

Endocrine pathology

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Physiology

Endocrine pancreatic disorders

- DM1
- Diabetic ketoacidosis (DKA)
- DM2

Pituitary

Pituitary diseases

Prolactinoma

Acromegaly

Pituitary failure

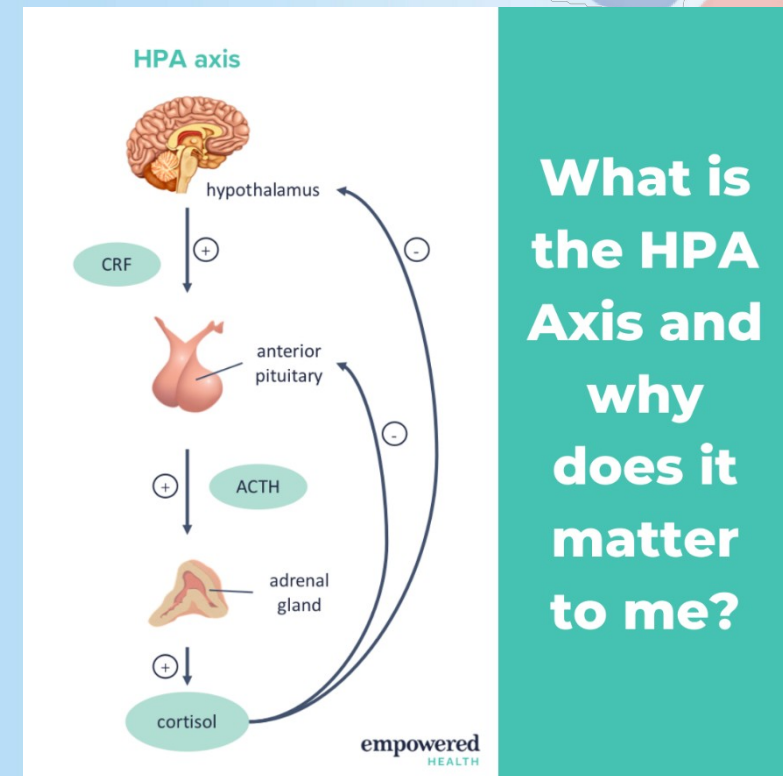
Diabetes

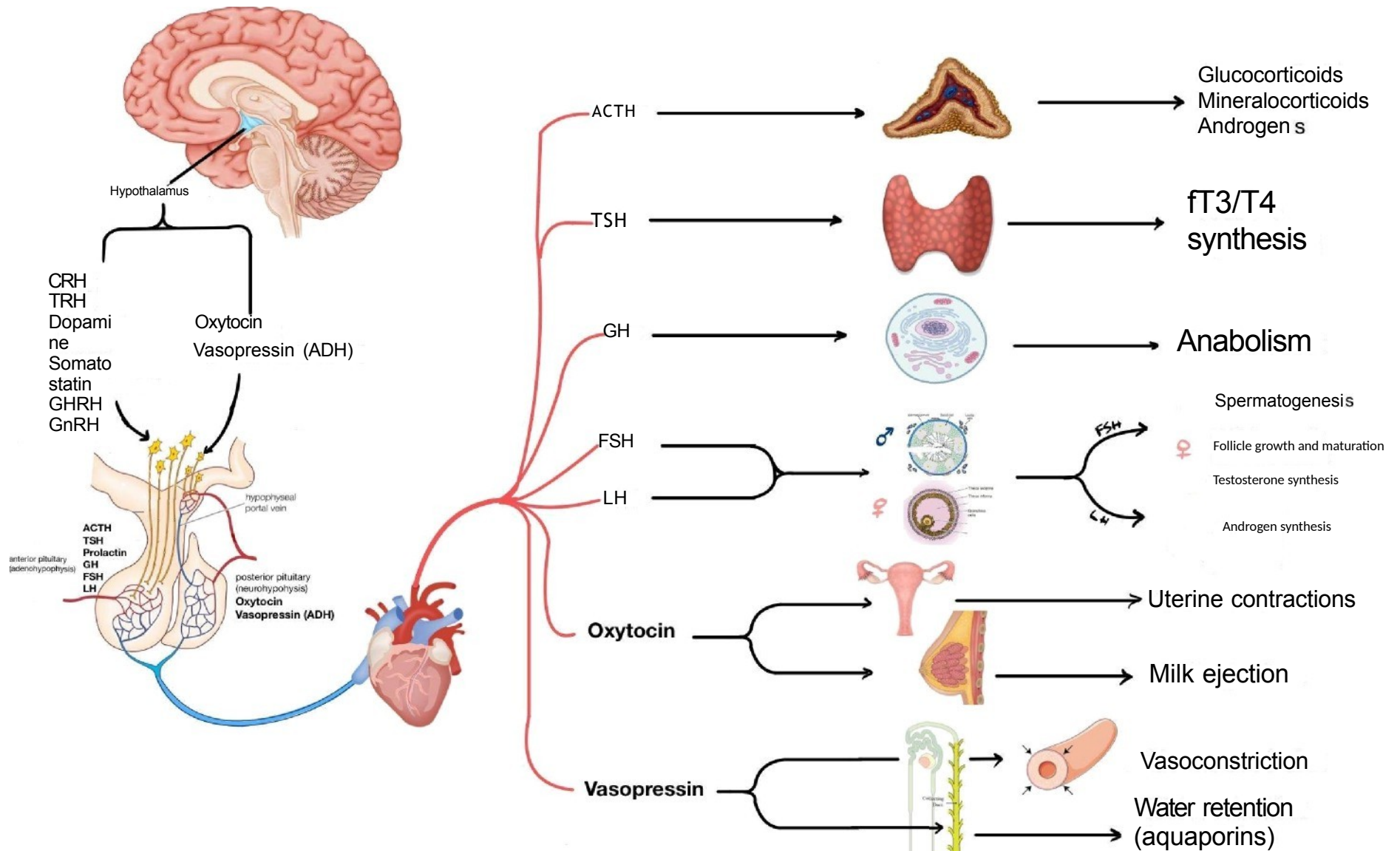
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Hypothalamic-pituitary axis

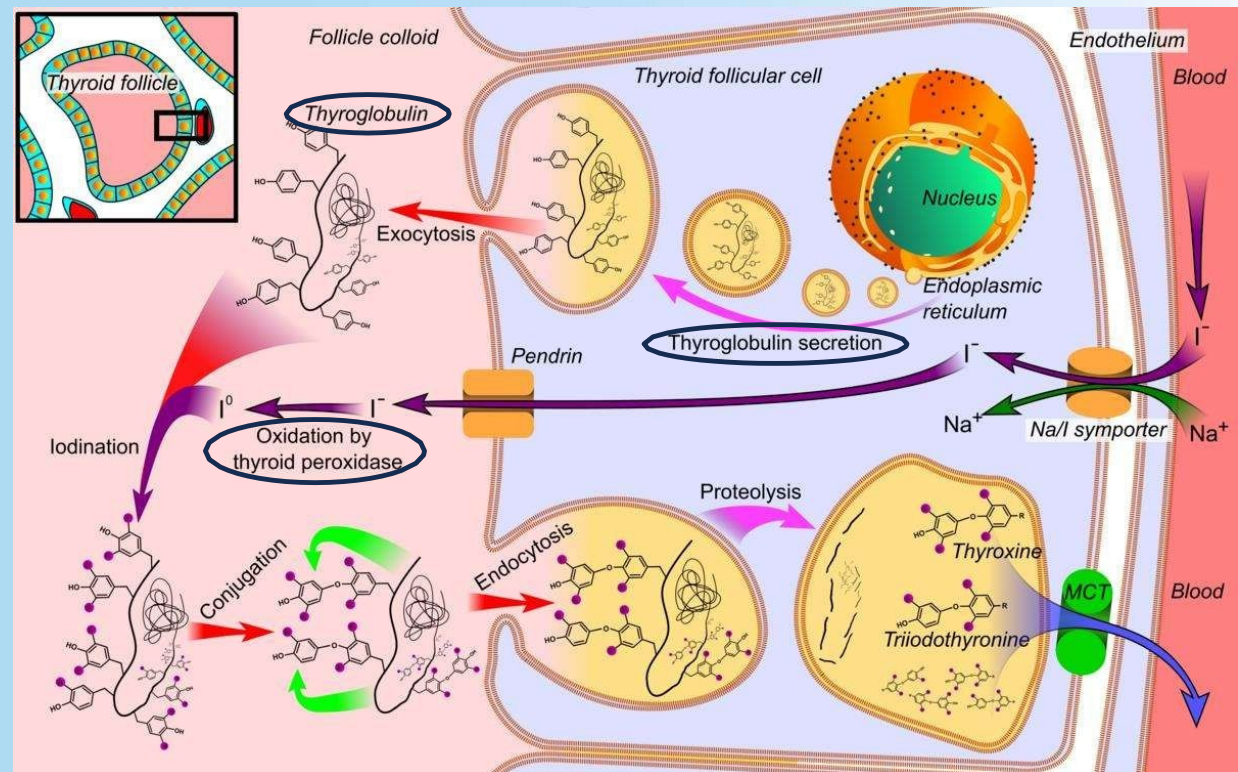
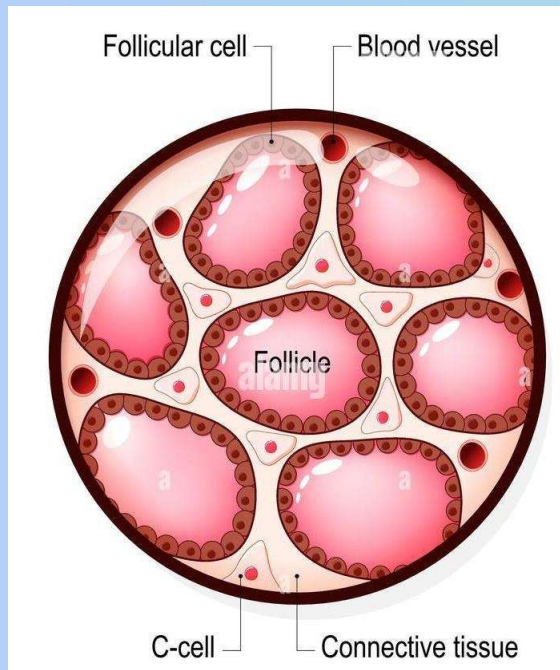
- Hypothalamus - a group of nuclei lying inferior to the thalamus
 - Overall control of the ANS and endocrine system
- Pituitary gland (hypophysis) - a two-lobed organ with neuroendocrine function
 - Ant. and post. lobe share a PORTAL system, just like the GI-tract and liver
 - Ant. and post. Lobe also called the adenohypophysis and neurohypophysis

Target organ - effect (often secretion)
directly stimulated by hormones





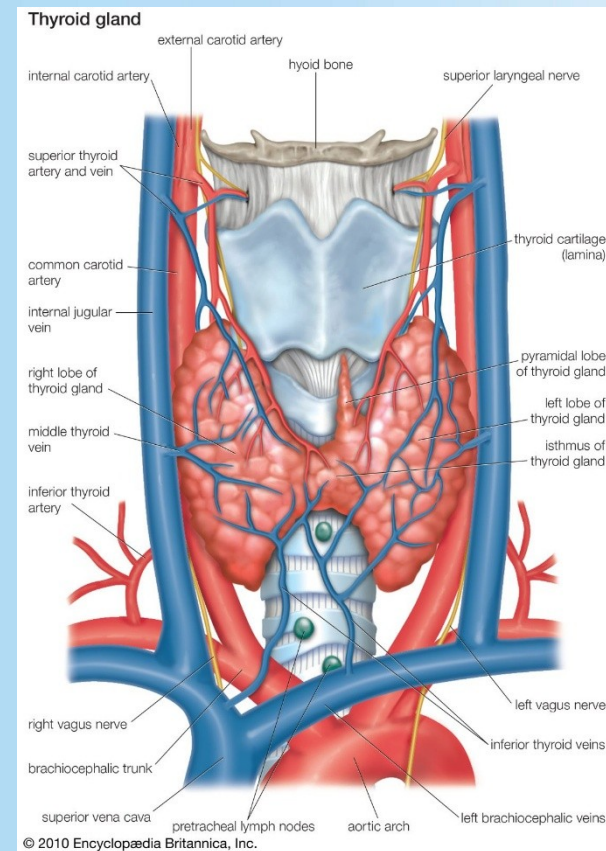
Thyroid physiology recap



		Thyroid activity (function)			
		Hormone overproduction (thyrotoxicosis)		Normal	Hormone insufficiency (hypothyroidis m)
		Hyperthyroidism	Destructive thyroiditis		
Thyroid shape	Swelling (diffuse goiter)	Basedow's disease		Simple diffuse goiter	
				Hashimoto's disease	
	Normal	During pregnancy (transitory)	Subacute thyroiditis		
	Develop lumps (nodular goiter)	Functional nodule		Benign tumors Malignant tumors	

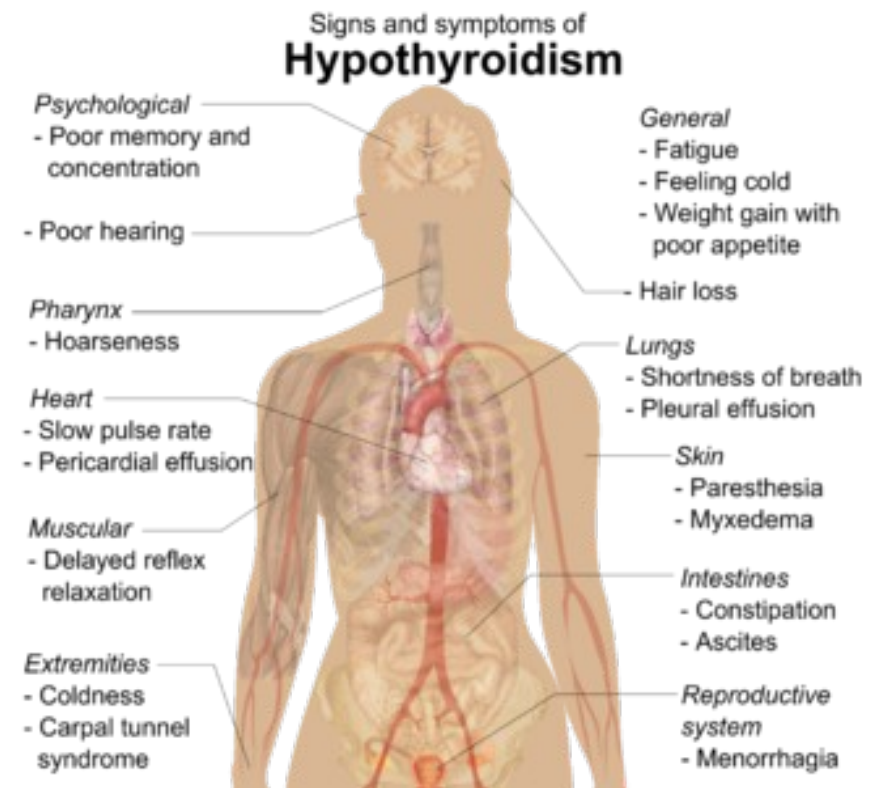
Hypothyroidism - causes

- Causes can be divided into
- Problems with the gland itself (primary hypothyroidism), inadequate stimulation from pituitary (secondary hypothyroidism) and inadequate release of TRH (tertiary)
- Primary causes:
 - Iodine deficiency
 - Hashimoto's thyroiditis
 - Postpartum (first hyperthyroidism)
 - Radiotherapy
- Secondary
 - Lesions compressing pituitary
 - Craniopharyngioma
 - Sheehan's syndrome



Hypothyroidism - symptoms

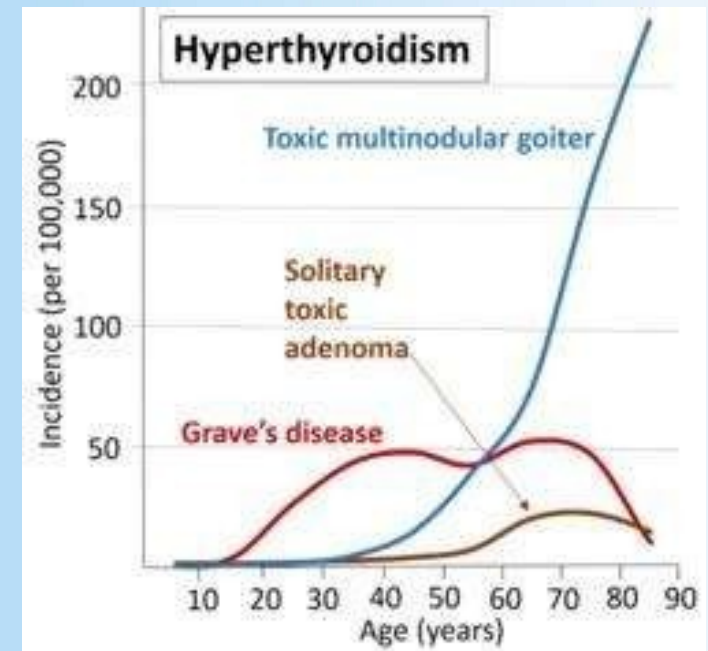
- Memory loss
- Obesity (weight gain)
- Menorrhagia
- Slowness and mental problems (depression, anxiety, irritability)
- Skin and hair dryness and brittleness
- Bradycardia low CO, ECG changes
- Exit difficulties of feces (constipation)
- Tiredness
- Intolerance to cold
- Raised BP (or Really low energy)
- Enlarged gland (goiter)
- Dopamine (Hyperprolactinemia)



Mnemonic: MOM'S BE TIRED

Hyperthyroidism - causes

- Graves disease (diffuse toxic goiter) (60-80%)
 - Autoantibodies against TSH receptor (TSI)
 - Stimulates thyroid to produce and release fT_3/T_4
- Toxic multinodular goiter (TNMG) (15-20%)
Induced thyroid cell hyperplasia following iodine deficiency
- Toxic thyroid adenoma (3-5 %)
Benign tumor, may function under stimulation or completely autonomously
- TSH-producing pituitary adenoma (<1%)



Hyperthyroidism - symptoms

- Everything is in overdrive



- Sweating excessively
- Weight loss
- Emotional lability
- Appetite increase
- Tremors
- Intolerance to heat
- Nervousness
- Gastrointestinal issues

Mnemonic: SWEATING

Graves' disease

- B and T cell-mediated autoimmune attack
 - IgG against TSH-receptor is formed (TRAb)
 - IgG stimulates thyroid gland to release its hormones (T3/T4), as well as promoting growth of the gland with goiter formation



Exophthalmos



Pretibial myxedema



Thyroid
acropachy

Thyroid storm

- Acute exacerbation of hyperthyroidism, LIFE-THREATENING
- Causes

iatrogenic: thyroid surgery, RAIA, exogenous iodine from medications, discontinuation of treatment

Stress-related: other kinds of surgery, anesthesia, induction, labor, concomitant illness

- High fever ($>40^{\circ}\text{C}$)
- Tachycardia +- arrhythmia, increased BP
- Shock, secondary to strain on heart and water loss from intestines
- Severe nausea, vomiting, diarrhea, psychosis, seizures, coma

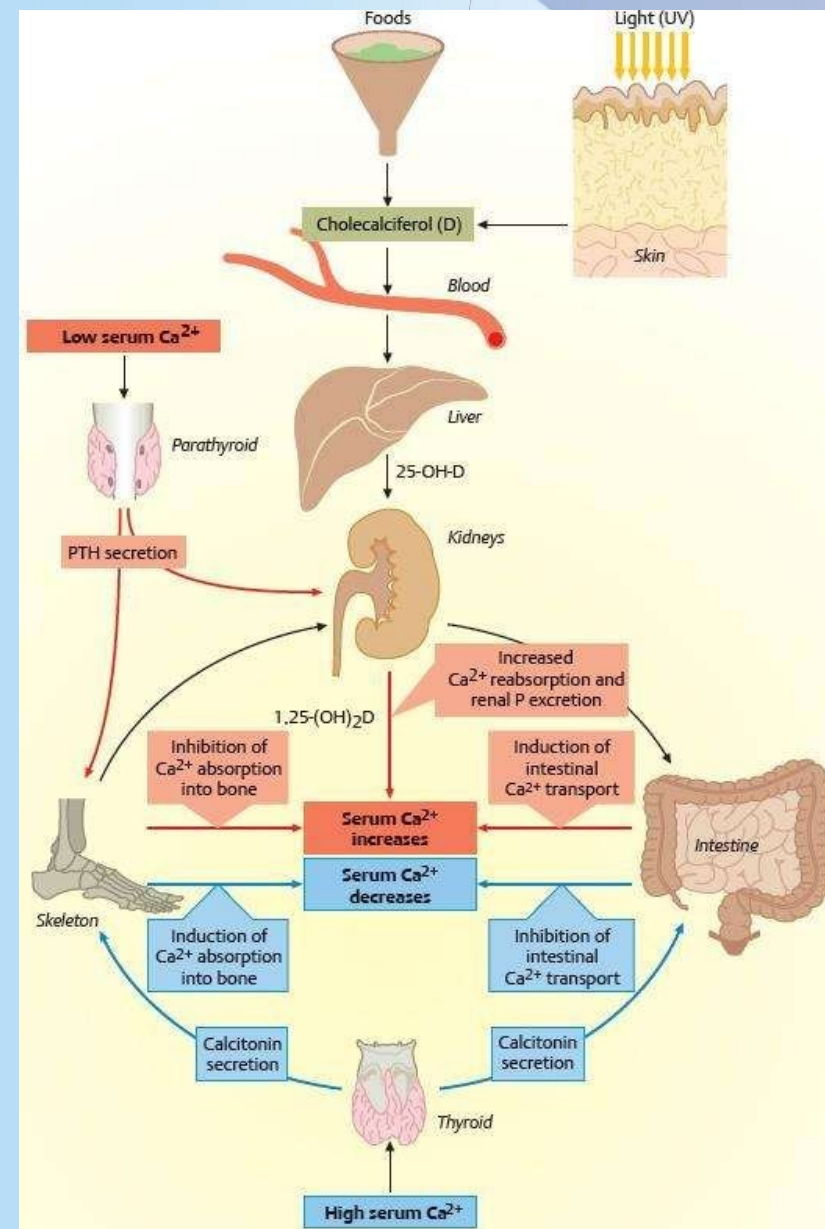
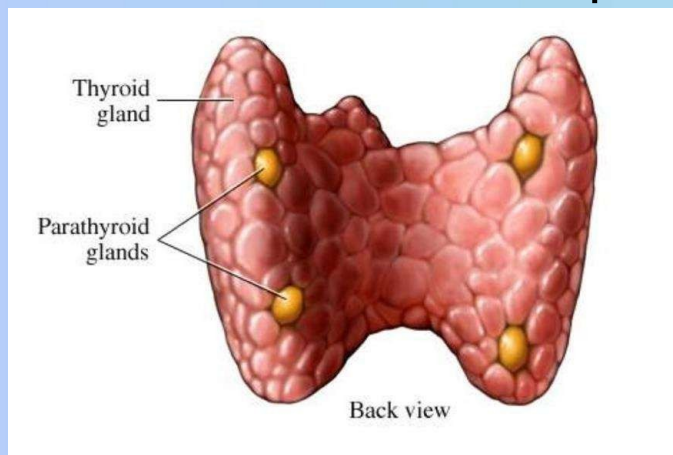


Thyroid labs

	TRH	TSH	ft3/T4	Antibodies
Graves' disease	↓	↓	↑	TSI/TRAb
Hashimoto's disease	↑	↑	↓	TPO Thyroglobulin (Tg)
Pituitary adenoma	↓	↑	↑	-
Toxic multinodular goiter	↓	↓	↑	-

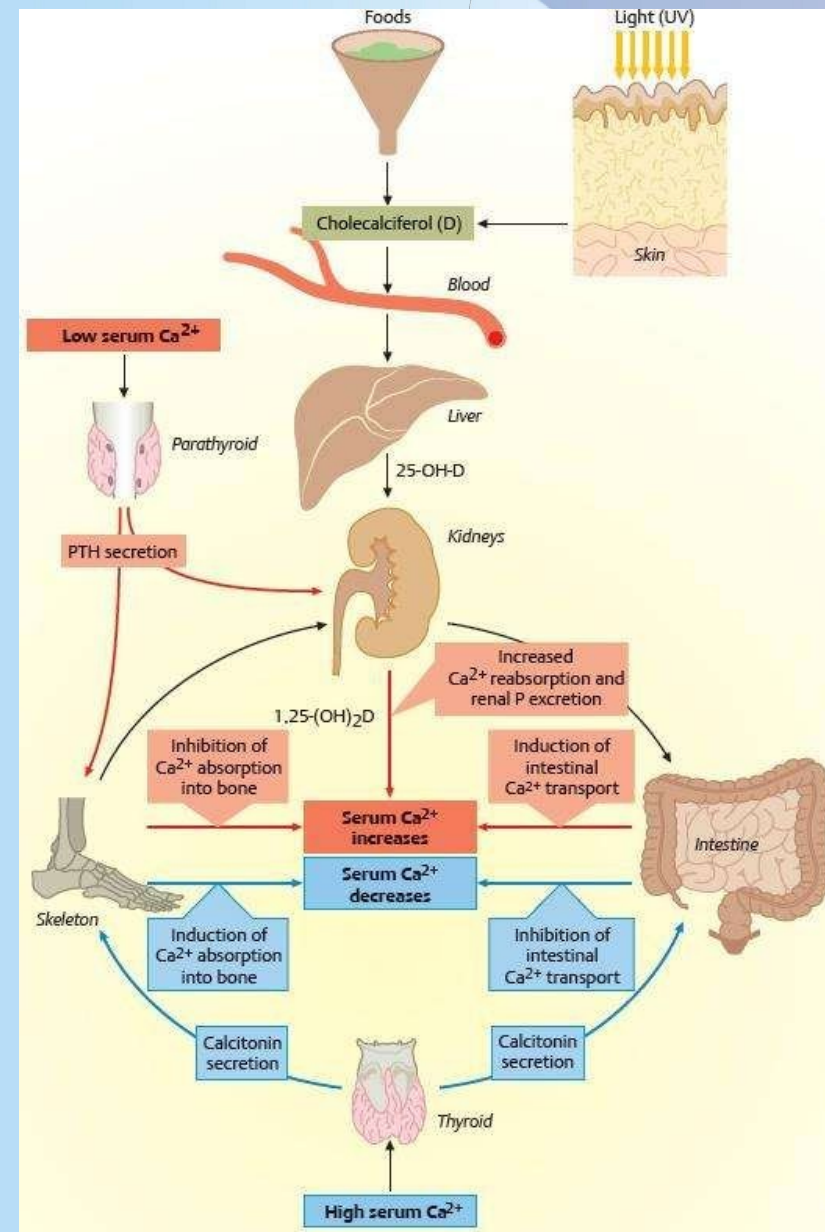
Parathyroid physiology recap

- The point of PTH is to maintain normal Ca^{2+} levels in blood
 - Bone lysis through osteoclast activity leads to increased Ca^{2+} in blood
 - Increased Ca^{2+} reabsorption in kidneys



Hypoparathyroidism

- Causes
 - Iatrogenic (injury during thyroid surgery)
 - Autoimmune
 - Nonautoimmune
 - Congenital (DiGeorge syndrome)
- Common for all is {PTH



Hypoparathyroidism

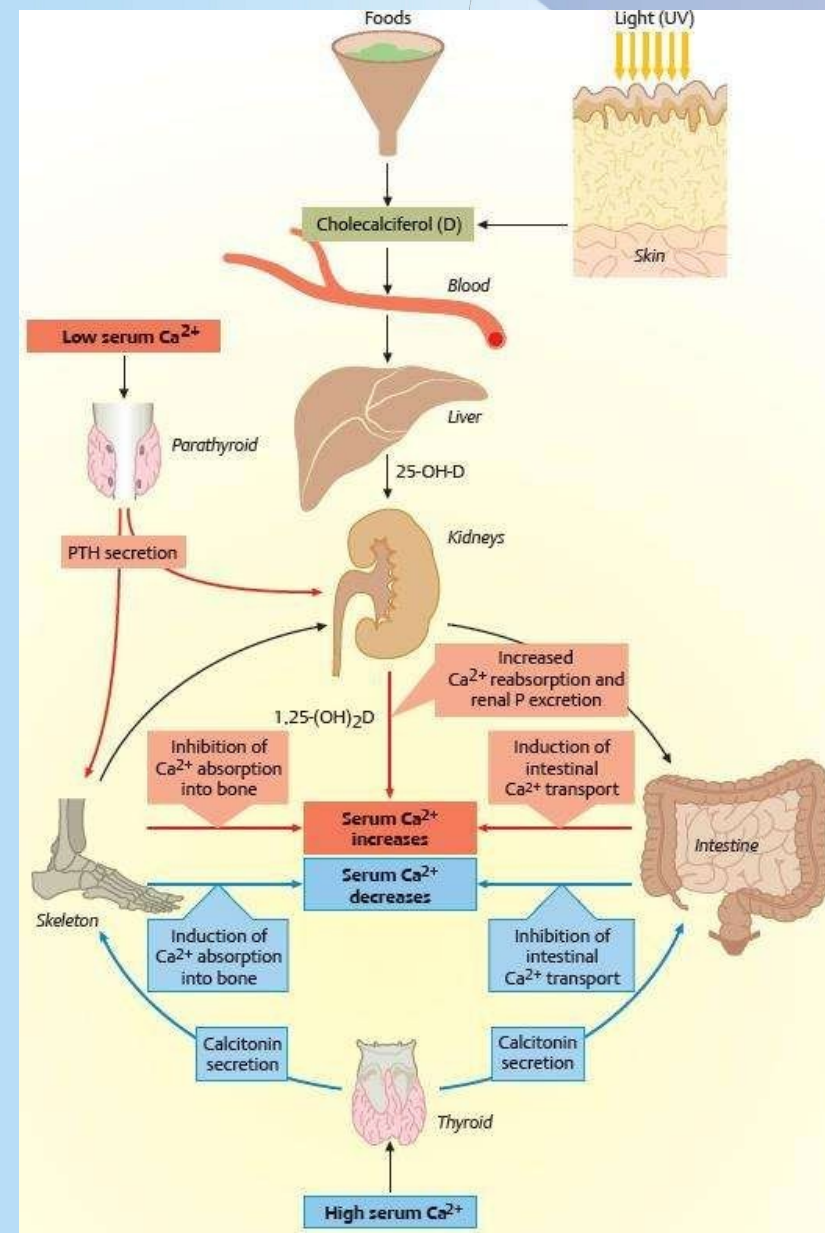
- Signs and symptoms

Acute

Tetany, laryngospasm, seizures
Arrhythmias

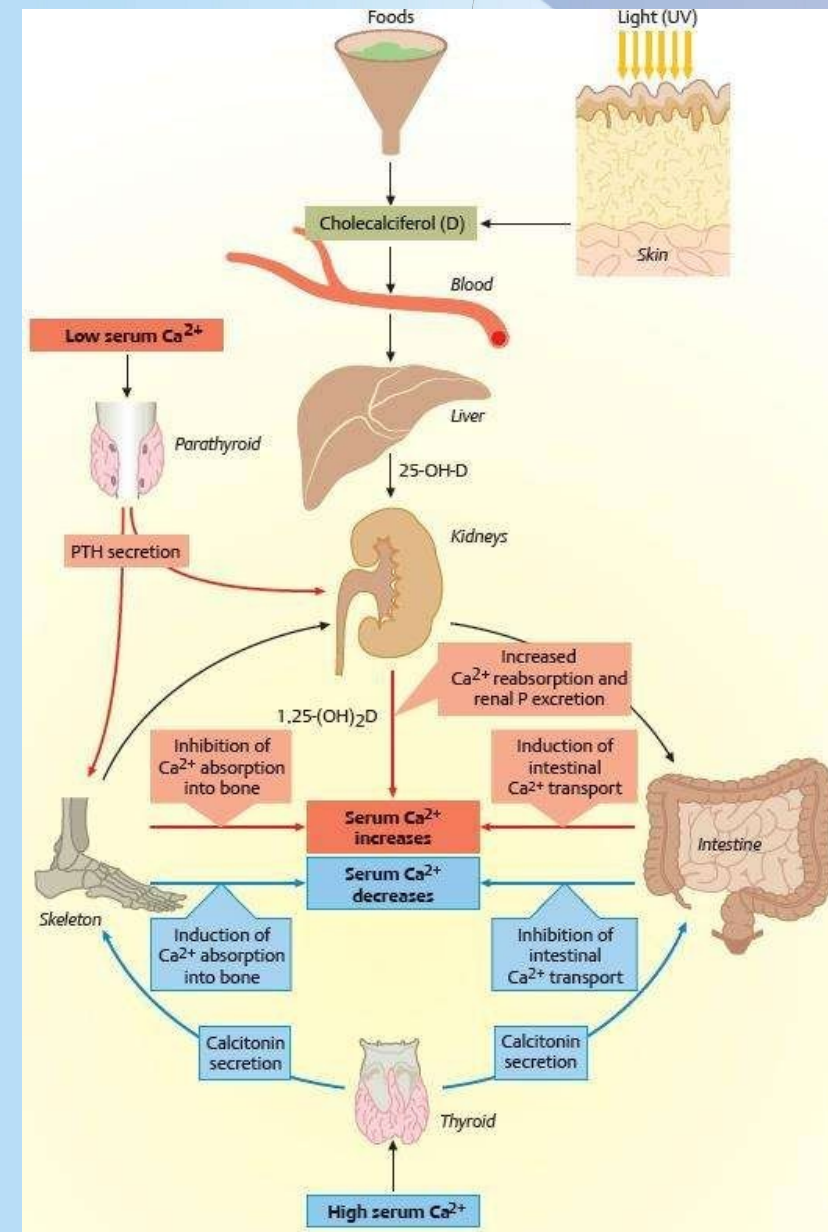
Chronic

Extrapyramidal
Parkinsonism,
hemiballismus, dystonia, dementia
Ocular (cataracts and conjunctivitis)
Skeletal (increased bone density)
Dental abnormalities



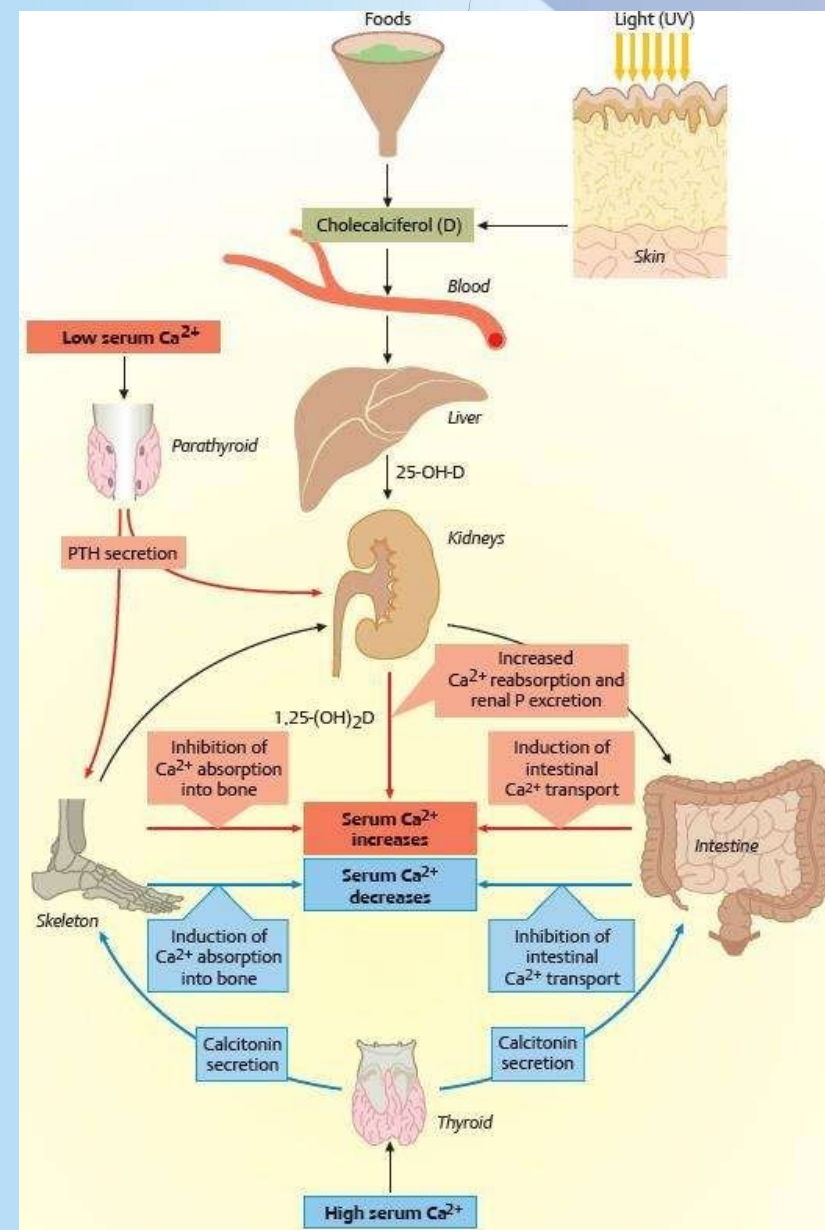
Hyperparathyroidism

- Three types:
 - Primary - problem in parathyroid glands (most often adenoma)
 - Secondary - problem with hypocalcemia, usually CKD (leading to a reflex hyperparathyroidism)
 - Tertiary - problem with parathyroid glands after years of overstimulation
- Common for all is ↑PTH
 - Induces RANKL-expression in osteoblasts
 - Binding RANKL with RANK on osteoclasts
 - Bone destruction -> release of $\text{Ca}_3(\text{PO}_4)_2$
 - Binds to kidneys -> phosphaturia



Hyperparathyroidism

- Primary: majority are asymptomatic
General weakness
LVH, increased BP
Kidney stones
Bone, muscle and joint pain
Decreased appetite, weight loss,
nausea, constipation, ulcers,
acute pancreatitis
- Primary: majority are asymptomatic



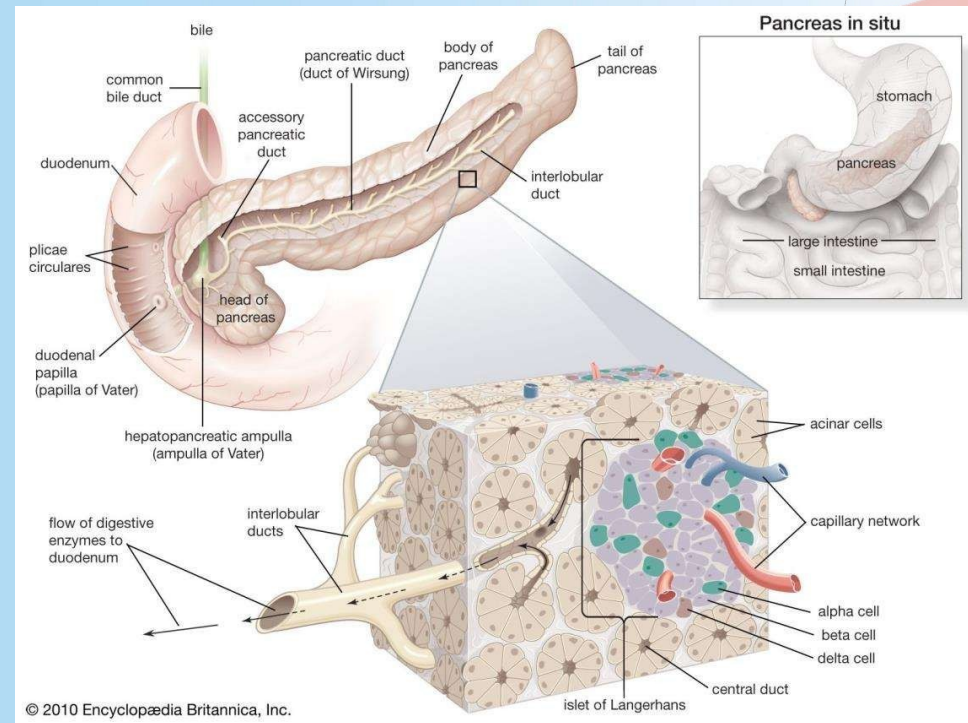
Parathyroid labs

	Calcium	PTH	Vitamin D	Phosphate
Primary hyper	↑	↑	↑	↓
Secondary hyper	↓ or normal	↑	↓	↑ or ↓
Tertiary hyper	↑	↑ ↑	↓	↑
Hypo	↓	↓	normal	↑

Endocrine pancreas physiology

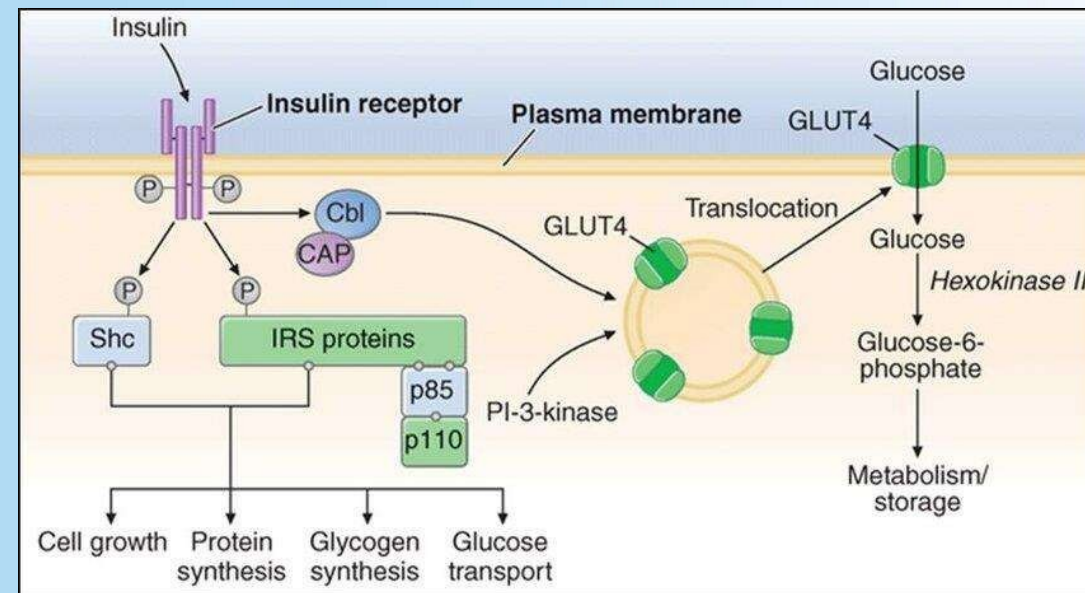
recap

- β -cells (65%) - insulin
- α -cells (20%) - glucagon
- δ -cells (10%) - somatostatin
- PP-cells (5%) pancreatic polypeptide
- Insulin and glucagon have an inverse relationship



Diabetes mellitus

- Hallmark of diabetes mellitus is HYPERGLYCEMIA
- Endogenous insulin secretion from Langerhans islet beta-cells:
 - Rapid, short-acting (peak 10 minute) in response to glucose
 - Sustained, long-acting (peak 2-3 hours)
- Insulin works on a tyrosine kinase to stimulate expression and translocation of GLUT4 transporter to the cell membrane
- Glucose enters through this transporter, eventually matching the extracellular glucose level



DM1 vs DM2

DM1

- Mechanism: autoimmune destruction of beta cells

{ INSULIN

- Young age
- Sudden onset
- Thin or normal
- Diabetic ketoacidosis (DKA)
- Less prevalent
- Treatment: INSULIN (lifelong)

DM2

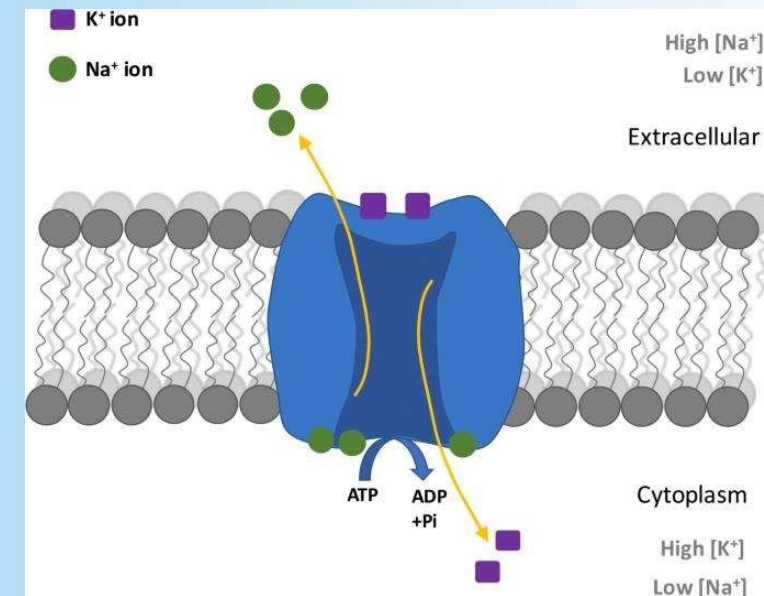
- Mechanism: insulin resistance (downregulation of insulin receptor expression)
t INSULIN RECEPTOR
- Older age
- Gradual onset
- Obese
- Hyperosmolar hyperglycemic state (HSS)
- Highly prevalent
- Treatment: initially oral metformin

Metabolic syndrome

- Need to meet 3 out of 5 criteria:
 - Abdominal obesity
 - Hypertension
 - Hyperglycemia
 - Hypertriglyceridemia
 - Low HDL
- Risk factor for developing cardiovascular disease and DM2
- Underlying cause for metabolic syndrome? We don't know.
Probably an underlying disease of energy utilization and storage. Overlaps with insulin resistance and prediabetes.

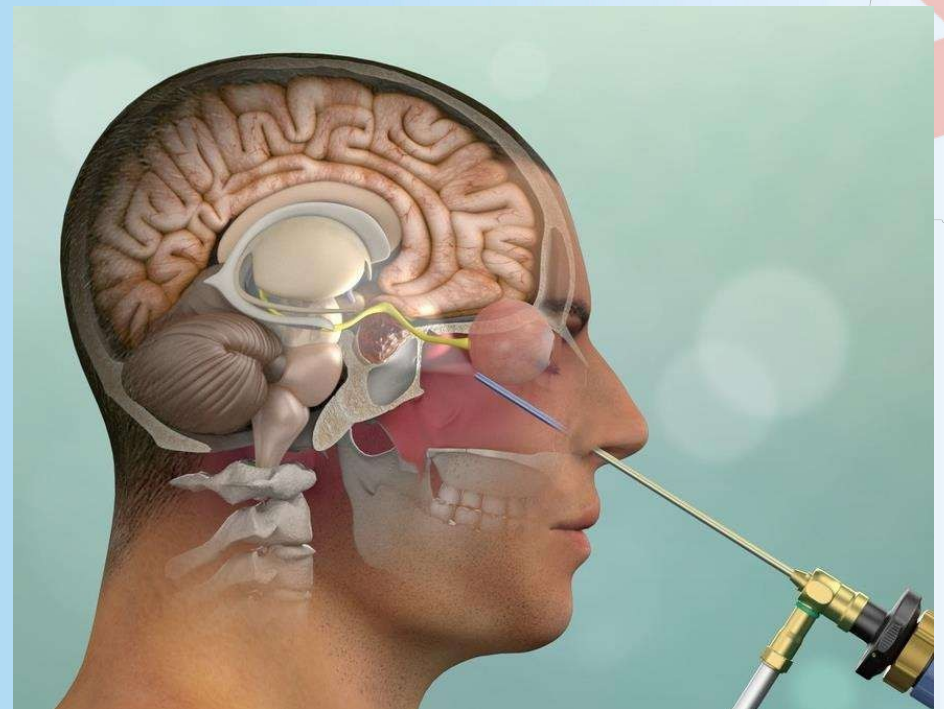
Diabetic ketoacidosis (DKA)

- Life-threatening complication of DM (mostly type 1)
 - ↓ insulin → ↓ glucose intracellularly → switch to beta-oxidation of fatty acids into ketone bodies → ↓ pH → metabolic acidosis (DKA)
- DEHYDRATION
- HYPOKALEMIA
- HYPERGLYCEMIA
- Treatment is rehydration, K⁺-repletion, and insulin



Pituitary adenomas

- Symptoms depends on what cells the adenoma consists of:
 - Prolactinoma (40%)
 - Somatotroph adenoma (10-15%)
 - Corticotroph adenoma (Cushing disease) (5%)
 - Thyrotroph adenoma (1%)
 - Gonadotroph adenoma (very rare)



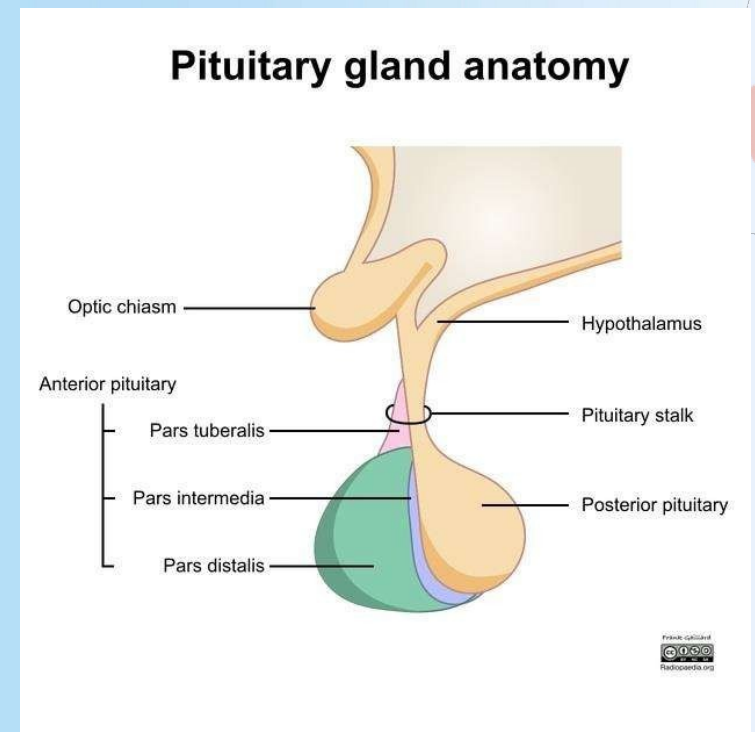
Prolactinoma

- Tumor arises in pituitary gland from lactotrophs (prolactin-producing cells)
- Causes ↑ prolactin levels
♀
- Anovulatory infertility, menstrual changes (oligo- /amenorrhea), galactorrhea
♂
- ↓ Libido, erectile dysfunction, infertility, gynecomastia



Hyperprolactinemia from other causes

- Dopamine is normally meant to inhibit prolactin-production
- It flows usually from the hypothalamus down the pituitary stalk to the adenohypophysis (ant. pituitary)
- If compressed by a tumor, ↑ dopamine transport -> ↑ prolactin secretion

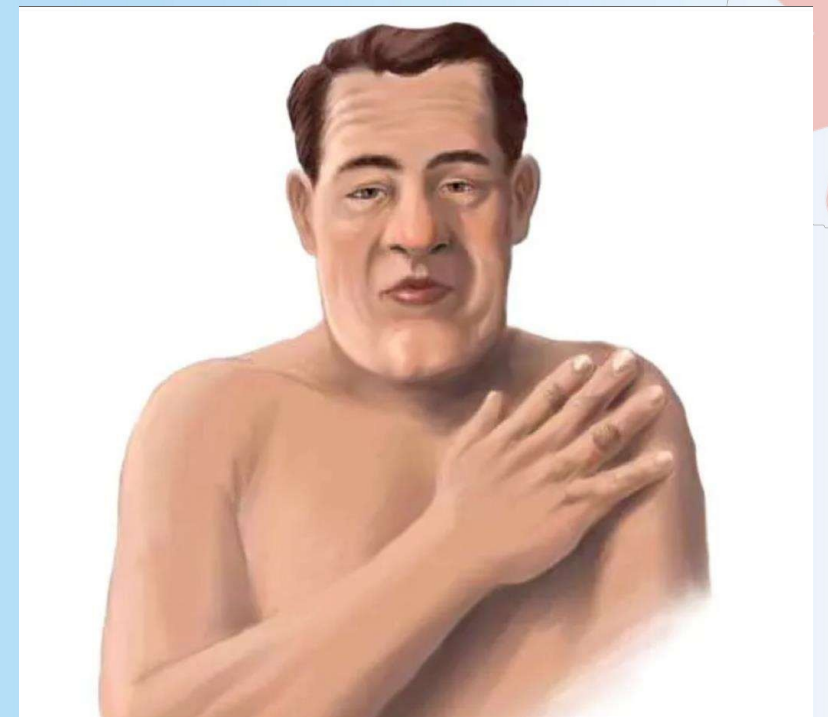


Acromegaly

- Tumor arises in pituitary gland from somatotrophs (GH-producing cells)

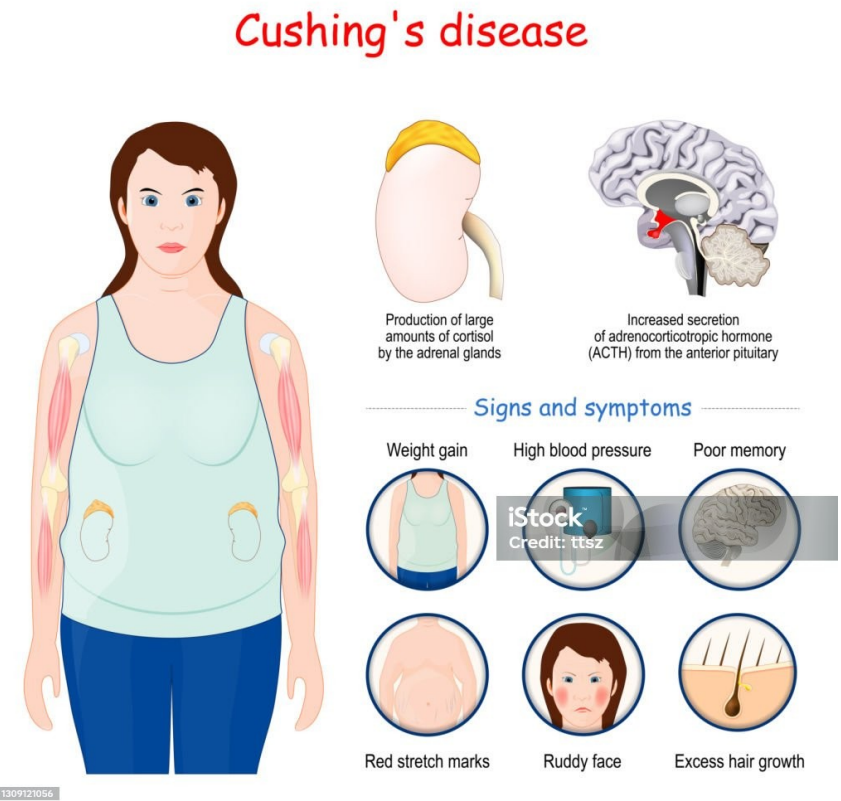
Somatotrophs produce GH $\rightarrow$ $\uparrow$ IGF-1 $\rightarrow$ cell growth and replication
“Especially on bone, cartilage, skeletal muscle, skin, soft tissue, organs”

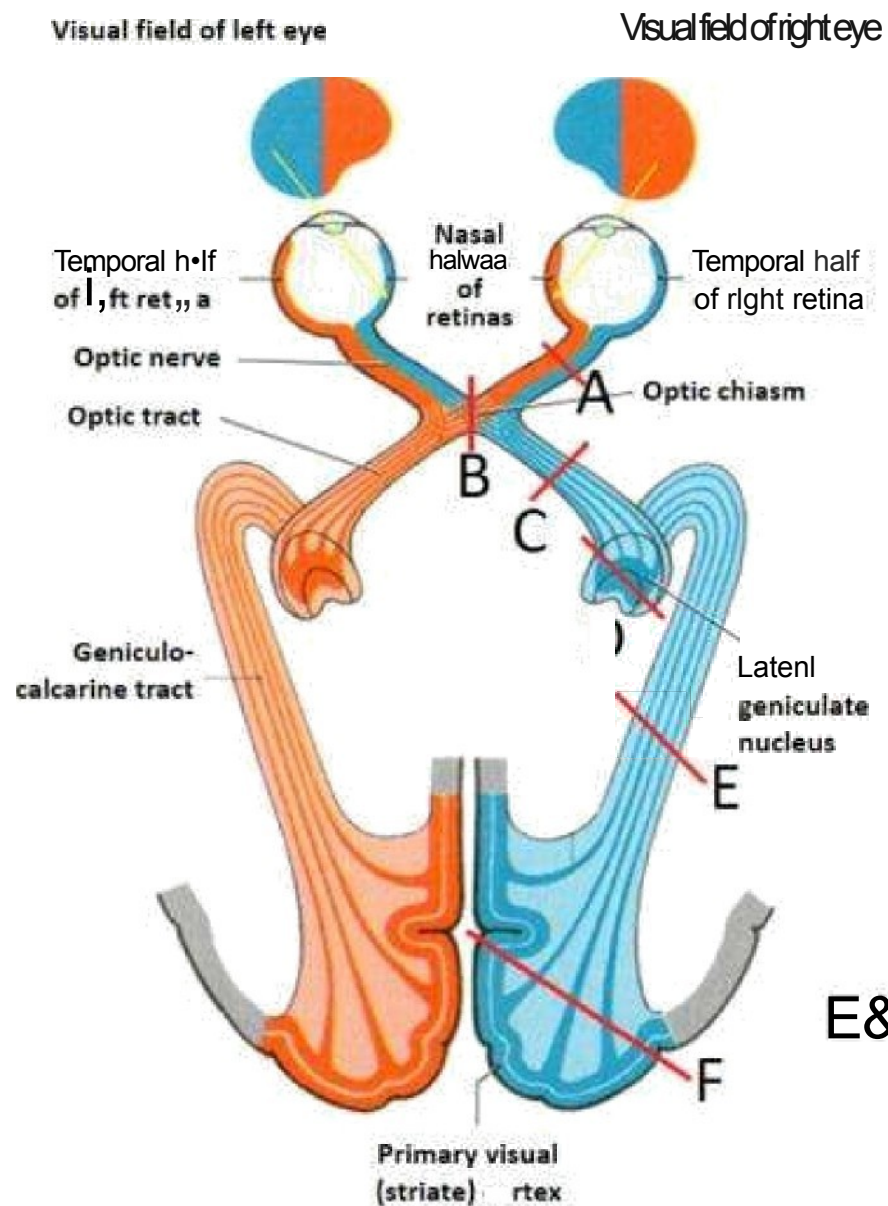
- If this happens to a child $\rightarrow$ gigantism
- If this happens to an adult $\rightarrow$ acromegaly
- In young, they grow tall because the epiphyseal plate has not yet closed
- In adolescents/adults with closed epiphyseal plates, height stays the same



Corticotroph adenoma (Cushing's disease)

- Adenoma from corticotrophic cells in the anterior pituitary
- A.k.a. Cushing's disease
- Leads to **Cushing syndrome**
- Cushing's disease $\neq$ Cushing syndrome
- ACTH-dependence: whether the cortisol release is driven from ACTH (in case of pituitary adenoma) or other causes





	left	right
A		
B		
C		
D		
E&F		

Blood supply

ophthalmic a.

Superior = anterior cerebral a.
Inferior = internal carotid a.
posterior communicating a.
posterior cerebral a.
basilar a.

posterior communicating a.
anterior choroidal a.

anterior choroidal a.
lateral posterior choroidal a.

posterior cerebral aa.

deep branches of middle cerebral a.

posterior cerebral a.
calcarine
parieto-occipital
posterior temporal

middle cerebral a.
anastomosing
frenches

