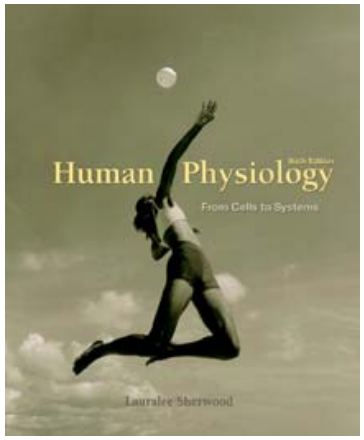
Chapter 18
The Central Endocrine Glands



Outline

- General Principles of Endocrinology
  - Free vs. bound, disorders, receptors
- Hypothalamus and pituitary
  - Relationship
  - Anterior pituitary
  - Posterior pituitary
- Endocrine control of growth
- Pineal gland and circadian rhythms

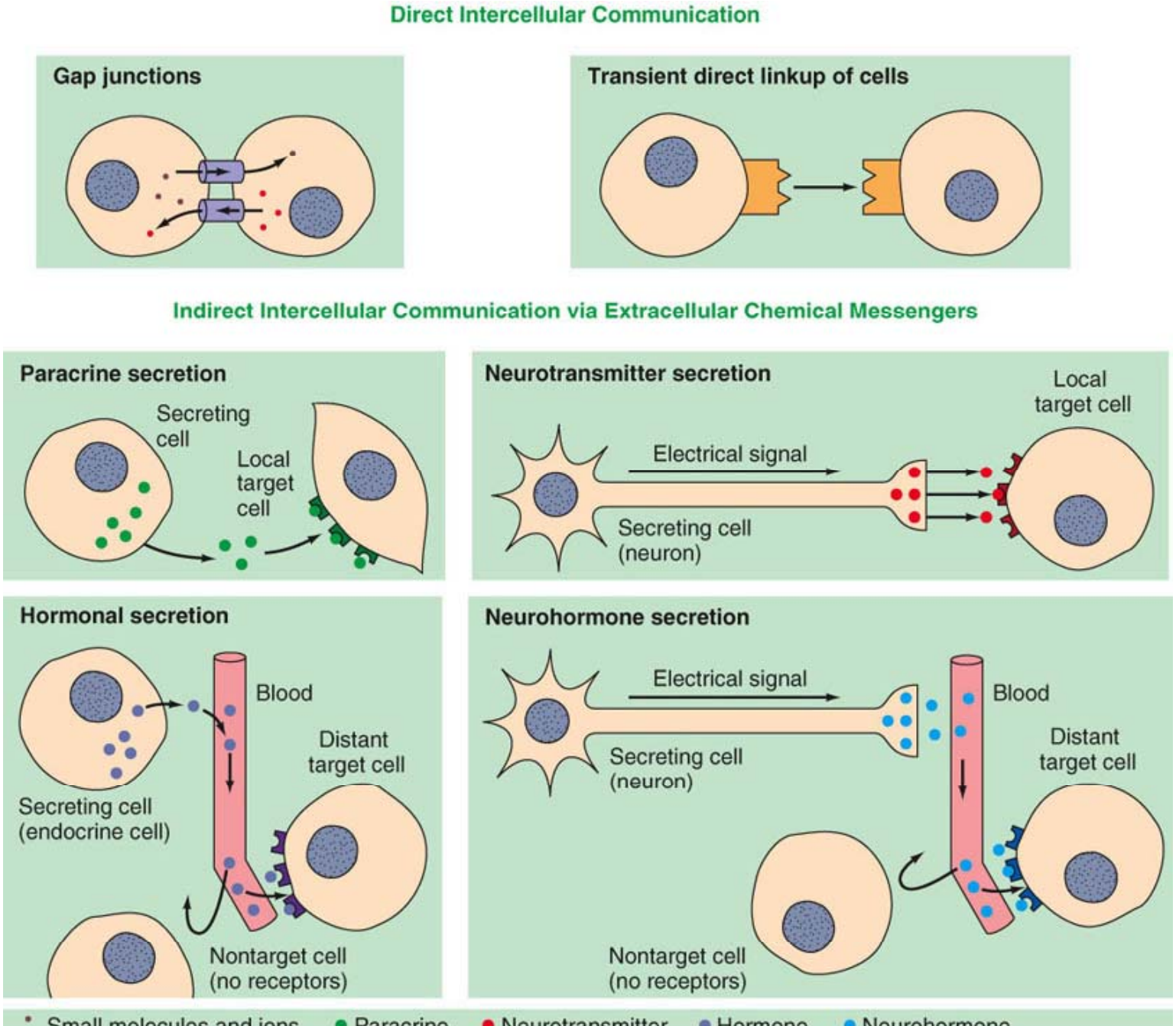


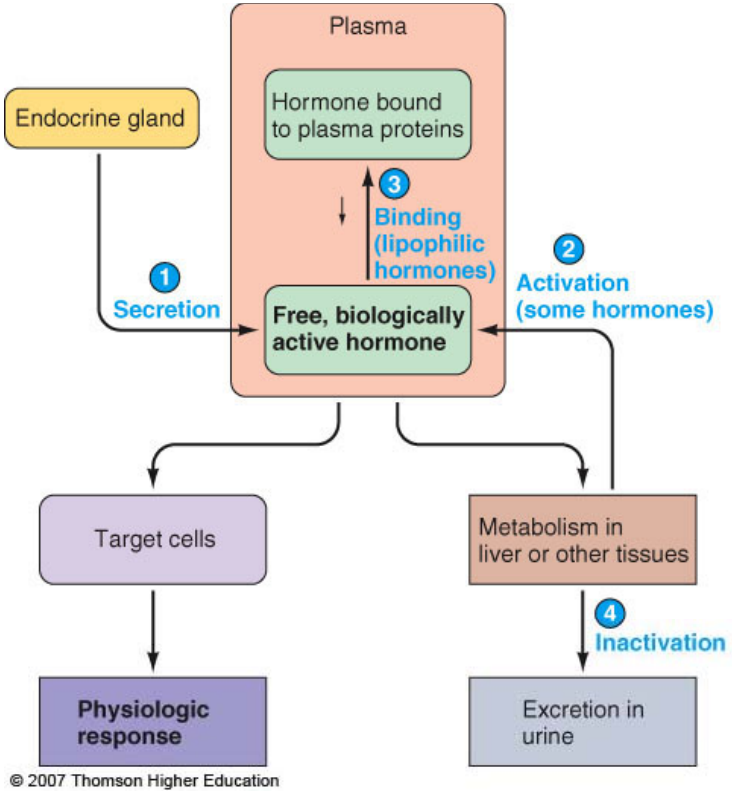
Fig. 4-21, p. 112

Endocrine System

- Overall functions
  - Regulate organic metabolism and H_2O and electrolyte balance (think of resting potentials)
  - help body cope with stressful situations (what is stress?)
  - Promote smooth, sequential growth and development (hypo/hyper)
  - Control reproduction (birth control/agriculture)
  - Regulate red blood cell production (EPO)
  - Along with autonomic nervous system, control and integrate both circulation and the digestion and absorption of food

GENERAL PRINCIPLES OF ENDOCRINOLOGY

- Hormones exert regulatory effects throughout the body.
- The effective plasma concentration of a hormone is regulated by:
  - rate of secretion
  - transport,
  - metabolism
  - excretion.
- Endocrine disorders result from hormone excess or deficiency or decreased target-cell responsiveness.
- The responsiveness of a target cell can be varied by regulating the number of hormone-specific receptors.



The plasma concentration of free, biologically active hormone, which can interact with its target cells to produce a physiologic response, depends on

1. the hormone's rate of secretion by the endocrine gland (for all hormones; the major factor)
2. its rate of metabolic activation (for a few hormones)
3. its extent of binding to plasma proteins (for lipophilic hormones)
4. its rate of metabolic inactivation and excretion (for all hormones)

- Plasma concentration of each hormone is normally controlled by regulated changes in rate of hormone secretion
- Direct regulatory inputs that influence secretory output of endocrine cells
  - Neural input
  - Input from another hormone
- Effective plasma concentration also influenced by
  - Rate of removal from blood by metabolic inactivation and excretion
  - Rate of activation or its extent of binding to plasma proteins
  - Being bound or free. Many hormones are not transported in their active form. They can be bound to a carrier or chemically modified

Fig. 18-2, p. 655

Hormones

- Two distinct groups of hormones based on their solubility properties
  - Hydrophilic hormones (Proteins, peptides)
    - Highly water soluble
    - Low lipid solubility
  - Lipophilic hormones (Steroids)
    - High lipid solubility
    - Poorly soluble in water
- Peptides/catecholamines/iodinated tyrosines

Steroid Hormones

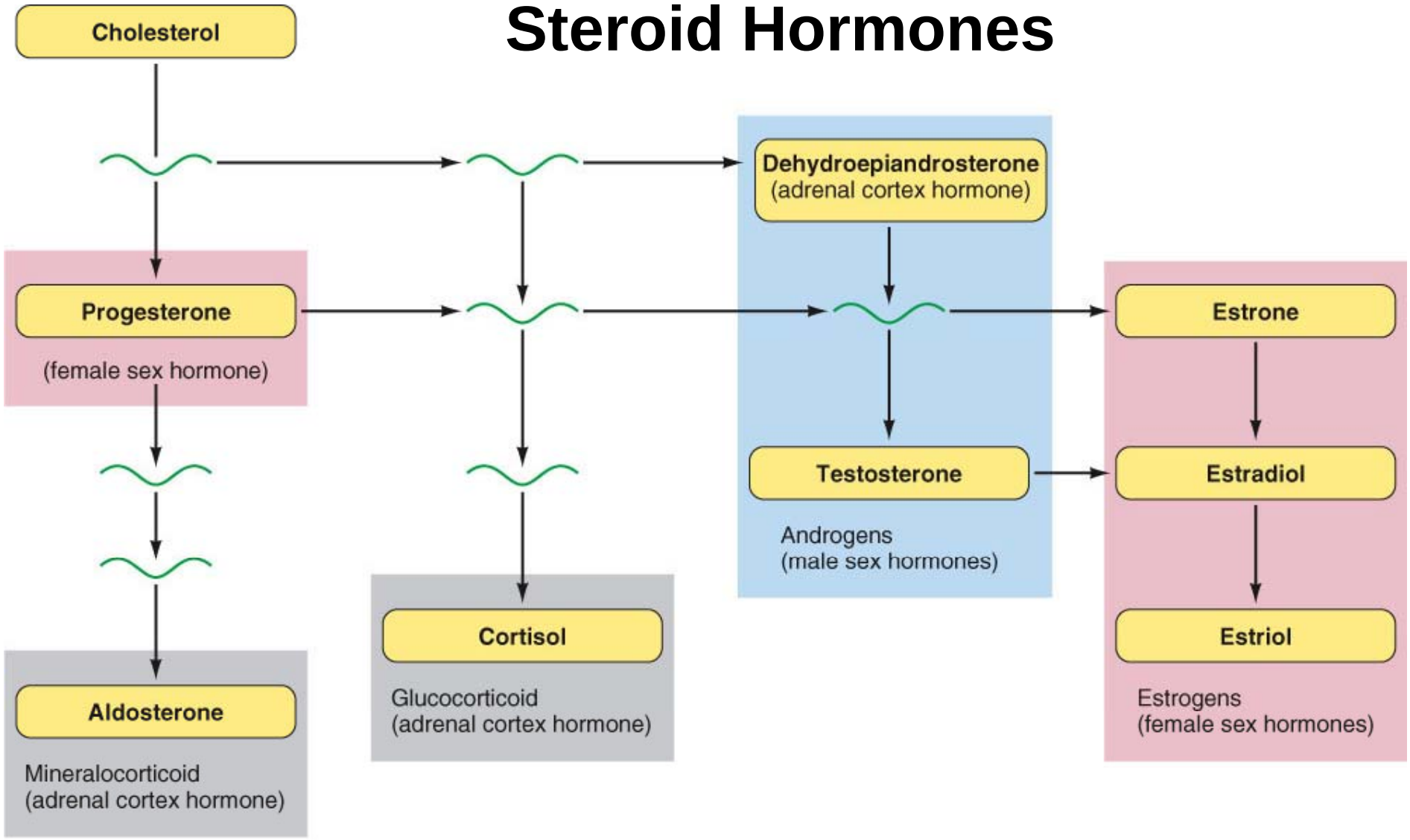
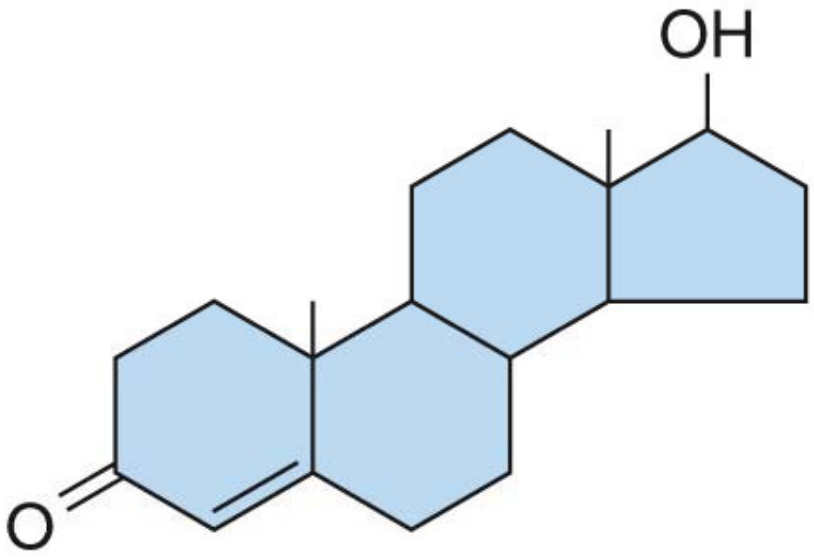
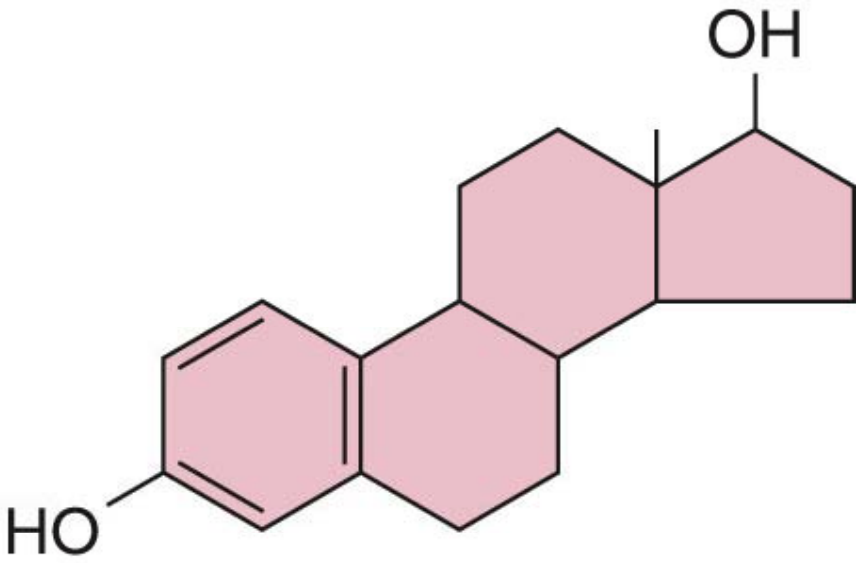


Fig. 4-23, p. 116

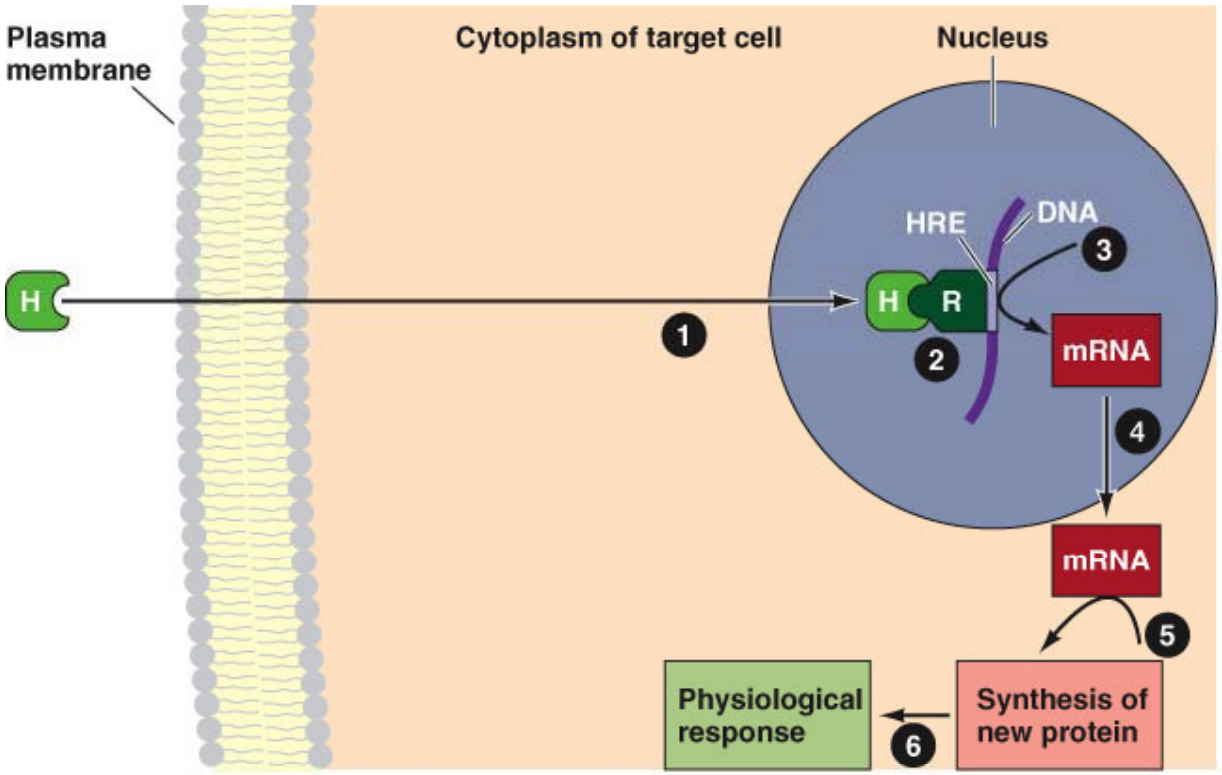


Testosterone,
a masculinizing
hormone



Estradiol,
a feminizing
hormone

Fig. 4-22, p. 115



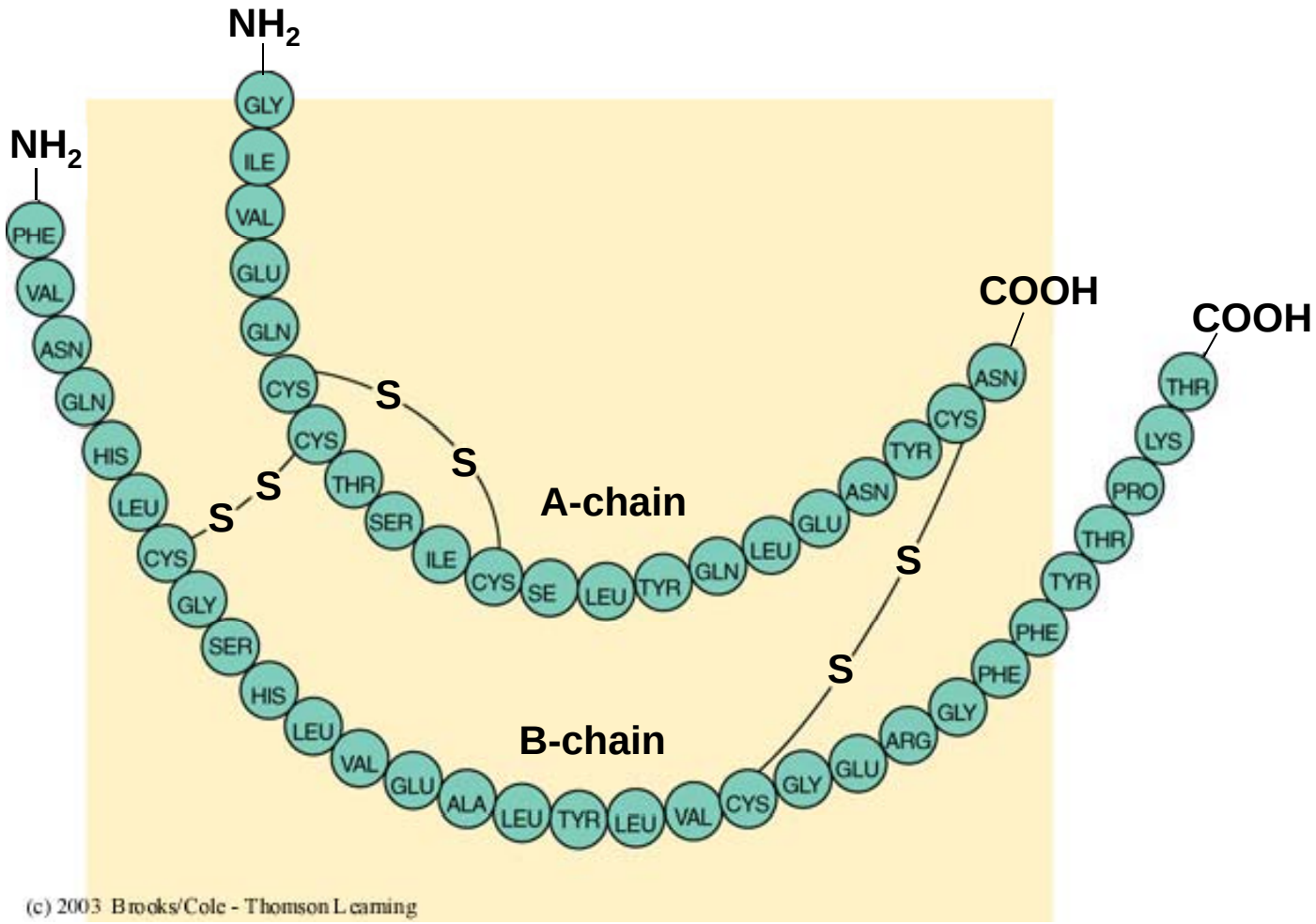
1. A lipophilic hormone diffuses through the plasma and nuclear membranes of its target cells and binds with a nuclear receptor specific for it.
2. The hormone receptor complex in turn binds with the hormone response element, a segment of DNA specific for the hormone receptor complex.
3. DNA binding activates specific genes, which produce complementary messenger RNA.
4. Messenger RNA leaves the nucleus.
5. In the cytoplasm, messenger RNA directs the synthesis of new proteins.
6. These new proteins, either enzymatic or structural, accomplish the target cell's ultimate physiologic response to the hormone.

H = Free lipophilic hormone
R = Lipophilic hormone receptor

HRE = Hormone response element
mRNA = Messenger RNA

Fig. 4-26, p. 122

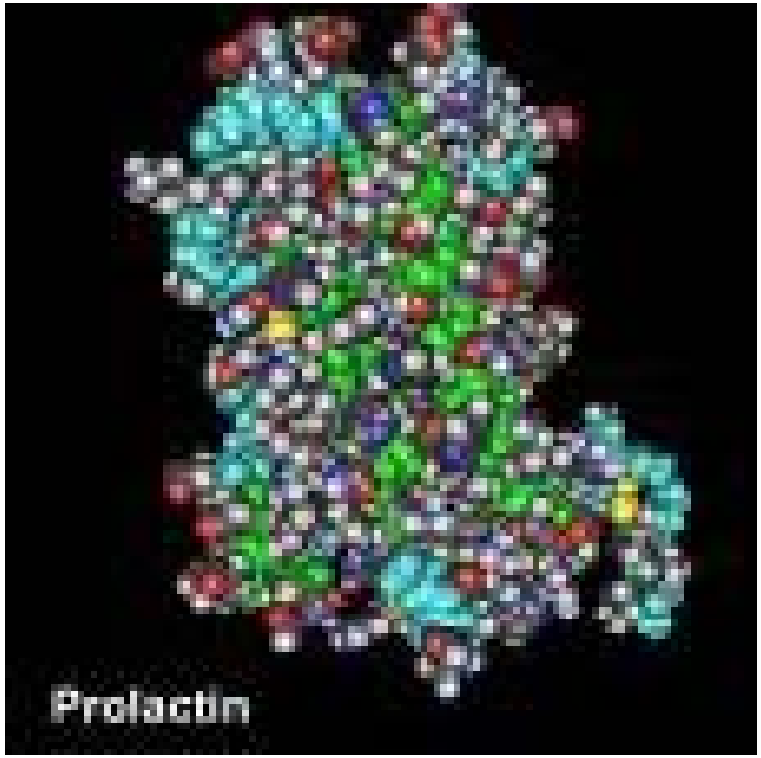
Protein Hormones

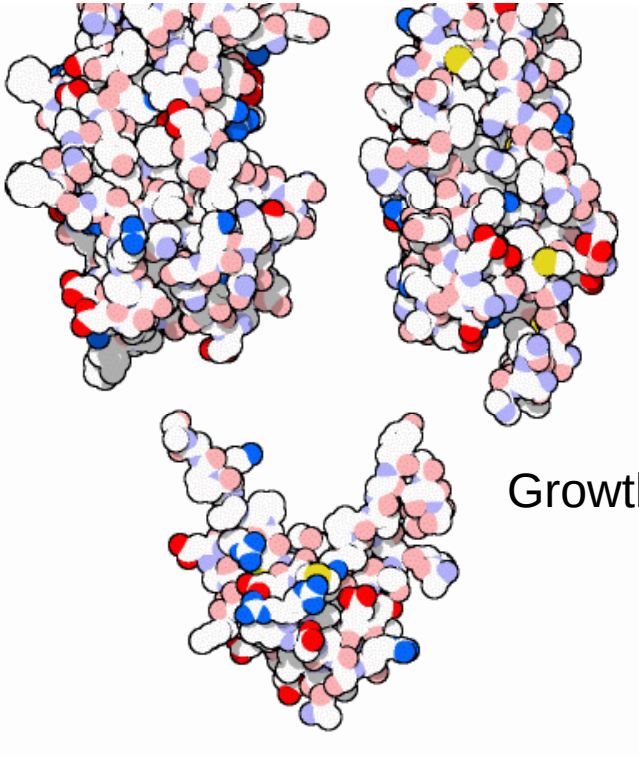


A chain and B-chain

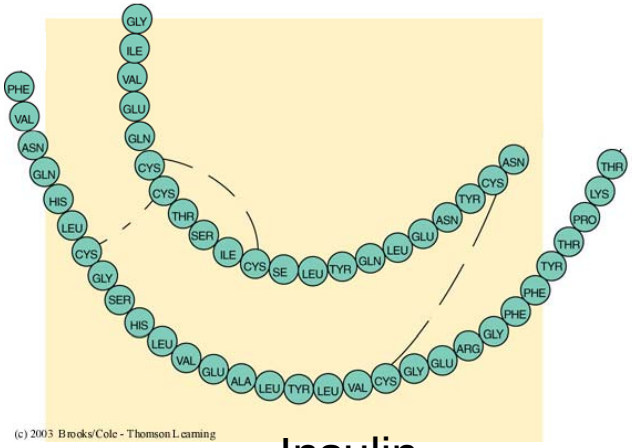
C- peptide

Fig 15-4, pg 456

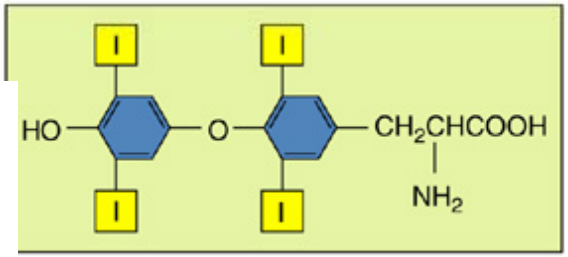




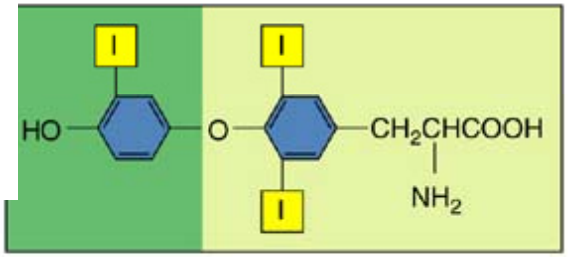
Growth hormone



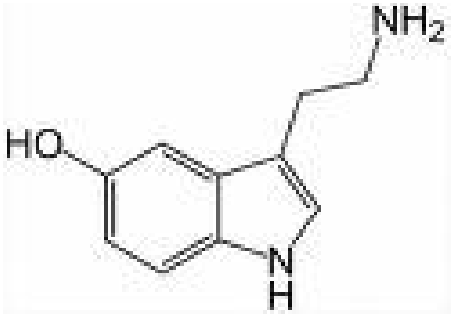
Insulin



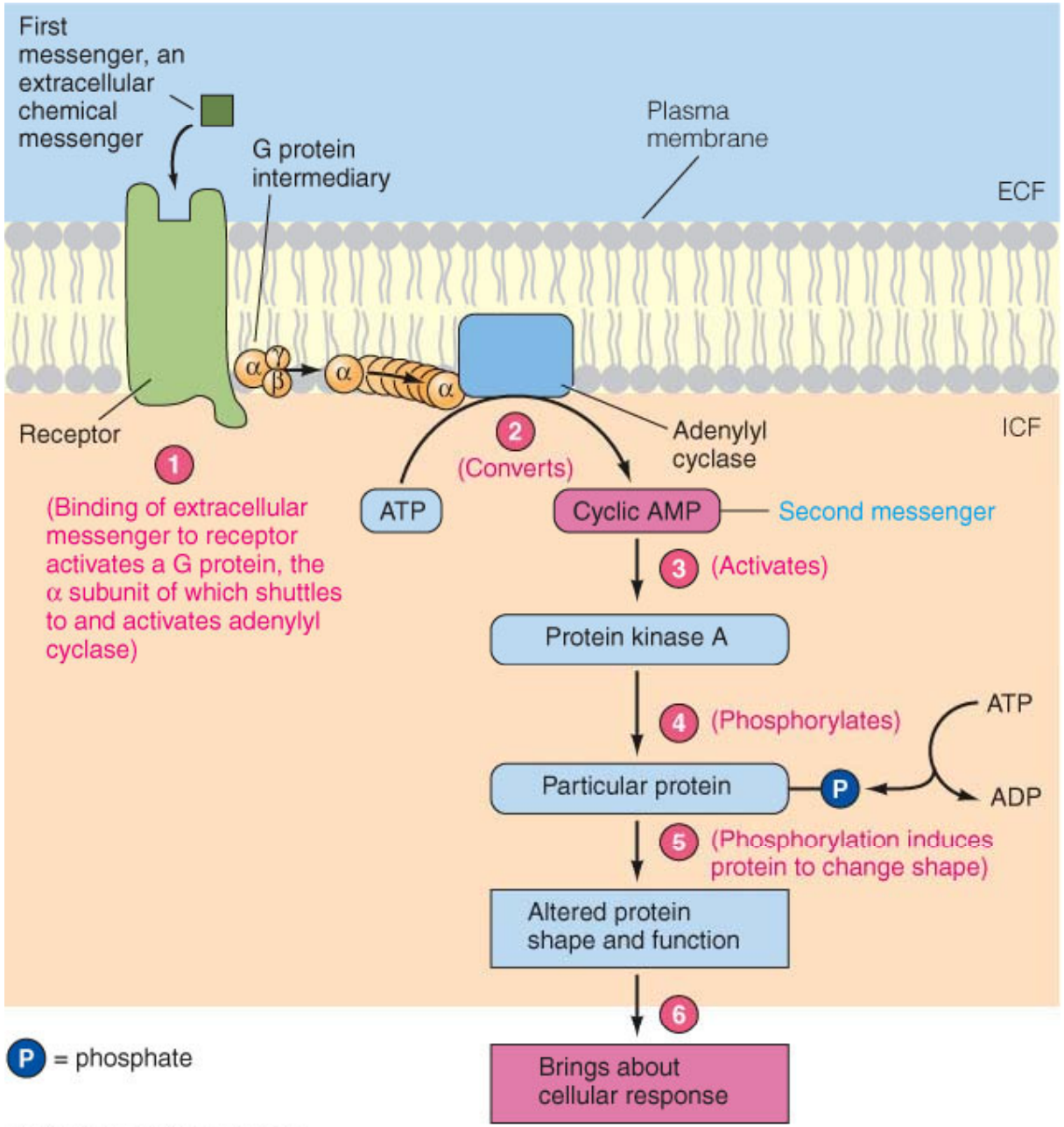
T_4 (thyroxine)



T_3

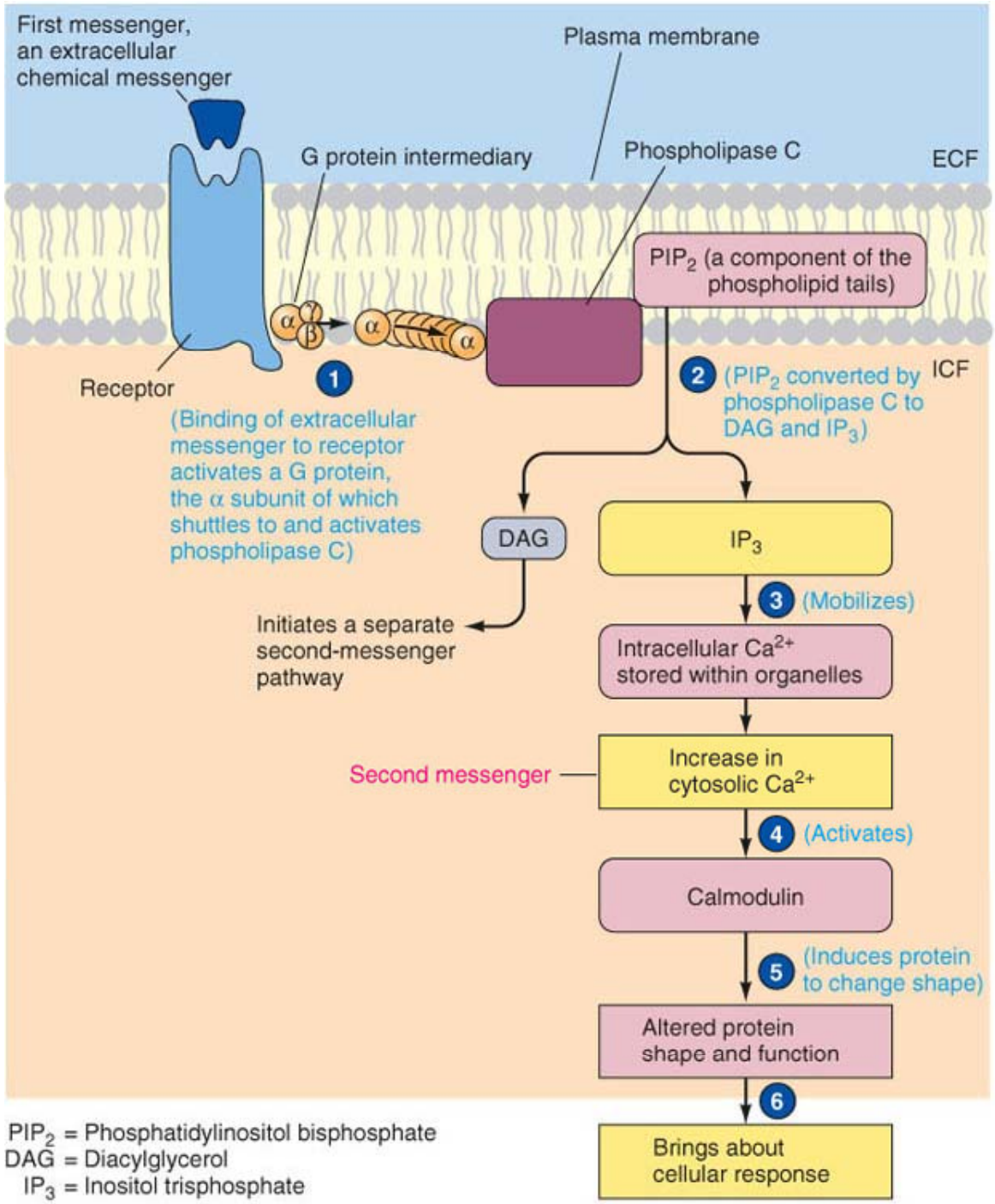


Serotonin



1. Binding of an extracellular messenger, the *first messenger*, to a surface membrane receptor activates by means of a G protein intermediary the membrane-bound enzyme adenylyl cyclase.
2. Adenylyl cyclase converts intracellular ATP into cyclic AMP.
3. Cyclic AMP acts as an intracellular *second messenger*, triggering the desired cellular response by activating protein kinase A.
4. Protein kinase A in turn phosphorylates a particular intracellular protein.
5. Phosphorylation induces a change in the shape and function of the protein.
6. The altered protein then accomplishes the cellular response dictated by the extracellular messenger.

Fig. 4-24, p. 118



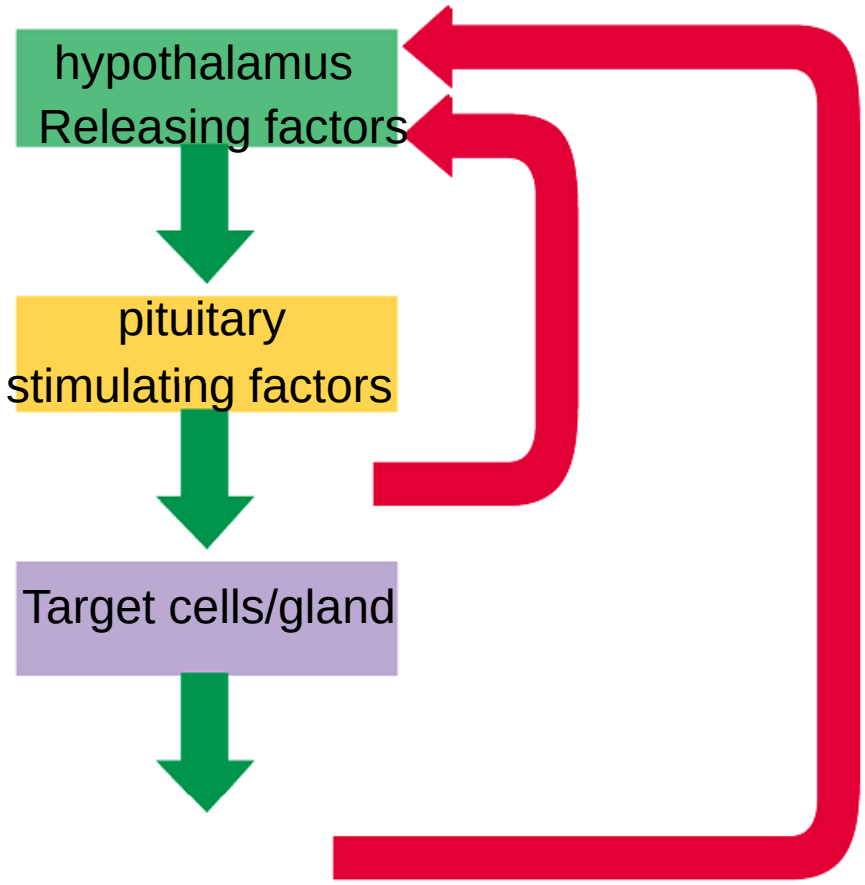
PIP_2 = Phosphatidylinositol bisphosphate
DAG = Diacylglycerol
IP_3 = Inositol trisphosphate

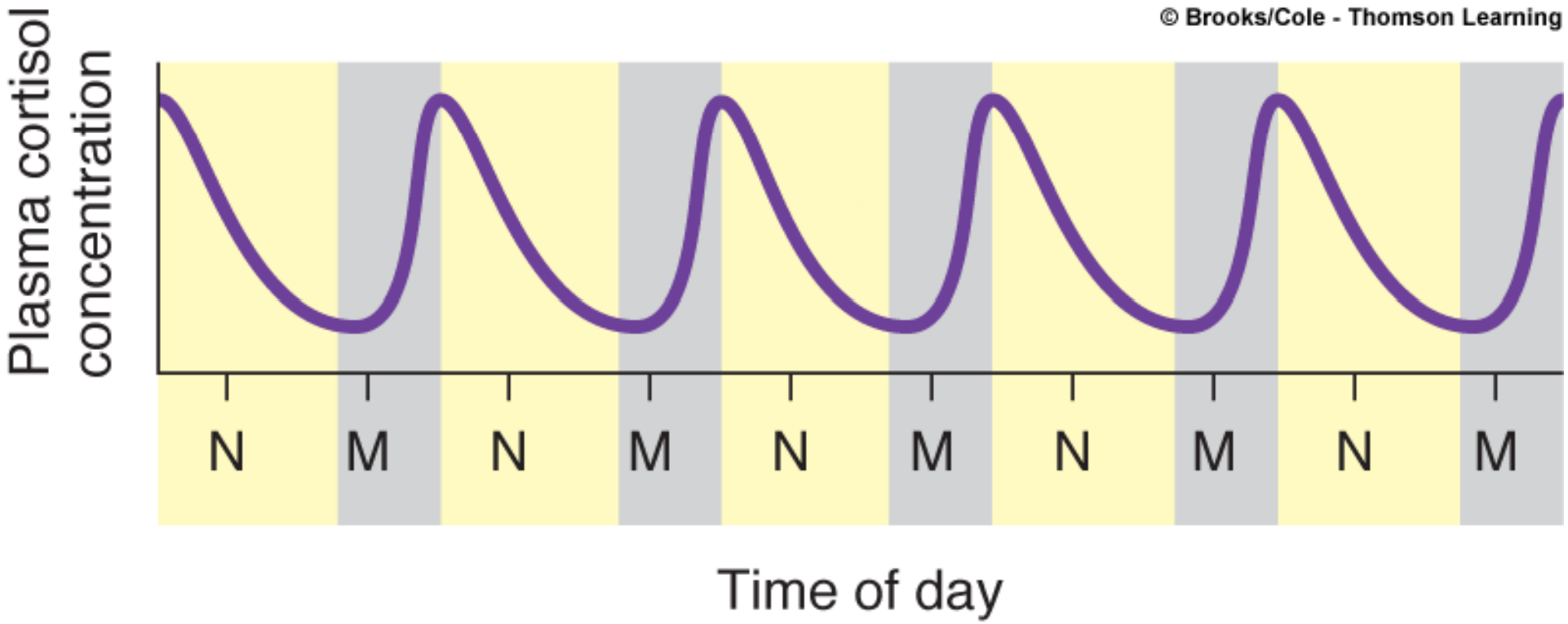
1. Binding of an extracellular messenger to a surface membrane receptor activates by means of a G protein intermediary the membrane-bound enzyme phospholipase C.
2. Phospholipase C converts PIP_2, a membrane component, into DAG and IP_3.
3. IP_3 in turn mobilizes Ca^{2+} stored within organelles.
4. Ca^{2+}, acting as a second messenger, activates calmodulin.
5. Calmodulin induces a change in the shape and function of a particular intracellular protein.
6. The altered protein then produces the desired cellular response dictated by the extracellular messenger.

Fig. 4-25, p. 119

Tropic Hormones

- Regulate hormone secretion by another endocrine gland
- Stimulates and maintains their endocrine target tissues
- Example
  - Thyroid-stimulating hormone (TSH) secreted from anterior pituitary stimulates thyroid hormone secretion by thyroid gland
    - Also maintains structural integrity of thyroid gland





N = noon
M = midnight

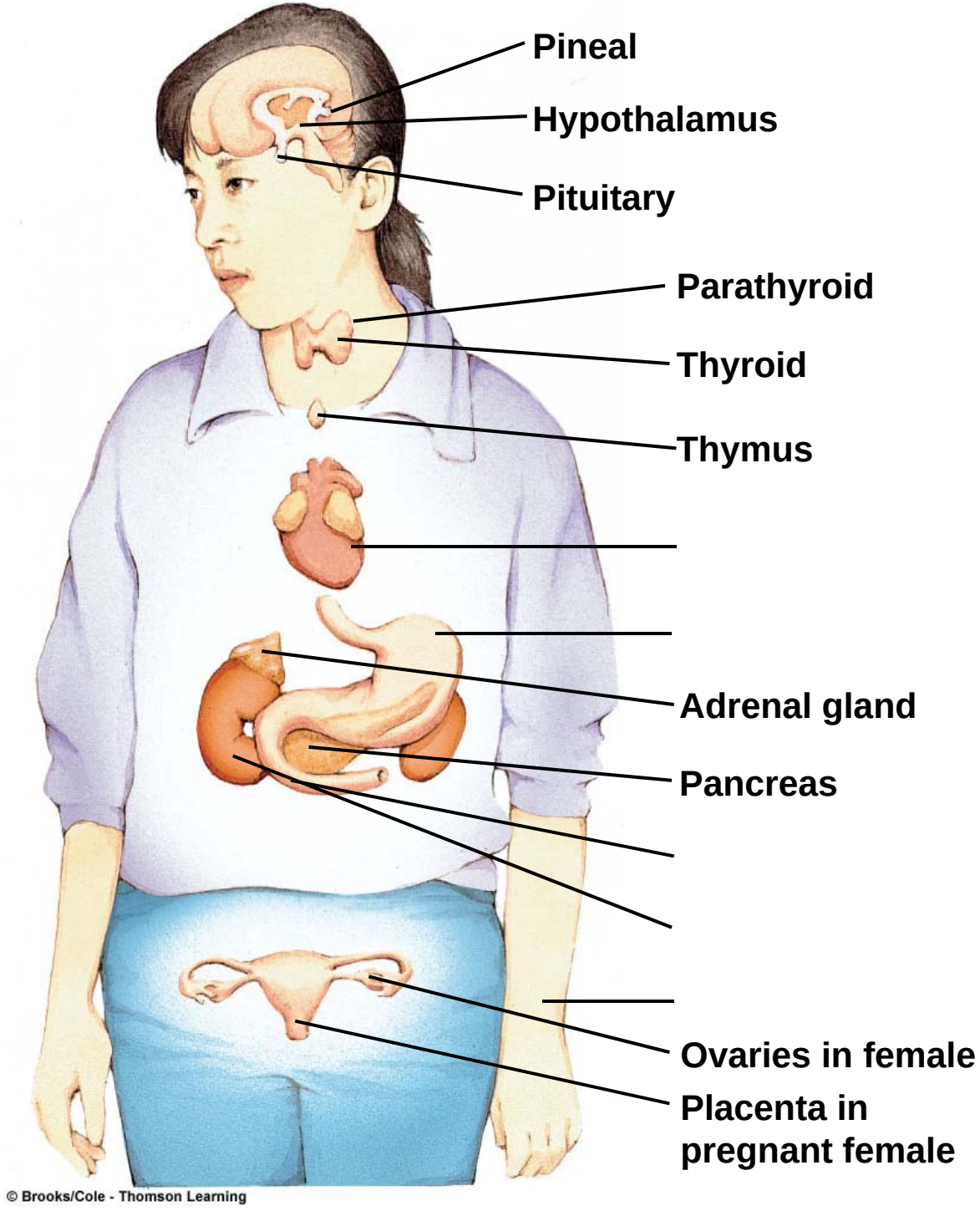
Light

Dark

Fig. 18-4, p. 656

Hormone Influence at Target Cell

- Hormone can influence activity of another hormone at given target cell in one of three ways
  - Permissiveness
    - One hormone must be present in adequate amounts for full exertion of another hormone's effect
  - Synergism
    - Occurs when actions of several hormones are complimentary
    - Combined effect is greater than the sum of their separate effects
  - Antagonism
    - Occurs when one hormone causes loss of another hormone's receptors
    - Reduces effectiveness of second hormone



Know

Hormones
function
regulation
transduction

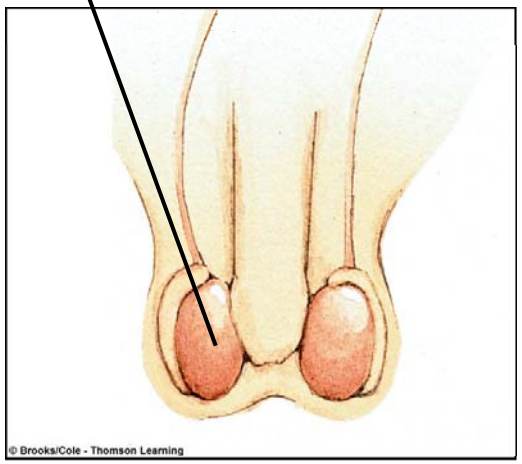
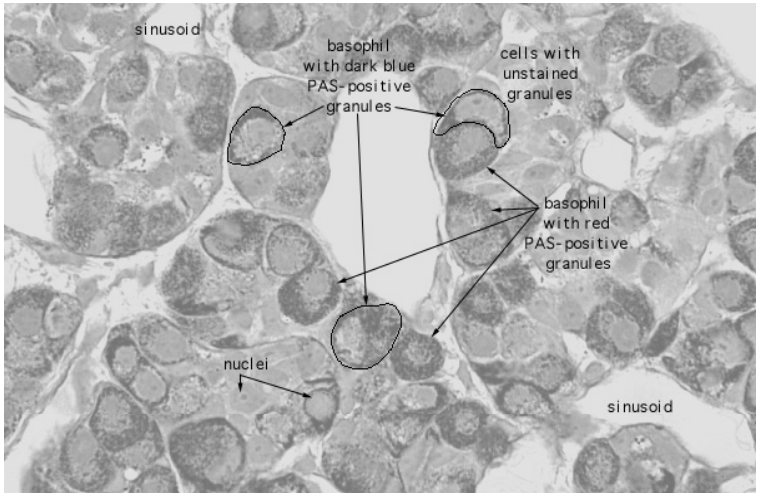
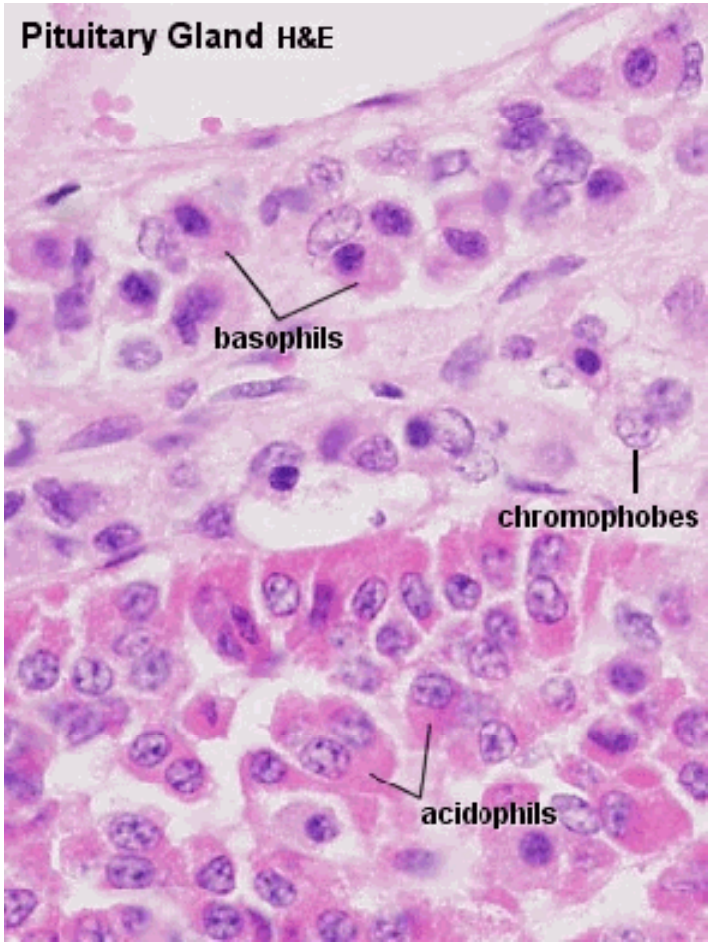
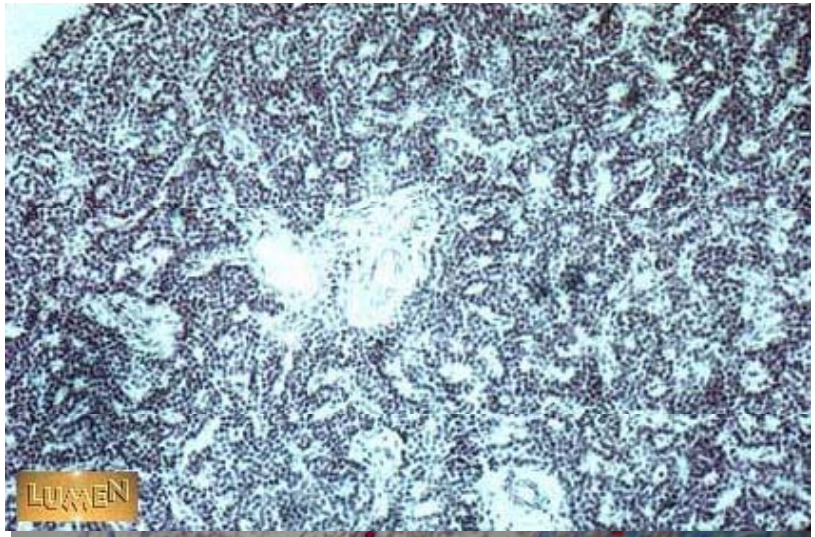


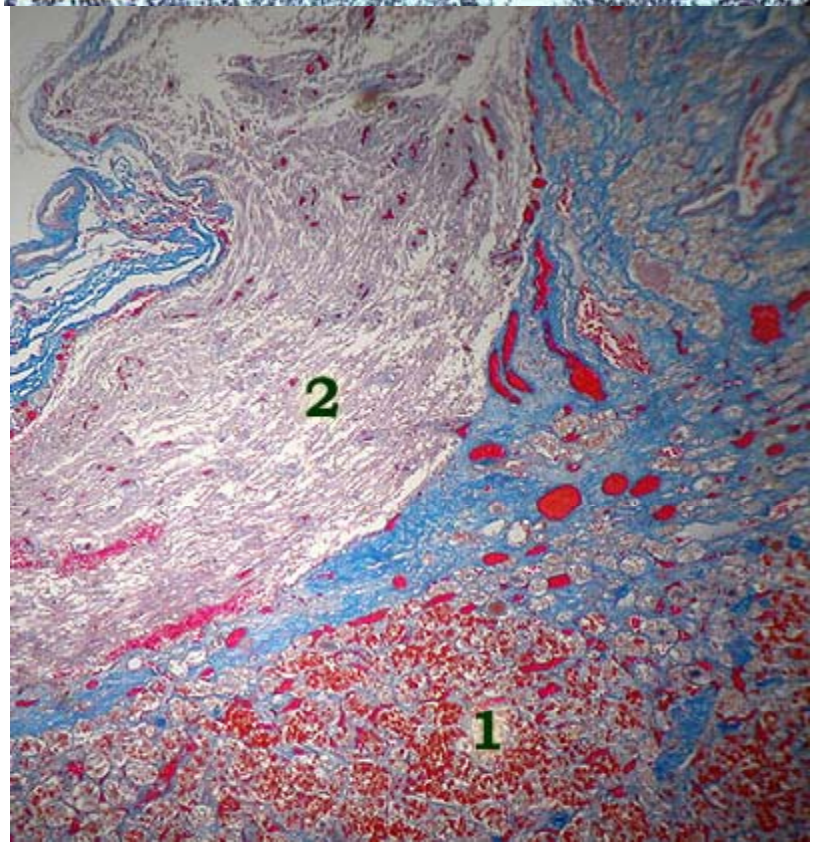
Fig. 18-1, p. 654

ENDOCRINE GLAND	HORMONES	TARGET CELLS	MAJOR FUNCTIONS OF HORMONES
Hypothalamus	Releasing and inhibiting hormones (TRH, CRH, GnRH, GHRH, GHIH, PRH, PIH)	Anterior pituitary	Controls release of anterior pituitary hormones
Posterior Pituitary (hormones stored in)	Vasopressin (antidiuretic hormone)	Kidney tubules	Increases H_2O reabsorption
		Arterioles	Produces vasoconstriction
	Oxytocin	Uterus	Increases contractility
		Mammary glands (breasts)	Causes milk ejection
Anterior Pituitary	Thyroid-stimulating hormone (TSH)	Thyroid follicular cells	Stimulates T_3 and T_4 secretion
	Adrenocorticotropic hormone (ACTH)	Zona fasciculata and zona reticularis of adrenal cortex	Stimulates cortisol secretion
	Growth hormone	Bone; soft tissues	Essential but not solely responsible for growth; stimulates growth of bones and soft tissues; metabolic effects include protein anabolism, fat mobilization, and glucose conservation
		Liver	Stimulates somatomedin secretion
	Follicle-stimulating hormone (FSH)	*Females:* ovarian follicles	Promotes follicular growth and development; stimulates estrogen
Anterior Pituitary (*continued*)	Follicle-stimulating hormone (FSH) (*continued*)	*Males:* seminiferous tubules in testes	Stimulates sperm production
	Luteinizing hormone (LH) (interstitial cell-stimulating hormone—ICSH)	*Females:* ovarian follicle and corpus luteum	Stimulates ovulation, corpus luteum development, and estrogen and progesterone secretion
		Males: interstitial cells of Leydig in testes	Stimulates testosterone secretion


sinusoid
basophil with dark blue PAS-positive granules
cells with unstained granules
basophil with red PAS-positive granules
nuclei
sinusoid


Pituitary Gland H&E
basophils
chromophobes
acidophils


LUMEN


2
1

Thyroid Gland C Cells	Calcitonin	Bone	Decreases plasma Ca^{2+} concentration
Adrenal Cortex			
Zona glomerulosa	Aldosterone (mineralocorticoid)	Kidney tubules	Increases Na^+ reabsorption and K^+ secretion
Zona fasciculata and zona reticularis	Cortisol (glucocorticoid)	Most cells	Increases blood glucose at the expense of protein and fat stores; contributes to stress adaption
	Androgens (dehydroepiandrosterone)	*Females:* bone and brain	Responsible for the pubertal growth spurt and sex drive in females
Adrenal Medulla	Epinephrine and norepinephrine	Sympathetic receptor sites throughout the body	Reinforces the sympathetic nervous system; contributes to stress adaptation and blood pressure regulation
Endocrine Pancreas (Islets of Langerhans)	Insulin (β cells)	Most cells	Promotes cellular uptake, use, and storage of absorbed nutrients
	Glucagon (α cells)	Most cells	Important for maintaining nutrient levels in blood during postabsorptive state
	Somatostatin (D cells)	Digestive system	Inhibits digestion and absorption of nutrients
		Pancreatic islet cells	Inhibits secretion of all pancreatic hormones

(*continued*)

Table 18-2c, p. 660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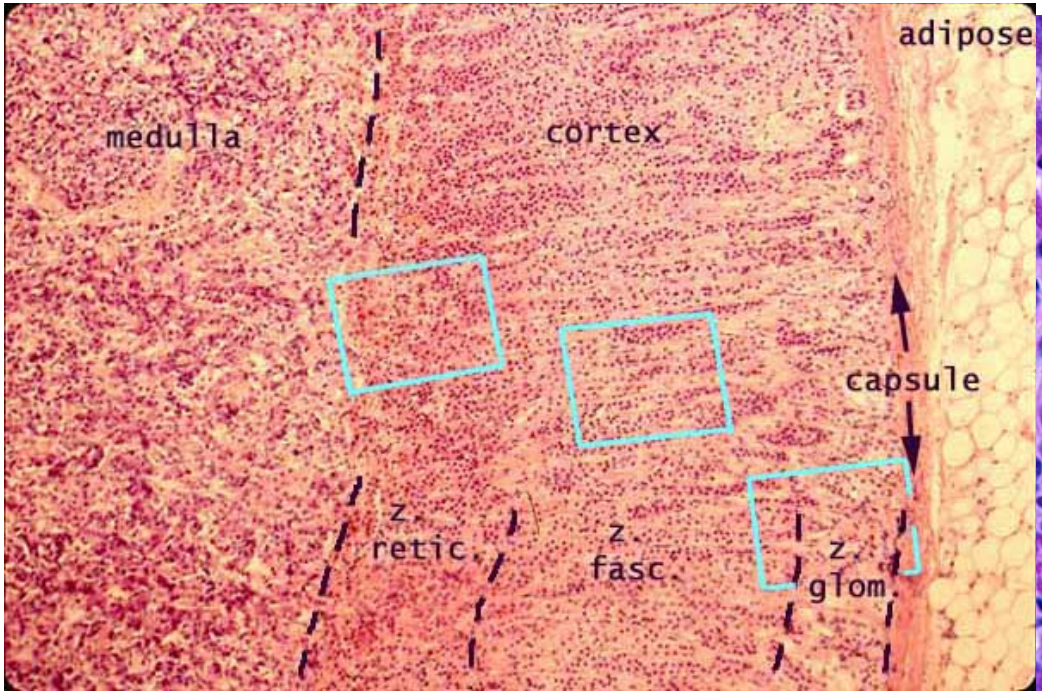
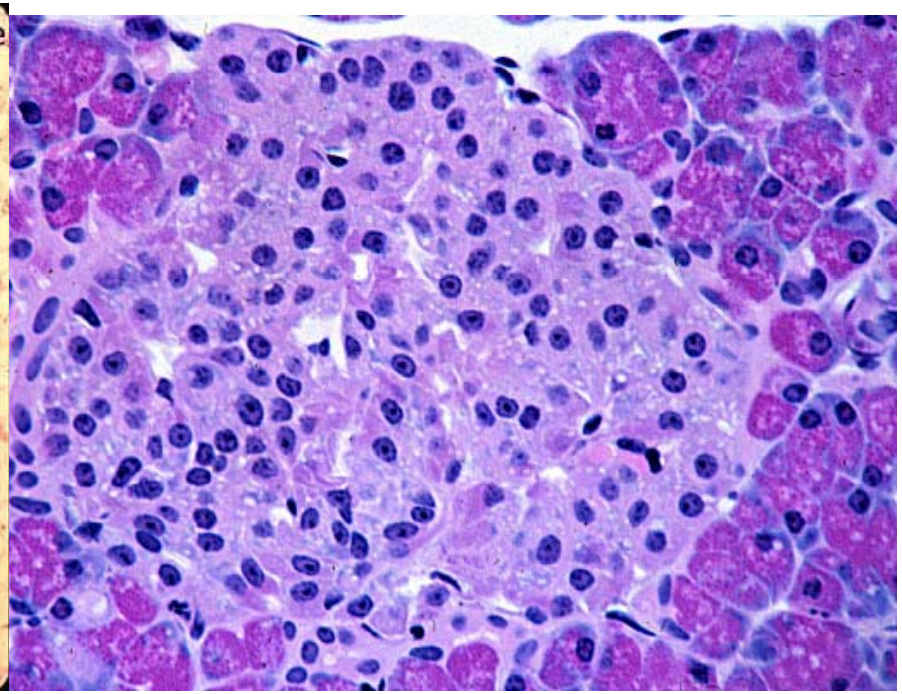
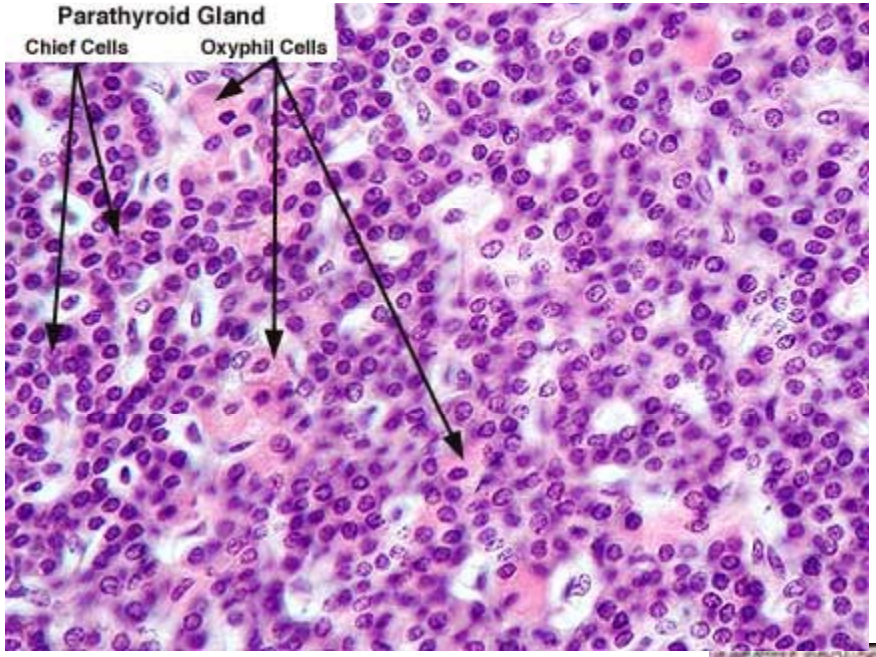
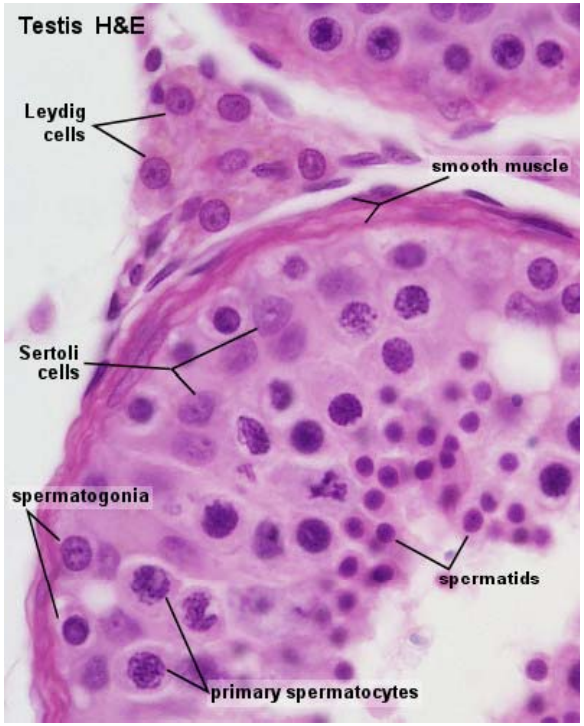

adipose
medulla
cortex
capsule
z
retic
z
fasc
z
glom.

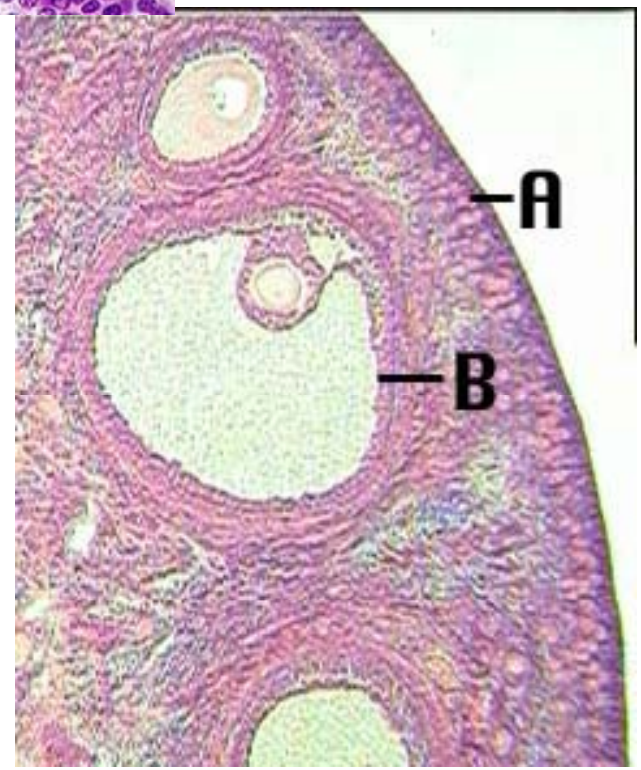


ENDOCRINE GLAND	HORMONES	TARGET CELLS	MAJOR FUNCTIONS OF HORMONES
Parathyroid Gland	Parathyroid hormone (PTH)	Bone, kidneys, intestine	Increases plasma Ca^{2+} concentration; decreases plasma PO_4^{3-} concentration; stimulates vitamin D activation
Gonads			
Female: ovaries	Estrogen (estradiol)	Female sex organs; body as a whole	Promotes follicular development; governs development of secondary sexual characteristics; stimulates uterine and breast growth
		Bone	Promotes closure of the epiphyseal plate
	Progesterone	Uterus	Prepares for pregnancy
Male: testes	Testosterone	Male sex organs; body as a whole	Stimulates sperm production; governs development of secondary sexual characteristics; promotes sex drive
		Bone	Enhances pubertal growth spurt; promotes closure of the epiphyseal plate
Testes and ovaries	Inhibin	Anterior pituitary	Inhibits secretion of follicle-stimulating hormone

Table 18-2d, p. 661


Parathyroid Gland
Chief Cells
Oxyphil Cells

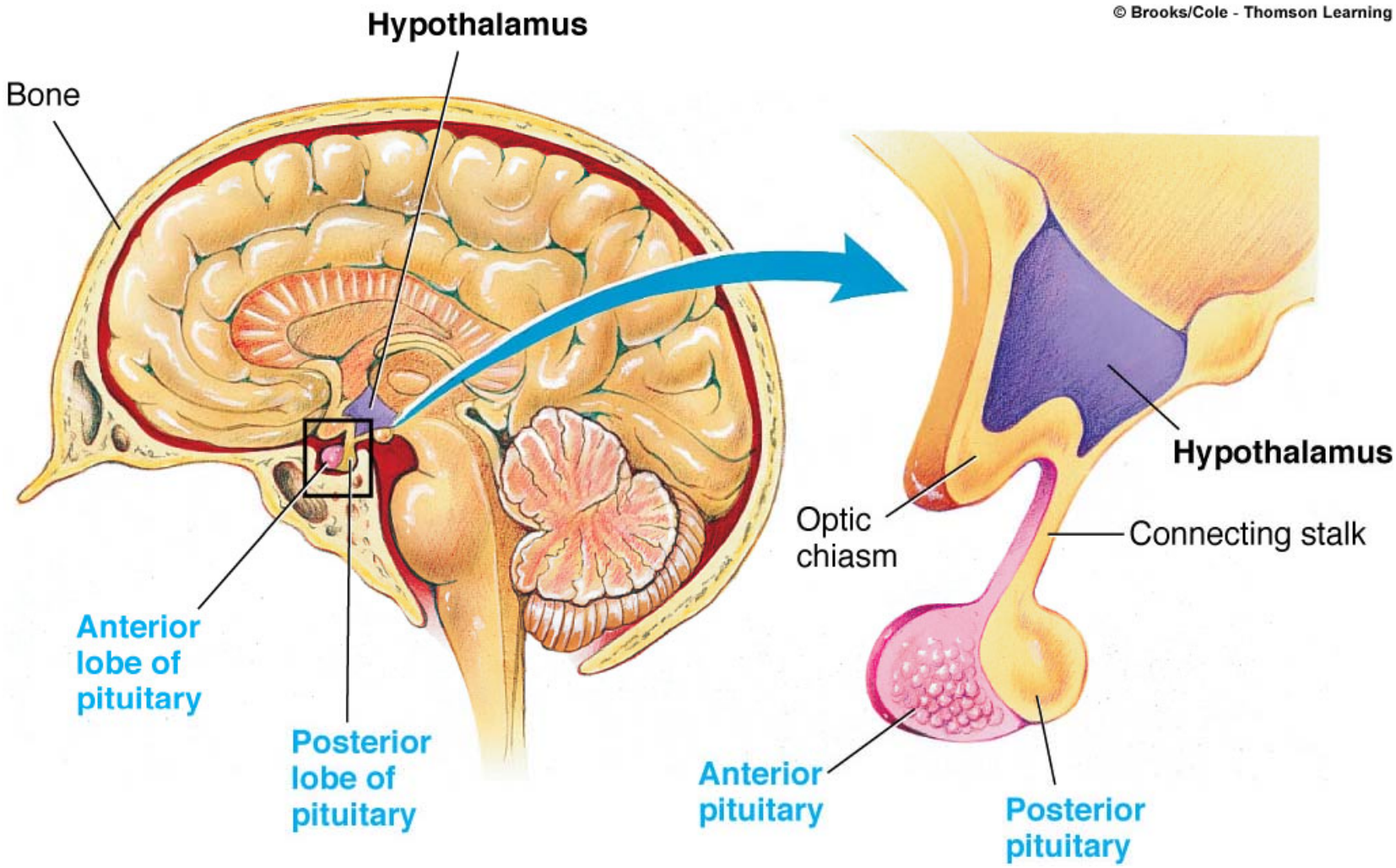

Testis H&E
Leydig cells
smooth muscle
Sertoli cells
spermatogonia
spermatids
primary spermatocytes


A
B

Placenta	Estrogen (estriol); progesterone	Female sex organs	Help maintain pregnancy; prepare breasts for lactation
	Chorionic gonadotropin	Ovarian corpus luteum	Maintains corpus luteum of pregnancy
Kidneys	Renin (→ angiotensin)	Zona glomerulosa of adrenal cortex (acted on by angiotensin, which is activated by renin)	Stimulates aldosterone secretion
	Erythropoietin	Bone marrow	Stimulates erythrocyte production
Stomach	Gastrin	Digestive tract exocrine glands and smooth muscles; pancreas; liver; gallbladder	Controls motility and secretion to facilitate digestive and absorptive processes
Duodenum	Secretin; cholecystokinin		
	Glucose-dependent insulinotropic peptide	Endocrine pancreas	Stimulates insulin secretion
Liver	Somatomedins (insulin-like growth factors (IGF)	Bone; soft tissues	Promotes growth
	Thrombopoietin	Bone marrow	Stimulates platelet production
Skin	Vitamin D	Intestine	Increases absorption of ingested Ca^{2+} and PO_4^{3-}
Thymus	Thymosin	T lymphocytes	Enhances T lymphocyte proliferation and function
Heart	Artrial natriuretic peptide	Kidney tubules	Inhibits Na^+ reabsorption
Adipose tissue	Leptin	Hypothalamus	Suppresses appetite; important in long-term control of body weight
	Other adipokines	Multiple sites	Play role in metabolism and inflammation

Table 18-2e, p. 661

Anatomy of the Pituitary Gland



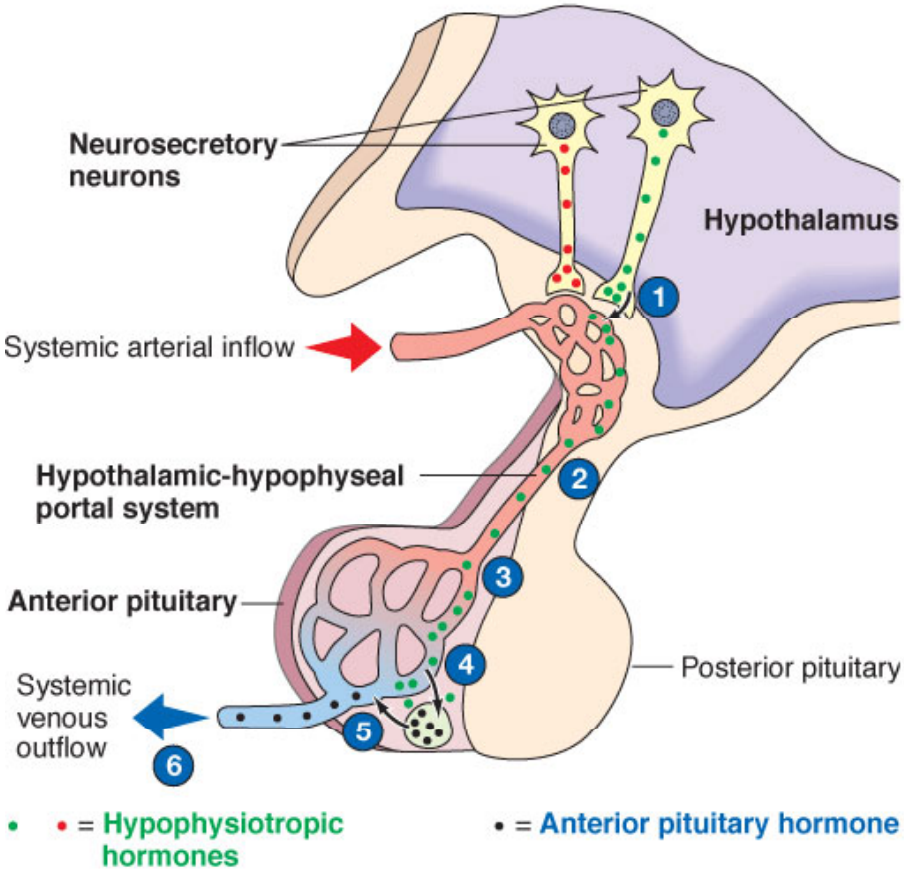
Anterior

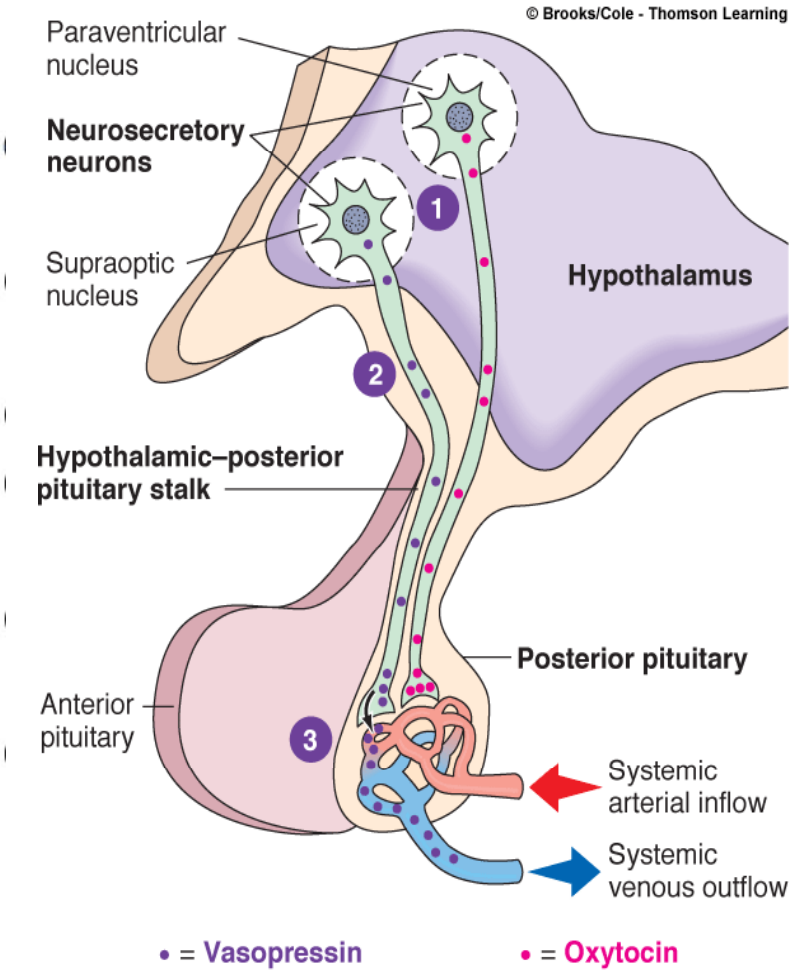
- Releasing and inhibiting hormones are secreted bu the hypothalamus into the capillaries
- The hormone travels through the hypothalamic hypophysial portal system
- Corresponding pituitary hormone released into the blood

- Vascular

Posterior

- vasopressin and oxytocin are synthesized the hypothalamus.
- The hormone travels down the axon to be stored in the posterior pituitary.
- the stored hormone is released blood.
- Hardwired



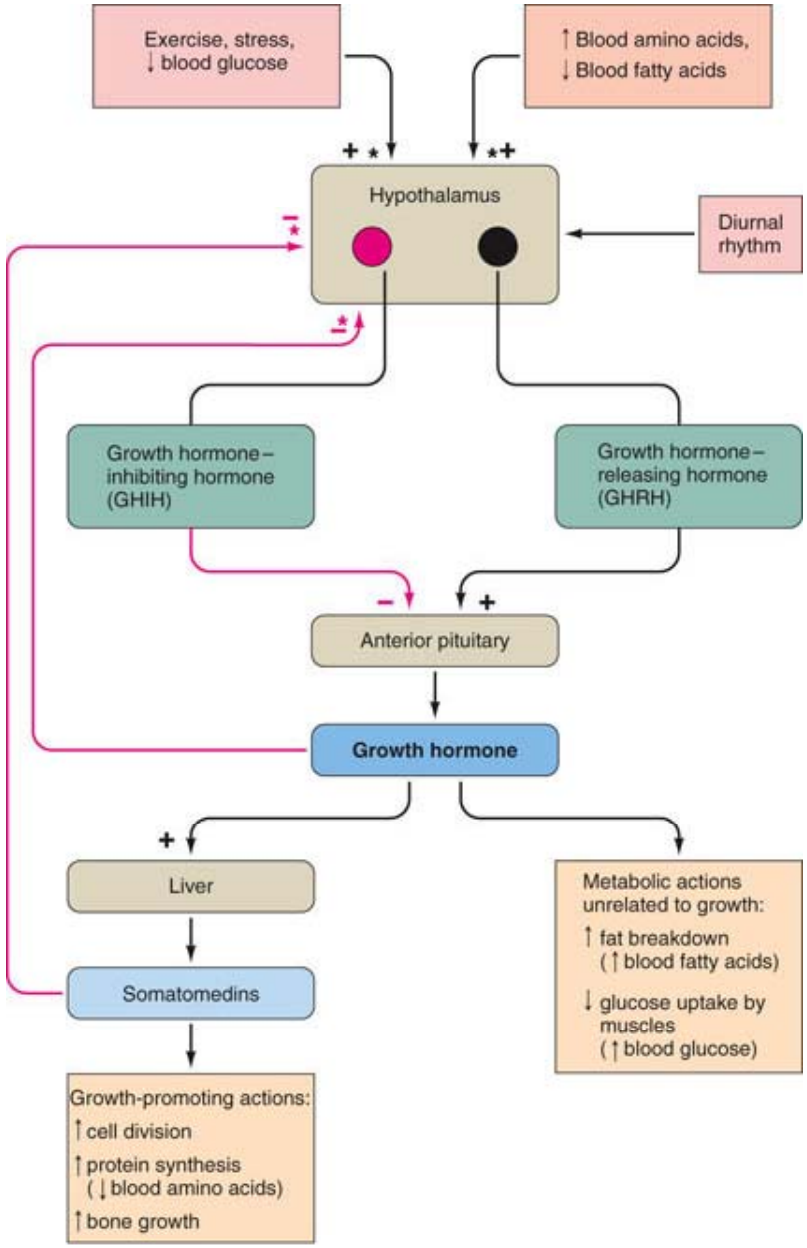


Hypothalamic Releasing and Inhibiting Hormones

Hypothalamic Hormone	**Effect on Anterior Pituitary**
Thyrotropin-Releasing hormone (TRH)	Stimulates release of TSH
Corticotropin-Releasing hormone (CRH)	Stimulates release of ACTH
Gonadotropin-releasing hormone (GnRH)	Stimulates release of FSH and LH
Growth-hormone releasing hormone (GHRH)	Stimulates release of growth hormone
Growth-hormone inhibiting hormone (GHIH)	Inhibits release of growth hormone and TSH
Prolactin-releasing hormone (PRH)	Stimulates release of prolactin
Prolactin-inhibiting hormone (PIH)	Inhibits release of prolactin

Endocrine Control of Growth

- Growth depends on growth hormone but is influenced by other factors as well
  - Genetic determination of an individual's maximum growth capacity
  - An adequate diet
  - Freedom from chronic disease and stressful environmental conditions
  - Normal levels of growth-influencing hormones
    - Including insulin, thyroid and steroid hormones



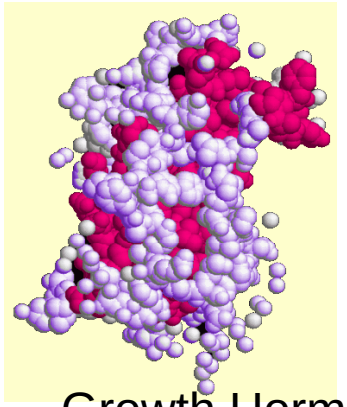
*These factors all increase growth hormone secretion, but it is unclear whether they do so by stimulating GHRH or inhibiting GHIH, or both.

*These factors inhibit growth hormone secretion in negative-feedback fashion, but it is unclear whether they do so by stimulating GHIH or inhibiting GHRH or inhibiting the anterior pituitary itself.

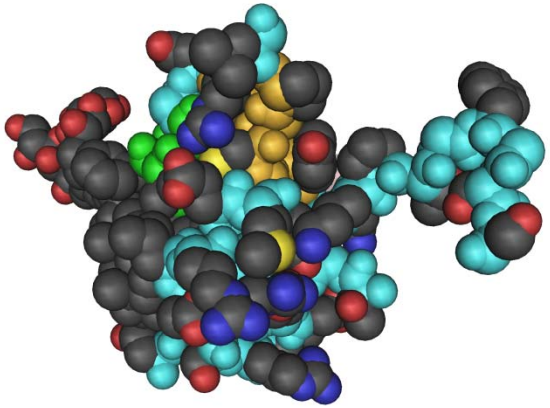
Fig. 18-12, p. 673

Growth Hormone

- Primarily promotes growth indirectly by stimulating liver's production of somatomedins
  - Primary somatomedin is insulin-like growth factor (IGF-1)
    - Acts directly on bone and soft tissues to bring about most growth-promoting actions
    - Stimulates protein synthesis, cell division, bone growth
    - Inhibits apoptosis
- Exerts metabolic effects not related to growth
  - Increases fatty acid levels in blood
  - Increases blood glucose



Growth Hormone



(IGF-1)

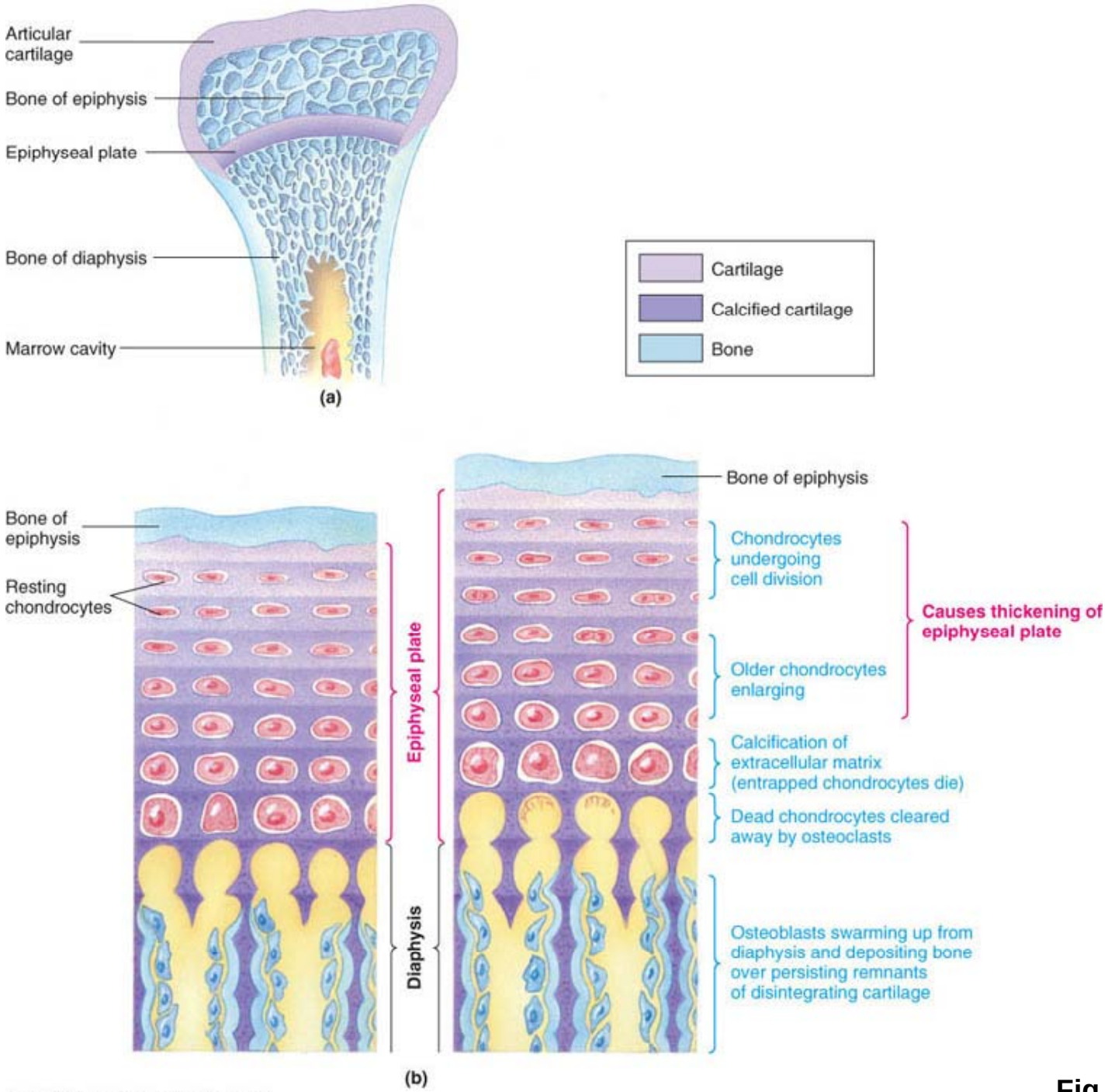


Fig. 18-11, p. 671

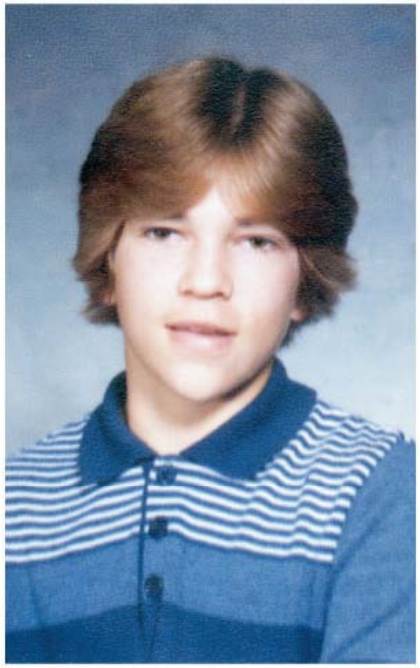
Endocrine Dysfunction

- Can arise from a variety of factors
- Most commonly result from abnormal plasma concentrations of a hormone caused by inappropriate rates of secretion
  - Hyposecretion - Too little hormone is secreted
  - Hypersecretion - Too much hormone is secreted
  - Primary hyposecretion
    - Too little hormone is secreted due to abnormality within gland
    - Causes - Genetic, Dietary, Chemical or toxic, Immunologic, cancer, Idiopathy
  - Secondary hyposecretion
    - Gland is normal but too little hormone is secreted due to deficiency of its tropic hormone
  - Causes
    - Tumors that ignore normal regulatory input and continuously secrete excess hormone, Immunologic factors
  - Primary hypersecretion
    - Too much hormone is secreted due to abnormality within gland
  - Secondary hypersecretion
    - Excessive stimulation from outside the gland causes oversecretion

Growth Hormone Abnormalities

- Growth hormone deficiency
  - Due to pituitary defect or hypothalamic dysfunction
  - Hyposecretion of GH in child is one cause of dwarfism
  - Deficiency in adults produces relatively few symptoms
- Growth hormone excess
  - Most often caused by tumor of GH-producing cells of anterior pituitary
  - Symptoms depend on age of individual when abnormal secretion begins
    - Gigantism
      - Caused by overproduction of GH in childhood before epiphyseal plates close
    - Acromegaly
      - Occurs when GH hypersecretion occurs after adolescence

The world's tallest man (7.9 feet) and smallest man (2.4 feet)



Growth

- Other hormones besides growth hormone are essential for normal growth
  - Thyroid hormone
    - Growth severely stunted in hypothyroid children
    - Hypersecretion does not cause excessive growth
  - Insulin
    - Deficiency often blocks growth
    - Hyperinsulinism often spurs excessive growth
  - Androgens
    - Play role in pubertal growth spurt, stimulate protein synthesis in many organs
    - Effects depend on presence of GH
  - Estrogens
    - Effects of estrogen on growth prior to bone maturation are not well understood poorly

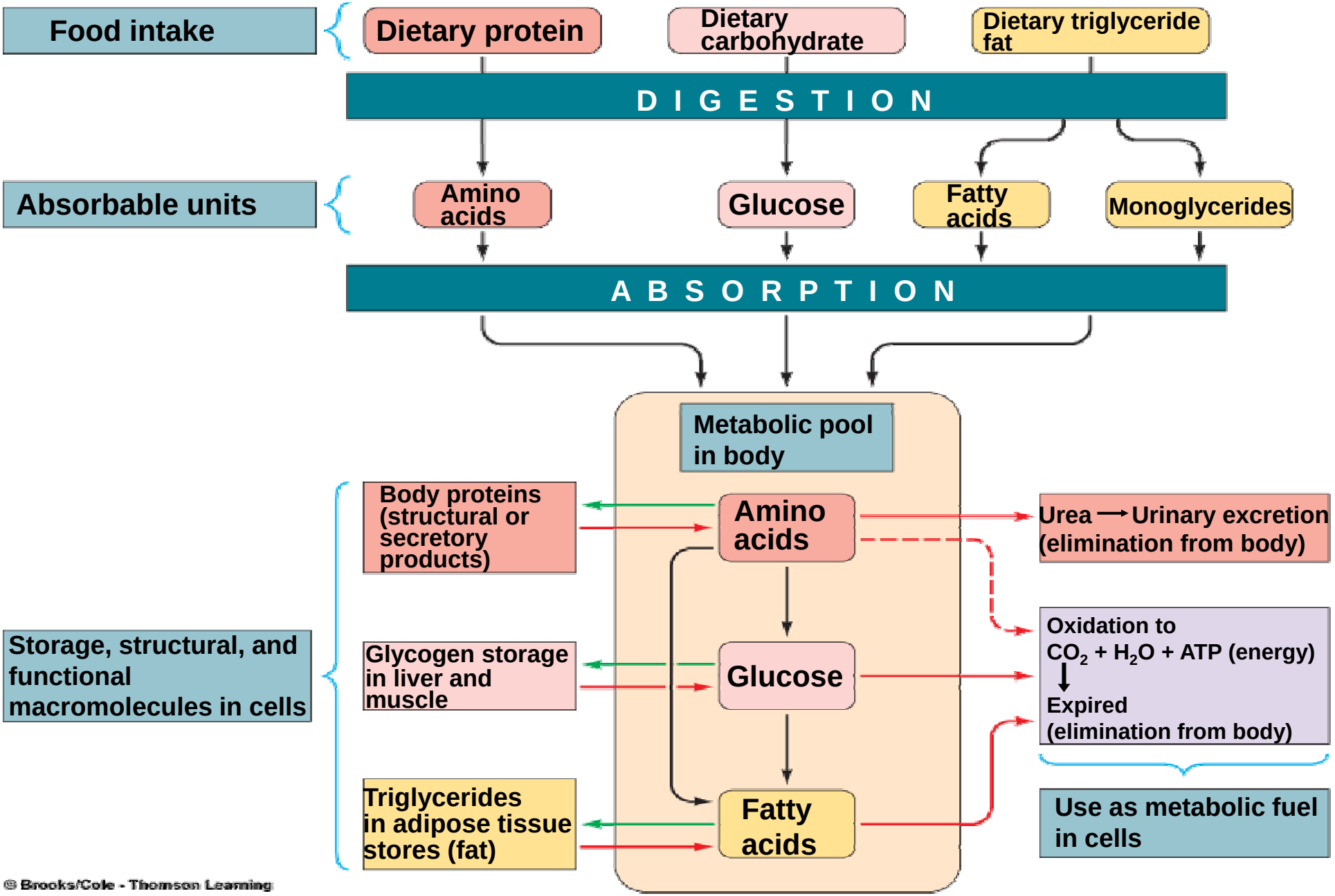


Fig. 19-13, p. 702