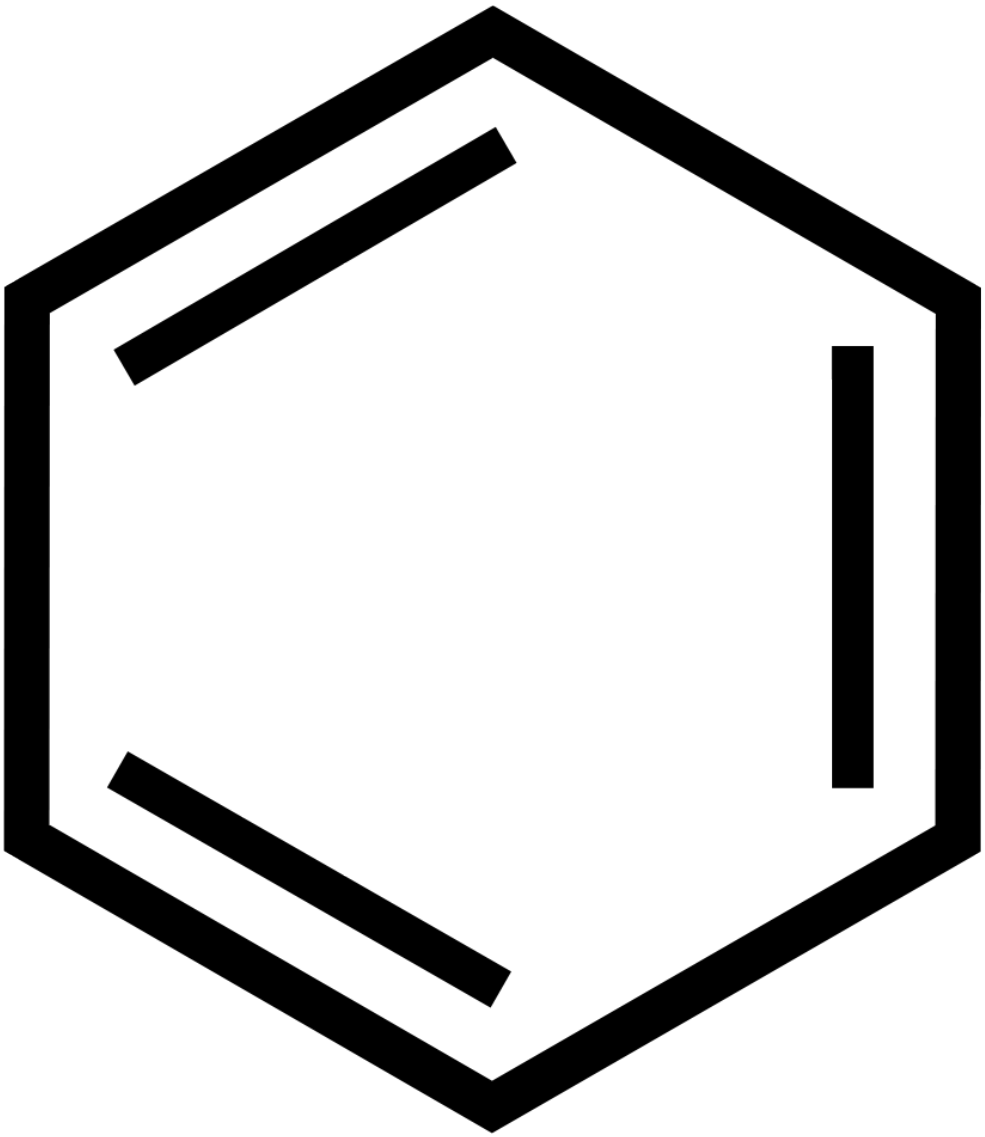

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CONCEPT: BASICS OF HORMONE FUNCTION

General Definitions and Functional Notes:

● An **endocrine hormone** is a molecule—protein or steroid—secreted *into the bloodstream* to affect distant body parts.

□ Can have effects even at very low concentrations—nanomolar (10^{-9}) or picomolar (10^{-12}) range.

□ Circulation in bloodstream means spread to every corner of body→*can* have very global effects.

● Hormones exert effects on target cells by binding to _____.

□ Either in the cell or on the cell's membrane (more later).

□ A cell *MUST* have the proper receptor for a hormone to have an effect.

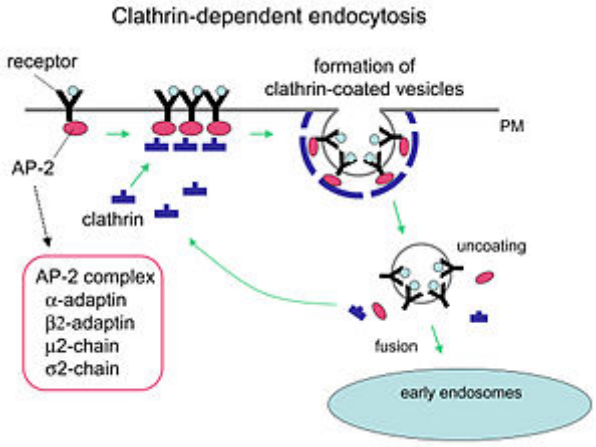
-How hormones can have specific effects, even when in general circulation.

EXAMPLE: Vasopressin specifically affects the kidneys and blood vessels, while epinephrine has more global effects.

Clearance and Termination:

- To stop their effects from lasting forever, hormones must be cleared from the blood.
    - □ Most metabolic clearance is done by the liver and/or kidneys.
    - □ In individual cells, activated receptors stop being activated when hormone unbinds and diffuses away.
        - -Or, receptor:hormone complex may be endocytosed and degraded.

EXAMPLE: Endocytosis of an activated receptor.

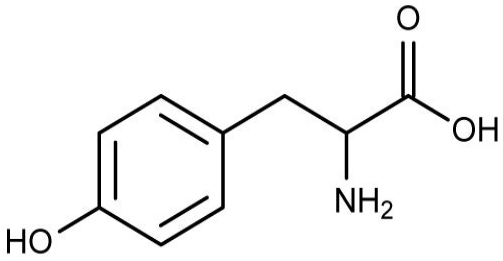


CONCEPT: HORMONE CLASSIFICATION AND MECHANISM OF ACTION

Structural Classification of Hormones:

● Based on molecular structure, there are 3 major categories of hormones: *amines*, *peptides*, and *steroids.*

● **Amines** are made from the amino acid tyrosine.



□ (So, they all are small and have an aromatic ring).

□ Highly polar—probably can't cross cell membranes.

□ They include:

-The **Catecholamines: epinephrine, norepinephrine** and **dopamine.** (But, norepi and dopa are NTs.)

-Thyroid Hormone (aka T_3, T_4).

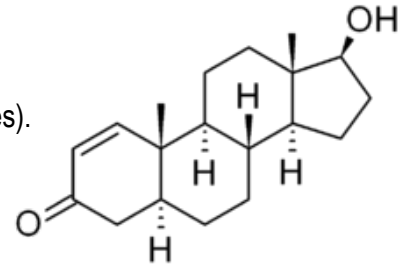
● **Peptide hormones** are _____ made by specific hormone-secreting cells.

□ Transcribed/translated in cells, packaged into vesicles, and secreted into blood when signaled.

□ Usually about 10 amino acids in size (see Example below)—10× larger than an amine hormone.

□ Large size and polarity means they dissolve in water but definitely can't cross cell membranes.

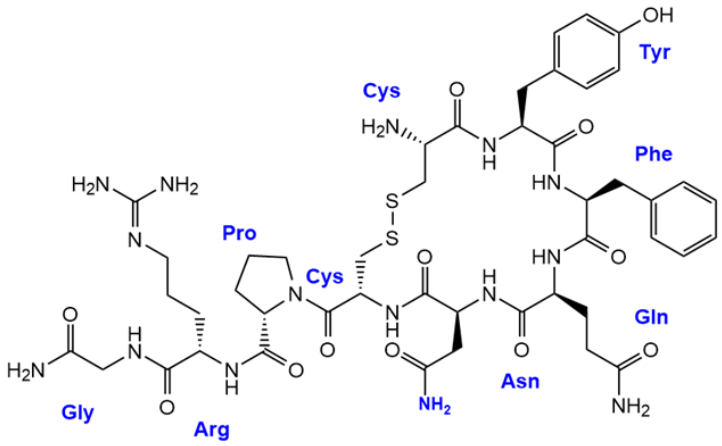
● **Steroid hormones** are complex, highly-cyclized _____.



□ Made mostly by the adrenal cortex and gonads (testes or ovaries).

□ Lipophilicity means they *can* cross cell membranes.

EXAMPLE: Vasopressin is a 10-amino acid peptide hormone:

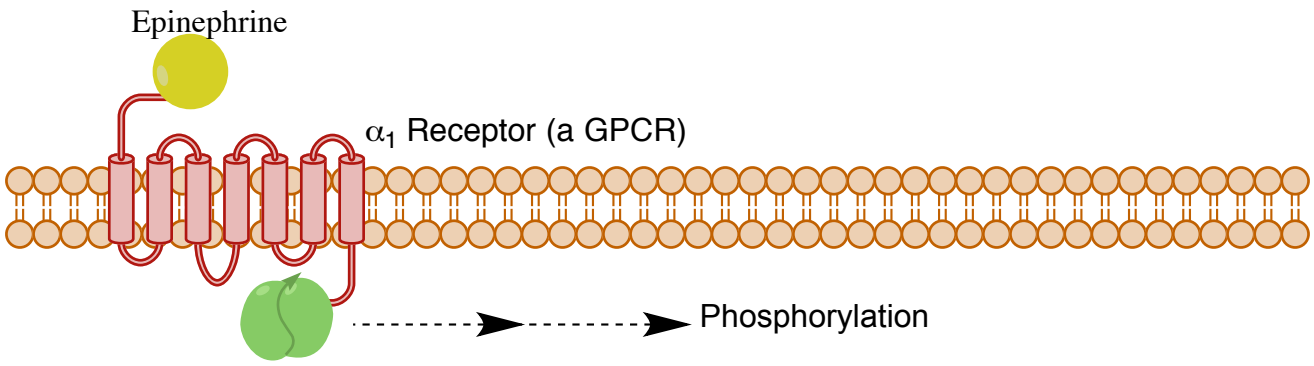


- Structure of a hormone largely determines its mechanism of action—*how* it exerts its effects on cells.
    - □ Mechanism of action, in turn, determines how quickly the effects happen and how long they last.

Mechanism of Action of Catecholamines and Peptides:

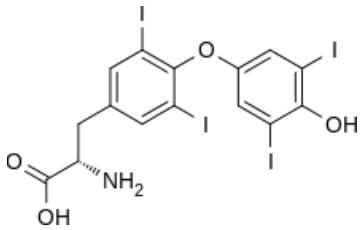
- The catecholamine epinephrine and all the peptide hormones are large and hydrophilic.
    - □ Exert their effects by *binding and activating a membrane receptor*—cannot cross cell membranes themselves.
        -Usually work via GPCRs, though sometimes Ca^{2+}.
- These intracellular pathways modify the activity of *already existing* proteins, usually by phosphorylation.
    - □ Onset of effects is very fast— seconds to minutes to activate transduction pathway and make modifications.
    - □ Duration of effects is short— minutes to hours to deactivate receptor and dephosphorylate proteins.

EXAMPLE: Epinephrine affects cells by binding and activating α_1 receptors.

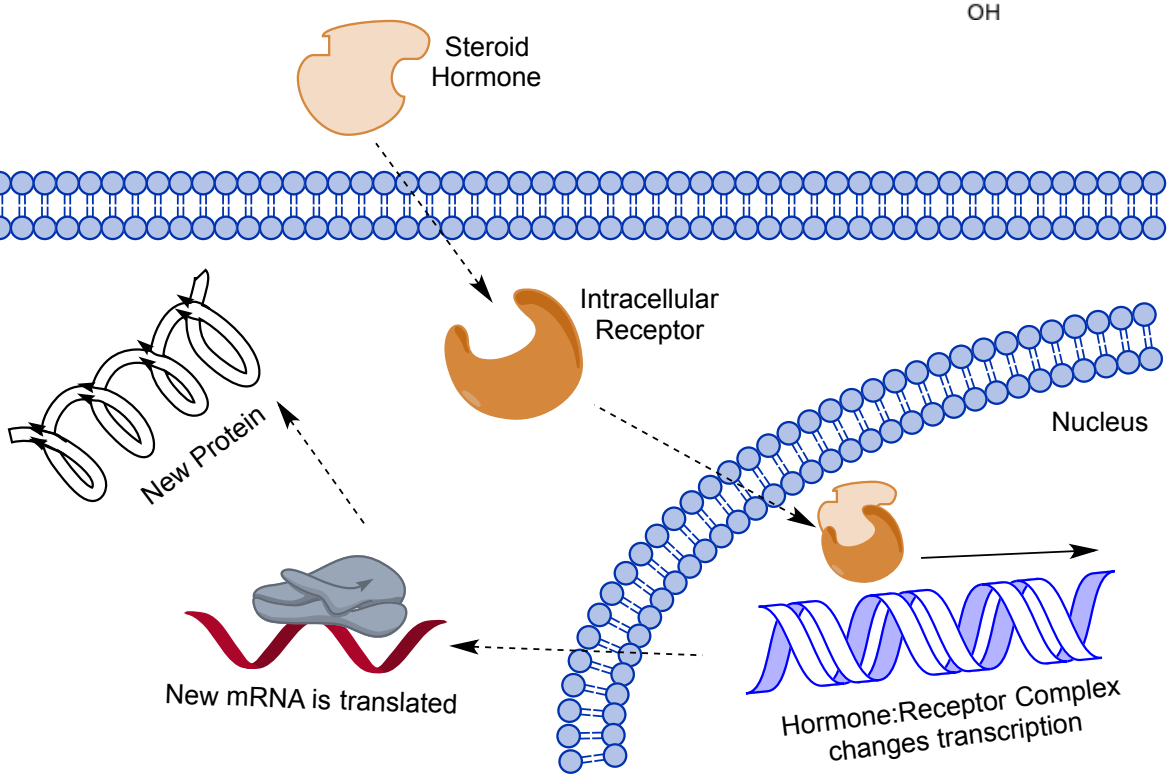


Mechanism of Action of Steroids and Thyroid Hormone:

- Steroid hormones are lipophilic, allowing them to diffuse across membranes from the blood into cells.
    - □ Exert their effects by crossing cell membranes and binding to an *intracellular* receptor.
    - □ This complex then either acts as a *transcription factor* or activates other transcription factors.
        - -Change which genes are being transcribed (or how much they're being transcribed).
        - -So, change the proteins a cell is actually making.
- For steroid hormones to take effect, a lot has to happen—transcription, translation, protein modification, etc.
    - □ Onset of effects is slow—hours to days for these protein changes to take place.
    - □ Duration of effects is pretty long—days to weeks, depending on how long cell keeps its proteins around.
- Thyroid hormone is weird—it looks like a catecholamine, but has big iodine atoms on it.
    - □ I atoms "shield" the molecule, making it nonpolar→acts like a steroid hormone.



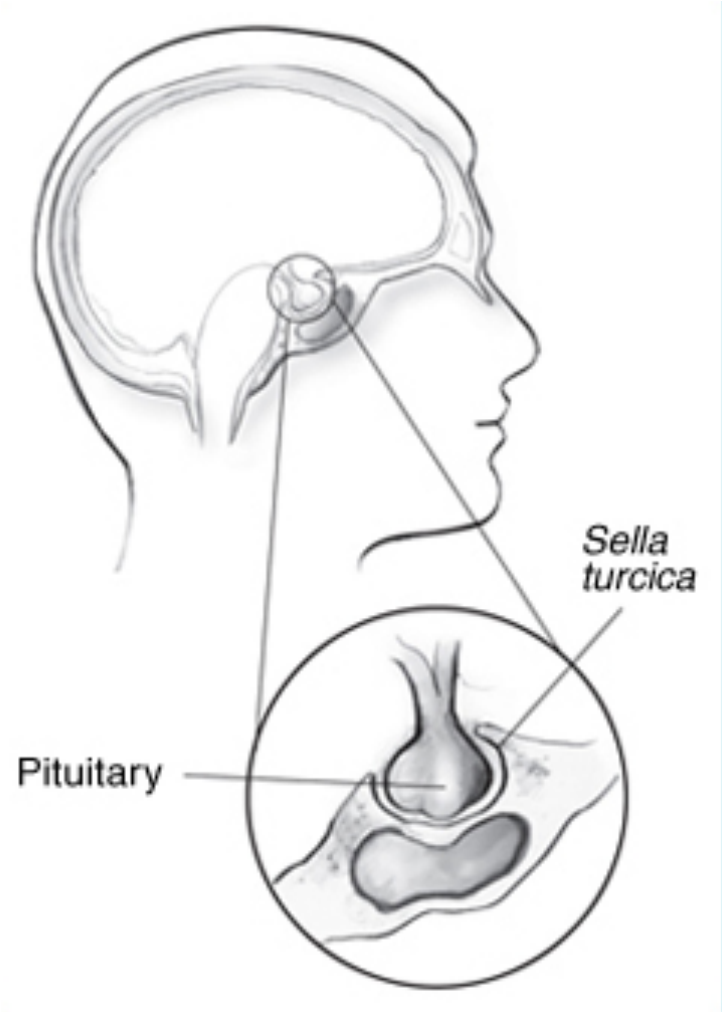
EXAMPLE: Mechanism of action of a general steroid hormone



CONCEPT: PITUITARY GLAND

- The **pituitary gland** (hypophysis) is _____- to the hypothalamus
  - □ Small gland located in the sella tucica of sphenoid bone

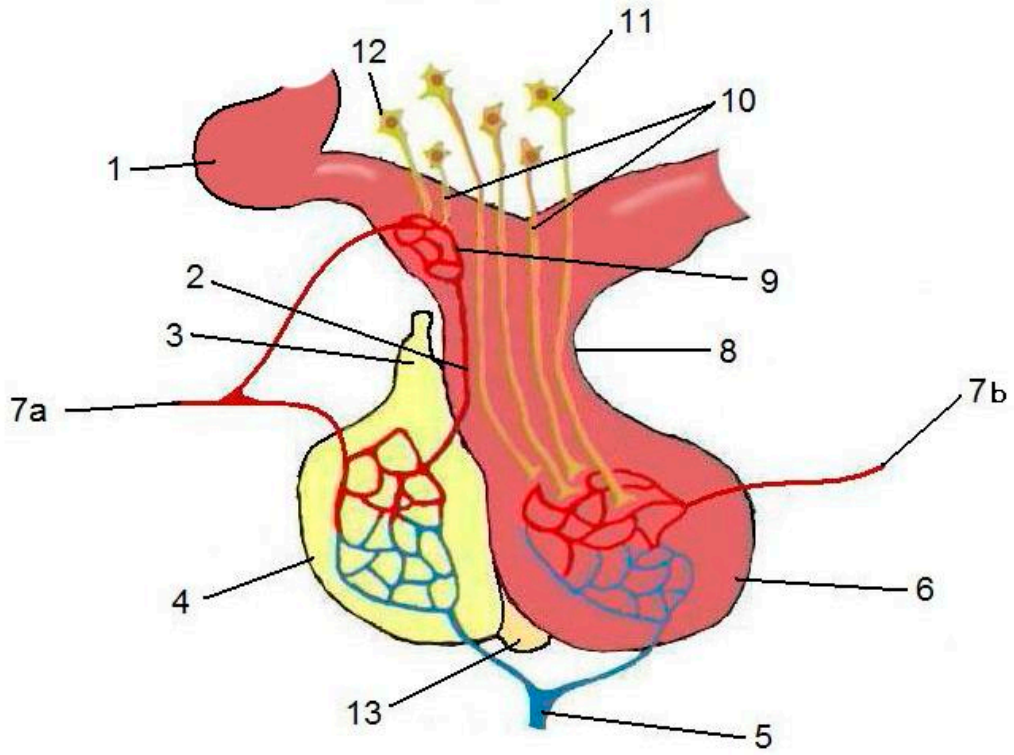
EXAMPLE:



□ The **anterior pituitary** (adenohyophysis) makes up _____ of the pituitary gland mass

- The **pars distalis** is the anterior rounded portion
- The **pars tuberalis** is the wrapping around the infundibulum
- The **pars intermedia** is a tiny region between the anterior and posterior pituitary
- A capillary system called the **hyopthalmo-hypophyseal portal system** connects to the hypothalamus
    - Blood drains from **primary capillary plexus** into **portal veins** and then into the **secondary plexus**

EXAMPLE:



□ The **posterior pituitary** (neurohypophysis) is one quarter of the pituitary gland mass

- The **pars nervosa** is the posterior rounded lobe

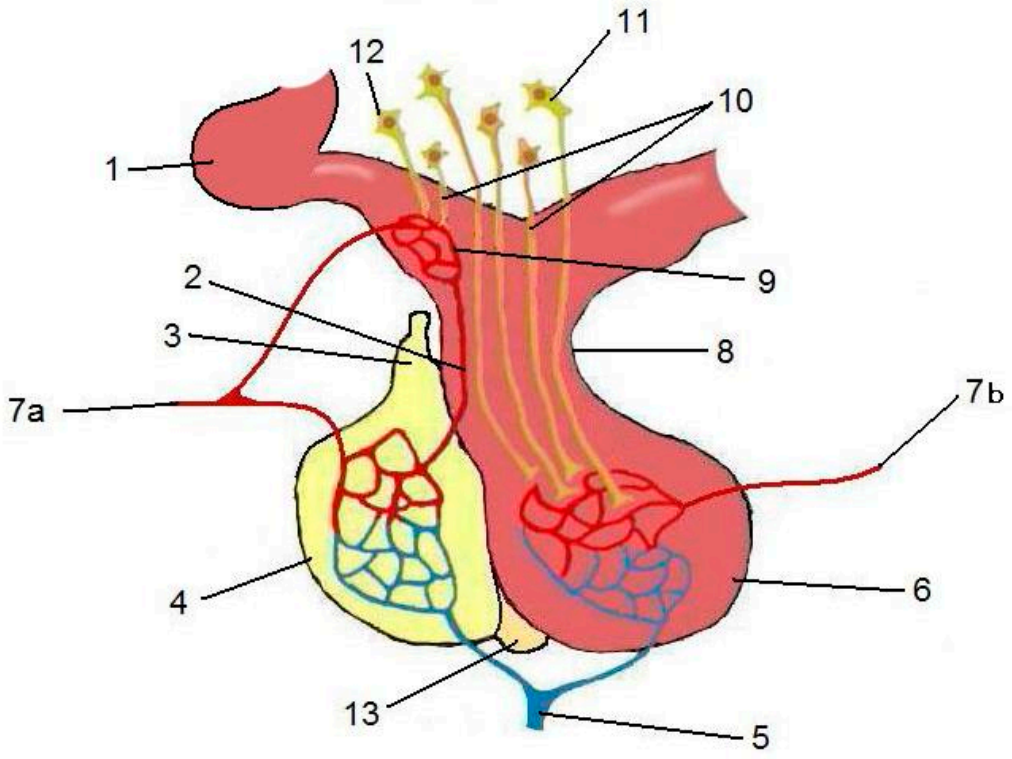
- The **infundibulum** connects the pituitary gland to the hypothalamus

- The **hypothalamo-hypophyseal tract** is a group of unmyelinated axons in the posterior pituitary

  - Connects the _____ to the pituitary gland

- The **inferior hypophyseal arteries** provides blood to the posterior pituitary

EXAMPLE:



CONCEPT: THE HYPOTHALAMUS AND PITUITARY GLAND

Hypothalamus and Pituitary Anatomy:

● **Hypothalamus** is an important regulatory/homeostatic center on the underside of the brain.

□ Controls many functions—body temperature, reproduction, blood pressure, growth and puberty, etc.

□ Much of this control is endocrine/hormonal, through interactions with the *pituitary gland.*

● **Pituitary Gland** is a cluster of cells hanging off the hypothalamus.

□ Actually 2 totally separate glands fused together:

-**Anterior pituitary** (aka **adenohypophysis**) and **posterior pituitary** (aka **neurohypophysis**).

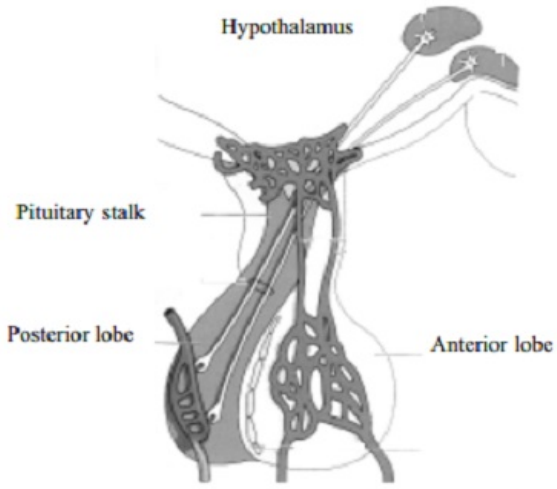
□ Stalk of tissue called **infundibulum** connects the pituitary gland to the hypothalamus.

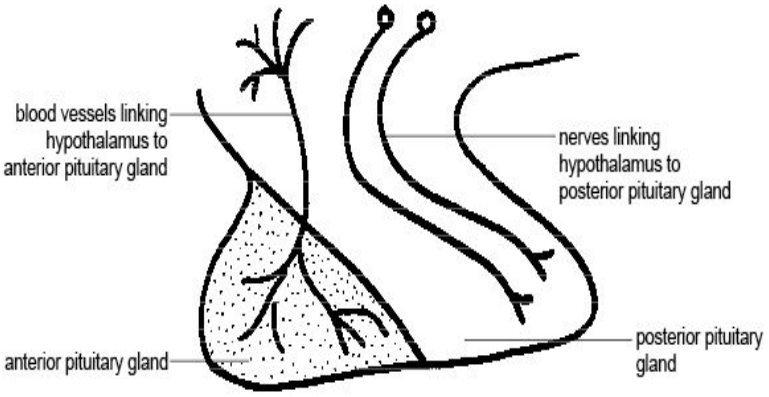
● The infundibulum is made of different types of tissue for the two halves of the pituitary.

□ In anterior pituitary, *blood vessels* link the hypothalamus to the pituitary.

□ In posterior pituitary, *axons of neurons* link the hypothalamus to the pituitary.

EXAMPLE: The anterior and posterior pituitary glands.

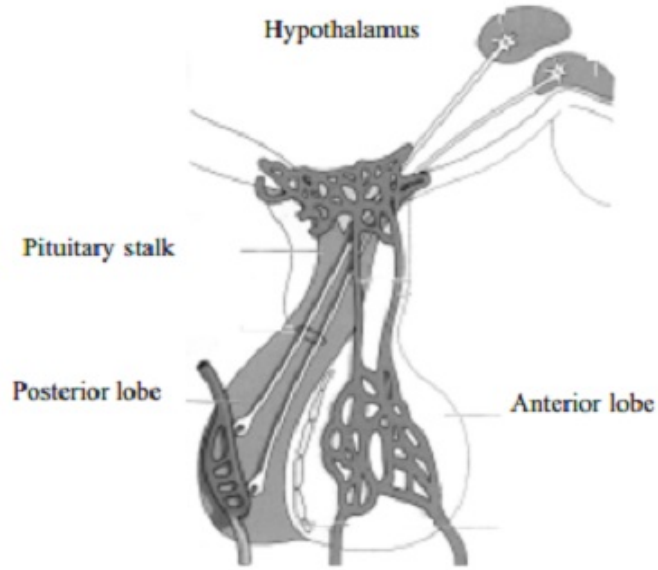




The Posterior Pituitary and Neurohormone Secretion:

- The posterior pituitary is connected to the hypothalamus by *axons of hypothalamic neurons.*
    - □ These axons make synapses onto *capillary beds* in the posterior pituitary itself.
    - □ The "NT" they release is a _____—synaptic transmission releases it into the bloodstream.
        -Called a **neurohormone** because it's a hormone that came from a neuron.
- The posterior pituitary secretes two neurohormones:
    - □ **Oxytocin** is important in child birth and lactation (breastfeeding).
    - □ **Vasopressin** (aka **Anti-diuretic hormone** [ADH]) helps maintain blood pressure, volume, and osmolarity.

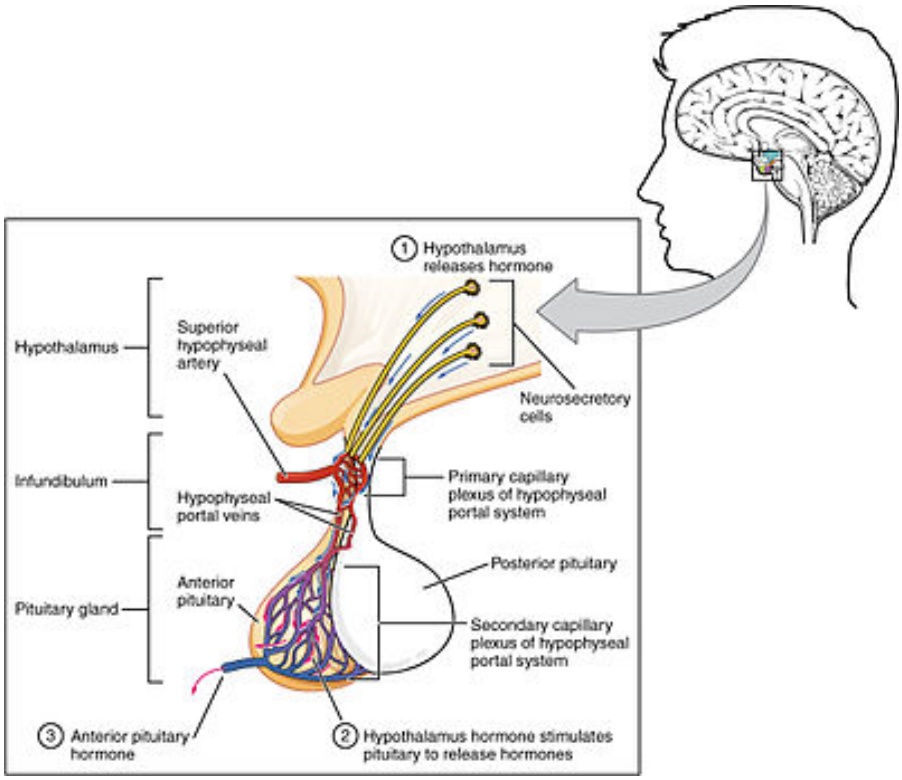
EXAMPLE: Neurons connect the hypothalamus and the posterior pituitary.



The Anterior Pituitary and the Hypothalamo-Hypophyseal Portal System:

- The anterior pituitary is connected to the hypothalamus by *two capillary beds in series with each other.*
    - □ One capillary bed in the hypothalamus, linked by blood vessels to a second in the anterior pituitary.
    - □ **Portal System** is the general name for this highly unusual arrangement of two capillary beds in a row.
        - -"**Hypothalamo-Hypophyseal Portal System"** because it connects hypothalamus and adenohypophysis.
- Anterior pituitary itself is made of classic endocrine cells—make, package, and secrete peptide hormones when signaled.
- **Releasing Hormones**—secreted by hypothalamic neurons into the portal system—are the signals.
    - □ Hypothalamic neurons make synapses onto capillaries in hypothalamic side of portal systems.
        - -When active, release a releasing hormone into the portal system.
    - □ Releasing hormone travels down portal system into capillaries in anterior pituitary side.
        - -Activates anterior pituitary cells to release their hormones into the *general* circulation.

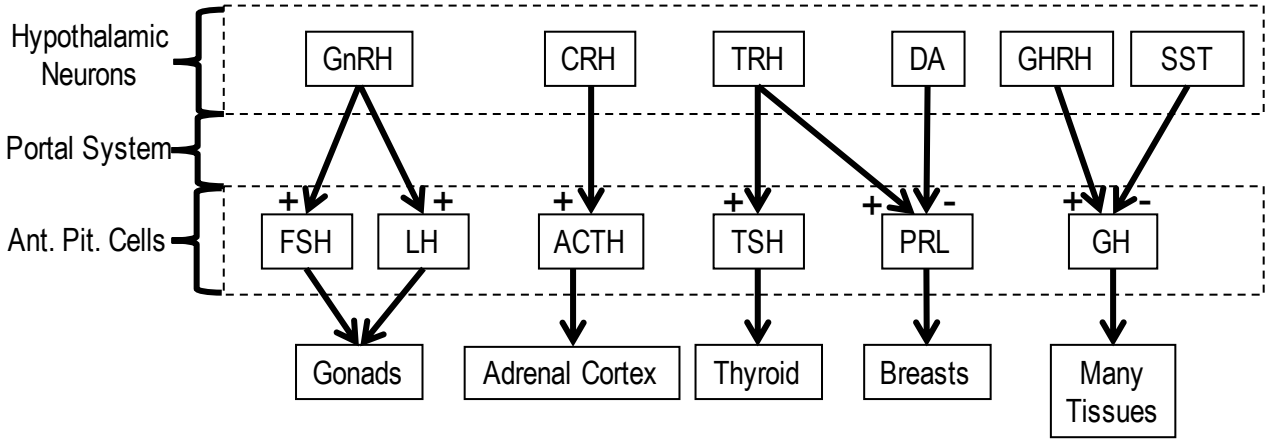
EXAMPLE: The anterior pituitary and they hypothalamo-hypophyseal portal system.



The Anterior Pituitary Hormones and their Releasing Hormones:

- The anterior pituitary can release 6 hormones into the circulation:
  - □ Follicle-stimulating hormone (FSH), luteinizing hormone (LH), adrenocorticotrophic hormone (ACTH), thyroid stimulating hormone (TSH), prolactin (PRL), and growth hormone (GH).
- The release of each hormone above is controlled by a specific releasing hormone from the hypothalamus.
  - □ Most releasing hormones are named for the hormone they activate in the anterior pituitary.
    - -e.g. Corticotrophin Releasing Hormone (CRH)→Adrenocorticotrophic Hormone (ACTH) release.

EXAMPLE: A flow diagram of all anterior pituitary hormones and their hypothalamic releasing hormones.

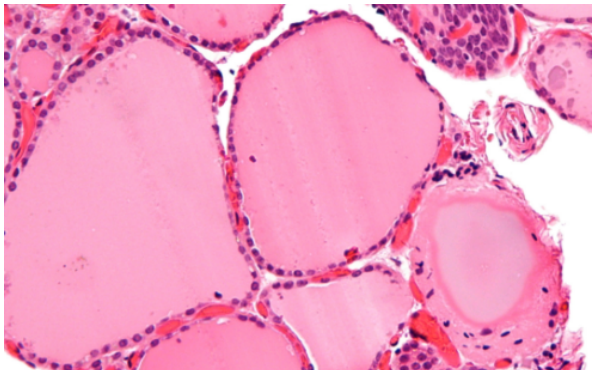


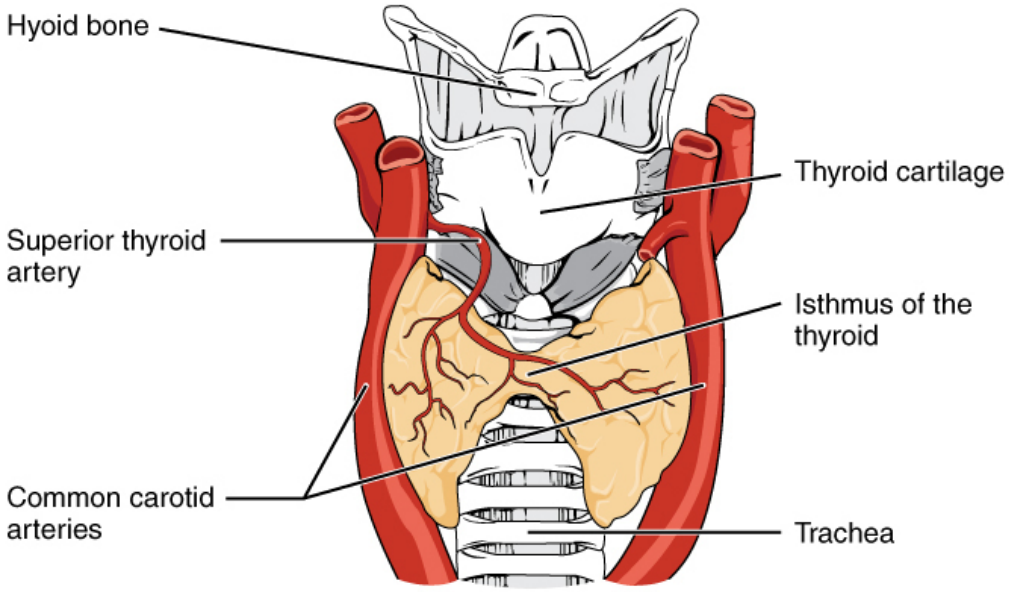
GnRH=Gonadotrophin Releasing Hormone
FSH=Follicle Stimulating Hormone
LH=Luteinizing Hormone
CRH= Corticotrophin Releasing Hormone
ACTH= Adrenocorticotrophic Hormone
TRH= Thyroid Hormone Releasing Hormone
TSH= Thyroid Stimulating Hormone
DA= Dopamine
PRL= Prolactin
GHRH= Growth Hormone Releasing Hormone
SST= Somatostatin
GH= Growth Hormone

CONCEPT: THYROID GLAND

- The **thyroid gland** is a butterfly-shaped organ inferior to the larynx, anterior to the trachea; it is highly _____
  - □ It has a right and left **lateral lobe** connected by the **isthmus**
    - About half of thyroid glands have a *pyramidal lobe* as a third lobe
  - □ **Thyroid follicles** make up most of the thyroid gland
    - Are circular structures filled with colloid and lined with **follicular cells**
      - Secretes T_3 and T_4
      - Active cells are cuboidal or columnar and _____ cells are squamous
    - Also have a few *parafollicular cells* (C cells) which synthesizes calcitonin hormone for calcium regulation

EXAMPLE:

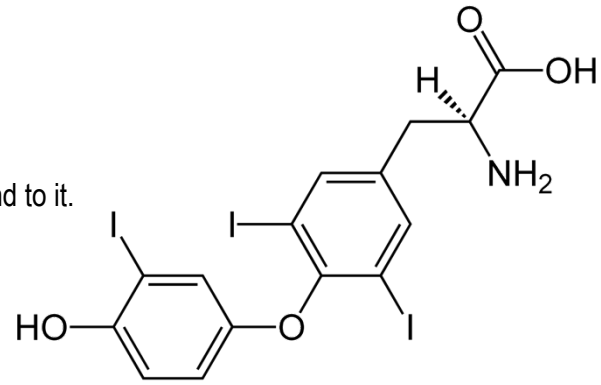




CONCEPT: THE THYROID GLAND

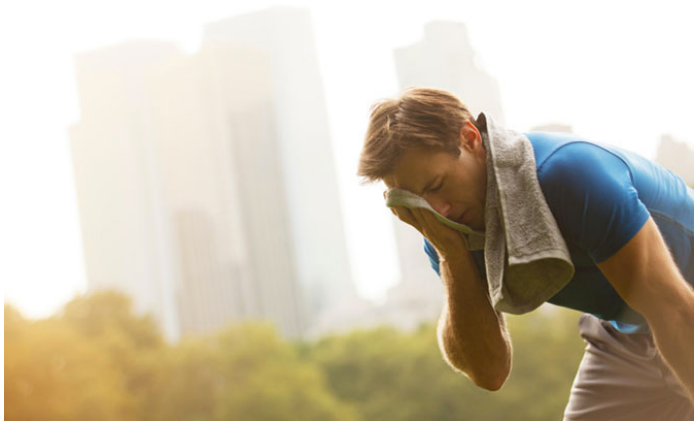
The Thyroid Gland and Thyroid Hormone:

- **Thyroid** is a gland in the neck, just below larynx. Produces two hormones: triiodothyronine (T_3) and Thyroxine (T_4).
    - □ Usually, target cells make T_3 from T_4 when they get it.
        - -Effects of T_3 and T_4 are essentially identical.
- Structurally, T_3 and T_4 are the amino acid tyrosine with 3 or 4 iodines bound to it.



    - □ Large I atoms "shield" the hormone, making it nonpolar.
    - □ Nonpolar→acts like a steroid hormone.
        - -Diffuses across membrane, interacts with transcription factors→change in gene expression.
- Thyroid hormones have *many* effects on the body, mostly result from ↑transcription/translation of Na^+/K^+ ATPases.
    - □↑Na^+/K^+ ATPases→↑ATP use.
        - -↑Heat production, ↑Aerobic Metabolism to replace ATP.

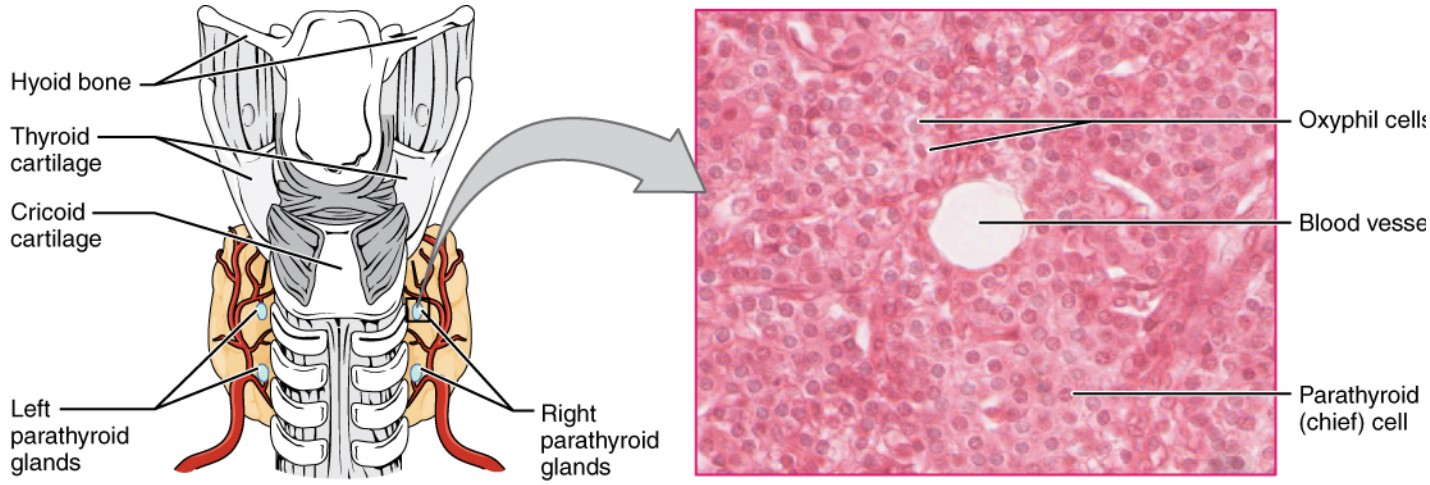
EXAMPLE: Hyperthyroidism (too much T_3) leads to weight loss and sensitivity to heat.



CONCEPT: PARATHYROID GLAND

- The **parathyroid gland** is made of small reddish-brown nodules, located on the posterior surface of the thyroid gland
  - □ Can range from 2-6 small _____ (average is 4); has a connective tissue capsule
  - □ The superior thyroid arteries supply the superior glands, and the inferior thyroid arteries supply the inferior glands
  - □ Their venous drainage is the same drainage that is used by the thyroid gland
  - □ There are two main types of _____
    - **Chief cells** (principal cells) synthesis parathyroid hormone (PTH), which increase blood calcium levels
    - **Oxyphil cells** have an unknown function

EXAMPLE:



a) Thyroid gland, posterior view

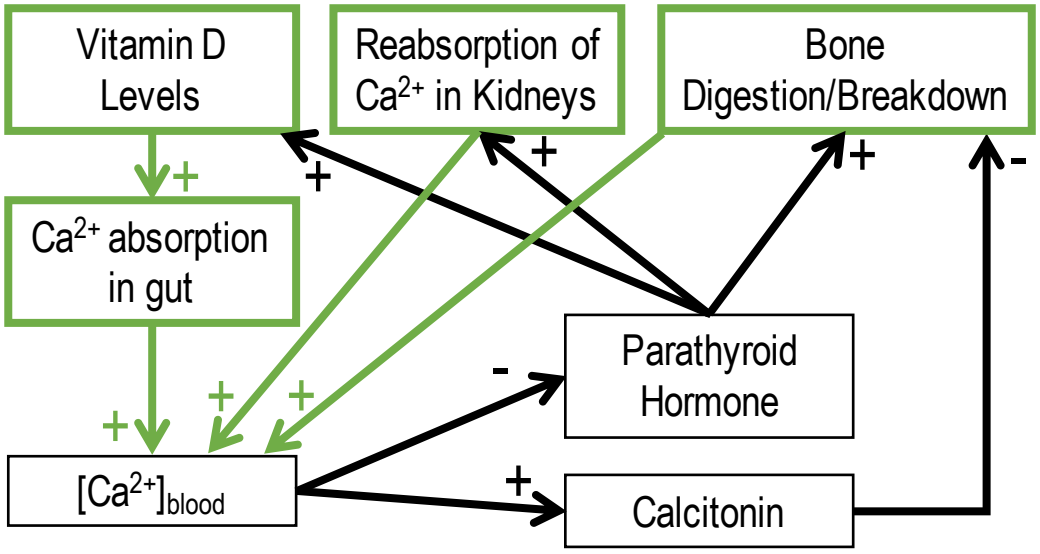
b) Micrograph of parathyroid tissue

CONCEPT: THE PARATHYROID GLAND

The Parathyroid Gland—Parathyroid Hormone and Calcitonin:

- **Parathyroid gland**, on the back side of the thyroid, secretes *parathyroid hormone* and *calcitonin.*
  - □ These two hormones generally function in controlling _____ levels in the blood.
- **Parathyroid Hormone (PTH)** is secreted in response to ↓$[Ca^{2+}]_{blood}$.
  - □ ↑PTH⟶↑Bone "Digestion" to release Ca^{2+}.
    - -Also: ↑Vitamin D absorption/production⟶↑Ca^{2+} absorption in gut.
    - -And: ↑Ca^{2+} reabsorption in the kidneys (stop peeing out Ca^{2+}).
- **Calcitonin** is secreted in response to ↑Ca^{2+}.
  - □ ↑Calcitonin⟶↑Bone Growth and ↓Bone Digestion/Breakdown.

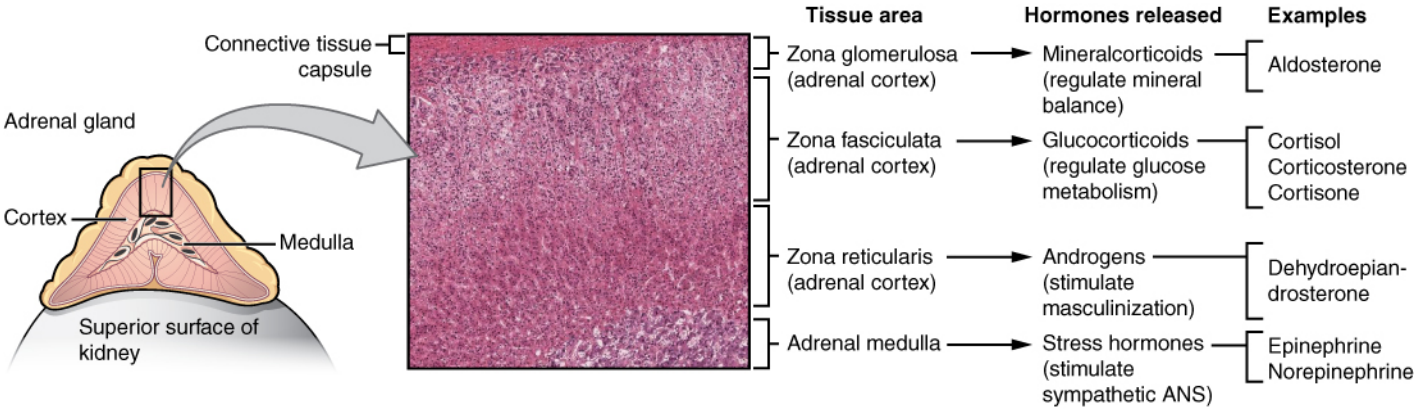
EXAMPLE: The negative feedback loop(s) for PTH and calcitonin.



CONCEPT: ADRENAL GLANDS

- The **adrenal glands** are paired pyramidal endocrine glands that sit on the superior surface of each _____
  - □ The glands are retroperitoneal and are anchored down with fascia and fat to reduce their movement
  - □ It has two main regions
    - The **adrenal cortex** makes up 80-90% of the adrenal gland
      - The high _____ content gives it a distinct yellow color and synthesizes corticosteroids
      - Is separated into 3 zones: glomerulosa, fasciculata, and reticularis
    - The **adrenal medulla** makes up 10-20% of the adrenal gland
      - Is highly vascularized giving it a red color; forms the inner core
      - Respond to sympathetic simulation by releasing catecholamines

EXAMPLE:



CONCEPT: THE ADRENAL GLANDS

Anatomy of the Adrenal Glands:

- **Adrenal Gland=** a pair of glands, one sitting atop each _____.
    - □ Adrenals are actually 2 glands in one—*adrenal cortex* on the outside and *adrenal medulla* on the inside.

EXAMPLE: The adrenal glands.

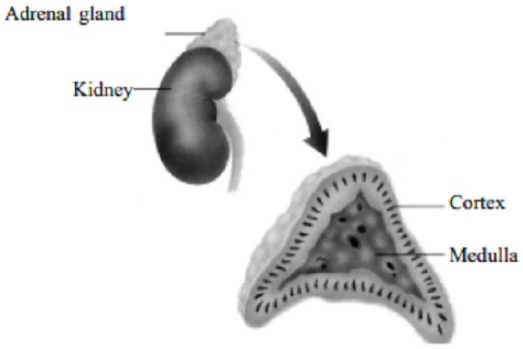
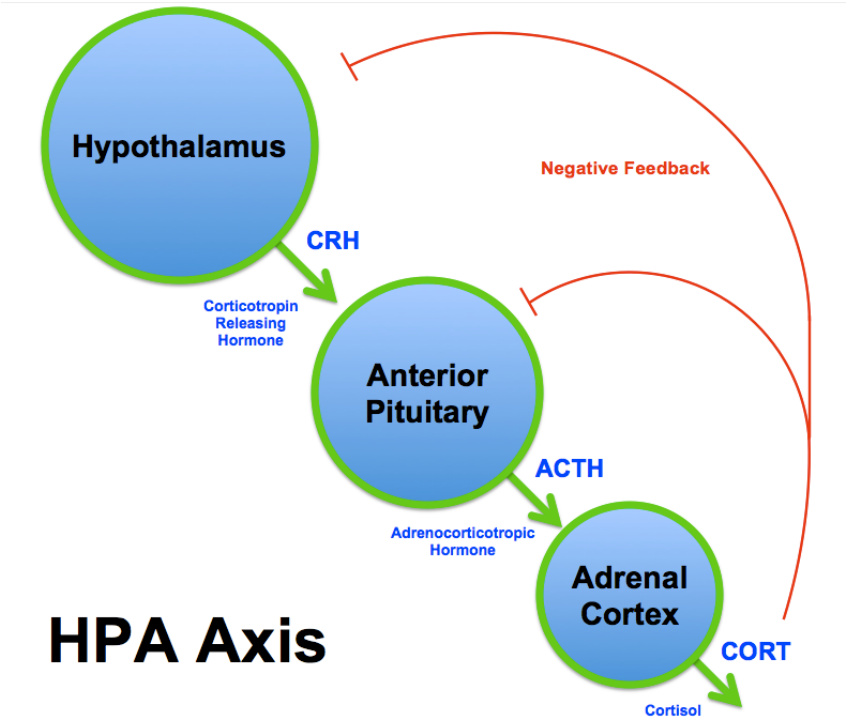


Fig. 29 : Adrenal Gland

The Adrenal Cortex and its Steroid Hormones:

- **Adrenal Cortex** secretes *steroid*s: *aldosterone*, the sex hormones (*testosterone*, *estrogen*, etc.), and *cortisol.*
  - □ **Aldosterone** acts on kidneys, promotes H_2O and Na^+ retention→↑Blood pressure.
    - -Controlled via massively-complicated Renin-Angiotensin-Aldosterone System (RAAS).
  - □ The sex hormones determine secondary sexual characteristics:
    - -**Testosterone**→↑Muscle production, ↑Body Hair ("manly" things).
    - -**Estrogen**→↑Body Fat (especially hips, thighs, breasts), role in control of menstrual cycle.
  - □ **Cortisol** is important part of the "stress" response:
    - -↑Gluconeogenesis and ↑β-oxidation→more energy.
    - -↑Muscle breakdown→use proteins for energy.
    - -↓Inflammation (that's the clinical use).
    - -Controlled by **Hypothalamus-Anterior Pituitary-Adrenal (HPA) Axis,** a classic negative feedback loop.

EXAMPLE: The HPA Axis: ↑Cortisol→↓CRH and ↓ACTH.



The Adrenal Medulla and Epinephrine:

- **Adrenal Medulla** secretes the catecholamine *epinephrine* into the general circulation.
    - □ **Epinephrine** (aka **adrenaline**) is the major *hormone* of the sympathetic nervous system→"fight-or-flight" effects.
        - -↑Heart rate, ↑Blood pressure, ↑Glycogenolysis, ↑β-oxidation, etc.
        - -(Similar effects to the sympathetic NT norepinephrine.)
    - □ Secretion controlled by pre-ganglionic sympathetic neurons.
        - -(Epinephrine-secreting cells in adrenal medulla actually modified post-ganglionic sympathetic neurons.)
        - -↑SNS Activity→↑Epinephrine secretion from adrenal medulla→↑$[Epinephrine]_{blood}$.

EXAMPLE: Epinephrine prepares the body for (stressful?) activity.

PRACTICE 1: Prednisone is a drug that is given to reduce inflammation. It acts exactly like—and binds at the same receptors as—cortisol. Levels of which of the following hormones will be *reduced* by the administration of prednisone? (Choose all that apply.)

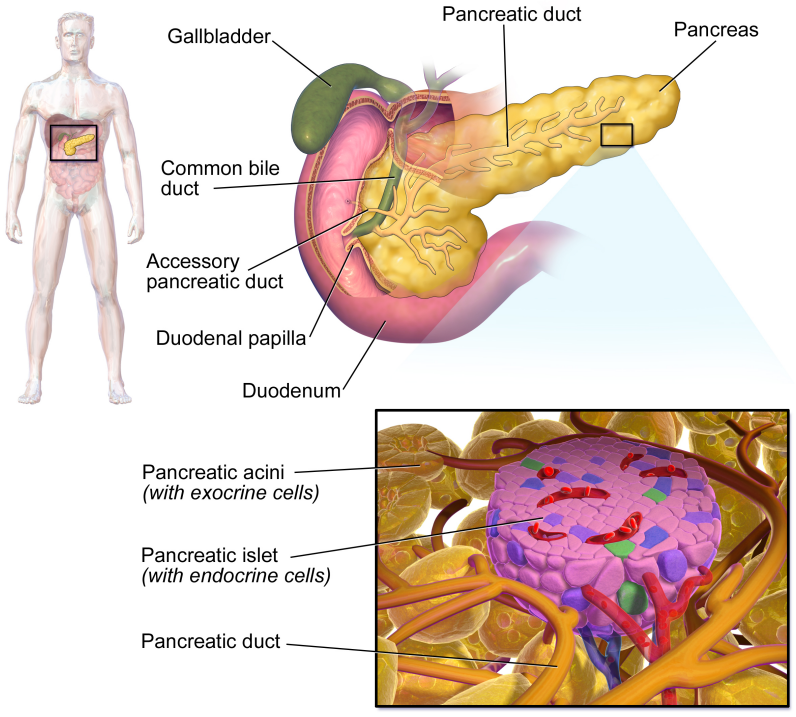
a) Corticotrophin releasing hormone (CRH).
b) Adrenocorticotrophic hormone (ACTH).
c) Cortisol.
d) Aldosterone.
e) Epinephrine.

CONCEPT: THE ENDOCRINE PANCREAS

The Endocrine Pancreas and Islets of Langerhans:

- **Pancreas** is a small glandular organ behind the _____.
  - □ Function revolves almost entirely around making and secreting proteins to be used by rest of body.
- Two general functions—as an *exocrine* gland and an *endocrine* gland.
  - □ As exocrine, secretes digestive hormones into small intestine (more much later, with digestive physiology).
- **Endocrine Pancreas** secretes three hormones: *glucagon*, *insulin*, and *somatostatin.*
- **Islets of Langerhans** are the clusters of endocrine cells in pancreas that secrete the above hormones. Three cell types:
  - □ α cells→glucagon □ β cells→insulin □δ cells→somatostatin

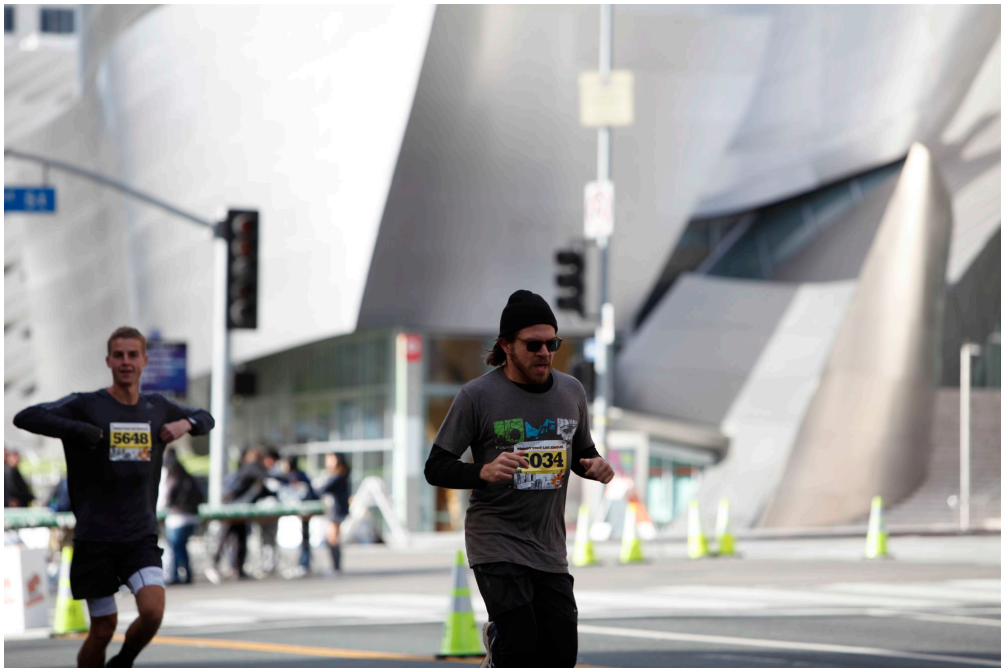
EXAMPLE: The pancreas and a close up of an islet.



Glucagon:

- **Glucagon** is secreted by pancreatic α cells in response to low blood _____.
  - □ Mostly affects liver, causing changes that ↑$[Glucose]_{blood}$.
    - -↑Glycogenolysis, ↑Gluconeogenesis

EXAMPLE: Glucagon levels increase when blood glucose is low, like in endurance exercise.



Insulin:

● **Insulin** is secreted from pancreatic β cells in response to high blood _____.

□ Acts on many cell types, especially liver and skeletal muscle. Generally:

-↑Glucose uptake from blood into cells, ↑Glycogen synthesis.

- ↓Gluconeogenesis, ↓Lipolysis/β-oxidation

EXAMPLE: Insulin levels rise when blood glucose levels increase, like after a large meal.

Somatostatin:

● **Somatostatin** (SST, aka growth hormone inhibiting hormone) is a complicated and not-deeply-understood hormone.

□ Works in opposition to growth hormone (from the anterior pituitary) throughout the body.

□ From pancreas, SST is released during meal absorption and slows the absorption process

-Slows absorption→prevents too much nutrients from amassing in blood.

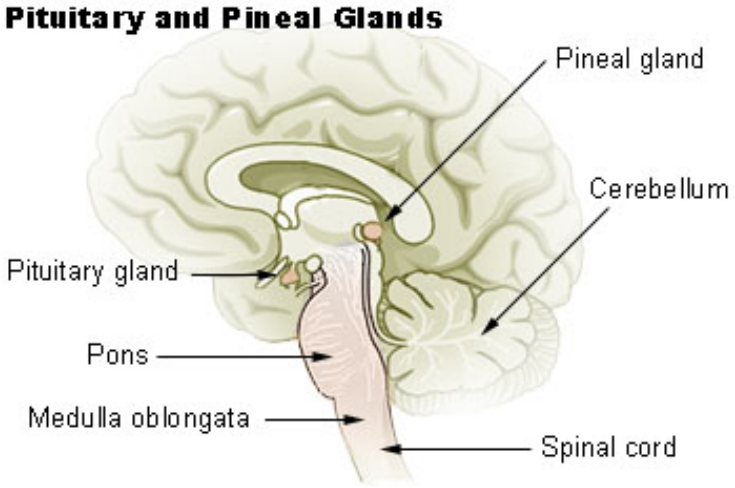
PRACTICE 1: Type I diabetes is caused by immune attack on the cells that produce insulin. Which of the following cell types are attacked by the immune systems of patients with Type I diabetes?

a) α cells.
b) β cells.
c) δ cells.

CONCEPT: PINEAL GLAND

- The **pineal gland** is a cone-shaped structure that makes up the _____ of the epithalamus
  - □ The pineal gland secretes melatonin, which regulates sleep patterns
    - Melatonin may also regulate the synthesis of some anterior pituitary hormones

EXAMPLE:



CONCEPT: THYMUS

- The **thymus** is found superior anterior to the heart, posterior to the sternum
  - □ Is a _____ organ, that may differ in size but are commonly fused, where T cells mature
  - □ Is pinkish-grey color with lobules that are held together by delicate areolar tissue
  - □ Is a specialized primary lymphoid organ of the immune system
  - □ It is comparatively large in babies, grows larger during _____, and then shrinks in adulthood
  - □ It is speculated that the regression of the thymus may make the elderly more susceptible to diseases

EXAMPLE: