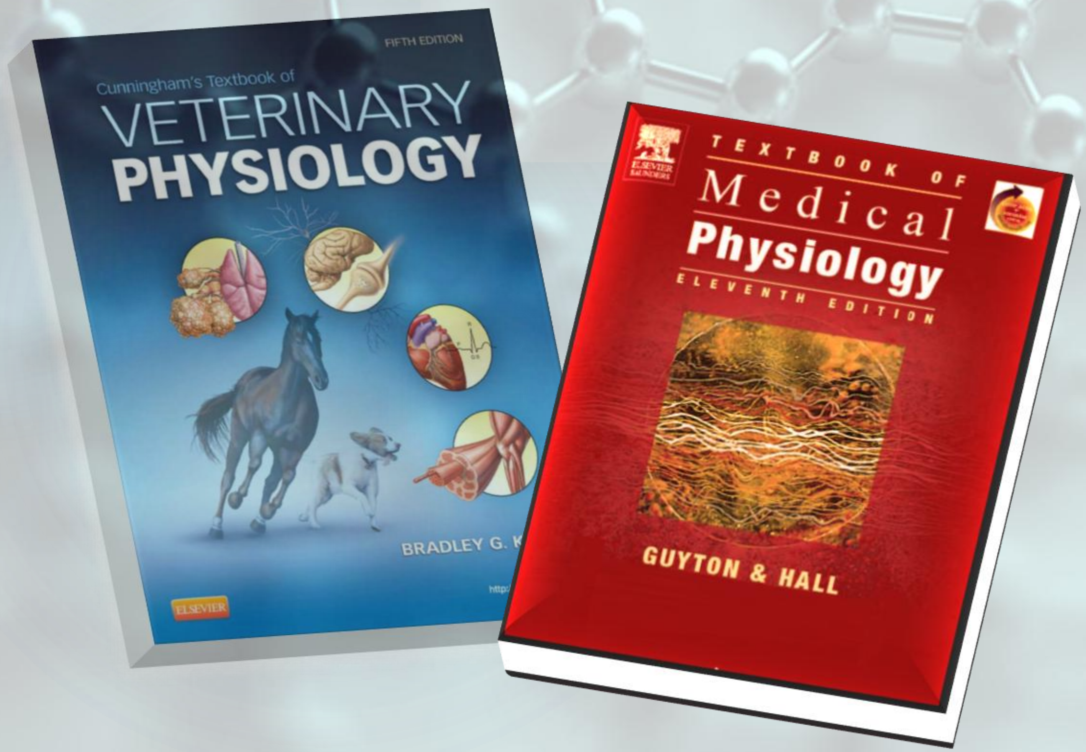
Endocrine Physiology

Dr. A. K.Goudrazi , D.V.M. Ph.D
Department of basic sciences
Faculty of veterinary medicine
I.A.University



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Section One:

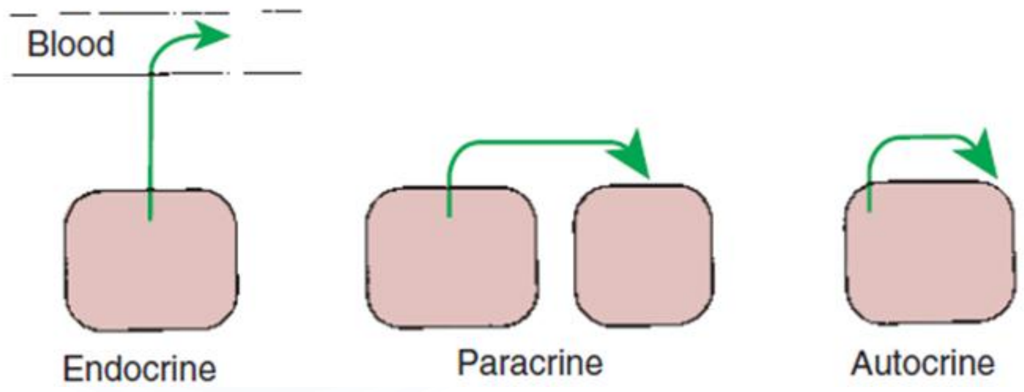
General Concepts of Endocrinology

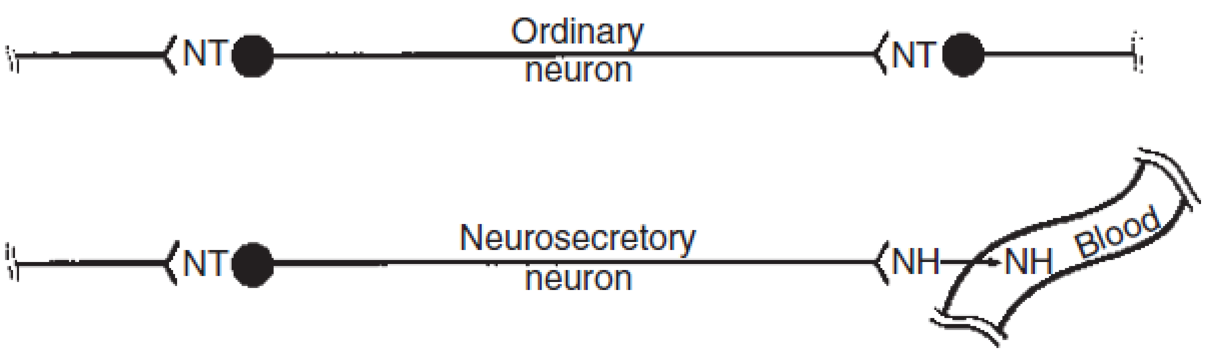
Introduction to Endocrinology

- The endocrine system has evolved to allow physiological processes to be coordinated and regulated.
- The system uses chemical messengers called hormones. Hormones have traditionally been defined as "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.

Introduction to Endocrinology

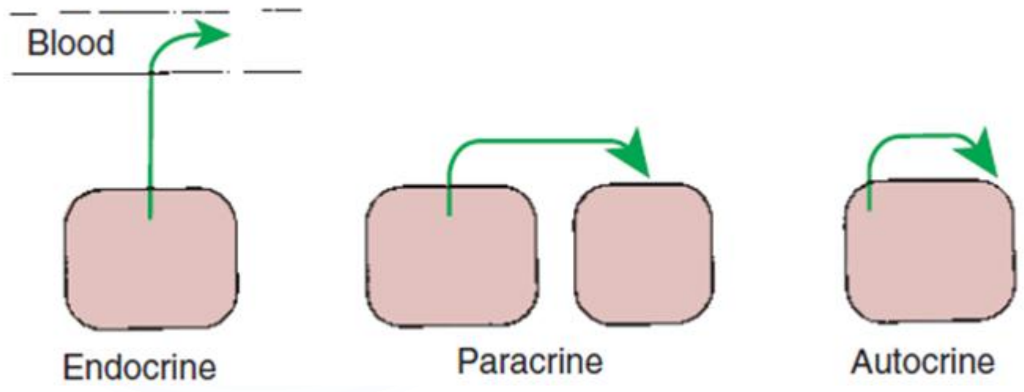
- Other types of control systems:
  - Paracrine effectors, in which the messenger diffuses through the interstitial fluids, usually to influence adjacent cells; if the messenger acts on the cell of its origin, the substance is called an autocrine effector
  - Neurotransmitters, which affect communication between neurons, or between neurons and target cells; the substances are limited in the distance traveled and the area of the cell influenced
  - Exocrine effectors, such as hormones produced by the pancreas, are released into the gastrointestinal tract.

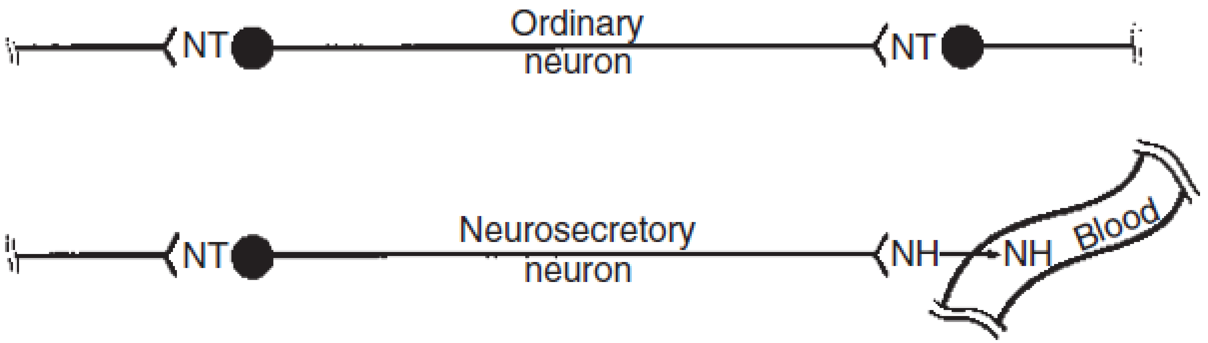




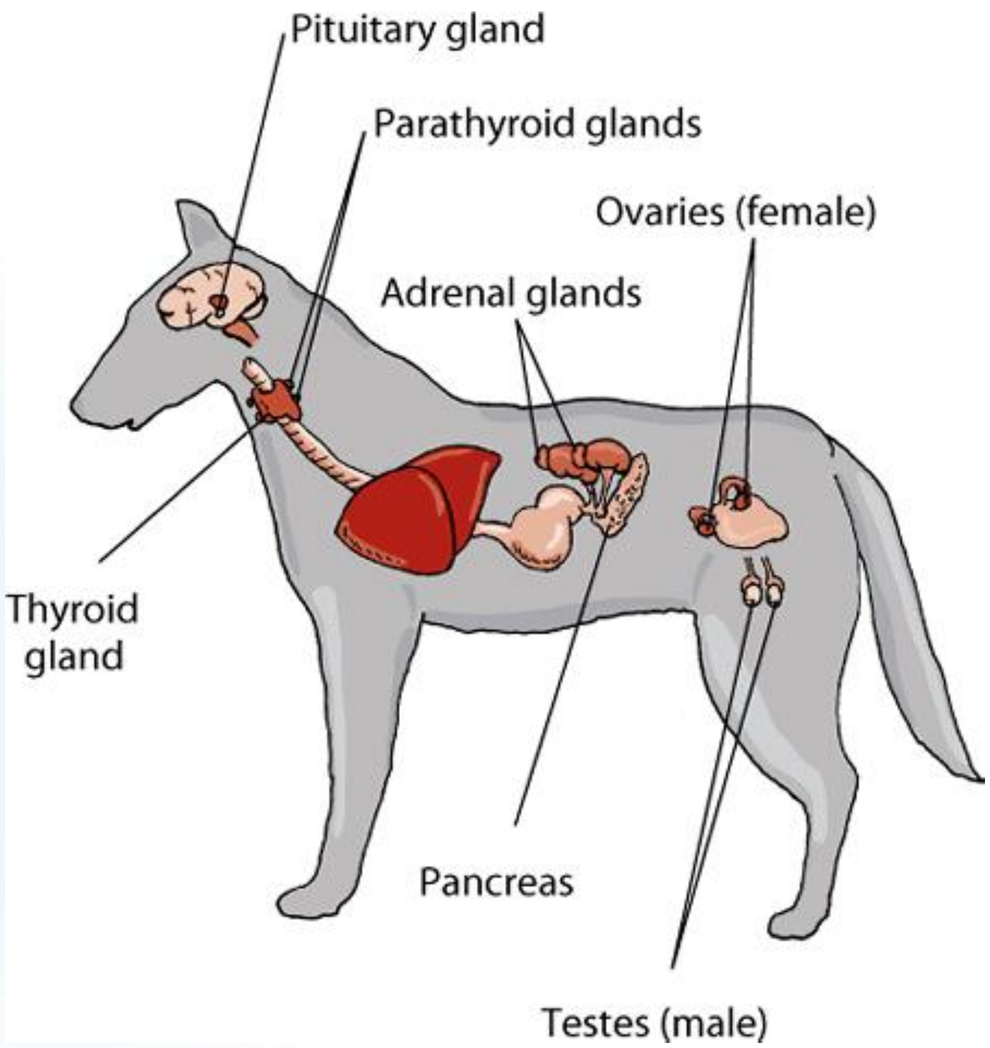
Introduction to Endocrinology

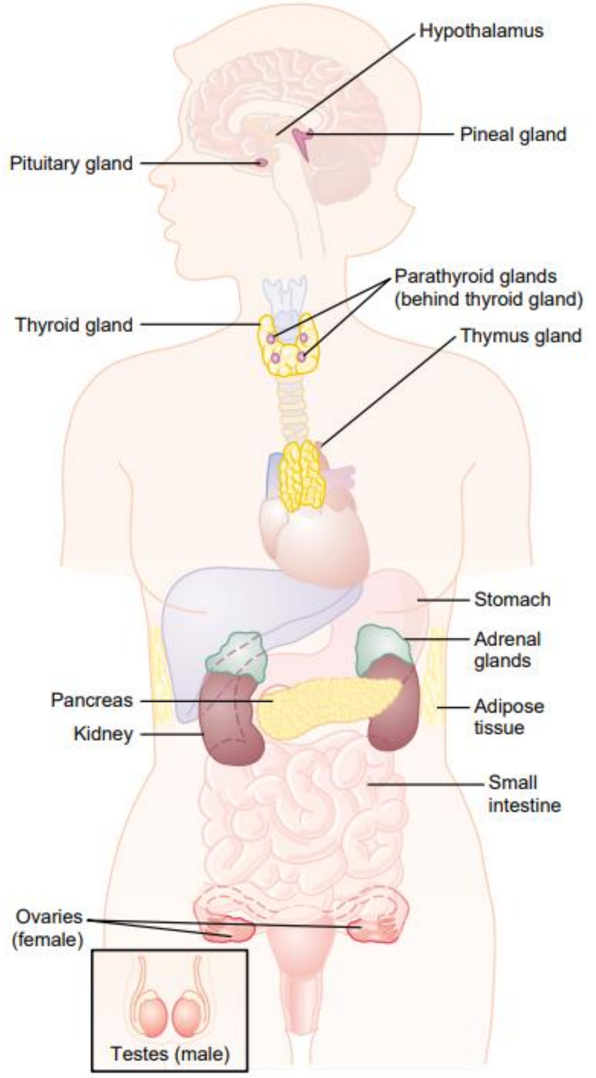
- Other types of control systems:
  - Neuroendocrine hormones are secreted by neurons into the circulating blood and influence the function of cells at another location in the body.
  - Cytokines are peptides secreted by cells into the extracellular fluid and can function as autocrines, paracrines, or endocrine hormones.
    - Examples of cytokines include the interleukins and other lymphokines that are secreted by helper cells and act on other cells of the immune system. Cytokine hormones (e.g., leptin) produced by adipocytes are sometimes called adipokines.





Hormone production: "Classic" glands





Overview of Endocrine Glands and Hormones

Gland/Tissue	Hormones	Major Functions	Chemical Structure
Hypothalamus	Thyrotropin-releasing hormone (TRH)	Stimulates secretion of TSH and prolactin	Peptide
	Corticotropin-releasing hormone (CRH)	Causes release of ACTH	Peptide
	Growth hormone–releasing hormone (GHRH)	Causes release of growth hormone	Peptide
	Growth hormone inhibitory hormone (GHIH) (somatostatin)	Inhibits release of growth hormone	Peptide
	Gonadotropin-releasing hormone (GnRH)	Causes release of LH and FSH	
	Dopamine or prolactin-inhibiting factor (PIF)	Inhibits release of prolactin	Amine
Anterior pituitary	Growth hormone	Stimulates protein synthesis and overall growth of most cells and tissues	Peptide
	Thyroid-stimulating hormone (TSH)	Stimulates synthesis and secretion of thyroid hormones (thyroxine and triiodothyronine)	Peptide
	Adrenocorticotropic hormone (ACTH)	Stimulates synthesis and secretion of adrenocortical hormones (cortisol, androgens, and aldosterone)	Peptide
	Prolactin	Promotes development of the female breasts and secretion of milk	Peptide
	Follicle-stimulating hormone (FSH)	Causes growth of follicles in the ovaries and sperm maturation in Sertoli cells of testes	Peptide
	Luteinizing hormone (LH)	Stimulates testosterone synthesis in Leydig cells of testes; stimulates ovulation, formation of corpus luteum, and estrogen and progesterone synthesis in ovaries	Peptide
Posterior pituitary	Antidiuretic hormone (ADH) (also called vasopressin)	Increases water reabsorption by the kidneys and causes vasoconstriction and increased blood pressure	Peptide
	Oxytocin	Stimulates milk ejection from breasts and uterine contractions	Peptide

Overview of Endocrine Glands and Hormones

Gland/Tissue	Hormones	Major Functions	Chemical Structure
Thyroid	Thyroxine (T_4) and triiodothyronine (T_3)	Increases the rates of chemical reactions in most cells, thus increasing body metabolic rate	Amine
	Calcitonin	Promotes deposition of calcium in the bones and decreases extracellular fluid calcium ion concentration	Peptide
Adrenal cortex	Cortisol	Has multiple metabolic functions for controlling metabolism of proteins, carbohydrates, and fats; also has anti-inflammatory effects	Steroid
	Aldosterone	Increases renal sodium reabsorption, potassium secretion, and hydrogen ion secretion	Steroid
Adrenal medulla	Norepinephrine, epinephrine	Same effects as sympathetic stimulation	Amine
Pancreas	Insulin (β cells)	Promotes glucose entry in many cells, and in this way controls carbohydrate metabolism	Peptide
	Glucagon (α cells)	Increases synthesis and release of glucose from the liver into the body fluids	Peptide
Parathyroid	Parathyroid hormone (PTH)	Controls serum calcium ion concentration by increasing calcium absorption by the gut and kidneys and releasing calcium from bones	Peptide
Testes	Testosterone	Promotes development of male reproductive system and male secondary sexual characteristics	Steroid
Ovaries	Estrogens	Promotes growth and development of female reproductive system, female breasts, and female secondary sexual characteristics	Steroid
	Progesterone	Stimulates secretion of "uterine milk" by the uterine endometrial glands and promotes development of secretory apparatus of breasts	Steroid
Placenta	Human chorionic gonadotropin (HCG)	Promotes growth of corpus luteum and secretion of estrogens and progesterone by corpus luteum	Peptide
	Human somatomammotropin	Probably helps promote development of some fetal tissues as well as the mother's breasts	Peptide
	Estrogens	See actions of estrogens from ovaries	Steroid
	Progesterone	See actions of progesterone from ovaries	Steroid

Chemical characteristics of hormones

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

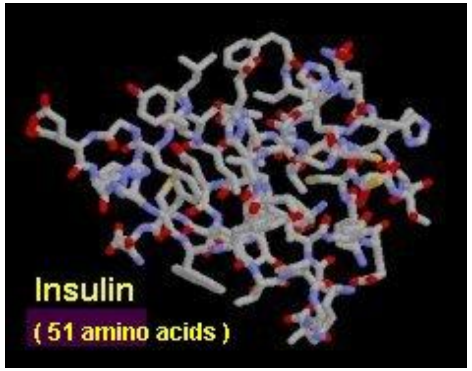
  anterior and posterior pituitary

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

  PTH, GH, PRL (proteins)

  FSH, LH,TSH (glycoproteins)

  the pancreas (insulin and glucagon),



Chemical characteristics of hormones

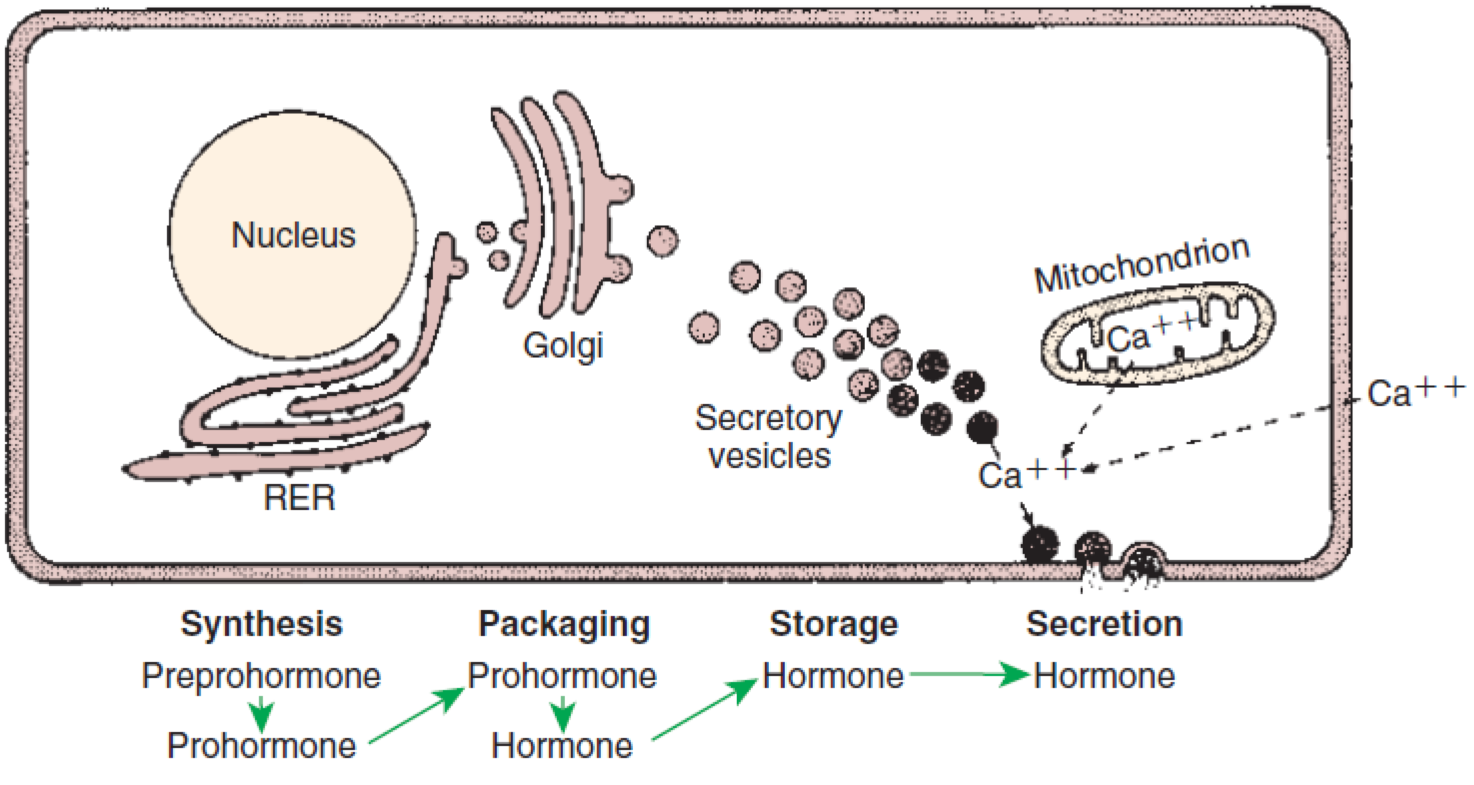
- Steroids (from cholesterol)
  - adrenal cortex (cortisol and aldosterone)
  - sex hormones

    the testes (testosterone),

    ovaries (estrogen and progesterone),

    placenta (estrogen and progesterone)

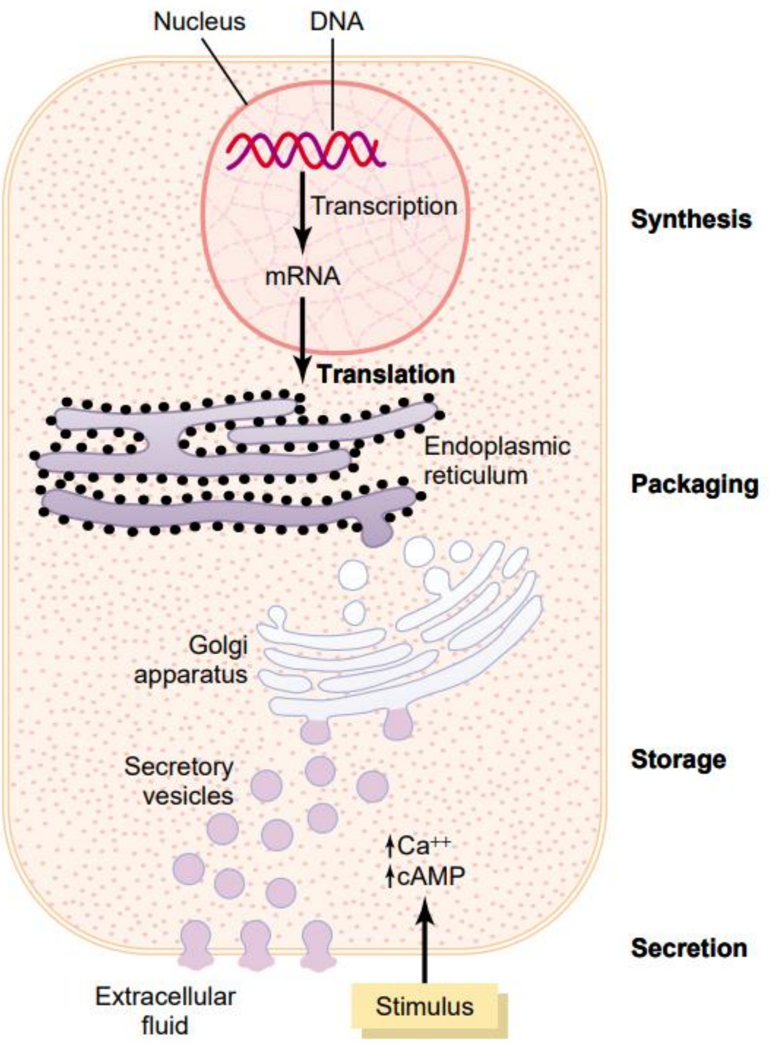
Synthesis of hormones



Subcellular components of peptide hormone synthesis and secretion.

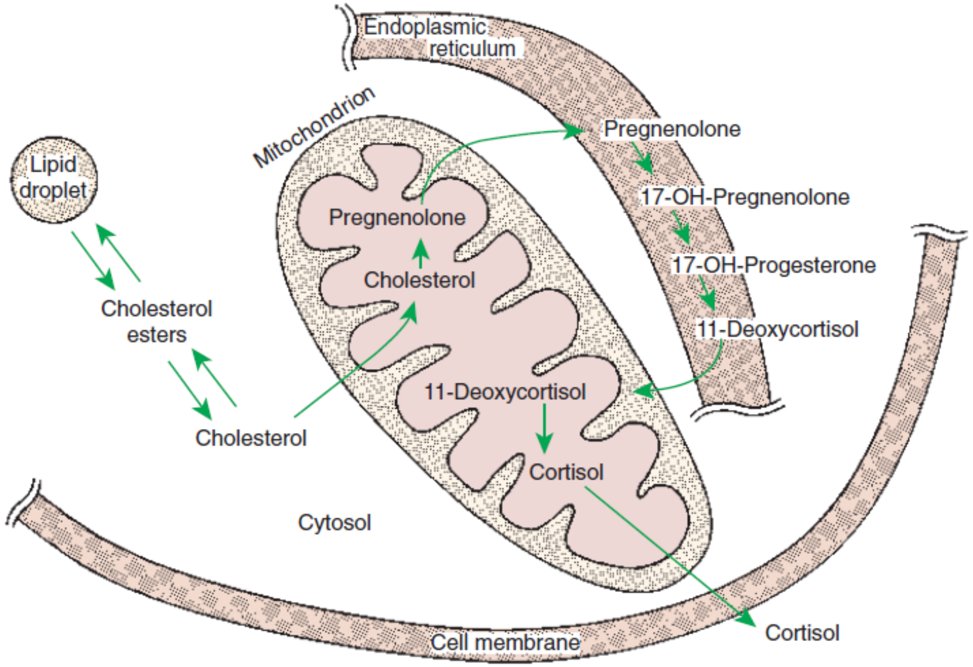
Hormone release

- 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



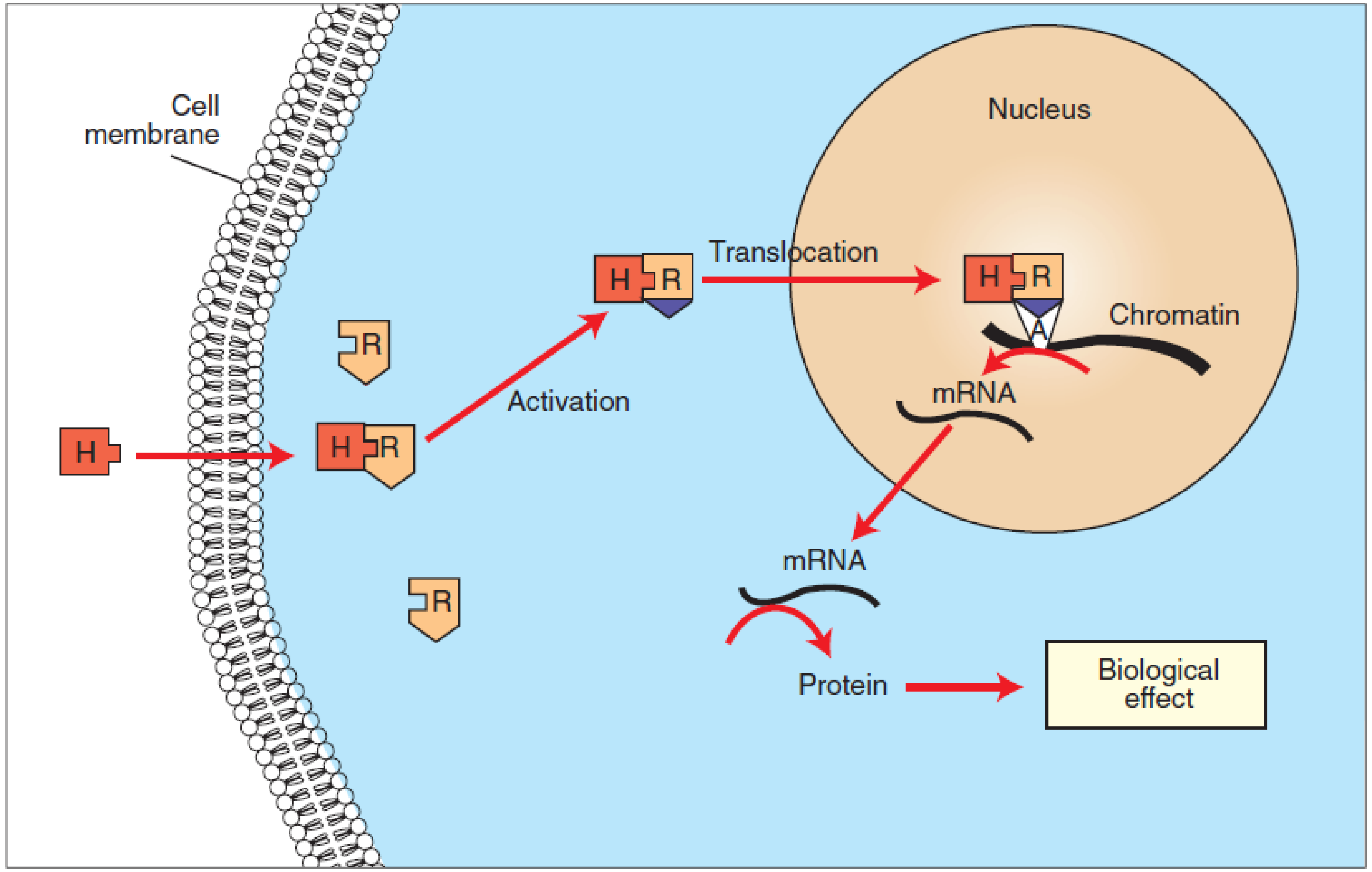
Hormone release

- Thyroid hormones:
  - made as part of thyroglobulin
  - stored in follicles
  - T3 & T4 secreted by enzymatic cleavage
- Steroid hormones:
  - leave the cell across cell membrane right after synthesis (no storage)



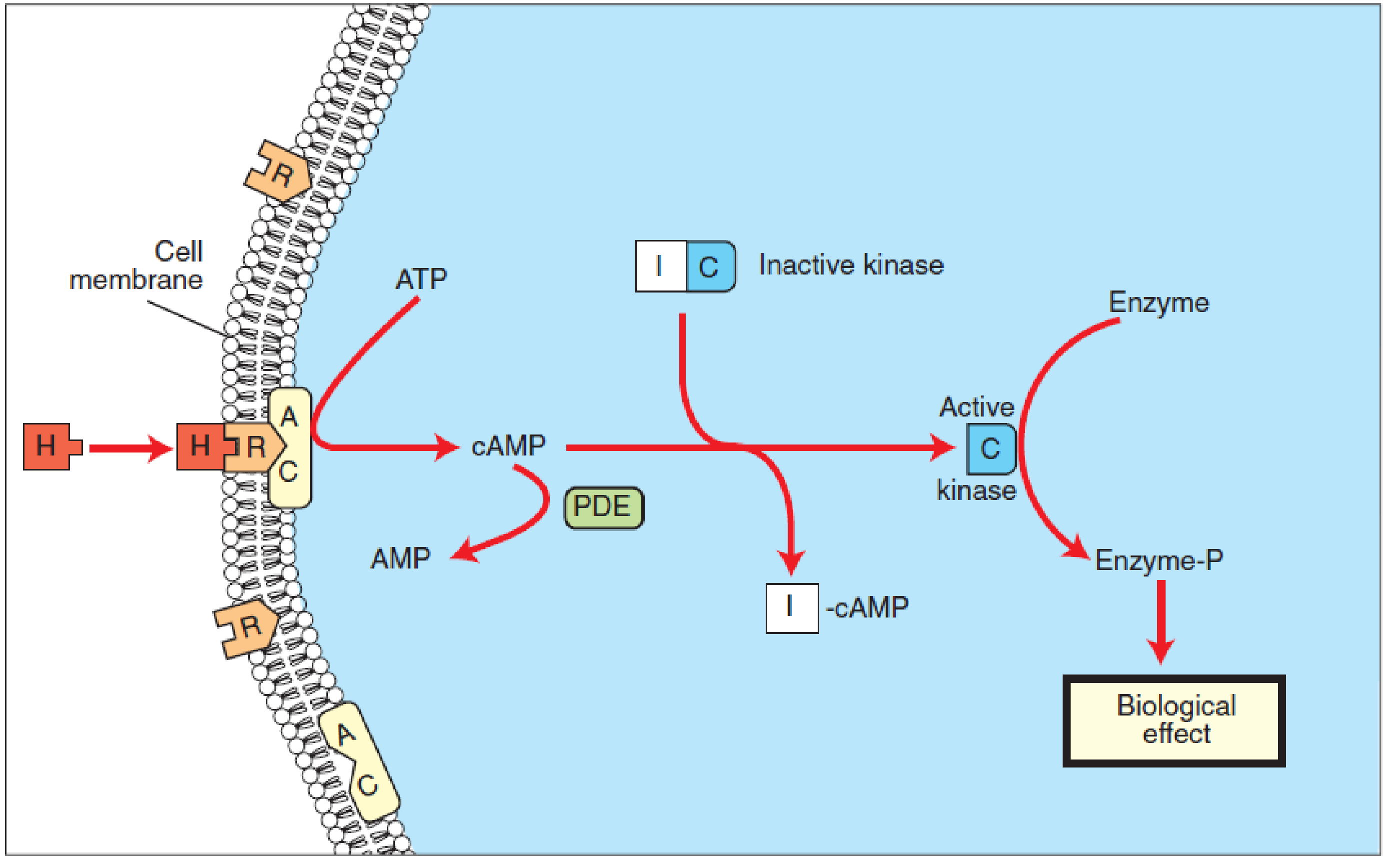
Subcellular compartmentalization of cortisol biosynthesis.

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.

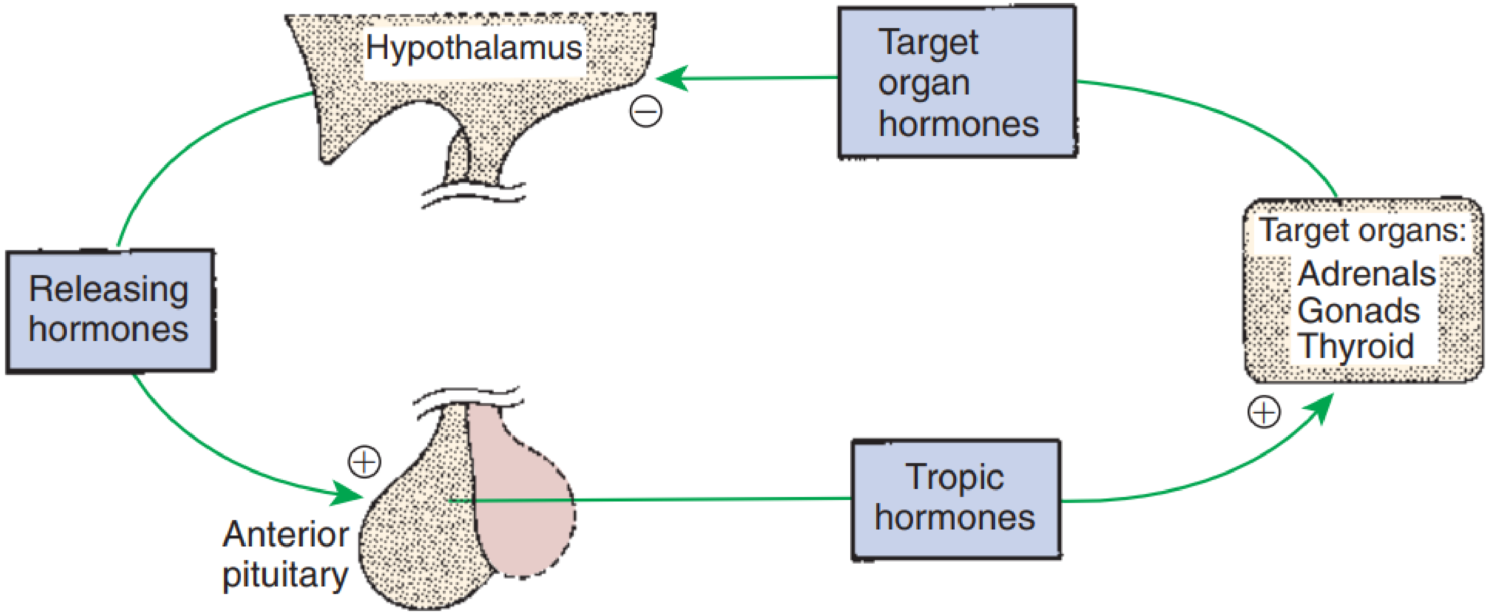
Postreceptor cell response to hormones



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

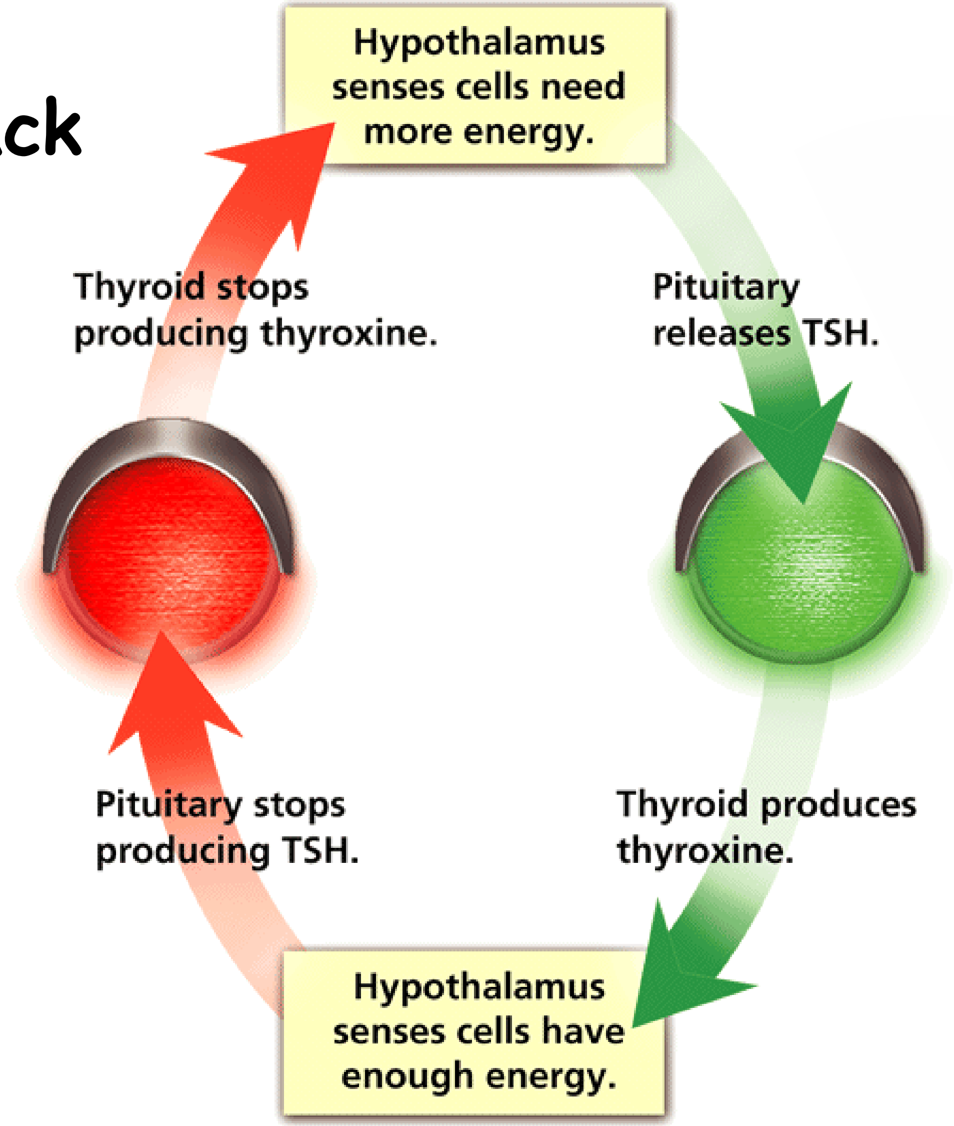
1. Negative feedback



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)

One example is the preovulatory release of LH, in which the pulsatile rate of LH secretion greatly increases during the late stages of ovarian follicular development because of increased estrogen production by the follicle.

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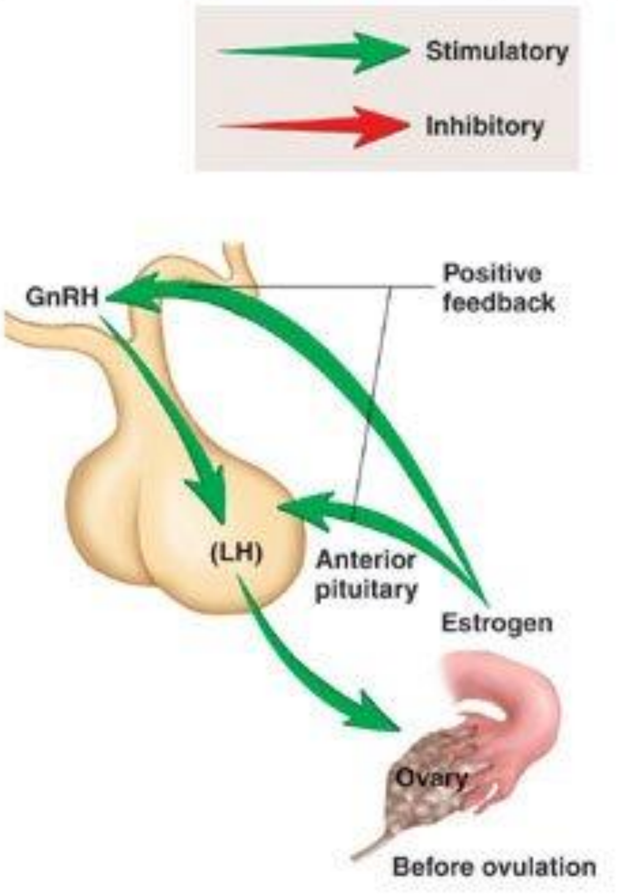


Regulation of hormone release

3. Nerve regulation

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

Combined feedback

Stress etc.

CRH secretion in hypothalamus

stimulation

ACTH secretion in pituitary

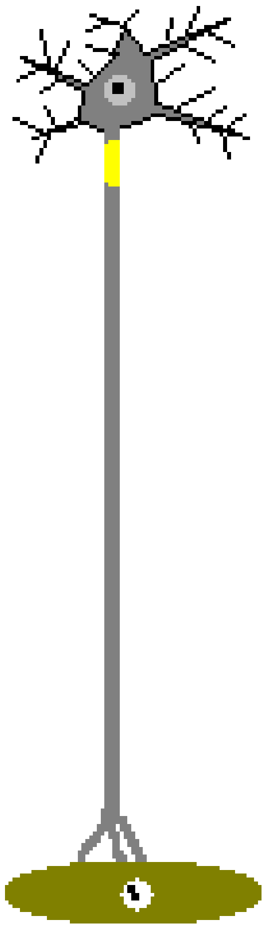
↑ plasma ACTH

inhibition

cortisol secretion in adrenals

↑ plasma cortisol

The Nervous System vs. Endocrine System



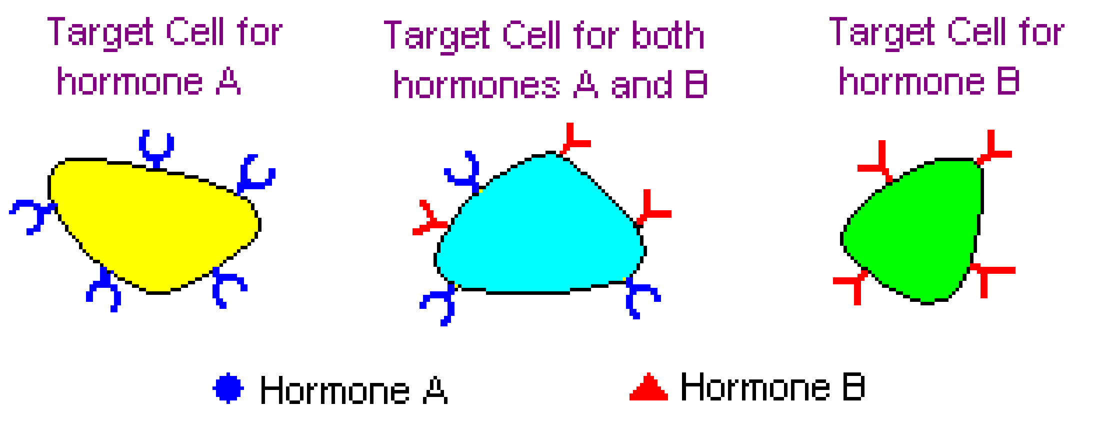
The nervous system
exerts point-to-point control through nerves, similar to sending messages by conventional telephone. Nervous control is electrical in nature and fast.

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?

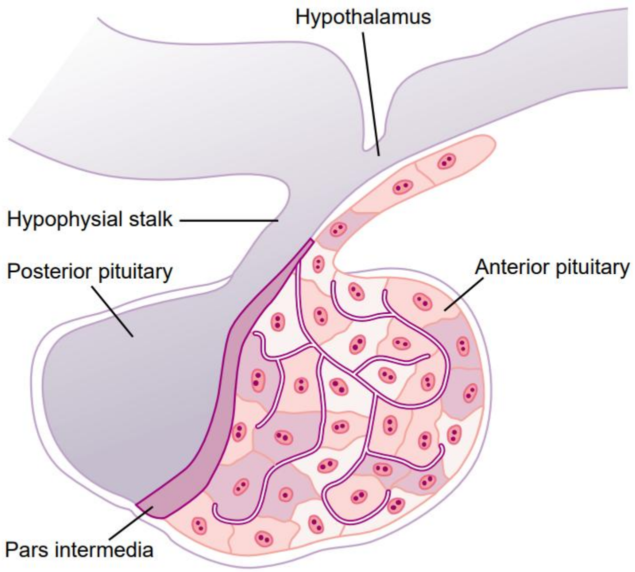
Section Two:

Pituitary Hormones and Their Control by the Hypothalamus

Pituitary Gland and Its Relation to the Hypothalamus

- The pituitary gland, also called the hypophysis, is a small gland—about 1 centimeter in diameter and 0.5 to 1 gram in weight—that lies in the sella turcica, a bony cavity at the base of the brain, and is connected to the hypothalamus by the pituitary (or hypophysial) stalk.

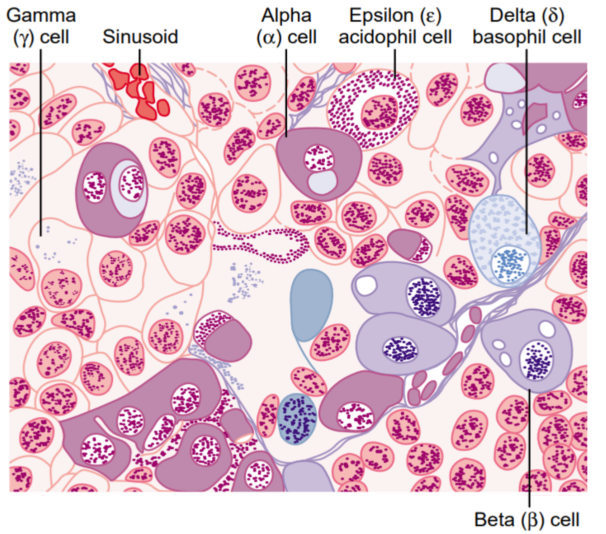
- Is divisible into two distinct portions: the anterior pituitary, also known as the adenohypophysis, and the posterior pituitary, also known as the neurohypophysis.

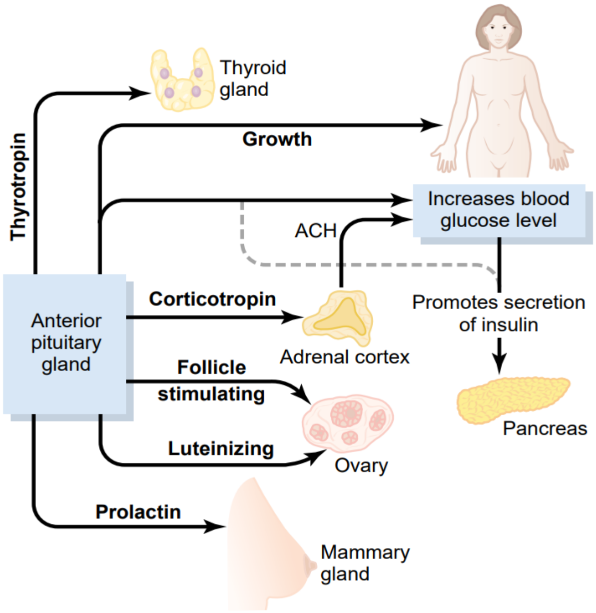


Pituitary Gland and Its Relation to the Hypothalamus

- Anterior Pituitary Gland Contains Several Different Cell Types That Synthesize and Secrete Hormones.

  - 1. Somatotropes—human growth hormone (hGH)
  - 2. Corticotropes—adrenocorticotropin (ACTH)
  - 3. Thyrotropes—thyroid-stimulating hormone (TSH)
  - 4. Gonadotropes—gonadotropic hormones, which include both luteinizing hormone (LH) and follicle stimulating hormone (FSH)
  - 5. Lactotropes—prolactin (PRL)





Pituitary Gland and *Its Relation to the* *Hypothalamus*

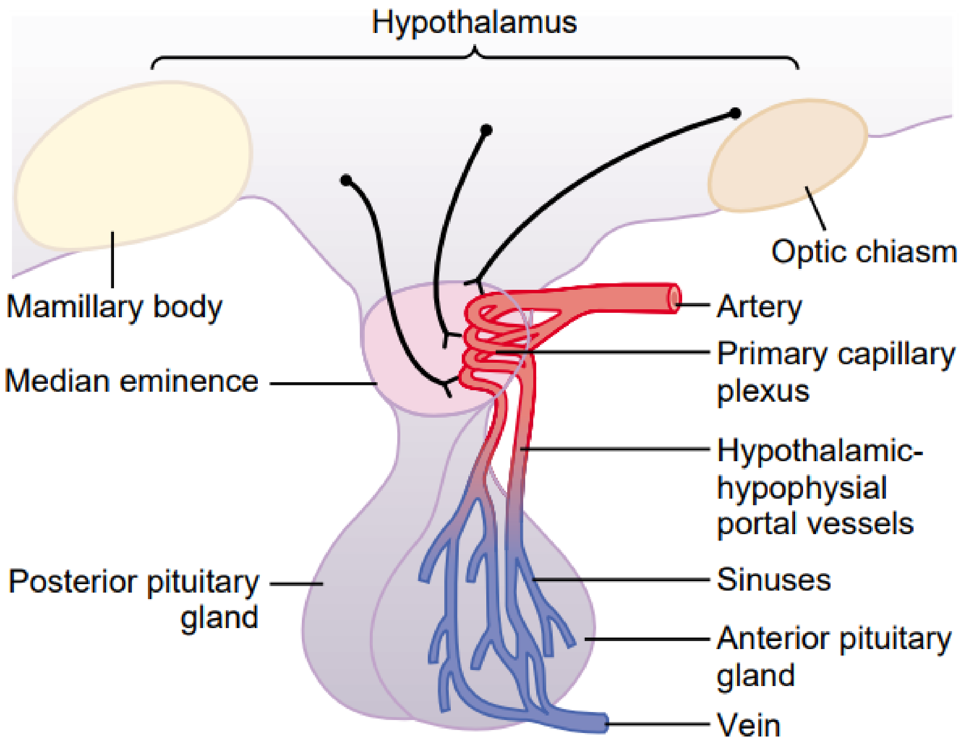
Cells and Hormones of the Anterior Pituitary Gland and Their Physiological Functions

Cell	Hormone	Chemistry	Physiological Actions
Somatotropes	Growth hormone (GH; somatotropin)	Single chain of 191 amino acids	Stimulates body growth; stimulates secretion of IGF-1; stimulates lipolysis; inhibits actions of insulin on carbohydrate and lipid metabolism
Corticotropes	Adrenocorticotropic hormone (ACTH; corticotropin)	Single chain of 39 amino acids	Stimulates production of glucocorticoids and androgens by the adrenal cortex; maintains size of zona fasciculata and zona reticularis of cortex
Thyrotropes	Thyroid-stimulating hormone (TSH; thyrotropin)	Glycoprotein of two subunits, α (89 amino acids) and β (112 amino acids)	Stimulates production of thyroid hormones by thyroid follicular cells; maintains size of follicular cells
Gonadotropes	Follicle-stimulating hormone (FSH)	Glycoprotein of two subunits, α (89 amino acids) and β (112 amino acids)	Stimulates development of ovarian follicles; regulates spermatogenesis in the testis
	Luteinizing hormone (LH)	Glycoprotein of two subunits, α (89 amino acids) and β (115 amino acids)	Causes ovulation and formation of the corpus luteum in the ovary; stimulates production of estrogen and progesterone by the ovary; stimulates testosterone production by the testis
Lactotropes, Mammotropes	Prolactin (PRL)	Single chain of 198 amino acids	Stimulates milk secretion and production

IGF, insulin-like growth factor

Pituitary Gland and Its Relation to the Hypothalamus

- The anterior pituitary is a highly vascular gland with extensive capillary sinuses among the glandular cells.
- Almost all the blood that enters these sinuses passes first through another capillary bed in the lower hypothalamus.
- The blood then flows through small *hypothalamic-hypophysial* portal blood vessels into the anterior pituitary sinuses.



Hypothalamus as a gland

Hypothalamic Releasing and Inhibitory Hormones That Control Secretion of the Anterior Pituitary Gland

Hormone	Structure	Primary Action on Anterior Pituitary
Thyrotropin-releasing hormone (TRH)	Peptide of 3 amino acids	Stimulates secretion of TSH by thyrotropes
Gonadotropin-releasing hormone (GnRH)	Single chain of 10 amino acids	Stimulates secretion of FSH and LH by gonadotropes
Corticotropin-releasing hormone (CRH)	Single chain of 41 amino acids	Stimulates secretion of ACTH by corticotropes
Growth hormone–releasing hormone (GHRH)	Single chain of 44 amino acids	Stimulates secretion of growth hormone by somatotropes
Growth hormone inhibitory hormone (somatostatin)	Single chain of 14 amino acids	Inhibits secretion of growth hormone by somatotropes
Prolactin-inhibiting hormone (PIH)	Dopamine (a catecholamine)	Inhibits secretion of prolactin by lactotropes

ACTH, adrenocorticotropic hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; TSH, thyroid-stimulating hormone.

Anterior pituitary

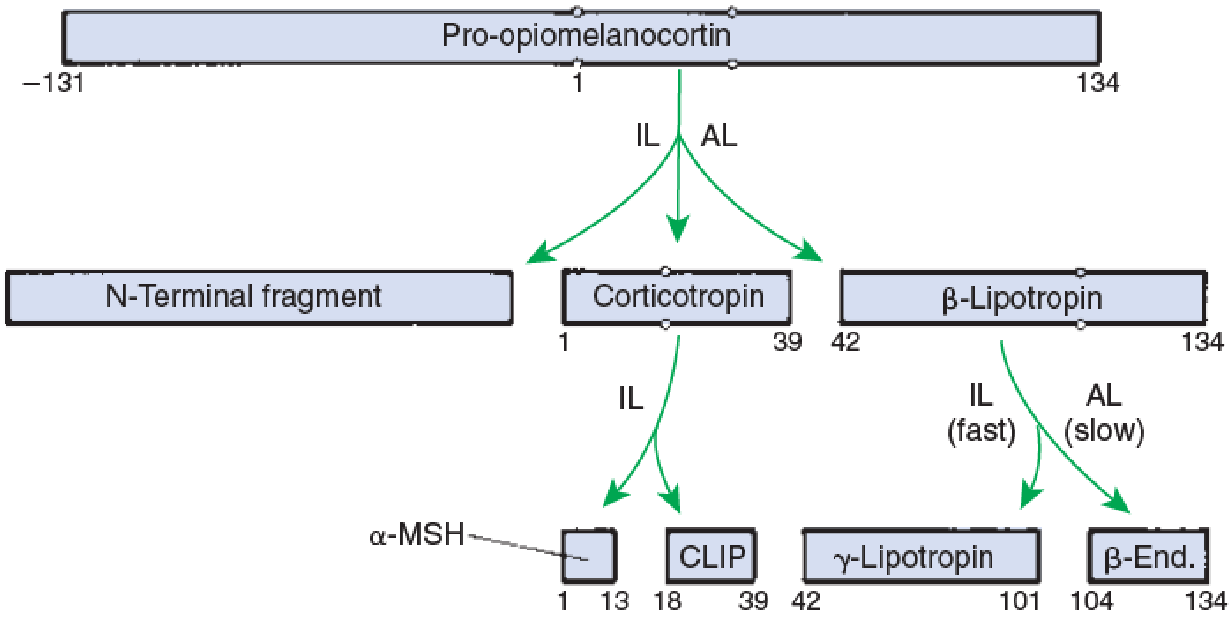
- GH and PRL are single-chain proteins that contain two and three disulfide bonds, respectively.
- There is overlap of activity between GH and PRL; this overlap is based on the approximately 50% homology of their amino acid sequences.
- Of these two major somatomammotropins, GH is uniquely species specific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

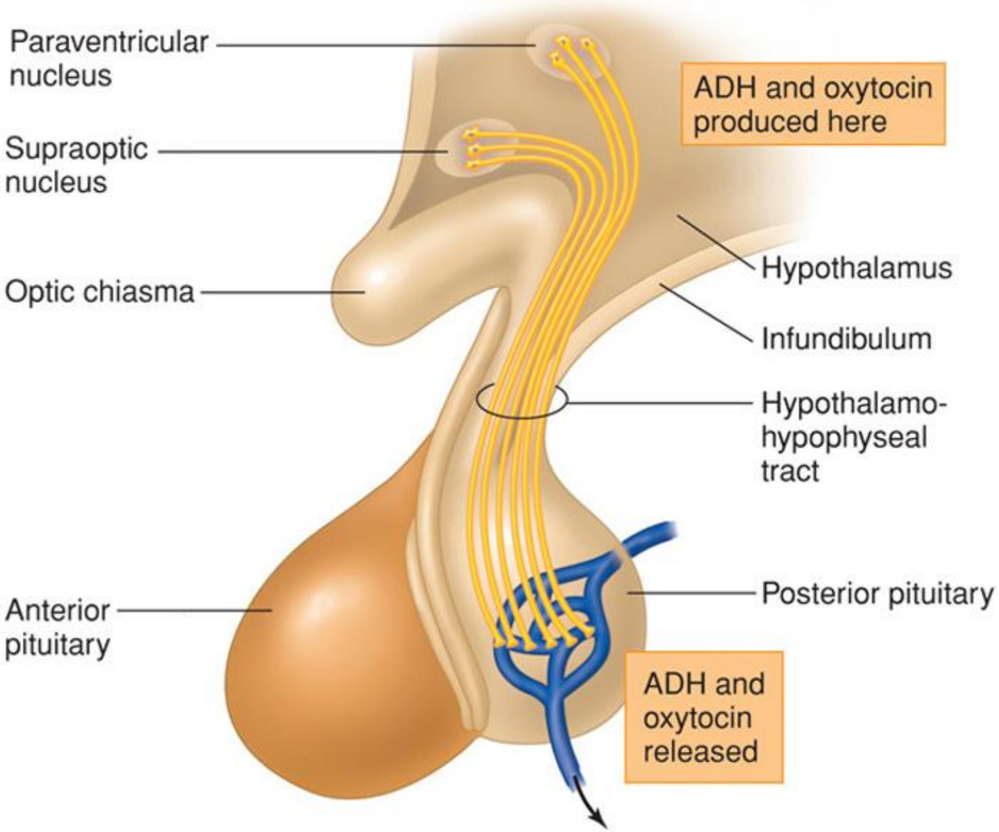


Cleavage of pro-opiomelanocortin to yield corticotropin and related peptides.
By convention, the numbering of the amino acids begins
with the first one of corticotropin and then increases positively toward the carboxy terminal and negatively toward the amino terminal.
Cleavage occurs at pairs of basic 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.

Posterior pituitary

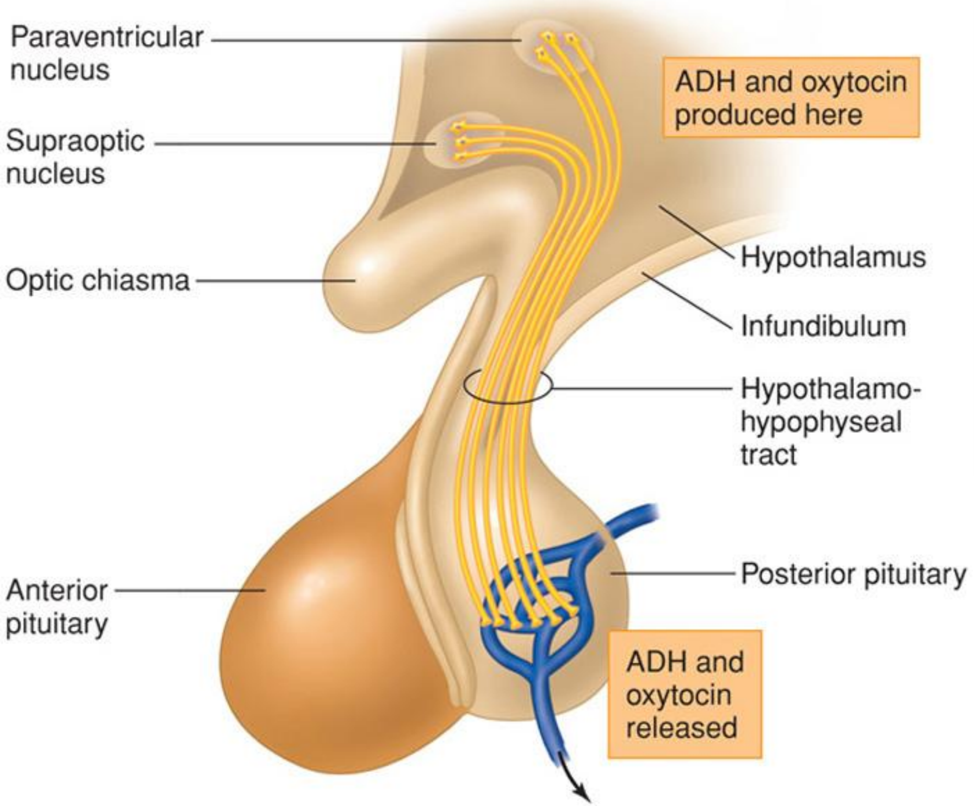
Stores and releases vasopressin (ADH) and oxytocin

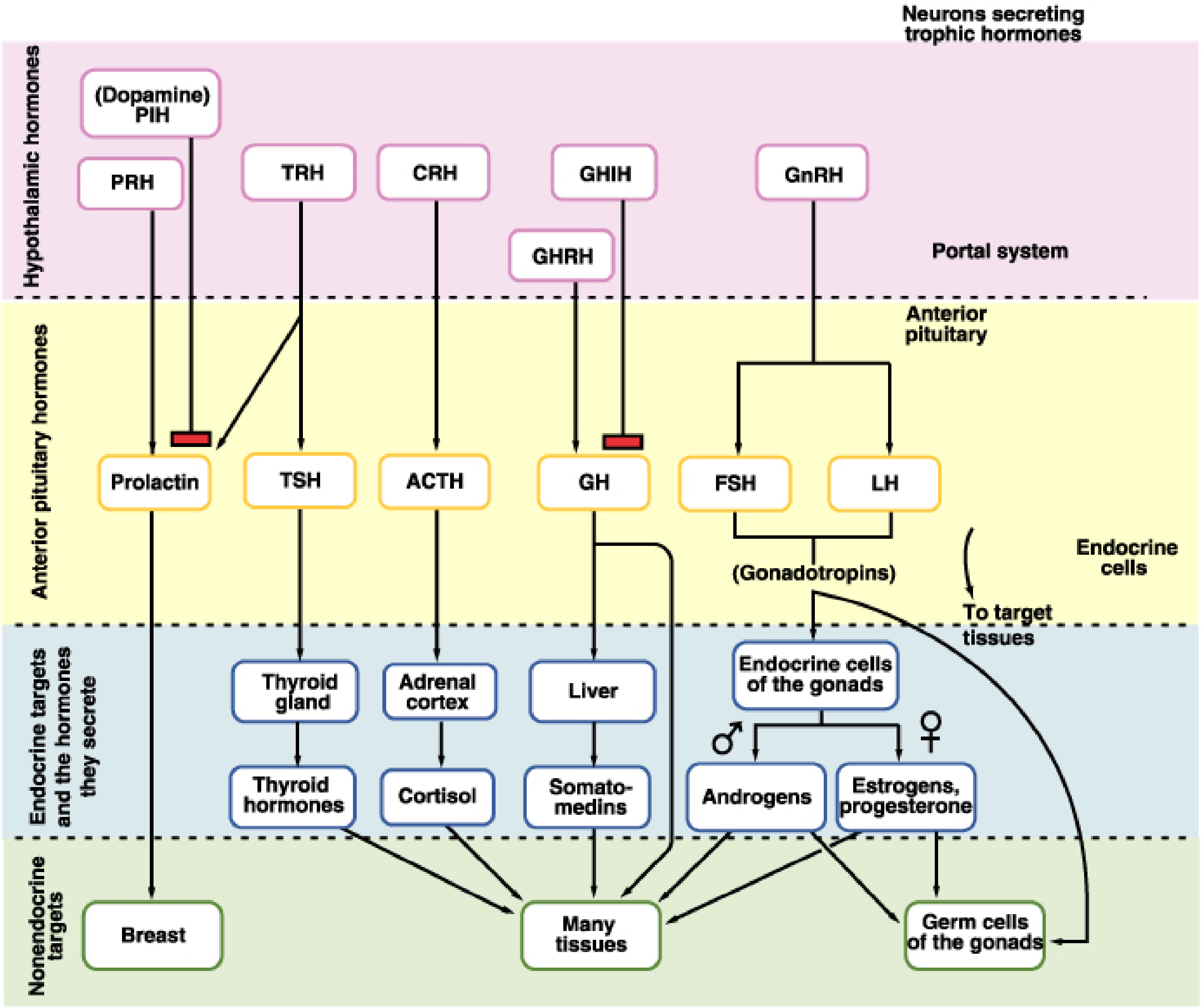
- hormones made in the hypothalamus



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
GHRH
GnRH
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 Three:

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.

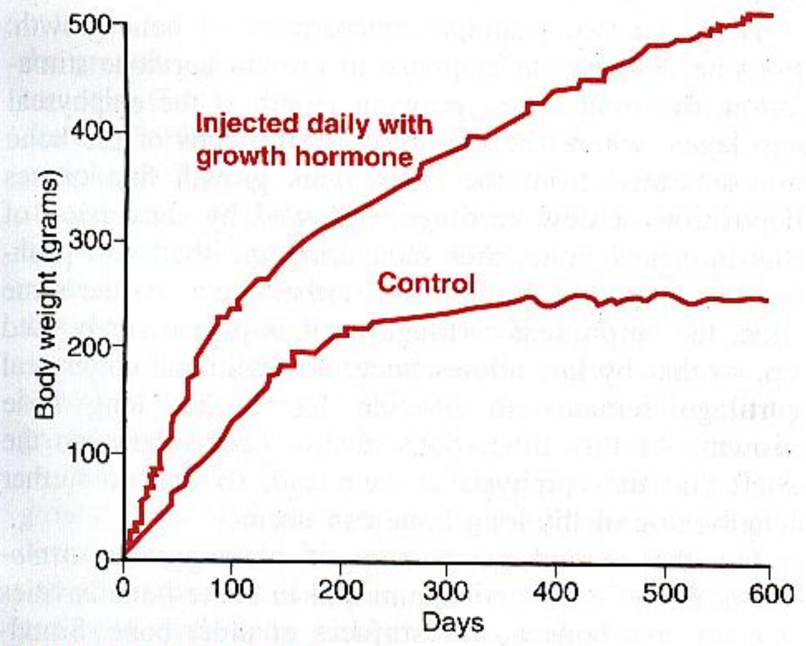


FIGURE 75–5

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

Growth Hormone

1.Physiological effects on growth

- it has been found that growth hormone causes the liver (and, to a much less extent, other tissues) to form several small proteins called somatomedins that have the potent effect of increasing all aspects of bone growth.
- Many of the somatomedin effects on growth are similar to the effects of insulin on growth.
  - Therefore, the somatomedins are also called insulin-like growth factors (IGFs).

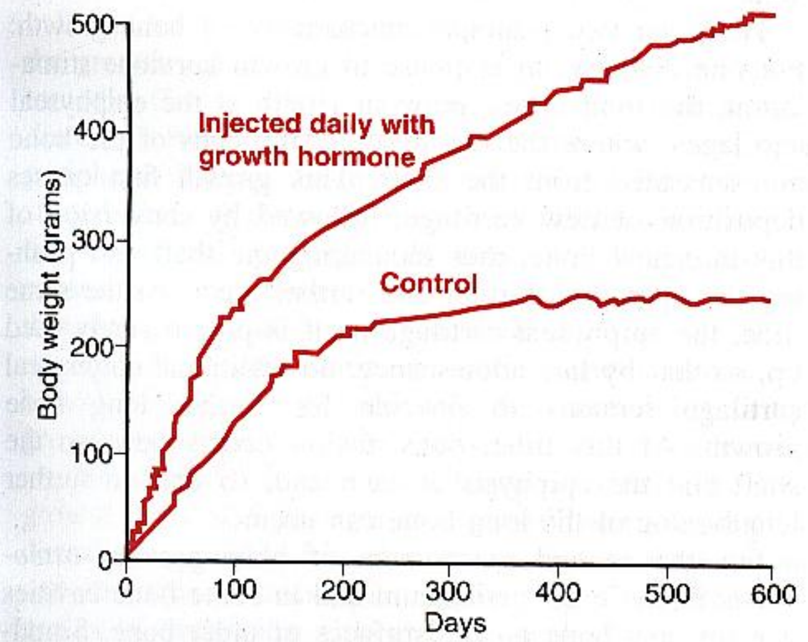


FIGURE 75 – 5

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

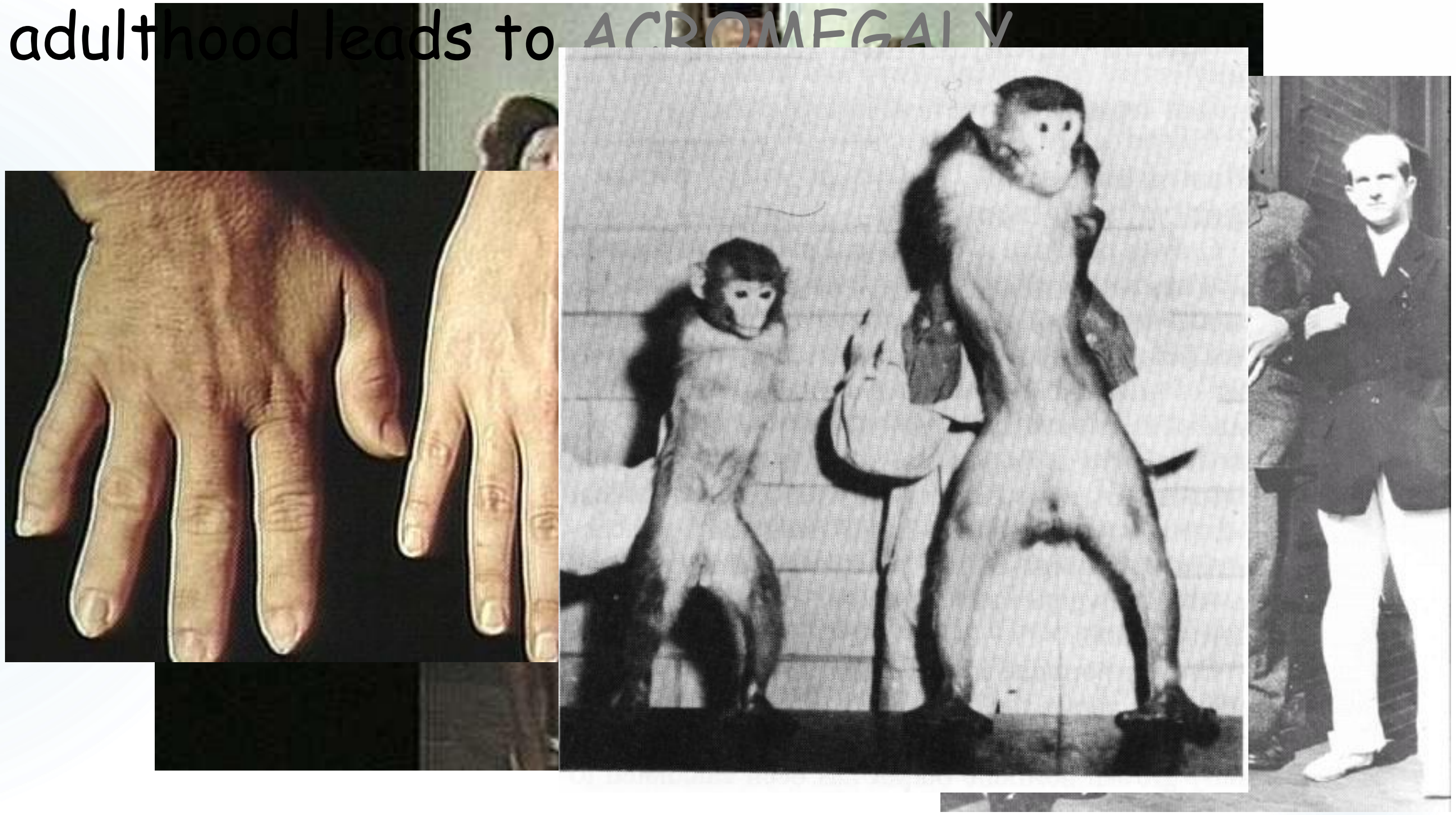
Growth Hormone

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

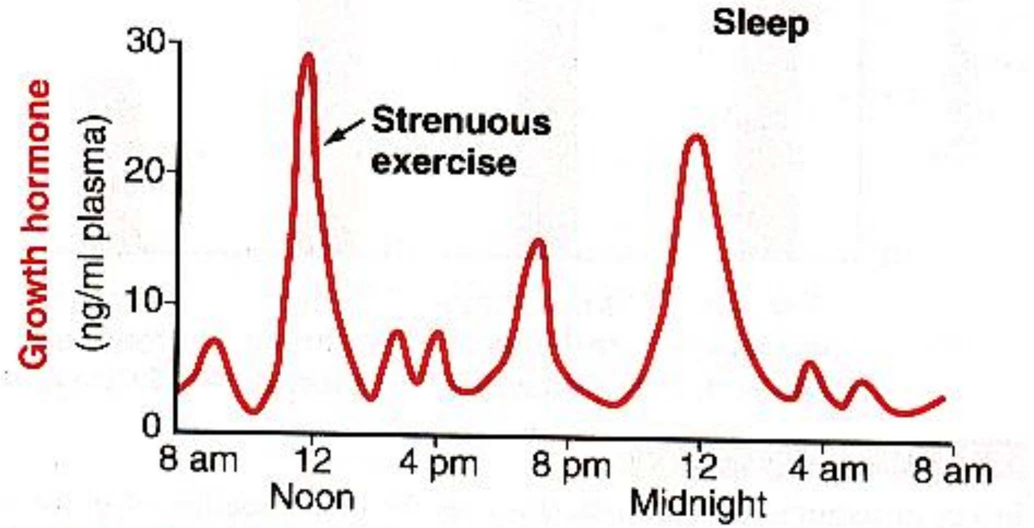
3) Regulation of GH secretion

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.

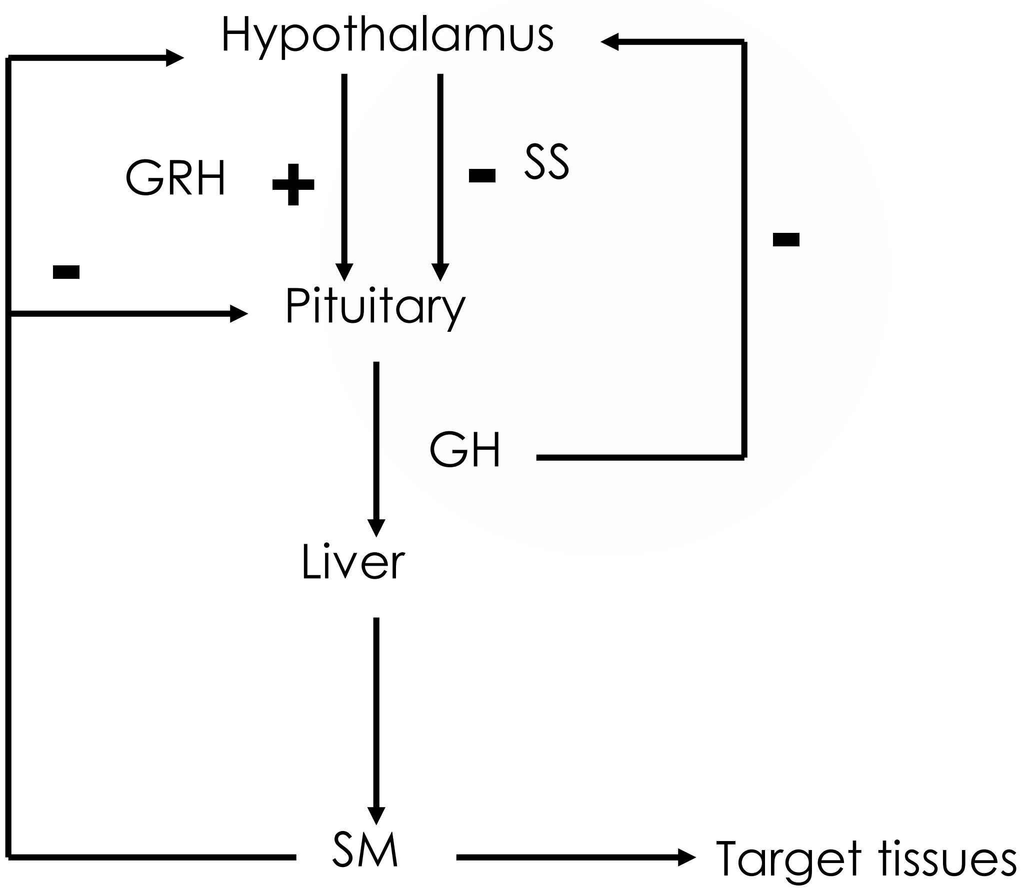


Growth Hormone

3) Regulation of GH secretion

Factors That Stimulate or Inhibit Secretion of Growth Hormone

Stimulate Growth Hormone Secretion	Inhibit Growth Hormone Secretion
Decreased blood glucose	Increased blood glucose
Decreased blood free fatty acids	Increased blood free fatty acids
Starvation or fasting, protein deficiency	Aging
Trauma, stress, excitement	Obesity
Exercise	Growth hormone inhibitory hormone (somatostatin)
Testosterone, estrogen	Growth hormone (exogenous)
Deep sleep (stages II and IV)	Somatomedins (insulin-like growth factors)
Growth hormone–releasing hormone	

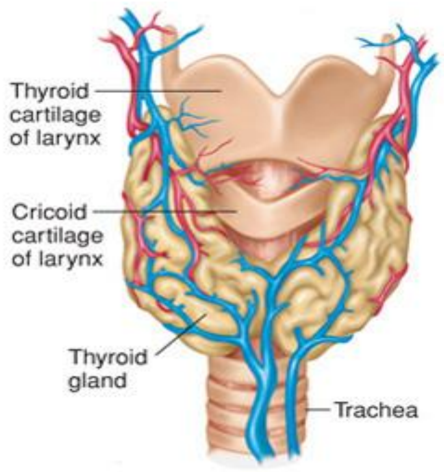


Section Four:

The 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



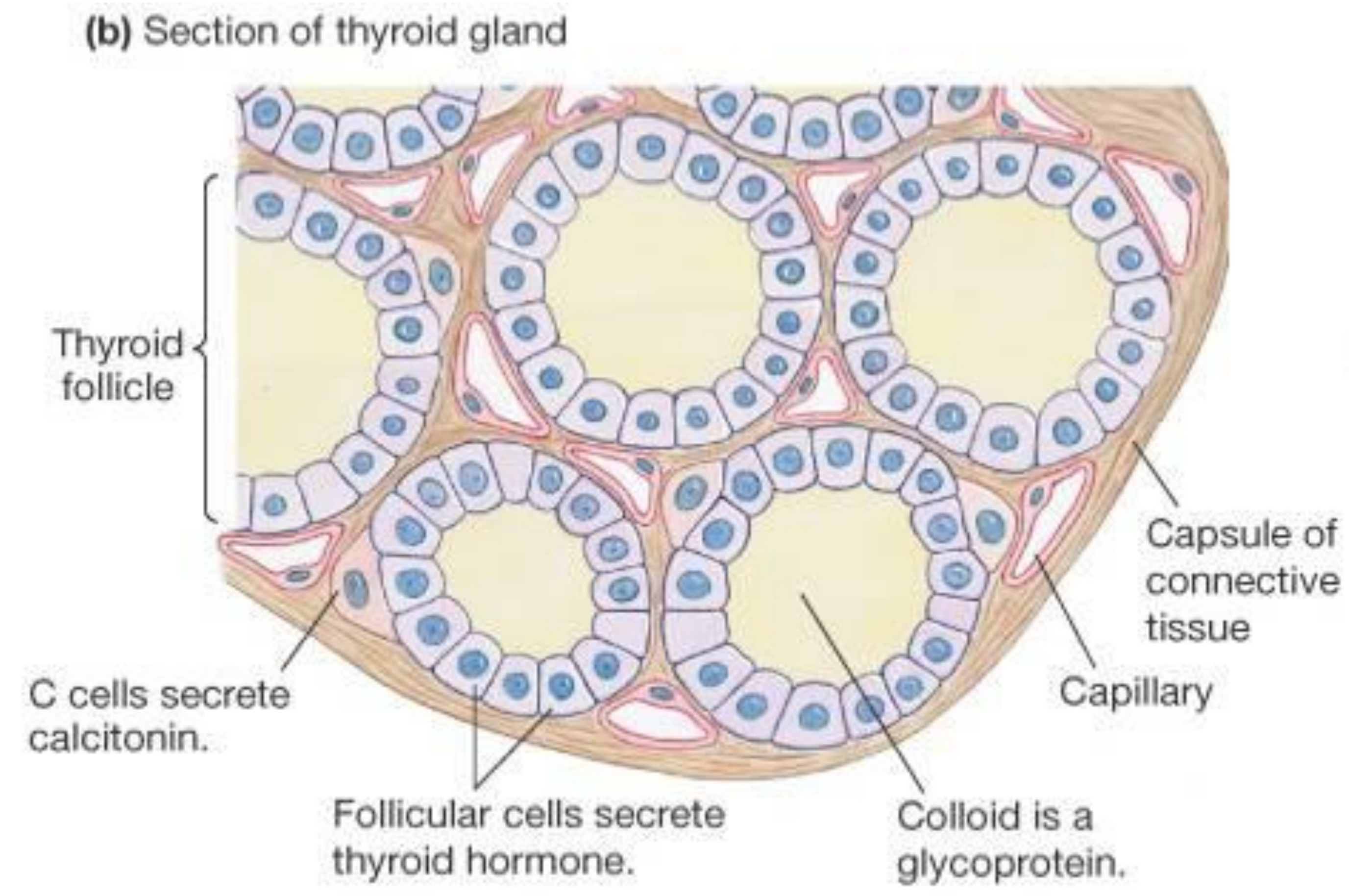
(a)

(b)

b:© Nawrocki Stock Photo, Inc.

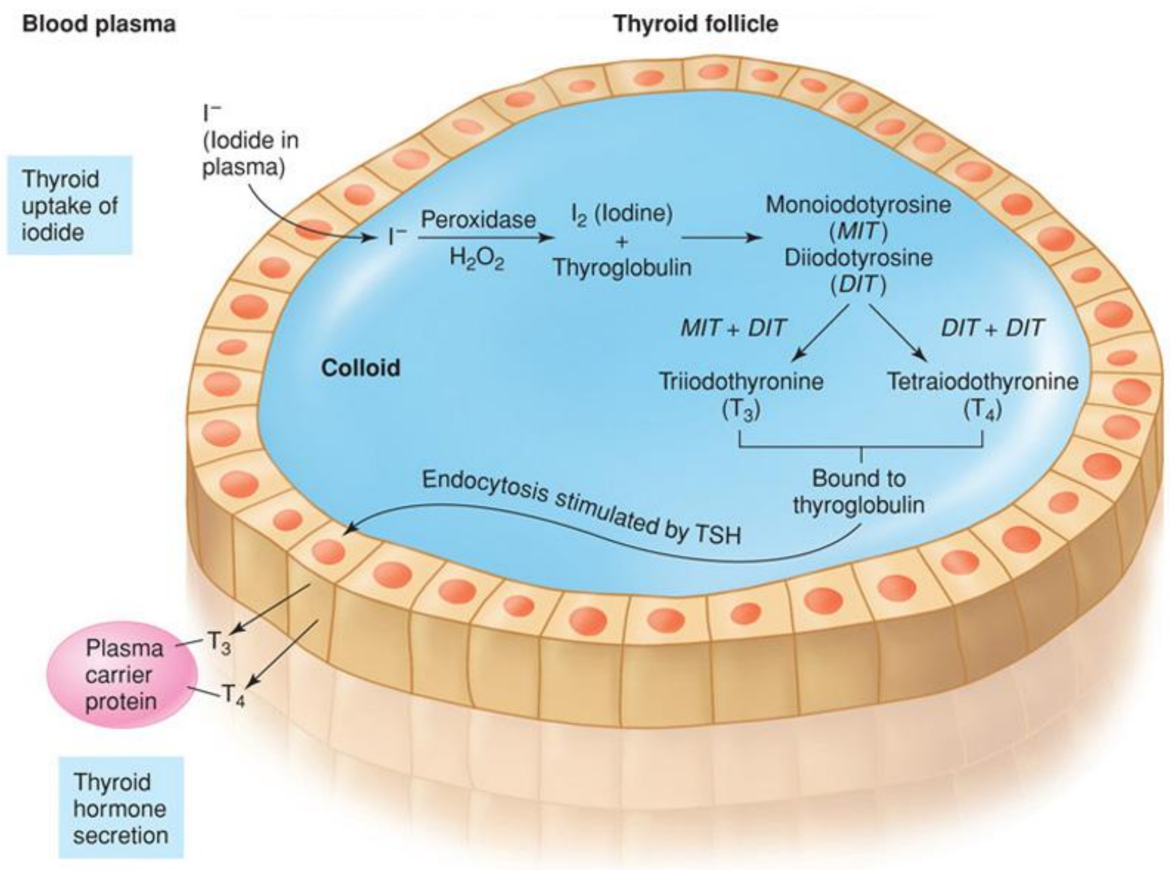
A scan of the thyroid 24 hrs. after intake of radioactive iodine

Thyroid Gland

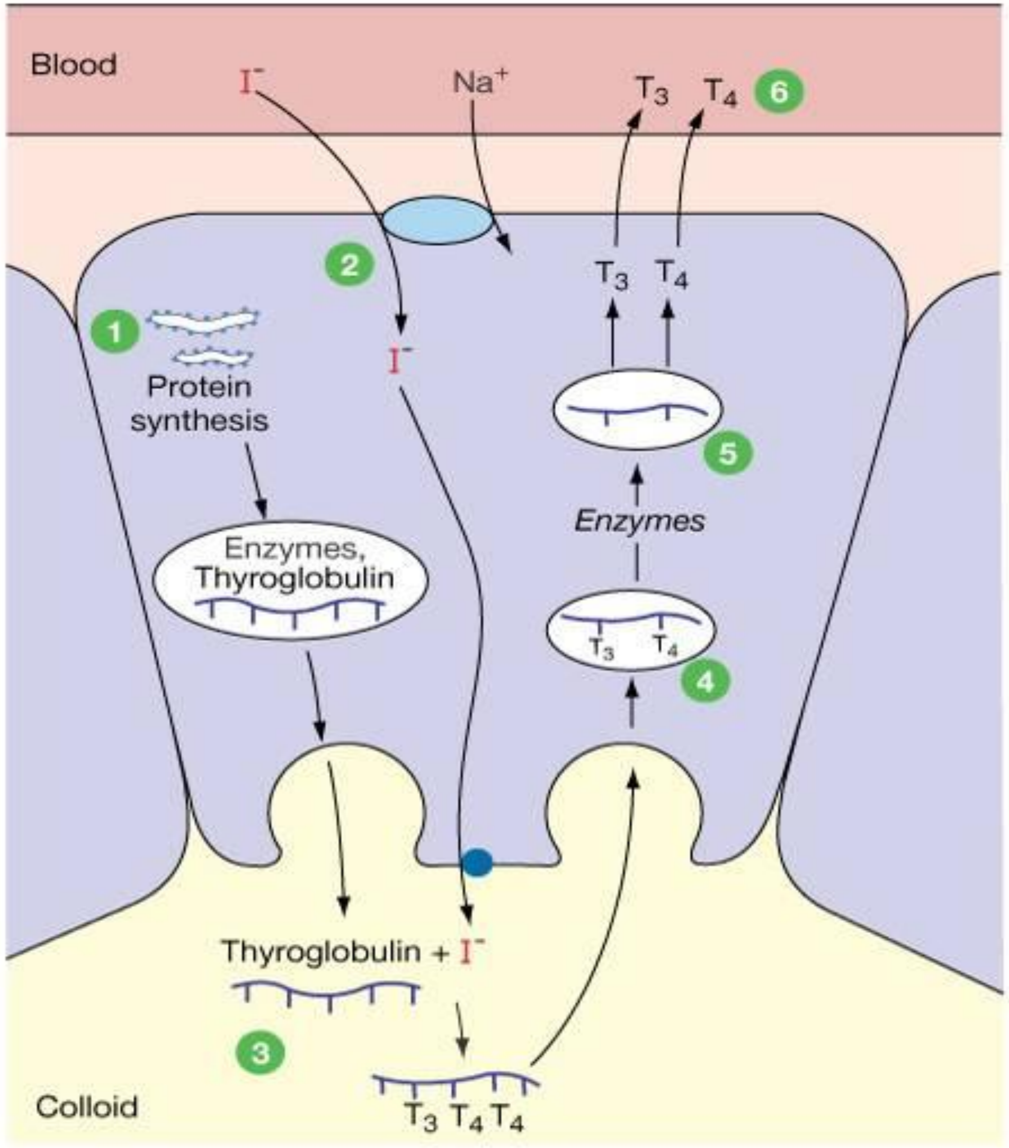


Thyroid Gland

- 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

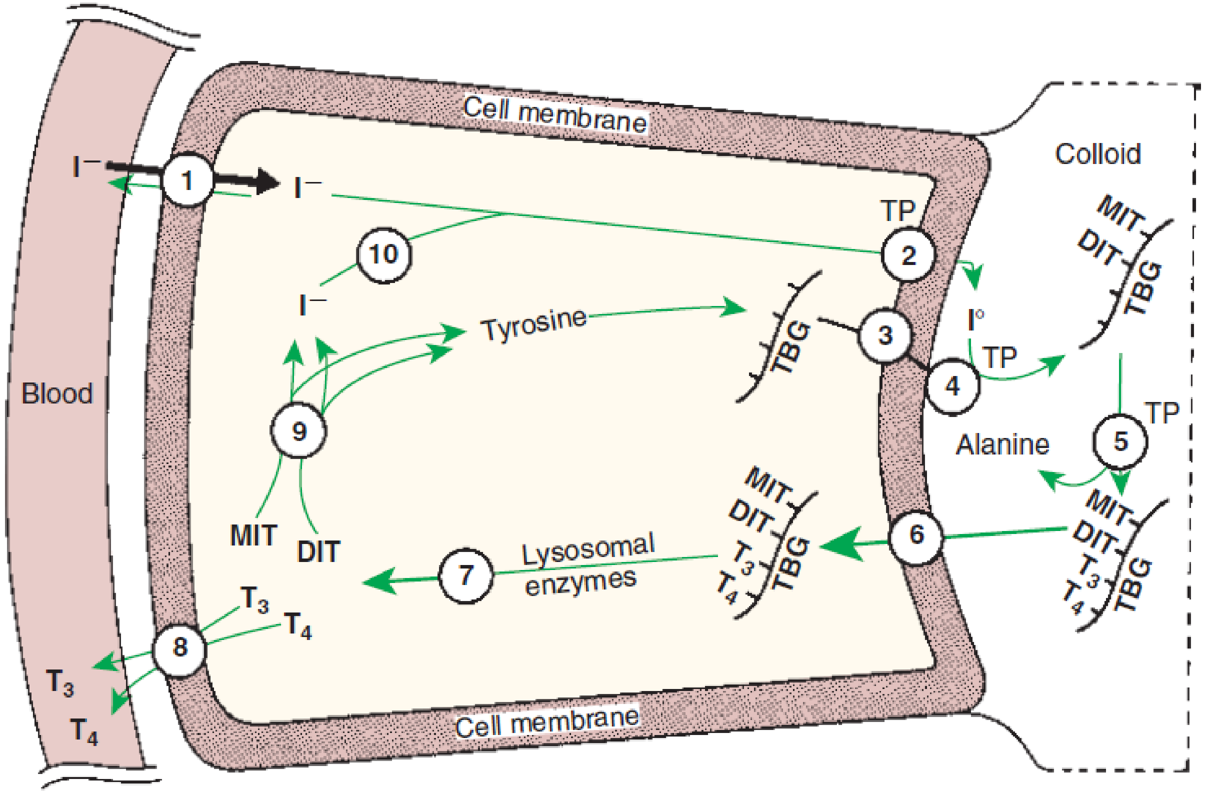


1. Follicular cell synthesizes enzymes and thyroglobulin for colloid.
2. I^- is co-transported into the cell with Na^+ and transported into colloid.
3. Enzymes add iodine to thyroglobulin to make T_3 and T_4.
4. Thyroglobulin is taken back into the cell.
5. Intracellular enzymes separate T_3 and T_4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

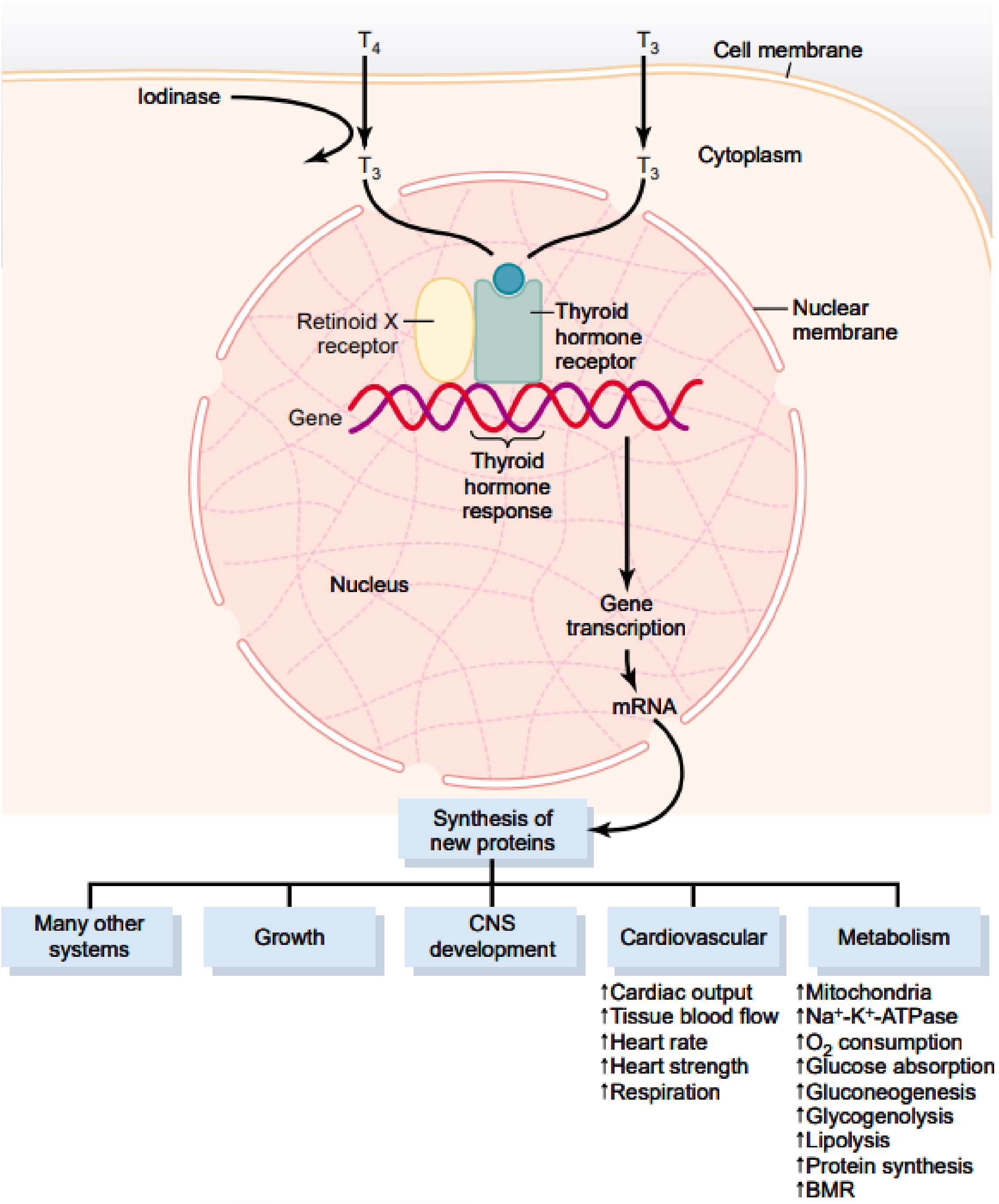
T_3 and T_4 formation and release

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.



T_3 and T_4 effects



- Thyroid hormone activation of target cells. Thyroxine (T4) and triiodothyronine (T3) readily diffuse through the cell membrane.

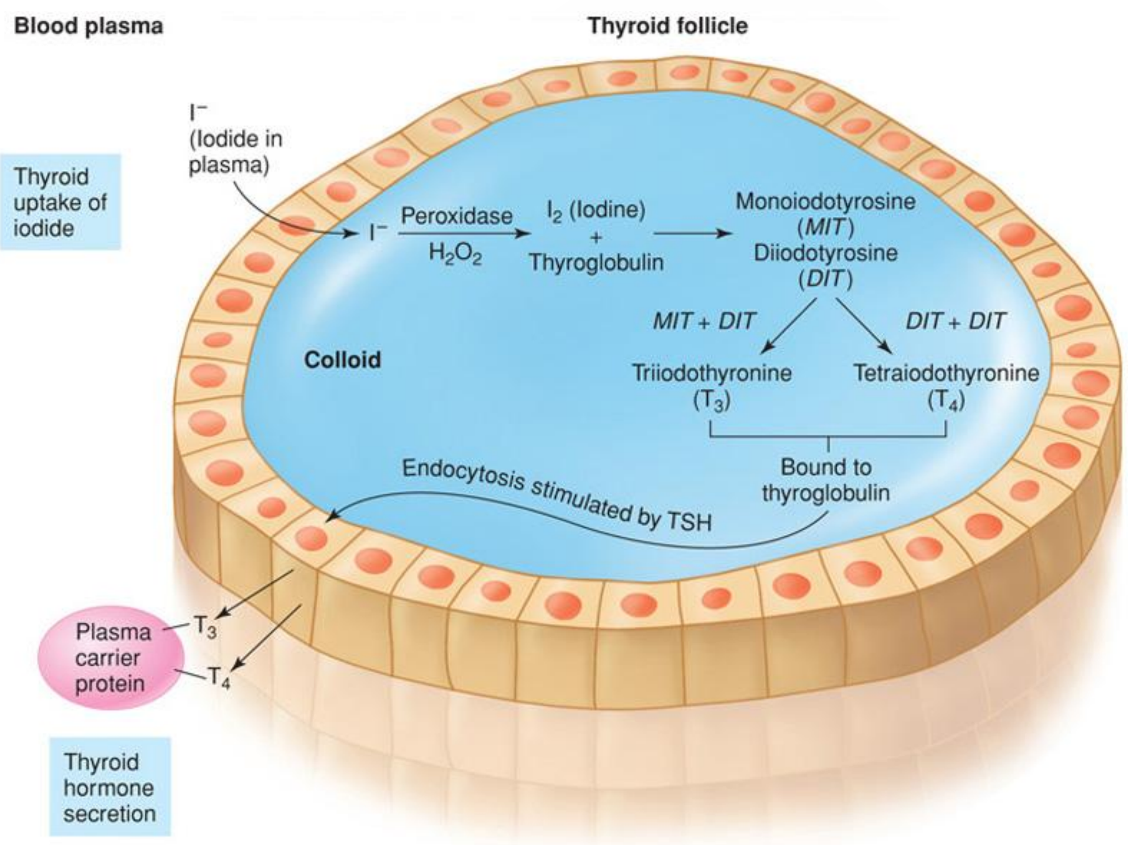
- Much of the T4 is deiodinated to form T3, which interacts with the thyroid hormone receptor, bound as a heterodimer with a retinoid X receptor, of the thyroid hormone response

- element of the gene.
- This causes either increases or decreases in transcription of genes that lead to formation of proteins, thus producing the thyroid hormone response of the cell.

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.



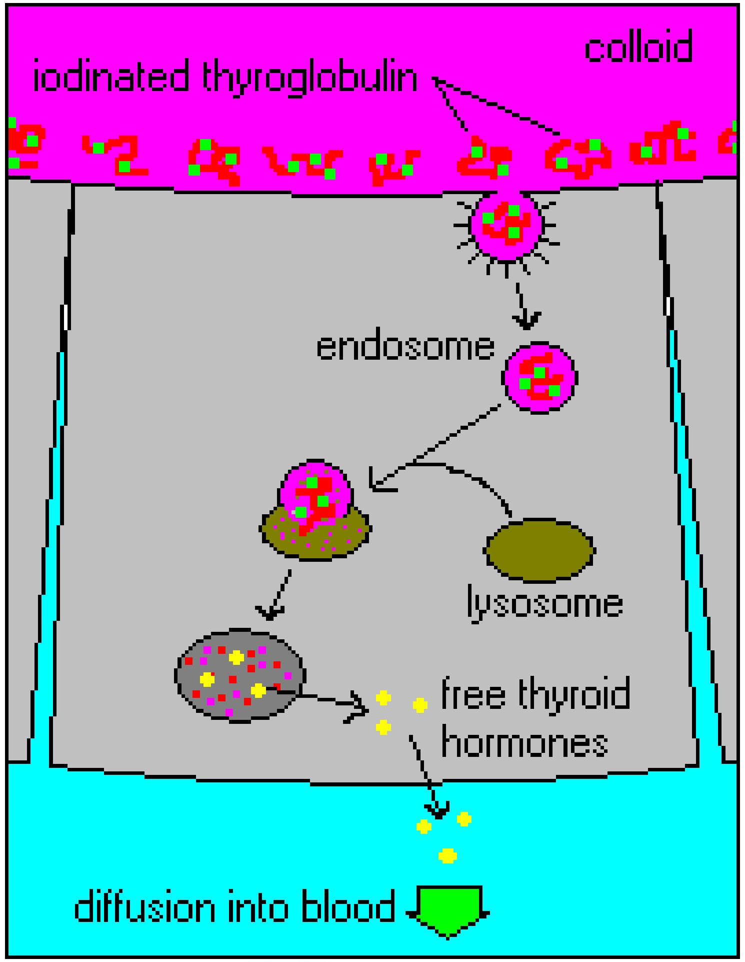
T_3 & T_4

- 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.

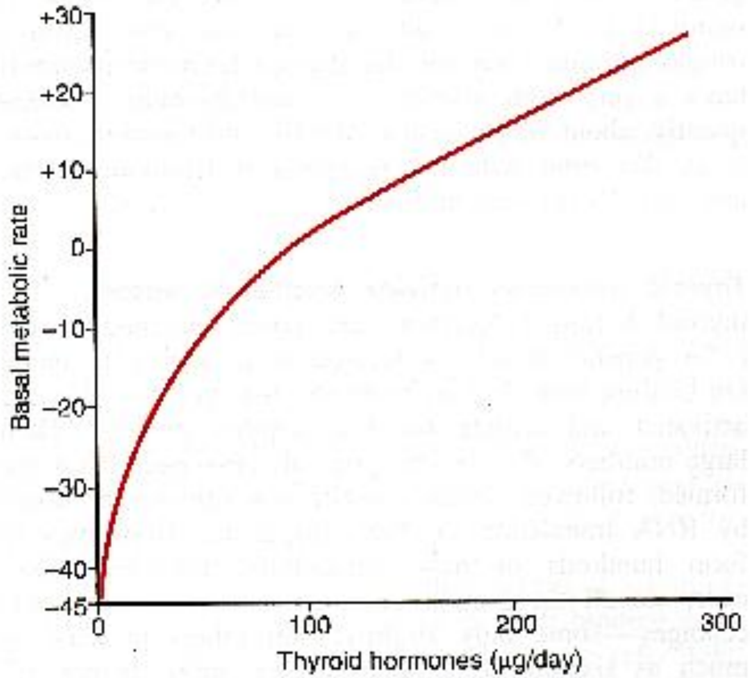


FIGURE 76-5

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.

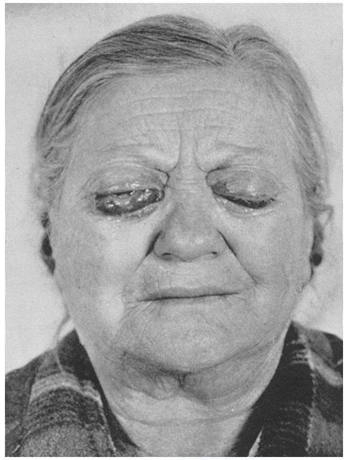
- Normally, T_4 and T_3 stimulates synthesis of proteins and enzymes, increasing anabolism of protein and causing positive balance of nitrogen

- 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

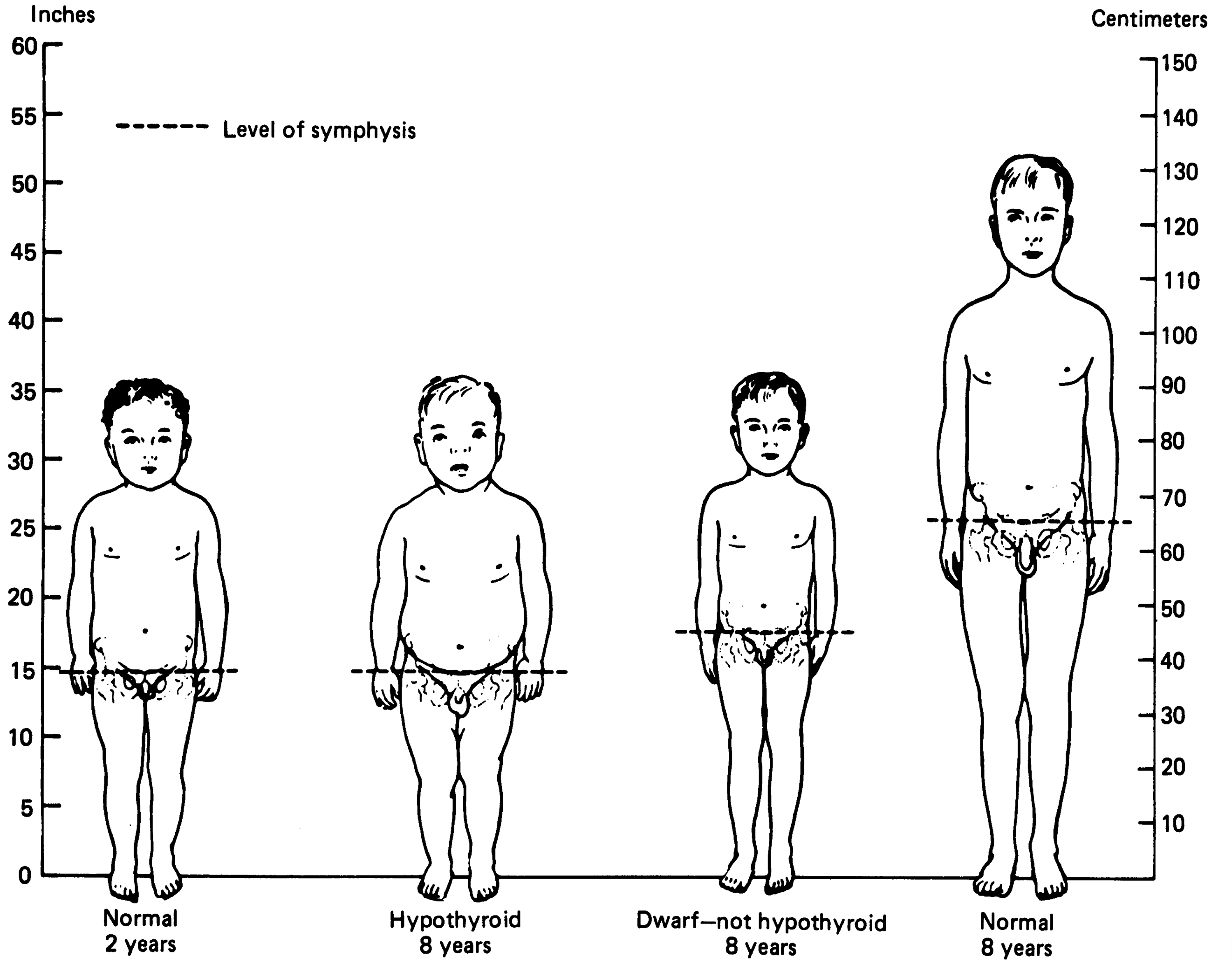
Thyroid hormone is essential for normal growth and development especially skeletal growth and development.

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

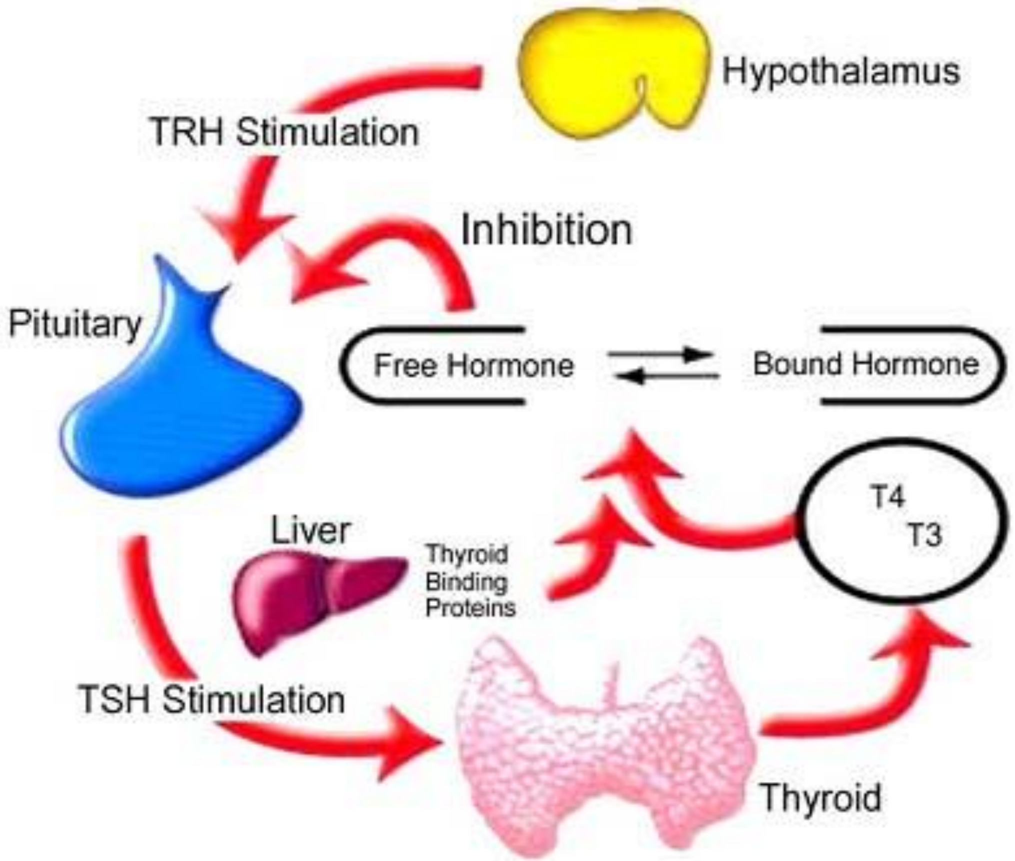
- Thyroid hormones increase the heart rate and force of contraction, probably through their interaction with the catecholamines by increasing the responsiveness of tissues to β-adrenergic receptors.
- Blood pressure is elevated because of increased systolic pressure, with no change in diastolic pressure;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

- 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.



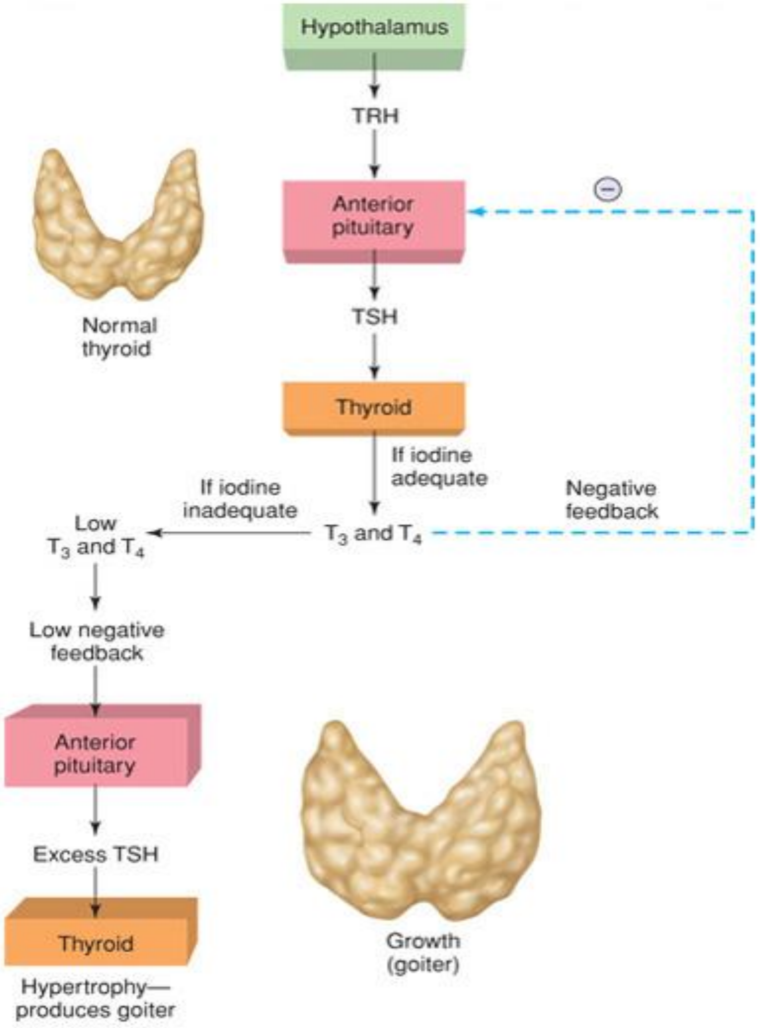
T_3 & T_4 secretion disorders

- 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

- Insufficient dietary iodide, T_4 and T_3 cannot be made and levels are low
  - Low T_4 and T_3 provide negative feedback and TSH levels go up
    - Because TSH is a trophic hormone, thyroid gland grows
    - Resulting in a goiter



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.

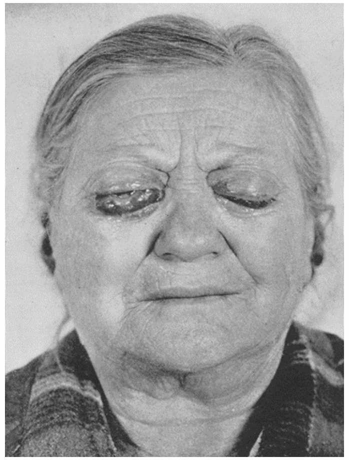
Hyperthyroidism in Cats

- 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)

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

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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 Five:

The Adrenal Gland

Adrenal Gland

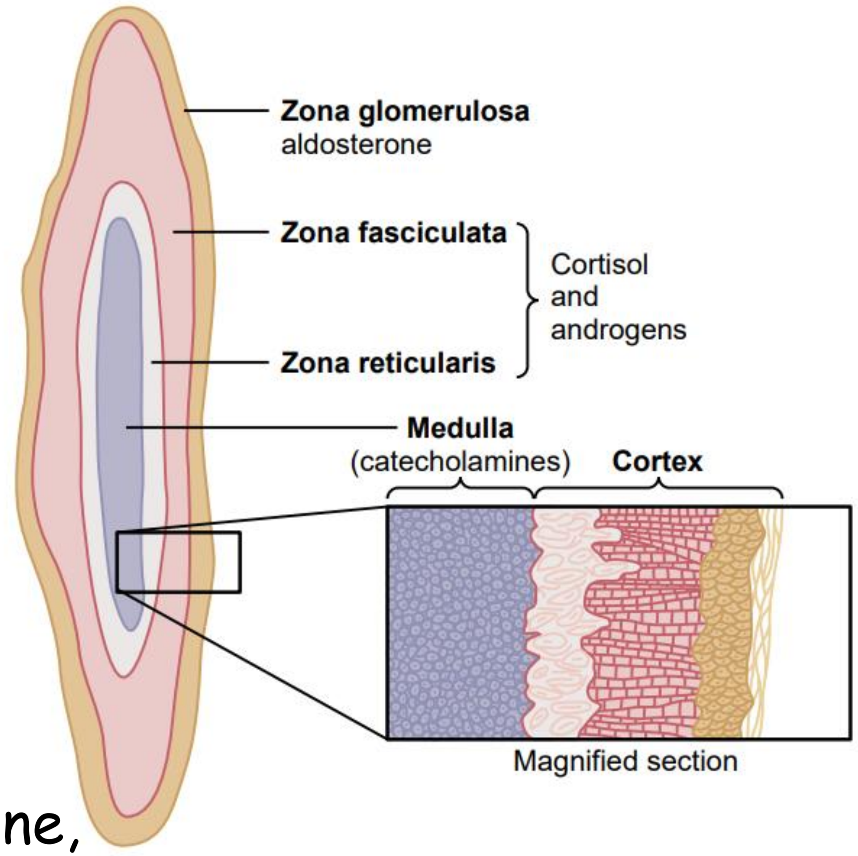
- The adrenal glands are two bilaterally symmetric endocrine organs located just anterior to the kidneys. Each gland is divided into two separate entities, a **medulla** and a **cortex**.
  - The medulla arises from the neuroectoderm and produces amines such as norepinephrine and epinephrine.
  - The 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).

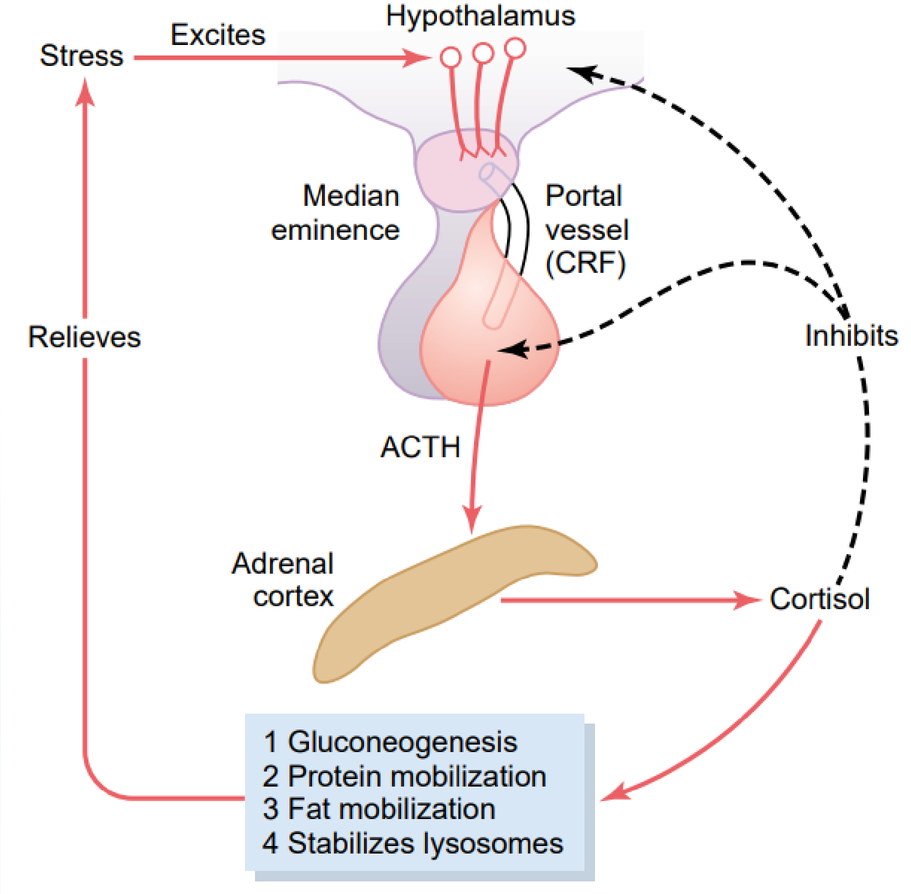
Adrenocortical Hormones

1. **The zona glomerulosa:**
   - The only cells that contain aldosterone synthase enzyme ⟶ secret aldosterone
   - Secretion is controlled by angiotensin II and K^+

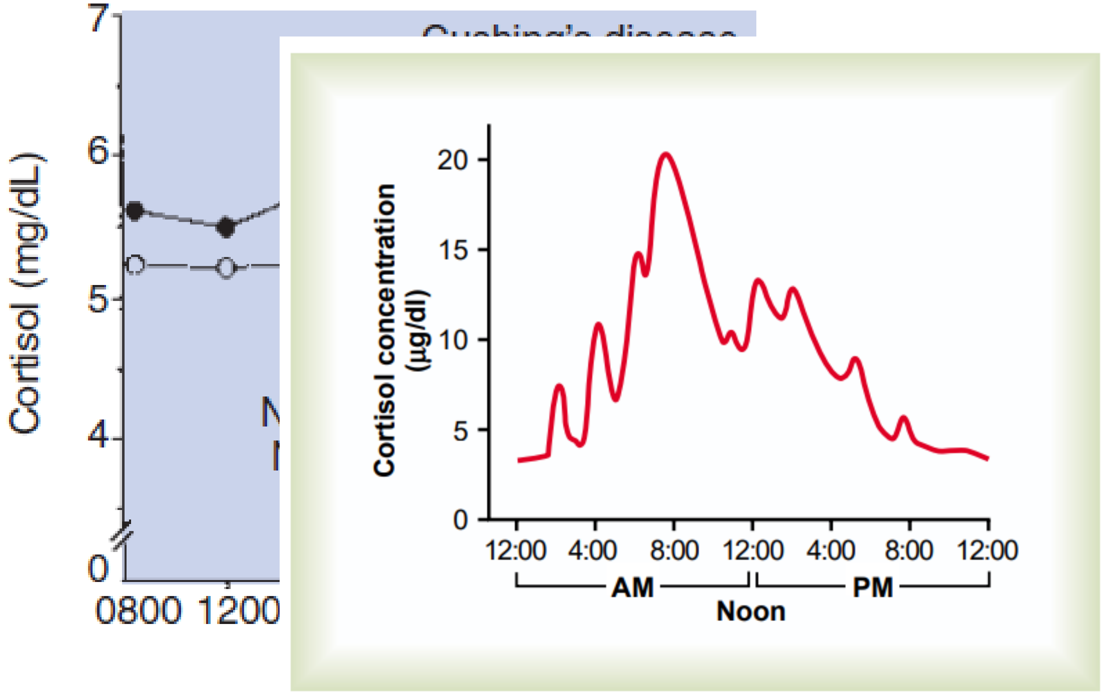
- **The zona fasciculata**
  - secretes the glucocorticoids cortisol and corticosterone, as well as small amounts of adrenal androgens and estrogens
  - Secretion is controlled by ACTH
- **The zona reticularis**
  - secretes the adrenal androgens dehydroepiandrosterone (DHEA) and androstenedione, and small amounts of estrogen
  - Secretion is controlled by ACTH



Glucocorticoid secretion



Regulation of cortisol secretion by the hypothalamopituitary axis. *CRF,* Corticotropin-releasing factor.



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

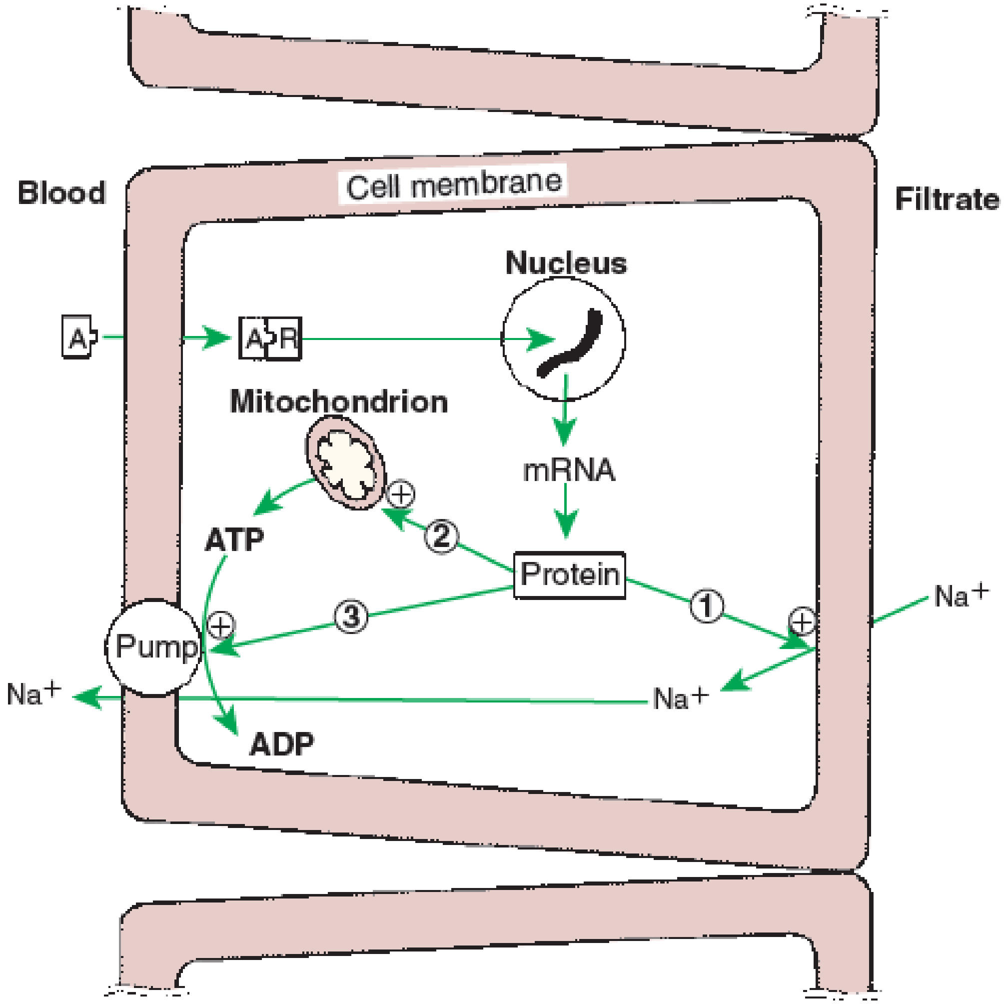
- The most common clinical signs:
  - polydipsia, polyuria, polyphagia, abdominal enlargement or "potbelly," alopecia (especially truncal), thin skin, . . .

- 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.

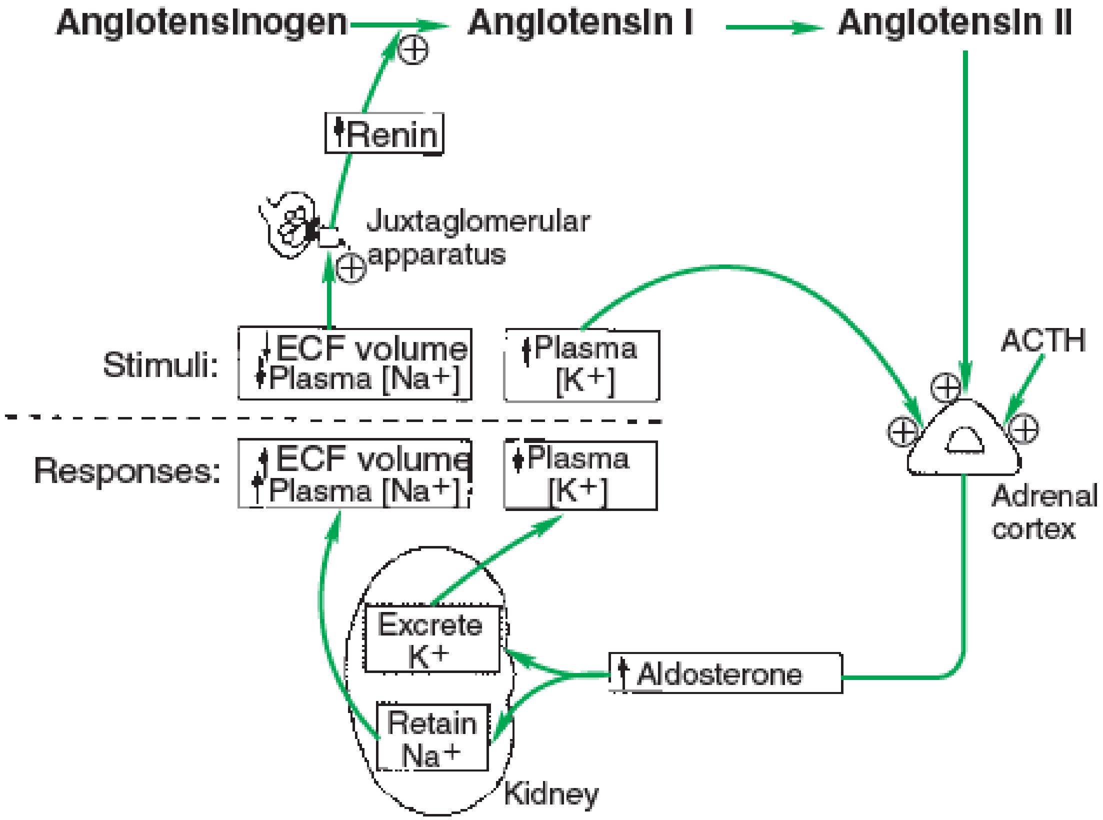
The *numbered arrows* indicate the three putative sites of action of aldosterone: *1,* increasing the permeability of the luminal membrane to sodium; *2,* increasing mitochondrial adenosine triphosphate *(ATP)* production; *3,* increasing Na^+,K^+-ATPase activity in the contraluminal membrane. *Plus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



Mineralocorticoids

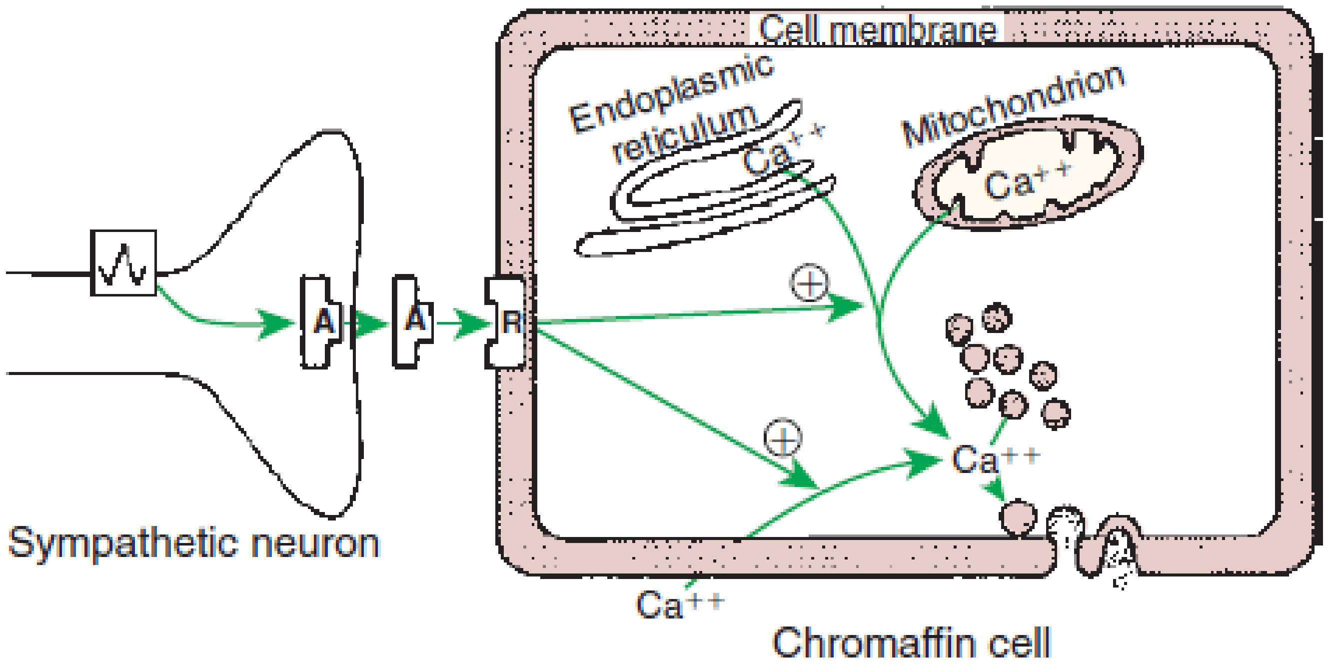
Effect	Site of Action
Stimulates Na^+ reabsorption	Kidney, salivary glands, sweat glands
Stimulates K^+ excretion	Kidney, salivary glands, sweat glands
Stimulates H^+ excretion	Kidney

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

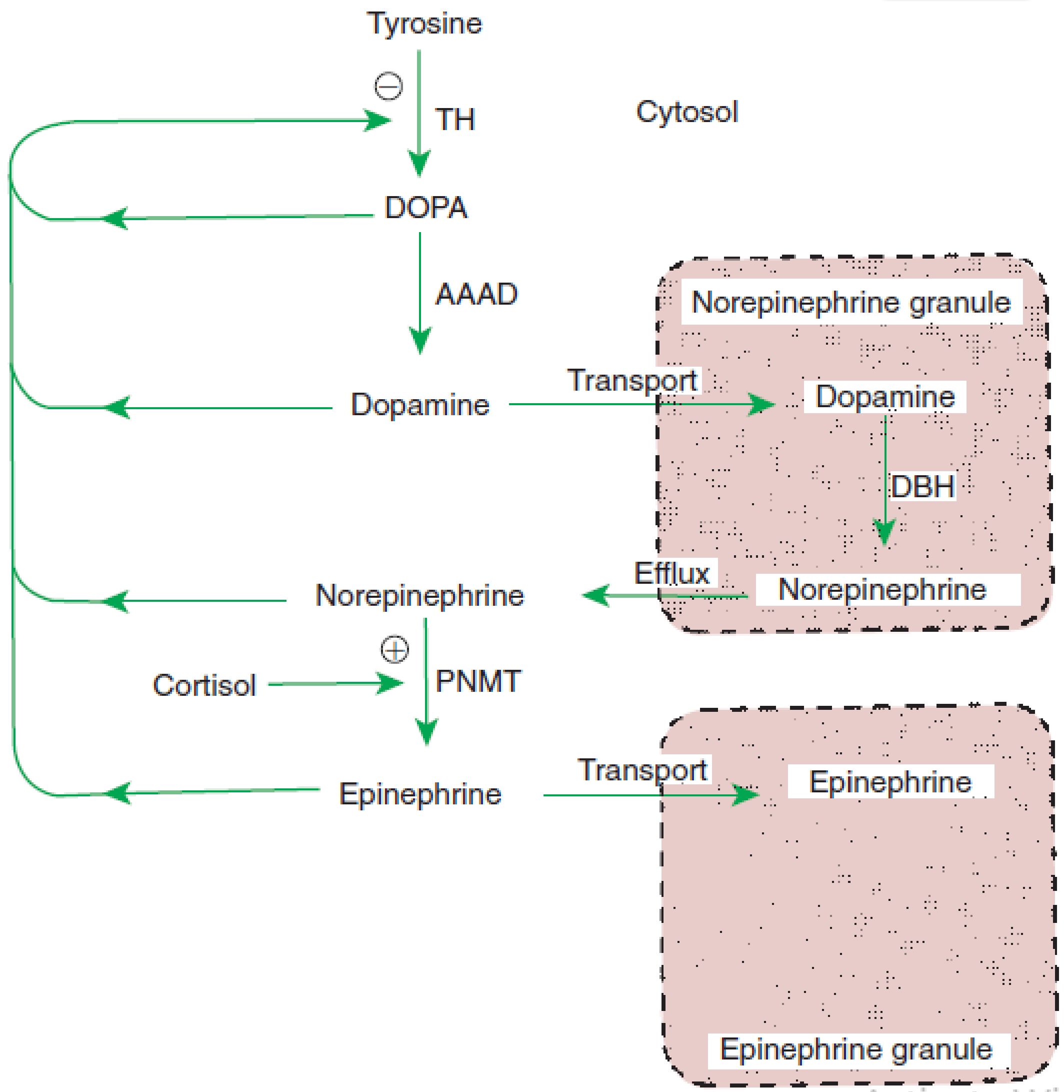
The Adrenal Medulla



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.



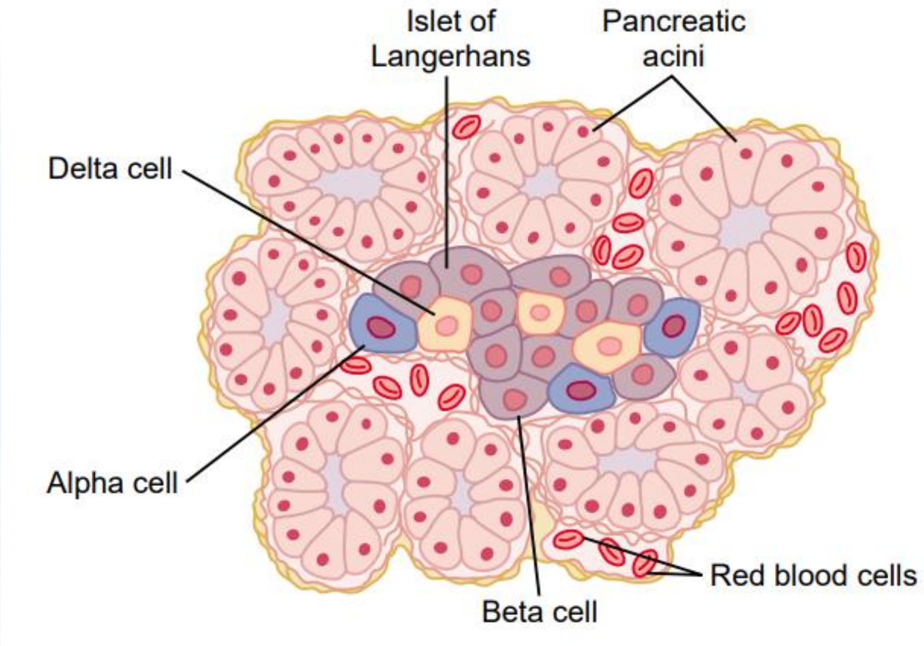
Activate Win

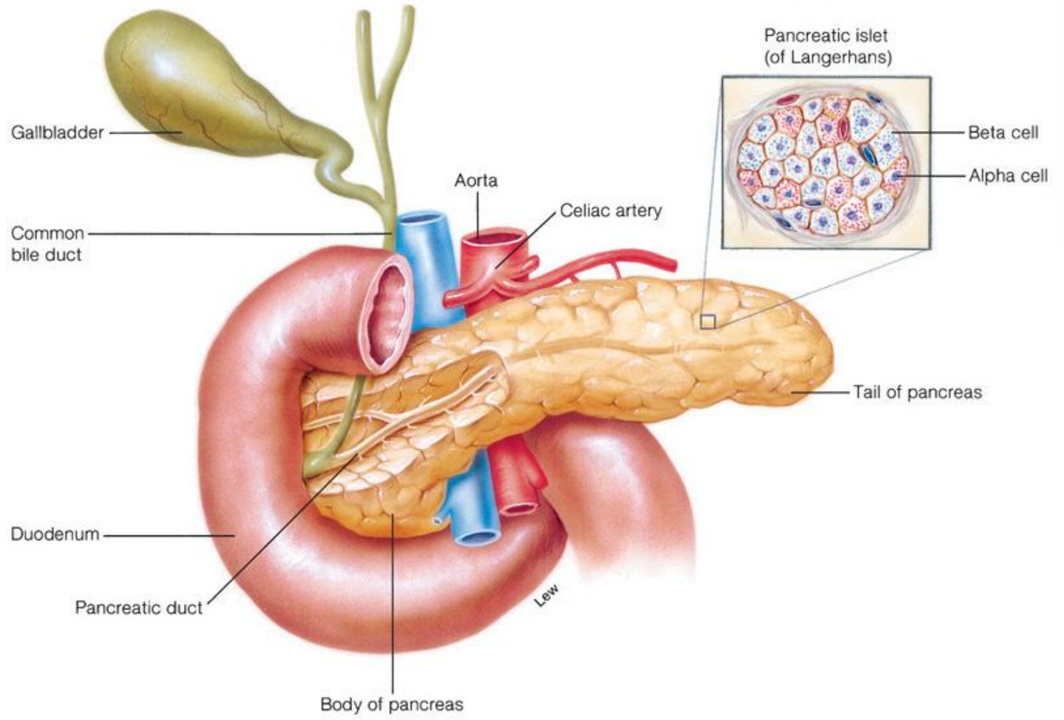
Section Six:

The Islets of Langerhans

Islets of Langerhans

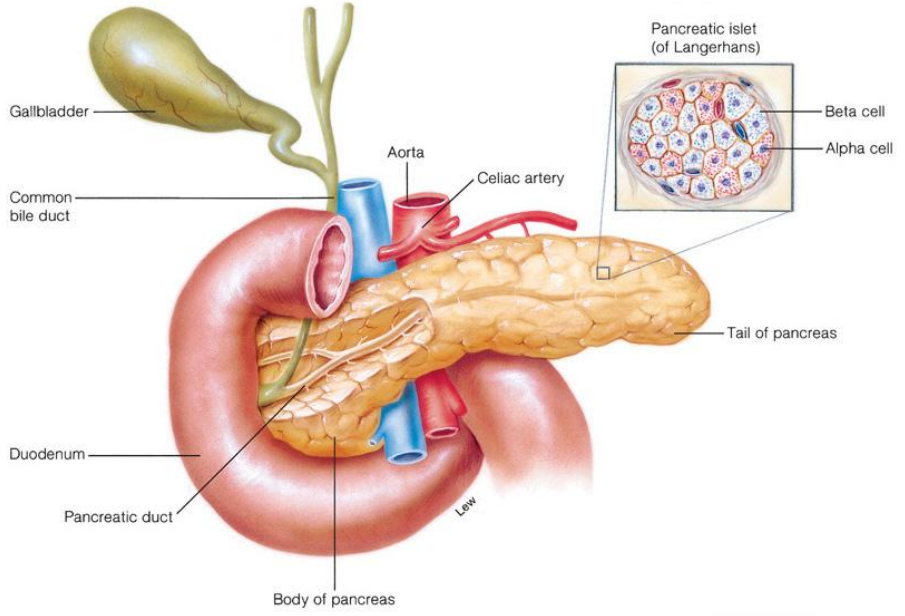
- Scattered clusters of endocrine cells in pancreas
- Contain alpha and beta cells

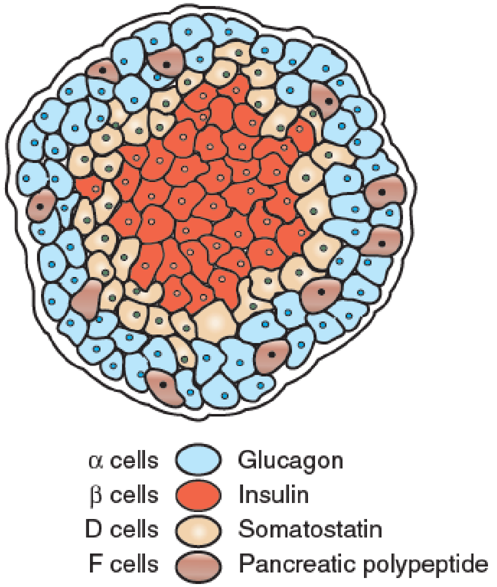




Islets of Langerhans

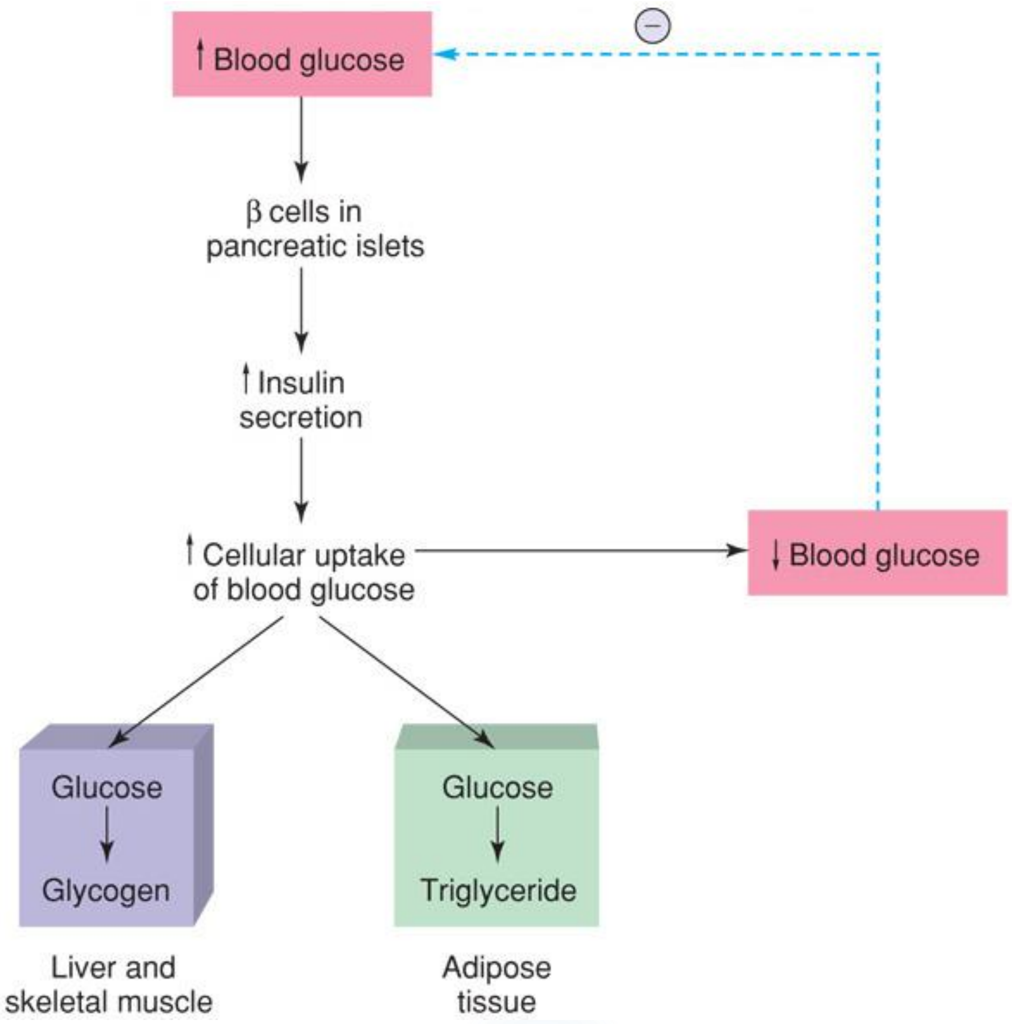
- The pancreas, in addition to its digestive functions, secretes two important hormones, insulin and glucagon, that are crucial for normal regulation of glucose, lipid, and protein metabolism.
- Although the pancreas secretes other hormones, such as amylin, somatostatin, and pancreatic polypeptide, their functions are not as well established.





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 high blood glucose
  - Promotes entry of glucose into cells
  - And conversion of glucose into glycogen and fat
  - Decreases blood glucose



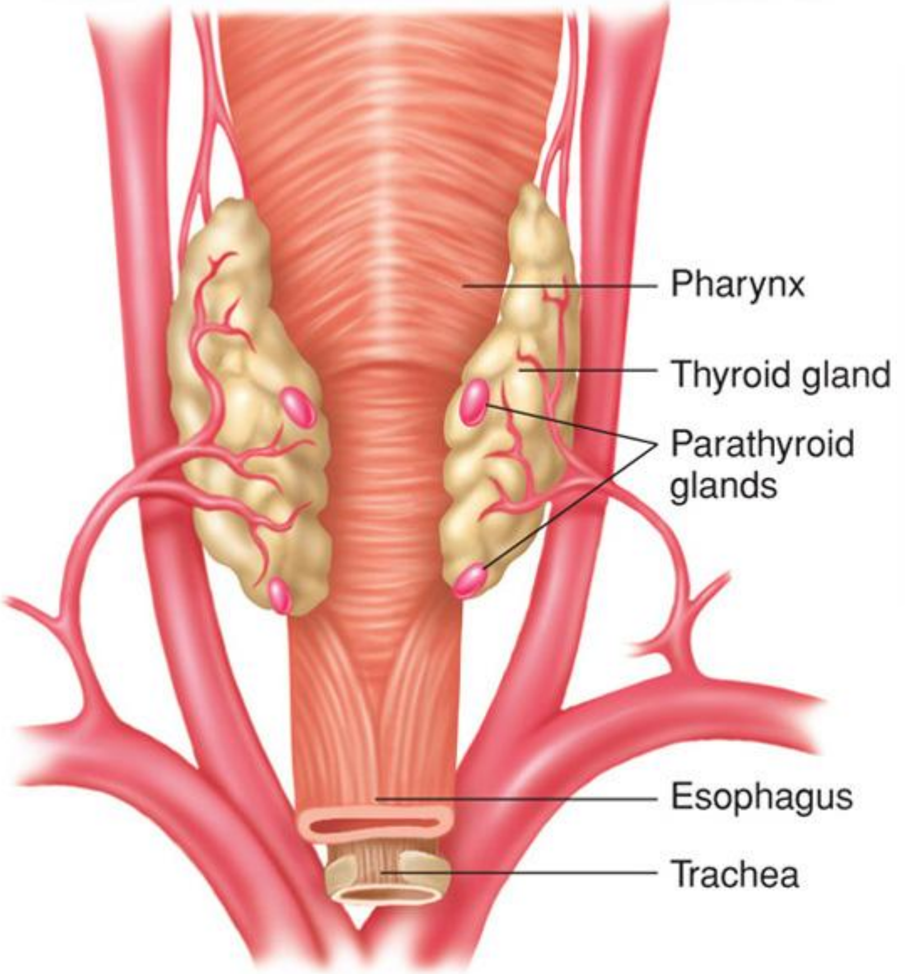
Section Seven:

Parathyroid Glands

Parathyroid Glands

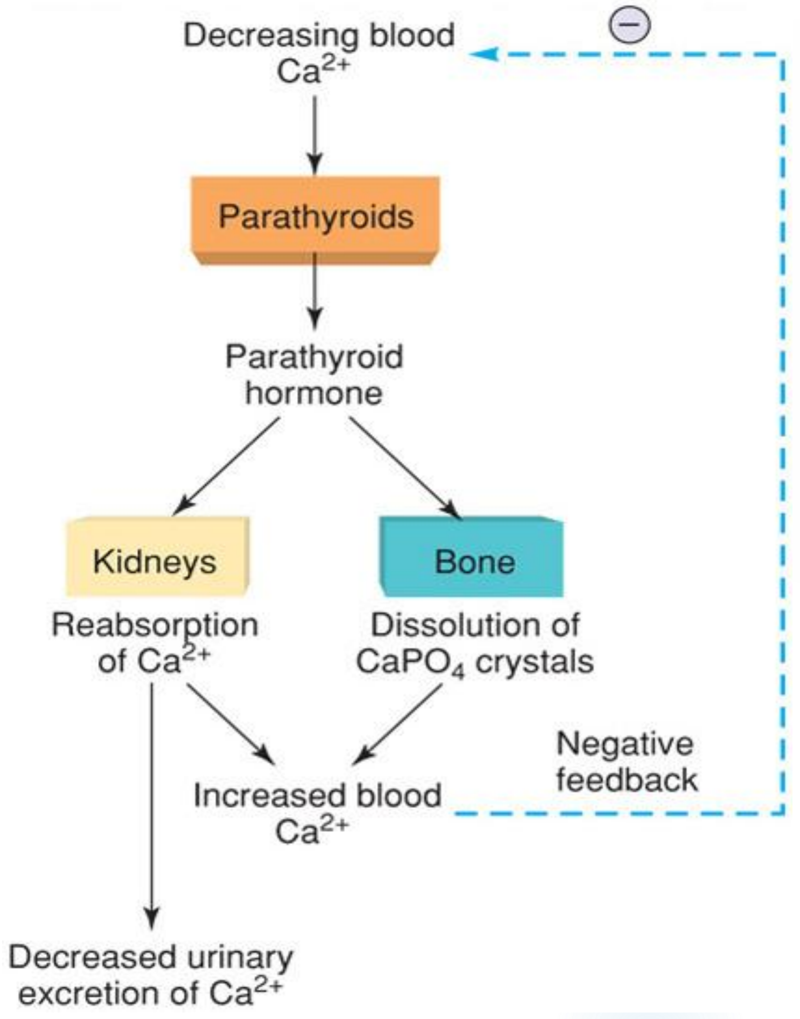
- 4 glands embedded in lateral lobes of posterior side of thyroid gland

- 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



Good Luck!