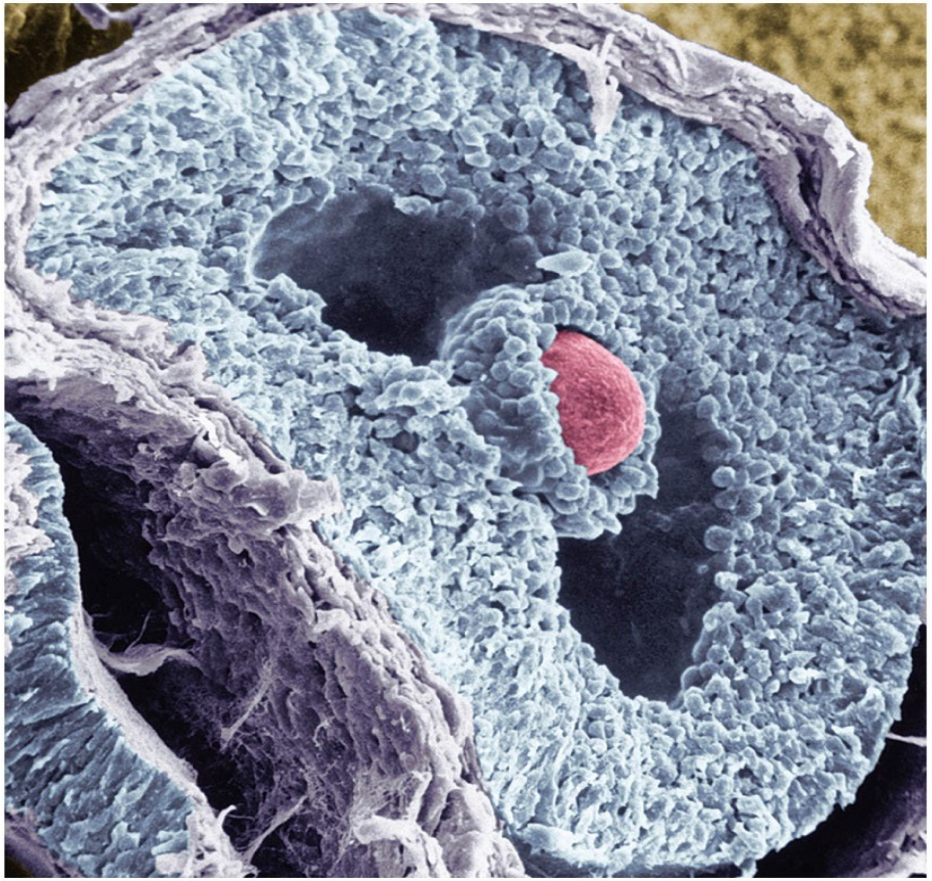
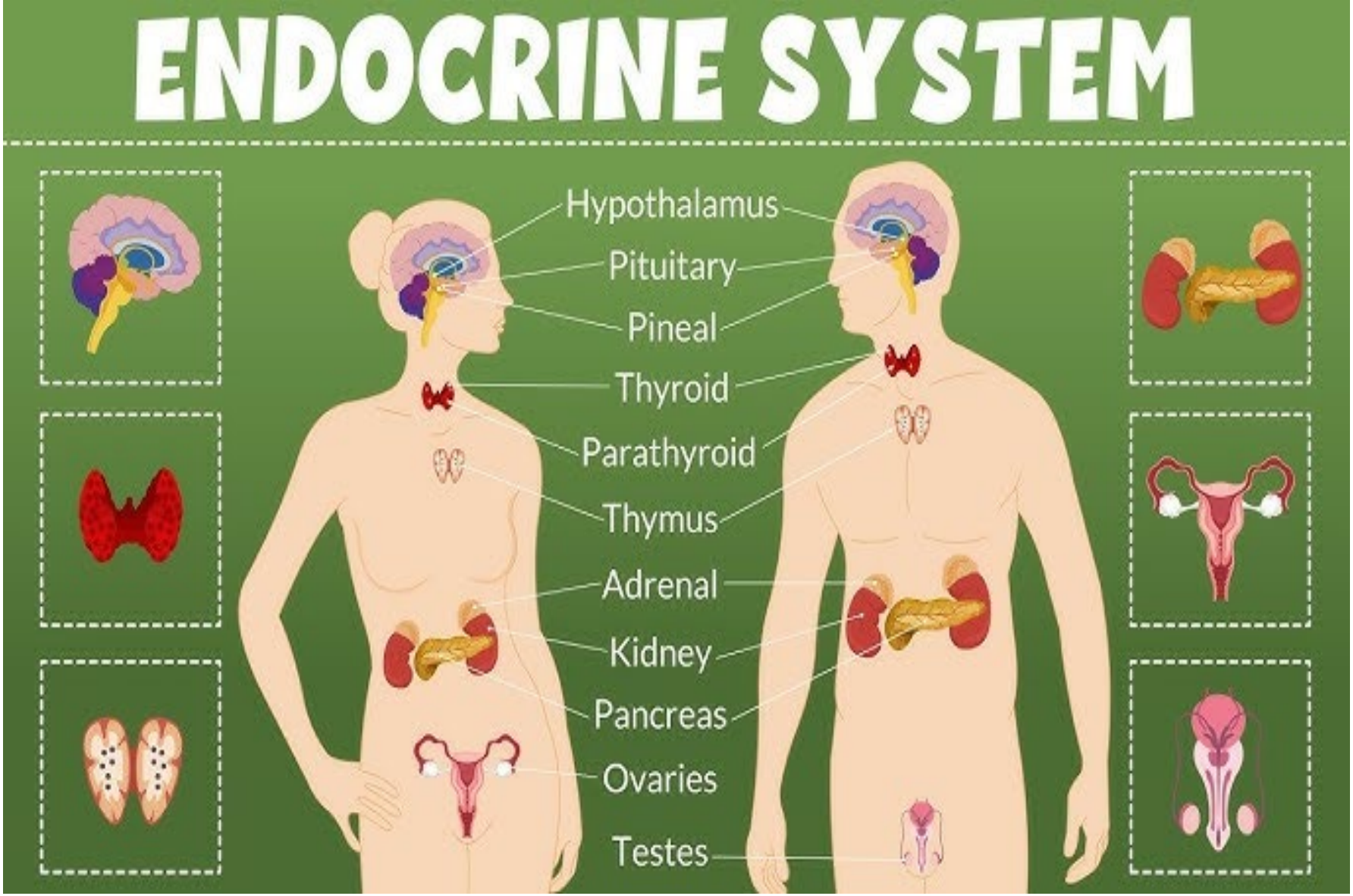
Chapter 17.2

Review of Endocrine Hormones
(Origin / Target Tissues / Effect)



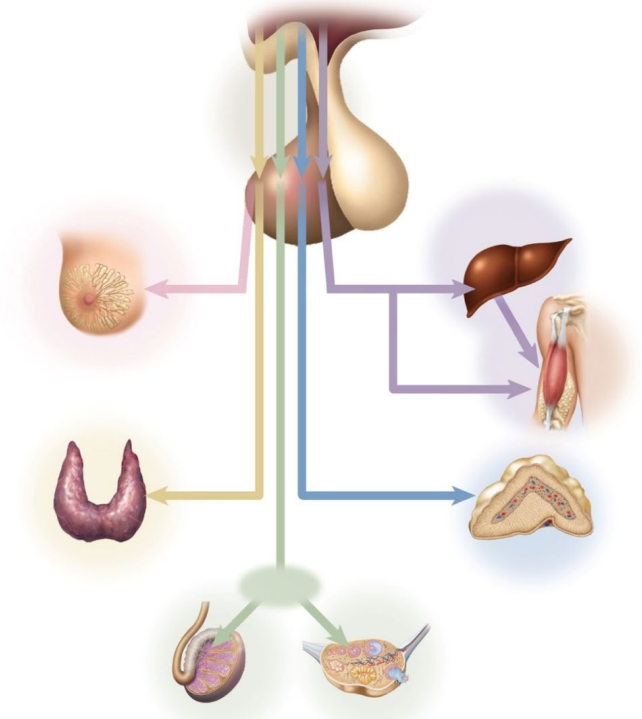


The endocrine system uses the blood to transport hormones to target tissues throughout the body. The target tissue has a receptor matched to the hormones. The metabolism of the target tissue is changed when the hormone docks to the receptor on the target tissue.

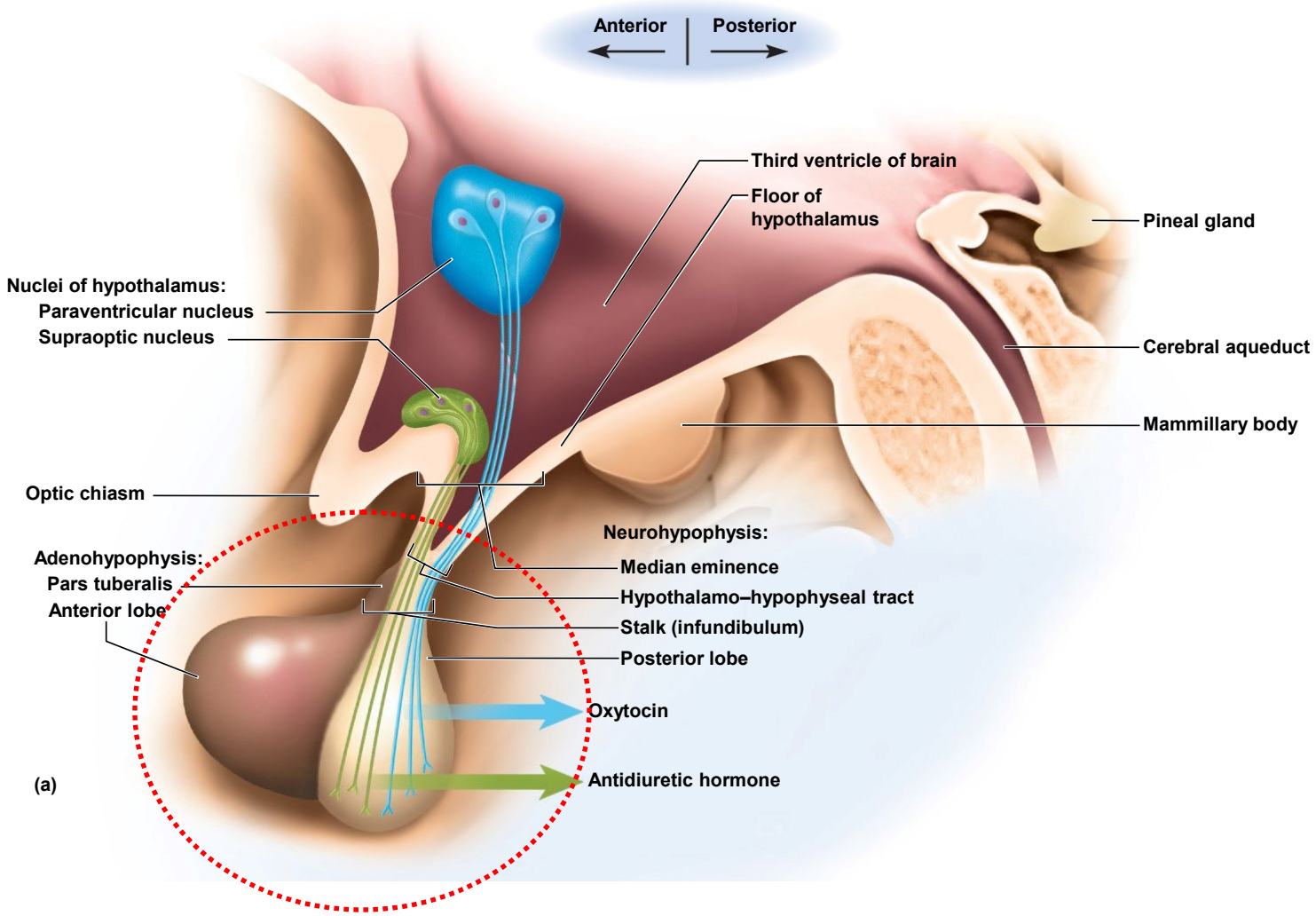
Why is the Pituitary Gland Called the *Master Endocrine Gland?*

Pituitary produces many hormones with target tissue located throughout the body.

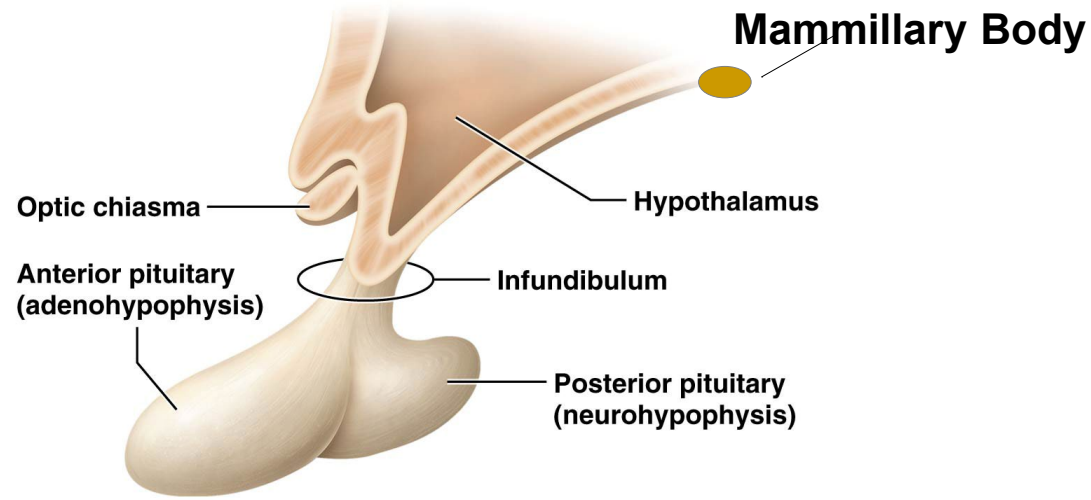
The pituitary hormones regulate the secretion of other endocrine glands located throughout the body.



Pituitary Gland is Called the Master Endocrine Gland



Structure of the hypothalamus and pituitary gland.



(b) Structure of hypothalamus, and anterior and posterior pituitary glands

Pituitary gland (also called the hypophysis) is suspended from the hypothalamus by a stalk of tissue called the infundibulum

Pituitary is in the sella turcica of sphenoid bone // size and shape of kidney bean

Pituitary composed of two histologically different tissues with independent origins and separate functions /// adenohypophysis (anterior pituitary) -- arises from hypophyseal pouch (outgrowth of pharynx / epithelial tissue) -- neurohypophysis (posterior pituitary) // downward growth from brain (nervous tissue)

Anatomy and Function of Hypothalamus

Shaped like a flattened funnel // area between opitic chiasma and mammillary bodies /// Forms floor and walls for the third ventricle of the brain

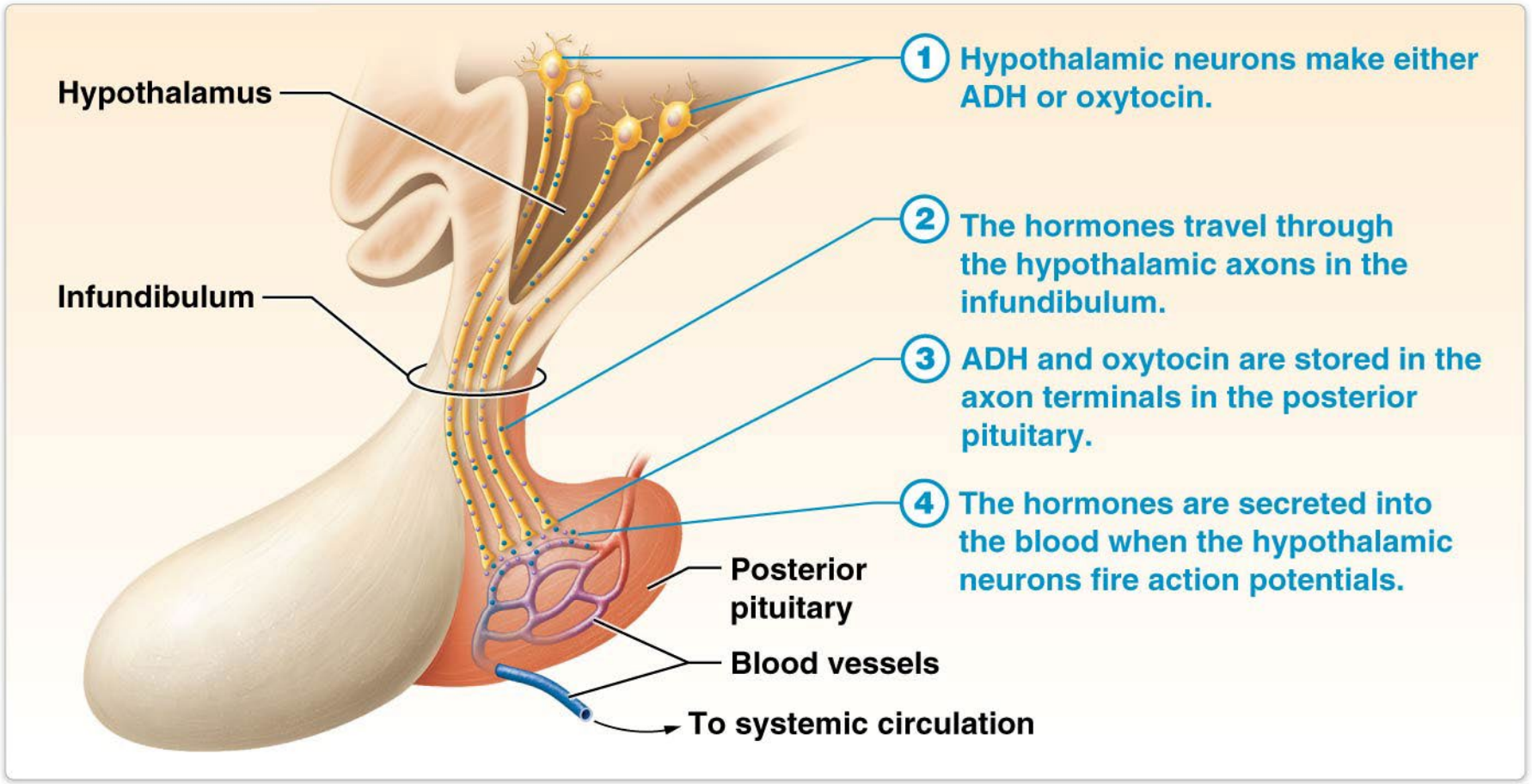
Regulates functions of the body that are more "advanced" than the "medulla oblongata" functions

Functions include water balance, thermoregulation, sexual cycles, childbirth // these functions are regulated by hormones secreted by the hypothalamus

Hormones released by the hypothalamus regulate the release of other hormones from the anterior pituitary gland into the blood

The hypothalamus hormones may inhibit or cause the release of the anterior pituitary hormones

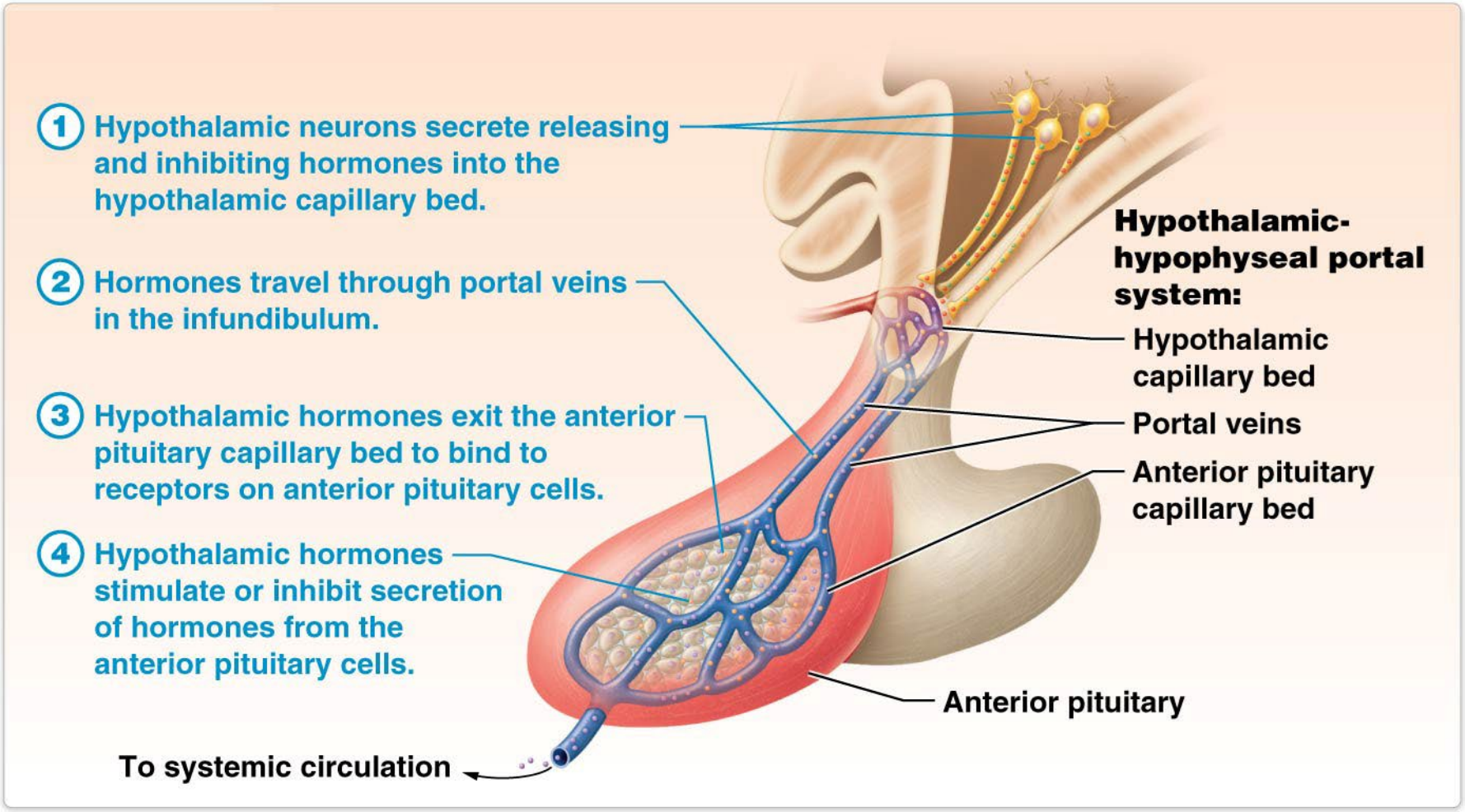
Structural relationships between the hypothalamus and posterior pituitary gland.



(a) Relationship between the hypothalamus and posterior pituitary

Hypothalamo–Hypophyseal Tract

Structural relationships between the hypothalamus and anterior pituitary gland.



(b) Relationship between the hypothalamus and anterior pituitary

Hypophyseal Portal System

Anterior and Posterior Pituitary
(Adenohypophysis & Neurohypophysis)

Adenohypophysis constitutes anterior three-quarters of pituitary

two segments // anterior lobe (pars distalis) and pars tuberalis
small mass of cells adhering to stalk

linked to hypothalamus by the hypophyseal portal system

- a portal system is two capillary beds between an artery and a vein.
- first capillary bed in hypothalamus connected to secondary capillary bed in adenohypophysis by portal venules
- hypothalamic hormones regulate metabolism of the adenohypophysis cells

Adenohypophysis & Neurohypophysis

Neurohypophysis constitutes the posterior one-quarter of the pituitary

has 3 parts /// median eminence, infundibulum, and the posterior lobe (pars nervosa) // nerve tissue /// not a typical glandular tissue

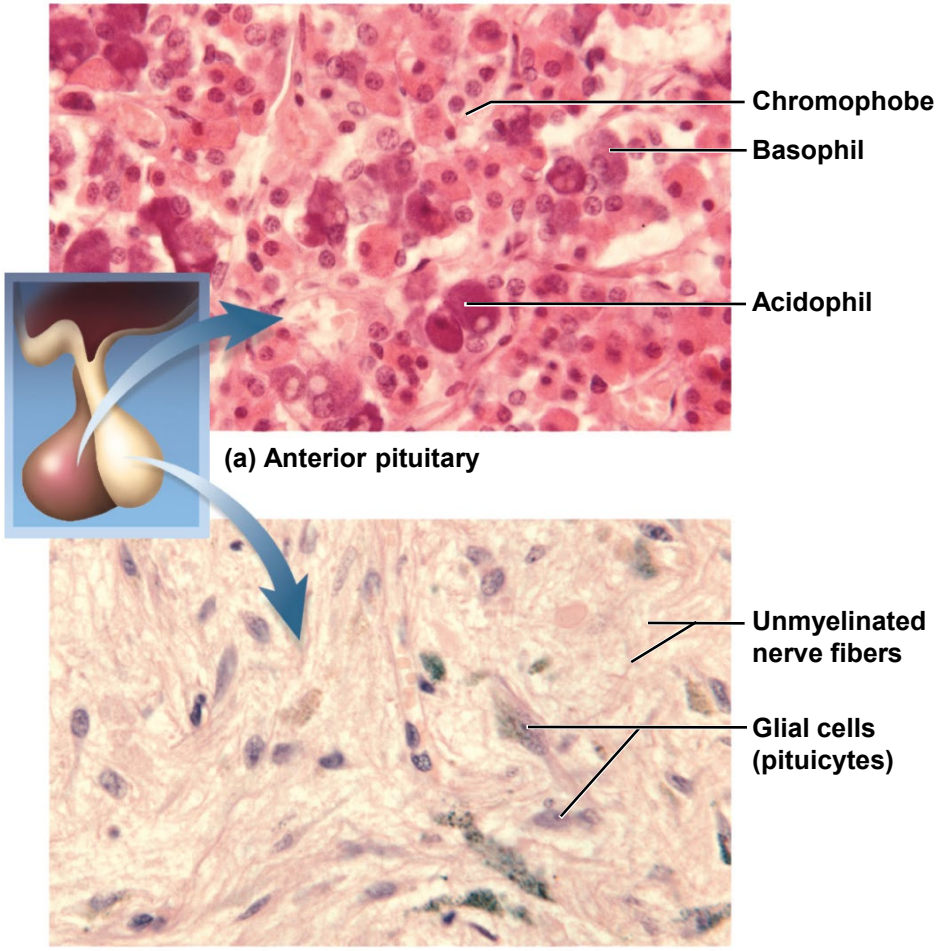
- The nerve soma is in hypothalamus, and its axon passes down the stalk as the hypothalamo-hypophyseal tract

- terminates in posterior lobe // hypothalamic neurons secrete hormones that are stored in neurohypophysis until the hormones are released into blood

Histology of Pituitary Gland

Epithelial tissue

Nervous tissue



Hypothalamic Hormones

Eight hormones are synthesized in the hypothalamus

Six of these hormones are delivered to the anterior pituitary // these hormones are called inhibiting or releasing hormones // they regulate the synthesis and release of other hormones from the anterior pituitary.

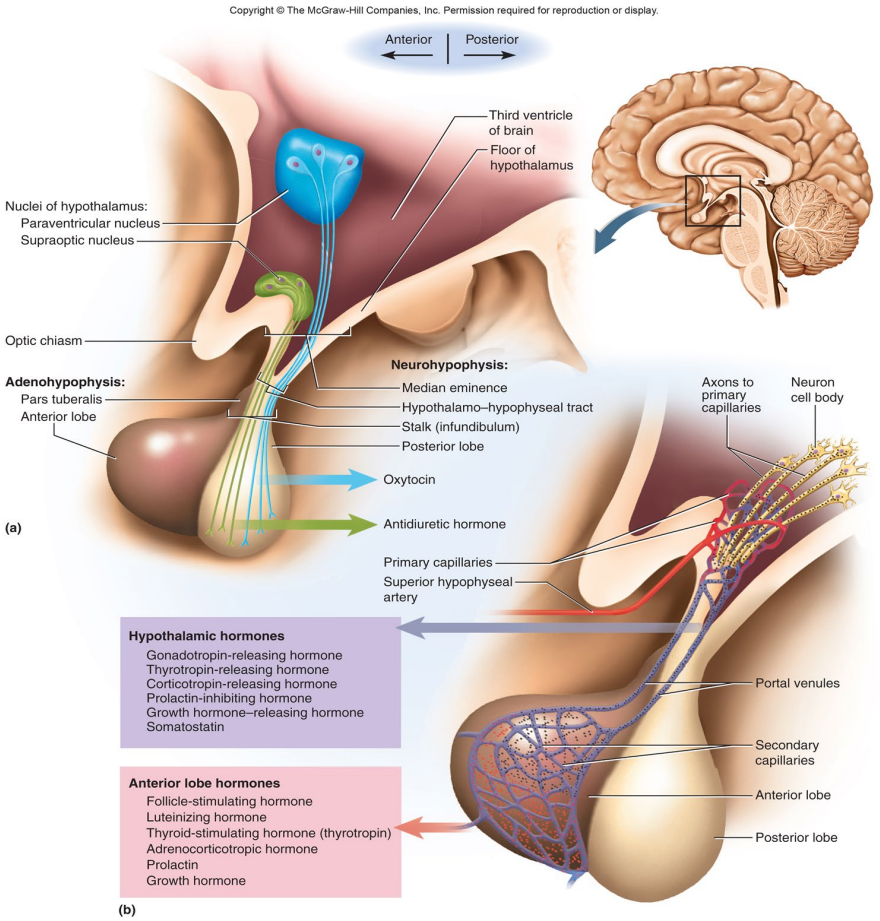
Two hormones are transported to the posterior pituitary and later released into the blood.

Hypothalamic Hormones

Six of the hypothalamic hormones either stimulate or inhibit the release of anterior pituitary hormones

> Thyroid Releasing Hormone (TRH) - TSH
> Corticotropin Releasing Hormone (CRH) - ACTH
> Gonadaltropin Releasing Hormone (GnRH) – FSH and LH
> Growth Hormone Releasing Hormone (GHRH) - GH
> Prolactin Inhibiting Hormone - inhibits secretion of prolactin
> Somatostatin inhibits secretion of growth hormone and thyroid stimulating hormone by the anterior pituitary

Posterior Pituitary Hormones



Oxytocin

Antidiuretic Hormone

Hypothalamic Hormones Released From the Posterior Pituitary Gland

Oxytocin (OT) & Antidiuretic Hormone (ADH)

These hormones are synthesized in hypothalamus, stored in posterior pituitary, and are released upon nerve signal from the hypothalamus

Right and left paraventricular nuclei produce oxytocin (OT)

Supraoptic nuclei produce antidiuretic hormone (ADH)

Posterior pituitary do not synthesize these hormones but only stores them for future use

Hypothalamic Hormones

ADH (antidiuretic hormone)

Increases water retention thus reducing urine volume and prevents dehydration

Also called vasopressin because it can cause vasoconstriction

Hypothalamic Hormones

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

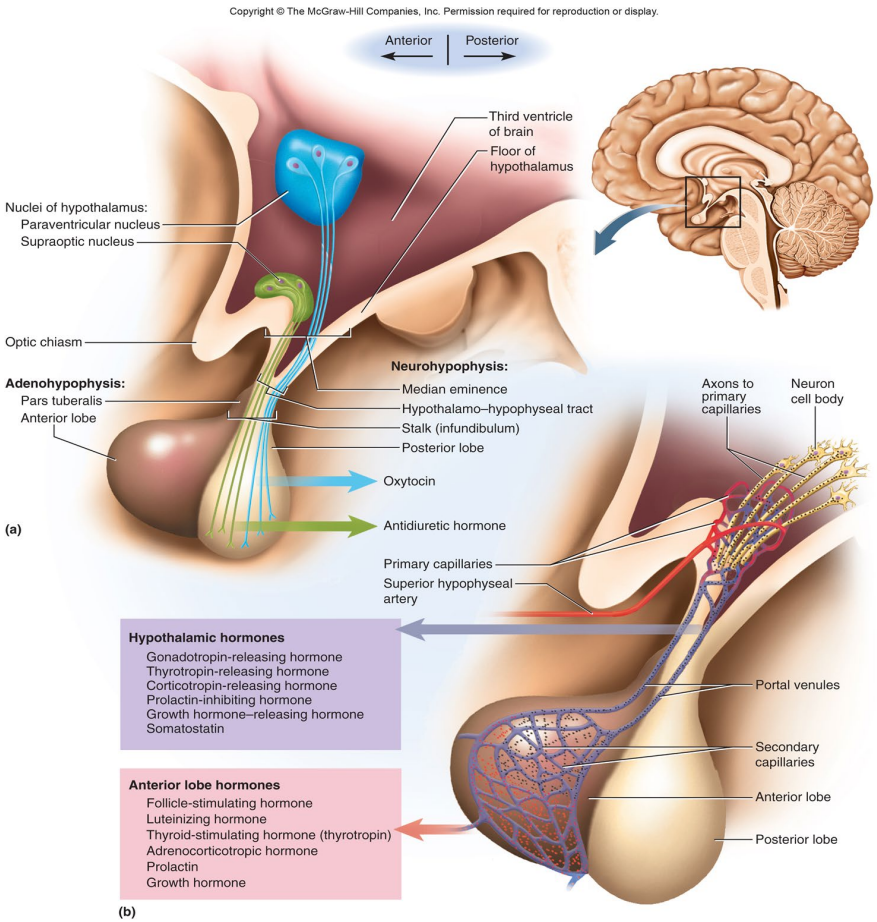
stimulates labor contractions during childbirth

stimulates flow of milk during lactation

promotes emotional bonding between lactating mother and infant (love hormone!)

Guess what happens to you and/or your pet when you "comfort your pet"!

Anterior Pituitary Hormones



Follicle stimulating hormone

Lutenizing hormone

Thyroid stimulating hormone

Adrenocoricotropic hormone

Prolactin

Growth hormone

What is the origin, target tissue, and action of these anterior pituitary hormones?

Anterior Pituitary Hormones

Two gonadotropin hormones target male and female gonadal tissues

FSH (follicle stimulating hormone) // in female stimulates ovaries to form follicles which secrete estrogen // in males FSH stimulate Sertolli cells in testes to produce androgen binging proteins necessary for sperm production

LH (luteinizing hormone) // in females stimulates ovulation resulting in formation of corpus luteum which then secretes progesterone necessary to maintain endometrium // in male targets testes interstitial cells to produce testosterone

Anterior Pituitary Hormones

TSH (thyroid stimulating hormone) // stimulates secretion of thyroid hormone // gas pedal of body // all cells in body have receptors for TSH

ACTH (adrenocorticotropic hormone) // stimulates adrenal cortex to secrete glucocorticoids (cortisol) // anti-inflammatory, reduce protein synthesis, gluconeogenisis

PRL (prolactin) // normally inhibited // after birth secreted and stimulates mammary glands to synthesize milk // believed to enhances secretion of testosterone by testes

GH (growth hormone) // stimulates mitosis and cellular differentiation // all cells in body have receptors for GH

About Growth Hormone

GH has widespread effects on various body tissues /// especially cartilage, bone, muscle, and fat

GH 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

Growth Hormone

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

Growth Hormone

GH Regulates:

GH has different effects in the short term and long term.

Protein synthesis increases -- boosts transcription of DNA, production of mRNA

Amino acid uptake into cells /// suppresses protein catabolism Protein-sparing effect
//

Lipid catabolism /// shifts metabolism towards fat catabolism by adipocytes – provides energy for growth // spares glucose metabolism

Initial increase than a decrease in blood glucose concentration

Growth Hormone

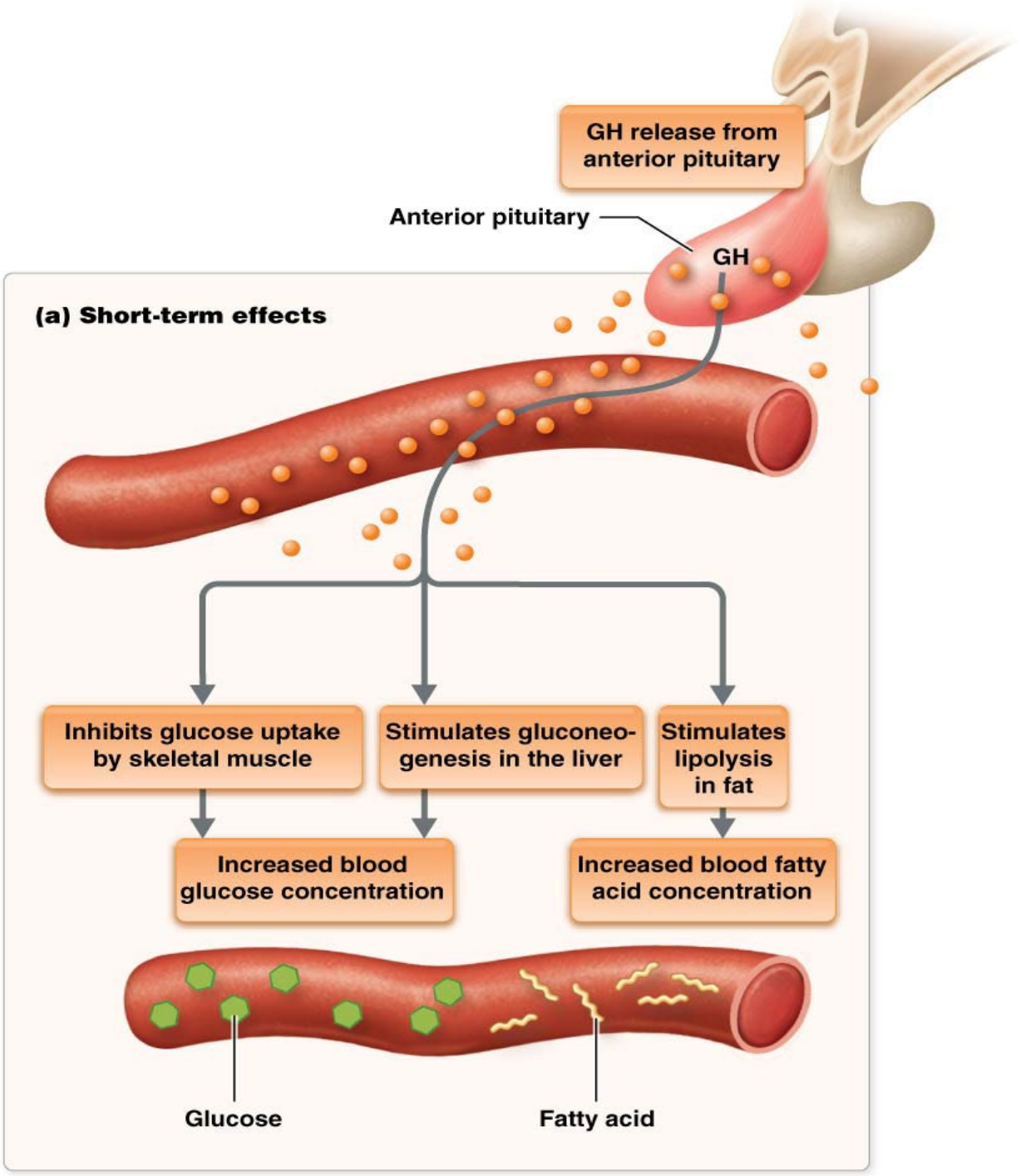
Carbohydrate metabolism – by mobilizing fatty acids for energy, GH functions as a glucose-sparing hormone // makes glucose available for brain energy source and/or glycogen synthesis and storage

Electrolyte balance – promotes Na^{+}, K^{+}, & Cl^{-} retention by kidneys, enhances Ca^{+2} absorption in intestine

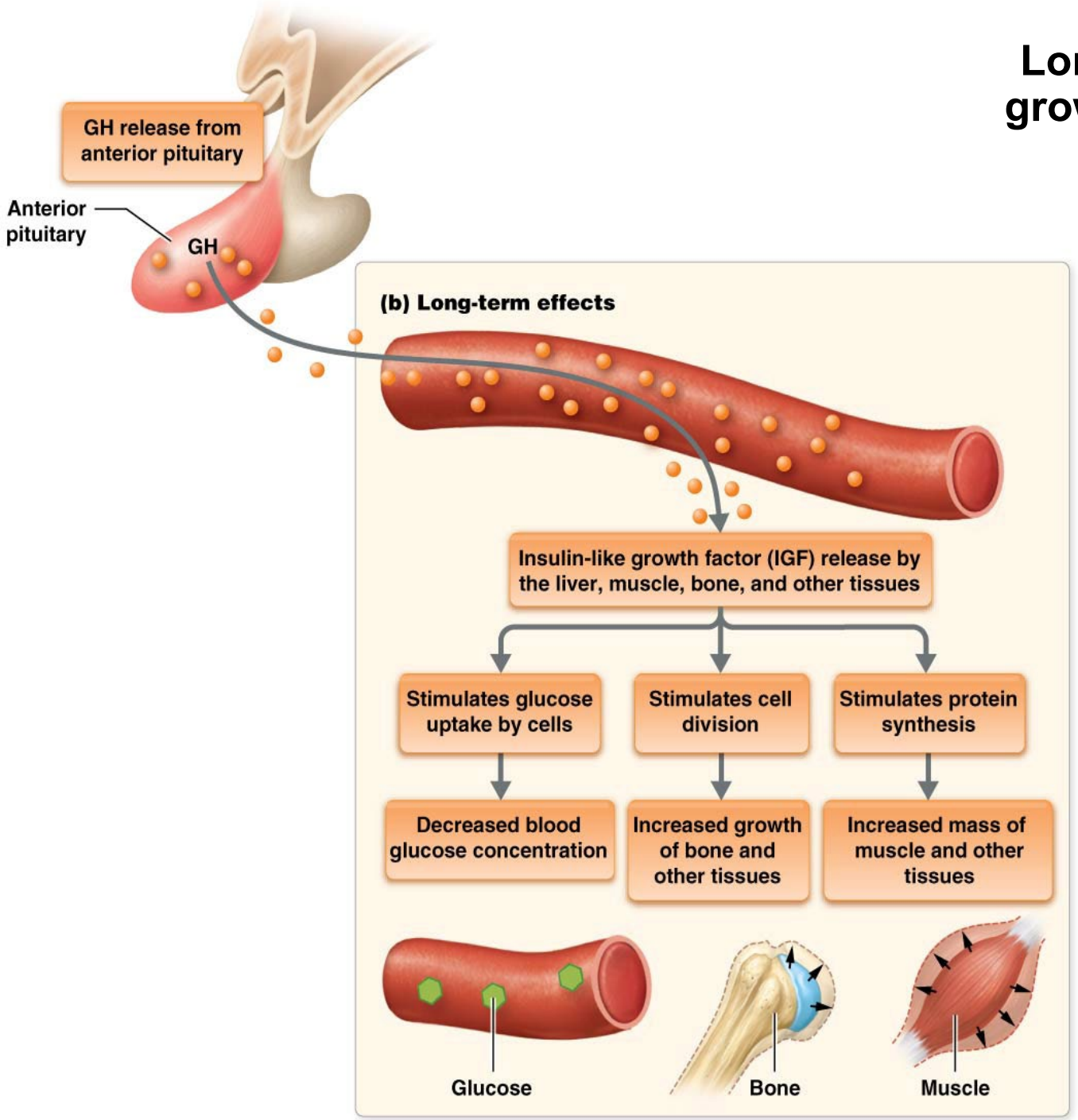
Bone growth - thickening and remodeling influenced, especially during childhood and adolescence

How will GH “reshape” appearance of body when GH taken as a supplement? (build muscle and burn fat so better definition of the muscle mass)

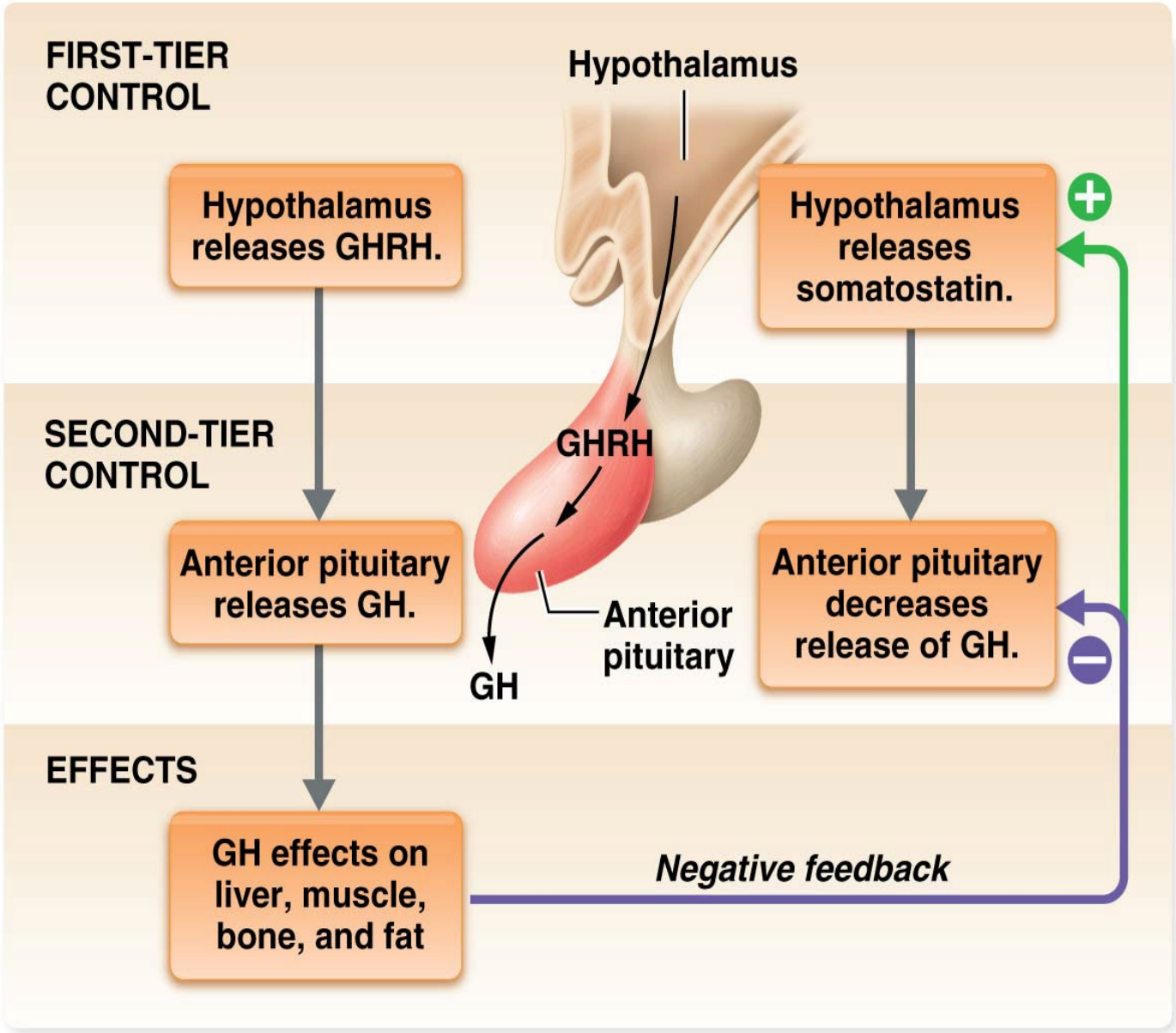
Short term effects of growth hormone (GH)



Long term effects of growth hormone (GH)



The regulation of growth hormone (GH) release.



Pituitary Growth Hormone Disorders

Hypersecretion of growth hormone (GH)

Late onset in adult = acromegaly - thickening of bones and soft tissues // especially in hands, feet and face

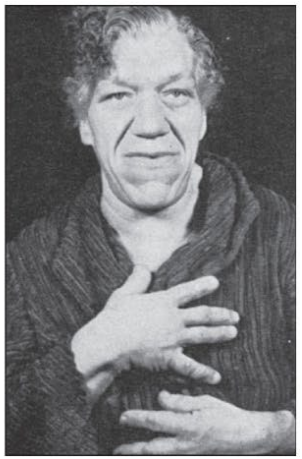
Early onset / childhood or adolescence = gigantism

Hyposecretion of GH // Pituitary dwarfism - rare today since growth hormone is now made by genetically engineered bacteria

Age 9

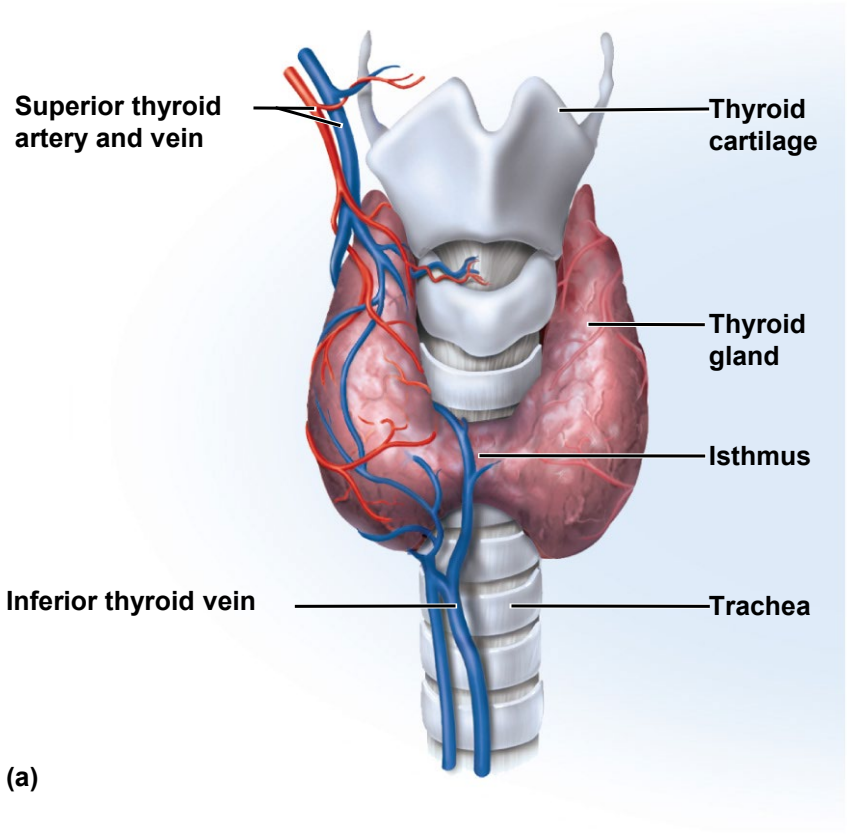
Age 16

Age 33



Age 52

Thyroid Gland Anatomy



Largest endocrine gland

composed of two lobes and an isthmus below the larynx

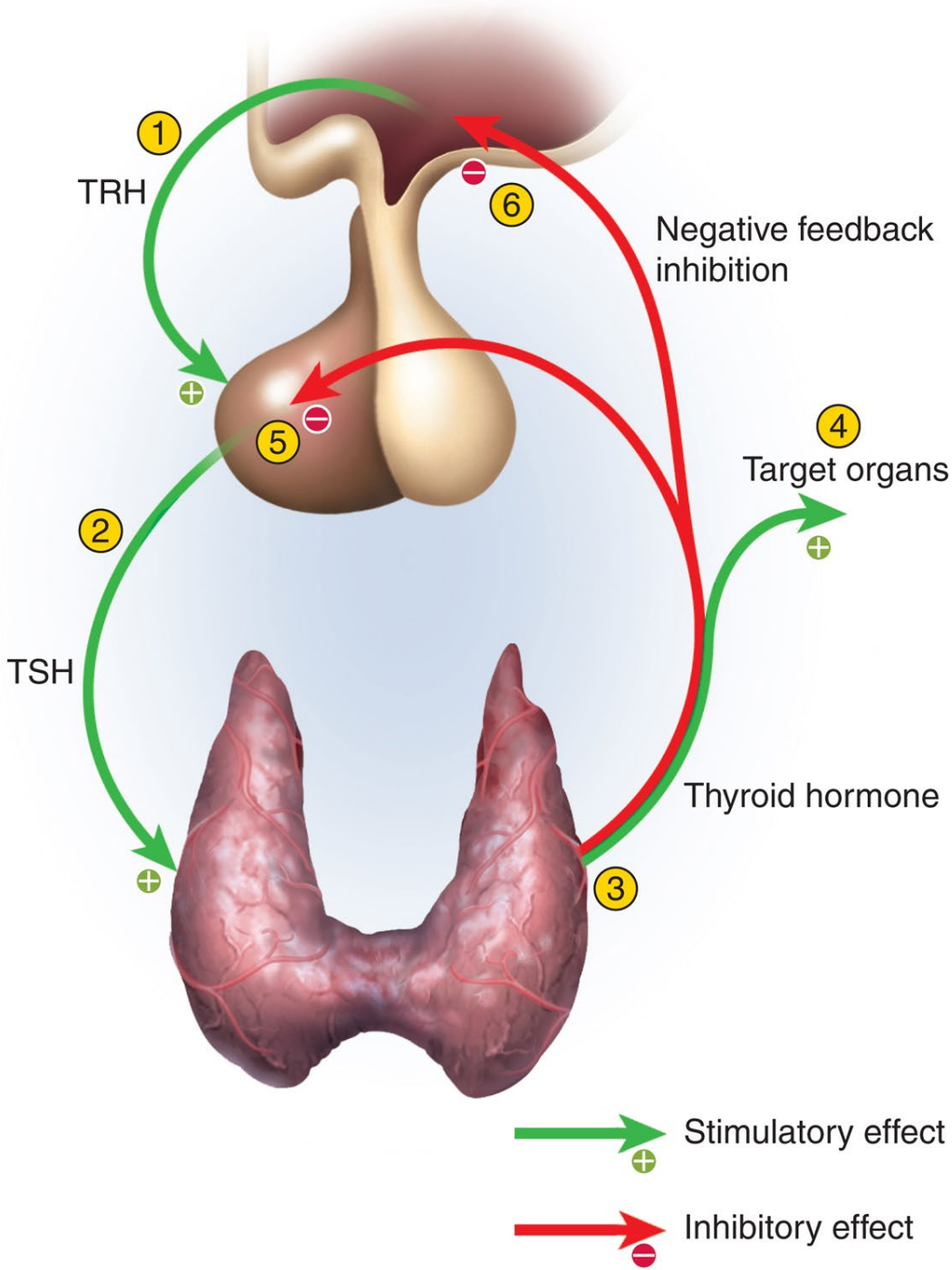
dark reddish-brown color due to rich blood supply

thyroid follicles – sacs that store most of thyroid // contain protein rich colloid

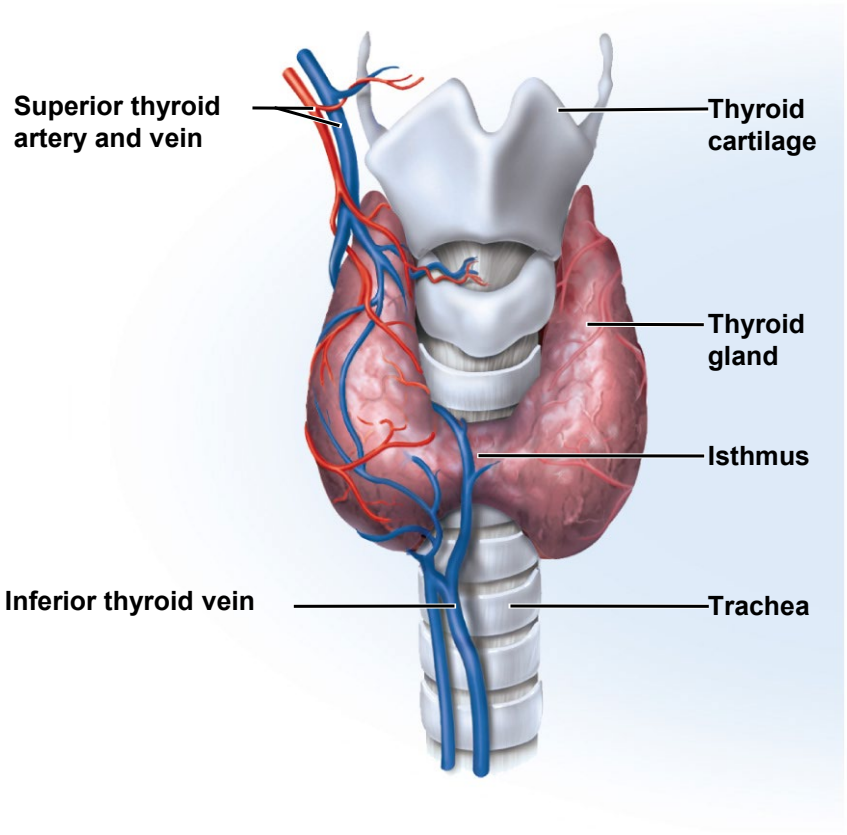
follicular cells – simple cuboidal epithelium that lines follicles

Three hormones secreted from this location (two different glands) // thyroid hormone and calcitonin from the thyroid gland and parathyroid hormone from the parathyroid gland.

Negative Feedback Mechanism to Regulate Thyroid Hormone



Thyroid Gland Hormone



Thyroid Hormone

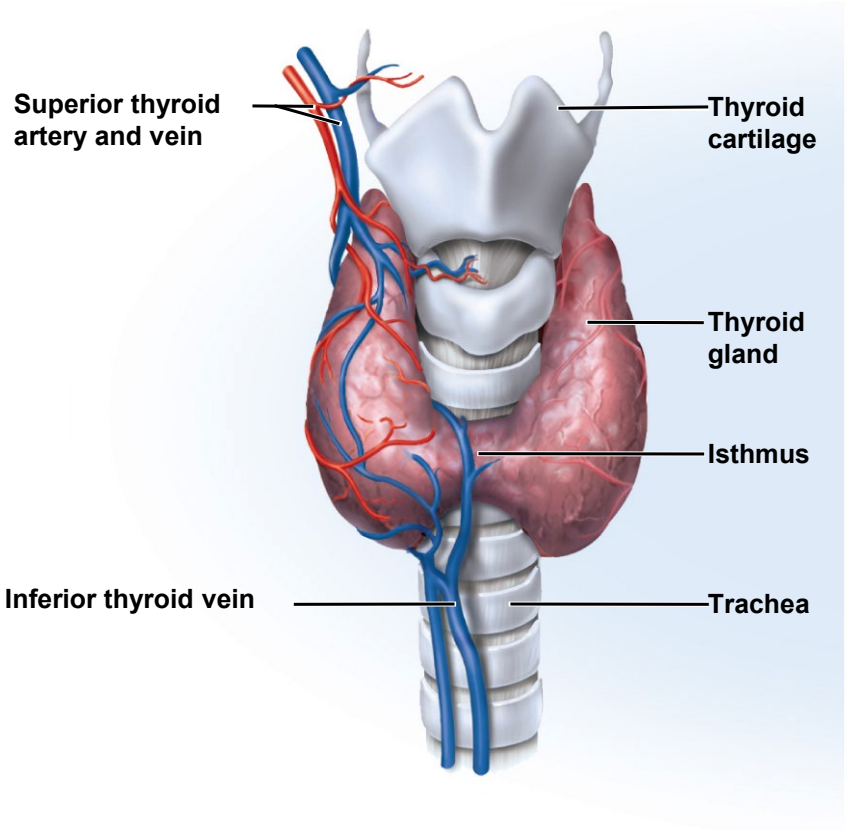
secretes **thyroxine** (T_4 because of 4 iodine atoms)

Secretes triiodothyronine (T_3) – (T_4 is converted to T_3) // T3 active hormone

All cells have receptors for T3

increases metabolic rate, O_2 consumption, heat production (**calorigenic effect**), increase appetite, growth hormone secretion, alertness and quicker reflexes

Thyroid Gland Hormone



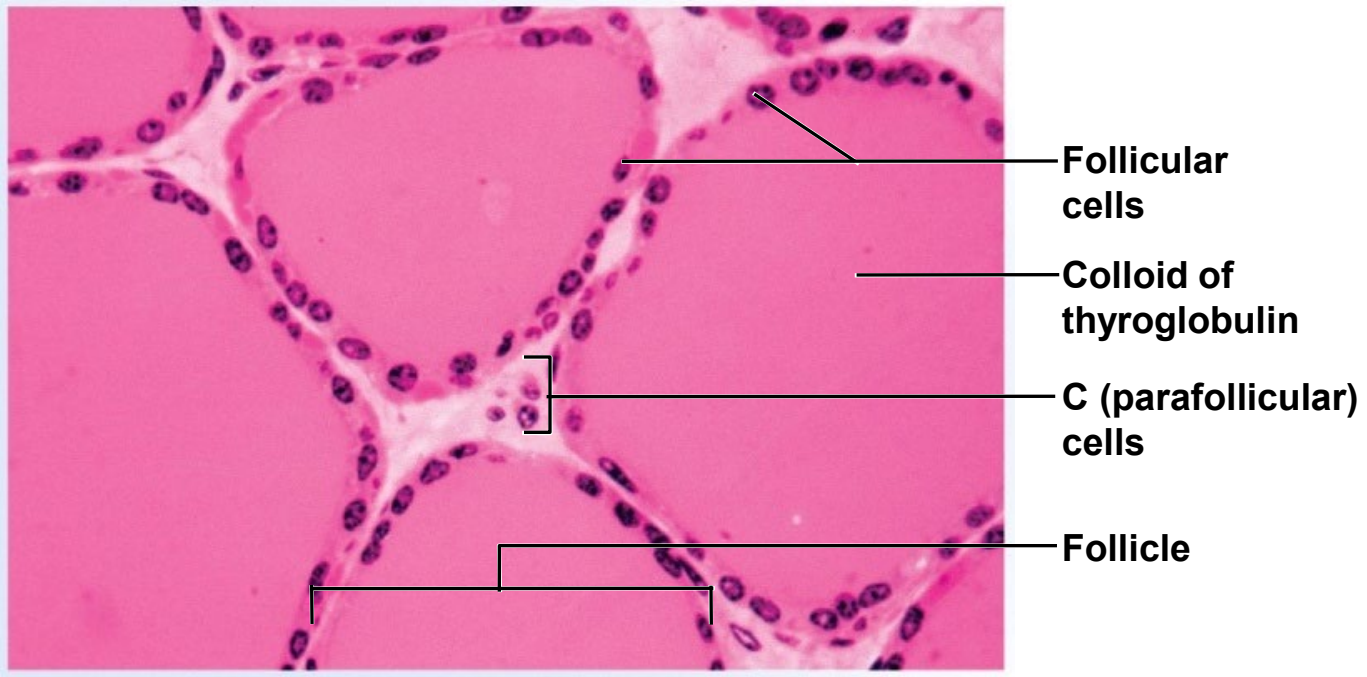
Calcitonin Hormone

parafollicular cells (C cells) secrete calcitonin

if blood calcium increases // stimulates bone growth so calcium moved from blood to make more bone matrix

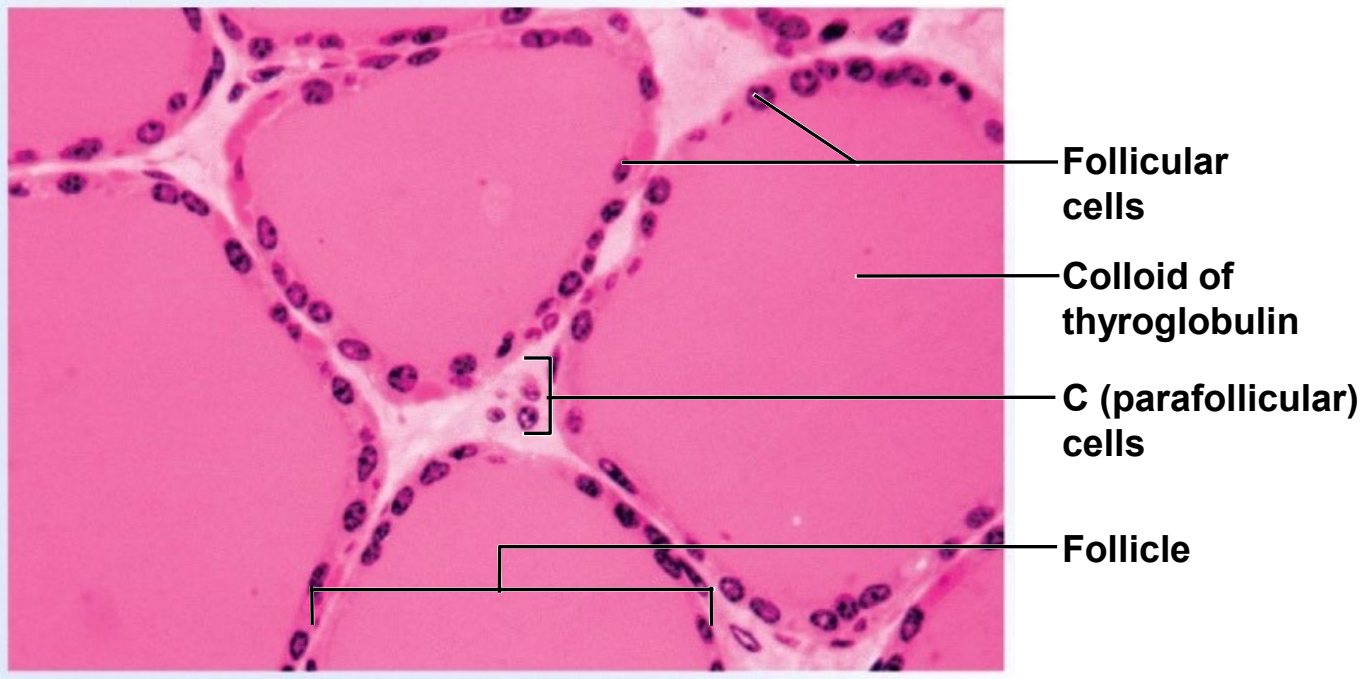
stimulates osteoblast activity and new bone formation

Histology of the Thyroid Gland



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

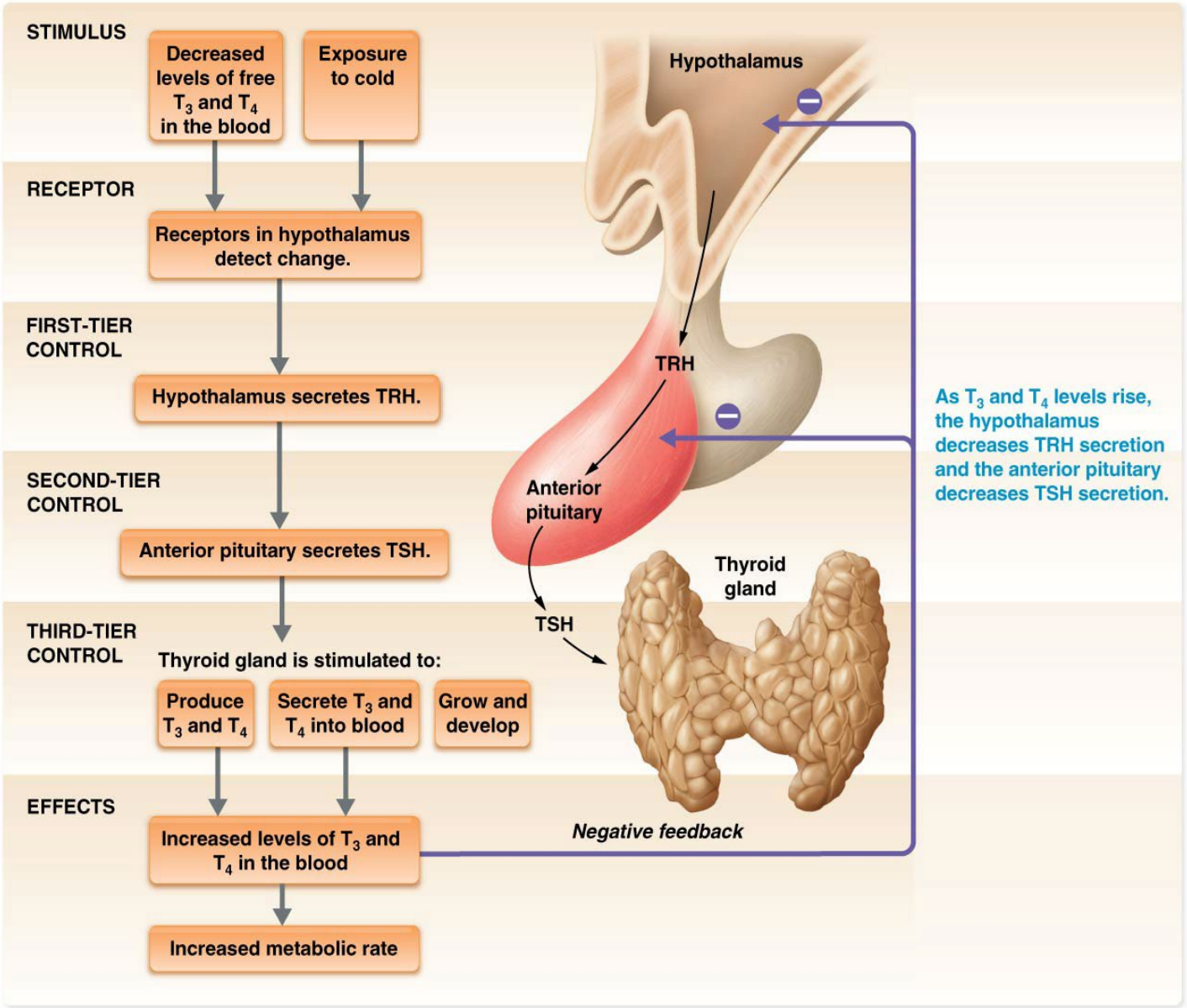
Calcitonin



C cells produce calcitonin when blood calcium levels are high.

Calcitonin reduces blood calcium levels by stimulating osteoblasts // use blood calcium to make new bone.

Maintaining homeostasis: regulation of thyroid hormone production by a negative feedback loop.



Hypo-Thyroidism Disorders

Congenital hypothyroidism (decreased TH)
–hypo-secretion present a birth (formerly called cretinism)
–If not treated results in cognitive disorders
–treat with oral thyroid hormone

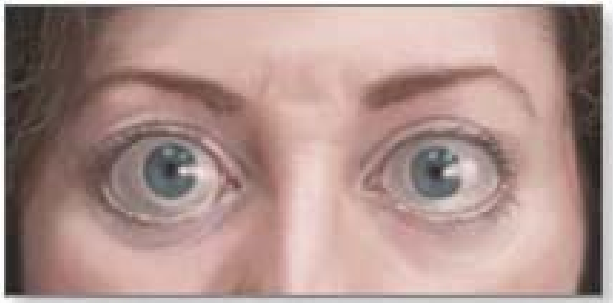
Myxedema (decreased TH)
–adult hypothyroidism
–treat with oral thyroid hormone

Before / After Treatment

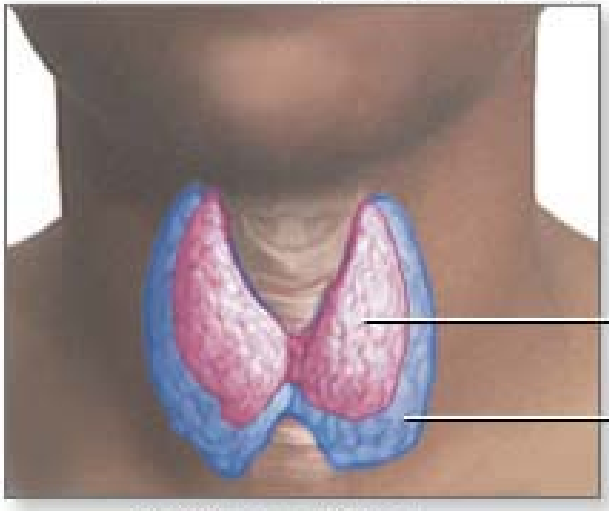
Myxedema: describes a specific form of cutaneous and dermal edema secondary to increased deposition of connective tissue components (like glycosaminoglycans, hyaluronic acid, and other mucopolysaccharides) in subcutaneous tissue as seen in various forms of hypothyrodism.

It is more common in women than in men.

Hyperthyroidism = Graves' Disease



Exophthalmos (bulging eyes)



Diffuse goiter

Graves' disease is a common cause of hyperthyroidism, an over-production of thyroid hormone, which causes enlargement of the thyroid and other symptoms such as exophthalmos, heat intolerance and anxiety

A.D.A.M.

Graves' ophthalmopathy (a protrusion of one or both eyes), caused by inflammation of the eye muscles by attacking auto-antibodies)

Goiter – A Thyroid Gland Disorder

Any pathological enlargement of the thyroid gland

–Endemic goiter

- Continued secretion of thyroid stimulating hormone, hypertrophy of thyroid gland
- Caused by dietary iodine deficiency
- Unable to produce TH
- Without TH / no negative feedback to stop TSH secretion

–**Toxic goiter** (Graves disease)

- auto-antibodies mimic the effect of TSH on the thyroid causing hyper-secretion
- overgrown thyroid produces functional TH

Endemic Goiter

Parathyroid Glands

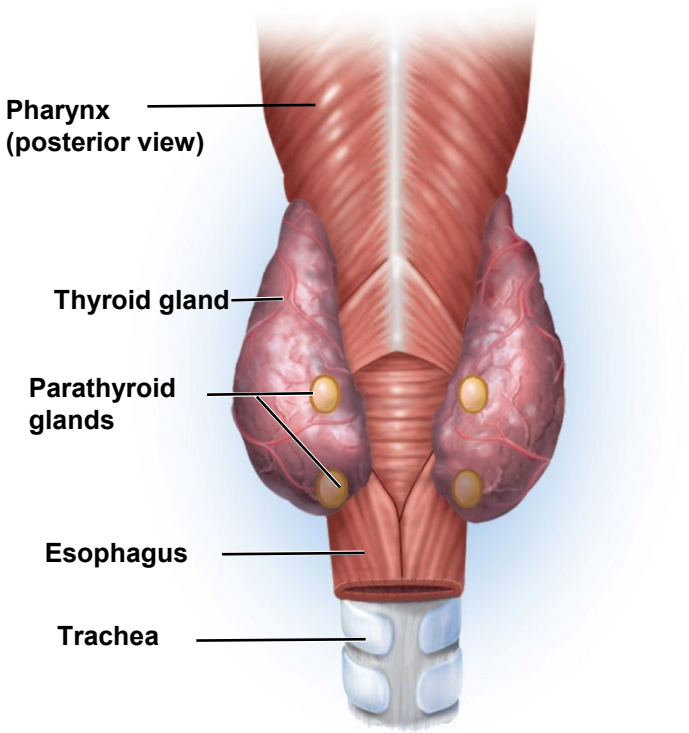
Four glands partially embedded in posterior surface of thyroid gland

Can be found from as high as hyoid bone to as low as aortic arch

Secretes parathyroid hormone when blood calcium is low

Stimulate osteoclast activity // breaks down bone matrix

increase Ca ions in blood

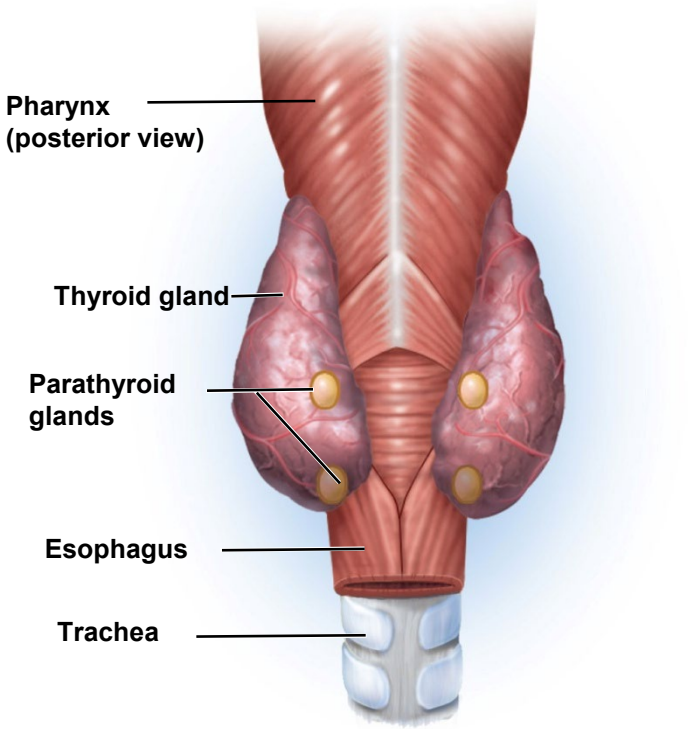


Parathyroid Hormone

Promotes synthesis of calcitriol (vitamin D) /// increases absorption of Ca^{2+}

Decreases urinary excretion

Increases bone resorption



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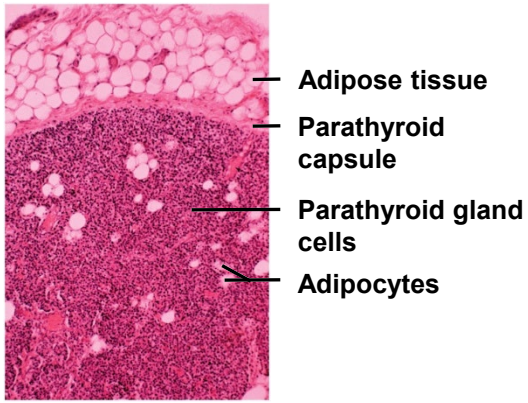
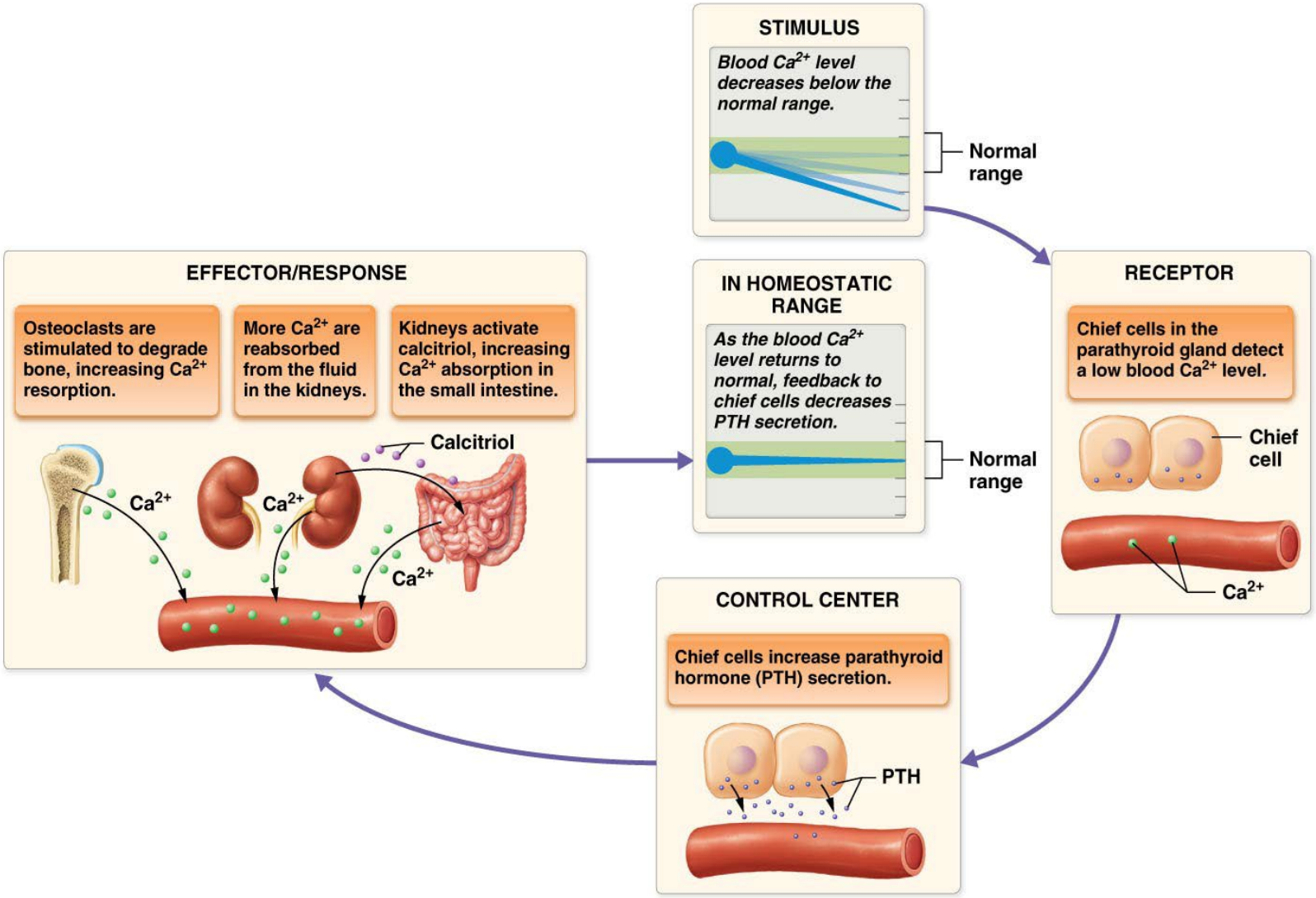


Maintaining Calcium Homeostasis
Parathyroid Hormone



Adrenal Cortex

Surrounds adrenal medulla and produces more than 25 steroid hormones called corticosteroids or corticoids

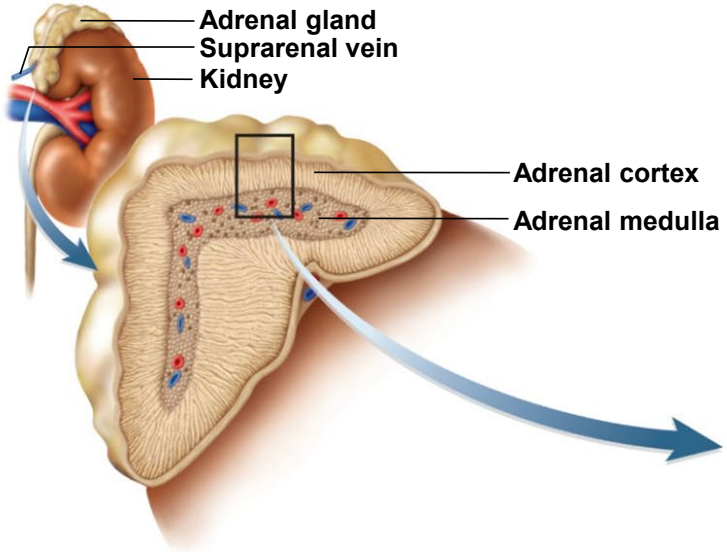
Secretes 5 major steroid hormones from three layers of glandular tissue

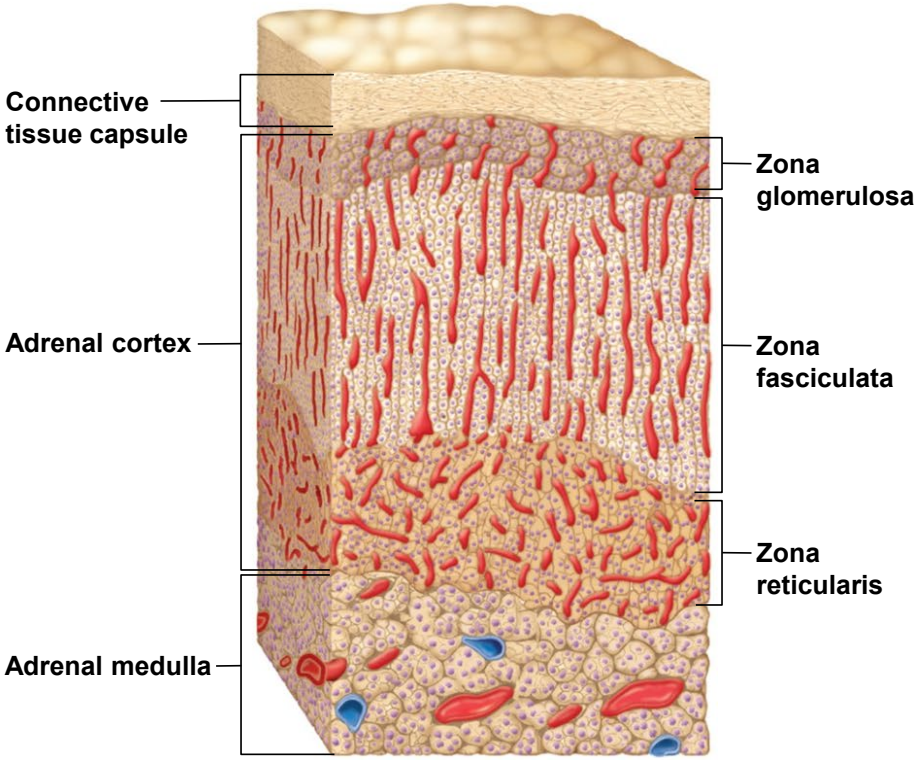
zona glomerulosa (thin, outer layer) /// cells are arranged in rounded clusters /// secretes mineralocorticoid – regulate the body's electrolyte balance

zona fasciculata (thick, middle layer) /// cells arranged in fascicles separated by capillaries /// secretes glucocorticoids

zona reticularis (narrow, inner layer) // cells in branching network // secretes sex steroids

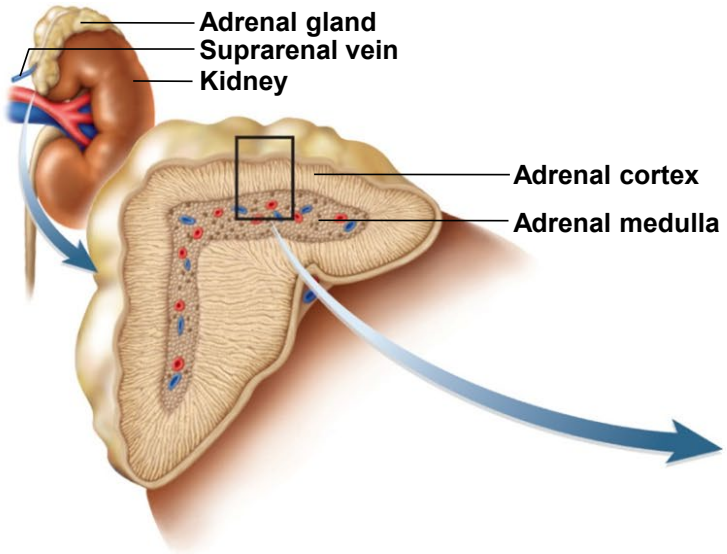
Adrenocorticotropic hormone (ACTH) Released by the Pituitary and Targets the Adrenal Gland's Cortex

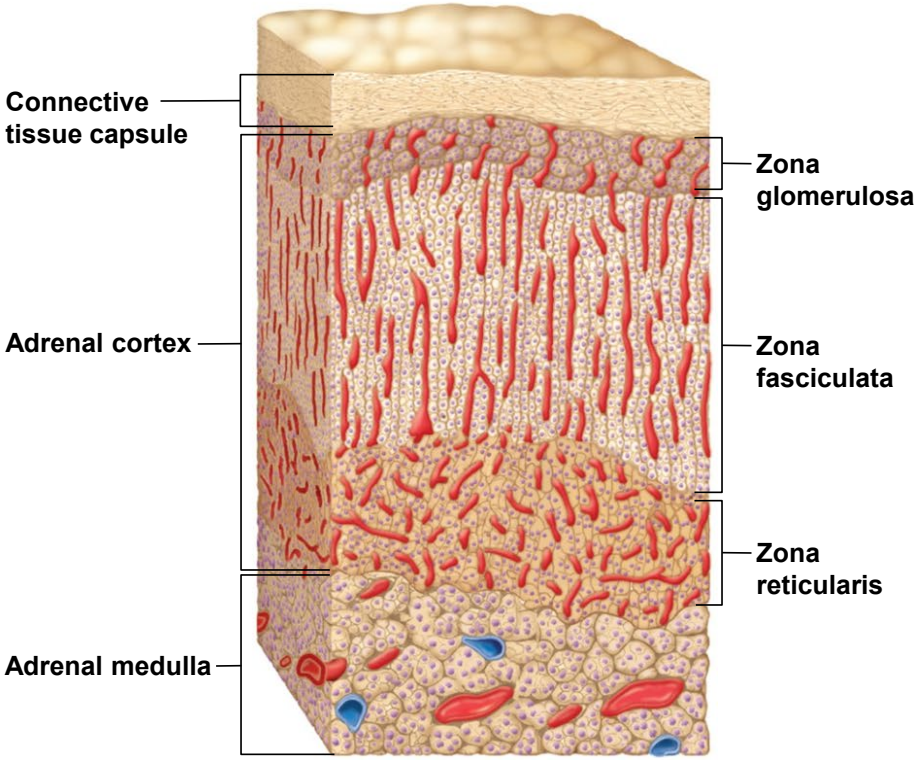




Adrenal gland is small gland that sits on top of each kidney

Adrenocorticotropic hormone (ACTH) Released by the Pituitary and Targets the Adrenal Gland's Cortex





Adrenal cortex secretes mineralocorticoid and glucocorticoid hormones

Adrenal medulla classified as a SNS ganglia (releases epinephrine and norepinephrine)

Secretions by the Adrenal Gland Medulla

Adrenal medulla – inner core, 10% to 20% of gland

Has **dual nature** /// acting as **an endocrine gland** plus acting as a **sympathetic ganglion** of sympathetic nervous system

Innervated by **sympathetic preganglionic fibers**

Consists of modified sympathetic postganglionic neurons called **chromaffin cells**

When stimulated by ANS release **catecholamines** (**epinephrine** and **norepinephrine**) and a trace of **dopamine** directly into the bloodstream

Catecholamines Released by Adrenal Medulla

Effect is longer lasting than effects of norepinephrine released as a neurotransmitters release

Increases alertness and prepares body for physical activity

Mobilize high energy fuels /// lactate, fatty acids, and glucose

Glycogenolysis and gluconeogenesis both boost glucose levels

Glucose-sparing effect /// catecholamines *inhibits insulin secretion* /// therefore muscles use fatty acids for energy and save glucose for brain (brain tissue does not need insulin to uptake glucose)

Increases blood pressure, heart rate, blood flow to muscles, pulmonary air flow to alveoli and overall metabolic rate

Decreases digestion and urine production /// maintenance type functions in favor of systems of “action”

Corticosteroids

Glucocorticoids (zona fasciculata)

regulate metabolism of glucose and other fuels

especially important is **cortisol** /// stimulates fat and protein catabolism to drive **gluconeogenesis** (glucose from amino acids and fatty acids)

cause release of fatty acids and glucose into blood

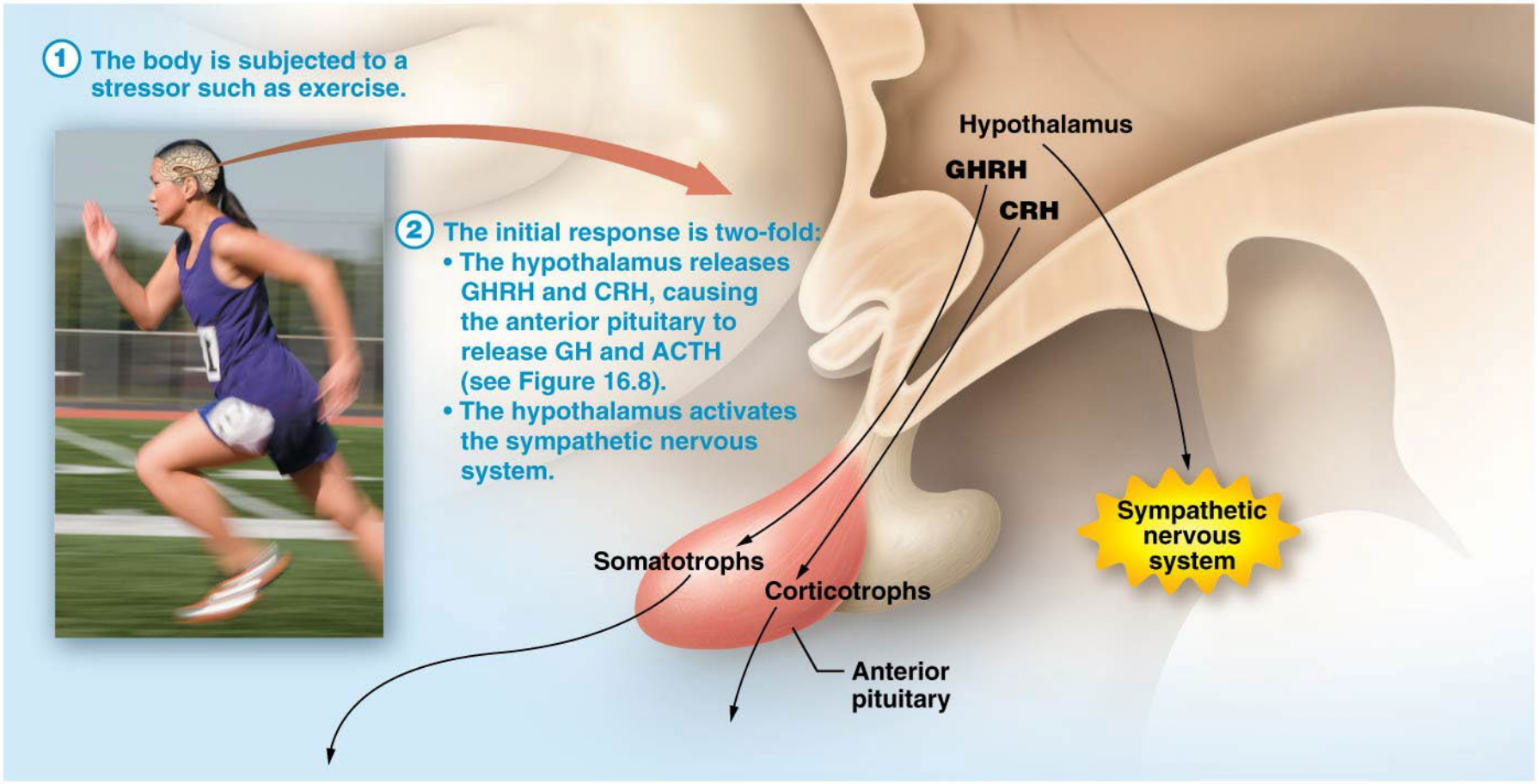
helps body adapt to stress and repair tissues

anti-inflammatory effect // reduce edema

suppressing protein synthesis = **inhibit antibody formation** /// result in immune suppression with long-term use of cortisol

The Big Picture of the Hormonal Response to Stress

Stress is not a disease but a condition that makes all diseases worst.



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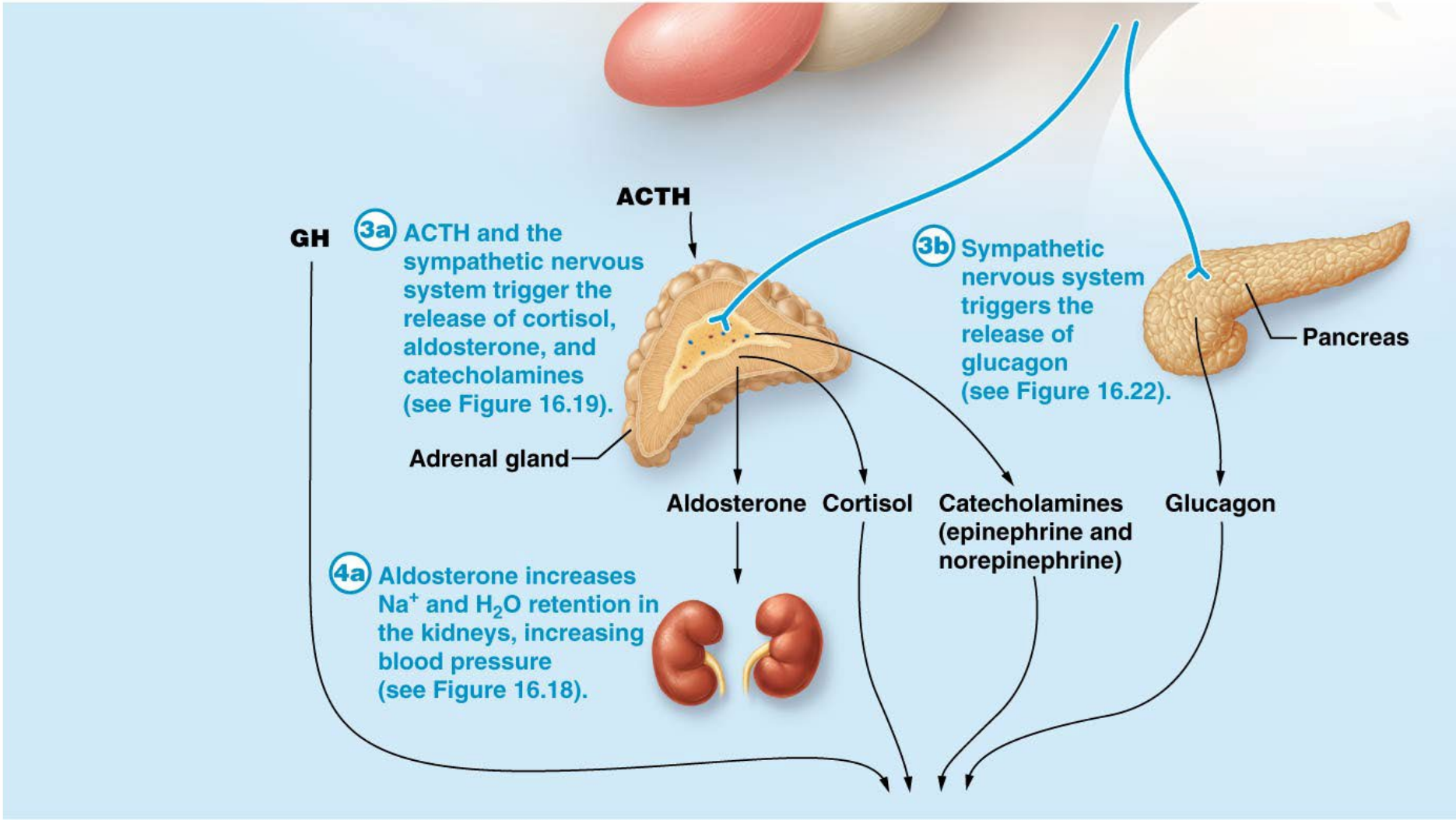
The Big Picture of the Hormonal Response to Stress



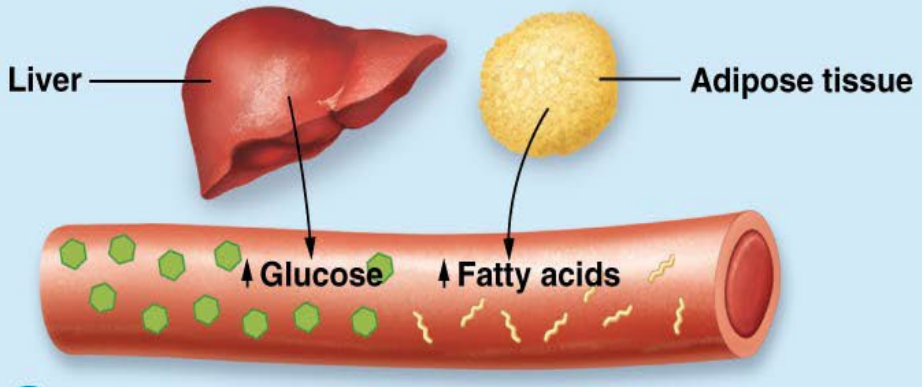
The Big Picture of the Hormonal Response to Stress

GHRH = Growth hormone–releasing hormone

CRH = Corticosteroid-releasing hormone

GH = Growth hormone

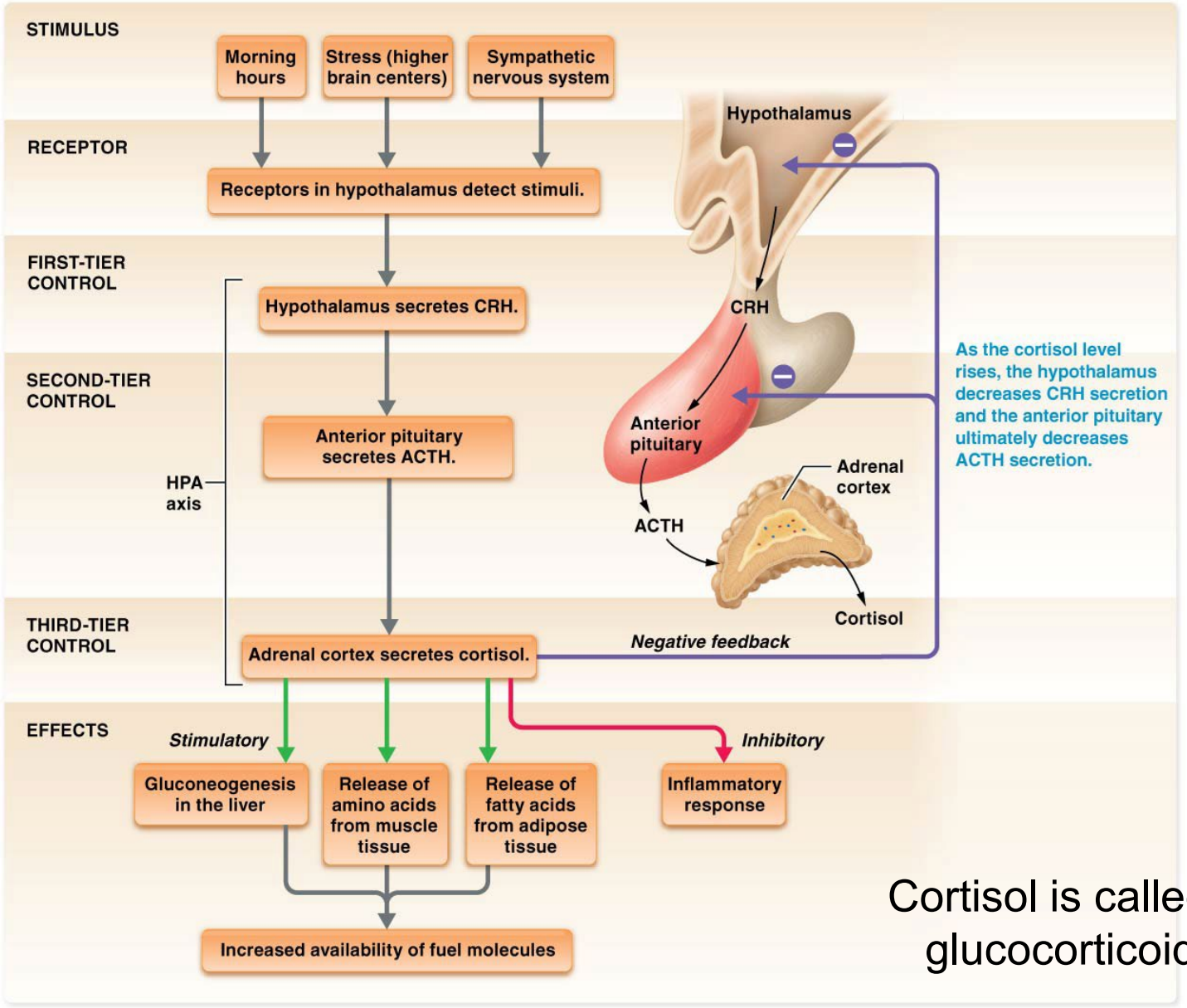
ACTH = Adrenocorticotropic hormone



4b GH, cortisol, catecholamines, and glucagon trigger an increased release of metabolic fuels from the liver and adipose tissue.

ACTH and Cortisol Regulation Using Negative Feedback Loop

What are the end results of cortisol secretions?



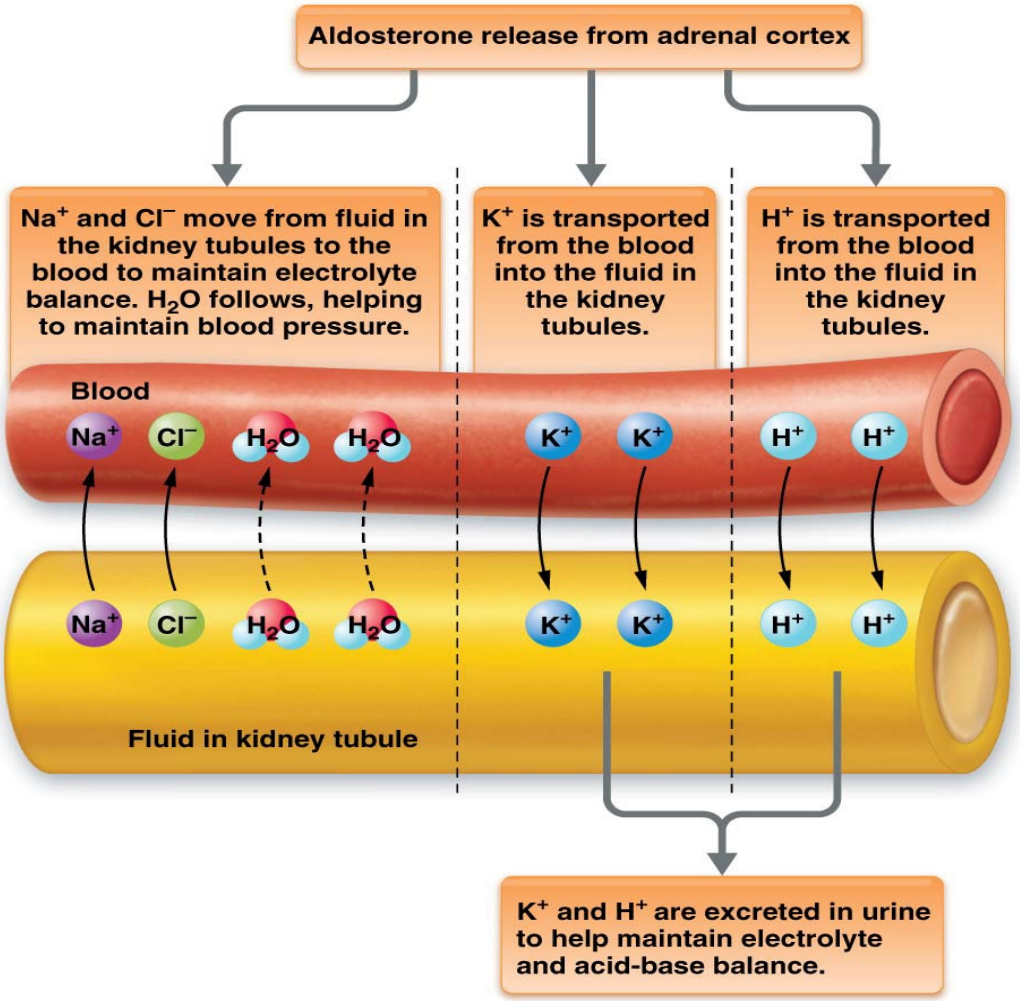
Cortisol is called a glucocorticoid.

Aldosterone

- **Aldosterone is called a mineralocorticoids**

- Regulate electrolyte balance /// stimulates retention of Na^+ while increasing excretion of K^+ plus H+

- water is retained with sodium by osmosis, helps to maintain blood volume and blood pressure



Other Adrenal Cortex Hormones

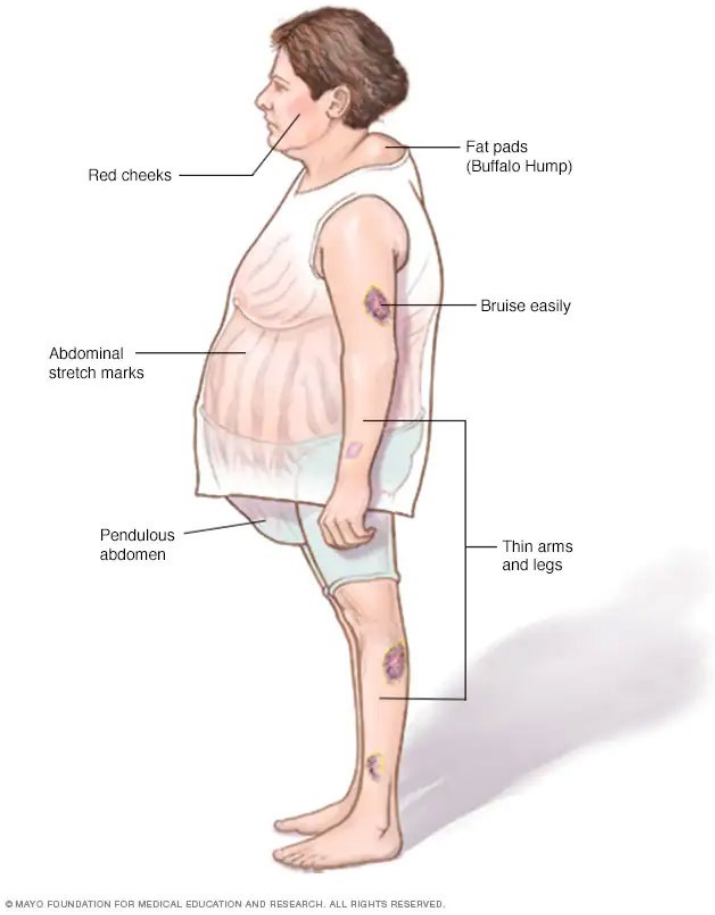
Sex steroids (zona reticularis)

Androgens – sets libido throughout life; large role in prenatal male development (includes DHEA which other tissues convert to testosterone)

Estradiol – small quantity, but important after menopause for sustaining adult bone mass; fat converts androgens into estrogen

Cushing Syndrome

(Not a lecture objective)



Cushing's syndrome is a disorder that occurs when your body makes too much cortisol over a long period of time.

Cortisol is sometimes called the “stress hormone” because it helps your body respond to stress. Cortisol also helps maintain blood pressure, and regulate blood glucose

Excess cortisol may cause enlargement of external sexual organs in children and early onset of puberty

Newborn girls exhibit masculinized genitalia

Women masculinizing effects – body hair, deeper voice, beard growth

Adrenal Gland Disorder

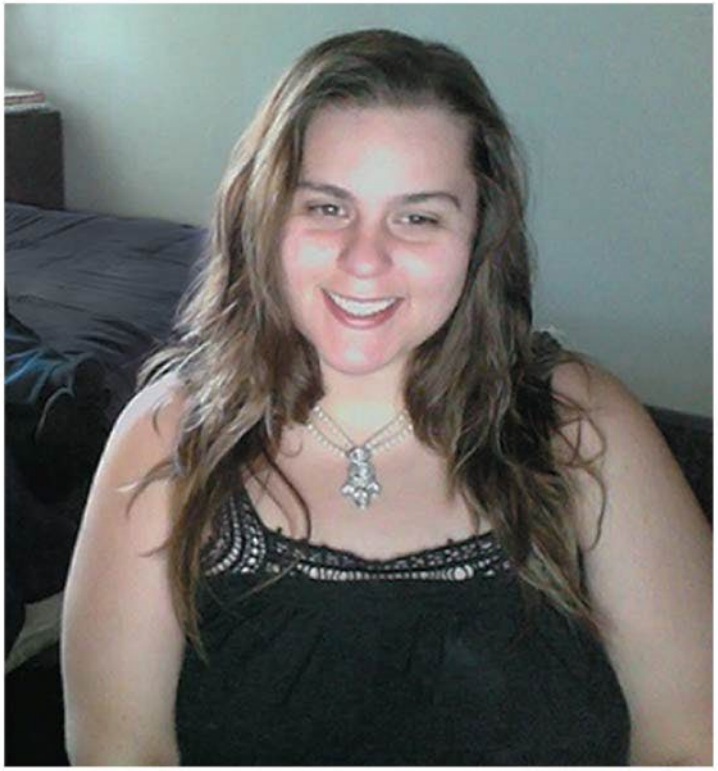
Cushing syndrome - excess cortisol secretion

- hyperglycemia, hypertension, weakness, edema
- rapid muscle and bone loss due to protein catabolism
- abnormal fat deposition // moon face and buffalo hump
- Inhibits protein synthesis // increase infections // atrophy of lymph nodes

(a) (b)

a-b: From: Atlas of Pediatric Physical Diagnosis, 3/e by Zitelli & Davis, fig 9-17 1997, with permission from Elsevier

Cushing's syndrome.



(a) Patient before development of Cushing's syndrome

(b) Patient 3 years after the onset of Cushing's syndrome

Cushing Syndrome - excess cortisol secretion

Adrenal Gland Interactions

Medulla and cortex of adrenal gland are not functionally independent

Medulla atrophies without the stimulation of cortisol (made in cortex)

Some chromaffin cells of medullary origin extend into the cortex

Chromaffin cells stimulate the cortex to secrete corticosteroids when stress activates the sympathetic nervous system

Adrenogenital Syndrome (AGS)

Congenital adrenal hyperplasia is a term used to represent a group of inherited adrenal gland disorder. Patients with this condition produce an excess of the androgen hormone and insufficient amounts of cortisol and aldosterone hormones.

It is a condition that results in a lack of a specific enzyme necessary for the adrenal glands to make the necessary cortisol and aldosterone hormones within the body.

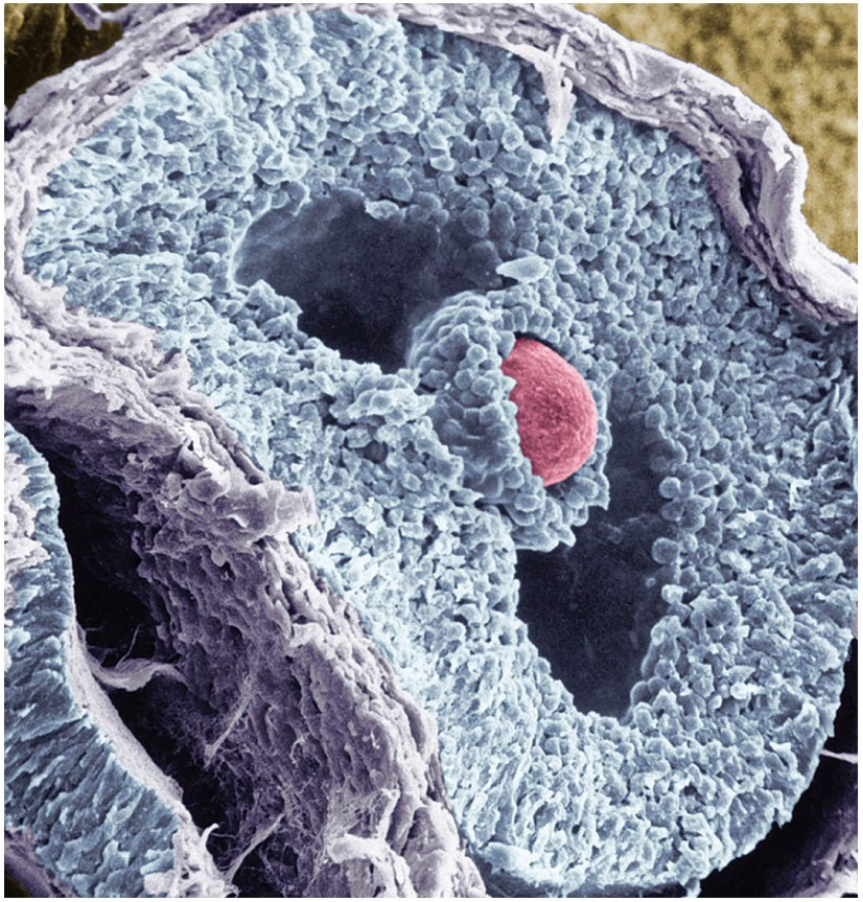
In lacking these two hormones, the body instead produces an excess amount of androgen, a kind of male sex hormone.

With this excess of androgen, early or inappropriate appearance of male characteristics are present. 1 in 50,000 +/- are affected

Masculinizing effects on women // increased body hair, deeper voice and beard growth

Congenital Adrenal Hyperplasia

Endocrine System's Tissues & Organs



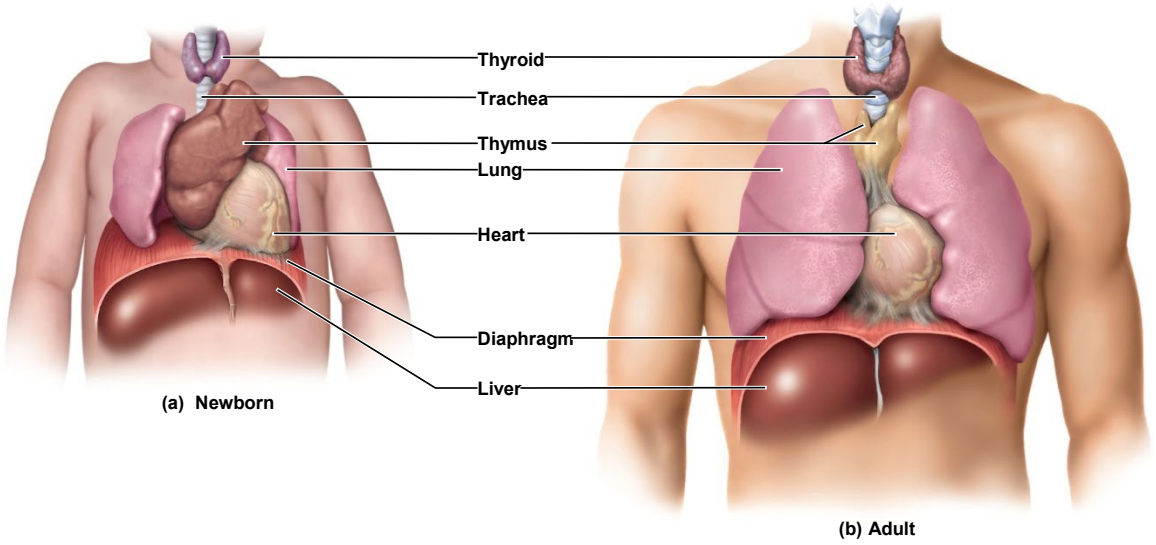
Thymus

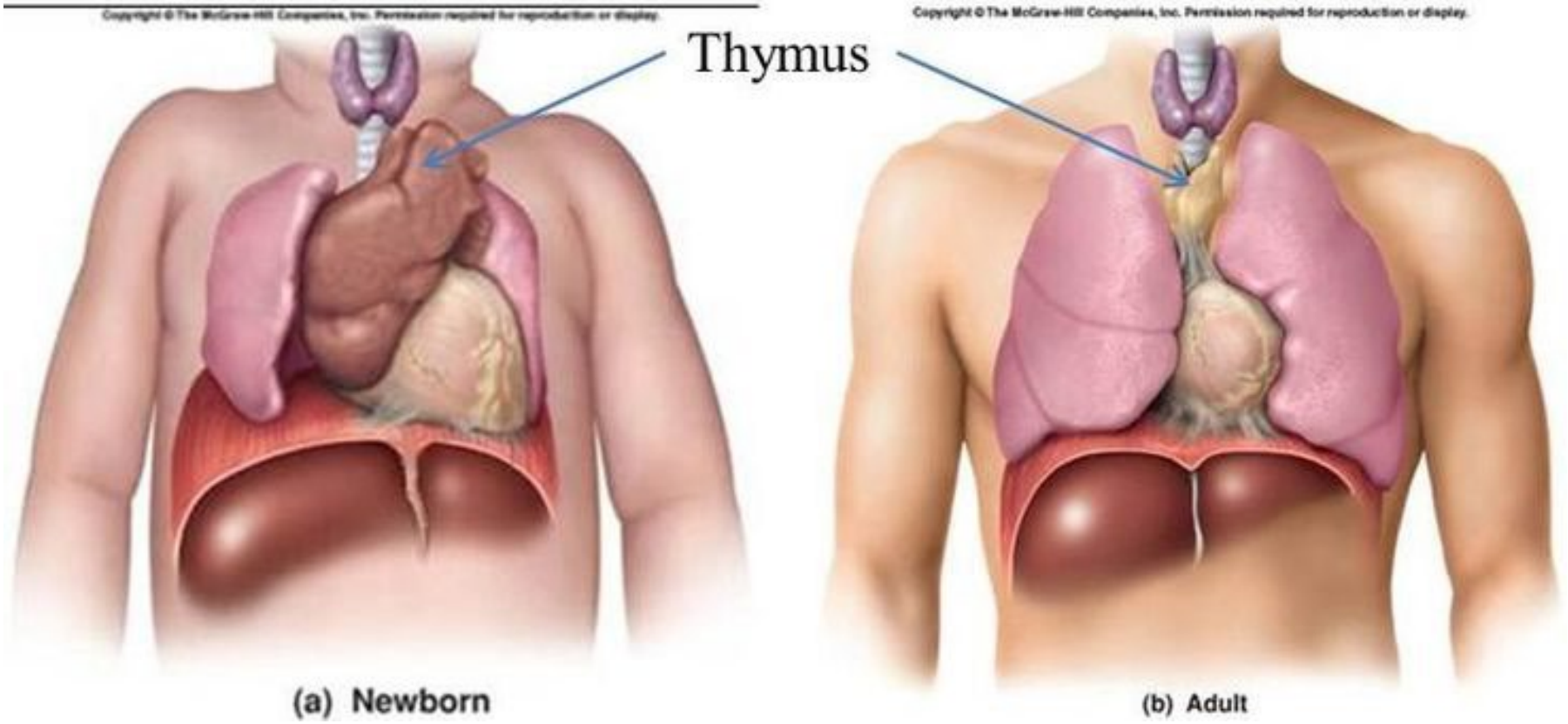
Thymus plays a role in three systems: endocrine, lymphatic, and immune

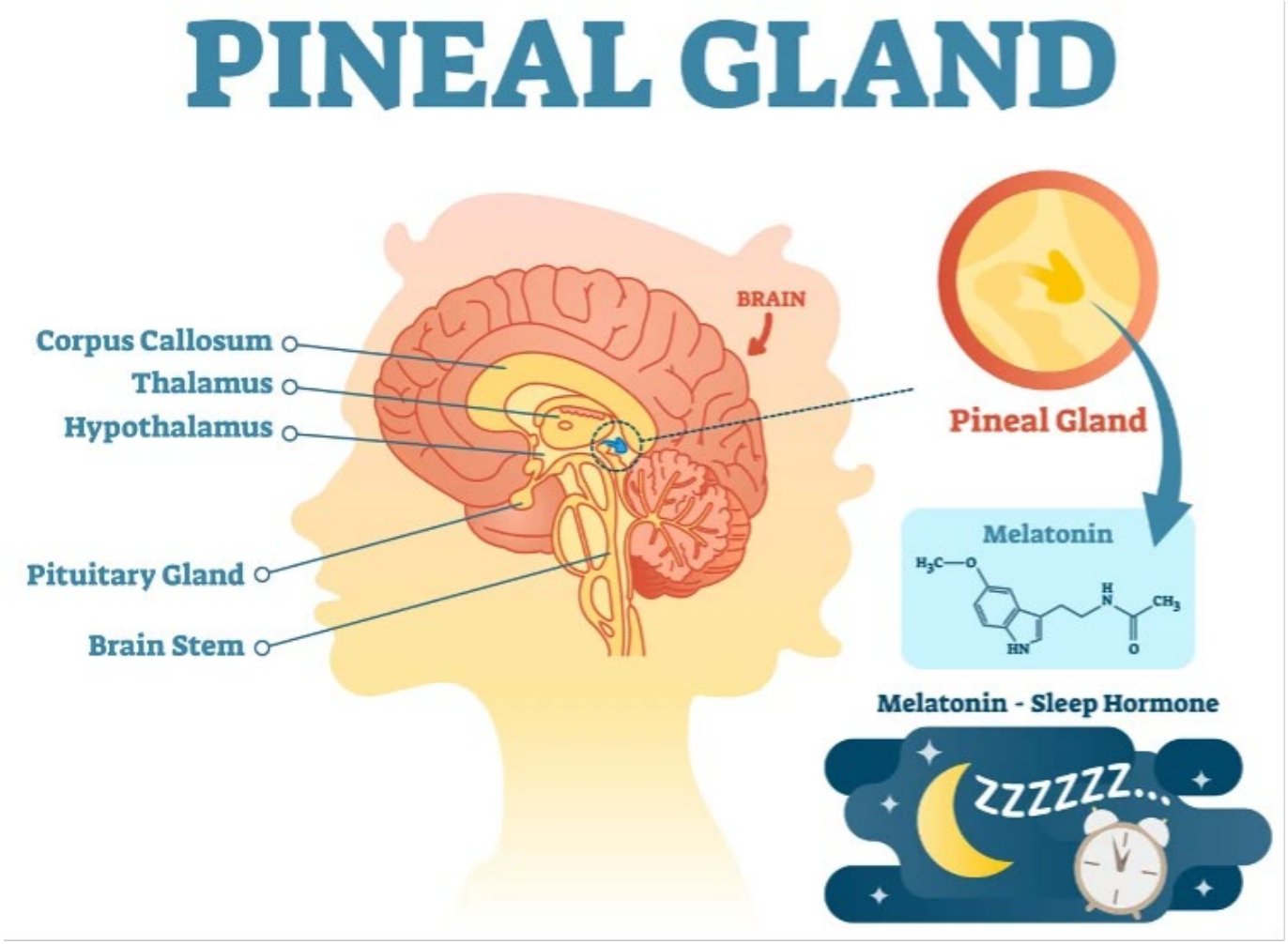
Bilobed gland in the mediastinum superior to the heart // goes through involution after puberty

Site of maturation of T cells important in immune defense

Secretes hormones (thymopoietin, thymosin, and thymulin) that stimulate development of other lymphatic organs and helps to complete development of T-lymphocytes




Thymus
(a) Newborn
(b) Adult



Attached to roof of third ventricle beneath the posterior end of the corpus callosum

Synchronize physiological function with 24-hour **circadian rhythms** of daylight and darkness

Pineal Gland

Pineal gland produces melatonin

Hormone nicknamed the SAD (seasonal adjusted disease) hormone

Synthesized from serotonin during the night ///
longer nights more melatonin – more "mood change" or sadness

Fluctuates seasonally with changes in day length ///
longer nights more melatonin

May regulate timing of puberty in humans // melatonin also thought to be associated with female mood swings associated with menses

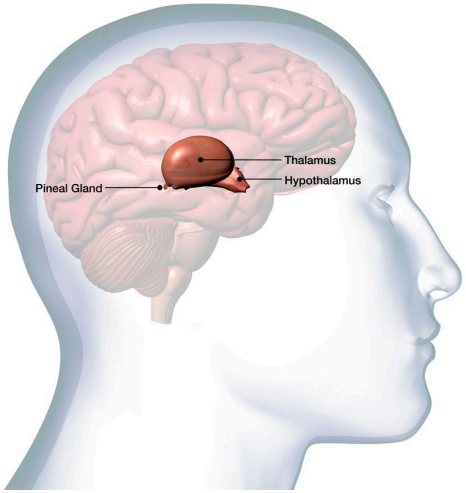
Pineal Gland

Seasonal affective disorder (SAD)

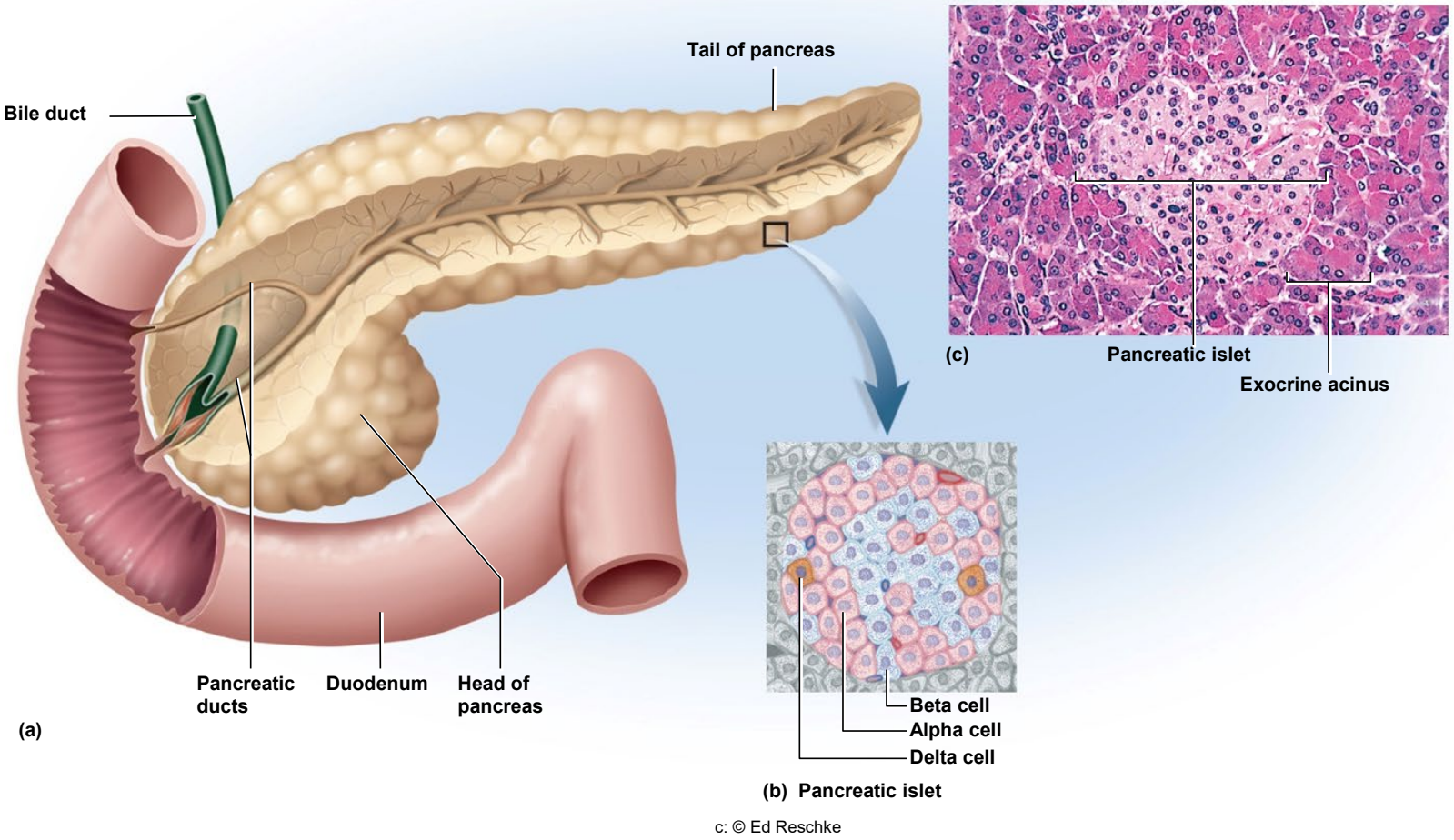
occurs in winter or northern climates // greater darkness increases melatonin production

symptoms - depression, sleepiness, irritability and carbohydrate craving

corrective action = 2 to 3 hours of exposure to bright light each day reduces the melatonin levels and the symptoms (phototherapy)



Pancreas



Dual Gland: Exocrine gland producing digestive enzymes and endocrine gland producing hormones to regulate blood glucose. Cell clusters (pancreatic islets) // retroperitoneal, inferior and posterior to stomach.

Pancreatic Hormones

1-2 million **pancreatic islets** (Islets of Langerhans) produce hormones // 2% of pancreas

Other 98% of pancreas cells produces digestive enzymes

Insulin secreted by **beta (β) cells** // secreted during and after meal when glucose and amino acid blood levels are rising

Glucagon is produced by alpha cells // released when hypoglycemic // target tissue is liver // breaks down stored glycogen into glucose which is released into blood

Insulin

Insulin stimulates cells to absorb glucose and amino acids from GI tract and cells of body to either store or metabolize them /// this will **lower *blood glucose levels***

*Also, p*romotes synthesis glycogen, fat, and protein

Suppresses use of already stored fuels

Note; Brain, liver, kidneys and RBCs absorb glucose without insulin. All other tissues in body require insulin to transport glucose into their cells.

Diabetes mellitus occurs when there is an insufficiency (not enough produced) or cells become resistant to insulin's function

Glucagon

Glucagon – secreted by A or **alpha (α) cells**

Released between meals when blood glucose concentration in the blood is falling

Glucagon in liver, stimulates gluconeogenesis and glycogenolysis

The release of glucose into the circulation raising blood glucose level

In adipose tissue, stimulates fat catabolism and release of free fatty acids // spares the metabolism of glucose for energy

Glucagon also released in response to rising amino acid levels in blood /// promotes amino acid absorption, and provides cells with raw material for gluconeogenesis

Hyperglycemic VS Hypoglycemic Hormones

Hyperglycemic hormones // raise blood glucose concentration

- glucagon
- growth hormone
- epinephrine & norepinephrine
- cortisol & corticosterone

Hypoglycemic hormone // lower blood glucose /// only insulin

Two Types of Diabetes Mellitus

Type 1 (Insulin Dependent Diabetes Mellitus / IDDM) – 5 to 10% of cases in US // Beta cells do not make insulin

Insulin is required to treat Type 1

Insulin provided by injections, insulin pump, or dry insulin inhaler

Must monitoring blood glucose levels and control diet

Hereditary susceptibility if infected with certain viruses (rubella, cytomegalovirus)

Caused by auto-immune disease // destroy pancreatic beta cells

Associated as “early onset” diabetes

Two Types of Diabetes Mellitus

Type 2 (Non-insulin dependent diabetes mellitus - NIDDM) – 90 to 95% of diabetics // Beta cells produce insulin by cells resistant to insulin.

Cells throughout body become resistant to **insulin //** failure of target cells to respond to insulin // problem with glucose transporter (transmembrane protein)

Risk factors are heredity, age (40+),obesity, and ethnicity – Native American, Hispanic, and Asian

Treated first with weight loss program and exercise since: loss of muscle mass causes difficulty with regulation of glycemia adipose signals interfere with glucose uptake into most cells

Oral medications may improve insulin secretion or target cell sensitivity

Use to be associated as late development (after 30-40 year old) but now epidemic of young children develop Type 2. Believed to be cause by increased use of high fructose sugar in our diet.

Diabetes Mellitus

Most prevalent metabolic disease in the world // *Ancient Greeks 400 BCE described diabetes as a "disease that turns the body into water".*

Disruption of metabolism due to hyposecretion or inaction of insulin

Revealed by elevated blood glucose, glucose in urine and ketones in the urine // Early doctors diagnosed diabetes by tasting urine for sweetness.

Symptoms:

- **polyuria** (excess urine output)
- **polydipsia** (intense thirst)
- **polyphagia** (hunger)

Diabetes Mellitus

DM causes elevated glucose blood levels

Kidneys filter plasma and filtration moves glucose into kidney tubules

Under normal glucose concentrations // all filtered glucose reabosorbed back into body and no glucose is excreted in urine

High glucose concentrations // exceed kidney's proximal convoluted tubule transport maximum // glucose now becomes an osmotic diuretic

DM limit to how fast the glucose transporters can work to reabsorb glucose from filtrate (urine)

Excess glucose enters urine and water follows // polyuria (excess urine output), polydipsia (intense thirst), polyphagia (hunger)

Pathology of Diabetes

Pathogenesis:

- cells cannot absorb glucose
- must rely on fat and proteins for energy needs
- results in weight loss and weakness

Fat catabolism increases free fatty acids and ketones in blood

Ketonuria -- promotes osmotic diuresis, loss of Na^+ and K^+, irregular heartbeat, and neurological issues

Ketoacidosis -- occurs as ketones decrease blood pH (make more acidic) // deep, gasping breathing and diabetic coma are terminal result // breath smells “fruity” or “alcoholic”

Result of Chronic Hyperglycemia From Diabetes

Leads to neuropathy and cardiovascular damage

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

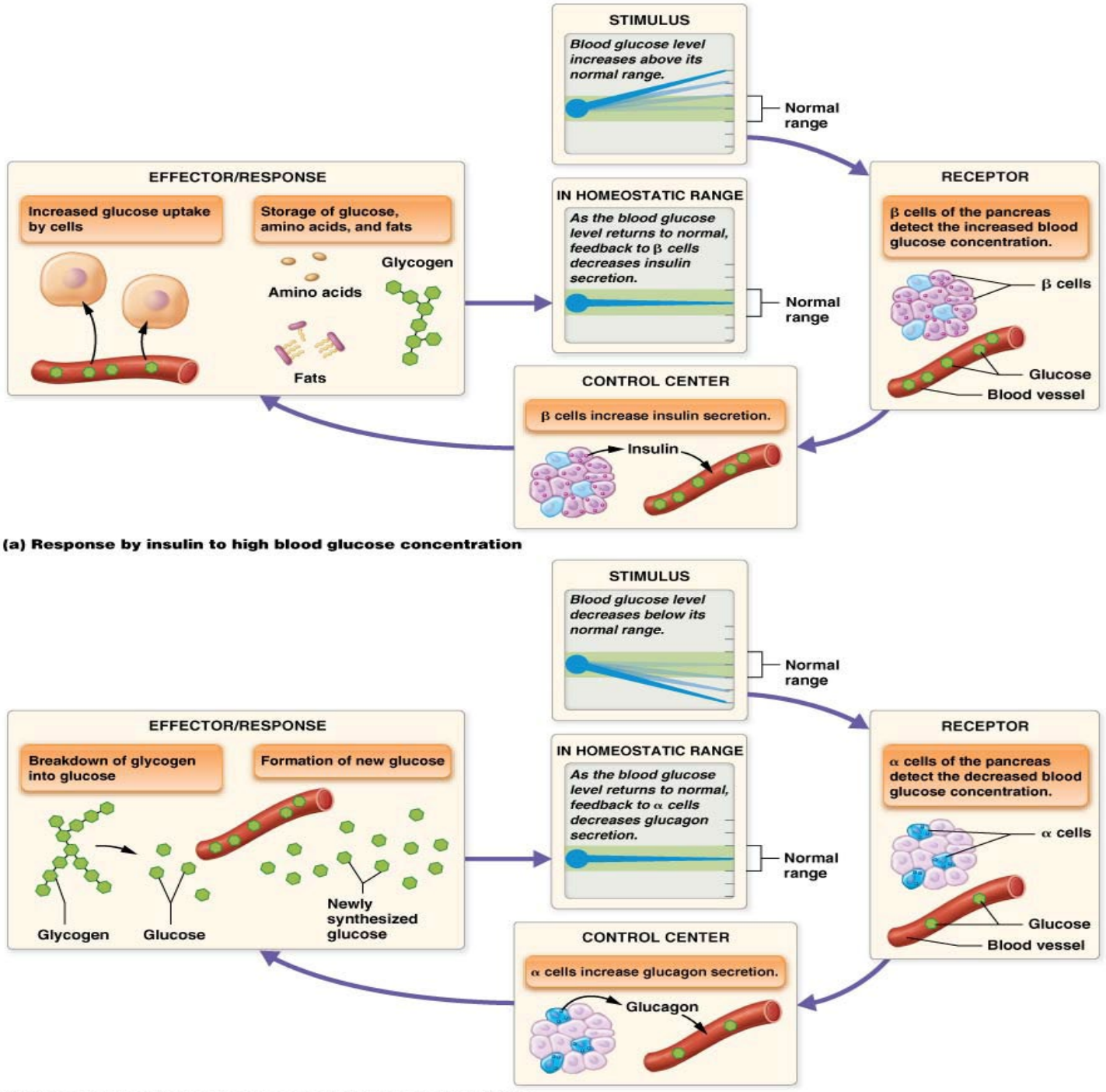
Vascular problems related to “thickening” of the basement membrane in the capillaries

Other Types of Diabetes

Gestational Diabetes – somatic cells of pregnant woman become “insensitive” to insulin // her blood glucose level increases

Diabetes Insipidus – normal insulin – glucagon - blood glucose levels /// ADH levels too low – results in large urine volume

Regulation of blood glucose concentration by negative feedback loops.



Other Hormones

The following hormones are not included in this exam.

We will cover these hormones as we cover the different systems of the human body.

The following slides preview some of the hormones we will study in Unit Three and Unit Four.

Other Hormones

somatostatin secreted by D or **delta (δ) cells**

- partially suppresses secretion of glucagon and insulin
- inhibits nutrient digestion
- absorption which prolongs absorption of nutrients

pancreatic polypeptide secreted by PP cells or **F cells**

- inhibits gallbladder contraction
- secretion of pancreatic digestive enzymes

gastrin secreted by **G cells**

- stimulates stomach acid secretion, motility and emptying

Endocrine Functions of the Skin

Skin

keratinocytes convert a cholesterol like steroid into cholecalciferol using UV from sun

This molecule is eventually converted to Vitamin D / the sunshine hormone!

Endocrine Functions of the Liver

Liver

involved in the production of at least five hormones

converts cholecalciferol into **calcidiol (pro Vitamin D)**

secretes **angiotensinogen** (a prohormone) // precursor of angiotensin II (a regulator of blood pressure)

secretes 15% of **erythropoietin** (stimulates bone marrow) – primary source are kidneys

hepcidin – promotes intestinal absorption of iron

source of insulin like growth factor (**IGF-I)** that controls action of growth hormone

Endocrine Functions of the Kidneys

Kidneys

plays role in production of three hormones

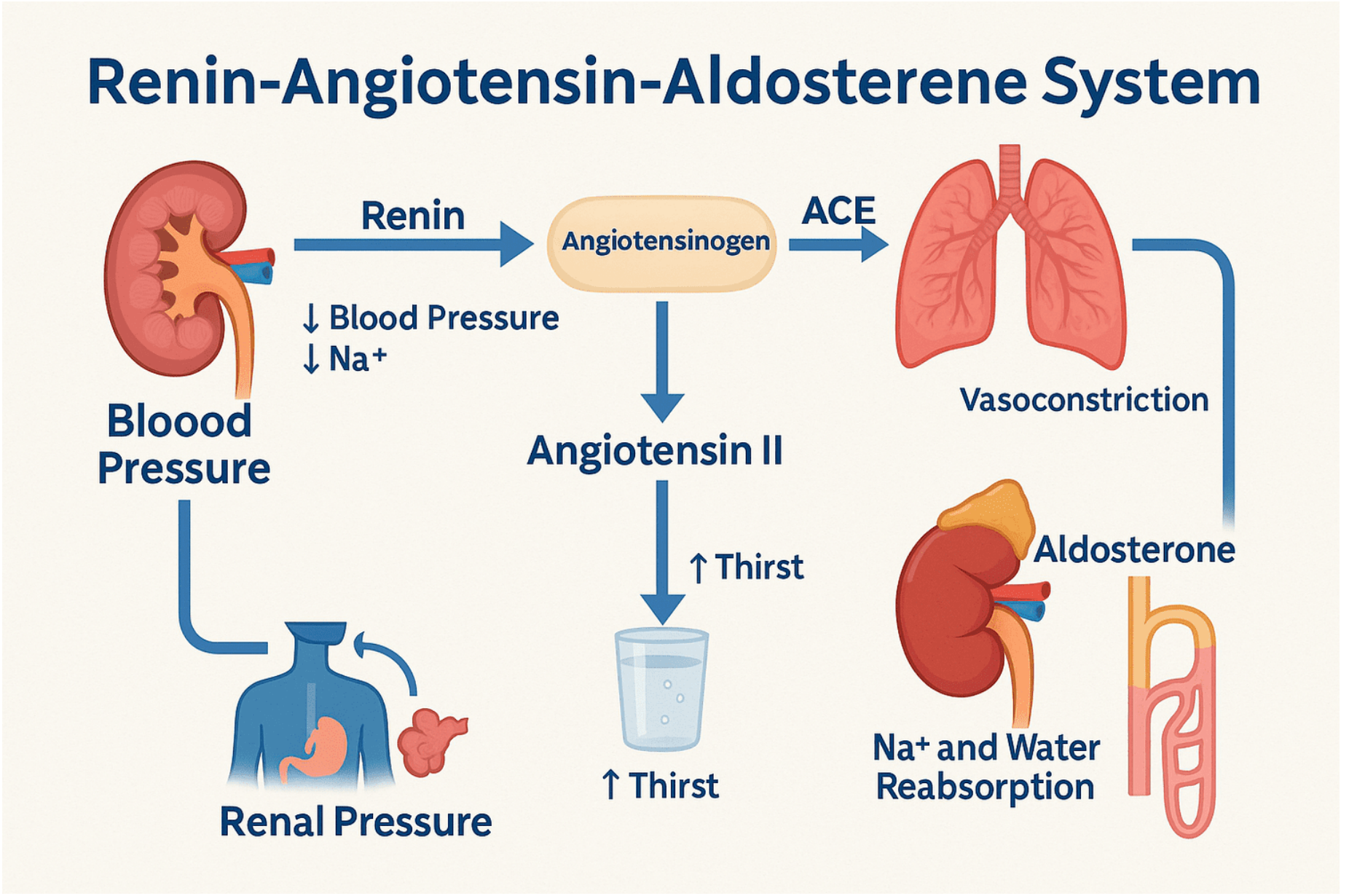
converts calcidiol to calcitriol, the active form of vitamin D /// increases Ca^{2+} absorption by intestine and inhibits loss in the urine

secrete renin that converts angiotensinogen to angiotensin I

enzyme in lungs (angiotensin converting enzyme) converts angiotensin I into angiotensin II / the active form

Angiotensin II constricts blood vessels and raises blood pressure

Kidneys


Renin-Angiotensin-Aldosterene System
Renin
Angiotensinogen
ACE
↓ Blood Pressure
↓ Na+
Bloood Pressure
Angiotensin II
Vasoconstriction
↑ Thirst
Aldosterone
Renal Pressure
↑ Thirst
Na+ and Water Reabsorption

Endocrine Functions of the Kidney

Kidneys

erythropoietin

- produces 85% of this hormone
- (liver produces other 15%)

- stimulates bone marrow to produce RBCs

Endocrine Functions of the Heart, Stomach & Intestine

Heart

cardiac muscle secretes atrial and brain natriuretic peptides (ANP and BNP) 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

lowers blood pressure

Stomach and small intestine secrete at least ten enteric hormones secreted by enteroendocrine cells

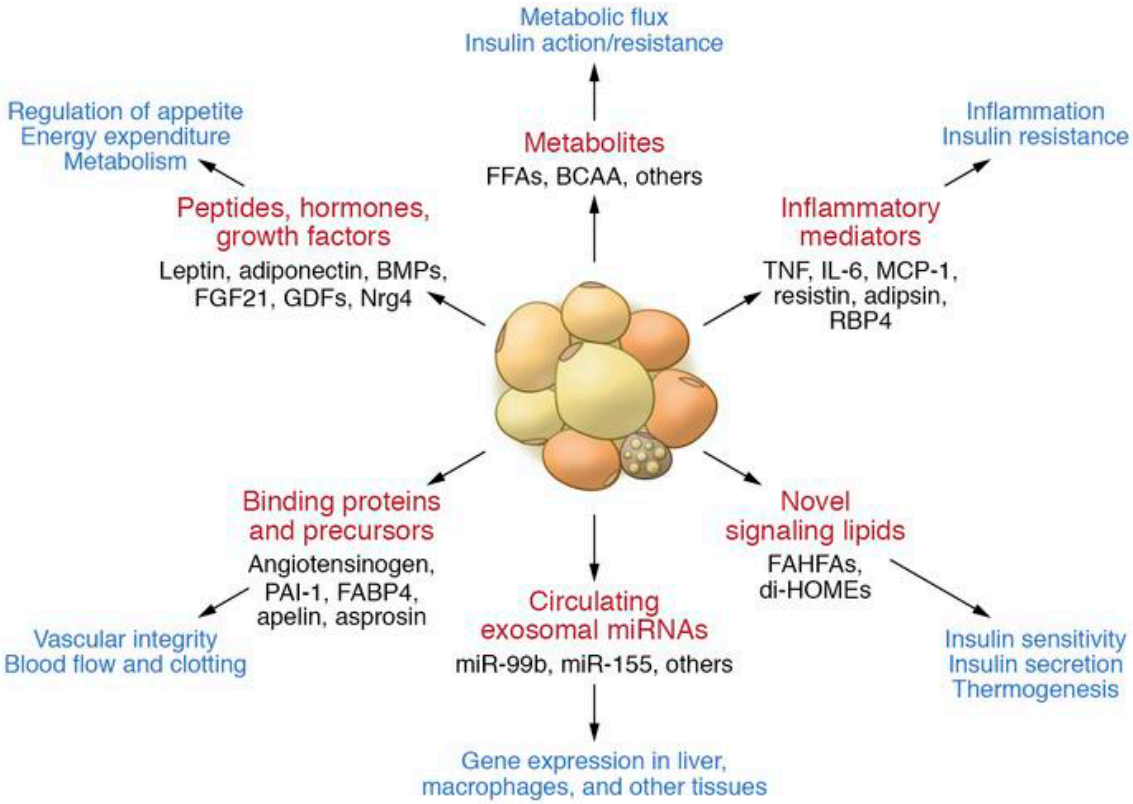
– coordinate digestive motility and glandular secretion

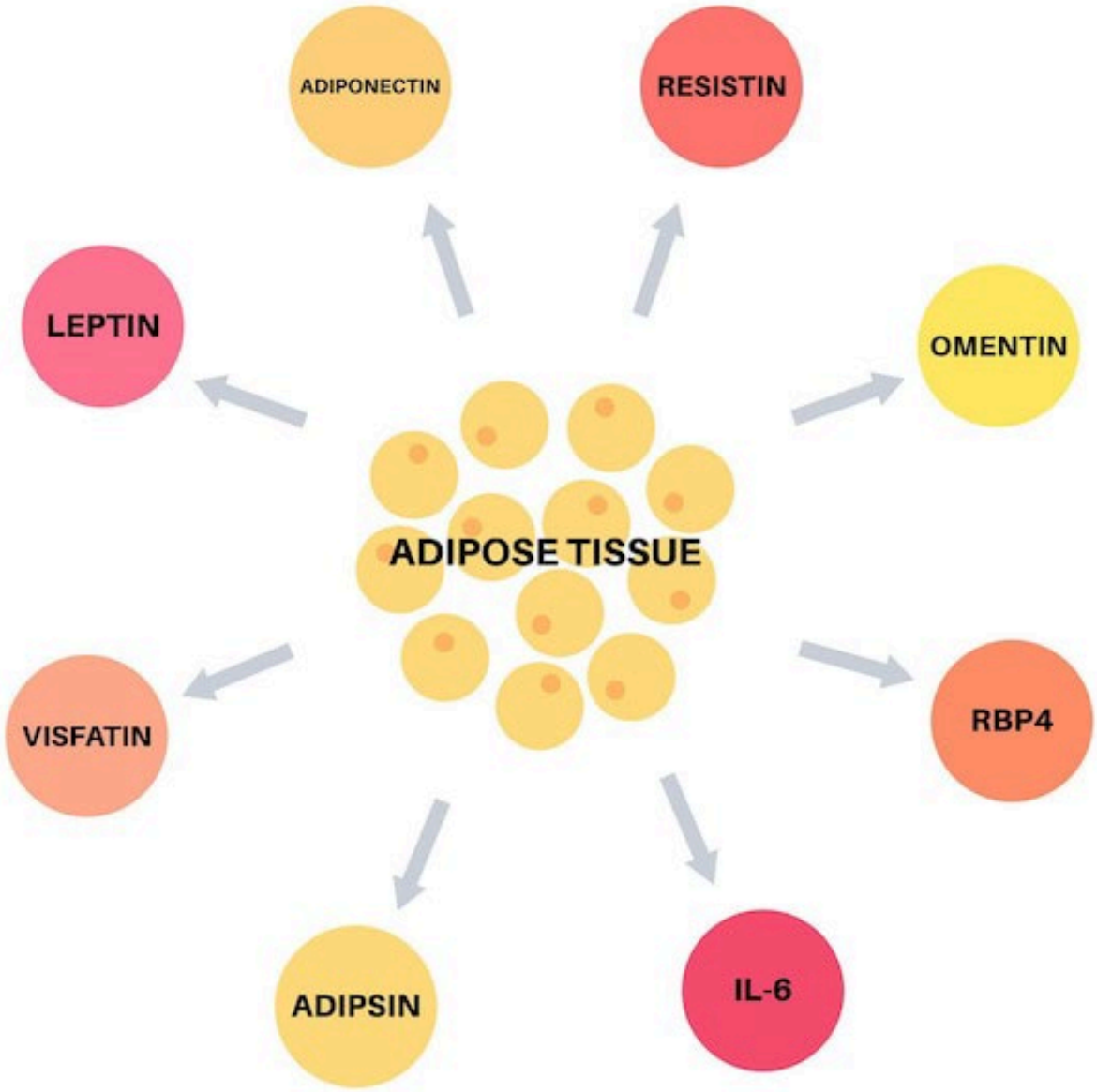
– cholecystokinin, secretin, gastrin, Ghrelin, and peptide YY

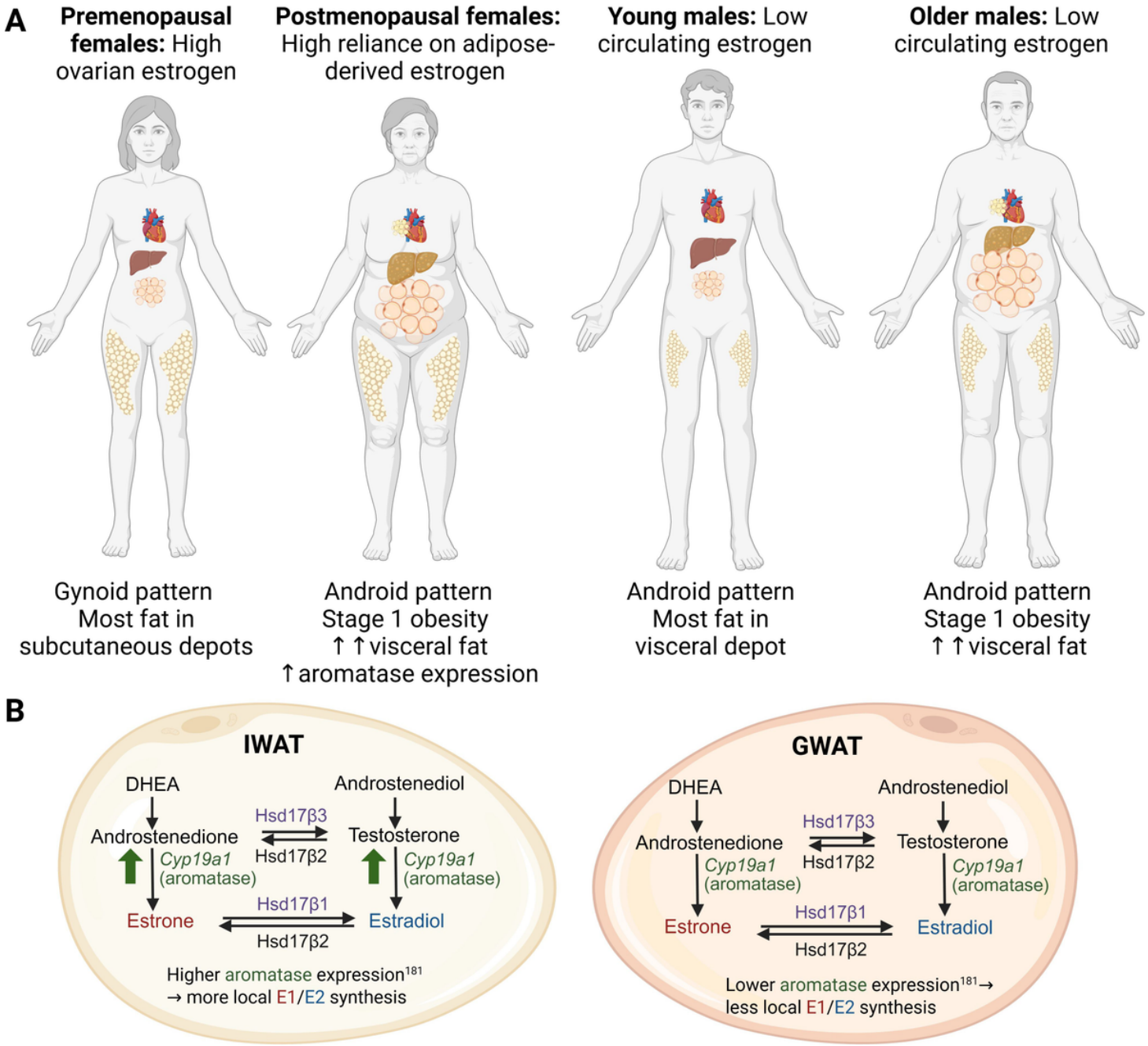
Endocrine Functions of Other Organs

Adipose tissue secretes leptin /// slows appetite

Adipose tissue also secretes many other hormones and regulatory molecules




ADIPONECTIN
RESISTIN
LEPTIN
OMENTIN
ADIPOSE TISSUE
VISFATIN
RBP4
ADIPSIN
IL-6


A
Premenopausal females: High ovarian estrogen
Postmenopausal females: High reliance on adipose-derived estrogen
Young males: Low circulating estrogen
Older males: Low circulating estrogen
Gynoid pattern
Most fat in subcutaneous depots
Android pattern
Stage 1 obesity
↑ ↑ visceral fat
↑ aromatase expression
Android pattern
Most fat in visceral depot
Android pattern
Stage 1 obesity
↑ ↑ visceral fat
B
IWAT
DHEA
Androstenediol
Androstenedione
Hsd17β3
Hsd17β2
Testosterone
Cyp19a1 (aromatase)
Cyp19a1 (aromatase)
Estrone
Hsd17β1
Hsd17β2
Estradiol
Higher aromatase expression[181]
→ more local E1/E2 synthesis
GWAT
DHEA
Androstenediol
Androstenedione
Hsd17β3
Hsd17β2
Testosterone
Cyp19a1 (aromatase)
Cyp19a1 (aromatase)
Estrone
Hsd17β1
Hsd17β2
Estradiol
Lower aromatase expression[181]→
less local E1/E2 synthesis

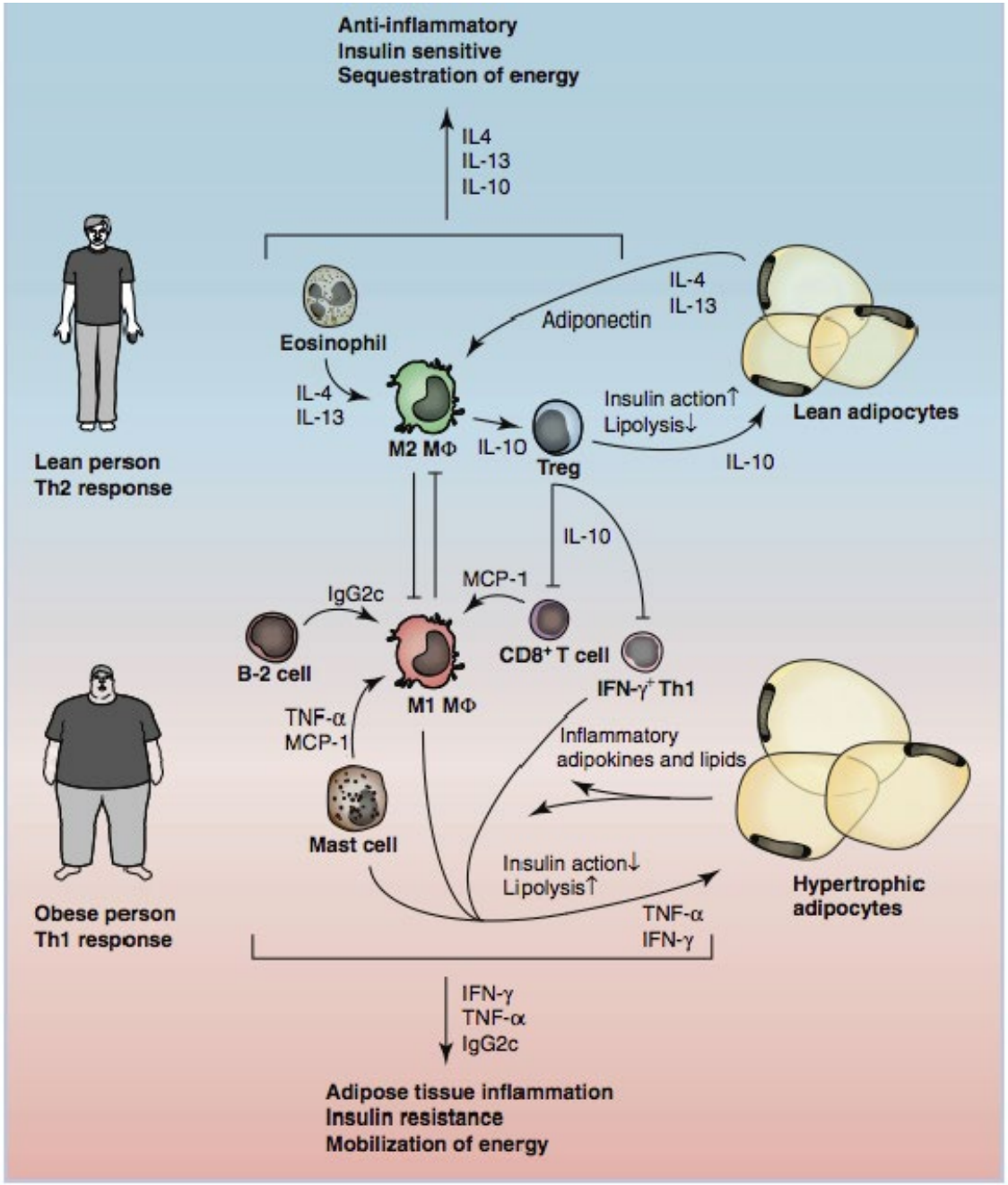


Figure 2.

Adipose tissue - resident immune cells: key players in immunometabolism. Trends in Endocrinology and Metabolism. August 2012.

Endocrine Functions of Other Organs

Osseous tissue – osteocalcin secreted by osteoblasts

– increases number of pancreatic beta cells, pancreatic output of insulin, and insulin sensitivity of other body tissues

– inhibits weight gain and onset of type II diabetes mellitus

Placenta // secretes estrogen, progesterone and others /// regulate pregnancy, stimulate development of fetus and mammary glands

The Gonads as Endocrine Glands

Ovaries and testes are both endocrine and exocrine glands

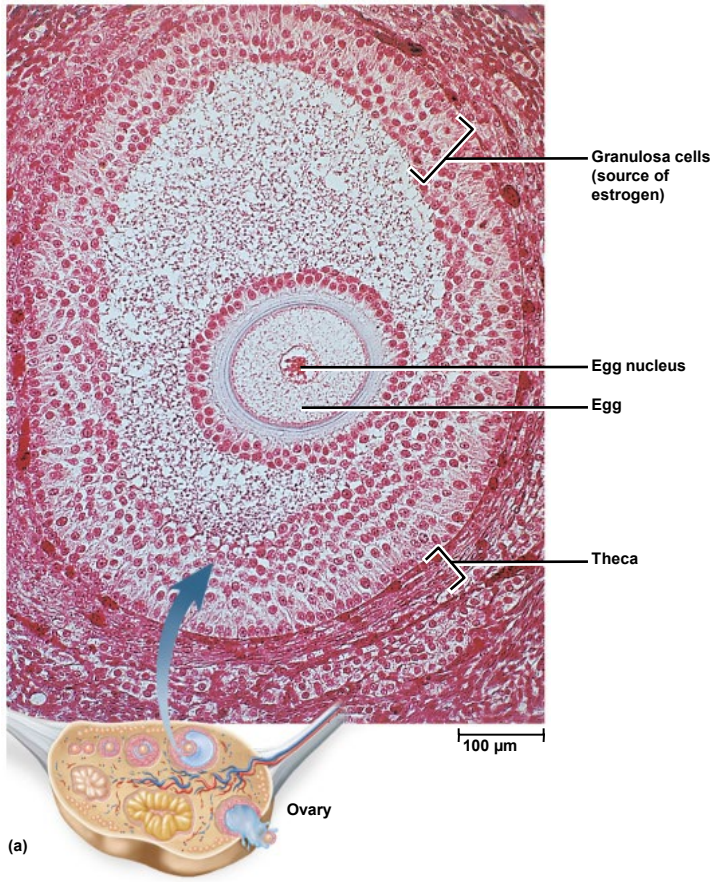
exocrine product – whole cells - eggs and sperm (cytogenic glands)

endocrine product - gonadal hormones – mostly steroids

Ovarian hormones (female ovaries) // estradiol, progesterone, and inhibin

Testicular hormones (male testes) // testosterone, weaker androgens, estrogen and inhibin

Histology of Ovary



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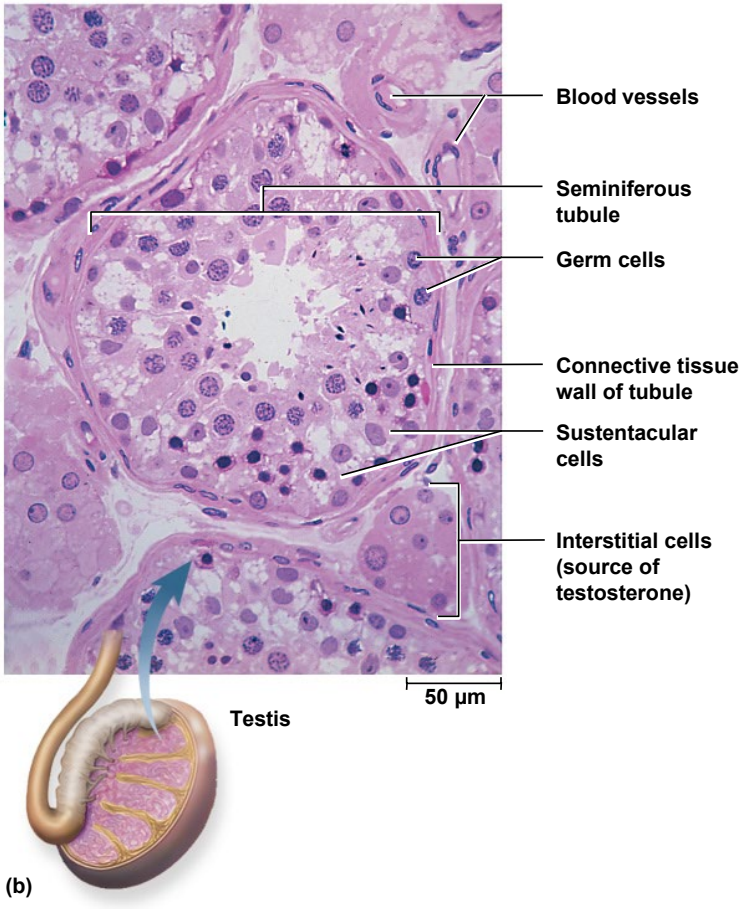


© Ed Reschke

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

Ovary

theca cells synthesize androstenedione

converted to mainly estradiol by theca and granulosa cells

functions of estradiol and progesterone

development of female reproductive system and physique including adolescent bone growth

regulate menstrual cycle, sustain pregnancy

prepare mammary glands for lactation

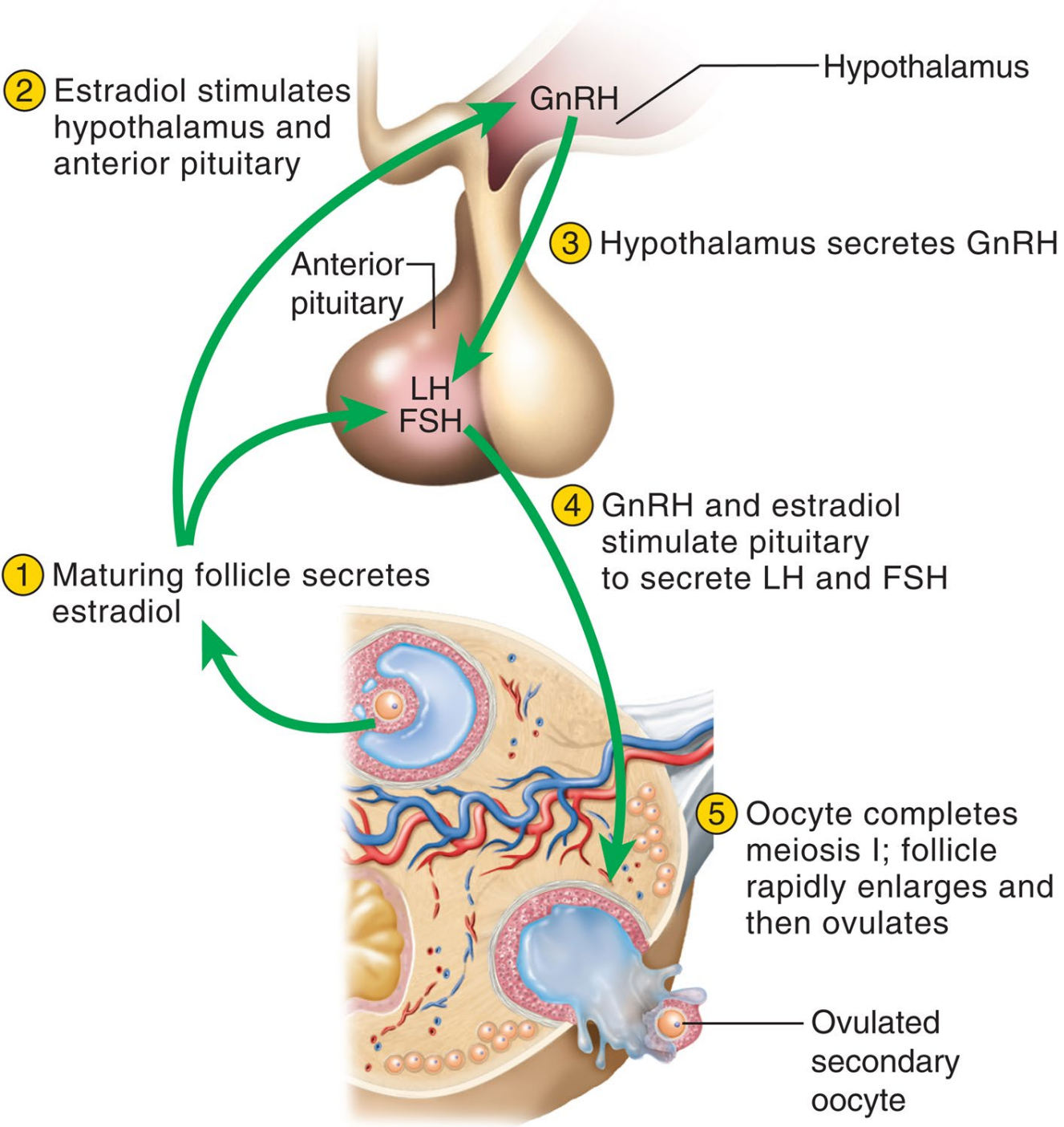
Ovary

anterior pituitary after ovulation /// the remains of the follicle becomes the corpus luteum

secretes progesterone for 12 days following ovulation

Follicular cells and corpus luteum also secrete inhibin

inhibin suppresses FSH secretion from



After ovulation corpus luteum produces progesterone and inhibin

Inhibin's negative feedback on anterior pituitary stops FSH secretion so another follicle does not mature

LH secretion continues

LH stimulates CL to produce progesterone which maintains endometrium

Testes

microscopic **seminiferous tubules** produce sperm

tubule walls contain sustentacular (Sertoli) cells

Leydig cells (interstitial cells) lie in clusters between tubules

Testes

testicular hormones

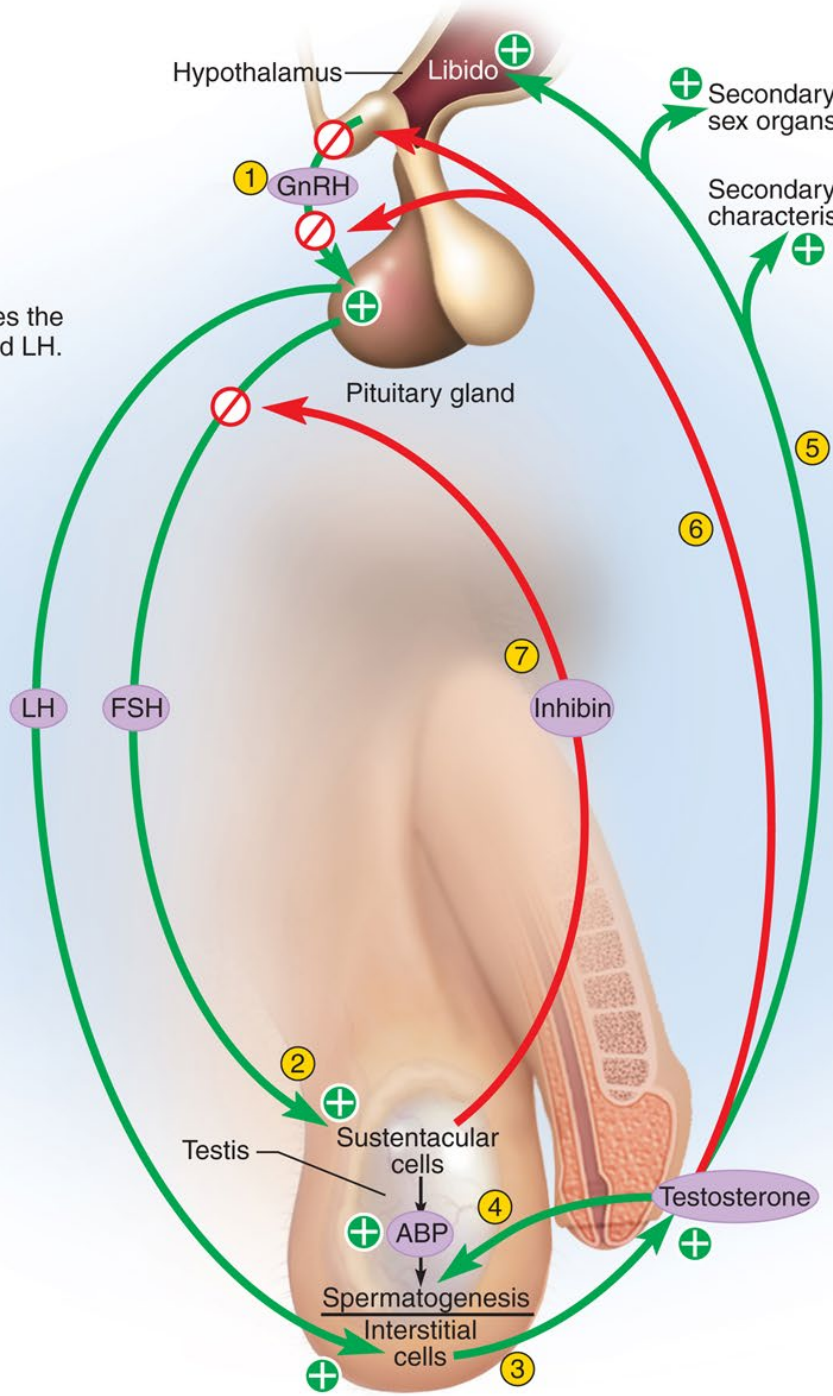
testosterone and other steroids from interstitial cells (cells of Leydig) nestled between the tubules

stimulates development of male reproductive system in fetus and adolescent, and sex drive

sustains sperm production

inhibin from sustentacular (Sertoli) cells

limits FSH secretion in order to regulate sperm production

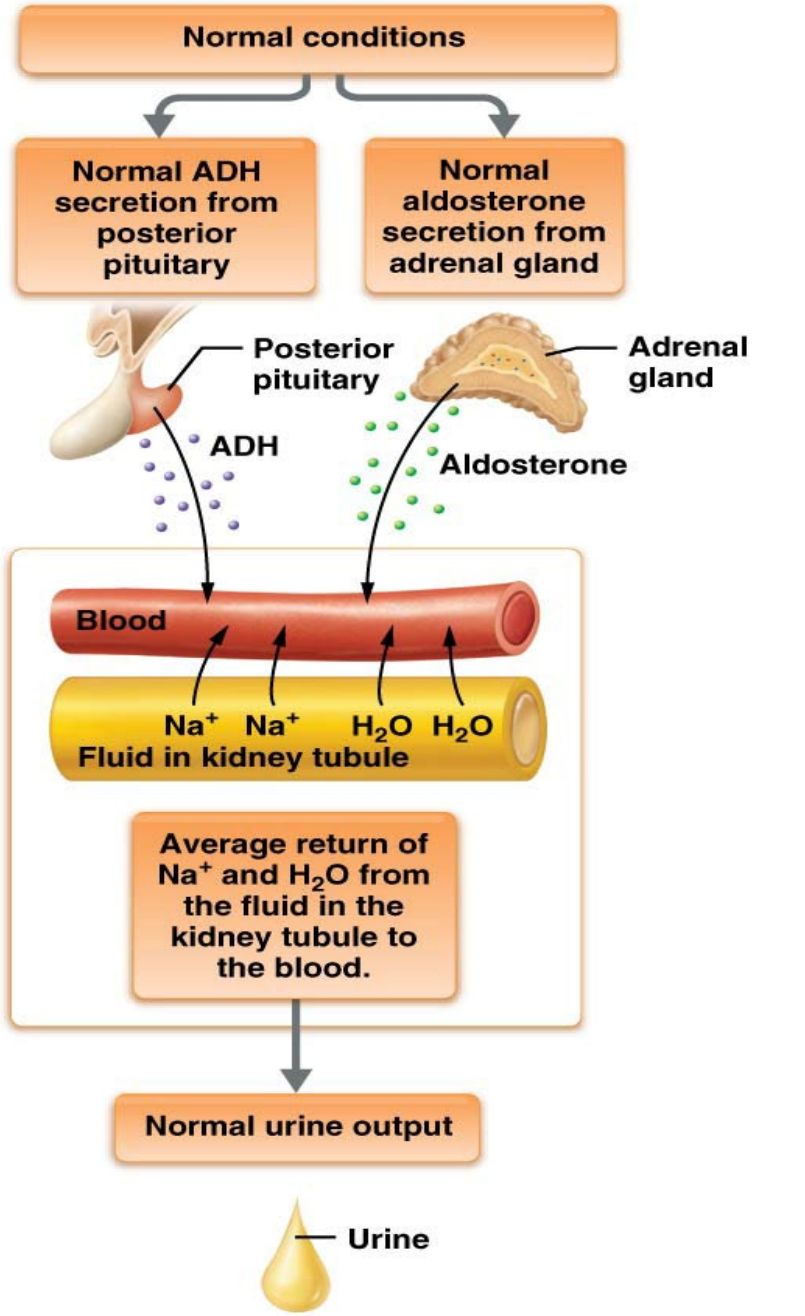


1. GnRH from hypothalamus stimulates the anterior pituitary to secrete FSH and LH.
2. FSH stimulates sustentacular cells to secrete androgen-binding protein (ABP).
3. LH stimulates interstitial cells to secrete testosterone (androgen).
4. In the presence of ABP, testosterone stimulates spermatogenesis.
5. Testosterone also stimulates the libido and the development of secondary sex organs and characteristics.
6. Testosterone has negative feedback effects that reduce GnRH secretion and pituitary sensitivity to GnRH.
7. Sustentacular cells also secrete inhibin, which selectively inhibits FSH secretion and thus reduces sperm production without reducing testosterone secretion.

Key

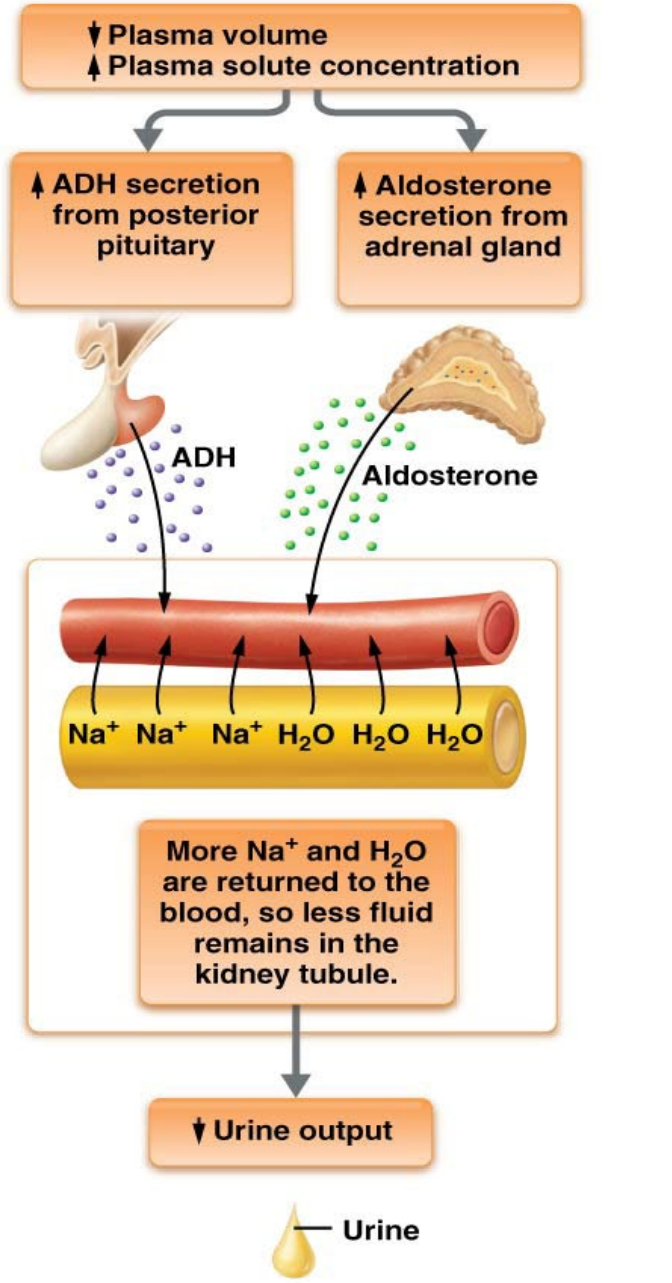
- Stimulation
- Inhibition

Summary of endocrine control of fluid homeostasis.



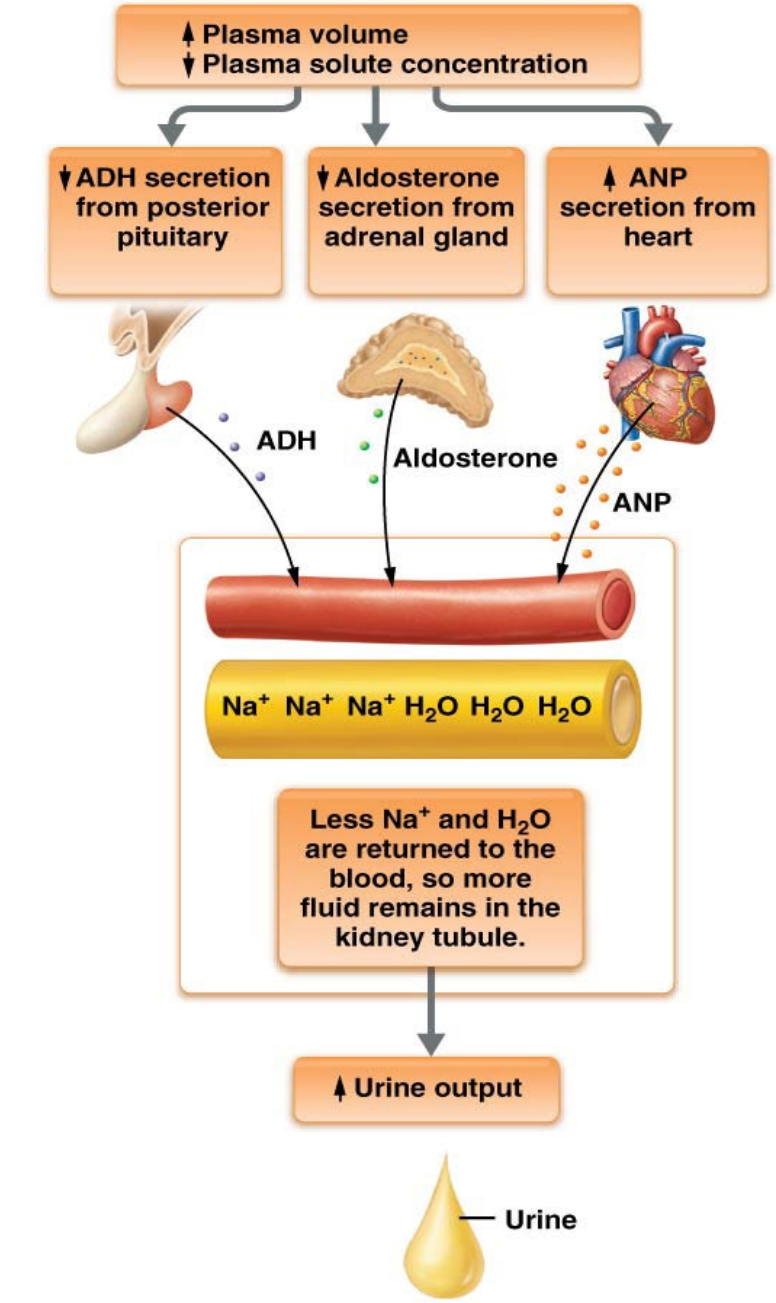
(a) Normal conditions: low ADH and aldosterone

Summary of endocrine control of fluid homeostasis.



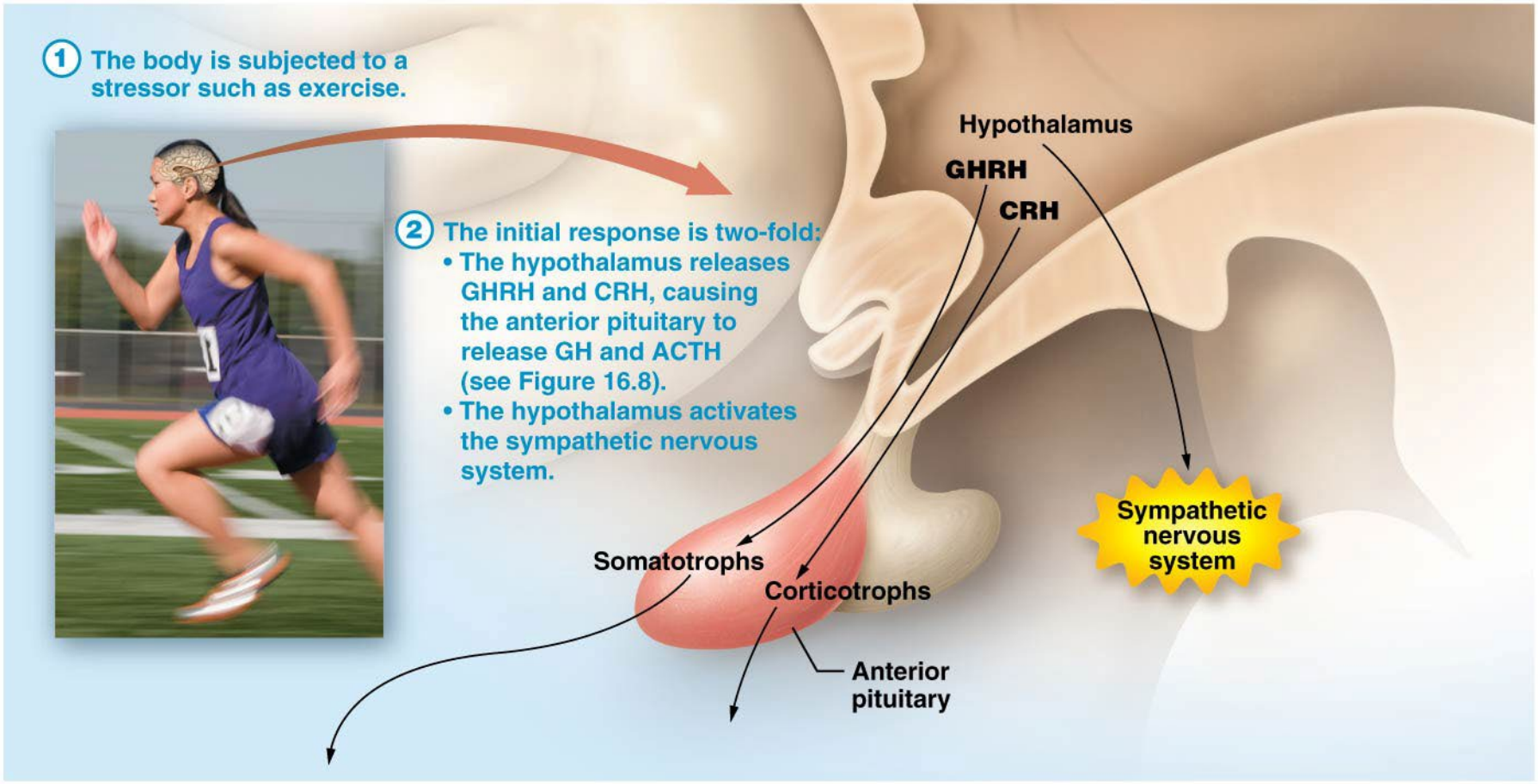
(b) Decreased plasma volume and increased plasma solute concentration: high ADH and aldosterone

Summary of endocrine control of fluid homeostasis.



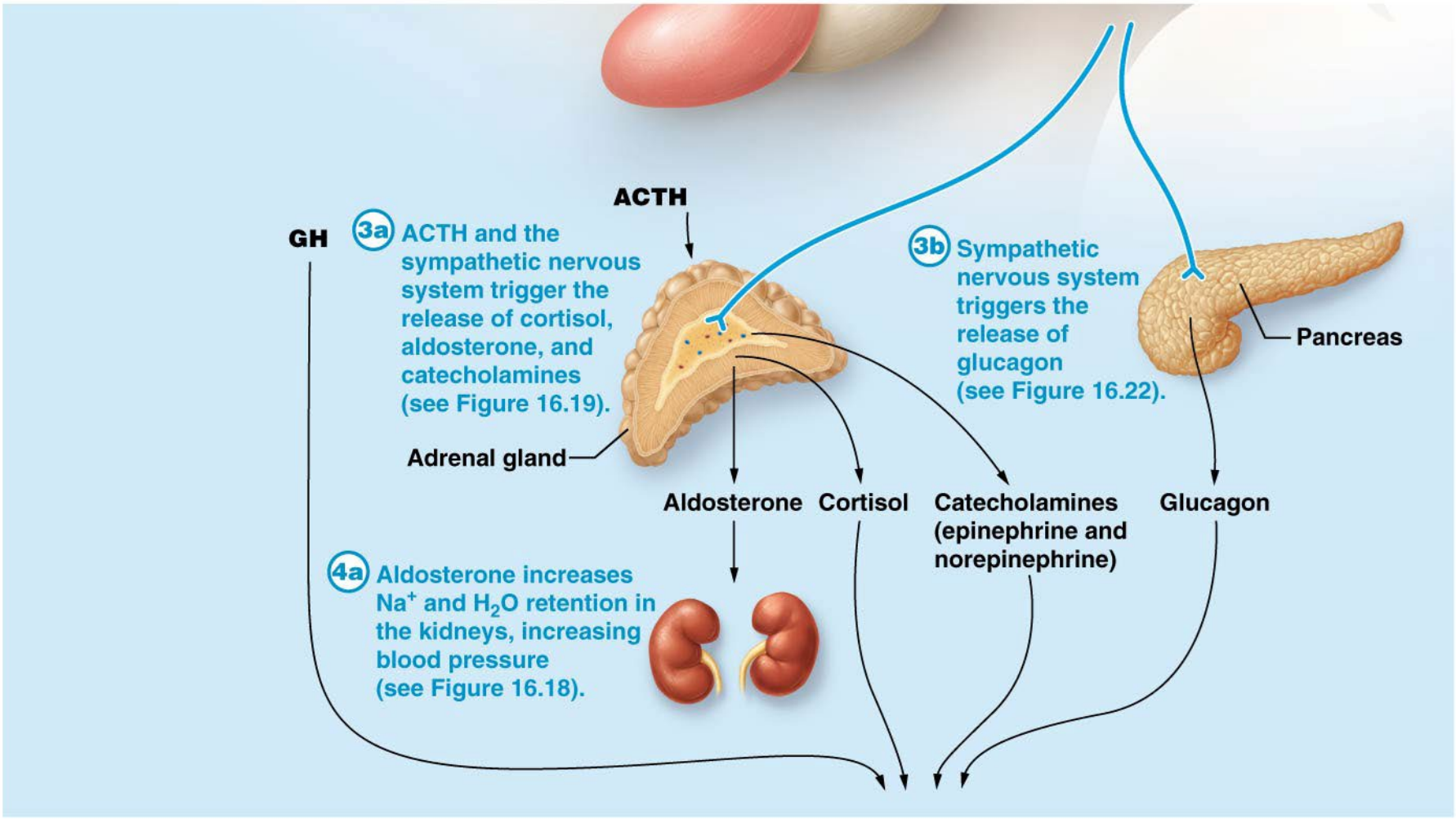
(c) Increased plasma volume and decreased plasma solute concentration: very low ADH and aldosterone, high ANP

The Big Picture of the Hormonal Response to Stress



See Next Two Slides

The Big Picture of the Hormonal Response to Stress



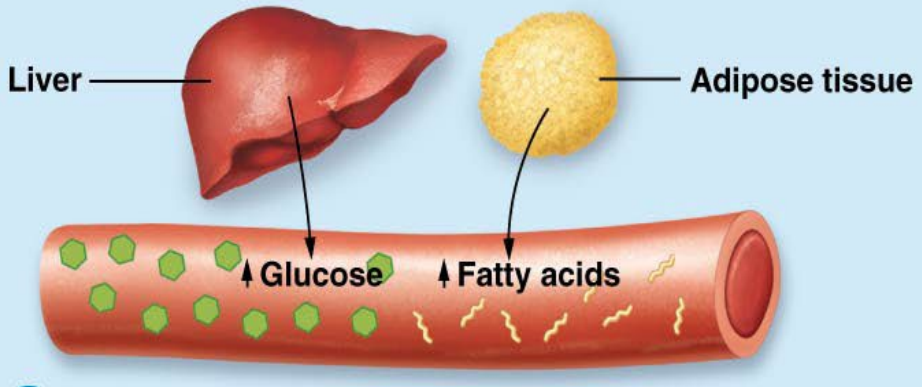
The Big Picture of the Hormonal Response to Stress

GHRH = Growth hormone–releasing hormone

CRH = Corticosteroid-releasing hormone

GH = Growth hormone

ACTH = Adrenocorticotropic hormone



4b GH, cortisol, catecholamines, and glucagon trigger an increased release of metabolic fuels from the liver and adipose tissue.