Pathology of Pituitary, Adrenal and pancreas

Disorders of the anterior pituitary

I Hyperpitutary syndromes

Caused by: -Hyperplasia.

-**Functioning adenomas** of anterior pituitary is the **most cause**, may produce Prolactin, Growth Hormone, and ACTH

-Carcinoma (rare).

II Hypopituitarism

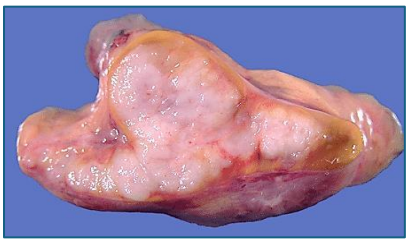
(1) Congenital anomalies (agenesis-Aplasia-hypoplasia).

(2) Sheehan's syndrome which is Post-partum Pituitary Necrosis; Coagulative necrosis, followed by fibrosis.

(3) Destruction of the pituitary by a pituitary adenoma, surgery, radiation or trauma, metastatic tumors.

Tumors of the anterior pituitary

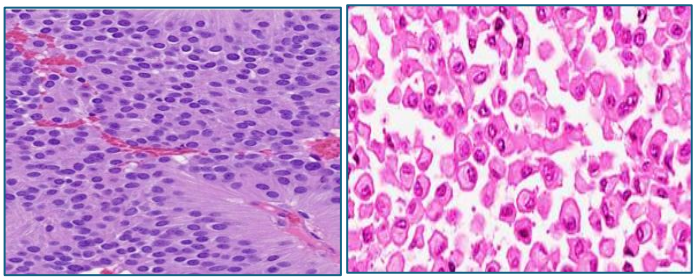
	Pituitary Adenoma	Craniopharyngioma
Site & incidence	---	They are **benign** epithelial neoplasm of Sellar region, arise from epithelial remnants of Rathke's Pouch. **Age:** children and young adults
N/E	Adenomas appear as a **lobulated** mass covered by a thin, attenuated shiny **capsule**	**-**Craniopharyngiomas are **calcified yellow (due to cholesterol crystal deposits).** **-Cross-sections** reveal multiple cystic areas containing oily fluid.
M/E	**-Tumors have a uniform** fibrovascular stroma; cells classified as acidophilic, basophilic or chromophobic based on content of hormone secretory cells. **- Crooke hyaline change** is characterized by large cells with a glassy hyaline appearance (due to accumulation of keratin filaments)	- **May appear well circumscribed** Cords, lobules, nodular whorls and trabeculae of well differentiated squamous epithelium bordered by palisading columnar epithelium - **Peripheral cells** surround looser plumper cells called stellate reticulum - **Nodules of plump**, anucleate squamous cells (ghost cells) and wet keratin



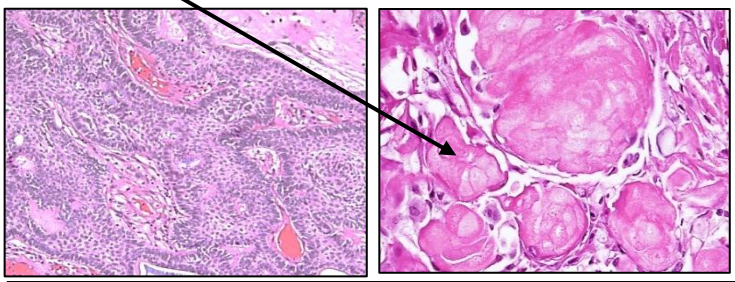
N/E of pituitary adenoma

Ghost cells

N/E of Craniopharyngioma



M/E of pituitary adenoma



M/E of Craniopharyngioma

Diseases of supra-renal gland

I Hyperpitutary syndromes

Due to Hyperplasia, adenoma or carcinoma of the adrenal cortex.

Effects:

Conn's disease	Cushing syndrome	Adrenogenital syndrome
aldosterone hypersecretion	glucocorticoids hypersecretion	androgen hypersecretion

II Cortical hypofunction

A. Acute adrenal insufficiency leads to shock and death.

Waterhouse-Friederichsen Syndrome: Acute Hypofunction occurs in association with overwhelming bacteremia (usually Meningococcus).

B. Chronic adrenal insufficiency leads to Addison's disease

Causes: 1-Idiopathic Atrophy (60-75%)

2- an autoimmune disease

3-Tuberculosis

4-Amyloidosis

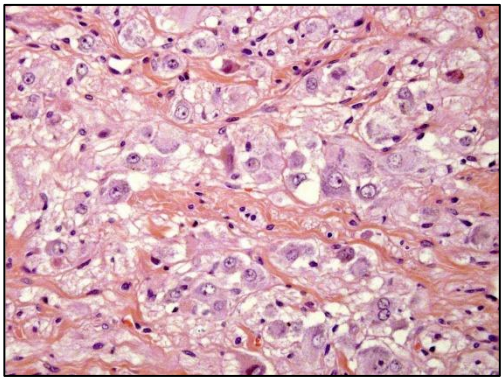
5-Metastatic Carcinoma [lung]

Tumors of supra-renal gland

Primary	Secondary
Cortex	-Lung -Breast -Melanomas
-Cortical Adenoma -Cortical carcinoma	
Medulla	
-Ganglioneuroma -Pheochromocytoma -Neuroblastoma	

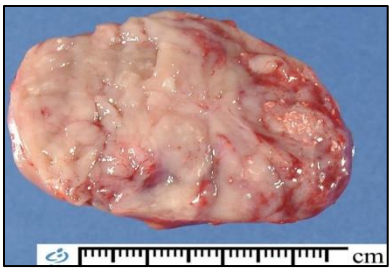
Ganglioneuroma

Benign tumor composed of ganglion cells and nerve fibers (schwanian stroma)



Neuroblastoma

Highly malignant tumor of children under the age of 4 years.

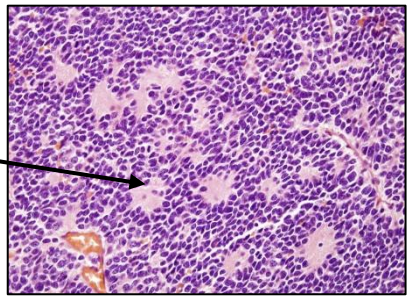


N/E:

Large, soft mass with yellow areas of necrosis and red areas of hemorrhage.

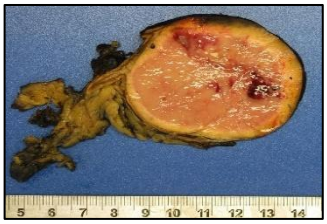
M/E:

The tumor consists of small blue malignant round cells with dark nuclei "neuroblasts" arranged in sheets or in **rosettes**.



Pheochromocytoma

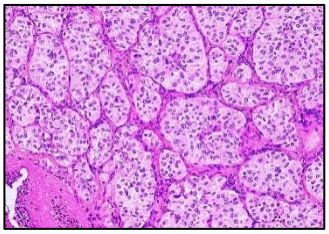
Paraganglioma of the adrenal medulla composed of chromaffin cells that produce catecholamines.



ME: Nested, trabecular or solid arrangement.

Cells: large, polygonal, uniform or extensively vacuolated.

Cytoplasm: abundant fine, granular red-purple cytoplasm.



Diseases of Endocrine Pancreas

Diabetes Mellitus (DM)

• **A group of metabolic disorders** characterized by hyperglycemia caused by defects in insulin secretion, insulin action, or both.

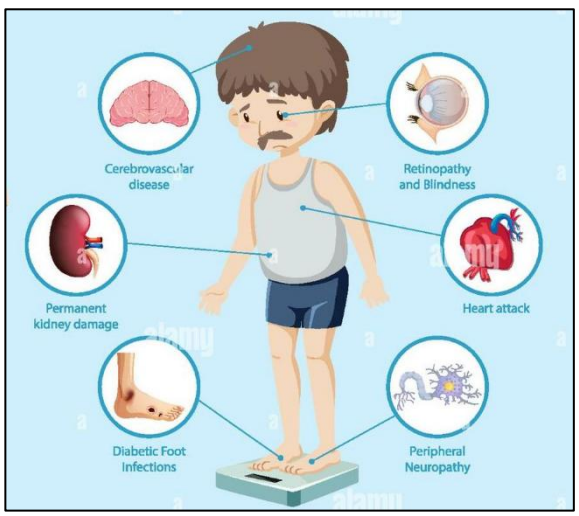
• **DM causes** secondary damage in multiple organ systems, especially the blood vessels, kidneys, eyes, and nerves.

I Clinically

A. Classic triad of symptoms: Polyuria +polydipsia +polyphagia

B. Elevated plasma glucose level confirmed by:

- Fasting plasma glucose >126 mg/dL.
- Random plasma glucose ≥ 200 mg/dL (in a patient with classic clinical signs or in repeated measures).
- Glycated hemoglobin (HbA1C) level ≥6.5%



II Types

Types	T1DM	T2DM
Etiopathogenesis	**1) Autoimmune disease** due to production of autoantibodies against ß cell antigens. **2) ß cell destruction.** **3) Absolute insulin deficiency**. **4) Associated with:** • Specific class I, MHC genes (HLA-DR 3,4). • Environmental factors: as mumps, rubella, and coxsackie B virus infections	**1. Insulin resistance** (failure of target tissues to respond normally to insulin) associated with obesity. **2. Beta cell dysfunction**: B cells compensate for insulin resistance by hypersecretion, followed by ß cell failure, and diabetes

III Mechanism of complication

Formation of advanced glycation end products (AGEs) that bind to receptors (RAGE) on inflammatory, endothelial and vascular smooth muscle cells leads to:

- Release of cytokines, growth factors, reactive oxygen species.
- Inflammation.
- Deposition of basement membrane material, extracellular matrix.
- Neovascularization increased vascular permeability.
- Trapping of low-density lipoprotein (LDL) within AGE-modified large-vessel walls → accelerated atherosclerosis.

IV complication

1. Diabetic Macrovascular Disease (Macroangiopathy)

2. Diabetic Microangiopathy:
   a) Diabetic nephropathy.
   b) Ocular complications.
   c) Diabetic neuropathy.

3. Increased liability for infections.

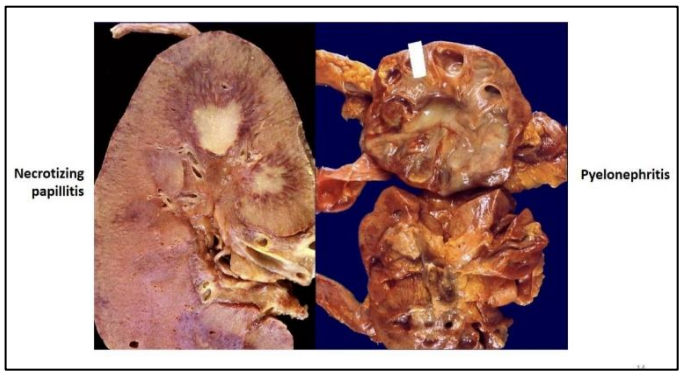
4. Impaired wound healing.

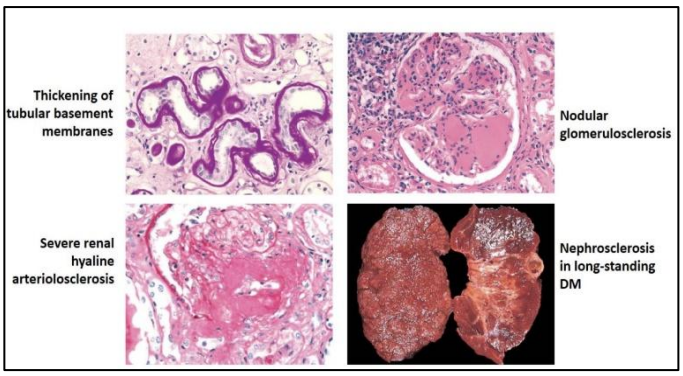
5. Diabetic foot

6. Diabetic coma

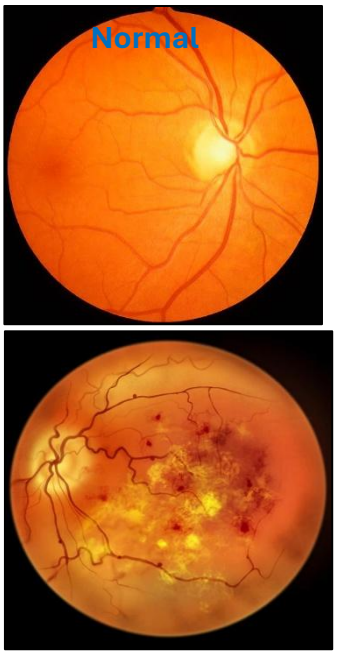
	1-Diabetic Macrovascular Disease (Macroangiopathy)	2-Diabetic Microangiopathy
Characters and site	• **Its hallmark is accelerated atherosclerosis** (greater severity and earlier age at onset). • Affect the aorta and large- and medium-sized arteries.	• Its **hallmark is diffuse thickening of basement membranes**. **Affects:** • Capillaries of the skin, skeletal muscle, retina, renal glomeruli, and renal medulla. • Non-vascular structures: renal tubules, Bowman capsule, nerves.
Outcomes	1. **Myocardial infarction** (coronary atherosclerosis) is the **most common cause of death** in diabetics. 2. Cerebral ischemia and infarction. 3. Peripheral vascular diseases: intermittent claudications and gangrene of the lower extremities. 4. Renal artery atherosclerosis	a. Diabetic nephropathy. b. Diabetic retinopathy and ocular complications. c. Diabetic neuropathy

3- Diabetic Nephropathy	• Renal failure is the **second cause of death in diabetics**.	**Categories**	**1.Glomerular lesions:** • Thickening of glomerular capillary basement membranes • Nodular glomerulosclerosis (Kimmelstiel-Wilson lesion) **2. Thickening** of tubular basement membrane **3.Renal vascular lesions:** atherosclerosis and hyaline arteriolosclerosis. **4. Pyelonephritis** is more severe than non-diabetics. **5. Necrotizing papillitis** (acute papillary necrosis): special pattern of acute pyelonephritis more frequent in diabetics than in non-diabetics.).





4. Ocular complications of DM



1. Cataract

2. Glaucoma

3. Non proliferative retinopathy: edema, hemorrhage, exudate, aneurysms and thickening of retinal papillae.

4. Proliferative retinopathy: Neovascularization and fibrosis, vitreous hemorrhages (more risk of blindness and retinal detachment).

Outcomes: Visual impairment, retinal detachment, total blindness.

5. Diabetic Neuropathy

• Due to microangiopathy +direct axonal damage.

Includes:

1. Peripheral, symmetric neuropathy: of the lower extremities (mainly sensory than motor function).

2. Autonomic neuropathy: disturbances in bowel and bladder function.

3. Mononeuropathy: footdrop or wrist drop or isolated cranial nerve palsies

6. Other complications:

A. Increased liability to infections:

- Due to hyperglycemia + defects in leukocyte functions and cytokine production.
- Skin, respiratory and urinary tract infections.
- Tuberculosis, fungal infections and AIDS.

B. Impaired wound healing (sensory loss, poor circulation and immune response, infection).

C. Diabetic foot: ulceration, infection, gangrene due to neuropathy, poor circulation and increased liability to infection

D. Diabetic coma:

• Diabetic ketoacidosis **(common in type 1 DM).**

• Hypoglycemic coma

Features	T 1DM	T 2DM
Age Incidence Weight/ass. diseases Risk of coma	▪ Childhood and adolescence ▪ 5% to 10% of cases ▪ Normal or weight loss ▪ Diabetic ketoacidosis	▪ Usually in adulthood (40y) ▪ 90% of cases ▪ Obesity and metabolic syndrome ▪ Non-ketotic hyperosmolar coma
Beta cell mass	▪ Depletion	▪ Mild depletion
Insulin level	▪ Reduced	▪ Increased (early); normal or moderate decrease (late)
Islet autoantibodies	▪ Present	▪ Absent
Etiology	▪ Autoimmune destruction and loss of β cells due to failure of self-tolerance	▪ Insulin resistance ▪ β cell dysfunction
Genetic linkage	▪ MHC class I and II genes; HLADR3, 4	▪ Diabetogenic and obesity-related genes
Pathology (islets of Langerhans)	▪ Insulitis ▪ Decreased number and size of islets	▪ Normal islets at early stage ▪ Amyloid deposition in islets (late)