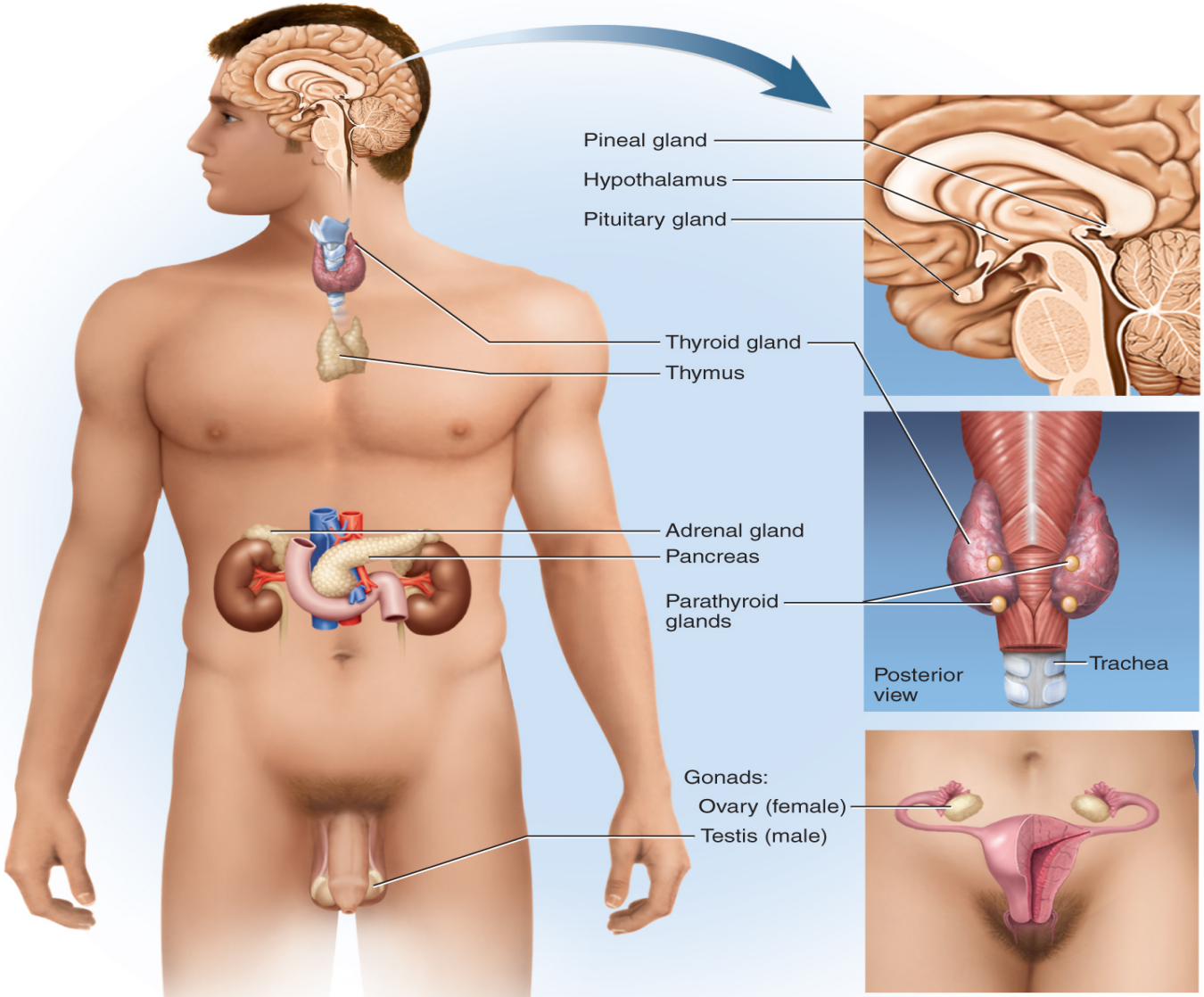
Chapter 17

Endocrine System Components

- endocrine system
- endocrinology
- endocrine glands
- hormones



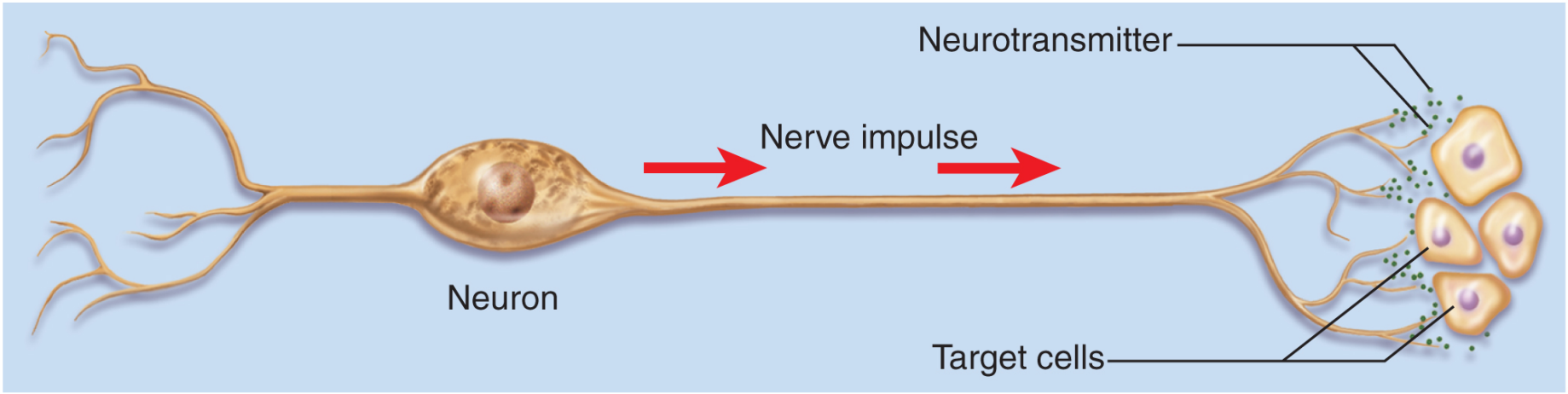
Comparison of Endocrine and Exocrine Glands

- **exocrine glands**
  - have ducts – ‘external secretions’
  - extracellular effects (food digestion)
- **endocrine glands**
  - no ducts
  - fenestrated capillary networks
  - ‘internal secretions’
  - intracellular effects
- **liver acts like both**

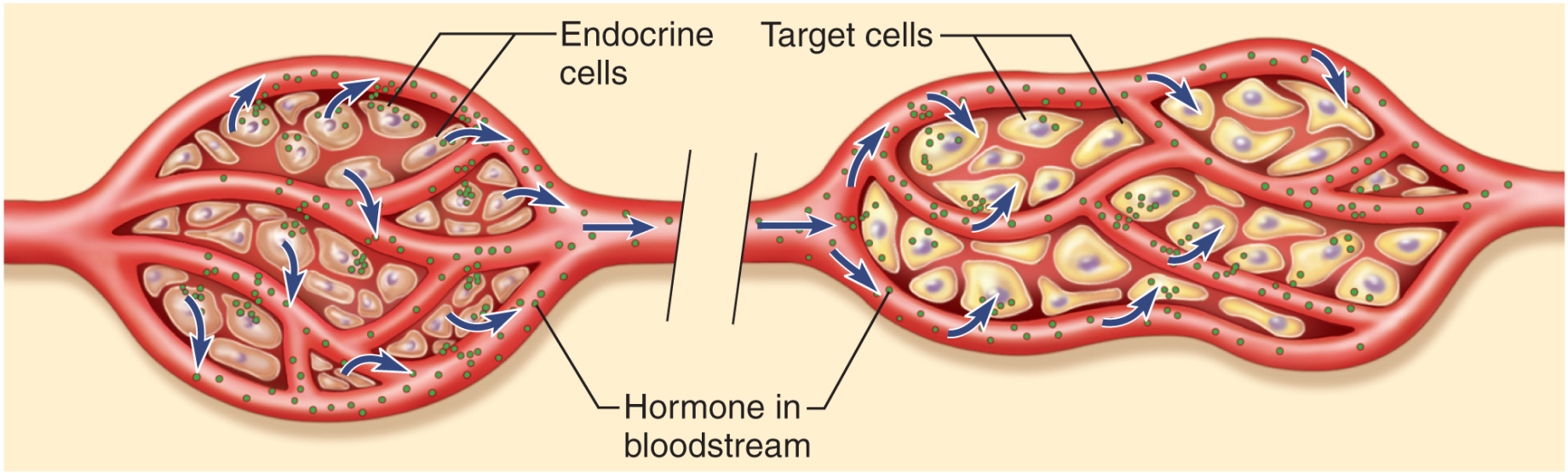
Comparison of Nervous and Endocrine Systems (Differences)

- **internal communication**
  - nervous - both electrical and chemical
  - endocrine - only chemical
- **speed and persistence of response**
  - nervous – quick, short lived response
  - endocrine – slow, long term response
- **adaptation to long-term stimuli**
  - nervous - response declines (adapts quickly)
  - endocrine - response persists (adapts slowly)
- **area of effect**
  - nervous - targeted and specific
  - endocrine - general, widespread effects

Communication by the Nervous and Endocrine Systems



(a) Nervous system



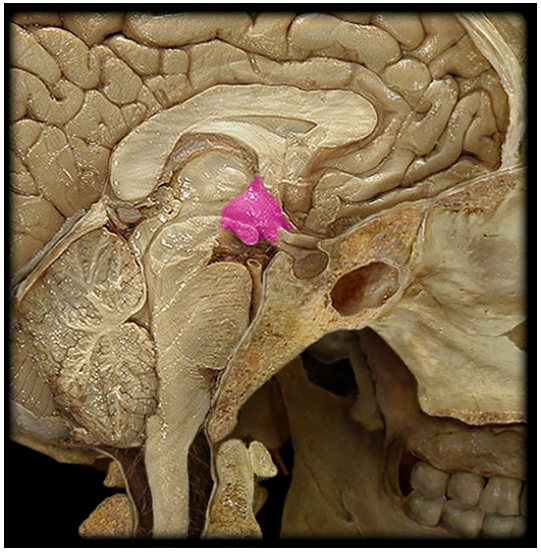
(b) Endocrine system

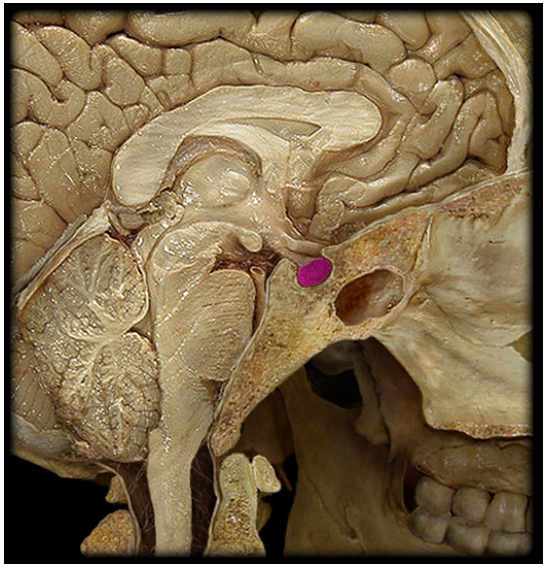
Nervous and Endocrine Systems (Similarities)

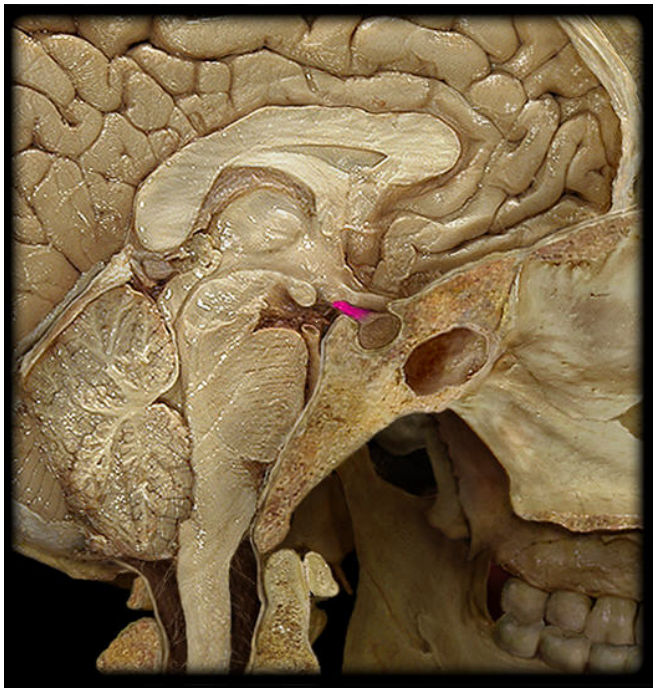
- **chemicals that are both hormones and neurotransmitters**
  - norepinephrine, cholecystokinin, thyrotropin-releasing hormone, dopamine and antidiuretic hormone
- **neuroendocrine cells secrete hormones into the bloodstream**
  - oxytocin and catecholamines
- **overlapping effects on same target cells**
  - norepinephrine and glucagon cause glycogen hydrolysis in liver
- **systems regulate each other**
- **target organs or cells**

Hypothalamus & Pituitary Gland

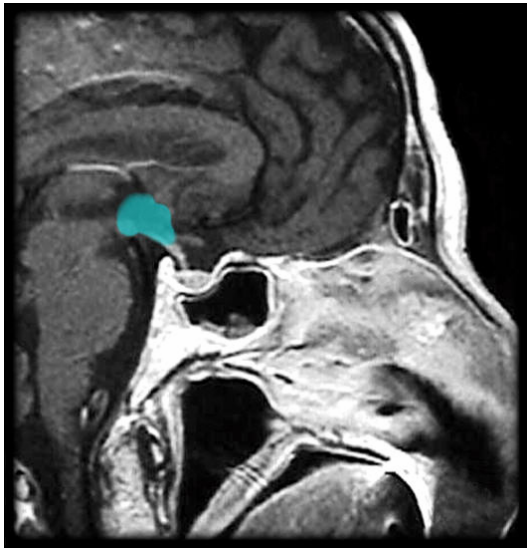
Hypothalamus & Pituitary Gland

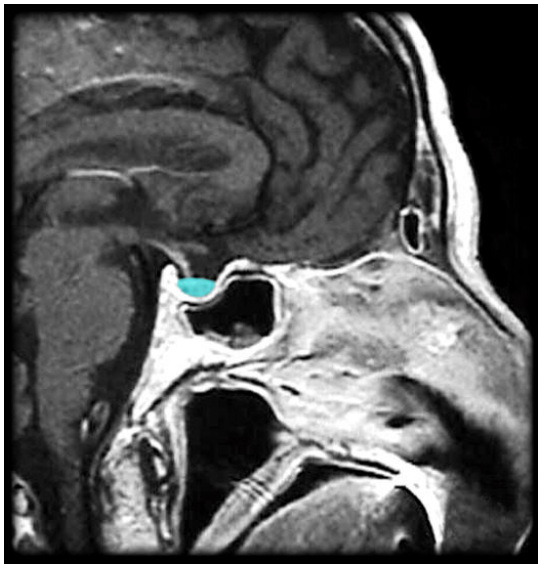






infundibulum





Pituitary Gland (Hypophysis)

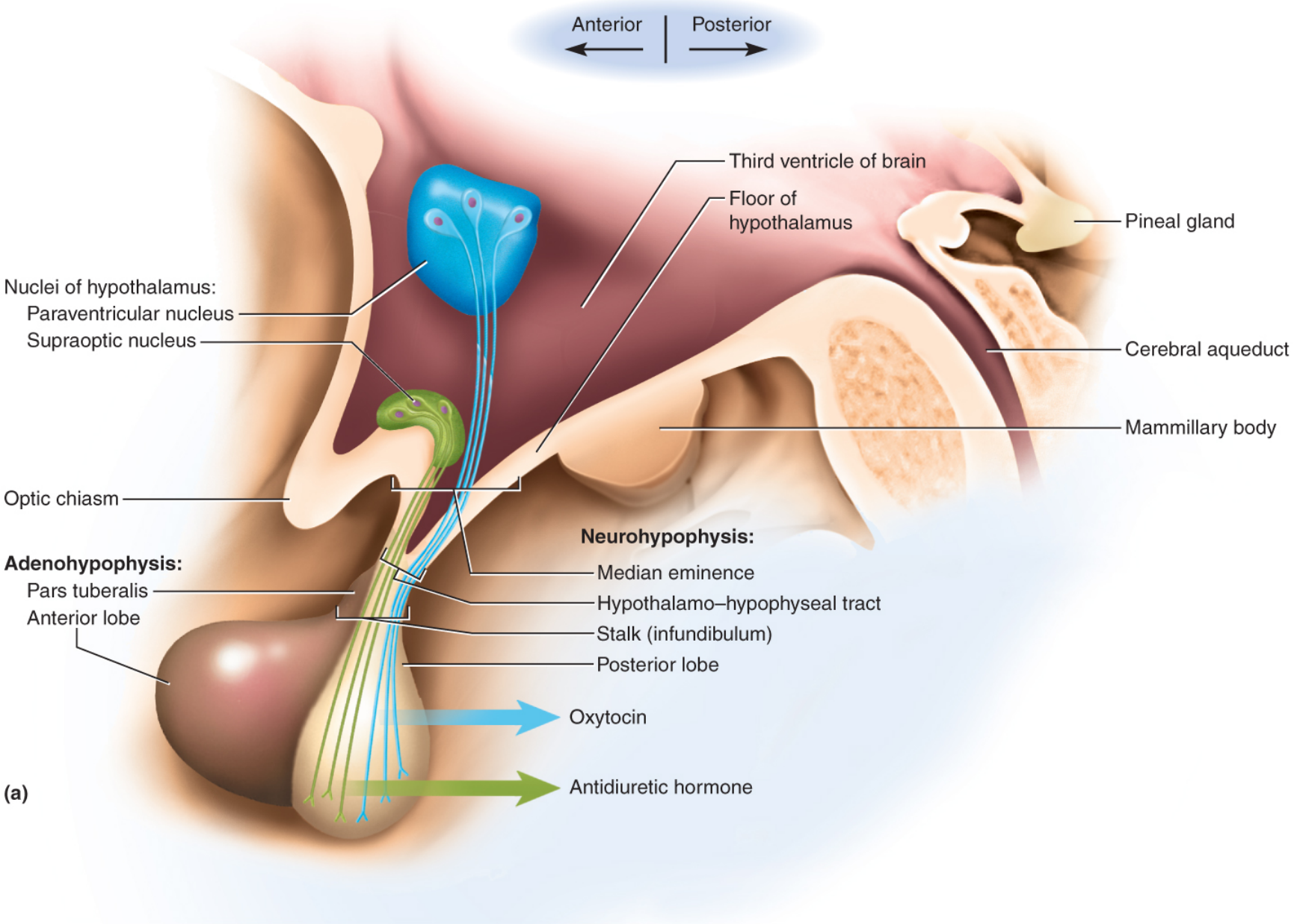
- **adenohypophysis** (anterior pituitary)
  - arises from hypophyseal pouch (outgrowth of pharynx)
- **neurohypophysis** (posterior pituitary)
  - downgrowth from brain

Embryonic Development

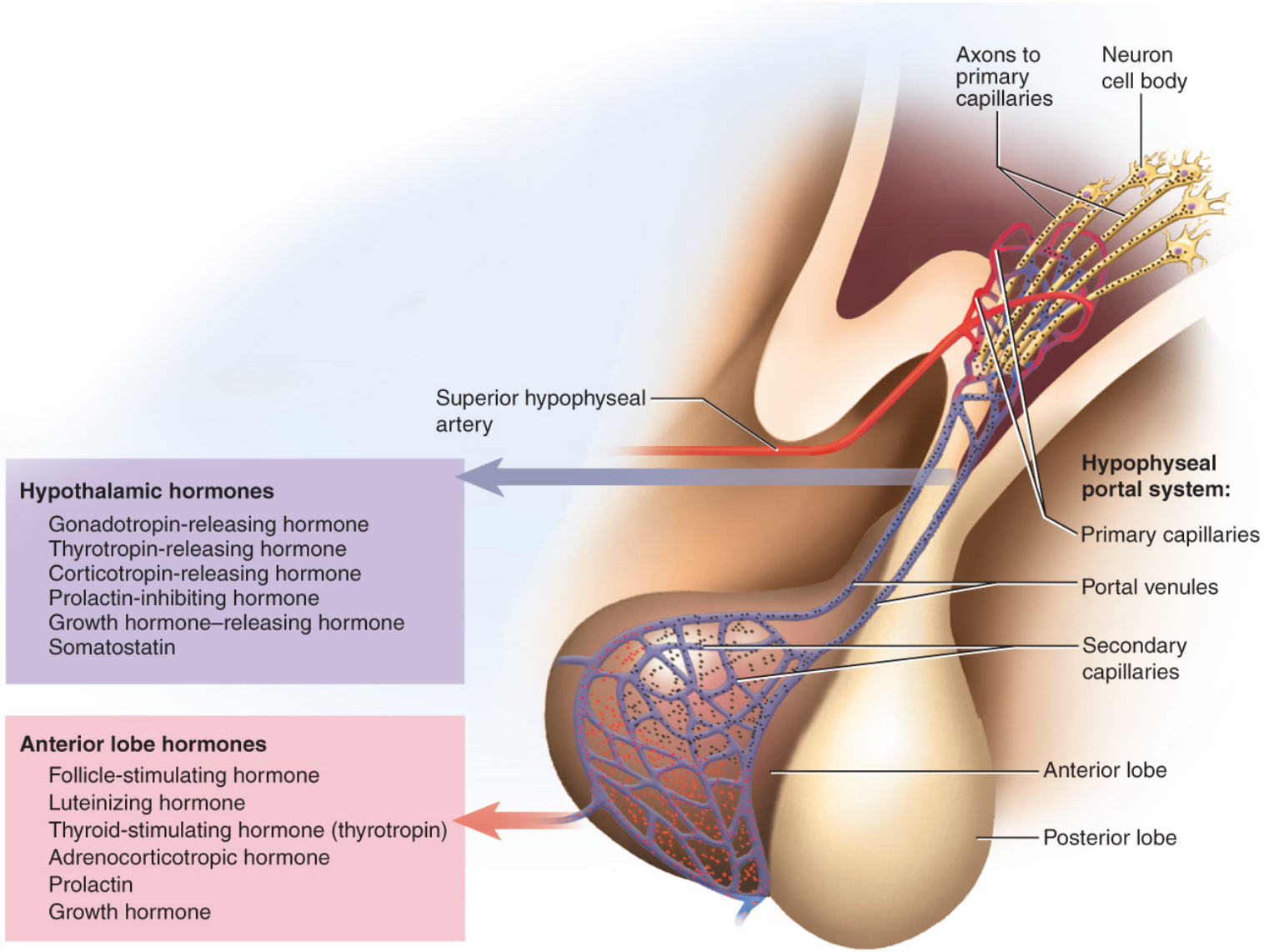
Adenohypophysis & Neurohypophysis

- **adenohypophysis** - anterior three-quarters of pituitary
  - anterior lobe (pars distalis)
  - pars tuberalis small mass of cells adhering to stalk
    - linked to hypothalamus by **hypophyseal portal system**
- **neurohypophysis** - posterior one-quarter of the pituitary
  - median eminence, infundibulum, and the posterior lobe (pars nervosa)
  - nerve tissue, not a true gland

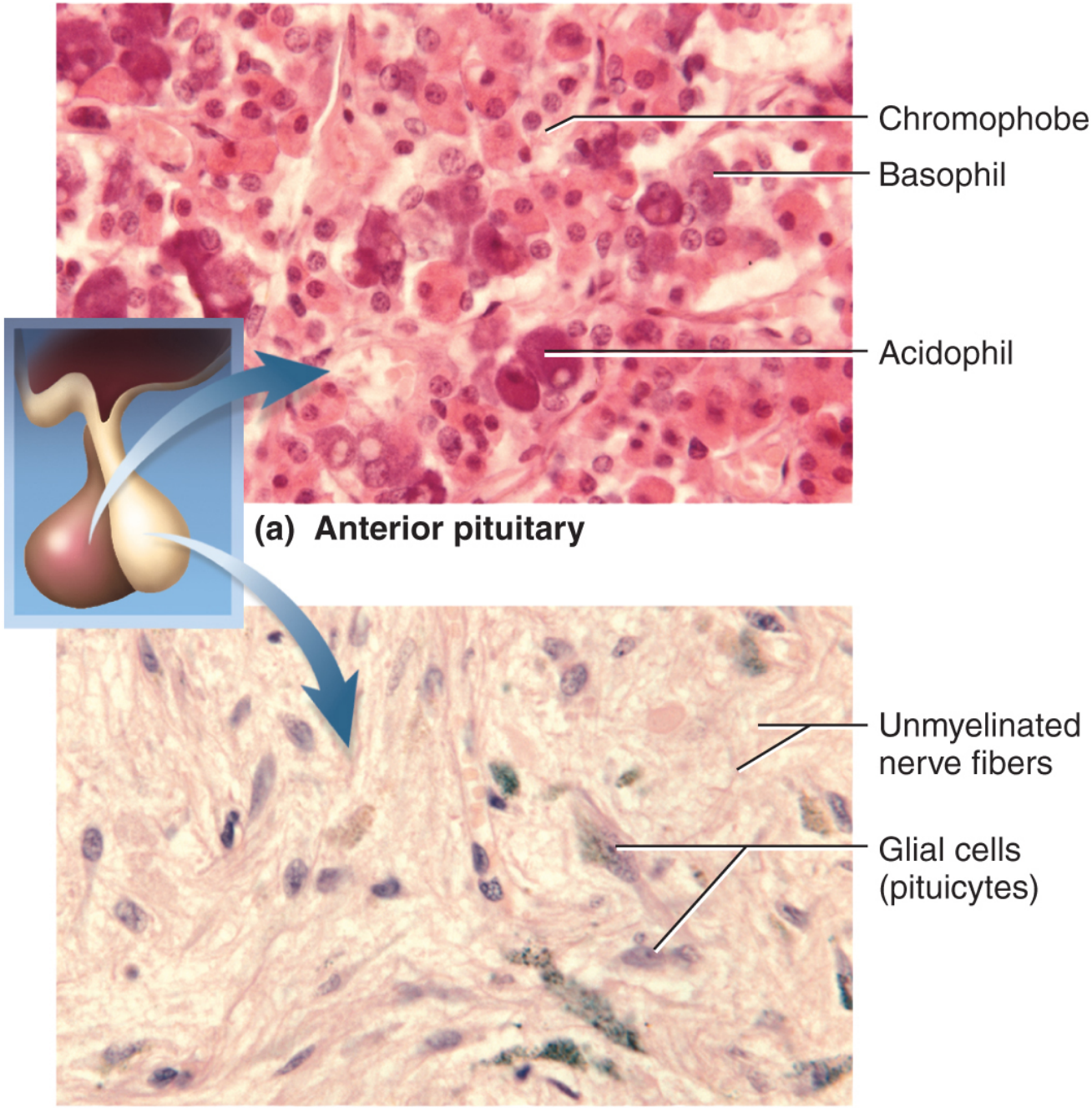
Posterior Pituitary Hormones



Hypophyseal Portal System

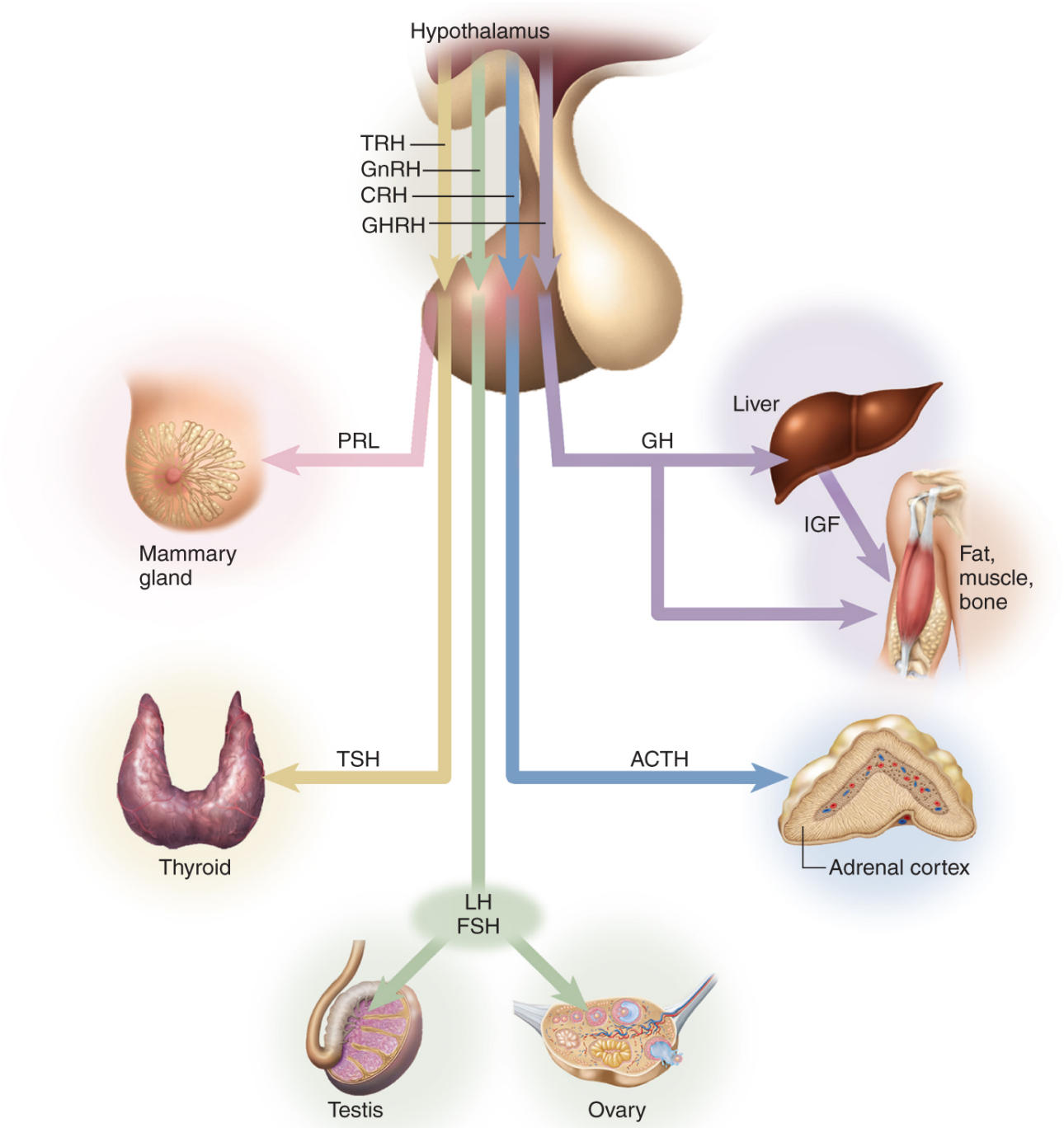


Histology of Pituitary Gland



Anterior Pituitary Hormones

- **Gonadotropin hormones** that target gonads
  - **FSH (follicle stimulating hormone)**
    - stimulates secretion of ovarian sex hormones, development of ovarian follicles, and sperm production
  - **LH (luteinizing hormone)**
    - stimulates ovulation, stimulates corpus luteum to secrete progesterone, stimulates testes to secrete testosterone
- **TSH (thyroid stimulating hormone)**
  - stimulates secretion of thyroid hormone
- **ACTH (adrenocorticotropic hormone)**
  - stimulates adrenal cortex to secrete glucocorticoids
- **PRL (prolactin)**
  - after birth stimulates mammary glands to synthesize milk, enhances secretion of testosterone by testes
- **GH (growth hormone)**
  - stimulates mitosis and cellular differentiation



Posterior Pituitary Hormones

- produced in hypothalamus
  - transported by **hypothalamo-hypophyseal tract** to posterior lobe
  - releases hormones when hypothalamic neurons are stimulated

- **ADH** (antidiuretic hormone)
  - increases water retention thus reducing urine volume and prevents dehydration
  - also called vasopressin because it can cause vasoconstriction

- **OT** (oxytocin)
  - surge of hormone released during sexual arousal and orgasm
    - stimulate uterine contractions and propulsion of semen
  - promotes feelings of sexual satisfaction and emotional bonding between partners
  - stimulates labor contractions during childbirth
  - stimulates flow of milk during lactation
  - promotes emotional bonding between lactating mother and infant

Control of Pituitary Secretion

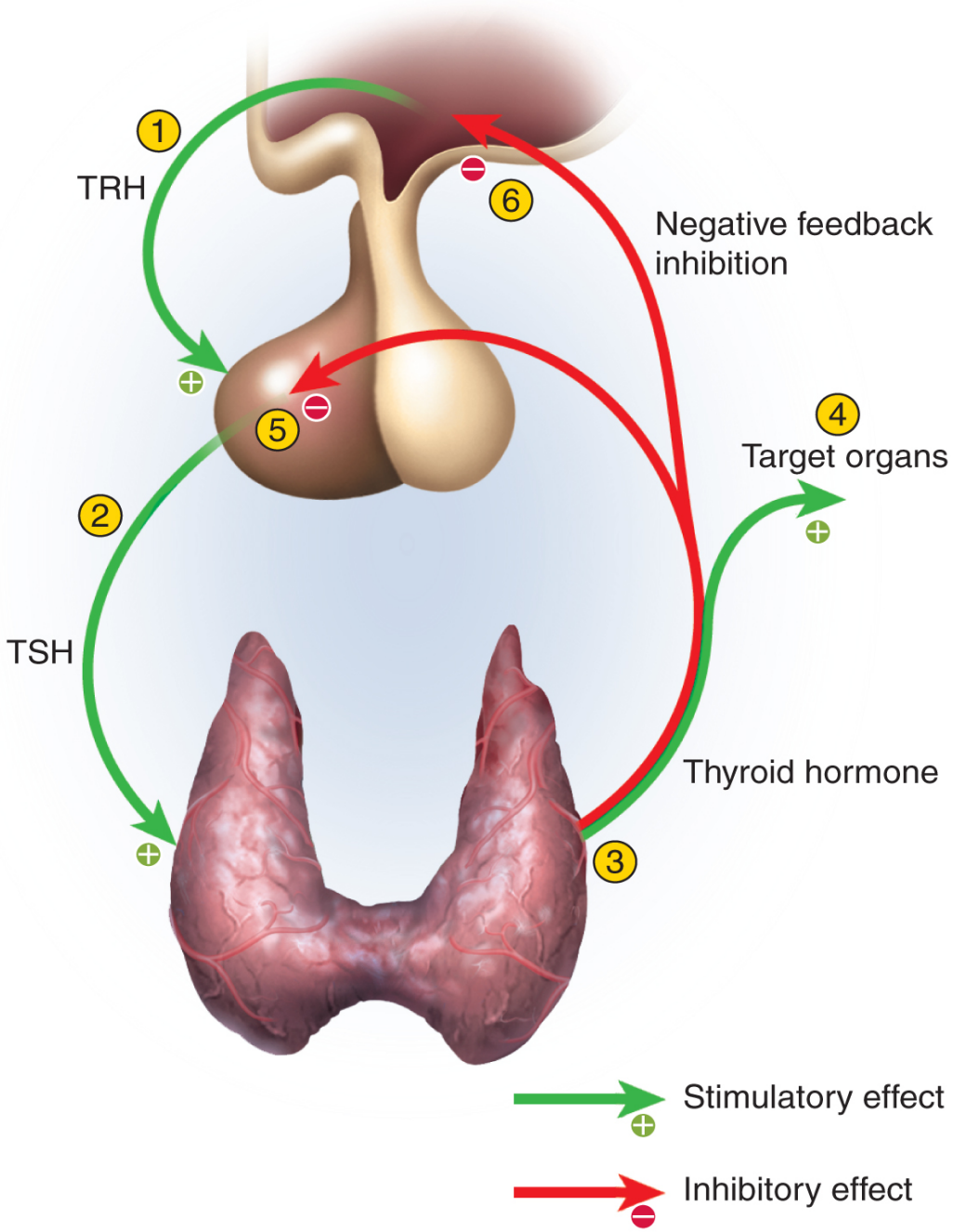
- rates of secretion are not constant
  - regulated by hypothalamus, other brain centers, and feedback from target organs

- **Hypothalamic and Cerebral Control**
  - **anterior lobe control** - releasing hormones and inhibiting hormones from hypothalamus
    - in cold weather, pituitary stimulated by hypothalamus to release TSH, leads to generation of body heat
  - **posterior lobe control** - neuroendocrine reflexes
    - **neuroendocrine reflex** - hormone release in response to nervous system signals
    - suckling infant ✹ stimulates nerve endings ✹ hypothalamus ✹ posterior lobe ✹ oxytocin ✹ milk ejection
    - hormone release in response to higher brain centers
    - milk ejection reflex can be triggered by a baby's cry
    - emotional stress can affect secretion of gonadotropins, disrupting ovulation, menstruation, and fertility

Control of Pituitary: Feedback from Target Organs

- **negative feedback -**increased target organ hormone levels inhibits release of hormones

- **positive feedback** stretching of uterus increases OT release, causes contractions, causing more stretching of uterus, etc. until delivery



Growth Hormone

- GH has widespread effects on the body tissues
  - especially cartilage, bone, muscle, and fat
- induces liver to produce growth stimulants
  - **insulin-like growth factors** (IGF-I) or **somatomedins** (IGF-II)
    - stimulate target cells in diverse tissues
    - IGF-I prolongs the action of GH
    - **hormone half-life** – the time required for 50% of the hormone to be cleared from the blood
      - **GH half-life** 6 – 20 minutes - **IGF-I half-life** about 20 hours
    - **protein synthesis increases** -- boosts transcription of DNA, production of mRNA, amino acid uptake into cells, suppresses protein catabolism
    - **lipid metabolism increased** – fat catabolized by adipocytes (protein-sparing effect) – provides energy for growing tissues

Growth Hormone

- **carbohydrate metabolism** – by mobilizing fatty acids for energy, GH produces **glucose-sparing** makes glucose available for glycogen synthesis and storage
- **electrolyte balance** – promotes Na^+, K^+, & Cl^- retention by kidneys, enhances Ca^{+2} absorption in intestine

– bone growth, thickening, and remodeling influenced, especially during childhood and adolescence
– secretion high during first two hours of sleep
– can peak in response to vigorous exercise
– GH levels decline gradually with age
– average 6 ng/ml during adolescence, 1.5 ng/mg in old age
  - lack of protein synthesis contributes to aging of tissues and wrinkling of the skin
  - age 30, average adult body is 10% bone, 30% muscle, 20% fat
  - age 75, average adult body is 8% bone, 15% muscle, 40% fat

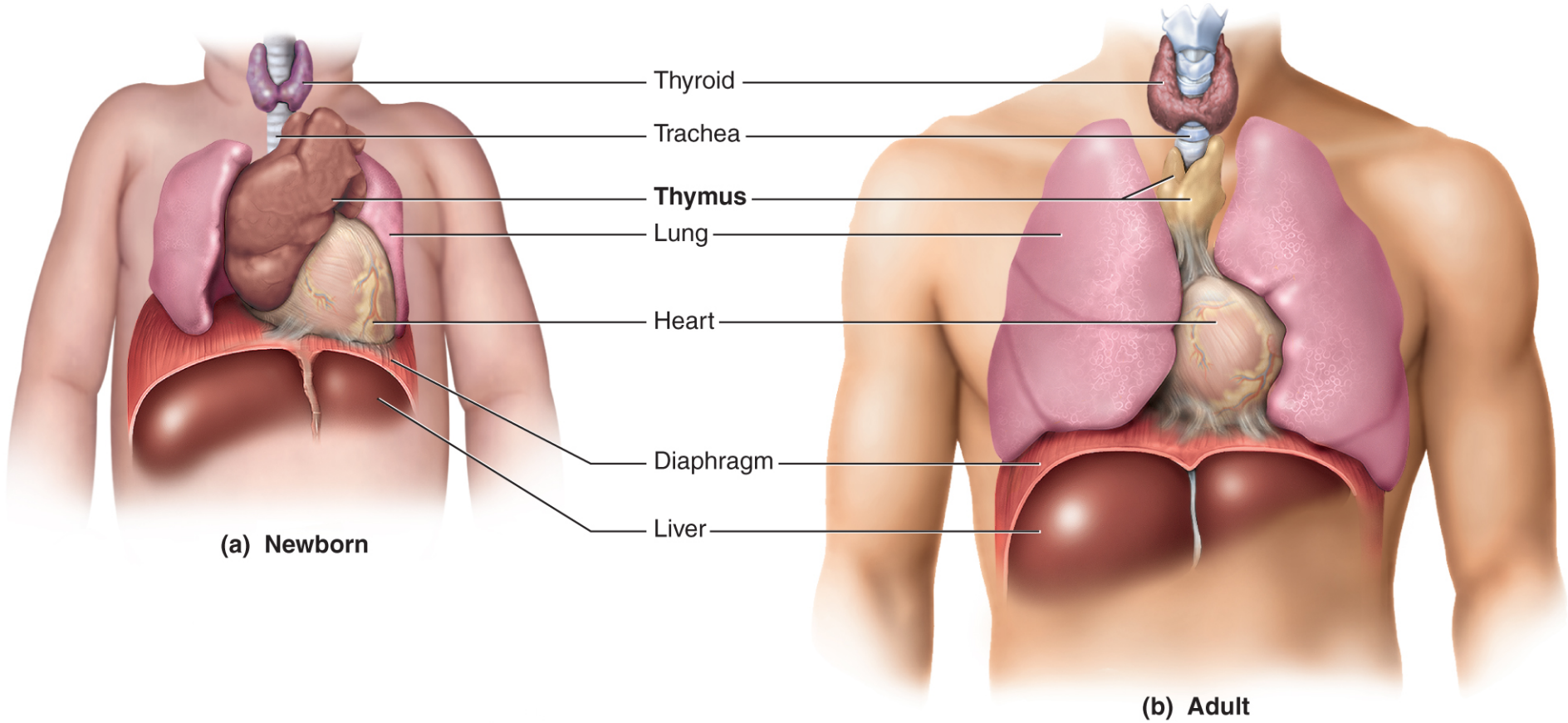
Pineal Gland

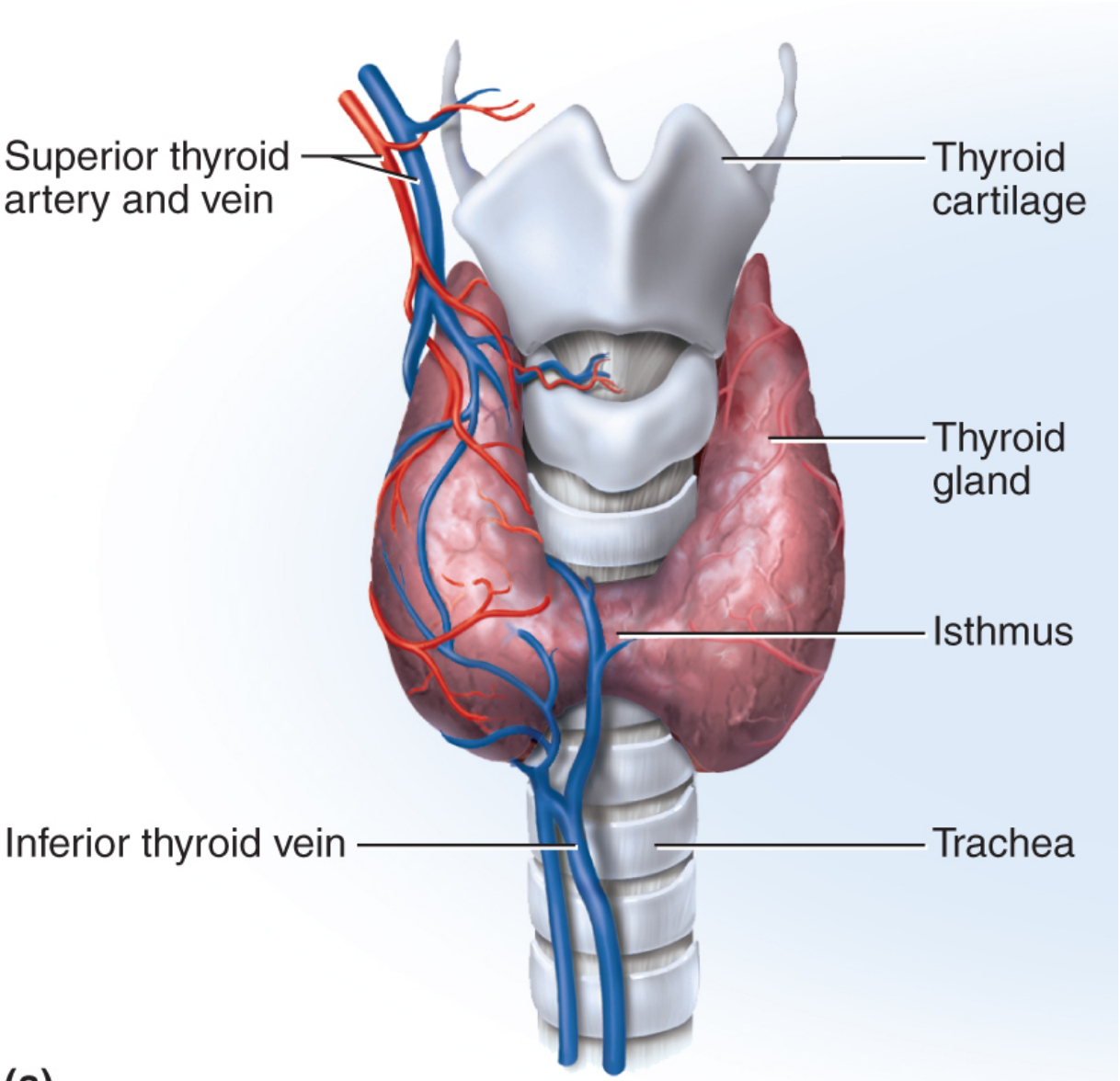
- after age 7, it undergoes **involution** (shrinkage)
  - down 75% by end of puberty
  - tiny mass of shrunken tissue in adults
- **circadian rhythms** of daylight and darkness
  - **synthesizes melatonin** from serotonin during the night
    - fluctuates seasonally with changes in day length
- may regulate timing of puberty in humans
- **seasonal affective disorder** (SAD) occurs in winter or northern climates
  - symptoms - depression, sleepiness, irritability and carbohydrate craving
  - Treatment - 2 to 3 hours of exposure to bright light each day

Pineal Gland

Thymus

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

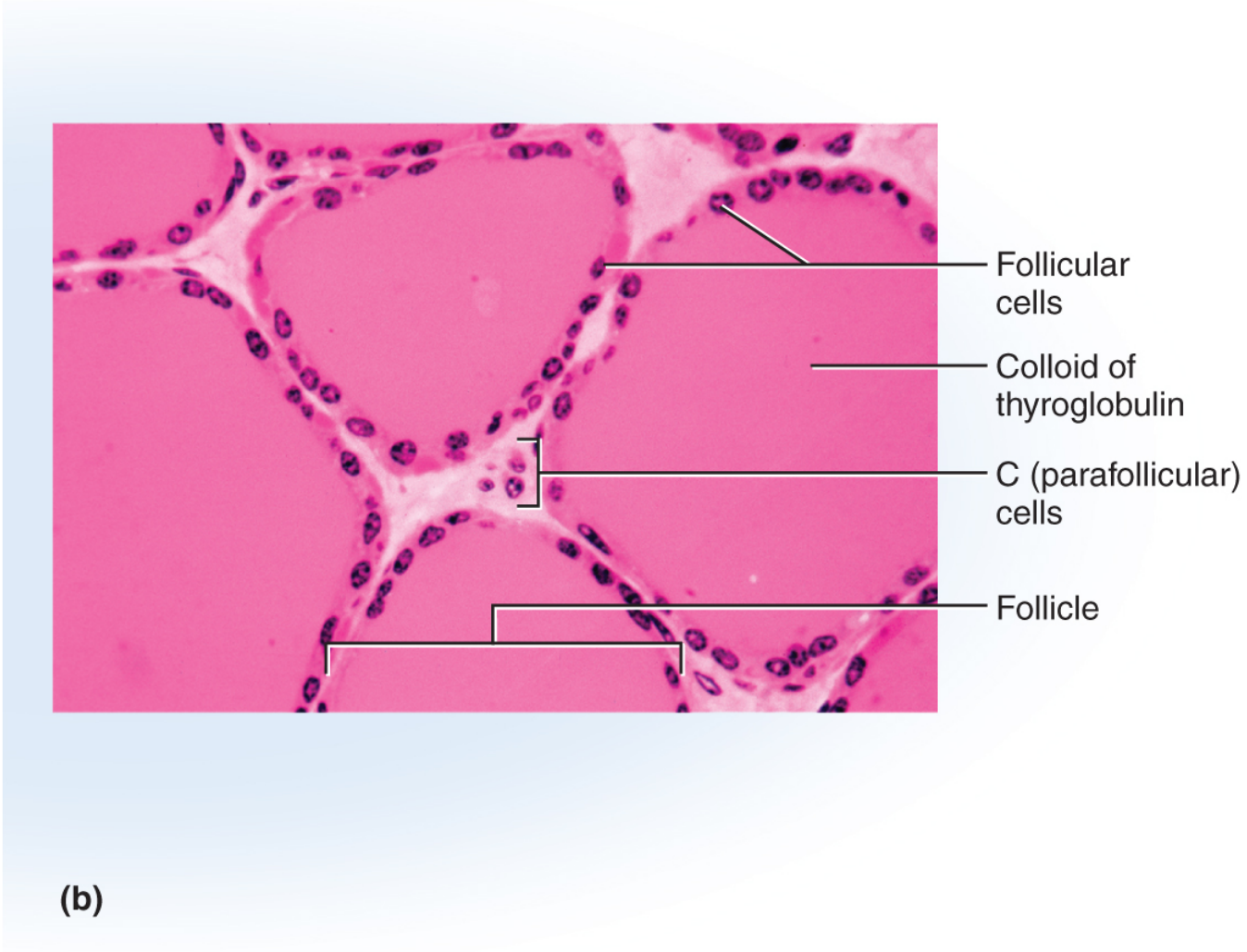




Thyroid Gland Anatomy

- **thyroid follicles** – sacs that compose most of thyroid
  - contain protein rich **colloid**
  - **follicular cells** – simple cuboidal epithelium that lines follicles
- secretes **thyroxine** (T_4) and **triiodothyronine** (T_3)
  - increases metabolic rate, O_2 consumption, heat production (**calorigenic effect**), appetite, growth hormone secretion, alertness and quicker reflexes
- **parafollicular** (C or clear) **cells** secrete **calcitonin** with rising blood calcium
  - stimulates osteoblast activity and bone formation

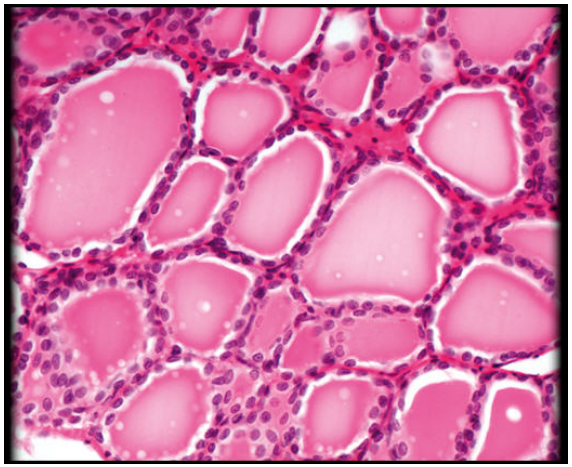
Histology of the Thyroid Gland



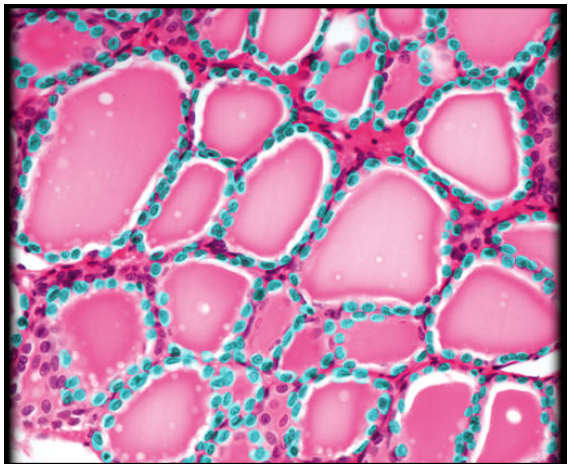
thyroid follicles are filled with colloid and lined with simple cuboidal epithelial cells (follicular cells).

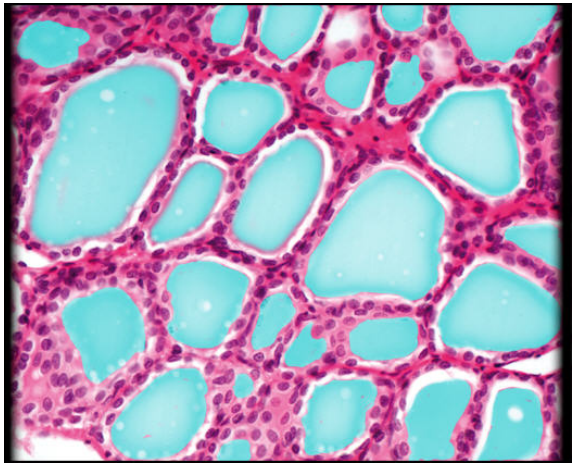
Thyroid Histology

thyroid follicles

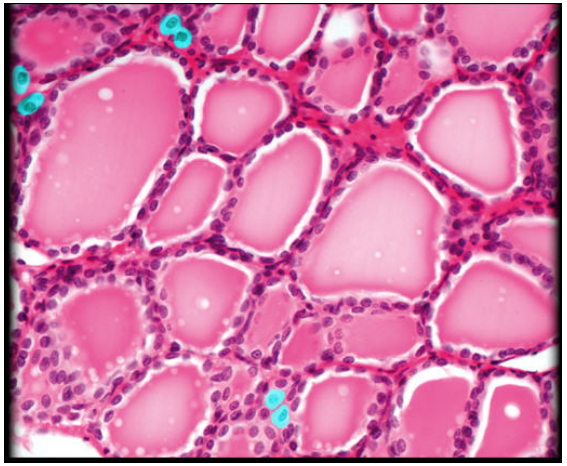


follicular cells





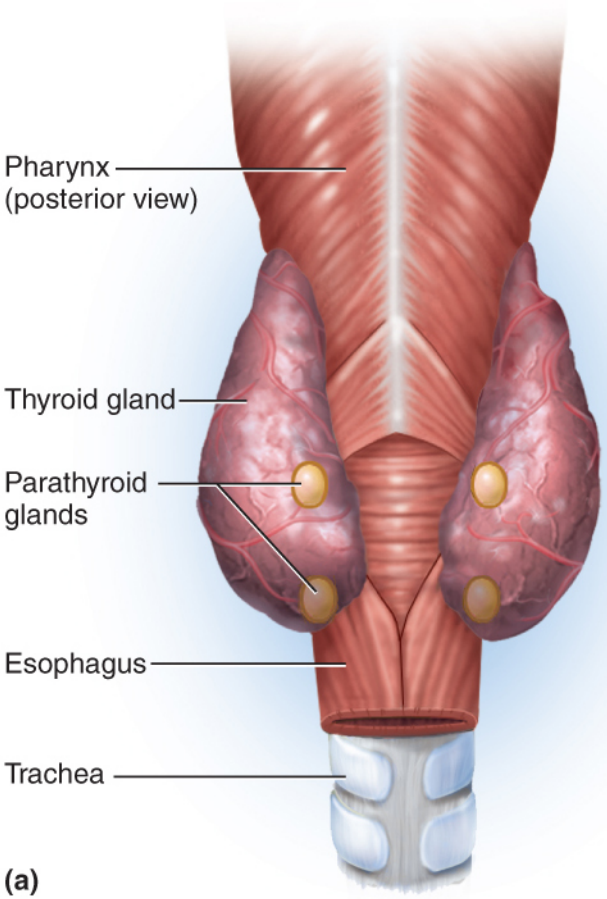
colloid



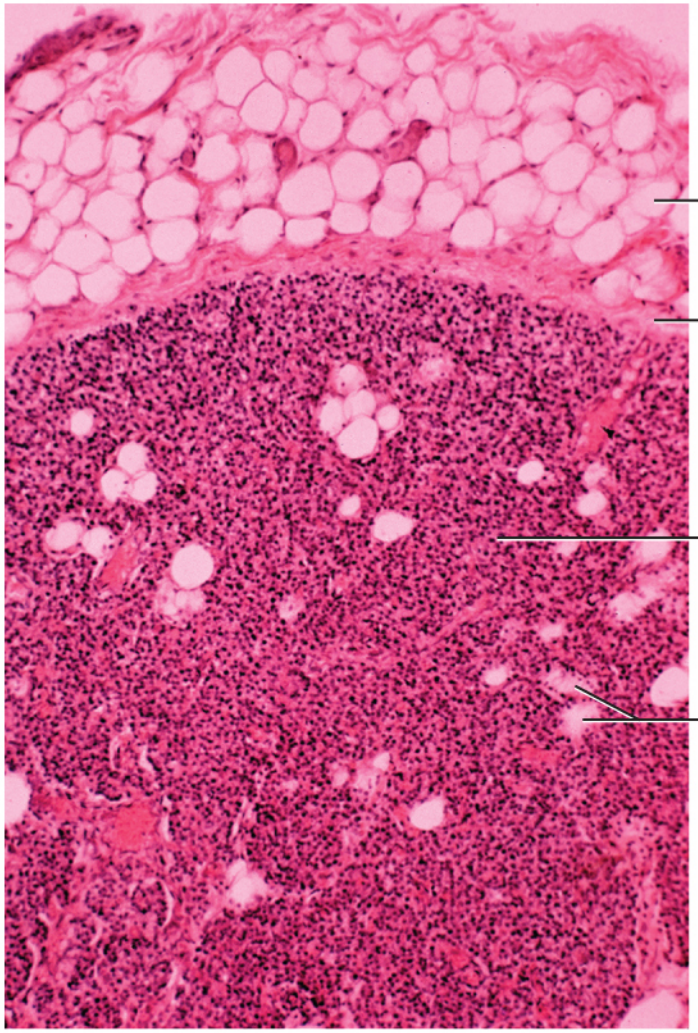
parafollicular (C) cells

Parathyroid Glands

- secrete parathyroid hormone (PTH)
  - increases blood Ca^{2+} levels
    - promotes synthesis of calcitriol
    - increases absorption of Ca^{2+}
    - decreases urinary excretion
    - increases bone resorption



(a)



(b)

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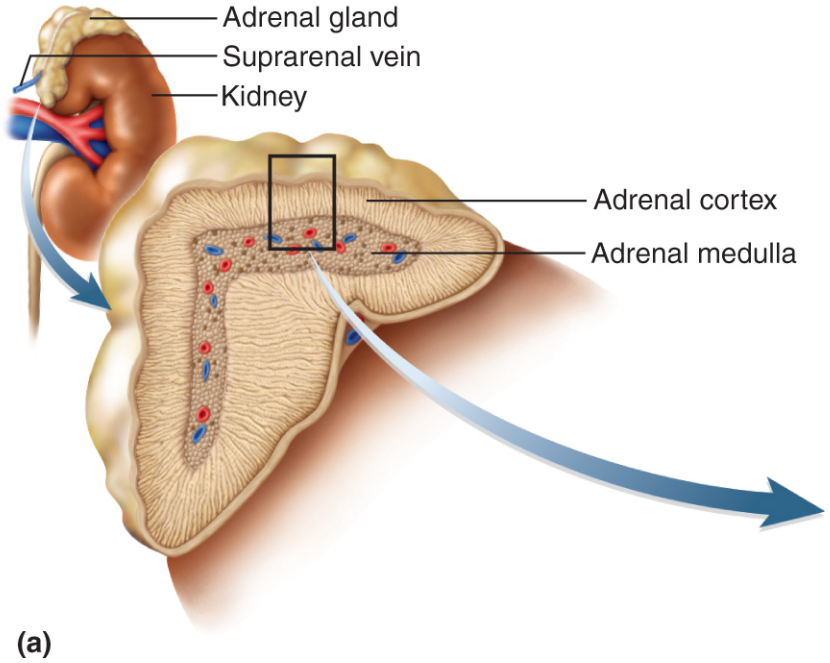
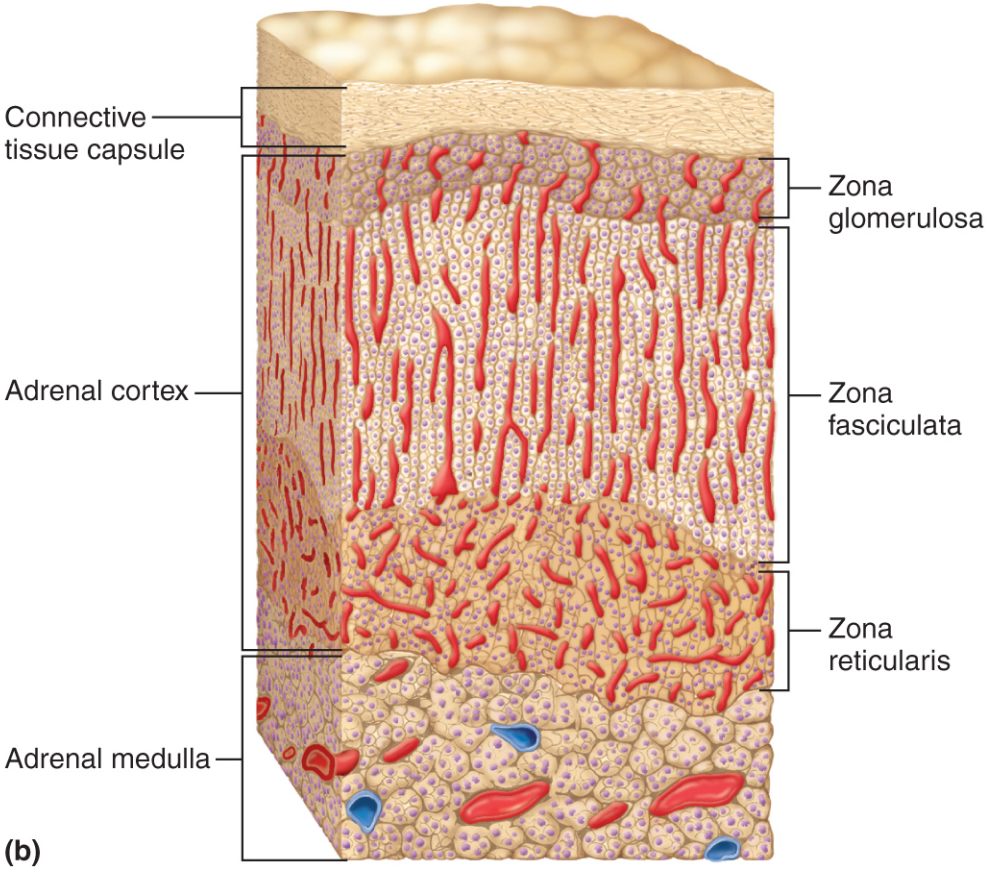
Adrenal Gland





Adrenal (Suprarenal) Glands

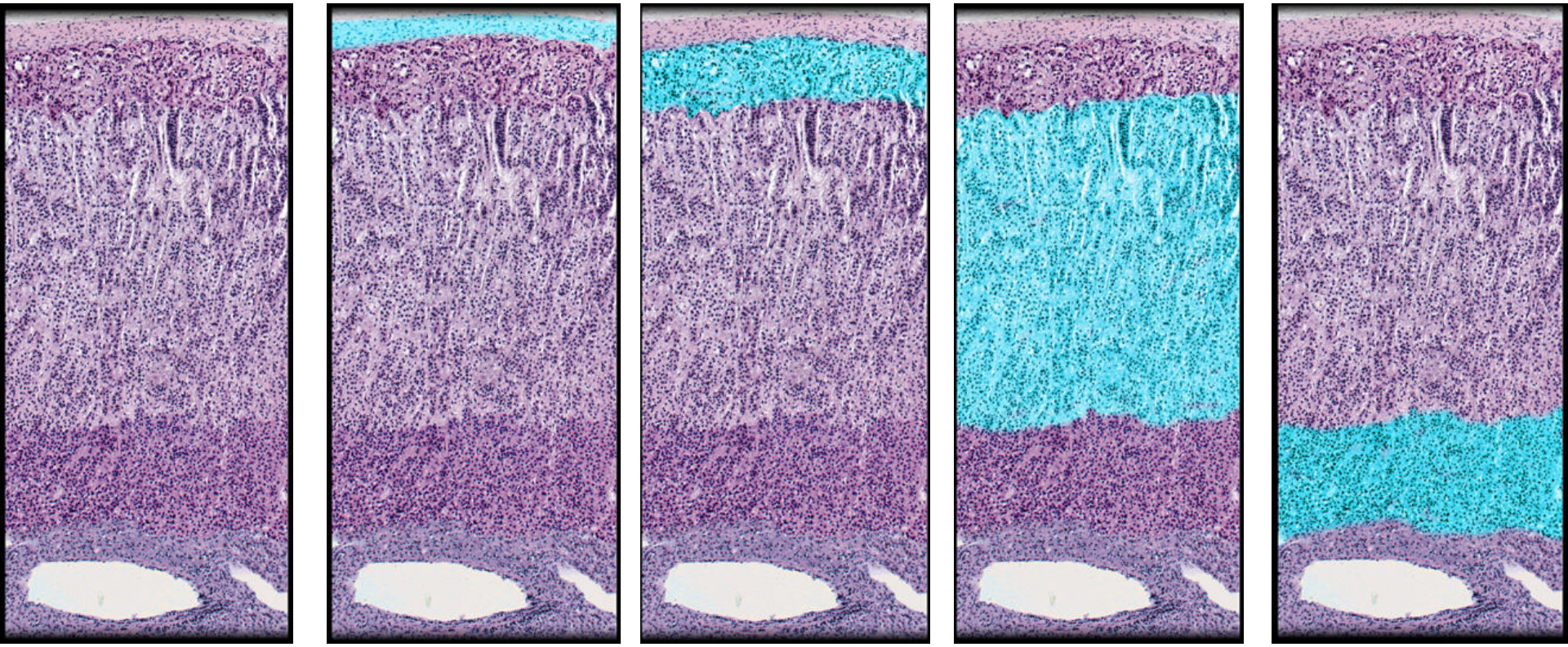
Adrenal Medulla

- **endocrine gland** and **sympathetic ganglion** of sympathetic nervous system
  - modified sympathetic postganglionic neurons called **chromaffin cells**
  - release **catecholamines** (**epinephrine** and **norepinephrine**) and a trace of **dopamine** directly into the bloodstream
- effect is longer lasting than neurotransmitters
  - increases alertness and prepares body for physical activity –
    - mobilize high energy fuels, lactate, fatty acids, and glucose
    - **glycogenolysis** and **gluconeogenesis** boost glucose levels
    - **glucose-sparing effect** because inhibits insulin secretion
      - muscles use fatty acids saving glucose for brain
  - **increases** blood pressure, heart rate, blood flow to muscles, pulmonary air flow and metabolic rate
  - **decreases** digestion and urine production

Adrenal Cortex

- secretes **5 major steroid hormones** from **three layers** of glandular tissue
  - **zona glomerulosa** (thin, outer layer)
    - secretes **mineralocorticoid** – regulate the body's electrolyte balance
  - **zona fasciculata** (thick, middle layer)
    - secretes **glucocorticoids**
  - **zona reticularis** (narrow, inner layer)
    - secretes **sex steroids**

Adrenal Histology



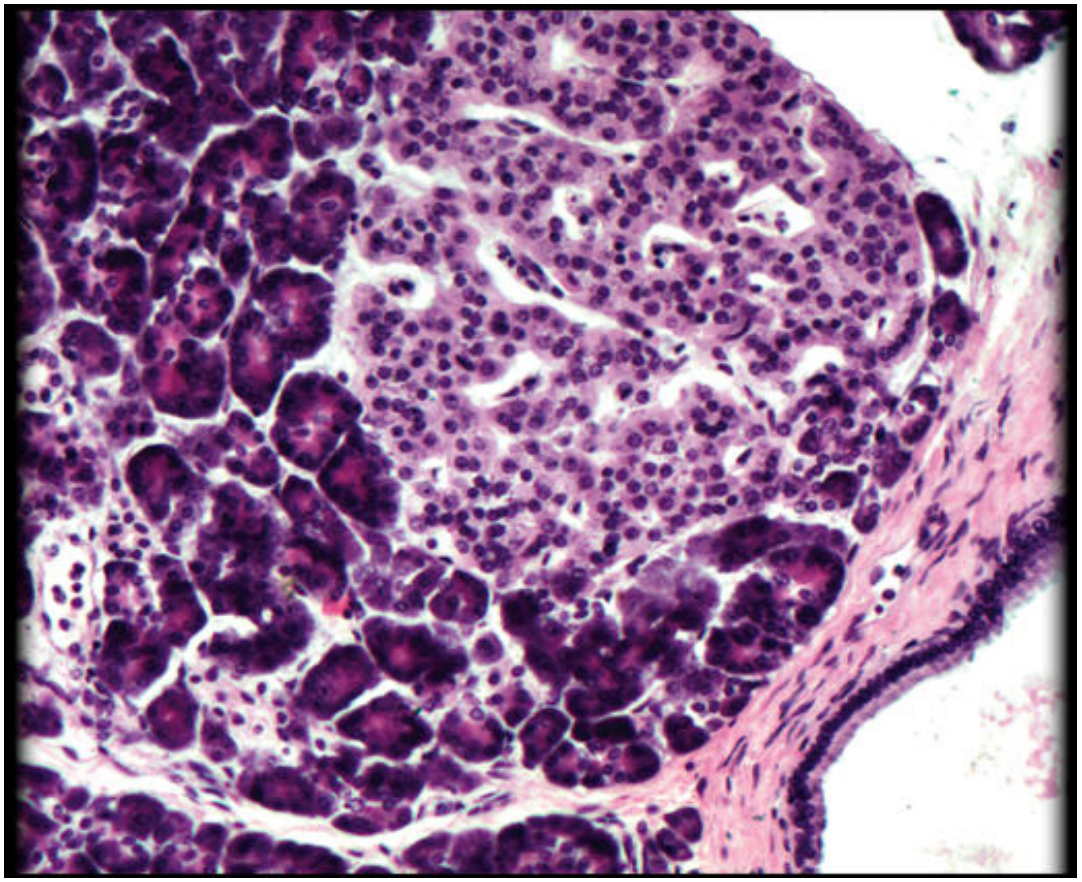
Categories of Corticosteroids

- **mineralocorticoids – zona glomerulosa**
  - regulate electrolyte balance
  - **aldosterone**
- **glucocorticoids – zona fasciculata**
  - regulate metabolism of glucose and other fuels
  - **Cortisol**
  - helps body adapt to stress and repair tissues
  - anti-inflammatory effect becomes immune suppression with long-term use
- **sex steroids – zona reticularis**
  - **androgens**
  - **estradiol**

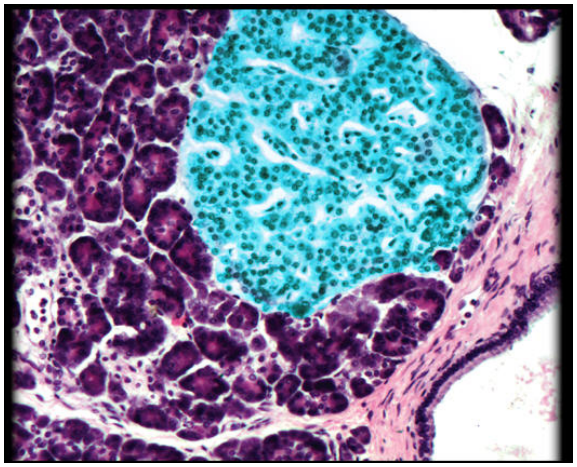
Adrenal Gland Interactions

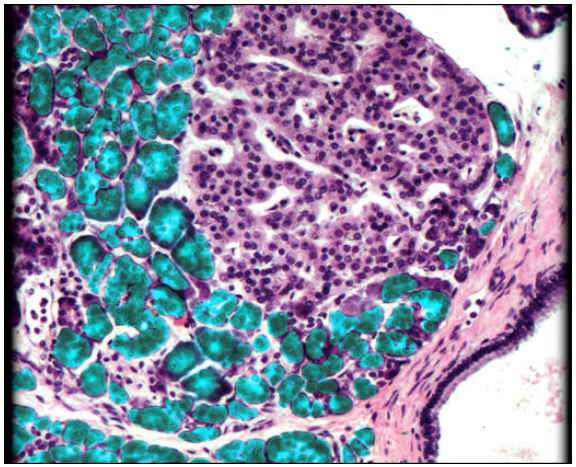
- medulla and cortex of adrenal gland are not functionally independent
- medulla atrophies without the stimulation of cortisol
- some chromaffin cells of medullary origin extend into the cortex
  - they stimulate the cortex to secrete corticosteroids when stress activates the sympathetic nervous system

Pancreas Histology



pancreatic islet





pancreas acini

- exocrine digestive gland and endocrine cell clusters (pancreatic islets).

Pancreatic Hormones

- **somatostatin** secreted by D or **delta (_)cells**
  - partially suppresses secretion of glucagon and insulin
  - inhibits nutrient digestion and absorption which prolongs absorption of nutrients
- **pancreatic polypeptide** secreted by PP cells or **F cells**)
  - inhibits gallbladder contraction and secretion pancreatic digestive enzymes
- **gastrin** secreted by **G cells**
  - stimulates stomach acid secretion, motility and emptying

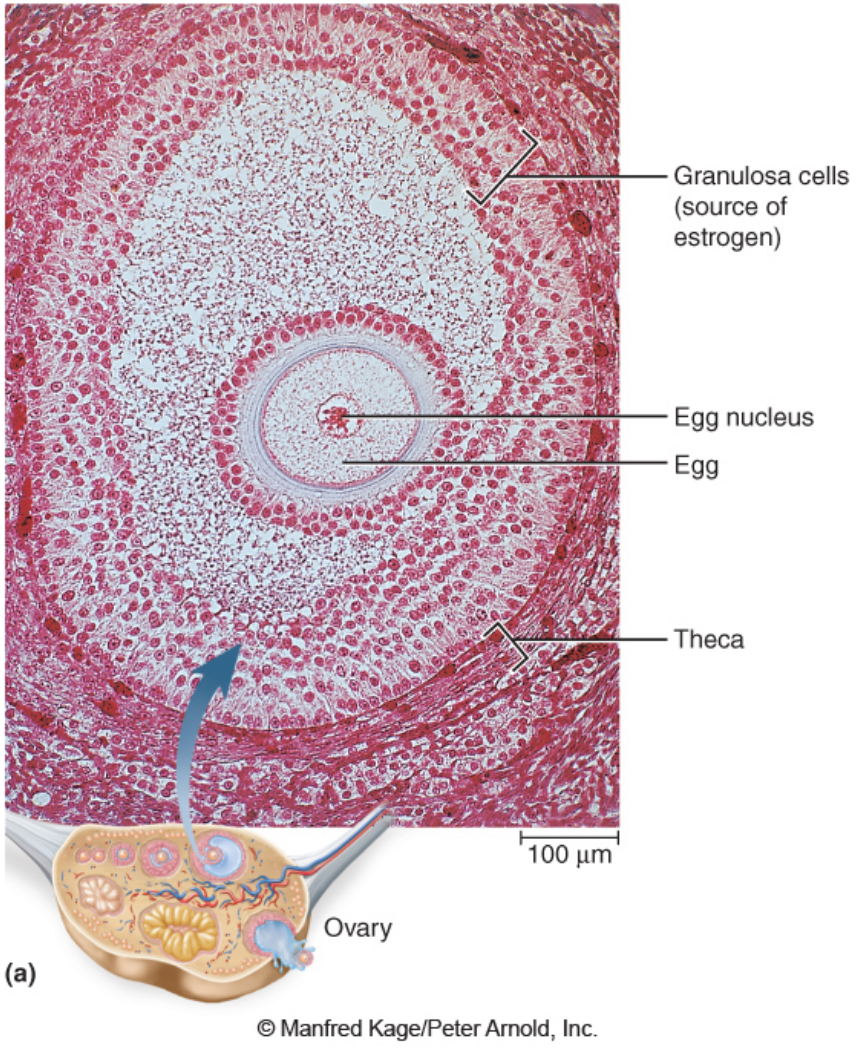
Hormones Affecting Glucose Metabolism

- **hyperglycemic hormones** raise blood glucose concentration
  - glucagon, growth hormone, epinephrine, norepinephrine, cortisol, and corticosterone
- **hypoglycemic hormones** lower blood glucose
  - insulin

The Gonads

- **ovaries** and **testes** are both endocrine and exocrine
  - **exocrine** product – whole cells - eggs and sperm (**cytogenic glands**)
  - **endocrine** product - gonadal hormones – mostly steroids
- **ovarian** hormones
  - estradiol, progesterone, and inhibin
- **testicular** hormones
  - testosterone, weaker androgens, estrogen and inhibin

Histology of Ovary and Testis



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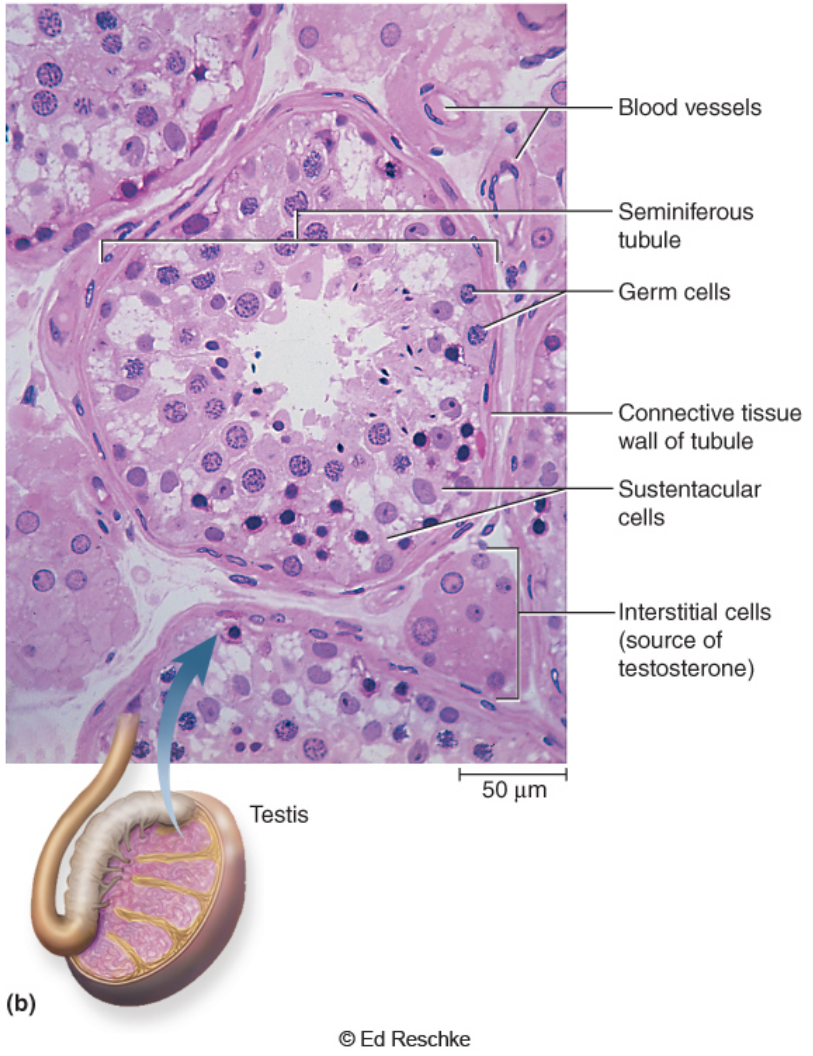


© Ed Reschke

follicle - egg surrounded by granulosa cells and a capsule (theca)

Endocrine Functions of Other Organs

- **skin**
  - keratinocytes convert a cholesterol-like steroid into cholecalciferol using UV from sun
- **liver**
  - converts cholecalciferol into **calcidiol**
  - secretes **angiotensinogen** (a prohormone)
    - precursor of angiotensin II (a regulator of blood pressure)
  - secretes 15% of **erythropoietin** (stimulates bone marrow)
  - **hepcidin** – promotes intestinal absorption of iron
  - source of **IGF-I** that controls action of growth hormone
- **kidneys**
  - converts calcidiol to **calcitriol,** the active form of vitamin D
    - increases Ca^{2+} absorption by intestine and inhibits loss in the urine
  - secrete **renin** that converts angiotensinogen to angiotensin I
    - angiotensin II created by converting enzyme in lungs
      - constricts blood vessels and raises blood pressure
  - produces 85% of **erythropoietin** –
    - stimulates bone marrow to produce RBCs

Endocrine Functions of Other Organs

- **heart**
  - cardiac muscle secretes **atrial natriuretic peptide (ANP)** in response to an increase in blood pressure
  - decreases blood volume and blood pressure by increasing Na^+ and H_2O output by kidneys
  - opposes action of angiotensin II
- **stomach and small intestine** secrete at least ten hormones
  - coordinate digestive motility and glandular secretion
  - cholecystokinin, gastrin, Ghrelin, and peptide YY
- ...and many others.

Hormone Chemistry

- three chemical classes
  - **steroids**
    - derived from cholesterol
    - secreted by gonads and adrenal glands
    - estrogens, progesterone, testosterone, cortisol, corticosterone, aldosterone, DHEA, and calcitriol
  - **peptides and glycoproteins**
    - created from chains of amino acids
    - secreted by pituitary and hypothalamus
    - oxytocin, antidiuretic hormone, releasing and inhibiting hormones, and anterior pituitary hormones
  - **monoamines (biogenic amines)**
    - derived from amino acids
    - secreted by adrenal, pineal, and thyroid glands
    - epinephrine, norepinephrine, melatonin, and thyroid hormone
- all hormones are made from either **cholesterol** or **amino acids** with carbohydrate added to make glycoproteins.

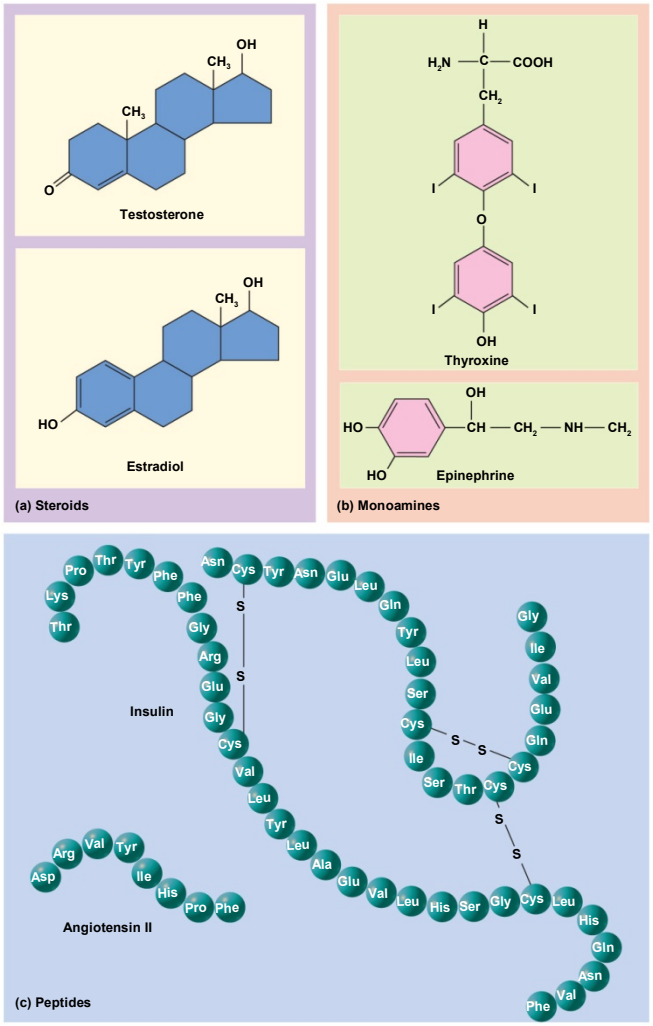


Figure 17.14 a-c

Hormone Synthesis: Steroid Hormones

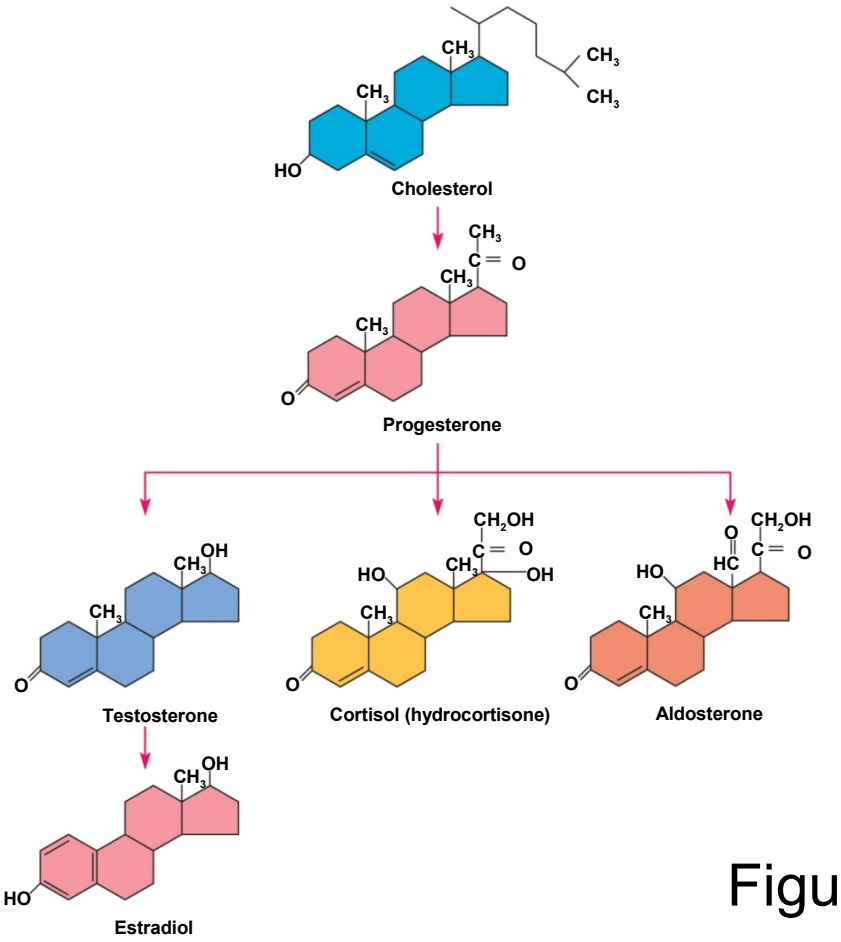


Figure 17.16

- synthesized from cholesterol – differs in functional groups attached to 4-ringed steroid backbone

Peptides

- synthesized in same way as any protein
- at first is an inactive **preprohormone**
- first several amino acids is a signal peptide that guides it into cisterna of rough endoplasmic reticulum
- signal peptide removed to form **prohormone**
- Golgi does final transformation to **hormone** packaged for secretion

Hormone Synthesis: Insulin

- begins as **preproinsulin**, then becomes **proinsulin**
- when **connecting peptide** is removed, two polypeptide chains are formed that make up insulin

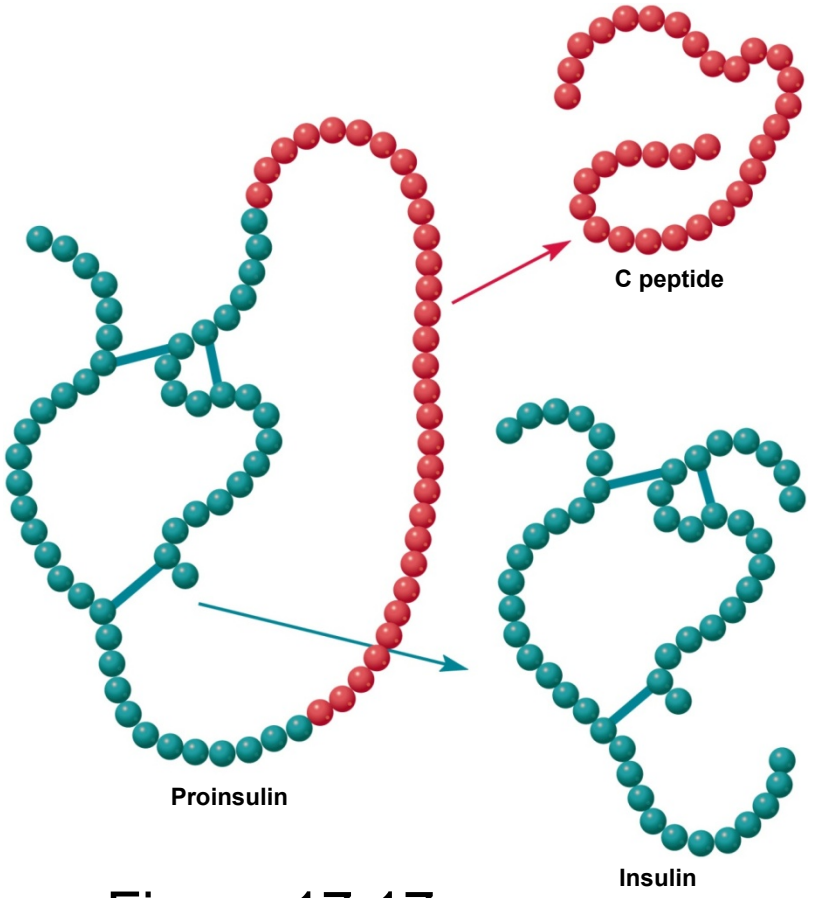
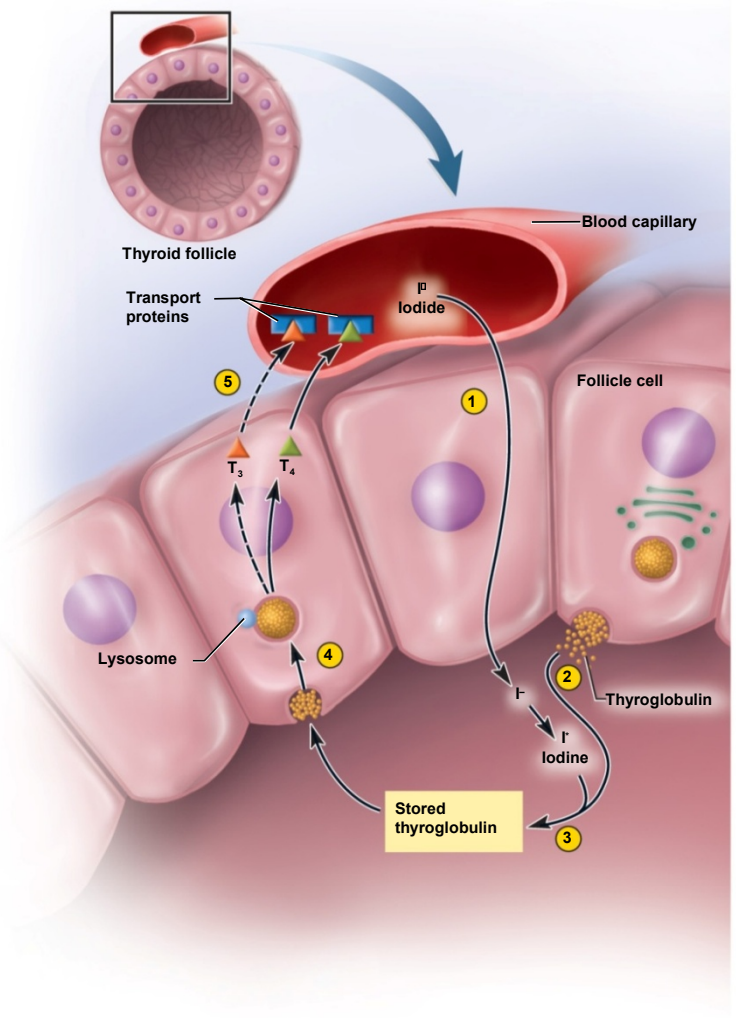


Figure 17.17

Monoamines

- **melatonin** is synthesized from amino acid **tryptophan**, and **other monoamines** from amino acid **tyrosine**
  - **thyroid hormone** is composed of 2 tyrosines

Thyroid Hormone Synthesis



1. Iodide absorption and oxidation
2. Thyroglobulin synthesis and secretion
3. Iodine added to tyrosines of thyroglobulin
4. Thyroglobulin uptake and hydrolysis
5. Release of T_4 and a small amount of T_3 into the blood

Figure 17.18

T_3 and T_4 Synthesis

- **follicular cells**
  - absorb **iodide** (I^-) **ions** from blood and store in lumen as a reactive form of iodine
  - synthesize **thyroglobulin** and store in lumen
    - forms colloid
    - contains lots of tyrosine
  - tyrosine and iodine combine to form thyroxine (T_4) bound to thyroglobulin
  - stored in follicle
- **TSH**
  - stimulates follicular cells to remove T_4 from thyroglobulin for release into plasma
  - most T_3 is produced in liver or by target cells removing an iodine from circulating T_4
  - 95% T_4 and 5% T_3

Hormone Receptors

- hormones stimulate only those cells that have receptors for them
- **receptors** are protein or glycoprotein molecules:
  - on plasma membrane, in the cytoplasm, or in the nucleus
- **receptors** act like switches turning on metabolic pathways when hormone binds to them
- usually each target cell has a few thousand receptors for a given hormone
- receptor-hormone interactions exhibit **specificity** and **saturation**
  - specific receptor for each hormone
  - saturated when all receptor molecules are occupied by hormone molecules

Hormone Mode of Action

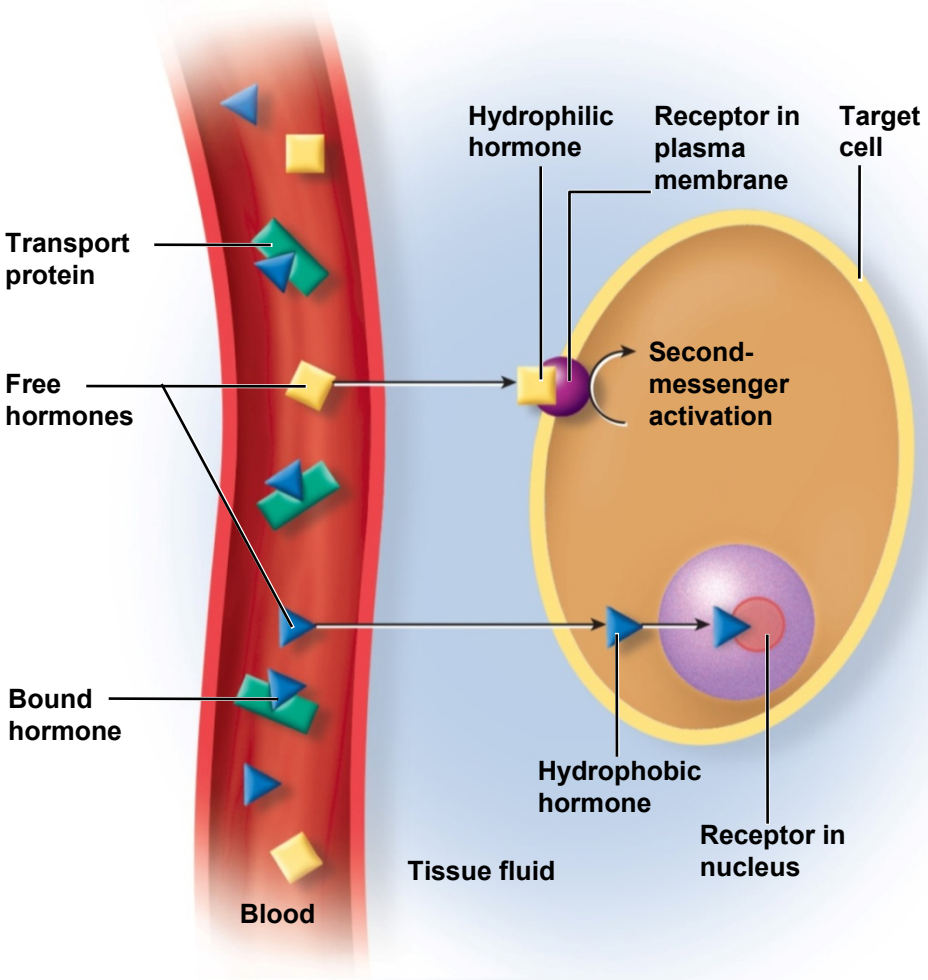


Figure 17.20

hydrophobic hormones

- penetrate plasma membrane and enter nucleus
- act directly on the genes changing target cell physiology
- estrogen, progesterone, thyroid hormone act on nuclear receptors
- take several hours to days to show effect due to lag for protein synthesis

hydrophilic hormones

- cannot penetrate into target cell
- must stimulate physiology indirectly

Thyroid Hormone

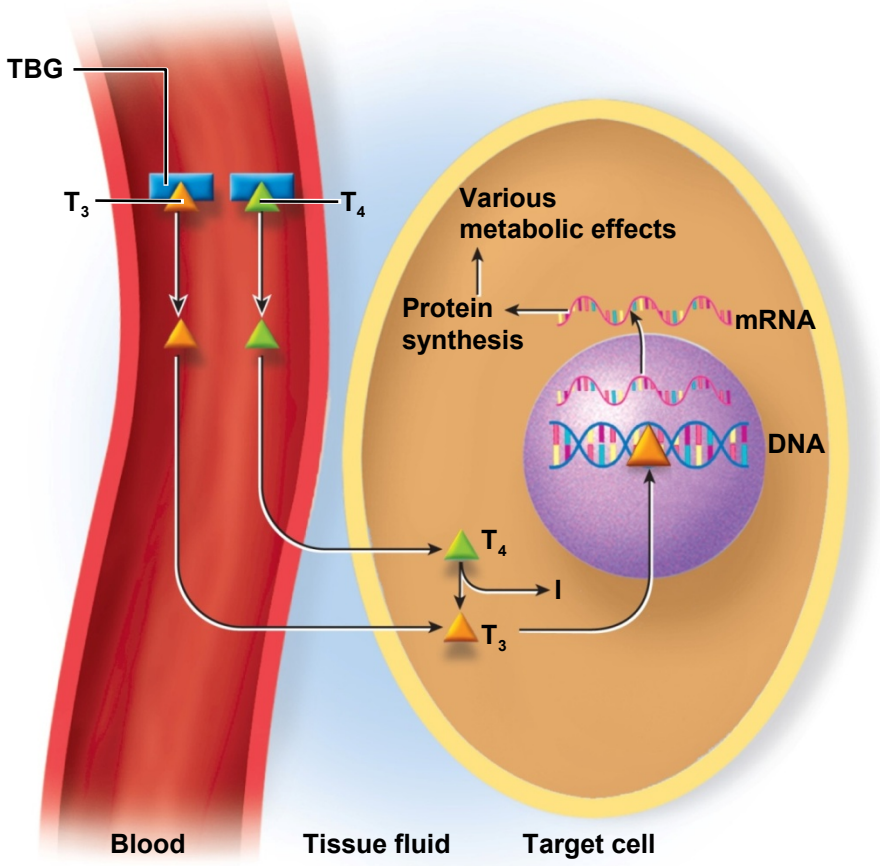
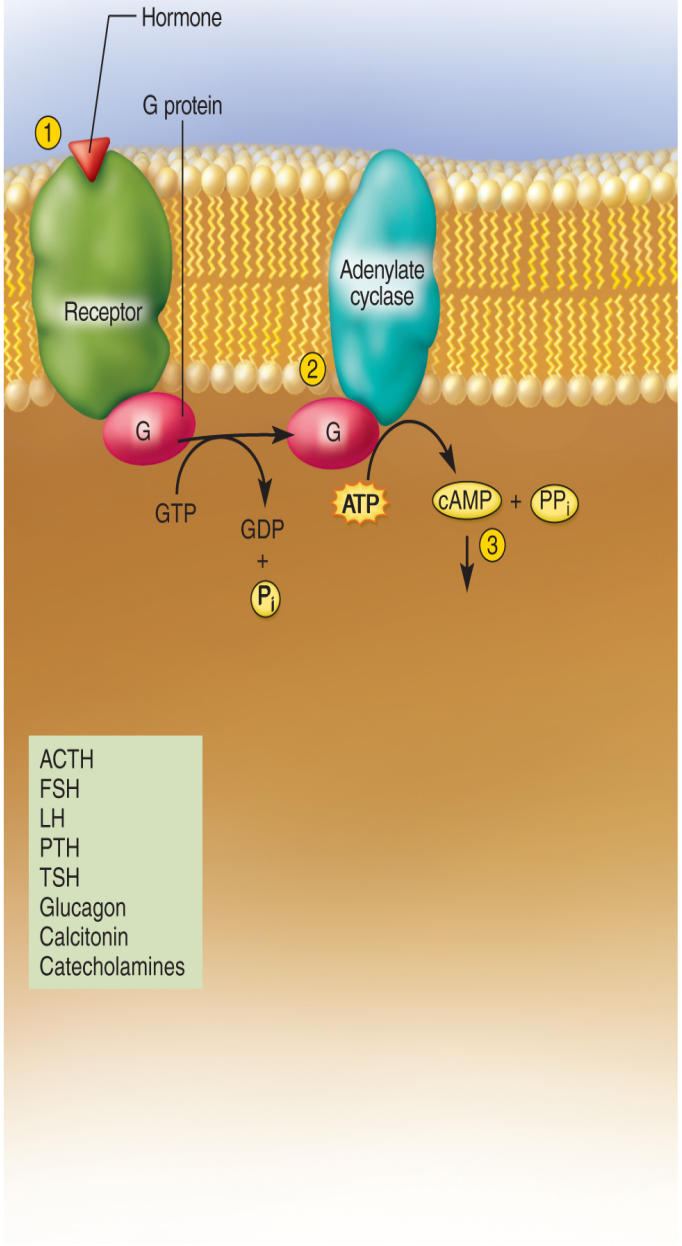


Figure 17.21

- thyroid hormone enters target cell by diffusion – mostly as T_4 with little metabolic effect
- within target cell, T_4 is converted to more potent T_3
- T_3 enters target cells and binds to receptors in chromatin
- activates genes
  - make a muscle protein (myosin) enhancing cardiac muscle response to sympathetic stimulation
  - strengthening heartbeat

Peptides and Catecholamines: Hydrophilic

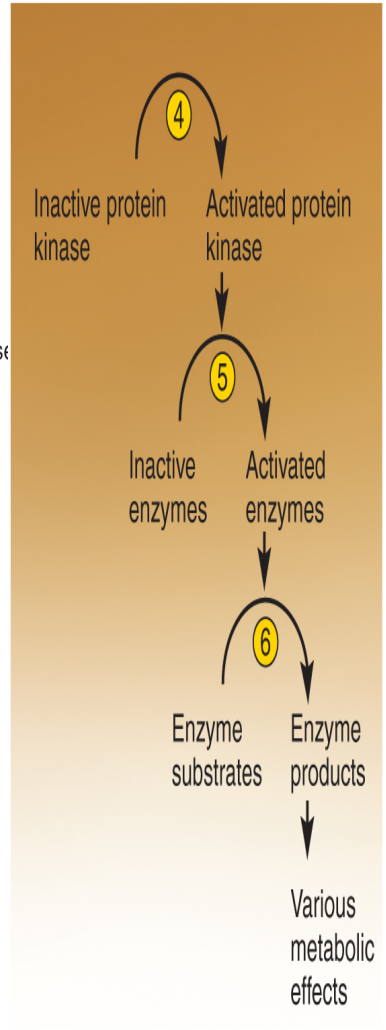
- hormone binds to cell-surface receptor
- receptor linked to second messenger system on other side of the membrane
- activates G protein which
- activates adenylate cyclase
- produces cAMP
- activates or inhibits enzymes
- metabolic reactions:
  - synthesis
  - secretion
  - change membrane potentials



1 Hormone–receptor binding activates a G protein.

2 G protein activates adenylate cyclase

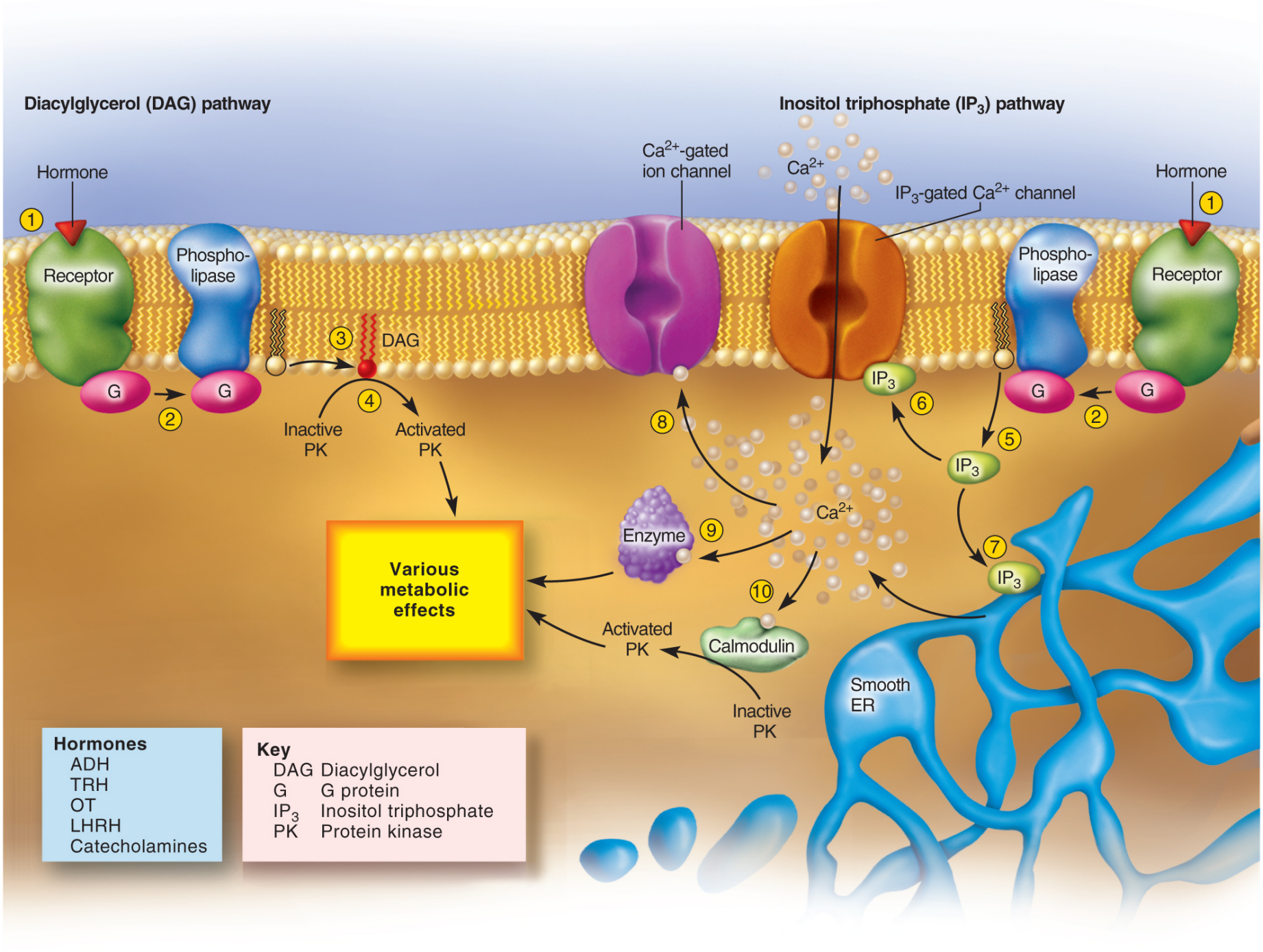
3 Adenylate cyclase produces cAMP.



4 cAMP activates protein kinases.

5 Protein kinases phosphorylate enzymes. This activates some enzymes and deactivates others.

6 Activated enzymes catalyze metabolic reactions with a wide range of possible effects on the cell.



Enzyme Amplification

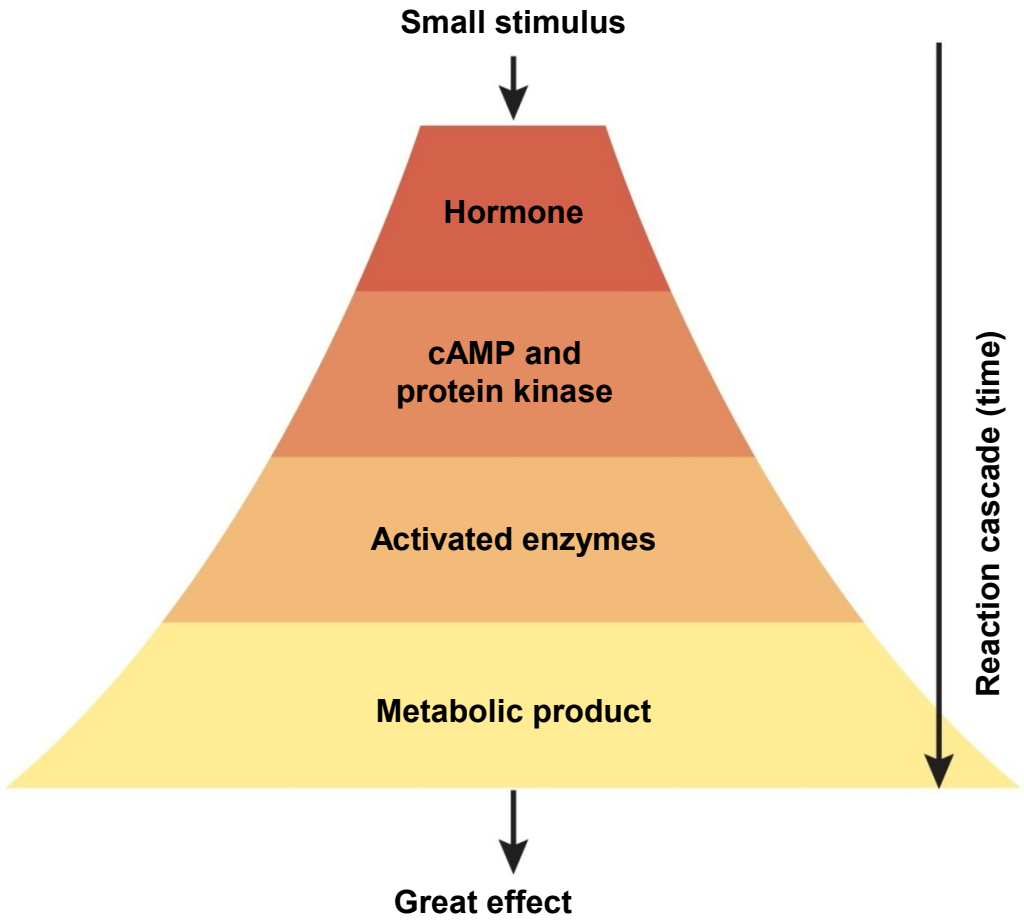
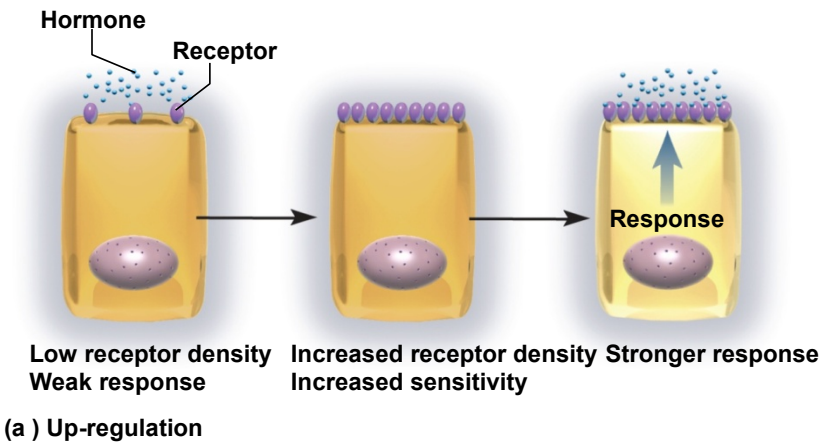


Figure 17.24

- hormones are extraordinarily potent chemicals
- one hormone molecule can trigger the synthesis of many enzyme molecules.
- very small stimulus can produce very large effect
- circulating concentrations very low

Modulation of Target Cell Sensitivity



- target cell sensitivity adjusted by changing the number of receptors
- **up-regulation** means number of receptors is increased
  - sensitivity is increased
- **down-regulation** reduces number of receptors
  - cell less sensitive to hormone
  - happens with long-term exposure to high hormone concentrations

Figure 17.25

Hormone Interactions

- most cells sensitive to more than one hormone and exhibit interactive effects
- **synergistic effects**
  - multiple hormones act together for greater effect
    - synergism between FSH and testosterone on sperm production
- **permissive effects**
  - one hormone enhances the target organ's response to a second later hormone
    - estrogen prepares uterus for action of progesterone
- **antagonistic effects**
  - one hormone opposes the action of another
    - insulin lowers blood glucose and glucagon raises it

Hormone Clearance

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

Endocrine Disorders

- **hyposecretion** – inadequate hormone release
- **hypersecretion** – excessive hormone release

Pituitary Disorders

- hypersecretion of growth hormone (GH)
  - **acromegaly** - thickening of bones and soft tissues in adults
    - especially hands, feet and face
  - problems in childhood or adolescence
    - **gigantism** if hypersecretion
    - pituitary **dwarfism** if hyposecretion – rare since growth hormone is now made by genetically engineered bacteria

Age 9 | Age 16 | Age 33 | Age 52

Figure 17.27 1-5

From *Clinical Pathological Conference Acromegaly, Diabetes, Hypermetabolism, Protein Use and Heart Failure* in American Journal of Medicine, 20:133, 1986. Copyright © 1986 by Excerpta Media, Inc.

Thyroid Gland Disorders

- **congenital hypothyroidism** (decreased TH)
  - hyposecretion present a birth
  - treat with oral thyroid hormone
- **myxedema** (decreased TH)
  - adult hypothyroidism
  - treat with oral thyroid hormone
- **goiter** – any pathological enlargement of the thyroid gland
  - **endemic goiter**
    - dietary iodine deficiency, no TH, no - feedback, increased TSH stimulates hypertrophy
  - **toxic goiter** (Graves disease)
    - autoantibodies mimic the effect of TSH on the thyroid causing hypersecretion
    - overgrown thyroid produces functional TH

Endemic Goiter

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Figure 17.28

Parathyroid Disorders

- **hypoparathyroidism**
  - surgical excision during thyroid surgery
  - fatal tetany in 3 - 4 days due to rapid decline in blood calcium level
- **hyperparathyroidism** - excess PTH secretion
  - parathyroid tumor
  - bones become soft, fragile, and deformed
  - Ca^{2+} and phosphate blood levels increase
  - promotes renal calculi formation

Adrenal Disorders

- **Cushing syndrome** - excess cortisol secretion
  - hyperglycemia, hypertension, weakness, edema
  - rapid muscle and bone loss due to protein catabolism
  - abnormal fat deposition

Diabetes Mellitus

- most prevalent metabolic disease in world
  - disruption of metabolism due to hyposecretion or inaction of insulin
  - symptoms:
    - **polyuria** (excess urine output), **polydipsia** (intense thirst) and **polyphagia** (hunger)
    - revealed by elevated blood glucose, glucose in urine and ketones in the urine

Types of Diabetes Mellitus

- **Type 1** (IDDM) – 5 to 10% of cases in US
  - **insulin** is always used to treat Type 1
    - insulin injections, insulin pump, or dry insulin inhaler
    - monitoring blood glucose levels and controlled diet
  - hereditary susceptibility if infected with certain viruses (rubella, cytomegalovirus)
  - autoantibodies attack and destroy pancreatic beta cells
- **Type 2** (NIDDM) – 90 to 95% of diabetics
  - problem is **insulin resistance**
    - failure of target cells to respond to insulin
  - risk factors are heredity, age (40+),obesity, and ethnicity – Native American, Hispanic, and Asian
  - treated with weight loss program and exercise
  - oral medications improve insulin secretion or target cell sensitivity

Pathology of Diabetes

- pathogenesis: cells cannot absorb glucose, must rely on fat and proteins for energy needs - weight loss and weakness
  - fat catabolism increases free fatty acids and ketones in blood
    - **ketonuria** irregular heartbeat, and neurological issues
    - **ketoacidosis** gasping breathing and diabetic coma
- chronic pathology (chronic hyperglycemia)
  - leads to neuropathy and cardiovascular damage from atherosclerosis and microvascular disease
    - arterial damage in retina and kidneys (common in type I), atherosclerosis leads to heart failure (common in type II)
    - **diabetic neuropathy** – nerve damage from impoverished blood flow can lead to erectile dysfunction, incontinence, poor wound healing, and loss of sensation from area