Endocrine system

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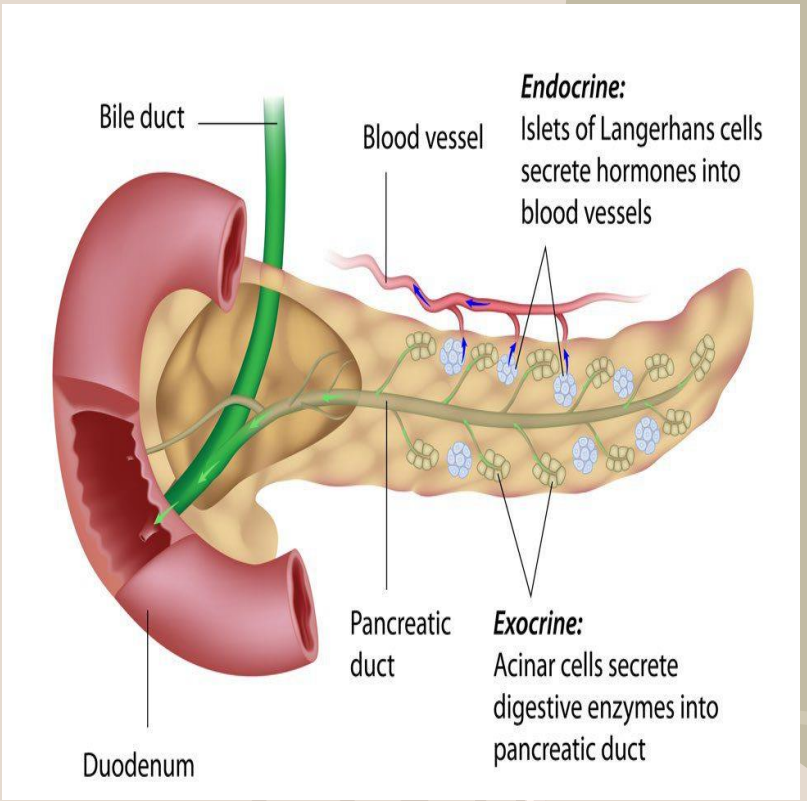
Pancreas

❖The exocrine pancreas

- Constitutes 80% to 85% of the organ
- Composed of acinar cells. These pyramidally shaped epithelial cells contain membrane-bound granules rich in proenzymes (zymogens), such as trypsinogen, chymotrypsinogen, and prophospholipase A and B, all of which contribute to digestion.
- Upon secretion, these proenzymes and enzymes are carried by a series of ductules and ducts to the duodenum, where they are activated by proteolytic cleavage

❖The endocrine pancreas

- Composed of about 1 million endocrine cell clusters, the islets of Langerhans, that are scattered throughout the gland. constitute only 1% to 2% of the organ mass
- The hormones released by the islet cells are essential regulators of systemic metabolism.



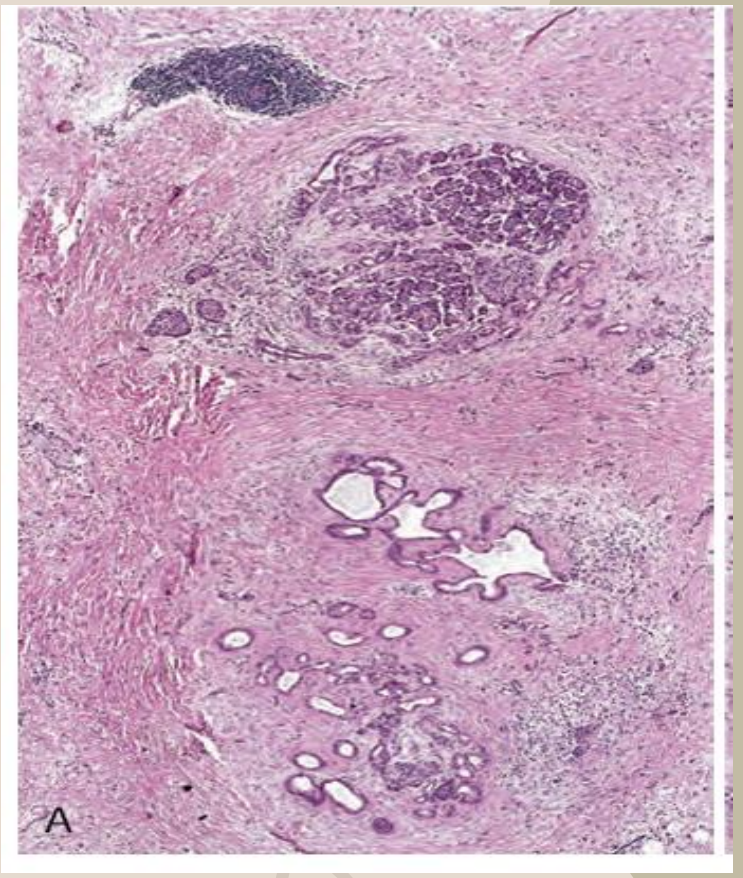
Acute pancreatitis (of the exocrine pancreas):

- Acute pancreatitis is characterized by reversible pancreatic parenchymal injury and inflammation
- Pathogenesis: inappropriate release and activation of pancreatic enzymes that, in turn, destroy pancreatic tissue and elicit an acute inflammatory reaction.
- Causes:
- 1) Pancreatic duct obstruction: is most commonly caused by gallstones.
- 2) Acinar cell injury: Alcohol, drugs, trauma, viruses.
- 3) Defective intracellular transport: Alcohol, drug obstruction.

- Clinically: abdominal pain (constant, intense, and referred to the upper or mid back and, occasionally, the left shoulder). Anorexia, nausea, and vomiting.
- Investigations: Laboratory findings include elevation of serum amylase and lipase levels during the first 4 to 12 hours following the onset of pain

Chronic pancreatitis (of the exocrine pancreas):

- Defined as prolonged inflammation of the pancreas associated with irreversible destruction of exocrine parenchyma, fibrosis, and, in the late stages, loss of endocrine parenchyma.
- The most common cause of chronic pancreatitis is long-term alcohol use.
- Chronic pancreatitis often follows repeated episodes of acute pancreatitis
- Clinically: features include intermittent or persistent abdominal pain, intestinal malabsorption, and diabetes



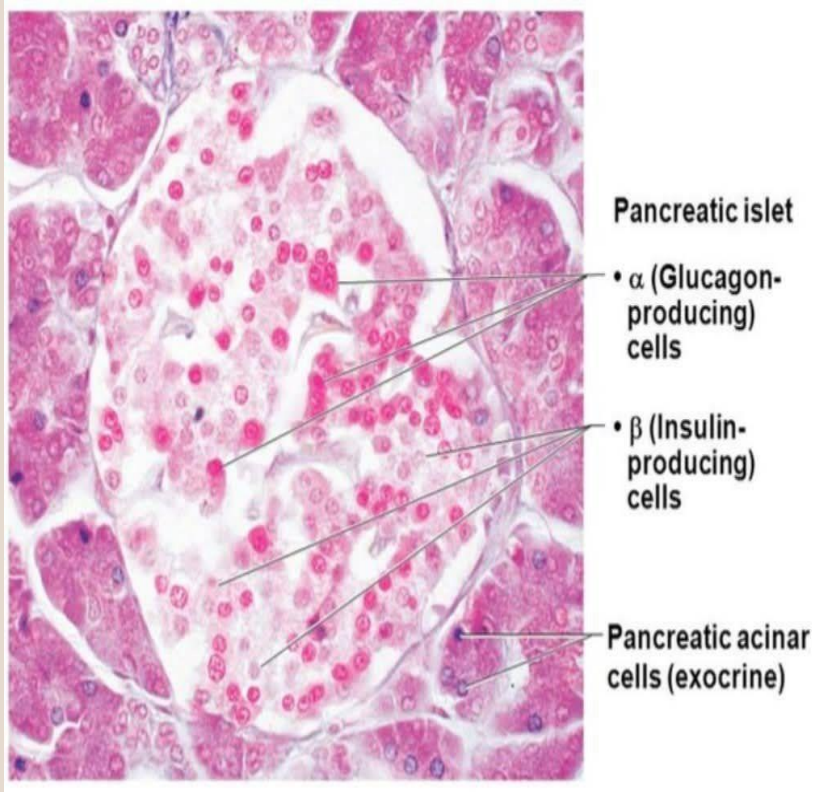
Extensive fibrosis and atrophy has left only residual islets (top) and ducts (bottom), with a sprinkling of chronic inflammatory cells

The Endocrine pancreas:

- The four main types are β, α, δ, and PP (pancreatic polypeptide) cells.
- They can be differentiated by the ultrastructural characteristics of their granules, and by their hormone content

- 1) The β cells produce insulin, which regulates glucose utilization in tissues and reduces blood glucose levels
- 2) The α cells secrete glucagon, which stimulates glycogenolysis in the liver and thus increases blood sugar.
- 3) The δ cells secrete somatostatin, which suppresses both insulin and glucagon release.
- 4) The PP cells secrete pancreatic polypeptide, which exerts several gastrointestinal effects, such as stimulation of secretion of gastric and intestinal enzymes and inhibition of intestinal motility.

- These cells not only are present in islets but also are scattered throughout the exocrine pancreas



Diabetes Mellitus:

- is a group of metabolic disorders sharing the common feature of hyperglycemia caused by defects in insulin secretion, insulin action, or, most commonly both.

- Diagnosis:

- Blood glucose is normally maintained in a very narrow range of 70 to 120 mg/dL. According to the ADA and WHO, diagnostic criteria for diabetes include the following:

1. A fasting plasma glucose ≥126 mg/dL
2. A random plasma glucose ≥200 mg/dL
3. A 2-hour plasma glucose ≥200 mg/dL during an oral glucose tolerance test (OGTT) with a loading dose of 75 g
4. A glycated hemoglobin (HbA1c) level ≥6.5%

➢ Classification:

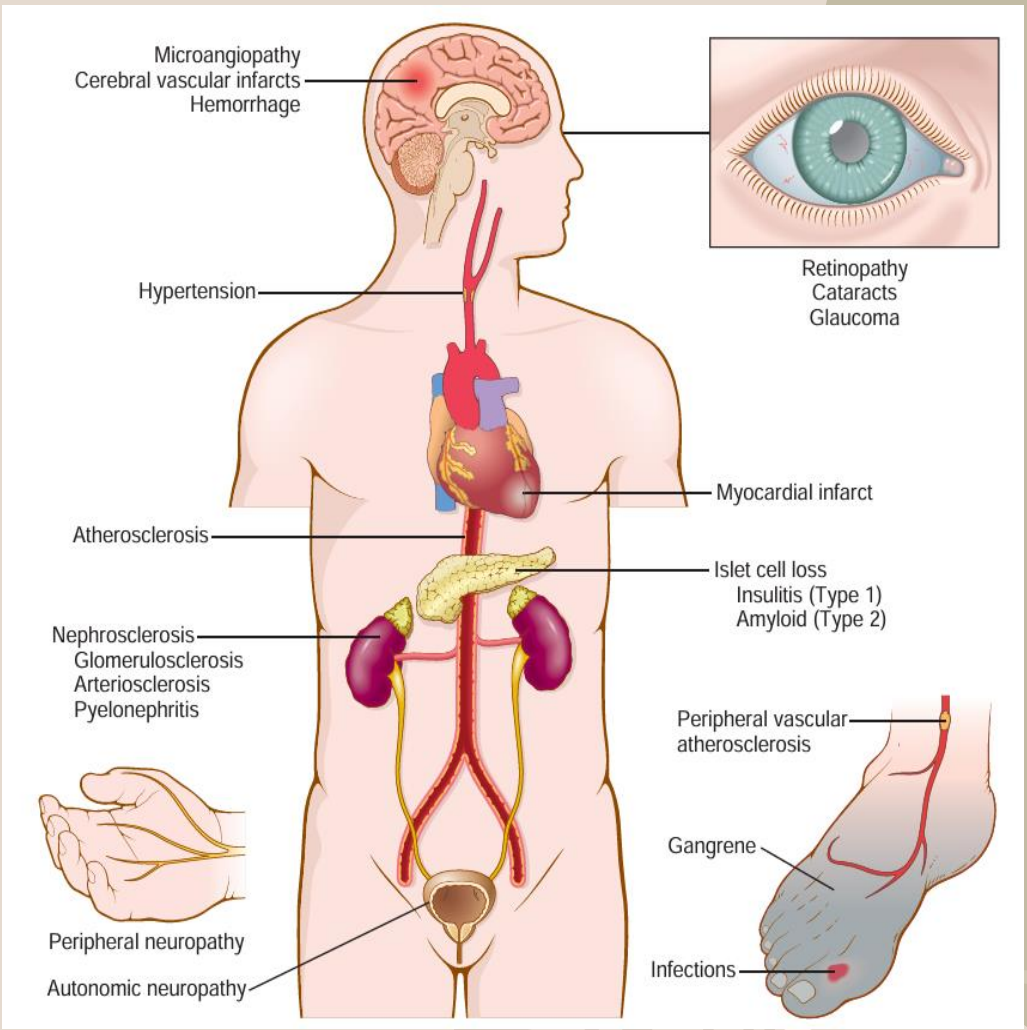
1) Type 1 diabetes (T1D) is an autoimmune disease characterized by pancreatic β-cell destruction and an absolute deficiency of insulin. is the most common subtype diagnosed in patients younger than 20 years of age.
2) Type 2 diabetes (T2D) is caused by a combination of peripheral resistance to insulin action and a secretory response by pancreatic β cells that is inadequate to overcome insulin resistance ("relative insulin deficiency"). Approximately 90% to 95% of diabetes patients have T2D, and the vast majority of such individuals are over weight.

➢ Clinically: The onset of T1D is usually marked by the triad of polyuria, polydipsia, polyphagia, and, when severe, diabetic ketoacidosis, all resulting from metabolic derangements.

- Diabetic Ketoacidosis: It is a life-threatening complication of diabetes and typically seen in patients with type-1 diabetes mellitus, though it may also occur in patients with type-2 diabetes mellitus. In most cases, the trigger is new-onset diabetes, an infection, or a lack of compliance with treatment.
- The liver processes the fat into a fuel called ketones, which causes the blood to become acidic.

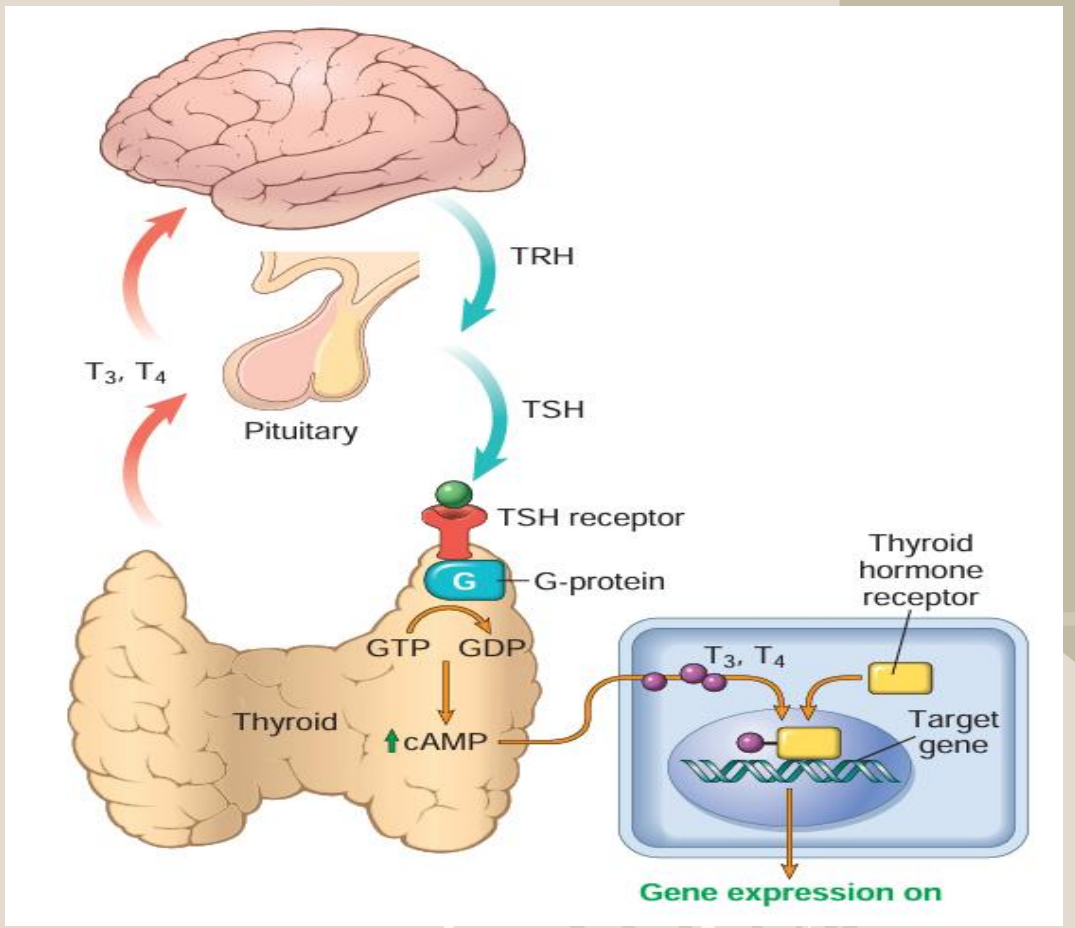
❖ Chronic Complications of Diabetes:

- The morbidity associated with long-standing diabetes of either type is due to damage induced in large- and medium sized muscular arteries (diabetic macrovascular disease) and in small vessels (diabetic microvascular disease) by chronic hyperglycemia.
- Macrovascular disease causes accelerated atherosclerosis among patients with diabetes, resulting in increased risk of myocardial infarction, stroke, and lower extremity ischemia.
- The effects of microvascular disease are most profound in the retina, kidneys, and peripheral nerves, resulting in diabetic retinopathy, nephropathy, and neuropathy, respectively



Thyroid gland

- Gland responsible for secretion of the thyroid hormones (T3 and T4) and calcitonin.
- Thyroid hormones are required for the development of brain and maintenance of basal metabolic rate
- Calcitonin is involved in calcium homeostasis.
- The two major disorders:
- 1) Hyperthyroidism
- 2) Hypothyroidism

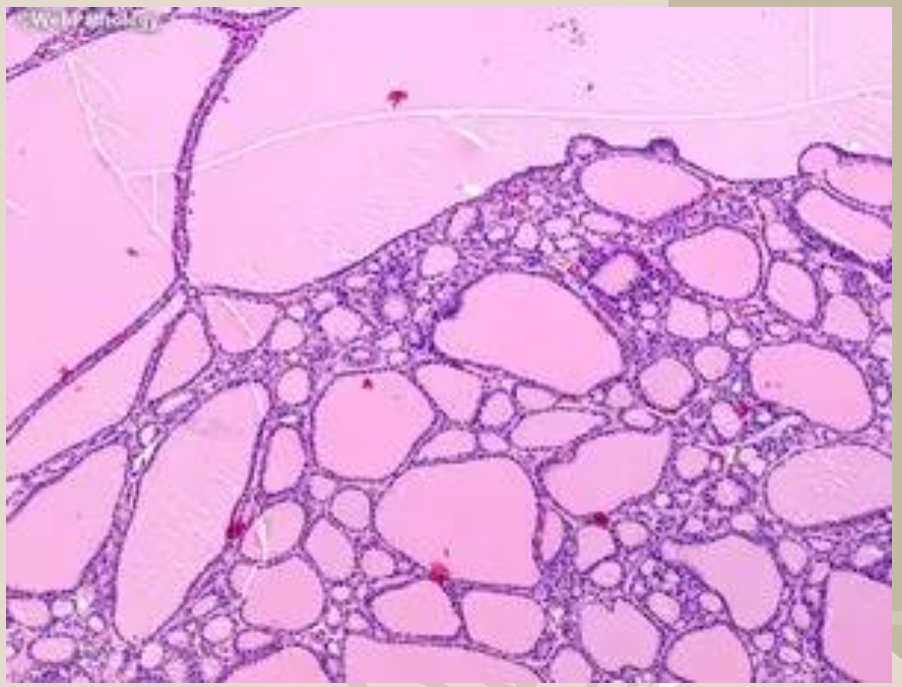


Hyperthyroidism:

- Definition: A state of hyperfunctioning of the thyroid gland
- Pathogenesis: Elevated levels of free T3 and T4 and associated with increased sympathetic activity.
- Causes:

1) Diffuse toxic hyperplasia (Graves disease), the most common.
2) Toxic multinodular goiter
3) Toxic adenoma
4) Uncommon causes: acute thyroiditis, thyroid cancer, TSH secreting pituitary adenoma.

- Clinically: Tachycardia, palpitation, increased sweating, heat intolerance, tremor, diarrhea and weight loss.
- Lab findings:
- In primary hyperthyroidism: serum TSH level is low, and free T4 is increased.
- In secondary hyperthyroidism: serum TSH level is high



Thyroid hyperplasia

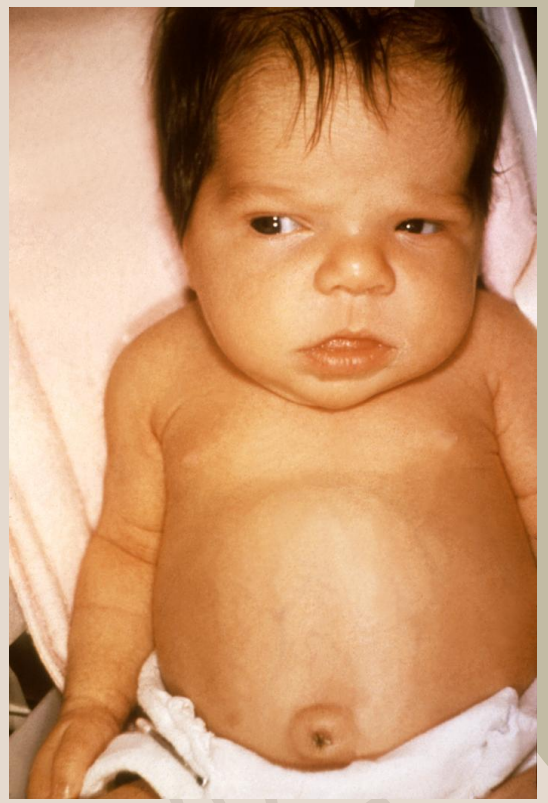
Hypothyroidism:

- Resulting from a deficiency of thyroid hormone
- Causes:

  1) Environmental iodine deficiency (most common etiology worldwide).
  2) Destruction or ablation of thyroid gland (surgery, radiation, developmental)
  3) Interference with thyroid hormone synthesis (idiopathic, genetic, drugs)
  4) Any pituitary or hypothalamic disorder that causes reduced TRF or TSH secretion
     - Include genetics, tumors (e.g., pituitary adenoma), infection, autoimmune disorders, drugs, pituitary surgery or radiotherapy, trauma.

- Clinically: Most common symptoms are dry skin, fatigue, muscle cramps, cold sensitivity, voice changes and constipation
- Myxedema, characterized by thickened, nonpitting edematous soft tissue

- Cretinism:
- Cretinism refers to hypothyroidism that develops in infancy or early childhood.
- Clinical features of cretinism include severe intellectual disability, short stature, coarse facial features, a protruding tongue, and umbilical hernia.
- Pathogenesis: Normally, maternal T3 and T4 cross the placenta and are critical for fetal brain development.
- If there is maternal thyroid deficiency before the development of the fetal thyroid gland, intellectual disability is severe.
- In contrast, maternal thyroid hormone deficiency later in pregnancy, after the fetal thyroid has become functional, does not affect normal brain development
- Early Diagnosis: Newborn screening for congenital hypothyroidism is crucial
- Hormone Replacement: Starting thyroid hormone (T4) treatment very early (within the first few months) can improve mental development, though severe cases may still have deficits,



Thyroid cancer:

❖ Papillary carcinomas are the most common form of thyroid cancer, accounting for nearly 85% of cases in the United States.

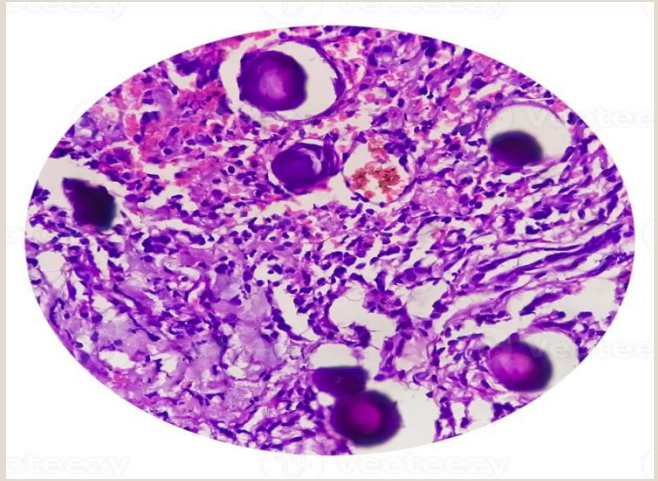
- They occur throughout life but most often between 25 and 50 years of age,
- account for the majority of thyroid carcinomas associated with previous exposure to ionizing radiation
- Microscopically:

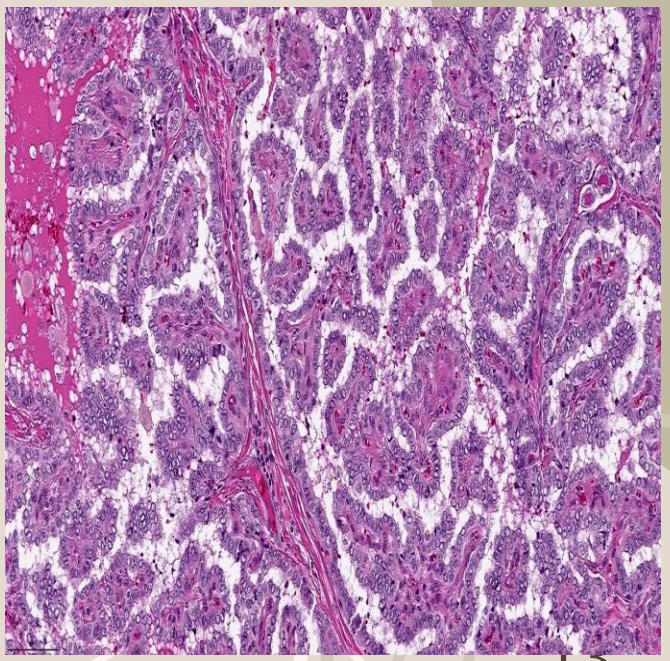
➢ *Branching papillae* having a fibrovascular stalk covered by a single to multiple layers of cuboidal epithelial cells.

➢ Nuclei with an optically clear or empty appearance, giving rise to the *Orphan Annie eye nuclei.*

➢ Concentrically calcified structures termed *psammoma bodies*

➢ Papillary thyroid cancers have an excellent prognosis, with a 10-year survival rate in excess of 95%.





Parathyroid gland

❖ Contains two types of cells:

- 1) Chief cells (secrete Parathyroid hormone PTH)
- 2) Oxyphil cells (secrete Glycogen)
- The function of the parathyroid glands is to regulate calcium homeostasis

❖ The activity of the parathyroid glands is controlled by the level of free (ionized) calcium in the blood.

➢ Normally, decreased levels of free calcium stimulate the synthesis and secretion of PTH.

❖ Several metabolic functions of PTH regulate serum calcium levels:

- 1) Increased renal tubular reabsorption of calcium
- 2) Increased conversion of vitamin D to its active dihydroxy form in the kidneys, which, in turn, augments gastrointestinal calcium absorption
- 3) Increased urinary phosphate excretion, thereby lowering serum phosphate levels and further increasing calcium (since phosphate binds to ionized calcium)
- 4) Enhanced osteoclastic activity (i.e., bone resorption, thus releasing ionized calcium)

➢ The net result of these activities is to elevate the level of free calcium, which, in turn, inhibits further PTH secretion in a classic feedback loop.

Hyperparathyroidism:

1 ## Primary (secrete PTH without stimulation by calcium levels)

- The most common cause of primary hyperparathyroidism is parathyroid adenoma

❖ Primary hyperparathyroidism is the most common cause of asymptomatic hypercalcemia (increased serum PTH and calcium without symptoms).

❖ Symptomatic hypercalcemia:

1) Bone disease and bone pain secondary to fractures of bones weakened by osteoporosis

2) Nephrolithiasis (renal stones) , Chronic renal insufficiency and abnormalities in renal function lead to polyuria and secondary polydipsia.

3) Gastrointestinal disturbances, including constipation, nausea, peptic ulcers, pancreatitis, and gallstones

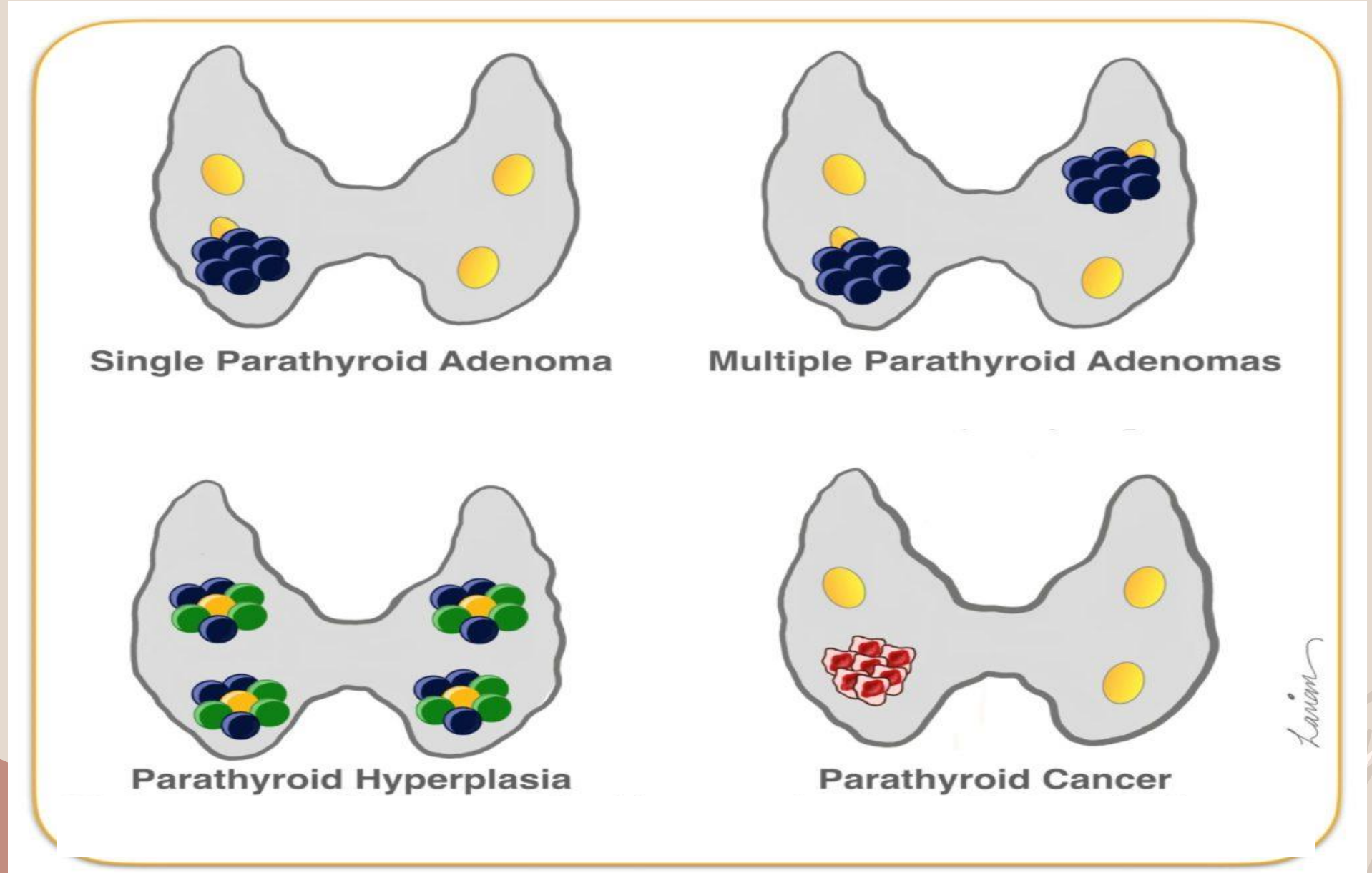
4) Central nervous system alterations, including depression, lethargy, and eventually seizures

5) Neuromuscular abnormalities, including weakness and fatigue

6) Cardiac manifestations, including aortic or mitral valve calcifications (or both)

2 ## Secondary:

- Renal failure, vitamin D insufficiency, nutritional deficiency.
- The hypocalcemia after these causes result in increase in PTH secretion.


Single Parathyroid Adenoma
Multiple Parathyroid Adenomas
Parathyroid Hyperplasia
Parathyroid Cancer

Hypoparathyroidism:

- Causes:

1) Surgical removal of the gland (the most common cause)

2) Congenital absence (Like in DiGeorge syndrome)

- Clinically: Due to hypocalcemia:

- 1) The hallmark of hypocalcemia is **tetany**, which is characterized by neuromuscular irritability, resulting from decreased serum calcium levels. The symptoms range from circumoral numbness or paresthesias (tingling) of the distal extremities and carpopedal spasm, to life threatening laryngospasm and generalized seizures.

- 2) Mental status changes include emotional instability, anxiety and depression

- 3) Ocular disease takes the form of calcification of the lens and cataract formation.

- 4) Dental abnormalities occur when hypocalcemia is present during early development. These findings are highly characteristic of hypoparathyroidism and include dental hypoplasia, failure of eruption, defective enamel and root formation, and abraded carious teeth.

Pituitary gland

❖ Structure that lies at the base of the brain within the sella turcica.

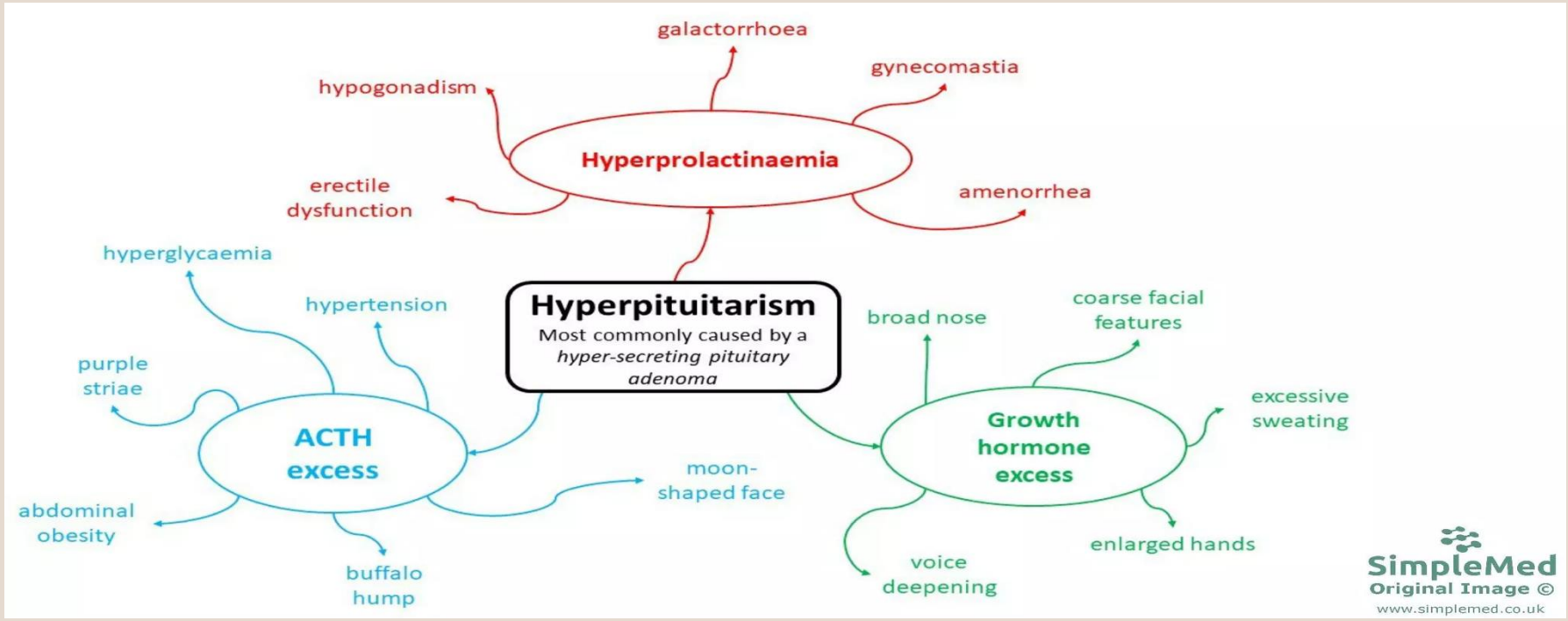
- Its function is controlled by the hypothalamus, to which it is connected by a stalk containing axons extending from the hypothalamus and a rich venous plexus.

❖ The pituitary gland is composed of two morphologically and functionally distinct components:

- 1) the anterior lobe (adenohypophysis): which constitutes about 80% of the gland, produces trophic hormones that stimulate the production of hormones from the thyroid, adrenal, and other glands.
- 2) the posterior lobe (neurohypophysis). two peptide hormones are secreted from the posterior pituitary, oxytocin and antidiuretic hormone (ADH), These hormones are actually synthesized in the hypothalamus and are transported through axons to the posterior pituitary.

❖ The manifestations of pituitary disorders are related to either excess or deficiency of pituitary hormones:

- 1) Hyperpituitarism arises from excess secretion of trophic hormones. The causes of hyperpituitarism include hyperplasias, adenomas, and carcinomas of the anterior pituitary, and certain hypothalamic disorders.
- 2) Hypopituitarism results from deficiency of trophic hormones. It may be caused by ischemic injury, surgery or radiation, inflammatory disorders,


galactorrhoea
hypogonadism
gynecomastia
Hyperprolactinaemia
erectile dysfunction
amenorrhea
hyperglycaemia
hypertension
Hyperpituitarism
Most commonly caused by a hyper-secreting pituitary adenoma
broad nose
coarse facial features
purple striae
ACTH excess
Growth hormone excess
excessive sweating
moon-shaped face
abdominal obesity
buffalo hump
voice deepening
enlarged hands
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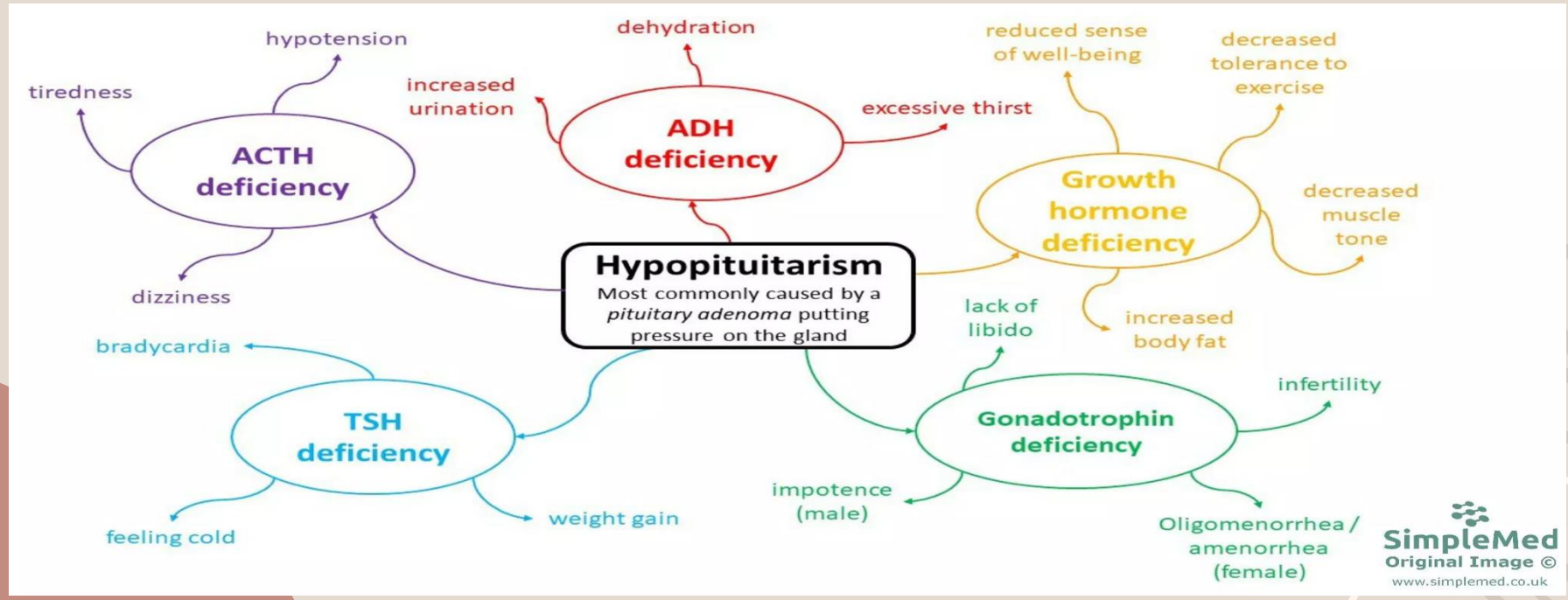
hypotension
dehydration
reduced sense of well-being
decreased tolerance to exercise
tiredness
increased urination
ADH deficiency
excessive thirst
ACTH deficiency
Growth hormone deficiency
decreased muscle tone
Hypopituitarism
Most commonly caused by a pituitary adenoma putting pressure on the gland
dizziness
lack of libido
increased body fat
bradycardia
infertility
TSH deficiency
Gonadotrophin deficiency
impotence (male)
weight gain
feeling cold
Oligomenorrhea / amenorrhea (female)
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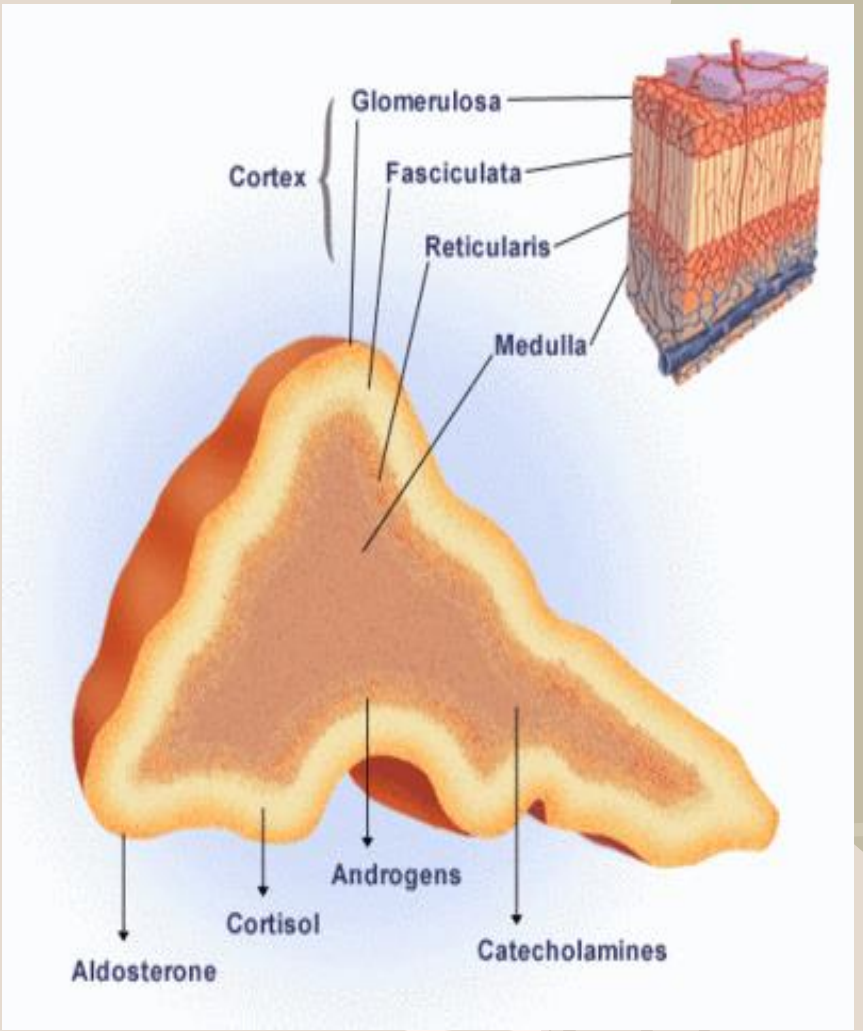
Adrenal gland

- Adrenal cortex has 3 layers that are histologically and physiologically distinct, listed below from superficial to deep
  - Zona glomerulosa: produces mineralocorticoids, specifically aldosterone, which increases sodium and water absorption and potassium secretion
  - Zona fasciculata: produces glucocorticoids (cortisol) and some sex hormones
  - Zona reticularis: produces estrogens and androgens, some glucocorticoids; this layer lies adjacent to the adrenal medulla

- Adrenal medulla is a neuroendocrine organ (paraganglia) composed of chromaffin cells, which secrete catecholamines;
- extra-adrenal paraganglia are aggregates of crest derived neuroendocrine cells that are dispersed throughout the body and are associated with autonomic function.



Hyperadrenalism:

1) Cushing syndrome:

- Excess of Glucocorticoid (cortisol)
- Causes of Cushing syndrome:

1) Exogenous: is the most common , are the result of the administration of exogenous glucocorticoids (iatrogenic Cushing syndrome).

2) The endogenous causes can, in turn, be divided into those that are ACTH dependent and those that are ACTH independent.

- The disorder affects women about four times more frequently than men

- Clinically: truncal obesity, moon facies, and accumulation of fat in the posterior neck and back (buffalo hump).
- Glucocorticoids induce gluconeogenesis and inhibit the uptake of glucose by cells, with resultant hyperglycemia, glucosuria, and polydipsia (secondary diabetes)

2) Hyperaldosteronism:

- Excess aldosterone secretion
- Primary hyperaldosteronism stems from an autonomous overproduction of aldosterone, with resultant hypertension,

3) Adrenogenital syndromes:

- Excess production of androgen resulting in virilization
- The adrenal cortex secretes dehydroepiandrosterone and androstenedione, two compounds that can be converted to testosterone in peripheral tissues.

❖ Causes:

1) adrenocortical carcinoma

2) congenital adrenal hyperplasia (the most common cause):

- Congenital adrenal hyperplasia stems from several autosomal recessive, inherited metabolic errors, each characterized by a deficiency of a particular enzyme involved in the biosynthesis of cortisol

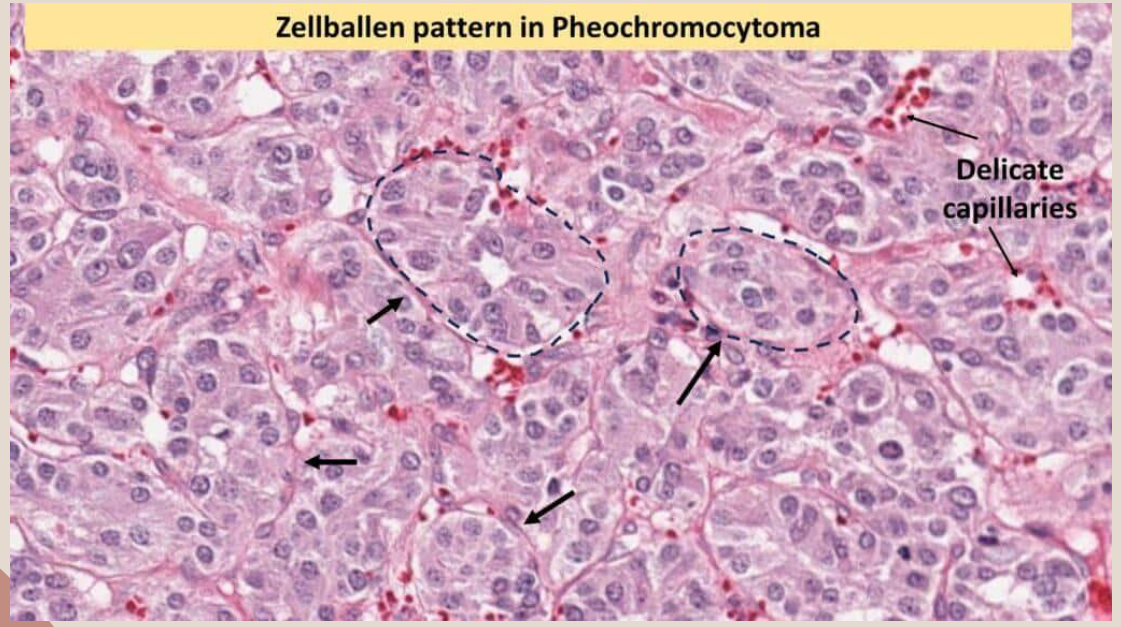
❖ in 21- α hydroxylase deficiency : Excessive androgenic activity causes signs of masculinization in **females** (Oligomenorrhea, hirsutism, acne)

❖ In **males**, Androgen excess is associated with enlargement of the external genetalia and precocious puberty in prepubertal patients and oligospermia in older patients

Pheochromocytoma:

- Pheochromocytomas are neoplasms composed of chromaffin cells, which synthesize and release catecholamines and, in some instances, peptide hormones.
- It is important to recognize these tumors because they are a rare cause of surgically correctable hypertension

The tumors are composed of clusters of polygonal shaped chromaffin cells , that are surrounded by supporting sustentacular cells, creating small nests or alveoli (zellballen), that are supplied by a rich vascular network



Pheochromocytoma

5 P's

Paroxysmal hypertension
Palpitations
Perspiration
Pain in head
Pallor

Rule of 10

10% malignant
10% bilateral/multiple
10% in children
10% familial
10% recurr
10% extra-adrenal
10% discovered incidentally


Thank
you