
The Endocrine System

Dr. Ali Ebneshahidi

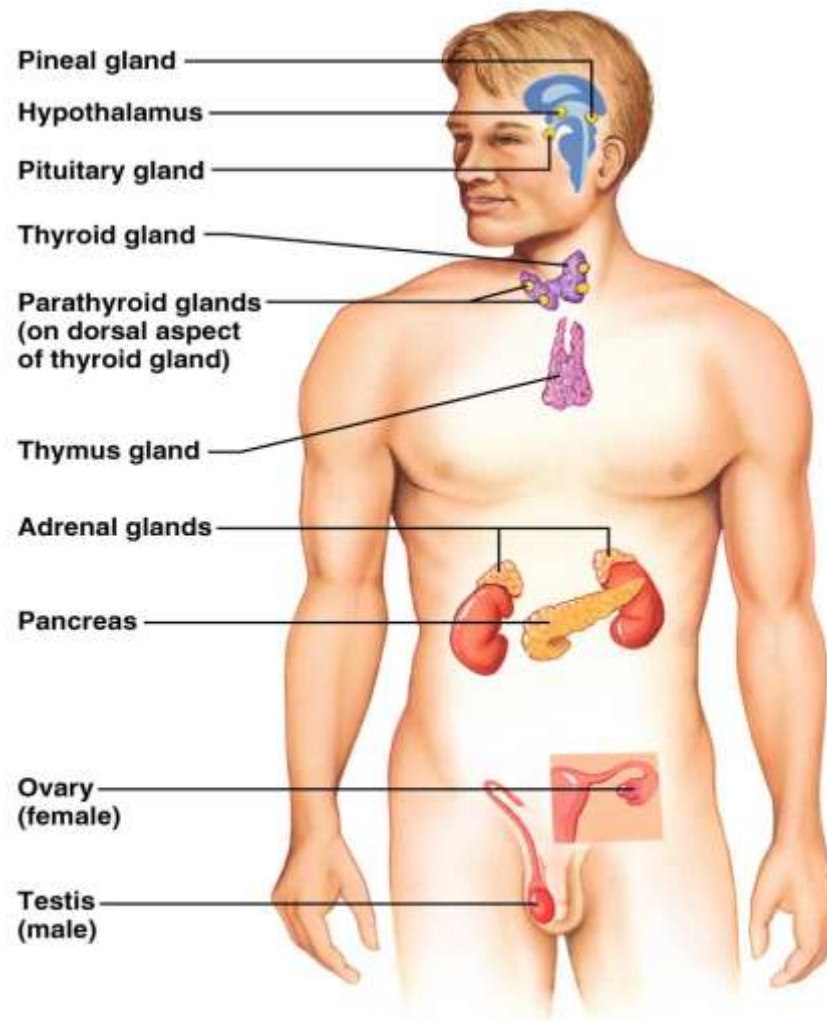
Endocrine System

- The endocrine system interacts with the nervous system to coordinate and integrate body activities by means of **hormones** .
- Endocrine tissues and organs secrete hormone into body fluids (mainly blood and lymph) **directly** using diffusion.
- Exocrine tissues, such as salivary glands, and sebaceous glands, secrete chemical substances through ducts into an open space.

Five major functions of hormones

- a) Regulate metabolic processes (e.g. thyroid hormones).
- b) Control the rate of chemical reactions (e.g. growth hormone).
- c) Aid in the transport of substances across the cell membrane of target cells (e.g. insulin and glucagon).
- d) Regulate water and electrolyte balances (e.g. antidiurectic hormone, calcitonin, and aldosterone).
- e) Play a vital role in reproduction, growth and development (e.g. estrogens , progesterone, and testosterone).

Major Endocrine Organs



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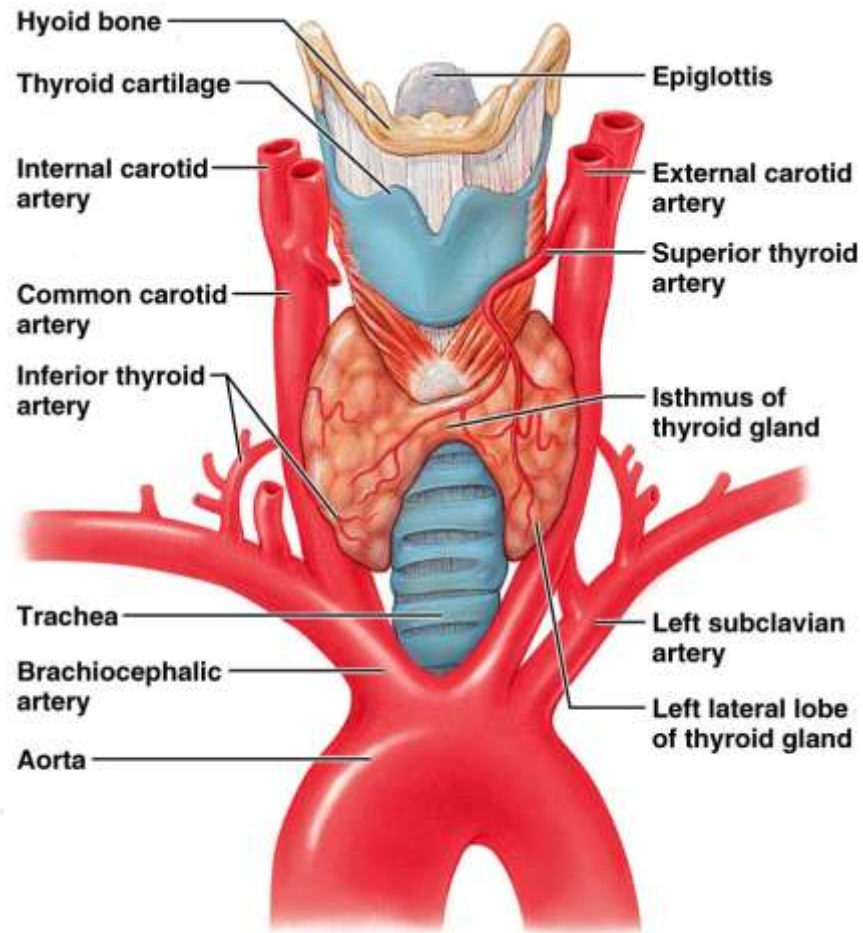
Chemistry of Hormones

- Hormones are organic compounds secreted by endocrine glands, that have a potent effect in target cells Two types of hormones:
- a) **Protein hormones**: made of amino acids joined by peptide bonds.
- fat – insoluble; as a result cannot diffuse across the membrane of target cells .
- most hormones belong to this group except hormones secreted by the gonads (testis and ovary) and the adrenal cortex.
- b) **Steroid hormones**: made of fatty acids using cholesterol as a functional group.
- Fat-soluble; as a result can diffuse into target cells .
- only hormones secreted by the gonads and adrenal cortex belong to this group .

Hormone Action

- 1. Most hormones adhere to the following action plan :
 - a) endocrine gland synthesizes the hormone .
 - c) Hormone diffuses into capillaries .
 - d) Hormone is transported by blood or lymph toward target cells .
 - e) Hormone diffuses out of capillaries at target tissue, and causes an effect in target cells .

Thyroid Gland



(a)

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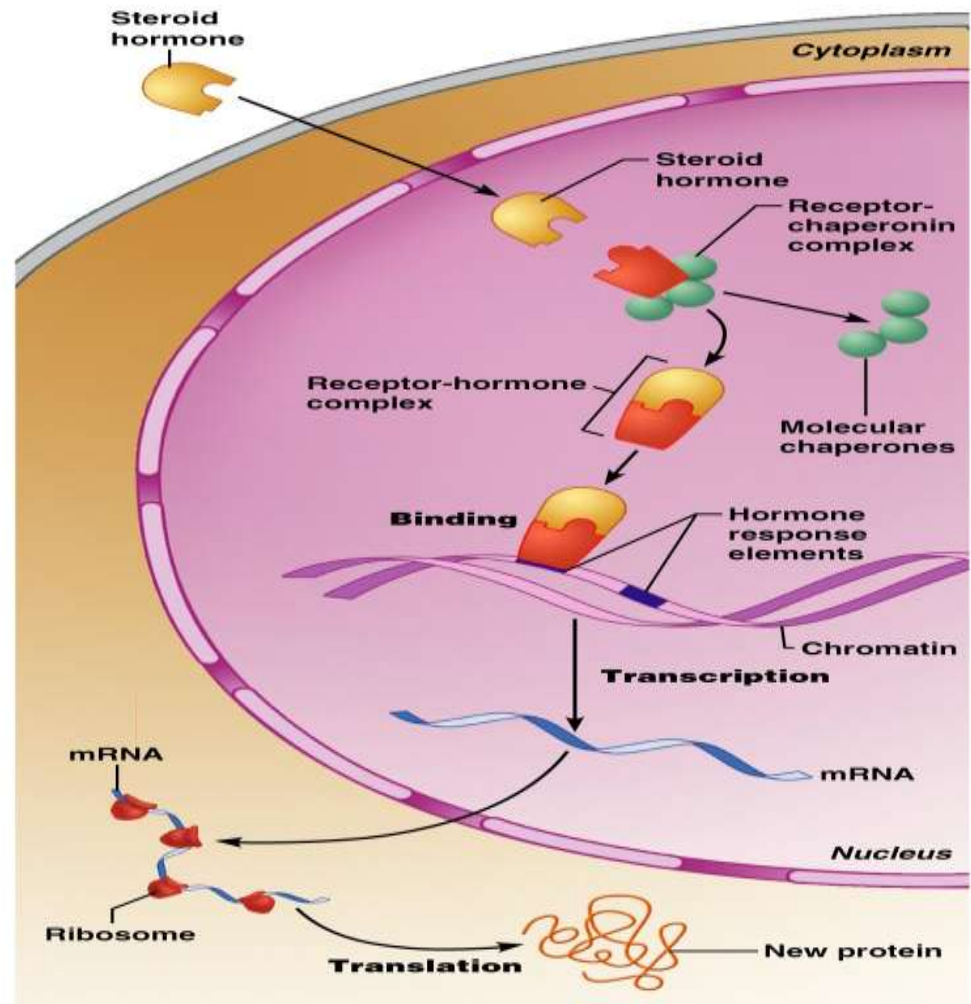
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- 2. Each step of this action plan is highly specific and carefully controlled by the endocrine and circulatory systems :
 - synthesis of hormone using protein or lipid anabolism.
 - secretion of hormone using exocytosis or diffusion .
 - transport of hormone in the blood or lymph (i.e. steroid hormones require a “protein transporter” during the transport).
 - interaction between the hormone and target cell (i.e. protein hormones require receptors at the cell membrane of target cells).

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- 3. Effects in the target cells caused by hormone action
 - a. A change in cell membrane permeability (e.g. insulin causes muscle cells to have a higher permeability for glucose).
 - b. A change in chemical reaction rate (e.g. growth hormone stimulates higher chemical reaction rates in muscle and bone cells).
 - c. Enzyme activation (e.g. epinephrine increases enzyme action in muscle cells).
 - d. Activation of cell secretion (e.g. melanocyte-stimulating hormone activates more melanin secretion from the melanocytes).

Actions of steroid hormones

- 1. Steroid hormones bind to a protein transporter during the transport in blood of lymph .
- 2. When they have arrived at the target cells , the protein transporter (being fat-insoluble) is repelled by the cell membrane, while the steroid hormone (being fat-soluble) diffuses into the cytoplasm of target cell.
- 3. Steroid hormone also diffuses across the nuclear envelope and enters into the nucleus of target cell.
- 4. Steroid hormone binds to a specific receptor located on a particular gene of target cell's DNA.
- 5. This binding alters the genetic information within that gene, resulting in a new messenger RNA (mRNA) being produced after transcription.

- 6. this new mRNA will be translated into a new protein (or enzyme) in the cytoplasm of target cell .
- 7. the new protein or enzyme causes a specific effect to occur within the target cells .

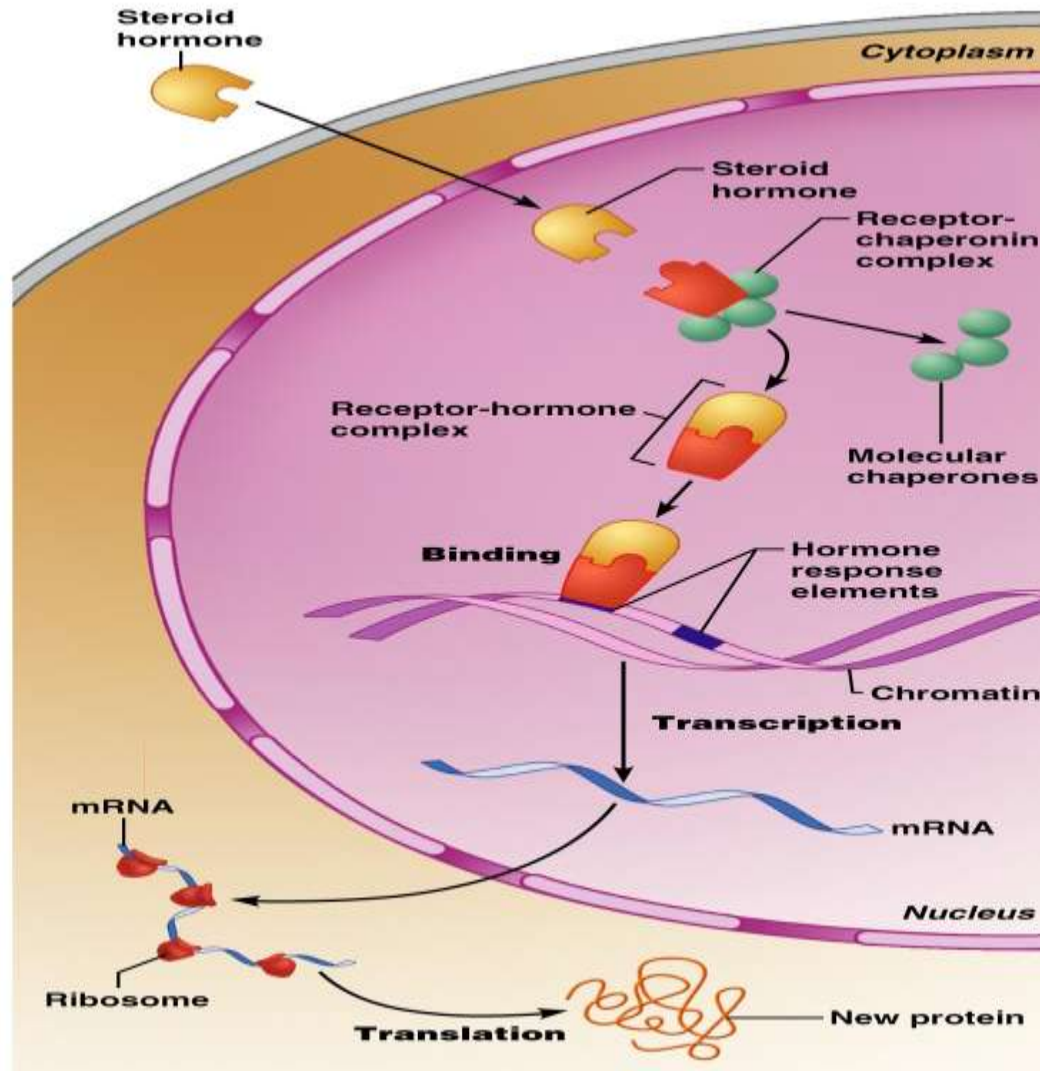


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Sequence of steroid hormone action - Summary

- 1. Endocrine glands secrete steroid hormone .
- 2. Steroid hormone diffuses through target cell membrane .
- 3. Hormone combines with a receptor molecule .
- 4. steroid hormone-receptor complex binds to DNA and promotes synthesis of mRNA.
- 5. mRNA enters the cytoplasm and directs protein synthesis .
- 6. Newly synthesized protein produce hormone's specific effects.
- 7. The new protein causes a specific effect to occur within the target cells.

Steroid Hormones

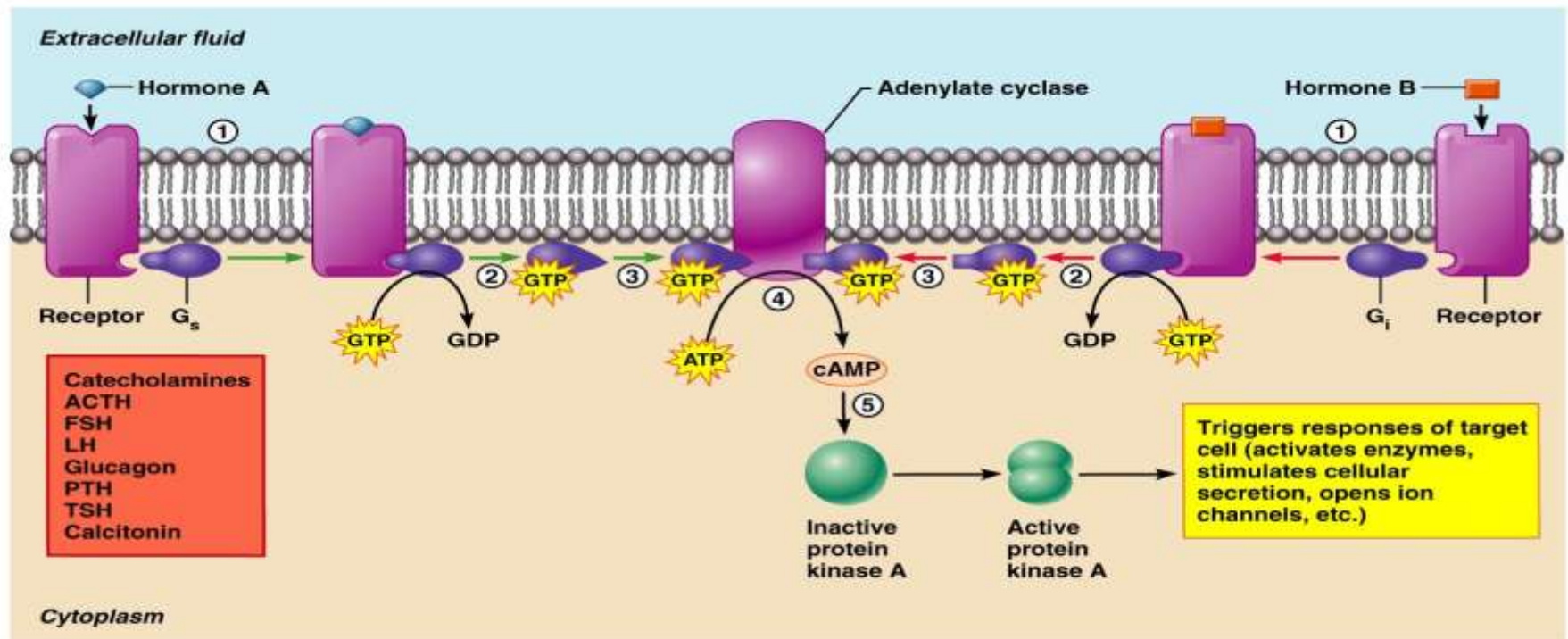


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Action of protein hormones

- 1. A protein hormone is transported in the blood or lymph by itself, without a transporter .
- 2. When it has arrived at the target cell, the protein hormone binds with a specific receptor embedded in the cell membrane of target cell. (The number of receptors changes in response to the amount of hormone released -- “**up-regulation**” refers to the phenomenon where more receptors will be produced to respond to a deficiency of the hormone; while “**down-regulation**” refers to the process of producing less receptors to respond to a large amount of hormone).
- 3. This binding activates a series of chemical reactions (“cascade reactions”) in the cytoplasm of target cell .

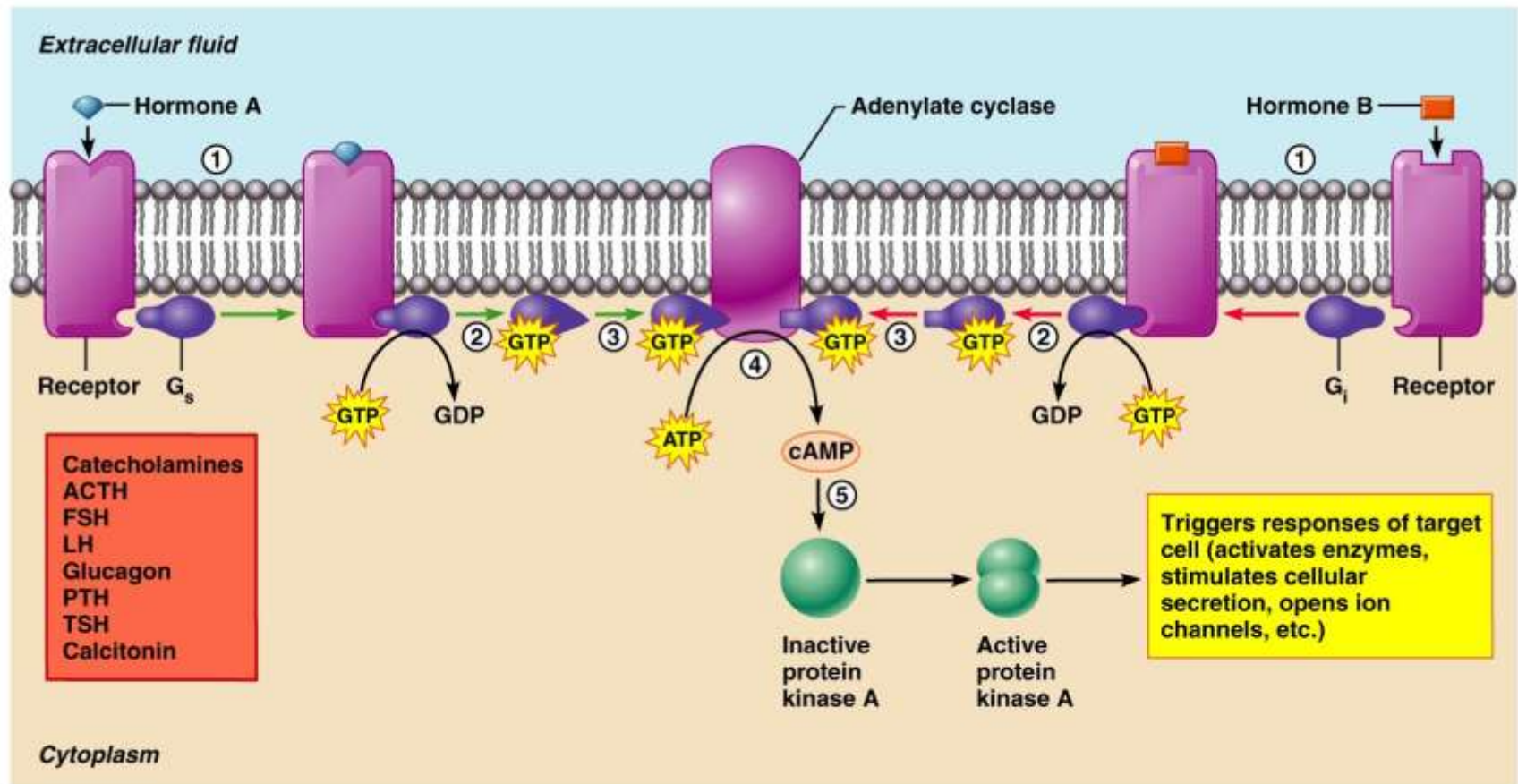
- 4. The product of these reactions is a substance known as the “secondary messenger” (usually cyclic adenosine monophosphate or cAMP), which acts on behalf of the protein hormone, causes a potent effect in the target cell (usually within the cytoplasm).
- 5. Since protein hormones never diffuse to the DNA of target cells, no new proteins or enzymes are made at the end.



Sequence of protein hormone action - summary

- 1. Endocrine gland secretes nonsteroid hormone.
- 2. Body fluid carries hormone to its target cell.
- 3. Hormone combines with receptor site on membrane of its target cell, activating G protein.
- 4. G protein activates an enzyme called adenylate cyclase within target cell's membrane.
- 5. Adenylate cyclase converts ATP into cyclic AMP.
- 6. Cyclic AMP activates protein kinases.
- 7. These enzymes activate protein substrate in the cell that change metabolic processes.
- 8. Cellular changes produce the hormone's effects.

Protein Hormones



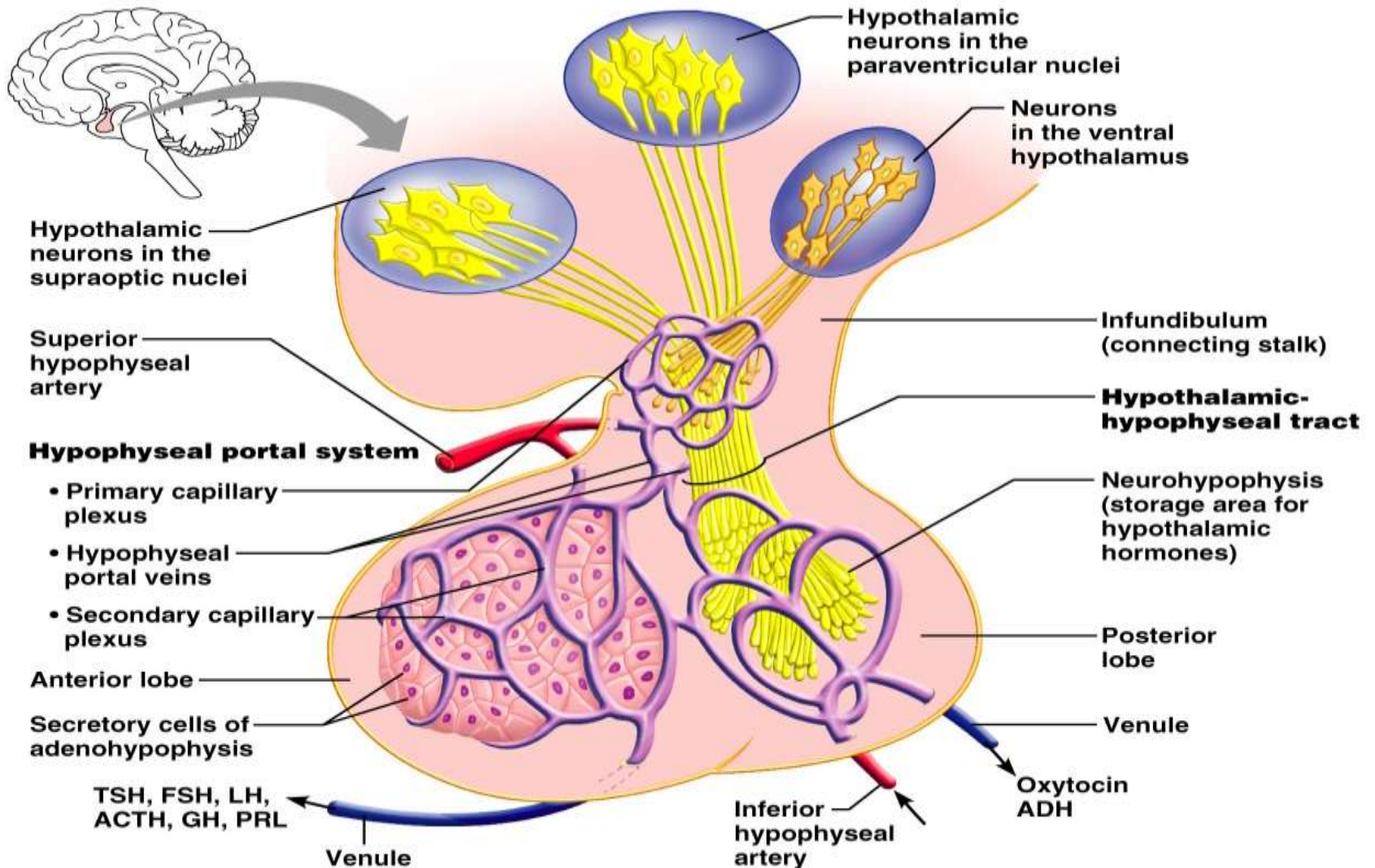
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Control of hormone secretion

- I. Negative feedback mechanism
- a) most secretion of hormones is regulated by negative feedback where once the desired effect is achieved in the target cell, an inhibitory signal (hormone, nerve impulse, or enzyme) will be sent from the target cells to the endocrine gland.
- b) hormones that are secreted by endocrine glands and travel to target cells directly are called **nontropic** hormones .
- c) hormones that are secreted by an endocrine gland (e.g. pituitary gland) and travels to another endocrine gland , causing the second gland to secrete another hormone, are referred to as **tropic** hormones .
- d) most hormones travel a long distance and act on target cells, they are called circulating (or endocrine) hormones; while other hormones travel a short distance, they are called local (paracrine) hormones.

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- II. Nervous control
 - a) Some hormone secretion is regulated by nerve impulse where **sympathetic** and **parasympathetic** nerves innervate the endocrine gland and control its secretion (e.g. sympathetic nerves cause the adrenal medulla to secrete epinephrine and nor epinephrine) .
 - b) Hormone release at the posterior pituitary gland is controlled by nerve fibers from the hypothalamus. In addition to transmitting nerve impulses, however, these specialized nerve fibers seem to also transport “**releasing hormones**” (e.g. gonadotropin releasing hormone or GnRH) to the pituitary gland.

Relationship of pituitary gland & Hypothalamus

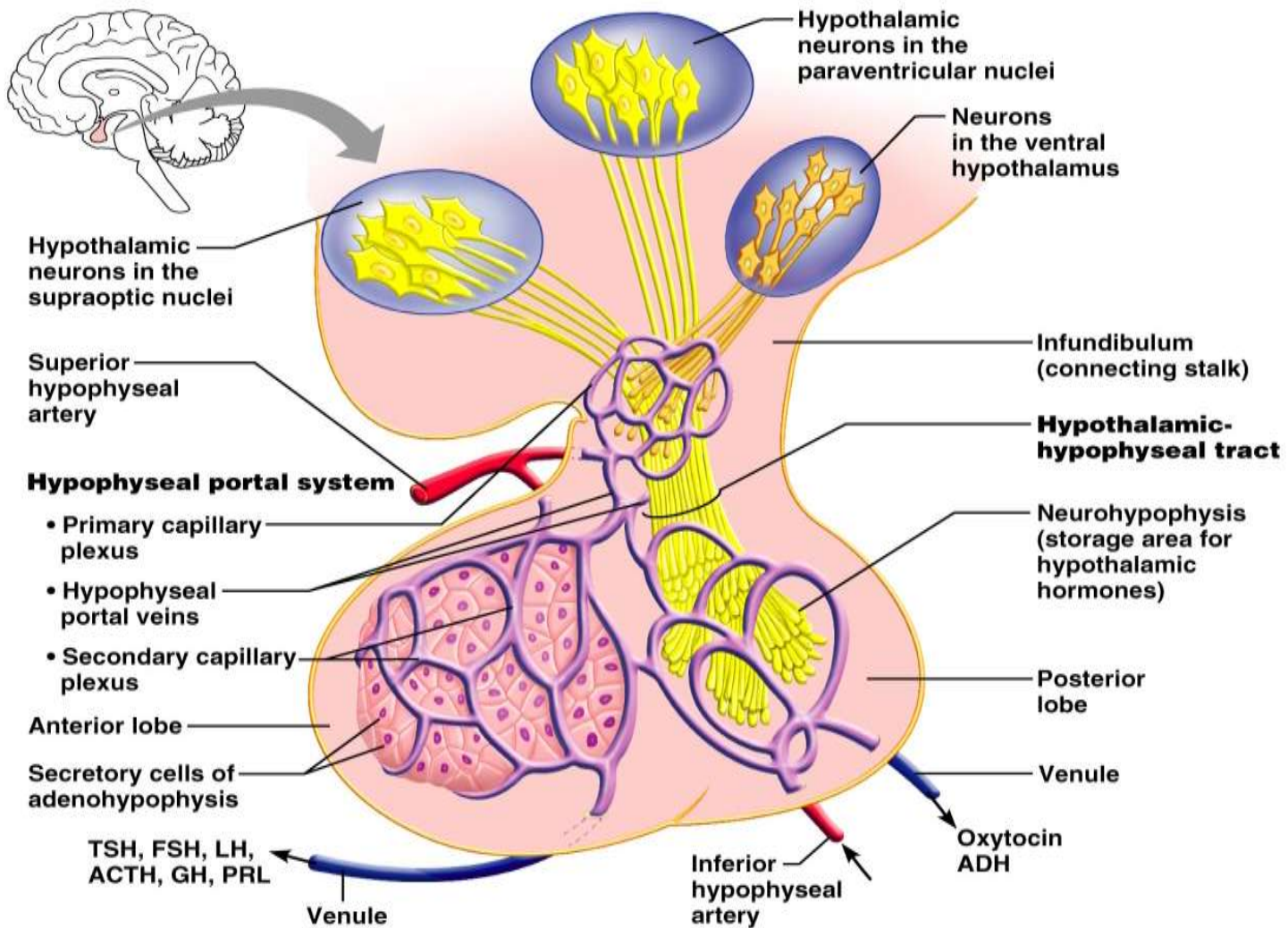


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Major endocrine glands & hormones

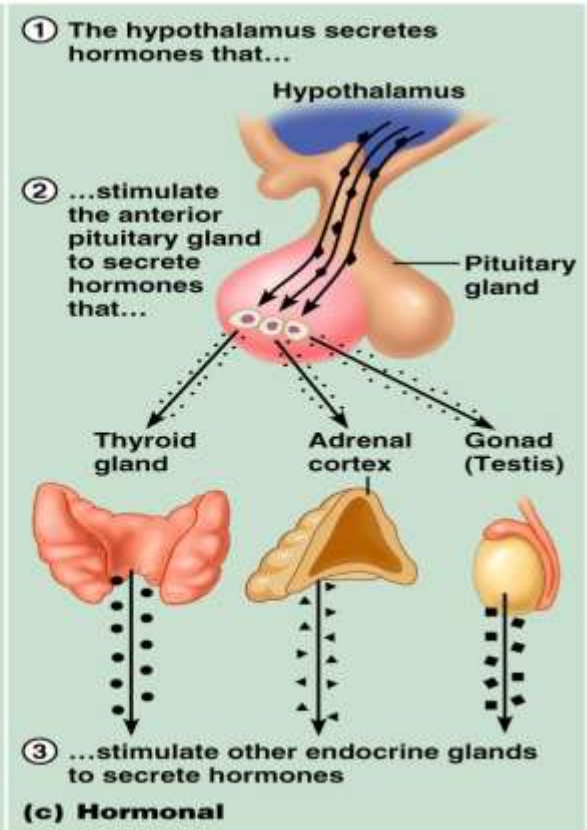
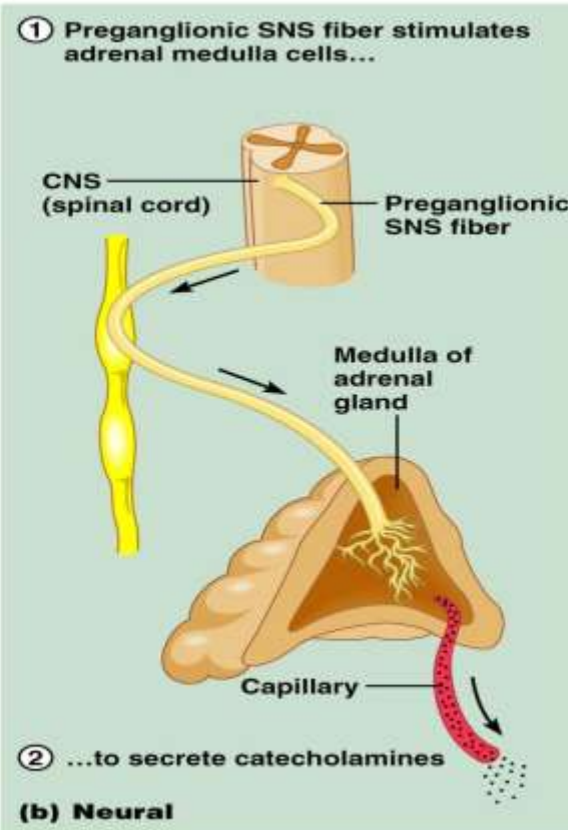
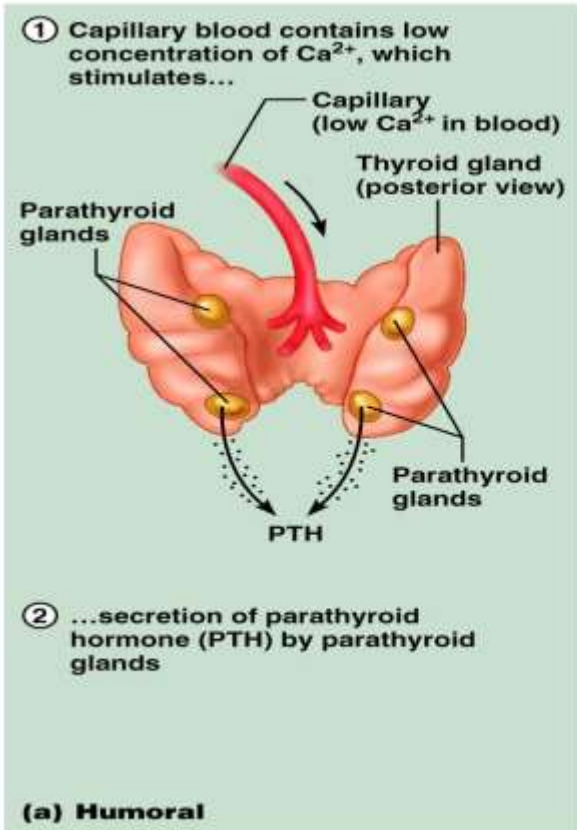
- The pituitary gland: attached to the hypothalamus by infundibulum.
 - Divided into anterior lobe (adenohypophysis) and posterior lobe (neurohypophysis). Anterior lobe is about 3 times larger than posterior lobe .
- 1. Anterior pituitary is under hormonal control by the hypothalamus where blood vessels transport “**releasing hormones**” to the anterior lobe. Anterior pituitary contains 5 types of glandular cells.
- Somatotrophs produce GH.
- Lactotrophs produce PRL.
- Corticotrophs produce ACTH and MSH.
- Thyrotrophs produce TSH.
- Gonadotrophs produce FSH and LH.

Relationship of the pituitary gland & Hypothalamus



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- 2. posterior pituitary is under nervous control by the hypothalamus where nerve fibers innervate the posterior lobe for its release of hormones (posterior pituitary does not produce hormones; it only release hormones made by the hypothalamus).



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Anterior pituitary gland – 7 hormones

- **Growth hormone (GH)** -- for normal growth and development of all body cells, especially muscle and bone cells. [Hyper secretion of it during childhood causes Gigantism, hypersecretion during adulthood causes Acromegaly, and hyposecretion causes Dwarfism].
- **Thyroid-stimulating hormone (TSH)** -- stimulates the thyroid gland to secrete thyroid hormones. [Hypersecretion causes Grave's disease, and hyposecretion causes cretinism in children and myxedema in adults].

a) Goiter b) Exophthalmos of graves disease



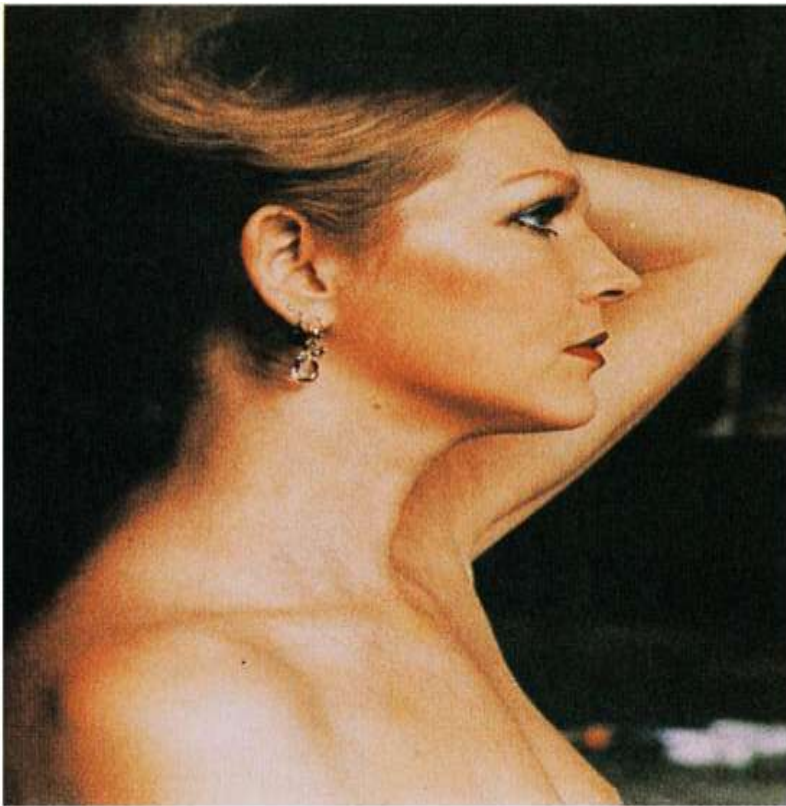
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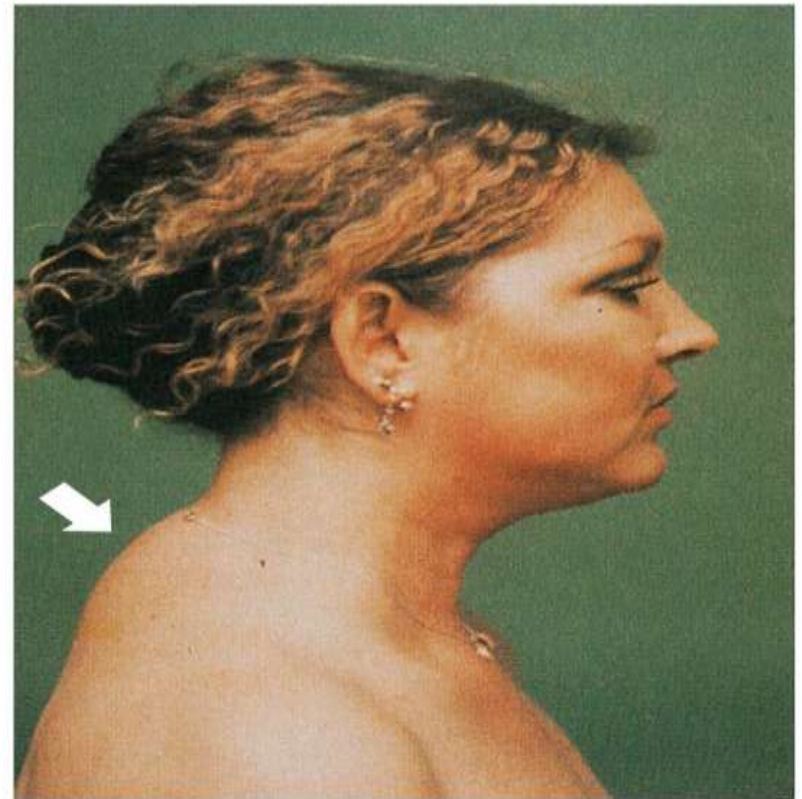
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- **Adrenocorticotrophic hormone (ACTH)** – stimulates the adrenal cortex to secrete mineralocorticoids, glucocorticoids, or gonadocorticoids. [Hypersecretion causes Cushing's disease, while hyposecretion is rare].



(a)



(b)

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- **Follicle-stimulating hormone (FSH)** -- stimulates the production of egg cells and sperm in the gonads. [Hypersecretion causes no known effects, while hyposecretion can cause failure of sexual maturation]
 - **Luteinizing hormone (LH)** -- triggers ovulation and stimulates the production of estrogens and progesterone in female, and promotes testosterone production in male. [Disorders are similar to those for FSH].
 - **Prolactin (PRL) or Lactogenic hormone (LTH)** -- stimulates milk production in the mammary glands. [Hypersecretion can disrupt normal menstrual cycles in female and causes impotence in male; and hyposecretion causes poor milk production in female].
 - **Melanocyte-stimulating hormone (MSH)** -- stimulates melanocytes in the epidermis and hair follicles to release melanin pigment. [Hypersecretion causes abnormally dark skin pigment, and hyposecretion causes abnormally light skin pigment].

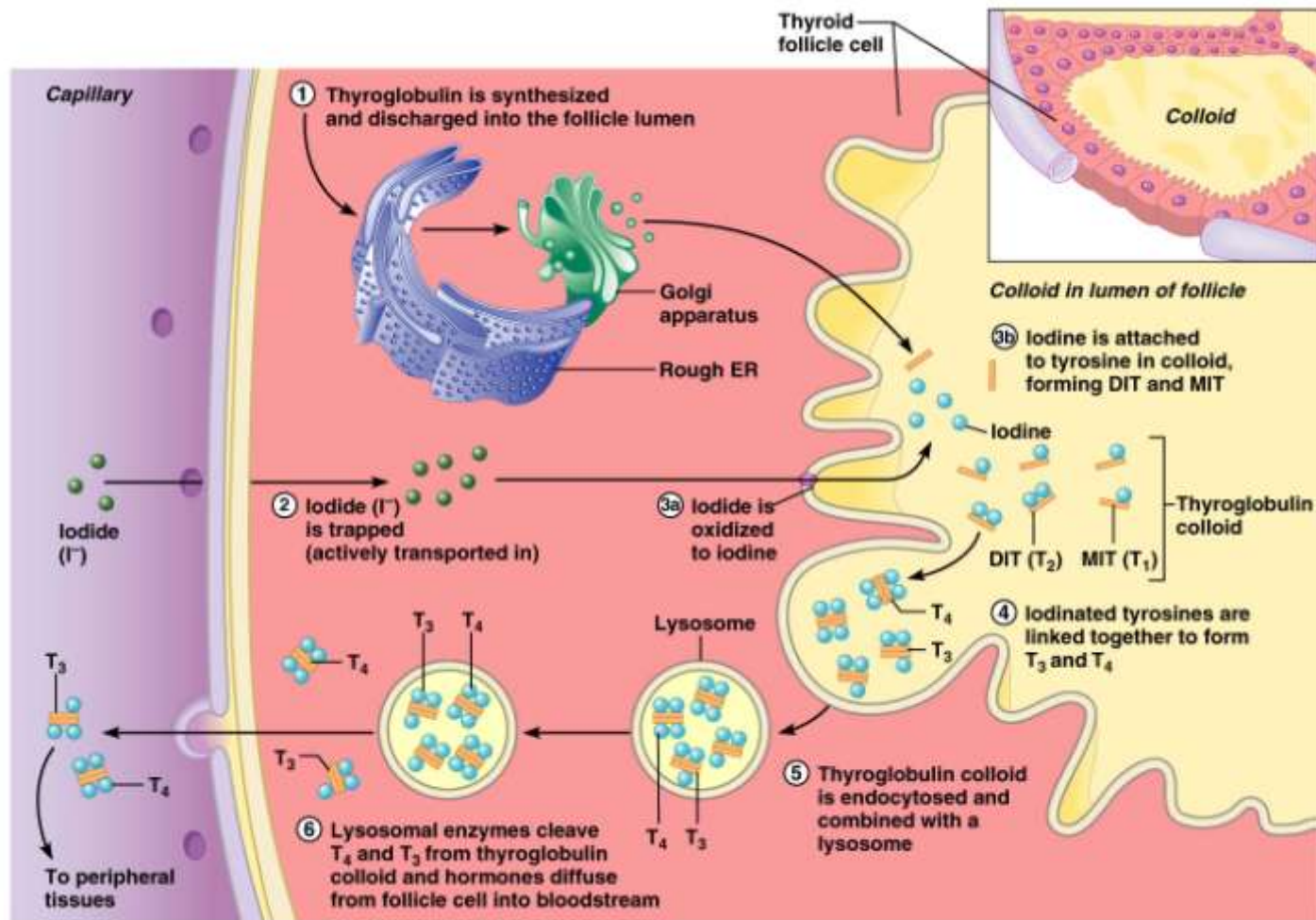
Posterior pituitary gland

- **Oxytocin (OT)** -- stimulates uterine contraction during the birth process, and activates milk ejection from the mammary glands. [Disorders are rare and have no known effects, except in some hyposecretion cases, weak labor contraction is reported].
- **Antidiurectic hormone (ADH)** -- stimulates water reabsorption in kidney tubules. [Hypersecretion has no known effects, and hyposecretion causes frequent urination called diabetes insipidus].

Thyroid gland

- a) located inferior to the larynx (voice box) and attached to the trachea.
- b) divided into two lateral lobes .
- c) thyroid follicles utilize iodine and synthesize thyroglobulin (TGB) to be stored in the colloids.
- d) upon stimulation of TSH, TGB is converted into two hormones -- **Triiodothyronine (T₃)** and **Thyroxine (T₄)** to promote normal metabolism. [Hyposecretion causes hypothyroidism, similar to cretinism and myxedema, and hypersecretion causes hyperthyroidism that results in a goiter or in Graves' disease].
- e) also secretes **Calcitonin** to lower blood calcium and phosphate levels and regulate digestive hormones. [Both hyposecretion and hypersecretion would affect normal balances of calcium and phosphate].

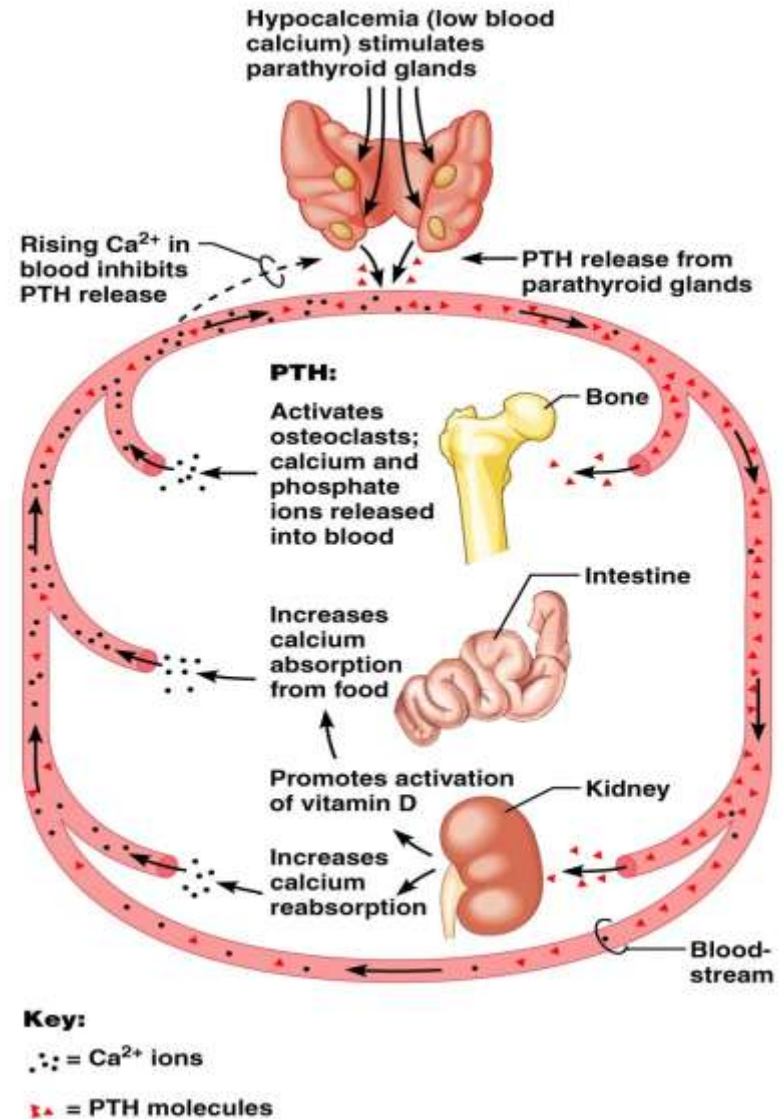
Synthesis of thyroid hormone



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Parathyroid glands

- Four oval-shaped glands embedded in the posterior surface of the thyroid gland.
- Secrete only 1 protein hormone called parathyroid hormone (PTH) or parathormone to raise blood calcium level and lower blood phosphate level. [Hyposecretion causes tetany, and hypersecretion causes osteitis fibrosa cystica].

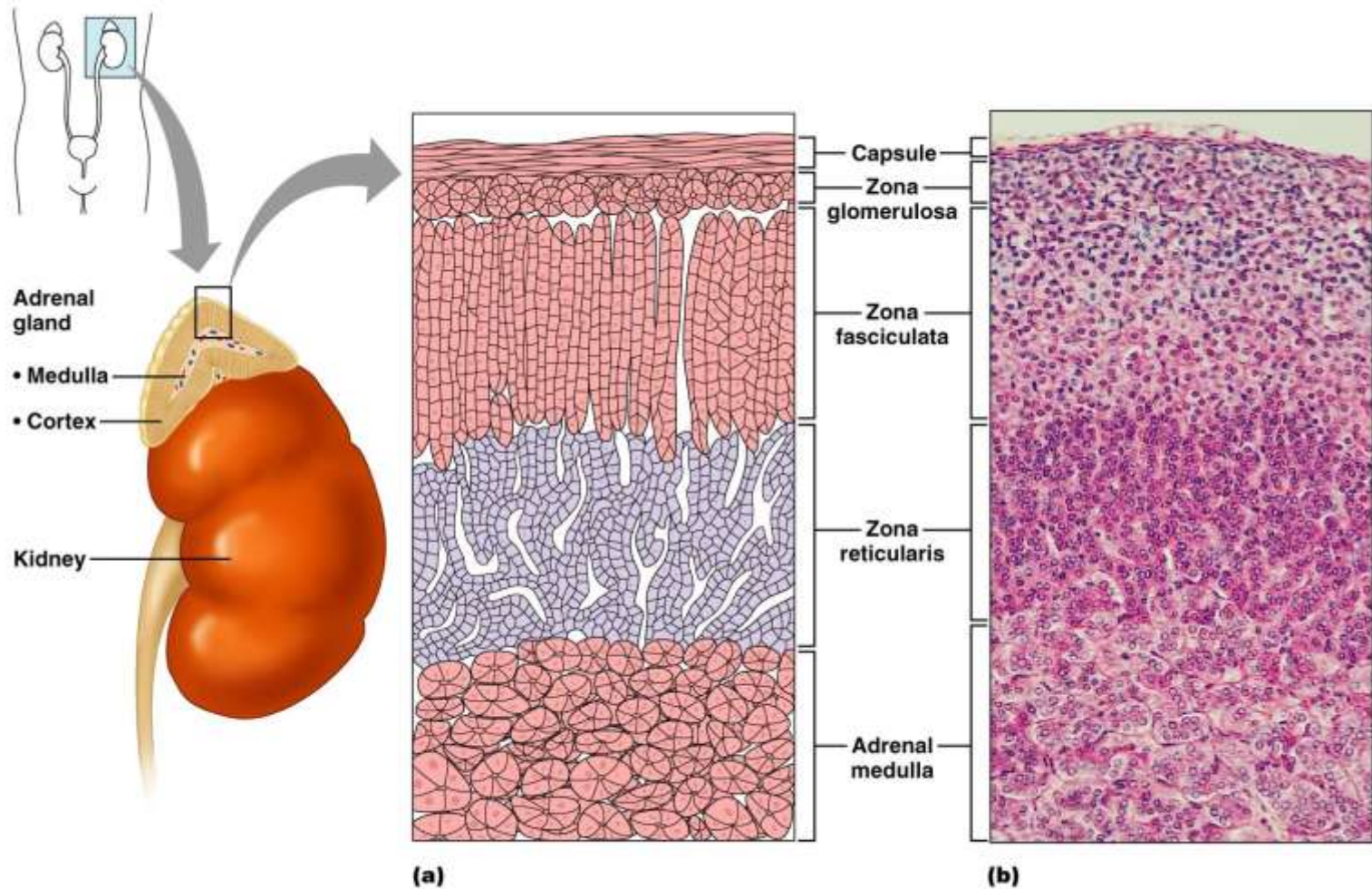


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Adrenal gland

- **A. Adrenal Cortex:** outer portion of the adrenal gland which is attached to the superior surface of the kidney.
- Divided into 3 regions, from outside to inside : **Zona glomerulosa**, **Zona fasciculata** , and **Zona reticularis**.
- Secretes over 30 steroid-based substances and several steroid hormones, all crucial for normal homeostasis .
- Zona glomerulosa secretes **mineralocorticoids** which help regulate the levels of minerals such as sodium, potassium, and magnesium. **Aldosterone** is the most important hormone in this group, where it raises blood levels of sodium and water, and lowers blood potassium level.

Adrenal gland



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- Zona fasciculata secretes **glucocorticoids** which affect glucose or carbohydrate metabolism. Cortisol is the most important hormone in this group, where it is involved in carbohydrate, lipid and protein metabolism, and also helps fight stress and inflammation. [Hyposecretion causes **Addison's disease**, and hypersecretion causes Cushing's syndrome].
 - Zona reticularis secretes **gonadocorticoids** which supplement sex hormones from the testes and ovaries and stimulate early development of reproductive organs. These hormones are male types (adrenal androgens), namely testosterone, but can be converted into female types, such as estrogens, by the skin, liver, and adipose tissues [Hyposecretion causes congenital adrenal hyperplasia, and hypersecretion causes gynecomastia in male].

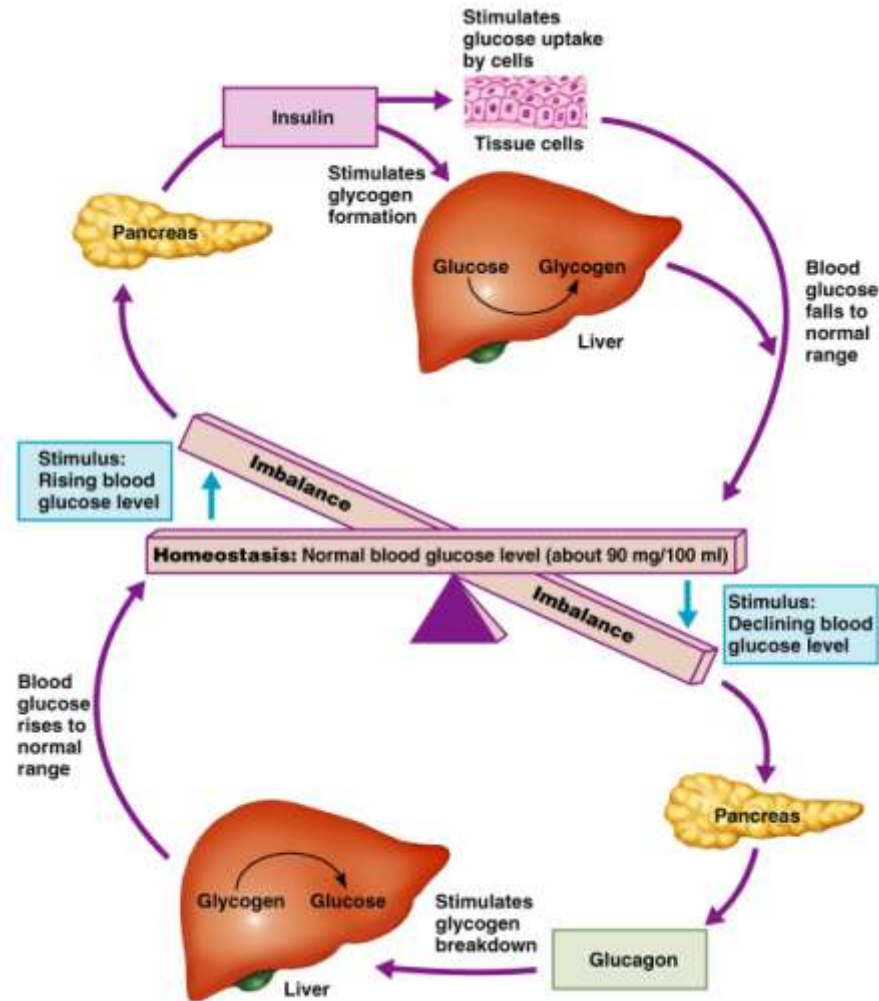
Adrenal gland

- **B. Adrenal Medulla:** inner portion of the adrenal gland.
- Made of modified nerve tissue that is under direct regulation of sympathetic nerves of the autonomic nervous system.
- Contains glandular cells called chromaffin cells which secrete 2 closely related hormones -- **Epinephrine** (or adrenaline) and **Norepinephrine** (or noradrenaline).
- Effects of these hormones resemble sympathetic stimulation, where body activities such as cardiac actions, blood pressure , and breathing rate are increased , while digestive processes are decreased. [No known effects are due to hyposecretion of these, but hypersecretion can caused hypertension, increased blood glucose level , and high heart rate].

Pancreas

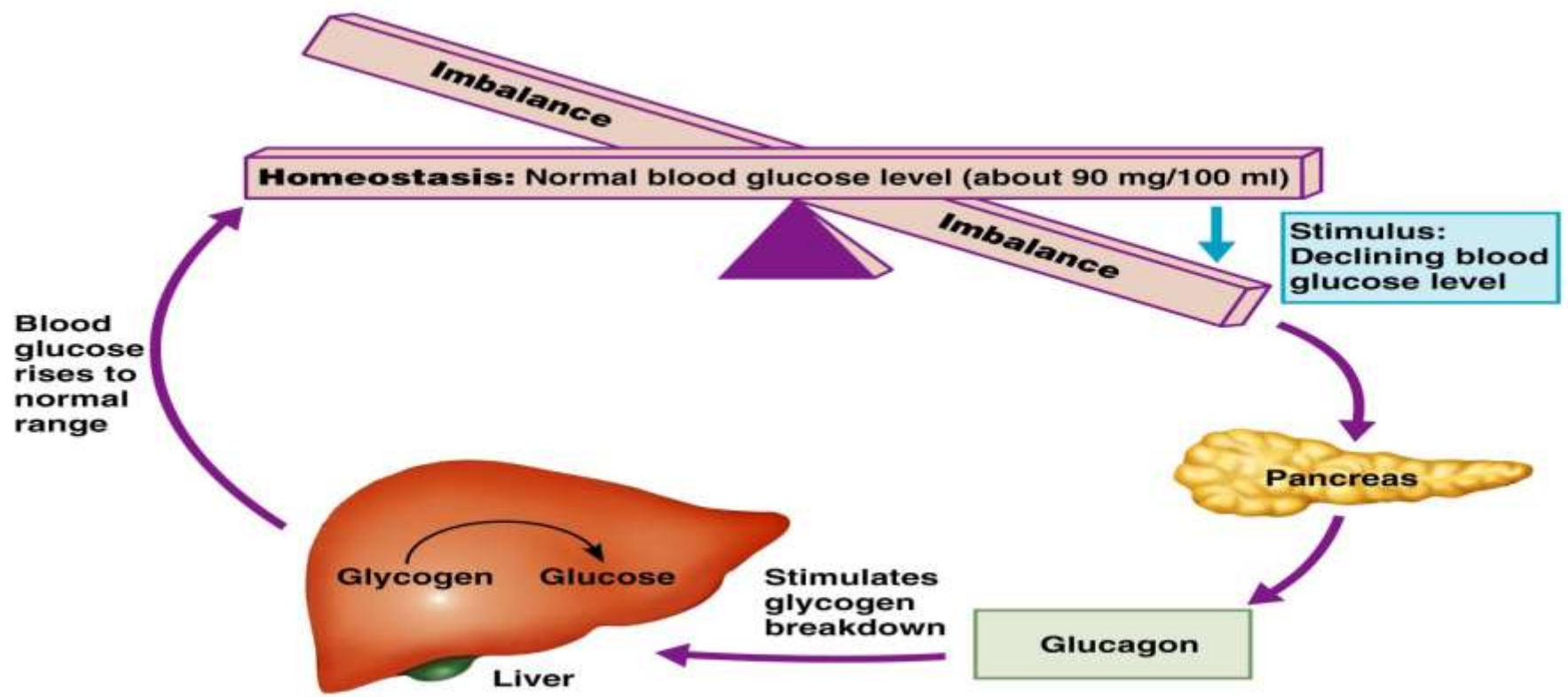
- The only gland that is both exocrine and endocrine in physiology.
- In its exocrine aspect, 99% of its mass is composed of cells called acini which secrete digestive enzymes and fluids into the small intestine through the pancreatic ducts.
- In its endocrine aspect, 1% of its mass is little groups of cells called islets of langerhans (or pancreatic islets) which secrete hormones to regulate blood glucose level.
- in each pancreatic islet , alpha cells (α cells) secrete glucagons to raise blood glucose level.
- beta cells (β cells) secrete insulin to lower blood glucose level.
[Hyposecretion causes diabetes mellitus where excessive glucose is present in urine, and hypersecretion causes hyperinsulinism].

Regulation of blood glucose



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- delta cells (δ cells) secrete **somatostatin** or **growth hormone inhibiting hormone (GHIH)** which helps regulate carbohydrate metabolism by inhibiting the secretion of glucagons.



Ovary

- The female sex organ that also serves as an endocrine gland.
- Contains follicular cells in its secondary and mature follicles, where they secrete **Estrogen** to develop and maintain female sexual characteristics, to regulate ovarian and menstrual cycles, to maintain pregnancy, and to develop secondary sexual characteristics. [Both hyposecretion and hypersecretion will have broad effects in female reproduction].
- Also contains degenerating scar tissue called **corpus luteum** which contain lutein cells that secrete **Progesterone** to help maintain ovarian and menstrual cycles, and pregnancy. [Discorders are similar to those for estrogens].

▪ Testis

- The male sex organ that also serves as an endocrine gland.
- Contains interstitial cells (or leydig's cells) that secrete **testosterone** to develop secondary sexual characteristics. [Both hyposecretion and hypersecretion and will have broad effects in male reproduction].

▪ Pineal gland

- -- pine cone shaped located deep in the cerebrum.
- -- secretes melatonin to regulate circadian rhythms which are necessary to keep track of day/night cycles, sleep/wake rhythm, menstrual and ovarian cycles.

-
- **Thymus gland:** A diminishing gland (over time) located between the lungs. secretes a group of hormones, such as **thymosin**, to affect the production and maturation of lymphocytes in body defenses.
 - **Heart :** The organ for pumping blood in the cardiovascular system. contains 2 small chambers called atrium which secrete **atrial natriuretic factor (ANF)** which helps regulate blood pressure.
 - **Digestive organs:** stomach secretes hormones such as **gastrin** to stimulate stomach activities .
 - --small intestine secretes hormones such as **cholecystokinin (CCK)** to stimulate gallbladder activities, and intestinal gastrin to regulate stomach activities.

- **kidneys**

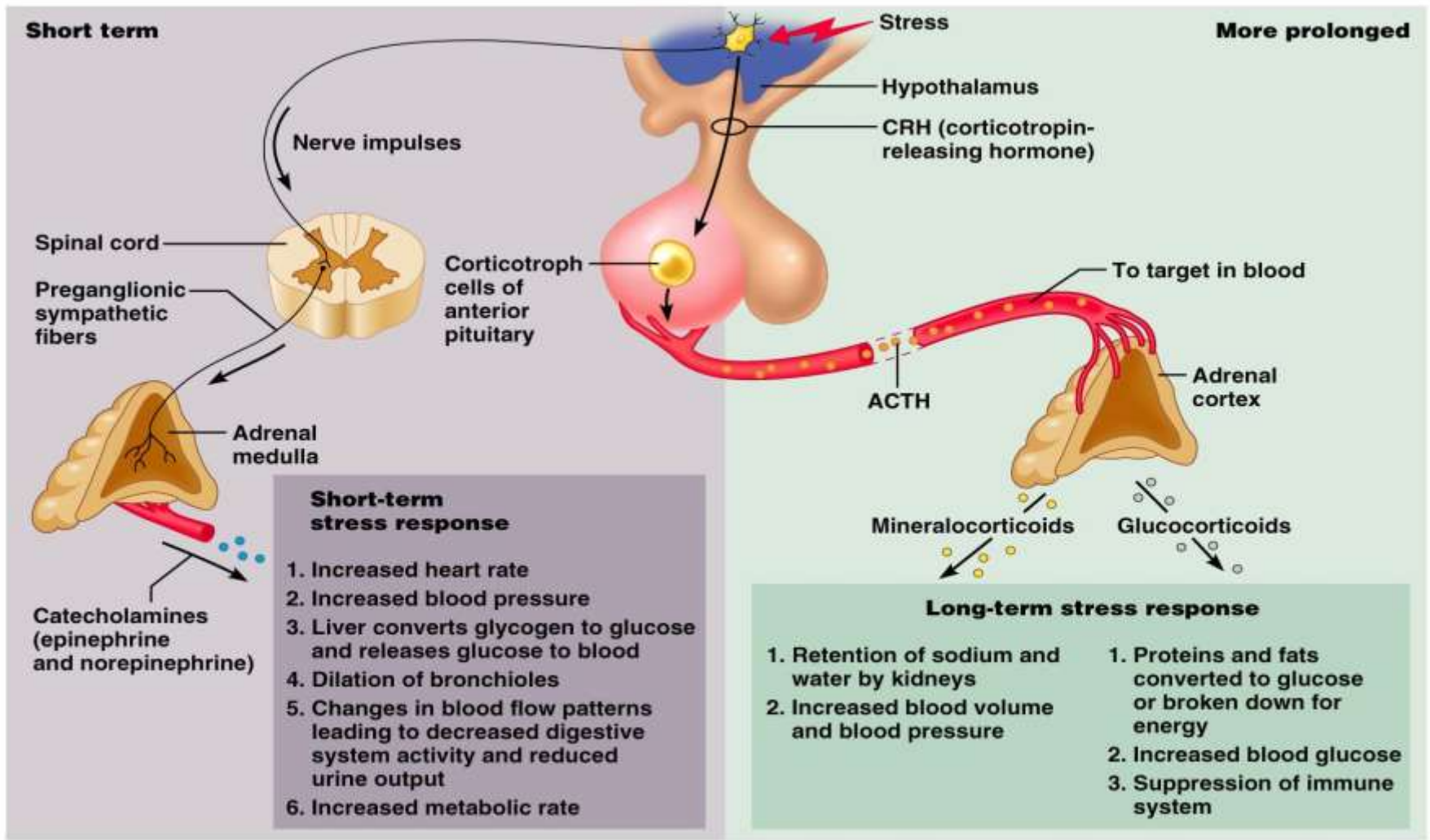
- -- organs for filtering and cleansing our blood and tissue fluids.
- -- secrete a hormone called **Erythropoietin** to stimulate red blood cell production in the red bone marrow .
- **placenta**
- -- protective sac around the fetus during pregnancy .
- -- secretes **estrogen** and **progesterone** to maintain normal pregnancy .

Major events in the general stress syndrome

- 1. As a result of stress , nerve impulses are transmitted to the hypothalamus .
- 2. **Sympathetic** impulses arising from the hypothalamus increases blood glucose conc. , blood glycerol conc. , blood fatty acid conc., heart rate, blood pressure , and breathing rate. They dilate air passages , shunt blood into skeletal muscles , and increase secretion of epinephrine from the adrenal medulla .
- 3. **Epinephrine** intensifies and prolongs sympathetic actions .
- 4. The hypothalamus secretes **CRH**, which stimulates secretion of **ACTH** by the anterior pituitary gland .

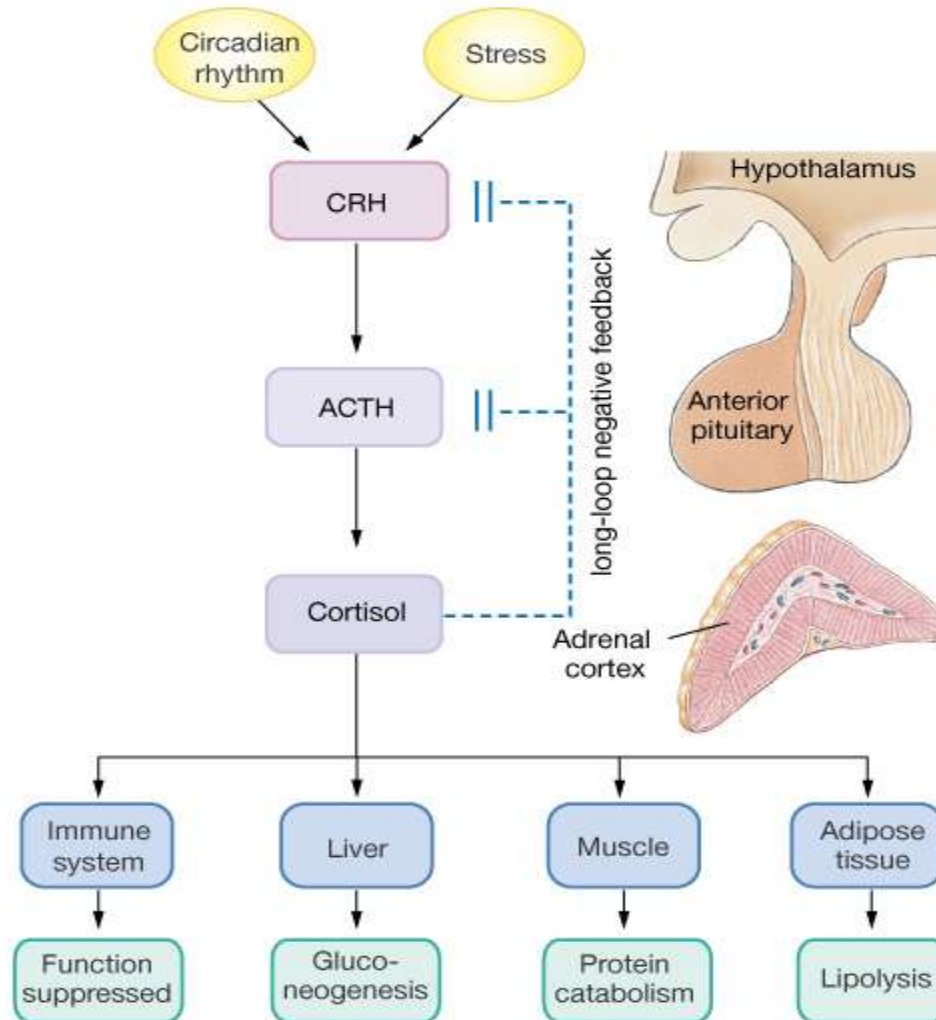
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- 5. ACTH stimulates release of **Cortisol** by the adrenal cortex .
 - 6. Cortisol increases the conc. of blood amino acids, releases fatty acids, and forms glucose from noncarbohydrate sources.
 - 7. Secretion of **glucagons** from the pancreas and **growth hormone** from the anterior pituitary increase .
 - 8. Glucagons and growth hormone aid mobilization of energy sources and stimulate uptake of amino acids by cells.
 - 9. Secretion of **ADH** from post. Pituitary increases .
 - 10. ADH promotes the retention of H₂O by the kidneys, which increases blood volume.
 - 11. **Renin** increases blood level of angiotnsin II, which acts as a vasoconstrictor and also stimulates **Aldosterone** secretion by the adrenal cortex .Aldosteron increase Na⁺ retention by the kidneys .

Stress and the adrenal gland



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The control pathway of Cortisol



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Disorders of the thyroid gland

- **Hyperthyroid** :
- Grave's disease : Auto antibodies (against self) bind TSH receptors on thyroid cell membranes , mimicking action of TSH, over stimulating gland (hyperthyroidism) ; This is an exophthalmic goiter.
- Hyperthyroidism : High metabolic rate, sensitivity to heat, restless ness, hyperactivity, weight loss , protruding eyes , goiter.

■ Hypothyroid :

- **Hashimoto's disease** : Auto antibodies (against self) attack thyroid cells, producing hypothyroidism .
- **Hypothyroidism** (infantile) : cretinism - stunted growth, abnormal bone formation , mental retardation , low body temperature , sluggishness.
- **Hypothyroidism** (adult) : Myxedema - low metabolic rate, sensitivity to colds, sluggishness, poor appetite , swollen tissue , mental dullness.
- **Simple goiter** : Deficiency of thyroid hormone due to iodine deficiency ; because no thyroid hormones inhibit pituitary release of TSH, thyroid is over stimulated and enlarges, but functions below normal (hypothyroidism).

Goiter and Myxedema



(a)



(b)

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Disorders of the parathyroid glands

- I. **Hyperparathyroidism** : fatigue , muscular weakness , painful joints, altered mental functions, depression, weight loss, bone weakening , increased PTH secretion over stimulates osteoclasts.
- cause : Tumor
- Treatment : Remove Tumor , correct bone deformities .
- II. **Hypoparathyroidism** : muscle cramps and seizures . Decreased PTH secretion reduces osteoclast activity , diminishing blood calcium ion concentration .
- cause : inadvertent surgical removal; injury .
- Treatment : calcium salt injections , massive doses of vitamin D.