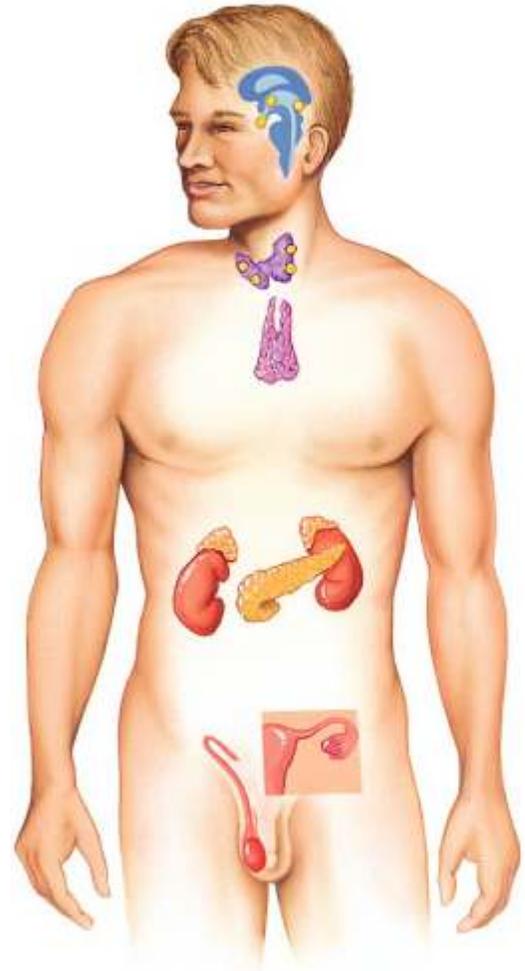


The Endocrine System

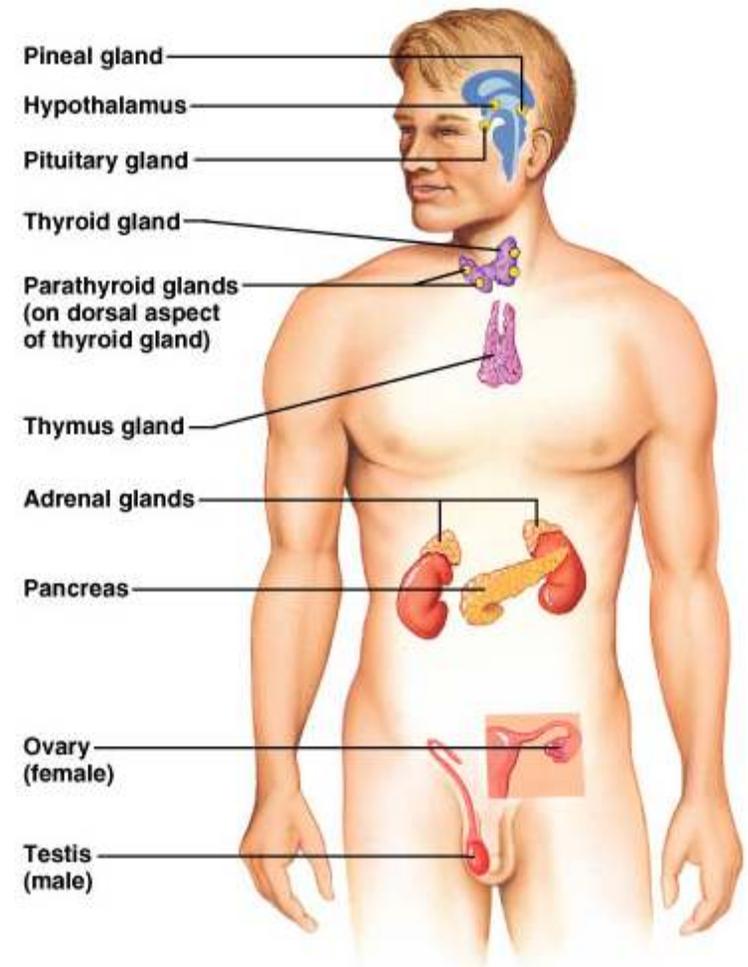


Overview of the Endocrine System

- System of ductless glands that secrete hormones
 - Hormones are “messenger molecules”
 - Circulate in the blood
 - Act on distant target cells
 - Target cells respond to the hormones for which they have receptors
 - The effects are dependent on the programmed response of the target cells
 - Hormones are just molecular triggers
- Basic categories of hormones
 - Amino acid based: modified amino acids (or *amines*), peptides (short chains of amino acids), and proteins (long chains of amino acids)
 - Steroids: lipid molecules derived from cholesterol

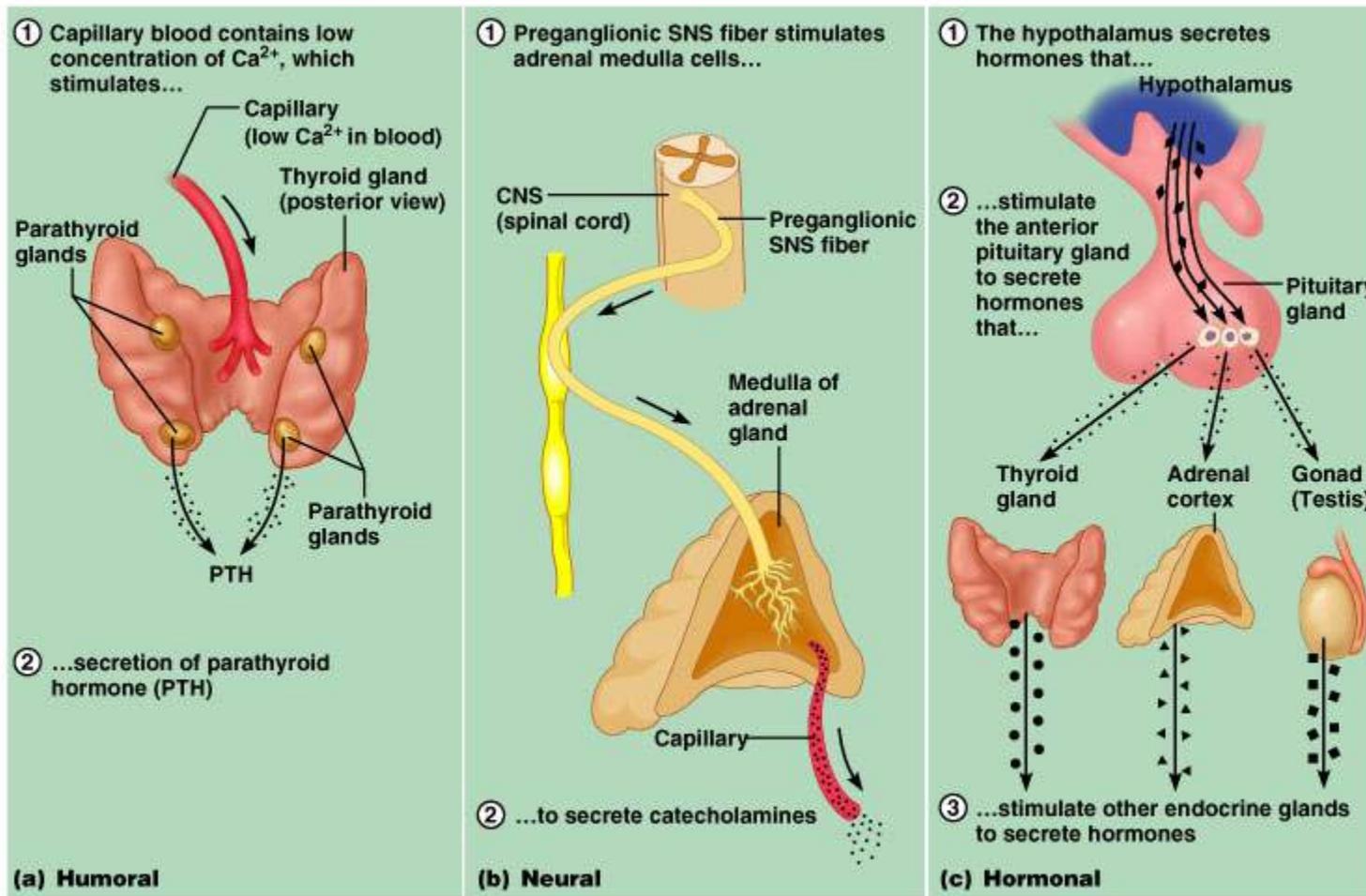
Endocrine Organs

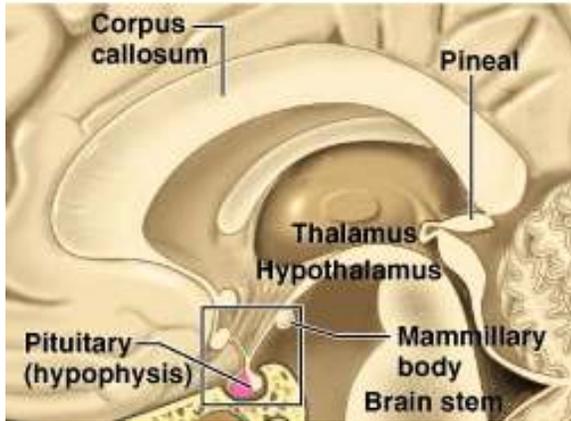
- Purely endocrine organs
 - Pituitary gland
 - Pineal gland
 - Thyroid gland
 - Parathyroid glands
 - Adrenal: 2 glands
 - Cortex
 - Medulla
- Endocrine cells in other organs
 - Pancreas
 - Thymus
 - Gonads
 - Hypothalamus



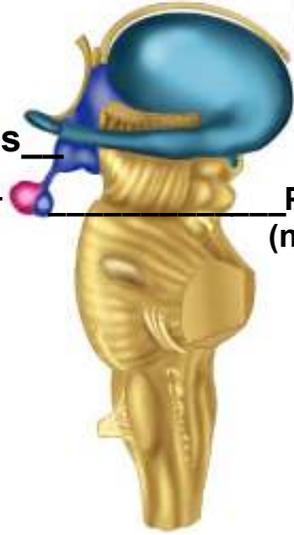
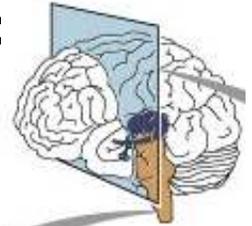
Mechanisms of hormone release

- (a) **Humoral:** in response to changing levels of ions or nutrients in the blood
- (b) **Neural:** stimulation by nerves
- (c) **Hormonal:** stimulation received from other hormones

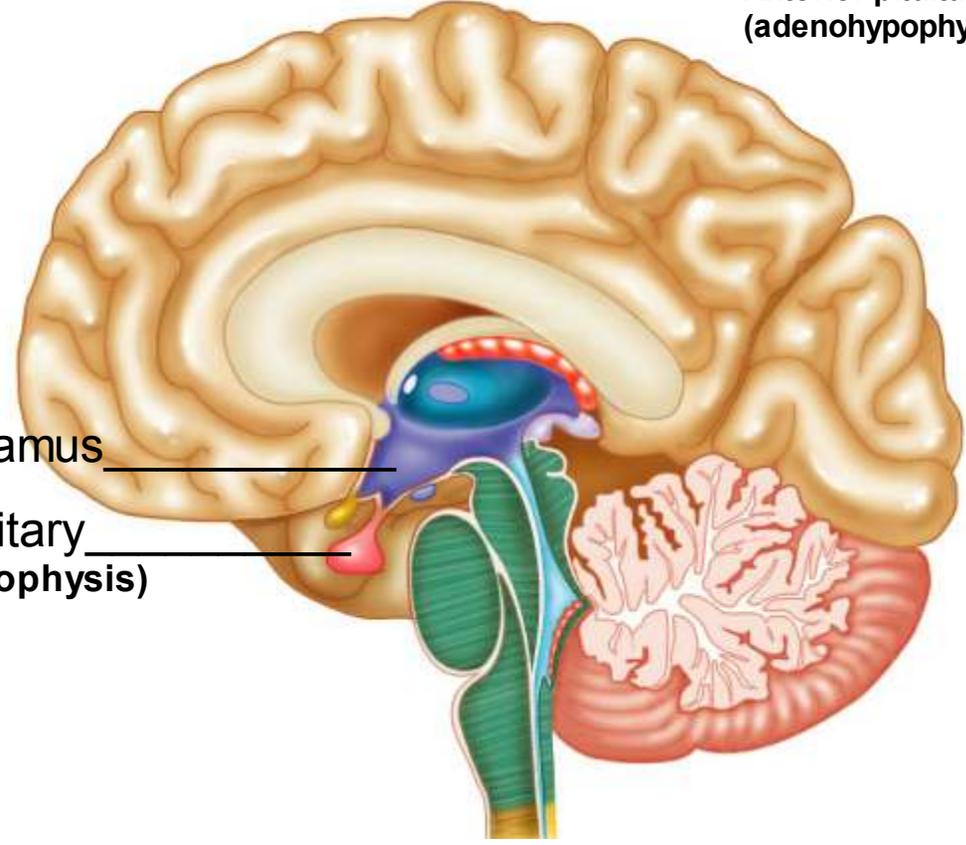




Learn the 3 endocrine organs on this slide:
Hypothalamus
Pituitary (hypophysis)
Pineal



Hypothalamus
Anterior pituitary (adenohypophysis)
Posterior pituitary (neurohypophysis)



Hypothalamus
Pituitary (hypophysis)

The Pituitary

Sits in hypophyseal fossa: depression in sella turcica of sphenoid bone

Pituitary secretes 9 hormones

Two divisions:

- Anterior pituitary
(adenohypophysis)

1. TSH

2. ACTH

3. FSH

4. LH

5. GH

6. PRL

7. MSH

The first four are “tropic” hormones, they regulate the function of other hormones

- Posterior pituitary
(neurohypophysis)

8. ADH (antidiuretic hormone), or vasopressin

9. Oxytocin

What the letters stand for...

- TSH: thyroid-stimulating hormone
- ACTH: adrenocorticotropic hormone
- FSH: follicle-stimulating hormone
- LH: luteinizing hormone
- GH: growth hormone
- PRL: prolactin
- MSH: melanocyte-stimulating hormone

- ADH: antidiuretic hormone
- Oxytocin

Hypothalamus controls anterior pituitary hormone release

- Releasing hormones (releasing factors)
 - Secreted like neurotransmitters from neuronal axons into capillaries and veins to anterior pituitary (adenohypophysis)
 - TRH**-----turns on TSH
 - CRH**-----turns on ACTH
 - GnRH** (=LHRH)---turns on FSH and LH
 - PRF**-----turns on PRL
 - GHRH**----turns on GH
- Inhibiting hormones
 - PIF**-----turns off PRL
 - GH inhibiting hormone** ---turns off GH

What the letters mean...

- Releasing hormones (releasing factors) of **hypothalamus**
Secreted like neurotransmitters from neuronal axons into capillaries and veins to anterior pituitary (adenohypophysis)
 - TRH (thyroid releasing hormone)** -----turns on* TSH
 - CRH (corticotropin releasing hormone)** -----turns on ACTH
 - GnRH (gonadotropin releasing hormone)** ---turns on FSH and LH
 - PRF (prolactin releasing hormone)** -----turns on PRL
 - GHRH (growth hormone releasing hormone)** ----turns on GH
- Inhibiting hormones of **hypothalamus**
 - PIF (prolactin inhibiting factor)** -----turns off PRL
 - GH (growth hormone) inhibiting hormone** ---turns off GH

The hypothalamus controls secretion of hormones which in their turn control the secretion of hormones by the thyroid gland, the adrenal cortex and gonads: in this way the brain controls these endocrine glands

*Note: “turns on” means causes to be released

So what do the pituitary hormones do?

The four tropic ones regulate the function of other hormones:

- TSH stimulates the thyroid to produce thyroid hormone
- ACTH stimulates the adrenal cortex to produce corticosteroids: aldosterone and cortisol
- FSH stimulates follicle growth and ovarian estrogen production; stimulates sperm production and androgen-binding protein
- LH has a role in ovulation and the growth of the corpus luteum; stimulates androgen secretion by interstitial cells in testes

The others from the anterior pituitary...

- GH (aka somatotropic hormone) stimulates growth of skeletal epiphyseal plates and body to synthesize protein
- PRL stimulates mammary glands in breast to make milk
- MSH stimulates melanocytes; may increase mental alertness

From the posterior pituitary (neurohypophysis)
structurally part of the brain

- ADH (antidiuretic hormone AKA vasopressin) stimulates the kidneys to reclaim more water from the urine, raises blood pressure
- Oxytocin prompts contraction of smooth muscle in reproductive tracts, in females initiating labor and ejection of milk from breasts

Can we put it all together?

Blue is from hypothalamus

Black is from pituitary

TRH (thyroid releasing hormone)

turns on TSH

CRH (corticotropin releasing hormone)

turns on ACTH

GnRH (gonadotropin releasing hormone)

turns on FSH and LH

PRF (prolactin releasing hormone)

turns on PRL

GHRH (growth hormone releasing hm)

turns on GH

TSH: thyroid-stimulating hormone

ACTH: adrenocorticotropin hormone

FSH: follicle-stimulating hormone

LH: luteinizing hormone

GH: growth hormone

PRL: prolactin

MSH: melanocyte-stimulating hormone

ADH: antidiuretic hormone

Oxytocin

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stimulates growth of skeletal epiphyseal plates and body to synthesize protein

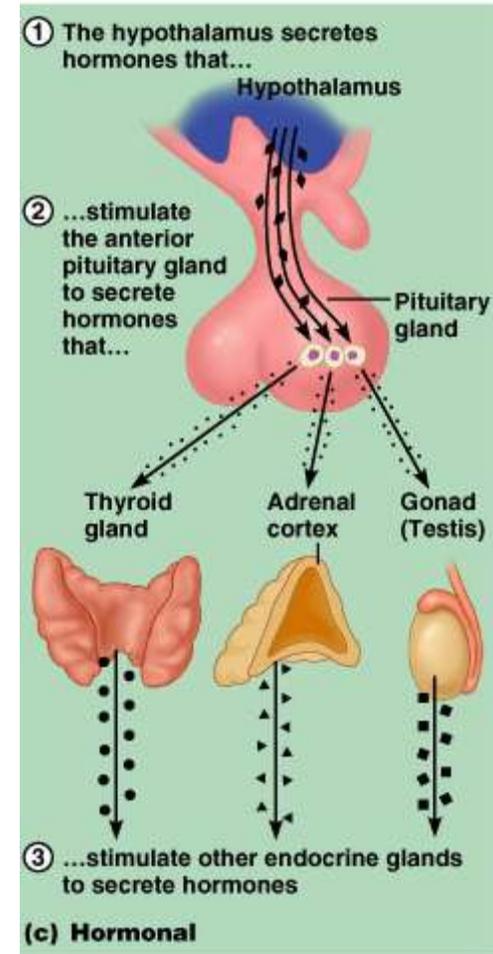
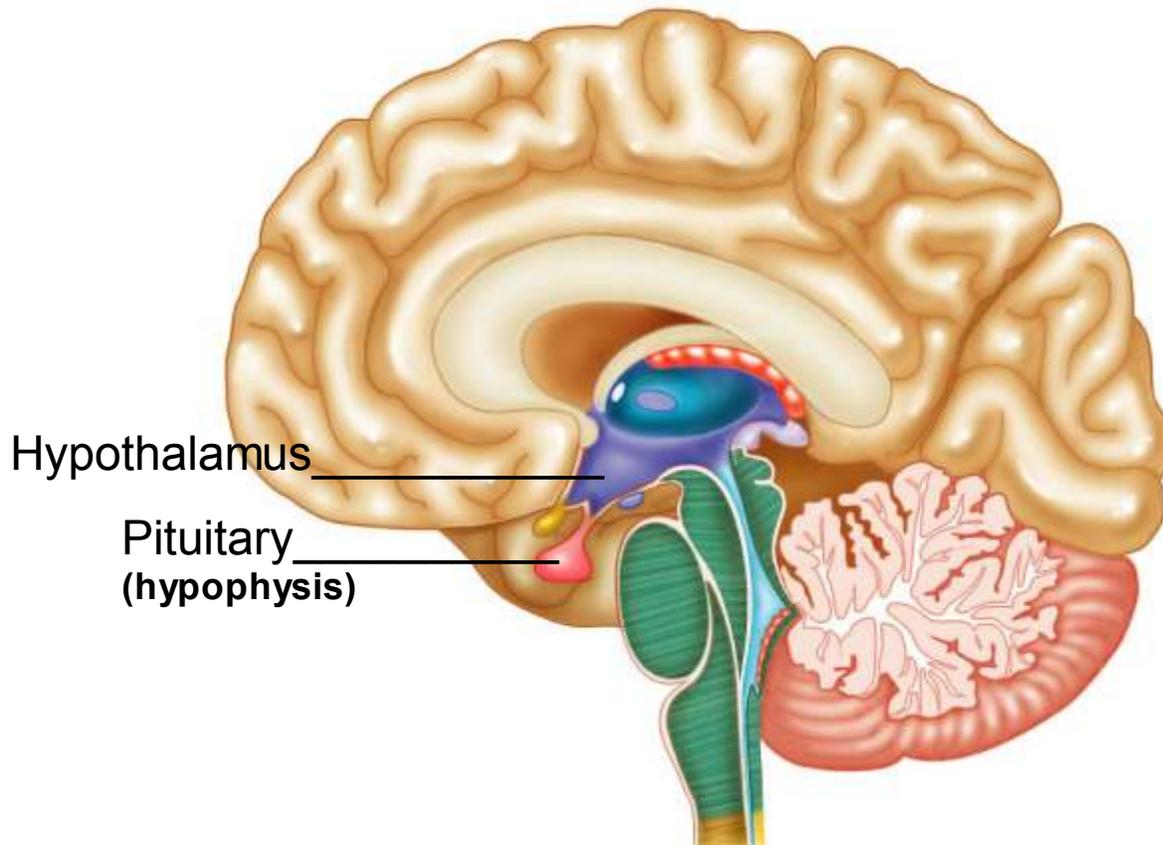
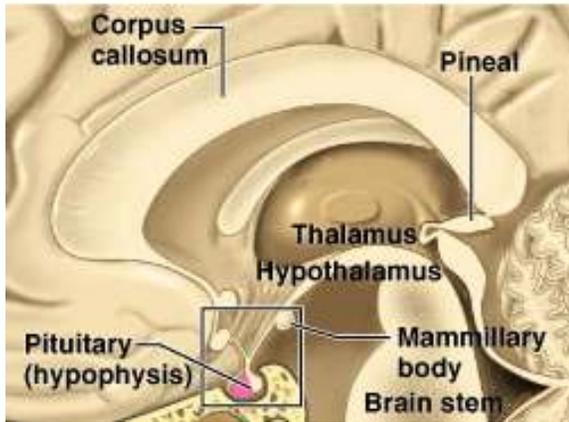
PRL stimulates mammary glands in breast to make milk

MSH stimulates melanocytes; may increase mental alertness

ADH (antidiuretic hormone or vasopressin) stimulates the kidneys to reclaim more water from the urine, raises blood pressure

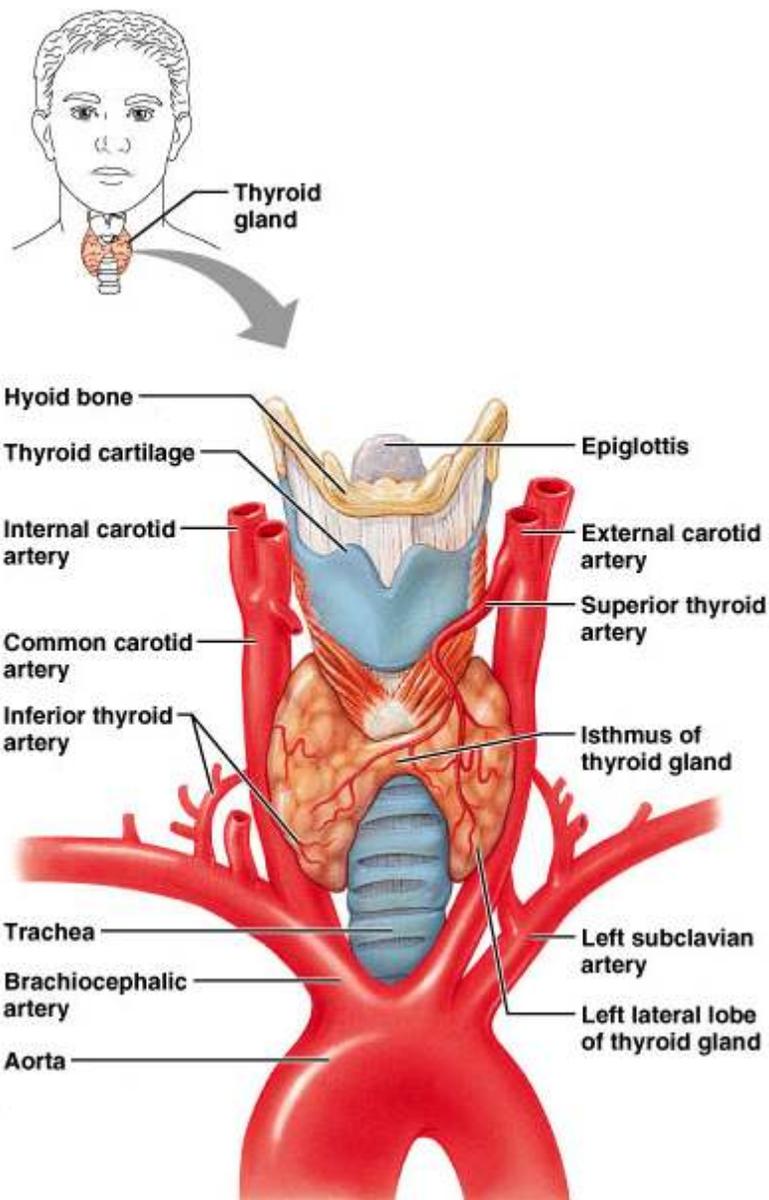
Oxytocin prompts contraction of smooth muscle in reproductive tracts, in females initiating labor and ejection of milk from breasts

Now try and remember the anatomy

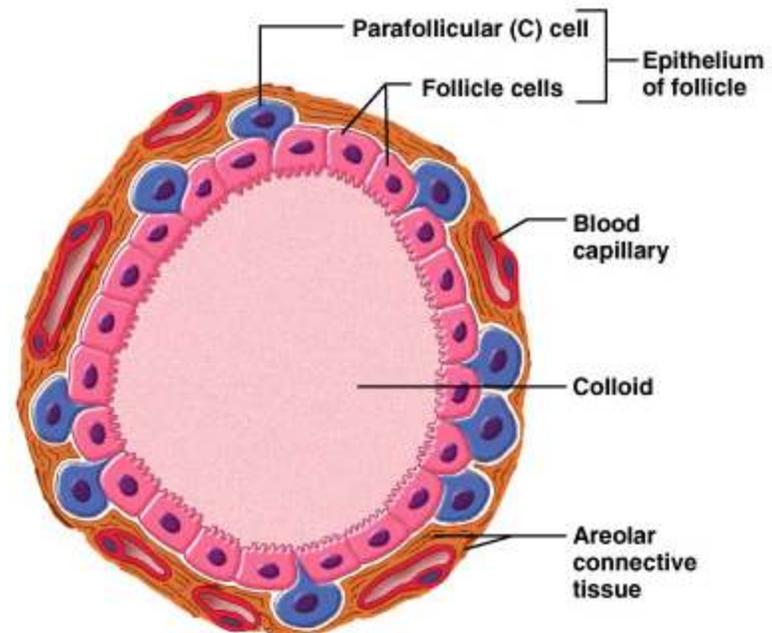
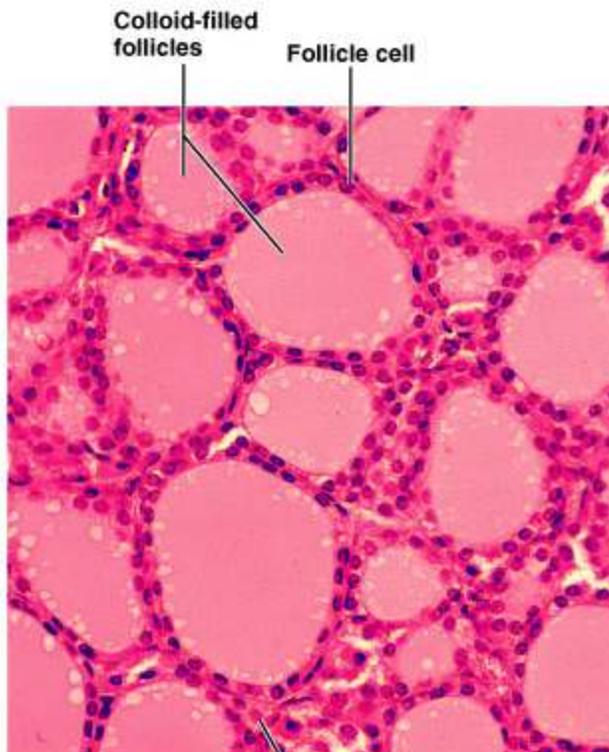


The Thyroid Gland

- Anterior neck on trachea just inferior to larynx
- Two lateral lobes and an isthmus
- Produces two hormones
 - Thyroid hormone: tyrosine based with 3 or 4 iodine molecules
 - T4 (thyroxine) and T3
 - Calcitonin involved with calcium and phosphorus metabolism



- Thyroid is composed of spherical follicles
 - Follicle cells: produce thyroglobulin, the precursor of thyroid hormone (thyroxin)
 - Colloid lumen is of thyroglobulin
 - Parafollicular “C” cells: produce calcitonin



An example of a feedback loop

generic

- A certain item in the blood decreases
- A certain area of the brain senses this decrease
- A certain hormone is released
- This hormone stimulates the release of another hormone
- This other hormone stimulates the release of the hormone which was sensed to be decreased in the first place, causing it to be increased to desired level

particular example: thyroid hormone

- Thyroxine (thyroid hormone)
- Hypothalamus
- TRF from the hypothalamus
- TSH from anterior pituitary
- Thyroxine from the thyroid (TSH has caused cleavage of thyroglobulin into thyroxine)

Some Effects of Thyroid Hormone (Thyroxine)

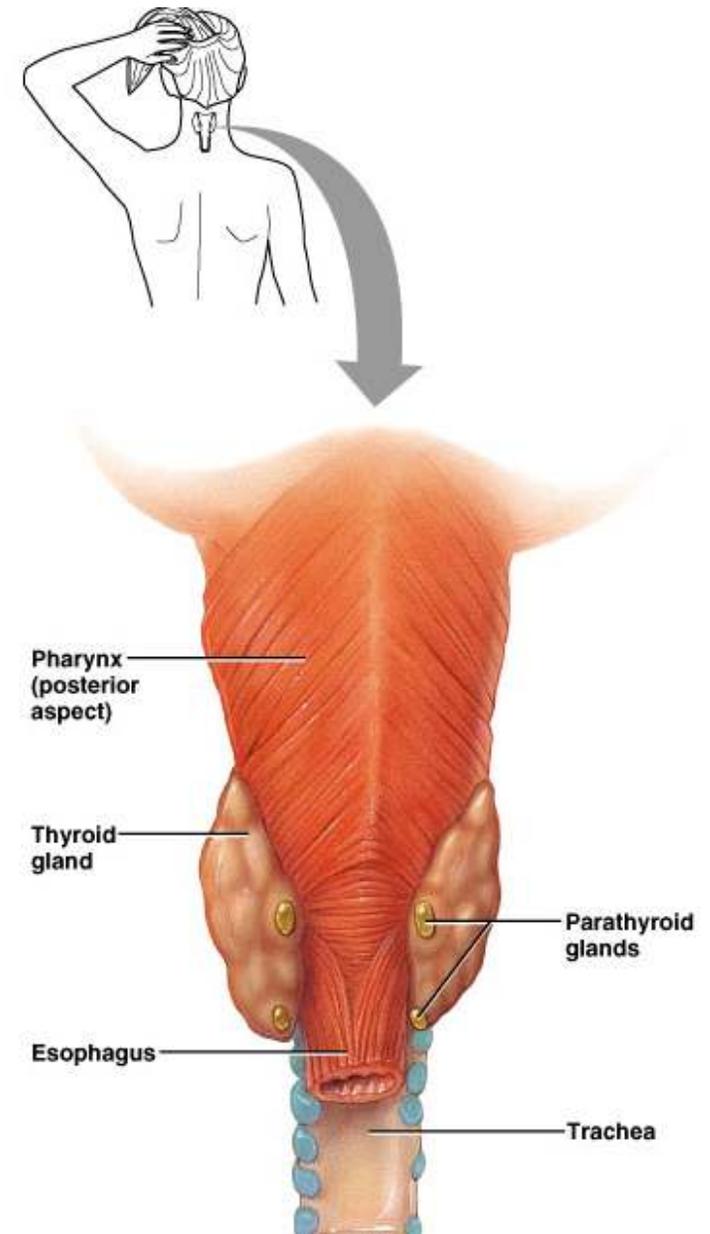
- Increases the basal metabolic rate
 - The rate at which the body uses oxygen to transform nutrients (carbohydrates, fats and proteins) into energy
- Affects many target cells throughout the body; some effects are
 - Protein synthesis
 - Bone growth
 - Neuronal maturation
 - Cell differentiation

The Effects of Calcitonin

- Secreted from thyroid parafollicular (C) cells when blood calcium levels are high
- Calcitonin lowers Ca^{++} by slowing the calcium-releasing activity of osteoclasts in bone and increasing calcium secretion by the kidney
- Acts mostly during childhood

The Parathyroid Glands

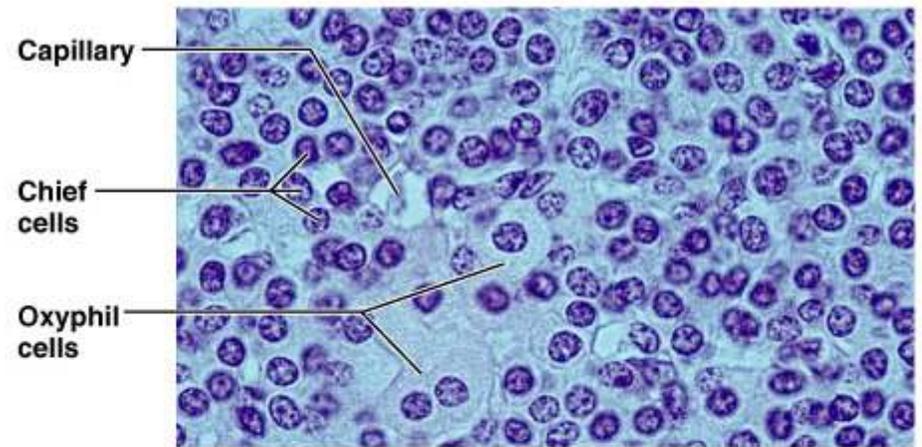
- Most people have four
- On posterior surface of thyroid gland (sometimes embedded)



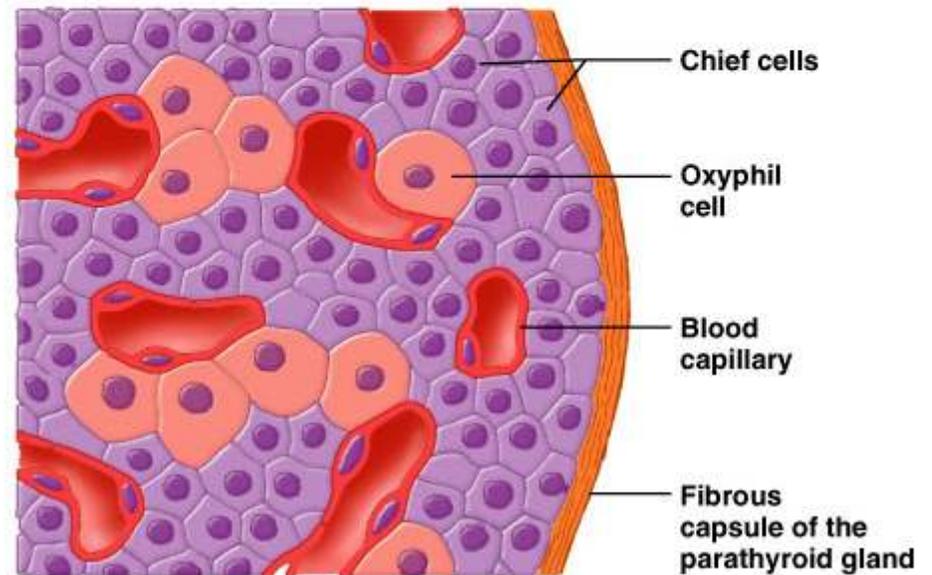
Parathyroids (two types of cells)

- Rare chief cells
- Abundant oxyphil cells (unknown function)

- Chief cells produce PTH
 - Parathyroid hormone, or parathormone
 - A small protein hormone



(b)



(c)

Function of PTH

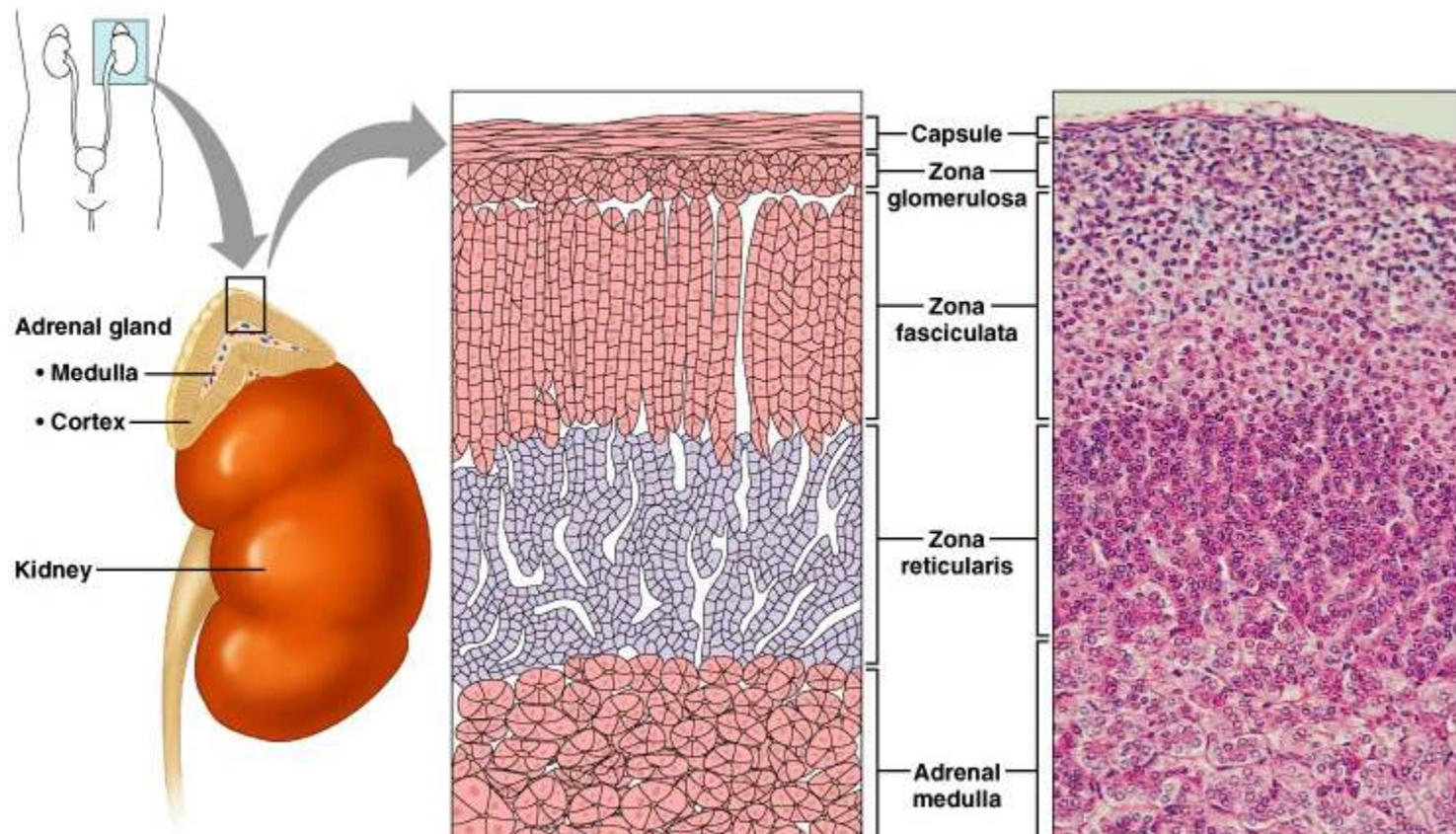
(parathyroid hormone or “parathormone”)

- ***Increases blood Ca^{++} (calcium) concentration when it gets too low***
- Mechanism of raising blood calcium
 1. Stimulates osteoclasts to release more Ca^{++} from bone
 2. Decreases secretion of Ca^{++} by kidney
 3. Activates Vitamin D, which stimulates the uptake of Ca^{++} from the intestine
- Unwitting removal during thyroidectomy was lethal
- ***Has opposite effect on calcium as calcitonin (which lowers Ca^{++} levels)***

Adrenal (suprarenal) glands

(“suprarenal” means on top of the kidney)

- Each is really two endocrine glands
 - Adrenal cortex (outer)
 - Adrenal medulla (inner)
- Unrelated chemicals but all help with extreme situations



Adrenal Gland

- Adrenal cortex
 - Secretes lipid-based steroid hormones, called “corticosteroids” – “cortico” as in “cortex”
 - MINERALOCORTICIDS
 - Aldosterone is the main one
 - GLUCOCORTICIDS
 - Cortisol (hydrocortisone) is the main one
- Adrenal medulla
 - Secretes epinephrine and norepinephrine

Aldosterone, the main *mineralocorticoid*

- Secreted by adrenal cortex in response to a decline in either blood volume or blood pressure (e.g. severe hemorrhage)
 - Is terminal hormone in renin-angiotensin mechanism
- Prompts distal and collecting tubules in kidney to reabsorb more sodium
 - Water passively follows
 - Blood volume thus increases

Cortisol, the most important *glucocorticoid*

(Glucocorticoid receptors are found in the cells of most vertebrate tissues)

- It is essential for life
- Helps the body deal with stressful situations within minutes
 - Physical: trauma, surgery, exercise
 - Psychological: anxiety, depression, crowding
 - Physiological: fasting, hypoglycemia, fever, infection
- Regulates or supports a variety of important cardiovascular, metabolic, immunologic, and homeostatic functions including water balance

People with adrenal insufficiency: these stresses can cause hypotension, shock and death: must give glucocorticoids, eg for surgery or if have infection, etc²⁶

Cortisol, continued

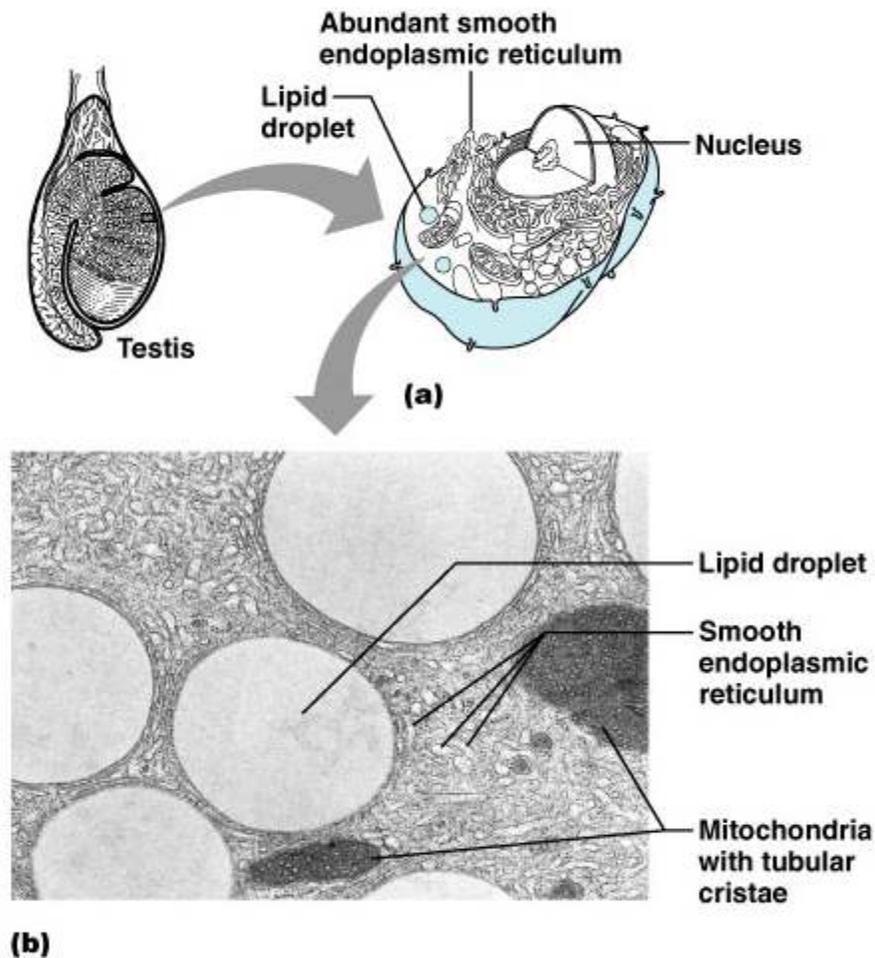
- Keeps blood glucose levels high enough to support brain's activity
 - Forces other body cells to switch to fats and amino acids as energy sources
- Catabolic: break down protein
- Redirects circulating lymphocytes to lymphoid and peripheral tissues where pathogens usually are
- In large quantities, depresses immune and inflammatory response
 - Used therapeutically
 - Responsible for some of its side effects

Hormonal stimulation of glucocorticoids

HPA axis (hypothalamic/pituitary/adrenal axis)

- With stress, hypothalamus sends CRH to anterior pituitary (adenohypophysis)
- Pituitary secretes ACTH
- ACTH goes to adrenal cortex where stimulates glucocorticoid secretion
 - Sympathetic nervous system can also stimulate it
- Adrenal cortex also secretes DHEA (dehydroepiandrosterone)
 - Converted in peripheral tissues to testosterone and estrogen (also steroid hormones)
 - Unclear function in relation to stress

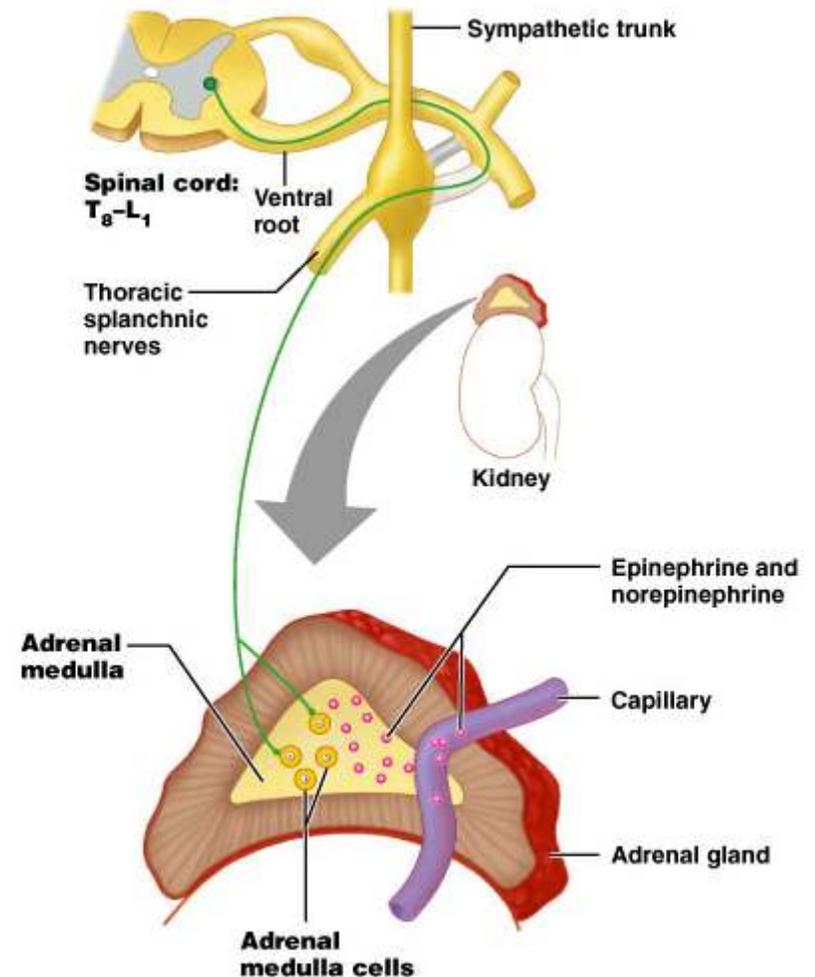
In general:



- Steroid-secreting cells have abundant smooth ER
 - As opposed to rough ER in protein-secreting cells
- Steroids directly diffuse across plasma membrane
 - Not exocytosis
- Abundant lipid droplets
 - Raw material from which steroids made

Adrenal medulla

- Part of autonomic nervous system
- Spherical chromaffin cells are modified postganglionic sympathetic neurons
 - Secrete epinephrine and norepinephrine
 - Amine hormones
 - Fight, flight, fright
- Vesicles store the hormones



The Pineal Gland

- At the end of a short stalk on the roof of the diencephalon
- Pinealocytes with dense calcium particles
- Can be seen on x-ray (because of Ca^{++})
- Melatonin helps regulate the circadian rhythm
 - The biological clock of the diurnal (night/day) rhythm
 - Complicated feedback via retina's visual input

The Pancreas

Exocrine and *endocrine* cells

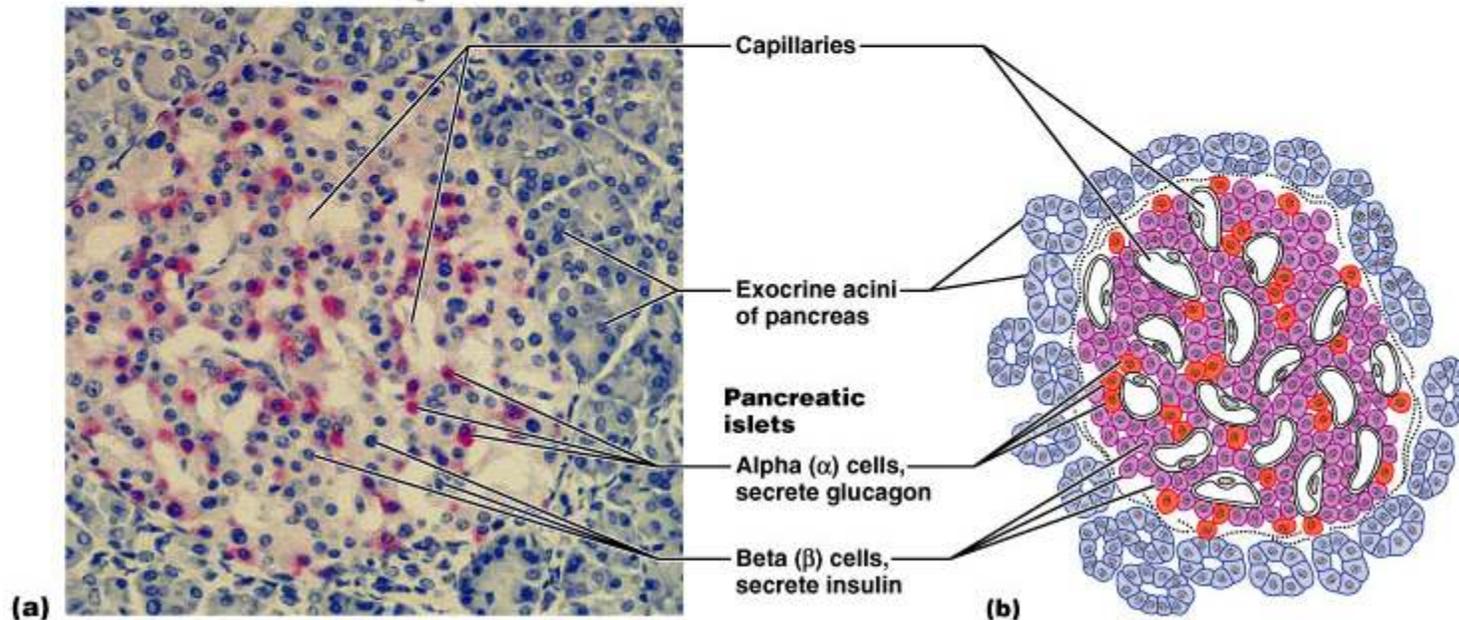
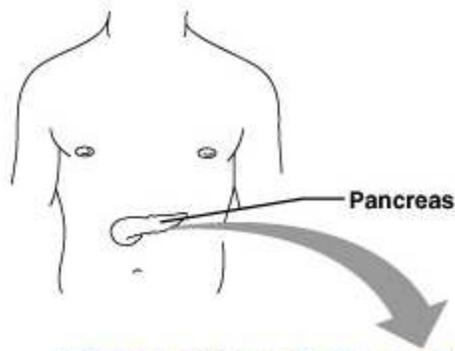
- *Acinar* cells (forming most of the pancreas)
 - *Exocrine* function
 - Secrete digestive enzymes
- *Islet* cells (of Langerhans)
 - *Endocrine* function

Pancreatic islet endocrine cells

Alpha cells: secrete **glucagon**
raises blood sugar
mostly in periphery

Beta cells: secrete **insulin**
lowers blood sugar
central part (are more abundant)

Also rare **Delta** cells: secrete
somatostatin
inhibits glucagon



The Gonads (testes and ovaries)

main source of the steroid sex hormones

- Testes
 - Interstitial cells secrete androgens
 - Primary androgen is testosterone
 - Maintains secondary sex characteristics
 - Helps promote sperm formation
- Ovaries
 - Androgens secreted by thecal folliculi
 - Directly converted to estrogens by follicular granulosa cells
 - Granulosa cells also produce progesterone
 - Corpus luteum also secretes estrogen and progesterone

Endocrine cells in various organs

- The heart: atrial natriuretic peptide (ANP)
 - Stimulates kidney to secrete more salt
 - Thereby decreases excess blood volume, high BP and high blood sodium concentration
- GI tract & derivatives: Diffuse neuroendocrine system (DNES)

Endocrine cells in various organs continued

- The heart: atrial natriuretic peptide (ANP)
 - Stimulates kidney to secrete more salt
 - Thereby decreases excess blood volume, high BP and high blood sodium concentration
- GI tract & derivatives: Diffuse neuroendocrine system (DNES)
- The placenta secretes steroid and protein hormones
 - Estrogens, progesterone
 - CRH
 - HCG
- The kidneys
 - Juxtaglomerular cells secrete renin
 - Renin indirectly signals adrenal cortex to secrete aldosterone
 - Erythropoietin: signals bone marrow to increase RBC production
- The skin
 - Modified cholesterol with uv exposure becomes Vitamin D precursor
 - Vitamin D necessary for calcium metabolism: signals intestine to absorb Ca^{++}

Pathology

- Pituitary
 - Gigantism –too much GH in childhood
 - Acromegaly – too much GH in adulthood
 - Pituitary dwarfs – too little GH in childhood
 - Diabetes insipidus - too much ADH
- Pancreas
 - Diabetes mellitus – one type of insulin (not enough)
- Thyroid
 - Hyperthyroidism, commonest is Grave's disease (autoimmune)
 - Hypothyroidism
 - In childhood leads to cretinism
 - Endemic goiter from insufficient iodine in diet
 - Adult hypothyroidism (myxedema): autoimmune



(a)

**Exophthalmos of
Grave's disease**



(b)

**Enlarged thyroid
(goiter) from
iodine deficiency**

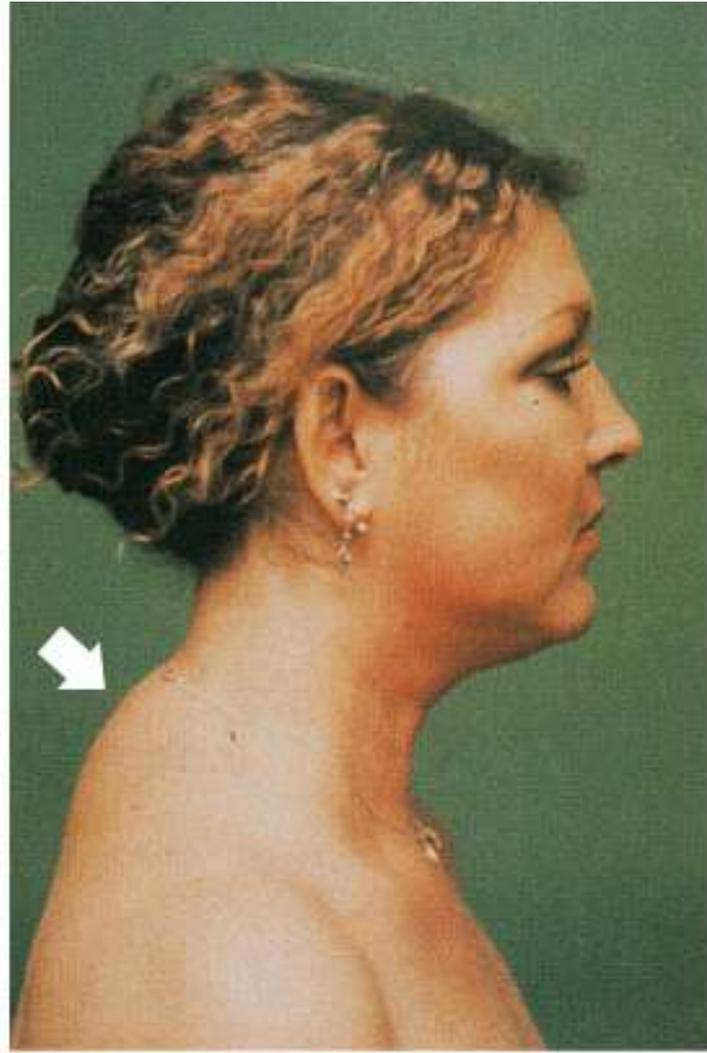
Pathology, continued

- Adrenal gland
 - Cushing's syndrome (see next pic)
 - Usually caused by an ACTH-secreting pituitary tumor
 - Rarely by tumor of adrenal cortex
 - Iatrogenic
 - Addison's disease
 - Hyposecretion (under secretion) of adrenal cortex
 - Usually involves cortisol and aldosterone: low blood glucose and sodium, severe dehydration, fatigue, loss of appetite, abdominal pain
(Jane Austin)

Before and after onset of Cushing's disease



(a) Before



(b) After