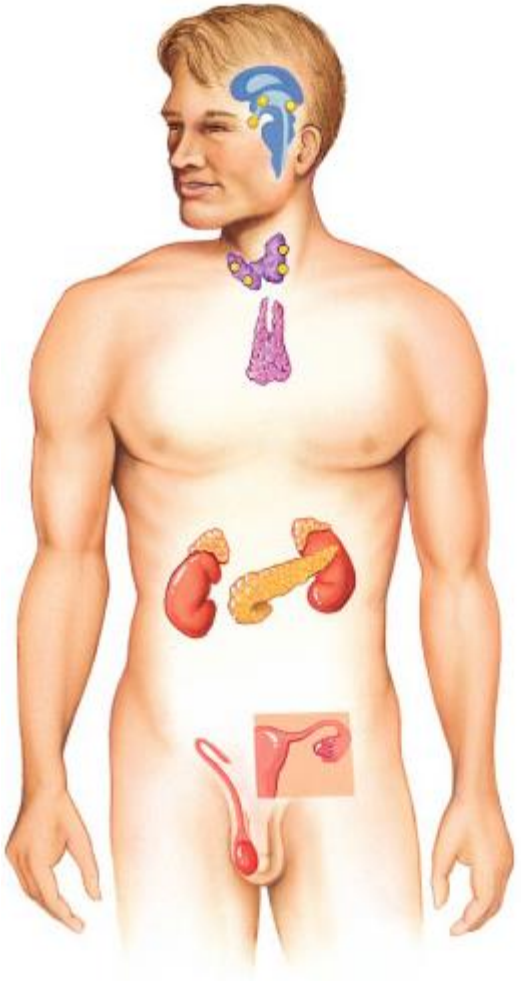
The Endocrine System

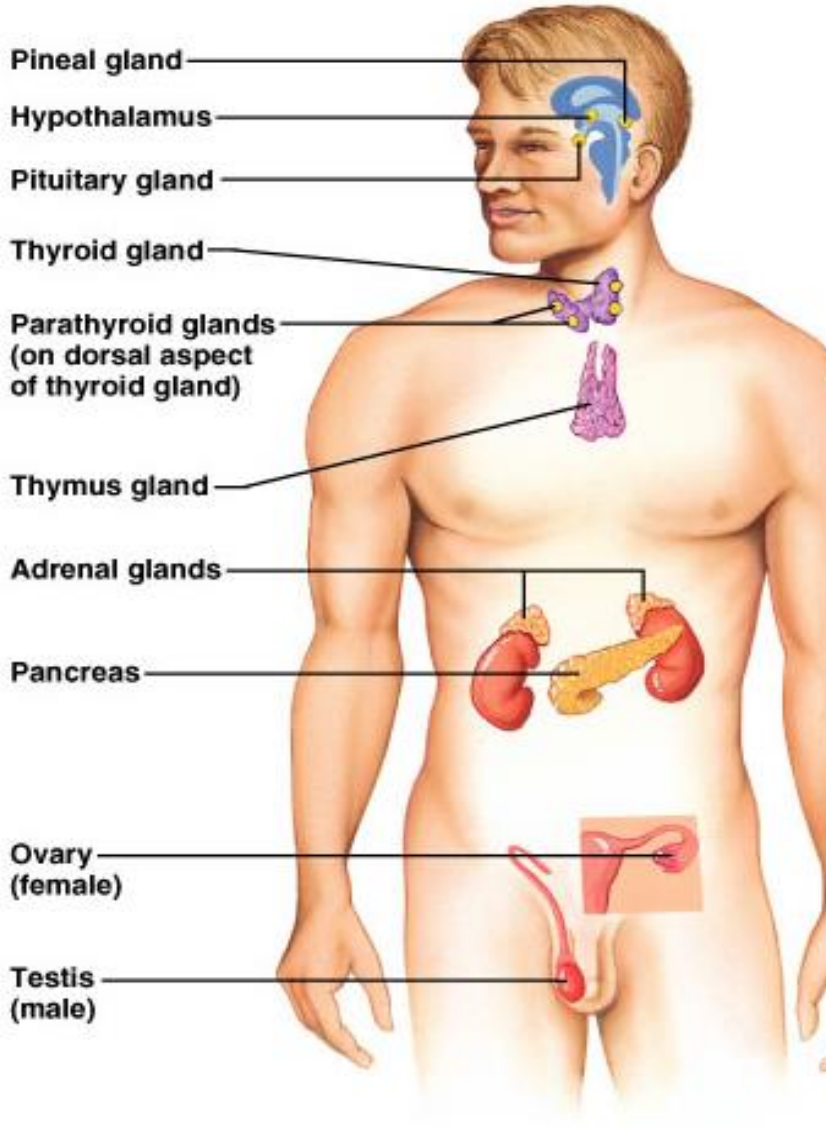


Overview of the Endocrine System

- 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

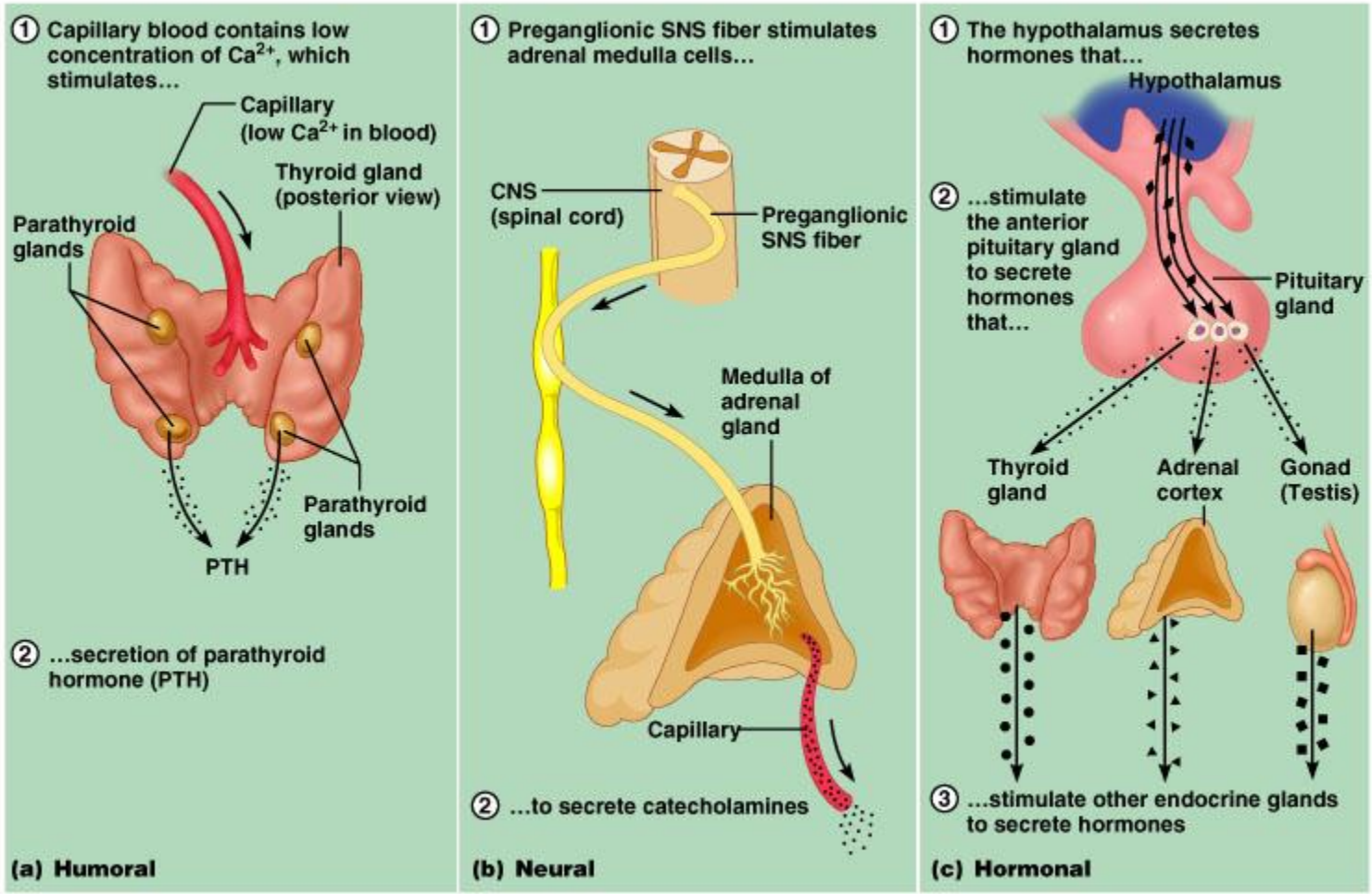


Mechanisms of hormone release

(a) Humoral: in response to changing levels of ions or nutrients in the blood

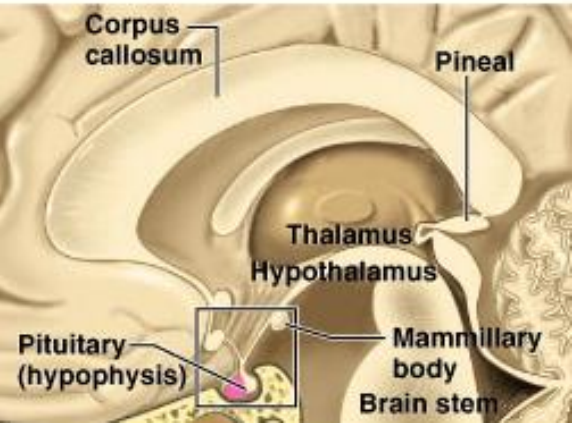
(b) Neural: stimulation by nerves

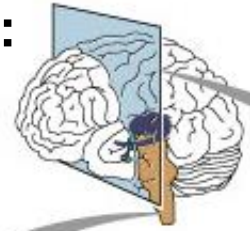
(c) Hormonal: stimulation received from other hormones

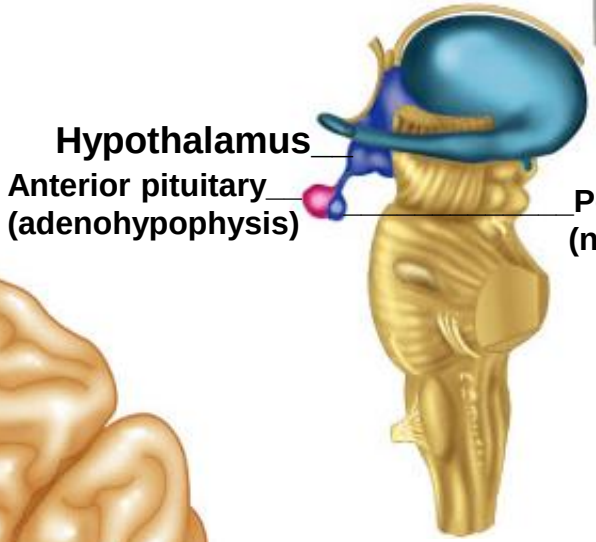


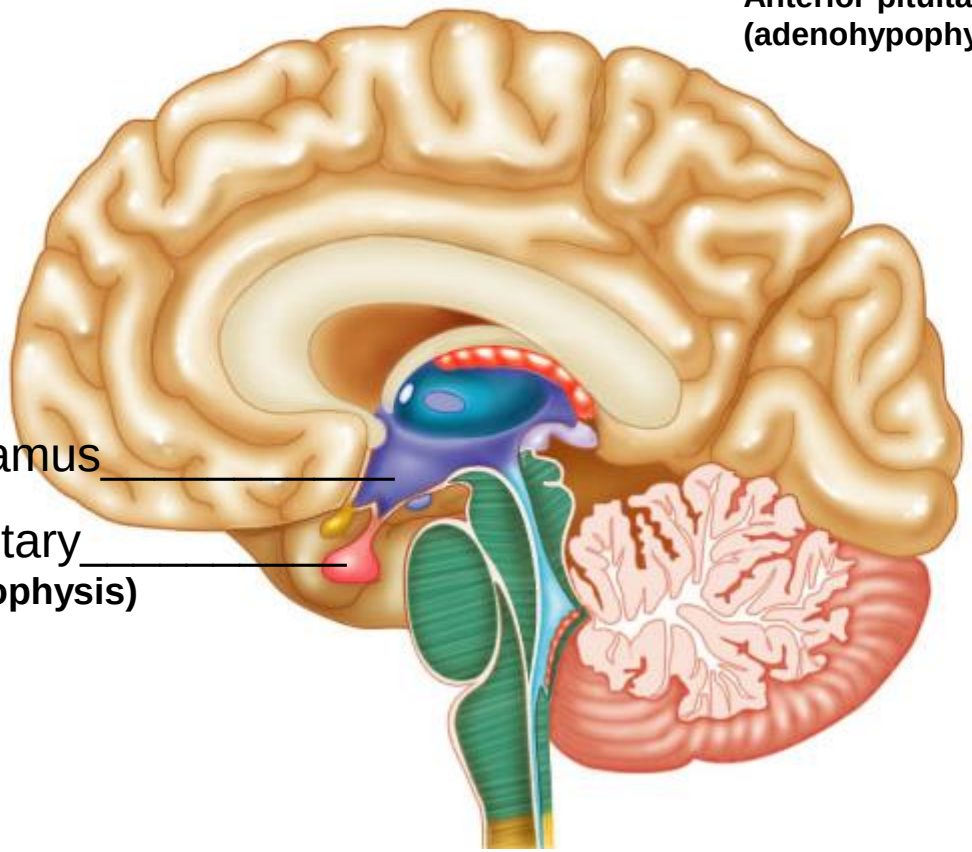
Learn the 3 endocrine organs on this slide:

Hypothalamus
Pituitary (hyophysis)
Pineal









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 somatrotropic hormone) stimulates growth of skeletal epiphyseal plates and body to synthesize protein http://primadonablog.blogspot.com/2014/03/you-know-about-gigantism.htmlhttp://primadonablog.blogspot.com/2014/03/you-know-about-gigantism.html
- PRL stimulates mammary glands in breast to make milk
- MSH stimulates melanocytes; may increase mental alertness

AFP/Getty Images


GIANTS AND GIRLS

When he was discovered at the age of four by P. T. Barnum little Charles stood a mere 25 inches in height and weighed 15 pounds. His father, long embarrassed by the miniscule stature of his offspring, gladly agreed to consign his son to a month-long trial as an attraction in Barnum's New York Museum. The agreed rate of pay was $3 as well as room and board. This was a modest financial arrangement but the elder Stratton was simply content to see his tiny toddler be of some use.

In the history of the world, little Pauline Musters is the smallest mature woman ever officially recorded. Pauline was listed in the Guinness Book of World Records as having stood only 1 foot 11.2 inches in height

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

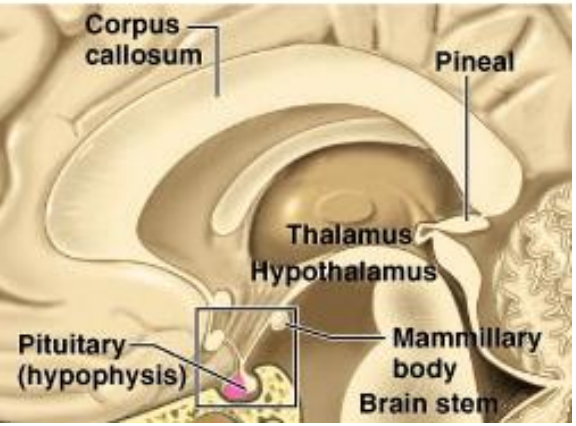
TRH (thyroid releasing hormone)
turns on TSH
CRH (corticotropin releasing hormone)
turns on ACTH
GnRH (gonadotropin releasing hormone)
turns on FSH and LH
PRF (prolactin releasing hormone)
turns on PRL
GHRH (growth hormone releasing hm)
turns on GH

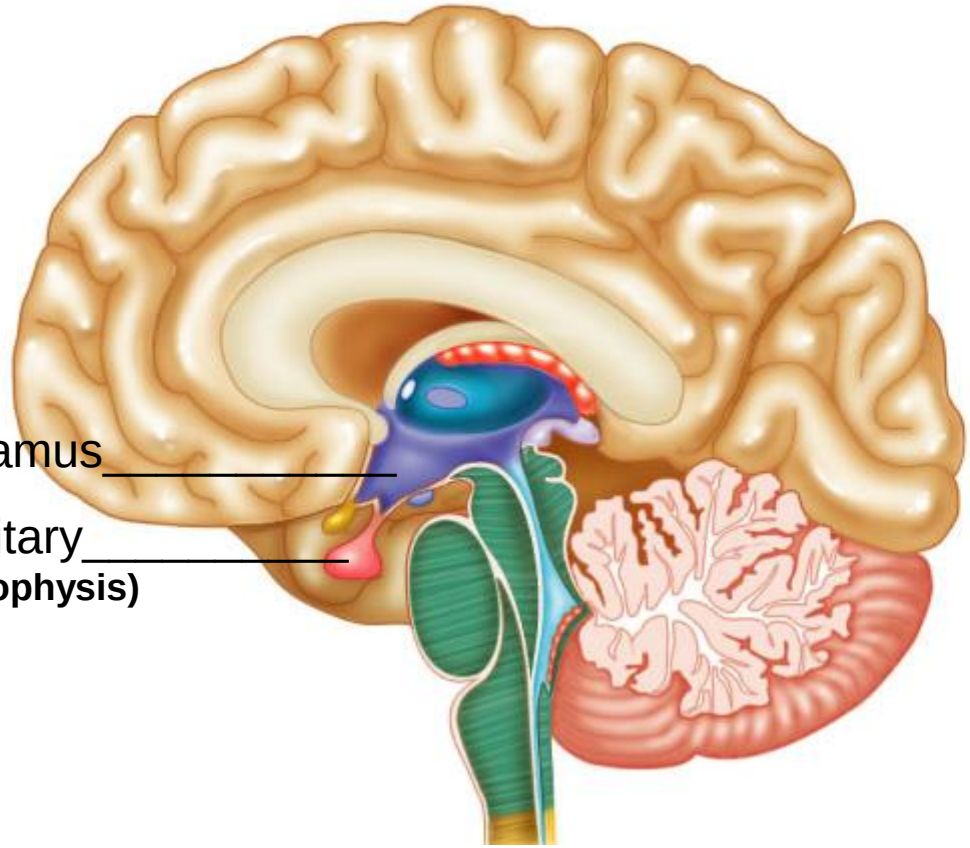
TSH: thyroid-stimulating hormone
ACTH: adrenocorticotropic hormone
FSH: follicle-stimulating hormone
LH: luteinizing hormone
GH: growth hormone
PRL: prolactin
MSH: melanocyte-stimulating hormone

ADH: antidiuretic hormone
Oxytocin

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
GH (aka somatrotropic 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
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

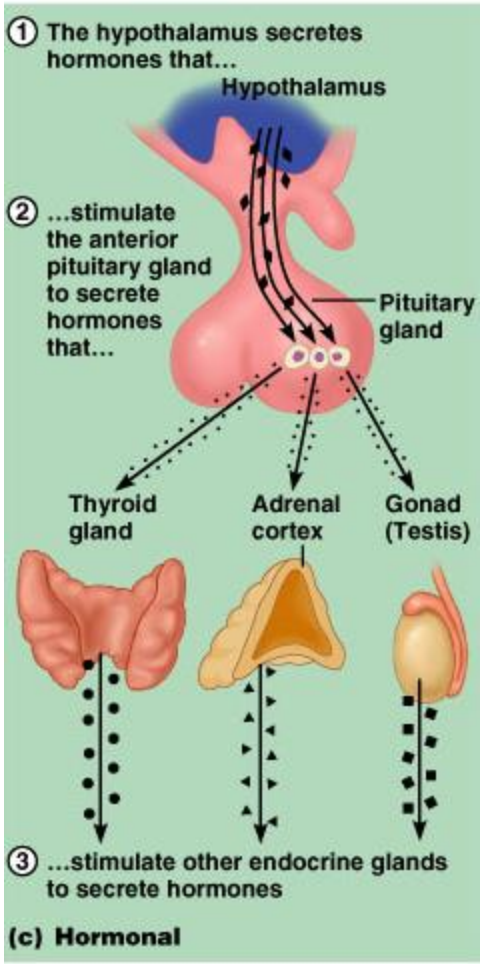
Now try and remember the anatomy





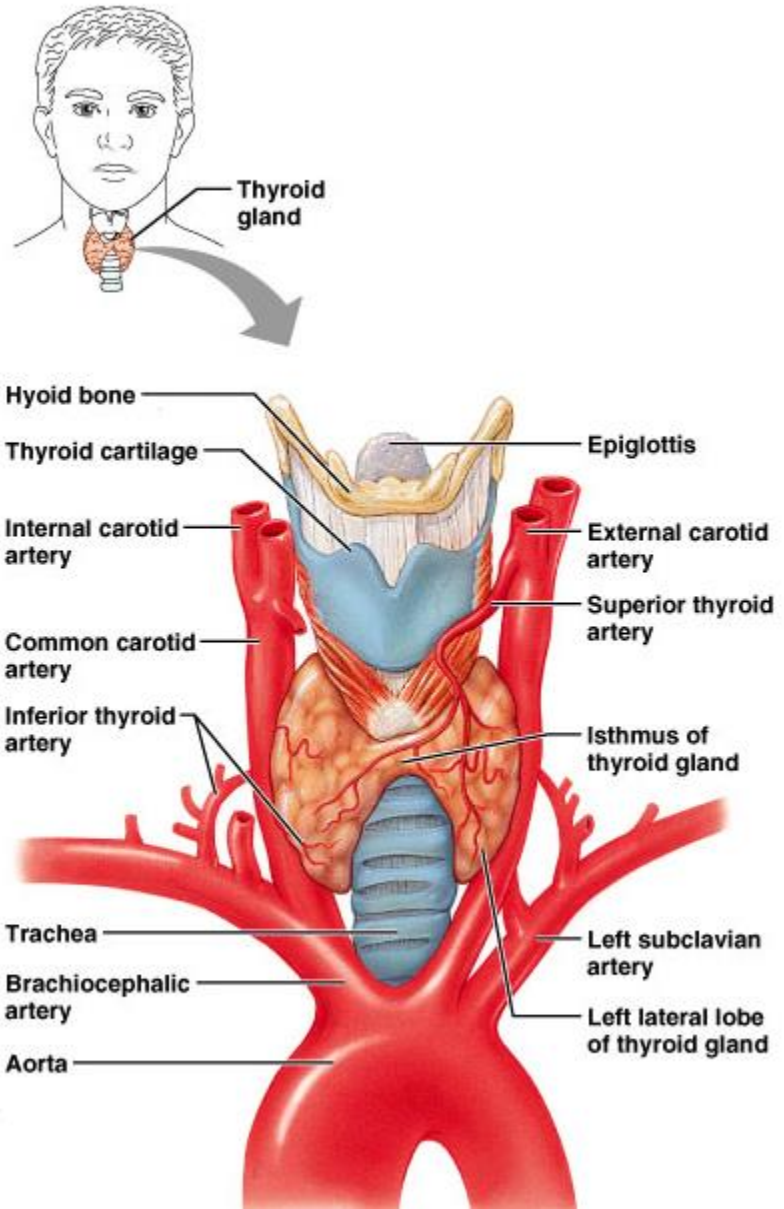
Hypothalamus_____

Pituitary_____
(hypophysis)

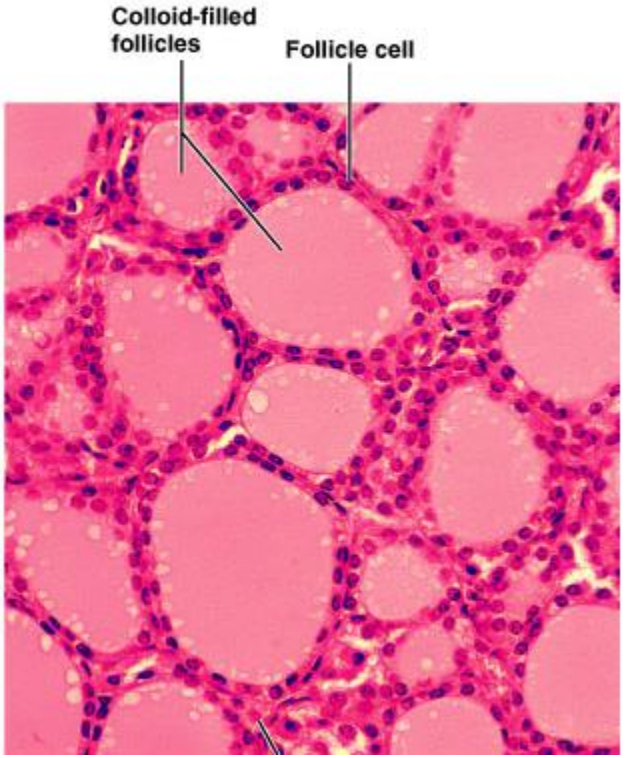


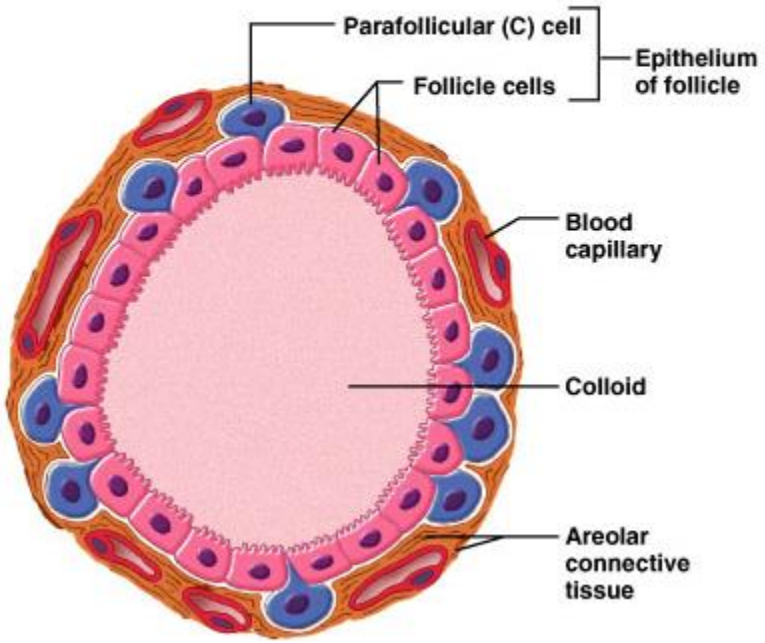
The Thyroid Gland

- 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 thryoid 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 thryroglobulin into thyroxine)

Some Effects of Thyroid Hormone (Thyroxine)

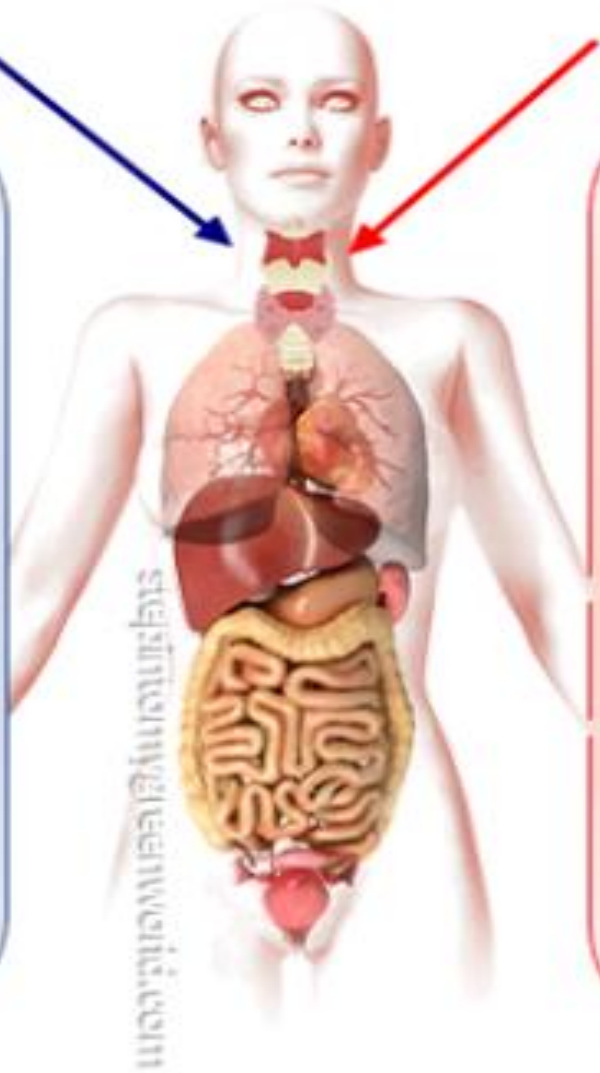
- Increases the basal metabolic rate
  - The rate at which the body uses oxygen to transform nutrients (carbohydrates, fats and proteins) into energy
- Affects many target cells throughout the body; some effects are
  - Protein synthesis
  - Bone growth
  - Neuronal maturation
  - Cell differentiation

THYROID DYSFUNCTION

stepintomygreenworld.com

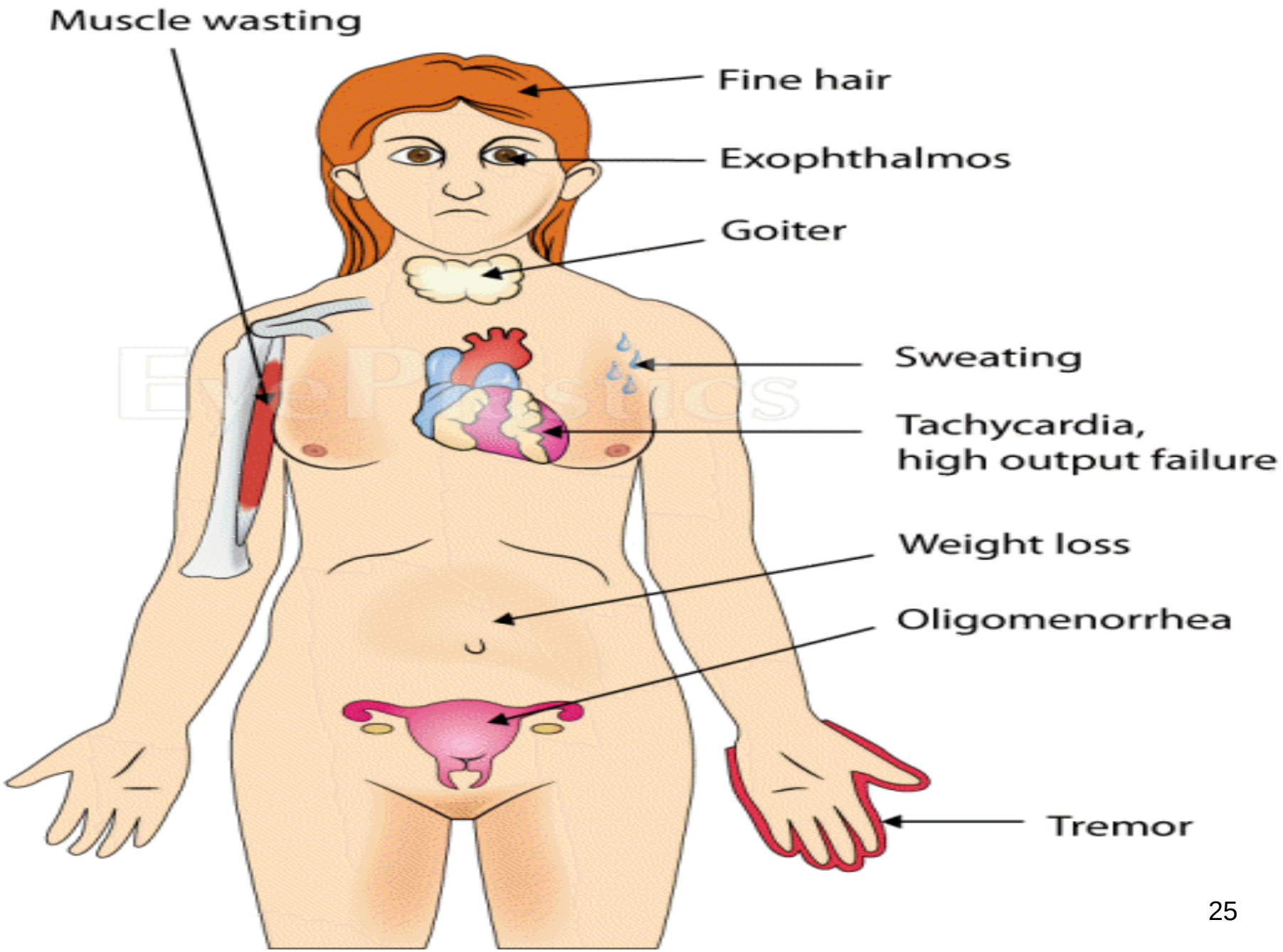
HYPO THYROIDISM

- DRY HAIR
- PUFFY FACE
- SLOW HEARTBEAT
- WEIGHT GAIN
- CONSTIPATION
- BRITTLE NAILS
- ARTHRITIS
- COLD INTOLEREANCE
- DEPRESSION
- DRY SKIN
- FATIGUE
- MEMORY LOSS
- HEAVY MENSTRUAL PERIODS
- MUSCLE ACHES

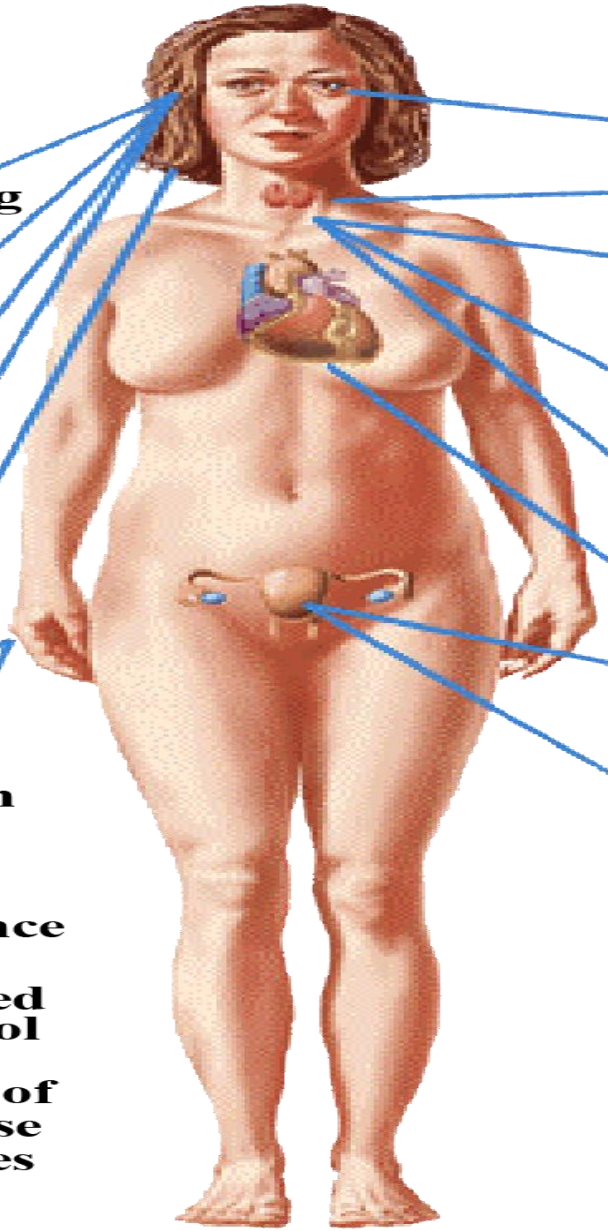


HYPER THYROIDISM

- HAIR LOSS
- BULGING EYES
- SWEATING
- RAPID HEARTBEAT
- WEIGHT LOSS
- REGULAR GAS
- SOFT NAILS
- SLEEPING DIFFICULTIES
- HEAT INTOLERANCE
- INFERTILITY
- IRRITABILITY
- MUSCLE WEAKNESS
- NERVOUSNESS
- SCANT MENSTRUAL PERIODS


Muscle wasting
Fine hair
Exophthalmos
Goiter
Sweating
Tachycardia,
high output failure
Weight loss
Oligomenorrhea
Tremor

Signs and Symptoms of HYPOTHYROIDISM



Tiredness

Forgetfulness/ Slower Thinking

Moodiness/ Irritability

Depression

Inability to Concentrate

Thinning Hair/ Hair Loss

Loss of Body Hair

Dry, Patchy Skin

Weight Gain

Cold Intolerance

Elevated Cholesterol

Family History of Thyroid Disease or Diabetes

Puffy Eyes

Swelling (Goiter)

Hoarseness/ Deepening of Voice

Persistent Dry or Sore Throat

Difficulty Swallowing

Slower Heartbeat

Menstrual Irregularities/ Heavy Period

Infertility

Constipation

Muscle Weakness/ Cramps

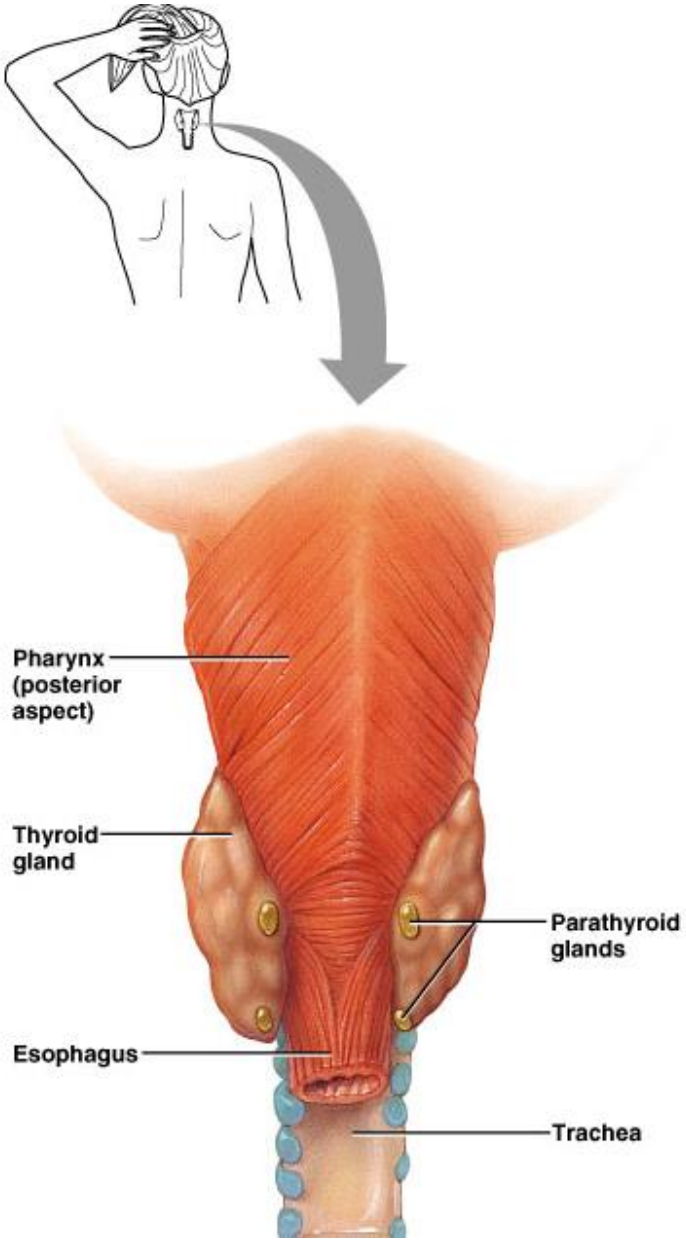
The Effects of Calcitonin

- 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

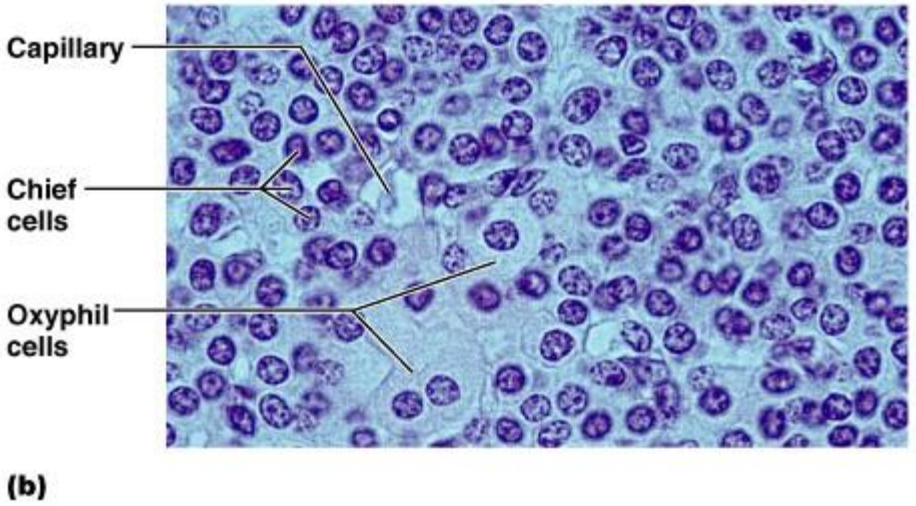
- Most people have four
- On posterior surface of thyroid gland

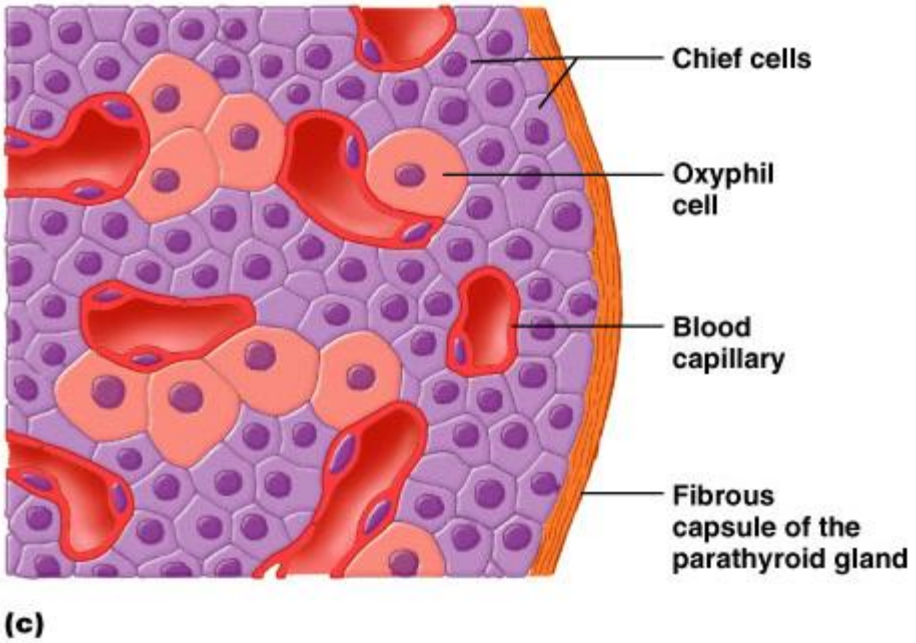
(sometimes embedded)



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



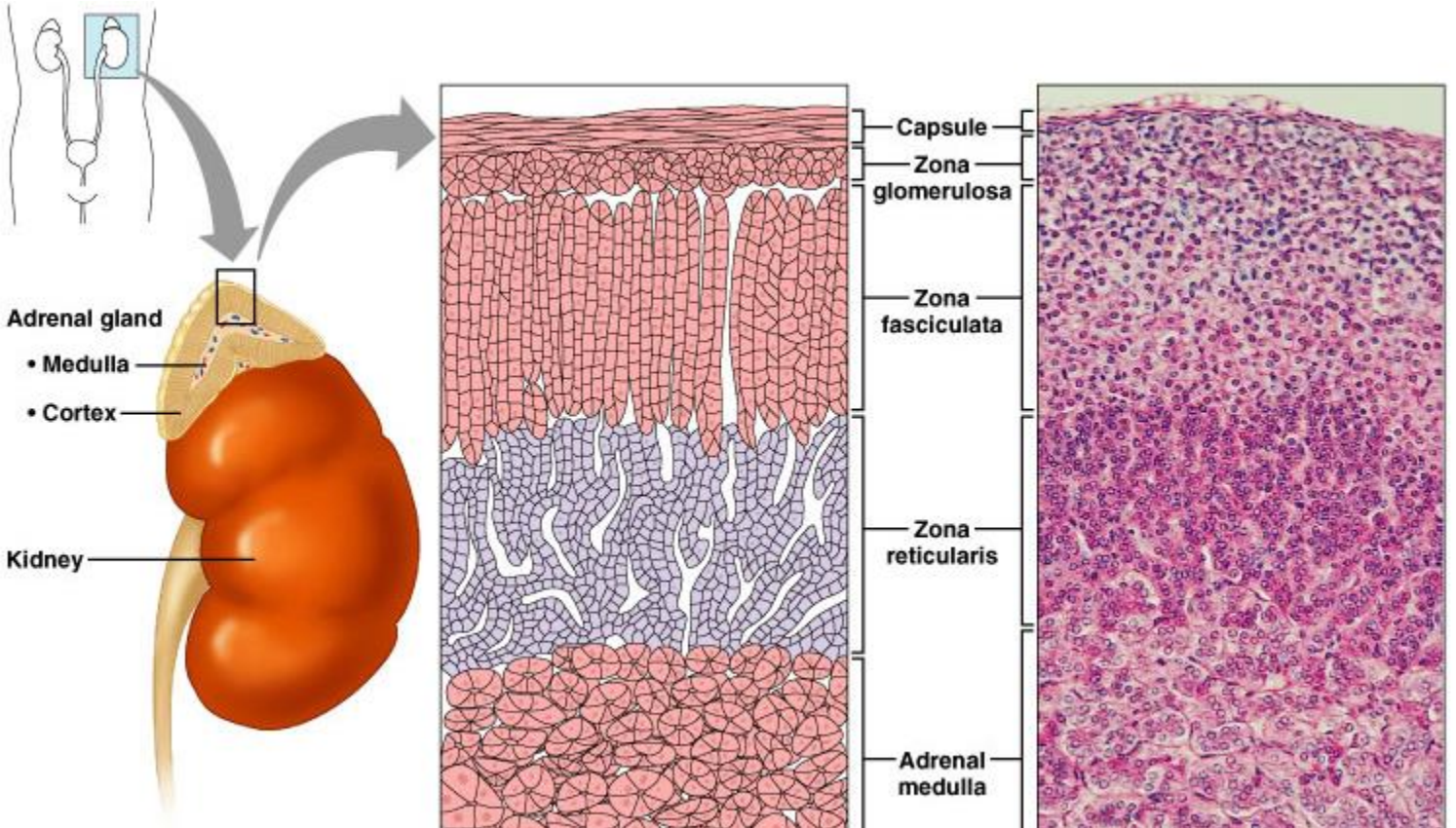


Function of PTH (**parathyroid hormone or "parathormone**")

- ***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 can be 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”
    - MINERALOCORTICOIDS
      - **Aldosterone is the main one**
    - GLUCOCORTICOIDS
      - **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, etc.

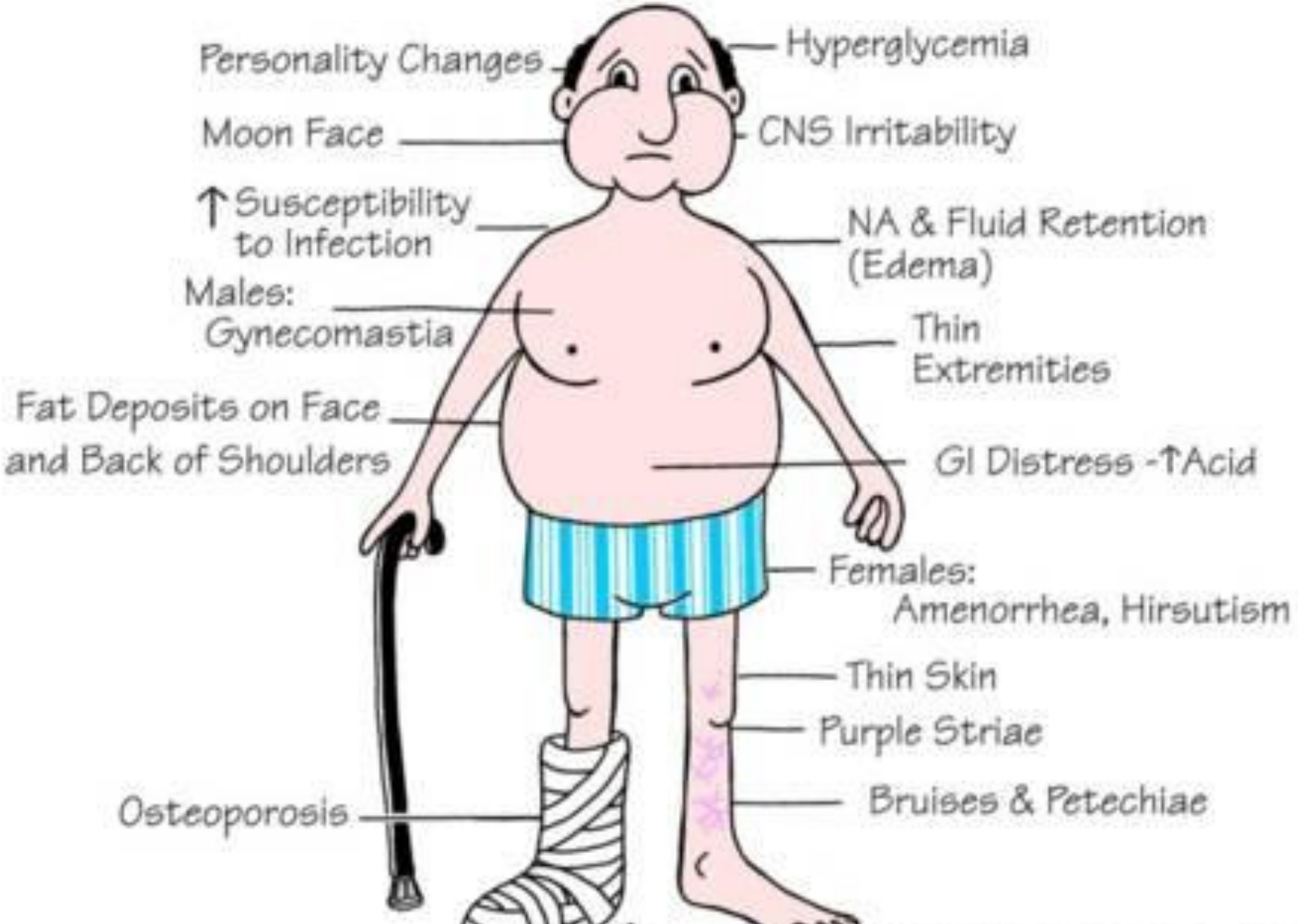
Cortisol, continued

- 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 (prednisone)
  - Responsible for some of its side effects

Cushing syndrome occurs when your body is exposed to high levels of the hormone cortisol for a long time. The most common cause of Cushing syndrome, sometimes called hypercortisolism, is the use of oral corticosteroid medication. The condition can also occur when your body makes too much cortisol.

Too much cortisol can produce some of the hallmark signs of Cushing syndrome >>>

CUSHING'S SYNDROME



Cushings

Other signs and symptoms include:

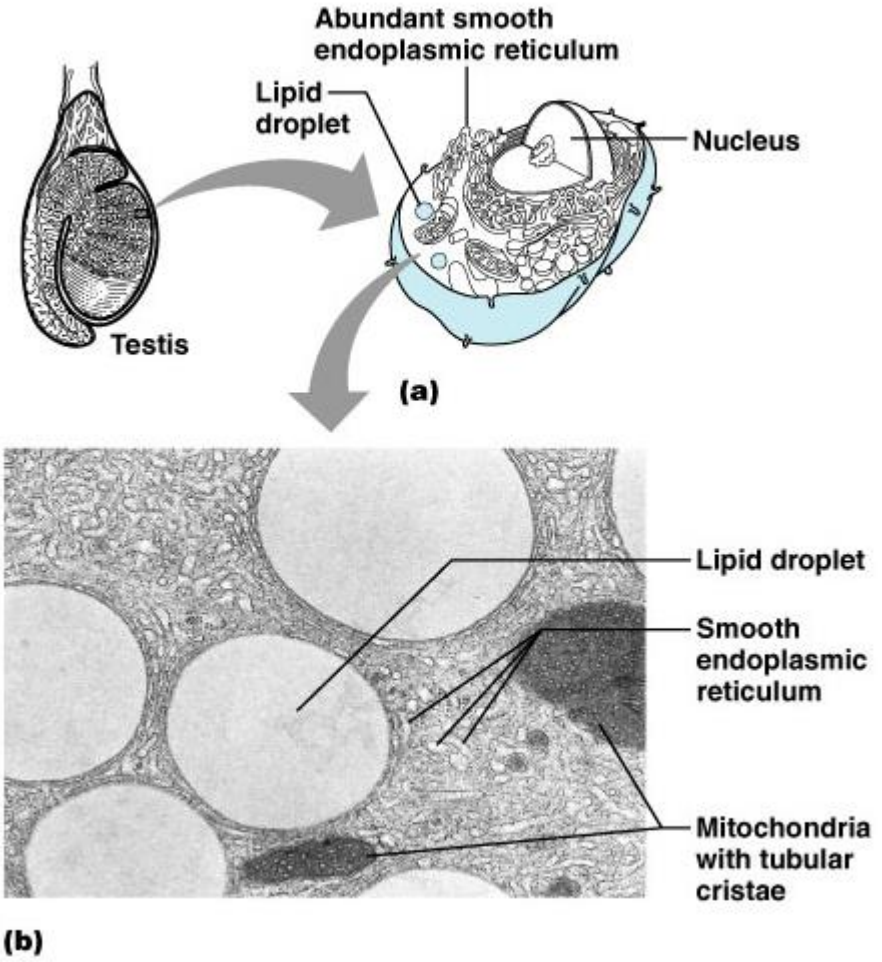
- **Fatigue**
- **Muscle weakness**
- **Depression, anxiety and irritability**
- **Loss of emotional control**
- **Cognitive difficulties**
- **New or worsened high blood pressure**
- **Glucose intolerance that may lead to diabetes**
- **Headache**
- **Bone loss, leading to fractures over time**

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**

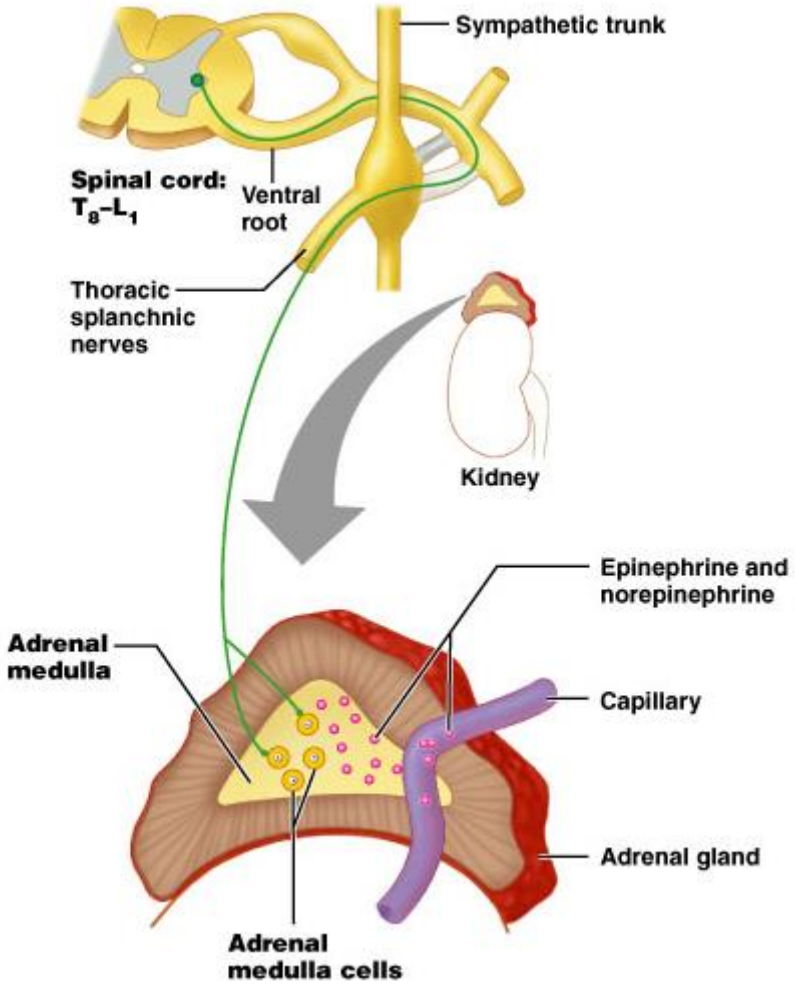
In general:



- 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 circadium rhythm
  - The biological clock of the diurnal (night/day) rhythm
  - Complicated feedback via retina's visual input

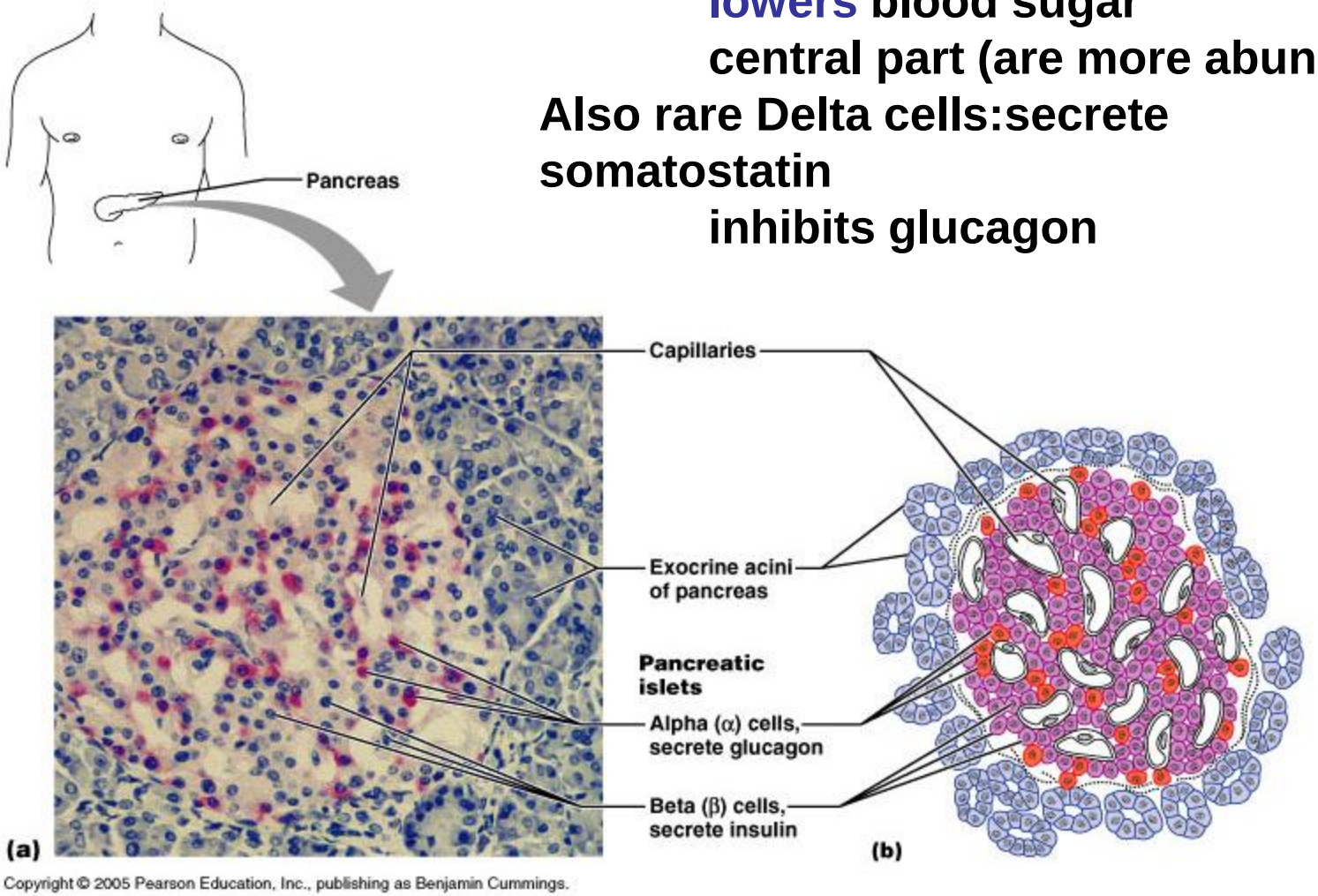
The Pancreas

Exocrine and endocrine cells

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

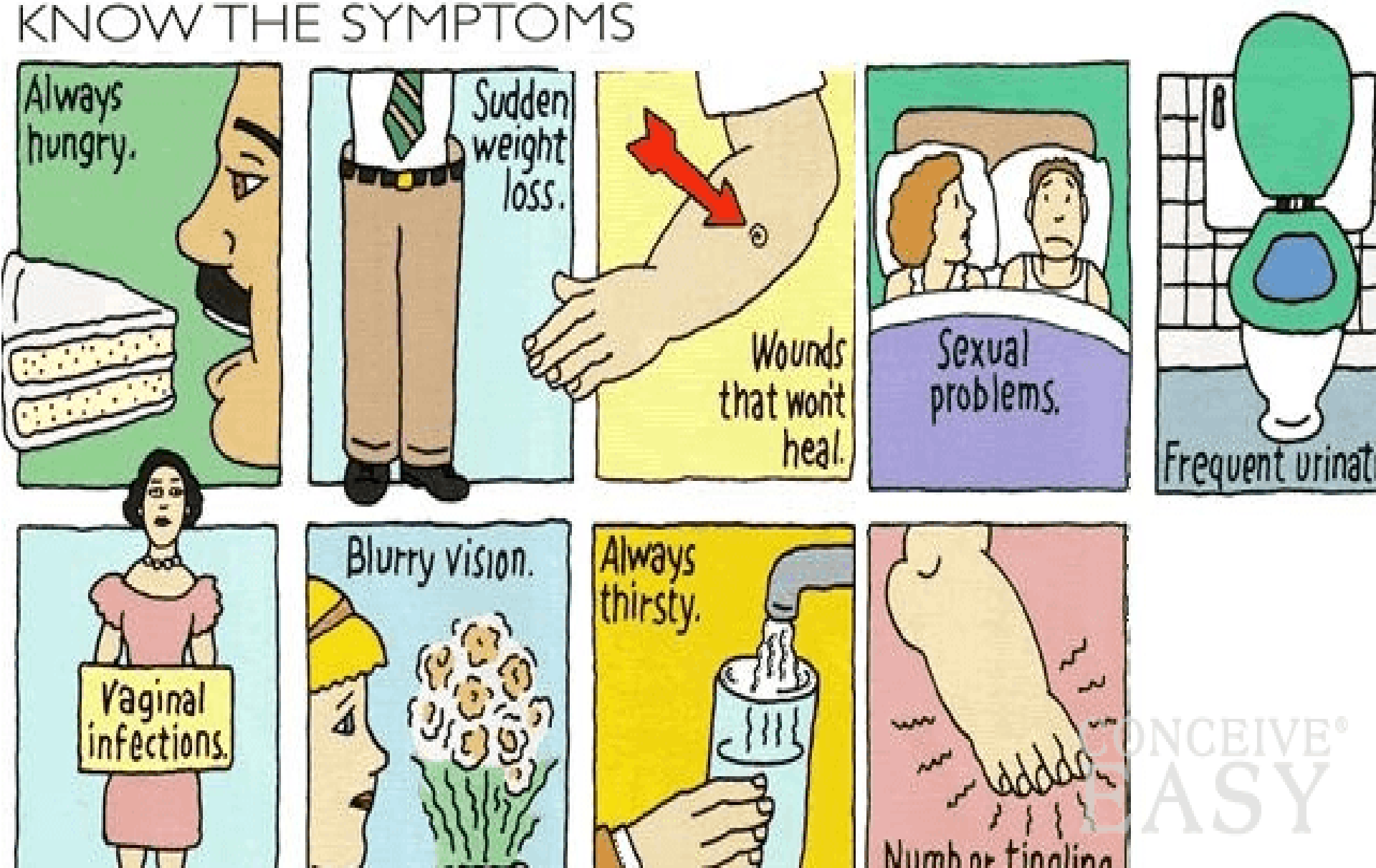
Pancreatic islet endocrine cells

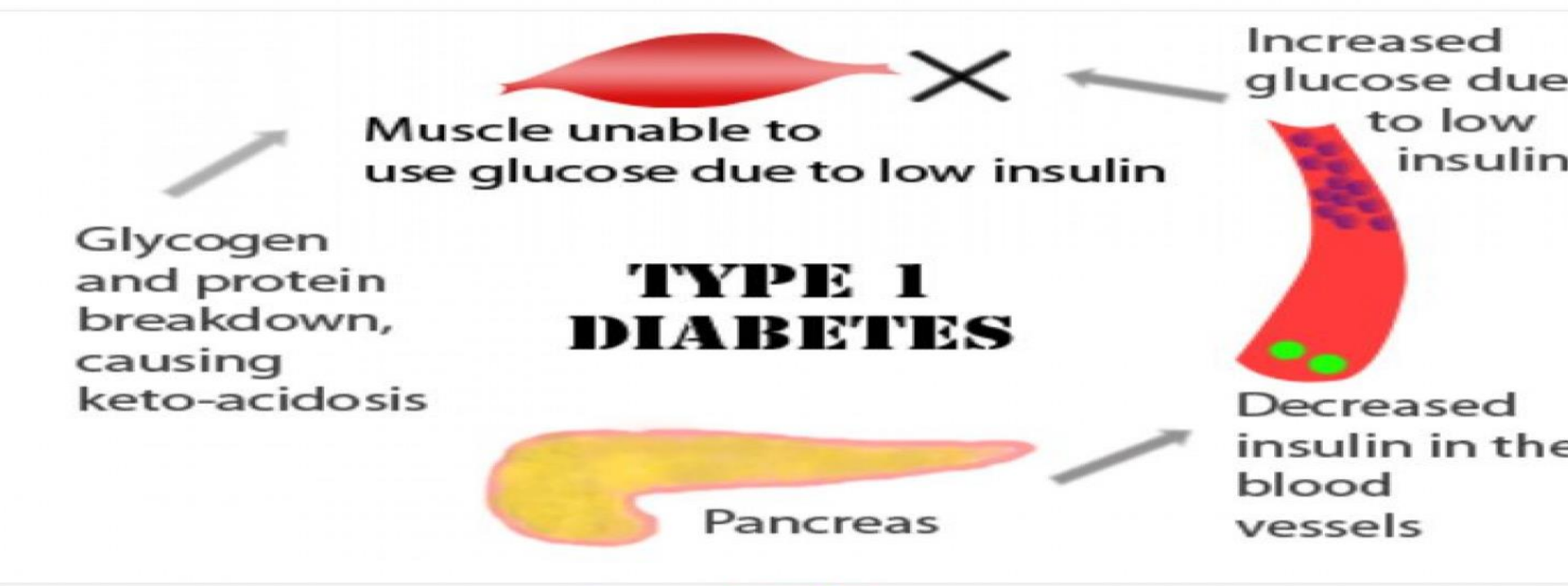
Alpha cells: secrete glucagon
raises blood sugar
mostly in periphery
Beta cells: secrete insulin
lowers blood sugar
central part (are more abundant)
Also rare Delta cells:secrete somatostatin
inhibits glucagon



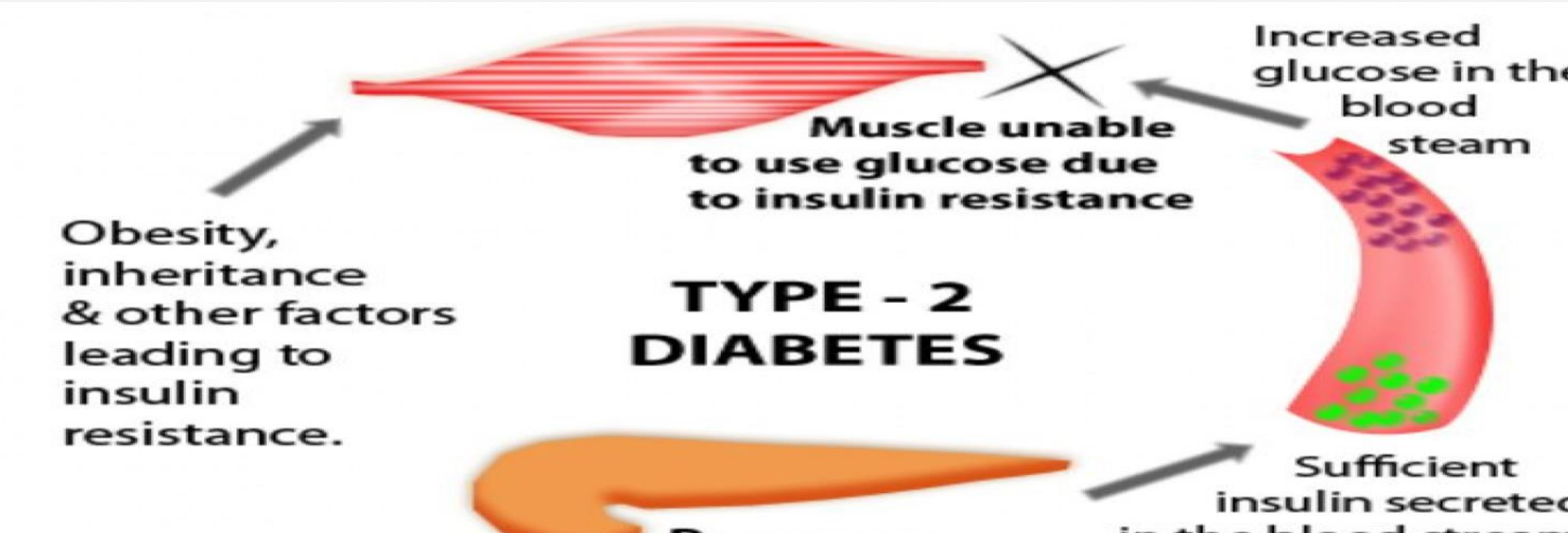
DIABETES

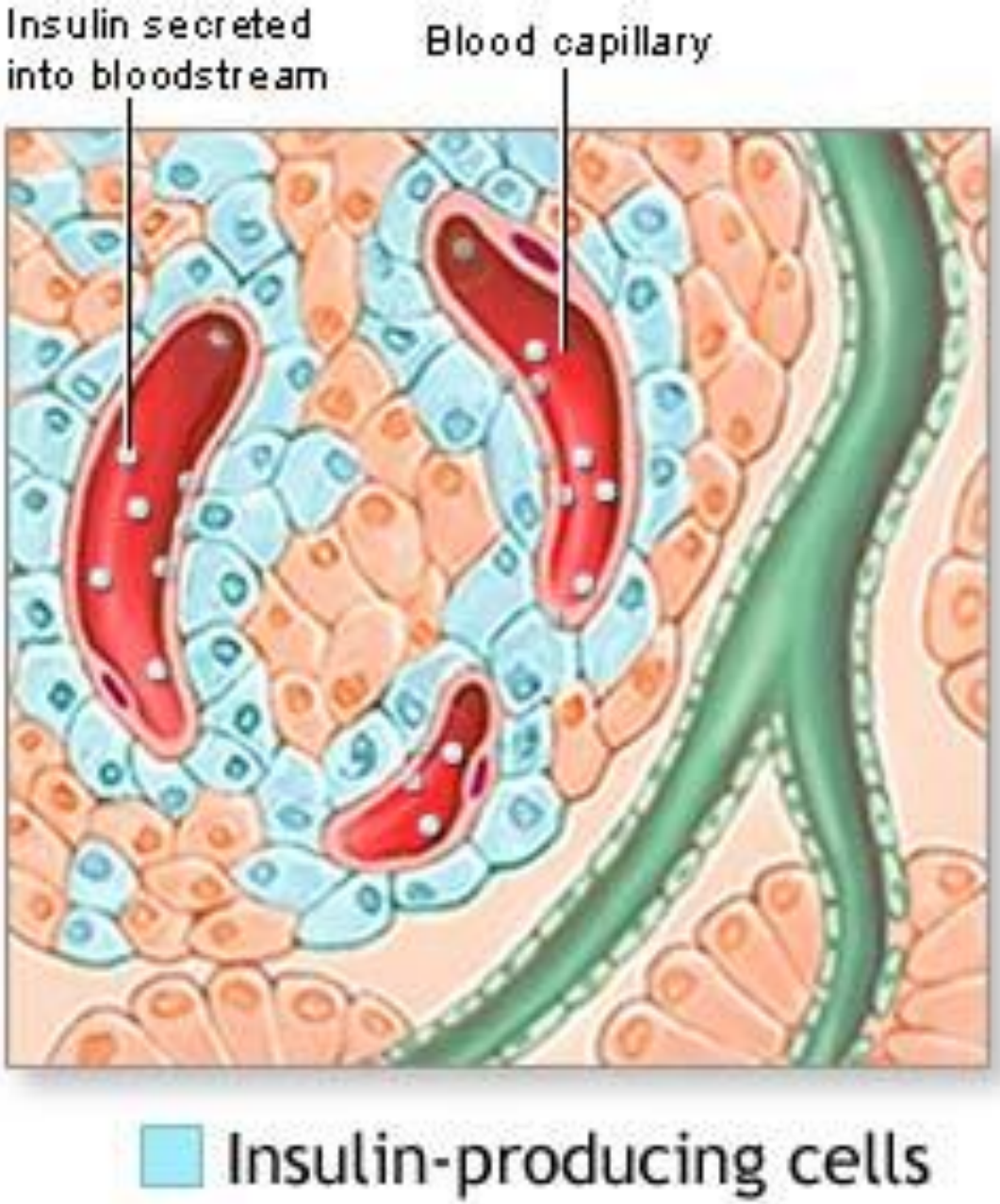
KNOW THE SYMPTOMS





Type 2 Diabetes




Insulin secreted into bloodstream
Blood capillary
Insulin-producing cells

Type 1 diabetes most often starts in childhood, before the age of 20. People with type 1 diabetes usually have a number of the following symptoms:

Frequent urination
Excessive thirst
Unexplained weight loss
Extreme hunger
Sudden vision changes
Tingling or numbness in hands or feet
Feeling very tired much of the time
Very dry skin
Sores that are slow to heal
More infections than usual
Nausea, vomiting, and stomach pains


Low blood sugar symptoms include:
Headache
Sweating
Shaking
Feeling tired
Weakness
Hunger
A.D.A.M.

Here are some of the symptoms that can signal type 2 diabetes:
Slow healing wounds and blisters that seem to take too long to recover.
Excessive lethargy and fatigue can indicate hypoglycemia and is an indication of type 2 diabetes if these symptoms are not associated with sudden lifestyle changes.
Unexplained increased hunger and or thirst can also be an indicator of onset of type 2 diabetes.
Sudden appearance of dark patches or changes in texture of small patches of skin can be an indicator especially appearing around the neck and armpits.
Rapid unexplained weight loss even when eating the same number of calories without changes in activity level.
Persistent blurred vision or headaches can be an indicator of type 2 diabetes and often accompanies irritability or confusion.
You should make a note of any sudden change in any of the above examples, especially if you are obese (BMI above 30).

Type 2 diabetes in children and teens is on the rise thanks to childhood obesity, poor nutrition and lack of exercise. We need to educate ourselves now about diabetes and children and what we can do to help reverse the trend. - See more at: http://www.losing-weight-and-the-glycemic-index.com/type-2-diabetes-in-children.html#sthash.0tih9WCI.dpuf

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

Hormones can be inadequate during or after each stage of development—embryonic and adolescent. During each stage, inadequate hormone stimulation will prevent normal development. After each stage, a decrease in hormone stimulation will result in failed function and perhaps some shrinkage. The organs affected principally by sex hormones are the male and female genitals, both internal and external, and the female breasts. Body hair, fat deposition, bone and muscle growth, and some brain functions are also influenced.

Read more: http://www.healthofchildren.com/G-H/Hypogonadism.html#ixzz3ER2YwOIc

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)

Atrial natriuretic peptide hormone of cardiac origin, which is released in response to atrial distension and serves to maintain sodium homeostasis and inhibit activation of the renin-angiotensin-aldosterone system. Congestive heart failure is a clinical syndrome characterized by increased cardiac volume and pressure overload with an inability to excrete a sodium load. Circulating atrial natriuretic peptide is greatly increased in congestive heart failure as a result of increased synthesis and release of this hormone. Atrial natriuretic peptide has emerged as an important diagnostic and prognostic serum marker in congestive heart failure. In early heart failure, it may play a key role in preserving the compensated state of asymptomatic left ventricular dysfunction. Despite increased circulating atrial natriuretic peptide in heart failure, the kidney retains sodium. The mechanism for the attenuated renal response is multifactorial and includes renal hypo perfusion, activation of the renin-angiotensin-aldosterone and sympathetic nervous system.

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, more about cushings)
    - 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 appetetie, abdominal pain

    (Jane Austin)

Addison's disease

Chronic Hypoadrenalism

Low [CORTISOL]
Hypoglycaemia
Hypercalcaemia & anaemia
High [ACTH] / [MSH]
Pigmentation

Low [SEX HORMONE]
Loss of body & pubes hair
Loss of libido/amenorrhoea
Muscle wasting & thin limbs

HYPOALDOSTERONISM
Low serum - [Na^+]
High serum - [K^+]
Dehydration (low ECV incl.TBV)
Postural hypotension
Weight loss
High plasma - [renin]

Adrenal Gland

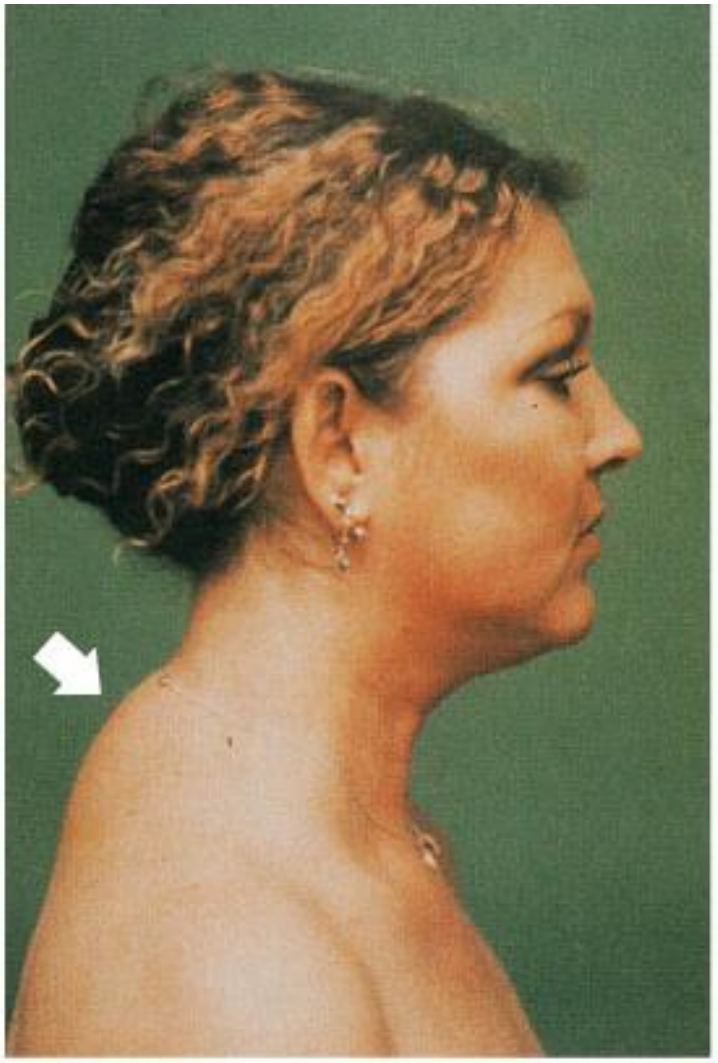
Video on Cushing's and Addisons

http://www.youtube.com/watch?v=sVLpROt1IoA

Before and after onset of Cushing's disease

(a)

Before



(b)

After