Section 1:

General principles of endocrine physiology

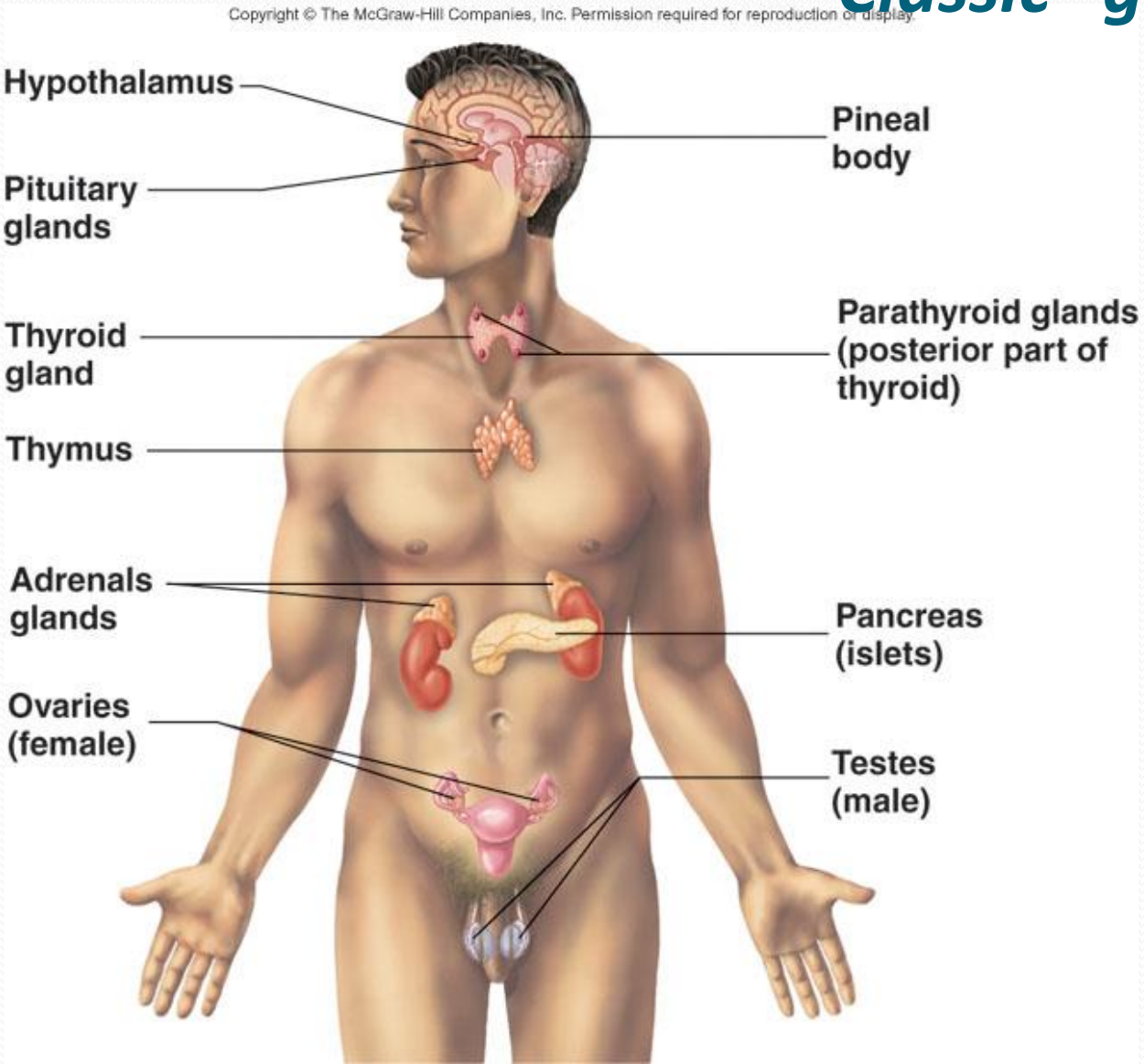
Regulation of homeostasis

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

Hormone

- Substance produced by a specific cell type usually accumulated in one (small) organ
- Transport by blood to target tissues
- Stereotypical response (receptors)

Hormone production: "Classic" glands



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

Chemical characteristics of hormones

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

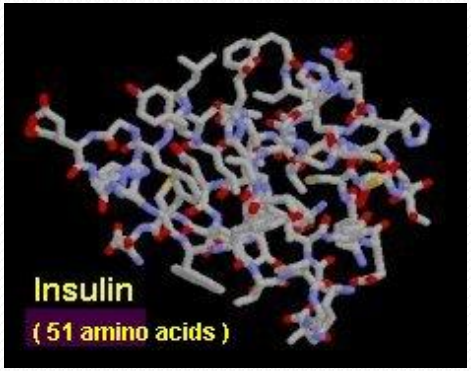
  anterior and posterior pituitary

  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)

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

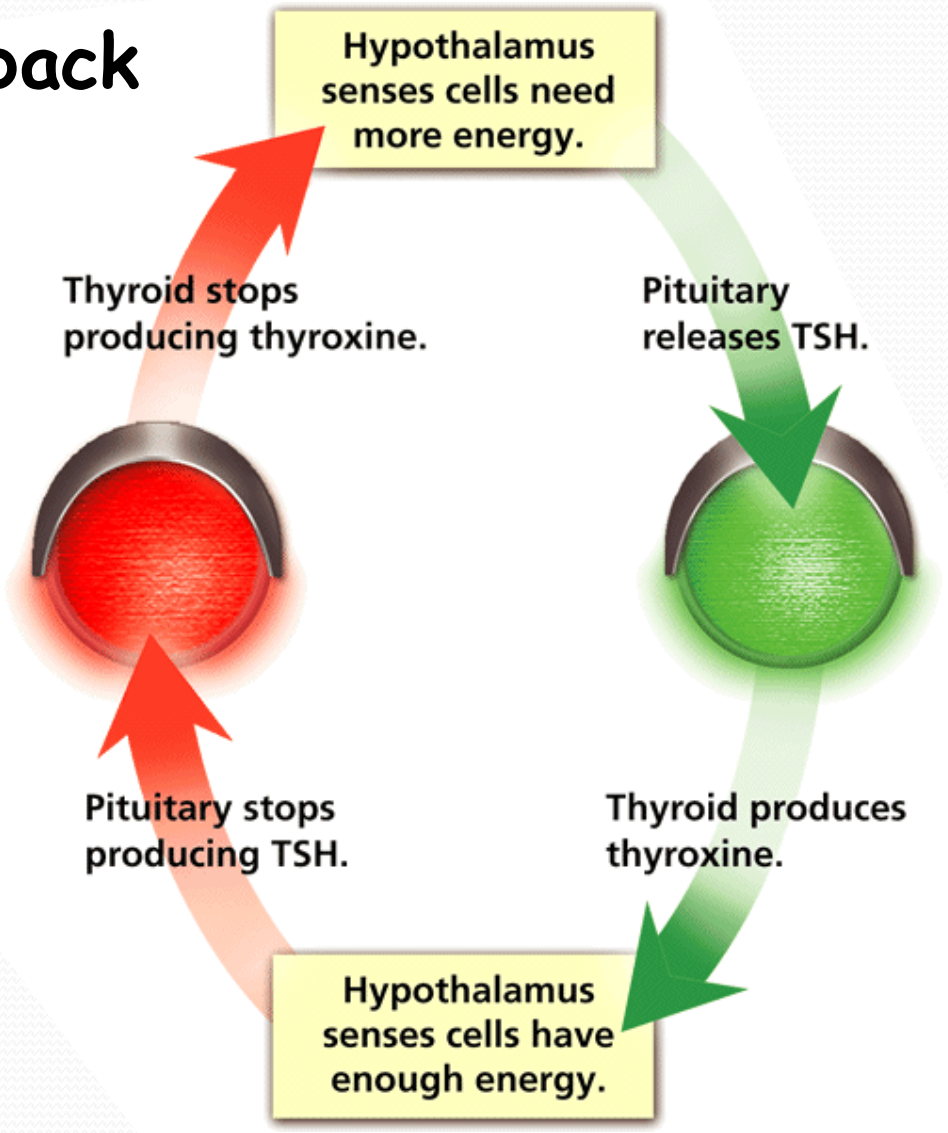
- Thyroid hormones:
  - made as part of thyroglobulin
  - stored in folicles
  - T3 & T4 secreted by enzymatic cleavage

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

Regulation of hormone release

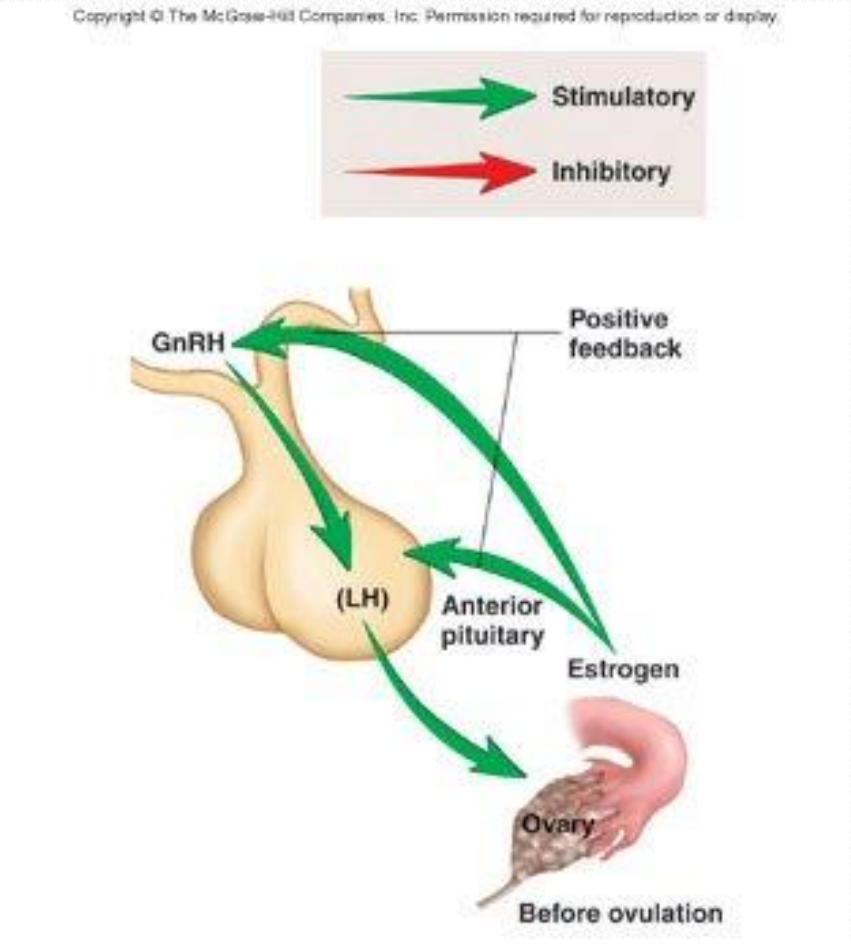
1. Negative feedback

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)

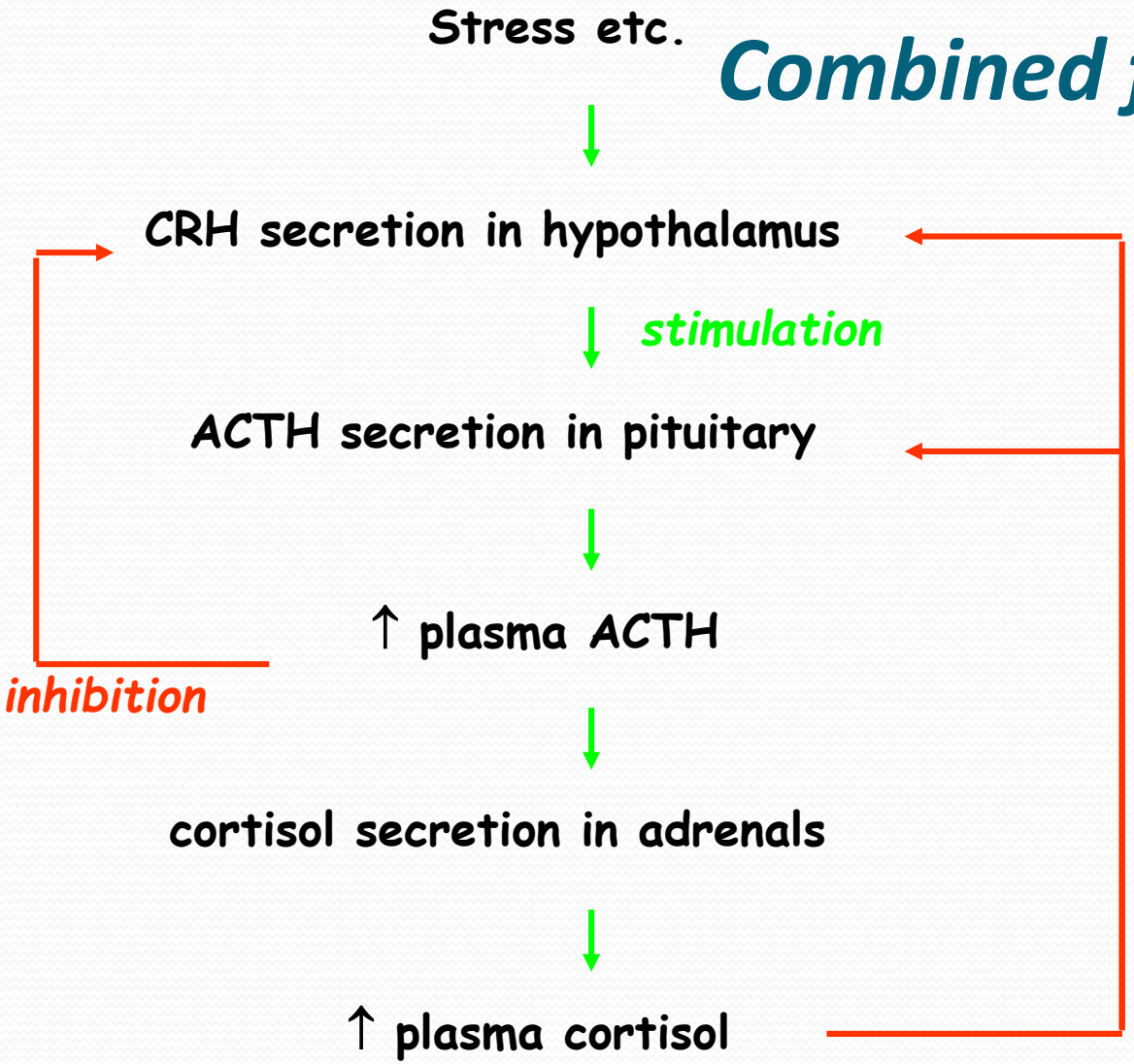


Regulation of hormone release

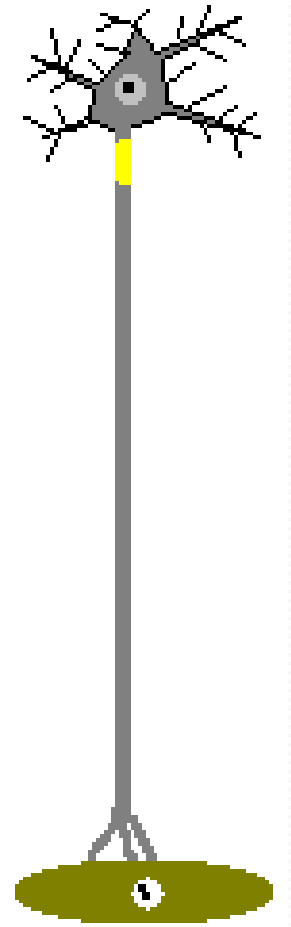
3. Nerve regulation

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

Combined feedback

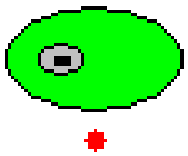


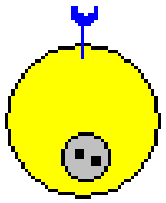
The Nervous System vs. Endocrine System



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

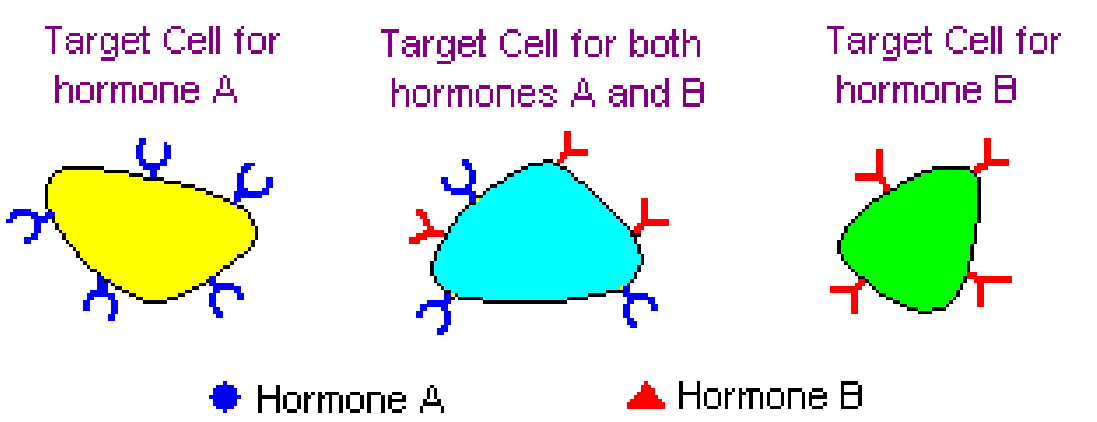




The endocrine system broadcasts its hormonal messages to essentially **all cells** by secretion into blood and fluid that surrounds cells. Like a radio broadcast, it requires a receiver to get the message - in the case of endocrine messages, cells must bear a *receptor* for the hormone being broadcast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

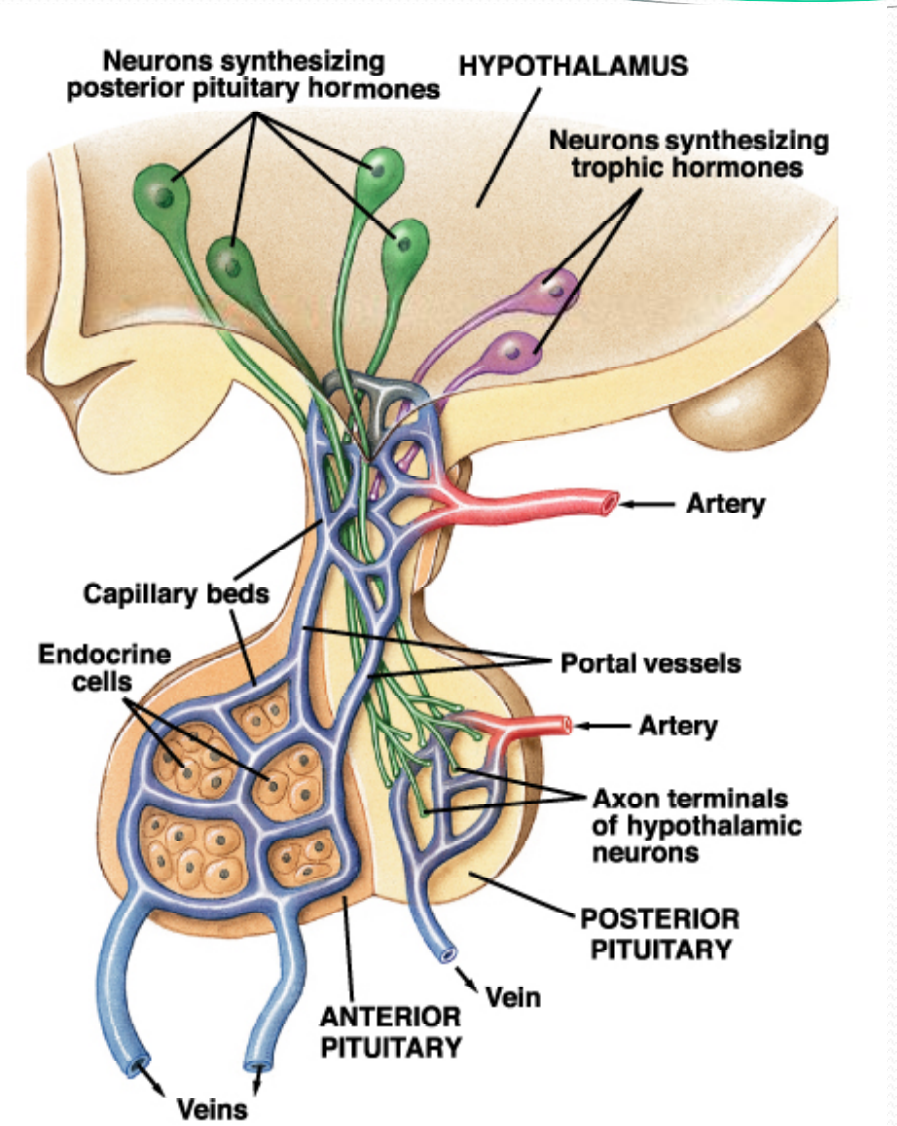
The Nervous System vs. Endocrine System

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.**



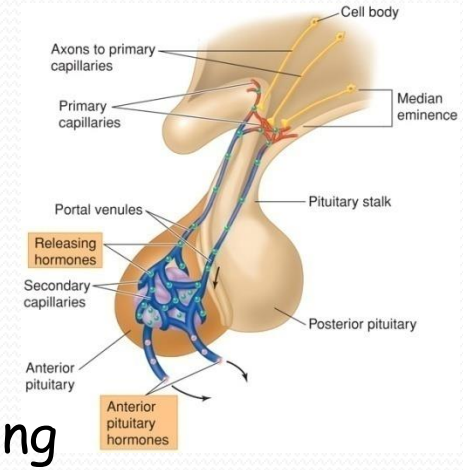
Section 2:

The hypothalamus-hypophysis axis



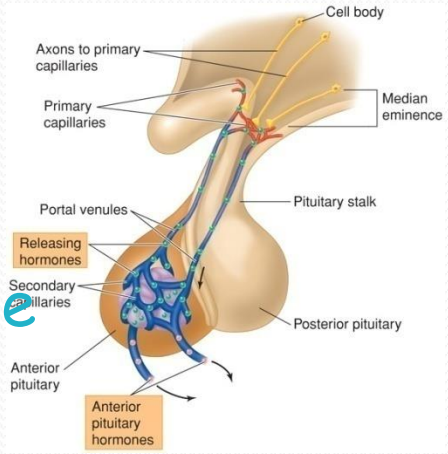
Anatomical and Functional Connection Between the Hypothalamus and Pituitary (hypothalamo- hypophyseal portal system and tract)

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)

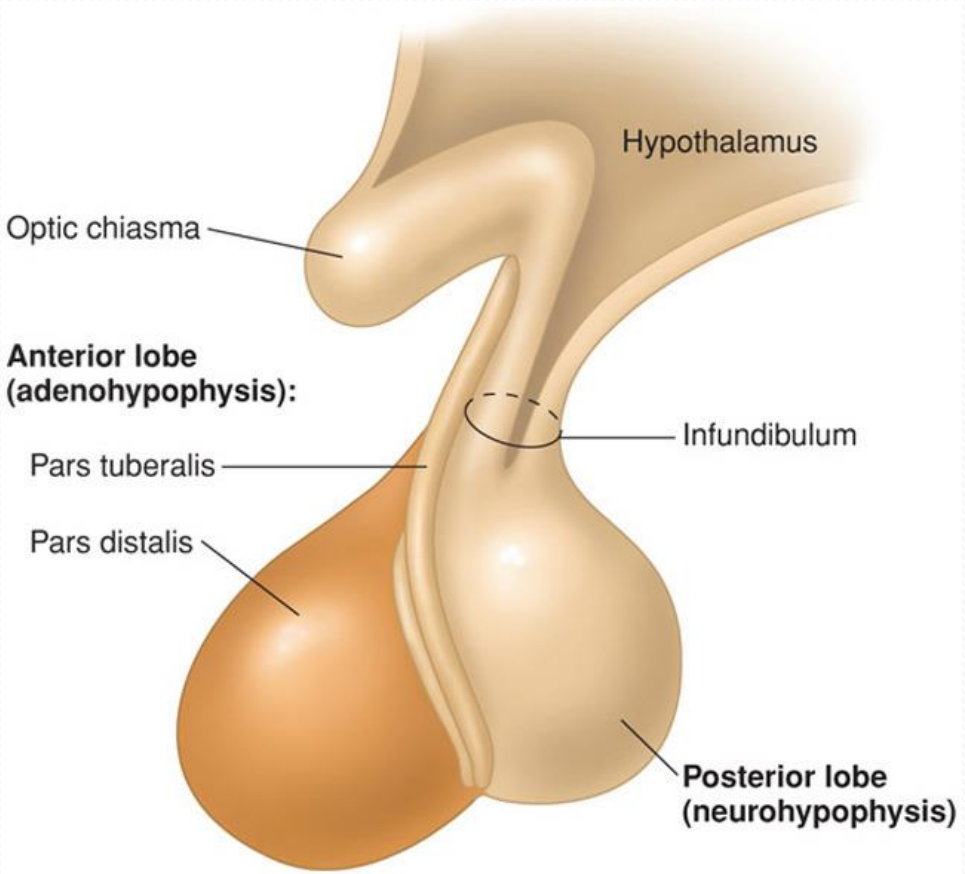
Hypothalamus as a gland



- 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

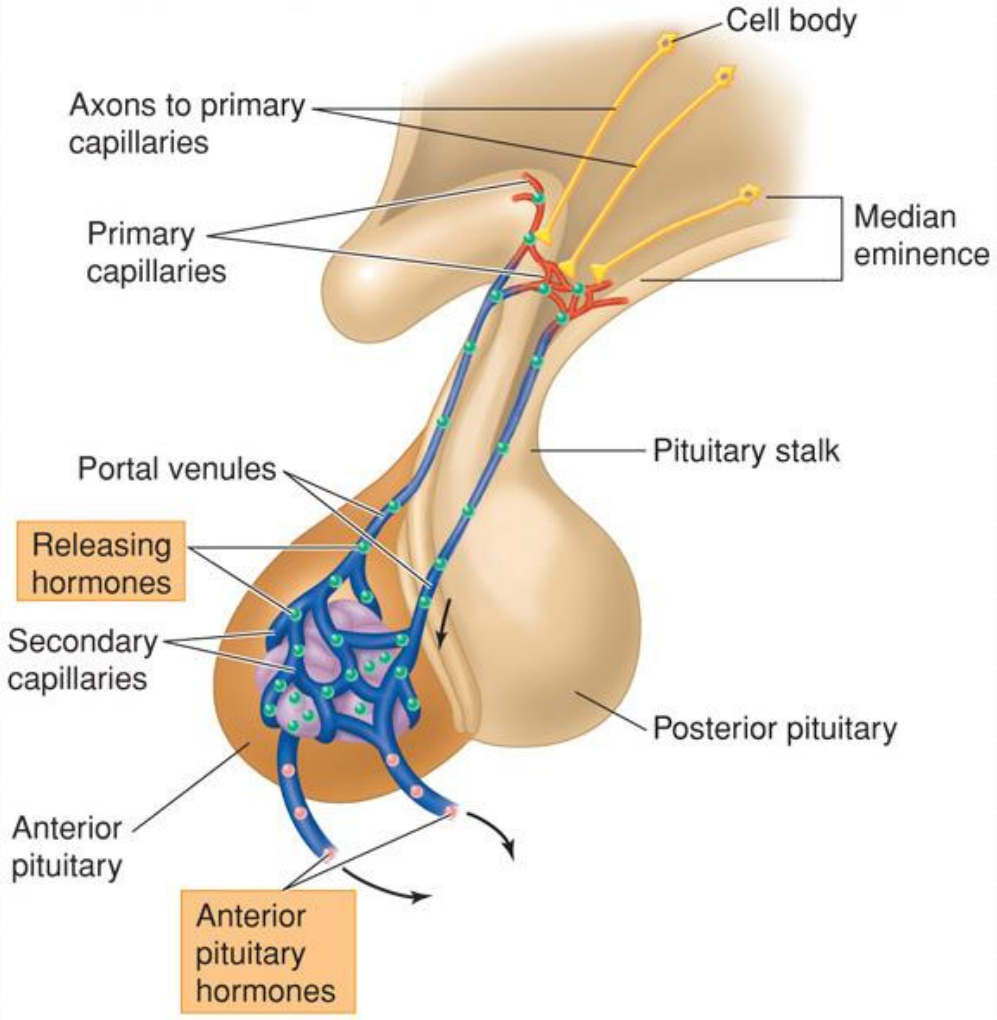
Pituitary gland

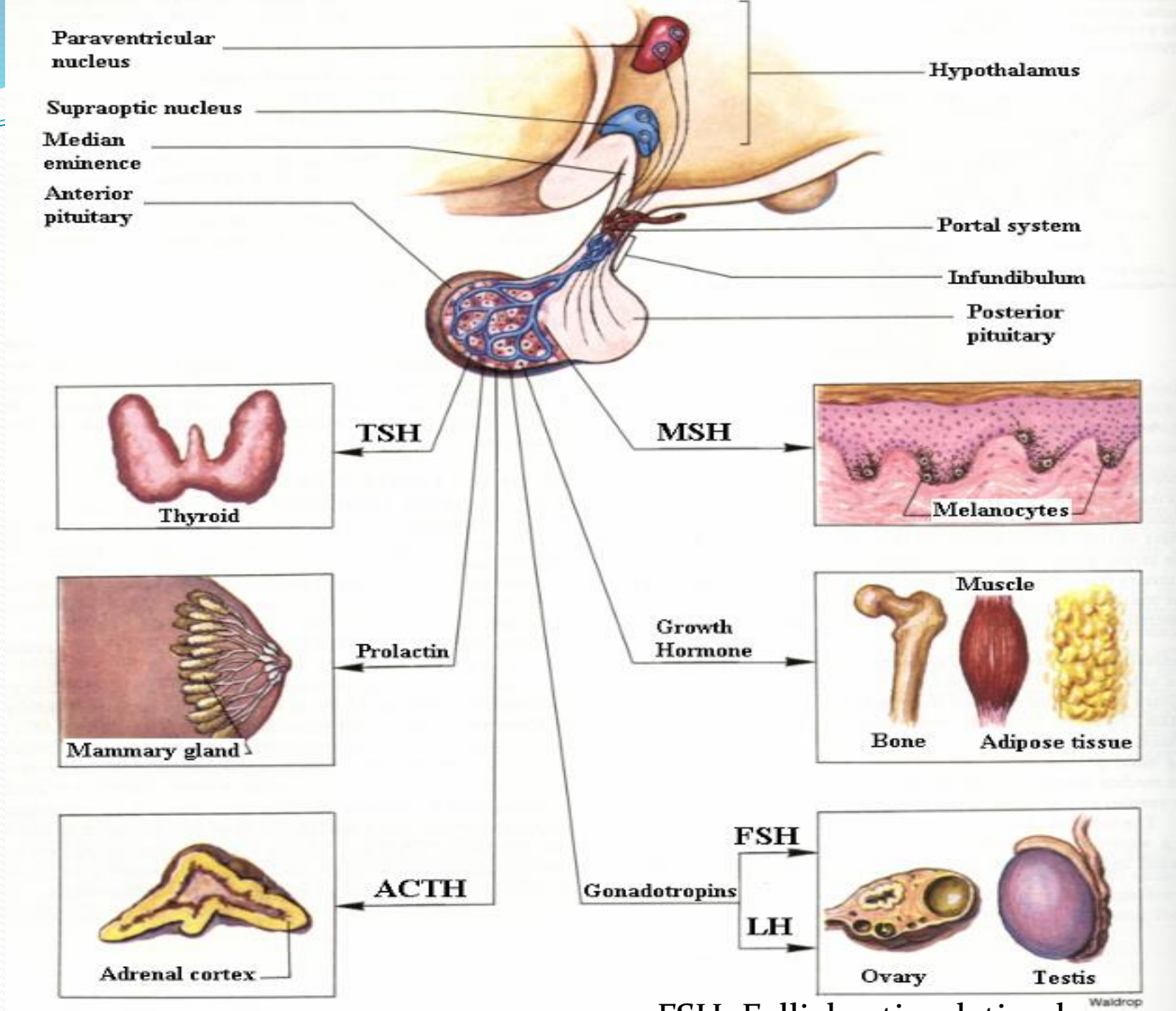
- Structurally & functionally divided into anterior and posterior lobes
- Hangs below hypothalamus by infundibulum
- Anterior produces own hormones
  - Controlled by hypothalamus
- Posterior stores and releases hormones made in hypothalamus



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

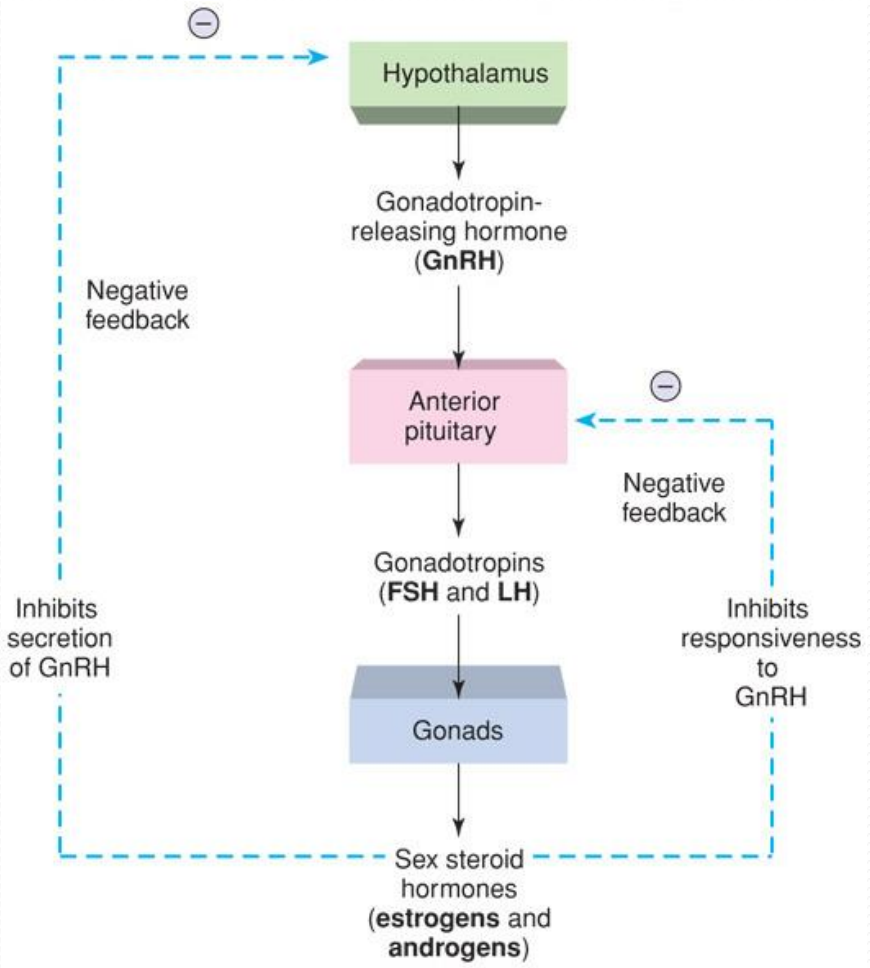
MSH, Melanophore-stimulating hormone

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

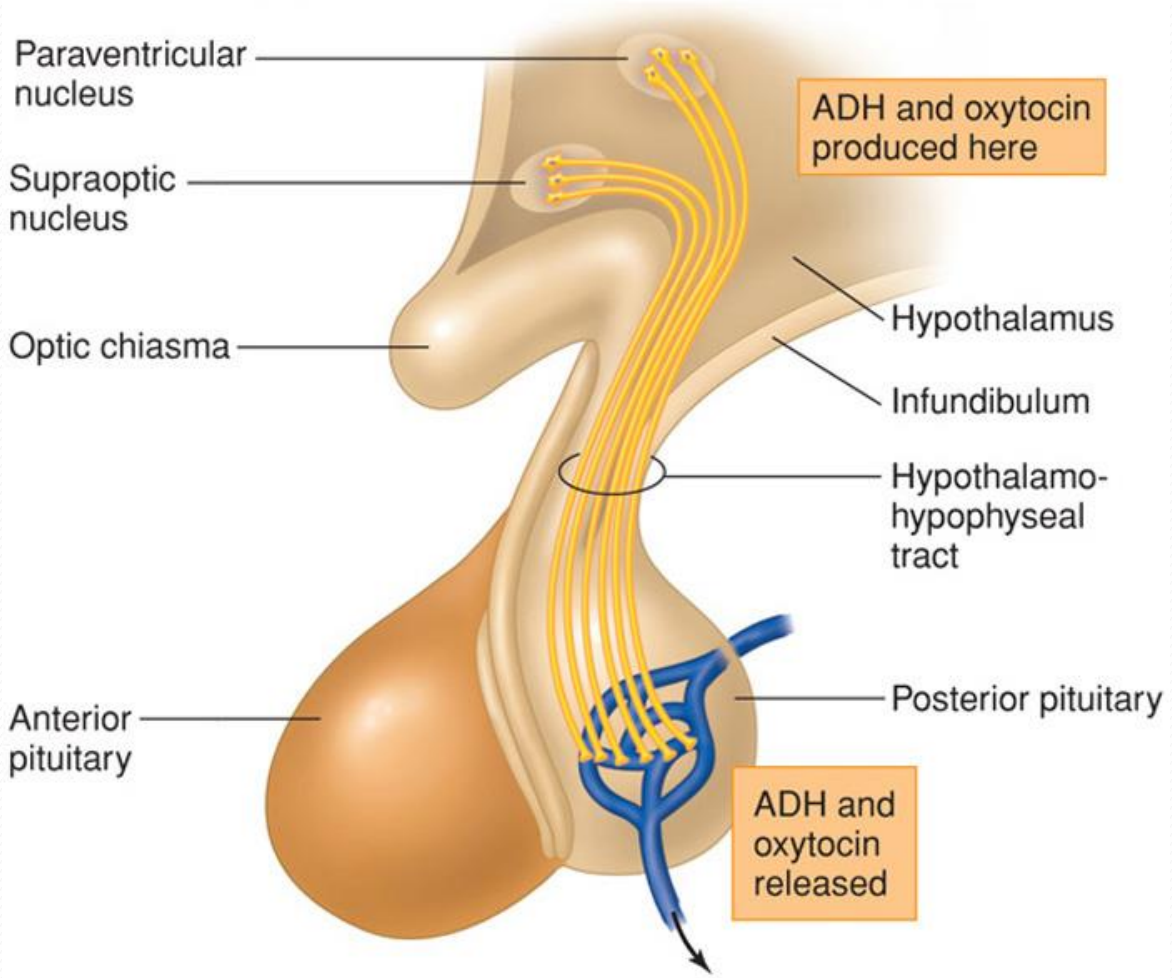
Anterior pituitary

- 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



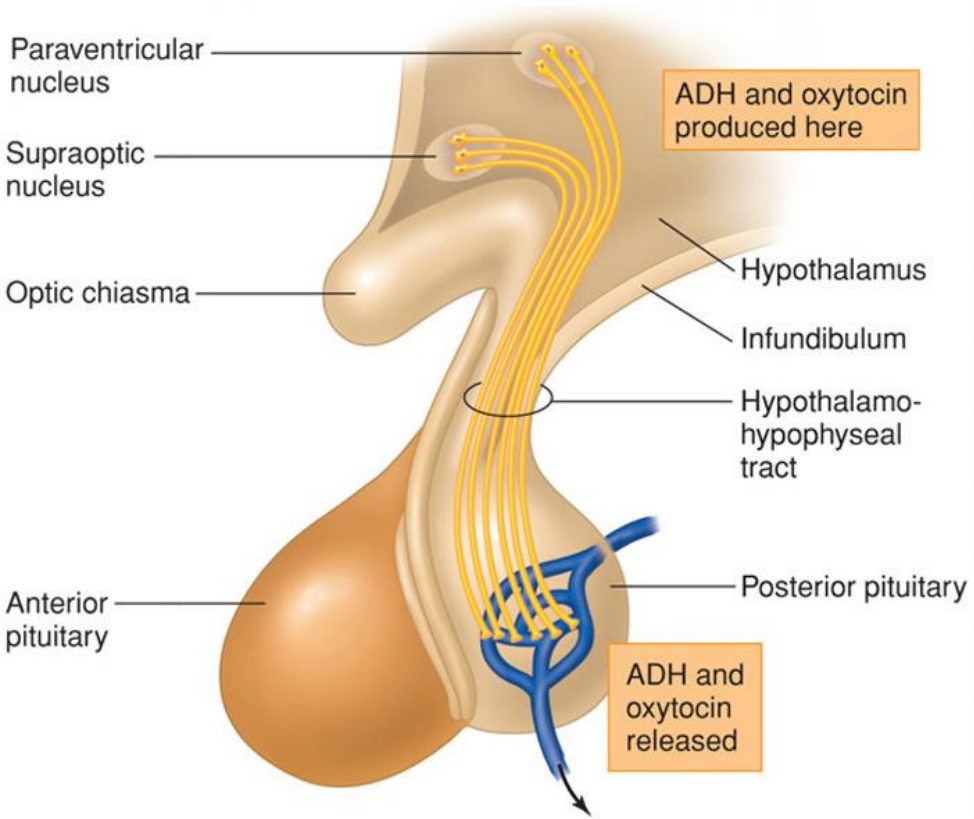
Posterior pituitary

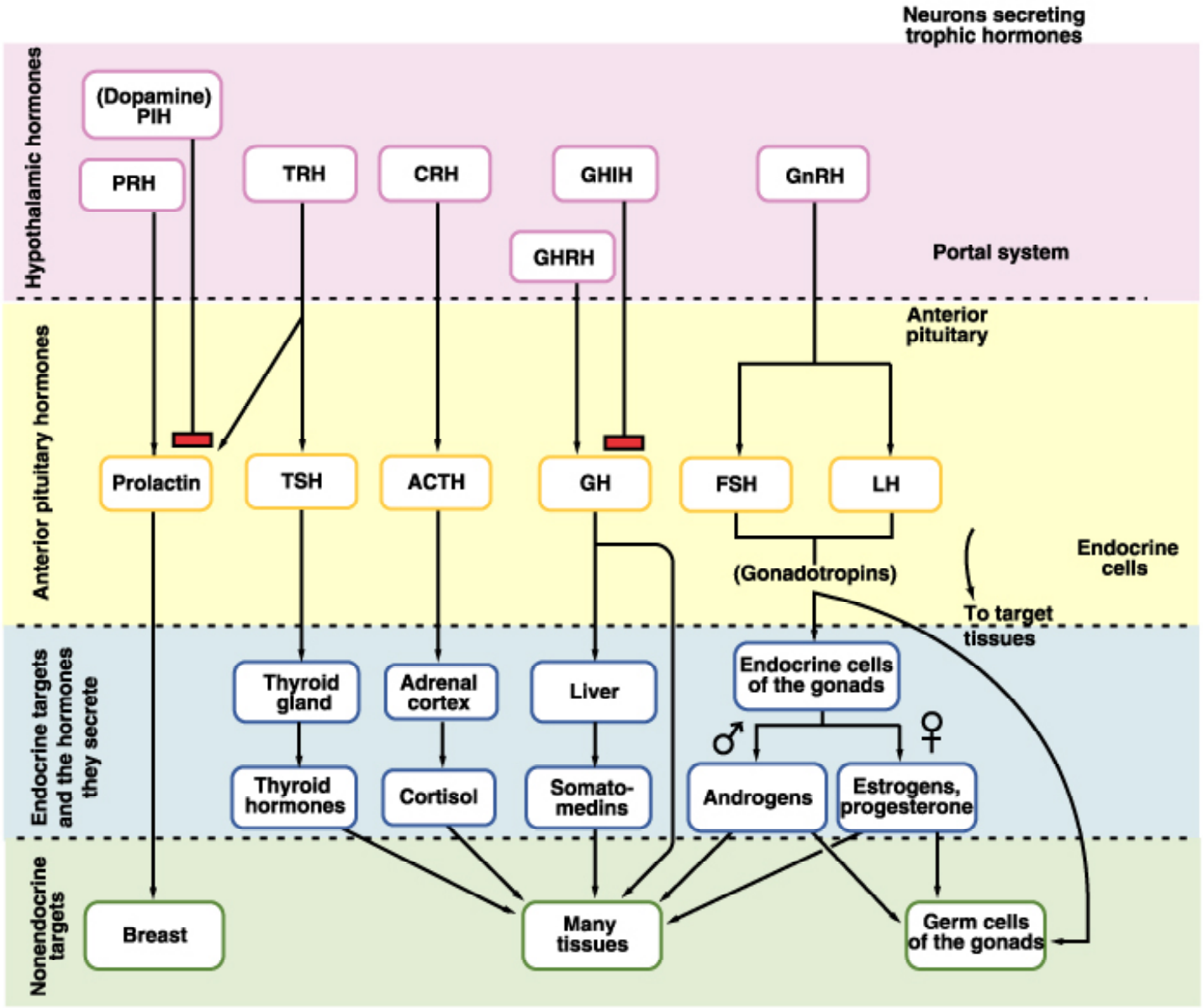
- Stores and releases vasopressin (ADH) and oxytocin
  - hormones made in the hypothalamus



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.

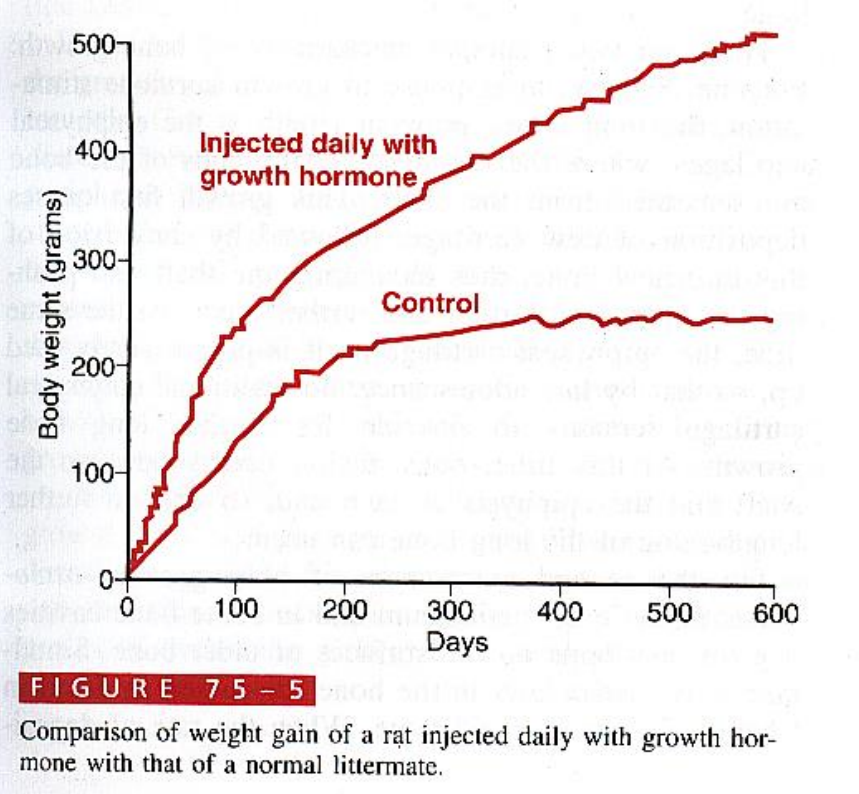


FIGURE 75–5

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.

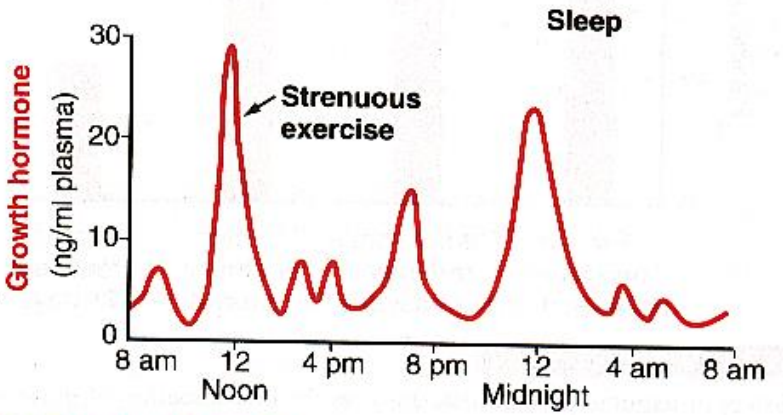
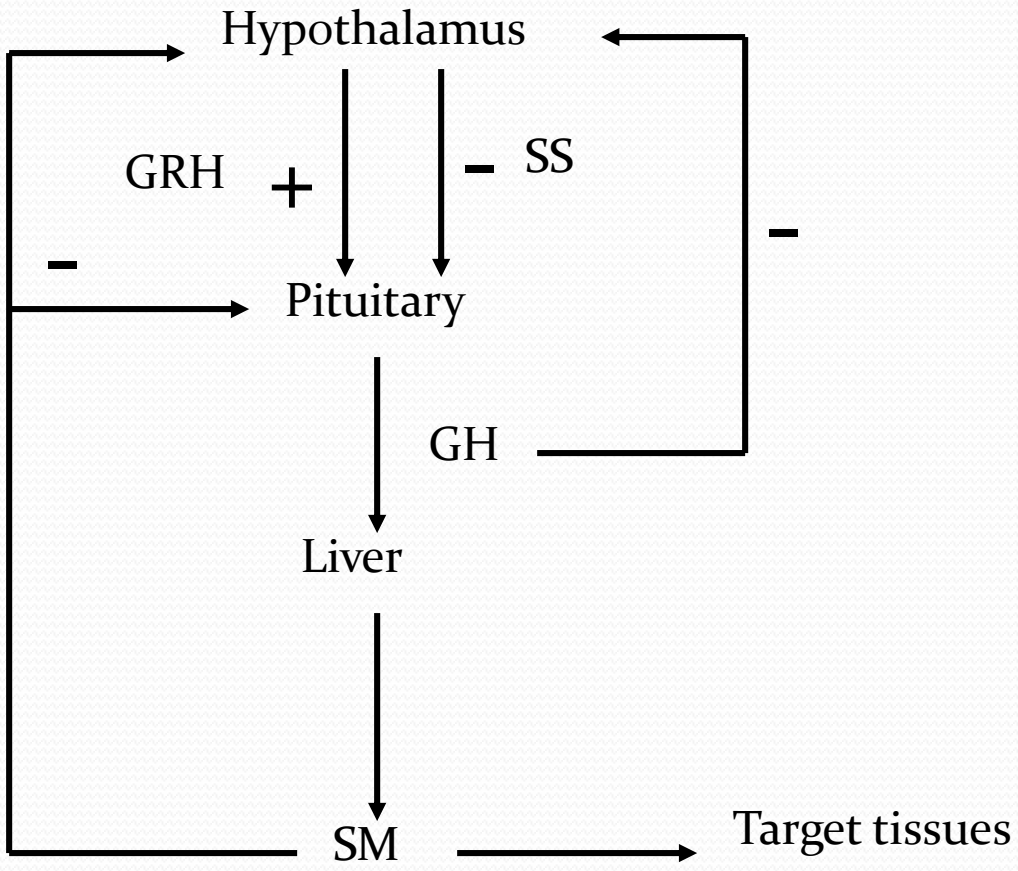


FIGURE 75-6

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

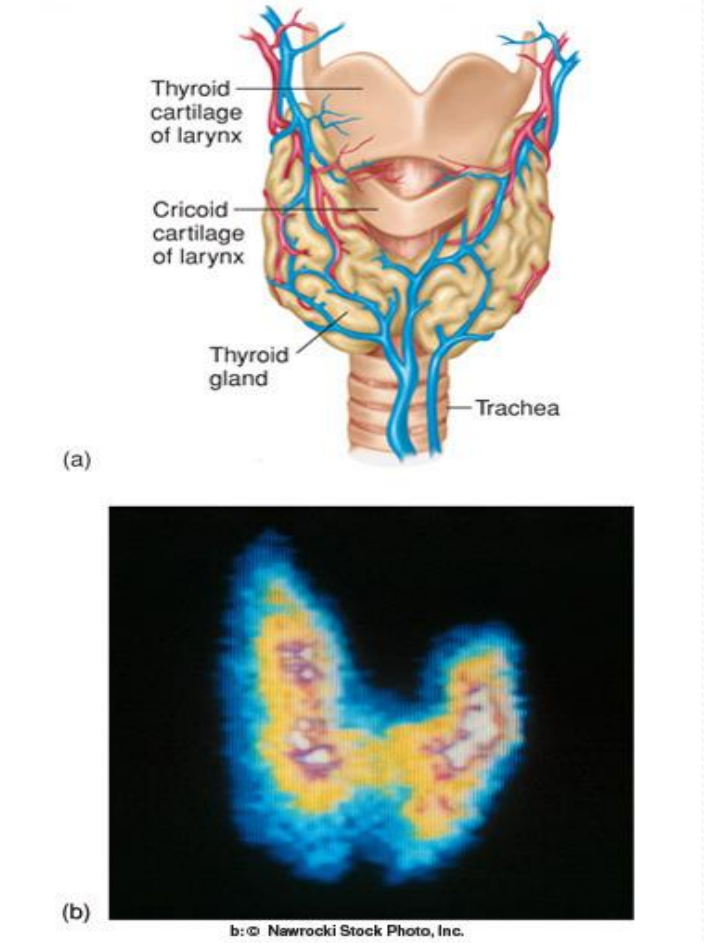
E, Trauma

Section 4:

Thyroid Gland

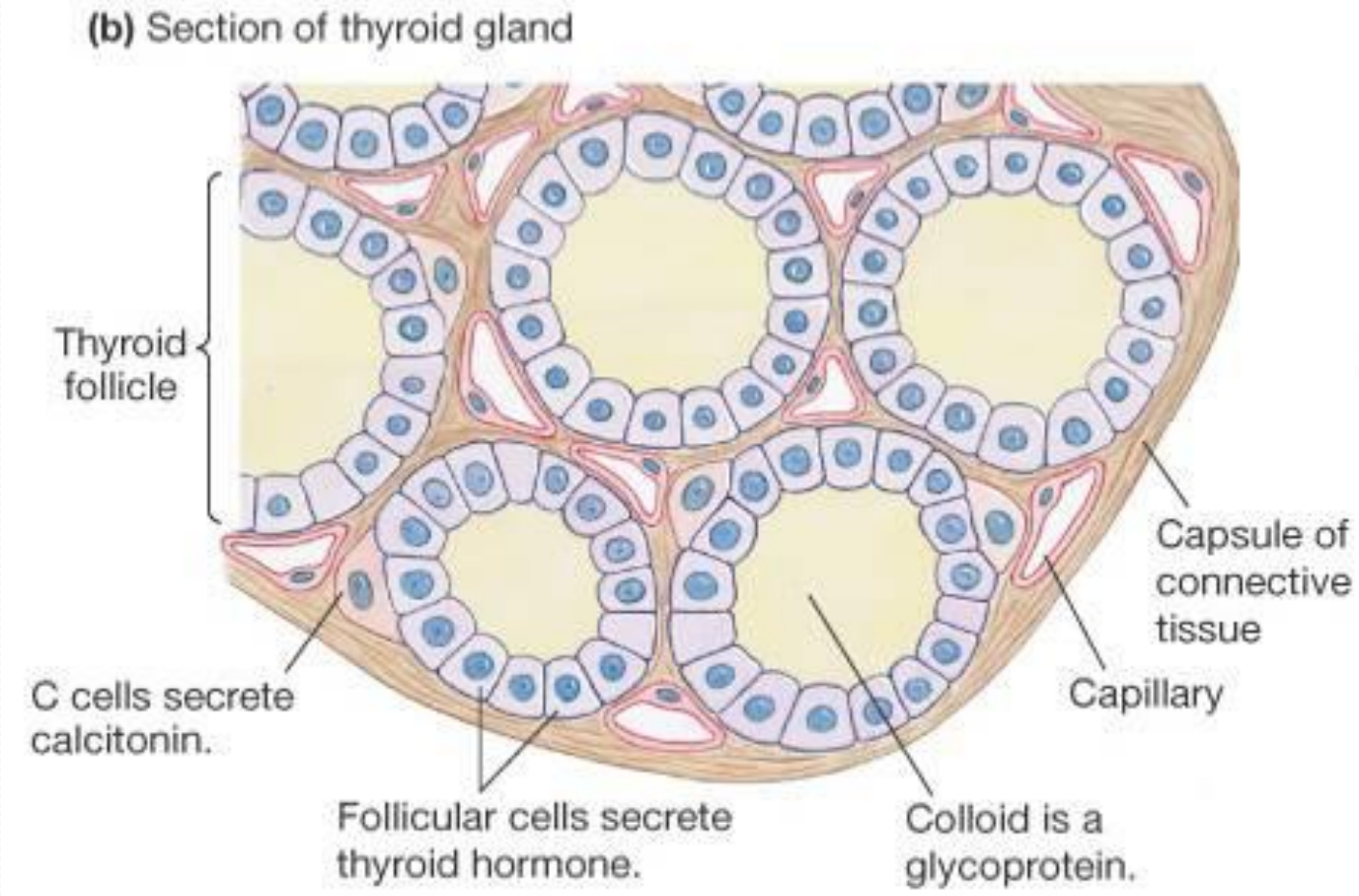
Thyroid Gland

- 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



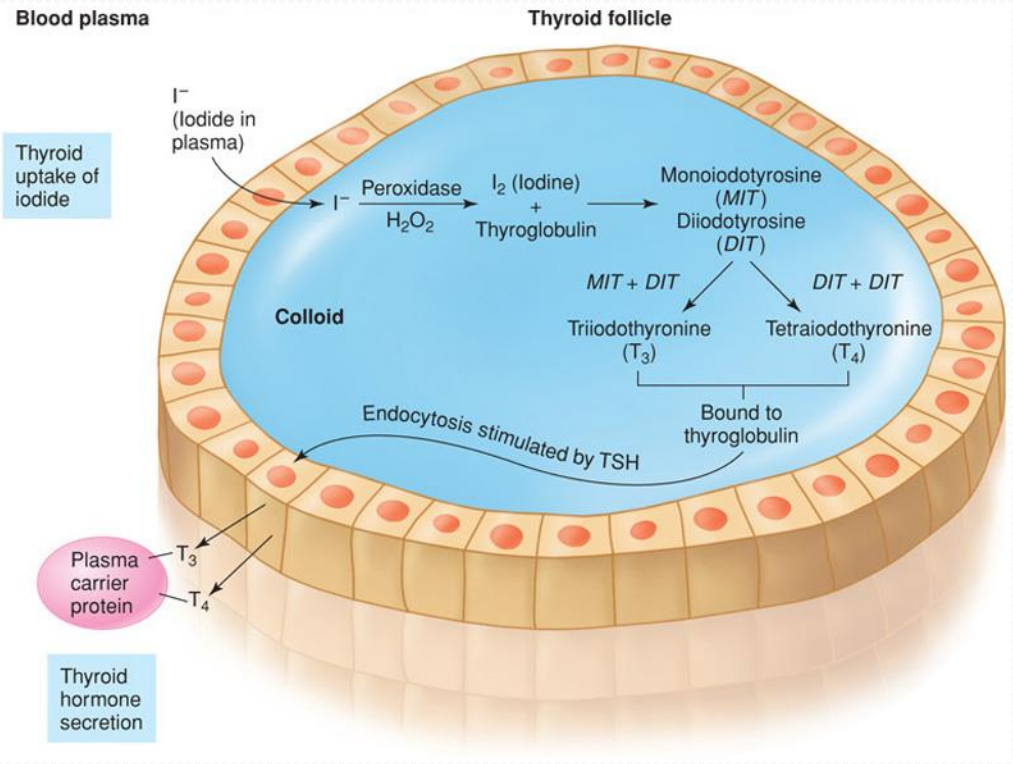
A scan of the thyroid 24 hrs. after intake of radioactive iodine

Thyroid Gland

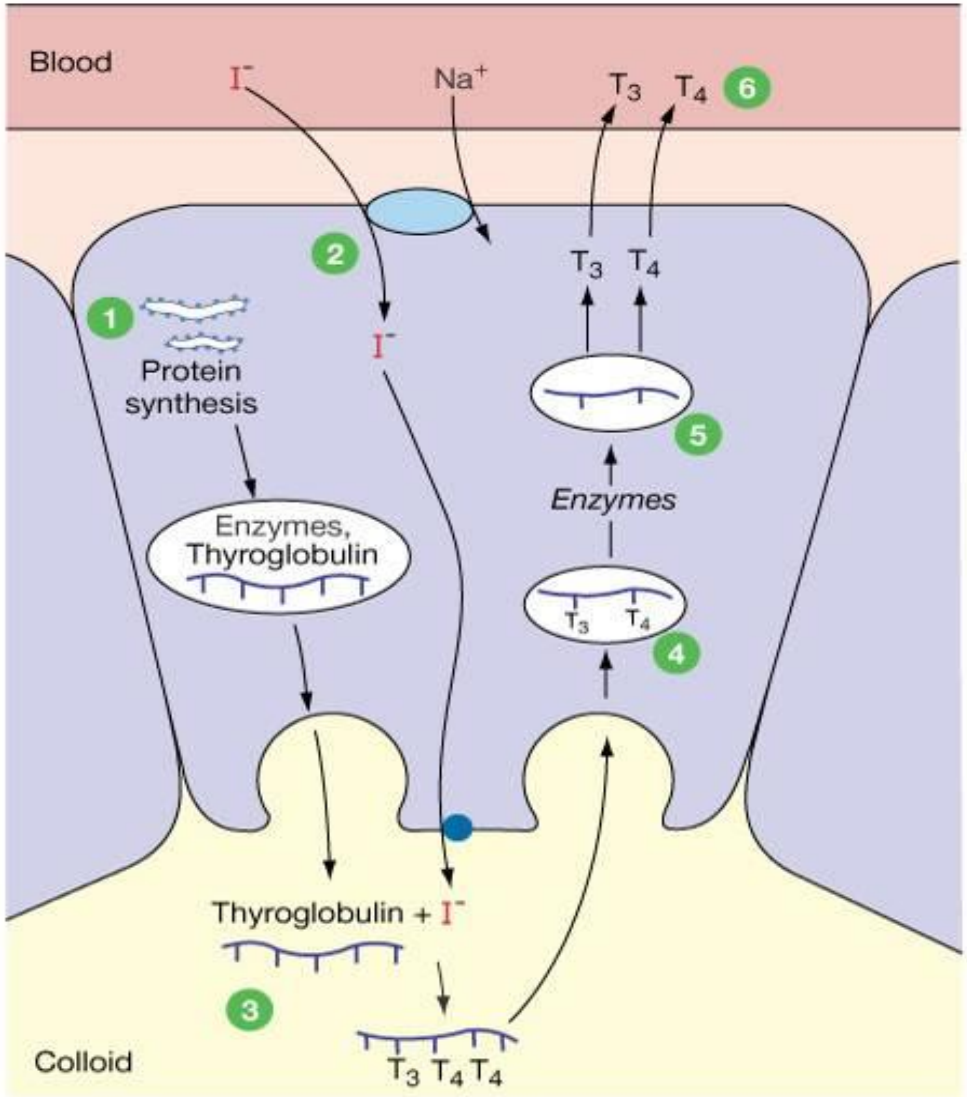


Thyroid Gland

- 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

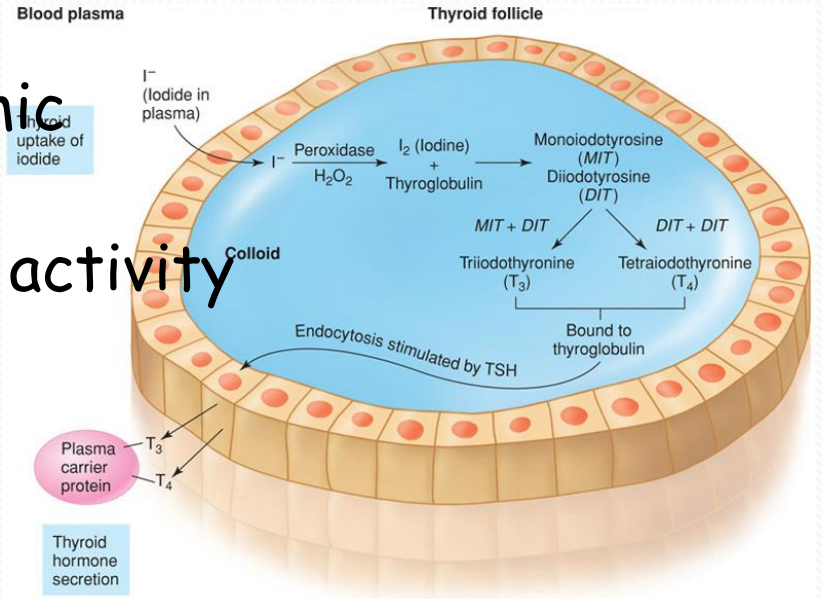


1. Follicular cell synthesizes enzymes and thyroglobulin for colloid.
2. I^- is co-transported into the cell with Na^+ and transported into colloid.
3. Enzymes add iodine to thyroglobulin to make T_3 and T_4.
4. Thyroglobulin is taken back into the cell.
5. Intracellular enzymes separate T_3 and T_4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

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.



Effects on Metabolism

T_3 & T_4

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.

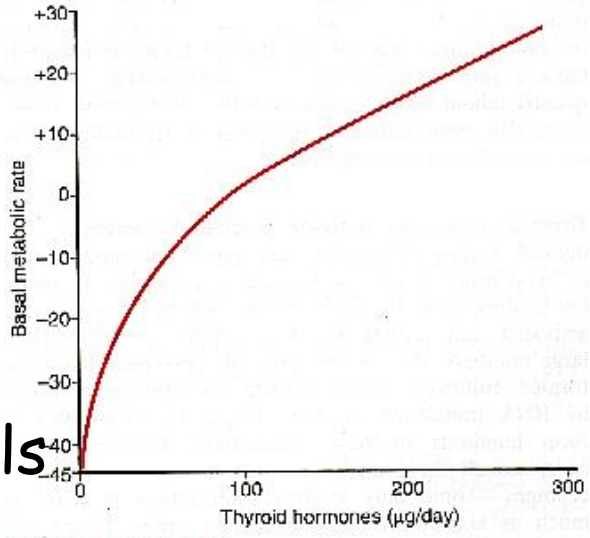


FIGURE 76–5

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

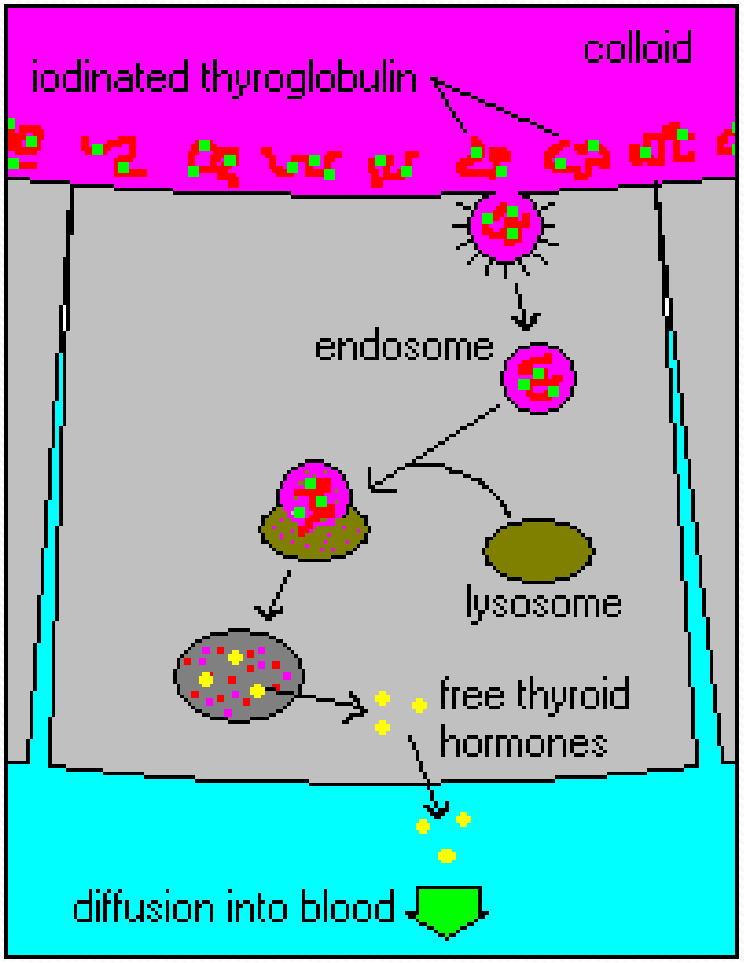
T_3 & T_4

- 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.



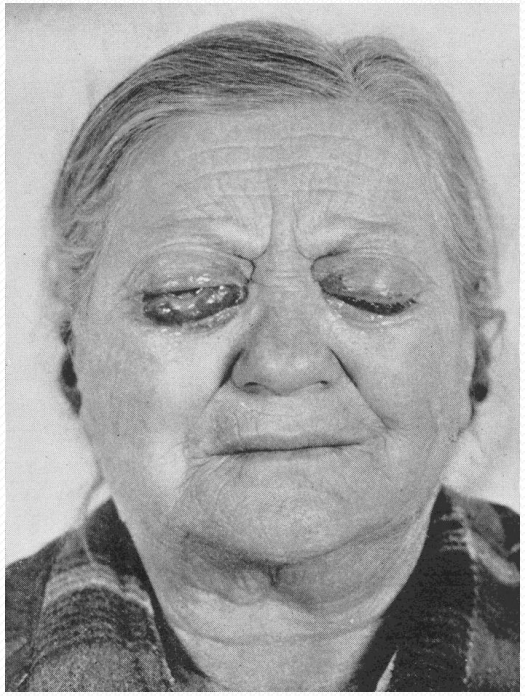
2. Effecs on Protein Metabolism.

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

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

T_3 & T_4

- 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.



T_3 & T_4

3. Effects on carbohydrate metabolism

A: Increase absorption of glucose from the gastrointestinal tract

E: Enhance glycogenolysis, and even enhanced diabetogenic effect of glucagon, cortisol and growth hormone.

C: Enhancement of glucose utilization of peripheral tissues.

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.

Effect of Thyroid Hormones on Growth and Development

T_3 & T_4

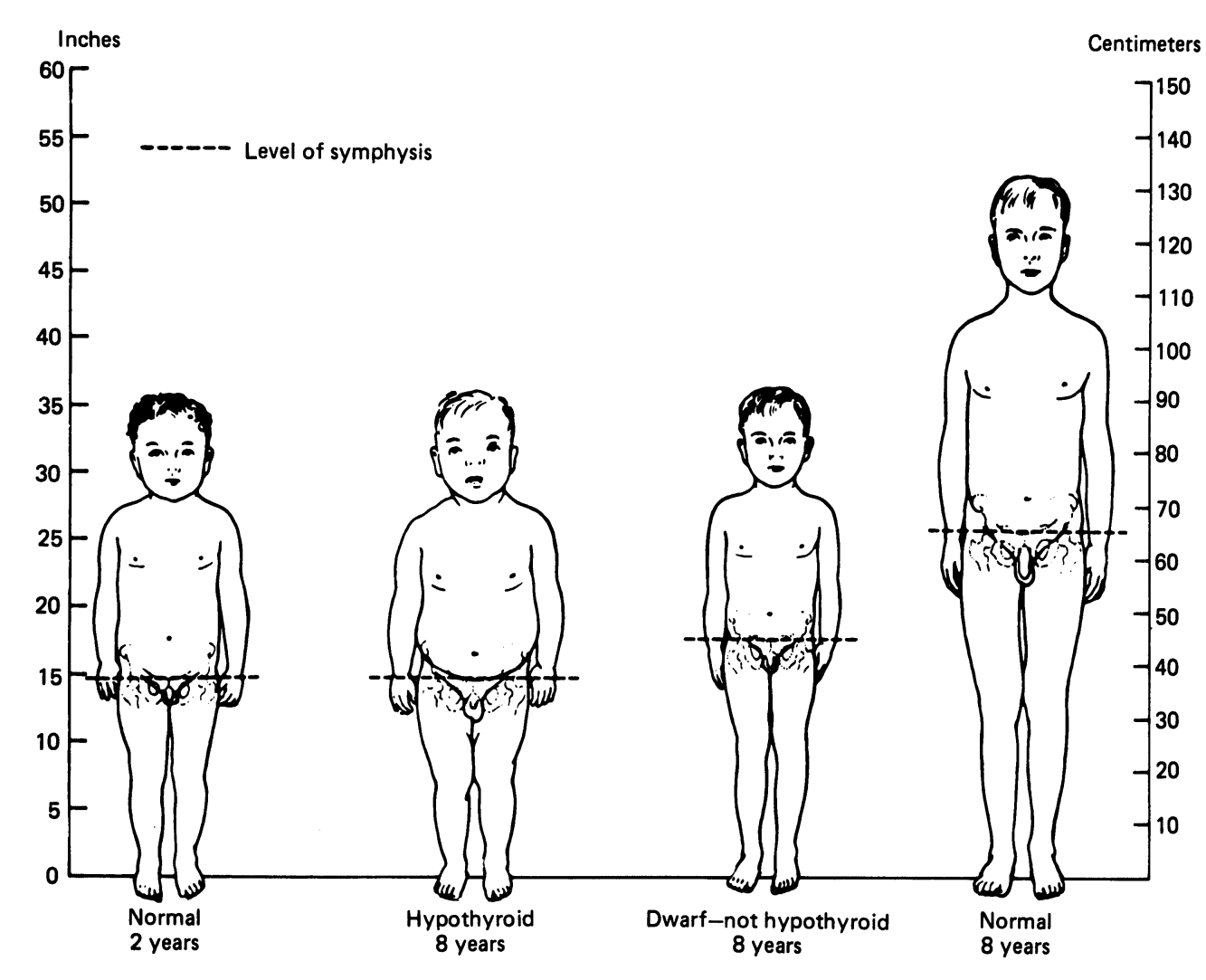
Thyroid hormone is essential for normal growth and development especially skeletal growth and development.

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.

T_3 & T_4


Inches
Centimeters
Level of symphysis
60
55
50
45
40
35
30
25
20
15
10
5
0
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Normal
2 years
Hypothyroid
8 years
Dwarf—not hypothyroid
8 years
Normal
8 years

T_3 & T_4

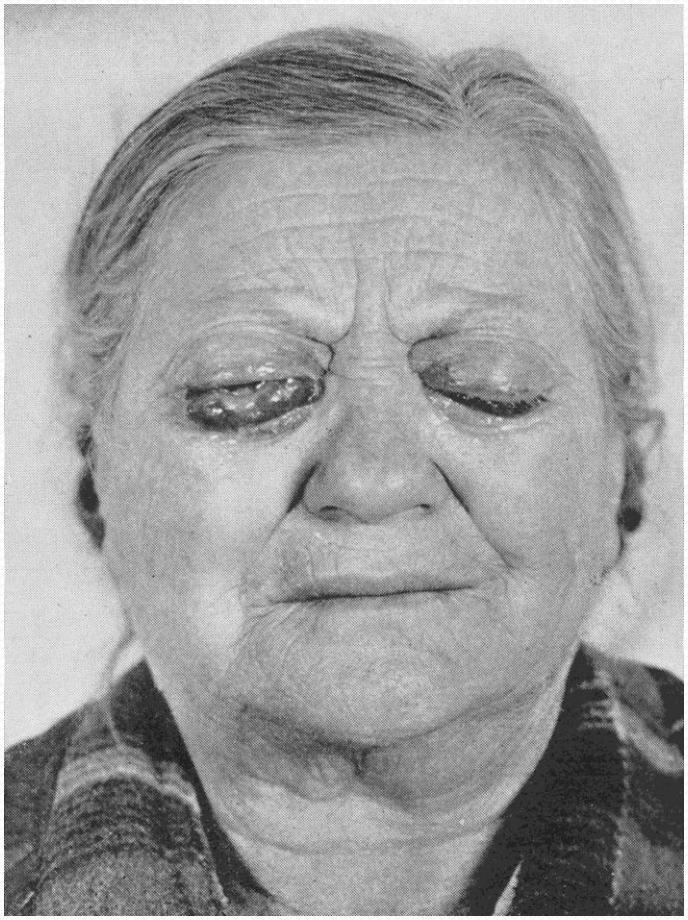
Effects of Thyroid Hormone on Nervous System

- increase excitability of central nervous system.
- In hyperthyroidism, the patient is likely to have extreme nervousness, many psychoneurotic tendencies including **anxiety complexes**, **extreme worry** and **paranoia**, and **muscle tremor**.

In addition, thyroid hormones can also stimulate the sympathetic nervous system.

T_3 & T_4

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



Effect on cardiovascular system

Thyroid hormones have a significant effect on cardiac output because of increase in heart rate and stroke volume, (may through enhance calcium release from sarcoplasmic reticulum).

Effect on gastrointestinal tract

Thyroid hormones increase the appetite and food intake by metabolic rate increased.

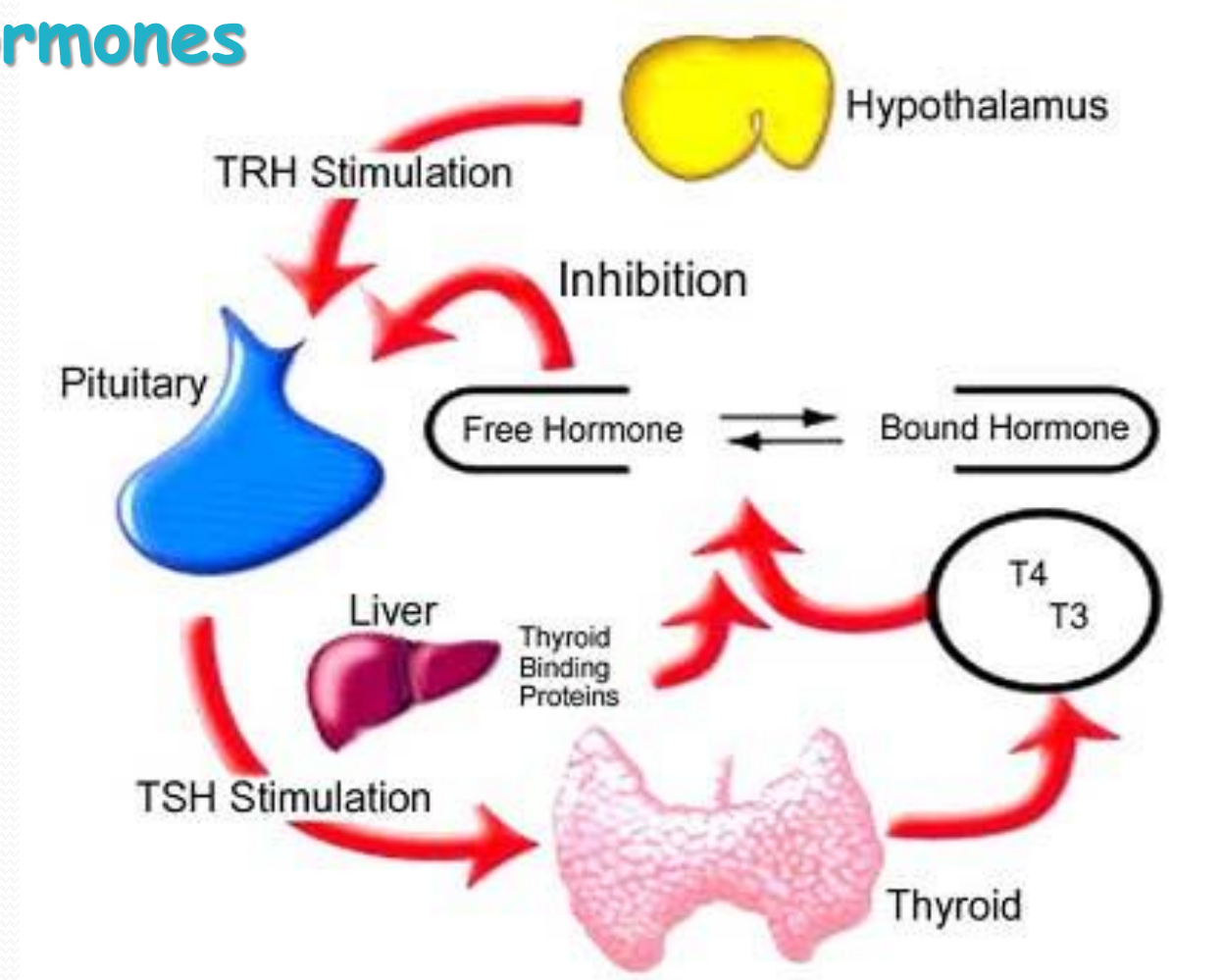
Thyroid hormones increase both the rate of secretion of the digestive juices and the motility of the gastrointestinal tract.

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



Diseases of the Thyroid - Goiter

T_3 & T_4

- In
  ioc
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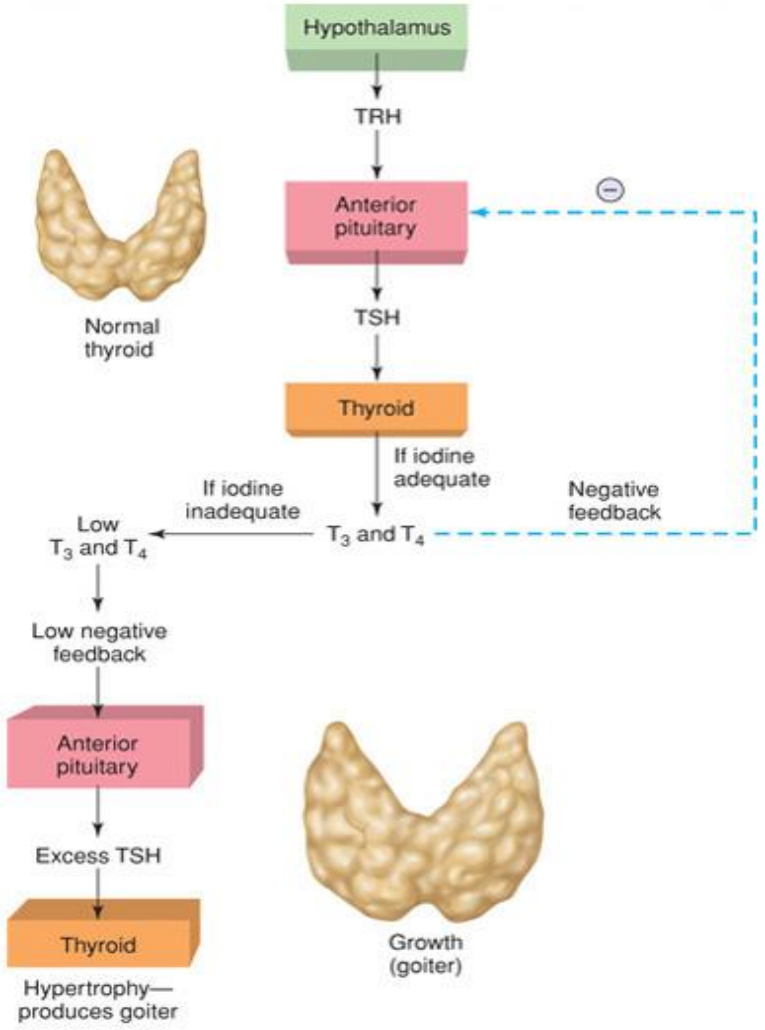


T_3 & T_4

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

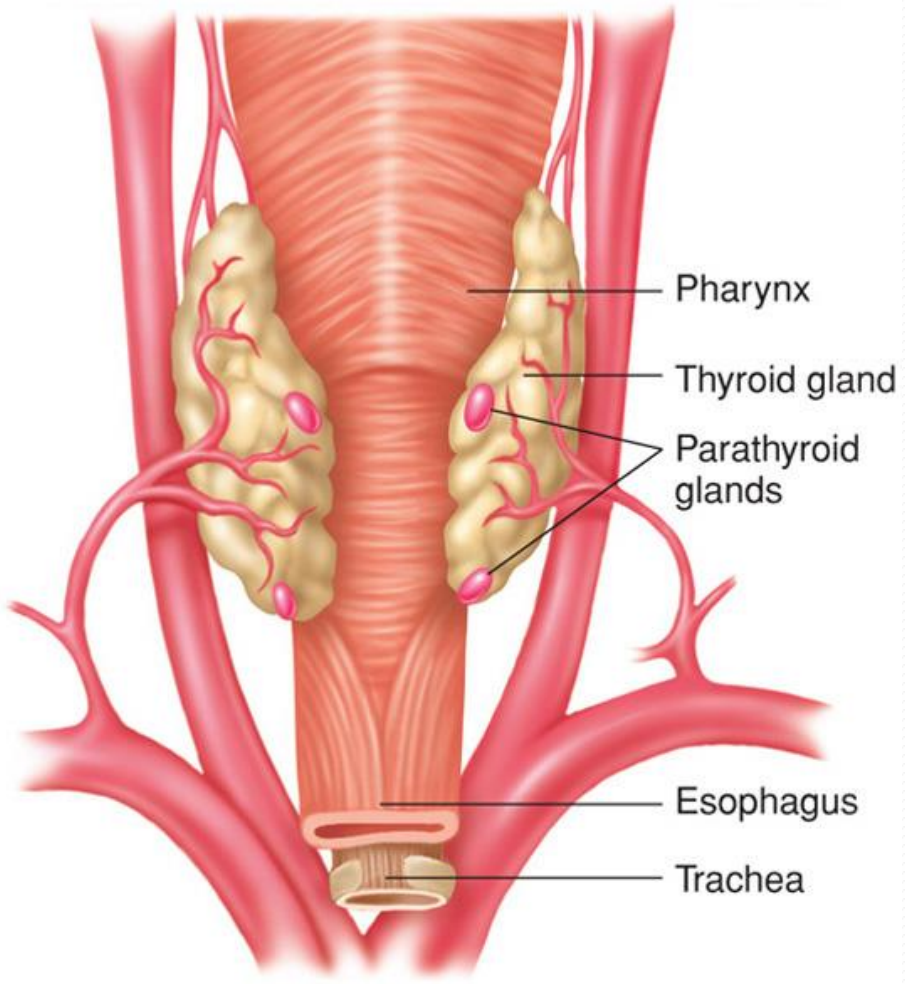
Feature	Hypothyroid	Hyperthyroid
Growth and development	Impaired growth	Accelerated growth
Activity and sleep	Lethargy; increased sleep	Increased activity; decreased sleep
Temperature tolerance	Intolerance to cold	Intolerance to heat
Skin characteristics	Coarse, dry skin	Normal skin
Perspiration	Absent	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

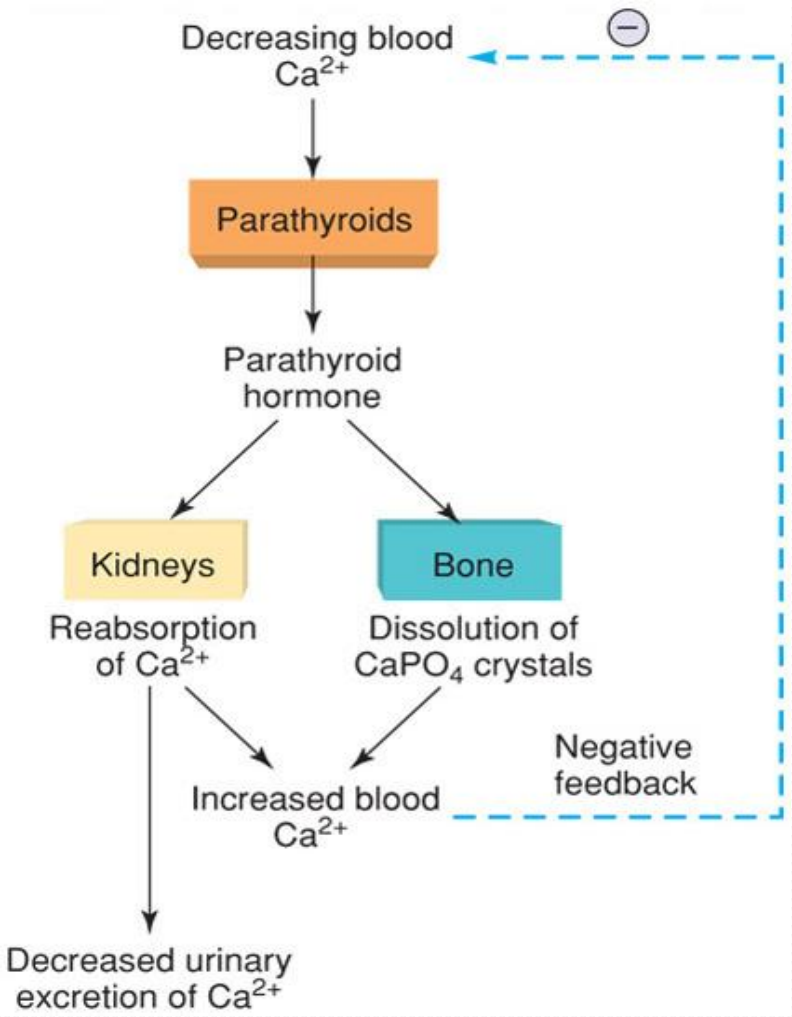
Parathyroid Glands

- 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

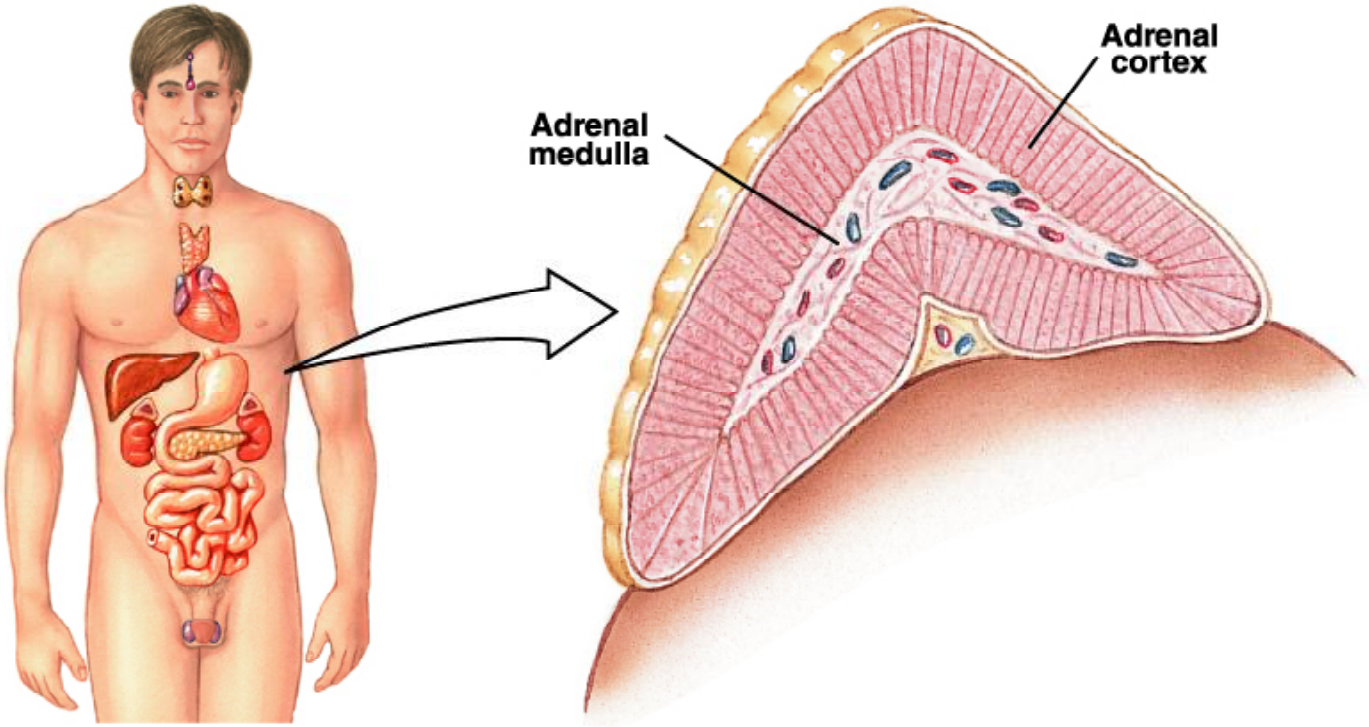
- Release stimulated by decreased blood Ca^{2+}
- Acts on bones, kidney, and intestines to increase blood Ca^{2+} levels



Section 6:

Adrenal Gland

Adrenal Gland



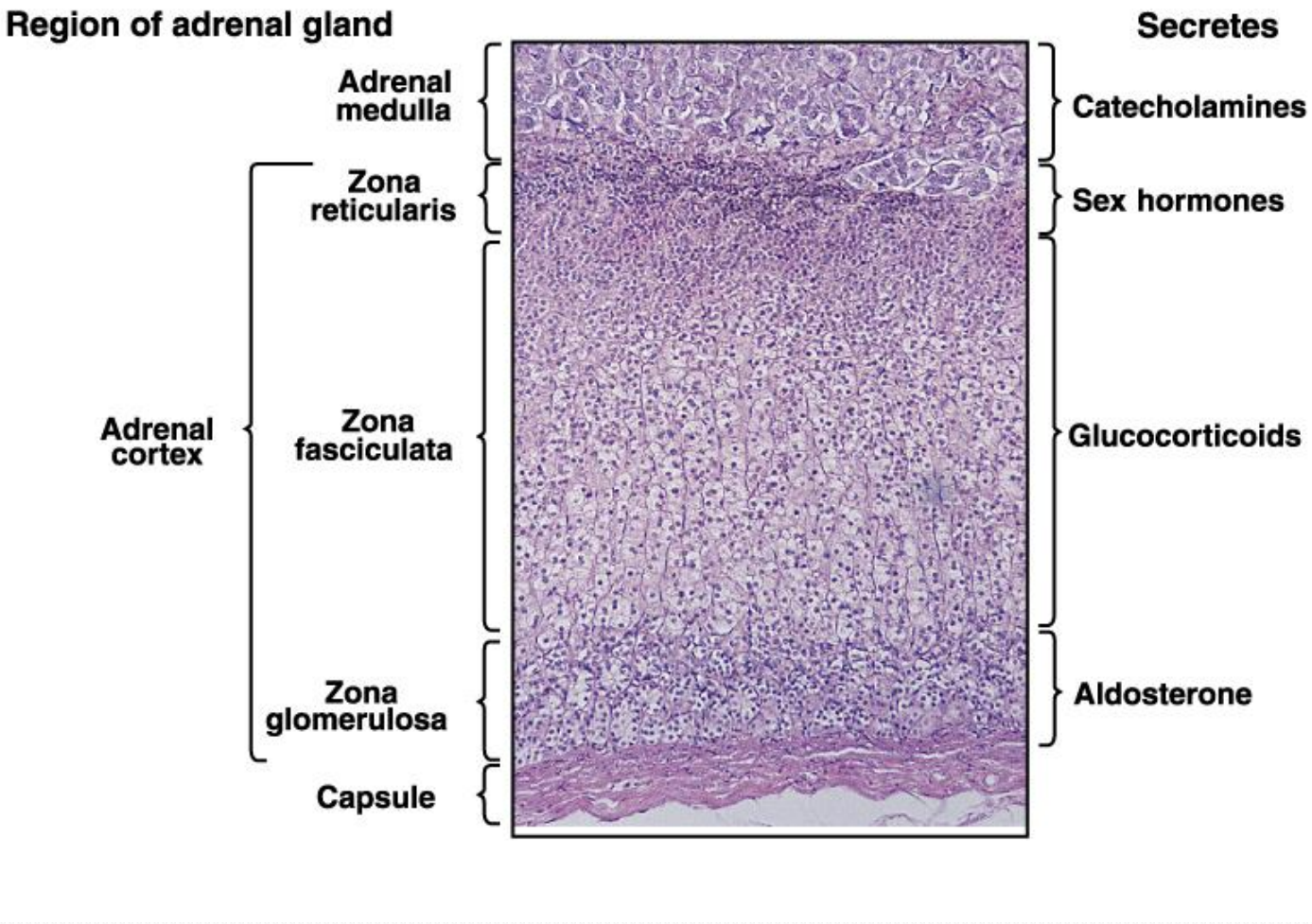
Adrenal Gland

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

Adrenal Gland

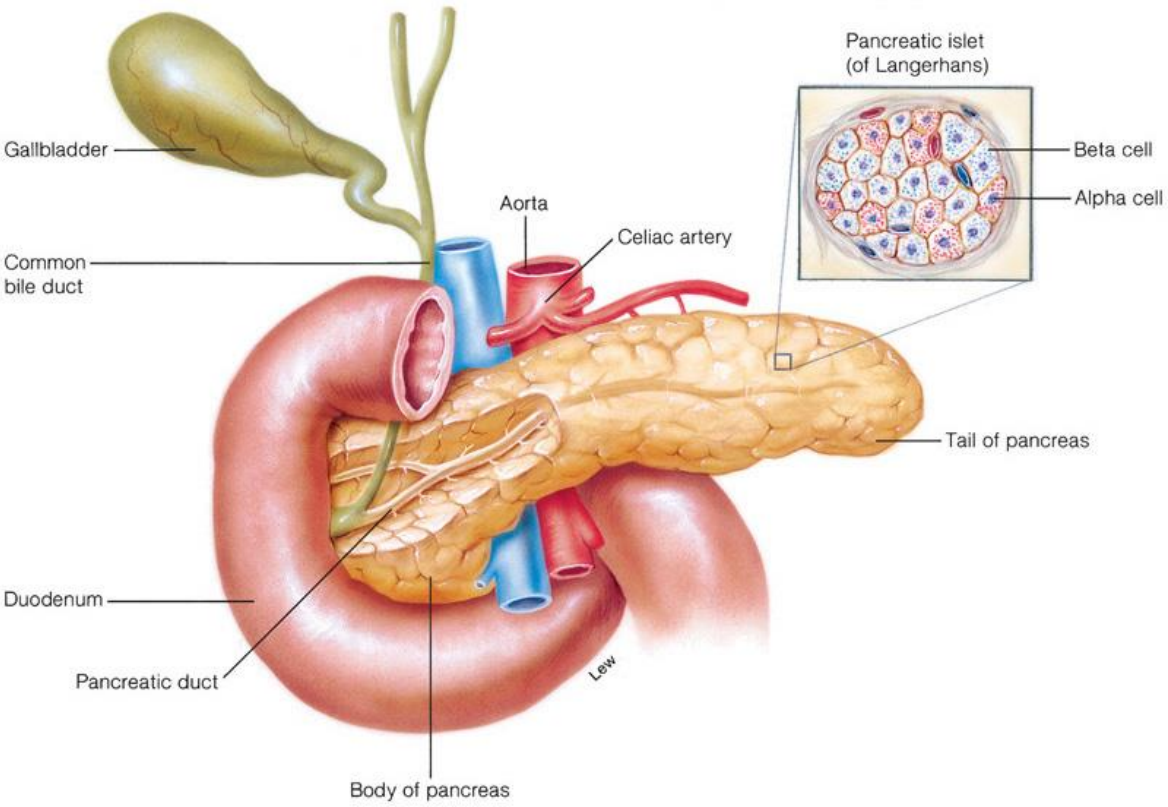


Section 7:

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