

Chapter 9

The Endocrine System

The endocrine system is all the organs of the body that are endocrine glands. An endocrine gland system is a system of ductless glands that secrete messenger molecules called hormones.

Endocrinology – study of hormones and endocrine glands. Hormones are able to maintain homeostasis because they are subject to negative feedback mechanisms. Frequently, very few molecules of a hormone are required to effect changes in a target cell because the mechanism of hormonal action involves an enzyme cascade that amplifies the response to a hormone. The endocrine system is a series of glands that release

Hormones are substances that are secreted by one group of cells into the blood, and affects the physiology of another group of cells (organs). The endocrine system is controlled by the pituitary gland and the hypothalamus. Compared to most other organs in the body, endocrine organs are well vascularized. They interact closely with the nervous system. A hormone is dissolved in plasma and transported throughout entire body within 60 seconds. Every cell is exposed to the hormone, but not every cell responds to it. For a cell to be able to respond to a hormone, the cell must have a functional hormone receptor. A cell that responds will do so in various ways. The cells in the heart, pancreas, and brain respond to epinephrine differently. One thing that always happens is that a cell will change its physiology in response to a hormone.

Major Endocrine Glands

Hypothalamus	Pituitary Gland
Thyroid Gland	Parathyroid Glands
Thymus Gland	Adrenal Glands
Pancreas	Ovaries
Testes	Pineal Gland

Endocrine Organs

Scattered throughout the body

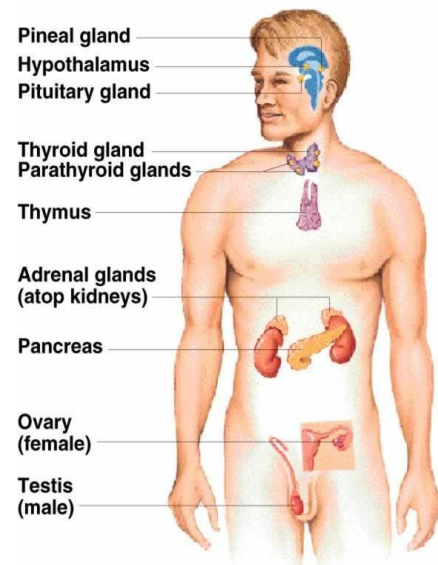
Pure endocrine organs:

- Pituitary, pineal, thyroid, parathyroid, and adrenal glands

Organs containing endocrine cells:

- Pancreas, thymus, gonads, and the hypothalamus

These are richly vascularized.



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Hormones:

Hormones can be synergistic; aldosterone and antidiuretic hormone (ADH) both help increase volume of fluid in body to raise blood pressure.

Some hormones are antagonists; Atrial natriuretic peptide (ANP, produced by heart cells) is released when you have high blood pressure. It causes the kidney to secrete more water, so blood pressure can decrease. That is the opposite of ADH, which makes you urinate less.

Some hormones are permissive; you need one in order for a second to do its job well. Thyroid hormone is permissive for growth hormone (you need thyroid hormone in order for

GH to work). Not enough thyroid hormone can cause stunted growth, even if enough growth hormone is present.

Basic hormone action

- Hormones are made by the gland's cells, possibly stored, then released
- Circulate throughout the body vasculature, fluids
- Influences only specific tissues: target cells that have a receptor for that particular hormone
- A hormone can have different effects on different target cells: depends on the receptor
- Some hormones are "permissive" for the actions of another (TH for GH)

Ultimate goal: alter cell activity by altering protein activity in the target cell.

Target Cell:

A target cell is only a target cell if it has a functional receptor (a protein) for the hormone.

Receptor:

It is a protein made by the target cell (protein synthesis after gene expression). The protein is made, then inserted into plasma membrane, or found in cytoplasm or nucleoplasm. What would happen if there were a gene defect in the DNA code for a receptor? The receptor becomes faulty, and will not respond to the hormone. The receptor will also not function properly if the cell is exposed to excess salt, heat, or pH. The active site on the protein "fits" the hormone and acts to convert the signal into a response.

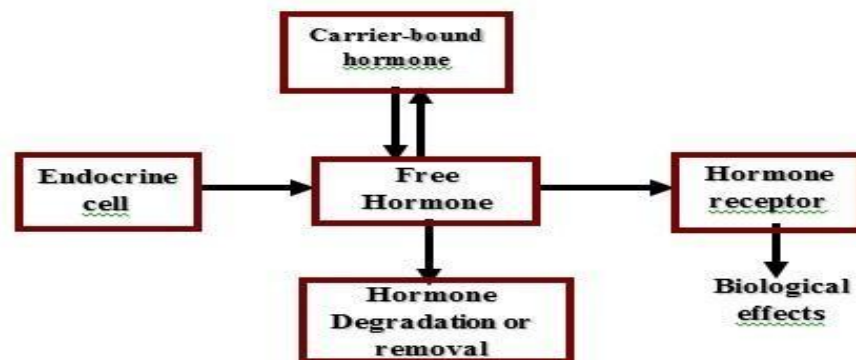
What happens to hormones?

Endocrine glands secrete hormones into the plasma. Then, several different events could occur. It could bind to its receptor on the target cell, causing a change.

Or, it could be destroyed by enzymes in the plasma. It could land in the kidneys and be filtered out before reaching its target.

What happens to a hormone once it's secreted?

- Degraded in bloodstream
- May be activated (turned from T_3 to T_4)
- May be excreted by kidneys/ liver
- May reach a target cell and cause a cell response
- May need carrier to reach target cell



Control of Hormone Secretion:

The endocrine system is controlled by the pituitary gland and the hypothalamus.

Always controlled by feedback loops.

Concentration declines below a minimum: more hormone is secreted

Concentration exceeds maximum: Hormone production is halted

MECHANISMS OF HORMONE SECRETION

a. Humoral Trigger

Something in the blood is being monitored. When the level of that substance is too low, it stimulates the release of the hormone.

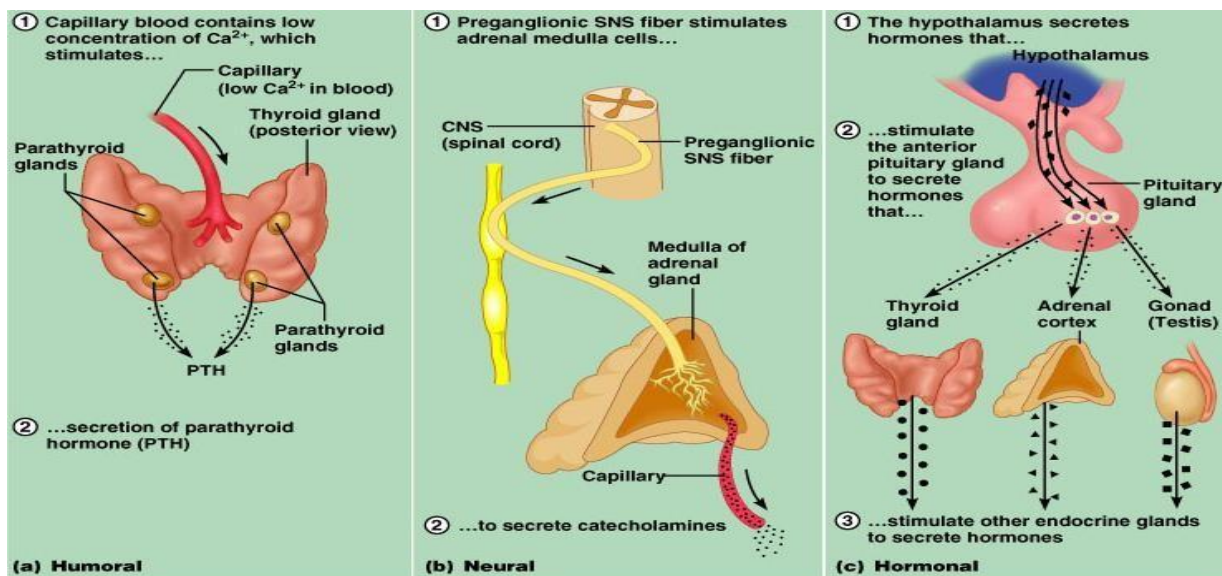
b. Neuronal Trigger

A neuron directly stimulates the gland to cause secretion of the hormone.

c. Hormonal Trigger

One endocrine gland releases a hormone that stimulates another endocrine gland to release its hormone.

CONTROL OF HORMONES RELEASE: THREE MECHANISMS



Hypothalamus:

LOCATION: - This is located at the base of the brain. It is part of the limbic system, which controls the autonomic nervous system and the endocrine systems.

The hypothalamus controls the endocrine system by controlling the pituitary gland.

- Secretes releasing hormones to cause the pituitary to release hormones
- Secretes inhibiting hormones to turn off secretion of pituitary hormones

Some people say the pituitary gland is the master gland because it controls many other endocrine glands, but the hypothalamus controls the pituitary gland, so really, maybe the hypothalamus is the Master Gland.

Hypothalamus Regulation:

The hypothalamus produces hormones which affect the anterior pituitary gland, for example:

- *Thyroid Stimulating Hormone Releasing Hormone (TSH-RH)*
 - Causes adenohypophysis to secrete TSH
 - TSH affects thyroid gland to secrete TH
- *Thyroid Stimulating Hormone Inhibiting Hormone (TSH-IH)*
 - Causes adenohypophysis to stop secreting TSH so thyroid gland stops secreting thyroid hormone

The hypothalamus affects the anterior pituitary gland, and that's about it.

Some Hypothalamus Hormones

Growth Hormone Releasing Hormone (GH-RH)
Prolactin Releasing Hormone (PRL-RH)
Thyroid Stimulating Hormone Releasing Hormone (TSH-RH)
Adrenocorticotrophic Hormone Releasing Hormone (ACTH-RH)
Melanocyte Stimulating Hormone Releasing Hormone (MSH-RH)
Follicle Stimulating Hormone Releasing Hormone (FSH-RH)
Luteinizing Hormone Releasing Hormone (LH-RH)

More Hypothalamus Hormones

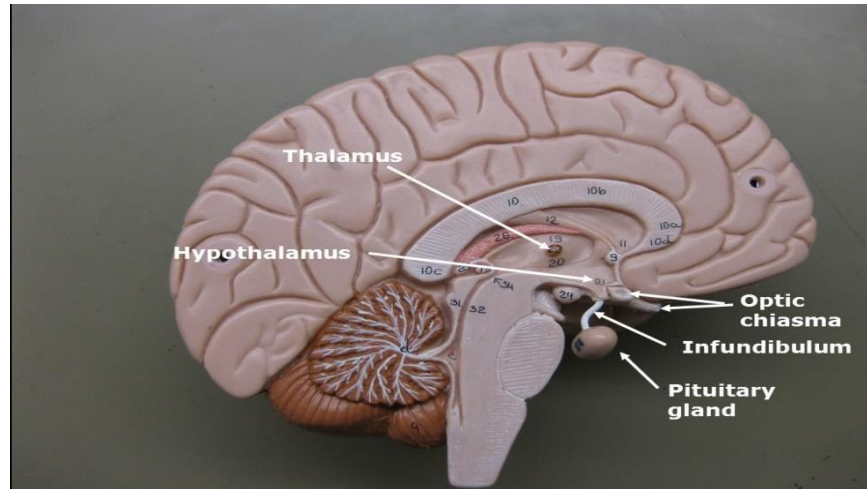
Growth Hormone Inhibiting Hormone (GH-IH)
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Luteinizing Hormone Inhibiting Hormone (LH-IH)

The Pituitary Gland

LOCATION: This is located in the sella tursica (totally encased in bone), which gives you a clue as to how important this gland is.

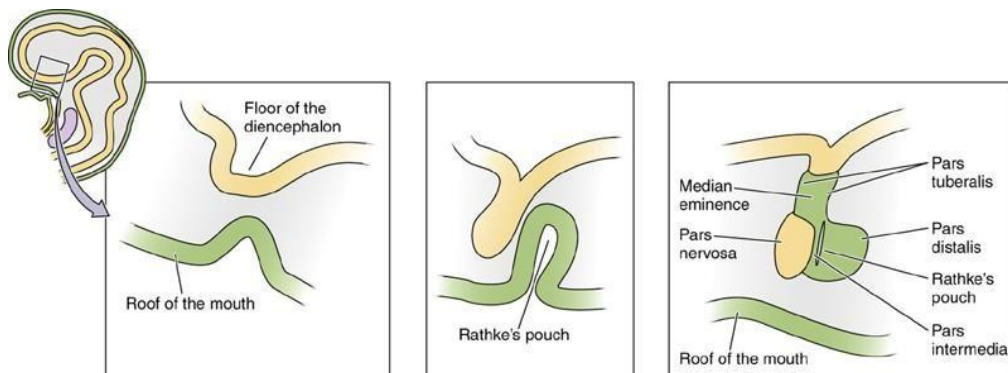
It has an anterior and a posterior lobe.

- The adenohypophysis portion of the pituitary gland (anterior lobe) actually develops from an embryonic pouch that grows upward from the ectoderm of the pharynx. One type of diabetes (insipidus) can be caused by trauma to the pituitary gland. A tumor of the pituitary gland can lead to blindness because it is so close to the optic chiasma.

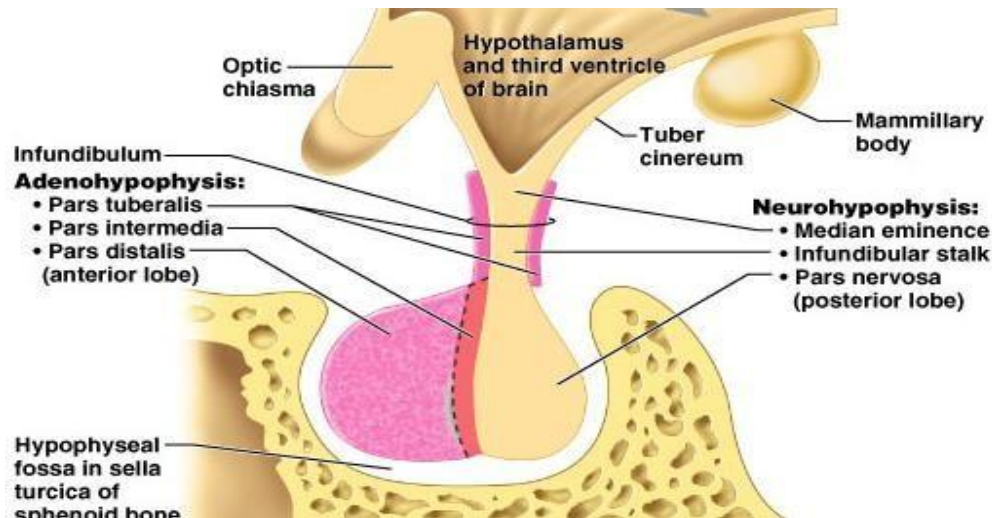


Origins of Pituitary(Hypophysis):

- *Adenohypophysis*
 - Rathke's pouch
 - Oral ectoderm
 - Loses attachment with oral cavity
- *Neurohypophysis*
 - Neuroectoderm
 - Outgrowth from floor of diencephalon
 - Remains attached to brain (HT) via infundibulum

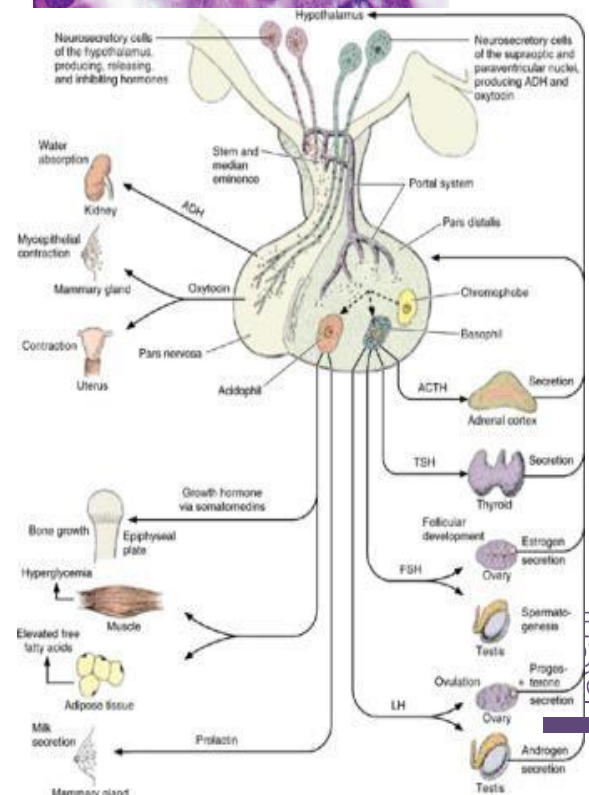
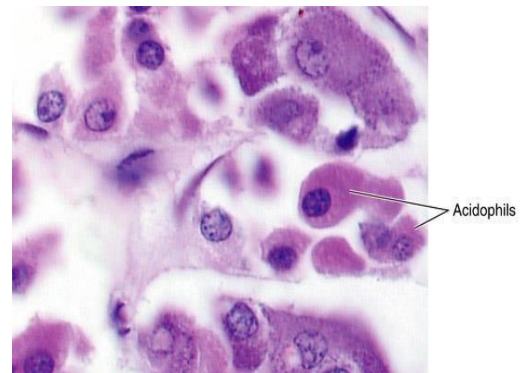


- Divisions of Hypophysis or pituitary:
 - *Adenohypophysis*
 - Pars distalis
 - Pars intermedia
 - Pars tuberalis
 - *Neurohypophysis*
 - Pars nervosa
 - Infundibulum



Adenohypophysis (pars distalis)

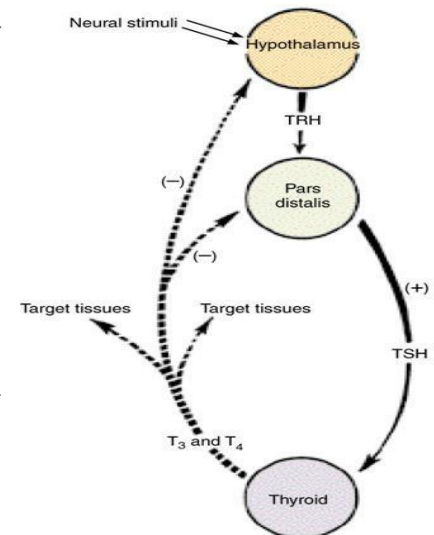
- ☐ 75% of pituitary
- ☐ Two major cell types upon staining
 - ☐ Chromophobes – resist stain (undiff. Cells)
 - ☐ Chromophils – important cells
 - Acidophils – eosinophilic
 - Basophils – basophilic
- Acidophils
- ☐ Important secretions produced
 - ☐ Somatotropes – somatotropin (hGH)
 - Affects for example epiphyseal plates of long bones
 - Human growth hormone (hGH) also coordinates growth in many other areas
 - ☐ Mammatropes – prolactin
 - Stimulates milk secretion from mammary glands
- Basophils
- ☐ General classes of secretion
 - ☐ Thyrotrophes – secrete thyroid stimulating hormone (TSH); causes thyroid to release T3 and T4 (thyroid hormones) setting basal metabolic rate
 - ☐ Gonadotropes
 - ☐ Corticotropes – promotes growth of adrenal cortex and stimulates release glucocorticoids and gonadocorticoids
- ☐ **Gonadotropes:**
- ☐ Gonadotropes of adenohypophysis



- FSH – females stimulates development of ovarian follicles ; in males stimulates Sertoli cells to produce androgen binding protein
- LH – in females promotes maturation of follicle and ovulation and maintains corpus luteum ; in males called interstitial cell secreting hormone (ICSH) promotes secretion of testosterone.

Regulation of Adenohypophysis

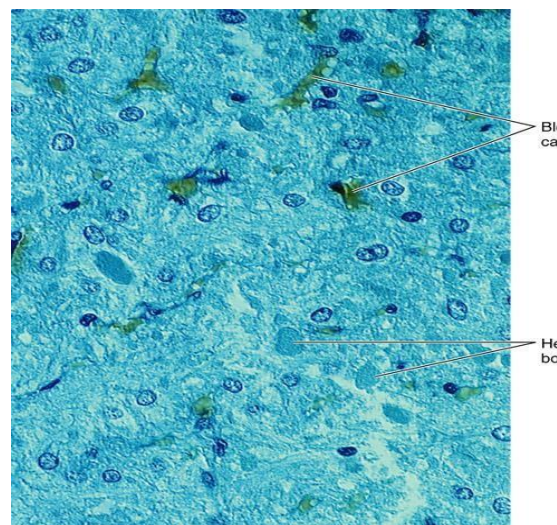
- Secretions of adenohypophysis are all regulated by Hypothalamic Releasing Hormones
 - These are given names based on the hormones they are encouraging the release of
 - Example Hormones of the thyroid gland are released upon release from the adenohypophysis of TSH. TSH is not released until stimulation of the thyrotrophs by thyroid releasing hormone (TRH) .
- Note: The releasing hormones are actually produced by neurosecretory cells. These cells function as receivers of action potential and they release hormones instead of neurotransmitters.
- Note also that this is a negative feedback system. The T₃ and T₄ released tend to inhibit both the release of TRH and TSH.



Neurohypophysis

- Hypothalamo-hypophyseal tract –
 - Neurosecretory cells axon processes
 - At the end of these axons are the
 - Herring bodies the swollen axon knobs
 - These distended tips are bigger than most axon knobs
 - Release either hormone or a releasing hormone

The neurohypophysis is a continuation of the Herring Bodies (pars nervosa) brain

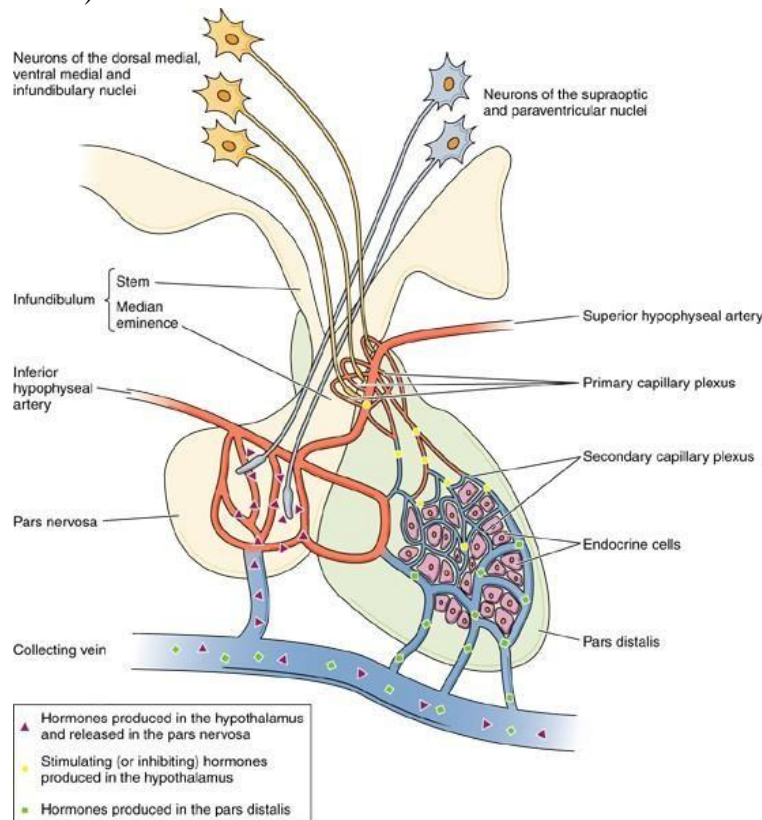


Neurosecretory Hormones

- ☐ Releasing Hormones
- ☐ Two other hormones
 - ☐ Oxytocin – paraventricular nucleus
 - Stimulates smooth muscle of uterus and myoepithelial cells of mammary glands
 - ☐ Antidiuretic hormone (ADH or Vasopressin)
 - Supraoptic nucleus release
 - Acts on distal and collecting tubules of kidney making them more permeable to water; generates more hypertonic urine

Blood Supply to Pituitary

- ☐ Inferior hypophyseal arteries to neurohypophysis
- ☐ Hypothalamo-hypophyseal portal system
 - ☐ Delivers hypothalamic regulating hormones to adenohypophysis (releasing hormones).



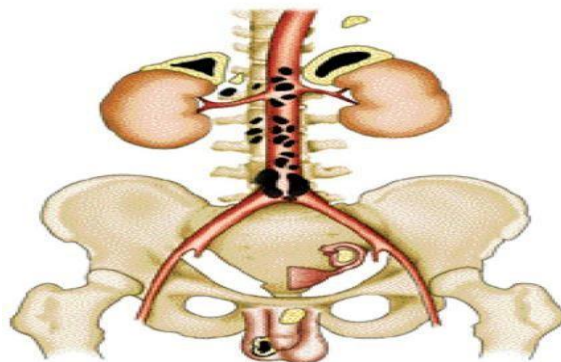
The Adrenal Glands

Location: Located on the superior surface of the kidneys

Two endocrine glands in one (different embryological origin)

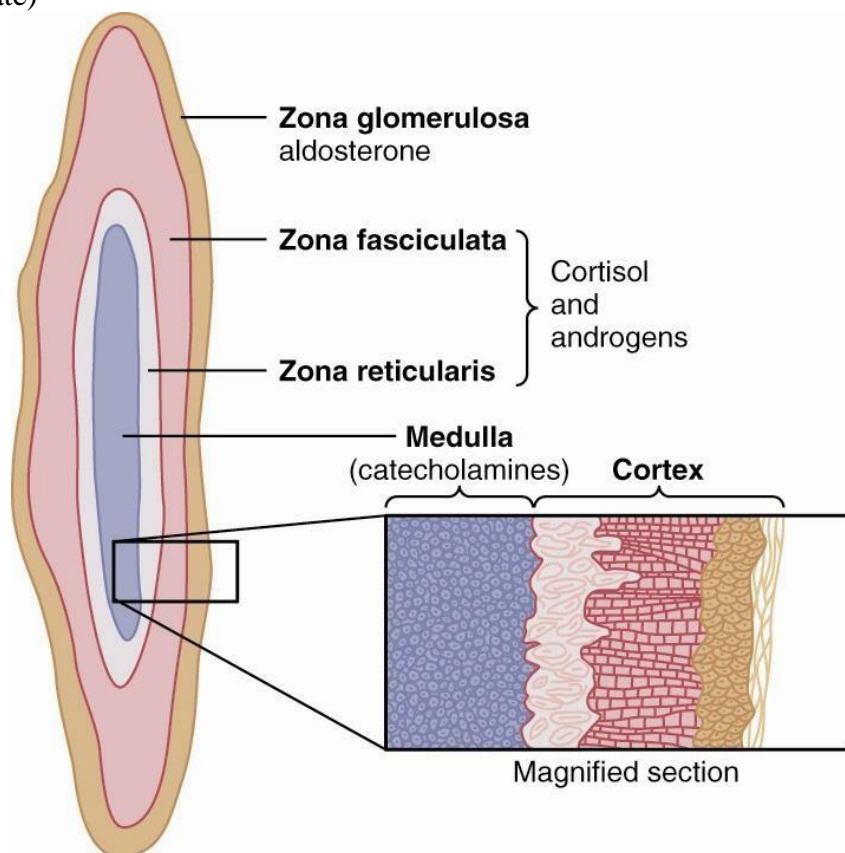
- ☐ ADRENAL MEDULLA – a knot of sympathetic nervous tissue
 - ☐ Secretes catecholamines (mostly epinephrine)
 - ☐ Active in “fight, flight, and fright” response
- ☐ ADRENAL CORTEX – bulk of the adrenal gland
 - ☐ Secretes aldosterone (salt and water balance for blood pressure)

- ☐ Secretes androgens and estrogens (sex hormones)
- ☐ Secretes cortisol (anti-stress and anti-inflammation hormone)



Adrenal Cortex layers:

- ☐ The bulk of the adrenal gland is the adrenal cortex. It has layers, from superficial to deep: “GFR”
- ☐ G = Zona glomerulosa: makes aldosterone
- ☐ F = Zona fasciculata
- ☐ R = Zona reticularis
 - ☐ The zona fasciculata and zona reticularis both make sex hormones and cortisol
- ☐ (Don’t confuse this mnemonic with “GFR” in the kidney, which stands for glomerular filtration rate)

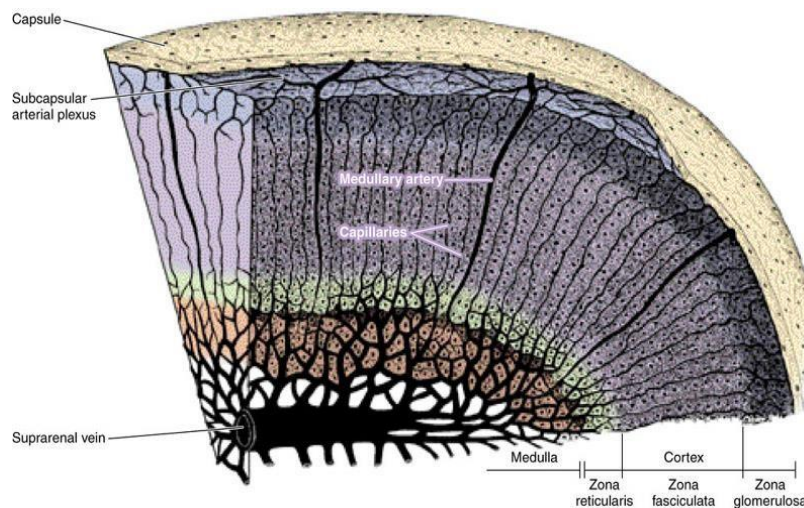


The Adrenal Cortex:

- ☐ **CORTISOL** helps the body deal with stressful situations like fasting, anxiety, trauma, and infection. It keeps the blood protein and glucose levels high enough to support the brain's activities. When the brain perceives a stressful situation, the hypothalamus tells the pituitary to secrete ACTH, which travels to the adrenal gland and signals it to release cortisol to most of the cells of the body. It is also known as hydrocortisone, which decreases inflammation.
- ☐ **ALDOSTERONE** increases blood volume during hemorrhage or drop in blood pressure. It causes kidney to reabsorb more sodium; water follows with it, so the blood volume increases.
- ☐ **SEX HORMONES** for the opposite sex: Males produce estrogen here, and females produce testosterone.

Glucocorticoids (cortisol):

- ☐ Glucocorticoids (GC) are a class of steroid hormones that bind to the glucocorticoid receptor (GR), which is present in almost every cell in the body.
- ☐ The name glucocorticoid (glucose + cortex + steroid) derives from their role in the raising glucose levels, their synthesis in the adrenal cortex, and their steroidal structure. They suppress the immune system (they are anti-inflammatory).
- ☐ Cortisol (also known as hydrocortisone) is one of the most important glucocorticoids.
- ☐ Others are prednisone, prednisolone, dexamethasone, and triamcinolone, which are also commonly used medicines for anti-inflammation.



Adrenal Cortex Hormones:

- ☐ Cortex utilizes
 - ☐ Cholesterol and acetate to synthesize steroid hormones

Zona Glomerulosa:

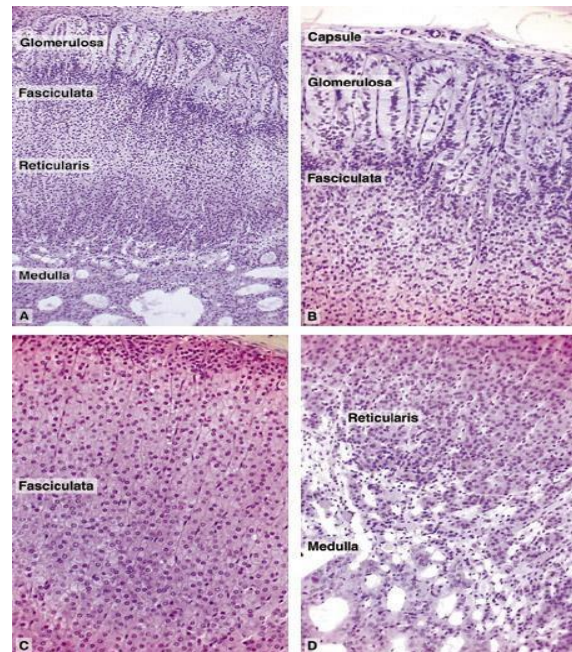
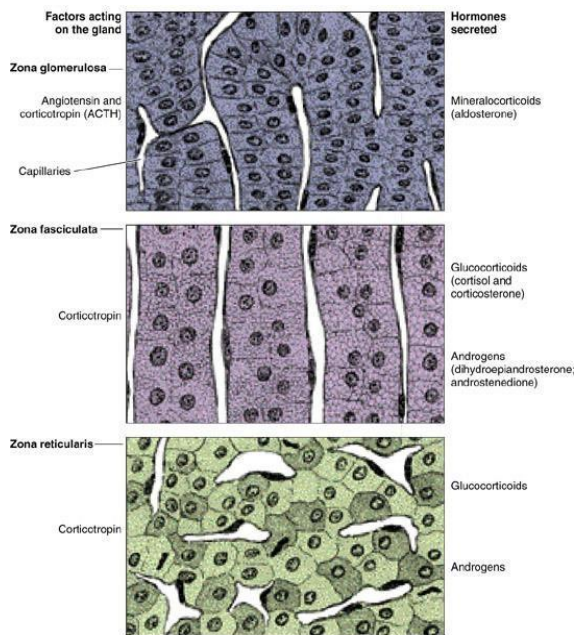
- ☐ Secretes mineralcorticoids – Aldosterone
 - ☐ Maintenance of electrolyte and water balance
 - ☐ Regulated by renin-angiotensin system
 - ☐ Unaffected by ACTH of pituitary

Zona Fasciculata:

- ☐ Secrete glucocorticoids – cortisol
 - ☐ Prepares body for maximal immediate energy demands; part of “fight or flight” stress response
 - ☐ Depresses immune function and inflammatory response
 - ☐ Regulated by ACTH of pituitary

Zona Reticularis:

- ☐ Secretes gonadocorticoids –
 - ☐ Dehydroepiandrosterone (DHEA) virilizing and an anabolic effect
 - ☐ Negligible amount compared to amount released from testis
 - ☐ Regulated by ACTH

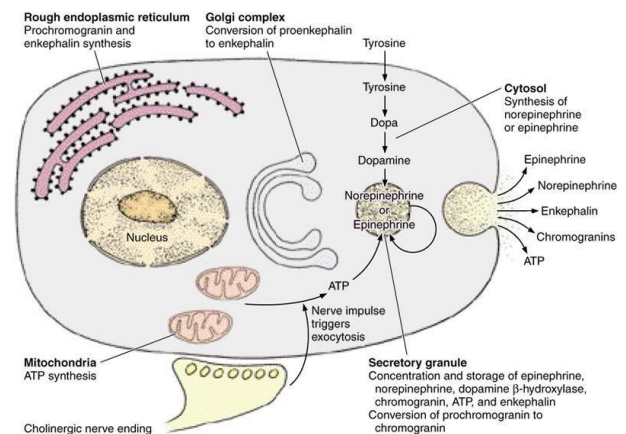
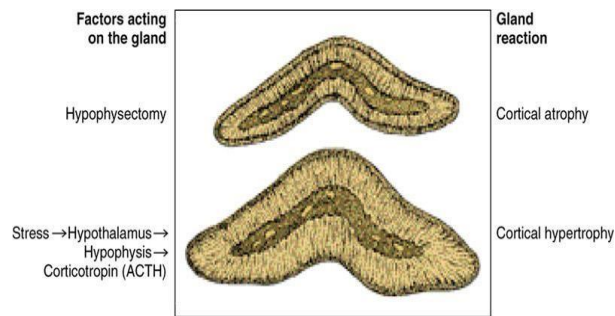


Adrenal Medulla:

- ☐ Derived from neural crest
- ☐ Modified sympathetic ganglion
 - ☐ Important cell type
 - Chromaffin cells – modified post-ganglionic neurons
 - These cells secrete epinephrine (80%) and norepinephrine (20%)
 - These cells regulated by preganglionic sympathetic neurons
- ☐ The adrenal medulla releases catecholamines (epinephrine and norepinephrine).
- ☐ These catecholamines are released when the sympathetic nervous system is activated (“fight or flight”).
- ☐ When you run from a predator, is that when you want insulin to take glucose from blood? No, you want to keep it there so the brain can get the glucose. The brain needs to think of a way to escape, and thinking burns glucose.
- ☐ Therefore, epinephrine is antagonistic to insulin

- Cells that don't get the glucose during fight or flight break down fatty acids to get their ATP. These fatty acids will be taken to the liver for gluconeogenesis to elevate the depleted blood glucose levels. Glycogen will also be broken down to glucose to elevate the depleted blood glucose levels.
- Epinephrine has the same effect as the sympathetic nervous system:
 - Heart rate and force increases.
 - BP goes up (from vasoconstriction in less-needed organs).
 - respiratory passages open (bronchiole dilation)
 - Digestion slows

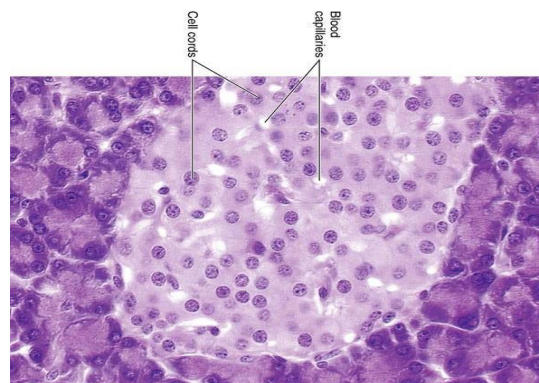
Adrenal Gland Atrophy & Hypertrophy



Pancreas:

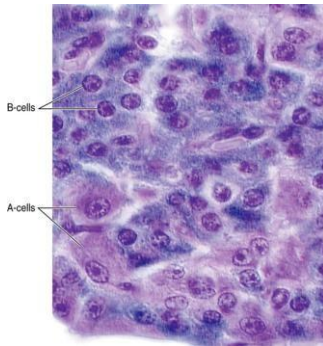
- Mixed Exocrine and Endocrine Gland
- Islets of Langerhans have endocrine
 - Islets 2% of entire gland
 - Alpha cells secrete glucagon; □ [blood glucose]
 - Beta cells secrete insulin; □ [blood glucose]
 - Delta cells secrete somatostatin; inhibits secretion of glucagon and insulin

Islets of Langerhans:



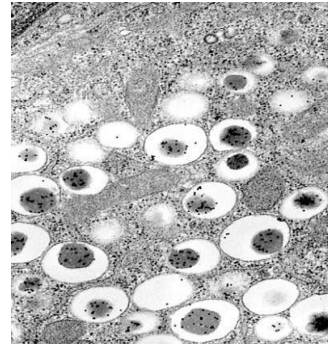
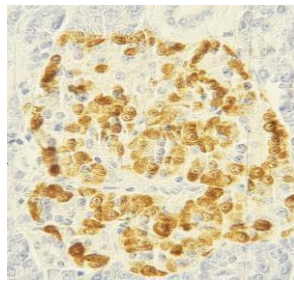
α and β cells:

β -cells secrete insulin



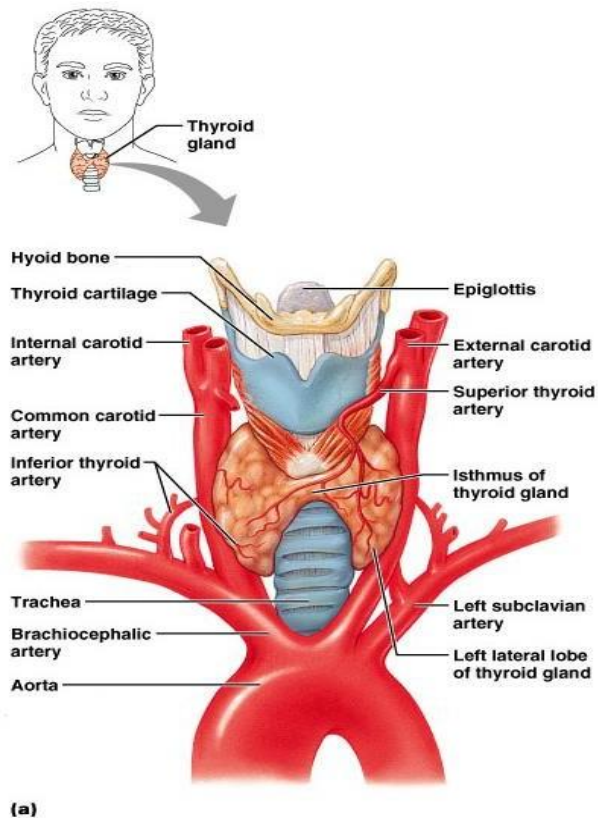
α -cells secrete glucagon

A-Cells stained



Thyroid Gland:

- ☐ Gross structure
 - ☐ Two lobes
 - ☐ Connected by isthmus
 - ☐ Connective Tissue Capsule
- ☐ Located in the anterior neck, inferior to thyroid cartilage
- ☐ Largest pure endocrine gland
- ☐ Produces two hormones
 - ☐ Thyroid hormone (TH)
 - ☐ Calcitonin



☐ **Thyroid hormone (TH)**

- ☐ Acts on most cells of the body
- ☐ Increases metabolic rate
- ☐ Controlled by hormonal mechanism
- ☐ Iodine is needed to make TH

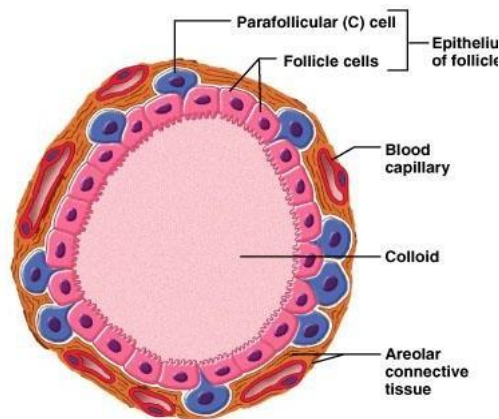
☐ **Calcitonin**

- ☐ Lowers blood calcium levels; especially secreted in children
- ☐ Slows osteoclasts to allow osteoblasts to deposit bone in the skeleton.

(Vitamin D is synthesized and secreted by the dermis)

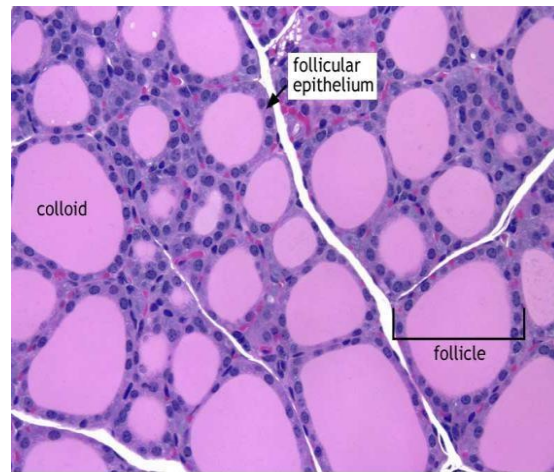
- ☐ The functional unit of the thyroid gland is the thyroid follicle. The cells making up the perimeter of the follicle are called follicular cells. They make and secrete the light purple liquid within the follicle, called colloid. Colloid is water, filled with a lot of protein called thyroglobulin, which is made by the follicular cells. Since thyroglobulin is a protein, there is a gene that codes for it, so there can be genetic mutations that affect its production.
- ☐ TSH is what stimulates the follicular cells to make thyroglobulin. TSH also increases the size of the follicle to accommodate all this protein.

Thyroid Follicle with Thyroid Hormone



(c)

Thyroid Gland



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Follicles of Thyroid:

- ☐ Structural and functional units of gland
 - ☐ Follicular cells simple cuboidal epithelium
 - ☐ Colloid collects in follicles
 - Precursor of Thyroid hormones
 - ☐ Thyroxine (T_4)
 - ☐ Triiodothyronine (T_3)
 - Thyroglobulin → secretory path built from tyrosine and iodinated to become T_3 and T_4

- Only endocrine gland to store its secretions; storage extracellular as colloid

Thyroid Gland Regulation:

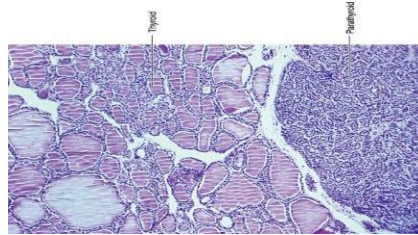
- Release of T_3 and T_4 stimulated
 - By TSH from pituitary

Parafollicular Cells:

- Also known as Interfollicular cells
 - Secrete calcitonin = inhibits osteoclast activity and stimulates osteoblast activity adding Ca^{+2} to boney matrix
 - Regulated by blood Ca^{+2} levels
 - Works in opposition to parathyroid hormone

Thyroid junctions with Parathyroid:

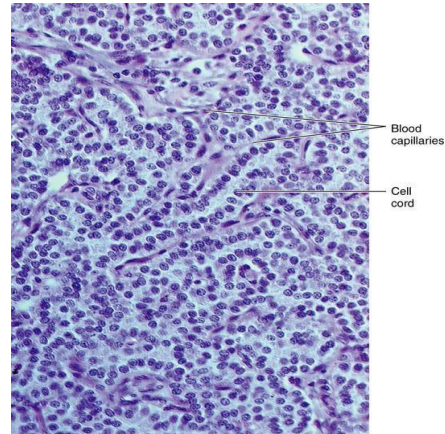
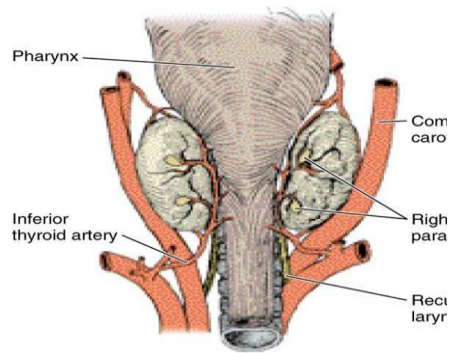
Thyroid junctions w Parathyroid



Parathyroid glands:

- Structure
 - Two pair
 - Embedded on posterior of thyroid gland
 - Cords of cells
 - Chief cells
 - Oxyphil cells – function unknown
- **Parathyroid hormone (PTH)**
 - Increases blood concentration of Ca^{2+}
 - There are three ways that the parathyroid hormone raises blood calcium levels
 - 1) Stimulates osteoclasts to move bone calcium from the skeleton to the bloodstream
 - 2) Stimulates the kidneys to stop excreting calcium
 - 3) Stimulates the intestines to absorb more calcium from diet.
 - It does that by activating vitamin D, which increases calcium uptake by intestines
 - Vitamin D is made in the dermis, requires 10 mins per day of sunlight to be produced.
 - **The antagonist of parathyroid hormone is calcitonin**, which is produced in the thyroid gland, and stimulates osteoblasts to take calcium from the blood and deposit it in bone.
 - Parathyroid hormone is released by a humeral mechanism.
 - If blood calcium levels are low, parathyroid hormone is released.
 - If blood calcium levels are high, parathyroid hormone stops being released.

Parathyroid Gland



Chief cells of parathyroid gland:

- ☐ Secrete parathyroid hormone
 - ☐ Low blood calcium stimulates secretion
 - ☐ Parathyroid hormone stimulates
 - Osteoclast increase in number and
 - Osteoclast to degrade bone and raise blood Ca^{+2}
 - ☐ Also decreases blood level of phosphate by decreasing resorption in kidney tubules, promoting excretion
 - ☐ Most important regulation blood Ca^{+2}

Pineal Gland:

- ☐ AKA epiphysis cerebri
- ☐ Pinealocytes secrete melatonin
 - ☐ Involved in diurnal rhythms
 - ☐ Innervated by neurons of the ANS
- ☐ Brain Sand
 - ☐ Crystallized deposits of calcium carbonates and calcium phosphates