Endocrine Physiology

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Section 1:

General principles of endocrine physiology

Regulation of homeostasis

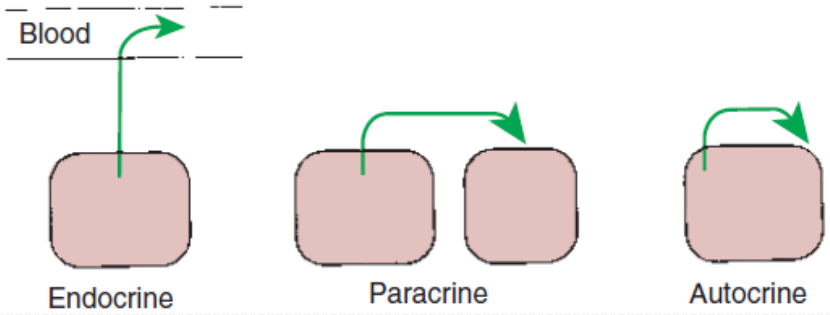
- Nerves
  - fast
  - governing
- Hormones
  - mainly metabolism, growth, differentiation, reproduction

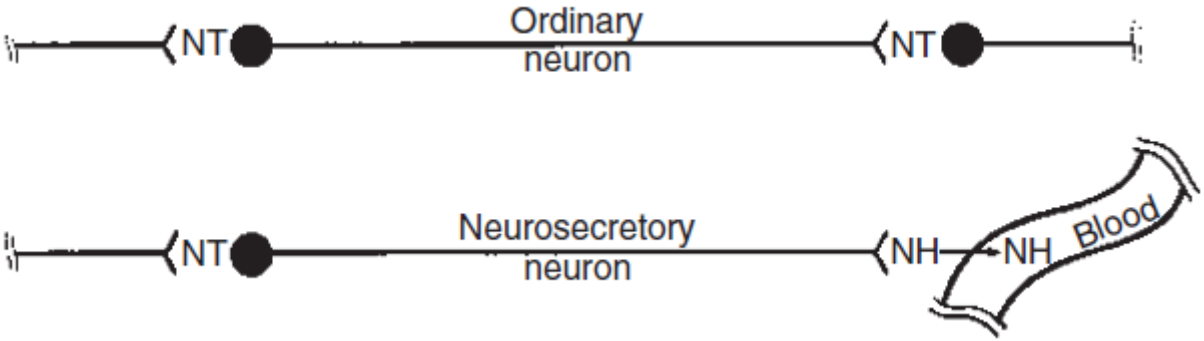
Hormone

- chemicals that are produced by specific endocrine organs, are transported by the vascular system and are able to affect distant target organs in low concentration
  - some substances, such as prostaglandins and somatomedins, are produced by many other tissues and are still considered hormones
- Stereotypical response (receptors)

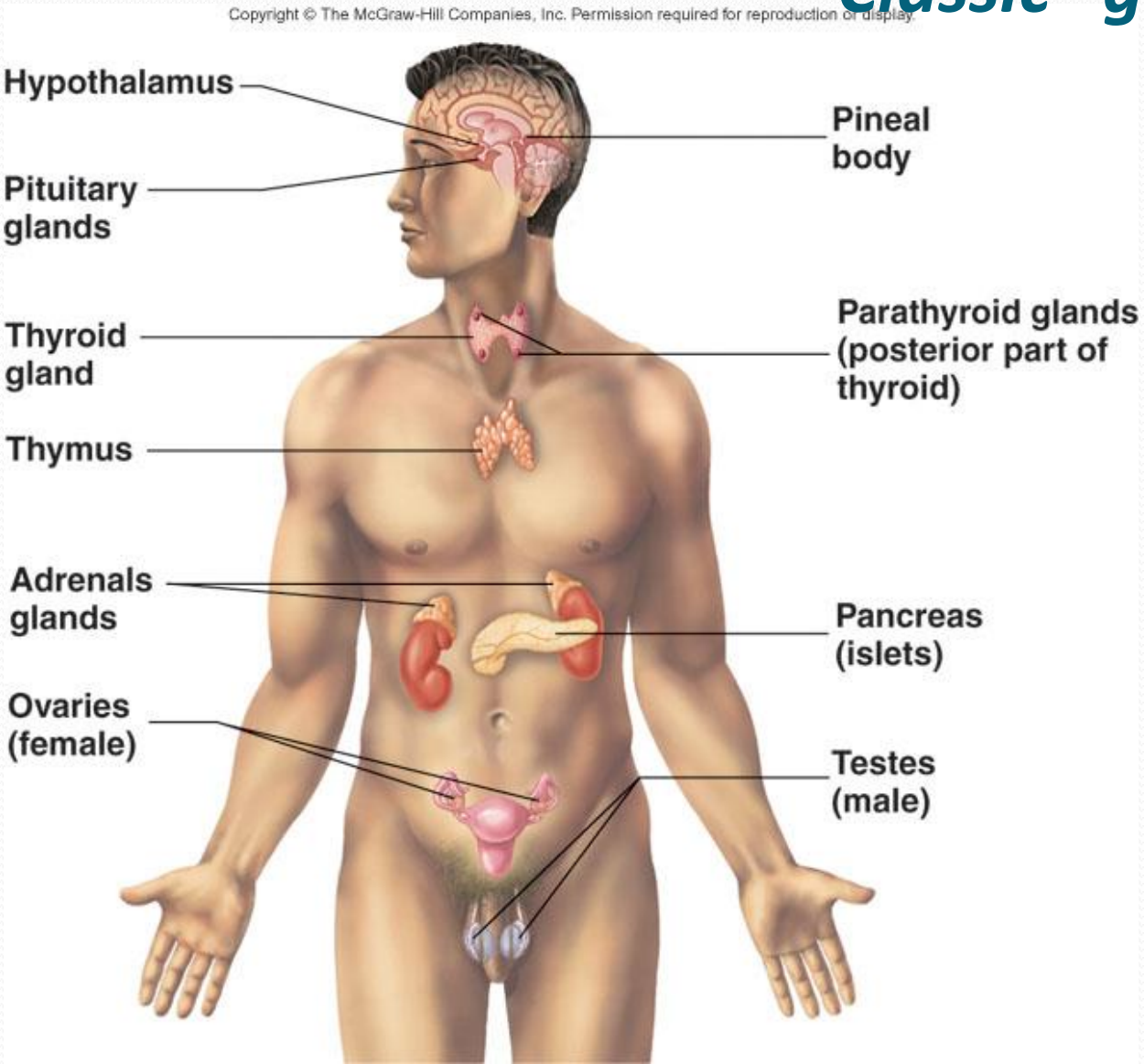
Types of hormonal signalization

- **Endocrine**
  - from gland via blood to a distance
- **Neurocrine**
  - via axonal transport and then via blood
- **Paracrine**
  - neighboring cells of different types
- **Autocrine**
  - neighboring cells of the same type or the secreting cell itself





Hormone production: "Classic" glands



Chemical characteristics of hormones

- Amines (from tyrosine)
  - Catecholamines from adrenal medullae (epinephrine and norepinephrine)
  - thyroid hormones (thyroxine and triiodothyronine)
- Peptides/proteins

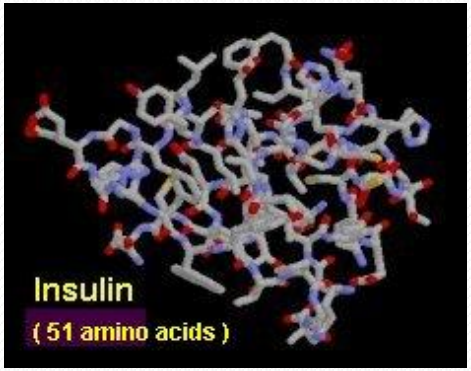
  anterior and posterior pituitary

  ADH, OT, TRH, SS, GnRH (peptides)

  PTH, GH, PRL (proteins)

  FSH, LH,TSH (glycoproteins)

  the pancreas (insulin and glucagon),



Chemical characteristics of hormones

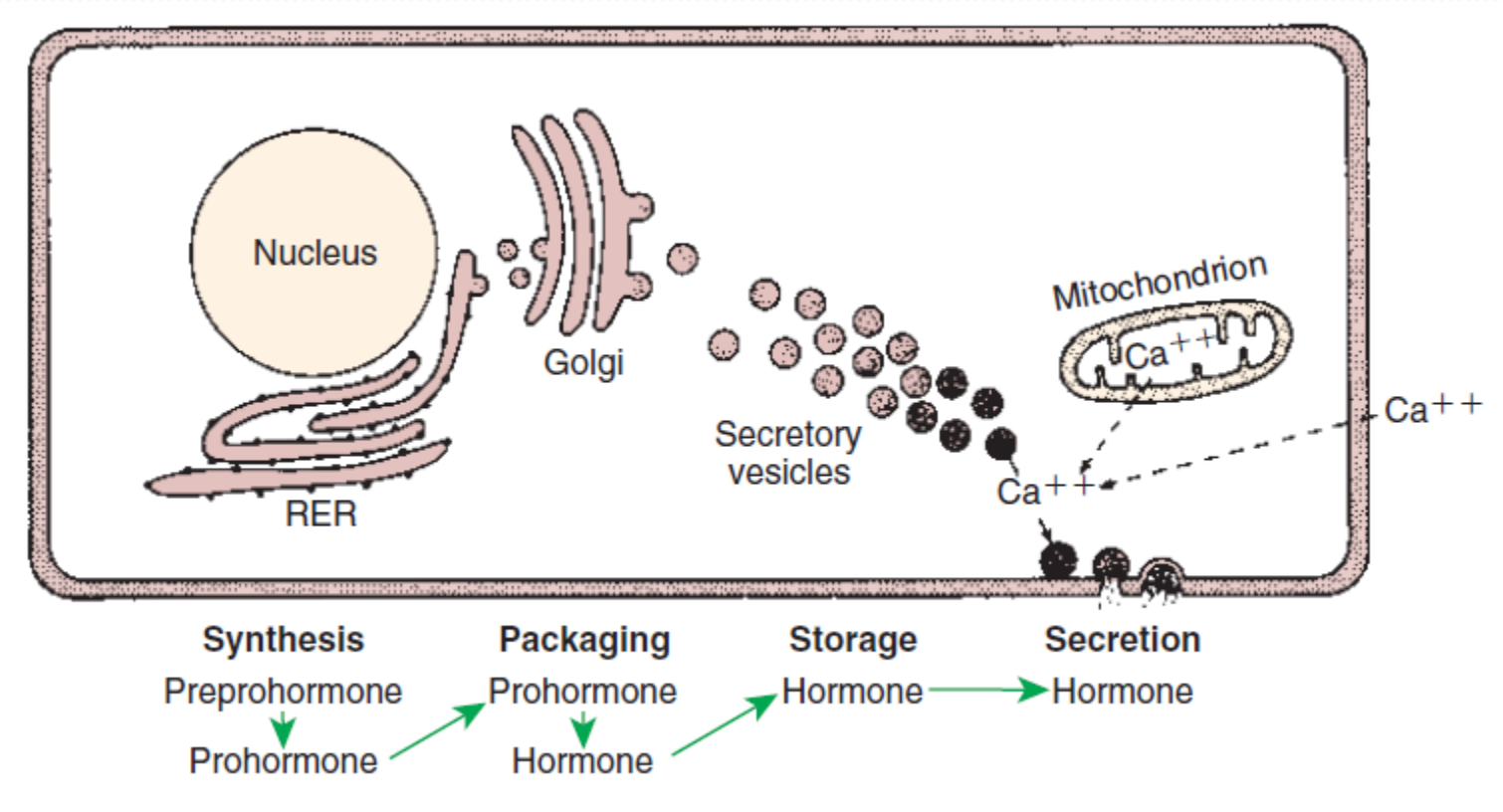
- Steroids (from cholesterol)
  - adrenal cortex (cortisol and aldosterone)
  - sex hormones

    the testes (testosterone),

    ovaries (estrogen and progesterone),

    placenta (estrogen and progesterone)

Synthesis of hormones



Subcellular components of peptide hormone synthesis and secretion.

Hormone release

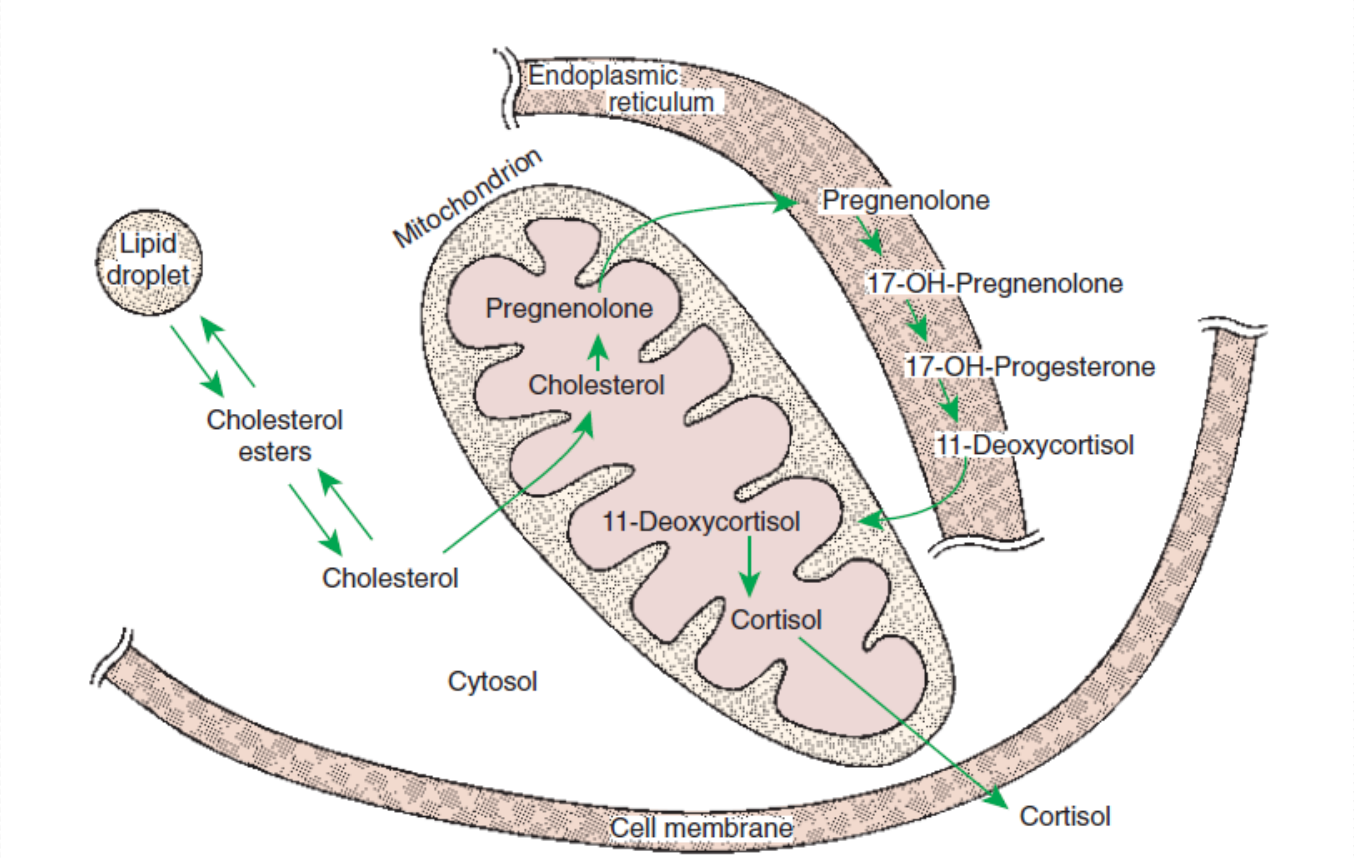
- Proteins & catecholamines:
  - secretory granules, exocytosis
    - for incorporation into granules often special sequences cleaved off in granules or after release
    - stimulus → ↑ $[Ca^{2+}]_i$ (influx, reticulum) → granules travel along microtubules towards cell membrane (kinesins, myosins) → fusion

Hormone release

- Thyroid hormones:
  - made as part of thyroglobulin
  - stored in folicles
  - T3 & T4 secreted by enzymatic cleavage

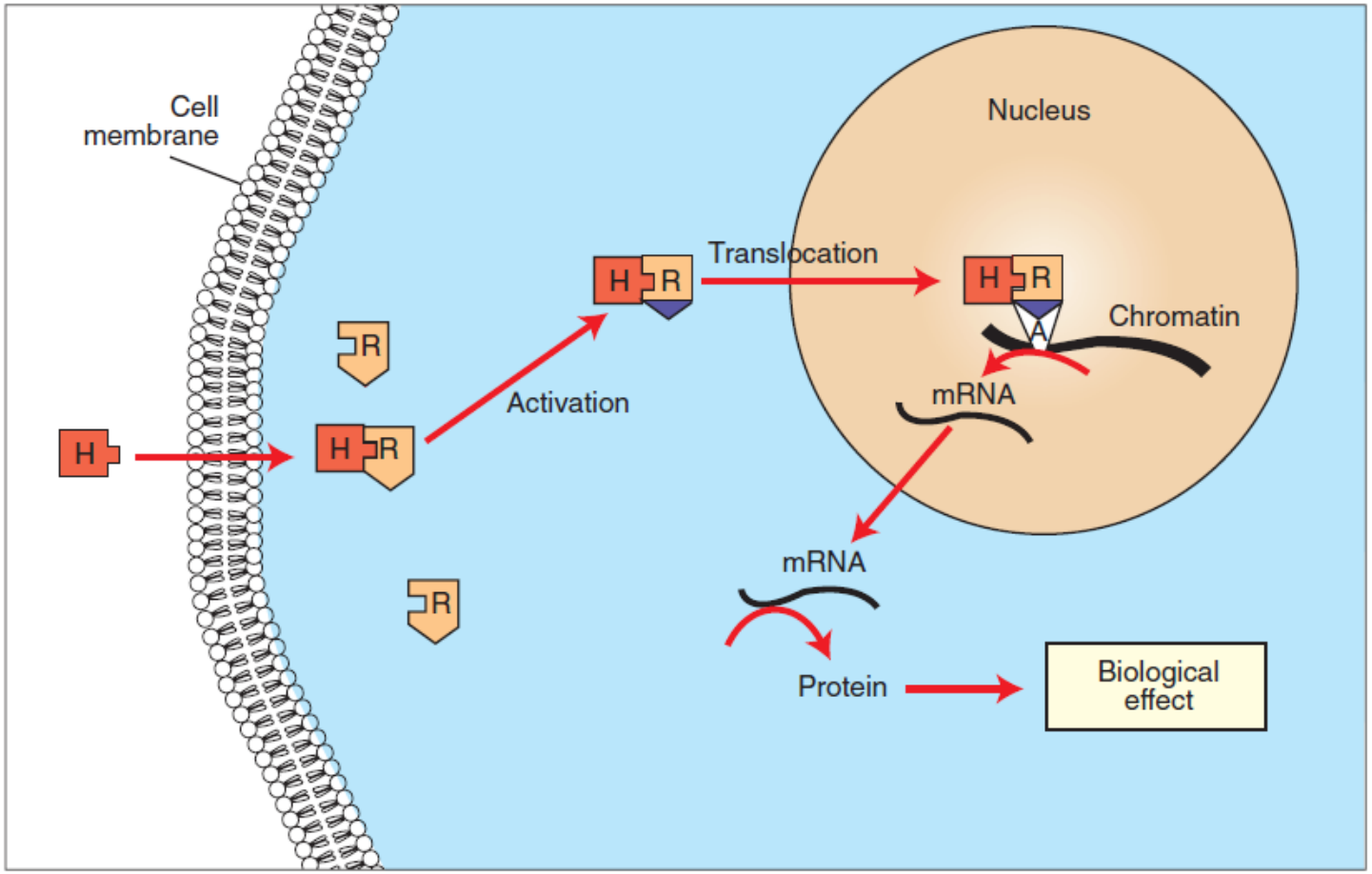
- Steroid hormones:
  - leave the cell across cell membrane right after synthesis (no storage)

Synthesis of hormones



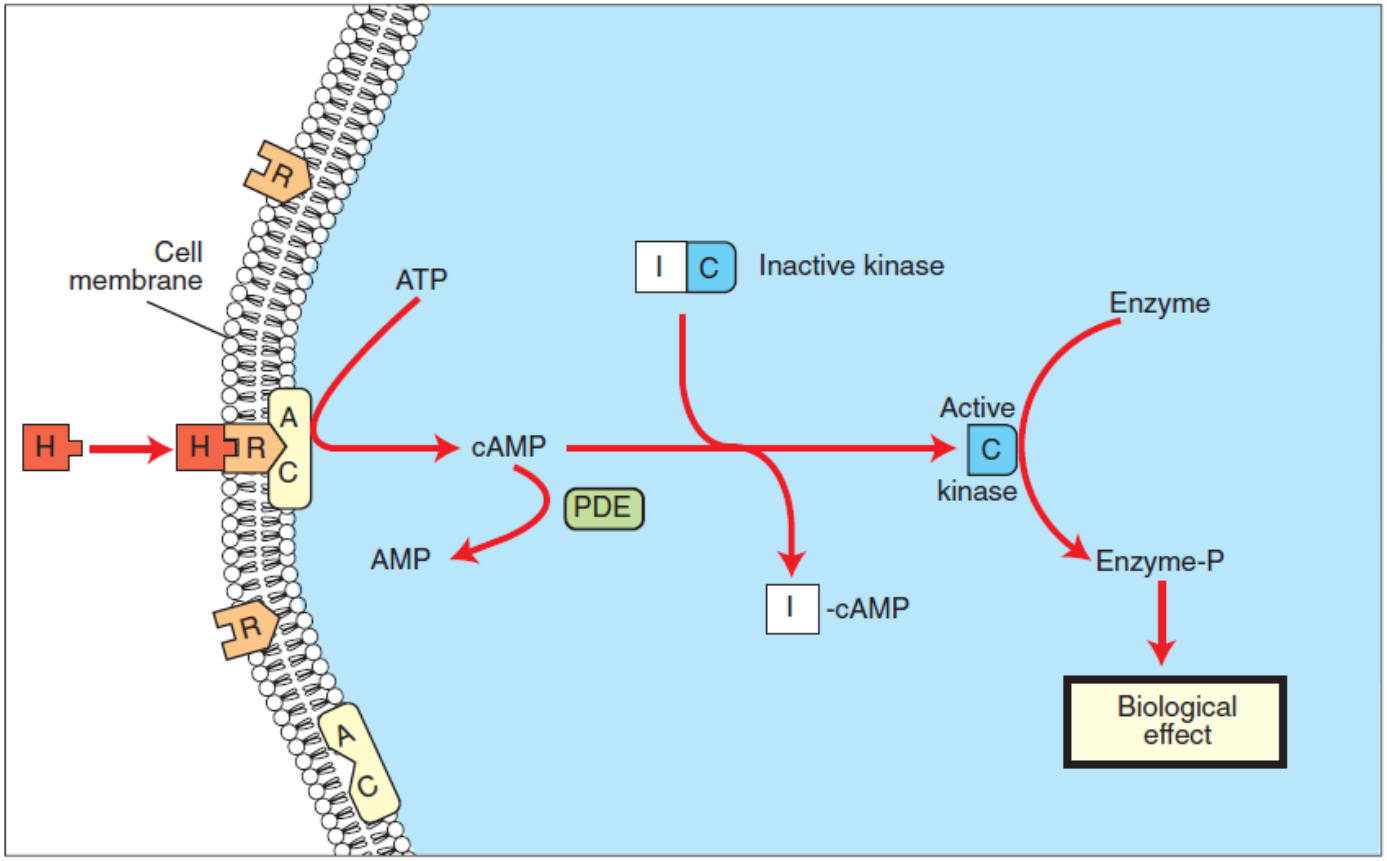
Subcellular compartmentalization of cortisol biosynthesis.

Postreceptor cell response to hormones



Subcellular mechanism of action of a lipophilic hormone *(H)* via an intracellular receptor *(R).* The H-R complex induces messenger ribonucleic acid *(mRNA)* synthesis by binding to an acceptor site *(A)* on the chromatin.

Postreceptor cell response to hormones

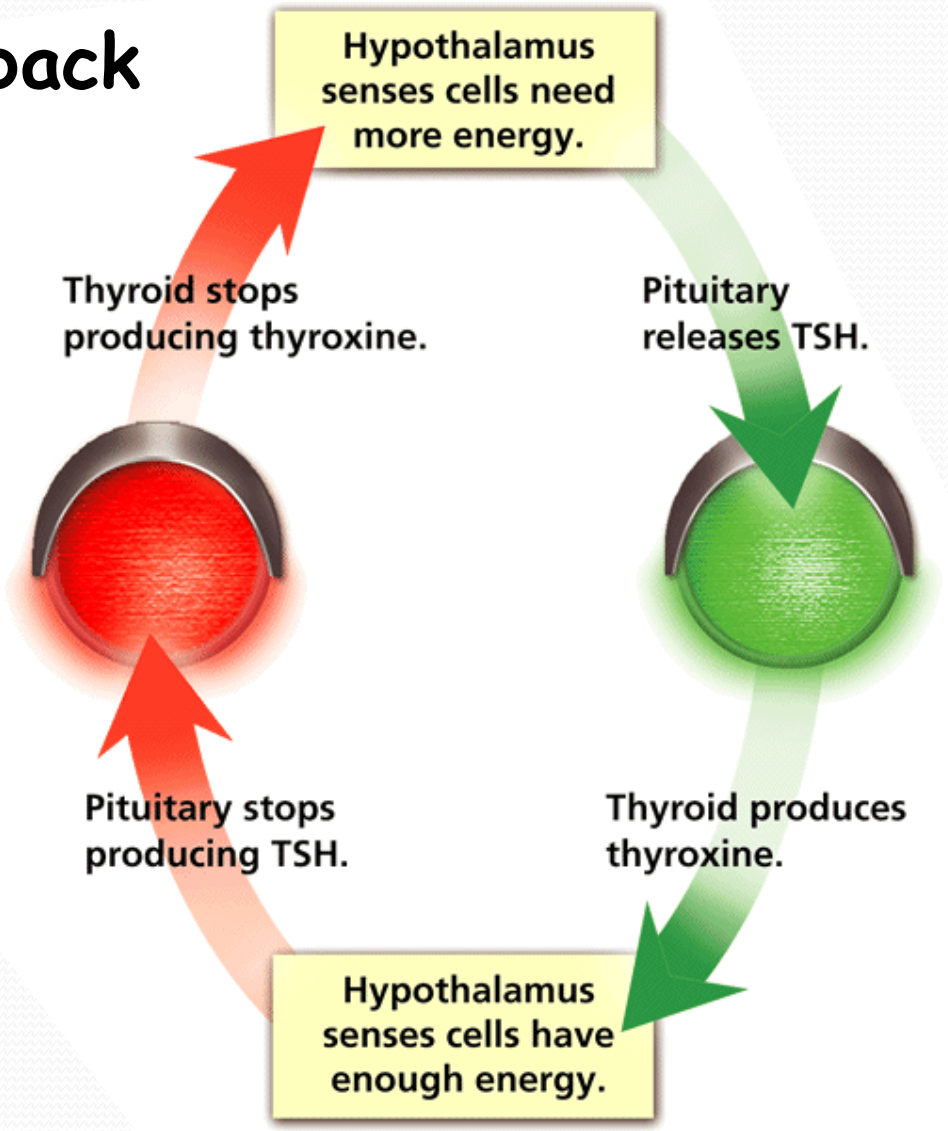


Subcellular mechanism of action of a hydrophilic hormone *(H)* via a membrane receptor *(R)* adenyl cyclase *(AC),* and cyclic adenosine monophosphate *(cAMP). ATP,* Adenosine triphosphate; *I* and *C,* inhibitory and catalytic subunits of the kinase, respectively; *PDE,* phosphodiesterase.

Regulation of hormone release

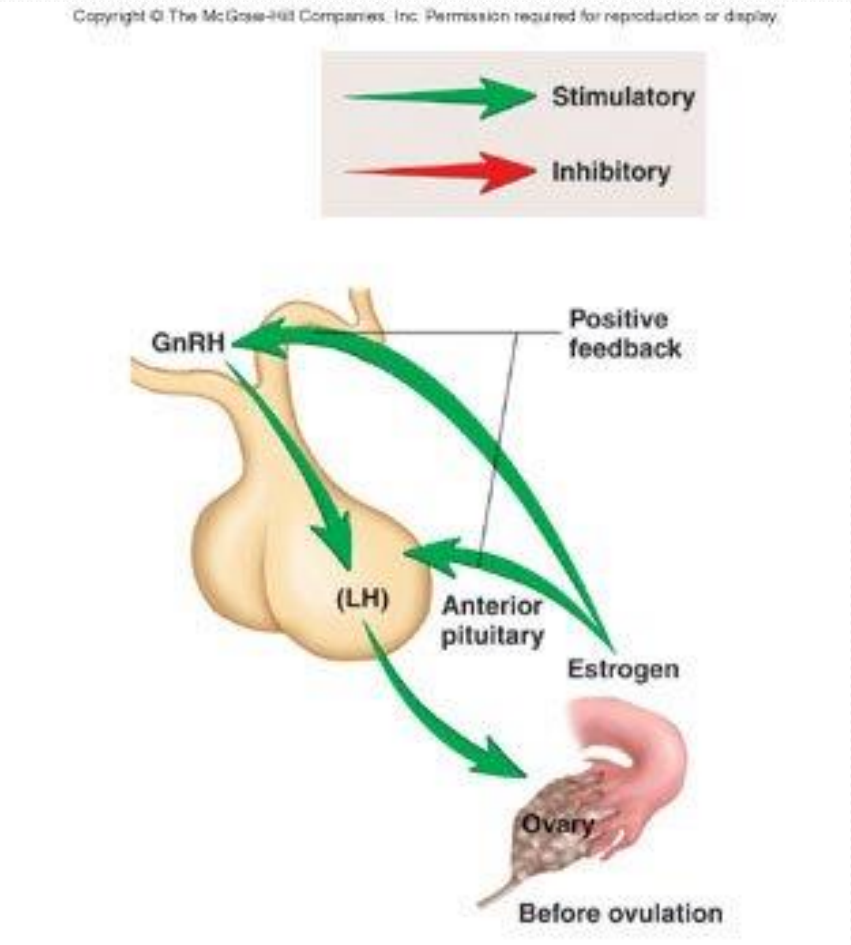
1. Negative feedback

Through negative feedback, when the amount of a particular hormone in the blood reaches a certain level, the endocrine system sends signals that stop the release of that hormone.



Regulation of hormone release

2. Positive feedback (only narrow dose range)

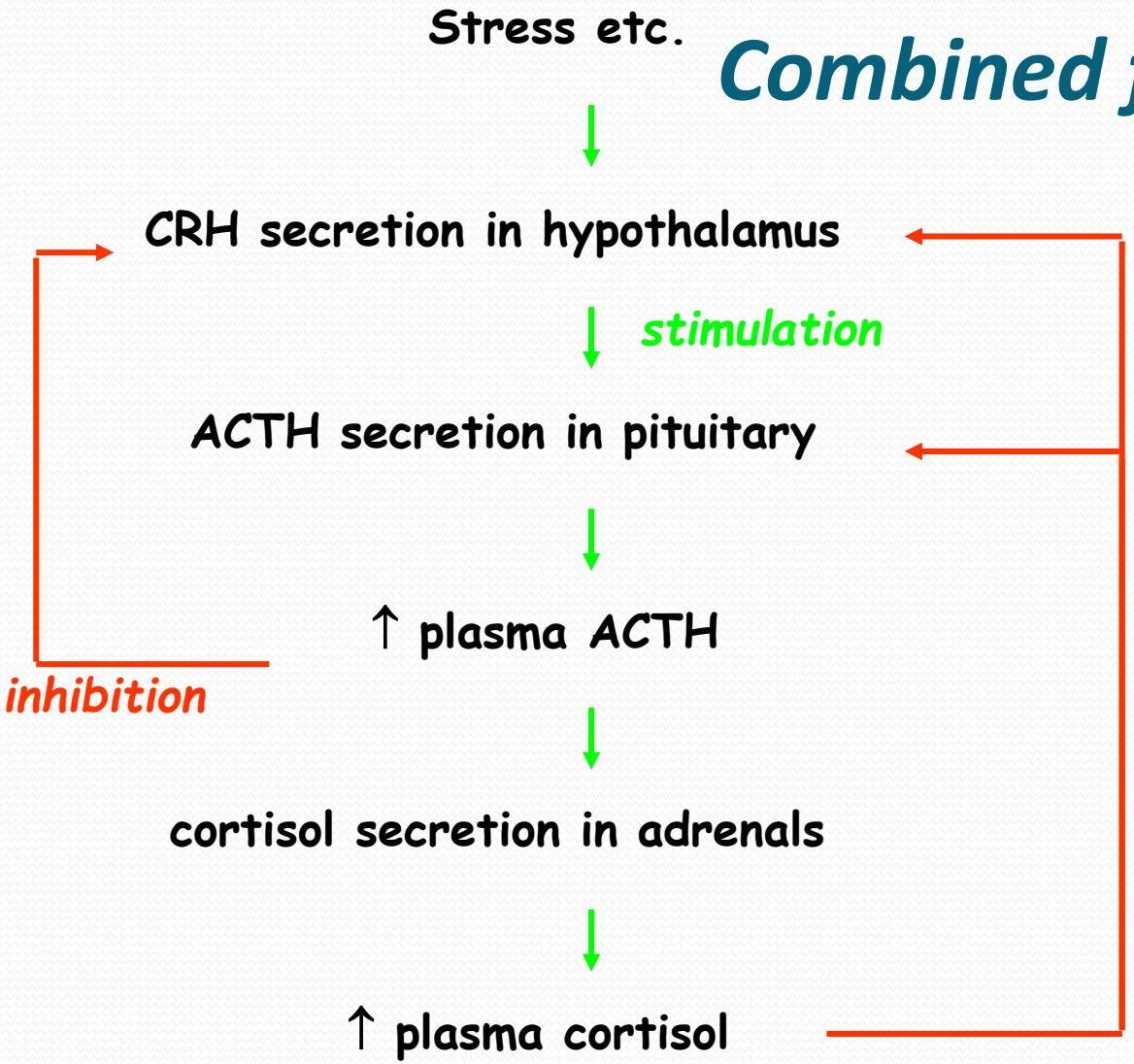


Regulation of hormone release

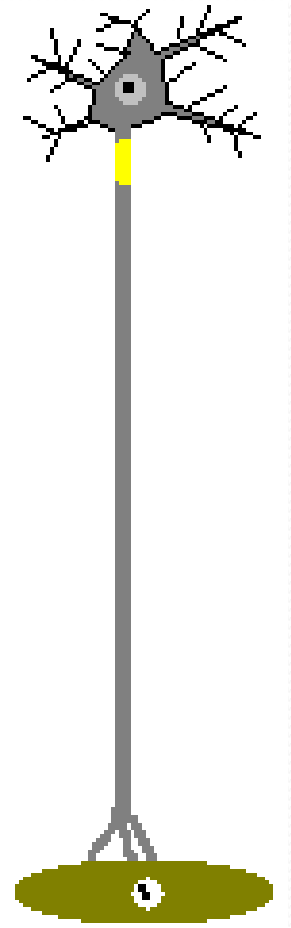
3. Nerve regulation

pain, emotions, sex, injury, stress,…
e.g. ↑ oxytocin with nipple stimulation

Combined feedback

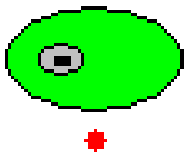


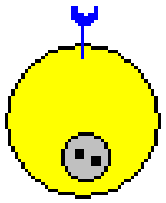
The Nervous System vs. Endocrine System



The nervous system exerts point-to-point control through nerves, similar to sending messages by conventional telephone. Nervous control is electrical in nature and fast.

The Nervous System vs. Endocrine System

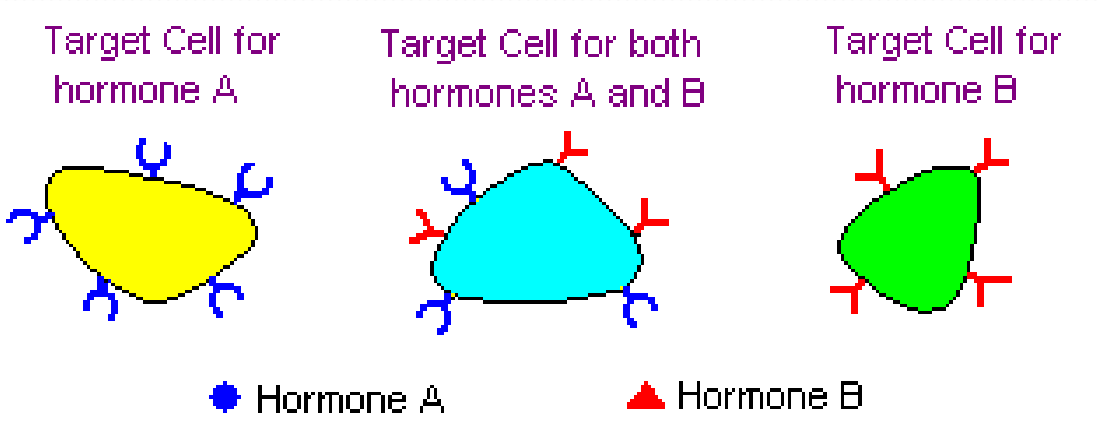




The endocrine system broadcasts its hormonal messages to essentially **all cells** by secretion into blood and fluid that surrounds cells. Like a radio broadcast, it requires a receiver to get the message - in the case of endocrine messages, cells must bear a *receptor* for the hormone being broadcast in order to respond.

The Nervous System vs. Endocrine System

Most hormones circulate in blood, coming into contact with essentially all cells. However, **a given hormone usually affects only a limited number of cells, which are called target cells. A target cell responds to a hormone because it bears receptors for the hormone.**



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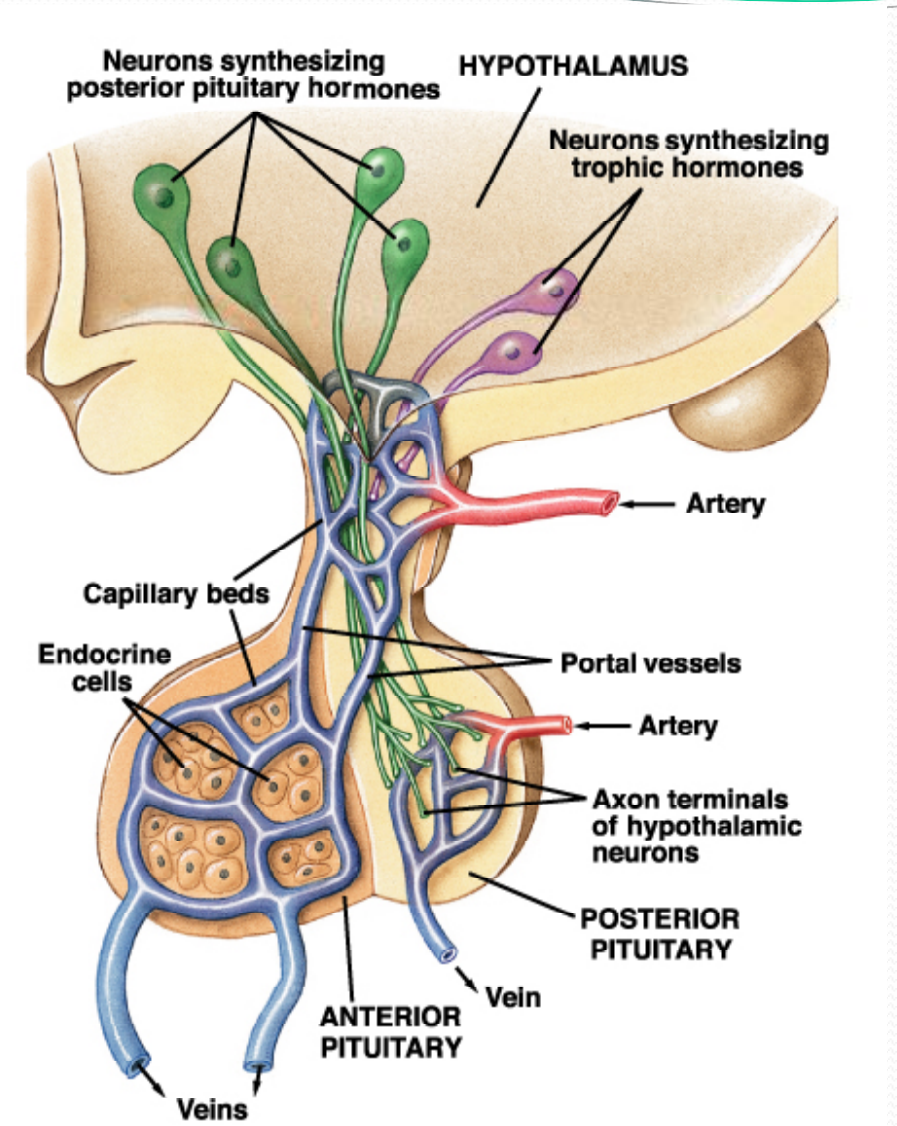
HOW DO YOUR HORMONES WORK?

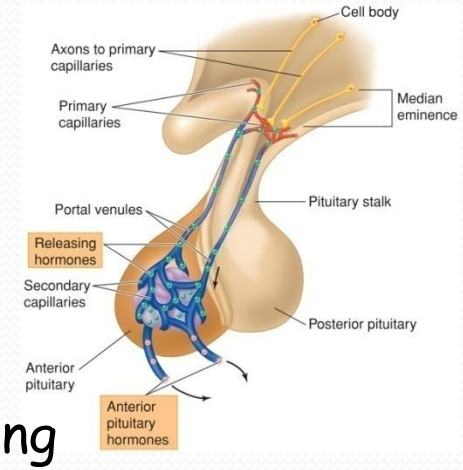
Section 2:

The hypothalamus-hypophysis axis



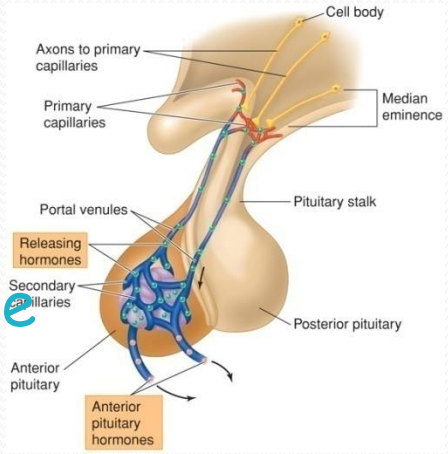
Anatomical and Functional Connection Between the Hypothalamus and Pituitary (hypothalamo- hypophyseal portal system and tract)

Hypothalamus as a gland



- Corticotropin-releasing hormone (CRH) - Stimulates secretion of ACTH (adrenocorticotropic hormone)
- Gonadotropin-releasing hormone (GnRH) Stimulates secretion of FSH (follicle-stimulating hormone) and LH (luteinizing hormone)
- Thyrotropin-releasing hormone (TRH)- stimulates secretion of TSH (thyroid-stimulating hormone)
- Melanocyte-stimulating hormone release inhibiting factor (MIF)-inhibits secretion of MSH (Melanocyte-stimulating hormone)

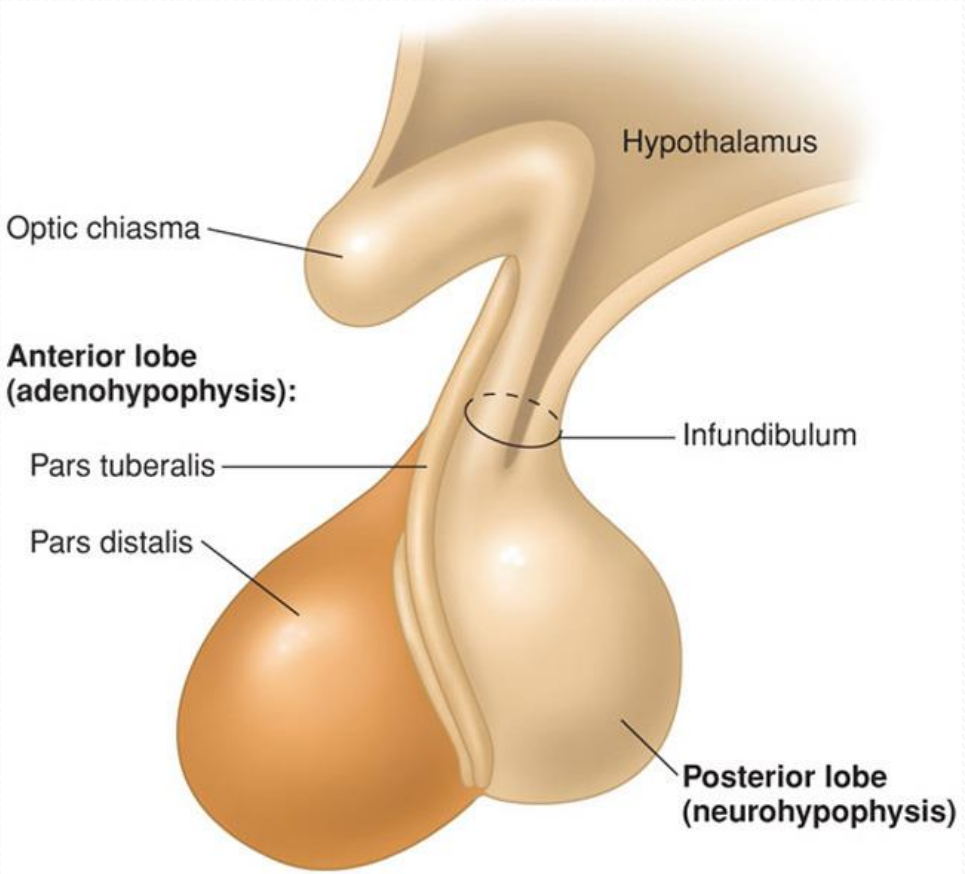
Hypothalamus as a gland



- Melanocyte-stimulating hormone releasing factor (MRF)-stimulate secretion of MSH
- Growth hormone release inhibiting hormone (GHRIH) or Somatostatin (SS) – inhibits secretion of growth hormone
- Growth hormone-releasing hormone (GHRH)- stimulates growth hormone secretion
- Prolactin-inhibiting factor (PIF)- inhibits prolactin secretion
- Prolactin-releasing factor (PRF)-stimulates prolactin secretion

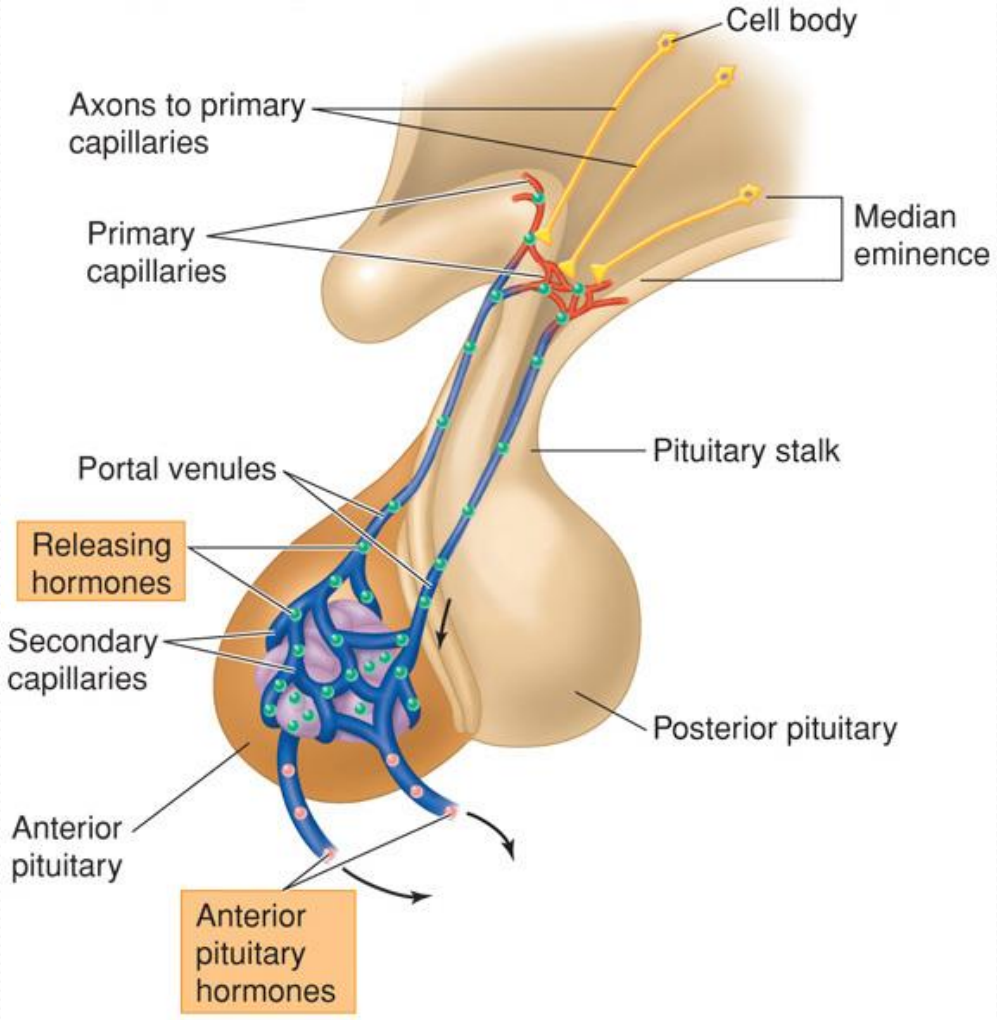
Pituitary gland

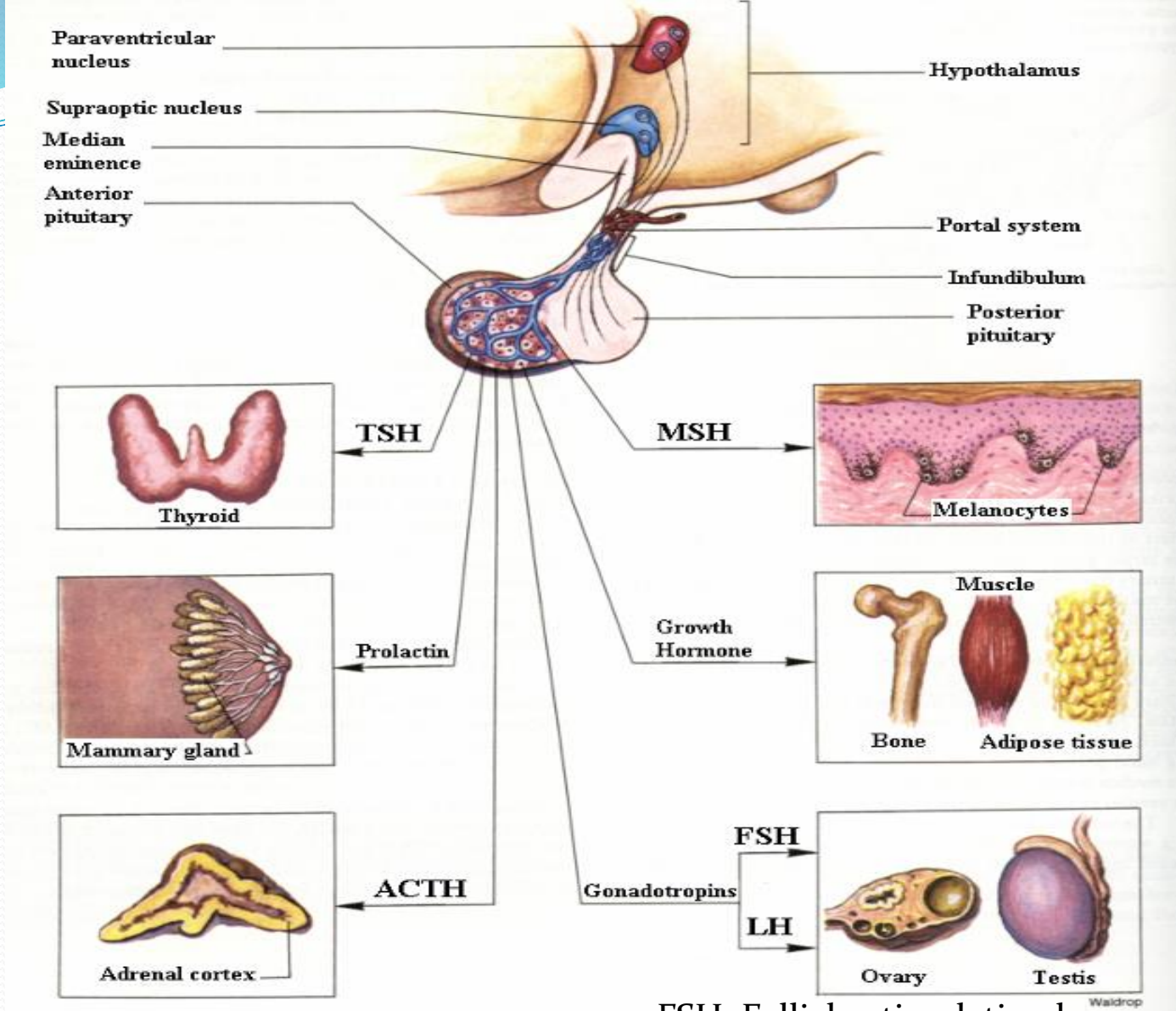
- Structurally & functionally divided into anterior and posterior lobes
- Hangs below hypothalamus by infundibulum
- Anterior produces own hormones
  - Controlled by hypothalamus
- Posterior stores and releases hormones made in hypothalamus



Anterior pituitary

- Releasing and inhibiting hormones from hypothalamus
  - released from axon endings into capillary bed in median eminence
  - Carried by **hypothalamo-hypophyseal portal system**
  - to another capillary bed
  - Diffuse into and regulate secretion of anterior pituitary hormones





TSH, Thyroid stimulating hormone

ACTH, Adrenocorticotropin hormone

FSH, Follicle-stimulating hormone

LH, Luteinizing hormone

MSH, Melanophore-stimulating hormone

Anterior pituitary

- Growth hormone (GH) promotes growth, protein synthesis, and movement of amino acids into cells
- Thyroid stimulating hormone (TSH) stimulates thyroid to produce and secrete T_4 and T_3
- Adrenocorticotrophic hormone (ACTH) stimulates adrenal cortex to secrete cortisol, aldosterone
- Follicle stimulating hormone (FSH) stimulates growth of ovarian follicles and sperm production
- Luteinizing hormone (LH) causes ovulation and secretion of testosterone in testes
- Prolactin (PRL) stimulates milk production by mammary glands

Anterior pituitary

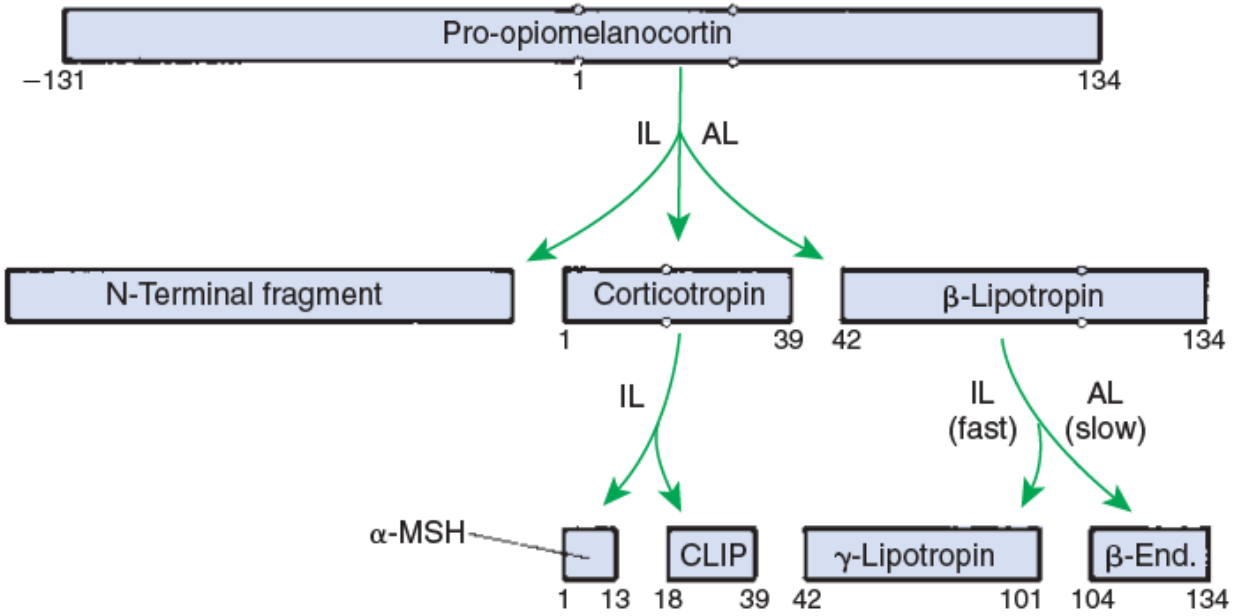
- GH and PRL are single-chain proteins that contain two and three disulfide bonds, respectively.
- There is overlap of activity between GH and PRL; this overlap is based on the approximately 50% homology of their amino acid sequences.
- Of these two major somatomammotropins, GH is uniquely species specific as to its activity.

Hormone	Abbreviations
Glycoproteins	
Follicle-stimulating hormone	FSH
Luteinizing hormone (interstitial cell–stimulating hormone)	LH (ICSH)
Thyroid-stimulating hormone (thyrotropin)	TSH
Somatotropins	
Growth hormone (somatotropin)	GH
Prolactin	PRL
Pro-opiomelanocortins	
β-Lipotropin	
Corticotropin (adrenocorticotropic hormone)	ACTH

Anterior pituitary

- TSH, produced by thyrotropes, and FSH and LH, produced by gonadotropes, are classified as glycoproteins because all three molecules have carbohydrate moieties.
- These hormones have α and β subunits that are linked by noncovalent binding.
  - The α subunits are identical (and interchangeable) among the three glycoproteins.
  - The β subunits, unique for each hormone, impart the specific action of each hormone.
- Other members of this family of hormones that are not of anterior pituitary origin include equine chorionic gonadotropin (also called pregnant mare's serum gonadotropin, PMSG) and primate chorionic gonadotropin or hCG, which are produced by cells of the placental chorion.

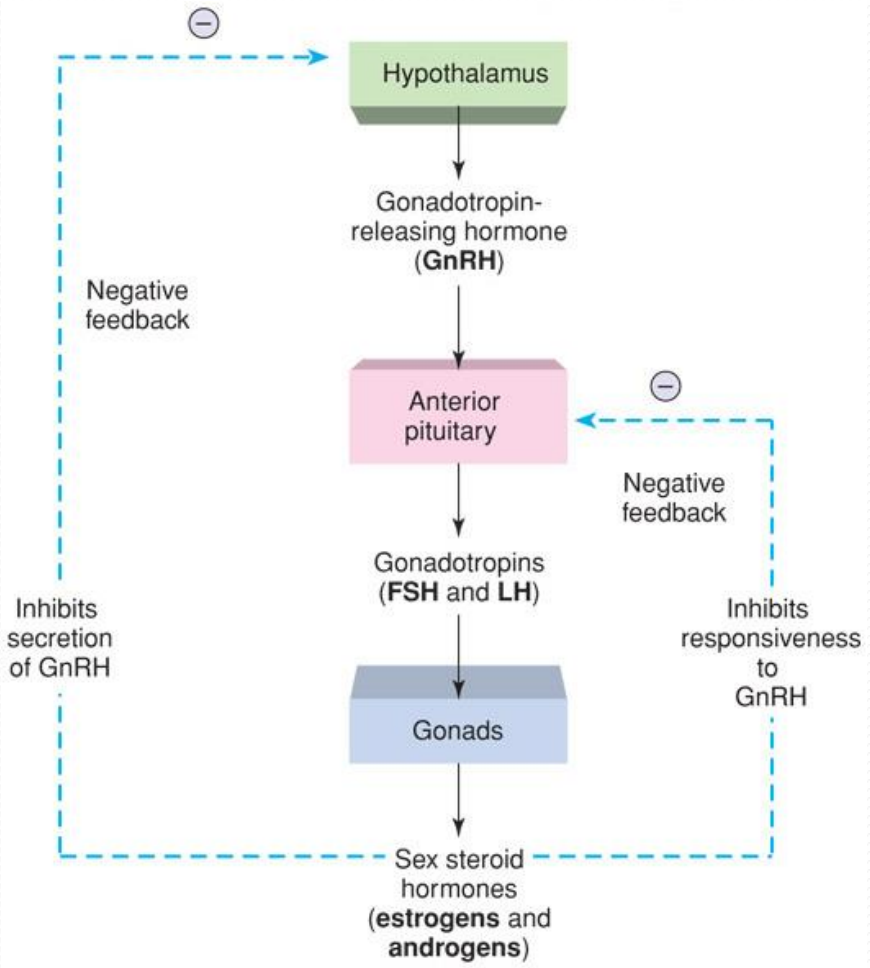
Anterior pituitary



Cleavage of pro-opiomelanocortin to yield corticotropin and related peptides. By convention, the numbering of the amino acids begins with the first one of corticotropin and then increases positively toward the carboxy terminal and negatively toward the amino terminal. Cleavage occurs at pairs of basic amino acids indicated by the circles. AL, Anterior lobe; α-MSH, alpha-melanocyte–stimulating hormone; β-End, beta-endorphin; CLIP, corticotropinlike intermediate lobe peptide; IL, intermediate lobe.

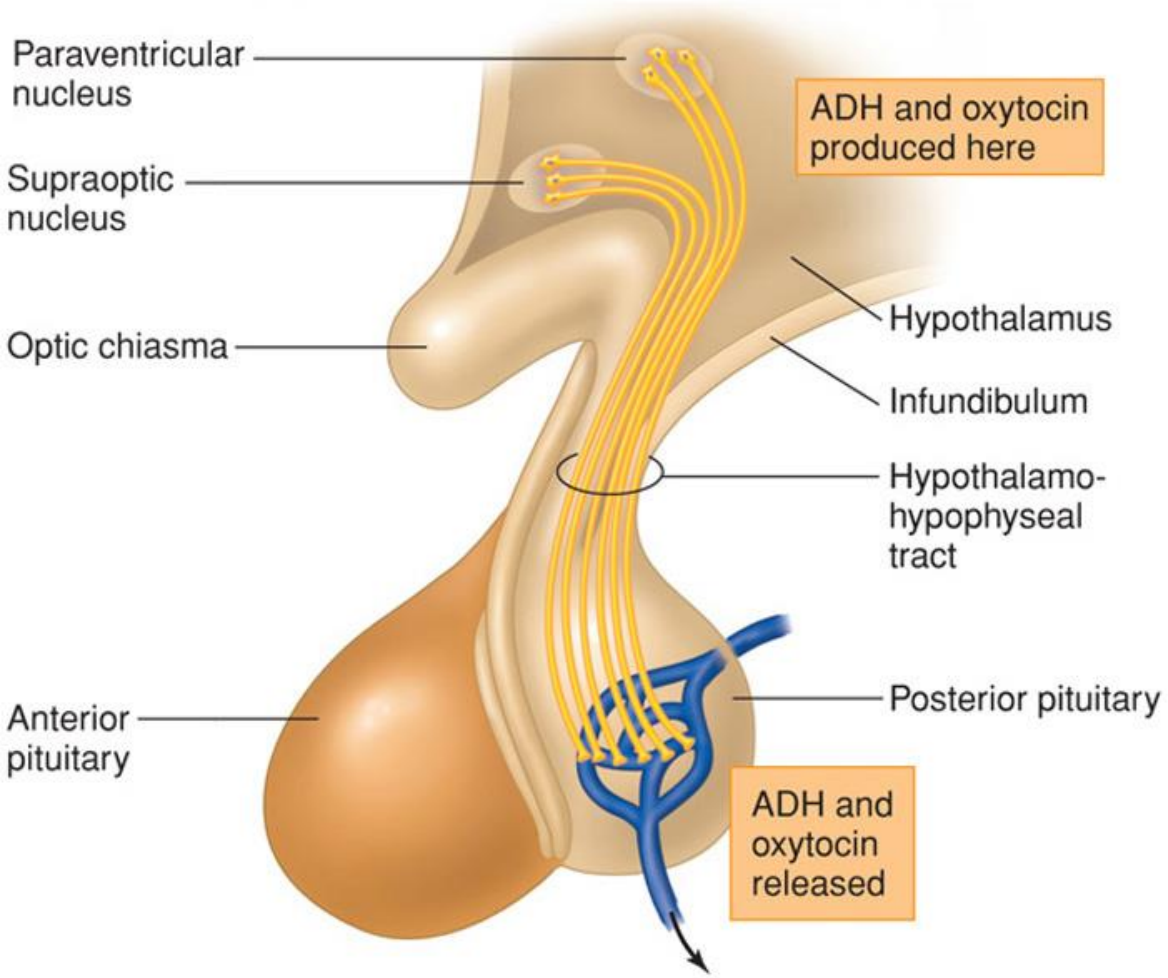
Anterior pituitary

- The hypothalamic-pituitary-gonad axis (control system)
- Involves short feedback loop
  - retrograde flow of blood and hormones back to hypothalamus
  - inhibits secretion of releasing hormone
- Involves negative feedback of target gland hormones
- And during menstrual cycle, estrogen stimulates "LH surge" by positive feedback



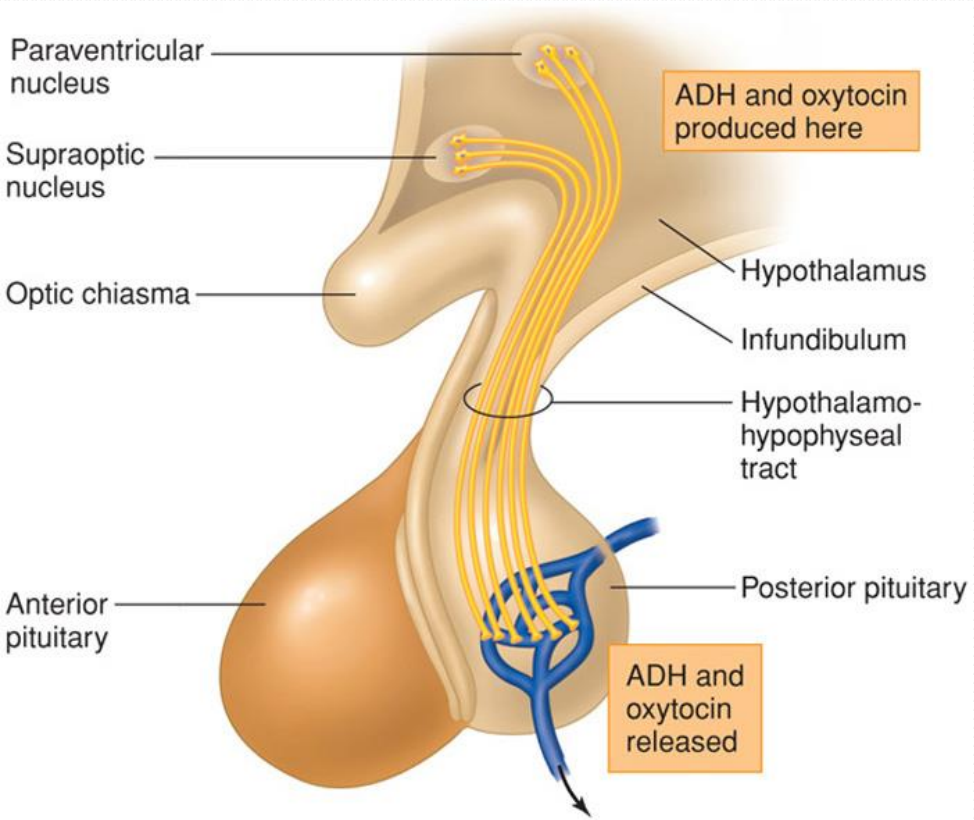
Posterior pituitary

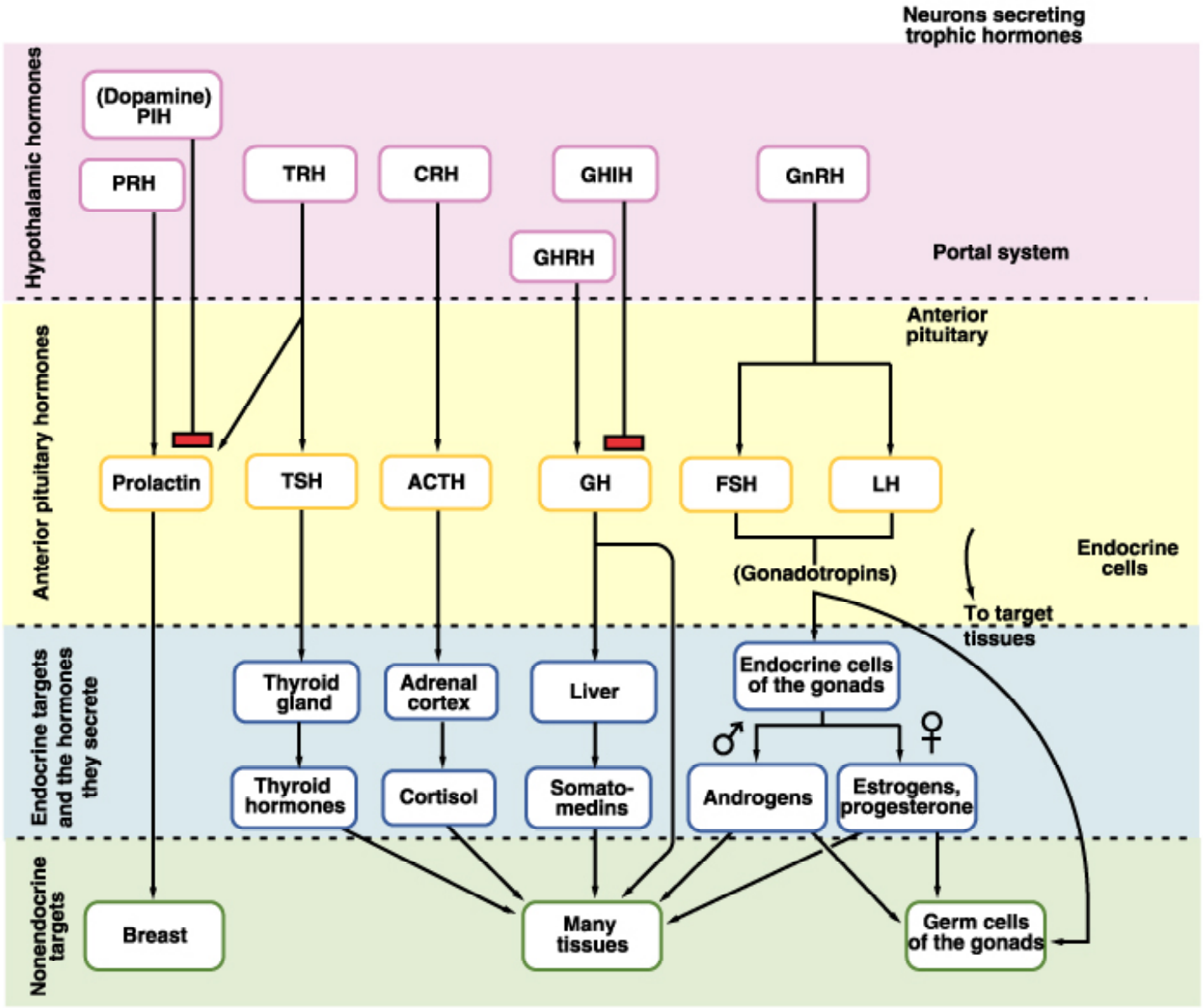
- Stores and releases vasopressin (ADH) and oxytocin
  - hormones made in the hypothalamus



Posterior pituitary

- Stores and releases 2 hormones produced in hypothalamus
- Antidiuretic hormone (ADH/vasopressin) which promotes H_2O conservation by kidneys
- Oxytocin which stimulates contractions of uterus during parturition
  - And contractions of mammary gland alveoli for milk-ejection reflex




Neurons secreting trophic hormones
Hypothalamic hormones
(Dopamine) PIH
PRH
TRH
CRH
GHIH
GnRH
GHRH
Portal system
Anterior pituitary
Anterior pituitary hormones
Prolactin
TSH
ACTH
GH
FSH
LH
(Gonadotropins)
Endocrine cells
To target tissues
Endocrine targets and the hormones they secrete
Thyroid gland
Adrenal cortex
Liver
Endocrine cells of the gonads
Thyroid hormones
Cortisol
Somato-medins
Androgens
Estrogens, progesterone
Nonendocrine targets
Breast
Many tissues
Germ cells of the gonads

Section 3:

The Growth Hormone

Growth Hormone

1.Physiological effects on growth

- stimulates cell division, especially in muscle and epiphyseal cartilage of long bones.
- The result is muscular growth as well as linear growth
- GH also stimulates growth in several other tissues:

skeletal muscle, heart, skin, connective tissue, liver, kidney, pancreas, intestines, adrenals and parathyroids.

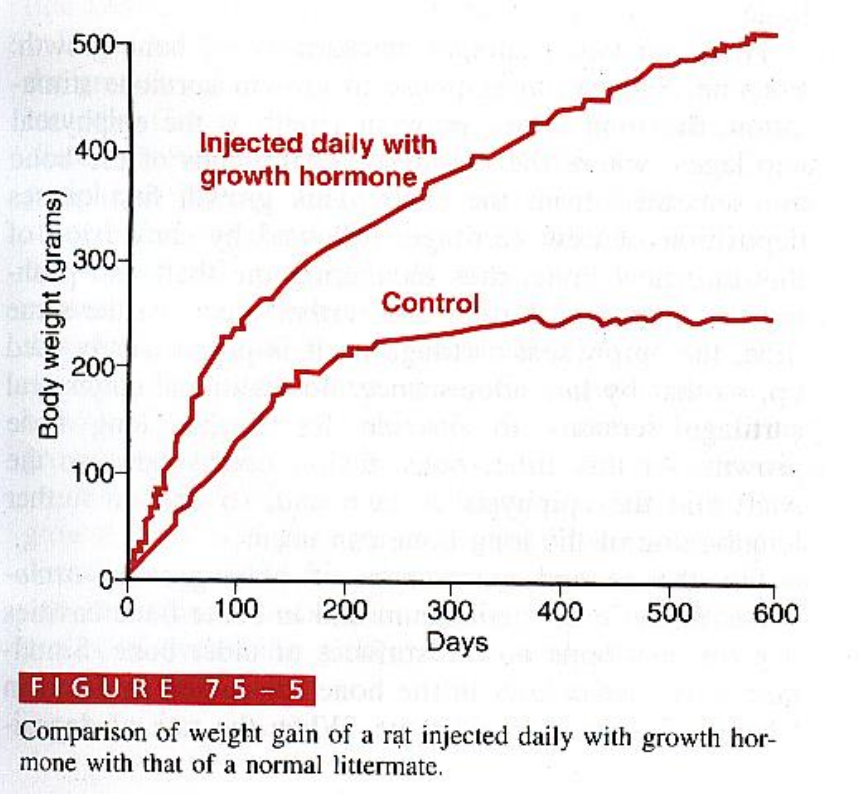


FIGURE 75–5

Comparison of weight gain of a rat injected daily with growth hormone with that of a normal littermate.

Growth Hormone

- Growth Hormone Excess
  - Hyposecretion of GH results in **dwarfism** during childhood.
  - in childhood leads to GIGANTISM
  - in adulthood leads to ACROMEGALY

2) Metabolic effects of GH

A, On Protein metabolism

- Enhance amino acid transport to the interior of the cells and increase RNA translation and nuclear transcription of DNA to form mRNA, and so increase rate of protein synthesis.
- GH also reduces the breakdown of cell proteins by decreasing catabolism of protein.

Growth Hormone

B, On fat metabolism

- Cause release of fatty acids from adipose tissue and then increasing the concentration of fatty acids.
- Therefore, utilization of fat is used for providing energy in preference to both carbohydrates and proteins.

Growth Hormone

C. On glucose metabolism

- Decreases cellular uptake of glucose and glucose utilization,
- leads to increase of the blood glucose concentration.

Growth Hormone

3) Regulation of GH secretion

The plasma concentration of GH changes with age. 5 – 20 years old, 6ng/ml; 20 – 40 years old, 3ng/ml; 40 –70 years old, 1.6ng/ml.

The change of GH concentration within one day.

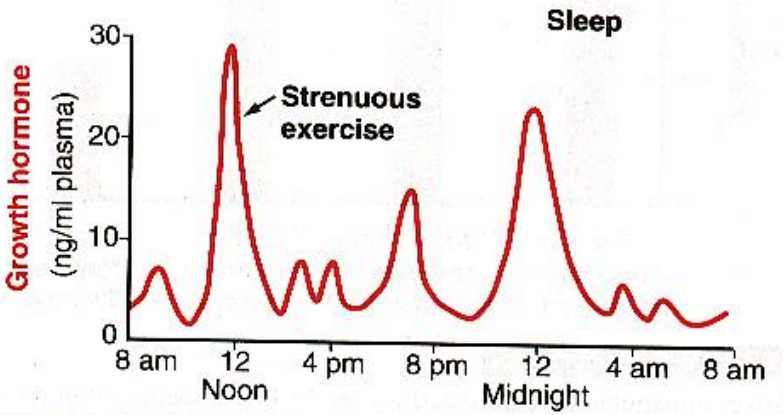
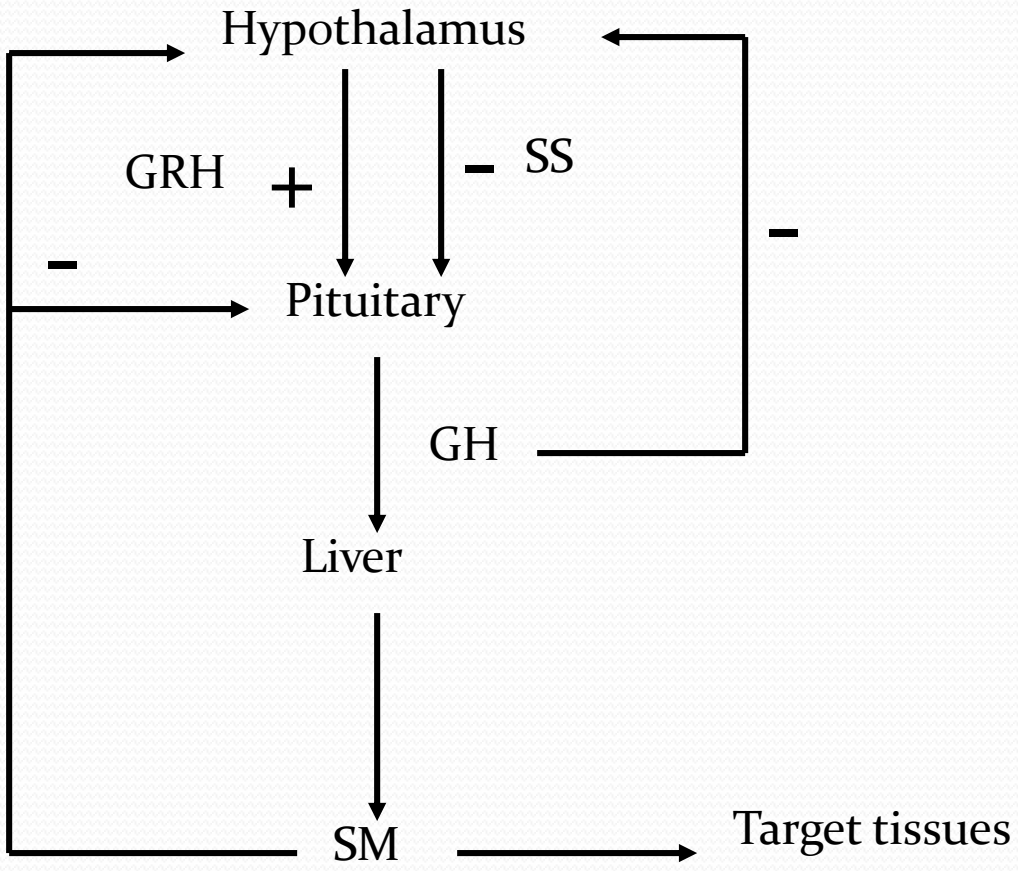


FIGURE 75–6

Typical variations in growth hormone secretion throughout the day, demonstrating the especially powerful effect of strenuous exercise and also the high rate of growth hormone secretion that occurs during the first few hours of deep sleep.

Growth Hormone

3) Regulation of GH secretion



Growth Hormone

- Other factors that affect the GH secretion

A, Starvation, especially with severe protein deficiency

B, Hypoglycemia or low concentration of fatty acids in the blood

C, Exercise

D, Excitement

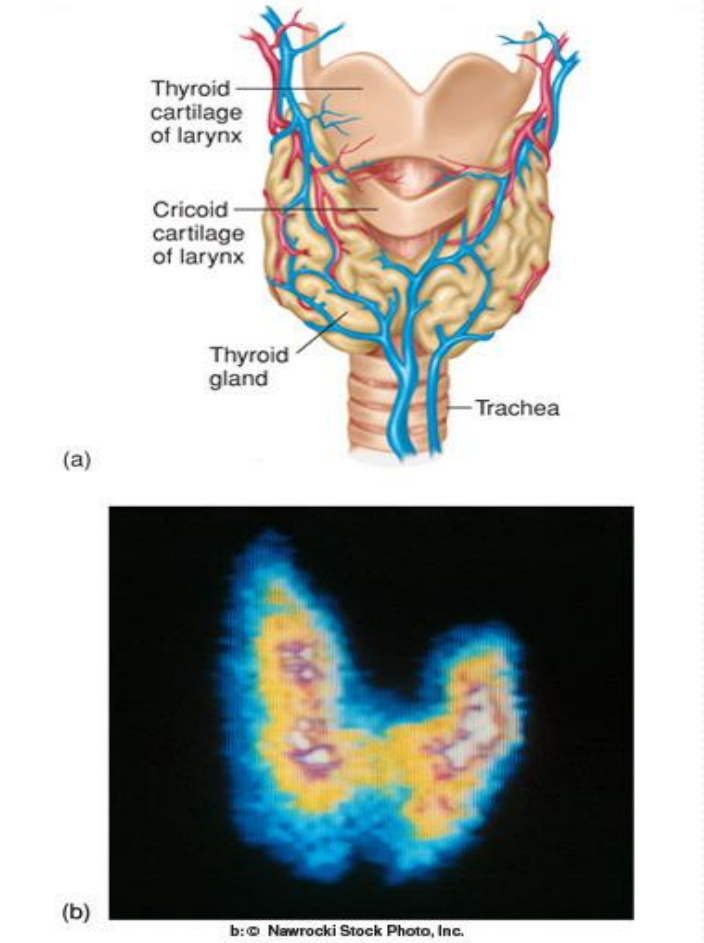
E, Trauma

Section 4:

Thyroid Gland

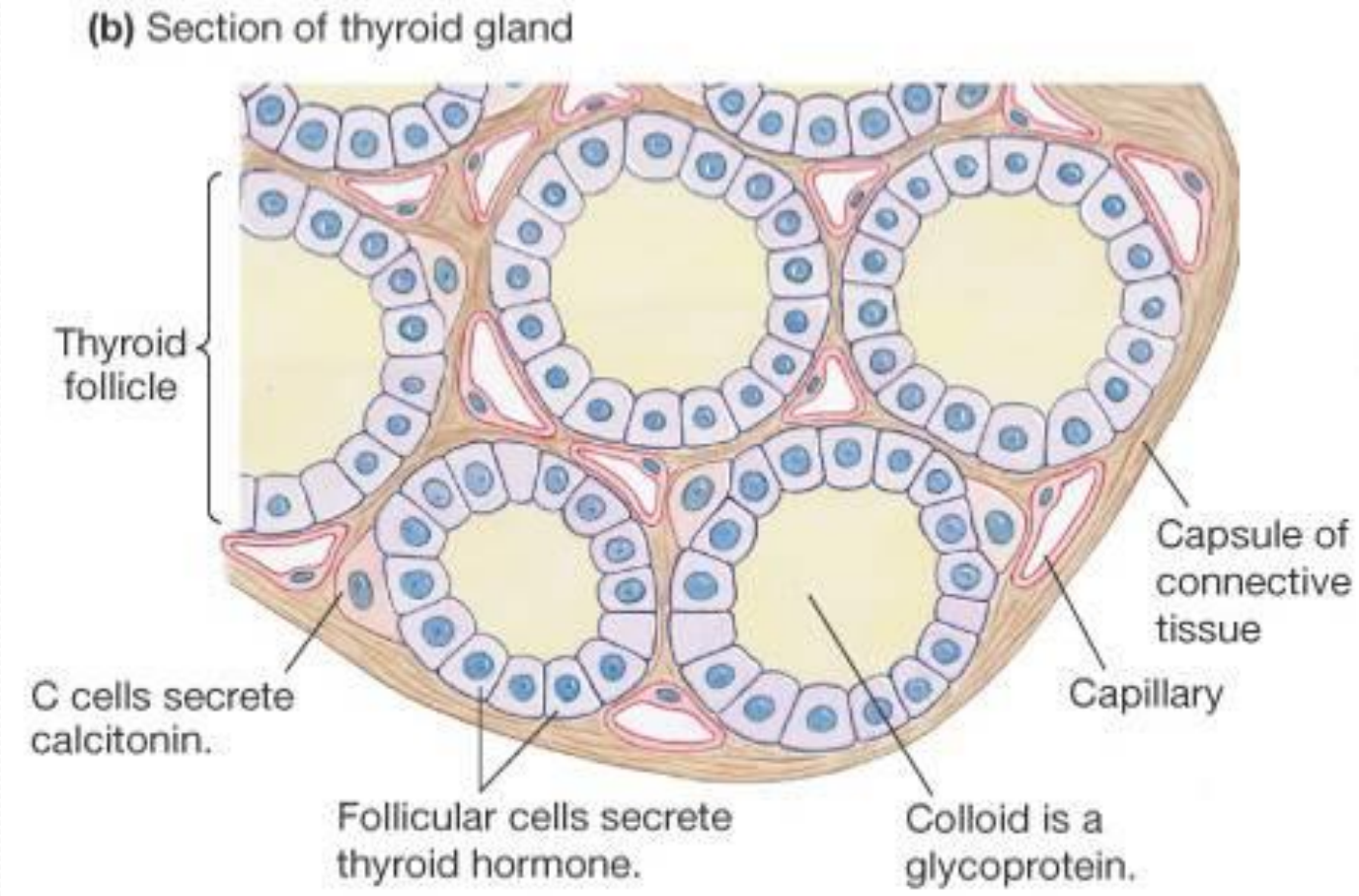
Thyroid Gland

- Located just below the larynx
- Secretes T_4 and T_3 which set BMR
  - needed for growth, development
- Consists of microscopic thyroid follicles
  - Outer layer **follicle cells** synthesize T_4
  - Interior filled with **colloid**, a protein-rich fluid



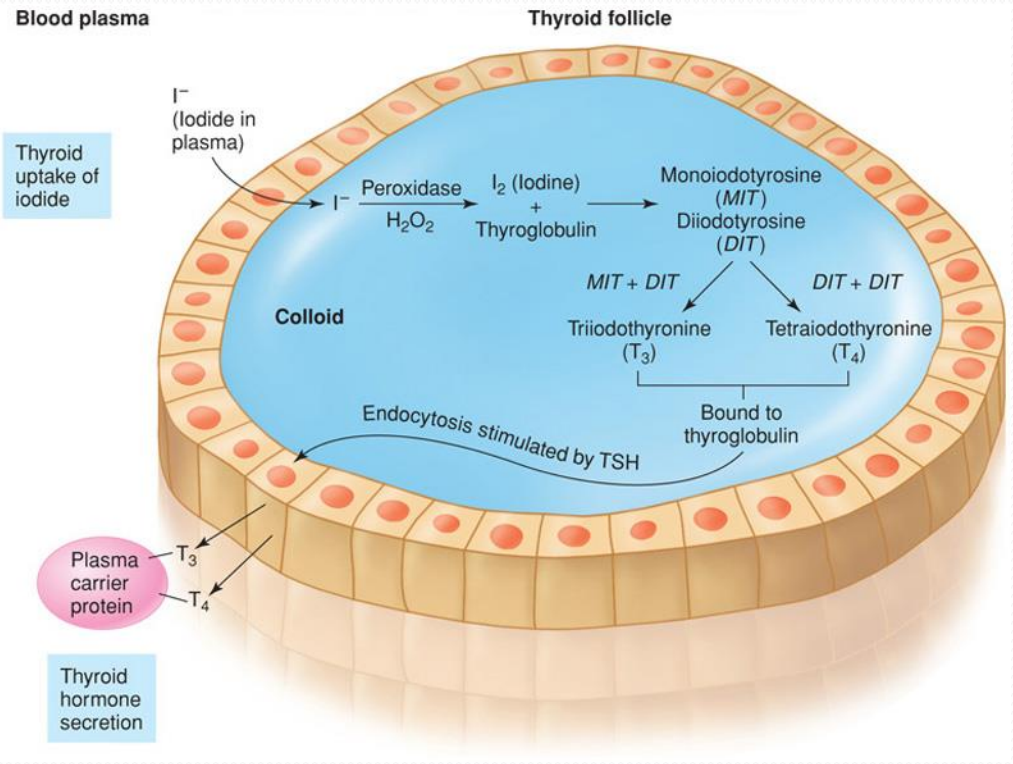
A scan of the thyroid 24 hrs. after intake of radioactive iodine

Thyroid Gland

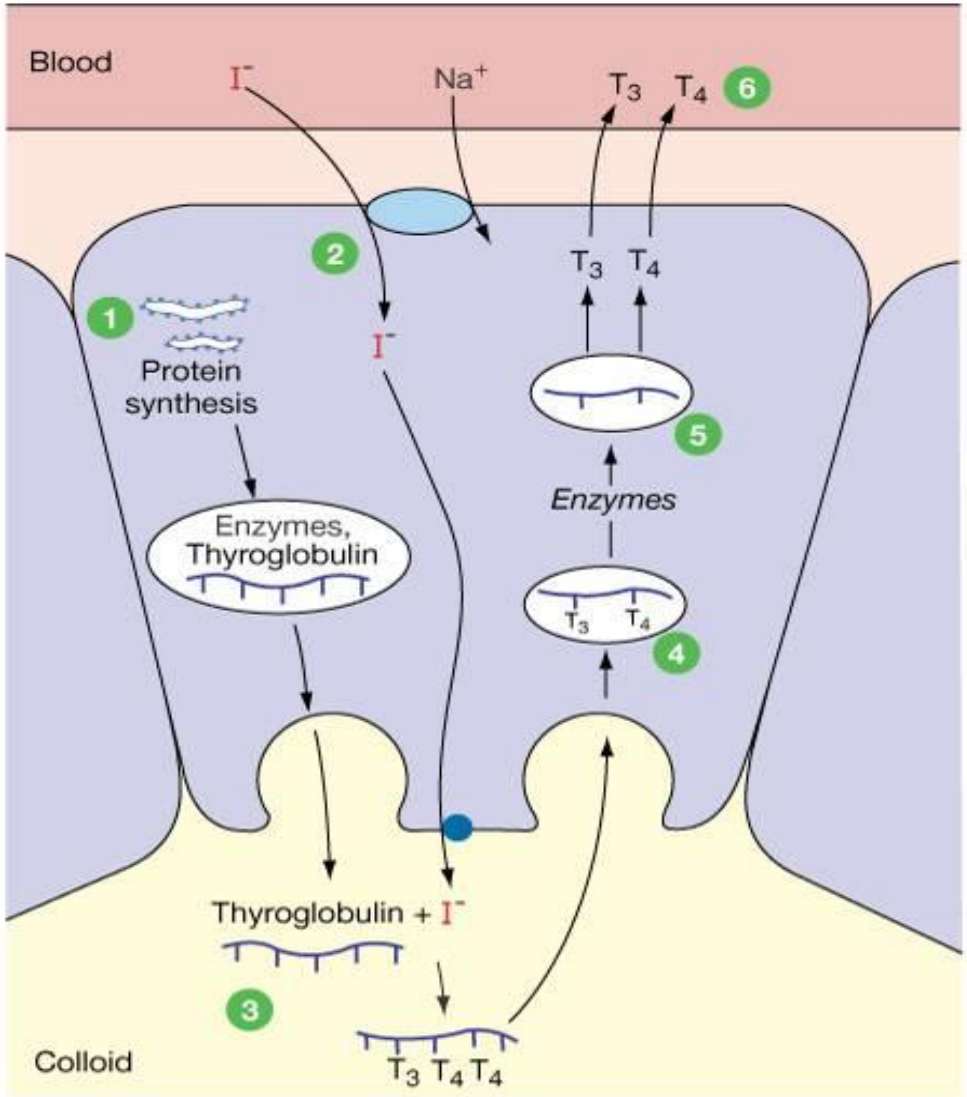


Thyroid Gland

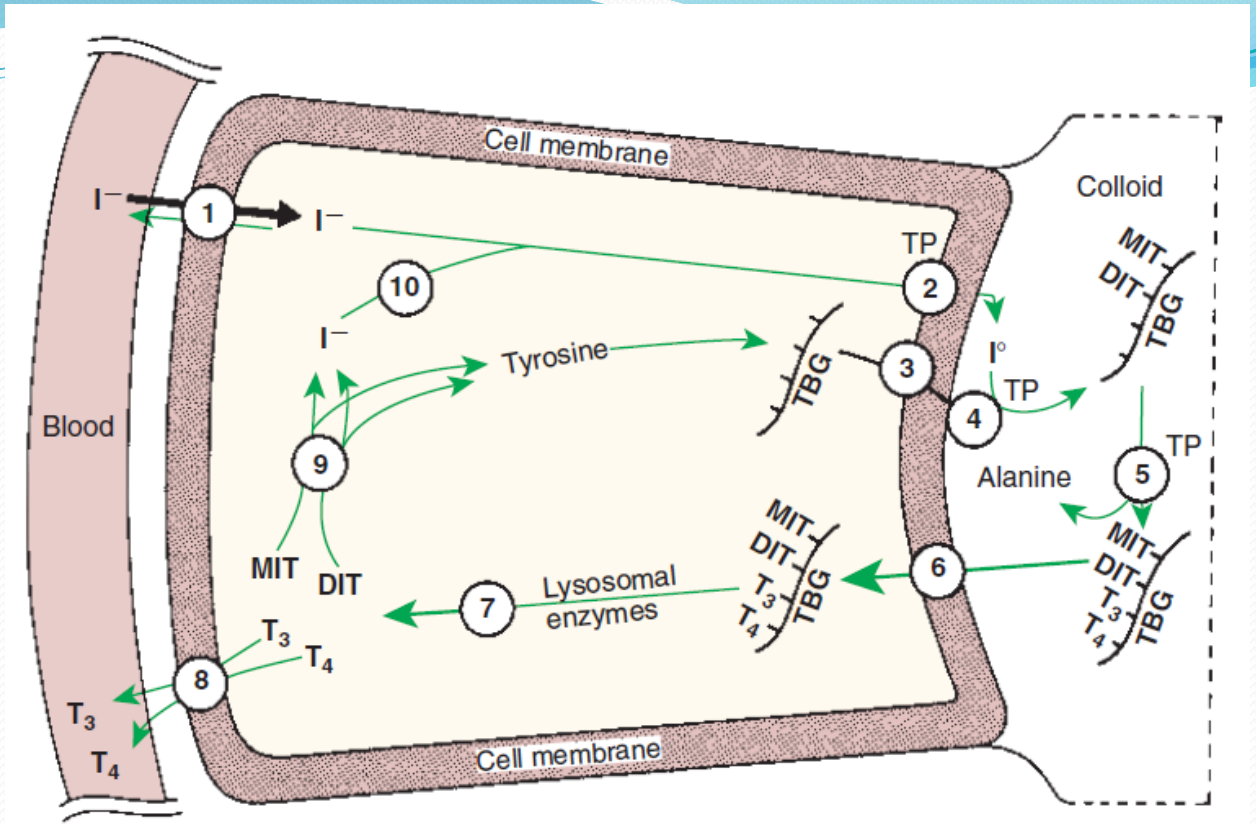
- Iodide (I^-) in blood actively transported into follicles and secreted into colloid
  - oxidized to iodine (I_2) and attached to tyrosines of thyroglobulin
  - large storage molecule for T_4 and T_3
  - TSH stimulates hydrolysis of T_4 and T_3 from thyroglobulin
  - and then secretion



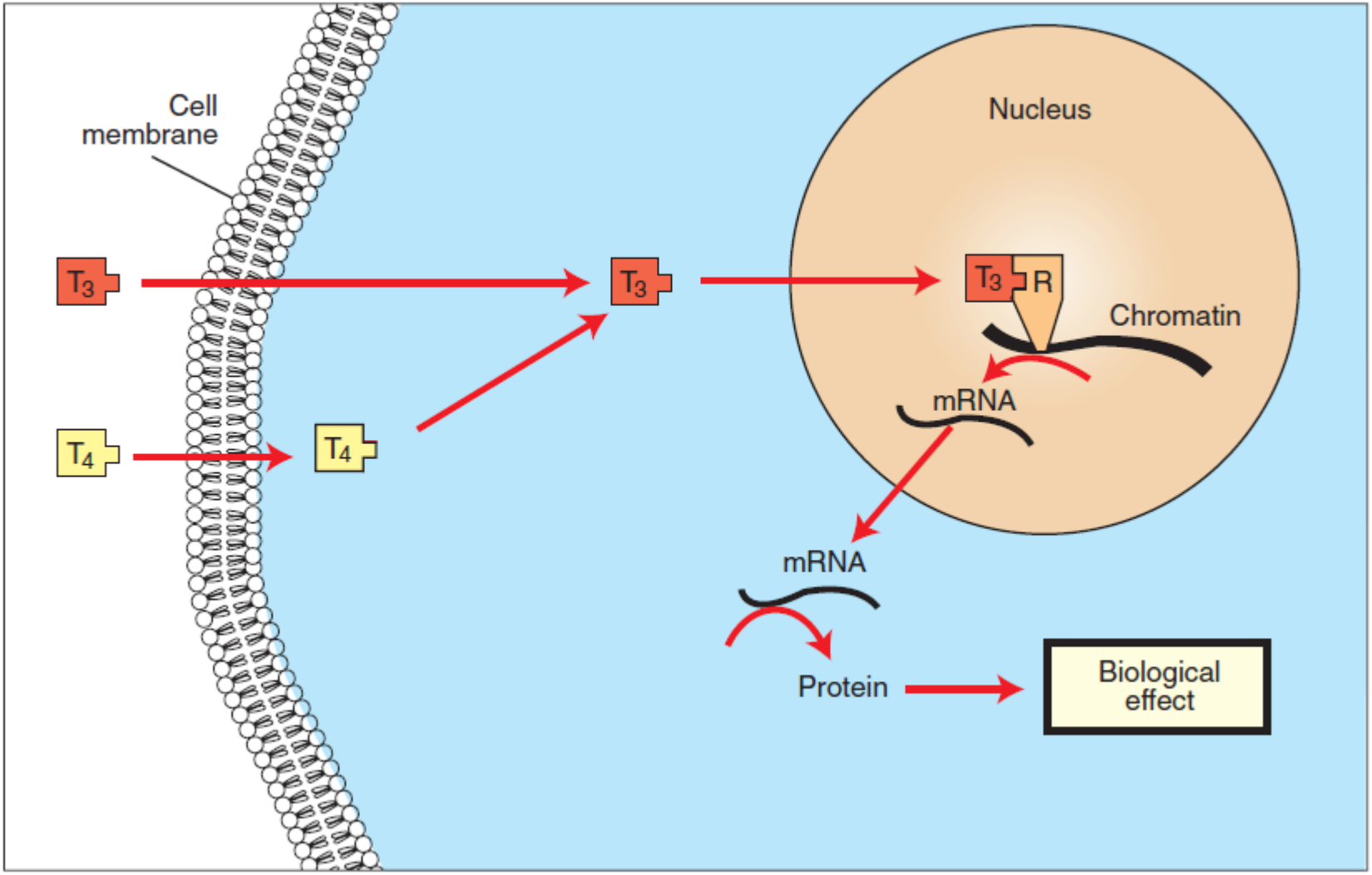
Thyroid Gland



1. Follicular cell synthesizes enzymes and thyroglobulin for colloid.
2. I^- is co-transported into the cell with Na^+ and transported into colloid.
3. Enzymes add iodine to thyroglobulin to make T_3 and T_4.
4. Thyroglobulin is taken back into the cell.
5. Intracellular enzymes separate T_3 and T_4 from the protein.
6. Free T_3 and T_4 enter the circulation.



1, trapping of iodide; 2, oxidation of iodide; 3, exocytosis of thyroglobulin; 4, iodination of thyroglobulin; 5, coupling of iodotyrosines; 6, endocytosis of thyroglobulin; 7, hydrolysis of thyroglobulin; 8, release of T3 and T4; 9, deiodination of monoiodotyrosine (MIT) and diiodotyrosine (DIT); and 10, recycling of iodide. TBG, Thyroxine-binding globulin; TP, thyroperoxidase.

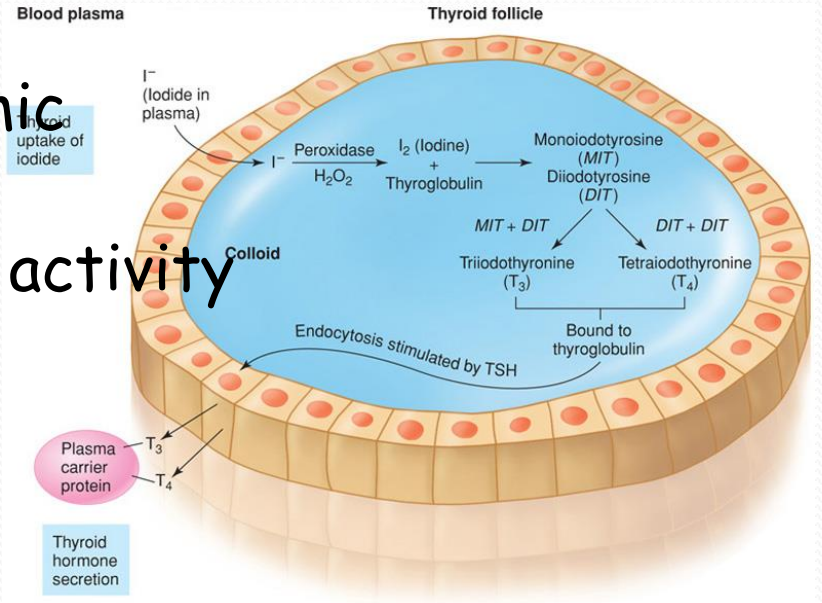


Proposed subcellular mechanism of thyroid hormone action. *mRNA*, Messenger ribonucleic acid; *R*, receptor.

Thyroid Gland

T_3 and T_4 (Almost all is deiodinated by one iodide ion, forming T_3) bind with nuclear receptor,

- activate and initiate genetic transcription. ---- mRNA
- protein synthesis in cytoplasmic ribosomes ----
- general increase in functional activity throughout the body.



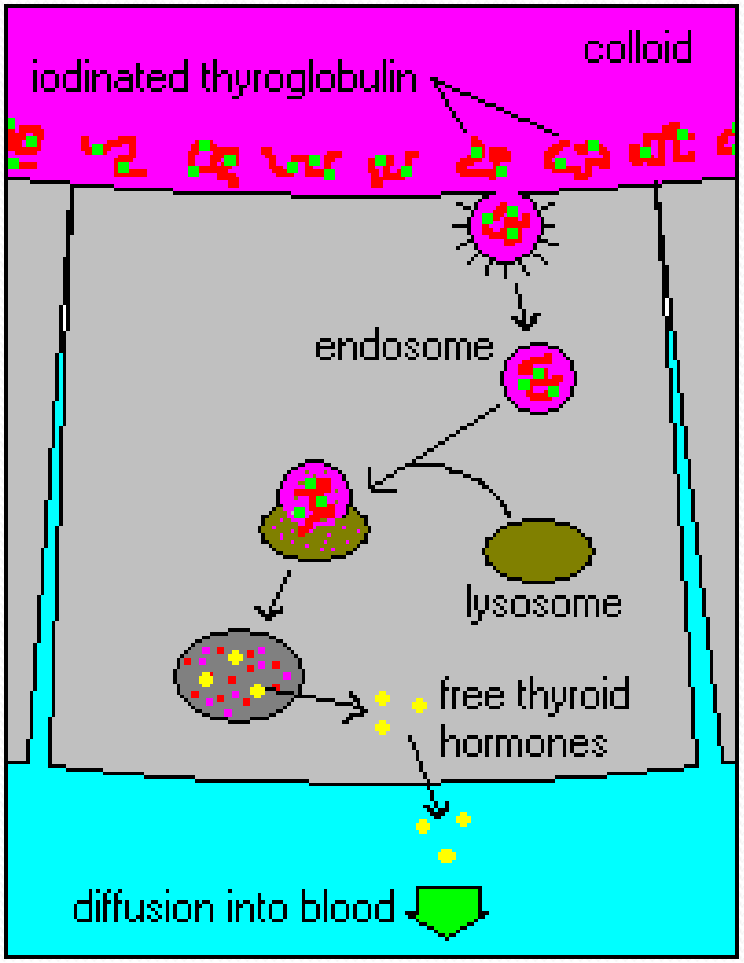
T_3 & T_4

- Note that within the colloid T_4 and T_3 are still attached to thyroglobulin.
- Upon stimulation by TSH,

the cells of the follicle take up a small volume of colloid by pinocytosis,

- hydrolyze the T_3 and T_4 from the thyroglobulin, and

secrete the free hormones into the blood.



Effects on metabolism

1. Calorigenic action

- increase O_2 consumption of most tissues in the body,
- increasing heat production and BMR.

The mechanism of calorigenic effect of thyroid hormones may be:

A: Enhances Na^+-K^+ ATPase activity

B: Causes the cell membrane of most cells to become leaky to Na^+ ions, which farther activates sodium pump and increases heat production.

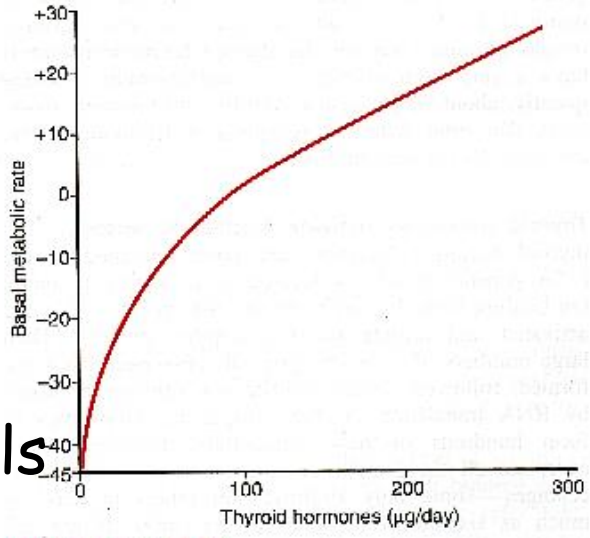


FIGURE 76–5

Approximate relation of daily rate of thyroid hormone (T_4 and T_3) secretion to the basal metabolic rate.

Effects on metabolism

2. Effects on Protein Metabolism.

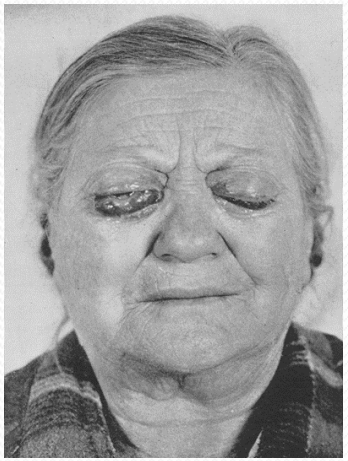
- Normally, T_4 and T_3 stimulates synthesis of proteins and enzymes, increasing anabolism of protein and causing positive balance of nitrogen

- Thyroid hormones in concert with growth hormone are essential for normal growth and development. This is accomplished in part by the enhancement of amino acid uptake by tissues and enzyme systems that are involved in protein synthesis.

Effects on metabolism

- In patient with **hyperthyroidism**, catabolism of protein increases, especially muscular protein, which leads weigh-loss and muscle weakness.

- In patients with **hypothyroidism**, myxedema develops because of deposition of mucoprotein binding with positive ions and water molecules in the interstitial spaces while protein synthesis decreases.



Effects on metabolism

3. Effects on carbohydrate metabolism

- Increase absorption of glucose from the gastrointestinal tract
- facilitating the movement of glucose into both fat and muscle.
- facilitate insulin-mediated glucose uptake by cells.
- Glycogen formation is facilitated by small amounts of thyroid hormones; however, glycogenolysis occurs after larger dosages

Effects on metabolism

4. Effects on fat metabolism

- accelerate the oxidation of free fatty acids by cells and increase the effect of catecholamine on decomposition of fat.

- not only promote synthesis of cholesterol but also increase decomposition of cholesterol by liver cells.

The net effect of T_3 and T_4 is to decrease plasma cholesterol concentration because the rate of synthesis is less than that of decomposition.

Effects on metabolism

4. Effects on fat metabolism

- Thyroid hormones affect all aspects of lipid metabolism, and the emphasis is placed on lipolysis.
- They reduce plasma cholesterol levels. This appears to involve both increased cell uptake of low density lipoproteins (LDLs) with associated cholesterol molecules and a tendency for increased degradation of both cholesterol and LDL.
- Hypercholesterolemia is a hallmark of thyroid deficiency.
- The effects of thyroid hormones on metabolic processes, including carbohydrate, protein, and lipid metabolism, are often described as catabolic.

Effects on Growth and Development

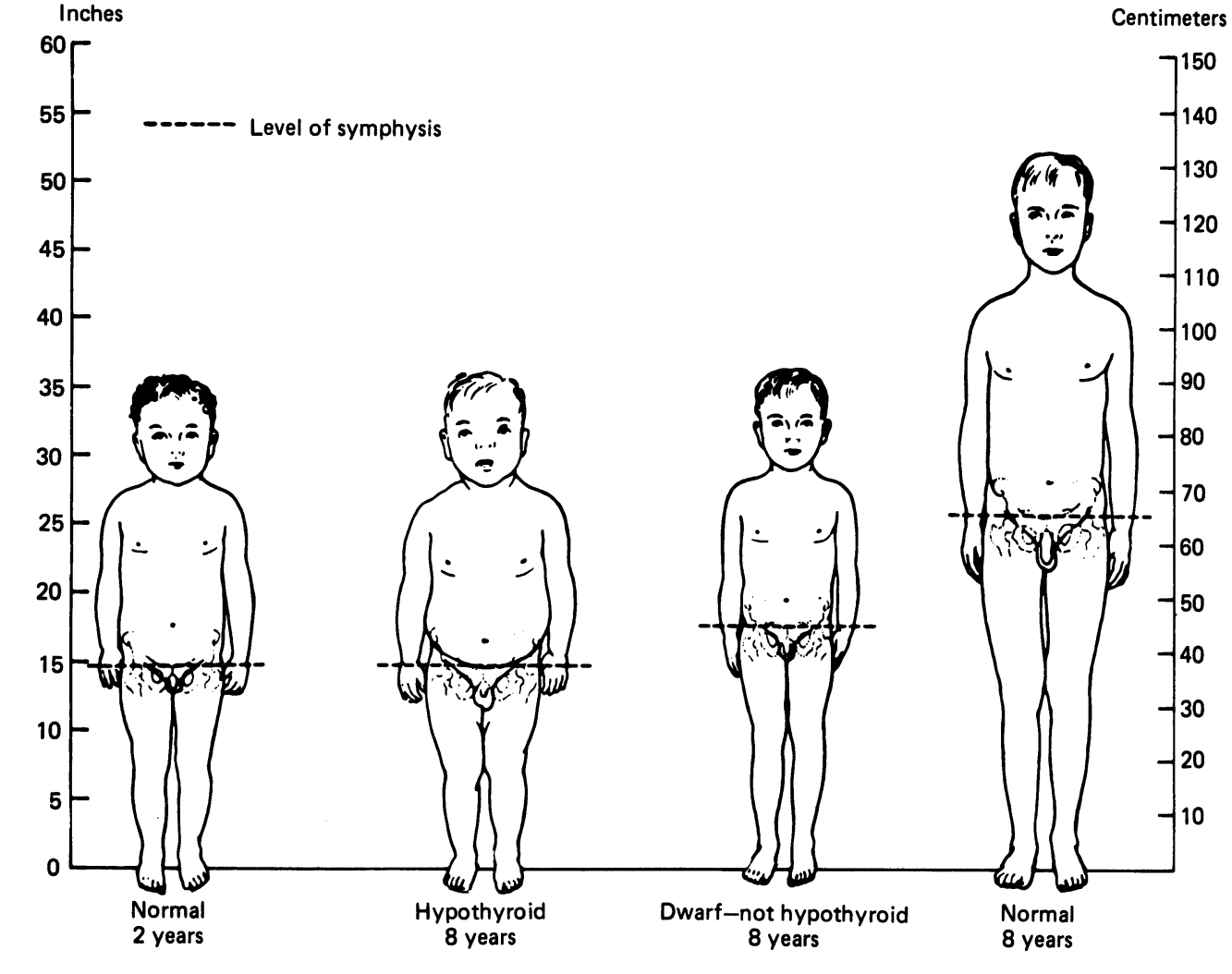
Thyroid hormone is essential for normal growth and development especially skeletal growth and development.

Thyroid hormones stimulate formation of dendrites, axons, myelin and neuroglia.

A child without a thyroid gland will suffer from **critinism**, which is characterized by **growth** and **mental** retardation.

Without specific thyroid therapy within three months after birth, the child with cretinism will remain mentally deficient throughout life.

Effects on Growth and Development



Effects on Nervous System

- Increase excitability of central nervous system.
- thyroid hormones can also stimulate the sympathetic nervous system.
- stimulation of β-adrenergic receptors in tissues that are targets for the catecholamines, such as epinephrine and norepinephrine.
- In the central nervous system (CNS), thyroid hormones are important for normal development of tissues in the fetus and neonate; inhibition of mental activity occurs when thyroid hormone exposure is inadequate.

Effects on Cardiovascular System

- Thyroid hormones increase the heart rate and force of contraction, probably through their interaction with the catecholamines by increasing the responsiveness of tissues to β-adrenergic receptors.
- Blood pressure is elevated because of increased systolic pressure, with no change in diastolic pressure; the end result is an increase in cardiac output.

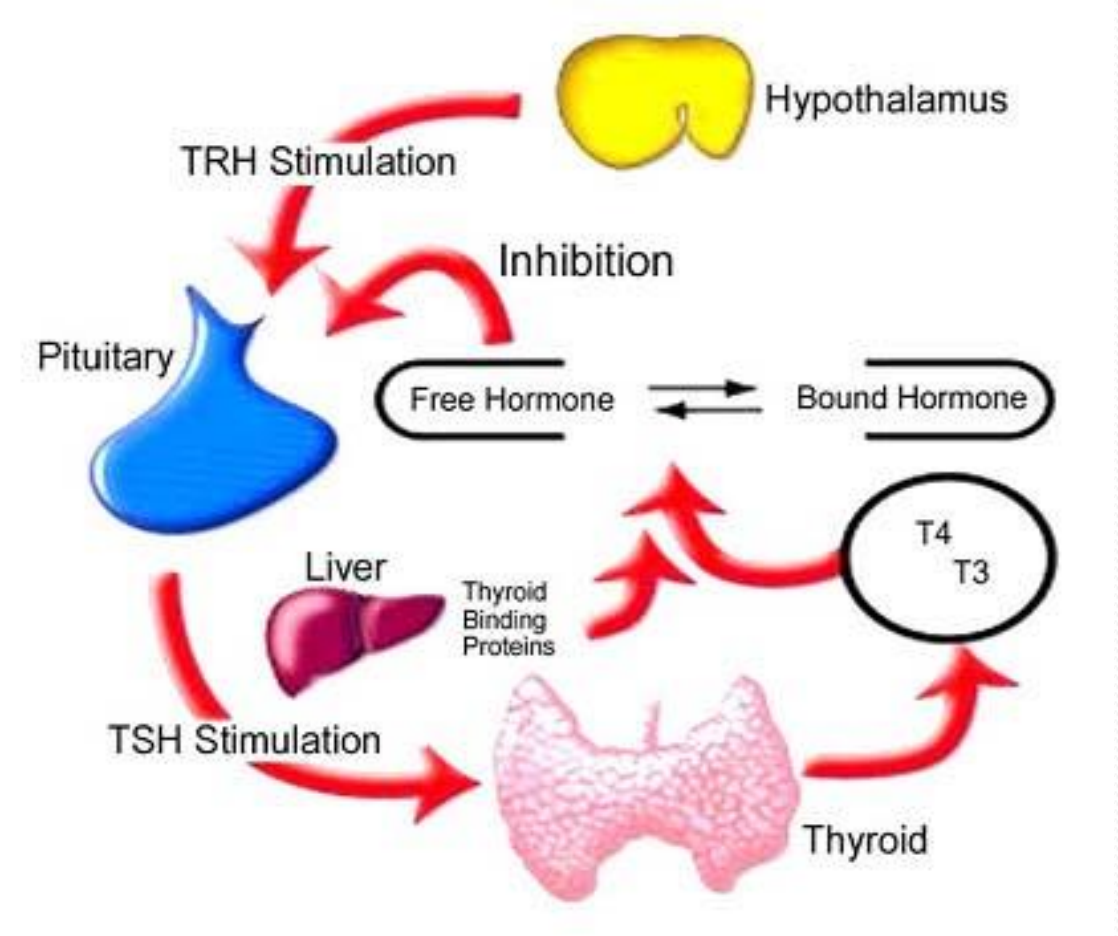
Effects on GI Tract

- Thyroid hormones increase the appetite and food intake by metabolic rate increased.
- Thyroid hormones increase both the rate of secretion of the digestive juices and the motility of the gastrointestinal tract.
- Lack of thyroid hormone can cause constipation.

Feedback Mechanisms of Thyroid Hormones

- T_3 and T_4 ⟶ **inhibitory protein** in anterior pituitary
- reduces production and secretion of TSH,
- decrease response of pituitary to TRH.
- Because of the negative mechanism, the concentration of free thyroid hormone in the blood can be maintained within a normal range.

Feedback Mechanisms of Thyroid Hormones



T_3 & T_4 secretion disorders

- In hyperthyroidism, the patient is likely to have extreme nervousness, many psychoneurotic tendencies including anxiety complexes, extreme worry and paranoia, and muscle tremor.

- The hypothyroid individual is to have fatigue, extreme somnolence, poor memory and slow mentation.

Diseases of the Thyroid - Goiter

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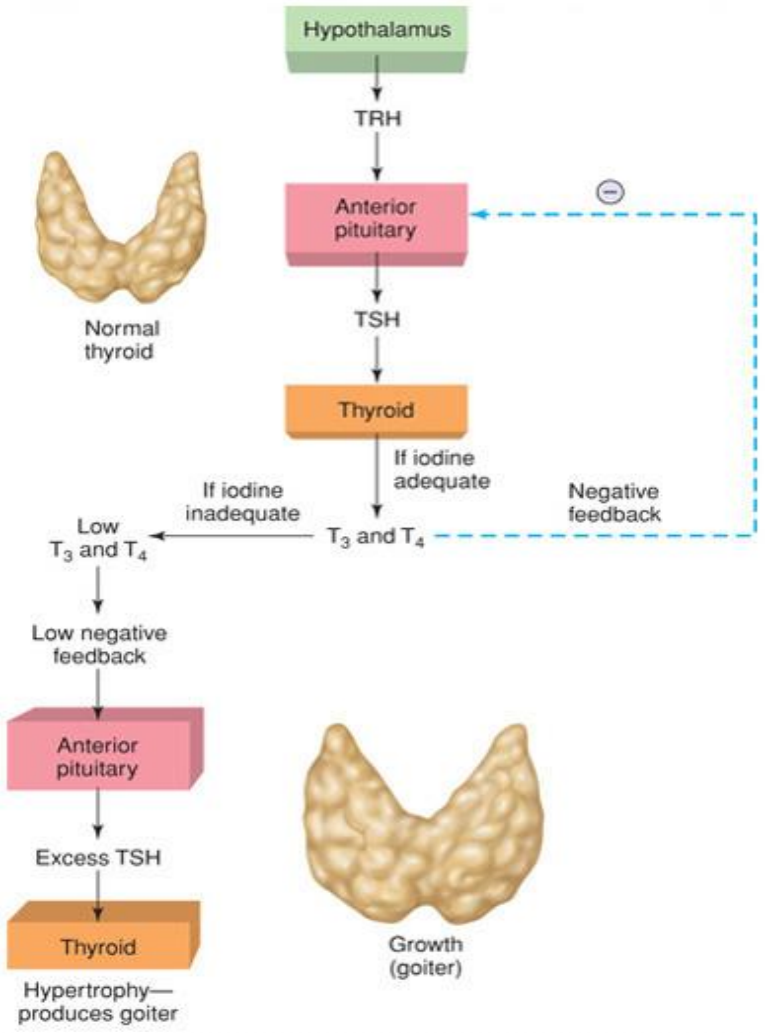


Diseases of the Thyroid - Goiter

- Certain plants, such as cruciferous plants (e.g., cabbage, kale, rutabaga, turnip, rapeseed)*, contain a potent antithyroid compound called progoitrin, which is converted into goitrin within the digestive tract.
- Goitrin interferes with the organic binding of iodine
- Many of the goitrogenic feeds also contain thiocyanates, which interfere with the trapping of iodine by the thyroid gland.
- Thiocarbamides, such as thiourea and thiouracil are most potent drugs for treatment of hyperthyroidism.
- Other antithyroid drugs include sulfonamides, p-aminosalicylic acid, phenylbutazone, and chlorpromazine.

* کلم، کلم پیچ، شلغم زرد، شلغم، دانه شلغم روغنی

Hypothyroidism in Dogs

- Hypothyroidism is most common in the dog
  - **Primary** hypothyroidism: etiology is lymphocytic thyroiditis.
  - **Congenital** hypothyroidism:
    - thyroid dysgenesis,
    - dyshormonogenesis,
    - T4 transport defects,
    - goitrogens,
    - or in rare cases, iodine deficiency.
  - **Secondary** hypothyroidism:
    - may be a secondary effect of pituitary tumors,
    - radiation therapy,
    - or ingestion of endogenous or exogenous glucocorticoids.
  - **Tertiary** hypothyroidism:
    - acquired, as in the case of hypothalamic tumors,
    - congenital as a result of defective TRH or TRH receptor defects.

Hypothyroidism in Dogs

- **Breeds predisposition:**
  - golden retrievers, Doberman pinschers, dachshunds, Irish setters, miniature schnauzers, Great Danes, miniature poodles, boxers , . . .

- ***Clinical signs***:
  - lethargy and obesity are most common.
  - truncal or tail head alopecia.
  - thickened skin because of myxedematous accumulations in the dermis.
  - hair coat changes include dull dry hair, poor hair regrowth after clipping, and presence or retention of puppy hair.

Hypothyroidism in Dogs

- **Diagnosis** is based on measurement of serum basal total thyroxine (T4) and triiodothyronine (T3) concentrations, serum free T4 and T3 concentrations, and endogenous canine serum thyrotropin (TSH) levels and/or results of dynamic thyroid function tests, including the TRH and TSH stimulation tests.

- In summary, diagnosis of canine hypothyroidism is based on signalment, historical findings, physical examination findings, clinicopathological features, and confirmation with a battery of thyroid function tests.

Hyperthyroidism in Cats

- Hyperthyroidism is the most common endocrinopathy of cats and is caused by adenomatous hyperplasia of the thyroid gland.
- As noted earlier, goitrogens can result in hypothyroidism. However, some have theorized that chronic exposure to goitrogens can lead to toxic nodular goiter resulting in hyperthyroidism.
- activation mutation (activation without ligand) of the TSH receptor may be part of the pathogenesis of feline hyperthyroidism in some cats.
- Furthermore, abnormalities of G proteins, specifically significantly decreased G inhibitory protein expression, have been described in tissues from hyperthyroid cats.

Hyperthyroidism in Cats

- Hyperthyroidism is characterized by hypermetabolism;
- **Clinical signs:**
  - polyphagia, weight loss, polydipsia, and polyuria are the most prominent features of the disease.
  - hyperactivity, tachycardia, pupillary dilation, and behavioral changes
  - Long-standing hyperthyroidism leads to hypertrophic cardiomyopathy, high-output heart failure, and cachexia, which may lead to death.

- **Diagnosis**: measurement of TT4 (and not TT3 or FT3)

T_3 & T_4

Diseases of the Thyroid - hypothyroidism

- Hypothyroid – inadequate T_4 and T_3 levels
  - Have low BMR, weight gain, lethargy, cold intolerance
  - Myxedema = puffy face, hands, feet
  - During fetal development hypothyroidism can cause cretenism (severe mental retardation)

Diseases of the Thyroid - hyperthyroidism

- Goiters are also produced by Grave's disease
  - Autoimmune disease: antibodies act like TSH and stimulate thyroid gland to grow and oversecrete = hyperthyroidism
    - Characterized by exopthalmos, weight loss, heat intolerance, irritability, high BMR

T_3 & T_4

Table 11.8 Comparison of Hypothyroidism and Hyperthyroidism

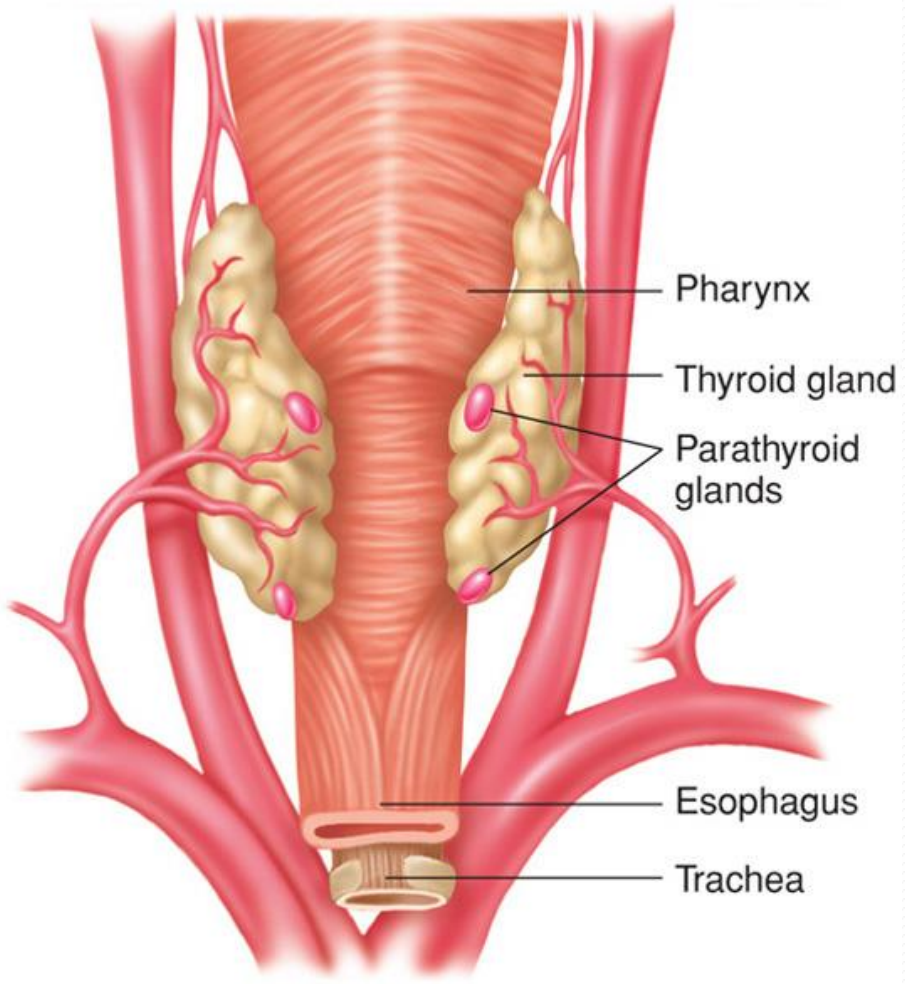
Feature	Hypothyroid	Hyperthyroid
Growth and development	Impaired growth	Accelerated growth
Activity and sleep	Lethargy; increased sleep	Increased activity; decreased sleep
Temperature tolerance	Intolerance to cold	Intolerance to heat
Skin characteristics	Coarse, dry skin	Normal skin
Perspiration	Absent	Excessive
Pulse	Slow	Rapid
Gastrointestinal symptoms	Constipation; decreased appetite; increased weight	Frequent bowel movements; increased appetite; decreased weight
Reflexes	Slow	Rapid
Psychological aspects	Depression and apathy	Nervous, "emotional" state
Plasma T_4 levels	Decreased	Increased

Section 5:

Patathyroid Glands

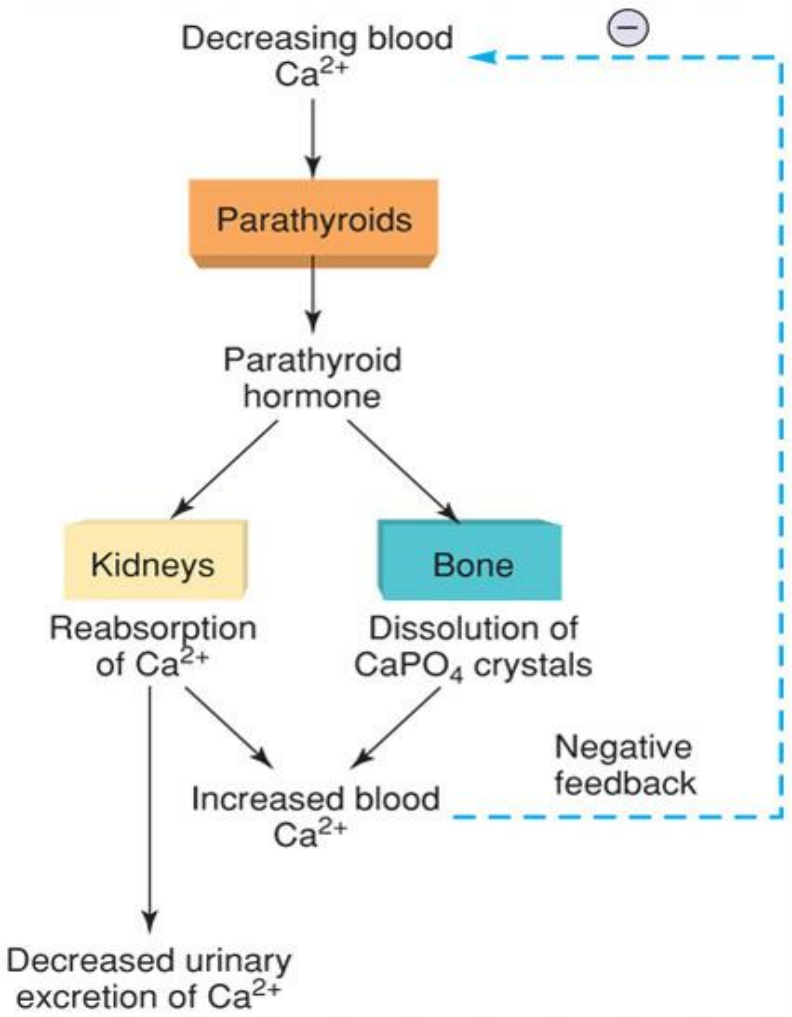
Parathyroid Glands

- 4 glands embedded in lateral lobes of posterior side of thyroid gland
- Secrete Parathyroid hormone (PTH)
  - Most important hormone for control of blood Ca^{2+} levels



Parathyroid Hormone

- Release stimulated by decreased blood Ca^{2+}
- Acts on bones, kidney, and intestines to increase blood Ca^{2+} levels



Section 6:

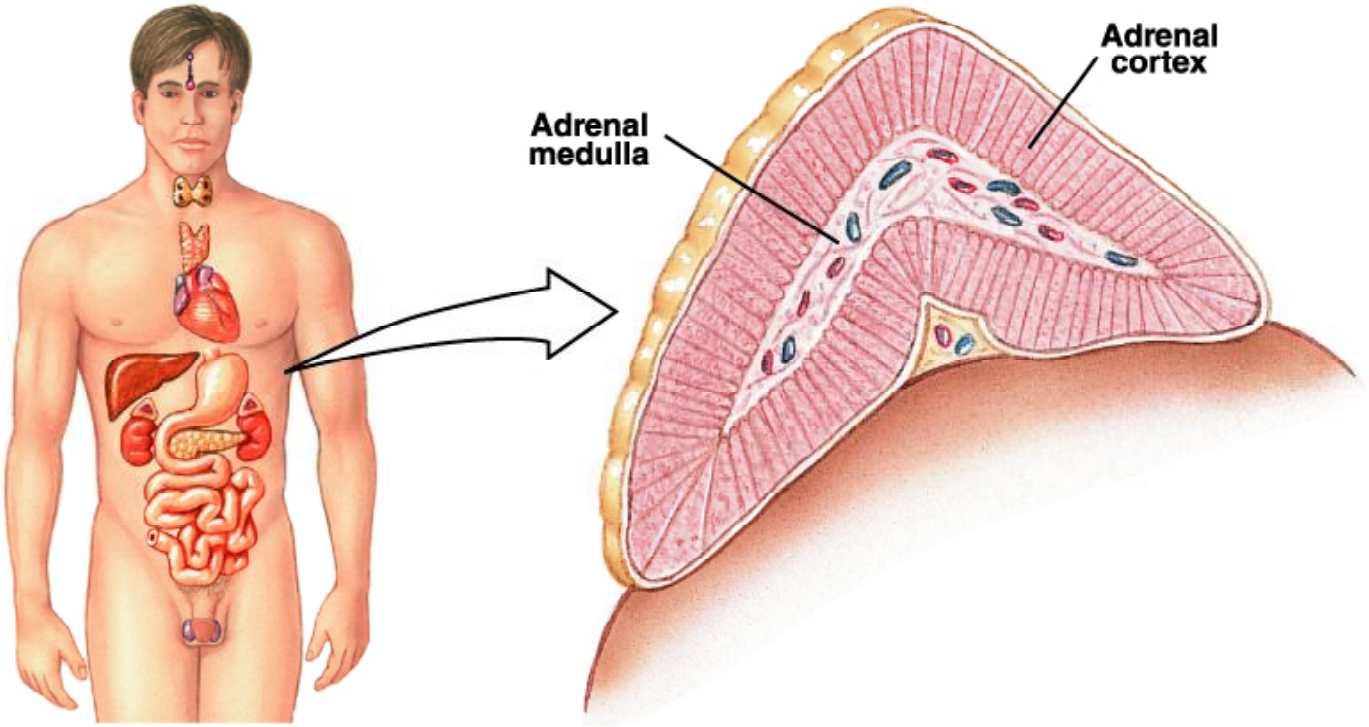
Adrenal Gland

Adrenal Gland

- The adrenal glands are two bilaterally symmetric endocrine organs located just anterior to the kidneys. Each gland is divided into two separate entities, a **medulla** and a **cortex**.
  - The medulla arises from the neuroectoderm and produces amines such as norepinephrine and epinephrine.
  - The cortex arises from the mesodermal coelomic epithelium and produces steroid hormones such as cortisol, corticosterone, sex steroids, and aldosterone.

- The common factor of these two sections is that both sets of hormones are important for adaptation to adverse environmental conditions (i.e., stress).

Adrenal Gland

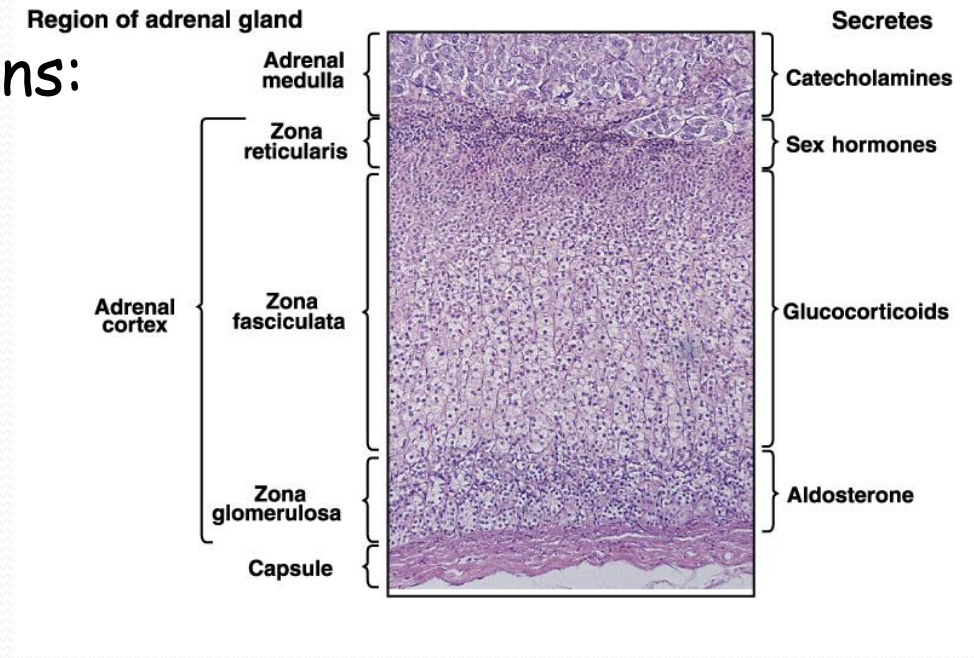


Adrenal Gland

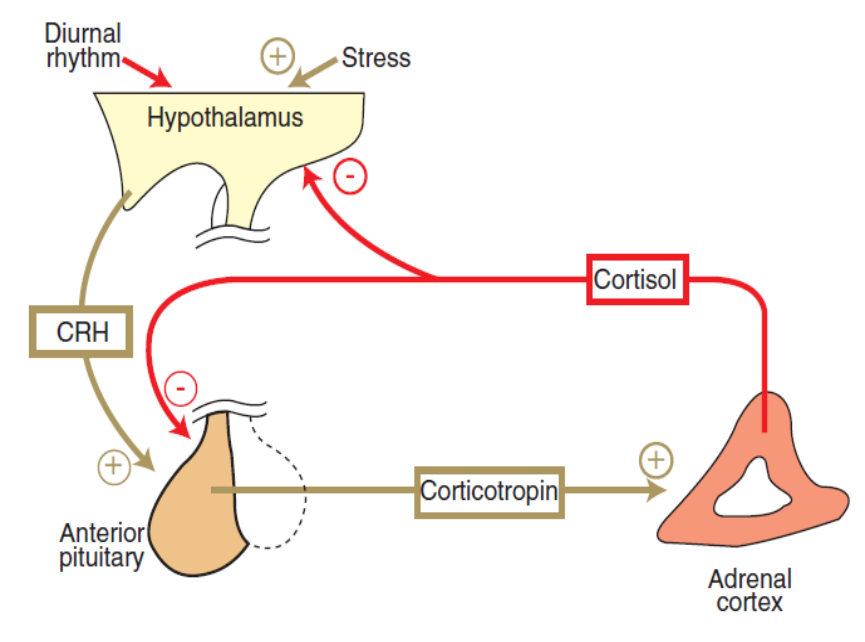
The **adrenal medulla** secretes **catecholamine hormones**.

The **adrenal cortex** secrete **steroid hormones**, which participate in the regulation of mineral balance, energy balance and reproductive function.

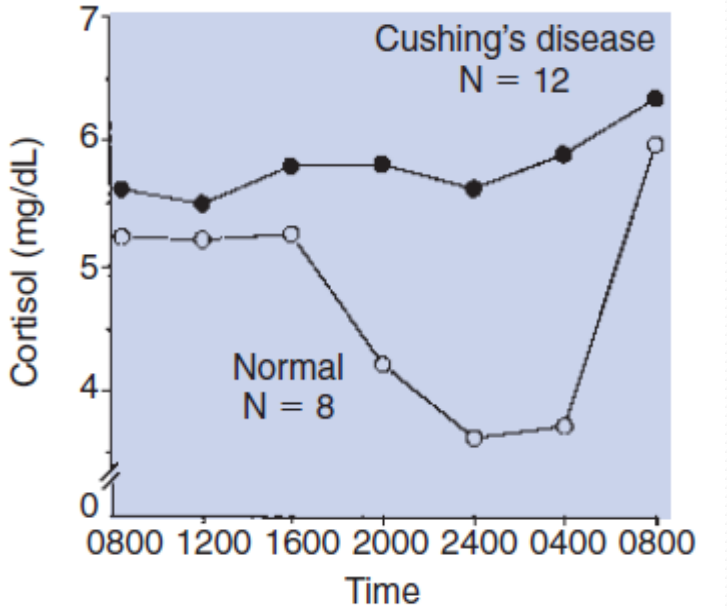
- Divided into three regions:
  - zona glomerulosa
    - secretes aldosterone
  - zona fasciculata
    - secretes glucocorticoids
  - zona reticularis
    - secretes androgens



Glucocorticoid secretion



Regulation of cortisol secretion by the hypothalamopituitary axis. *Plus signs* indicate stimulation; *minus signs* indicate inhibition. *CRH,* Corticotropin-releasing hormone.



Circadian changes in cortisol secretion in normal horses *(open circles),* in comparison with no circadian change in horses with equine Cushing's disease *(solid circles).*

Glucocorticoid hormone functions

Effect	Site of Action
Stimulates gluconeogenesis	Liver
Increases hepatic glycogen	Liver
Increases blood glucose	Liver
Facilitates lipolysis	Adipose tissue
Is catabolic (negative nitrogen balance)	Muscle, liver
Inhibits corticotropin secretion	Hypothalamus, anterior pituitary gland
Facilitates water excretion	Kidney
Blocks inflammatory response	Multiple sites
Suppresses immune system	Macrophages, lymphocytes
Stimulates gastric acid secretion	Stomach

Hyperadrenocorticism

- Hyperadrenocorticism (Cushing's syndrome) in the dog may be caused by a pituitary tumor, pituitary hyperplasia, adrenal tumors, adrenal hyperplasia, or nonendocrine tumors (usually of the lung), or it may be iatrogenic.
  - 85% of dogs have pituitary gland–dependent disease, whereas 15% exhibit adrenal tumors.

- Breeds predisposition:
  - by pituitary-dependent include: miniature poodles, dachshunds, boxers, Boston terriers, and beagles.
  - By adrenal tumors: large-breed dogs,
  - There is a predilection for females (3 : 1 ratio with males).

Hyperadrenocorticism

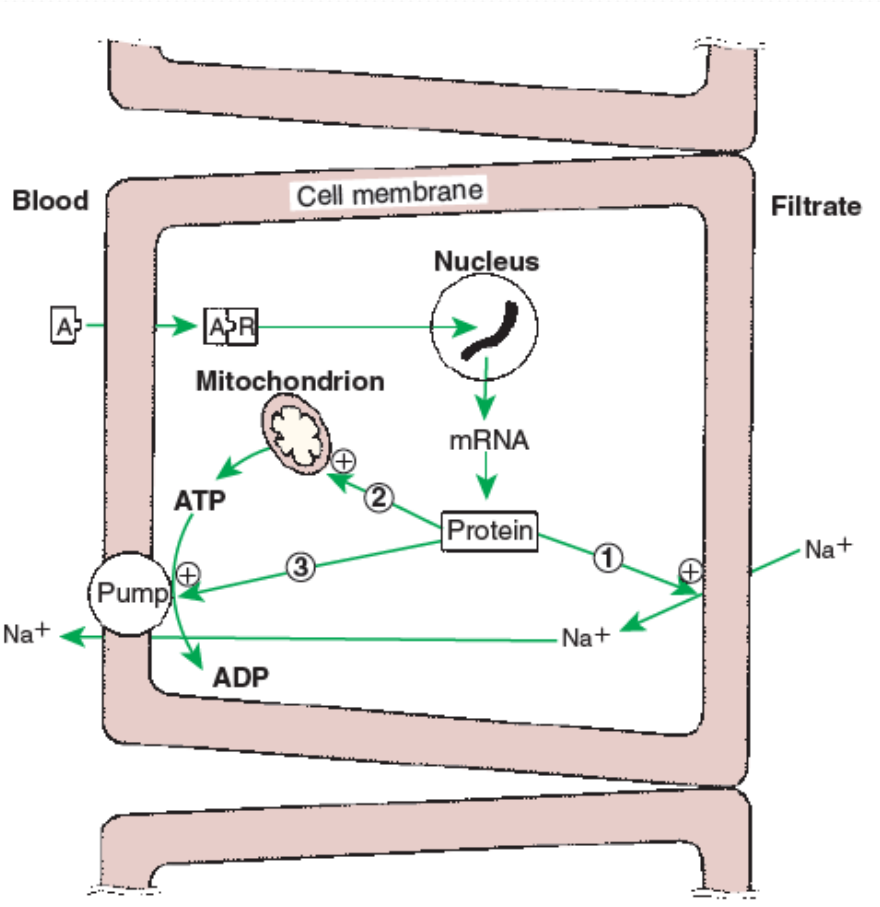
- The most common clinical signs:
  - polydipsia, polyuria, polyphagia, abdominal enlargement or "potbelly," alopecia (especially truncal), thin skin, . . .

- Diagnosis: based on clinical signs, lab tests (LDDS test, UC:CR, . . .

Mineralocorticoids

Mechanisms of action of aldosterone on sodium transport in the renal tubular cell.

The *numbered arrows* indicate the three putative sites of action of aldosterone: *1,* increasing the permeability of the luminal membrane to sodium; *2,* increasing mitochondrial adenosine triphosphate *(ATP)* production; *3,* increasing Na_+,K_+-ATPase activity in the contraluminal membrane. *Plus signs* indicate stimulation. *A,* Aldosterone; *ADP,* adenosine diphosphate; *mRNA,* messenger ribonucleic acid; *R,* receptor.

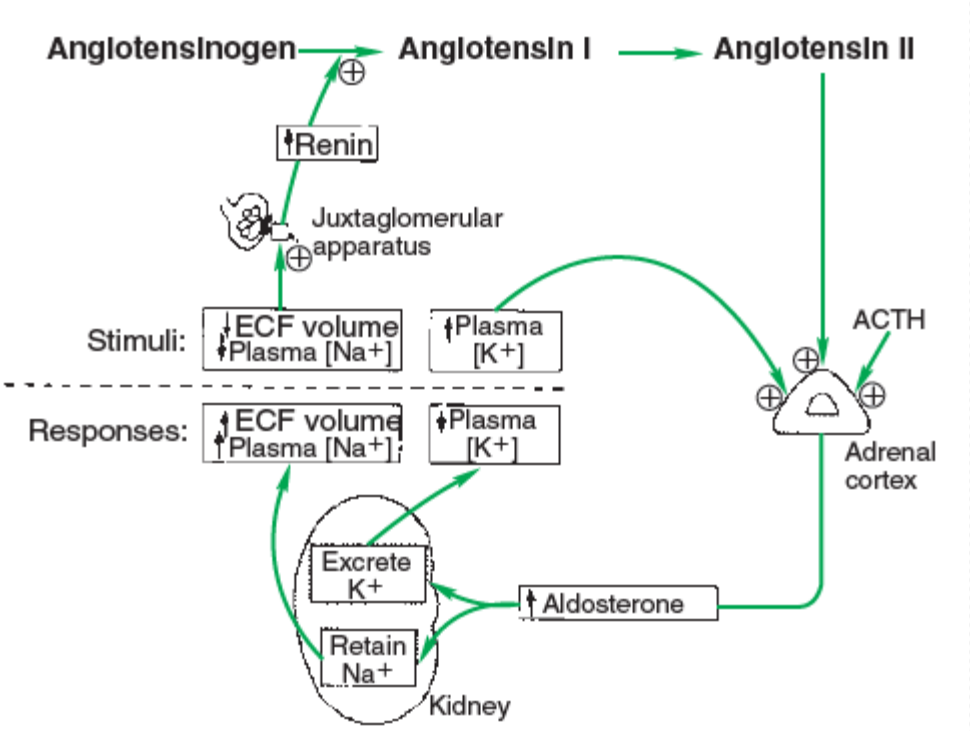


Mineralocorticoids

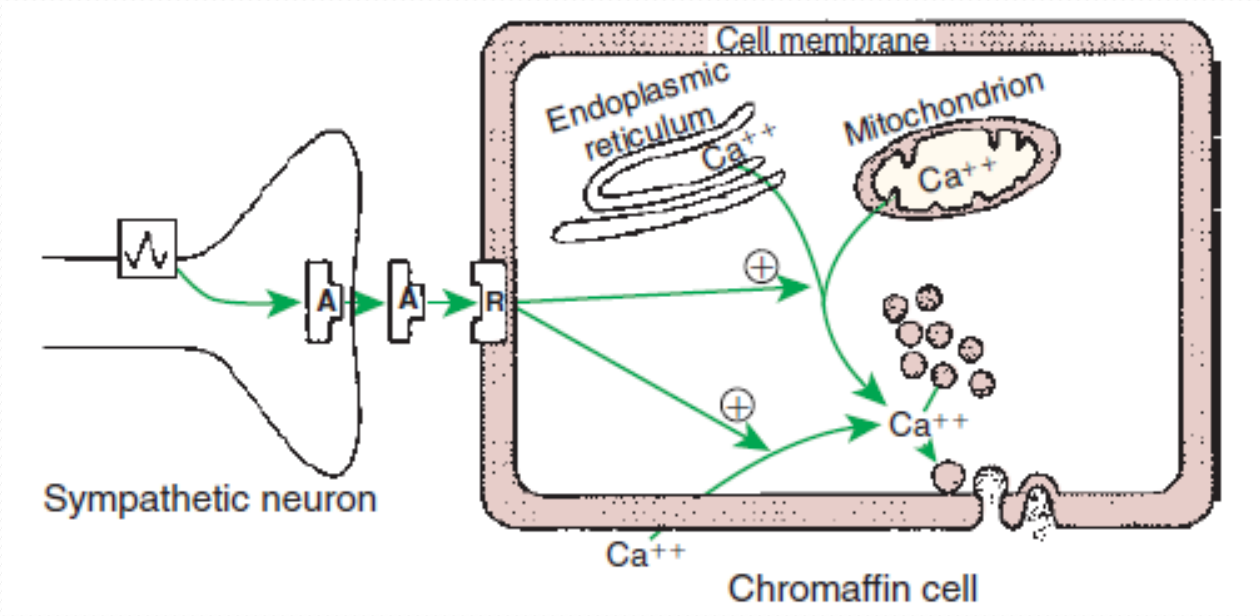
Effect	Site of Action
Stimulates Na^+ reabsorption	Kidney, salivary glands, sweat glands
Stimulates K^+ excretion	Kidney, salivary glands, sweat glands
Stimulates H^+ excretion	Kidney

Mineralocorticoid Effects and Target Tissues

Regulation of aldosterone secretion by the zona glomerulosa of the adrenal cortex. *Plus signs* indicate stimulation. *ACTH,* Corticotropin (adrenocorticotropic hormone); *ECF,* extracellular fluid



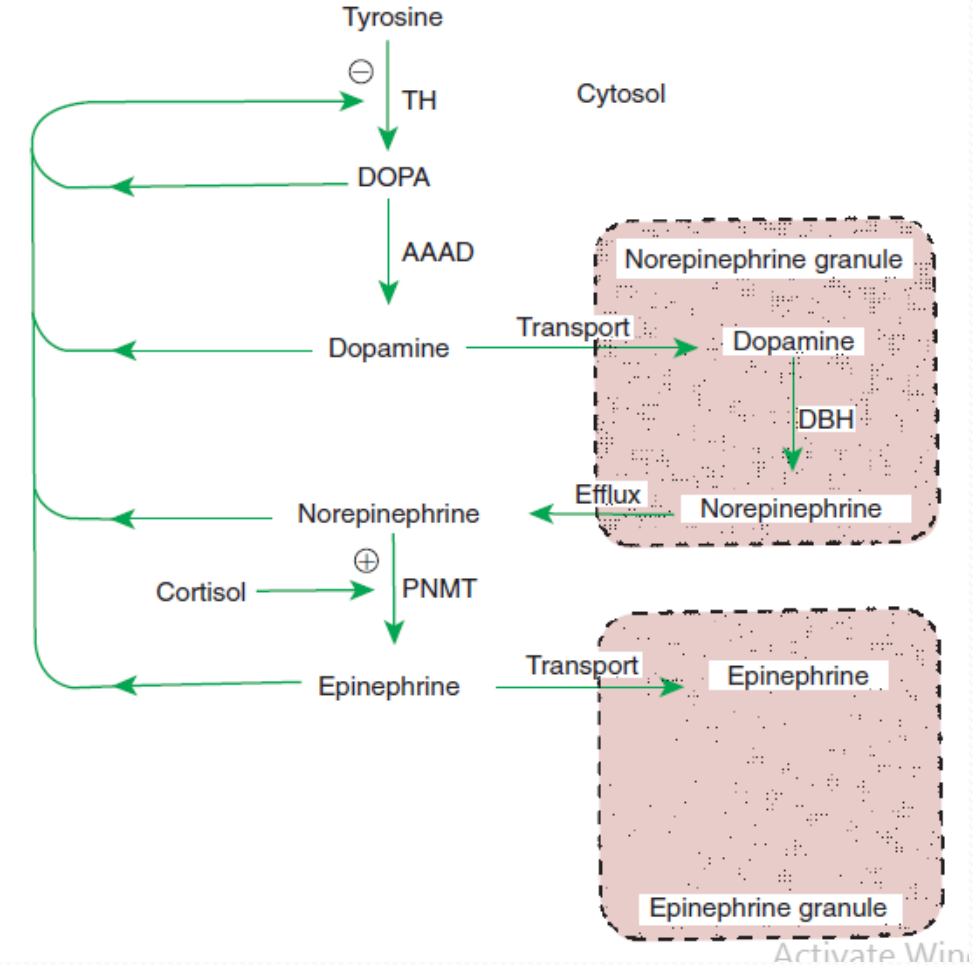
The Adrenal Medulla



Stimulus-secretion coupling in the adrenal chromaffin cell. Note that cytosolic calcium may be derived from intracellular or extracellular sources. *Circled plus signs* indicate stimulation. *A*, Acetylcholine; *R*, receptor.

The Adrenal Medulla

Regulation of catecholamine biosynthesis in the adrenal medulla. *Plus sign* indicates stimulation; minus sign indicates inhibition. *AAAD,* Aromatic-L-amino acid decarboxylase; *DBH,* dopamine-β-hydroxylase; *DOPA,* dihydroxyphenylalanine; *PNMT,* phenylethanolamine-*N*-methyltransferase; *TH,* tyrosine hydroxylase.

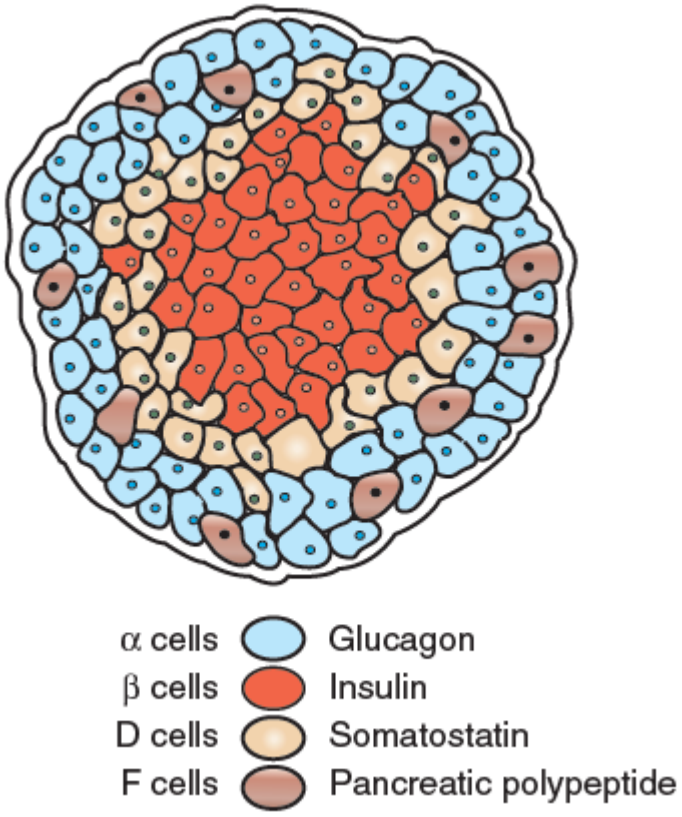


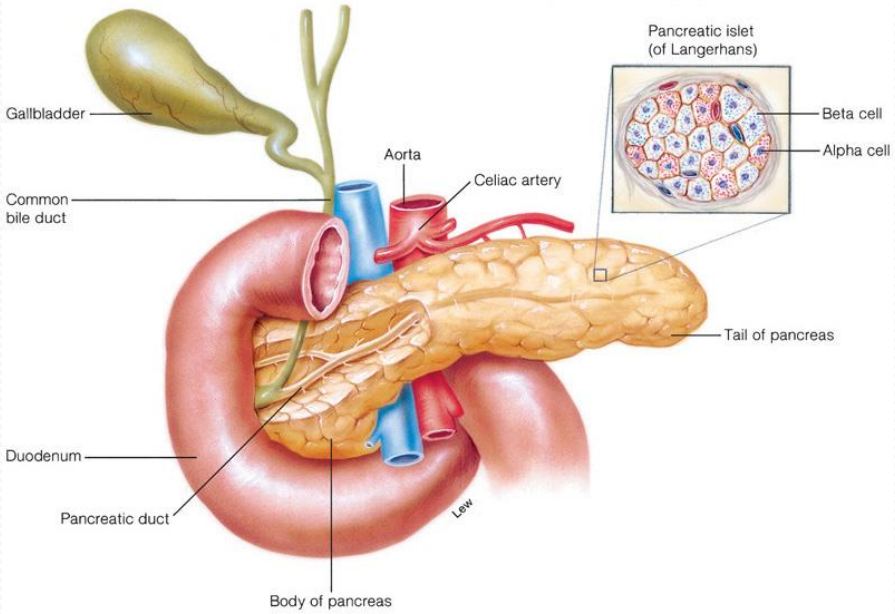
Section 7:

Islets of Langerhans

Islets of Langerhans

- Scattered clusters of endocrine cells in pancreas
- Contain alpha and beta cells





Islets of Langerhans

- Alpha cells secrete glucagon in response to low blood glucose
  - Stimulates glycogenolysis and lipolysis
  - Increases blood glucose

- Beta cells secrete insulin in response to low blood glucose
  - Promotes entry of glucose into cells
  - And conversion of glucose into glycogen and fat
  - Decreases blood glucose