Pathology

Pituitary , Adrenal and Pancreas

Learning Outcomes

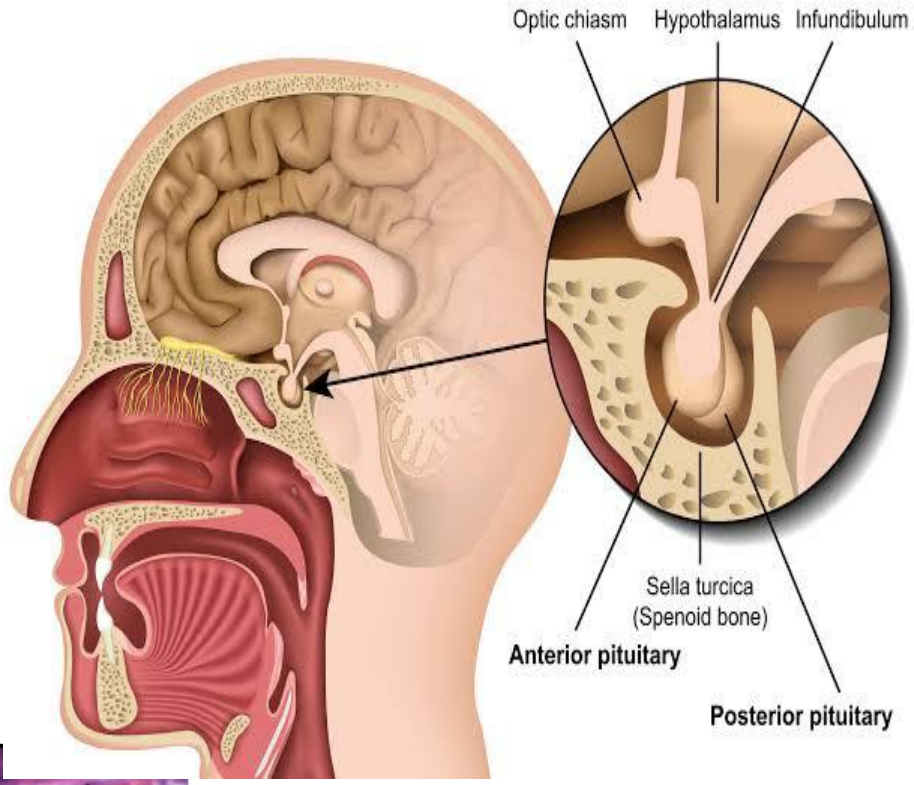
By the end of the lecture, you will be able to:

1. Identify non neoplastic disorders & Tumors of pitutary gland.
2. Identify Adrenal hypo and hyperfunction
3. Description of Adrenal tumors
4. Define diabetes mellitus (DM), Classify DM, Discuss the pathological effects, complications and causes of death.
5. Differentiate between type 1DM and type 2DM.

Agenda

- Pitutary gland Disorders
- Adrenal gland disorders
- Diabetes Mellitus and it's complications

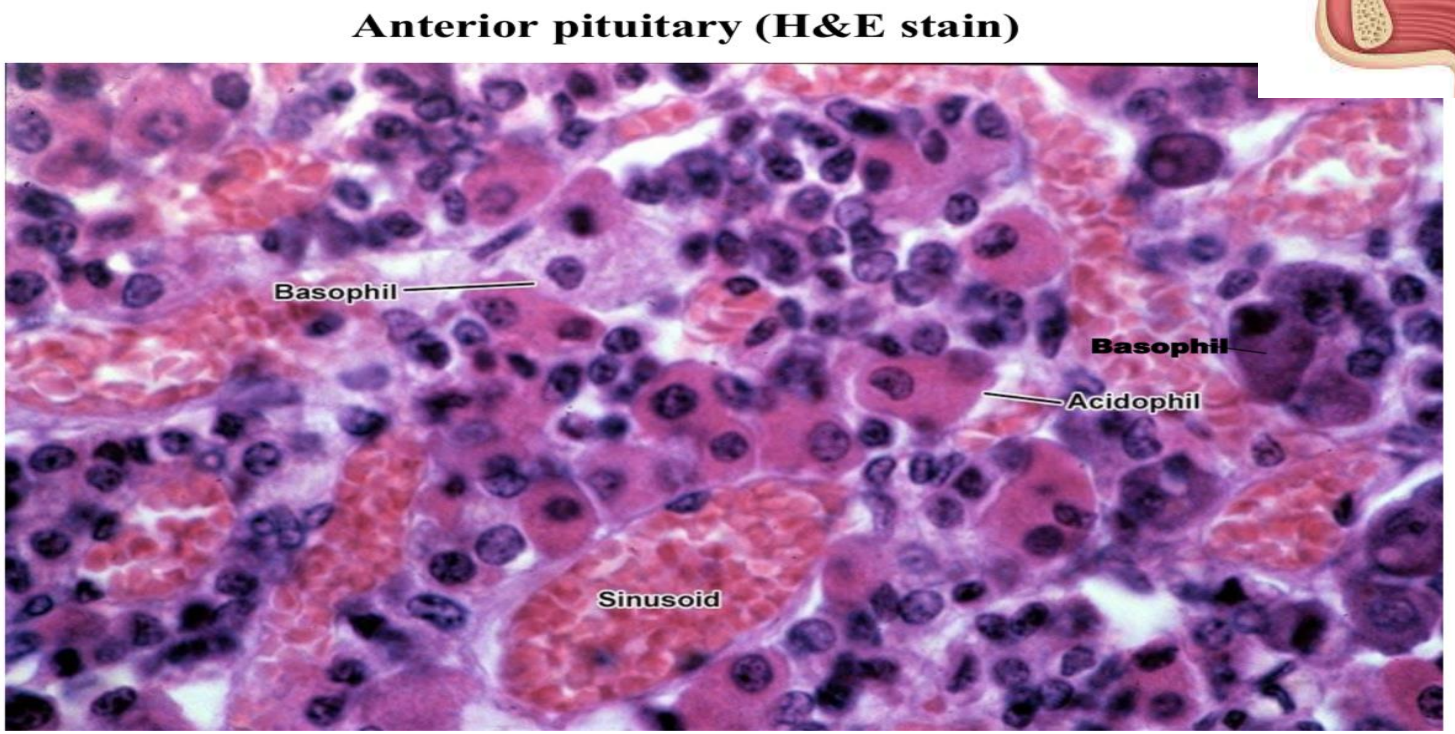
Pitutary gland



"Master endochrine gland ".

- Parts:

1. Adenohypothesis (Anterior pitutary).
2. Neurohypithesis (Posterior pitutary).



Disorders of the anterior pituitary

1-Hyperpitutary syndromes:

Caused by: -Hyperplasia,

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

-Carcinoma (rare).

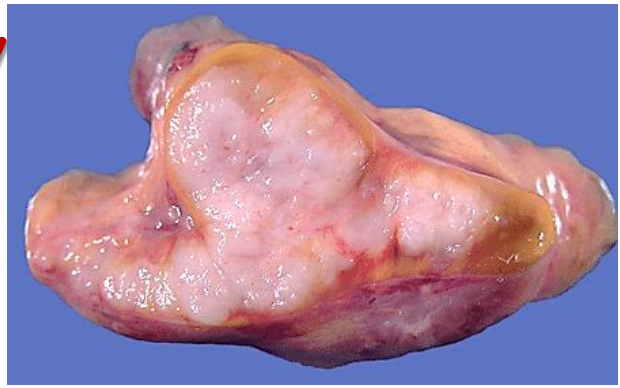
2-Hypopituitarism

(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.

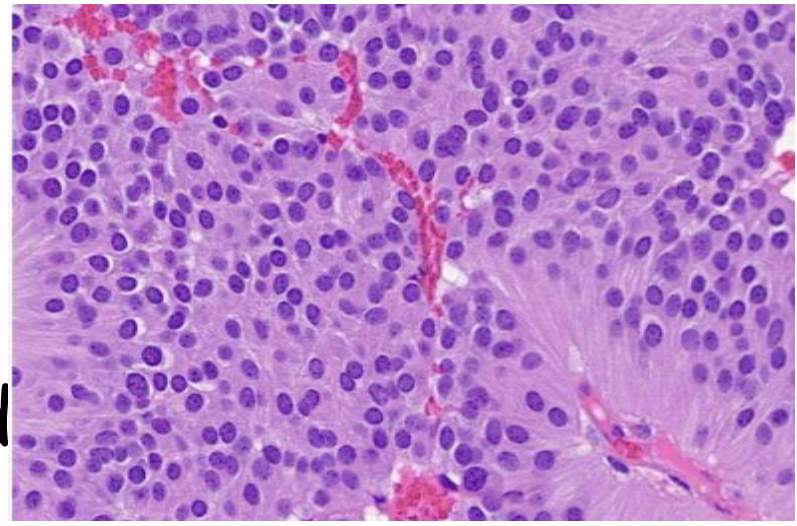
Tumors of the anterior pituitary
Pituitary Adenoma



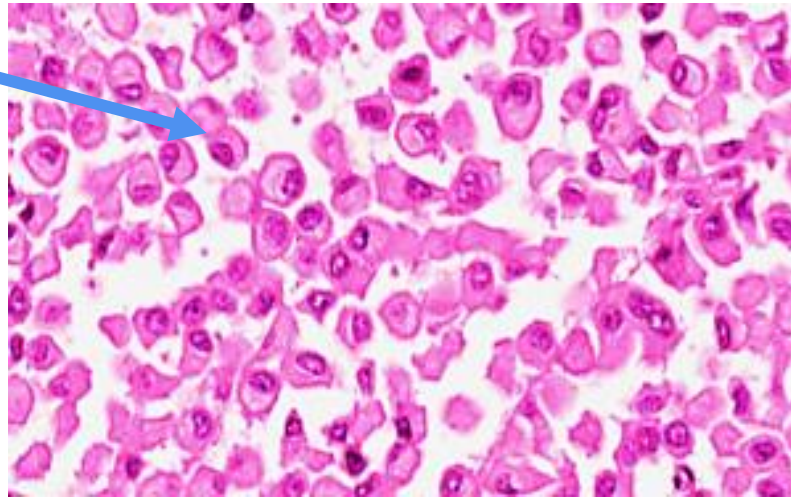
NE Adenomas appear as a lobulated mass covered by a thin, attenuated shiny capsule.

ME

Tumors have a uniform in appearance with fibrovascular stroma; cells classified as acidophilic, basophilic or chromophobic based on content of hormone secretory cells.

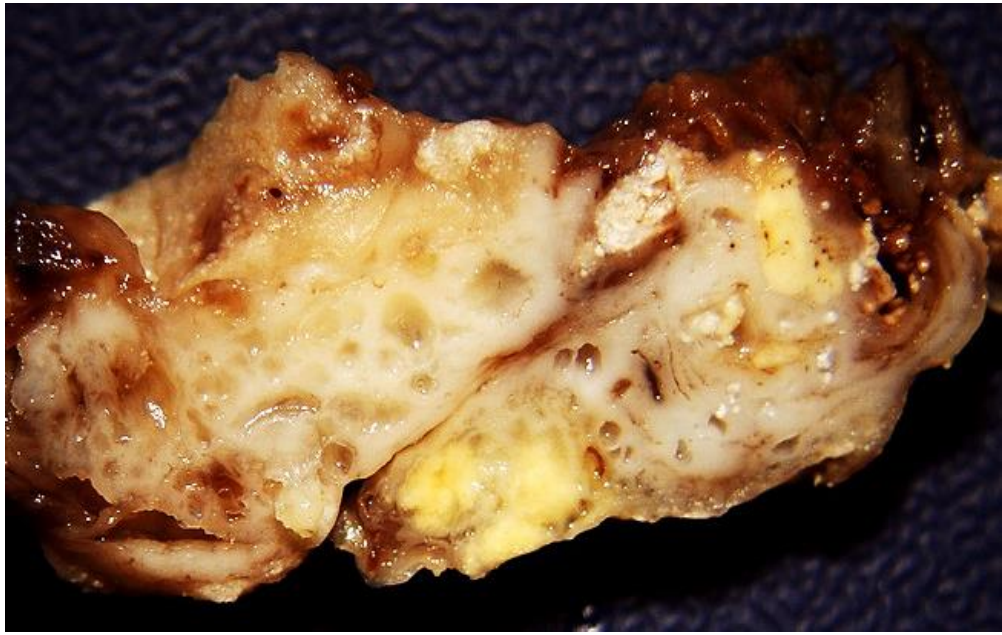


- Crooke hyaline change is characterized by large cells with a glassy hyaline appearance (due to accumulation of keratin filaments).



Tumors of the anterior pituitary
Craniopharyngioma

-They are benign epithelial neoplasm of sellar region, arise from epithelial remnants of Rathke's Pouch.
Age: children and young adults.



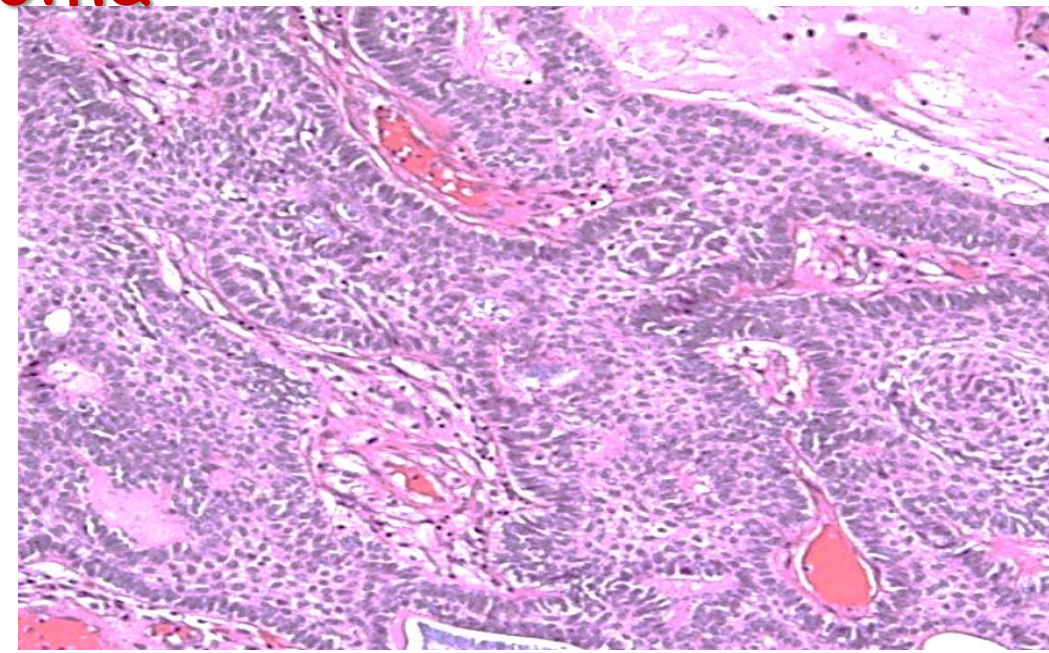
NE

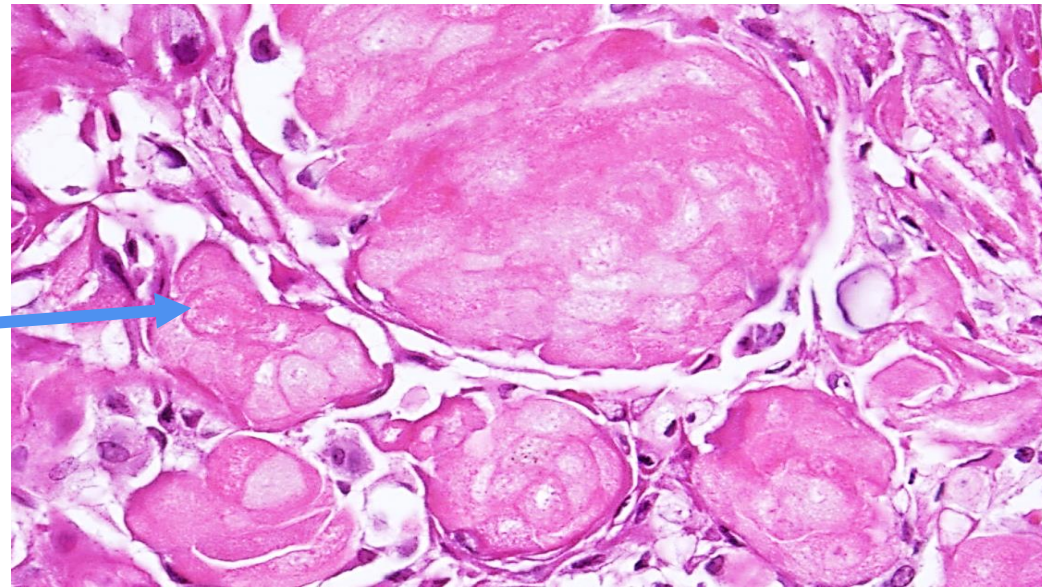
- Craniopharyngiomas are calcified yellow (due to cholesterol crystal deposits).
- Cross-sections reveal multiple cystic areas containing oily fluid.

Tumors of the anterior pituitary
Craniopharyngioma

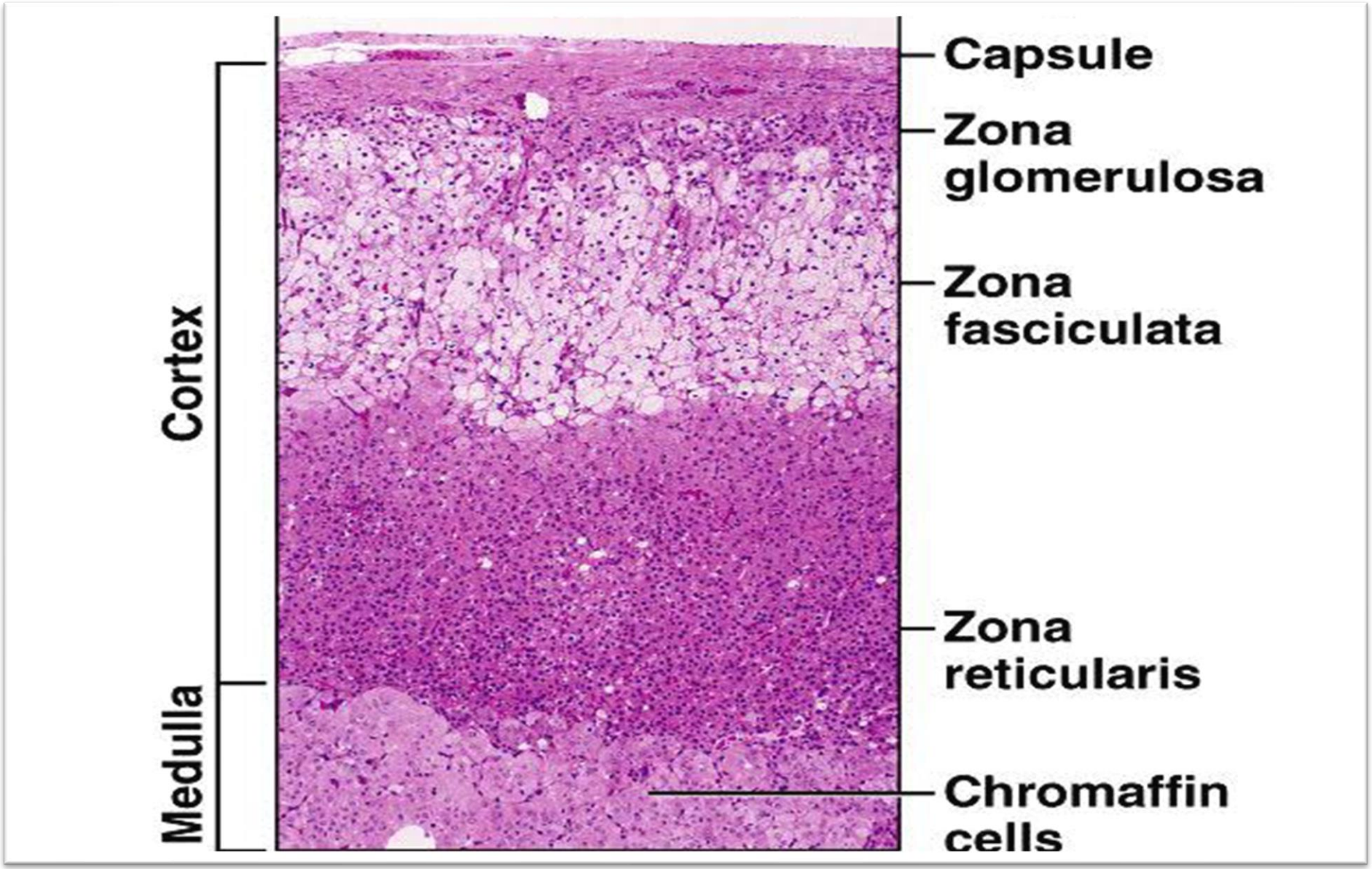
ME:

- 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**





Adrenal gland histology



Diseases of supra-renal gland

1. **Cortical hyperfunction:** due to Hyperplasia, adenoma or carcinoma of the adrenal cortex.

Effects:

1. **Conn's disease**:**aldosterone hypersecretion.**
2. **Cushing syndrome**:**glucocorticoides hypersecretion**
3. **Adrenogenital syndrome**:**androgen hypersecretion.**

Diseases of supra-renal gland

2. Cortical hypofunction

A. Acute adrenal insufficiency leads to shock and death

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

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 suprarenal gland

Primary

Cortex

*Cortical Adenoma

*Cortical carcinoma

Medulla

*Ganglioneuroma

*Pheochromocytoma

*Neuroblastoma

Secondary

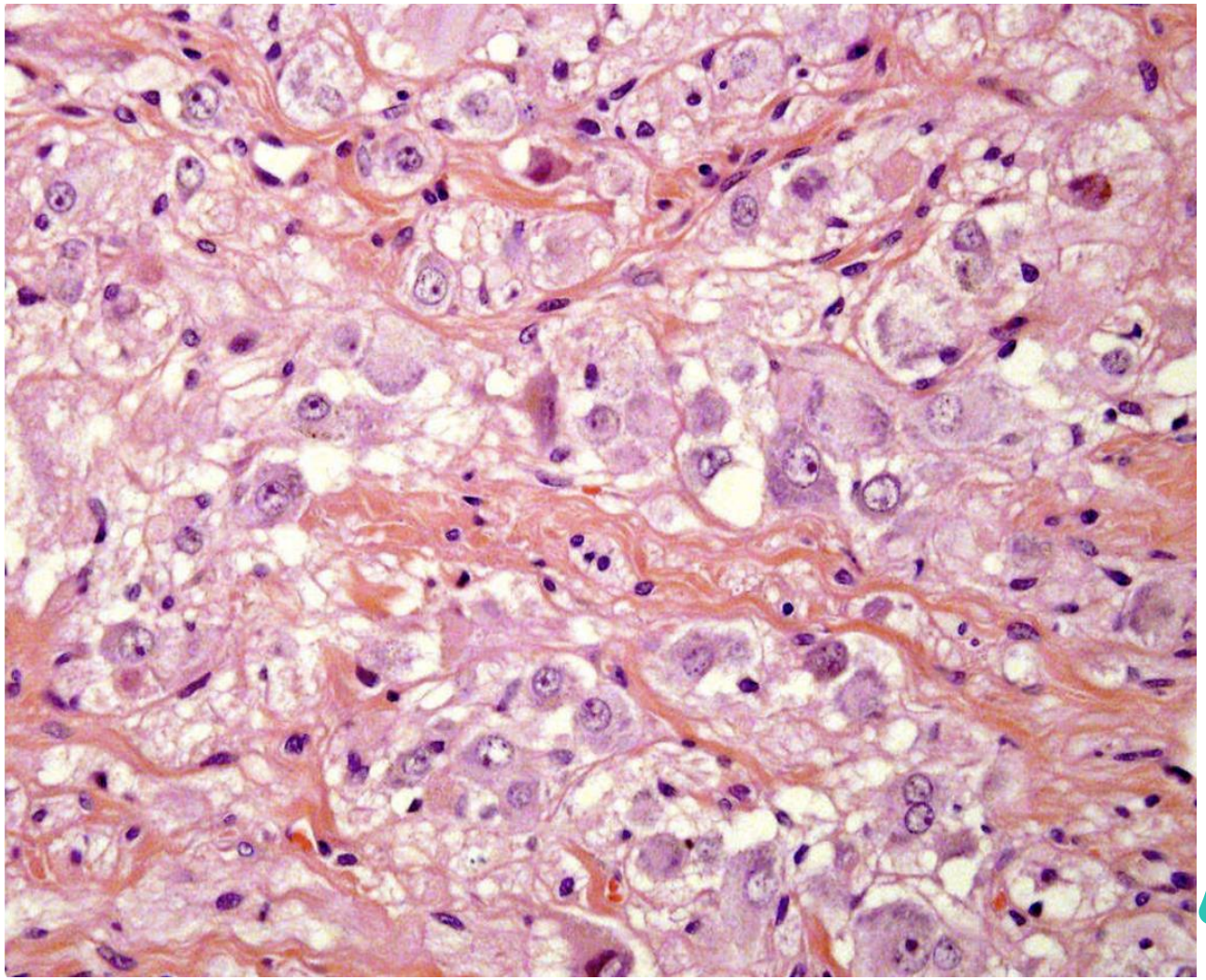
*lung

*breast

*melanomas

Ganglioneuroma

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

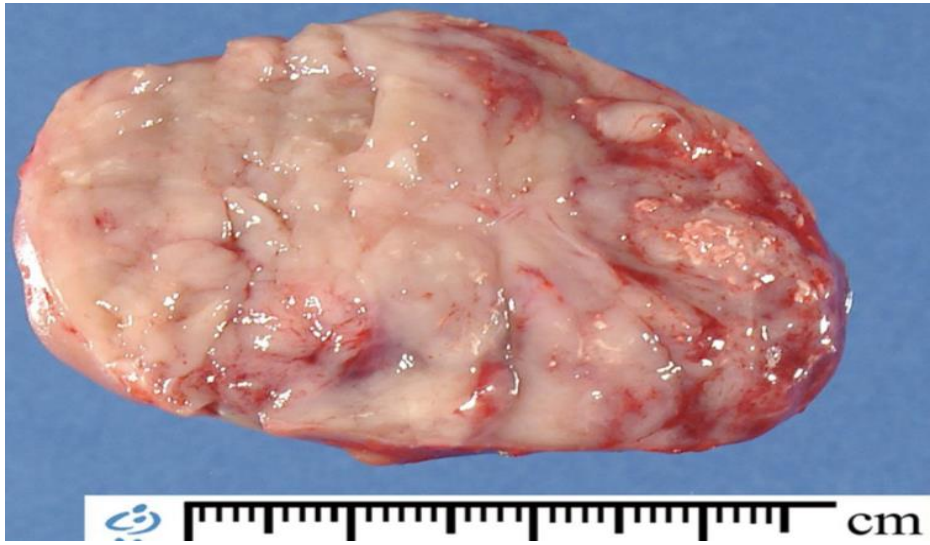


Neuroblastoma

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

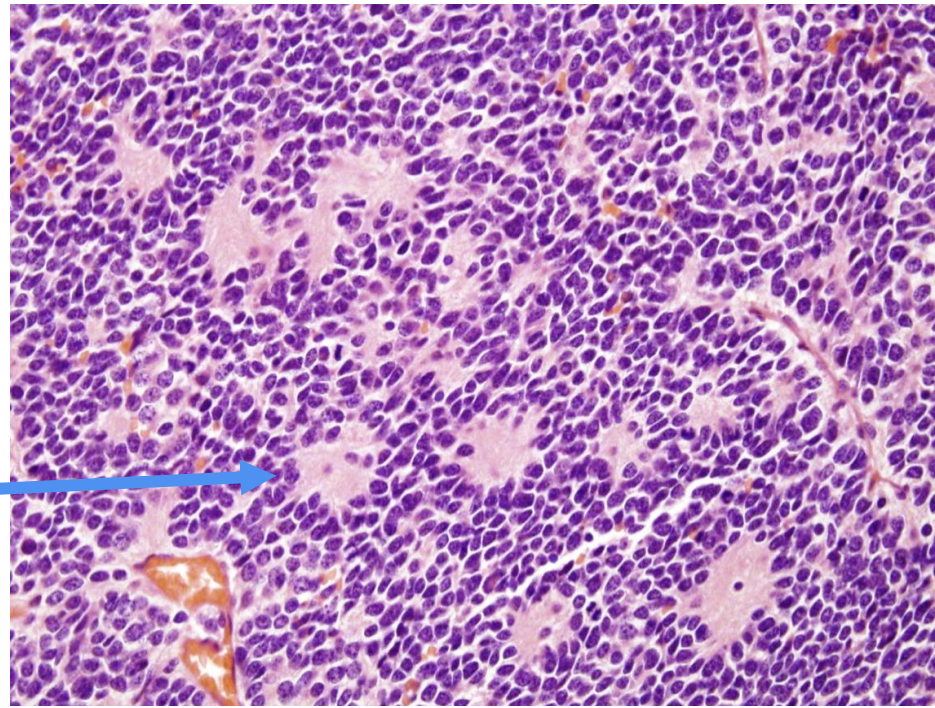
N/E:

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



M/E:

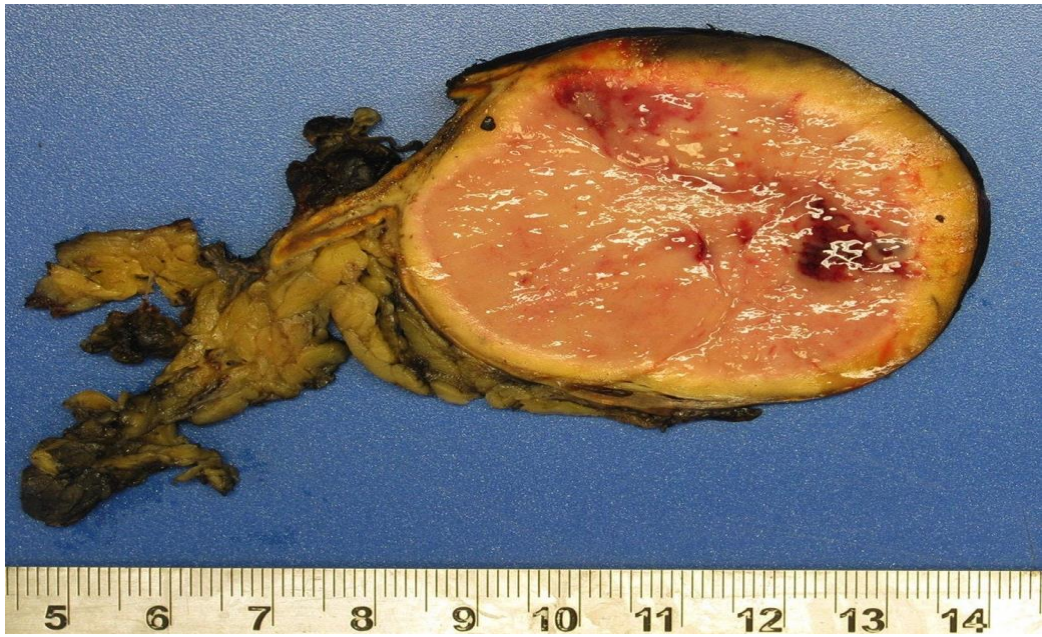
The tumor consists of small blue malignant round cells with dark nuclei "neuroblasts" arranged in sheets or in rosettes.

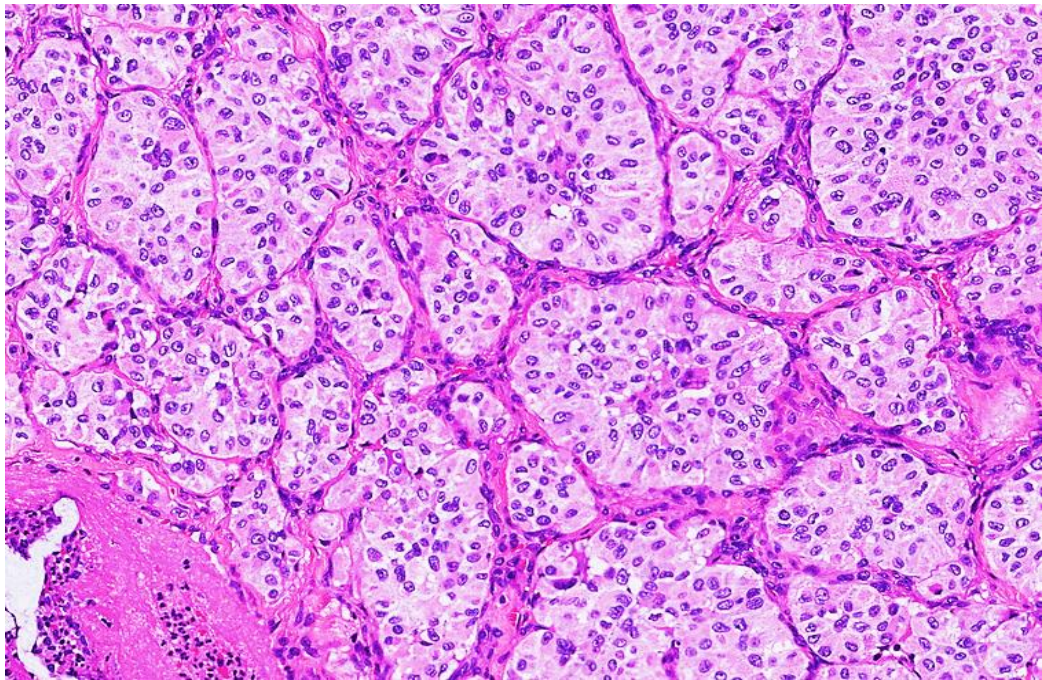


Pheochromocytoma

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.**

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%.

Diseases of Endocrine Pancreas

Diabetes Mellitus (DM)

Types:

I. Type 1 DM:

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.

Diseases of Endocrine Pancreas
Diabetes Mellitus (DM)

Types:

II Type 2 DM:

Etiopathogenesis:

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.

Diseases of Endocrine Pancreas
Diabetes Mellitus (DM)

Complications

Mechanism:

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

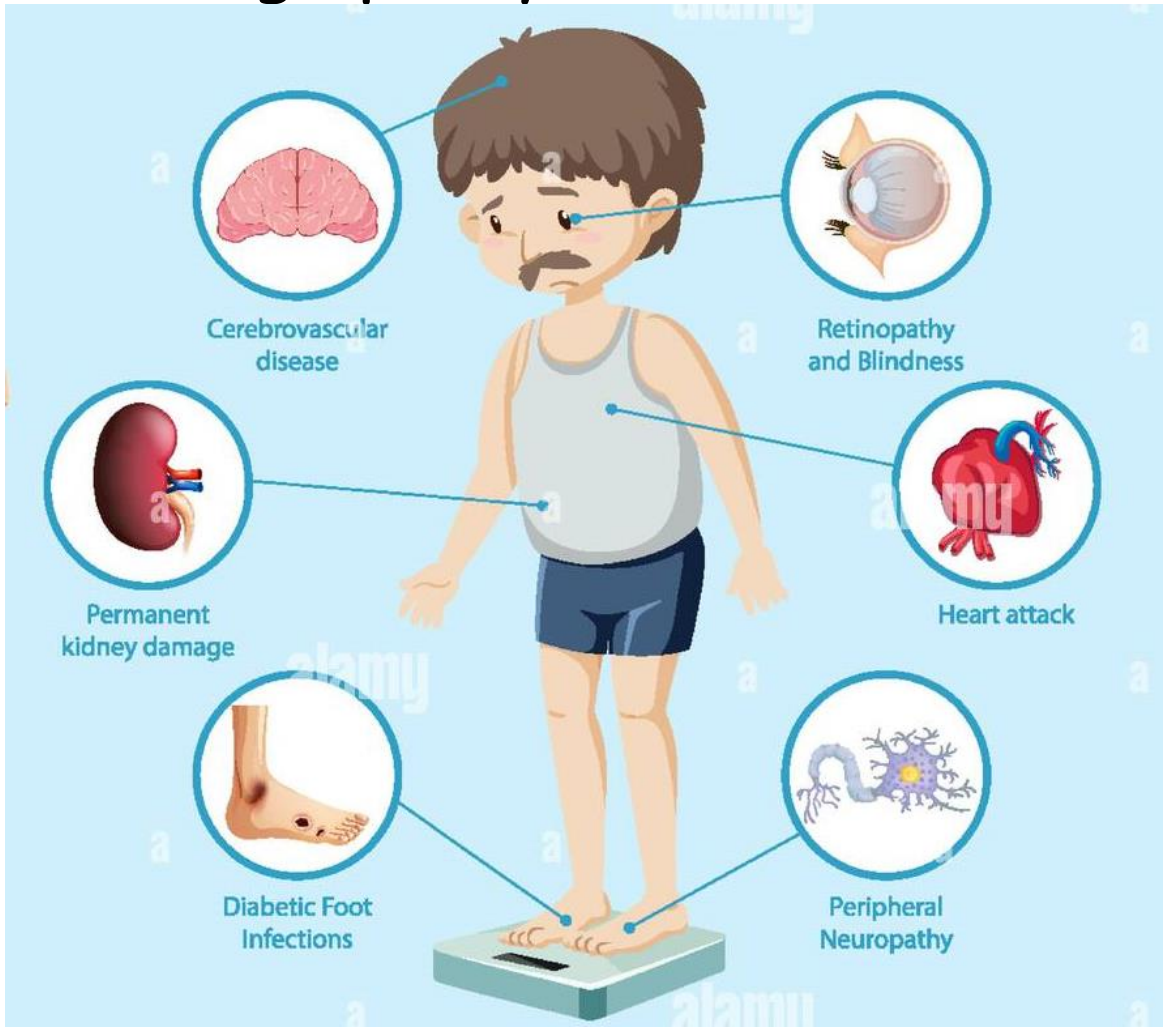
- Release of cytokines, growth factors, reactive oxygen species.
- Inflammation.
- Deposition of basement membrane material, extracellular matrix.
- Neovascularization, increased vascular permeability.
- Trapping of low-density lipoprotein (LDL) within AGE-modified large-vessel walls > accelerated atherosclerosis.

Diseases of Endocrine Pancreas
Diabetes Mellitus (DM)

Complications

1 .Diabetic Macrovascular Disease (Macroangiopathy)

2. Diabetic Microangiopathy:
   .a. Diabetic nephropathy.
   .b. Ocular complications.
   .c. Diabetic neuropathy.
3. Increased liability to infections.
4. Impaired wound healing.
5. Diabetic foot
6. Diabetic coma.



Diseases of Endocrine Pancreas
Diabetes Mellitus (DM)

1 .Diabetic Macrovascular Disease (Macroangiopathy)

- Its hallmark is accelerated atherosclerosis (greater severity and earlier age at onset).
- Affect the aorta and large- and medium-sized arteries.

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.**

Diseases of Endocrine Pancreas
Diabetes Mellitus (DM)

2. Diabetic Microangiopathy

- 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** development of:

.a. Diabetic nephropathy.
.b. Diabetic retinopathy and ocular complications.
.c. Diabetic neuropathy.

Diseases of Endocrine Pancreas
Diabetes Mellitus (DM)

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)**

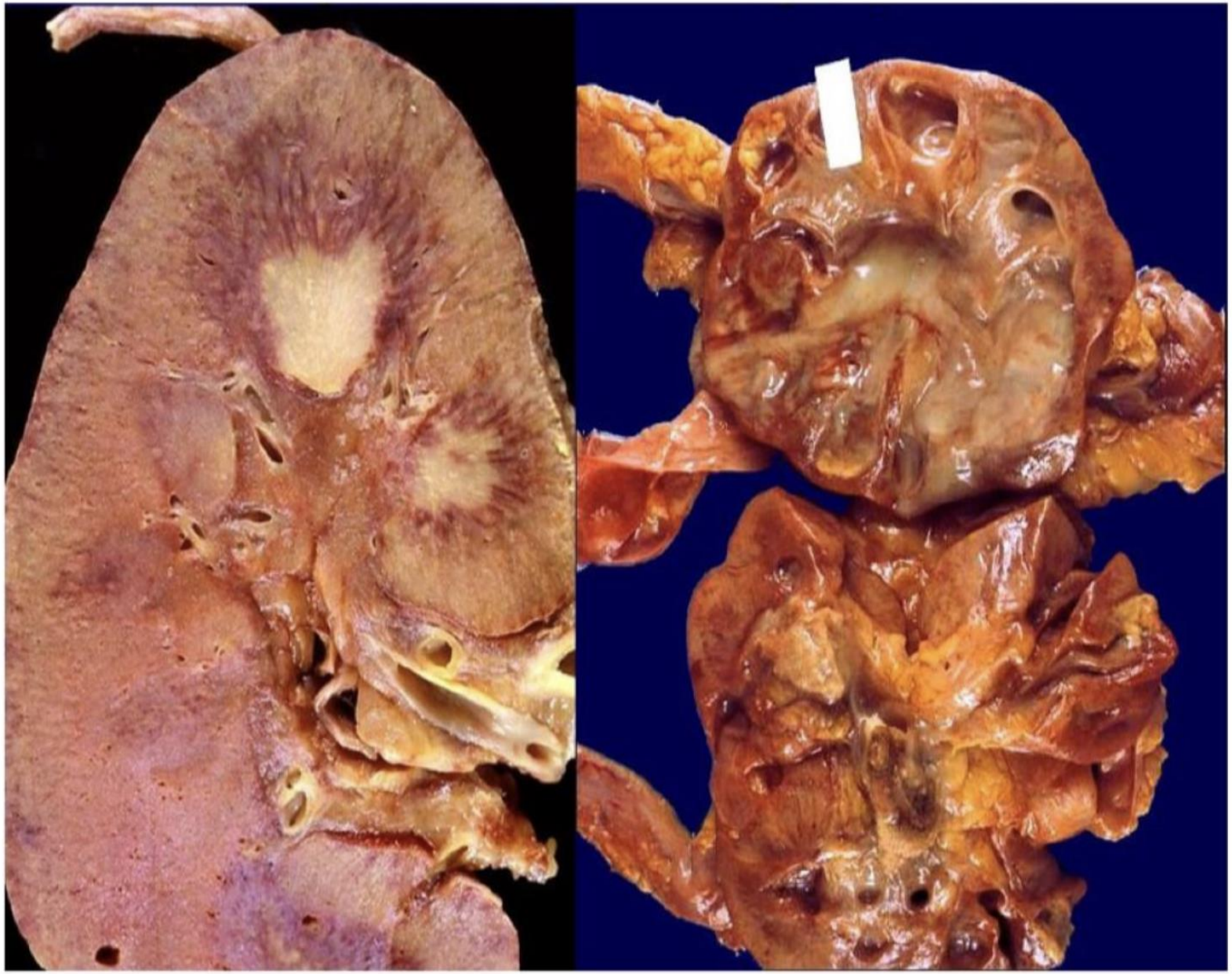
2. Thickening of tubular basement membrane

3.Renal vascular lesions: atherosclerosis and hyaline arteriolosclerosis.

4. Pyelonephritis more severe than non-diabetics.

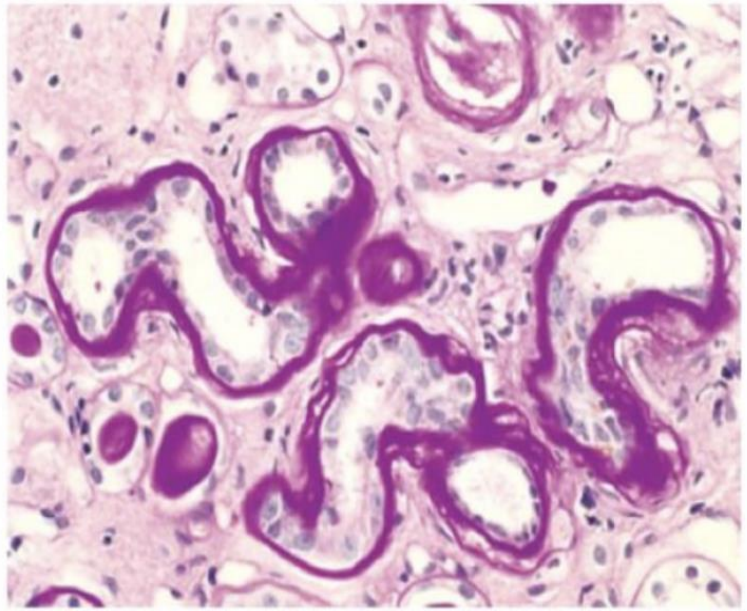
5. Necrotizing papillitis (acute papillary necrosis): special pattern of acute pyelonephritis more frequent in diabetics than in non-diabetics.).

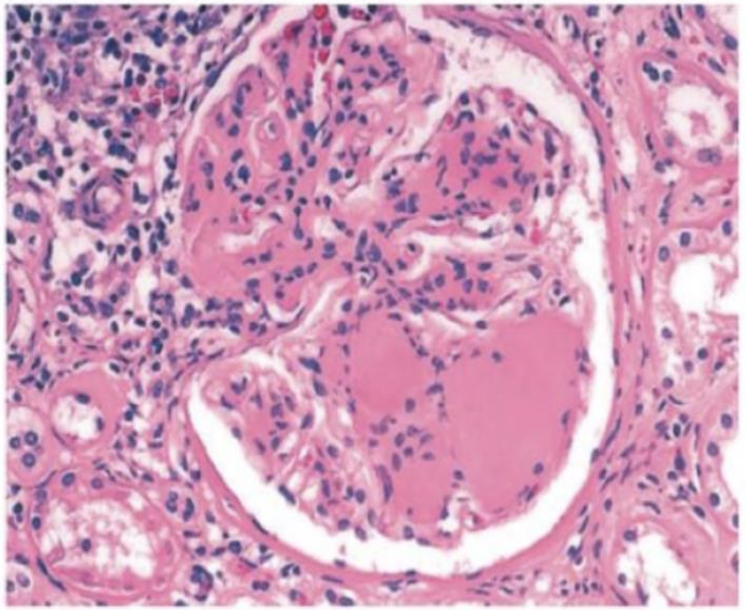
Necrotizing papillitis



Pyelonephritis

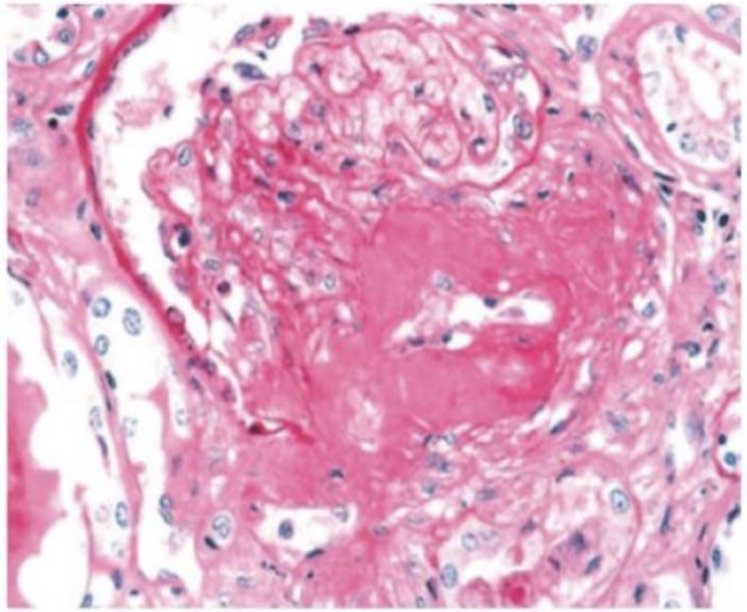
Thickening of tubular basement membranes

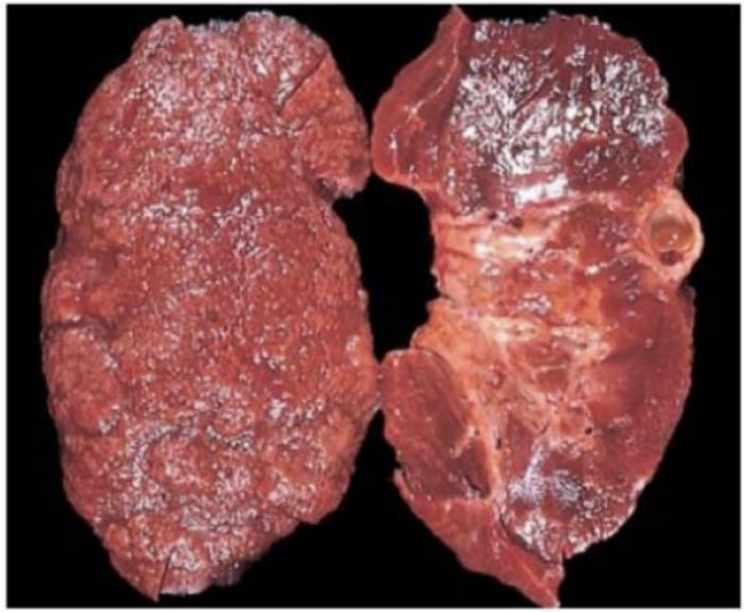




Nodular glomerulosclerosis

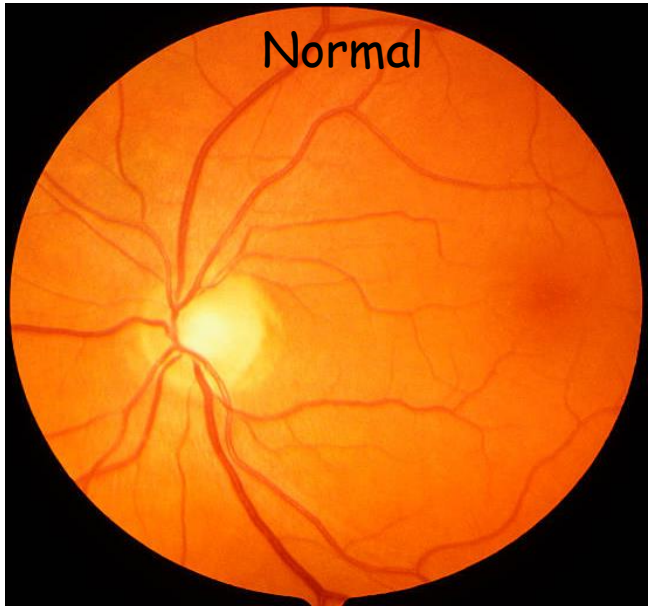
Severe renal hyaline arteriolosclerosis





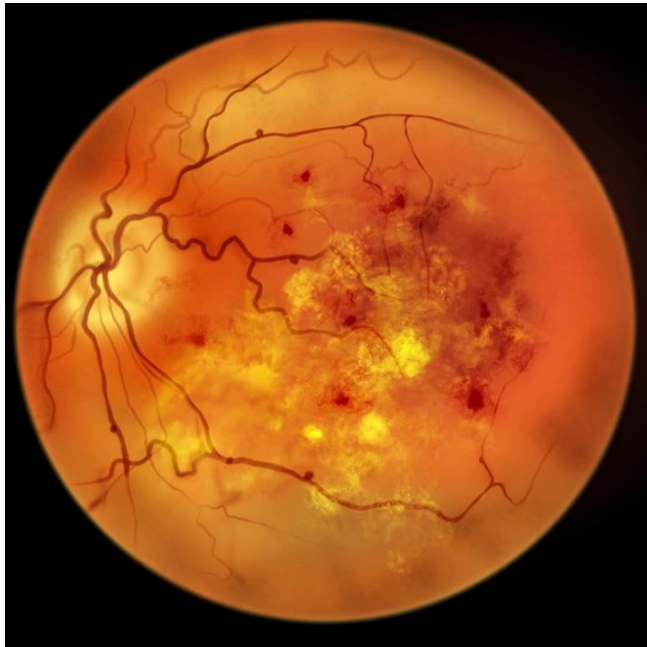
Nephrosclerosis in long-standing DM

Diseases of Endocrine Pancreas
Diabetes Mellitus (DM)



Occular complications of DM

- **1.Cataract**
- **2.Glucoma**
- **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.

Diseases of Endocrine Pancreas
Diabetes Mellitus (DM)

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 wristdrop or isolated cranial nerve palsies.

Diseases of Endocrine Pancreas
Diabetes Mellitus (DM)

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 1DM).
- Hypoglycaemic coma.

Type 1 Versus Type 2 Diabetes Mellitus

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)

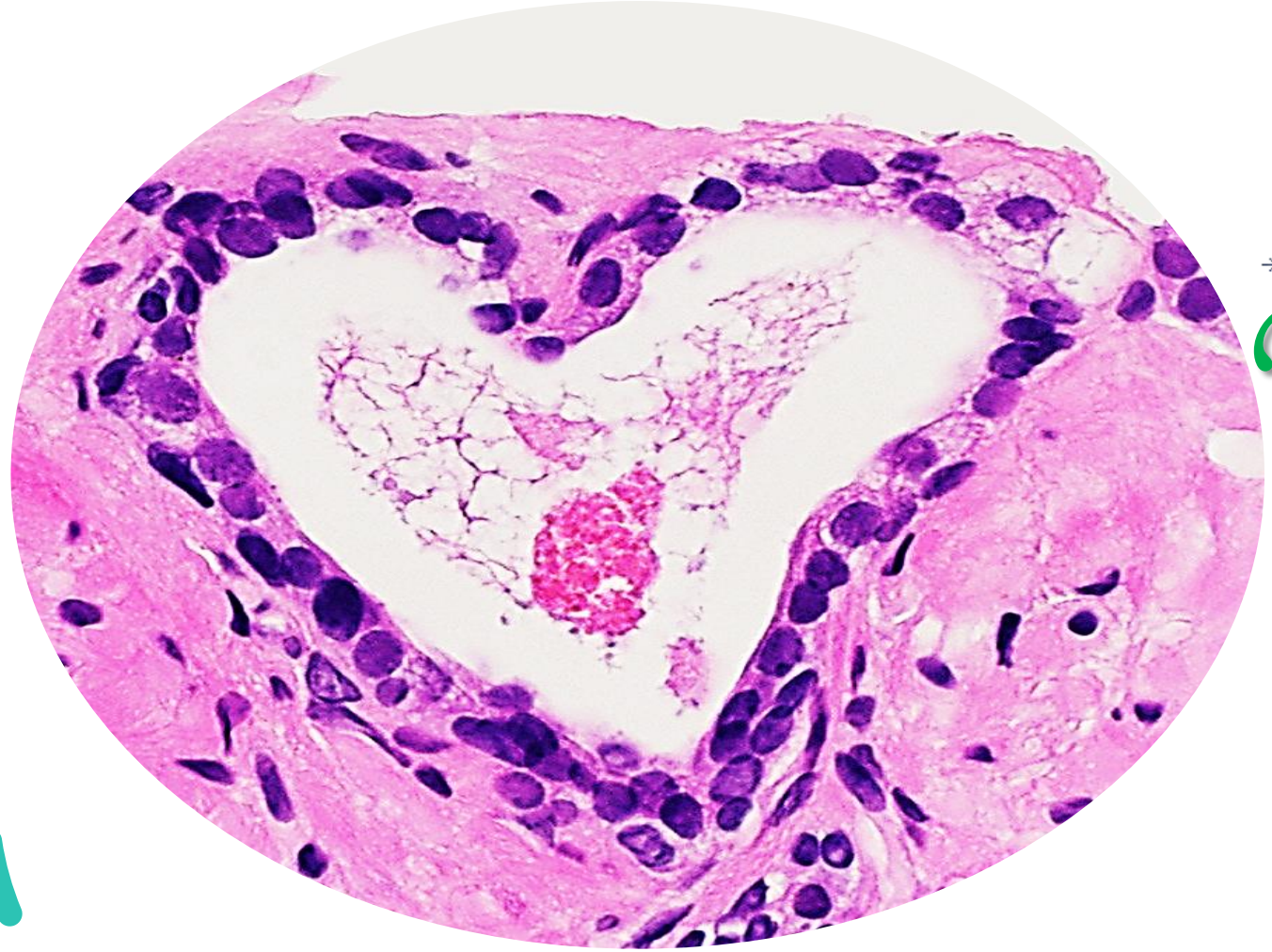
Discussion & Feedback

References & recommended readings

1. Robbins & Cotran Pathologic Basis of Disease, (Robbins Pathology), 2018 ISBN: 978-0-323-35317-5, Edition: 10th
2. Webpath:

   https://webpath.med.utah.edu/webpath.html

   https://www.pathologyatlas.ro/index.php



Thank you