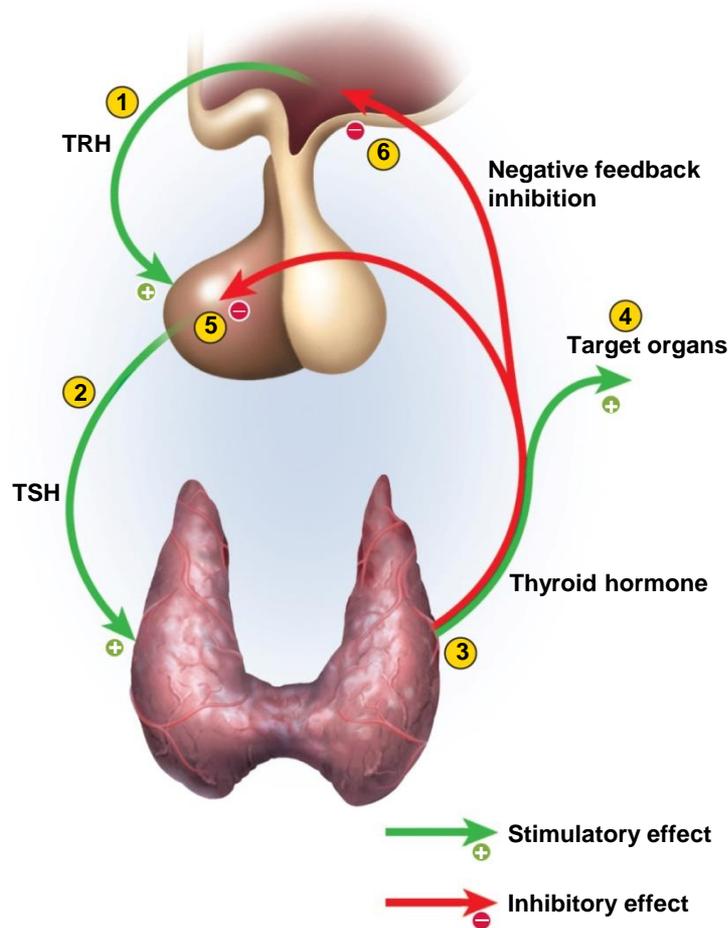
- Surge of hormone released during sexual arousal and orgasm
- Promotes feelings of sexual satisfaction and emotional bonding between partners
- Stimulates labor contractions during childbirth
- Stimulates flow of milk during lactation
- May promote emotional bonding between lactating mother and infant

Control of Pituitary Secretion

- **Rates of secretion are not constant**
 - Regulated by hypothalamus, other brain areas, and feedback from target organs
- **Hypothalamic and cerebral control:**
 - Brain monitors conditions and influences anterior pituitary accordingly
 - In times of stress, hypothalamus triggers release of ACTH
 - During pregnancy, hypothalamus triggers prolactin secretion
 - Posterior pituitary is controlled by neuroendocrine reflexes
 - Hypothalamic osmoreceptors trigger release of ADH when they detect a rise in blood osmolarity
 - Infant suckling triggers hypothalamic response to release oxytocin

Control of Pituitary Secretion

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- **Negative feedback**— increased target organ hormone levels inhibit release of hypothalamic and/or pituitary hormones
 - Example: thyroid hormone+ inhibits release of TRH by hypothalamus and of TSH by anterior pituitary

Figure 17.7

Control of Pituitary Secretion

- **Positive feedback** can also occur
 - Stretching of uterus increases OT release, causes contractions, causing more stretching of uterus, etc. until delivery

A Further Look at Growth Hormone

- **GH has widespread effects on the body tissues**
 - Especially cartilage, bone, muscle, and fat
- **Induces liver to produce growth stimulants**
 - **Insulin-like growth factors (IGF-I) or somatomedins (IGF-II)**
 - Stimulate target cells in diverse tissues
 - IGF-I prolongs the action of GH
 - **Hormone half-life**—the time required for 50% of the hormone to be cleared from the blood
 - **GH half-life:** 6 to 20 minutes
 - **IGF-I half-life:** about 20 hours

A Further Look at Growth Hormone

- **Induces liver to produce growth stimulants (continued)**
 - **Protein synthesis increases:** boosts transcription and translation; increases amino acid uptake into cells; suppresses protein catabolism
 - **Lipid metabolism increases:** stimulates adipocytes to catabolize fats (protein-sparing effect)
 - **Carbohydrate metabolism: glucose-sparing effect,** mobilizing fatty acids reduces dependence of most cells on glucose, freeing more for the brain; stimulates glucose secretion by liver
 - **Electrolyte balance:** promotes Na^+ , K^+ , and Cl^- retention by kidneys, enhances Ca^{2+} absorption in intestine; makes electrolytes available to growing tissues

A Further Look at Growth Hormone

- **Bone growth, thickening, and remodeling influenced, especially during childhood and adolescence**
- **Secretion high during first 2 hours of sleep**
- **Can peak in response to vigorous exercise**
- **GH levels decline gradually with age**
- **Average 6 ng/mL during adolescence, 1.5 ng/mL in old age**
 - Lack of protein synthesis contributes to aging of tissues and wrinkling of the skin
 - Age 30, average adult body is 10% bone, 30% muscle, 20% fat
 - Age 75, average adult body is 8% bone, 15% muscle, 40% fat

Other Endocrine Glands

- **Expected Learning Outcomes**
 - Describe the structure and location of the remaining endocrine glands.
 - Name the hormones these endocrine glands produce and state their functions.
 - Discuss the hormones produced by organs and tissues other than the classical endocrine glands.

The Pineal Gland

- **Pineal gland**—attached to roof of third ventricle beneath the posterior end of corpus callosum
- After age 7, it undergoes **involution (shrinkage)**
 - Down 75% by end of puberty
 - Tiny mass of shrunken tissue in adults
- May synchronize physiological function with 24-hour **circadian rhythms** of daylight and darkness
 - **Synthesizes melatonin** from serotonin during the night
 - Fluctuates seasonally with changes in day length

The Pineal Gland

- **Pineal gland may influence timing of puberty in humans**
- **May play a role in circadian rhythms**
 - It synthesizes **melatonin** at night
 - **Seasonal affective disorder (SAD)** occurs in winter or northern climates
 - Symptoms: depression, sleepiness, irritability, and carbohydrate craving
 - Two to 3 hours of exposure to bright light each day reduces the melatonin levels and the symptoms (phototherapy)

The Thymus

- **Thymus** plays a role in three systems: endocrine, lymphatic, immune
- **Bilobed gland in the mediastinum superior to the heart**
 - Goes through involution after puberty
- Site of **maturation of T cells** important in immune defense
- Secretes hormones (**thymopoietin, thymosin, and thymulin**) that stimulate development of other lymphatic organs and activity of T lymphocytes

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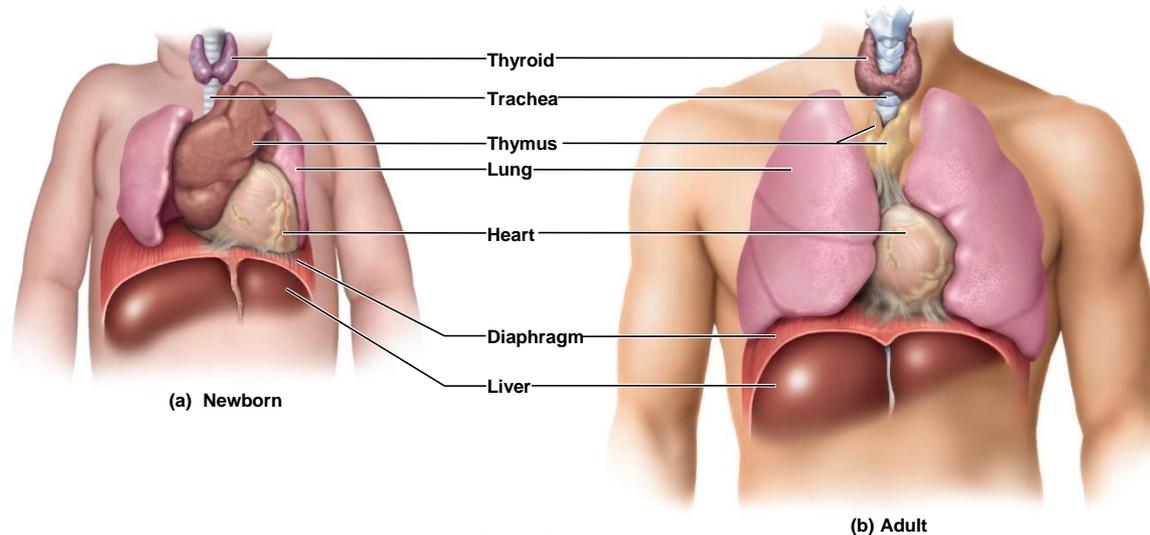
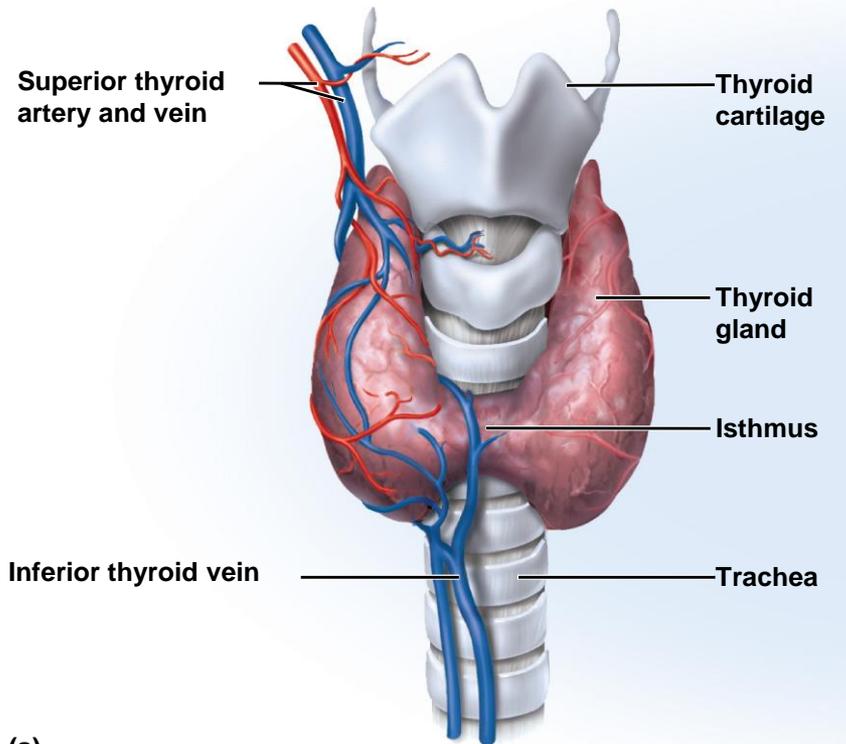


Figure 17.8a,b

The Thyroid Gland

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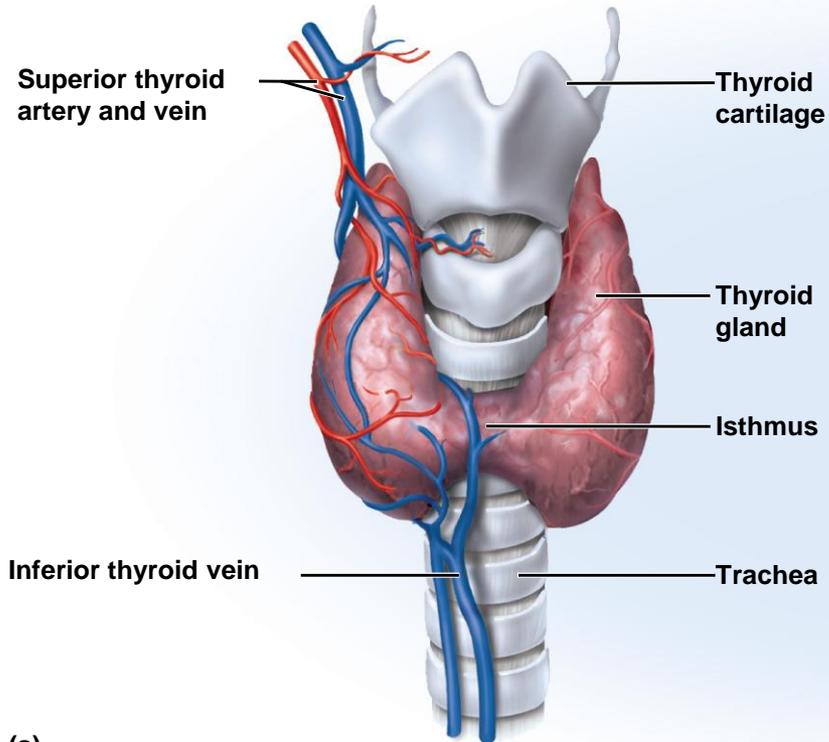
(a)

Figure 17.9a

- **Largest gland that is purely endocrine**
 - Composed of two lobes and an isthmus below the larynx
 - Dark reddish brown color due to rich blood supply
- **Thyroid follicles**—sacs that make up most of thyroid
 - Contain protein-rich **colloid**
 - **Follicular cells**: simple cuboidal epithelium that lines follicles

The Thyroid Gland

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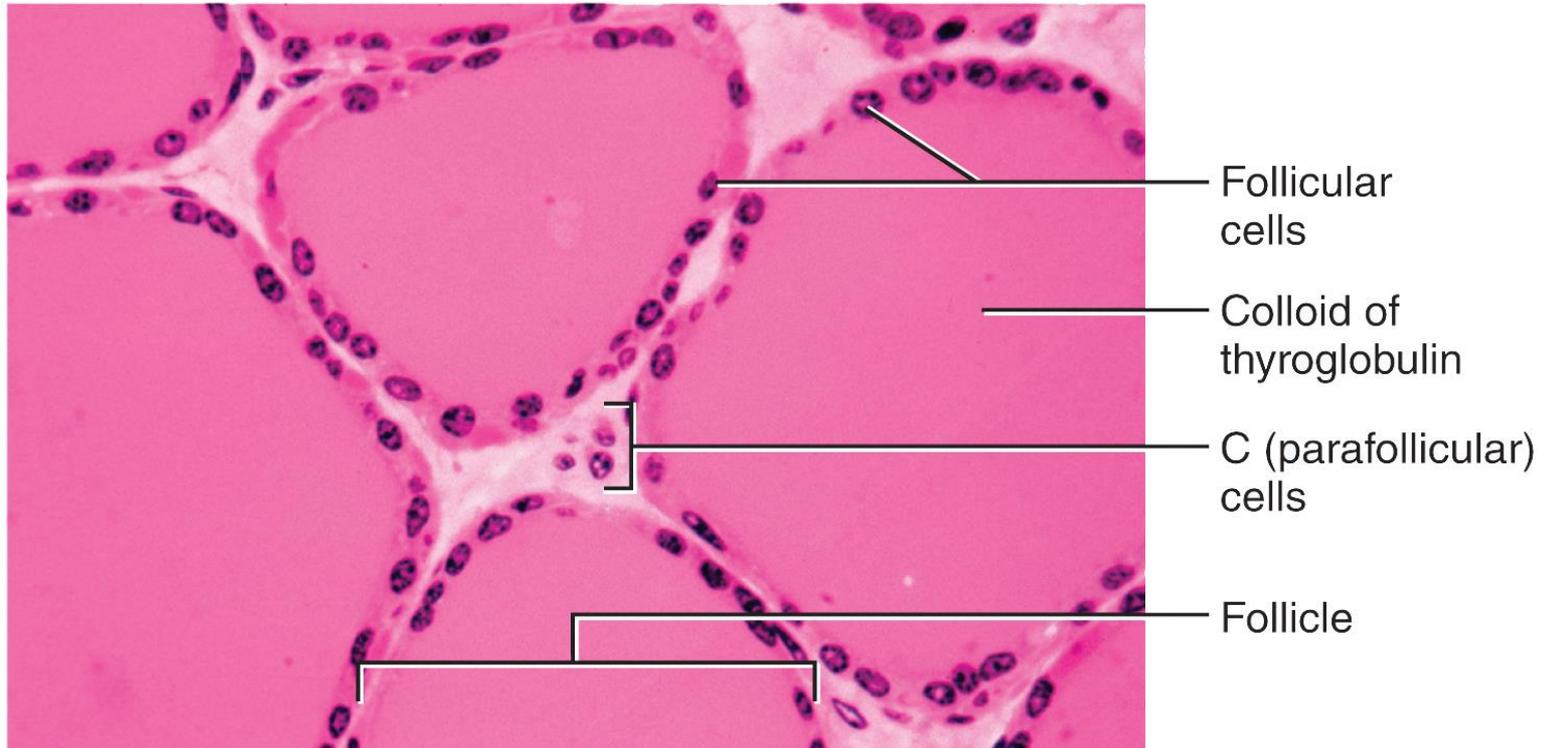
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Figure 17.9a

- Secretes **thyroxine** (T_4 because of four iodine atoms) and **triiodothyronine** (T_3) in response to TSH
 - Increases metabolic rate, O_2 consumption, heat production (**calorigenic effect**), appetite, growth hormone secretion, alertness, reflex speed
- **Parafollicular (C or clear) cells** secrete **calcitonin** with rising blood calcium
 - Stimulates osteoblast activity and bone formation in children

The Thyroid Gland

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(b)

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Figure 17.9b

Thyroid follicles are filled with colloid and lined with simple cuboidal epithelial cells (follicular cells).

The Parathyroid Glands

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- Usually four glands partially embedded in posterior surface of thyroid gland
 - Can be found from as high as hyoid bone to as low as aortic arch
- Secrete parathyroid hormone (PTH)
 - Increases blood Ca^{2+} levels
 - Promotes synthesis of calcitriol
 - Increases absorption of Ca^{2+}
 - Decreases urinary excretion
 - Increases bone resorption

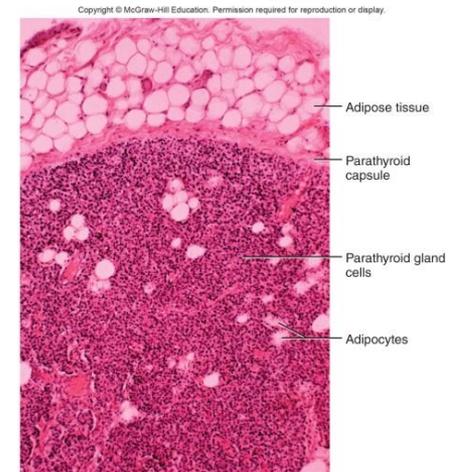
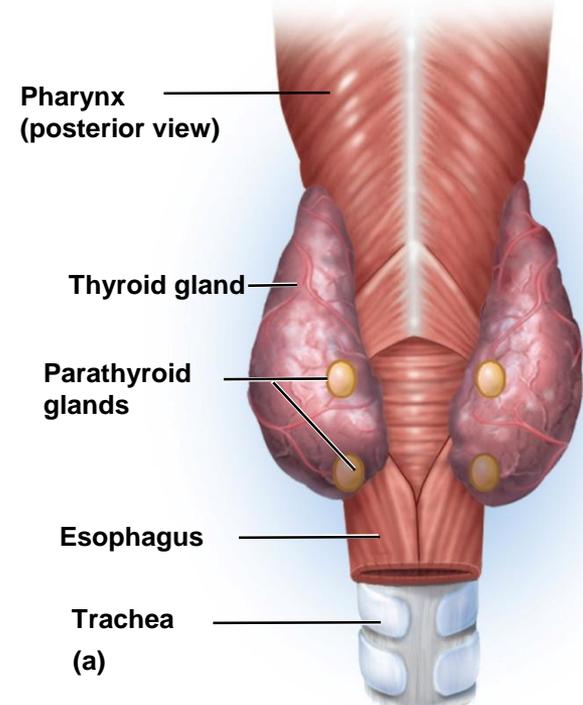


Figure 17.10a,b

The Adrenal Glands

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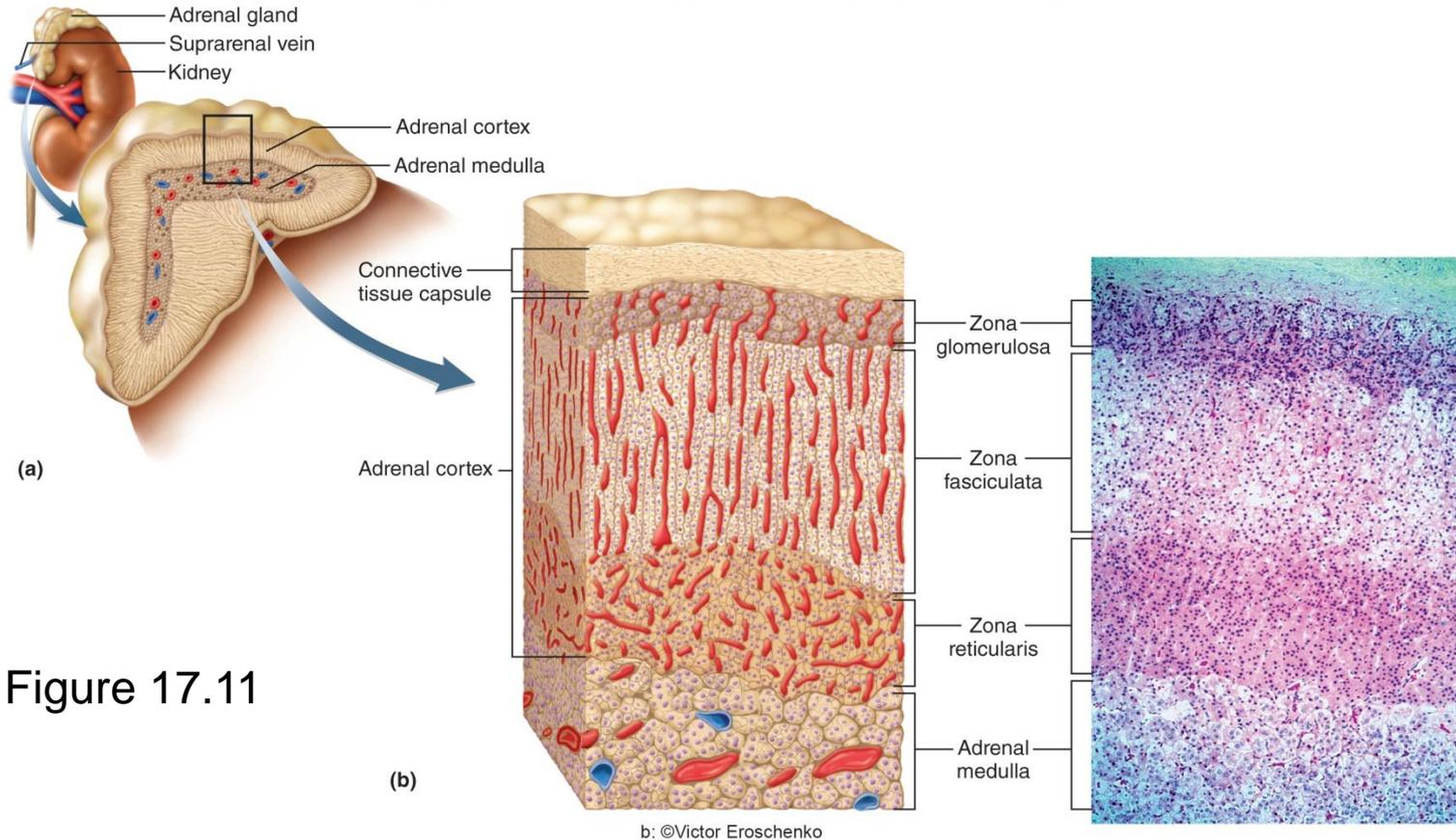


Figure 17.11

- **Small glands that sit on top of each kidney**
- **Retroperitoneal location**
- **Adrenal cortex and medulla formed by merger of two fetal glands with different origins and functions**

The Adrenal Medulla

- **Adrenal medulla**—inner core, 10% to 20% of gland
- Has **dual nature** acting as an **endocrine gland** and a **ganglion** of the sympathetic nervous system
 - Innervated by **sympathetic preganglionic fibers**
 - Consists of modified sympathetic postganglionic neurons called **chromaffin cells**
 - When stimulated, release **catecholamines** (**epinephrine** and **norepinephrine**) and a trace of **dopamine** directly into the bloodstream

The Adrenal Medulla

- **As hormones, catecholamines have multiple effects**
 - Increase alertness and prepare body for physical activity
 - Mobilize high-energy fuels, lactate, fatty acids, and glucose
 - **Glycogenolysis** and **gluconeogenesis** by liver boost glucose levels
 - Epinephrine inhibits insulin secretion and so has a **glucose-sparing effect**
 - Muscles use fatty acids, saving glucose for brain
 - **Increase** blood pressure, heart rate, blood flow to muscles, pulmonary airflow, and metabolic rate
 - **Decrease** digestion and urine production

The Adrenal Cortex

- Cortex surrounds medulla and secretes several **corticosteroids (hormones)** from **three layers** of glandular tissue
 - **Zona glomerulosa (thin, outer layer)**
 - Cells are arranged in rounded clusters
 - Secretes **mineralocorticoids**—regulate the body's electrolyte balance
 - **Zona fasciculata (thick, middle layer)**
 - Cells arranged in fascicles separated by capillaries
 - Secretes **glucocorticoids** and **androgens**
 - **Zona reticularis (narrow, inner layer)**
 - Cells in branching network
 - Secretes **glucocorticoids** and **sex steroids**

The Adrenal Cortex

- **Mineralocorticoids**—from **zona glomerulosa**
 - Steroid hormones that regulate electrolyte balance
 - **Aldosterone** stimulates Na^+ retention and K^+ excretion
 - Water is retained with sodium by osmosis, so blood volume and blood pressure are maintained
 - Part of the renin-angiotensin-aldosterone (RAA) system

The Adrenal Cortex

- **Glucocorticoids**

- Secreted by zona fasciculata and zona reticulata in response to ACTH
- Regulate metabolism of glucose and other fuels
- **Cortisol** and **corticosterone** stimulate fat and protein catabolism, **gluconeogenesis (glucose from amino acids and fatty acids)** and release of fatty acids and glucose into blood
- Help body adapt to stress and repair tissues
- Anti-inflammatory effect becomes immune suppression with long-term use

The Adrenal Cortex

- **Sex steroids**

- Secreted by zona fasciculata and zona reticularis
- **Androgens:** set libido throughout life; large role in prenatal male development (include DHEA which other tissues convert to testosterone)
- **Estradiol:** small quantity from adrenals, but this becomes important after menopause for sustaining adult bone mass

The Adrenal Glands

- **Medulla and cortex of adrenal gland are not functionally independent**
- **Medulla atrophies without the stimulation of cortisol**
- **Some chromaffin cells of medullary origin extend into the cortex**
 - They stimulate the cortex to secrete corticosteroids when stress activates the sympathetic nervous system

The Pancreatic Islets

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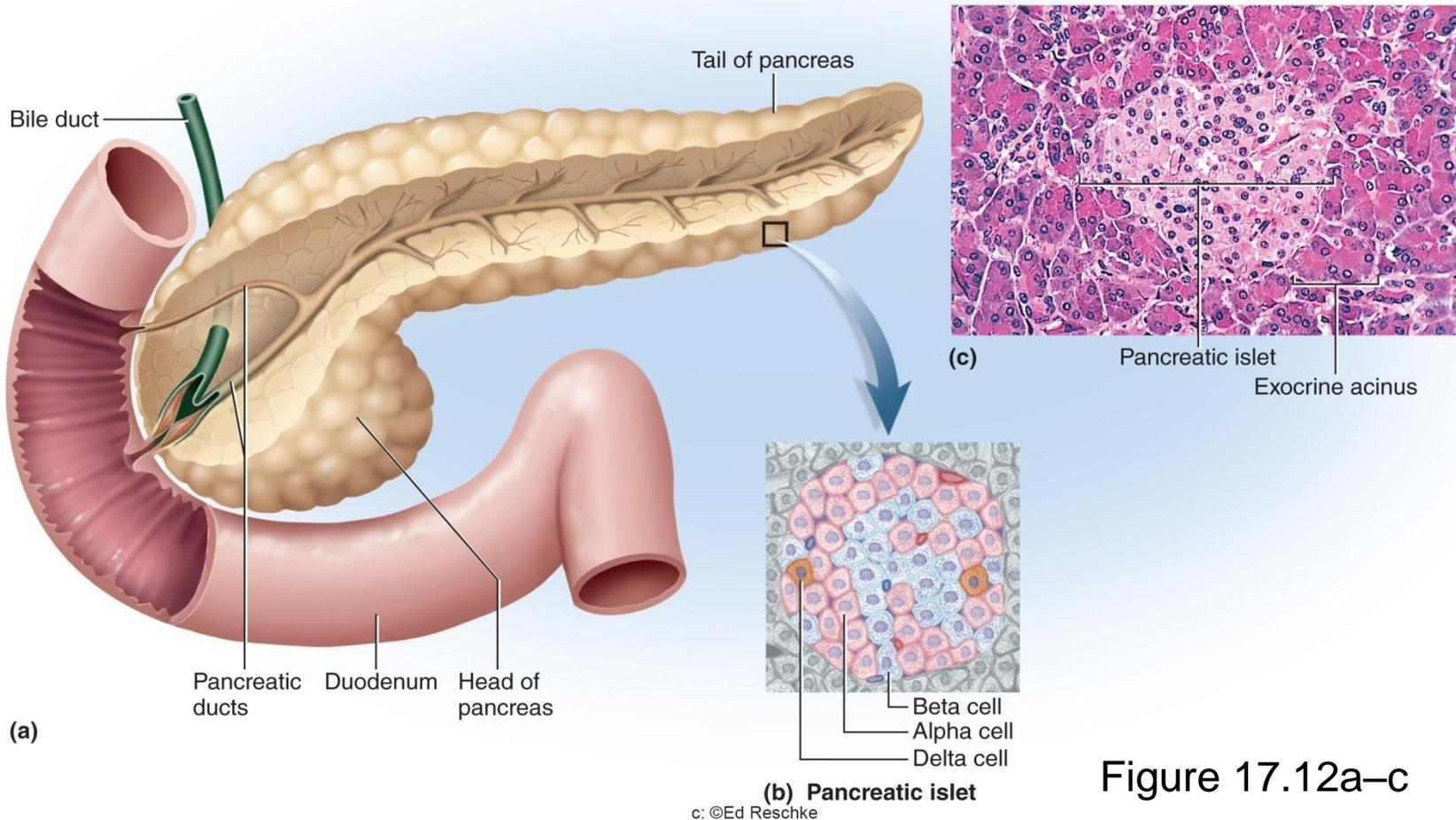


Figure 17.12a–c

- **Pancreas is elongated gland below and behind stomach**
- **It contains 1 to 2 million islets—clusters of endocrine cells that secrete hormones that regulate glycemia (blood sugar)**

The Pancreatic Islets

- **Glucagon**—secreted by **A** or **alpha (α) cells**
- Released between meals when blood glucose concentration is falling
- In liver, stimulates gluconeogenesis, glycogenolysis, and the release of glucose into the circulation raising blood glucose level
- In adipose tissue, stimulates fat catabolism and release of free fatty acids
- Glucagon also released to rising amino acid levels in blood, promotes amino acid absorption, and provides cells with raw material for gluconeogenesis

The Pancreatic Islets

- **Insulin** secreted by **B** or **beta (β) cells**
- Secreted during and after meal when glucose and amino acid blood levels are rising
- Stimulates cells to absorb these nutrients and store or metabolize them, **lowering blood glucose levels**
 - Promotes synthesis glycogen, fat, and protein
 - Suppresses use of already-stored fuels
 - Brain, liver, kidneys, and RBCs absorb glucose without insulin, but other tissues require insulin
- Insufficiency or inaction is cause of **diabetes mellitus**

The Pancreatic Islets

- **Somatostatin** secreted by **D** or **delta (δ) cells**

 - Partially suppresses secretion of glucagon and insulin
 - Inhibits nutrient digestion and absorption which prolongs absorption of nutrients

- **Pancreas also has PP and G cells of uncertain function**
- **Hyperglycemic hormones** raise blood glucose concentration (includes hormones from other glands)
 - Glucagon, growth hormone, epinephrine, norepinephrine, cortisol, and corticosterone
- **Hypoglycemic hormones** lower blood glucose
 - Insulin

The Gonads

- **Ovaries** and **testes** are both endocrine and exocrine
 - **Exocrine** product: whole cells—eggs and sperm (**cytogenic glands**)
 - **Endocrine** product: gonadal hormones—mostly steroids
- **Ovarian** hormones
 - Estradiol, progesterone, and inhibin
- **Testicular** hormones
 - Testosterone, weaker androgens, estrogen, and inhibin

The Gonads

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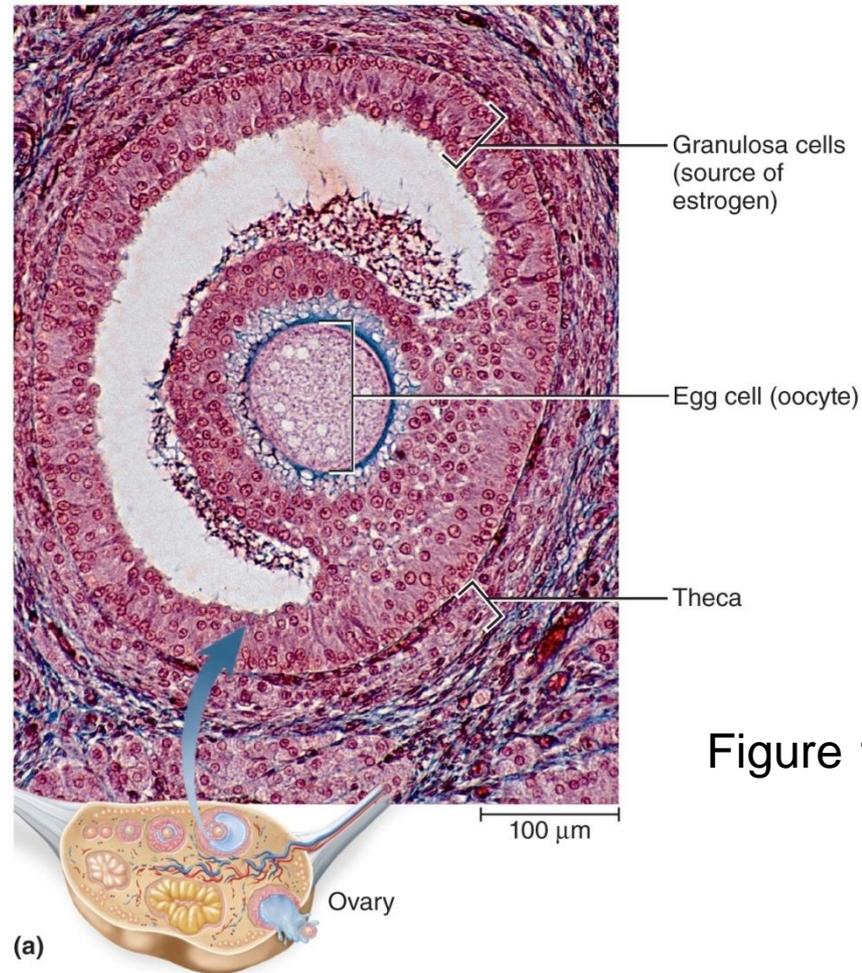


Figure 17.13a

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- **Follicle—egg surrounded by granulosa cells and a capsule (theca)**

The Gonads

- **Ovary**
 - Theca cells synthesize androstenedione
 - Converted to mainly estradiol by granulosa cells
- After ovulation, the remains of the follicle becomes the **corpus luteum**
 - Secretes **progesterone** for 12 days following ovulation
 - Follicle and corpus luteum secrete inhibin
- Functions of **estradiol** and **progesterone**
 - Development of female reproductive system and physique including adolescent bone growth
 - Regulate menstrual cycle, sustain pregnancy
 - Prepare mammary glands for lactation
- **Inhibin** suppresses FSH secretion from anterior pituitary

The Gonads

- **Testes**

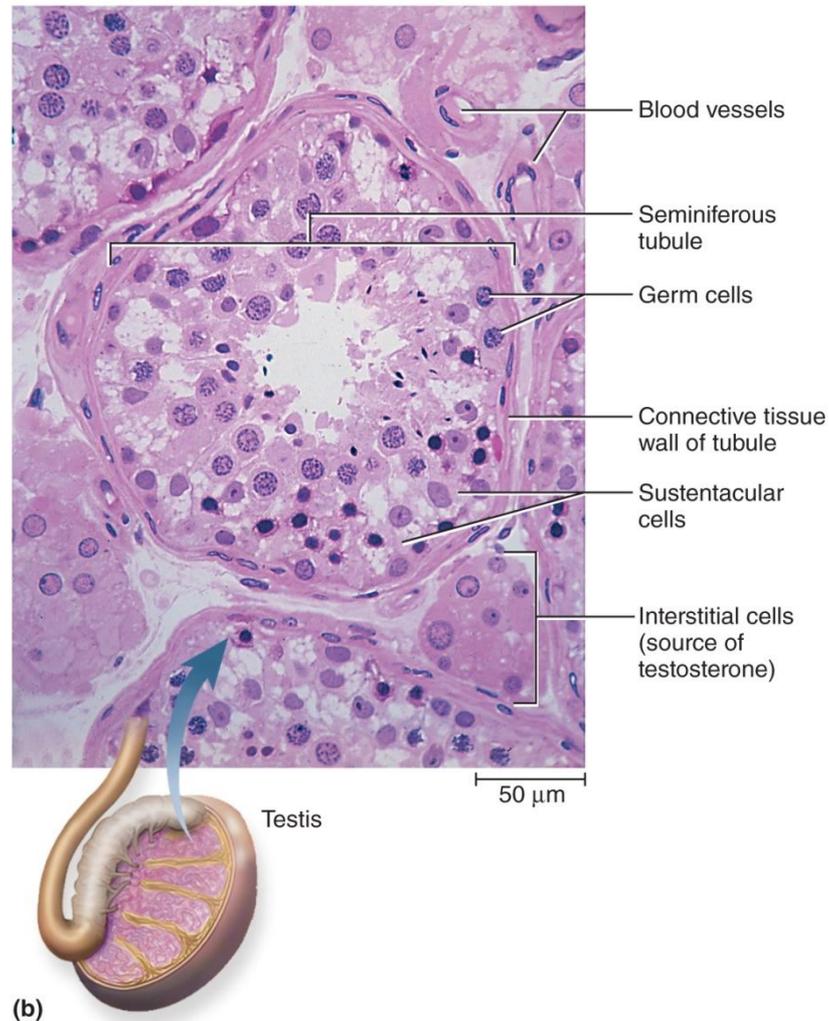
- Microscopic **seminiferous tubules** produce sperm
- Tubule walls contain sustentacular (Sertoli) cells
- Leydig cells (interstitial cells) lie in clusters between tubules

- **Testicular hormones**

- **Testosterone** and other steroids from interstitial cells (cells of Leydig) nestled between the tubules
 - Stimulates development of male reproductive system in fetus and adolescent, and sex drive
 - Sustains sperm production
- **Inhibin** from sustentacular (Sertoli) cells
 - Limits FSH secretion in order to regulate sperm production

The Gonads

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Figure 17.13b

Endocrine Functions of Other Tissues and Organs

- **Skin**

- Keratinocytes convert a cholesterol-like steroid into cholecalciferol using UV from sun

- **Liver**—involved in the production of at least five hormones

- Converts cholecalciferol into **calcidiol**
- Secretes **angiotensinogen (a prohormone)**
 - Precursor of angiotensin II (a regulator of blood pressure)
- Secretes 15% of **erythropoietin** (stimulates bone marrow)
- **Hepcidin**: promotes intestinal absorption of iron
- Source of **IGF-I** that controls action of growth hormone

Endocrine Functions of Other Tissues and Organs

- **Kidneys**—play role in production of three hormones
 - Convert calcidiol to **calcitriol**, the active form of vitamin D
 - Increases Ca^{2+} absorption by intestine and inhibits loss in the urine
 - Secrete **renin** that converts angiotensinogen to angiotensin I
 - Angiotensin II created by converting enzyme in lungs
 - Constricts blood vessels and raises blood pressure
 - Produces 85% of **erythropoietin**
 - Stimulates bone marrow to produce RBCs

Endocrine Functions of Other Tissues and Organs

- **Heart**
 - Atrial muscle secretes two **natriuretic peptides** in response to an increase in blood pressure
 - These decrease blood volume and blood pressure by increasing Na⁺ and H₂O output by kidneys and oppose action of angiotensin II
 - Lowers blood pressure
- **Stomach and small intestine** secrete at least 10 **enteric hormones** secreted by enteroendocrine cells
 - Coordinate digestive motility and glandular secretion
 - Cholecystokinin, gastrin, ghrelin, and peptide YY (PYY)

Endocrine Functions of Other Tissues and Organs

- **Adipose tissue** secretes **leptin**
 - Slows appetite
- **Osseous tissue—osteocalcin** secreted by osteoblasts
 - Increases number of pancreatic beta cells, pancreatic output of insulin, and insulin sensitivity of body tissues
 - Inhibits weight gain and onset of type 2 diabetes mellitus
- **Placenta**
 - Secretes estrogen, progesterone, and others
 - Regulate pregnancy, stimulate development of fetus and mammary glands

Hormones and Their Actions

- **Expected Learning Outcomes**

- Identify the chemical classes to which various hormones belong.
- Describe how hormones are synthesized and transported to their target organs.
- Describe how hormones stimulate their target cells.
- Explain how target cells regulate their sensitivity to circulating hormones.
- Describe how hormones affect each other when two or more of them stimulate the same target cells.
- Discuss how hormones are removed from circulation after they have performed their roles.

Hormone Chemistry

- **Three chemical classes: steroids, monoamines, and peptides**
 - **Steroids**
 - Derived from cholesterol
 - Sex steroids (such as estrogen) from gonads and corticosteroids (such as cortisol) from adrenals
 - **Monoamines (biogenic amines)**
 - Made from amino acids
 - Catecholamines (dopamine, epinephrine, norepinephrine), melatonin, thyroid hormone

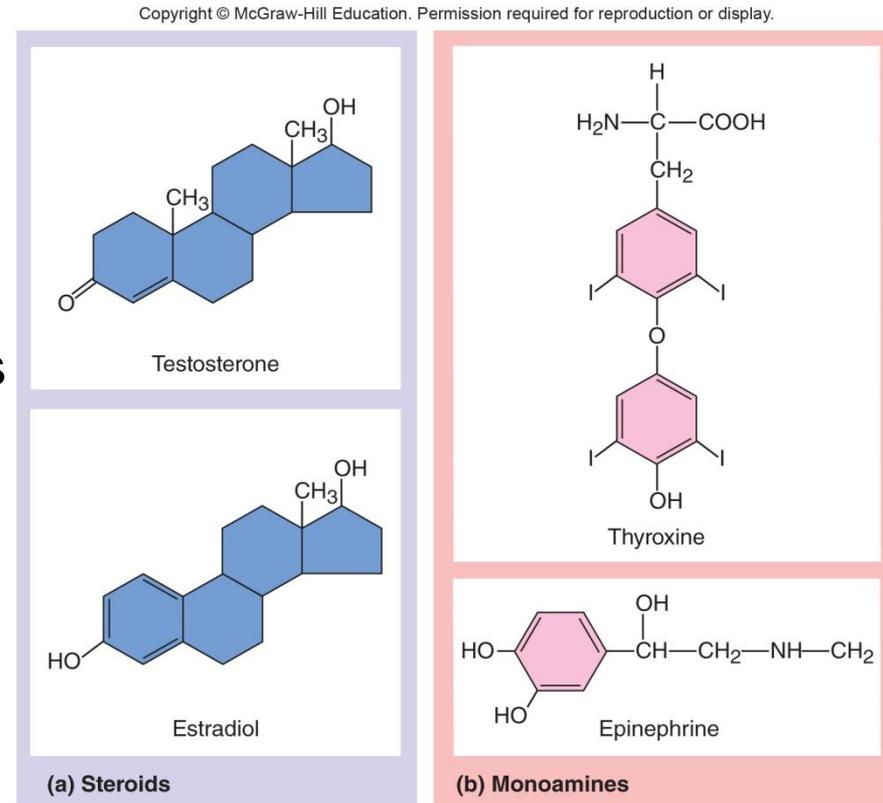


Figure 17.14a,b

Hormone Chemistry

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– Peptides and glycoproteins

- Created from chains of amino acids
- Examples include hormones from both lobes of the pituitary, and releasing and inhibiting hormones from hypothalamus
- Insulin is a large peptide hormone

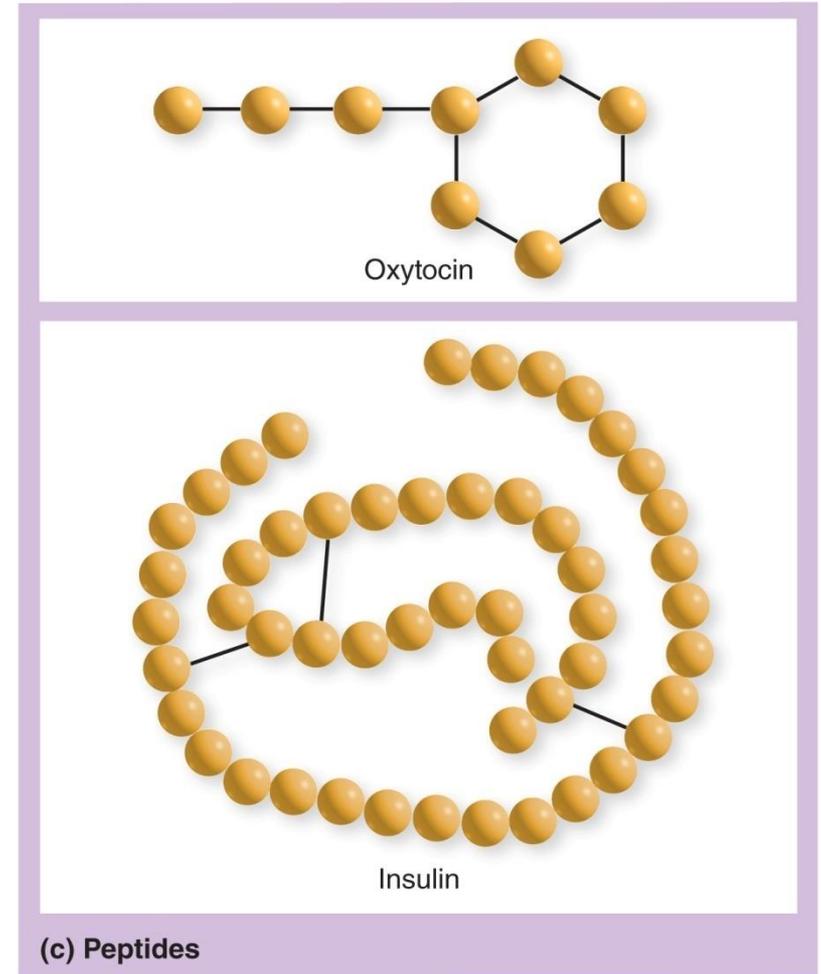


Figure 17.14c

Hormone Synthesis - Steroids

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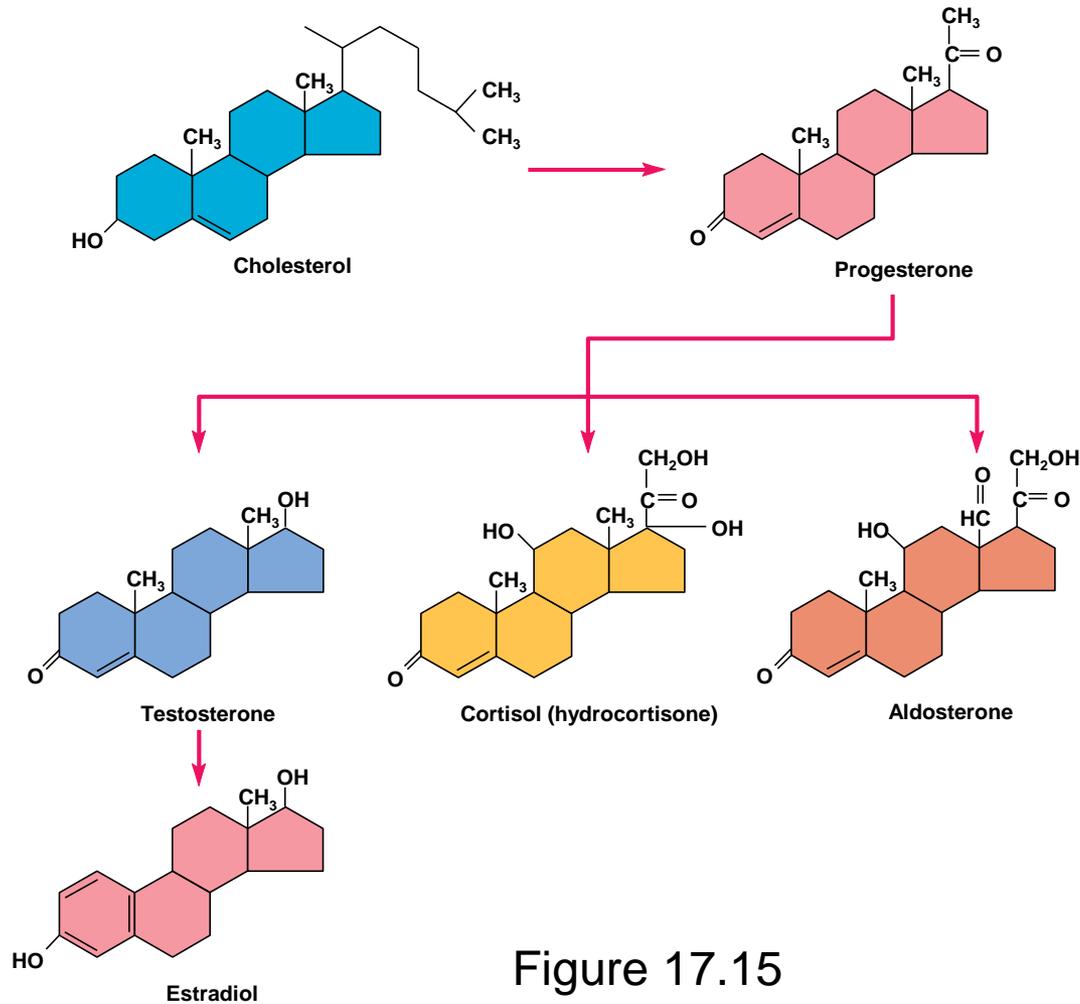


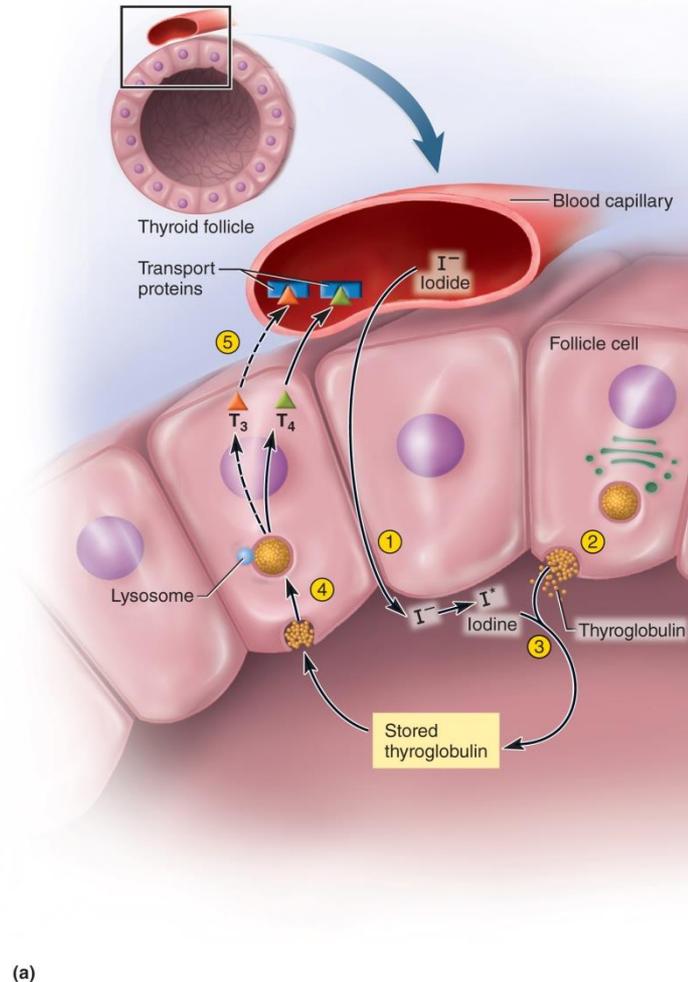
Figure 17.15

- **Steroids are synthesized from cholesterol and differ in functional groups attached to the four-ringed backbone**

Hormone Synthesis - Peptides

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- **Synthesized in same way as any protein**
 - Gene is transcribed to mRNA
 - Peptide is assembled from amino acids at ribosome
 - Rough ER and Golgi may modify peptide to form mature hormone
 - Example: Proinsulin has connecting peptide removed to form insulin (two peptide chains connected by disulfide bridges)



(a) Figure 17.17a

Hormone Synthesis - Monoamines

- **Melatonin** is synthesized from the amino acid **tryptophan**
- **Other monoamines** come from the amino acid **tyrosine**
- **Thyroid hormone** is composed of two tyrosines
 - Follicular cells absorb **iodide (I^-) ions** from blood and oxidize them to a reactive form
 - The cells also synthesize the large protein **thyroglobulin (Tg)** and store it in follicle lumen
 - Iodine (one or two atoms) is added to tyrosines within Tg
 - When two tyrosines within Tg meet, they link to each other forming forerunners of T_3 (three iodines) and T_4 (four iodines)
 - When follicle cell receives TSH, it absorbs Tg and employs lysosomal enzymes to split Tg and free thyroid hormone (TH)
 - TH (mostly as T_4) is released from basal side of follicle cell into blood capillary

Thyroid Hormone Synthesis and Secretion

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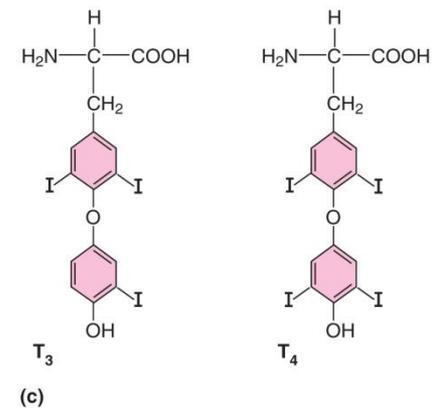
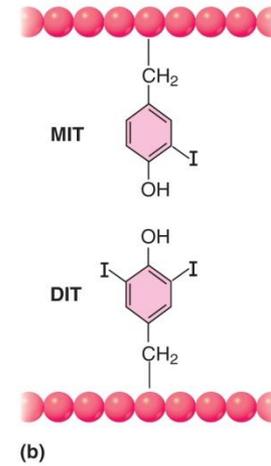
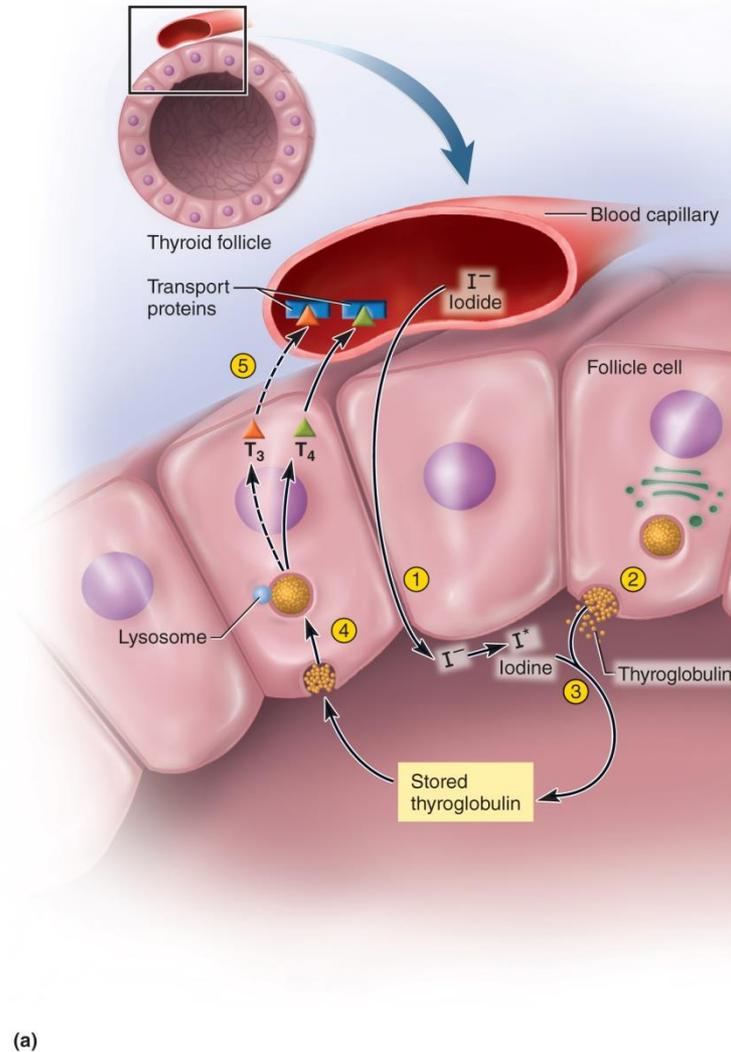


Figure 17.17

Hormone Transport

- Most monoamines and peptides are **hydrophilic**
 - Mix easily with blood plasma
- Steroids and thyroid hormone are **hydrophobic**
 - Bind to **transport proteins** (albumins and globulins synthesized by the liver)
 - **Bound hormones** have longer half-life
 - Protected from liver enzymes and kidney filtration
 - Only **unbound hormone** leaves capillaries to reach target cell
 - Transport proteins protect circulating hormones from being broken down by enzymes in the plasma and liver, and from being filtered out of the blood by the kidneys

Hormone Transport

- **Thyroid hormone binds to three transport proteins in the plasma**
 - **Albumin, thyretin, thyroxine-binding globulin (TGB)**
 - More than 99% of circulating TH is protein bound
- **Steroid hormones bind to globulins**
 - Transcortin: the transport protein for cortisol
- **Aldosterone**—short half-life; 85% unbound, 15% binds weakly to albumin and others

Hormone Receptors and Mode of Action

- **Hormones stimulate only those cells that have receptors for them**
- **Receptors** are protein or glycoprotein molecules
 - On plasma membrane, in the cytoplasm, or in the nucleus
- **Receptors** act like switches turning on metabolic pathways when hormone binds to them

Hormone Receptors and Mode of Action

- Usually each target cell has a few thousand receptors for a given hormone
- Receptor–hormone interactions exhibit **specificity** and **saturation**
 - Specific receptor for each hormone
 - Saturated when all receptor molecules are occupied by hormone molecules

Hormone Receptors and Mode of Action

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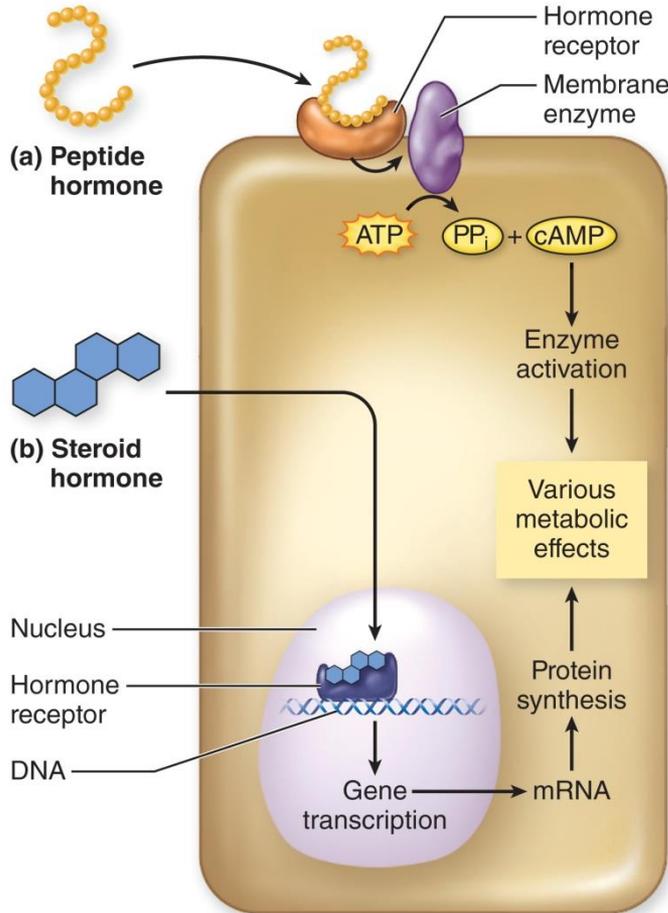


Figure 17.18

- **Peptide hormones**
 - Cannot penetrate target cell
 - Bind to surface receptors and activate intracellular processes through second messengers
- **Steroid hormones**
 - Penetrate plasma membrane and bind to internal receptors (usually in nucleus)
 - Influence expression of genes of target cell
 - Take several hours to days to show effect due to lag for protein synthesis

Steroids and Thyroid Hormone

- **Estrogen binds to nuclear receptors in cells of uterus**
 - It activates the gene for the progesterone receptor
 - Progesterone comes later in the menstrual cycle and binds to these receptors stimulating transcription of a gene for a nutrient synthesizing enzyme
- **Thyroid hormone enters target cell by means of an ATP-dependent transport protein**
 - Within target cell, T_4 is converted to more potent T_3
 - T_3 binds to nuclear receptors and activates gene for the sodium-potassium pump

Peptides and Catecholamines

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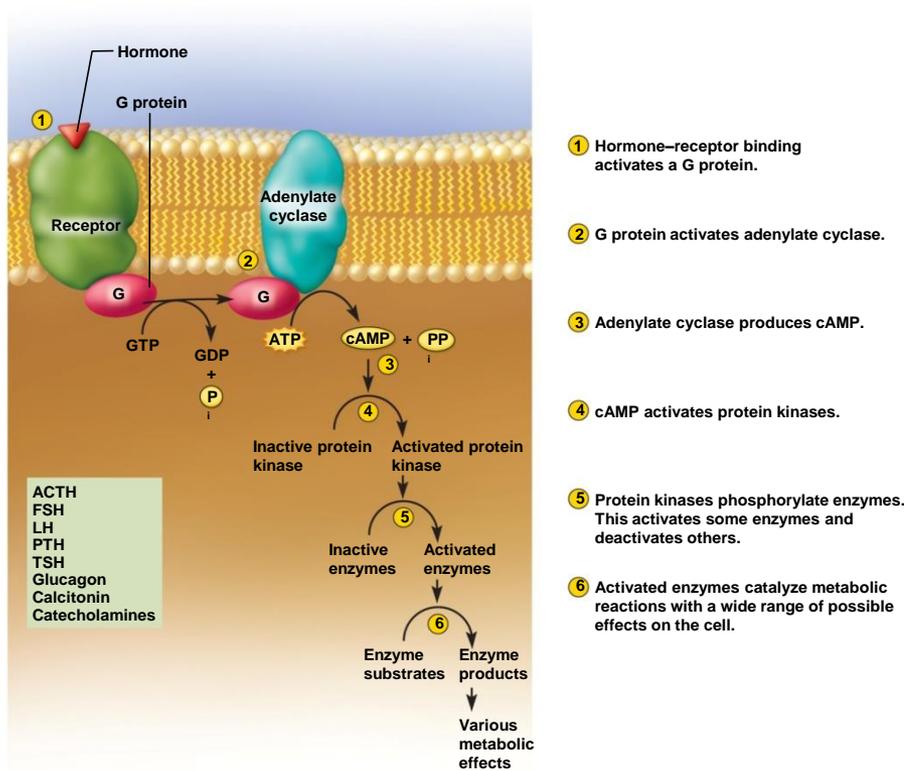


Figure 17.19

- Hormone binds to cell-surface receptor
- Activates G protein
- Activates adenylate cyclase
- Produces cAMP
- Activates or inhibits enzymes
- Metabolic reactions
 - Synthesis
 - Secretion
 - Change membrane potentials
- Phosphodiesterase breaks down cAMP

Peptides and Catecholamines

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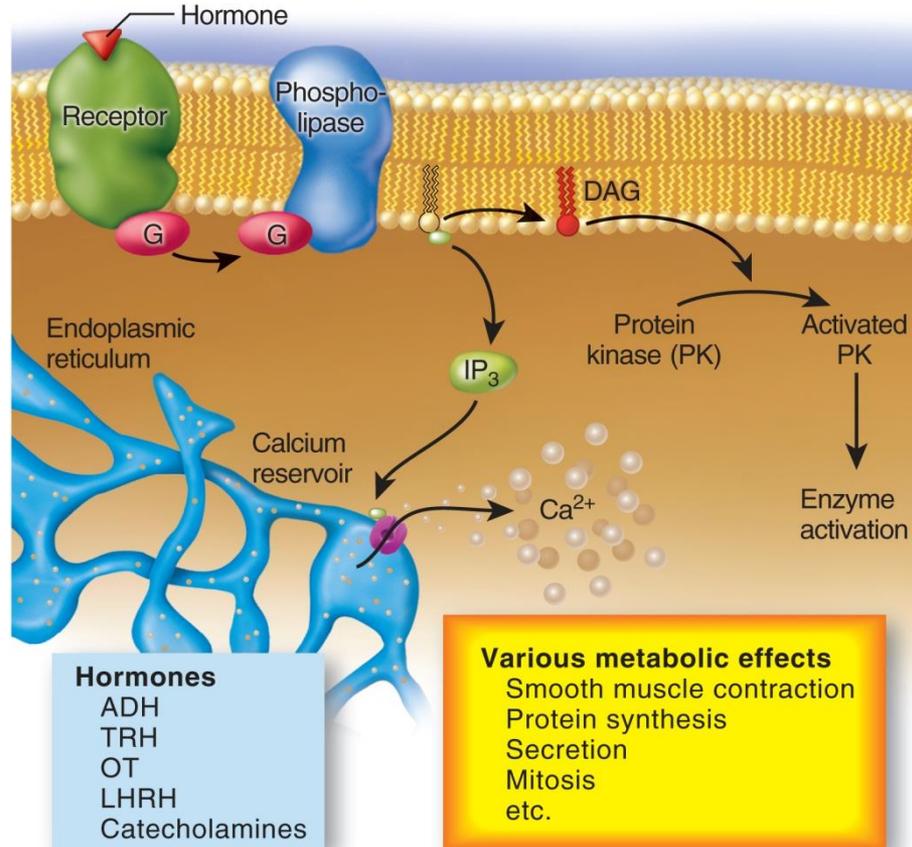


Figure 17.20

- Membrane receptors can alter metabolism through other second messenger systems causing varied effects
- Diacylglycerol (diglyceride) activates a protein kinase
- Inositol triphosphate system increases Ca⁺⁺

Signal Amplification

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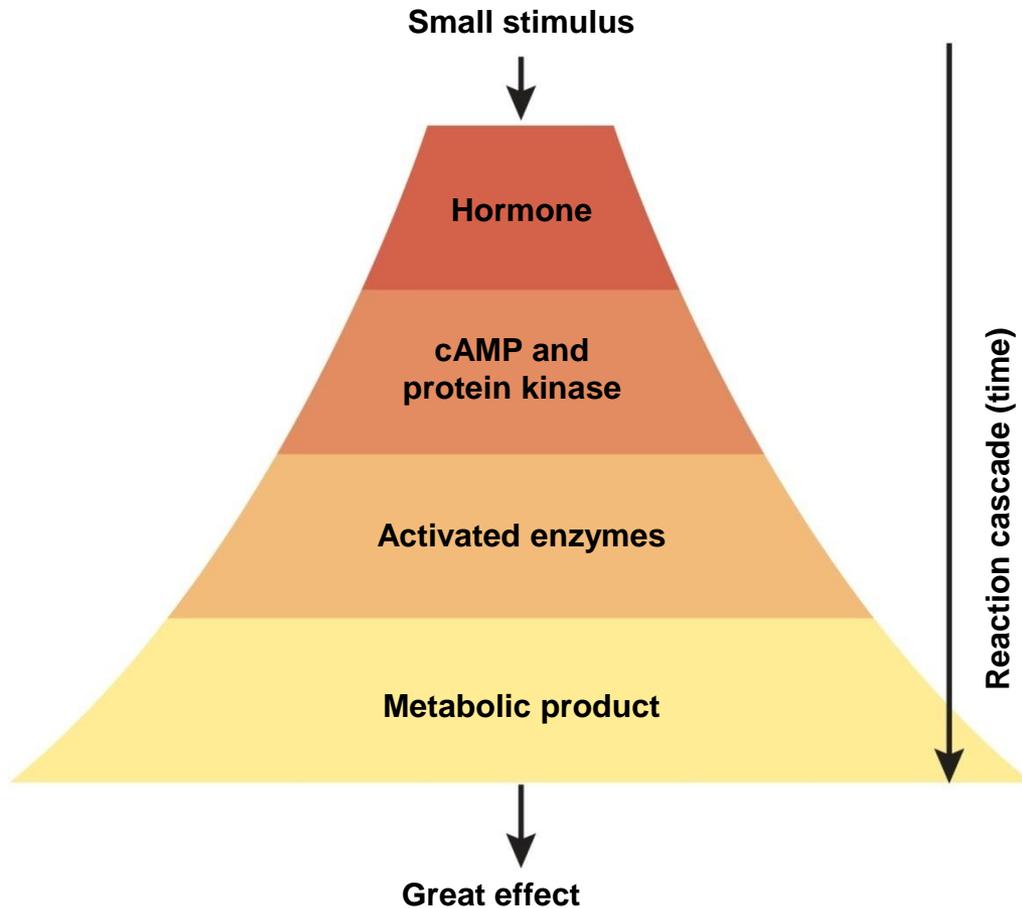
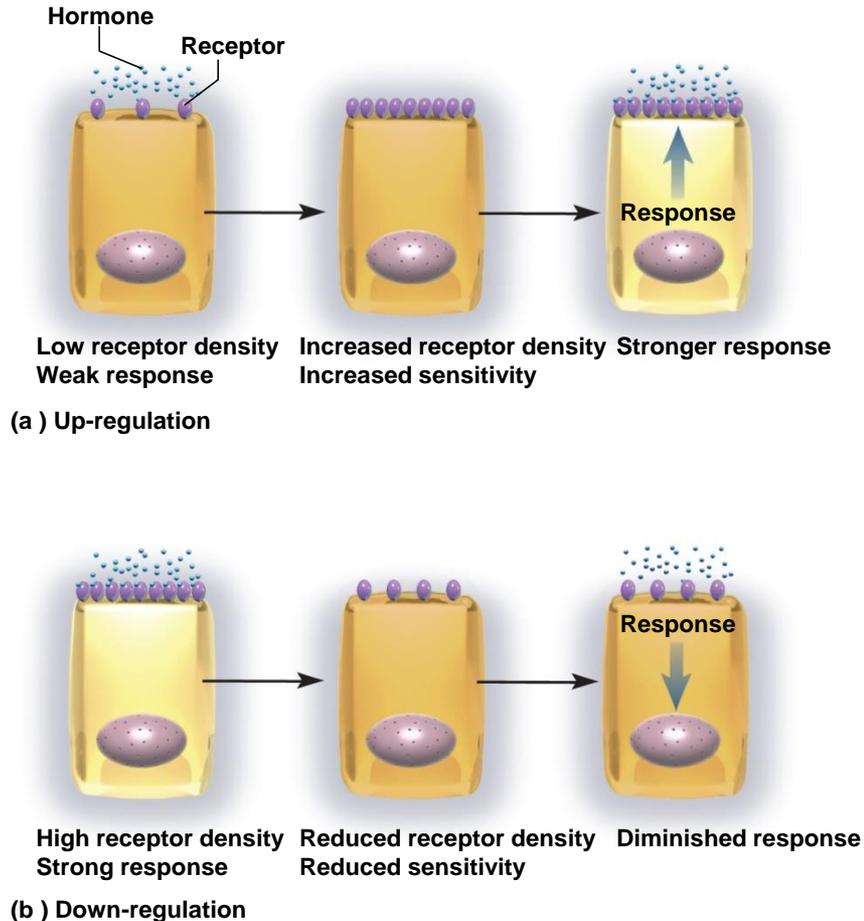


Figure 17.21

- **Hormones are extraordinarily potent chemicals**
- **One hormone molecule can activate many enzyme molecules**
- **Very small stimulus can produce very large effect**
- **Hormone concentrations in blood are low**

Modulation of Target-Cell Sensitivity

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- **Target-cell sensitivity adjusted by changing the number of receptors**
- **Up-regulation** means number of receptors is increased
 - Sensitivity is increased
- **Down-regulation** reduces number of receptors
 - Cell less sensitive to hormone
 - Happens with long-term exposure to high hormone concentrations

Figure 17.22

Hormone Interactions

- **Most cells sensitive to more than one hormone and exhibit interactive effects**
- **Synergistic effects**
 - Multiple hormones act together for greater effect
 - Synergism between FSH and testosterone on sperm production
- **Permissive effects**
 - One hormone enhances the target organ's response to a second later hormone
 - Estrogen prepares uterus for action of progesterone
- **Antagonistic effects**
 - One hormone opposes the action of another
 - Insulin lowers blood glucose and glycogen raises it

Hormone Interactions

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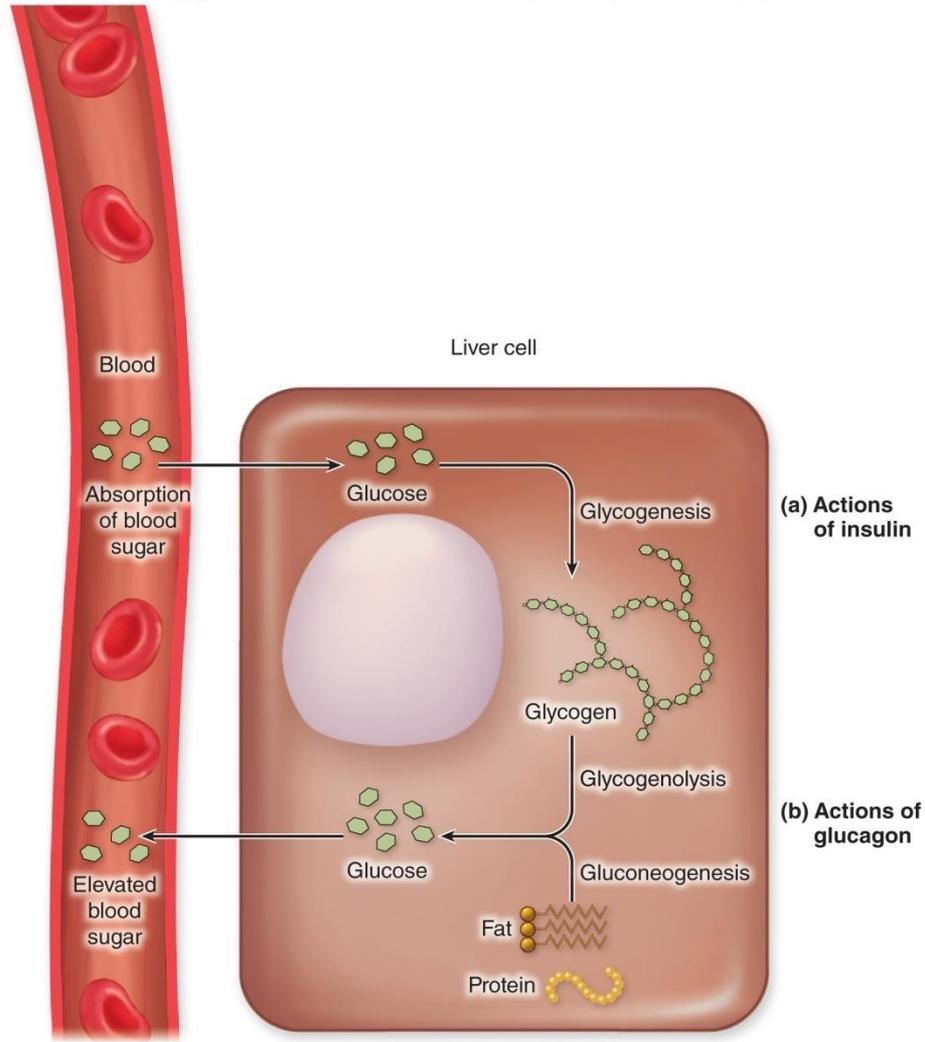


Figure 17.23

Hormone Clearance

- **Hormone signals must be turned off when they have served their purpose**
- Most hormones are taken up and degraded by **liver and kidney**
 - Excreted in bile or urine
- **Metabolic clearance rate (MCR)**
 - Rate of hormone removal from the blood
 - **Half-life:** time required to clear 50% of hormone from the blood
 - The faster the MCF, the shorter the half-life

Stress and Adaptation

- **Expected Learning Outcomes**
 - Give a physiological definition of stress.
 - Discuss how the body adapts to stress through its endocrine and sympathetic nervous systems.

Stress and Adaptation

- **Stress**—situation that upsets homeostasis and threatens one's physical or emotional well-being
 - Injury, surgery, infection, intense exercise, pain, grief, depression, anger, etc.
- **General adaptation syndrome (GAS)**
 - Consistent way the body reacts to stress; typically involves elevated levels of epinephrine and glucocorticoids (especially cortisol)
 - Occurs in three stages
 - **Alarm reaction**
 - **Stage of resistance**
 - **Stage of exhaustion**

The Alarm Reaction

- **Initial response**

- Mediated by **norepinephrine** from the **sympathetic nervous system** and **epinephrine** from the **adrenal medulla**
- Prepares body for fight or flight
- Stored glycogen is consumed
- Increases **aldosterone** and **angiotensin** levels
 - Angiotensin helps raise blood pressure
 - Aldosterone promotes sodium and water conservation

The Stage of Resistance

- After a few hours, glycogen reserves gone, but brain still needs glucose
- Provide alternate fuels for metabolism
- Stage dominated by **cortisol**
- Hypothalamus secretes **corticotropin-releasing hormone (CRH)**
- Pituitary secretes **ACTH**
 - Stimulates the adrenal cortex to secrete **cortisol** and other **glucocorticoids**
 - Promotes breakdown of fat and protein into glycerol, fatty acids, and amino acids, for **gluconeogenesis**

The Stage of Resistance

- Cortisol has **glucose-sparing effect**—inhibits protein synthesis leaving free amino acids for gluconeogenesis
 - Adverse effects of excessive cortisol:
 - Depresses immune function
 - Increases susceptibility to infection and ulcers
 - Lymphoid tissues atrophy, antibody levels drop, and wounds heal poorly

The Stage of Exhaustion

- **When stress continues for several months, and fat reserves are gone, homeostasis is overwhelmed**
 - Often marked by rapid decline and death
- **Protein breakdown and muscle wasting**
- **Loss of glucose homeostasis because adrenal cortex stops producing glucocorticoids**
- **Aldosterone promotes water retention and hypertension**
 - Conserves sodium and hastens elimination of K^+ and H^+
 - Hypokalemia and alkalosis leads to death
- **Death results from heart and kidney infection or overwhelming infection**

Eicosanoids and Paracrine Signaling

- **Expected Learning Outcomes**
 - Explain what eicosanoids are and how they are produced.
 - Identify some classes and functions of eicosanoids.
 - Describe several physiological roles of prostaglandins.

Eicosanoids and Paracrine Signaling

- **Paracrines**—chemical messengers that diffuse short distances and stimulate nearby cells
 - Histamine
 - From mast cells in connective tissue
 - Causes relaxation of blood vessel
 - Nitric oxide
 - From endothelium of blood vessels, causes vasodilation
 - Catecholamines
 - Diffuse from adrenal medulla to cortex
- **A single chemical can act as a hormone, paracrine, or even neurotransmitter in different locations**

Eicosanoids and Paracrine Signaling

- **Eicosanoids**—important family of paracrines
 - Derived from fatty acid called **arachidonic acid**
- **Lipoxygenase** converts arachidonic acid into leukotrienes
 - **Leukotrienes**
 - Mediate allergic and inflammatory reactions

Eicosanoids and Paracrine Signaling

(Continued)

- **Cyclooxygenase** converts arachidonic acid to three other types of eicosanoids
 - **Prostacyclin**
 - Inhibits blood clotting and vasoconstriction
 - **Thromboxanes**
 - Produced by blood platelets after injury
 - Overrides prostacyclin
 - Stimulates vasoconstriction and clotting
 - **Prostaglandins**
 - PGE—relaxes smooth muscle in bladder, intestines, bronchioles, uterus; stimulates contraction of blood vessels
 - PGF—causes opposite effects

Eicosanoid Synthesis

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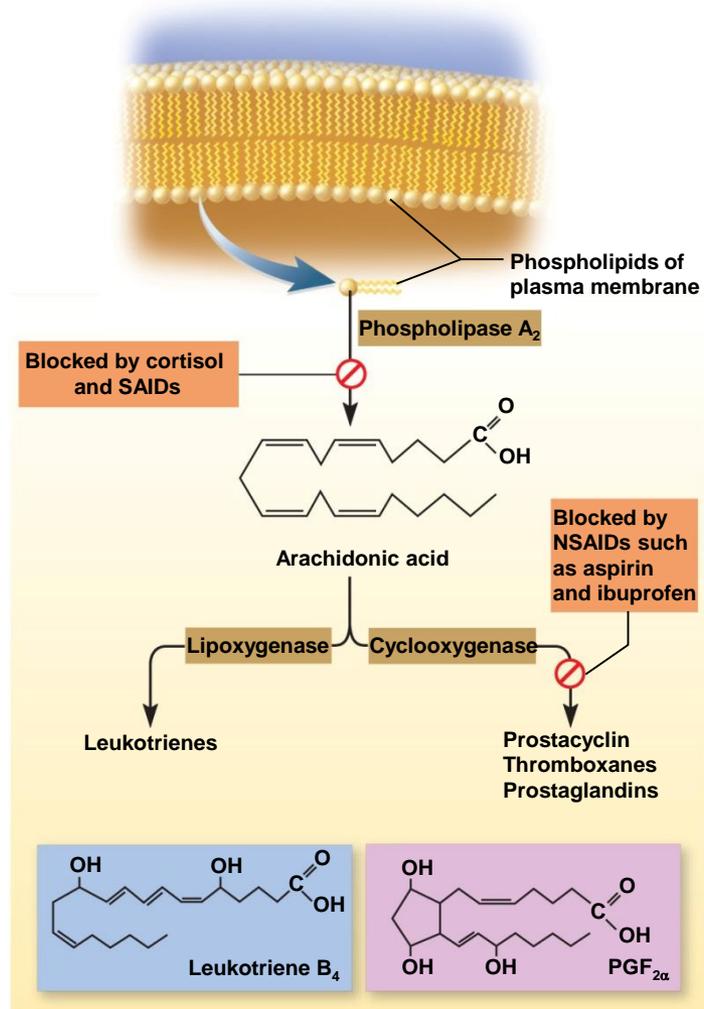


Figure 17.24

Anti-Inflammatory Drugs

- **Cortisol and corticosterone**
 - Steroidal anti-inflammatory drugs (SAIDs)
 - Inhibit inflammation by blocking release of arachidonic acid from plasma membrane and inhibit synthesis of eicosanoids
 - Disadvantage—produce symptoms of Cushing syndrome
- **Aspirin, ibuprofen, and celecoxib (Celebrex)**
 - Nonsteroidal anti-inflammatory drugs (NSAIDs)
 - **COX inhibitors** since block cyclooxygenase (COX)
 - Do not affect lipoxygenase function or leukotriene production
 - Useful in treatment of fever and thrombosis
 - Inhibit prostaglandin and thromboxane synthesis

Endocrine Disorders

- **Expected Learning Outcomes**
 - Explain some general causes and examples of hormone hyposecretion and hypersecretion.
 - Briefly describe some common disorders of pituitary, thyroid, parathyroid, and adrenal function.
 - In more detail, describe the causes and pathology of diabetes mellitus.

Endocrine Disorders

- **Variations in hormone concentration and target-cell sensitivity have noticeable effects on body**
- **Hyposecretion**—inadequate hormone release
 - Tumor or lesion destroys gland or interferes with its ability to receive signals from another gland
 - Head trauma affects pituitary gland's ability to secrete ADH
 - **Diabetes insipidus**: chronic polyuria
 - Autoantibodies fail to distinguish person's own gland from foreign matter
 - One cause of diabetes mellitus

Endocrine Disorders

- **Hypersecretion**—excessive hormone release
 - Tumors or autoimmune disorder
 - **Pheochromocytoma**—tumor of adrenal medulla secretes excessive epinephrine and norepinephrine
 - **Toxic goiter (Graves disease)**—autoantibodies mimic effect of TSH on the thyroid (bind and activate TSH receptor), causing thyroid hypersecretion

Pituitary Disorders

- **Hypersecretion of growth hormone (GH)**
 - **Acromegaly:** thickening of bones and soft tissues in adults
 - Especially hands, feet, and face
 - Problems in childhood or adolescence (before growth plates are depleted)
 - **Gigantism** if hypersecretion
 - Pituitary **dwarfism** if hyposecretion—rare since growth hormone is now made by genetically engineered bacteria

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Age 9



Age 16



Age 33



Age 52

(all): From Clinical Pathological Conference "Acromegaly, Diabetes, Hypermetabolism, Proteinuria and Heart Failure" in *American Journal of Medicine*, 20:133, 1956. Copyright © 1986 by Excerpta Media, Inc

Figure 17.25

Thyroid and Parathyroid Disorders

- **Congenital hypothyroidism (decreased TH)**
 - Hyposecretion present a birth
 - Treat with oral thyroid hormone
- **Myxedema (decreased TH)**
 - Adult hypothyroidism
 - Treat with oral thyroid hormone
- **Goiter**—any pathological enlargement of the thyroid gland
 - **Endemic goiter** (disease occurs in a geographic locality)
 - Dietary iodine deficiency, no TH, no feedback, increased TSH stimulates hypertrophy

Endemic Goiter

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Figure 17.26

Thyroid and Parathyroid Disorders

- **Hypoparathyroidism**

- Surgical excision during thyroid surgery
- Fatal tetany (spasms in larynx) in just a few days due to rapid decline in blood calcium level

- **Hyperparathyroidism: excess PTH secretion**

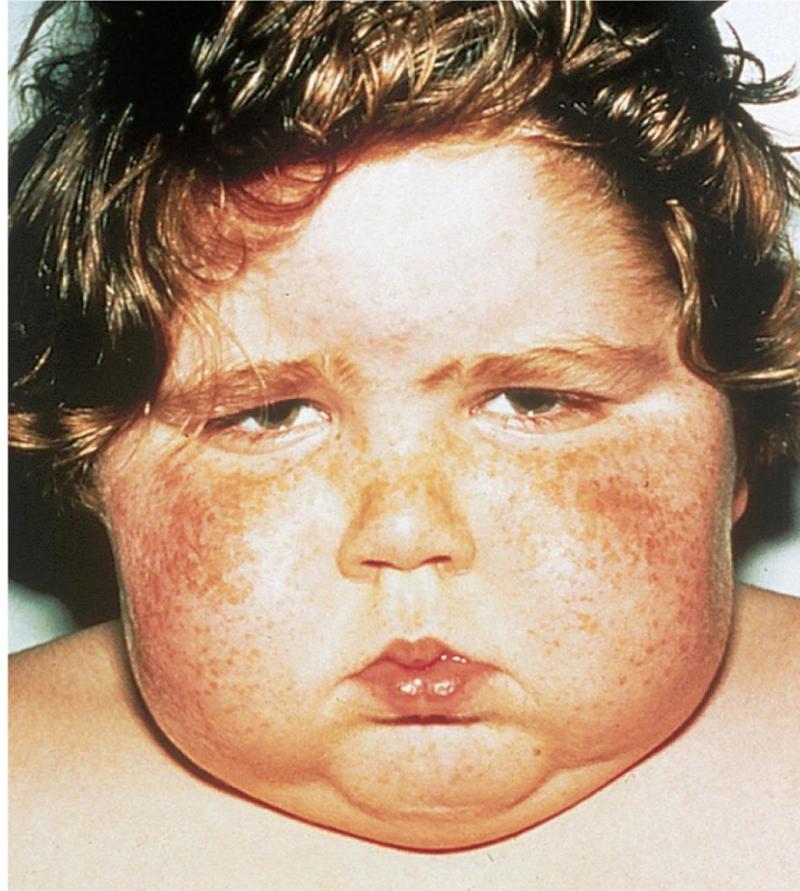
- Parathyroid tumor
- Bones become soft, fragile, and deformed
- Ca^{2+} and phosphate blood levels increase
- Promotes renal calculi formation

Adrenal Disorders

- **Cushing syndrome**—excess cortisol secretion
 - Hyperglycemia, hypertension, weakness, edema
 - Rapid muscle and bone loss due to protein catabolism
 - Abnormal fat deposition
 - Moon face and buffalo hump
- **Adrenogenital syndrome (AGS)**
 - Adrenal androgen hypersecretion (accompanies Cushing)
 - Enlargement of external sexual organs in children and early onset of puberty
 - Newborn girls exhibit masculinized genitalia
 - Masculinizing effects on women
 - Increased body hair, deeper voice, beard growth

Cushing Syndrome

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(b)

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Figure 17.27b

Diabetes Mellitus

- **Most prevalent metabolic disease in the world**
 - Disruption of metabolism due to hyposecretion or inaction of insulin
 - Symptoms
 - **Polyuria (excess urine output), polydipsia (intense thirst), and polyphagia (hunger)**
 - Revealed by elevated blood glucose, glucose in urine, and ketones in the urine
 - Polyuria (with thirst and dehydration) occurs because kidneys exhibit a **transport maximum**—limit to how fast the glucose transporters can work to reabsorb
 - Excess glucose enters urine and water follows it

Types and Treatment

- **Type 1 diabetes mellitus (IDDM)**—5% to 10% of cases in United States
 - **Insulin** is always used to treat type 1
 - Insulin injections, insulin pump, or dry insulin inhaler
 - Monitoring blood glucose levels and controlled diet
 - Hereditary susceptibility
 - If susceptible individual is infected with certain viruses (rubella, cytomegalovirus), autoantibodies attack and destroy pancreatic beta cells

Types and Treatment

- **Type 2 (NIDDM)**—90% to 95% of diabetics
 - Problem is **insulin resistance**
 - Failure of target cells to respond to insulin
 - Risk factors are heredity (36 genes so far known to increase risk), age (40+), obesity, and ethnicity (Native American, Hispanic, and Asian)
 - Treated with weight-loss program and exercise since:
 - Loss of muscle mass causes difficulty with regulation of glycemia
 - Adipose signals interfere with glucose uptake into most cells
 - If necessary, also use glycemia-lowering oral medications and, if still not enough, use insulin

Pathogenesis

- **Pathogenesis—cells cannot absorb glucose, must rely on fat and proteins for energy needs, thus weight loss and weakness**
 - Fat catabolism increases free fatty acids and ketones in blood
 - **Ketonuria** promotes osmotic diuresis, loss of Na^+ and K^+ , irregular heartbeat, and neurological issues
 - **Ketoacidosis** occurs as ketones decrease blood pH
 - Deep, gasping breathing and diabetic coma are terminal result

Pathogenesis

- **Chronic pathology (chronic hyperglycemia)**
 - Leads to neuropathy and cardiovascular damage from atherosclerosis and microvascular disease
 - Arterial damage in retina and kidneys (common in type 1), atherosclerosis leads to heart failure (common in type 2)
 - **Diabetic neuropathy**—nerve damage from impoverished blood flow can lead to erectile dysfunction, incontinence, poor wound healing, and loss of sensation from area