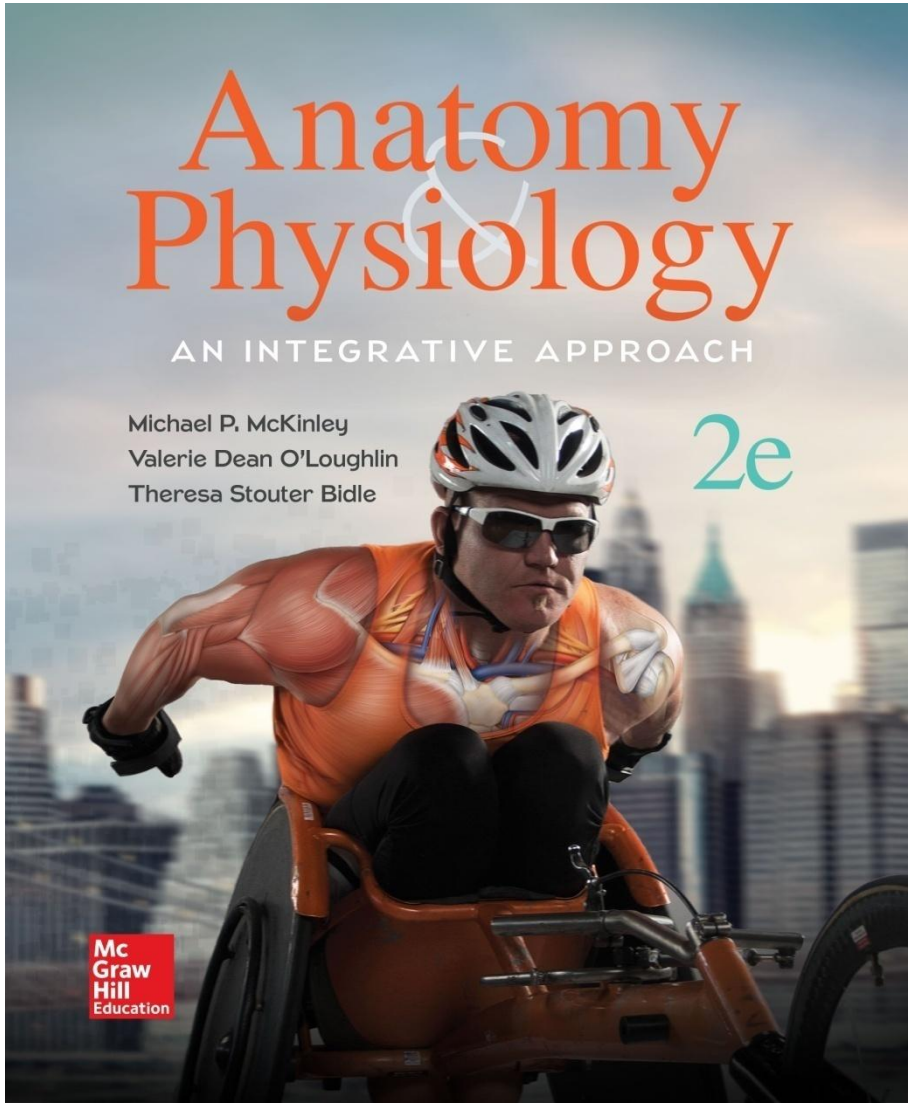
Chapter 17
Lecture Outline

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



17.1 Introduction to the Endocrine System

Learning Objectives:

1. Compare and contrast the actions of the endocrine system and the nervous system to control body function.
2. Describe the general functions controlled by the endocrine system.

17.1 Introduction to the Endocrine System

- **Endocrine system**
  - Composed of ductless glands that synthesize and secrete **hormones**
    - Hormones are released into the blood and transported throughout the body
  - **Target cells** have the specific receptors for a hormone
    - They bind hormone and respond
  - Endocrine and nervous systems are the two control systems of the body

17.1a Comparison of the Two Control Systems

- Both the endocrine and nervous system
  - Release **ligands**—chemical messengers
    - Ligands bind to cellular receptor on particular target cells
- Unlike the nervous system, the endocrine system
  - Transmits hormones through the blood
  - Targets any cells in the body with correct receptors
    - Can be very widespread
  - Exhibits longer reaction times
  - Has longer-lasting effects (minutes to days and weeks)

Nervous and Endocrine System Communication Methods

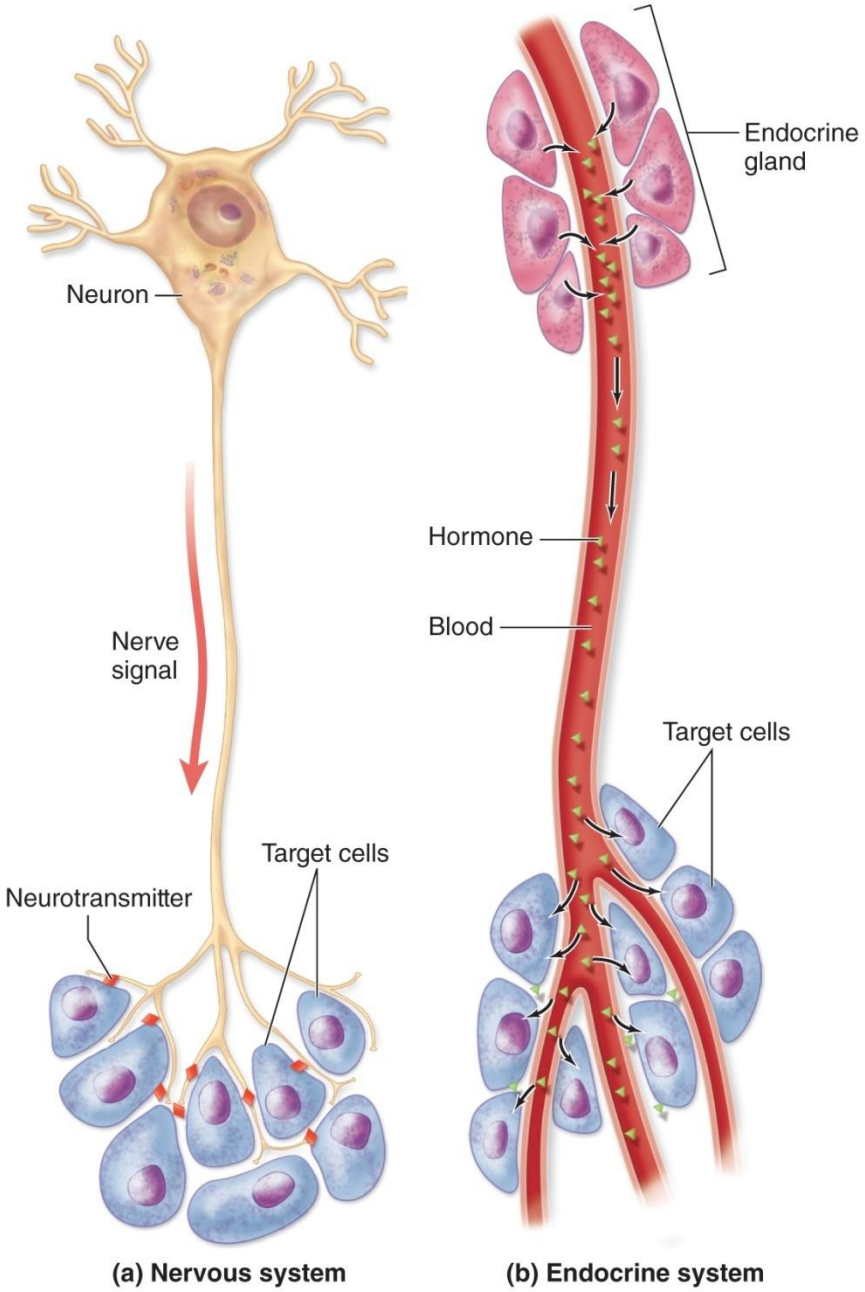


Figure 17.1

17.1b General Functions of the Endocrine System

- Regulating development, growth, and metabolism
  - Hormones help regulate embryonic cell division and differentiation
  - Hormones regulate metabolism (both anabolism and catabolism)
- Maintaining homeostasis of blood composition and volume
  - Hormones regulate blood solute concentrations (e.g., glucose, ions)
  - Hormones regulate blood volume, cellular concentration, and platelet number
- Controlling digestive processes
  - Hormones influence secretory processes and movement of materials in digestive tract
- Controlling reproductive activities
  - Hormones affect development and function of reproductive systems and the expression of sexual behaviors

What did you learn?

- Which control system typically has slower, longer-lasting effects?
- What general effects can hormones have on the characteristics of blood?

17.2 Endocrine Glands

Learning Objectives:

1. Distinguish between the two types of organization of endocrine cells.
2. Identify the major endocrine glands and their location within the body.
3. Explain the three reflex mechanisms for regulating secretion of hormones.

17.2a Location of the Major Endocrine Glands

- Glands contain epithelial tissue that makes and releases hormones
  - Some glands are **endocrine organs** with solely endocrine function
    - Include: pituitary, pineal, thyroid, parathyroid, and adrenal glands
  - Some "glands" are clusters of cells in organs with another function
    - Examples in: hypothalamus, skin, thymus, heart, liver, stomach, pancreas, small intestine, adipose connective tissue, kidneys, and gonads

Location of the Major Endocrine Glands and Organs Containing Endocrine Cells

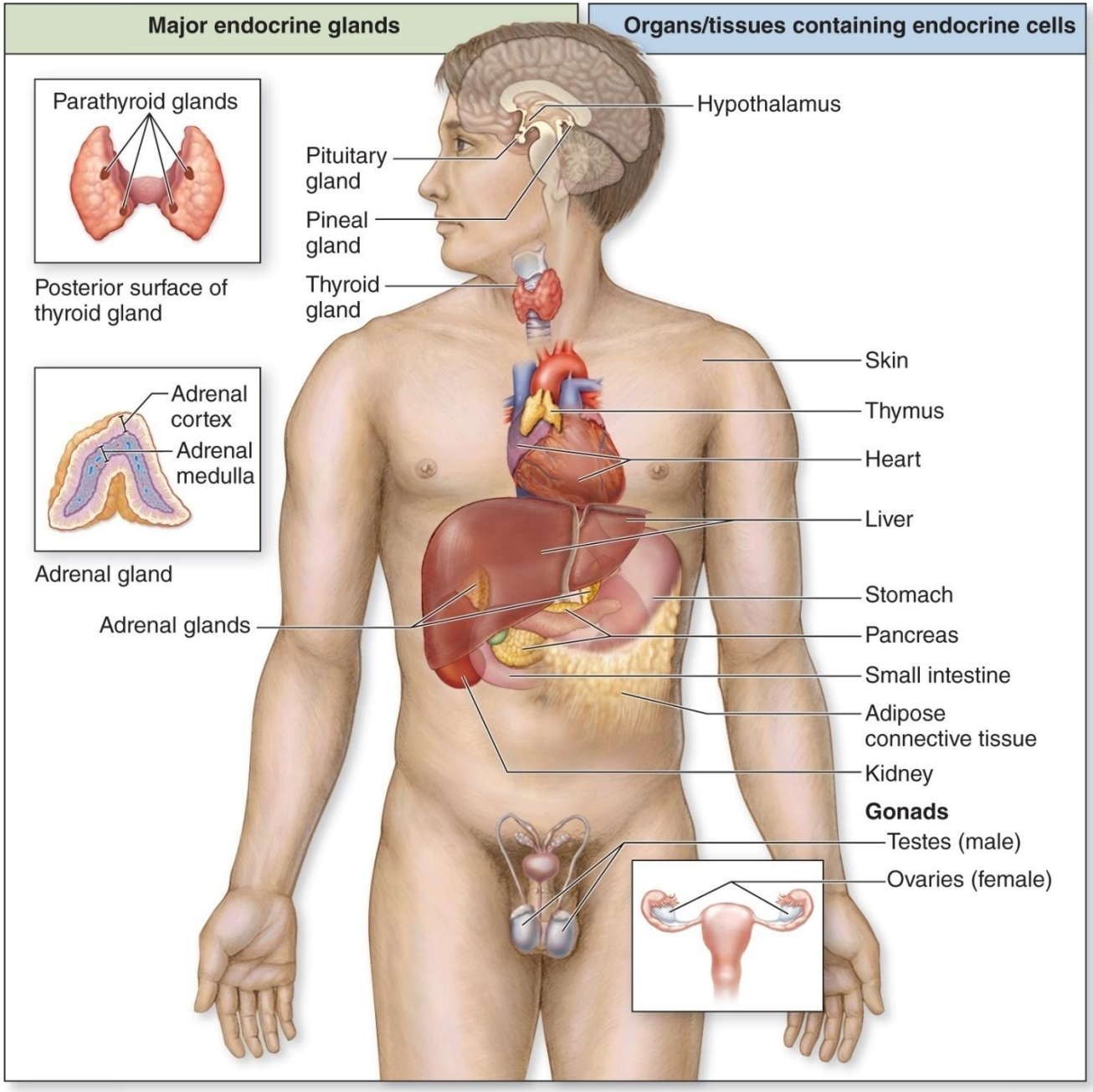
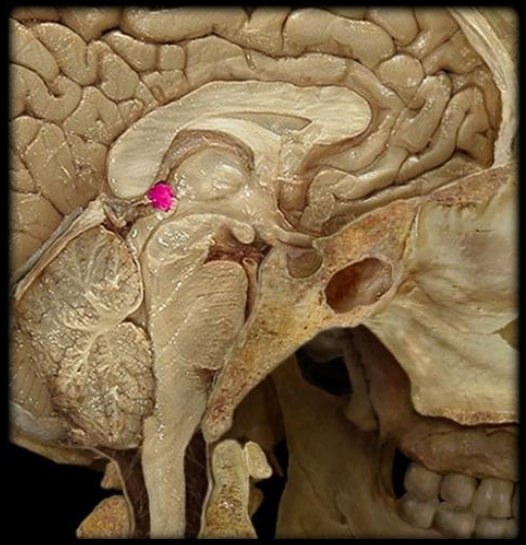


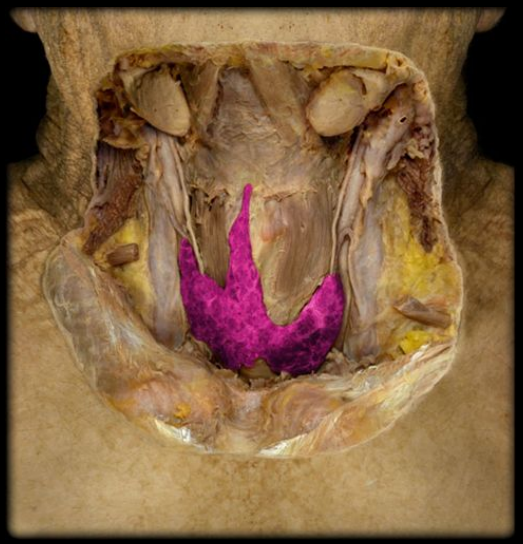
Figure 17.2

Endocrine Glands

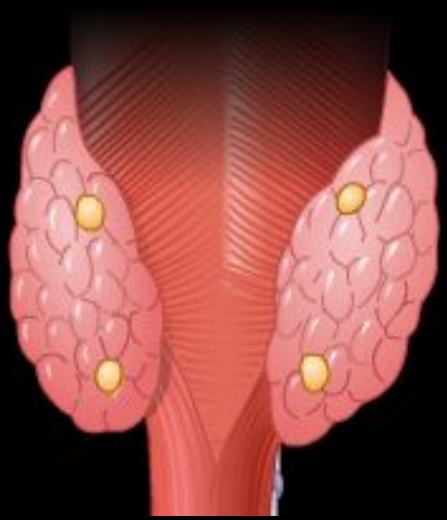


Pineal Gland

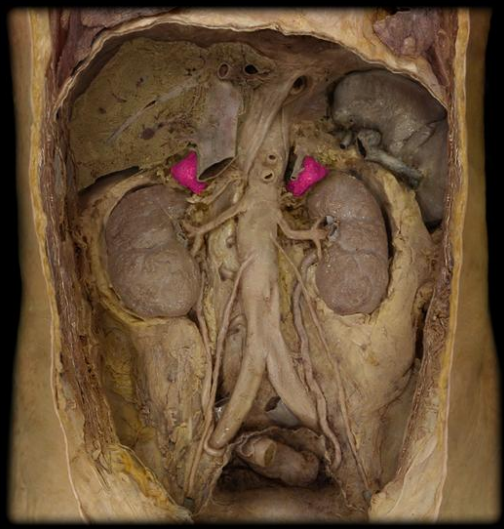
Pituitary Gland



Thyroid Gland

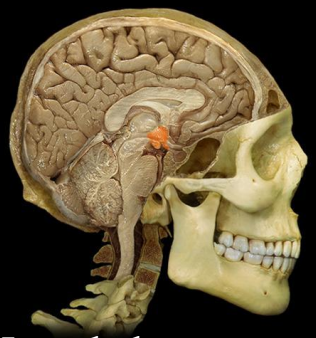


Parathyroid Glands

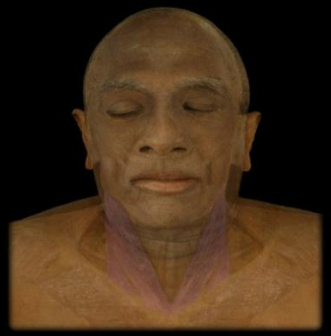


Adrenal Glands

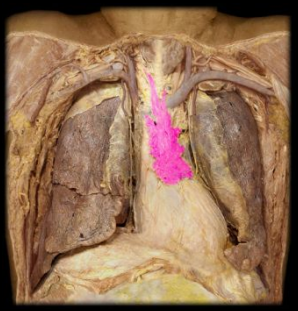
Organs Containing Endocrine Cells



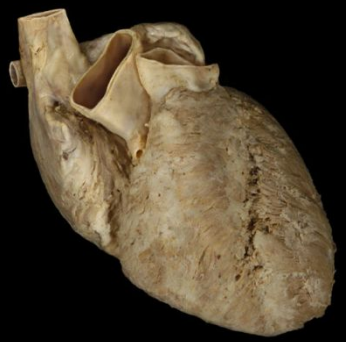
Hypothalamus



Skin

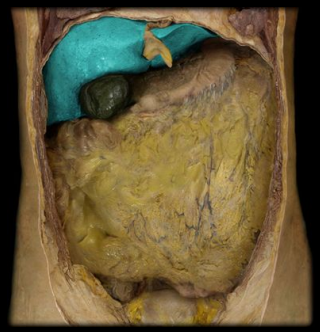


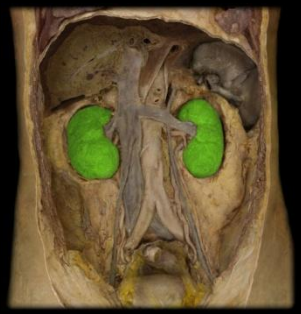
Thymus



Heart

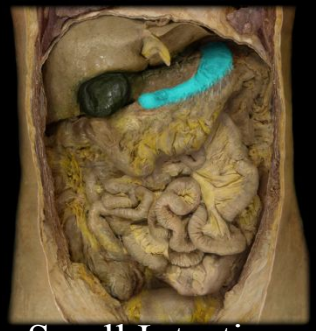
Liver





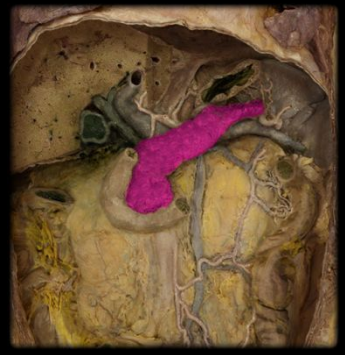
Kidneys

Stomach



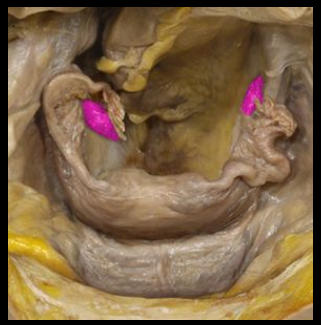
Small Intestines

Pancreas



Testis

Ovaries



17.2b Stimulation of Hormone Synthesis and Release

- Hormone release is regulated by reflexes to stimuli
- Hormonal, humoral, or nervous stimuli can initiate hormone release
  - **Hormonal stimulation**
    - A gland cell releases its hormone when some other hormone binds to it
  - **Humoral stimulation**
    - A gland cell releases its hormone when there is a certain change in levels of a nutrient or ion in the blood
  - **Nervous stimulation**
    - A gland cell releases its hormone when a neuron stimulates it

Types of Endocrine Stimulation

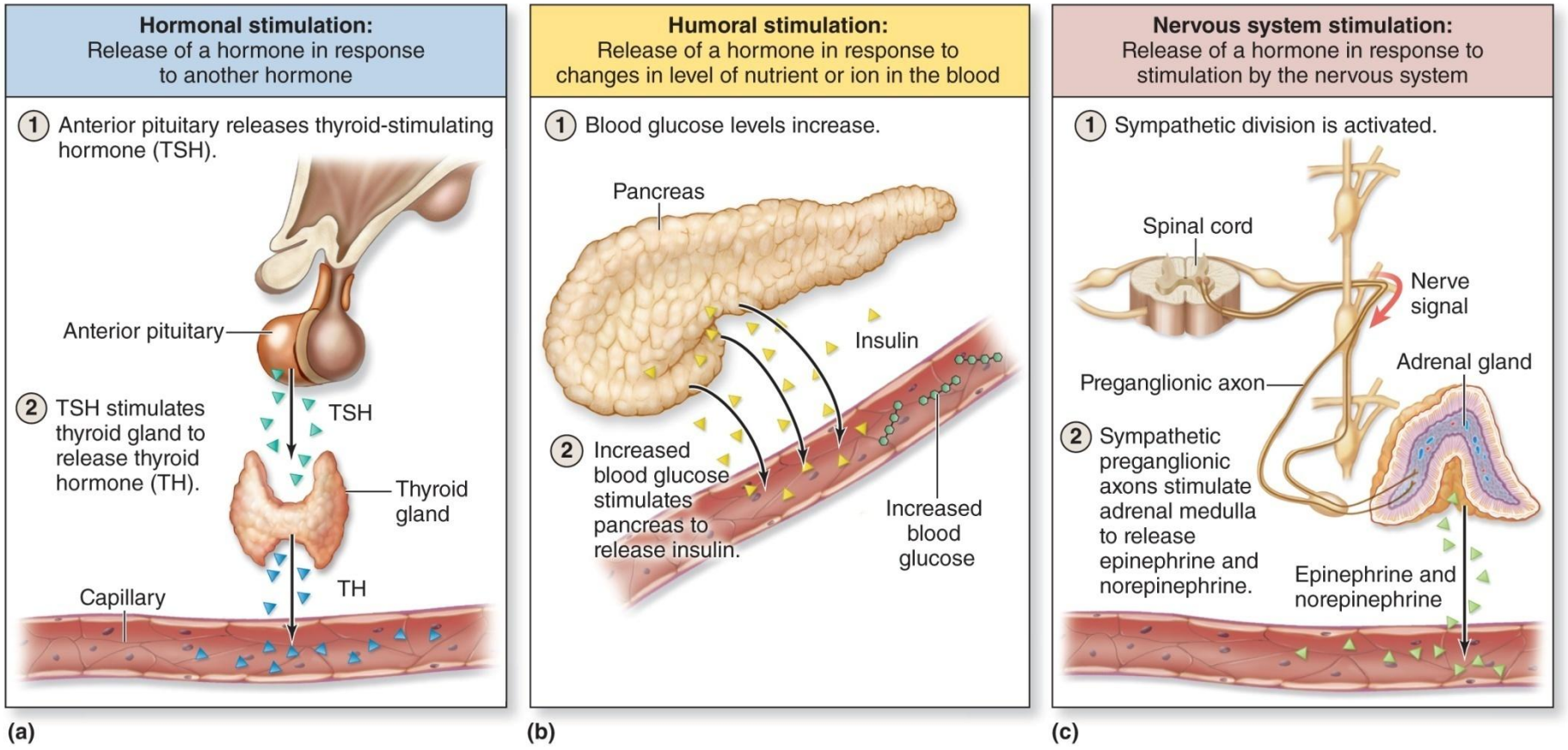


Figure 17.3

What did you learn?

- Is the entire pancreas an endocrine organ?
- Parathyroid hormone is secreted when blood calcium levels drop too low. What sort of stimulation is this?

17.3 Hormones

Learning Objectives:

1. Name the three structural categories of circulating hormones, and give examples within each category.
2. Distinguish the hormones that are lipid-soluble from those that are water-soluble.
3. Describe the general structure, formation, and function of local hormones.
4. Compare autocrine and paracrine signaling that occurs through local hormones.

17.3a Categories of Circulating Hormones

- **Steroids**
  - Lipid-soluble molecules synthesized from cholesterol
  - Includes gonadal steroids (e.g., estrogen)
  - Includes steroid synthesized by adrenal cortex (e.g., cortisol)
  - Calcitriol sometimes classified in this group, but more accurately called a *sterol*

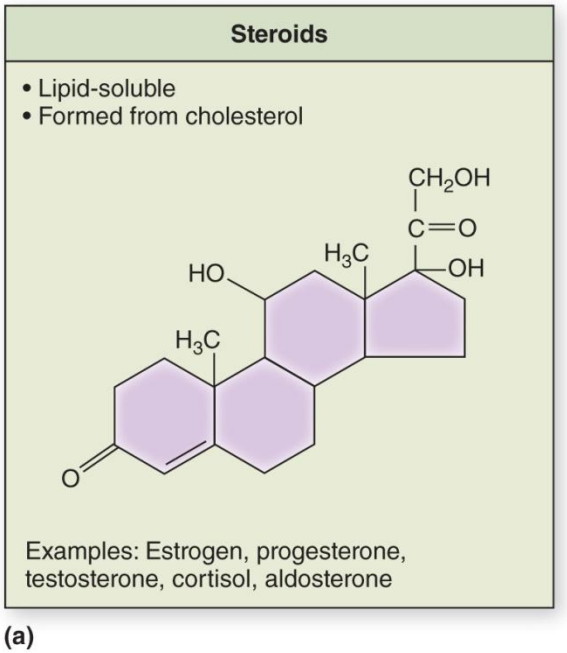


Figure 17.4a

17.3a Categories of Circulating Hormones

- **Biogenic amines** (*monoamines*)
  - Modified amino acids
  - Includes: catecholamines, thyroid hormone, melatonin
  - Water-soluble except for thyroid hormone (TH)
    - TH is nonpolar (made from a pair of tyrosines) and lipid soluble

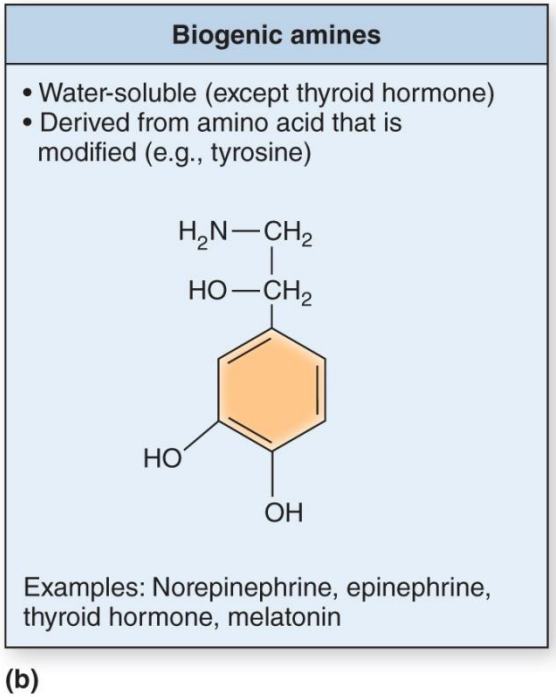


Figure 17.4b

17.3a Categories of Circulating Hormones

- **Proteins**
  - Most hormones are in this category
  - Water-soluble chains of amino acids

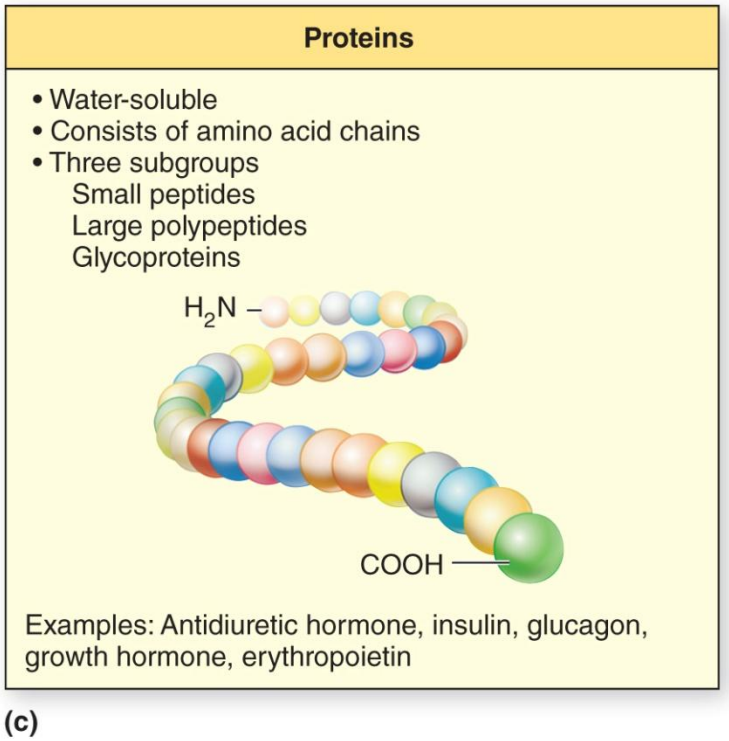


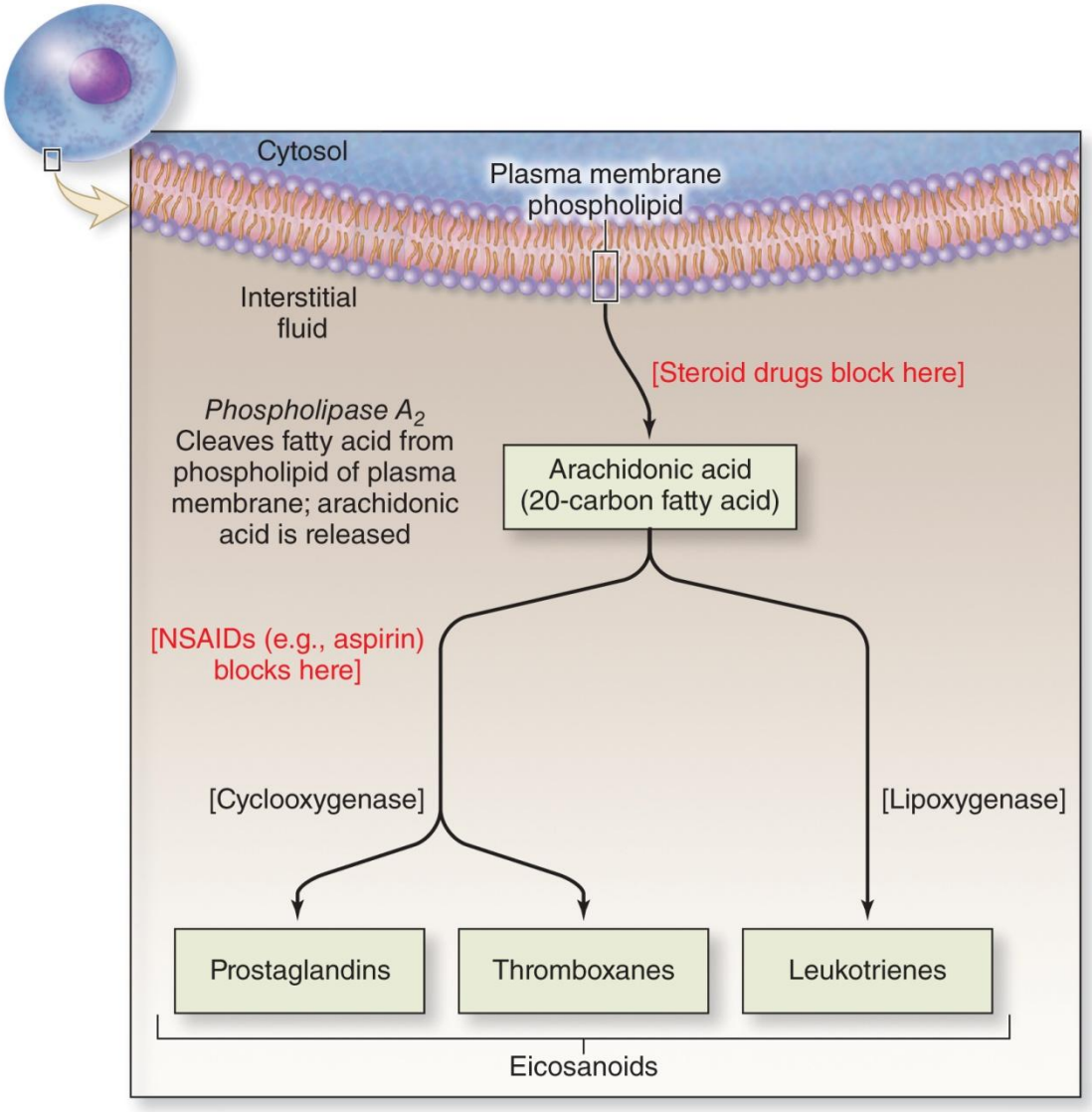
Figure 17.4c

17.3b Local Hormones

- **Local hormones**
  - Signaling molecules that don't circulate in blood
    - Some biologists don't consider them "hormones"
  - They bind to neighboring cells or the cells that release them
- **Eicosanoids:** a type of local hormone formed from fatty acids within phospholipid bilayer of membrane
  - Synthesized through an enzymatic cascade

17.3b Local Hormones

- **Eicosanoid** production
  - Phospholipase A_2 removes arachidonic acid from phospholipid
  - Other enzymes convert arachidonic acid to a subtype of eicosanoid



17.3b Local Hormones

- Eicosanoid effects
  - **Autocrine stimulation**
    - Effects on the same cell where messenger was formed
  - **Paracrine stimulation**
    - Effects on neighboring cells
- Prostaglandins are eicosanoids
  - Stimulate pain and inflammatory responses
  - Aspirin and other nonsteroidal anti-inflammatory drugs block prostaglandin formation

What did you learn?

- Insulin is made up of a chain of amino acids. What class of hormone is it? Is it water soluble or lipid soluble?
- How are prostaglandins synthesized?

17.4 Hormone Transport

Learning Objectives:

1. Compare the transport of lipid-soluble hormones with that of water-soluble hormones.
2. Describe the two primary factors that affect the concentration level of a circulating hormone.
3. Explain what is meant by the half-life of a hormone.

17.4a Transport in the Blood

- Lipid-soluble hormones use carrier molecules
  - Do not dissolve readily in blood
  - Carriers are water-soluble proteins made by the liver
  - Carriers protect hormones from early destruction
  - Binding between hormone and carrier is temporary
    - Attachment, detachment, reattachment are common
    - Most of the hormone (90% or more) is **bound hormone**
    - Only **unbound (free) hormone** is able to exit blood and bind to target cell receptors
- Most water-soluble hormones travel freely through blood
  - A few use carrier proteins to prolong their life

17.4b Levels of Circulating Hormone

- A hormone's blood concentration depends on how fast it is synthesized and eliminated
  - **Hormone synthesis** is done by the gland
    - The faster the synthesis rate, the higher the blood concentration
  - **Hormone elimination** occurs in multiple ways
    - Enzymatic degradation in liver cells
    - Removal from blood via kidney excretion or target cell uptake
    - The faster the elimination rate, the lower the blood concentration

17.4b Levels of Circulating Hormone

- **Half-Life—**time necessary to reduce a hormone's concentration to half of its original level
  - Depends on how efficiently it is eliminated
  - Hormones with short half-life must be secreted frequently to maintain normal concentration
  - Water-soluble hormones generally have short half-life
    - E.g., half-life of a few minutes for small peptide hormones
  - Steroid hormones generally have a long half-life
    - Carrier proteins protect them
    - E.g., testosterone half-life is 12 days

What did you learn?

- If hormone X and hormone Y had the same rate of synthesis, but X's elimination rate was faster, which would be at a higher level in the blood?
- Which type of hormone generally has a protein carrier in the blood?

17.5 Target Cells: Interactions with Hormones

Learning Objectives:

1. Describe how lipid-soluble hormones reach their target cell receptors and the type of cellular change they initiate.
2. Describe how water-soluble hormones induce cellular change in their target cells.

17.5a Lipid-Soluble Hormones

- Lipid-soluble hormones can diffuse across target cell membrane
  - Such hormones are small, nonpolar, and **lipophilic**
  - Their receptors are in the cytosol or nucleus
  - Once hormone enters cell it binds to receptor and forms **hormone-receptor complex**
  - The complex binds to a **hormone-response element** of DNA
    - Results in transcription of an mRNA, which is translated to a protein
    - The protein may have structural or metabolic effects

Lipid-Soluble Hormones and Intracellular Receptors

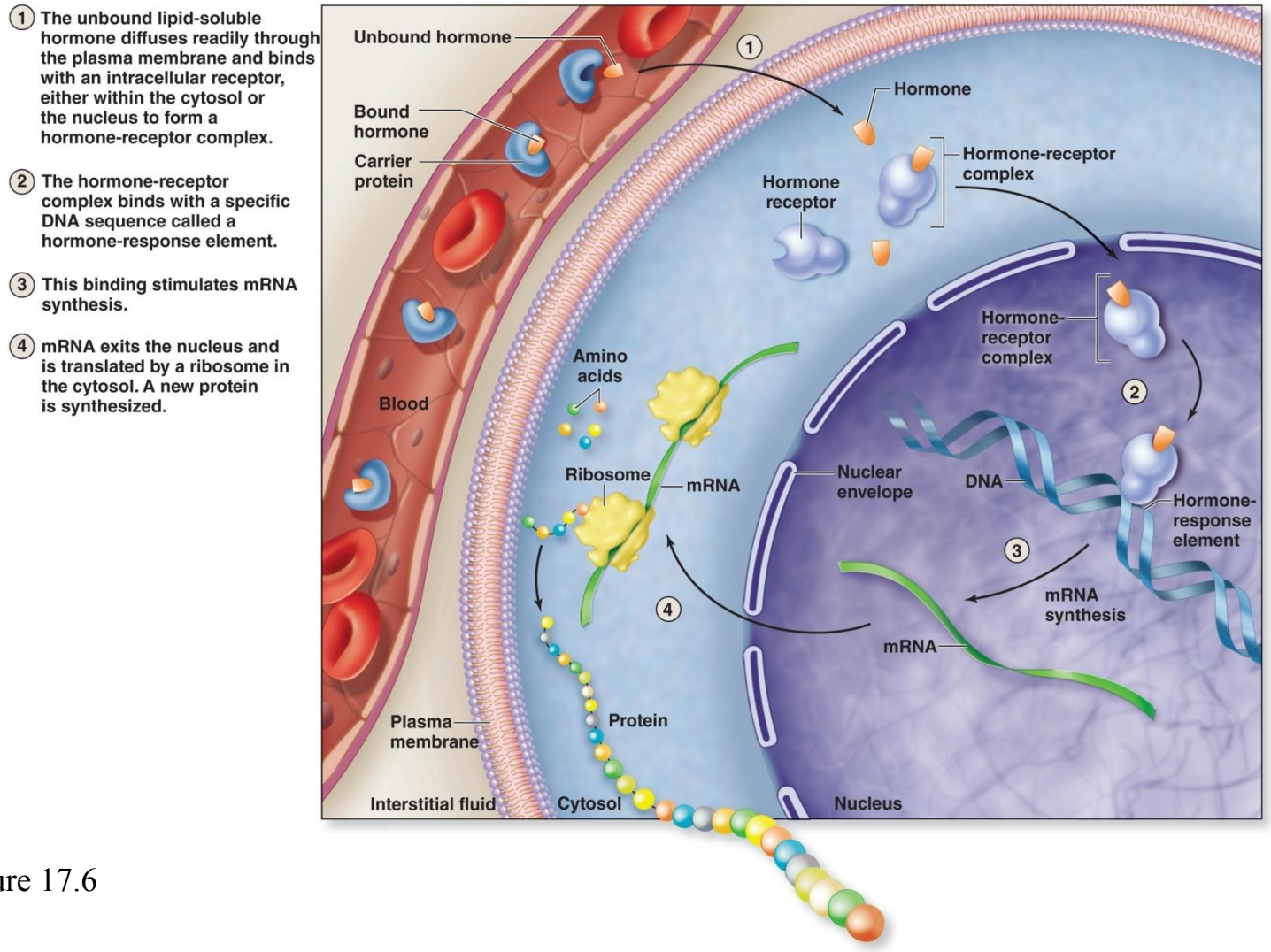


Figure 17.6

17.5b Water-Soluble Hormones

- Water-soluble hormones use membrane receptors
  - Such hormones are polar and can't diffuse through membrane
  - **Signal transduction pathway**
    - Hormone is **first messenger**—it initiates events by binding to receptor
    - Binding activates a **G-protein** (an internal membrane protein that binds a guanine nucleotide)
      - Activation results in binding of GTP instead of GDP
    - G-protein activation causes activation of a membrane enzyme such as adenylate cyclase or phospholipase C
    - Activated enzyme catalyzes the formation of a **second messenger—**a chemical that modifies cellular activity

Activation of G Proteins

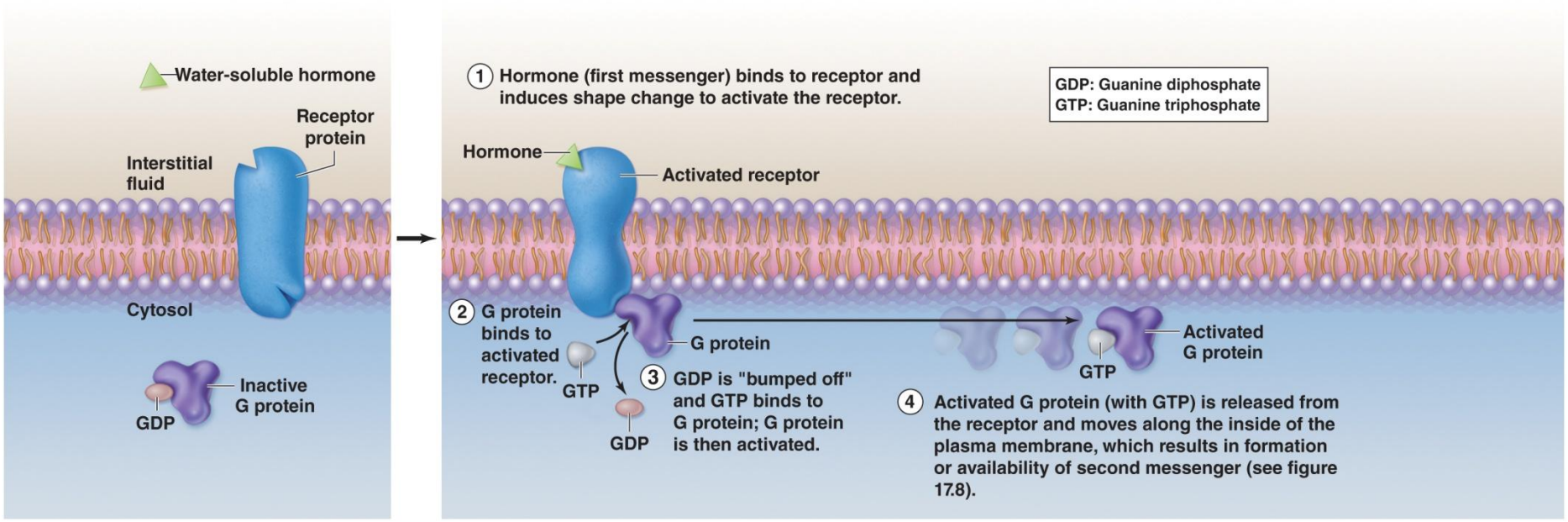
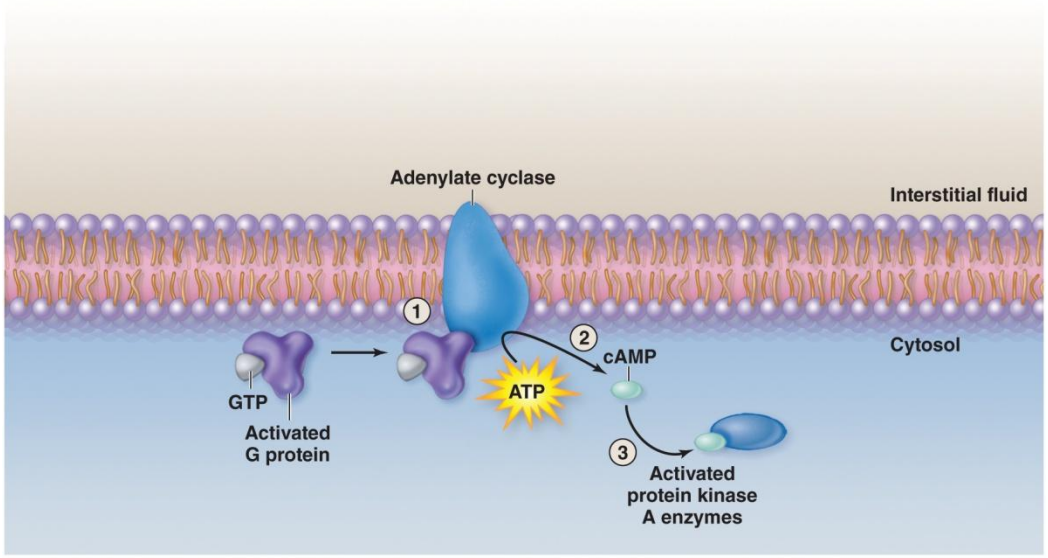


Figure 17.7

Action of G Proteins



(a) Activated G protein "turns on" adenylate cyclase.

Figure 17.8a

Adenylate cyclase pathway

- After hormone (e.g., glucagon) binds to its receptor, G protein is activated
- Activated G protein activates adenylate cyclase
- Adenylate cyclase generates cAMP
- cAMP activates protein kinase A
- Protein kinase A phosphorylates other molecules (activating or inhibiting them)

17.5b Water-Soluble Hormones

Phospholipase C pathway

- After hormone (e.g., epinephrine) binds to its receptor, G protein is activated
- Activated G protein activates **phospholipase C**
- Phospholipase C splits **PIP_2** into **diacylglycerol (DAG)** and **inositol triphosphate (IP_3)**
- DAG is a second messenger of the membrane that activates protein kinase C
  - Protein kinase C phosphorylates other molecules

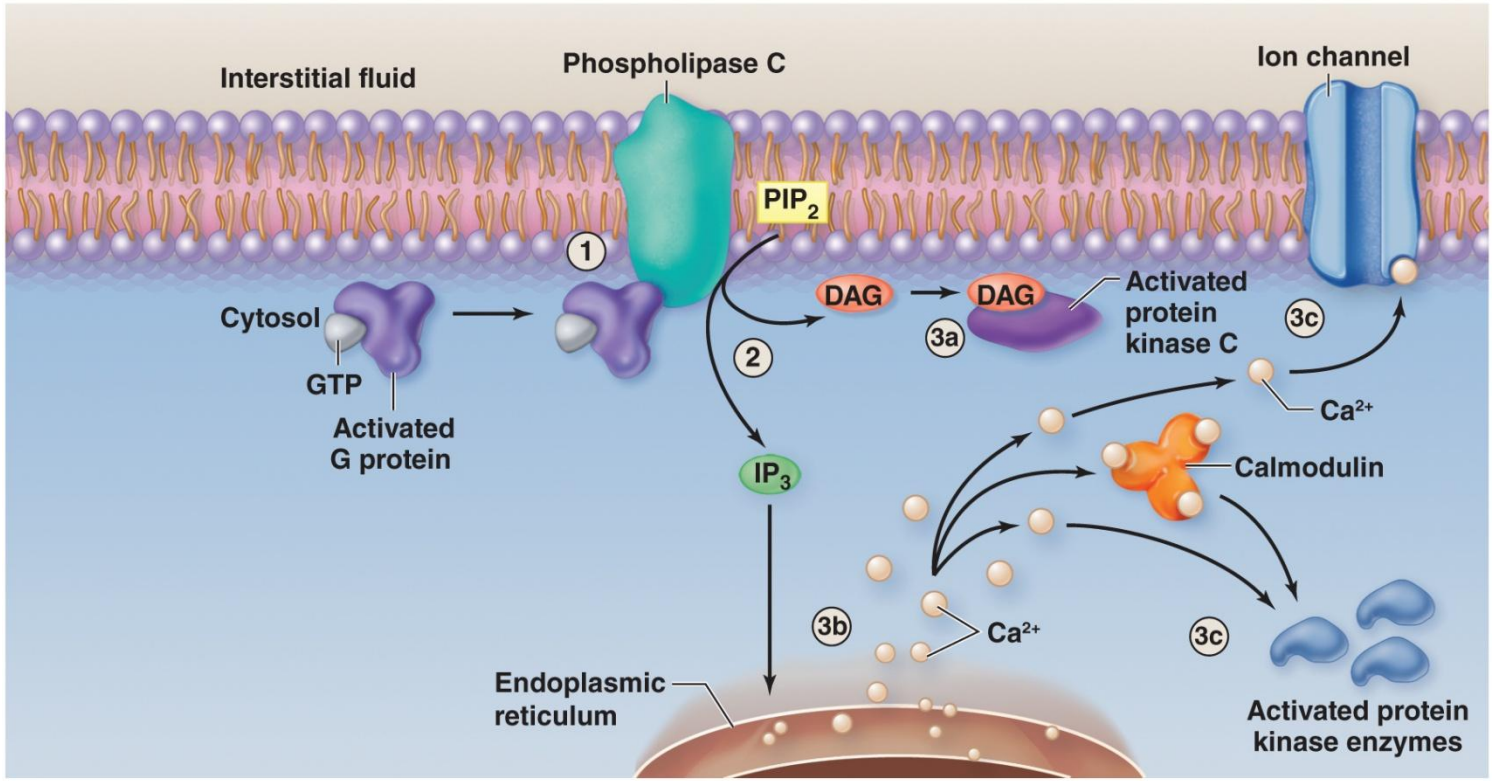
17.5b Water-Soluble Hormones

Phospholipase C pathway (*continued*)

- IP_3 is a second messenger that leaves the membrane and causes an increase in the levels of Ca^{2+} in the cytosol
  - Increase caused by effects on endoplasmic reticulum and cell membrane Ca^{2+} channels
  - Ca^{2+} acts as a third messenger, activating kinases (sometimes by binding to calmodulin) and interacting with ion channels

Action of G Proteins

Phospholipase C Pathway



(b) Activated G protein "turns on" phospholipase C.

Figure 17.8b

17.5b Water-Soluble Hormones

- Action of water-soluble hormones
  - Multiple results possible with different signal transduction pathways
    - Enzymes can be activated or inhibited
    - Growth can be stimulated (cell division)
    - Cellular secretions can be released
    - Membrane permeability can be changed
    - Muscles can be contracted or relaxed

17.5b Water-Soluble Hormones

- Action of water-soluble hormones (*continued*)
  - E.g., **glucagon** released from pancreas when blood sugar is low
    - Binds to receptors in membranes of liver cells
    - Liver cell increases cAMP synthesis, activating kinase A
    - Kinase A phosphorylates other enzymes leading to release of glucose from cell
  - E.g., **oxytocin** released from posterior pituitary during labor and delivery
    - Binds to receptors of smooth muscle cells in uterus
    - Muscle cell increases production of IP3 increasing intracellular Ca^{2+}
    - Uterine muscle contractions strengthen to expel baby

17.5b Water-Soluble Hormones

- Intracellular enzyme cascade and response amplification
  - Signaling pathway advantages
    - Signal is amplified at each enzymatic step
      - Just a few hormone molecules can change many molecules within cell
    - There are many places to regulate pathway activities
  - Signaling pathway controls
    - Cells possess mechanisms to quickly inactivate intermediate
      - E.g., to break down second messengers

What did you learn?

- Where are target cell receptors for lipophilic hormones located?
- What is protein kinase A, and what role does it have in a signal pathway?
- Where does DAG come from, and what function does it serve?

17.6 Target Cells: Degree of Cellular Response

Learning Objectives:

1. Describe the conditions that influence the number of receptors available for a specific hormone.
2. Define up-regulation and down-regulation.
3. Compare and contrast the three types of hormone interactions.

17.6 Target Cells: Degree of Cellular Response

- A cell's response to a hormone varies with
  - Its number of receptors for the hormone
  - Its simultaneous response to other hormones

17.6a Number of Receptors

- Receptor number fluctuates
  - **Up-regulation:** increases number of receptors
    - Increases sensitivity to hormone
      - Sometimes occurs when blood levels of hormone are *low*
      - Sometimes occurs with changes in development, cell cycle, cell activity
  - **Down-regulation:** decreases number of receptors
    - Decreases sensitivity to hormone
      - Sometimes occurs when blood levels of hormone are *high*
      - Sometimes occurs with changes in development, cell cycle, cell activity

Receptor Number

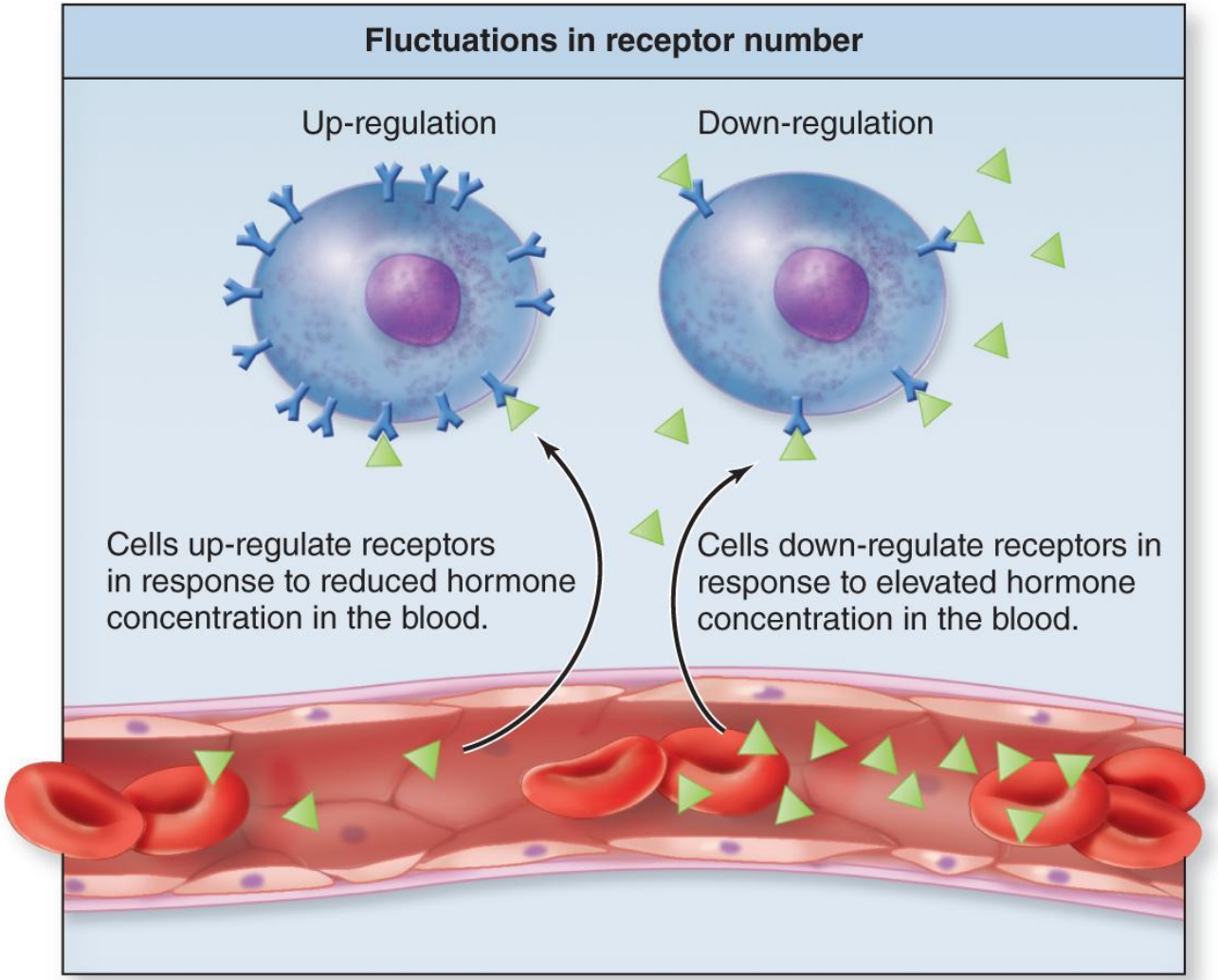


Figure 17.9a

17.6b Receptor Interactions

- Different hormones can simultaneously bind to a cell
  - **Synergistic** interactions
    - One hormone reinforces activity of another hormone
    - E.g., estrogen and progesterone effects on a target cell
  - **Permissive** interactions
    - One hormone requires activity of another hormone
    - E.g., oxytocin's milk ejection effect requires prolactin's milk generating effect
  - **Antagonistic** interactions
    - One hormone opposes activity of another hormone
    - E.g., glucagon increases blood glucose while insulin lowers it

Receptor Interactions

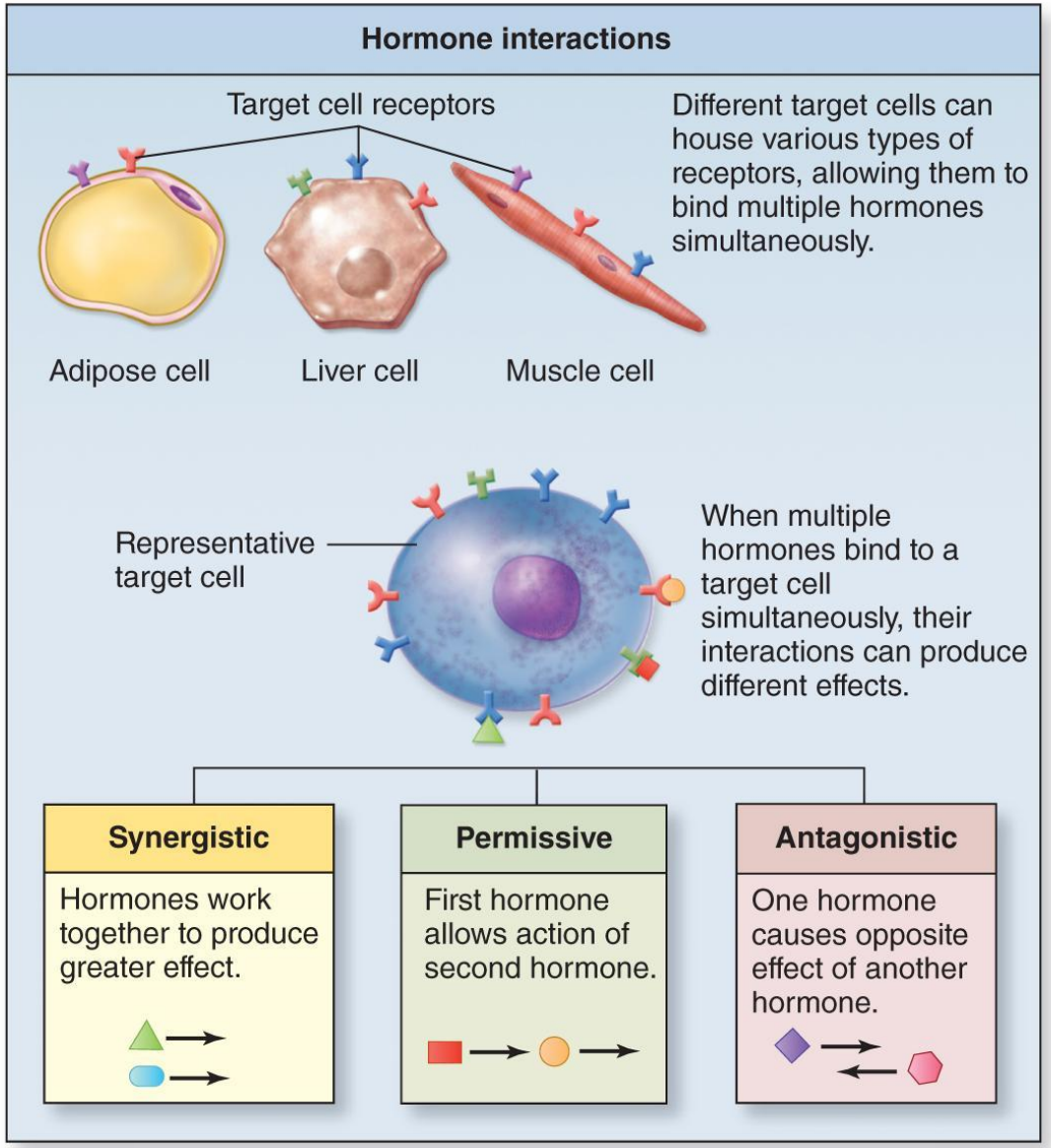


Figure 17.9b

What did you learn?

- If someone were to take a large dose of artificial hormone, how might target cells respond to maintain a normal level of response?
- What type of interaction occurs when a target cell has receptors for two hormones causing opposing effects?

17.7 The Hypothalamus and the Pituitary Gland

Learning Objectives:

1. Describe the anatomic relationship of the hypothalamus and the pituitary gland.
2. Identify the specific structures associated with the posterior pituitary and the anterior pituitary.
3. Identify the two hormones released from the posterior pituitary, and describe how the hypothalamus controls their release.
4. List the hormones released from the hypothalamus that control the anterior pituitary.
5. Explain how the hypothalamus controls the release of hormones from the anterior pituitary and the general function of each.

17.7a Anatomic Relationship of the Hypothalamus and the Pituitary Gland

- Hypothalamus controls pituitary, which controls thyroid, adrenal, liver, testes, ovaries
- **Pituitary gland** (*hypophysis*)
  - Lies inferior to hypothalamus in sella turcica of sphenoid bone
  - Pea sized
  - Connected to hypothalamus by **infundibulum** (stalk)
  - Partitioned into anterior and posterior pituitary (lobes)

Hypothalamus and Pituitary

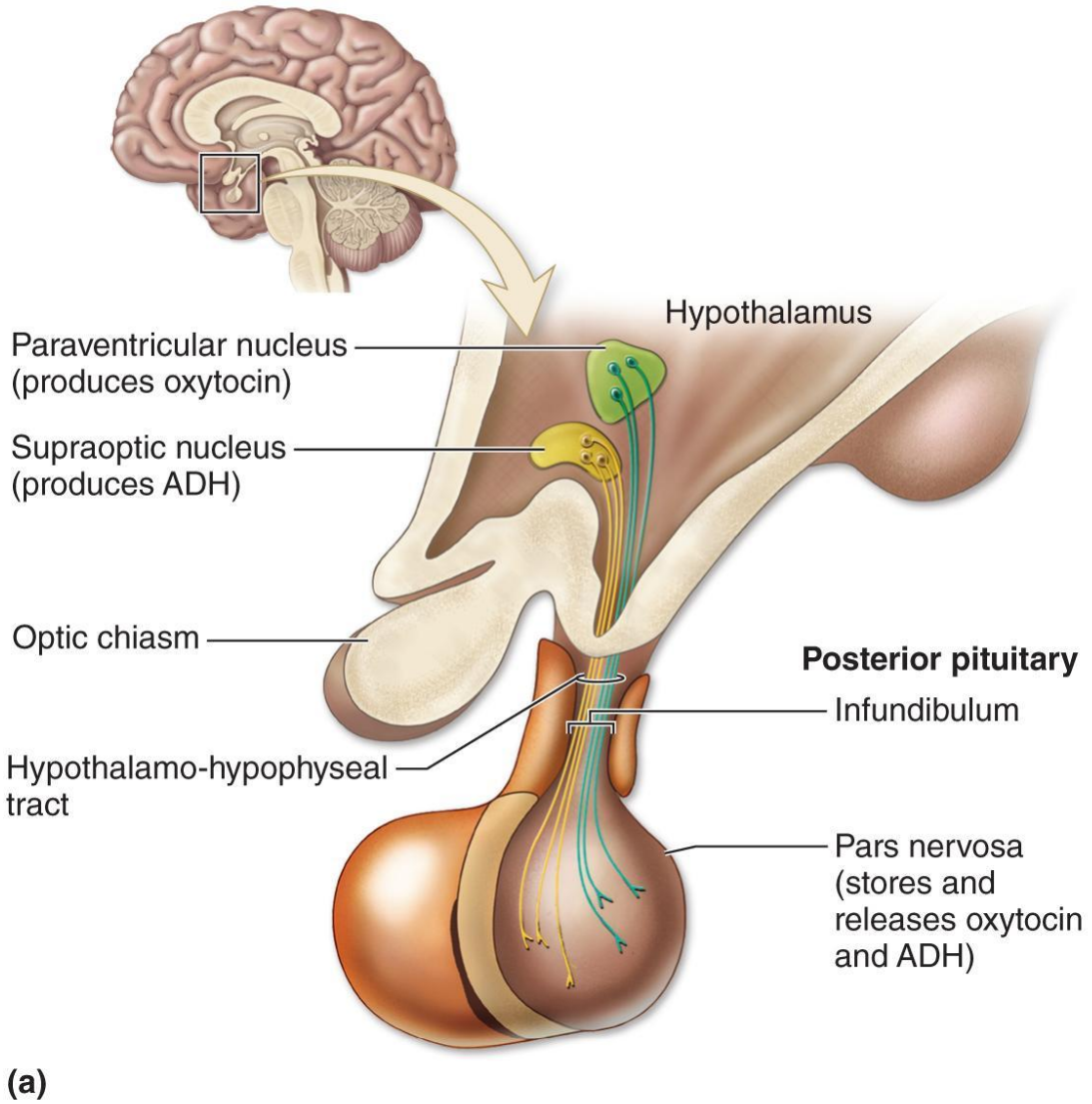


Figure 17.11a

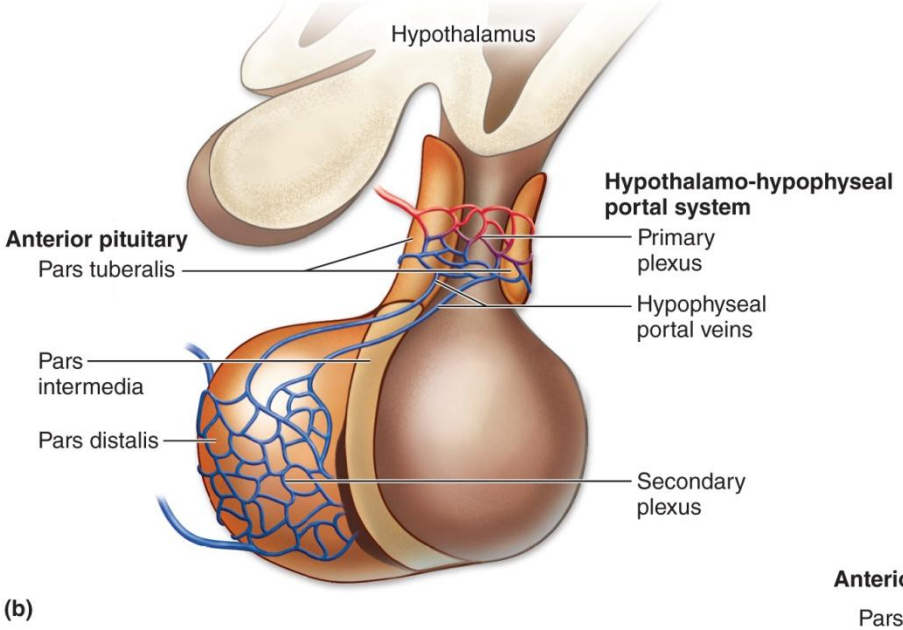
17.7a Anatomic Relationship of the Hypothalamus and the Pituitary Gland

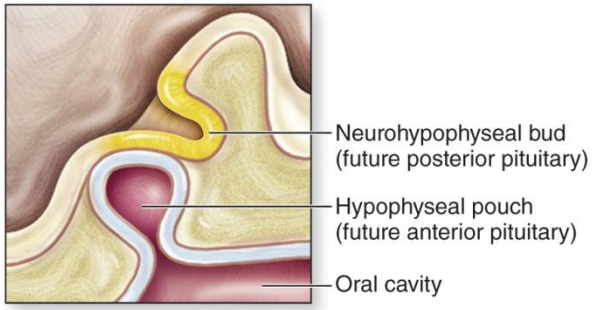
- **Posterior pituitary** (*neurohypophysis*)
  - Smaller, neural part of pituitary gland
  - Develops as a bud from the developing hypothalamus
  - Composed of *pars nervosa* (lobe) and infundibulum
  - Hypothalamic neurons project through infundibulum and release hormones in pars nervosa
    - Somas in **paraventricular nucleus** and **suprapotic nucleus**
    - Axons in **hypothalmo-hypophyseal tract** of infundibulum
    - Synaptic knobs in pars nervosa

17.7a Anatomic Relationship of the Hypothalamus and the Pituitary Gland

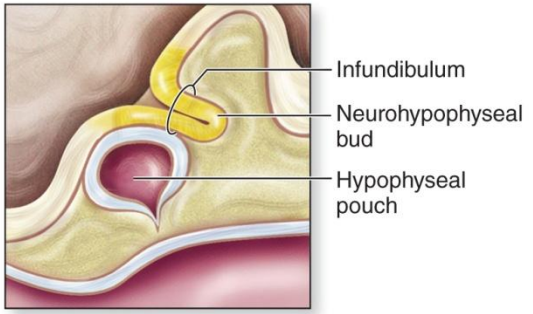
- **Anterior pituitary** (*adenohypophysis*)
  - Larger, glandular part of pituitary
  - Develops from ectoderm of oral cavity
  - Partitioned into three areas:
    - *Pars distalis,* large anterior rounded portion
    - *Pars tuberalis,* thin wrapping around infundibulum
    - *Pars intermedia,* scant region between the other two areas

Hypothalamus and Pituitary

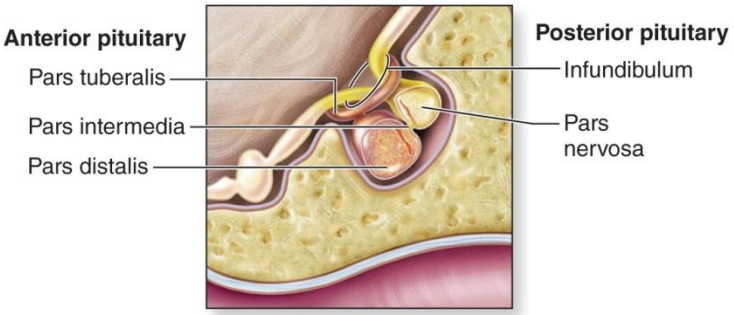




(c) Week 3: Hypophyseal pouch and neurohypophyseal bud form.



(d) Late second month: Hypophyseal pouch loses contact with roof of pharynx.



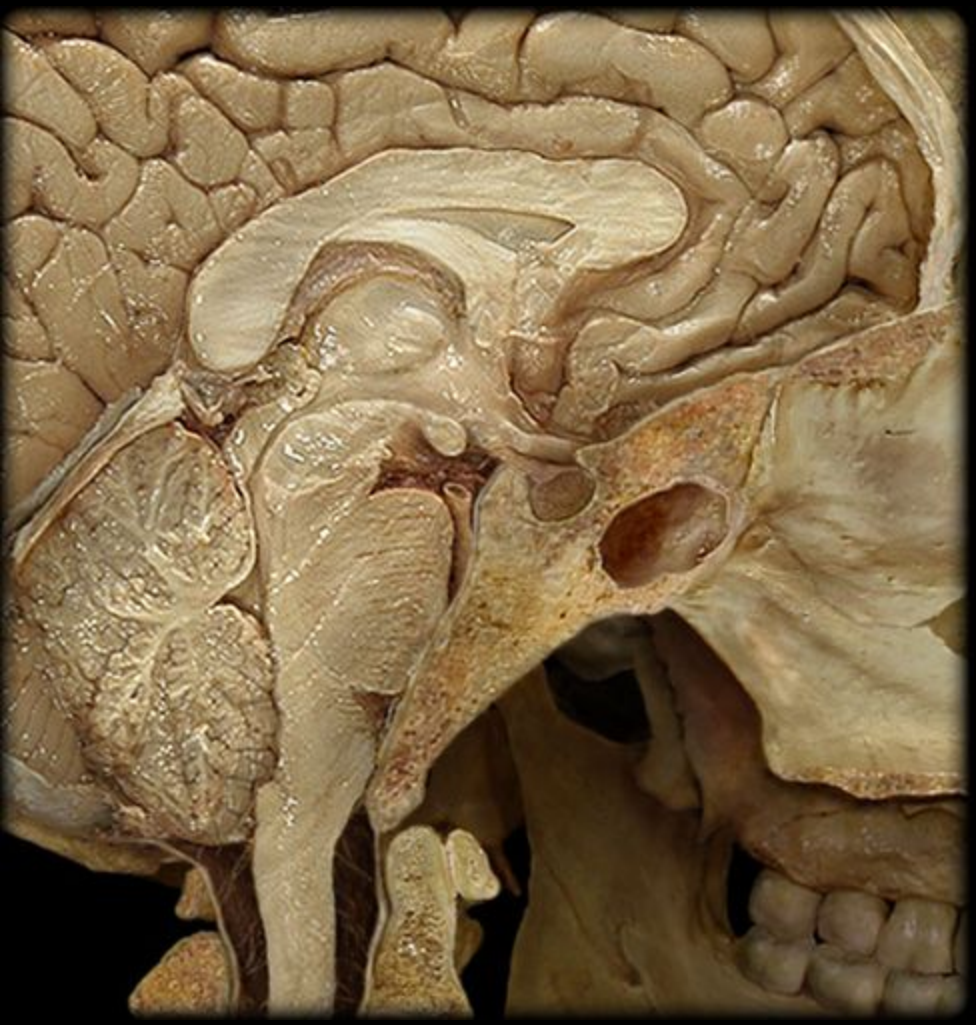
(e) Fetal period: Anterior and posterior pituitary have formed.

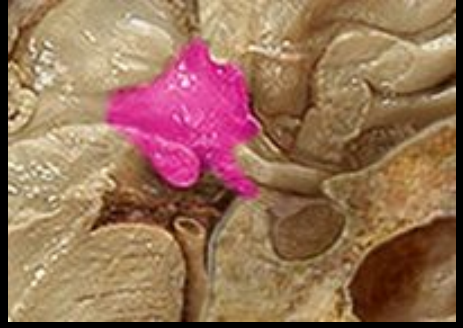
Figure 17.11b–e

17.7a Anatomic Relationship of the Hypothalamus and the Pituitary Gland

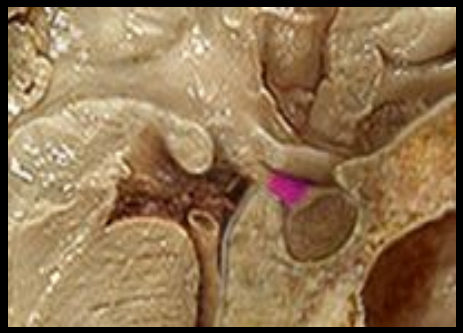
- **Anterior pituitary** (*continued*)
  - **Hypothalamo-hypophyseal portal system** of blood vessels
    - **Primary plexus**
      - Porous capillary network associated with hypothalamus
    - **Secondary plexus**
      - Capillary network associated with anterior pituitary
    - **Hypophyseal portal veins**
      - Drain primary plexus and transport to secondary plexus

Hypothalamus—Pituitary

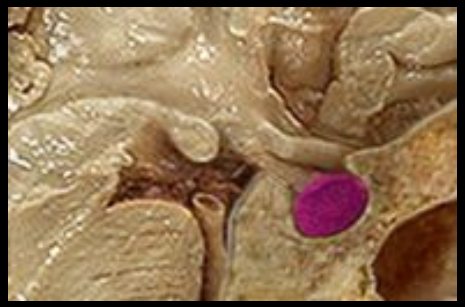




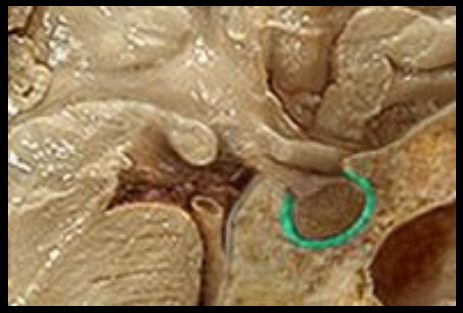
Hypothalamus



Infundibulum

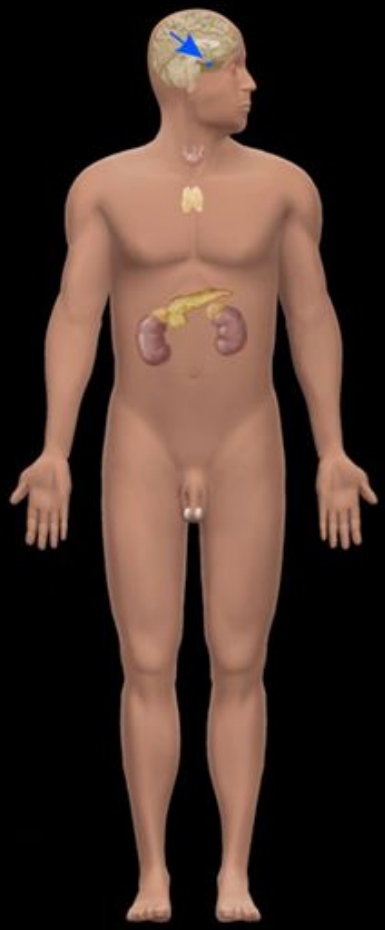


Pituitary gland



Sella turcica

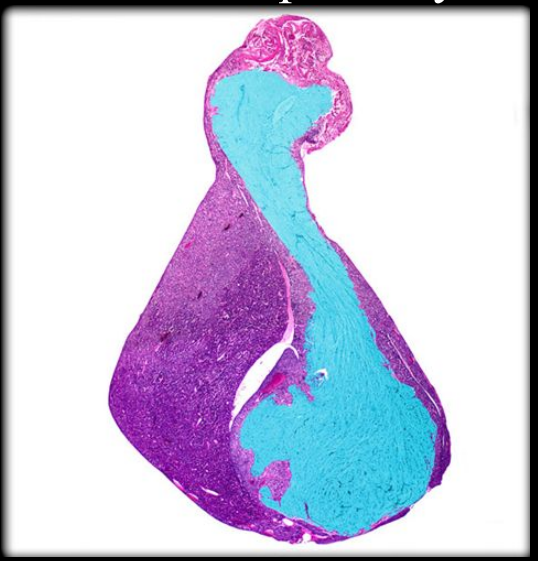
Pituitary Gland

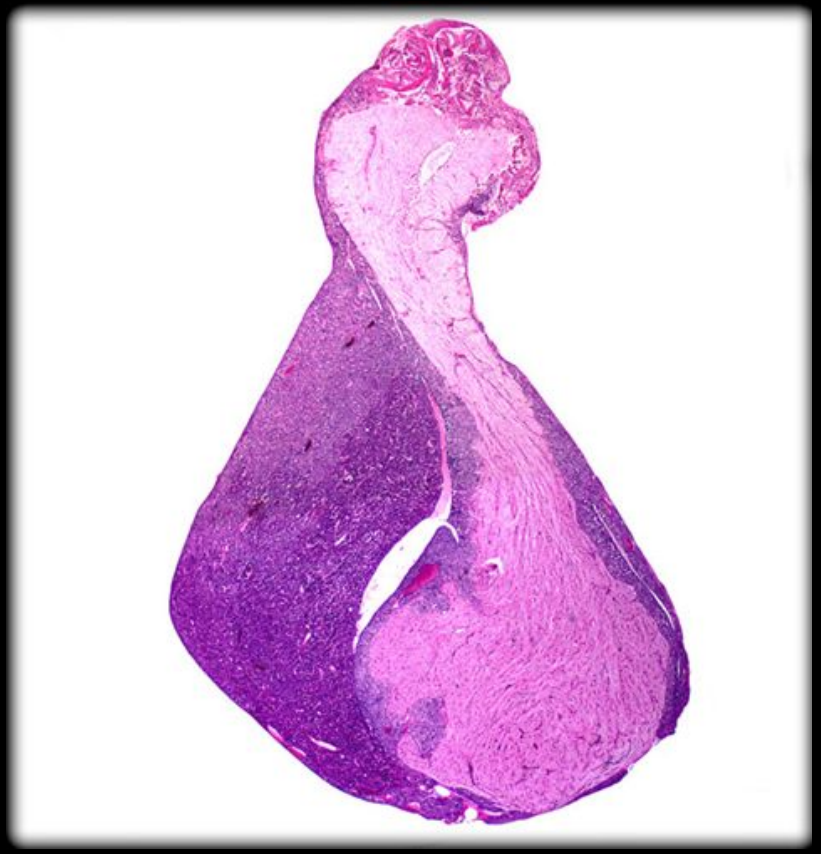


Pituitary Gland

Anterior pituitary

Posterior pituitary





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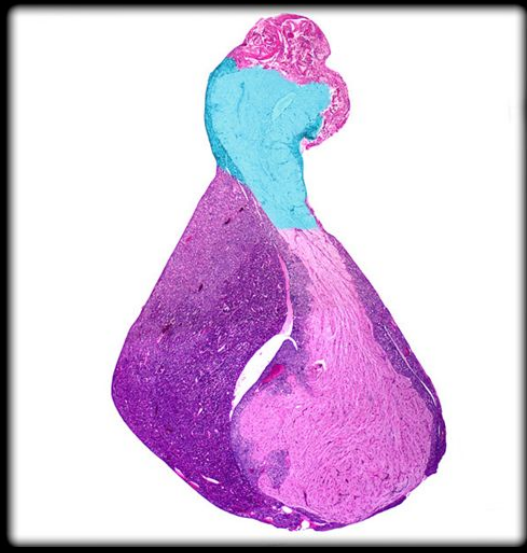
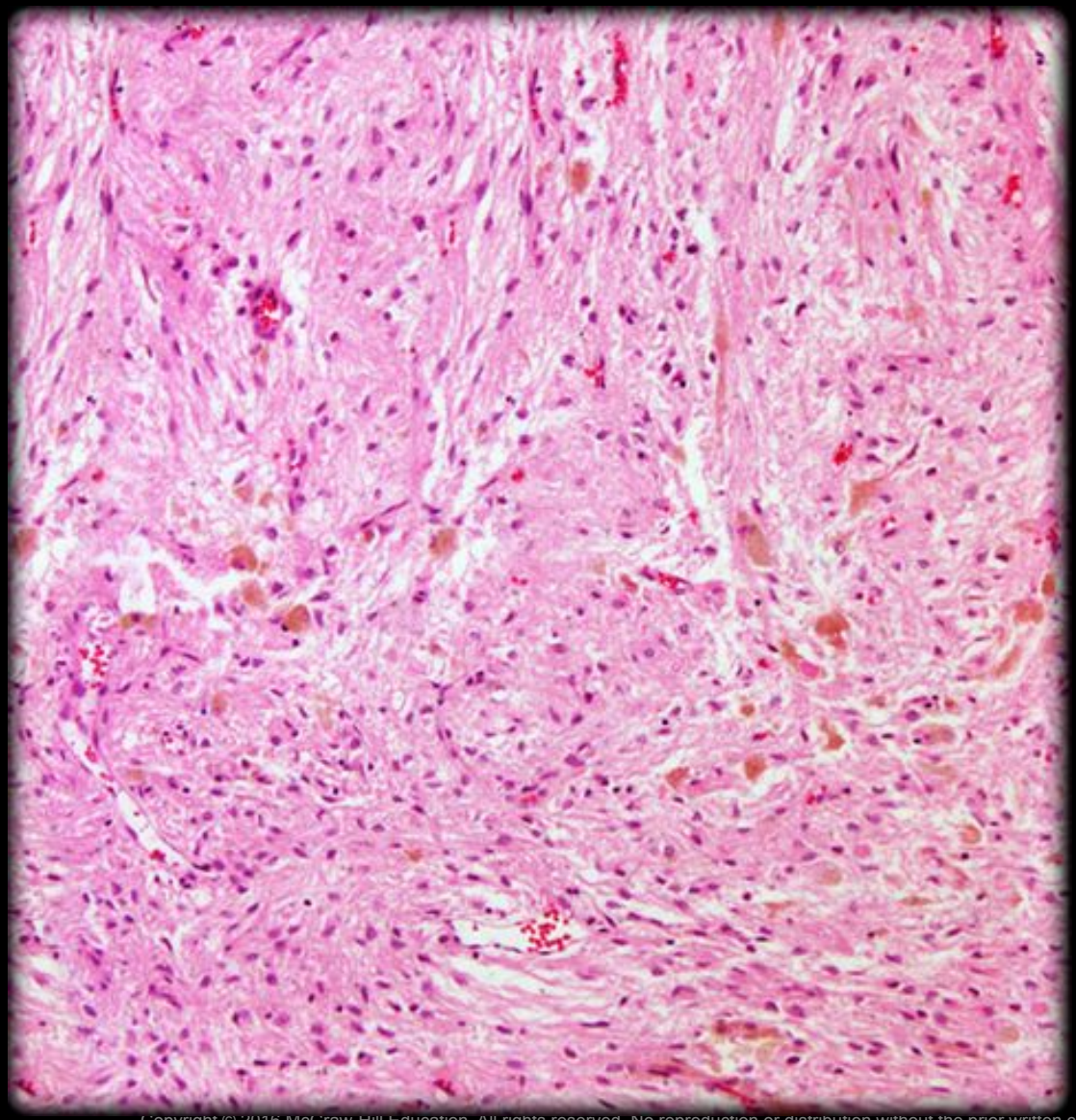
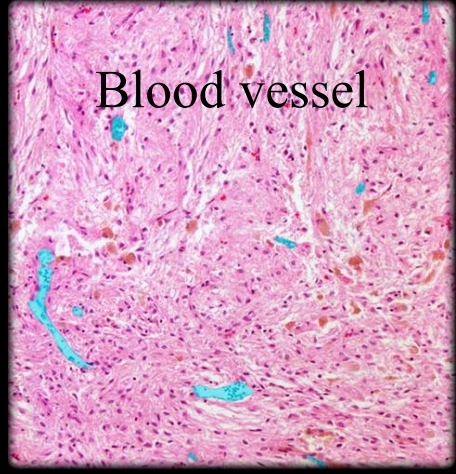
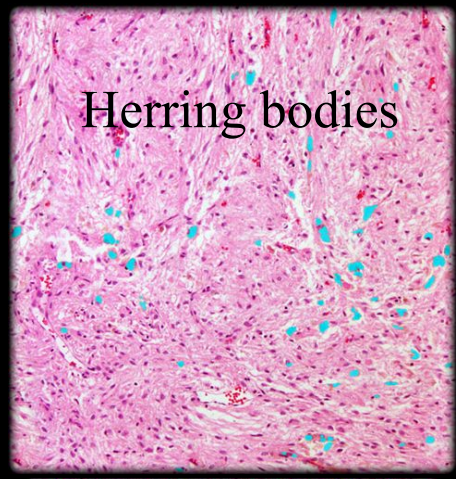


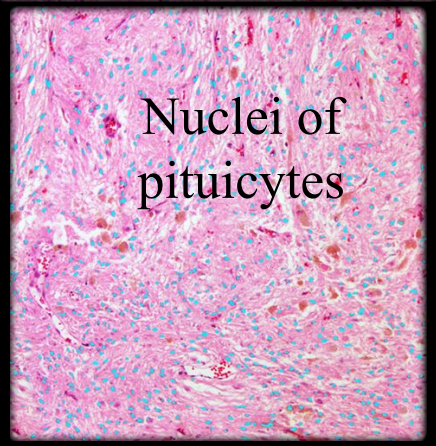
Posterior Pituitary

Medium Magnification



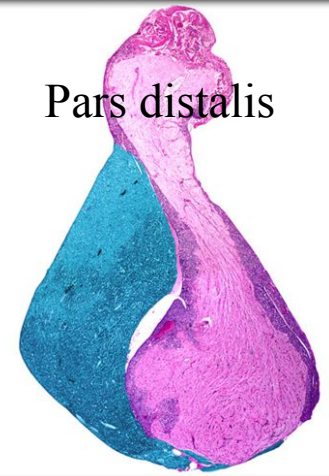




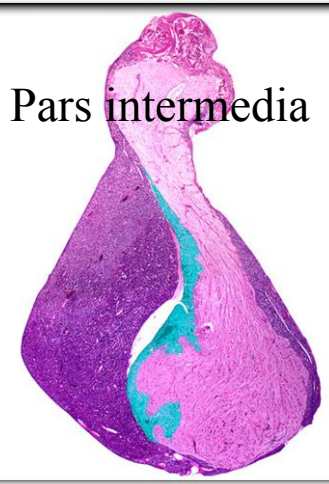


Pituitary Gland

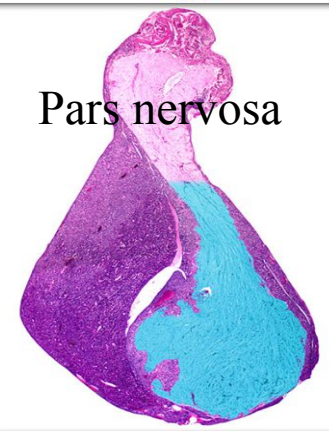
Pars distalis

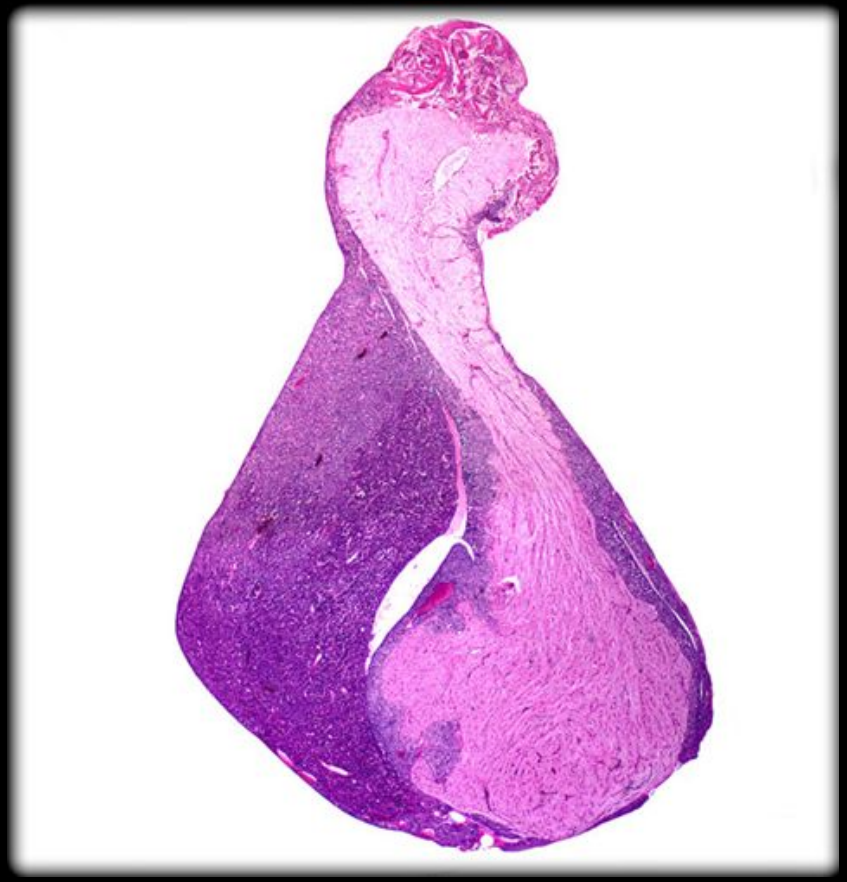


Pars intermedia

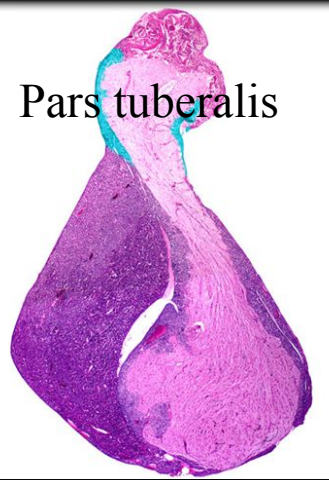


Pars nervosa

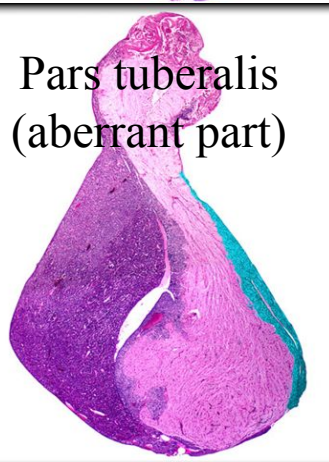




Pars tuberalis



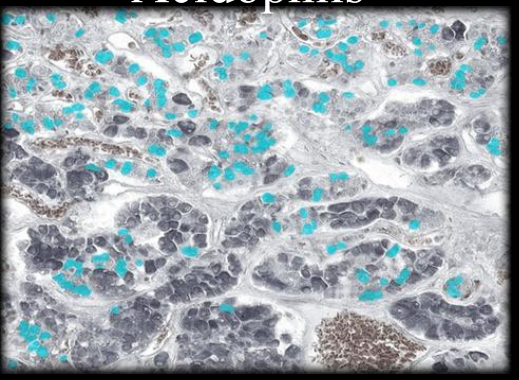
Pars tuberalis (aberrant part)

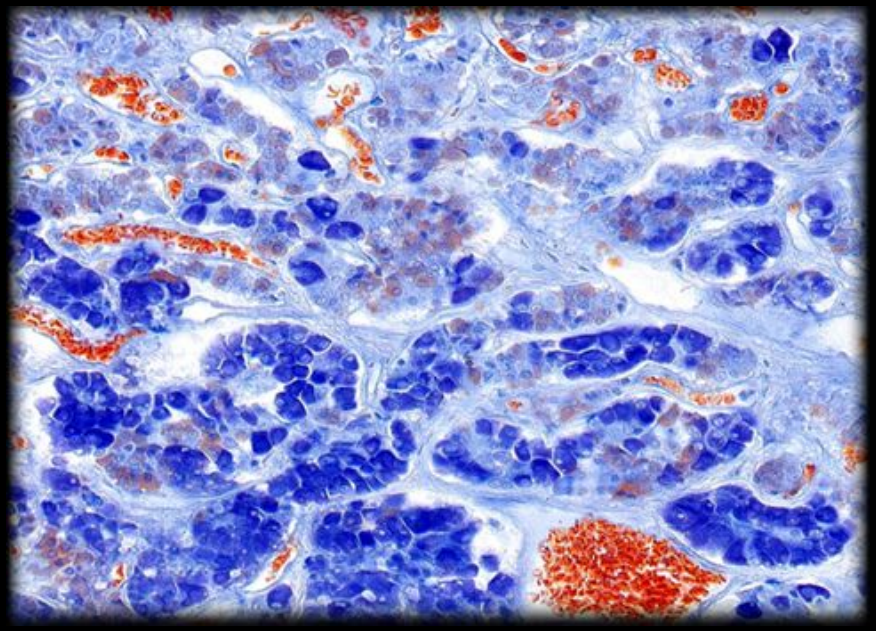


Vestige of Rathke's pouch

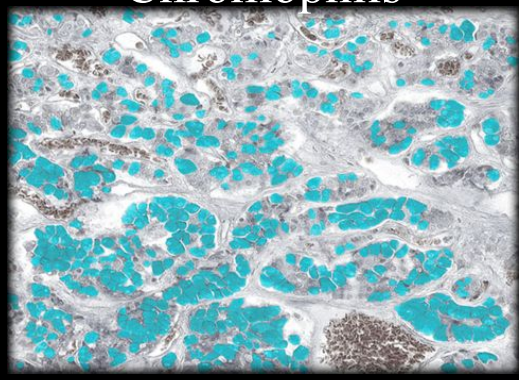
Anterior Pituitary

Acidophils

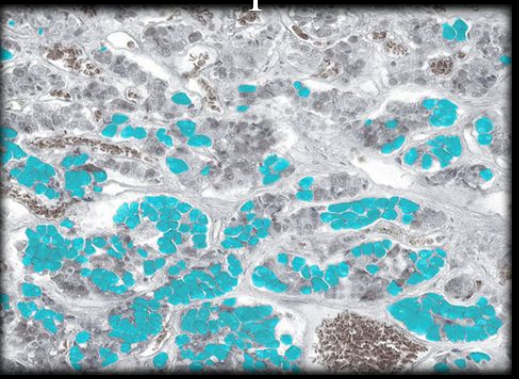




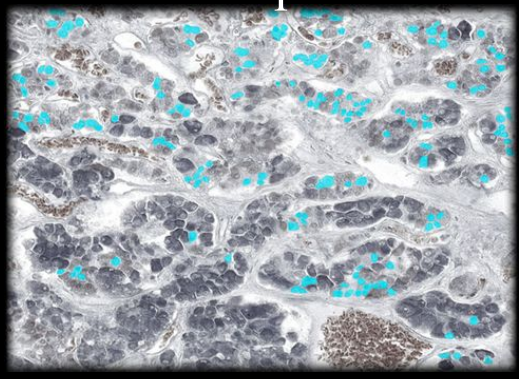
Chromophils



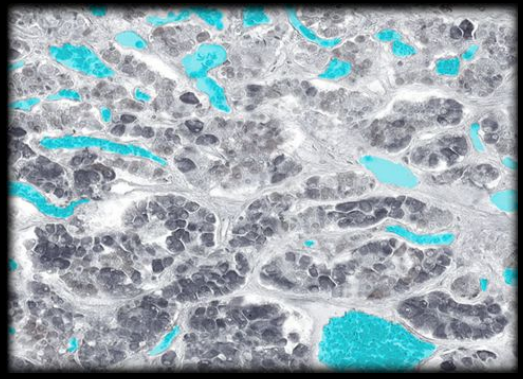
Basophils



Chromophobes



Blood vessel



17.7b Interactions Between the Hypothalamus and the Posterior Pituitary Gland

- Posterior pituitary is storage and release site for oxytocin (OT) and antidiuretic hormone (ADH)
  - Hormones made in hypothalamus by **neurosecretory cells**
    - Packed in secretory vesicles, transported by fast axonal transport
    - Released from synaptic knobs into blood when neurons fire impulses
  - **Oxytocin**
    - Made in paraventricular nucleus
    - Functions: uterine contraction, milk ejection , emotional bonding
  - **Antidiuretic hormone** (*vasopressin*)
    - Made in supraoptic nucleus
    - Functions: decrease urine production, stimulate thirst, constrict blood vessels

17.7c Interactions Between the Hypothalamus and the Anterior Pituitary Gland

- Hypothalamus hormonally stimulates anterior pituitary to release its hormones
  - Hypothalamus secretes **regulatory hormones**
    - Travel via portal blood vessels to pituitary
  - Anterior pituitary secretes hormones into general circulation

17.7c Interactions Between the Hypothalamus and the Anterior Pituitary Gland

- Regulatory hormones of the hypothalamus
  - **Releasing hormones**
    - Increase secretion of anterior pituitary hormones
    - Include: thyrotropin-releasing hormone (TRH), prolactin-releasing hormone (PRH), gonadotropin-releasing hormone (GnRH), corticotropin-releasing hormone (CRH), and growth hormone-releasing hormone (GHRH).
  - **Inhibiting hormones**
    - Decrease secretion of anterior pituitary hormones
    - Include: prolactin-inhibiting hormone (PIH) and growth-inhibiting hormone (GIH)

17.7c Interactions Between the Hypothalamus and the Anterior Pituitary Gland

- Anterior pituitary—tropic hormones and prolactin
  - **Thyroid stimulating hormone (TSH)**
    - Release triggered by TRH from hypothalamus
    - Causes release of thyroid hormone (TH) from thyroid gland
  - **Prolactin (PRL)**
    - Release triggered by PRH, inhibited by PIH from hypothalamus
    - Causes milk production, mammary gland growth in females
  - **Adrenocorticotropic hormone (ACTH;** corticotropin**)**
    - Release triggered by CRH from hypothalamus
    - Causes release of corticosteroids by adrenal cortex

17.7c Interactions Between the Hypothalamus and the Anterior Pituitary Gland

- Anterior pituitary—tropic hormones and prolactin (*continued*)
  - **Gonadotropins: follicle-stimulating hormone (FSH)** and **leutenizing hormone (LH)**
    - Release triggered by GnRH from hypothalamus
    - In female: regulate ovarian development and secretion of estrogen and progesterone
    - In male: regulate sperm development and secretion of testosterone
  - **Growth hormone (GH;** somatotropin**)**
    - Release triggered by GHRH, inhibited by GHIH from hypothalamus
    - Causes liver to secrete **insulin-like growth factors**

Anterior Pituitary Hormones

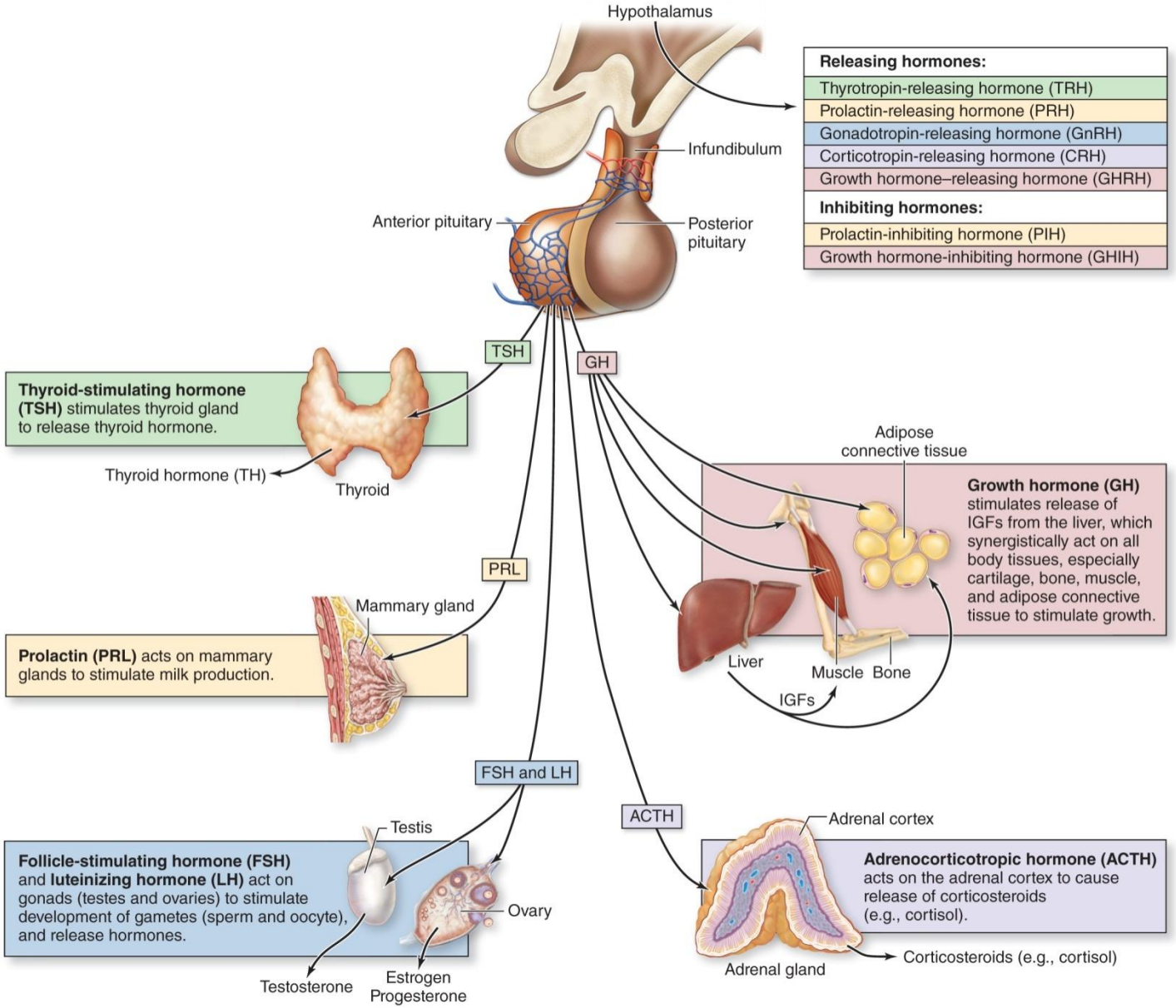


Figure 17.12

Clinical View: Hypophysectomy

- Surgical removal of the pituitary gland because of tumors
- Preferred surgical approach through nasal cavity
- Various hormones need to be replaced and their levels need to be monitored

What did you learn?

- Where are secondary plexus blood vessels located?
- Where are tropic hormones synthesized and what is their general function?
- Where is oxytocin synthesized and where is it released?

17.8 Representative Hormones Regulated by the Hypothalamus

Learning Objectives:

1. Describe the homeostatic system involving growth hormone.
2. Describe thyroid gland location and anatomy.
3. Discuss how thyroid hormones are produced, stored, and secreted.
4. Explain the control of thyroid hormone by the hypothalamus and pituitary.
5. Describe the structure and location of the adrenal glands.

17.8 Representative Hormones Regulated by the Hypothalamus (*continued*)

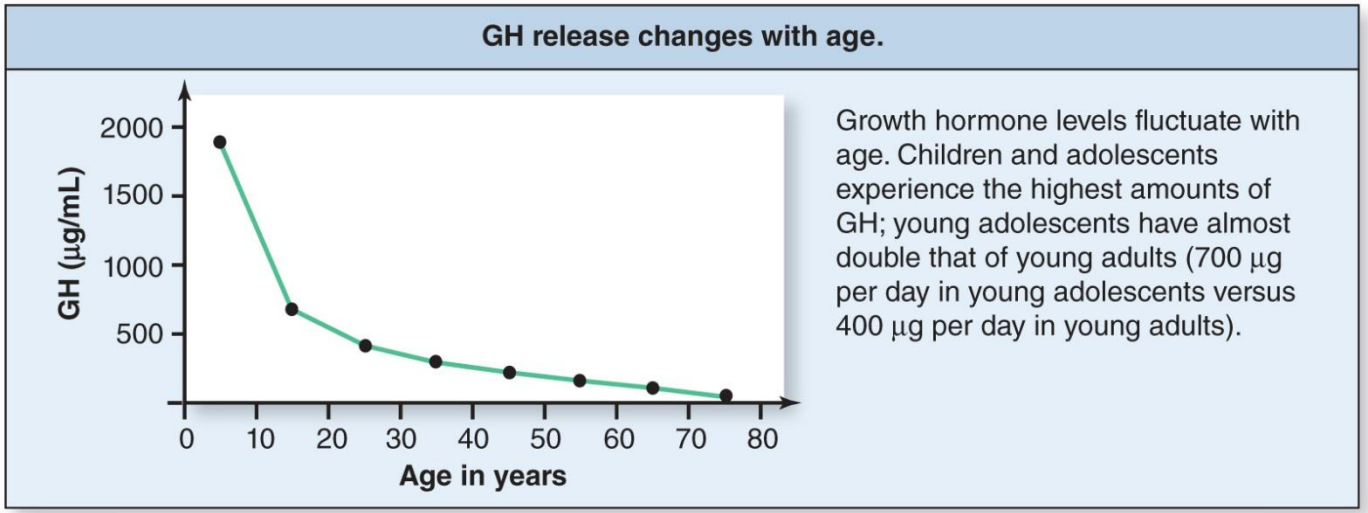
Learning Objectives:

6. Name the three zones of the adrenal cortex and the hormones produced in each zone.
7. Describe how the hypothalamus controls the release of glucocorticoid (cortisol) and the effects of cortisol.

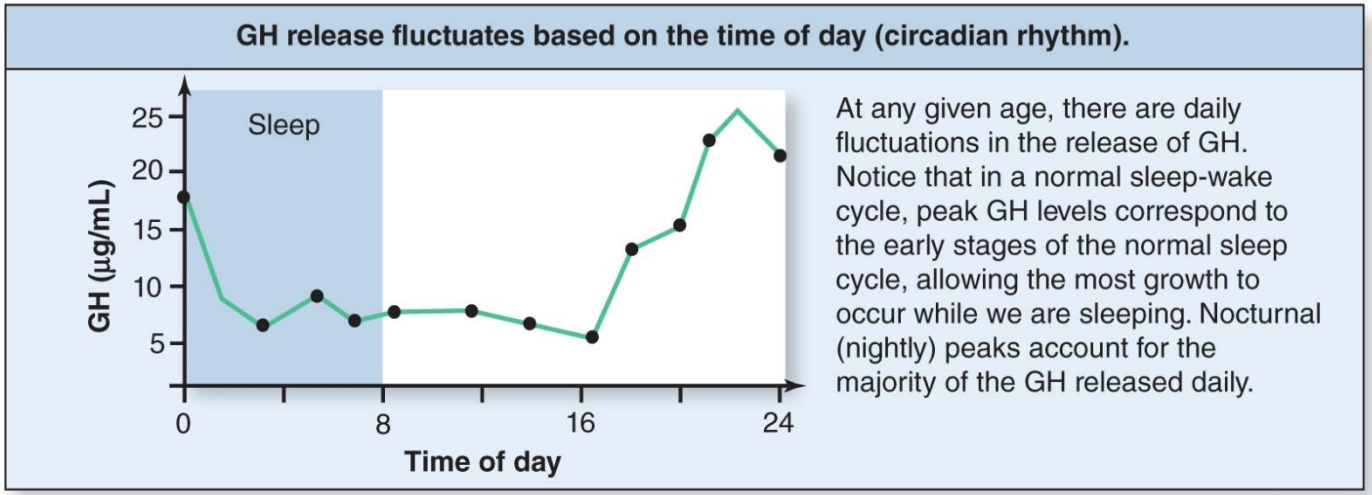
17.8a Growth Hormone

- Growth hormone (GH) functions include
  - Stimulation of linear growth at epiphyseal plate
  - Hypertrophy of muscle
  - Release of nutrients from storage into blood
- GHRH stimulates GH release
  - Release influenced by: age, time of day, and nutrient levels, stress and exercise

Growth Hormone Release



(a)

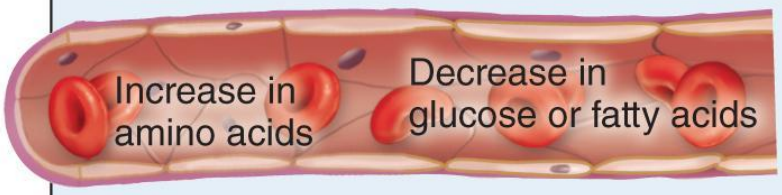


(b)

Figure 17.14a,b

Growth Hormone Release (*continued*)

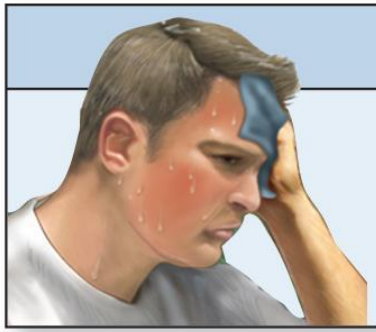
GH release changes in response to nutrient blood levels.



Growth hormone release is regulated by the level of nutrient molecules in the blood. Growth hormone levels increase in response to an increase in amino acid levels and to a decrease in glucose levels or fatty acids levels.

(c)

GH release is altered by stress.



Emotional, physical, and chemical stress, including surgery, trauma, exercise, or electroshock therapy increase GH release (although severe emotional stress can cause a decrease in its release in children).

(d)

Figure 17.14c,d

17.8a Growth Hormone

- GH targets hepatocytes
  - Hepatocytes release insulin-like growth factors (IGFs)
    - IGFs work synergistically with GH, enhancing response
    - IGFs have a longer half life than GH
  - Hepatocytes also increase glycogenolysis and gluconeogenesis
    - Results in **diabetogenic** increase in blood glucose levels
- All body cells have receptors for GH, IGF or both
  - Cause increases in cell division, protein synthesis, cell differentiation
  - Bone and muscle are particularly responsive

17.8a Growth Hormone

- GH and IGFs cause adipose cells to release nutrients
  - Cells increase lipolysis and decrease lipogenesis
  - Increases levels of glycerol and fatty acids in blood
    - Helps provide molecules necessary for generating ATP for growth
- Negative feedback regulation of GHRH, GH release
  - Increased levels of GH or IGF stimulate hypothalamus to release GHIH
  - GH release also inhibits its own release from pituitary

Regulation and Action of GH

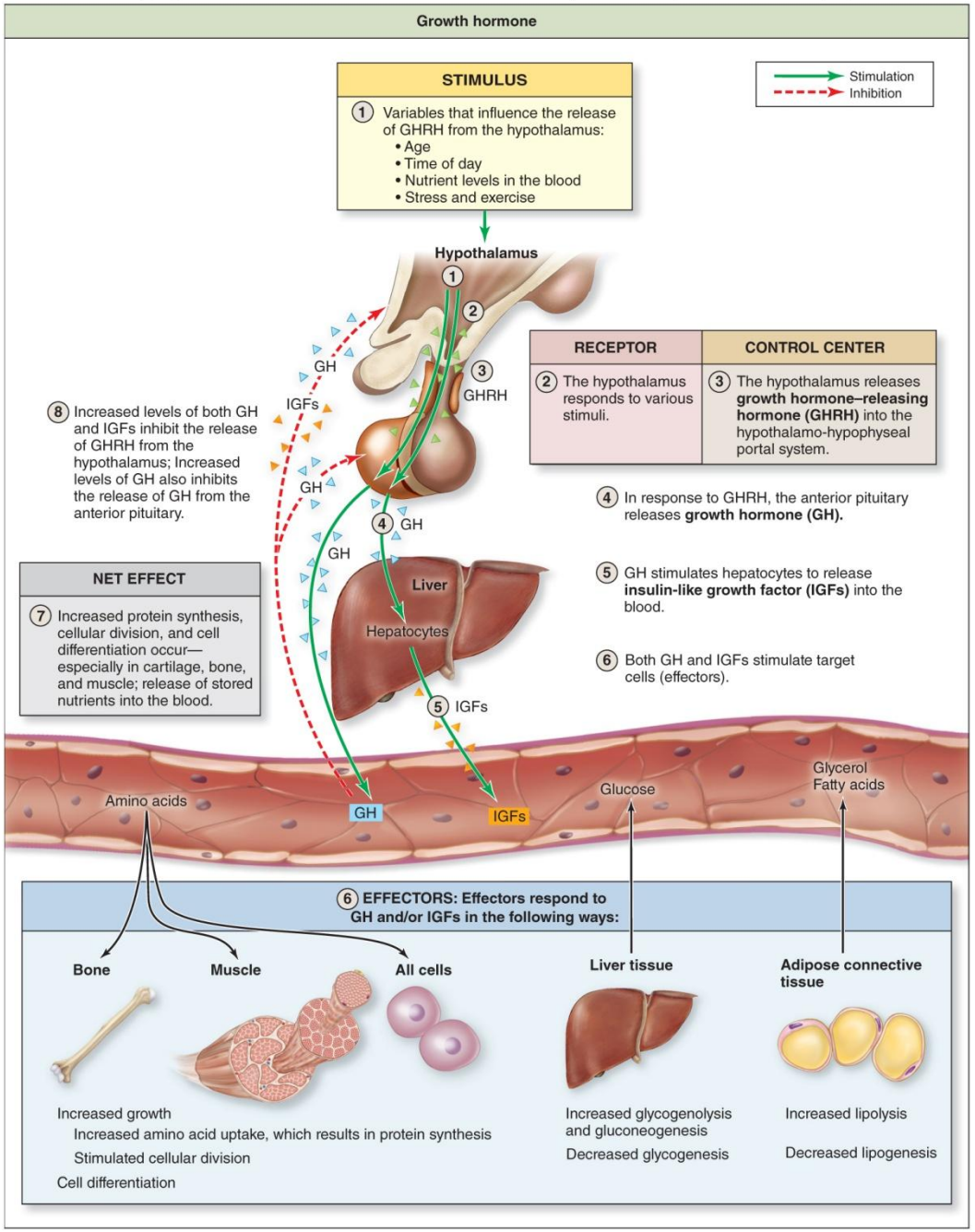


Figure 17.13

Clinical View: Disorders of Growth Hormone Secretion

- **Growth hormone deficiency** (*pituitary dwarfism*)
  - Inadequate growth hormone production
  - Due to hypothalamic or pituitary problem
  - Short stature and low blood sugar
- **Pituitary gigantism**
  - Too much growth hormone
  - Excessive growth and increased blood sugar
  - Enormous internal organs
  - Death at early age if untreated

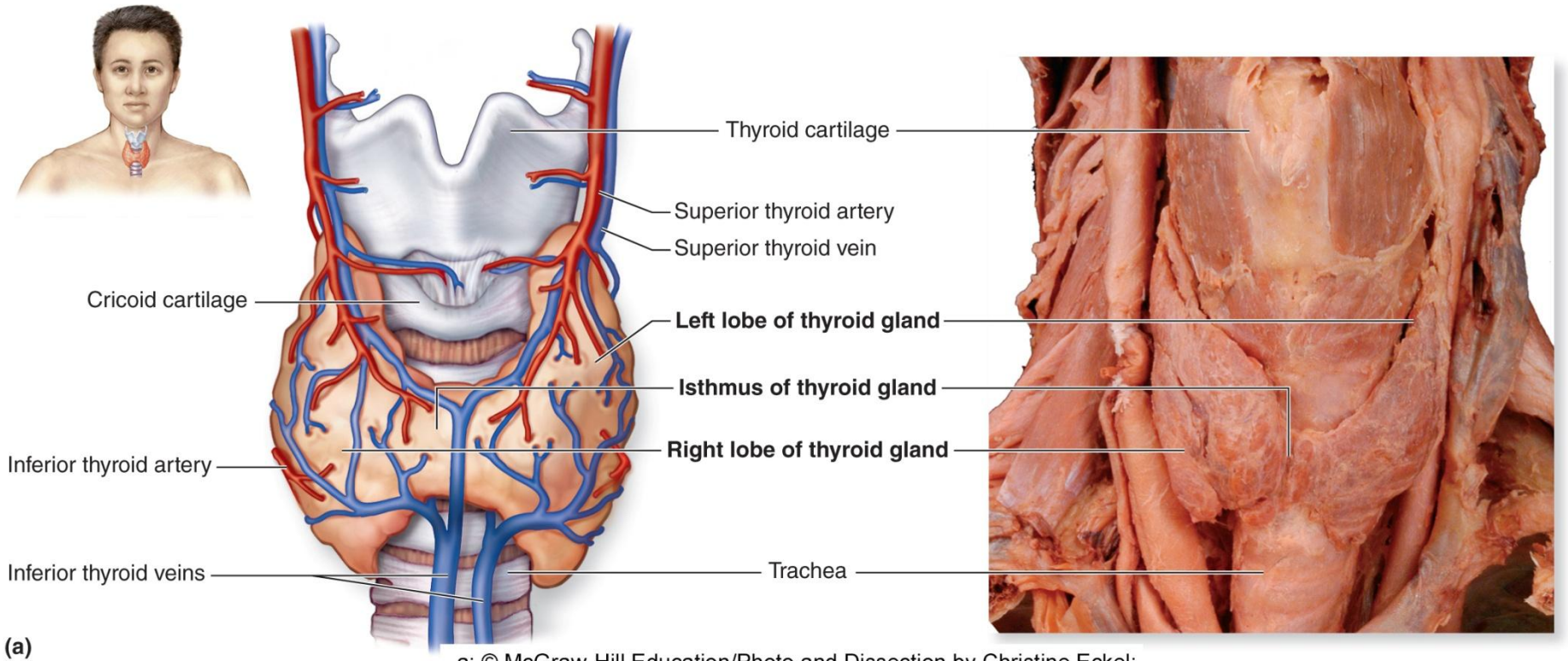
Clinical View: Disorders of Growth Hormone Secretion (*continued*)

- **Acromegaly**
  - Excessive growth hormone production in adult
  - Enlargement of bones of face, hands, and feet
  - Increased release of glucose
  - Internal organs increased in size
  - Results from loss of feedback control of growth hormone

17.8b Thyroid Gland and Thyroid Hormone

- Anatomy of the thyroid gland
  - Sits inferior to thyroid cartilage of larynx, anterior to trachea
  - **Left** and **right lobes**
    - Connected at midline by narrow **isthmus**
  - Rich vascularization gives it reddish color
  - Composed of microscopic follicles
    - **Follicular cells—**cuboidal epithelial cells that surround a central lumen
      - Produce and release thyroid hormone (TH)
    - Follicle lumen houses **colloid—**a viscous, protein-rich fluid
    - **Parafollicular cells—**cells around follicular cells that make **calcitonin**
      - Hormone that decreases blood calcium levels

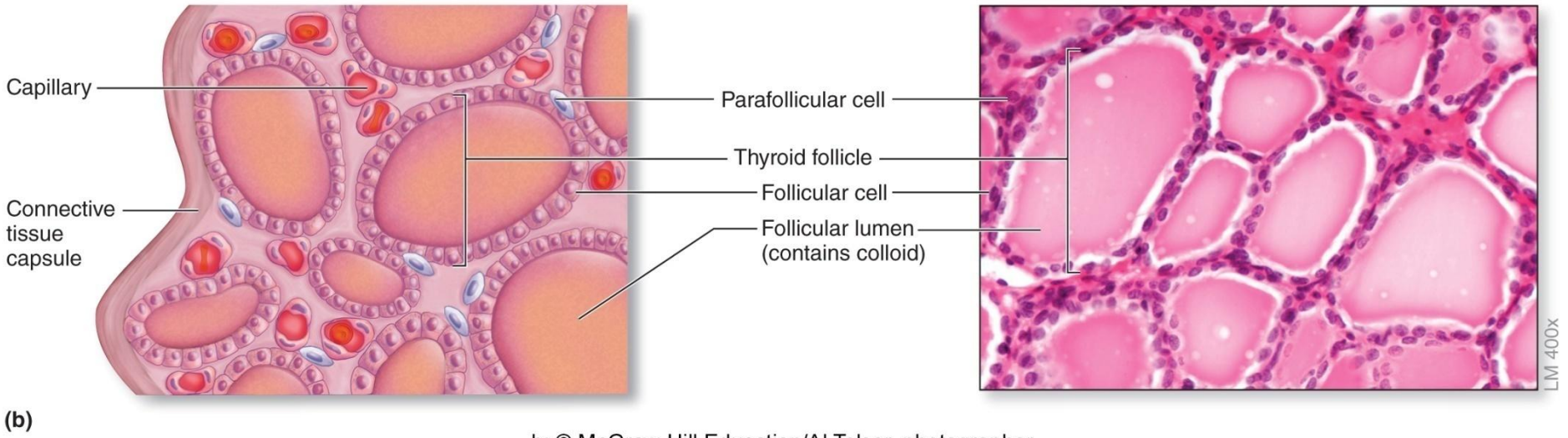
The Thyroid Gland



a: © McGraw-Hill Education/Photo and Dissection by Christine Eckel;

Figure 17.15a

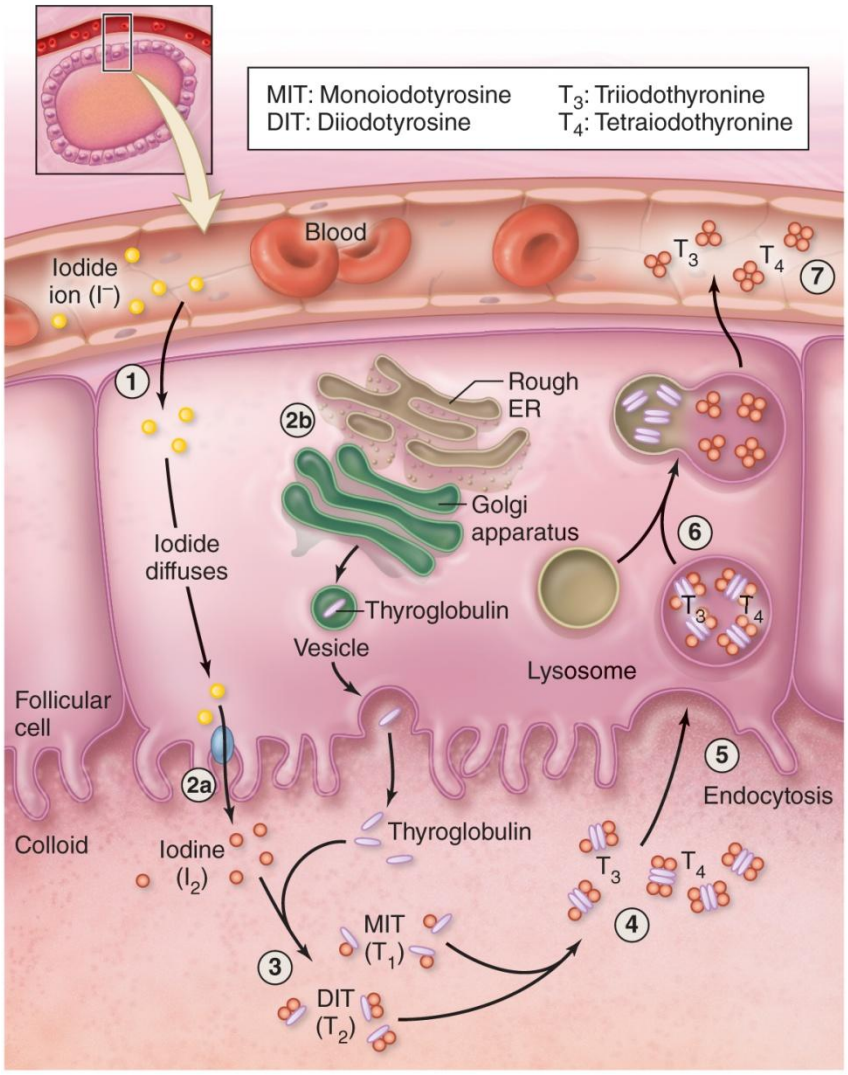
The Thyroid Gland



b: © McGraw-Hill Education/Al Telser, photographer

Figure 17.15b

Thyroid Hormone Synthesis, Storage, and Release



Follicular cell

(1) **Iodide ion uptake.** Iodide ion (I^-) is moved by active transport from the blood into a follicular cell (because iodide concentration is higher within the cell than within the blood), diffuses through the cell, and is transported by facilitated diffusion into the colloid, which fills the follicle lumen.

(2a) **Iodine molecule formation.** Two I^- are joined to form molecular iodine (I_2) at the plasma membrane of the follicular cell.

(2b) **Thyroglobulin synthesis.** Synthesis of thyroglobulin includes production of the protein within the rough ER, and shipping it to the Golgi apparatus for addition of carbohydrate. Thyroglobulin (a glycoprotein) is incorporated into a vesicle and released from the follicular cell into the colloid by exocytosis.

Colloid

(3) **MIT and DIT formation.** I_2 are attached specifically to tyrosine amino acids of thyroglobulin by peroxidase enzymes, which facilitate removal of electrons; one I_2 is added to form MIT or T_1 (monoiodotyrosine) or two I_2 are added to form DIT or T_2 (diiodotyrosine).

(4) **T_3 and T_4 formation.** Enzymes within the colloid facilitate the joining of MIT and DIT. One MIT and one DIT are joined to form T_3, whereas two MITs are joined to form T_4. Both T_3 and T_4 remain attached to thyroglobulin.

(5) **Endocytosis.** Thyroglobulin with attached T_3 and T_4 is endocytosed into a follicular cell.

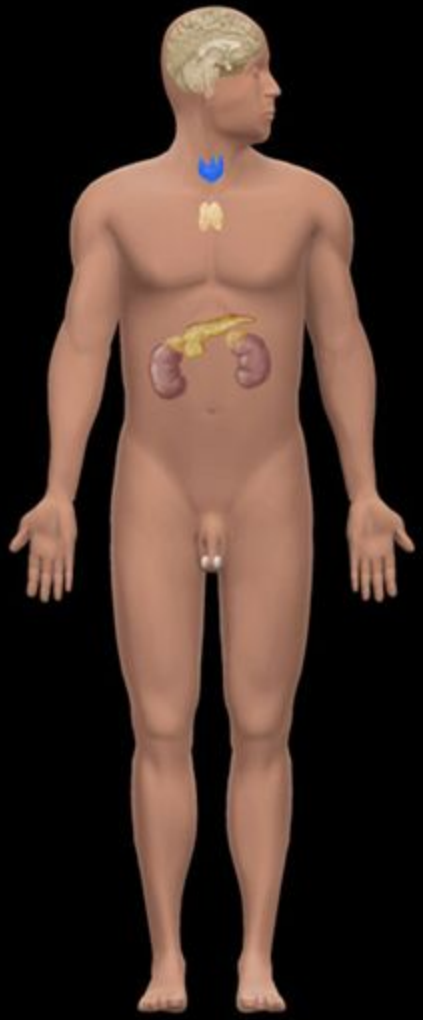
Follicular cell

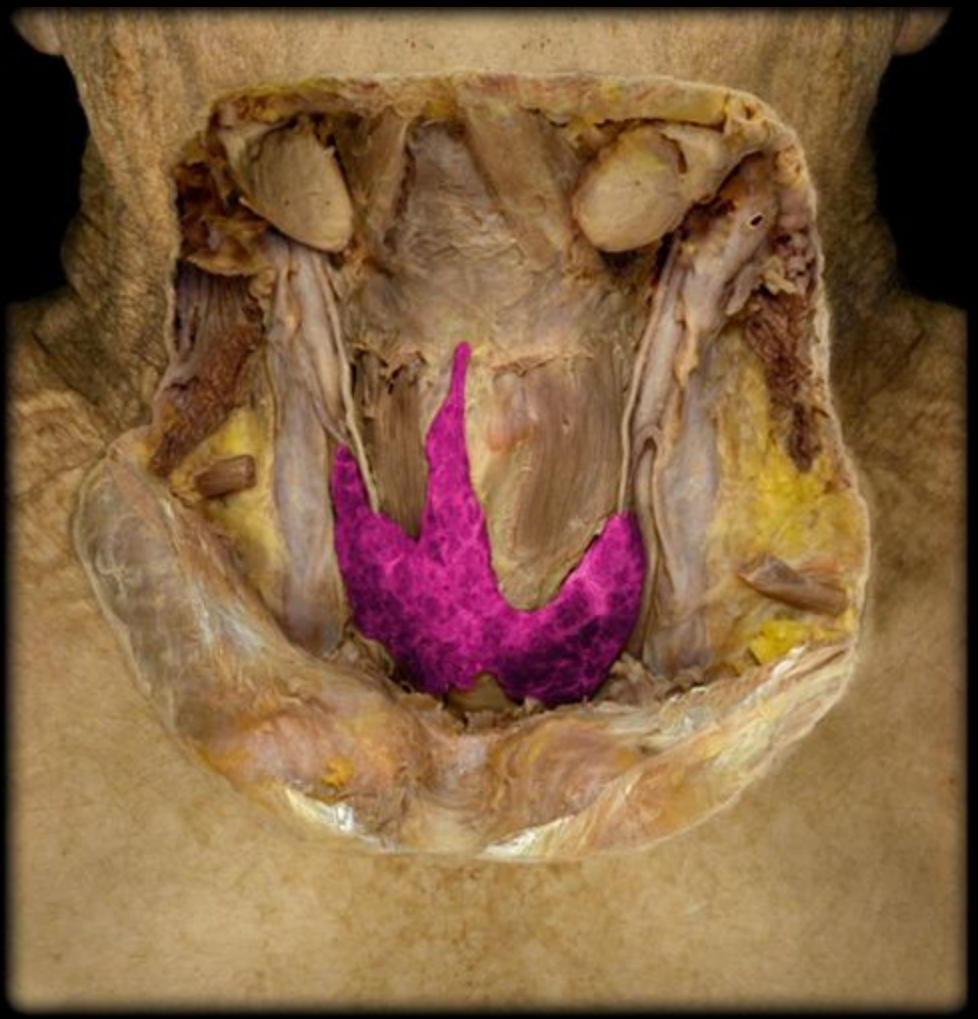
(6) **Release of T_3 and T_4 from thyroglobulin.** A vesicle containing thyroglobulin with attached T_3 and T_4 fuses with a lysosome. Lysosomal enzymes cleave T_3 and T_4 from thyroglobulin.

(7) **Release of T_3 and T_4 into the blood.** T_3 and T_4, which are lipid-soluble molecules, move from the follicular cell into the blood by simple diffusion. More T_4 is released than T_3. T_3 and T_4 are collectively called **thyroxine.**

Figure 17.16

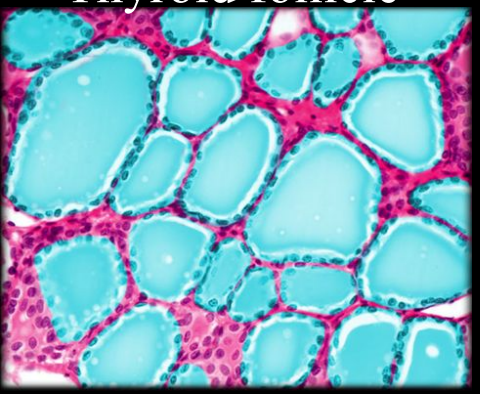
Thyroid Gland



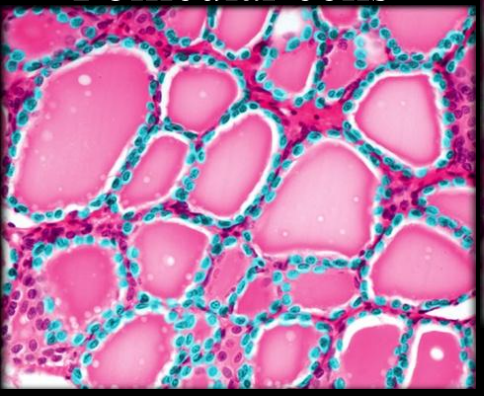


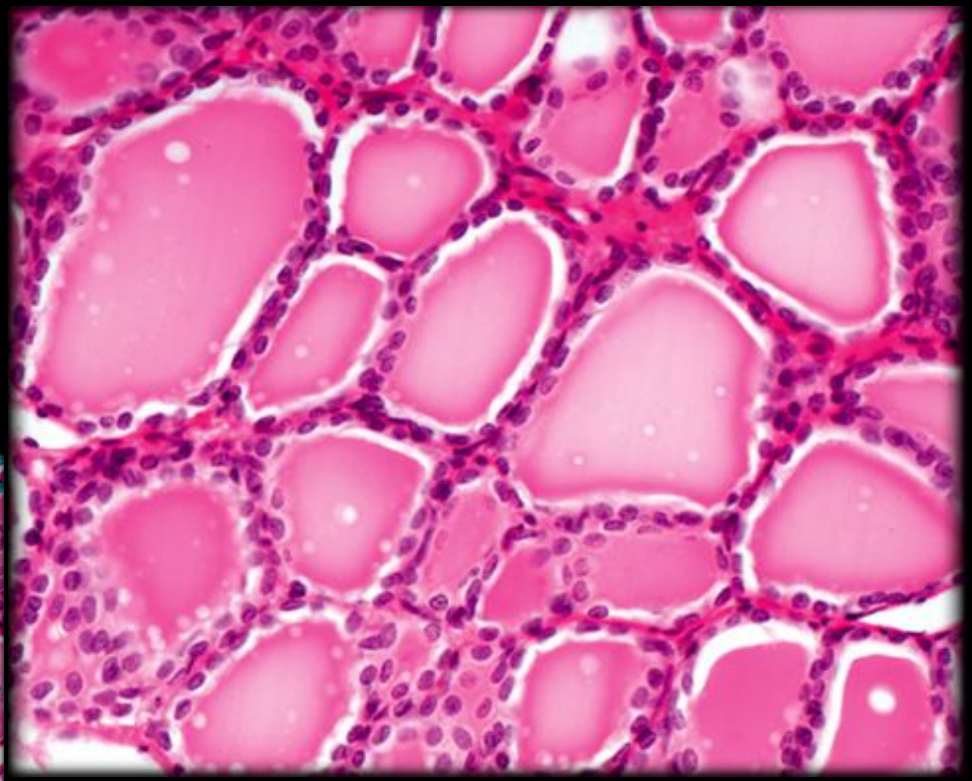
Thyroid Gland
Medium Magnification

Thyroid follicle

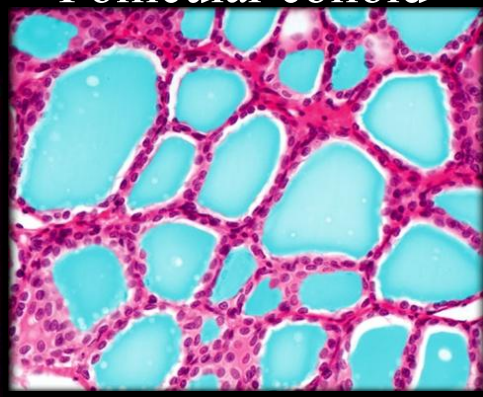


Follicular cells

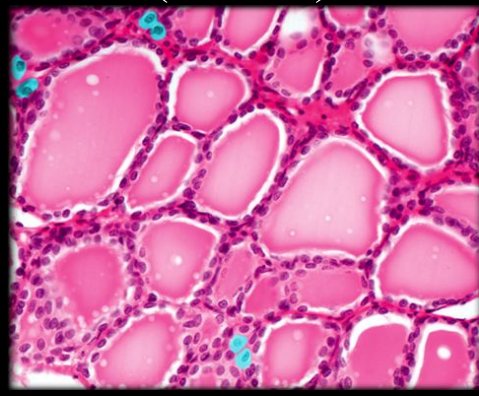




Follicular colloid

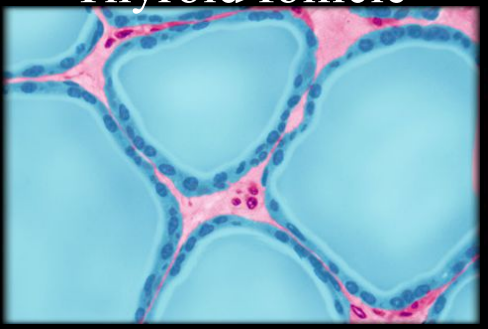


Extrafollicular cells (C cells)

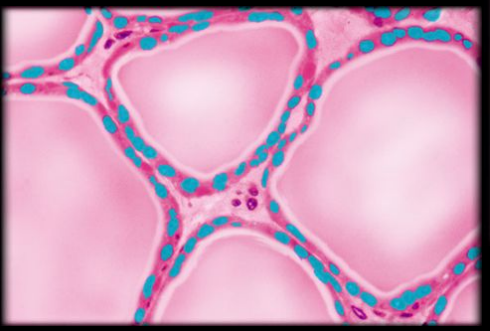


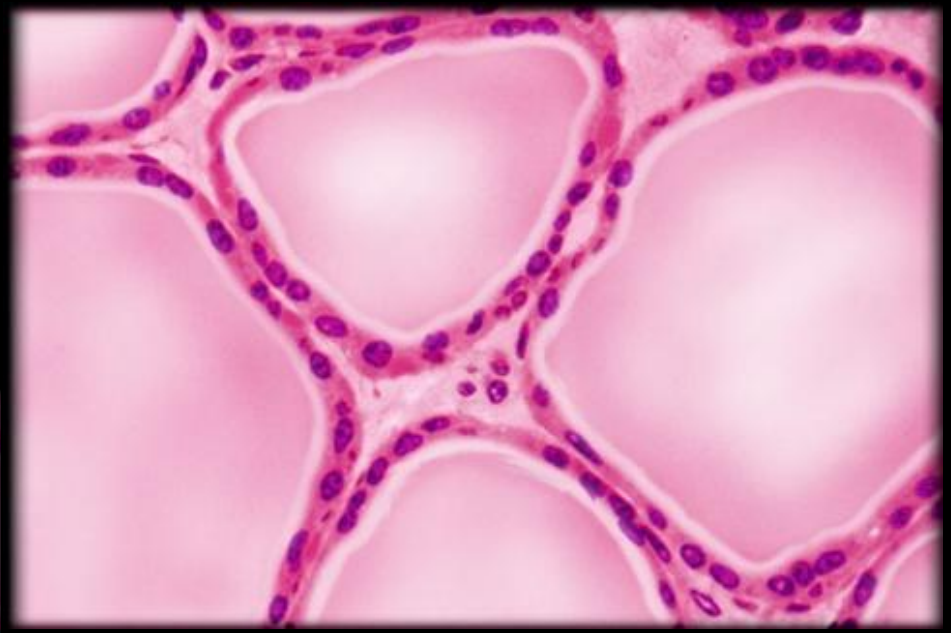
Thyroid Gland
High Magnification

Thyroid follicle

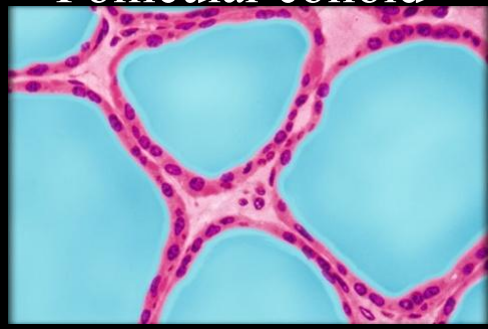


Nuclei of follicular cells

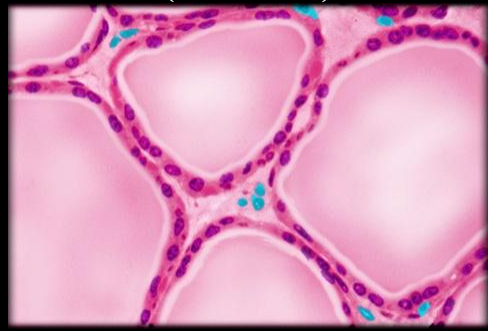




Follicular colloid



Extrafollicular cells (C cells)



17.8b Thyroid Gland and Thyroid Hormone

- Action of thyroid hormone (TH)
  - **Hypothalamic-pituitary-thyroid axis**
    - Cold temperature, pregnancy, high altitude, hypoglycemia, or low TH cause hypothalamus to release TRH
    - TRH causes anterior pituitary to release TSH
    - TSH binds to receptors of follicular cells and triggers release of TH
  - Follicular cells release two forms of TH to blood: T_3 and T_4
    - T_3 = triiodothyronine; T_4 = tetraiodothyronine
    - T_3 and T_4 are transported within blood by carrier molecules

17.8b Thyroid Gland and Thyroid Hormone

- Action of thyroid hormone (TH) (*continued*)
  - Some TH dissociates from carrier proteins and exits blood
  - Cellular transport brings TH into target cells where it binds to receptor
  - T_3 versus T_4
    - Thyroid gland produces more T_4 but T_3 is more active form
    - Most target cells convert T_4 to T_3
  - TH increases metabolic rate and protein synthesis in targets
    - Stimulates synthesis of sodium-potassium pumps in neurons
      - **Calorigenic:** generates heat, raises temperature
    - Stimulates increased amino acid and glucose uptake
    - Increases number of cellular respiration enzymes within mitochondria

17.8b Thyroid Gland and Thyroid Hormone

- Action of Thyroid Hormone (TH) (*continued*)
  - Fosters energy (ATP) production
    - Hepatocytes stimulated to increase blood glucose
      - TH causes increases in glycogenolysis and gluconeogenesis, and a decrease in glycogenesis
    - Adipose cells stimulated to increase blood glycerol and fatty acids
      - TH causes increase in lipolysis and decrease in lipogenesis
      - This saves glucose for the brain (**glucose-sparing effect**)
    - TH increases respiration rate
      - To meet additional oxygen demand
    - TH increases heart rate and force of contraction
      - Causes heart to increase receptors for epinephrine and norepinephrine

17.8b Thyroid Gland and Thyroid Hormone

- Negative feedback regulation of TH release
  - Increases in TH cause decreases in its release
    - TH inhibits release of TRH from hypothalamus
    - TH inhibits release of TSH from anterior pituitary
    - TH causes release of growth hormone inhibiting hormone further inhibiting TSH release

Regulation and Action of TH

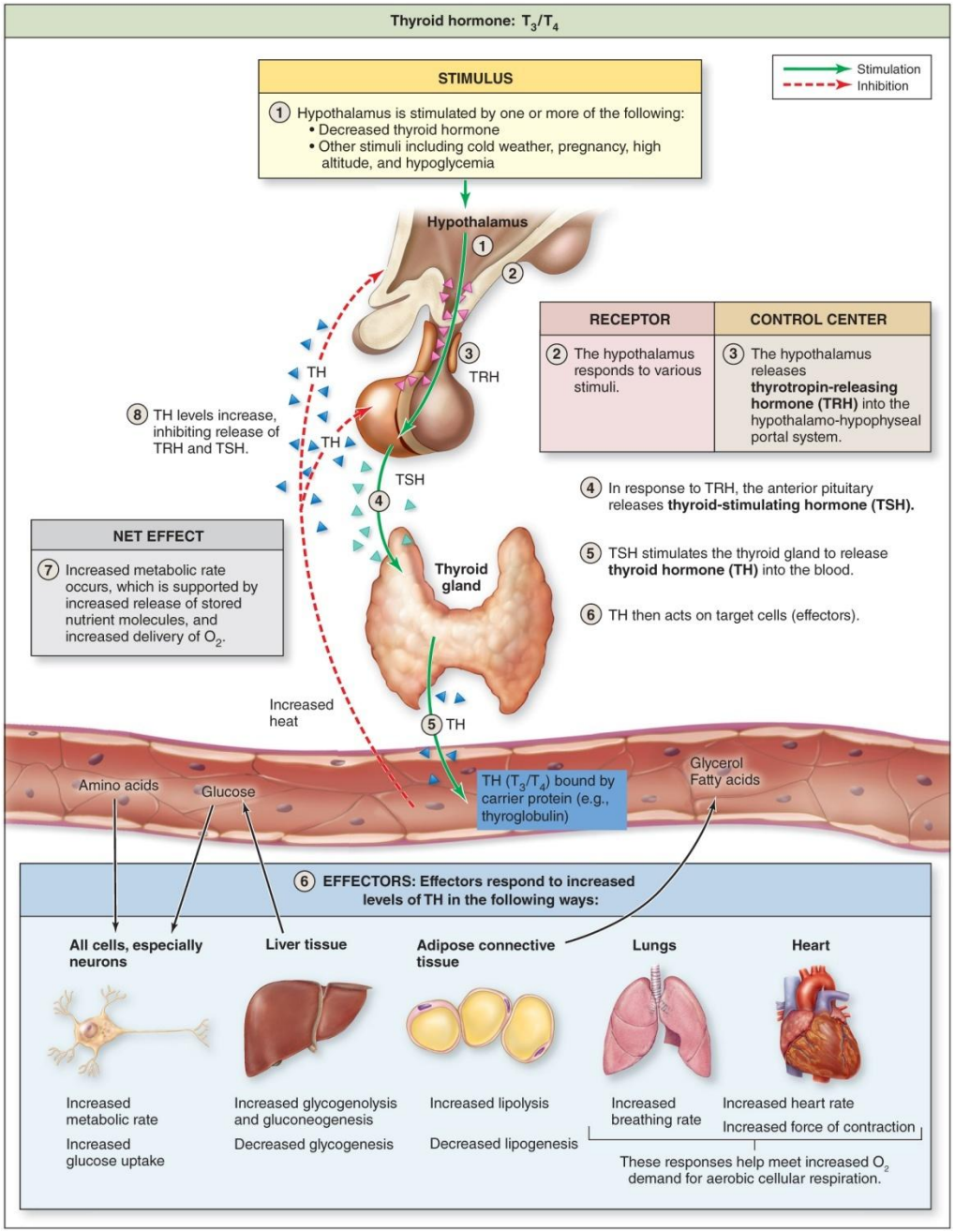


Figure 17.17

Clinical View: Disorders of Thyroid Hormone Secretion

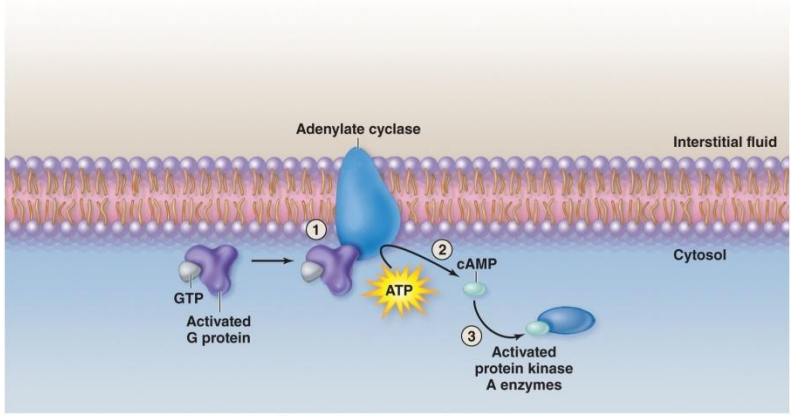
- **Hyperthyroidism**
  - Results from excessive production of TH
  - Increased metabolic rate, weight loss, hyperactivity, heat intolerance
  - Caused by T_4 ingestion, excessive stimulation by pituitary, or loss of feedback control in thyroid (**Graves disease**)
  - Treated by removing the thyroid (then giving hormone supplements)
- **Hypothyroidism**
  - Results from decreased production of TH
  - Low metabolic rate, lethargy, cold intolerance, weight gain, photophobia
  - Caused by decreased iodine intake, loss of pituitary stimulation of thyroid, postsurgical, or immune system destruction of thyroid
  - Treated with thyroid hormone replacement

Clinical View: Disorders of Thyroid Hormone Secretion *(continued)*

- **Goiter**
  - Enlargement of thyroid
  - Typically due to insufficient dietary iodine
  - Lack of dietary iodine preventing thyroid from producing thyroid hormone
  - Once relatively common in United States, but no longer now that iodine added to table salt

17.8c Adrenal Glands and Cortisol

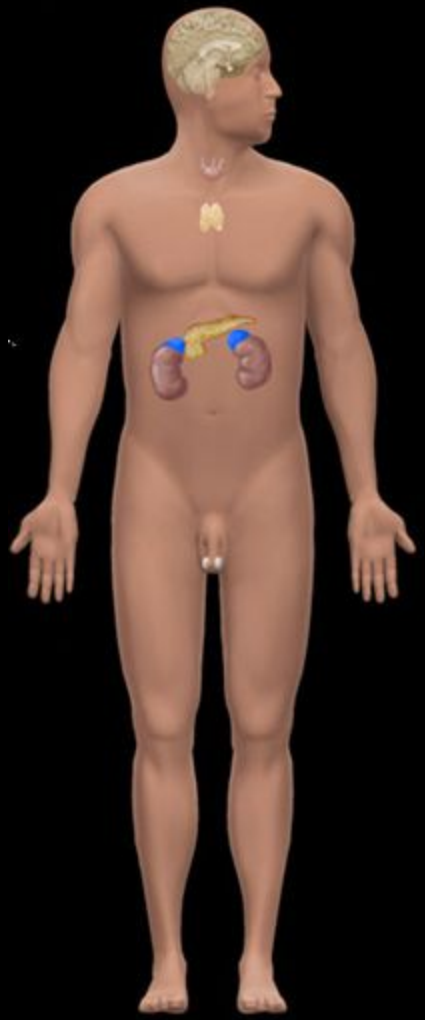
- Anatomy of the adrenal glands
  - Paired, pyramid-shaped endocrine glands
  - Located on superior surface of each kidney
  - Retroperitoneal, embedded within fat and fascia
  - Two regions: adrenal medulla and adrenal cortex

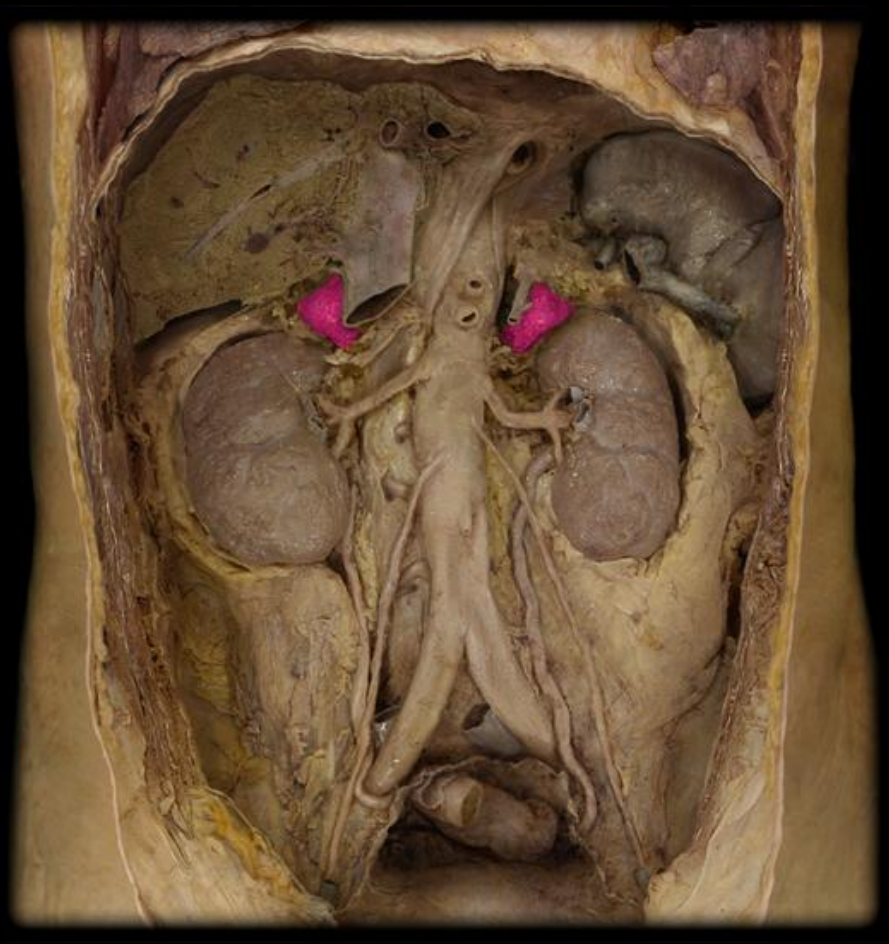


(a) Activated G protein "turns on" adenylate cyclase.

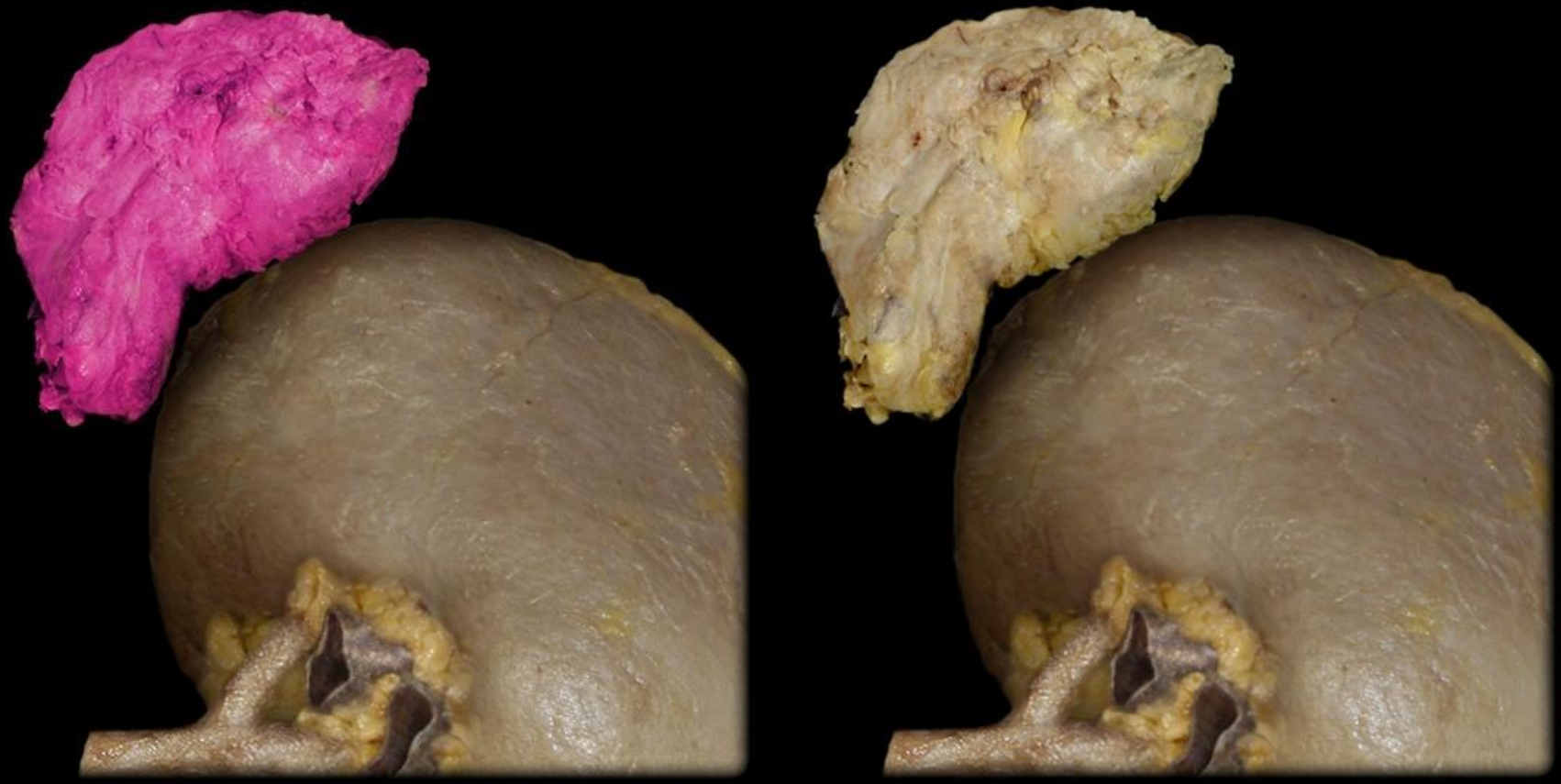
Figure 17.18a (part)

Adrenal Glands



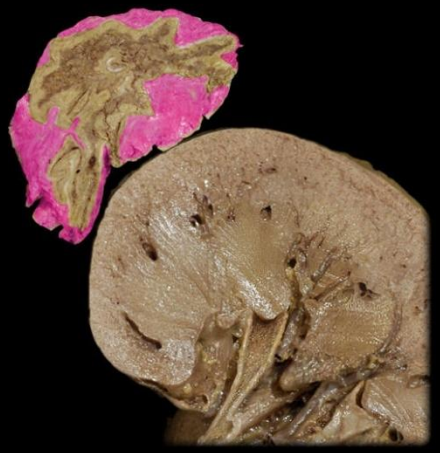


Adrenal (Suprarenal) Glands

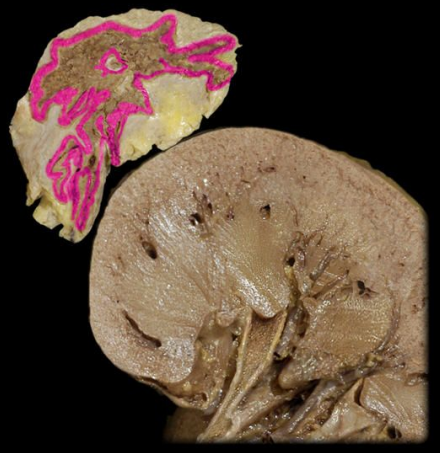


Adrenal (Suprarenal) Glands

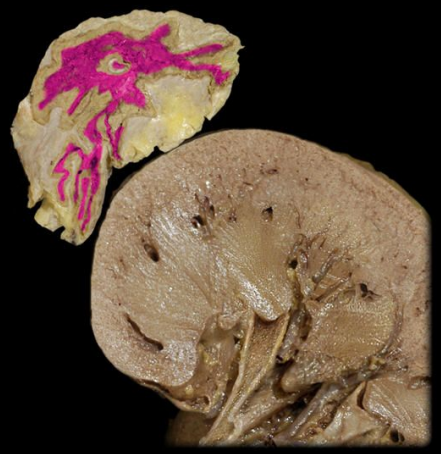
Cortex and Medulla



Capsule



Cortex

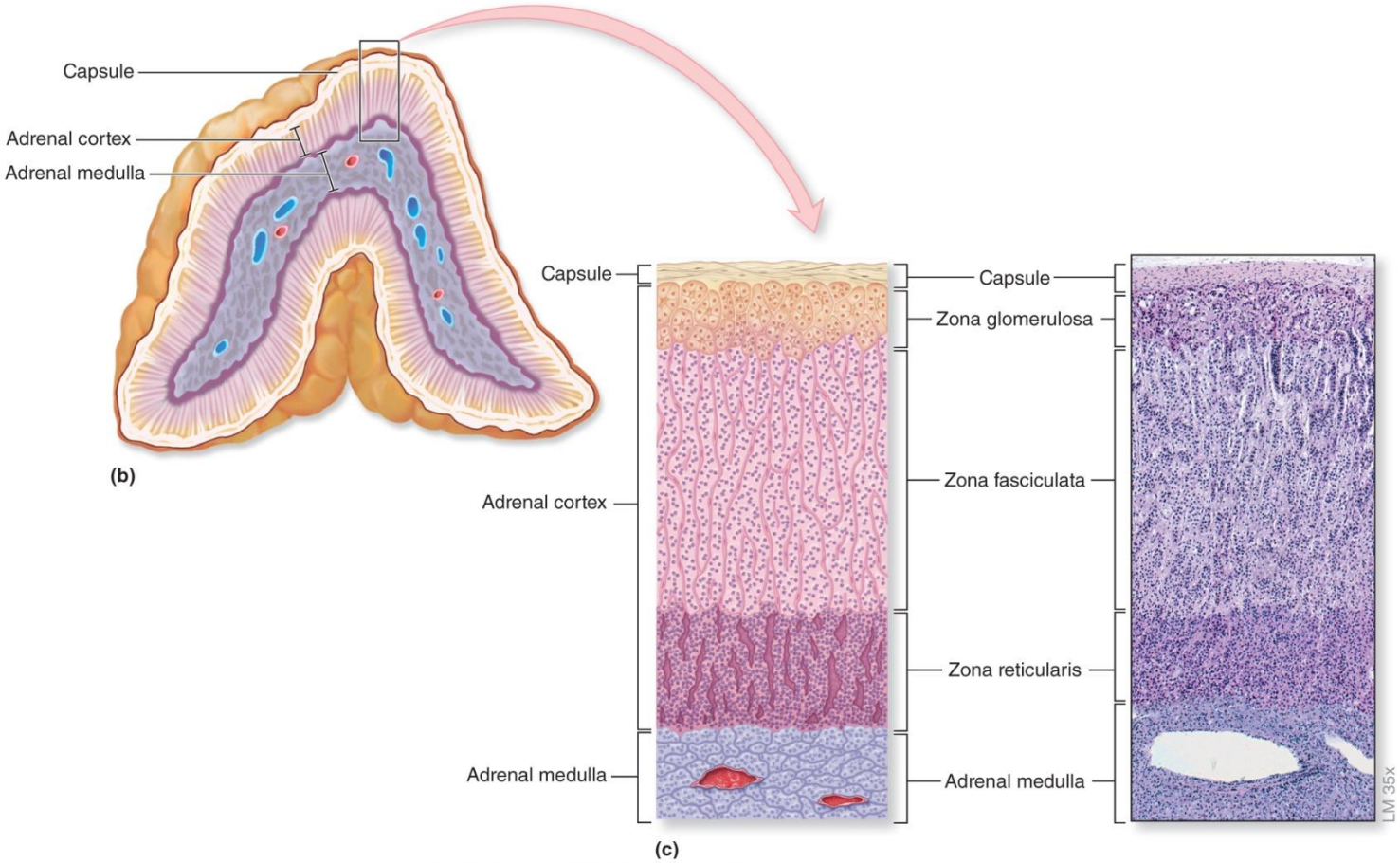


Medulla

17.8c Adrenal Glands and Cortisol

- Anatomy of the adrenal glands (*continued*)
  - **Adrenal medulla**
    - Forms inner core of each adrenal gland
    - Red-brown color due to extensive blood vessels
    - Releases epinephrine and norepinephrine with sympathetic stimulation
  - **Adrenal cortex**
    - Synthesizes more than 25 corticosteroids
    - Yellow color due to lipids within cells
    - Three regions producing different steroid hormones: zona glomerulosa, zona fasciculata, and the inner zona reticularis

Adrenal Glands



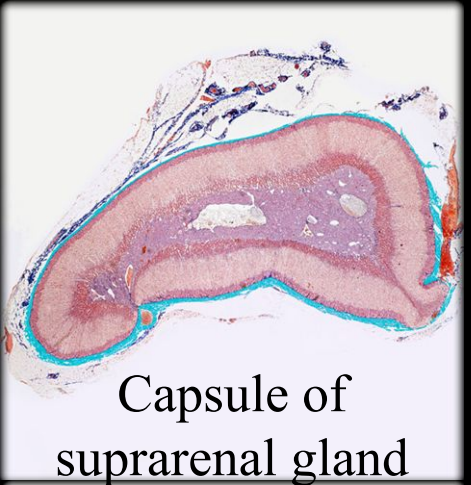
c: © McGraw-Hill Education/Al Telser, photographer

Figure 17.18b,c

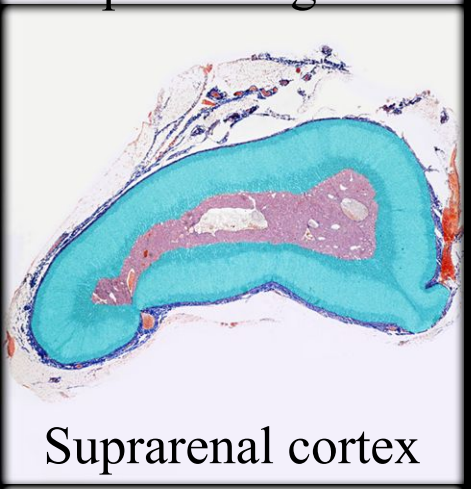
17.8c Adrenal Glands and Cortisol

- Hormones of the adrenal cortex
  - **Mineralocorticoids:** hormones that regulate electrolyte levels
    - Made in **zona glomerulosa:** thin, outer cortical layer
    - **Aldosterone** fosters Na^+ retention and K^+ secretion
  - **Glucocorticoids:** hormones that regulate blood sugar
    - Made in **zona fasciculata:** larger, middle cortical layer
    - **Cortisol** increases blood sugar
  - **Gonadocorticoids:** sex hormones
    - Made in **zona reticularis:** thin, inner cortical layer
    - **Androgens** are male sex hormones made by adrenals
      - Converted to estrogen in females
      - Amount of androgen produced by adrenals is less than amount from testes

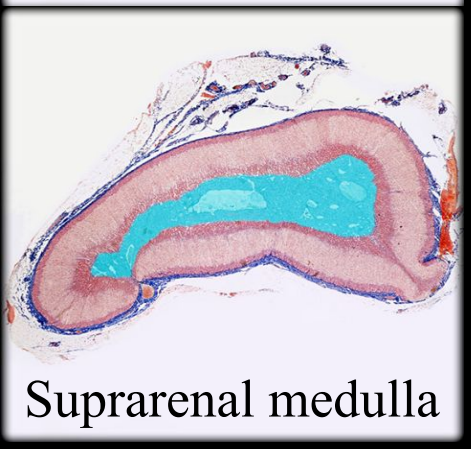
Suprarenal Gland
Low Magnification



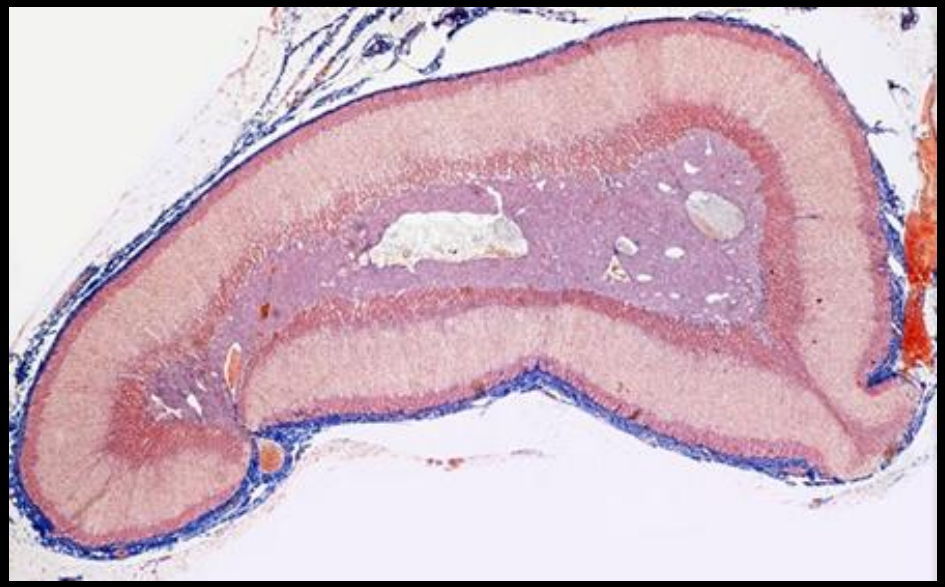
Capsule of suprarenal gland

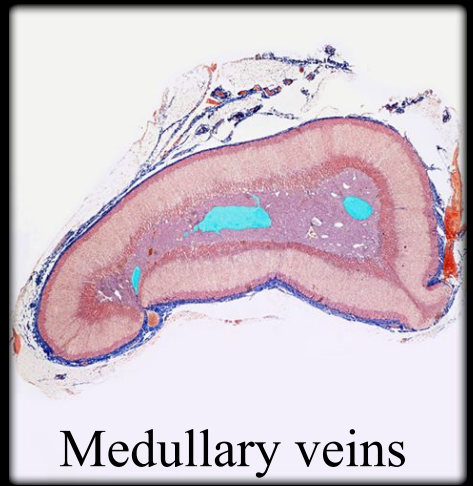


Suprarenal cortex

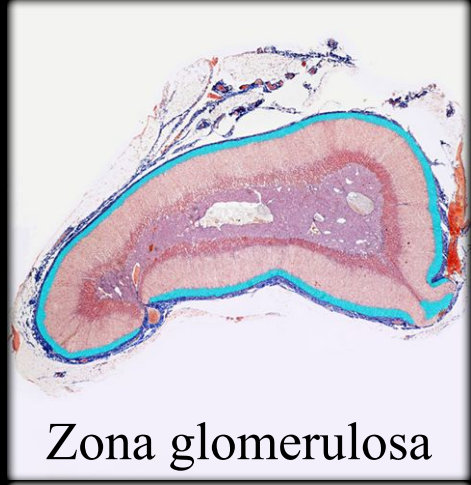


Suprarenal medulla

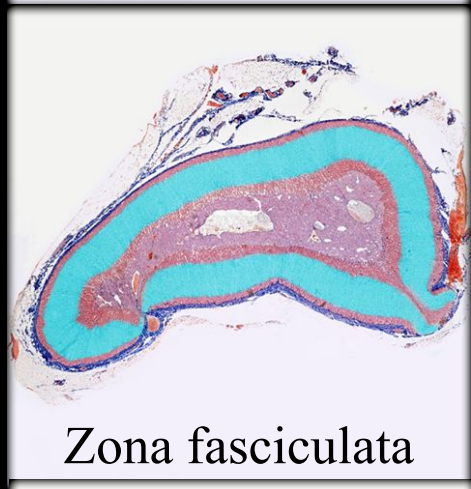




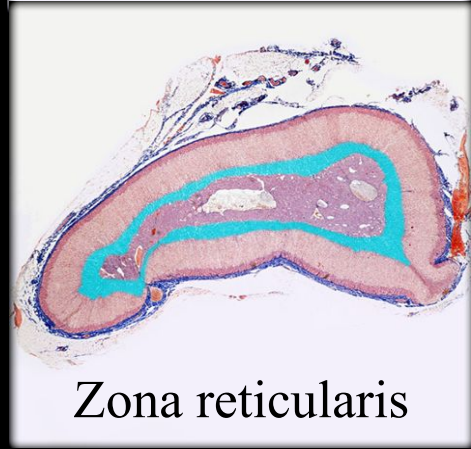
Medullary veins



Zona glomerulosa

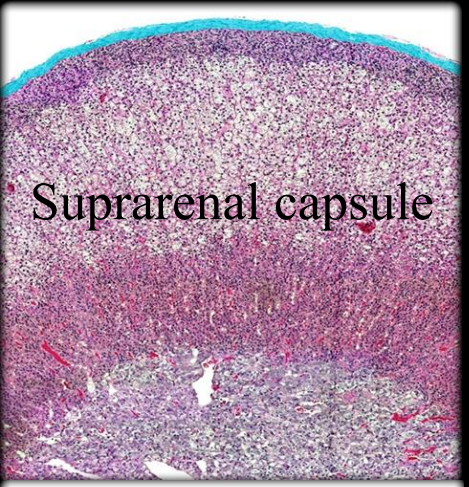


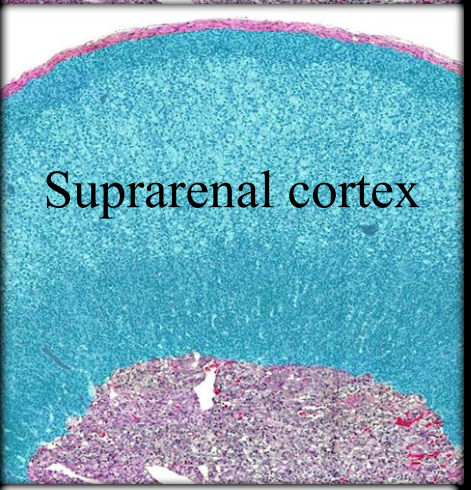
Zona fasciculata

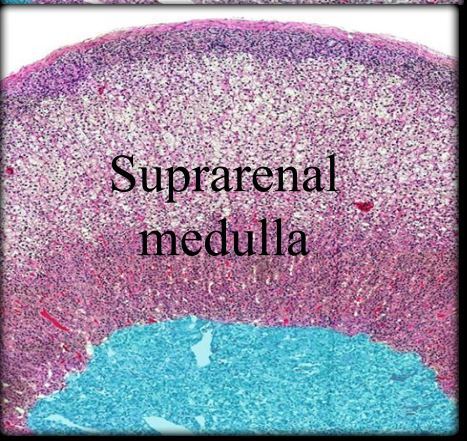


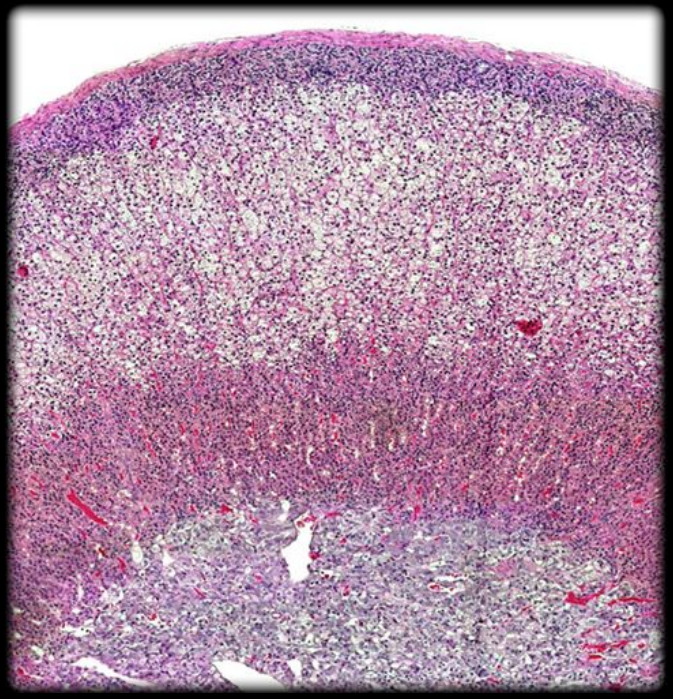
Zona reticularis

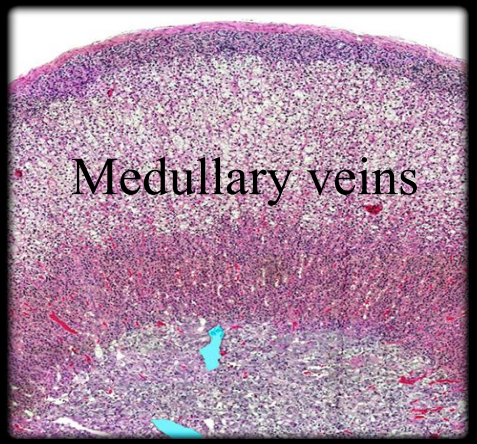
Suprarenal Gland
Medium Magnification

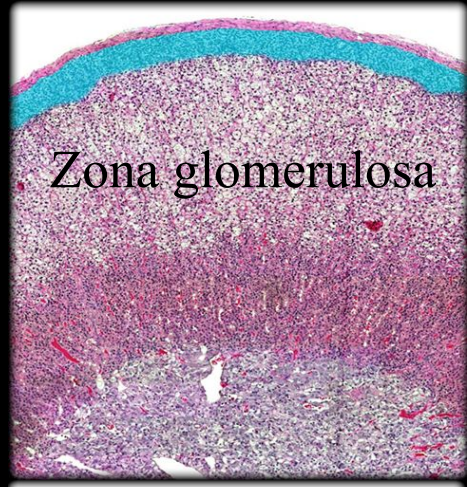


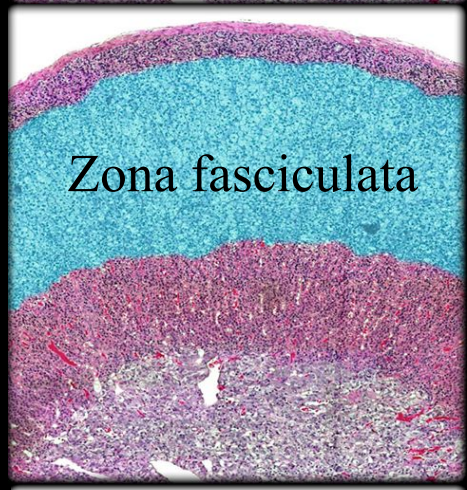


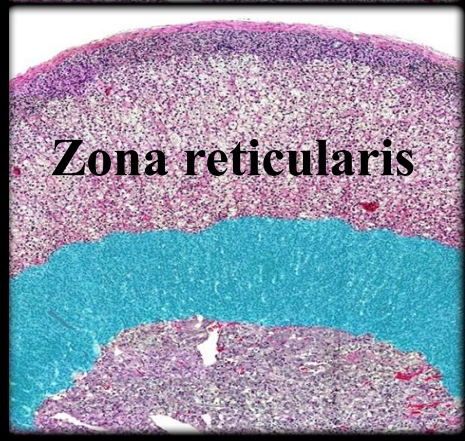












17.8c Adrenal Glands and Cortisol

- Action of cortisol
  - **Cortisol** and **corticosterone** increase nutrient levels in blood
    - To resist stress and repair injured tissue
  - Release regulated by **hypothalamic-pituitary-adrenal axis**
    - Stress, late stages of sleep, and low levels of cortisol stimulate hypothalamus to release CRH
    - CRH stimulates anterior pituitary to release ACTH
    - ACTH stimulates adrenal cortex to release cortisol and corticosterone
  - Cortisol travels through blood attached to carrier proteins
    - Small amounts of cortisol dissociate from carrier and leave bloodstream

Regulation and Action of Cortisol Hormone

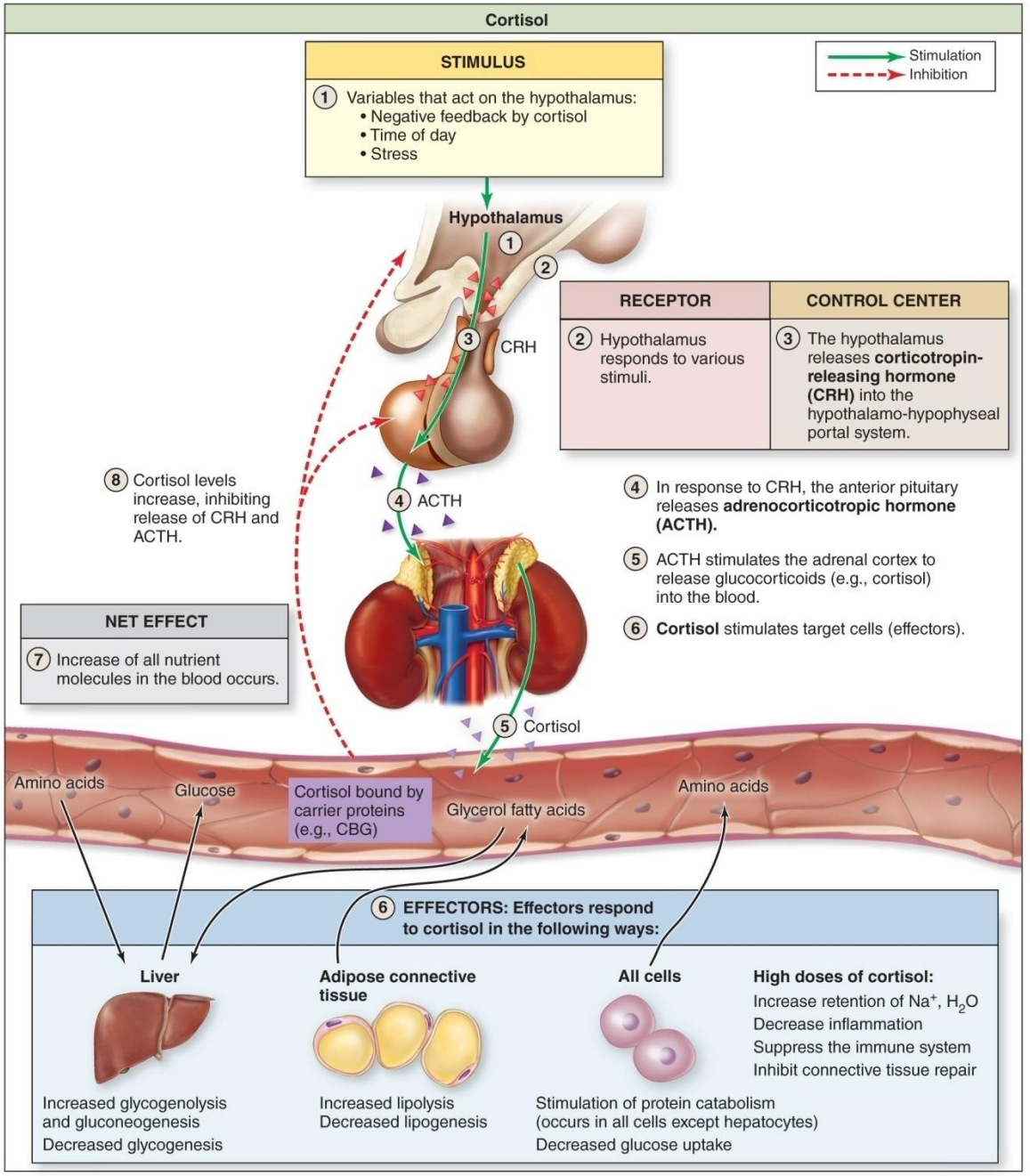
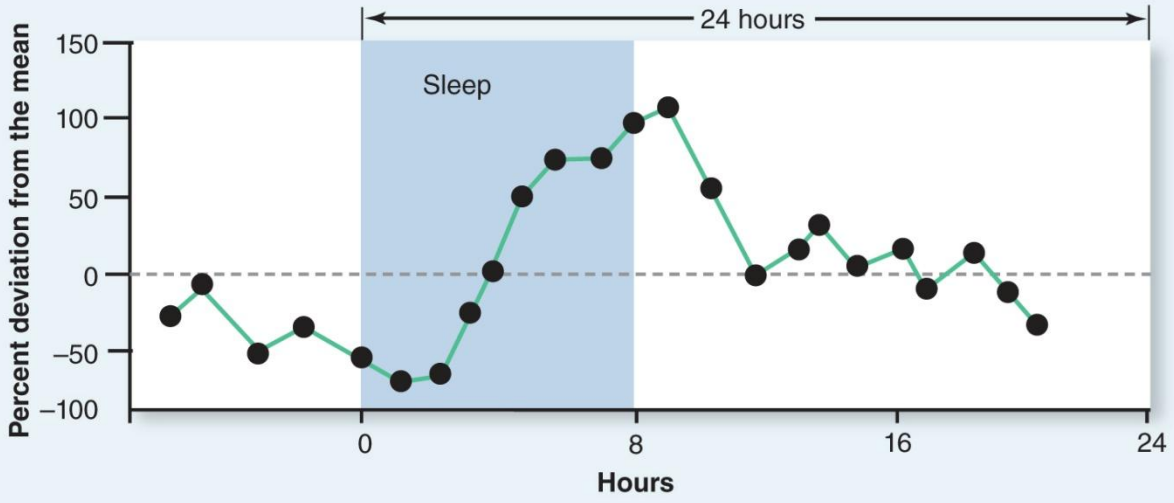


Figure 17.19

Variables That Influence Levels of Cortisol

Cortisol release fluctuates based on the time of day (circadian rhythm).

Cortisol levels fluctuate throughout the day. Notice that in a normal sleep-wake cycle, peak levels of cortisol correspond to the late stages of a normal sleep cycle. About half of all cortisol release occurs when you are asleep, with cortisol levels peaking right before waking in the morning. This rhythm of release is regulated by light and dark cycles detected by the retina as nerve signals are relayed to the hypothalamus. (Among individuals, there is significant variation in normal levels.)



(a)

Cortisol level is increased by stress.

Both emotional stress (e.g., anxiety, anger, fear) and physical stress (e.g., fever, trauma, or intense exercise) increase the release of cortisol.

(b)

Figure 17.20

17.8c Adrenal Glands and Cortisol

- Action of cortisol (*continued*)
  - Cortisol diffuses through target cell's membrane and binds to intracellular receptor
    - Hormone-receptor complex binds to DNA and activates genes
  - Cortisol causes target cells to increase blood nutrient levels
    - Liver cells increase glycogenolysis and gluconeogenesis; decrease glycogenesis
    - Adipose cells increase lipolysis and decrease lipogenesis
    - Many body cells break down proteins to amino acids
      - Liver cells use the amino acids for gluconeogenesis
    - Most cells decrease their glucose uptake, sparing it for brain

17.8c Adrenal Glands and Cortisol

- Cortisol levels are regulated by negative feedback
  - Cortisol inhibits release of CRH from hypothalamus and ACTH from anterior pituitary
- Corticosterone is used as a treatment for inflammation
  - It inhibits inflammatory agents and suppresses immune system
  - At high doses it has side effects
    - Increases risk of infections, cancer
    - Increases retention of sodium and water
    - Inhibits connective tissue repair

Clinical View: Disorders in Adrenal Cortex Hormone Secretion

- **Cushing syndrome**
  - Chronic exposure to excessive glucocorticoid hormones in people taking corticosteroids for therapy
  - Some cases when adrenal gland produces too much hormone
  - Obesity, hypertension, excess hair growth, kidney stones, and menstrual irregularities
- **Addison disease**
  - Form of adrenal insufficiency
  - Develops when adrenal glands fail
  - Chronic shortage of glucocorticoids and sometimes mineralocorticoids
  - May develop from lack of ACTH or lack of response to ACTH
  - Weight loss, fatigue and weakness, hypotension, and skin darkening
  - Therapy of oral corticosteroids

Clinical View: Disorders in Adrenal Cortex Hormone Secretion (*continued*)

- **Adrenogenital syndrome (congenital adrenal hyperplasia)**
  - Begins in embryo or fetus
  - Inability to synthesize corticosteroids leads to overproduction of ACTH
  - High ACTH causes increased size of adrenal gland and production of hormones with testosterone-like effects
    - Masculinizes newborn

Clinical View: Stress Response

- Stressors elicit a **stress response**
- Hypothalamus initiates neuroendocrine response
- Three stages
  - Alarm reaction
    - Initial response involving sympathetic nervous system activation, epinephrine, norepinephrine
  - Stage of resistance
    - After depletion of glycogen stores, adrenal secretes cortisol to raise blood sugar and help meet energy demands
  - Stage of exhaustion
    - After weeks or months, depletion of fat stores results in protein breakdown for energy leading to weakening of the body and illness

What did you learn?

- At what time of day are growth hormone levels highest?
- What is the function of thyroid follicular cells?
- What is the primary mineralocorticoid and what are its specific effects?

17.9 Pancreatic Hormones

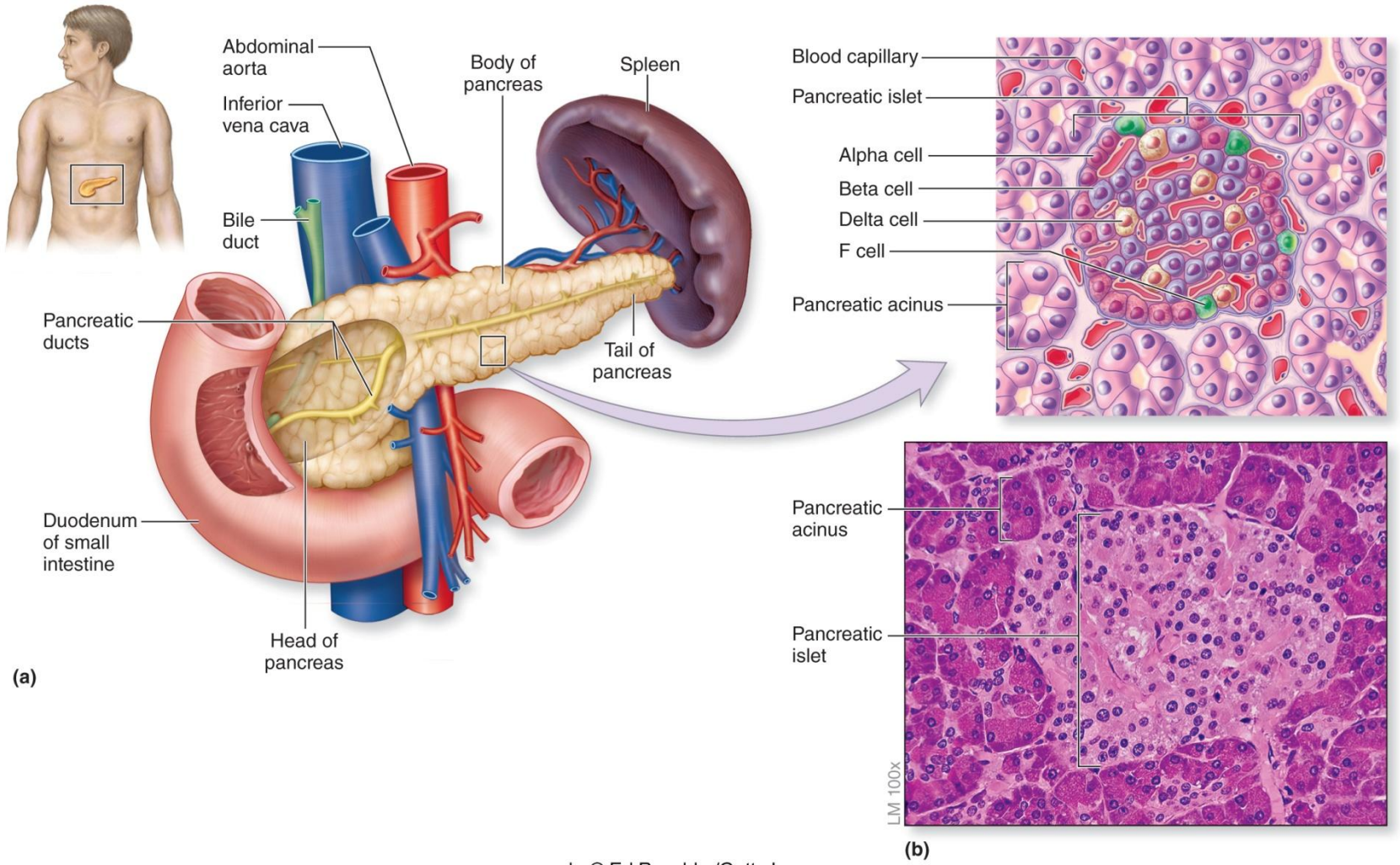
Learning Objectives:

1. Describe the gross anatomy and cellular structure of the pancreas.
2. Identify the primary types of pancreatic islet cells and the hormones they produce.
3. Describe the action of insulin in lowering blood glucose concentration.
4. Explain the action of glucagon in raising blood glucose concentration.

17.9a Anatomy of the Pancreas

- Sits behind stomach, between duodenum and spleen
- Pancreas has endocrine and exocrine functions
  - Acini cells generate exocrine secretions for digestion
    - They make up vast majority of pancreas
  - **Pancreatic islets** (of Langerhans) contain clusters of endocrine cells
    - **Alpha cells** secrete **glucagon**
    - **Beta cells** secrete **insulin**
    - Delta cells and F cells also present

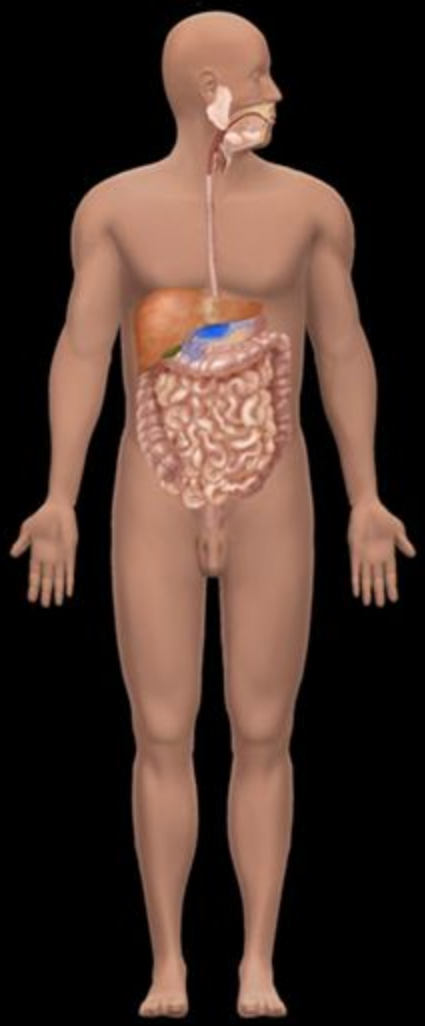
Pancreas

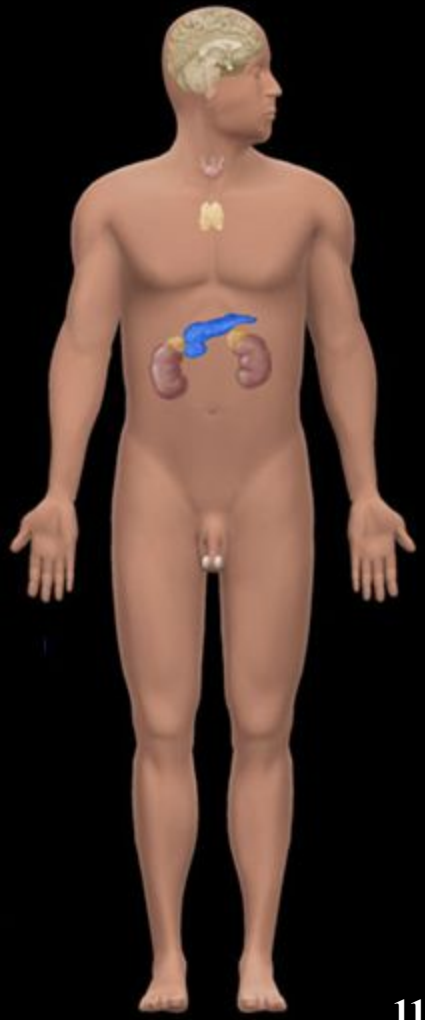


b: © Ed Reschke/Getty Images

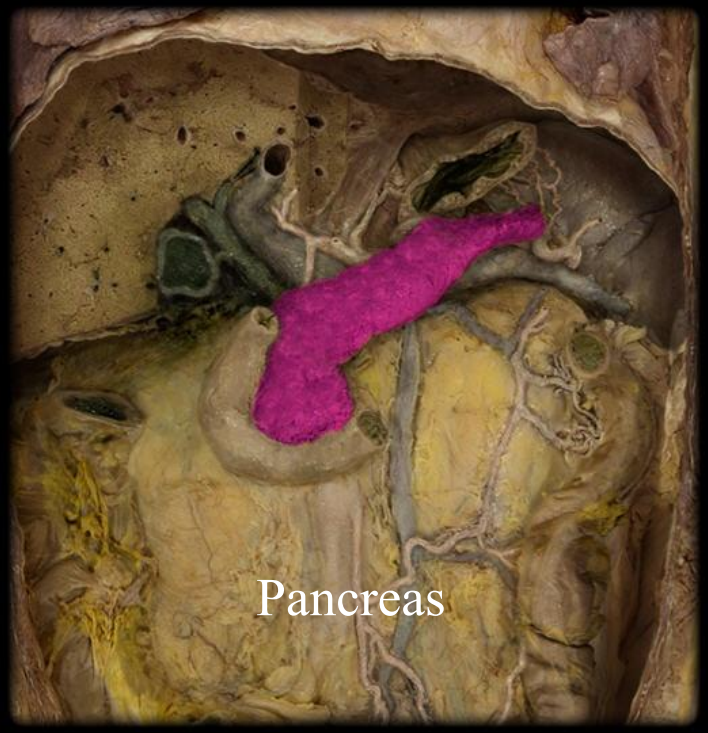
Figure 17.21

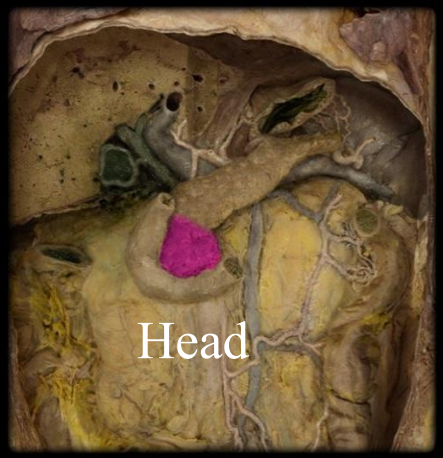
Pancreas

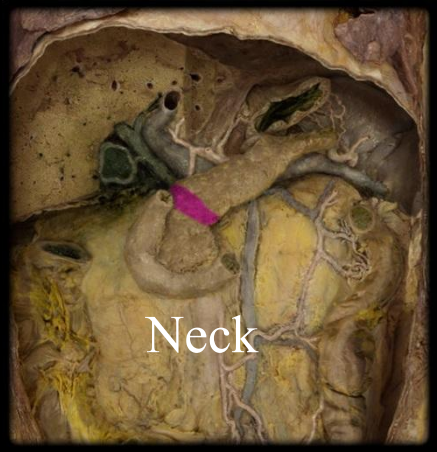


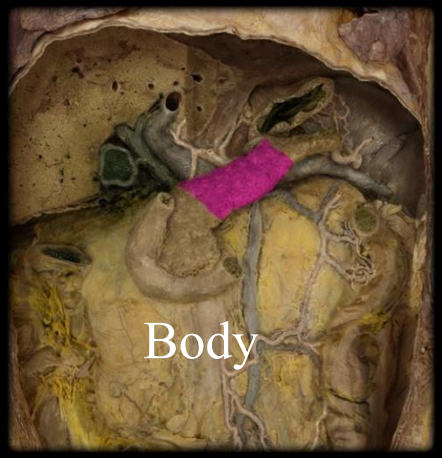


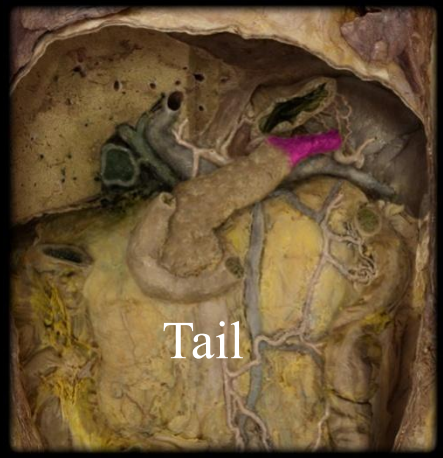
Pancreas











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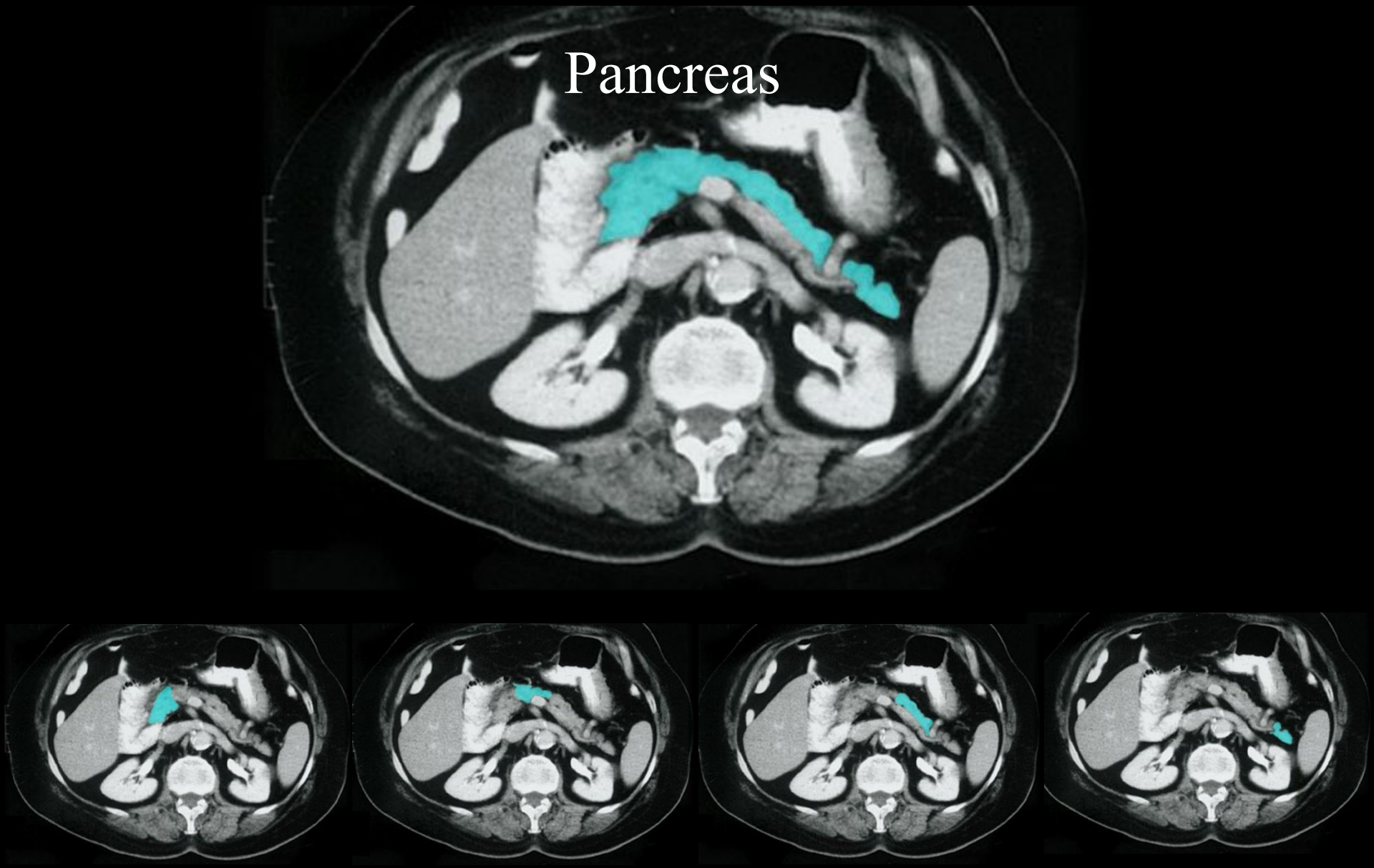
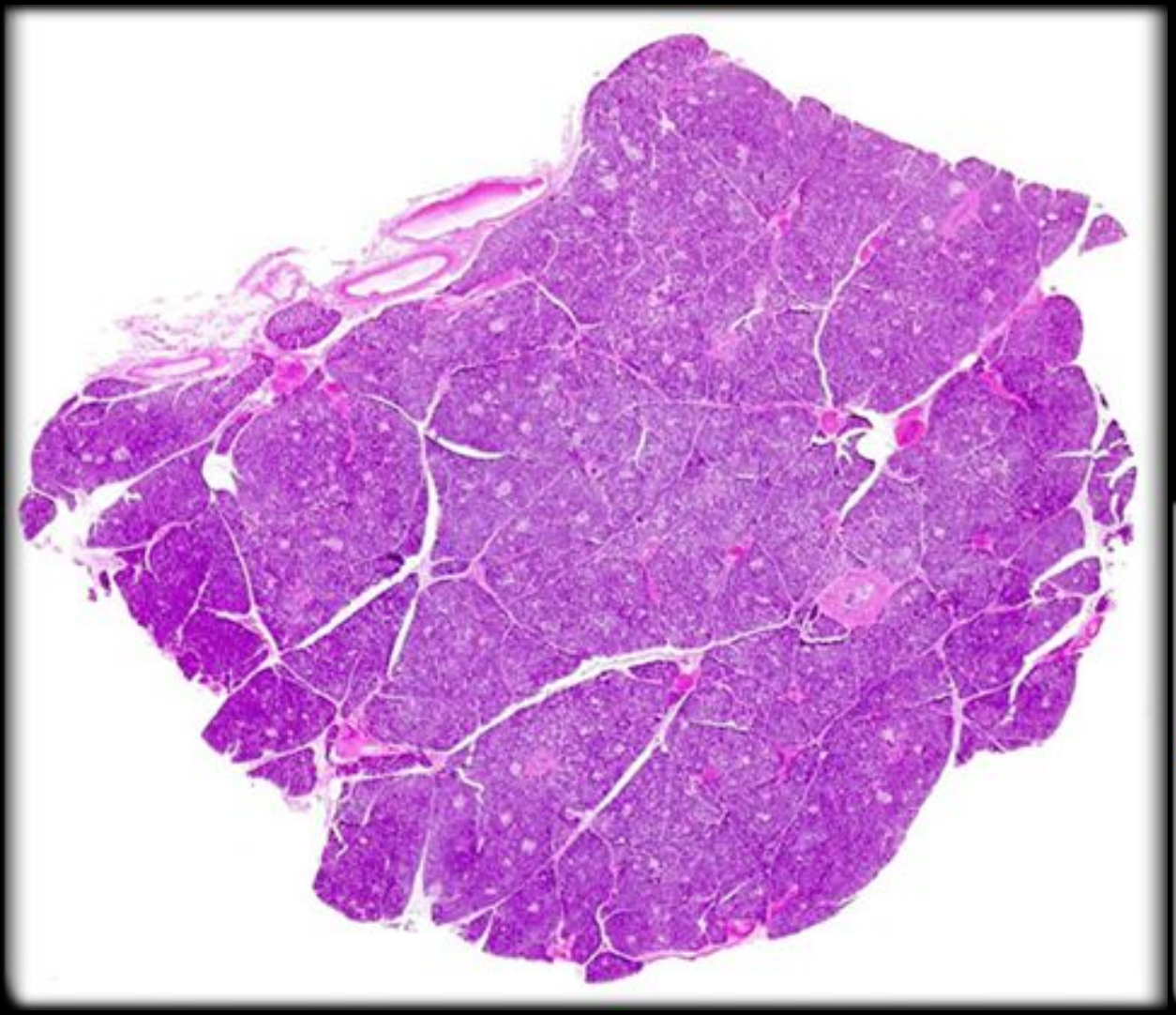
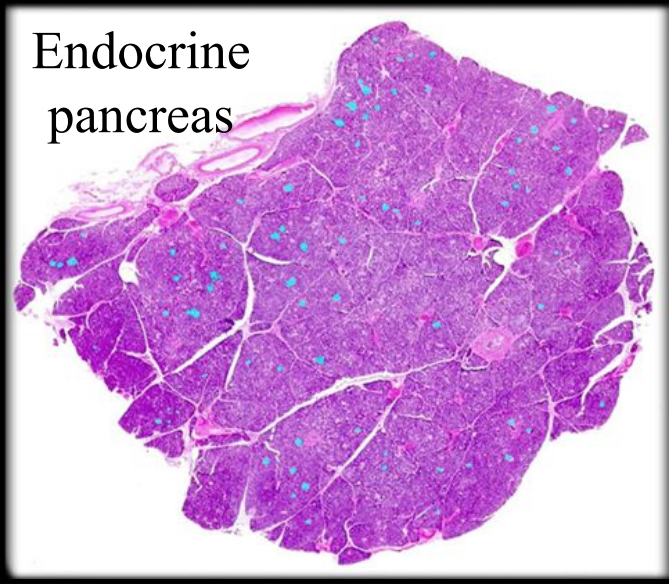
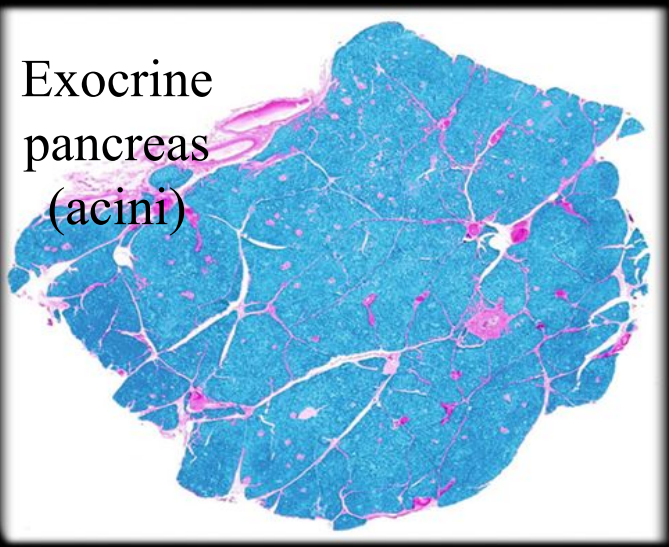


Head Neck Body Tail

Pancreas
Low Magnification



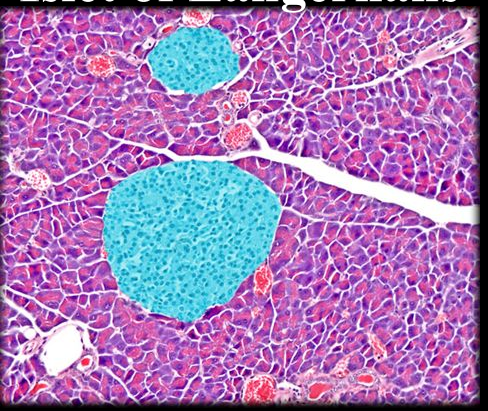


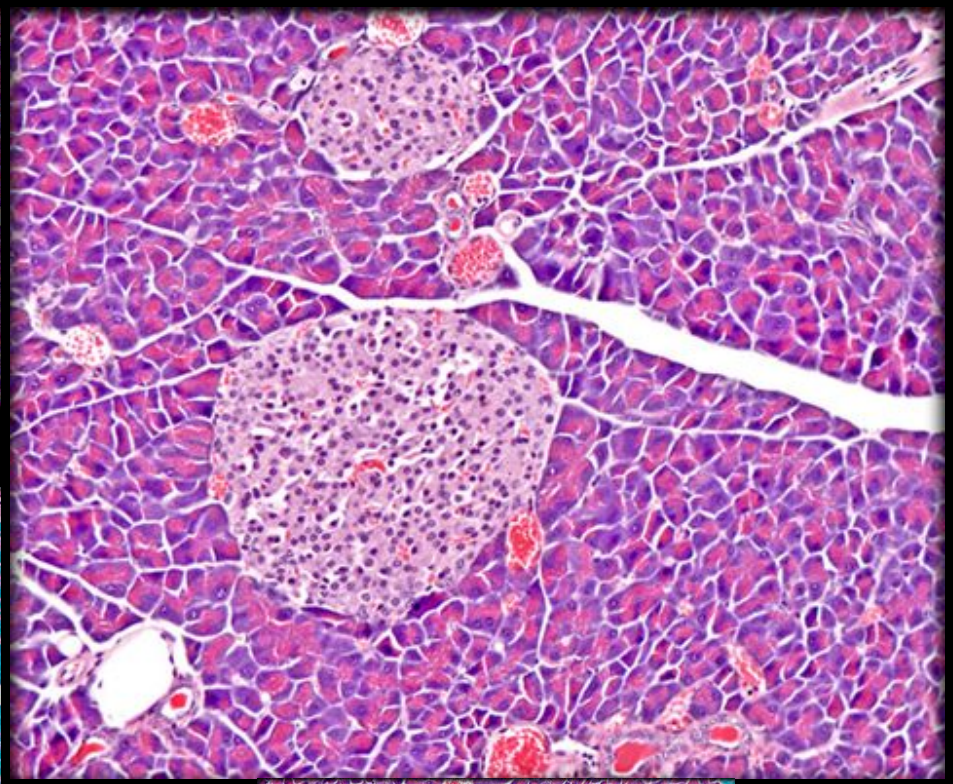


Pancreas

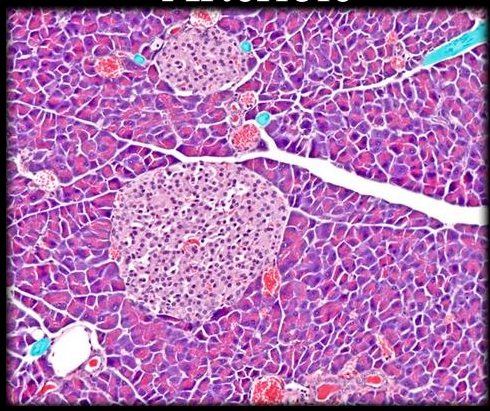
Medium Magnification

Islet of Langerhans

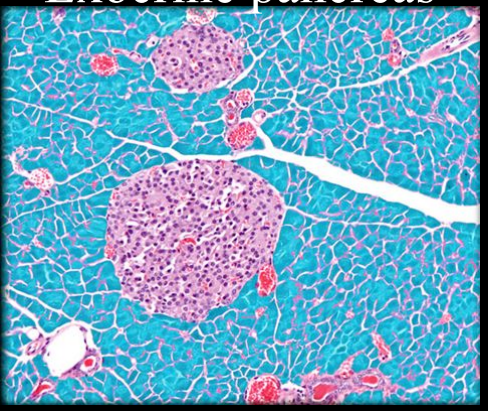




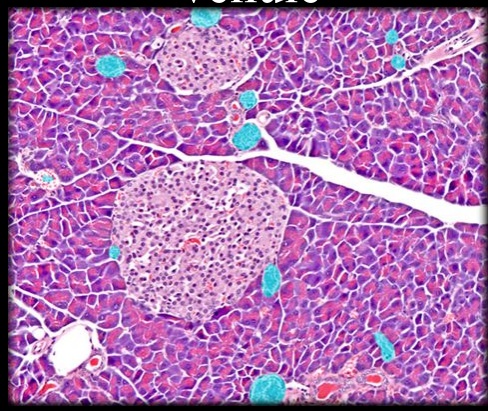
Arteriole



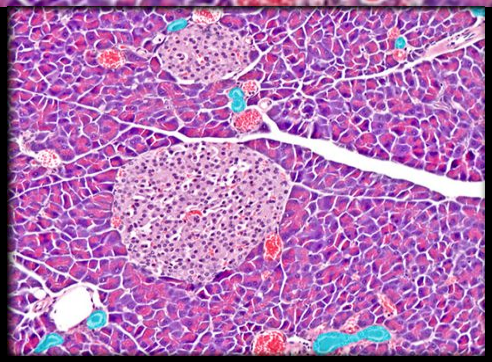
Exocrine pancreas



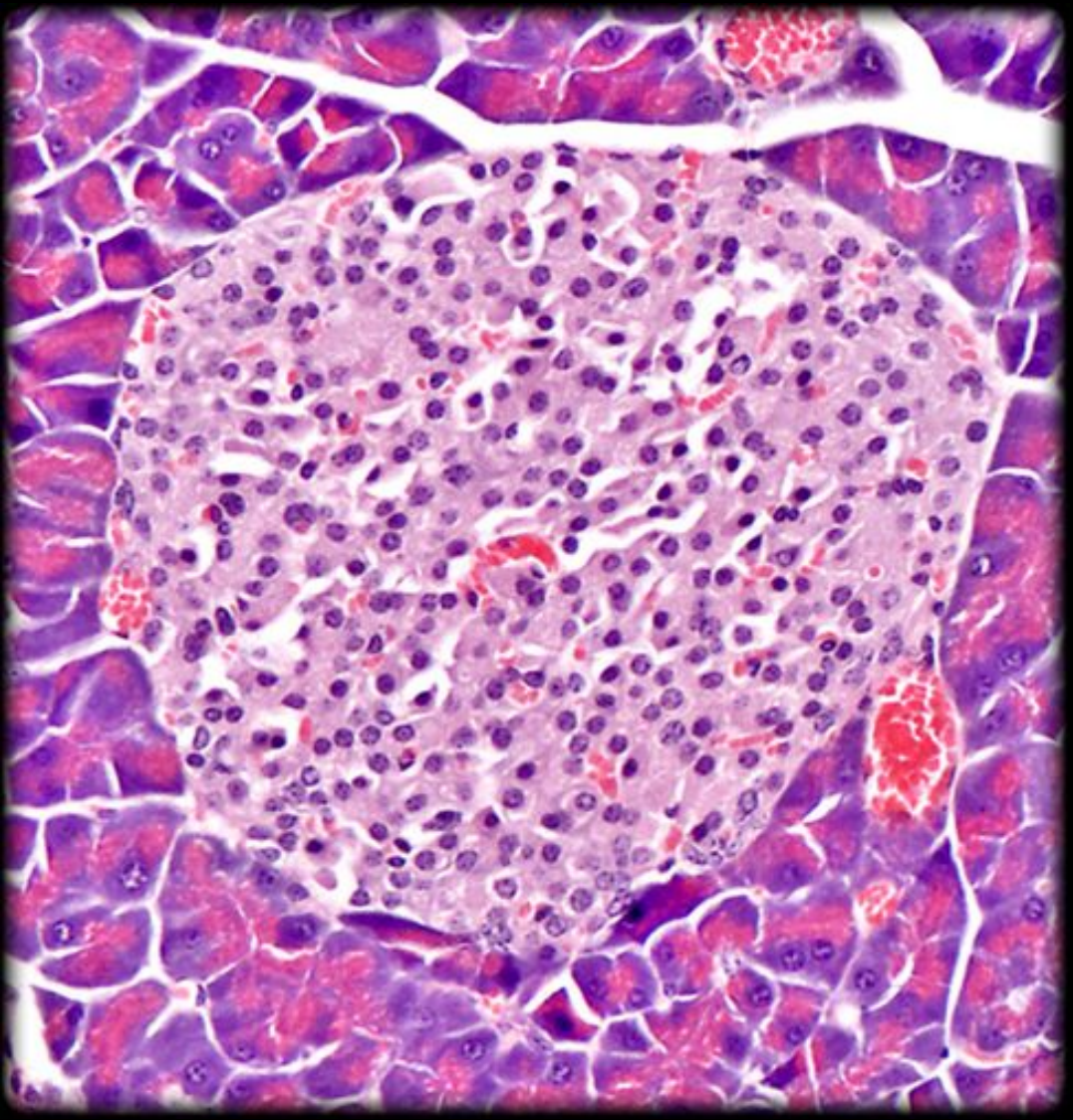
Venule

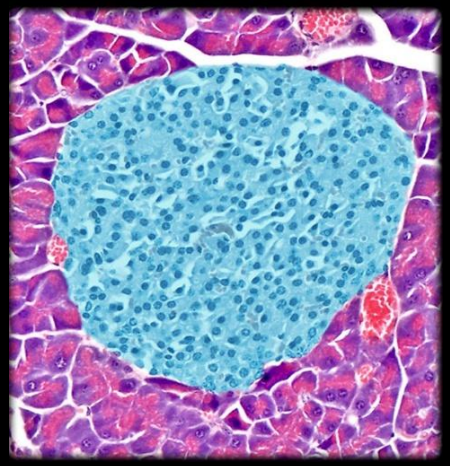


Intralobular ducts

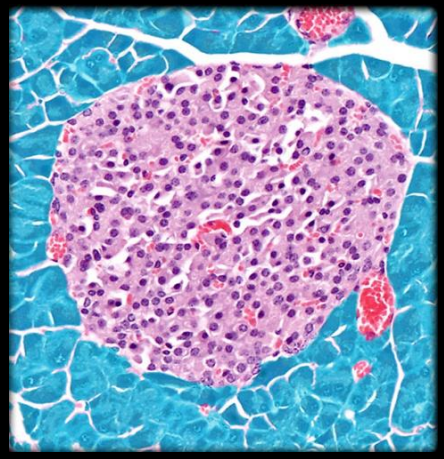


Pancreas
High Magnification

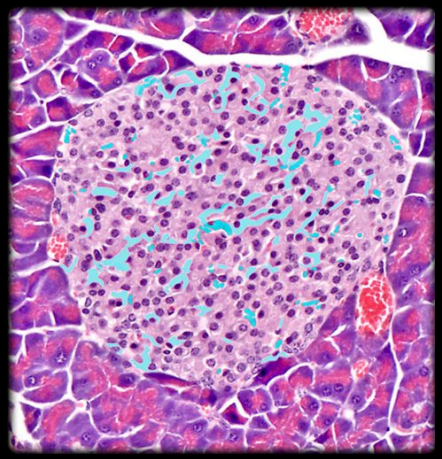




Islet of Langerhans

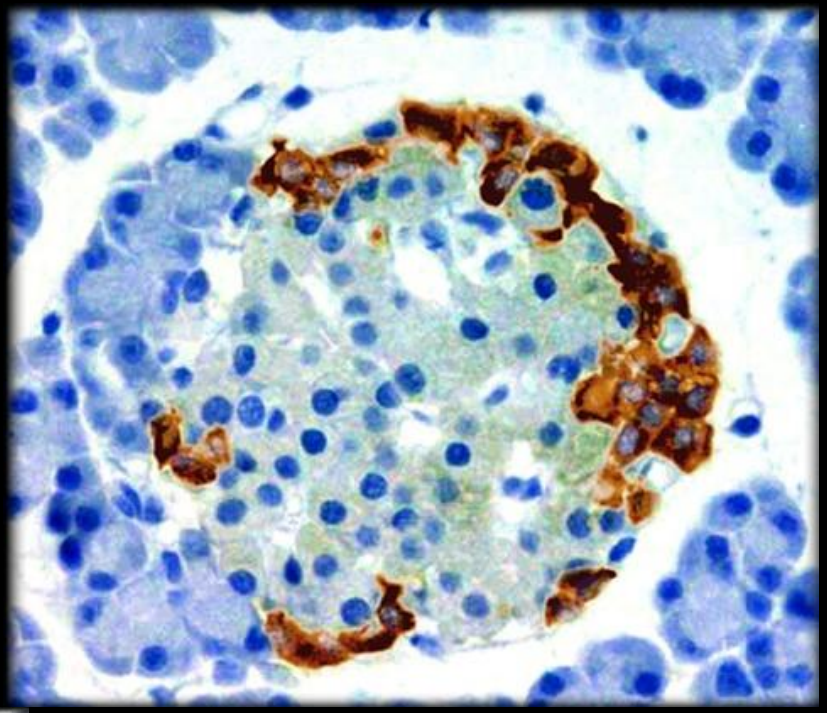


Exocrine pancreas

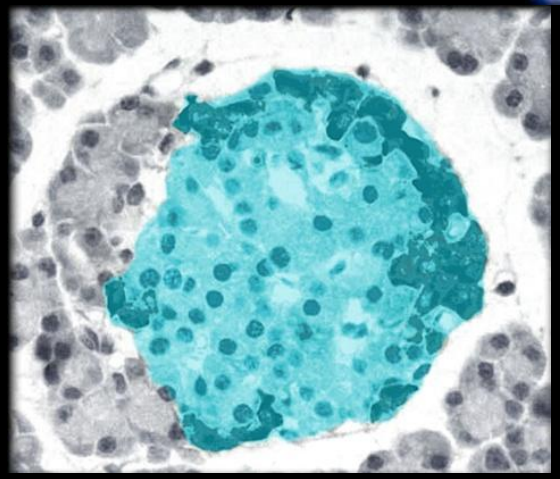


Capillaries in pancreatic islet of Langerhans

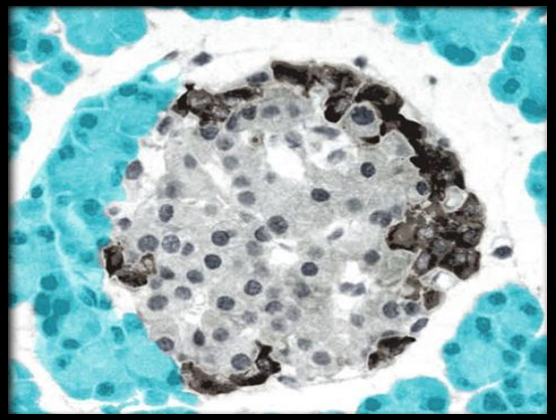
Pancreas—Alpha Cells



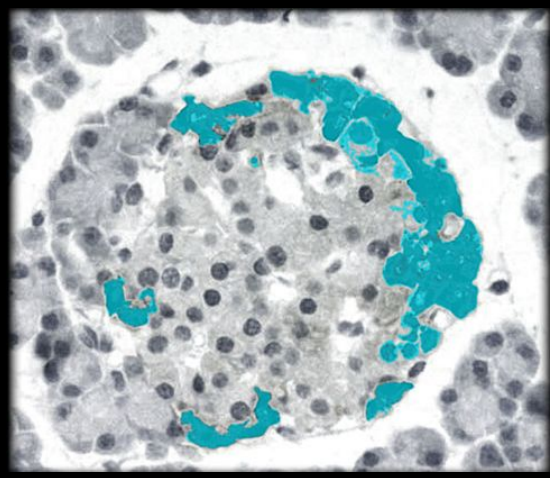
Pancreatic Islet of Langerhans



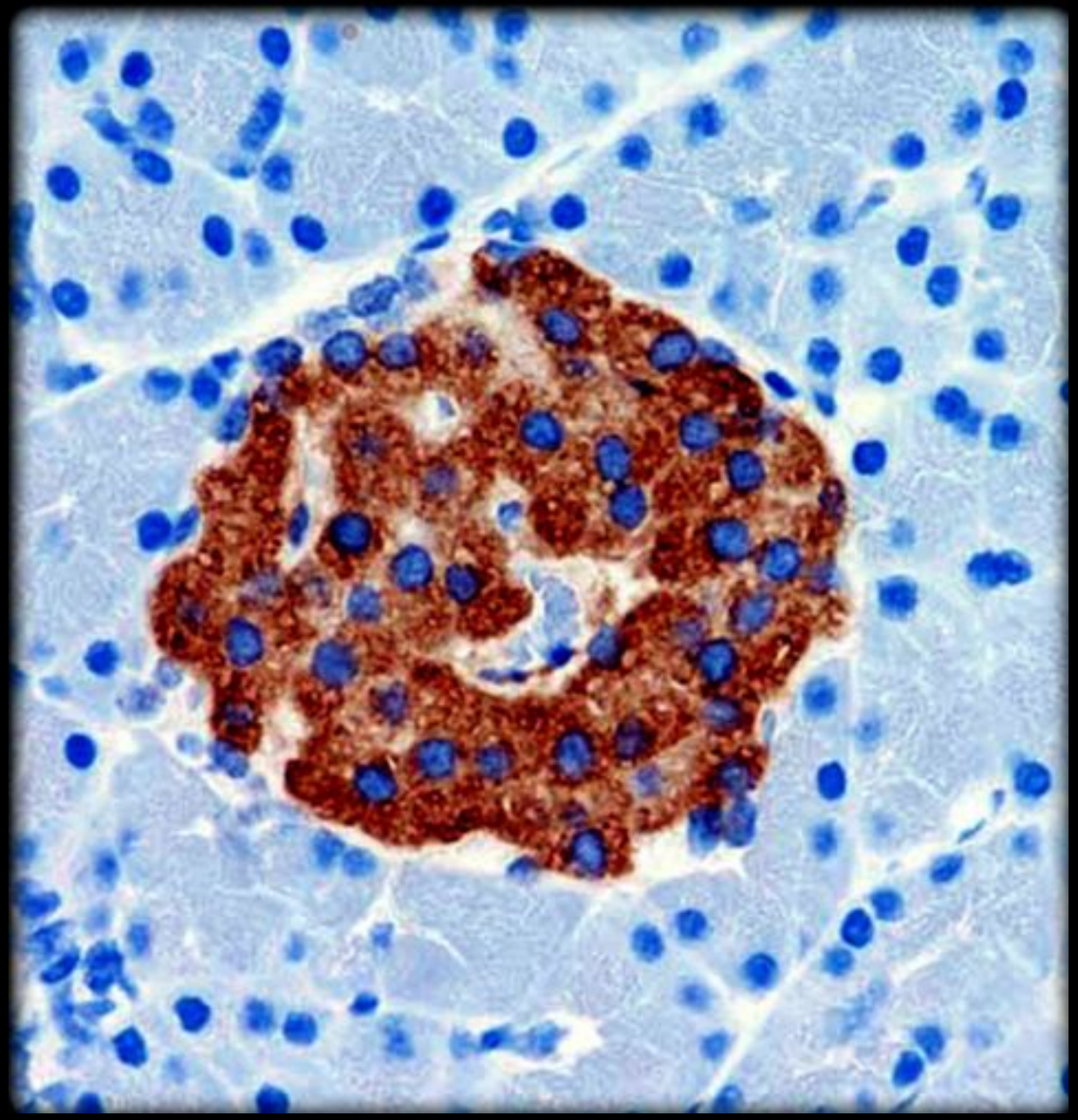
Exocrine pancreas

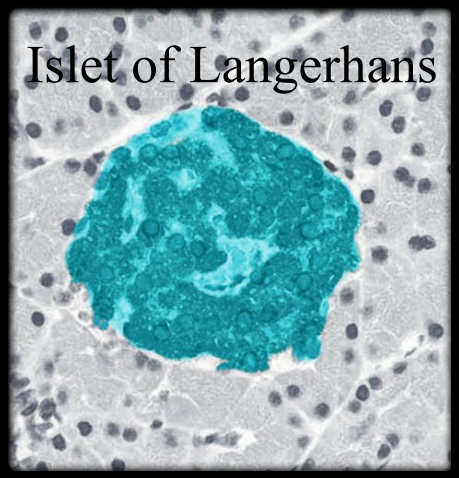


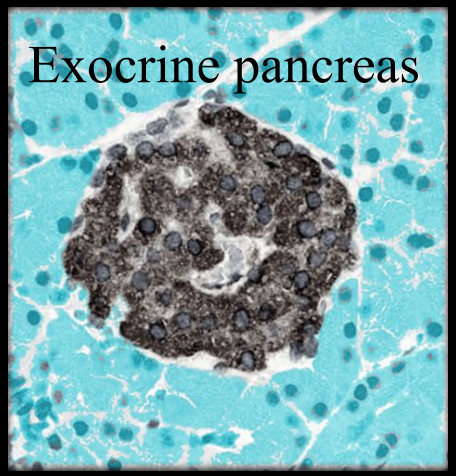
Alpha cells

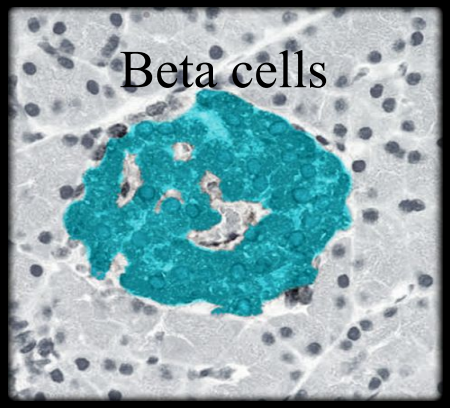


Pancreas—Beta Cells









17.9b Effects of Pancreatic Hormones

- Pancreatic hormones help maintain blood glucose
  - Normal range is 70 to 110 mg of glucose/deciliter
  - High levels damage blood vessels and kidneys
  - Low levels cause lethargy, mental and physical impairment, death
- Insulin lowers blood glucose
  - After food intake, beta cells detect rise in blood glucose and respond by secreting insulin
  - Insulin travels through blood and randomly leaves bloodstream to encounter target cells
  - Insulin binds to receptors and initiates 2nd messenger systems
  - Once blood glucose falls, beta cells stop secreting insulin

17.9b Effects of Pancreatic Hormones

- How insulin lowers blood glucose
  - Hepatocytes remove glucose from blood; store it as glycogen
    - Glycogenesis stimulated; glycogenolysis and gluconeogenesis inhibited
  - Adipose cells decrease fatty acid levels in blood; store fat
    - Lipogenesis stimulated and lipolysis inhibited
  - Most body cells increase nutrient uptake in response to insulin
    - Increased amino acid uptake, protein synthesis (especially in muscle)
    - Increased glucose uptake by incorporating more glucose transport proteins into plasma membrane
    - With less alternate fuels available (e.g., less fatty acids) more body cells use glucose
  - Some cells do not require insulin to take in glucose
    - Including: neurons, kidney cells, hepatocytes, red blood cells

Regulation and Action of Insulin

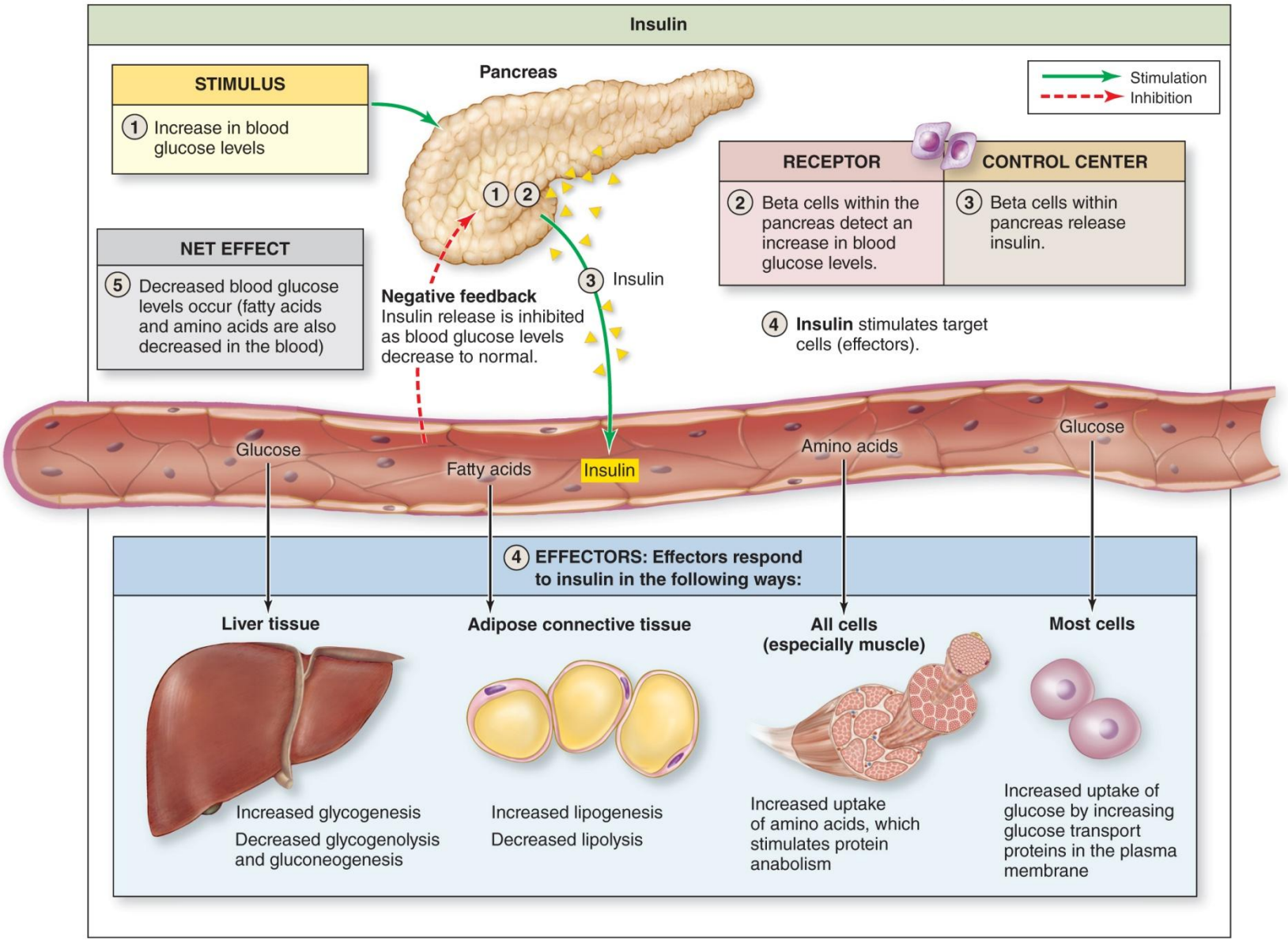


Figure 17.22

Clinical View: Conditions Resulting in Abnormal Glucose Levels

- **Diabetes mellitus**
  - Inadequate uptake of glucose from blood
  - Chronically elevated glucose, blood vessels damaged
  - Leading cause of retinal blindness, kidney failure, and nontraumatic amputations in the United States
  - Associated with increased heart disease and stroke
- **Type 1 diabetes**
  - Absent or diminished release of insulin by pancreas
  - Tends to occur in children and younger individuals
  - May have autoimmune component
  - Requires daily injections of insulin

Clinical View: Conditions Resulting in Abnormal Glucose Levels (*continued*)

- **Type 2 diabetes**
  - From decreased insulin release or insulin effectiveness
  - Obesity major cause in development
  - Tends to occur in older individuals, but can occur in young adults
  - Treatment with diet, exercise, and medications
- **Gestational diabetes**
  - Seen in some pregnant women
  - If untreated, causes risk to fetus and increases delivery complications
  - Increases chance of later developing type 2 diabetes

Clinical View: Conditions Resulting in Abnormal Glucose Levels (*continued*)

- **Hypoglycemia**
  - Glucose levels below 60 mg/DL
  - Numerous causes
    - Insulin overdose, prolonged exercise, alcohol use, liver or kidney dysfunction
    - Deficiency of glucocorticoids or growth hormone, genetics
  - Symptoms of hunger, dizziness, confusion, sweating, and sleepiness
  - Glucagon given if individual unconscious and unable to eat

17.9b Effects of Pancreatic Hormones

- Glucagon raises blood glucose
  - Alpha cells detect drop in blood glucose and release glucagon
  - Glucagon acts through membrane receptors and 2nd messengers causing body cells to release stored nutrients into blood
    - Hepatocytes release glucose
      - Glycogenolysis and gluconeogenesis stimulated; glycogenesis inhibited
    - Adipose cells release fatty acids and glycerol
      - Lipolysis stimulated, while lipogenesis inhibited
  - Glucagon does not affect protein composition
  - Glucagon can be given by paramedics to unconscious individuals with low blood sugar
- Once blood glucose rises, glucagon release is inhibited

Regulation and Action of Glucagon

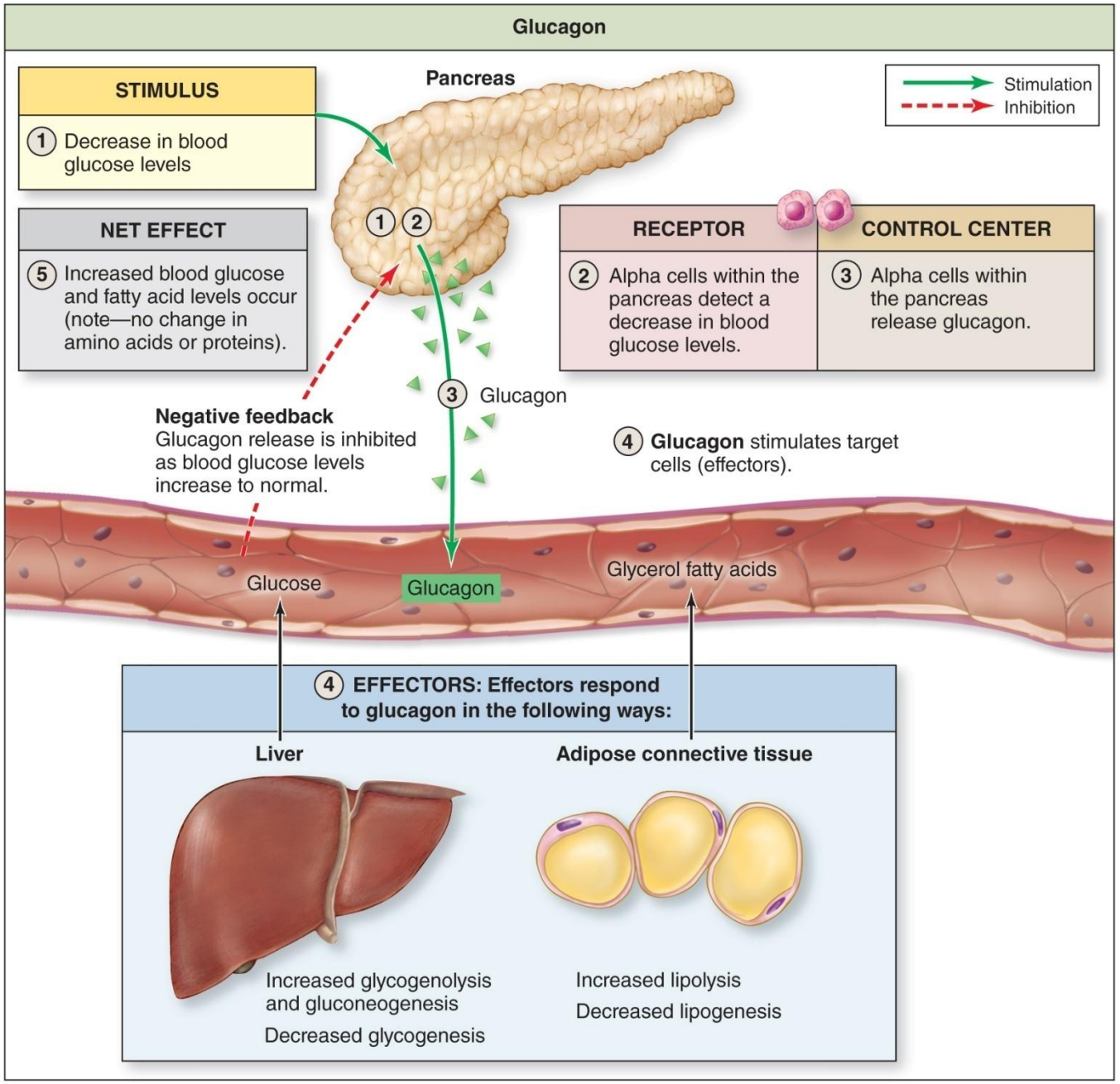


Figure 17.23

What did you learn?

- What function is served by the pancreatic islets?
- What effect would a decrease in insulin levels be expected to have on blood sugar?
- How is it that changes in the levels of fatty acids in the blood can affect blood sugar levels?

17.10 Other Endocrine Glands

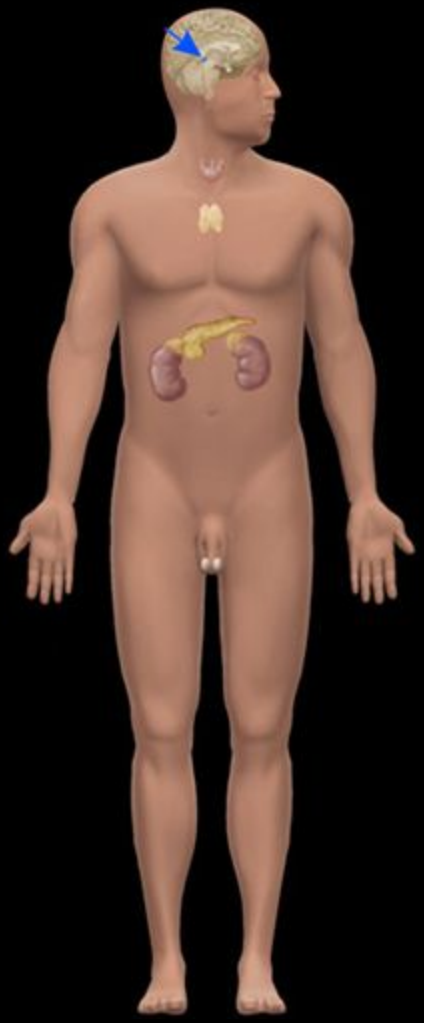
Learning Objectives:

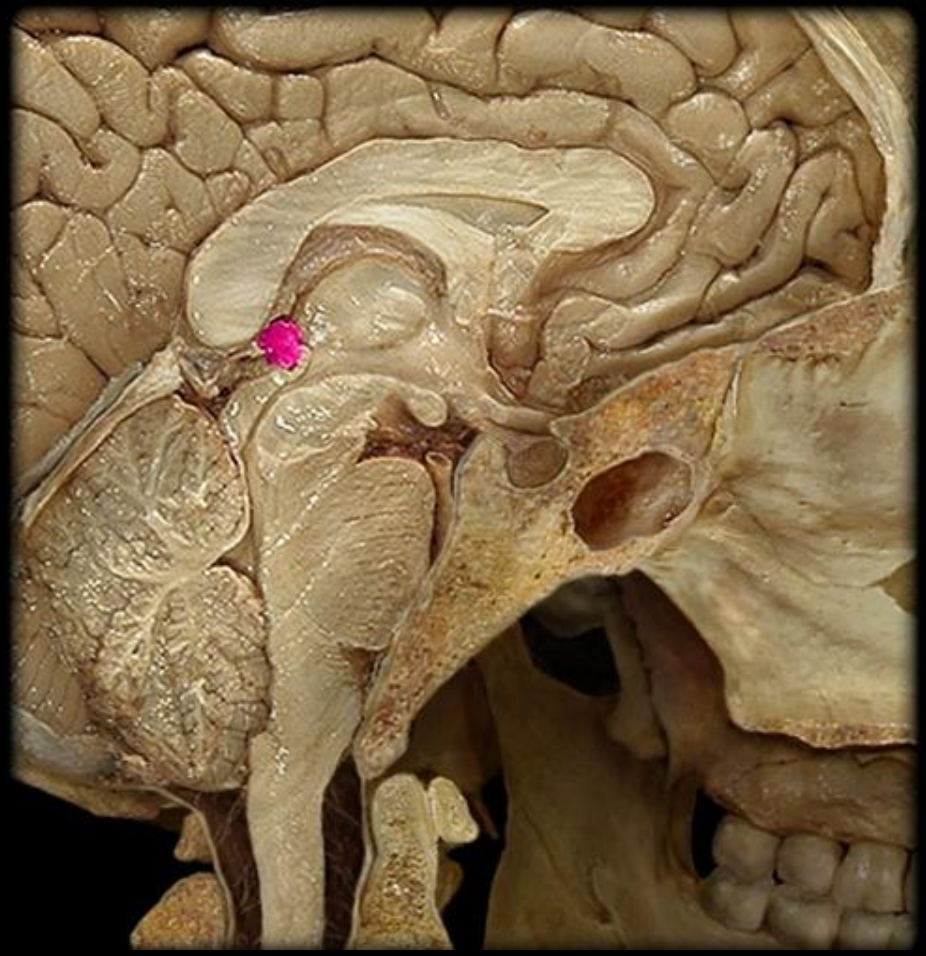
1. Describe the general structure, location, and function of the pineal gland.
2. Describe the general structure, location, and function of the parathyroid glands.
3. Identify and provide a description of the general function of the hormone(s) released from each of the organs discussed in this section.

17.10a Pineal Gland

- **Pineal gland** is a small unpaired body in the epithalamus of the diencephalon
- Pineal secretes **melatonin** at night
  - Causes drowsiness
  - Regulates circadian rhythm and has effects on mood
- Melatonin influences GnRH secretion
  - Has poorly understood effects on reproductive physiology

Pineal Gland

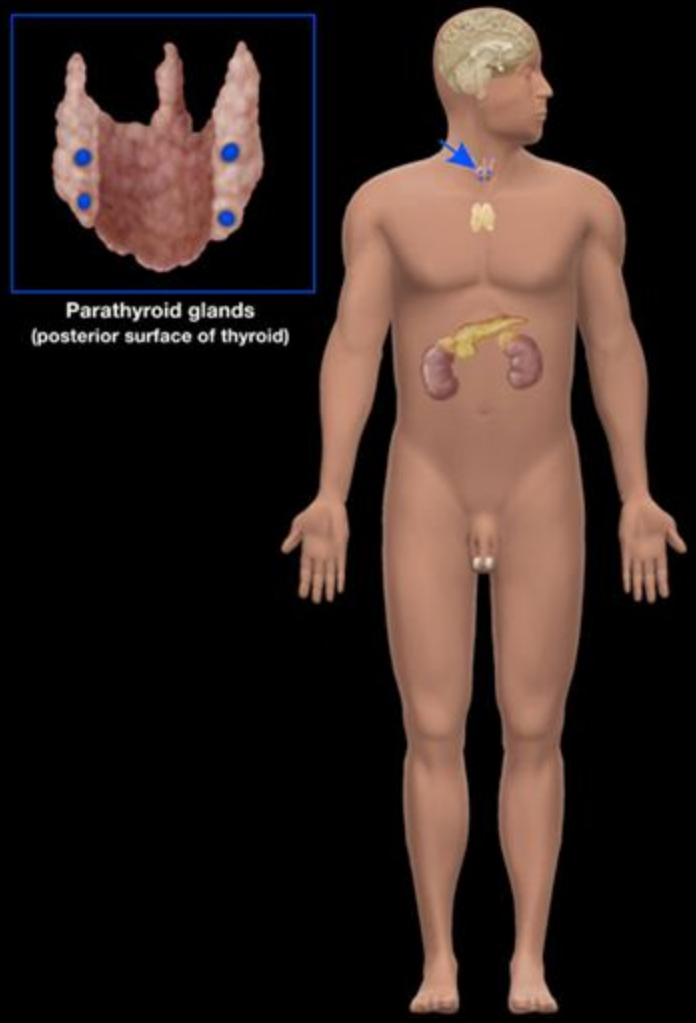




17.10b Parathyroid Glands

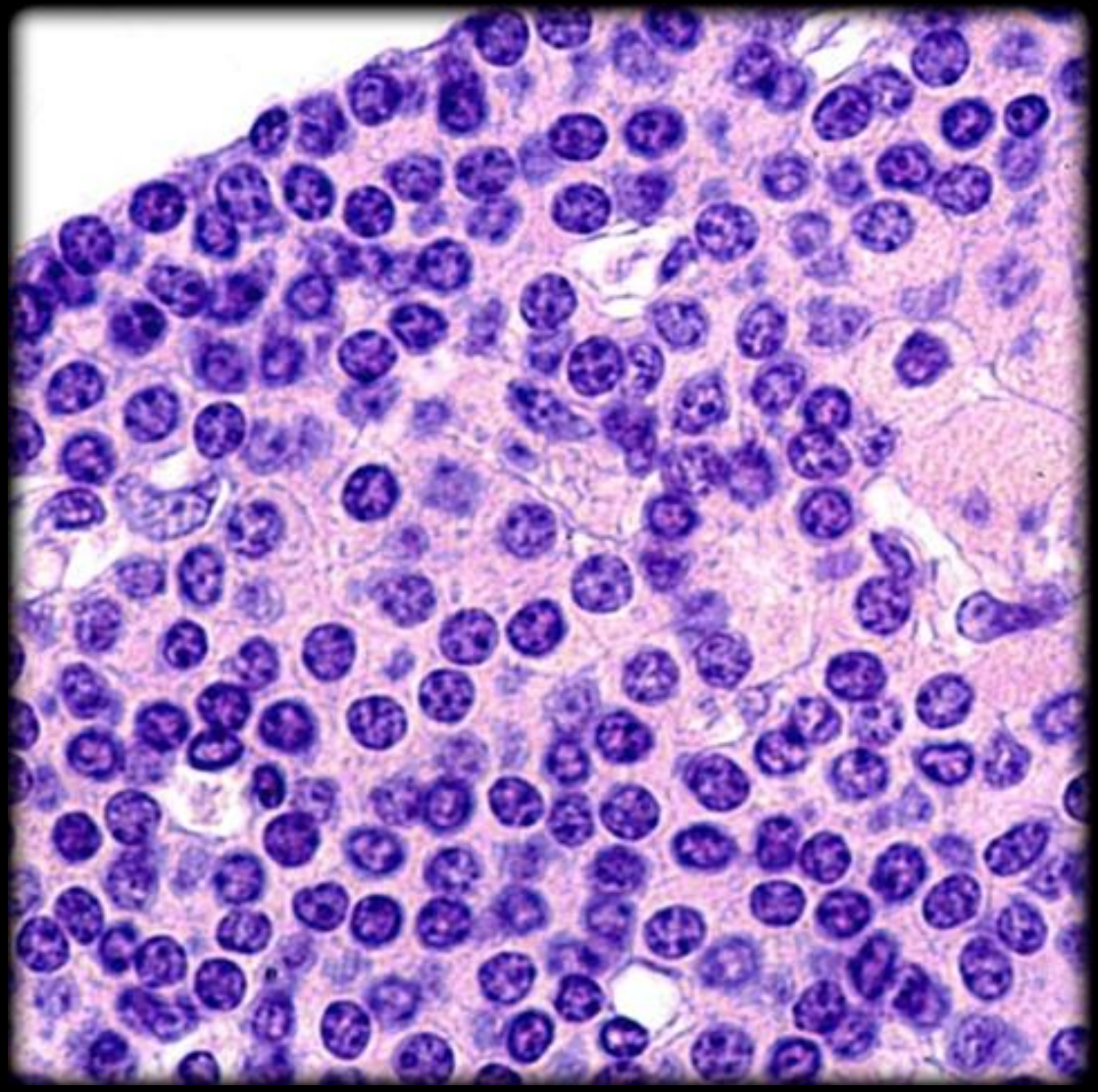
- **Parathyroid glands** are small structures on the back of the thyroid gland
  - There are between 2 and 6 of them (usually 4)
- Contain **chief cells** and oxyphil cells
  - Chief (principal) cells make parathyroid hormone (PTH)
  - PTH increases blood calcium
    - Liberates it from bone, decreases its loss in urine, activates calcitriol hormone

Parathyroid Glands

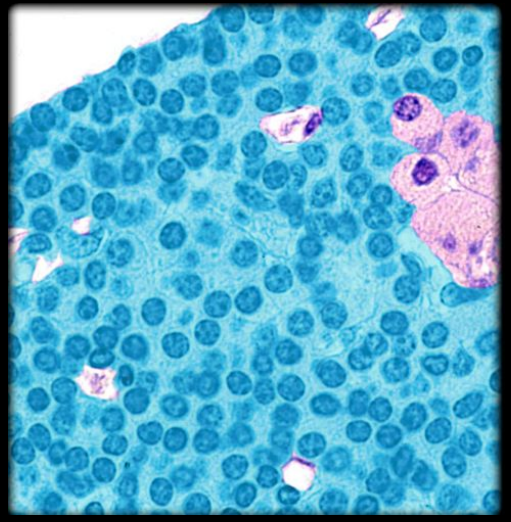


Parathyroid Glands

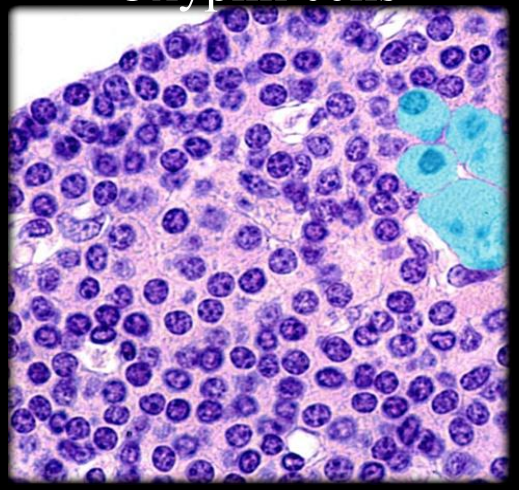
High Magnification



Chief cells



Oxyphil cells



17.10c Structures with an Endocrine Function

- **Thymus** epithelial cells secrete **thymic hormones**
  - Located anterior to top of heart
  - Grows during childhood but shrinks during adulthood
  - Maturation site for T-lymphocyte white blood cells
- Endocrine tissue in **heart** atria secretes **atrial natriuretic peptide (ANP)**
  - ANP is a hormone that lowers blood pressure
    - Kidneys increase urine output and blood vessels dilate
- **Kidney** endocrine cells release **erythropoietin (EPO)**
  - Secretion occurs in response to low blood oxygen
  - EPO causes increased red blood cell production

17.10c Structures with an Endocrine Function

- **Liver** secretions include insulin-like growth factors and the inactive hormone **angiotensinogen**
  - Angiotensinogen is converted to active **angiotensin II** by enzymes from the kidney and lung blood vessels
  - Angiotensin II helps raise blood pressure when it starts to fall
    - Causes vessel constriction, decreases urine output, stimulates thirst
- **Stomach** secretes **gastrin**
  - Gastrin increases secretion and motility in stomach for digestion

17.10c Structures with an Endocrine Function

- **Small intestine** secretes **secretin** and **cholecystokinin (CCK)** into blood
  - Secretin stimulates secretion of bile and pancreatic juice
  - CCK stimulates release of bile from gall bladder
- In skin cells, light converts modified cholesterol to **vitamin D_3,** which is then released into blood
  - Vitamin D_3 is converted to calcidiol by a liver enzyme
  - Calcidiol is converted to calcitriol by a kidney enzyme
  - **Calcitriol** is the active hormone that raises blood calcium
    - Stimulates Ca^{2+} from bone, decreases Ca^{2+} loss in urine, stimulates Ca^{2+} absorption in intestine

17.10c Structures with an Endocrine Function

- **Adipose** connective tissue secretes **leptin**
  - Leptin controls appetite by binding to neurons in hypothalamus
    - Lower body fat is associated with less leptin and this stimulates appetite
- Adipose has other endocrine effects
  - Excess adipose raises risk of cancer
  - Excess adipose delays male puberty
  - Abnormally low adipose interferes with female menstrual cycle

What did you learn?

- What gland secretes melatonin and what is its effect?
- What effect does PTH have on blood calcium levels?
- Why have dishonest endurance athletes taken exogenous EPO?
- How does sun exposure change hormone levels in the body?

17.11
Aging and the Endocrine System

Learning Objectives:

1. Describe how endocrine activity changes as people age.

17.11 Aging and the Endocrine System

- Endocrine changes with aging
  - Secretory activity wanes with age
  - Reduces efficiency of endocrine system functions
  - Decreased levels of normal hormones
    - E.g., decreased levels of GH and sex hormones
    - Reduced GH levels leading to loss of weight and body mass in elderly

What did you learn?

- How does hormone replacement therapy relate to aging?