

Molecular Endocrinology: health and environment

- 1. Overview of the endocrine system
- 2. Hypothalamus-pituitary axis; Adrenal Gland
- 3. Stress response, steroid hormone biosynthesis
- Exam
- 4. Cell surface receptors
- 5. Nuclear hormone receptors
- Exam
- 6. Diabetes-I
- 7. Diabetes-II, Obesity, metabolic syndrome
- 8. Sex determination, male development
- Exam
- 9. Female reproductive cycle
- 10. Endocrine disruption-I wild life
- 11. Endocrine disruption-II humans
- Movies

2024 Molecular Endocrinology: Grading

3 Written exams 30-40 minutes: 25% each : 75%

Group Project, 2-3 people: 25%

- 3 minute movie

Past movies are posted and available at:

<https://www.epfl.ch/labs/briskin-lab/bio-450/>

Course Plan

1. Overview of the endocrine system
2. Hypothalamus-pituitary axis; Adrenal Gland
3. Stress response, steroid hormone biosynthesis
Exam
4. Cell surface receptors
5. Nuclear hormone receptors
Exam
6. Diabetes-I
7. Diabetes-II, Obesity, metabolic syndrome
8. Sex determination, male development
Exam
9. Female reproductive cycle
10. Endocrine disruption-I wild life
11. Endocrine disruption-II humans
Movies

Literature suggestions

Crash Course Endocrine and Reproductive Systems

Gary Meszaros @ Elsevier Mosby

Endocrinology

Mac E. Hadley @ Prentice Hall

Textbook of Endocrine Physiology

Eds. James Griffin, Sergio Ojeda @ Oxford University Press

Color Atlas of Physiology

Agamemnon Despopoulos, Stefan Silbernagl @ Thieme

Vertebrate Endocrinology

David Norris, James Carr @ Academic Press

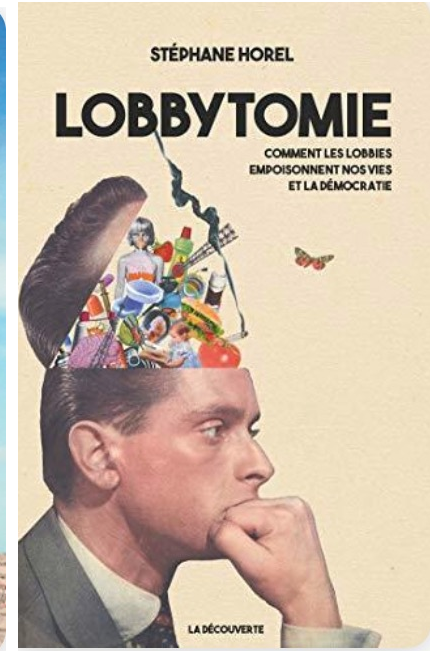
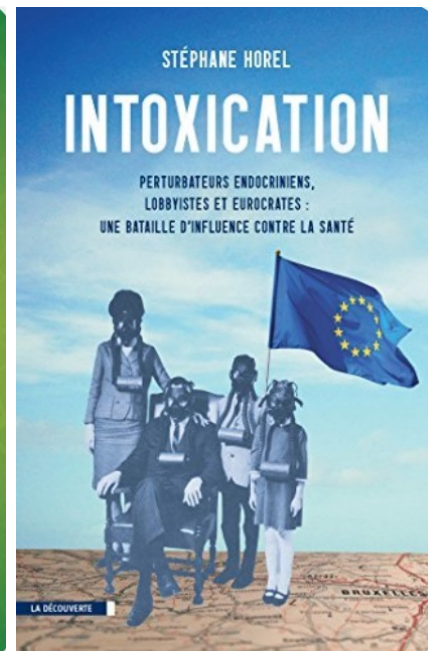
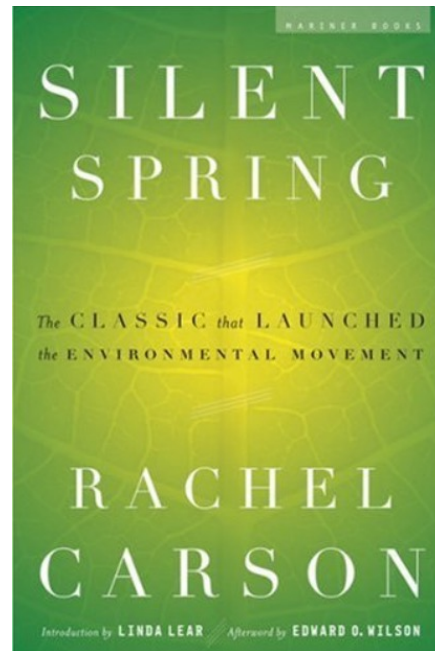
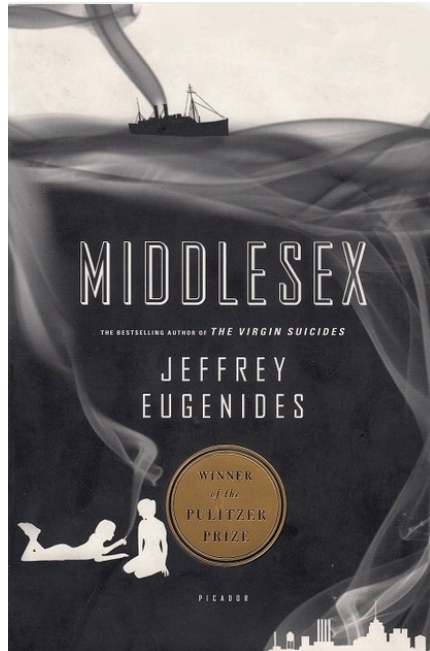
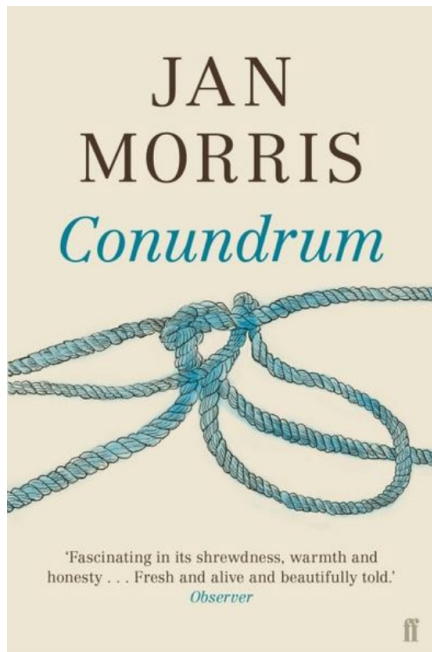
The Developing Human: clinically oriented embryology

Keith Moore et al. earlier edition pdf

Developmental Biology

Scott Gilbert

Further reading



Homeostasis

Claude Bernard (1813-1878)

“staying the same”

- "La fixité du milieu intérieur est la condition d'une vie libre et indépendante."
- "To have a free life, independent of the external environment, requires a constant internal environment".



The endocrine system

- **Hormaein:** to arouse, to excite

In humans there are about 10^{14} cells of 200 or more different types.

The endocrine and the nervous system constitute the two major communication systems. **The immune system**

Their functions are to:

1. allow appropriate adaptive changes
2. monitor internal and external environment
3. communicate via chemical messengers

All are required to maintain homeostasis.

Nervous versus endocrine system

- Nervous system performs short term crisis management
- Endocrine system regulates long term ongoing metabolic processes
 - Growth
 - Sexual development
 - Pregnancy
- Endocrine communication is carried out by endocrine cells releasing hormones
 - Alter metabolic activities of tissues and organs
 - Target cells

Nervous

vs

Endocrine System

- both send chemical signals
- both affect specific target organs or tissues
- both work to maintain homeostasis in the body

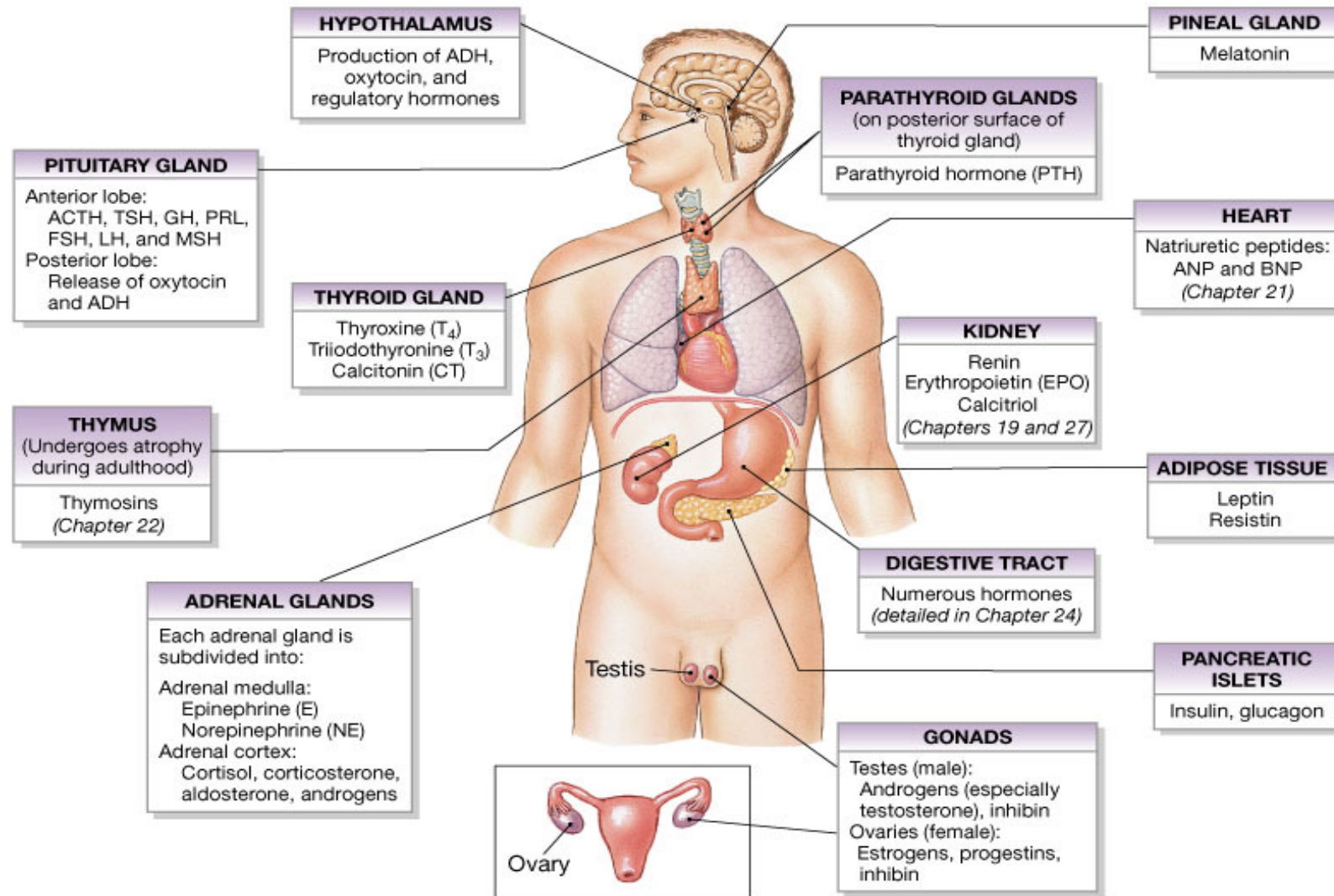
- Very rapid action
- Point to point, very specific
- Short duration
- Abrupt end to signal
- High energy expenditure (depolarization)
- Target cell mostly determined by locations

• Coarse & Rapid

- Slower response
- More diffuse
- Longer duration
- Effect or signal activity tails off
- Target cell determined by the receptors

• Fine & Slow

The Endocrine System



Brief History of Endocrinology-0

Eunuchs

China thousands of years widespread tradition
Korea, Vietnam, Thailand, India, Burma: royal courts
Ottoman empire: harem guards
Italy: opera singers

Used as:

Punishment

Remove threat of sexual interactions for those they were guarding

Political aids: perceived as no threat to power

Sensitive roles

-known for centuries that castration of cocks caused regression of the comb and wattles and changes in the plumage.

<https://youtu.be/IQo2PNnwOww>



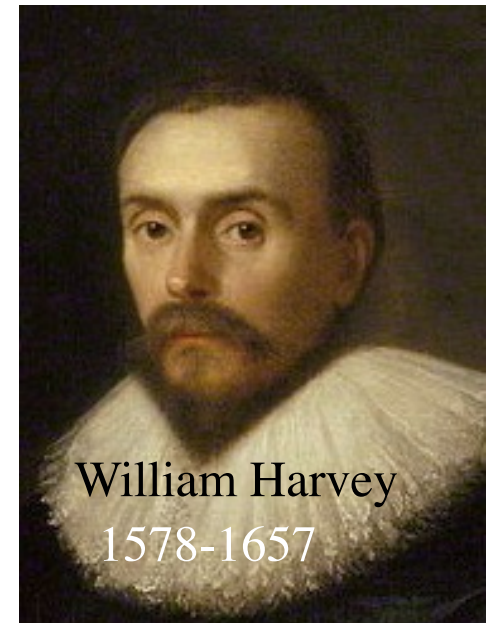
Brief History of Endocrinology-1: 17th century:

William Harvey described the heart as a four chambered pump that moves blood through arteries and veins, not air.

1628: *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus*

In addition he made significant contributions to embryology:

1651: *Exercitationes de Generatione Animalium*. "Ex ovo omnia."



William Harvey
1578-1657



Marcello Malpighi

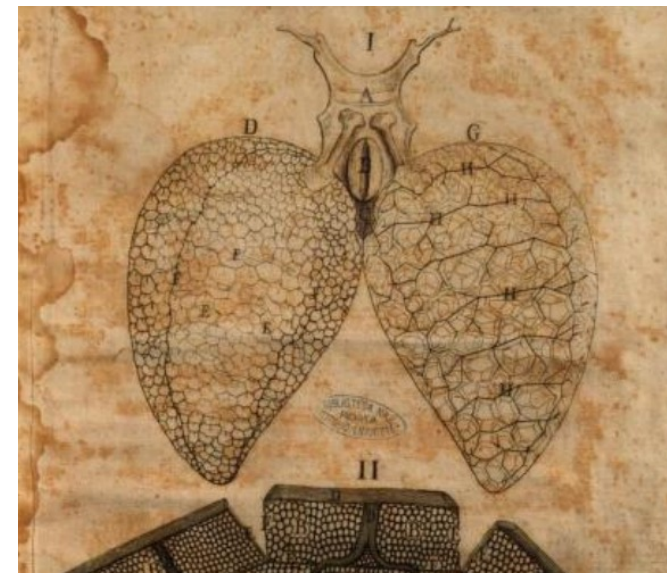
1628-
1694

Born in Folkstone, studied in Padova.

1661: Discovery of the capillaries, the link between arteries and veins

De pulmonibus observationes anatomicae

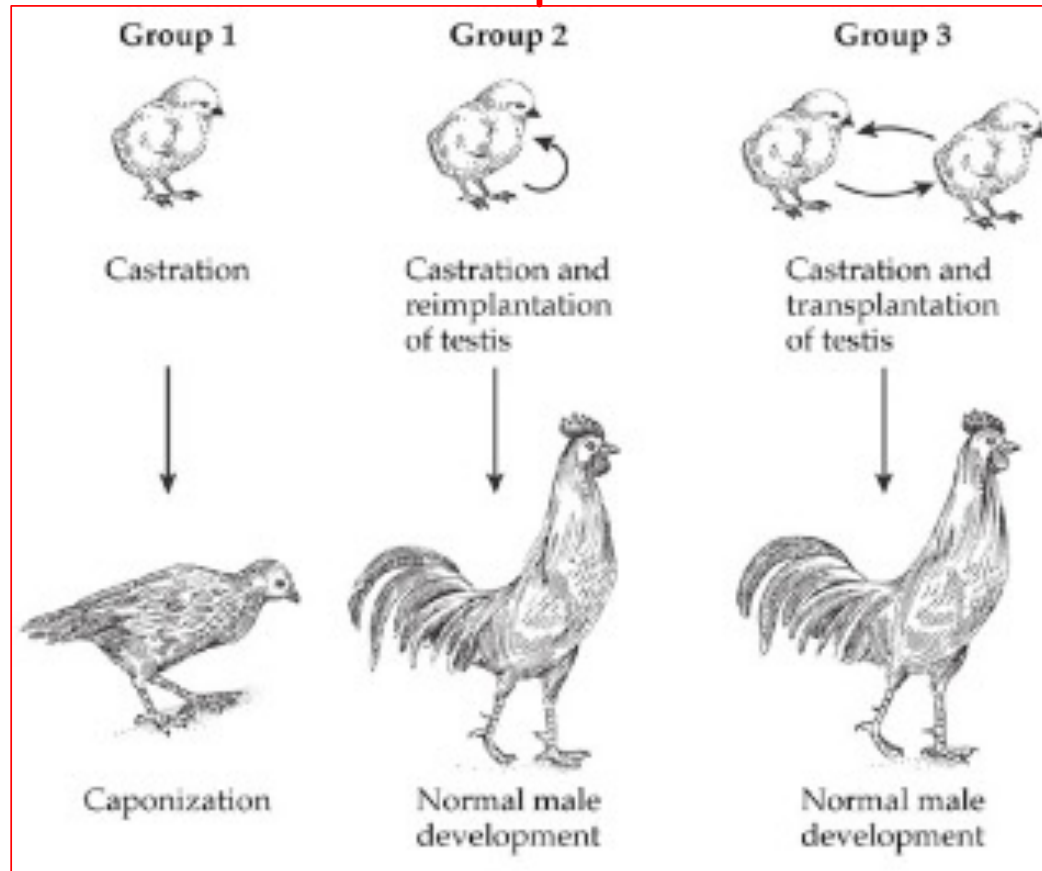
Mid 1800: idea that circulating blood carries substances from one part of the body to a distant part where they exert their effect.



Brief History of Endocrinology-2

First Experiment:

Arnold Adolph Berthold



1849: Berthold transplanted testes from normal cocks to capons:
cock-like feathers and cockscomb reappeared.

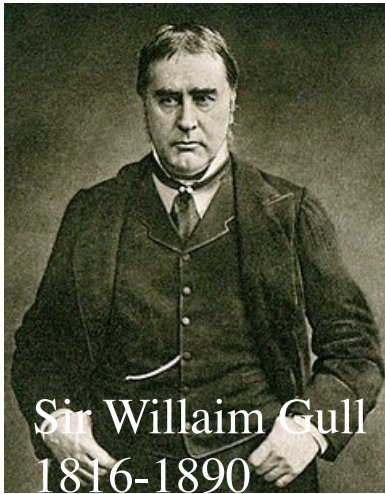
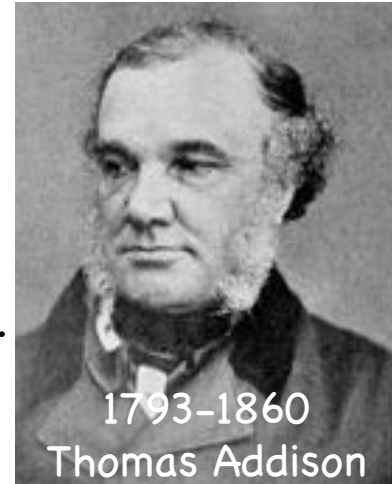
=> Proof of internal secretion

Brief History of Endocrinology-3

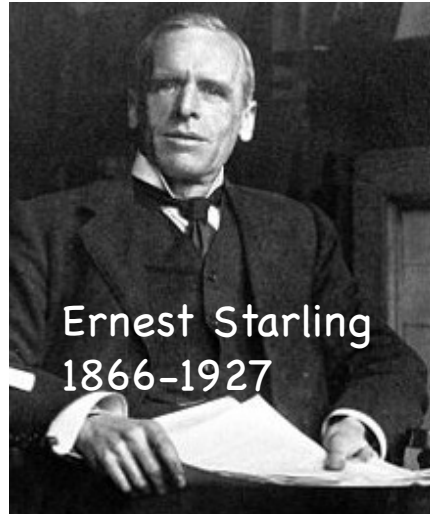
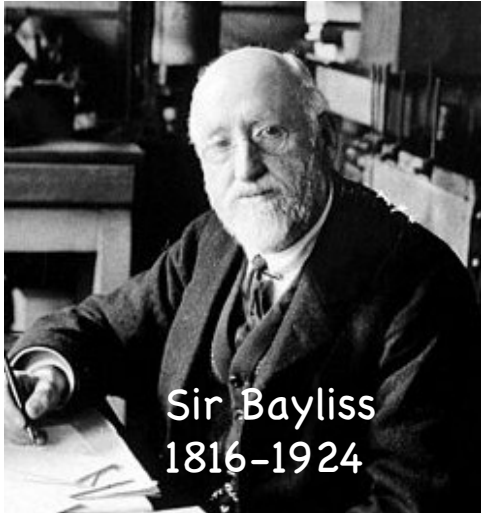
1855: Addison recognized the relationship between low blood pressure, muscular weakness, weight loss, bronzing of skin and the pathology of the adrenal gland.

1871: Hilton-Fagge related the cretinoid state to a congenital inadequacy of thyroid function in early childhood.

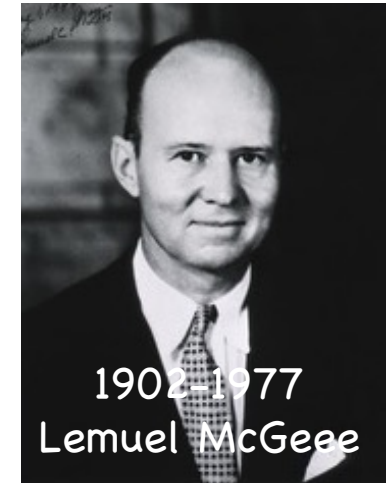
1879: Gull related dry skin, sparse hair, puffiness of face and hands, and a swollen tongue to myxedema, the pathological deficiency of thyroid function in adults. (goiter).



Brief History of Endocrinology-3



1902: Bayliss & Starling extracted and identified the first *hormone* secretin (secreted by cells in the intestinal mucosa).



1927: McGee isolated and purified substances that were androgenic in small amounts (microgram levels). Used a **bioassay**- applied to beak of sparrows and the beak darkened.

"Biological Activity of Testicular Extracts".

PhD thesis



Bernardo Houssay (1887-1971)

Nobel Prize 1947 (with Carl Ferdinand und Gerty Cori)

Buenos Aires

Hypophysectomized frogs and dogs.
Showed that the diabetes of a dog without pancreas improves when the hypophysis is removed ("Houssain's dog") because it results in decreased somatotropin secretion.

Definition of a Hormone:

- Secreted by living tissue
- Present in small or trace amounts (microgram= 10^{-6} , nanogram= 10^{-9} , picogram= 10^{-12})
- Secreted into and travel in the blood to a specific site of action (target organ)
- Not used as a source of energy but acts to regulate reactions to produce an appropriate response of the organism

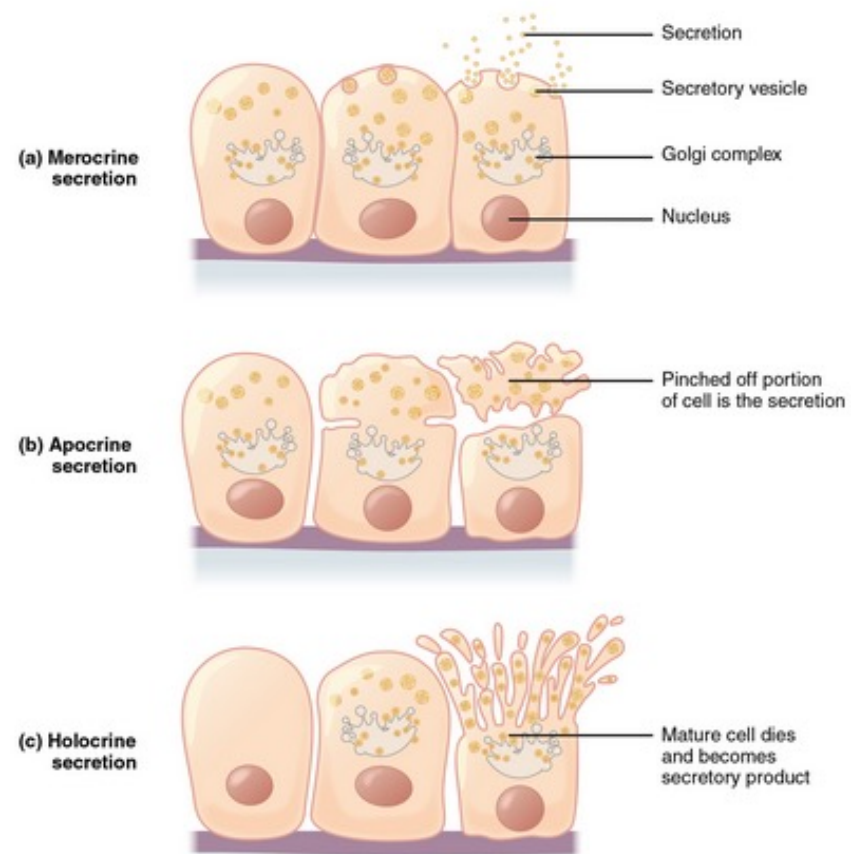
Endocrinology

- The study of the glands which secrete their products into the blood
- These glands are ductless (endocrine)
- The products secreted by these glands are called hormones

Types of glands

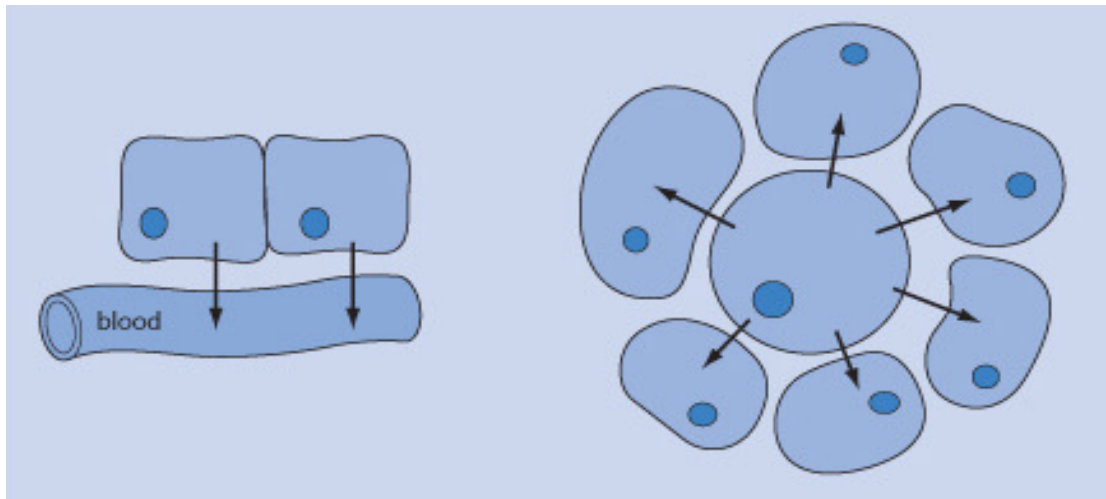
- *Endocrine*—ductless, secrete directly into the blood.
Ex. Thyroid, adrenal, etc.
- *Exocrine*—duct present, secrete their products through a duct onto a epithelial surface.
Ex. Salivary glands, mucous glands in intestine, etc.
- *Mixed*—contain both endocrine and exocrine functions in one gland.
Ex. Pancreas (trypsin-exocrine, insulin-endocrine)

Modes of glandular secretion

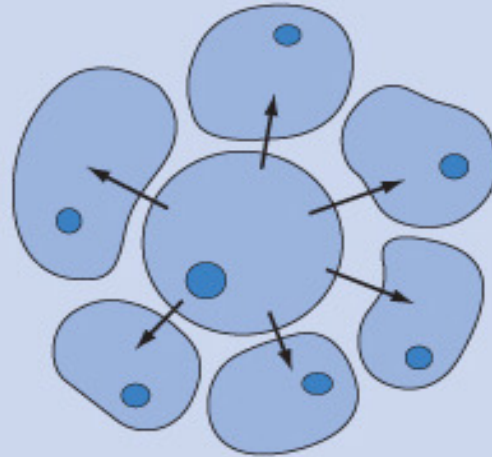


Modes of Delivery

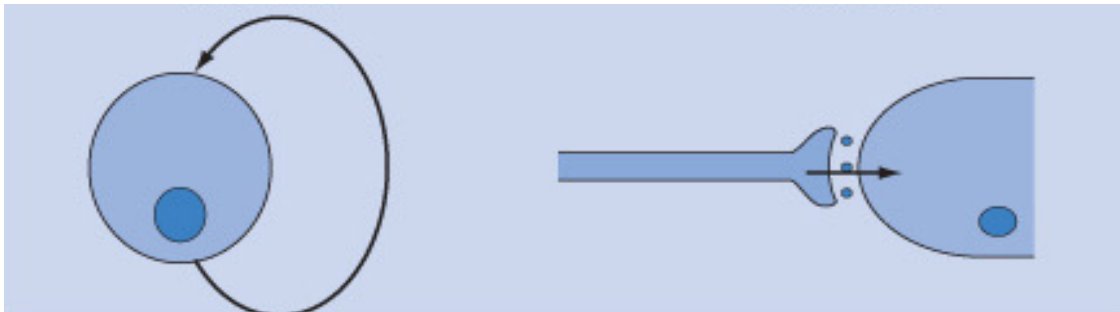
endocrine



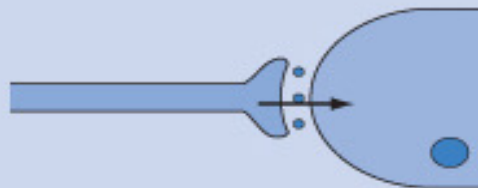
paracrine



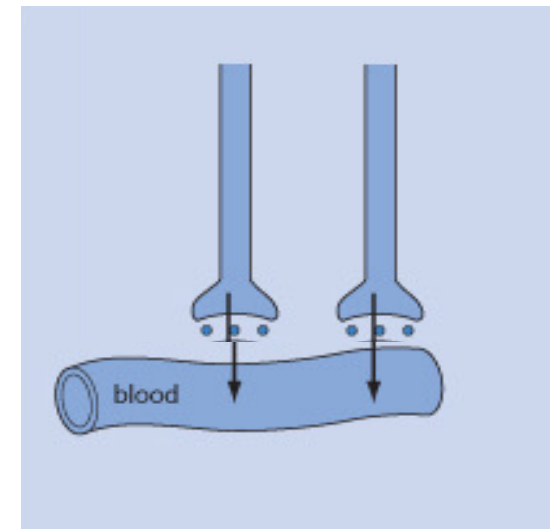
autocrine



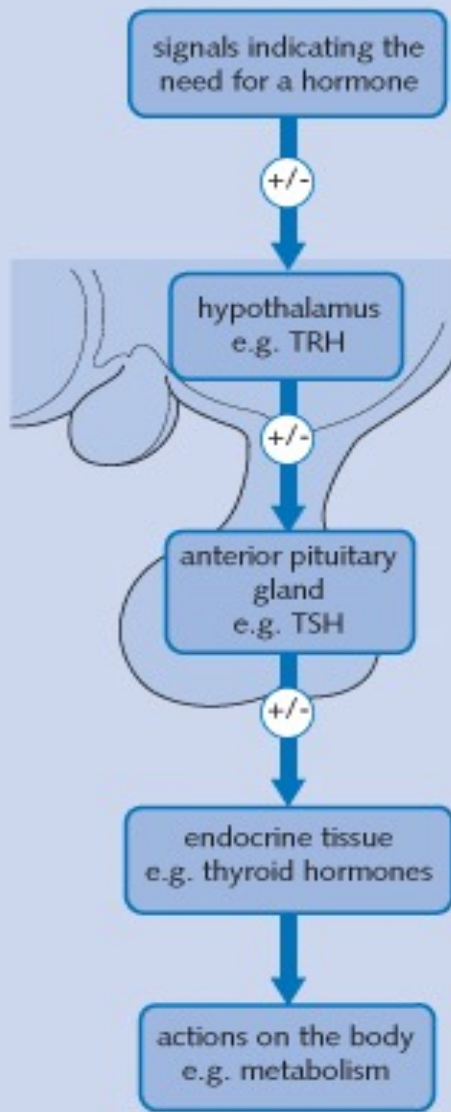
neurocrine



neuroendocrine



Organization of the endocrine system



hypothalamus:

-bridge between nervous system and endocrine system

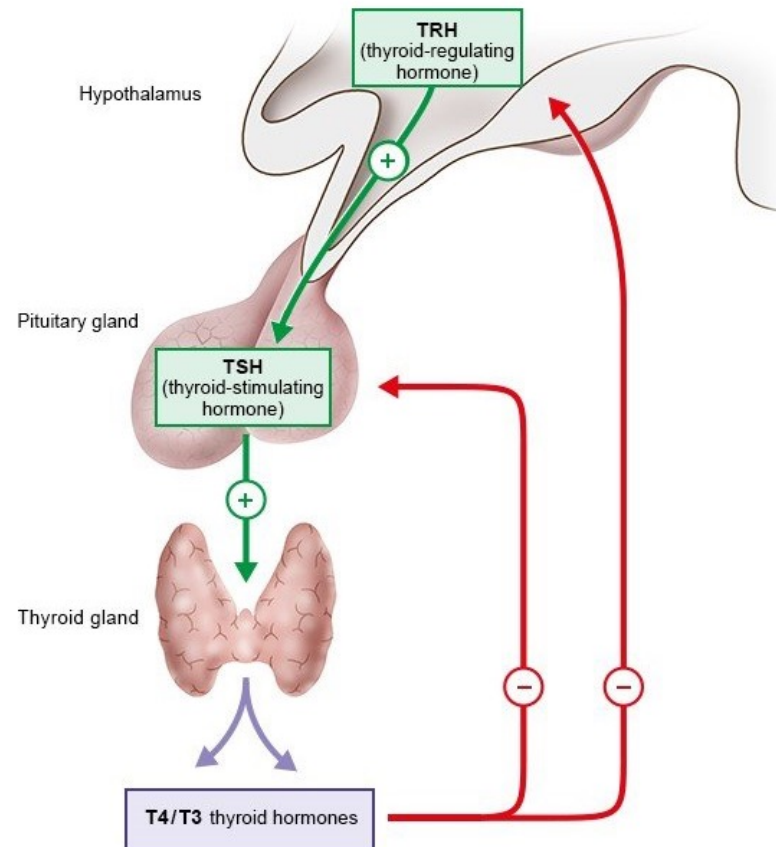
pituitary gland:

master endocrine gland

peripheral endocrine tissue

target cells

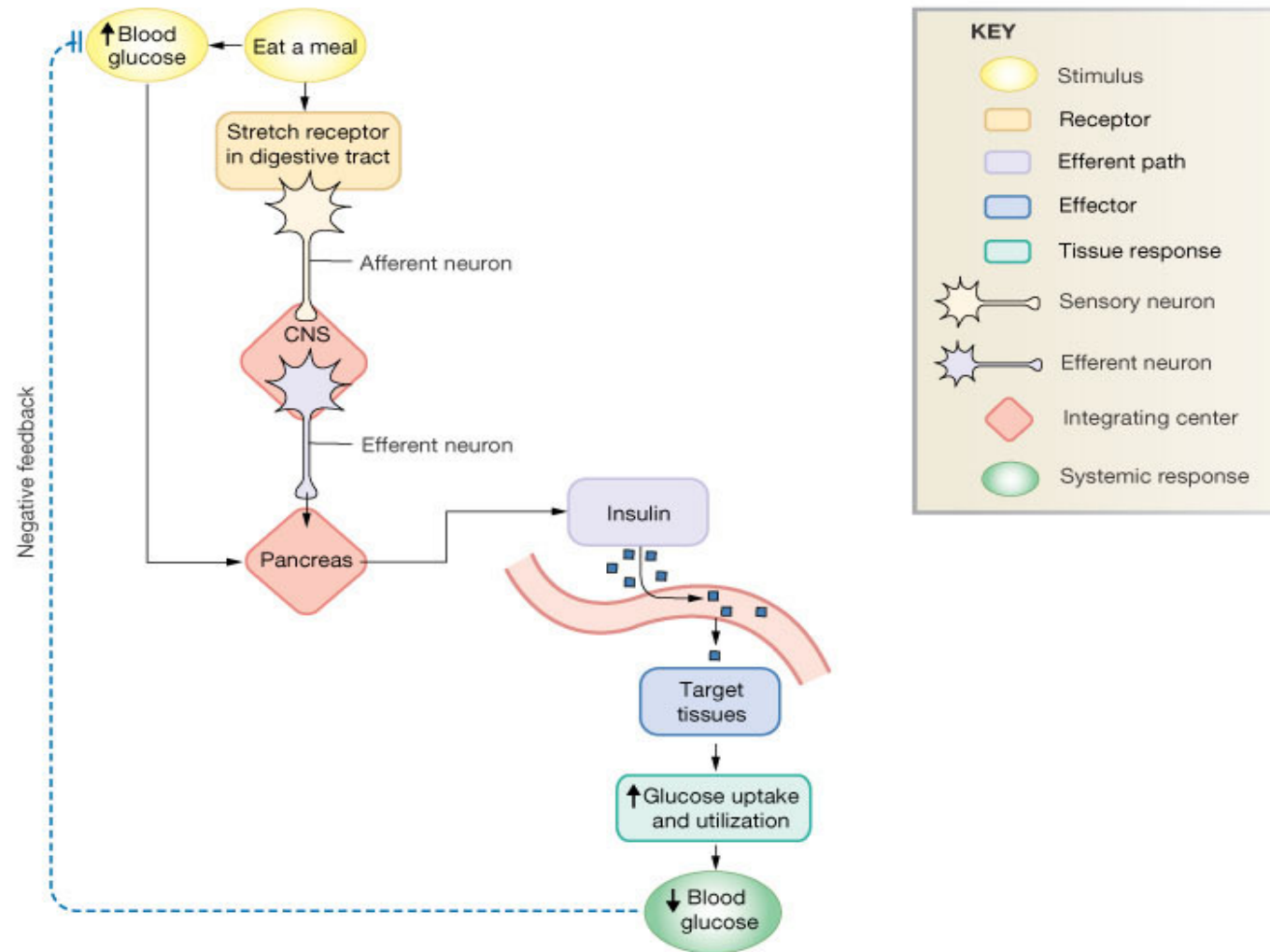
Negative Feedback loop (thyroid hormone production)



Endocrine Reflex Pathways: Overview

- Stimulus
- Afferent signal
- Integration
- Efferent signal (the hormone)
- Physiological action
- Negative feedback

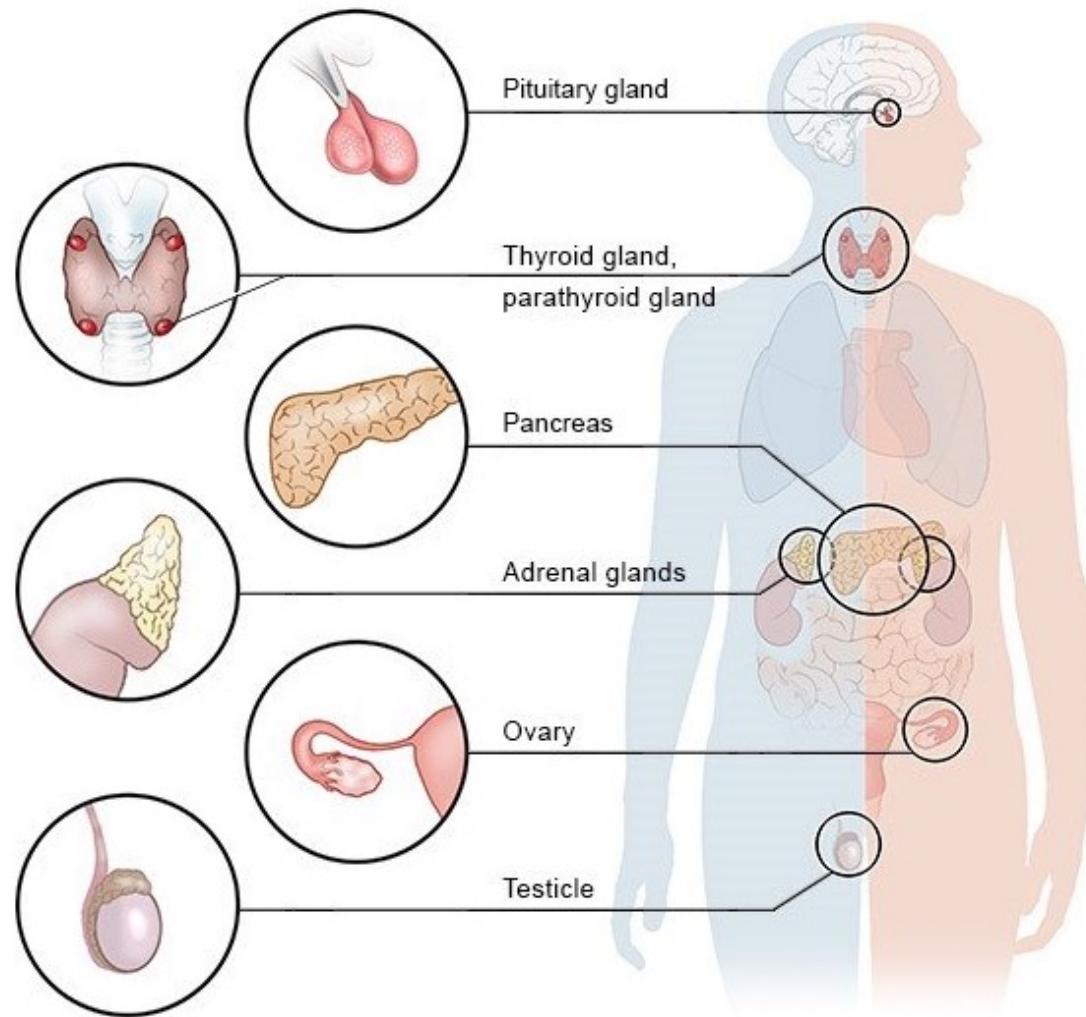
Endocrine Reflex Pathways: Overview

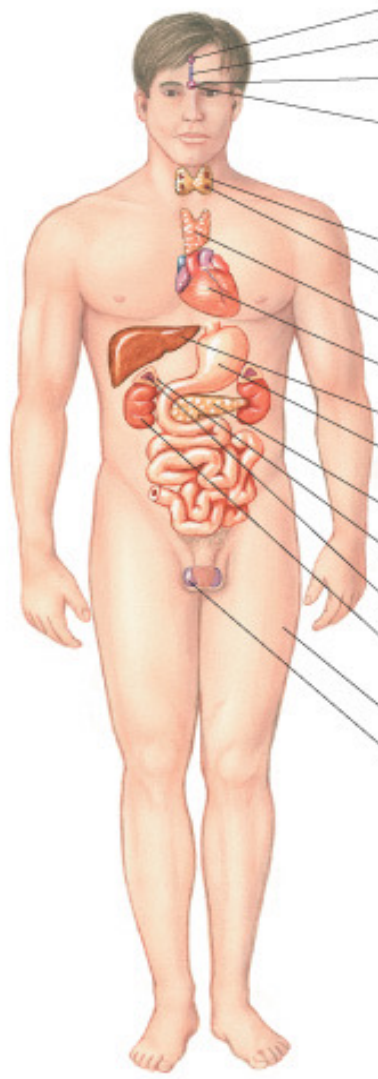


Tasks of the endocrine system:

- Glucose homeostasis
- Calcium homeostasis (clotting, muscle contraction)
- Sodium homeostasis
- Water balance
- Control of body temperature
- Control of feeding behavior
- Sexual behaviour
- Growth regulation

Main endocrine glands in the body:



	Location	Gland or cell?	Chemical class
	Pineal gland	Gland	Amine
	Hypothalamus	Clusters of neurons	Peptides
	Posterior pituitary	Extensions of hypothalamic neurons	Peptides
	Anterior pituitary	Gland	Peptides
	Thyroid	Gland	Iodinated amines Peptide
	Parathyroid	Gland	Peptide
	Thymus	Gland	Peptides
	Heart	Cells	Peptide
	Liver	Cells	Peptides
	Stomach and small intestine	Cells	Peptides
	Pancreas	Gland	Peptide
	Adrenal cortex	Gland	Steroids
	Adrenal medulla	Gland	Amines
	Kidney	Cells	Peptide Steroid
	Skin	Cells	Steroid
	Testes (male)	Glands	Steroids Peptide
	Ovaries (female)	Glands	Steroids Peptide
	Adipose tissue	Cells	Peptide
	Placenta (pregnant females only)	Gland	Steroids Peptide

Summary of the Endocrine System

<i>Hormone</i>	<i>Target</i>	<i>Main Effect</i>
Melatonin	Unclear in humans	Circadian rhythms. Other effects uncertain
Trophic hormones (see Fig. 7-13) See posterior pituitary	Anterior pituitary	Release or inhibit pituitary hormones
Oxytocin (OT)	Breast and uterus	Milk ejection; labor and delivery; behavior
Vasopressin (ADH) Prolactin (PRL) Growth hormone (GH, somatotropin) Corticotropin (ACTH) Thyrotropin (TSH) Follicle stimulating hormone (FSH) Luteinizing hormone (LH)	Kidney Breast Many tissues Adrenal cortex Thyroid gland Gonads Gonads	Water reabsorption Milk production Growth and metabolism Cortisol release Thyroid hormone synthesis and release Egg or sperm production; sex hormone production Sex hormone production; egg or sperm production
Triiodothyronine and thyroxine (T_3 , T_4) Calcitonin (CT)	Many tissues Bone	Metabolism, growth and development Plasma calcium levels (minimal effect in humans)
Parathyroid hormone (PTH)	Bone, kidney	Regulate plasma calcium and phosphate levels
Thymosin, thymopoietin	Lymphocytes	Lymphocyte development
Atrial natriuretic peptide (ANP)	Kidneys	Increase sodium excretion
Angiotensinogen Insulin-like growth factors (IGF)	Adrenal cortex, blood vessels, brain Many tissues	Aldosterone secretion, increase blood pressure Growth

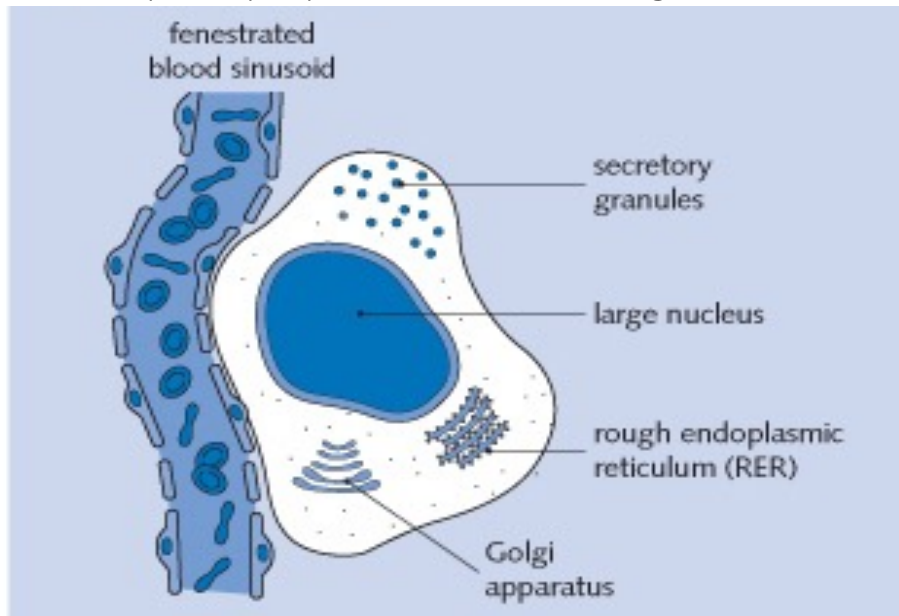
Hormone	Target	Main Effect
Gastrin, cholecystokinin (CCK), secretin, and others	GI tract and pancreas	Assist digestion and absorption of nutrients
Insulin, glucagon, somatostatin (SS), pancreatic polypeptide	Many tissues	Metabolism of glucose and other nutrients
Aldosterone Cortisol Androgens	Kidney Many tissues Many tissues	Na ⁺ and K ⁺ homeostasis Stress response Sex drive in females
Epinephrine, norepinephrine	Many tissues	Fight-or-flight response
Erythropoietin (EPO) 1,25 Dihydroxy-vitamin D ₃ (calciferol)	Bone marrow Intestine	Red blood cell production Increase calcium absorption
Vitamin D ₃	Intermediate form of hormone	Precursor of 1,25 dihydroxy -vitamin D ₃
Androgen Inhibin	Many tissues Anterior pituitary	Sperm production, secondary sex characteristics Inhibit FSH secretion
Estrogens and progesterone Ovarian inhibin Relaxin (pregnancy)	Many tissues Anterior pituitary Uterine muscle	Egg production, secondary sex characteristics Inhibit FSH secretion Relaxes muscle
Leptin	Hypothalamus, other tissues	Food intake, metabolism, reproduction
Estrogens and progesterone (P) Chorionic somatomammotropin (CS) Chorionic gonadotropin (CG)	Many tissues Many tissues Corpus luteum of ovary	Fetal and maternal development Metabolism Hormone secretion

Comparison of different types of hormones

	Polypeptides	Modified amino acids	Steroids
Size	Medium–large	Very small	Small
Ability to cross cell membrane	×	✓	✓
Receptor type	Cell-surface	Cell-surface or intracellular	Intracellular
Soluble in:	Water	Water	Fat
Action	Protein activation	Protein activation or synthesis	Protein synthesis
Transport in the blood	Dissolved in the plasma	Dissolved in the plasma or bound to plasma proteins	Bound to plasma proteins

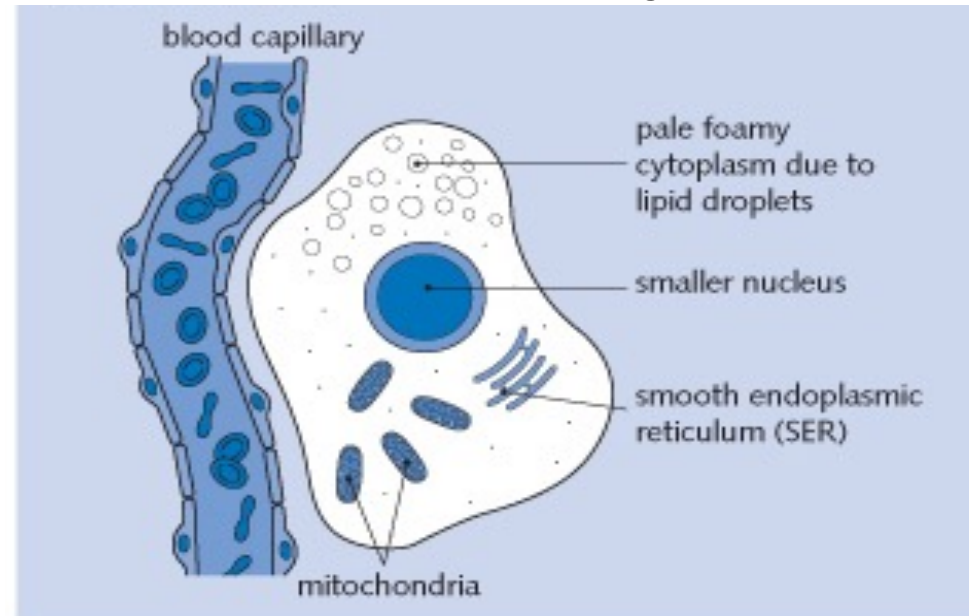
Hormone secretion

polypeptide secreting cell



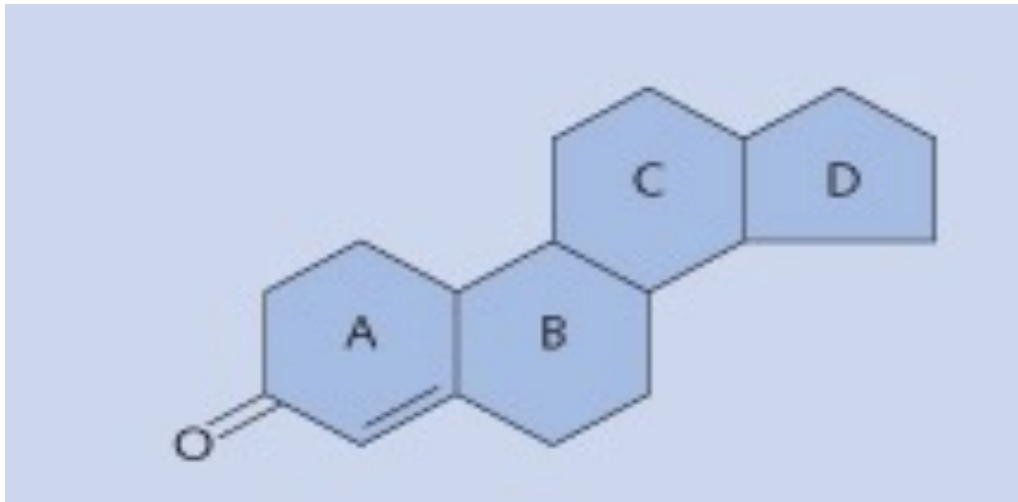
- Large prominent nuclei
- Small cytoplasm
- Large Golgi
- Abundant RER
- Many secretory granules
- fenestrated blood sinusoids

steroid secreting cell



- small rounded nuclei
- large cytoplasm
- lipid droplets “foamy”
- abundant ER
- many mitochondria
- highly vascularized

Basic structure of a steroid hormone



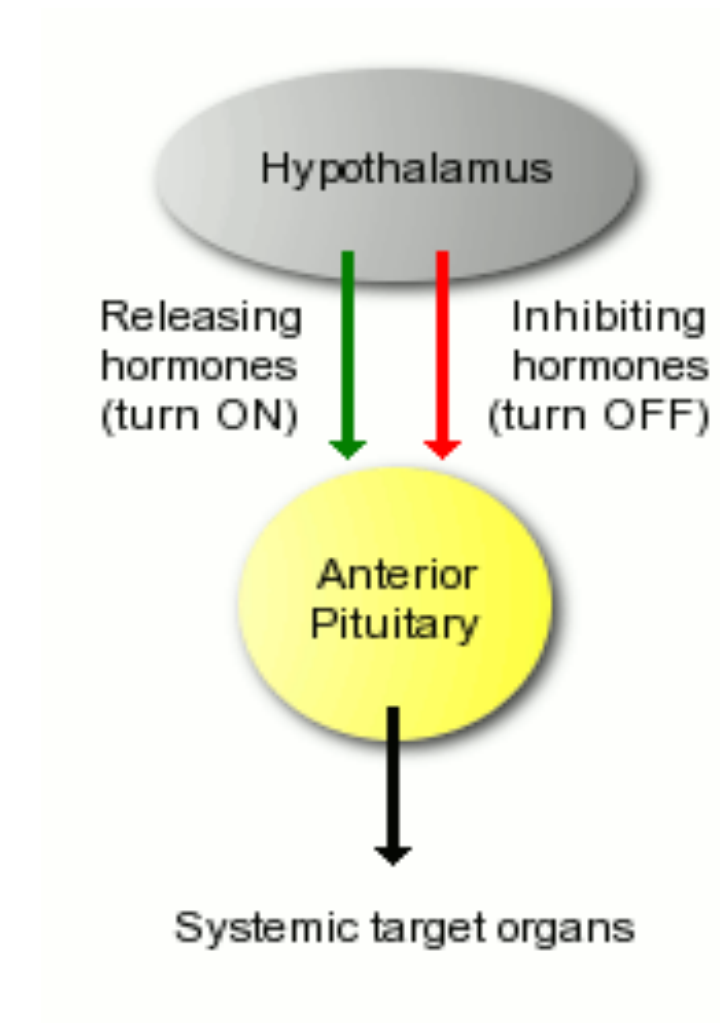
A, B, C = 6-carbon ring
D = 5-carbon ring

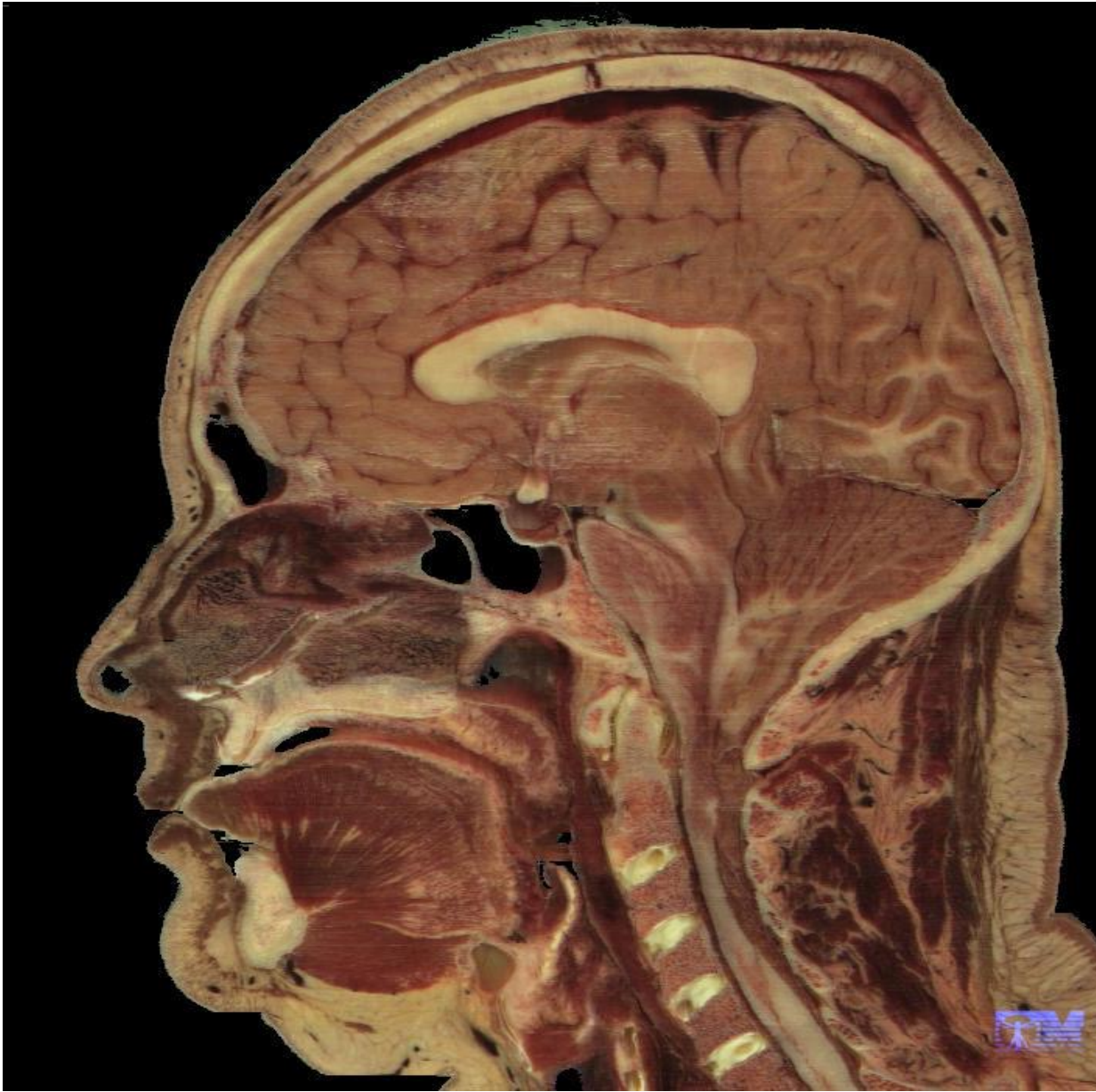
- small
- lipophilic
- circulate bound to plasma proteins

Steroid Hormones: Structure and Action

- from cholesterol, lipophilic, enter target cell,
- cytoplasmic or nuclear receptors (mostly)
- activate DNA for protein synthesis
- slower acting, longer half-life
- examples: cortisol, estrogen & testosterone

The Hypothalamus and the Pituitary Gland





Hypothalamus and pituitary gland -localization-

