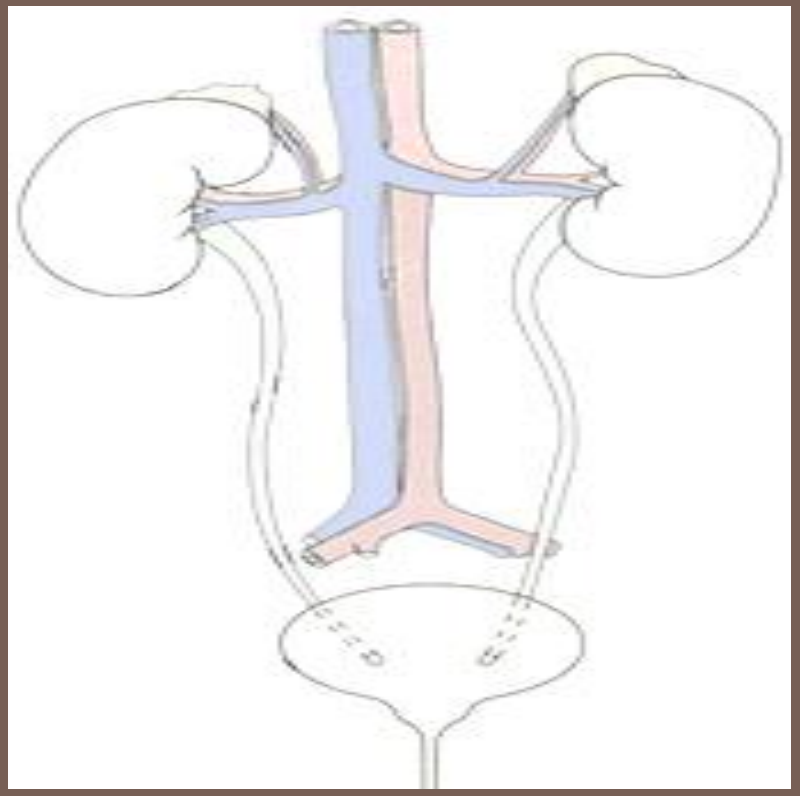
RENAL BLOCK



PATHOLOGY PRACTICAL 3

Prepared by:

- *Prof. Ammar Al Rikabi*
- *Dr. Sayed Al Esawy*

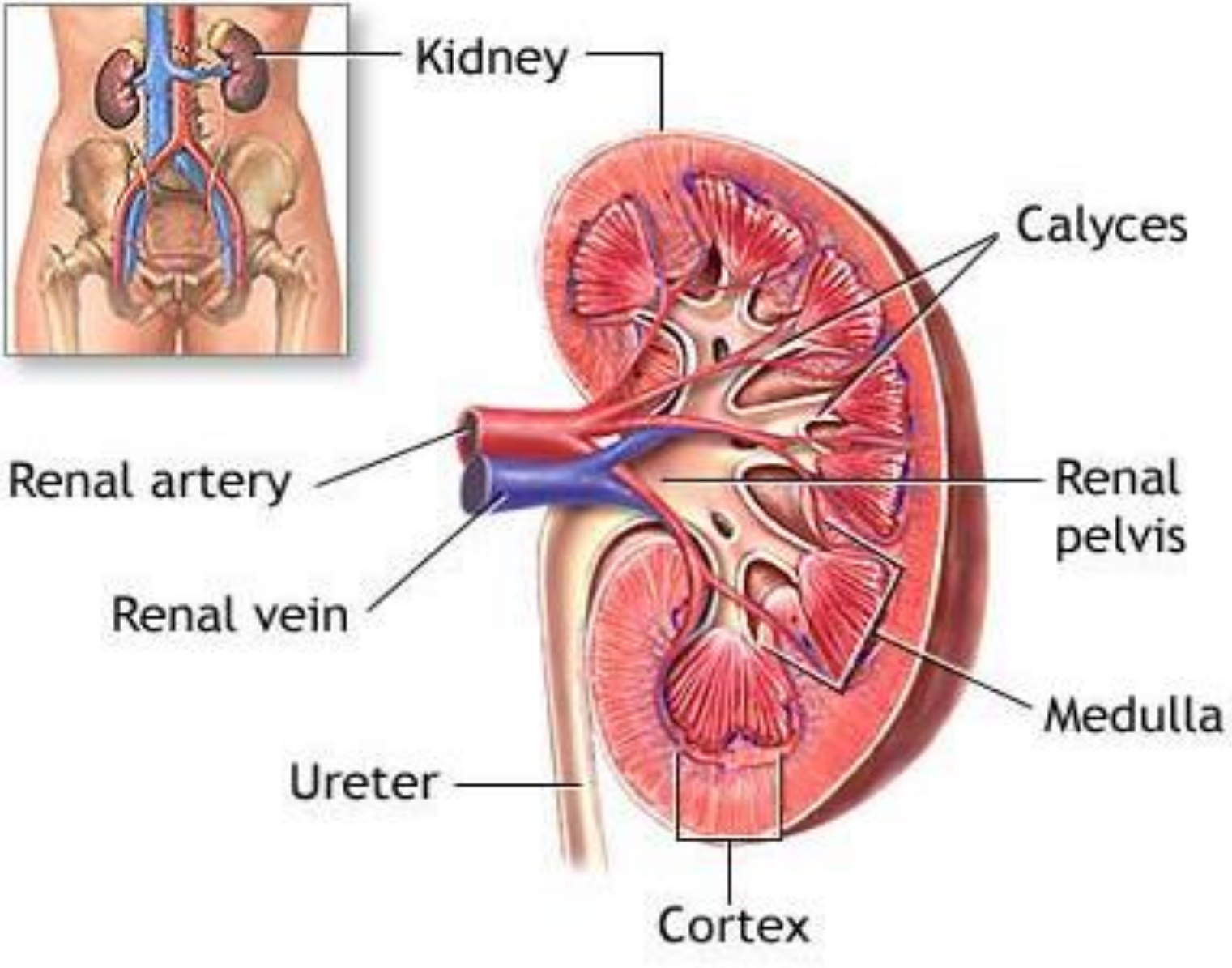
Objectives:

At the end of the practical sessions for the renal block, the students will be able to:

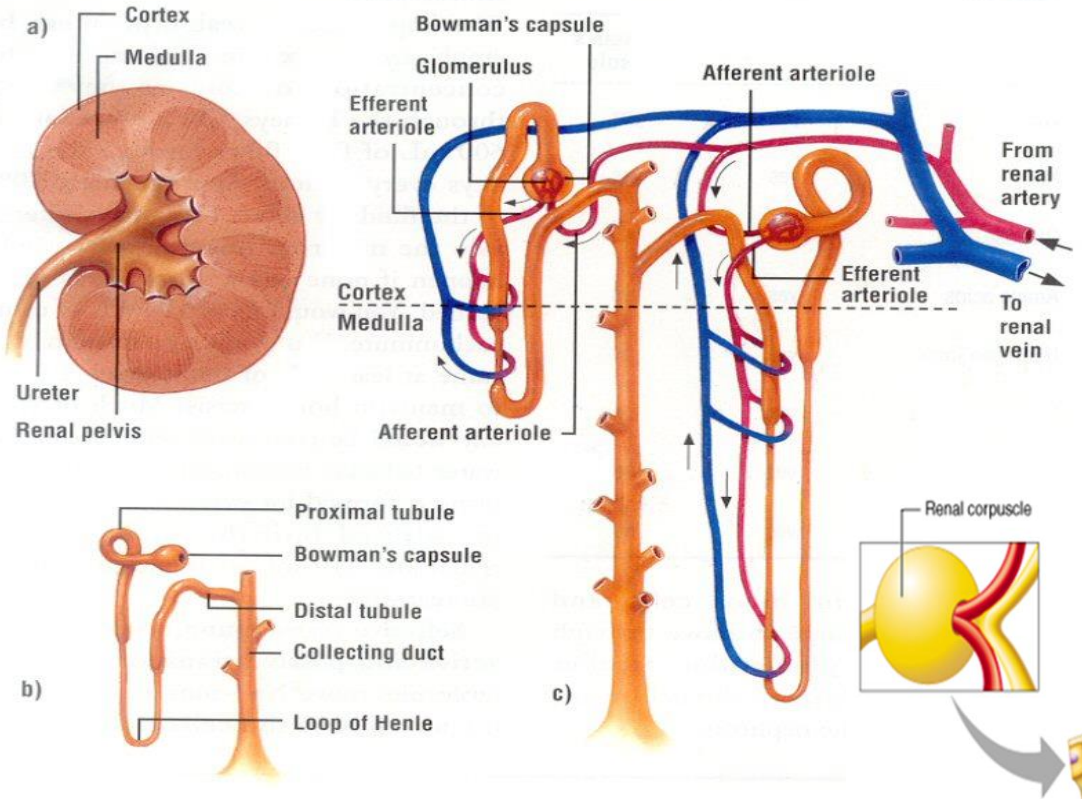
- Describe the normal constituents of the nephron, renal glomeruli and tubules.
- Identify the gross and microscopic features of:
  - Example of nephrotic syndrome: membranous nephropathy
  - Example of nephritic syndrome: post-streptococcal glomerulonephritis.
  - Rapid progressive (crescentic) glomerulonephritis
  - Tumors
    - Oncocytoma
    - Clear cell carcinoma of the kidney (renal cell carcinoma, clear cell type).
    - Wilm's tumor.
    - Urothelial carcinoma of the urinary bladder.
  - Transplanted kidney: acute cellular rejection.

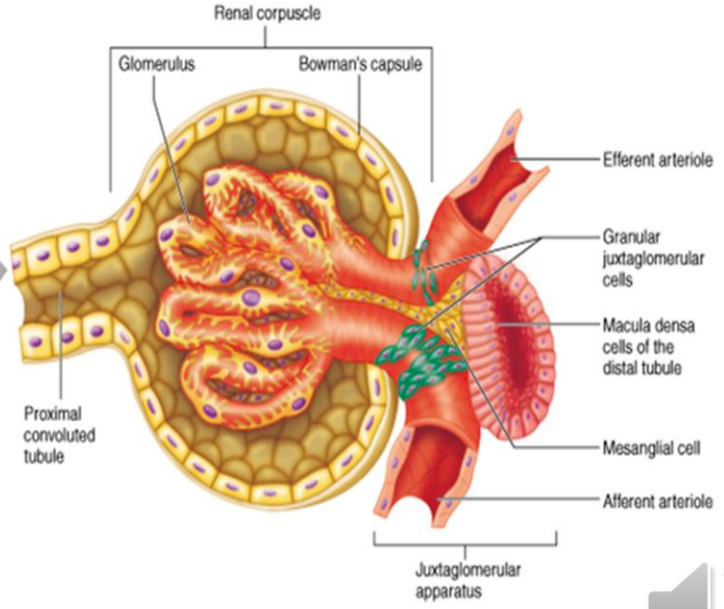
NORMAL ANATOMY AND HISTOLOGY

Anatomy of the Kidney

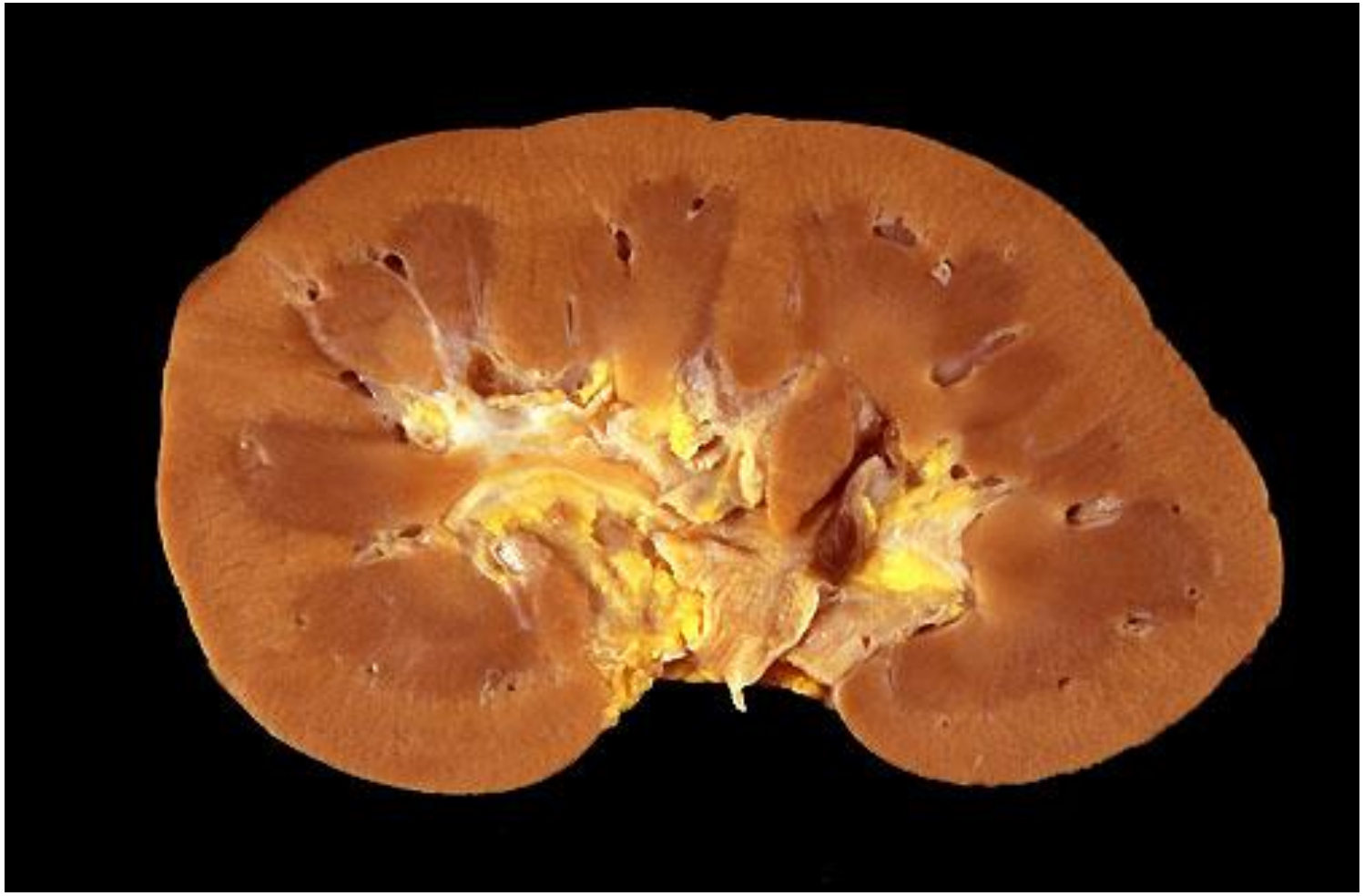


NEPHRON STRUCTURE



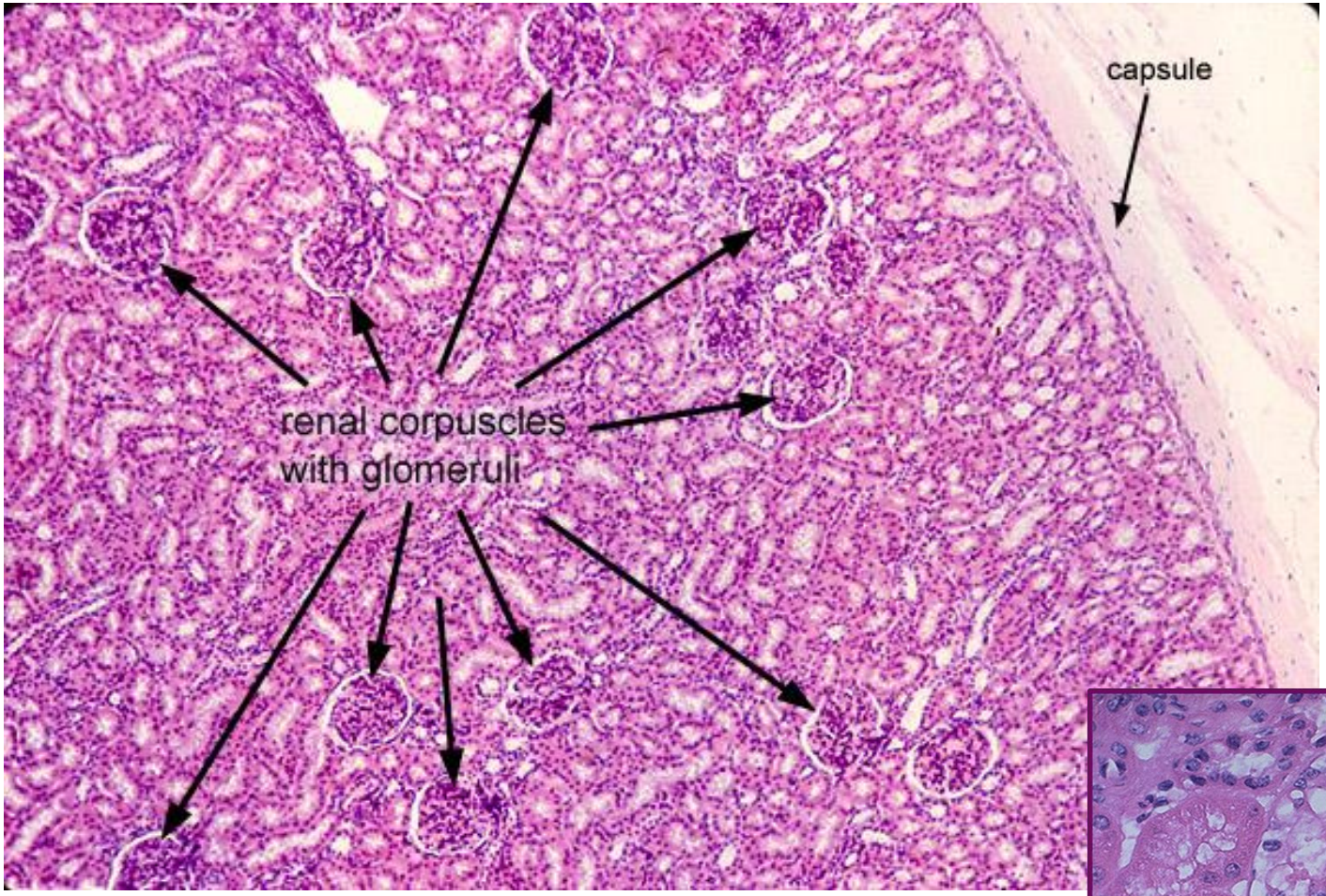


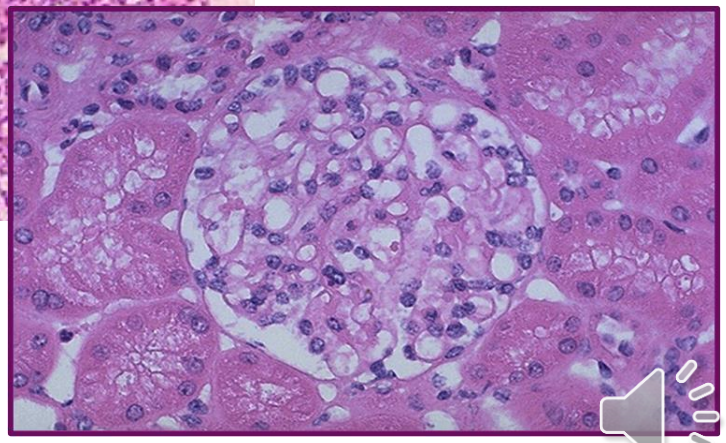
Normal Kidney - Gross



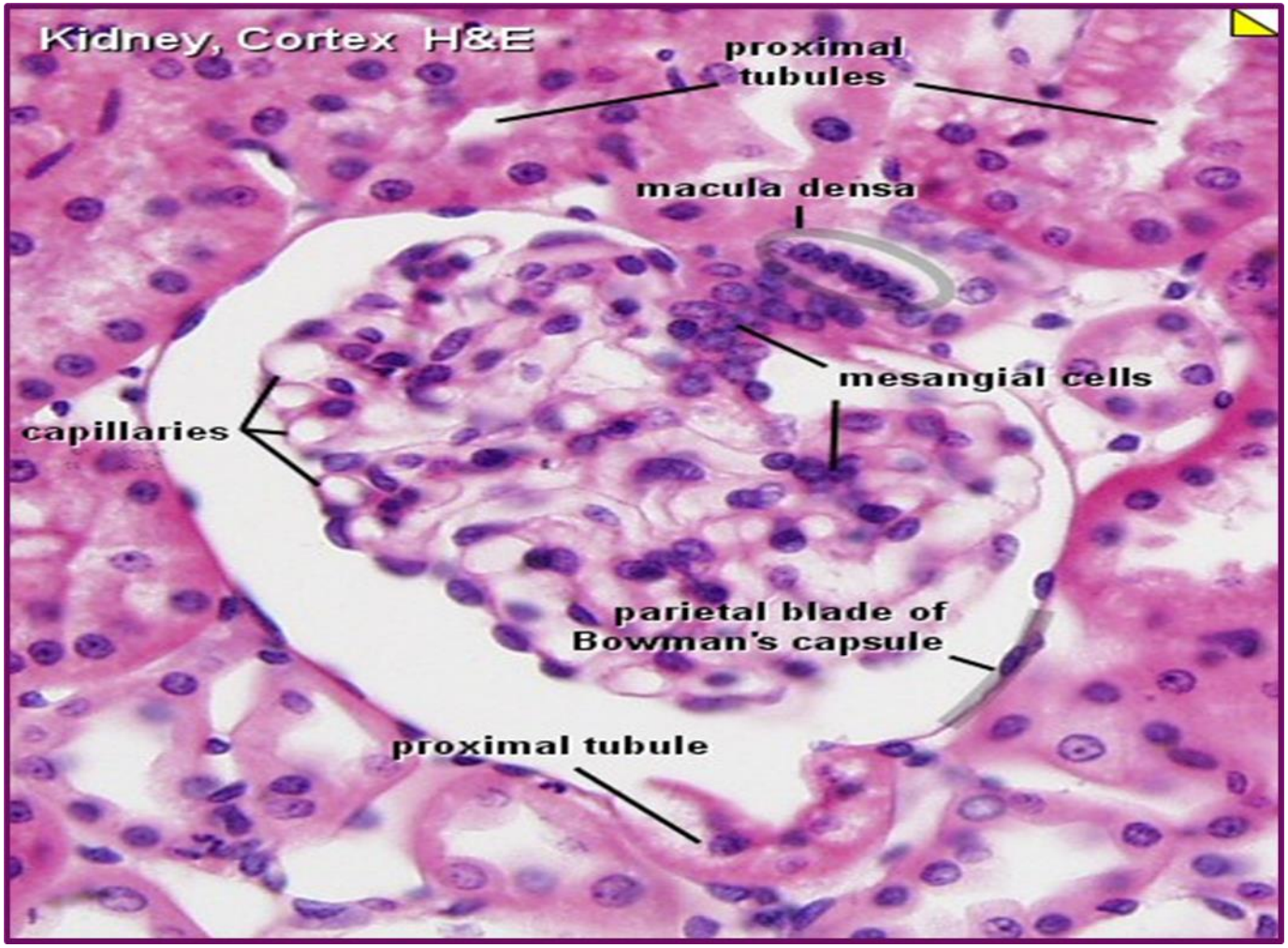
In cross section, this normal adult kidney demonstrates the lighter outer cortex and the darker medulla, with the renal pyramids into which the collecting ducts coalesce and drain into the calyces and central pelvis.

Kidney – Normal Histology



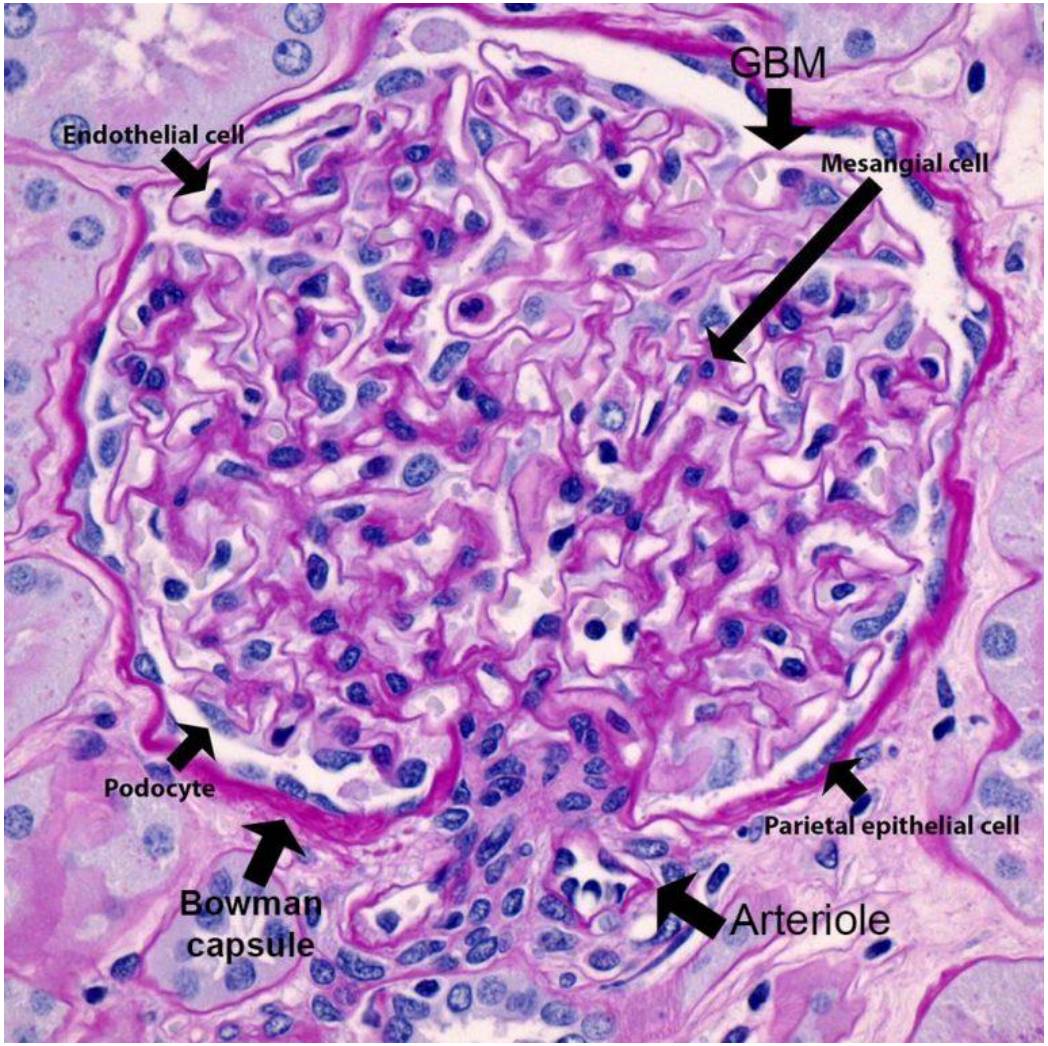


Renal Corpuscle – Normal Histology



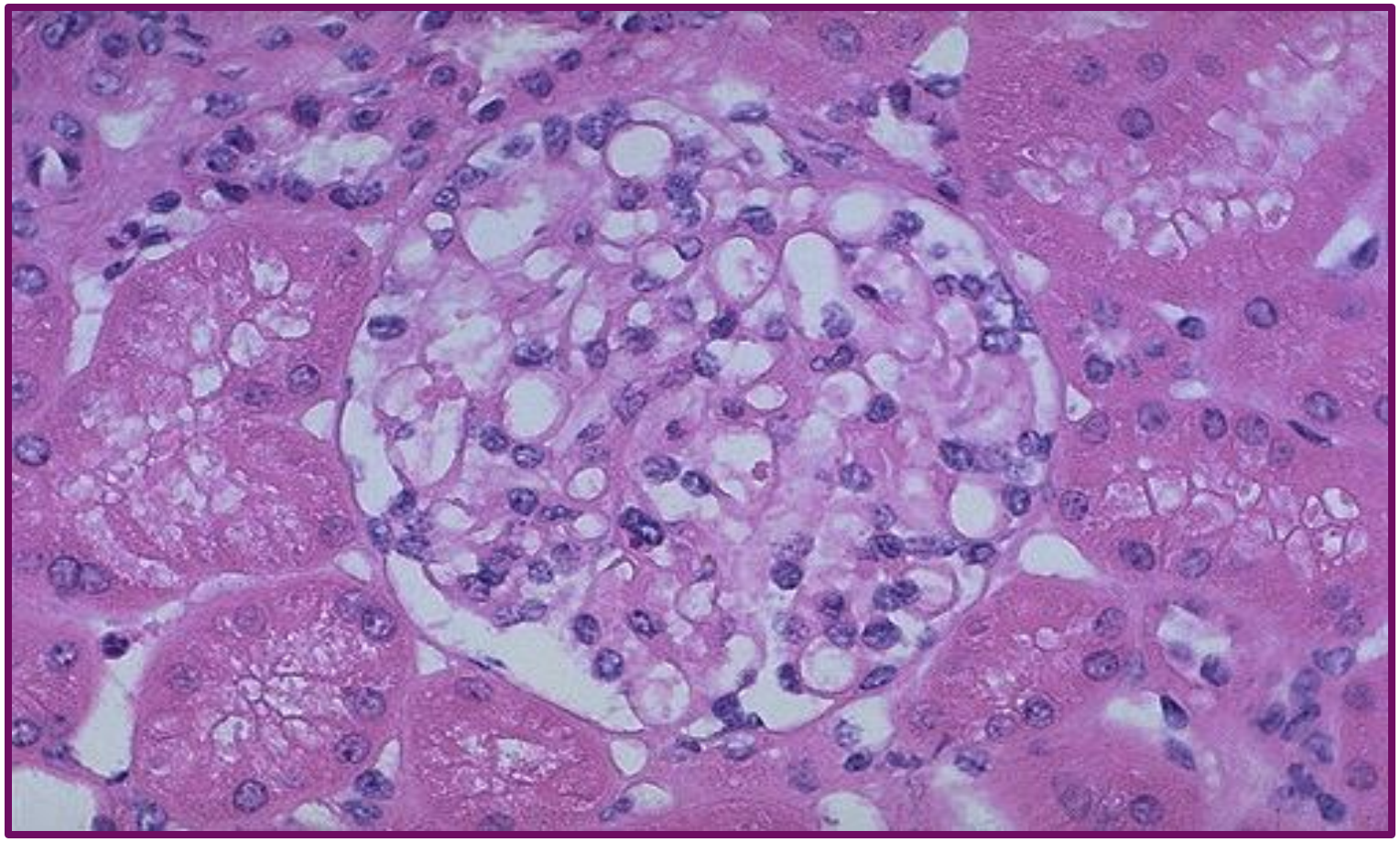
Normal glomerulus by light microscopy. The glomerular capillary loops are thin and delicate. Endothelial and mesangial cells are normal in number. The surrounding tubules are normal

Renal Corpuscle – Normal Histology



Normal glomerulus is stained with PAS to highlight basement membranes of glomerular capillary loops and tubular epithelium.

Renal Corpuscle – Normal Histology



Normal glomerulus by light microscopy. The glomerular capillary loops are thin and delicate. Endothelial and mesangial cells are normal in number. The surrounding tubules are normal

PRACTICAL SESSION : 3

- Example of nephrotic syndrome: membranous nephropathy
- Example of nephritic syndrome: post-streptococcal glomerulonephritis.
- Rapid progressive (crescentic) glomerulonephritis
- Tumors of kidney and urinary tract:
  - Oncocytoma
  - Clear cell carcinoma of the kidney.
  - Wilm's tumor.
  - Urothelial carcinoma of the urinary bladder.
- Transplanted kidney: acute cellular rejection.

Example of Nephrotic Syndrome

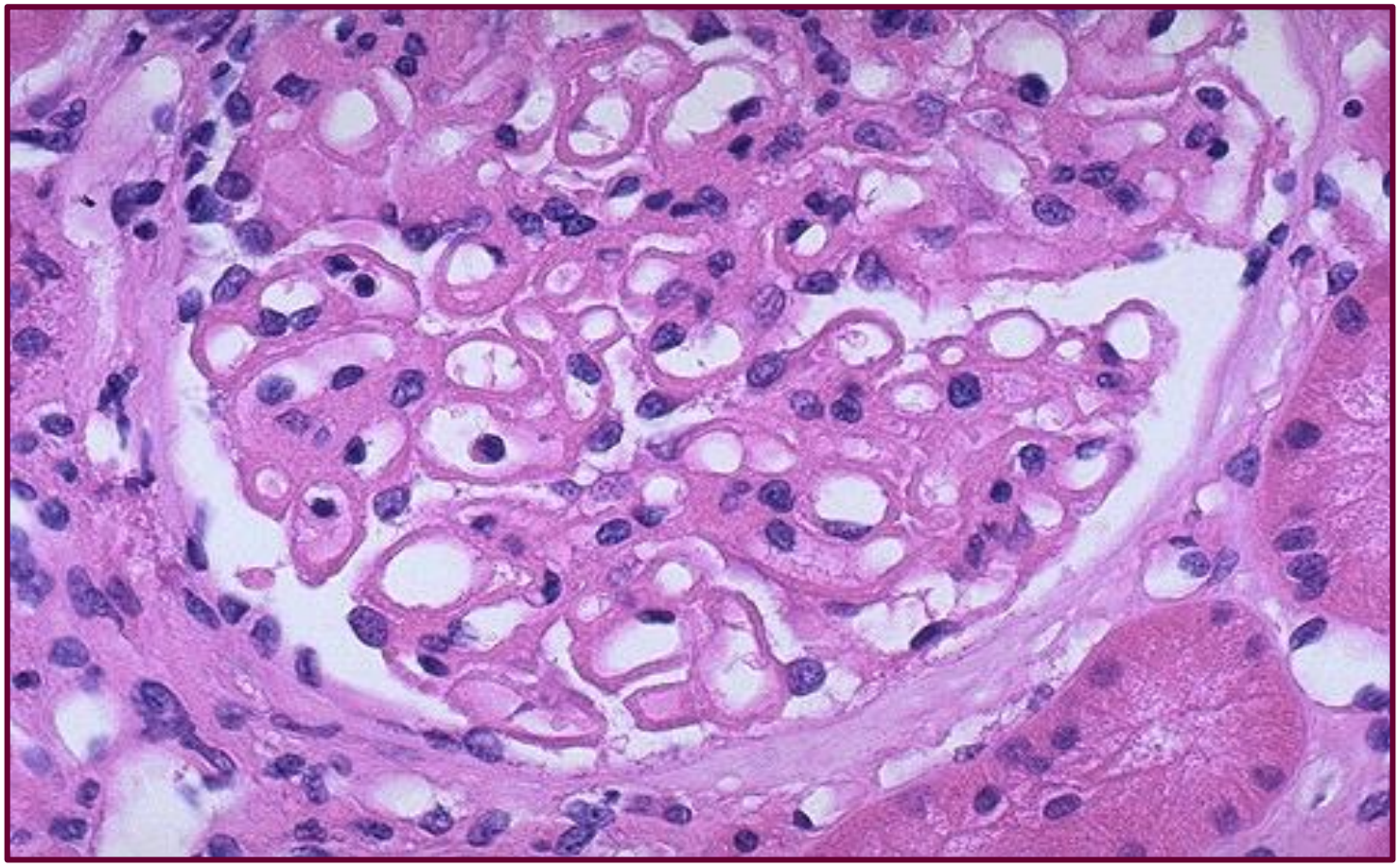
- Membranous nephropathy

Nephrotic syndrome

Nephrotic syndrome is a group of clinical features that include the following:

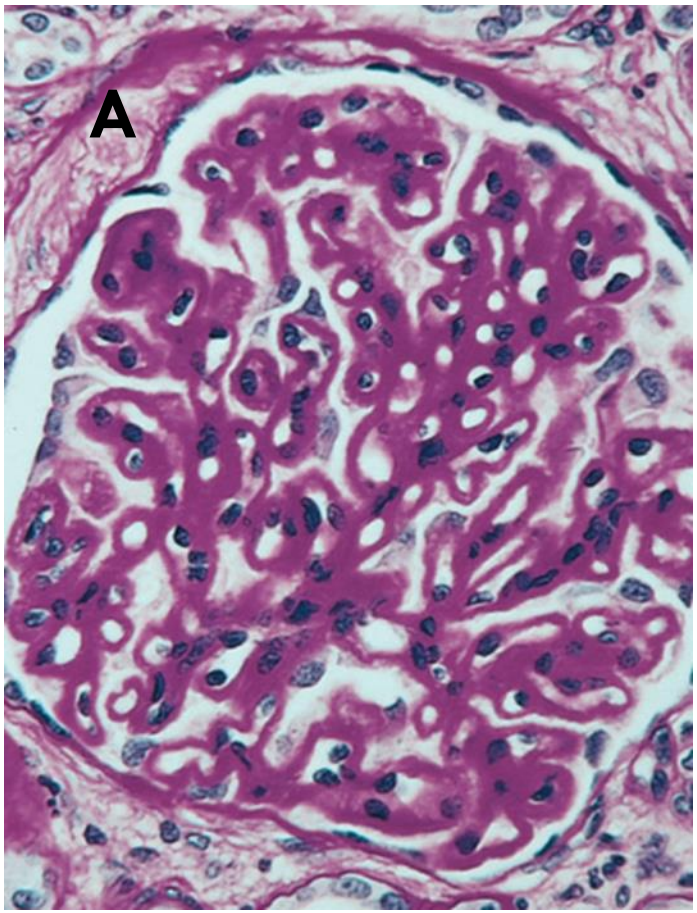
1. **Massive proteinuria**: >3.5 g of protein/day.
2. **Hypoproteinemia or hypoalbuminemia**
3. **Odema**
4. **Hyperlipidemia and lipiduria**.

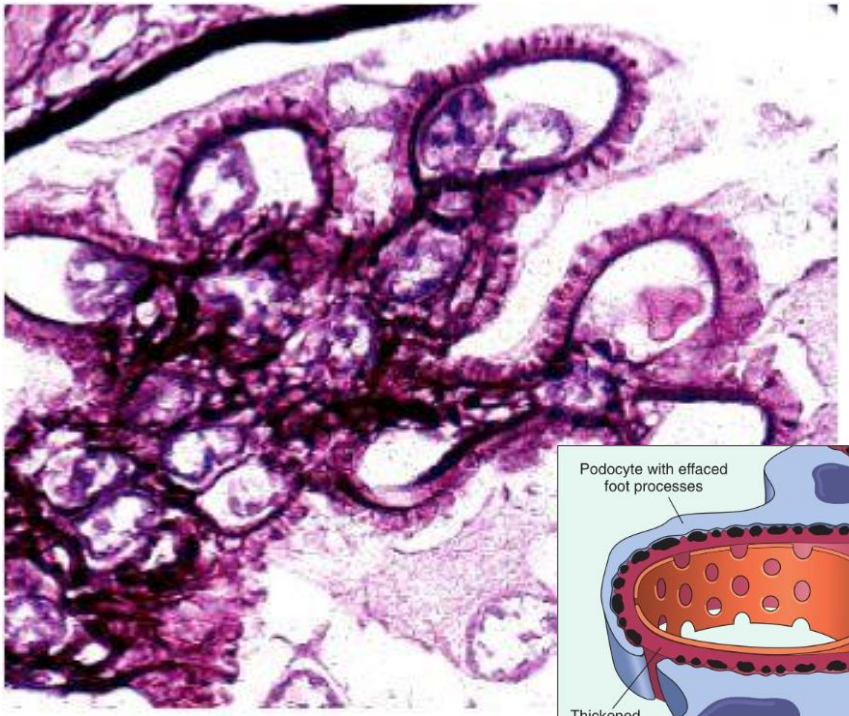
Membranous Nephropathy

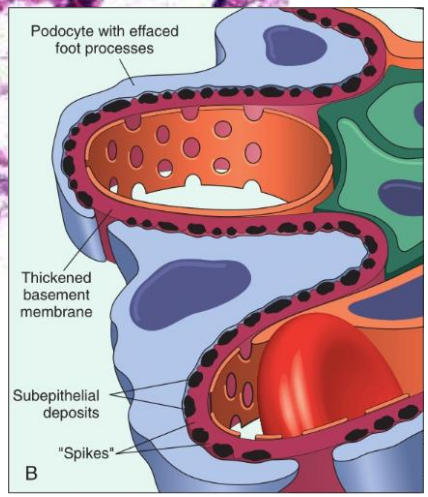


- *Membranous nephropathy is a common cause of Nephrotic syndrome in adults.*
- *It is commonly idiopathic/primary but it can be secondary to therapeutic drugs (penicillin), hepatitis B infection, malignancy, autoimmune diseases like SLE etc.*
- *The glomeruli show diffuse rigid thickened capillary loops.*

Membranous Nephropathy





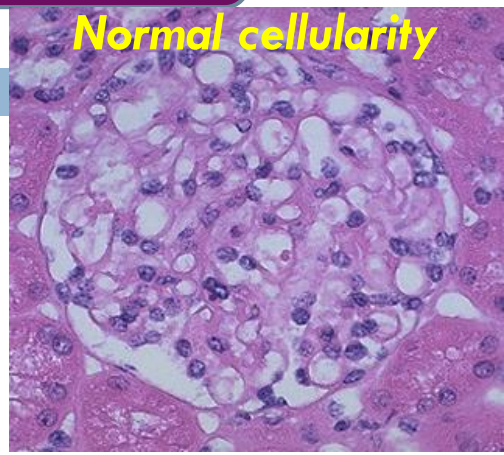


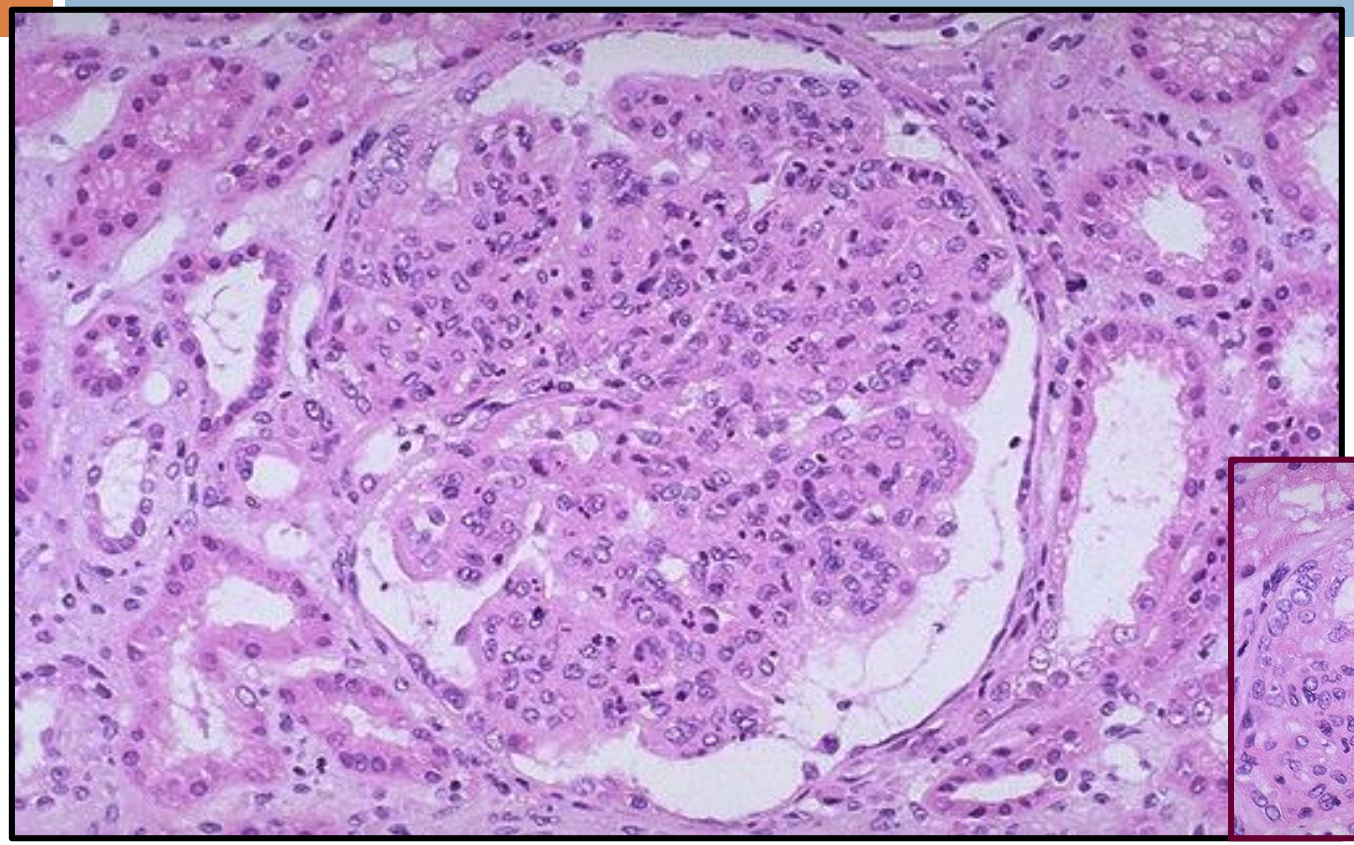
A. *The glomeruli show diffuse rigid thickened capillary loops.*
B. *A silver stain of the glomerulus highlights the glomerular basement membrane in black. There are characteristic projections arising from the basement membrane of the capillary loops called "spikes". These are projections around and in between subepithelial deposits (deposits do not take up the silver stain.)*

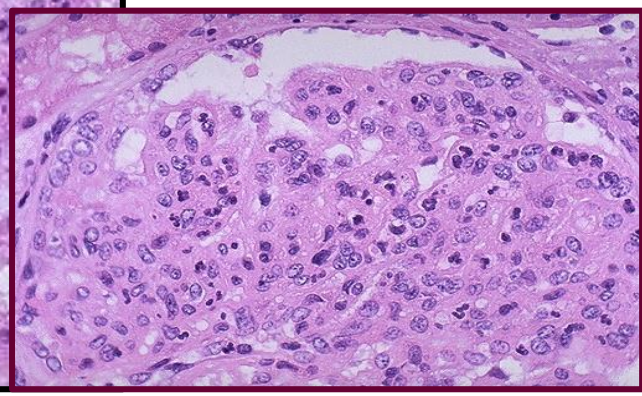
Example of Nephritic Syndrome

- Post infectious glomerulonephritis

Acute Post-infectious Glomerulonephritis

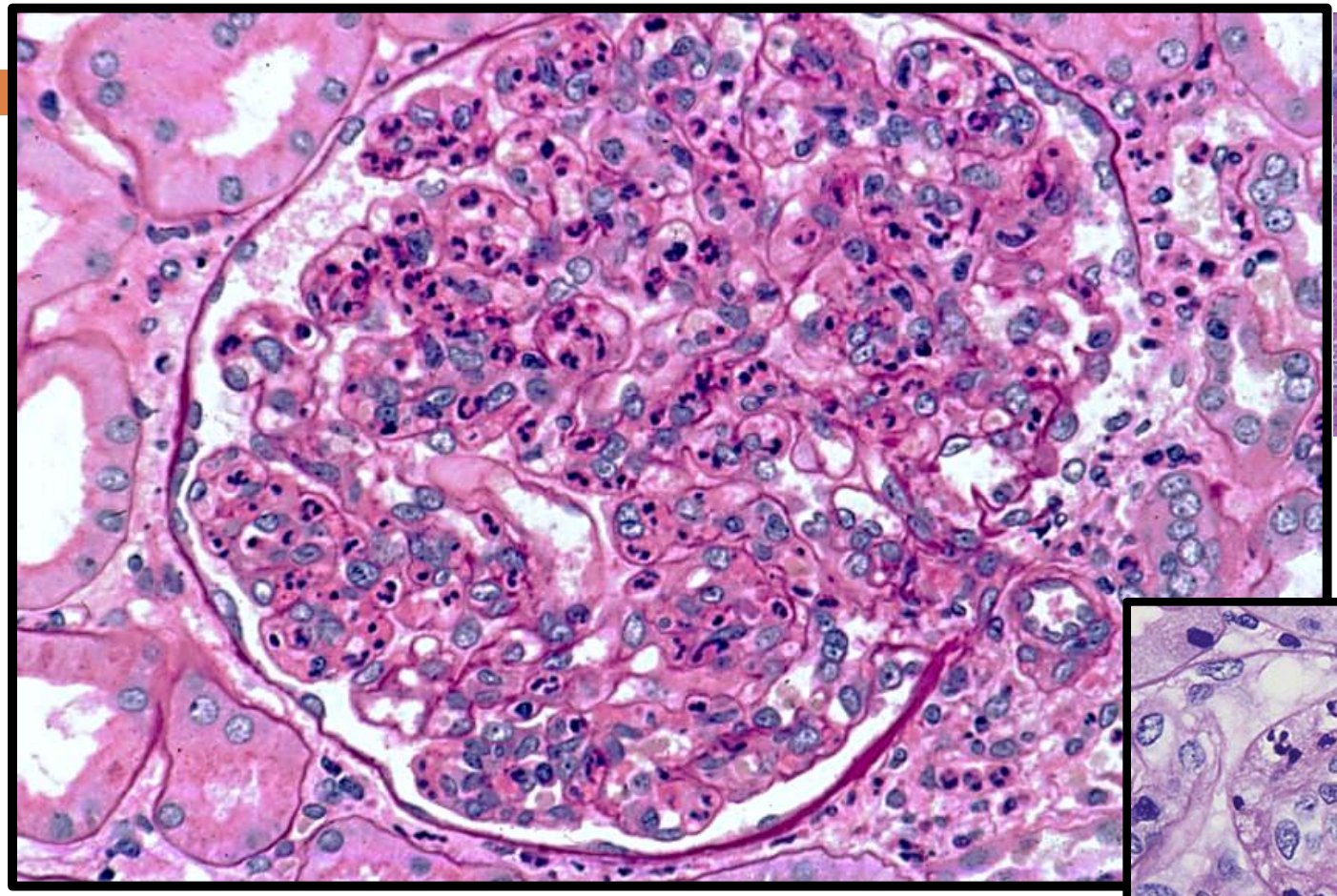


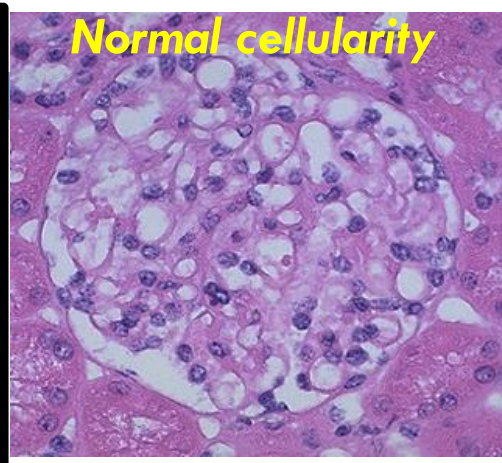


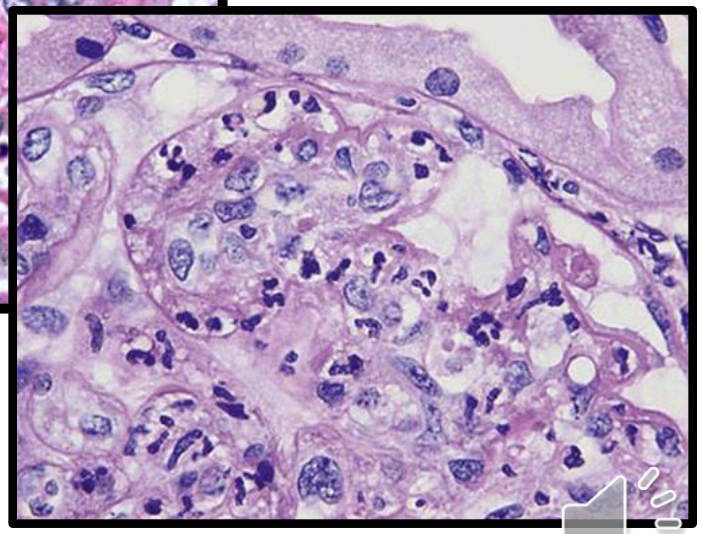


- *The glomerulus is enlarged, hypercellular and lobulated.*
- *The hypercellularity is due to increased numbers of endothelial and mesangial cells and there is infiltration of neutrophils and monocyte in and around the glomerular capillary loops.*
- *Post-infectious glomerulonephritis is typically follows a group A beta hemolytic streptococcal infection of the pharynx and thus it could be termed 'post-streptococcal glomerulonephritis'.*

Acute Post-infectious glomerulonephritis







Rapid progressive (crescentic) glomerulonephritis

Rapid Progressive Glomerulonephritis (RPGN)

- RPGN is a clinical syndrome, characterized by rapid and progressive loss of renal function within weeks to months. Patients present with acute renal failure with features of nephritic syndrome and severe oliguria.
- RPGN is commonly associated with severe glomerular injury with necrosis and GBM breaks and subsequent proliferation of parietal epithelium (crescents).
- Histologically there is severe glomerular injury. The characteristic finding in the glomeruli is the presence of extracapillary proliferations (i.e. proliferation outside the glomerular capillaries) called as crescents.
- Crescents are formed by
  - Proliferation of parietal epithelial cells that line the Bowman's capsule
  - and by migration of monocytes/macrophages into Bowman's space

The crescents eventually fill the Bowman's space, compress the glomeruli and can even rupture the GBM.
Segments of glomeruli may show necrosis.
In time with healing the crescents undergo fibrosis/scarring.

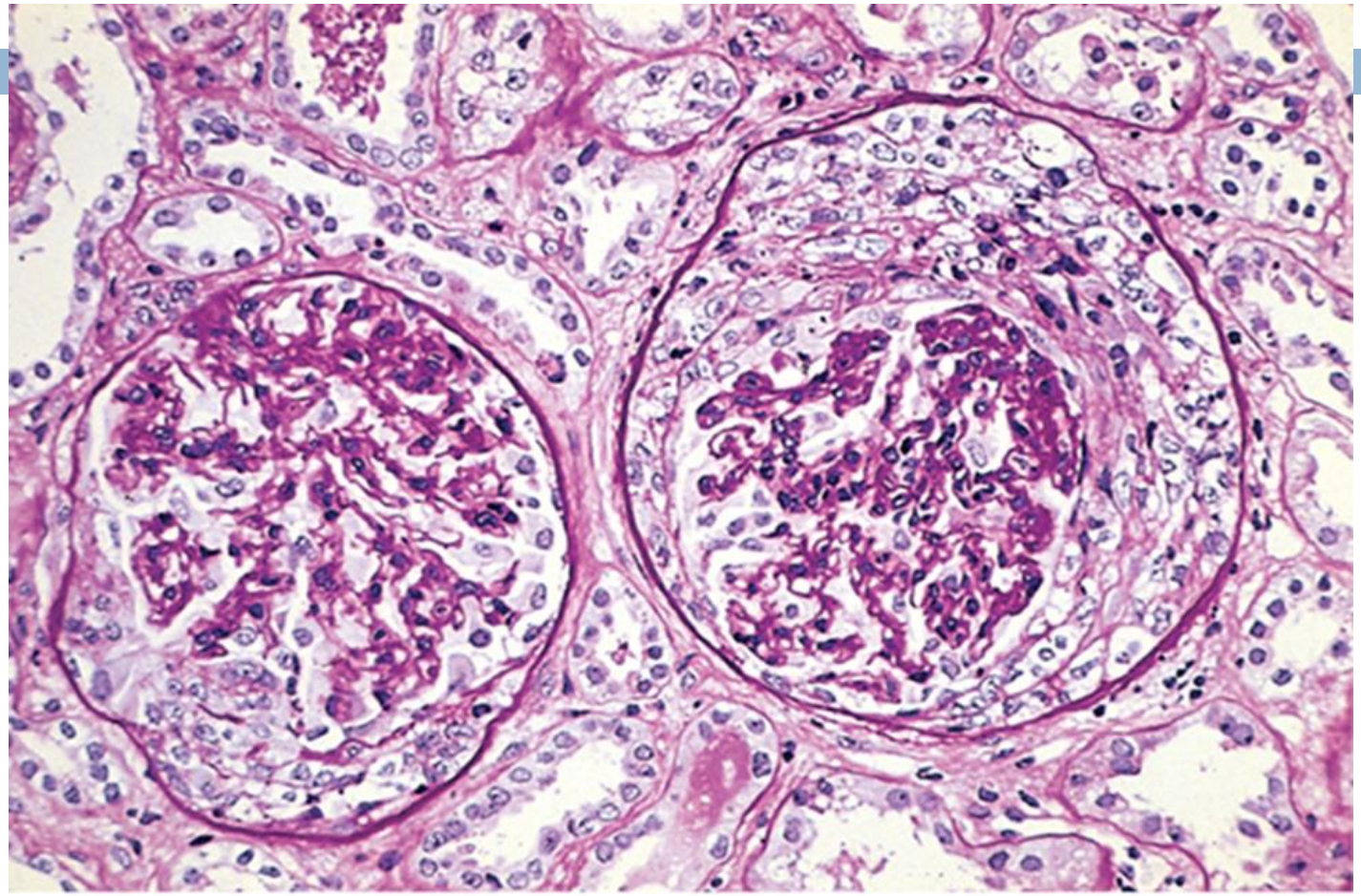
Types of RPGN/ CrGN

Type I RPGN = anti-glomerular basement membrane antibody–mediated crescentic GN (12%): has autoantibodies called anti GBM antibodies → anti-GBM disease, Goodpasture's Syndrome

Type II RPGN = immune complex mediated Crescentric GN (44%): is caused by the formation and deposition of antigen antibody immune complexes e.g. SLE, IgA nephropathy, post-infectious GN etc.

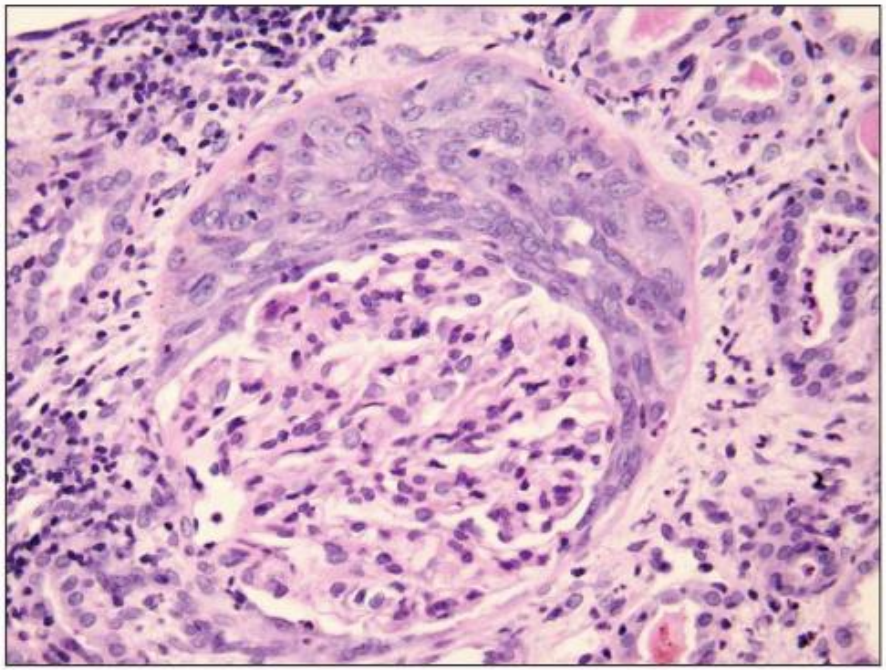
Type III RPGN (Pauci-immune) ANCA-Associated Crescentric GN (44%): the glomeruli are damaged by anti-neutrophil cytoplasmic antibodies e.g. Granulomatosis with polyangiitis (Wegener's) and Microscopic polyangitis

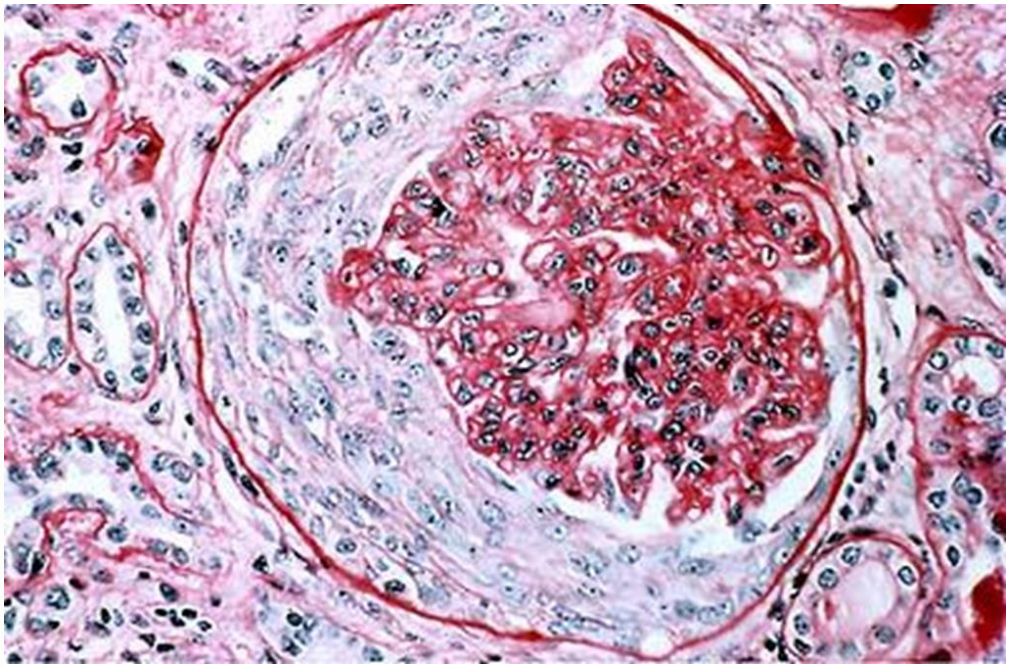
Rapid Progressive Glomerulonephritis (RPGN)



Crescents composed of proliferating epithelial cells.

Rapid Progressive Glomerulonephritis (RPGN)





All types of RPGN are characterized by glomerular injury and formation of crescents. The crescents are made up of proliferating parietal epithelial cells mixed with monocytes and macrophages forming a crescent-shaped proliferation. The crescents compress the glomerulus.

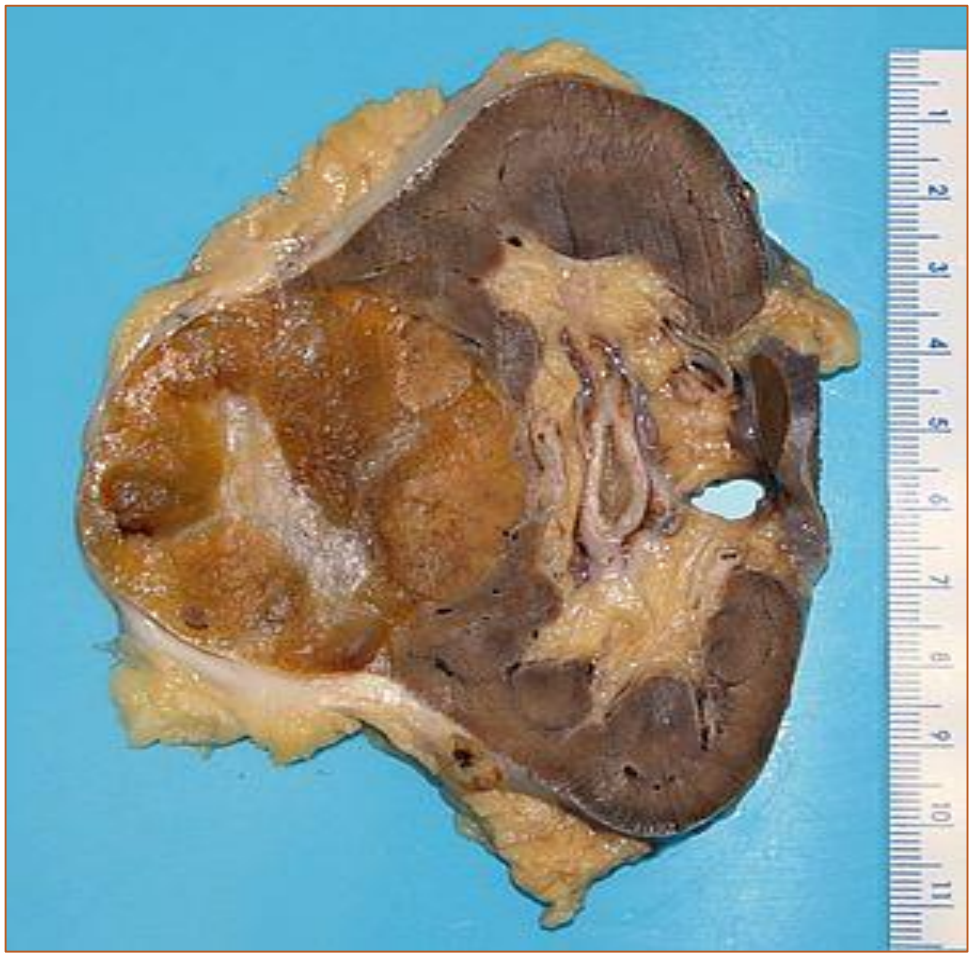
Epithelial cells of Bowman capsule are proliferated. Infiltrating WBCs such as monocytes and macrophages also proliferate compressing the glomerulus, forming a crescent.

Tumors of urinary tract

- Tumors of kidney
  - Benign: oncocytoma
  - Malignant: renal cell carcinoma & Wilm's tumor
- Tumors of urinary bladder: transitional cell carcinoma

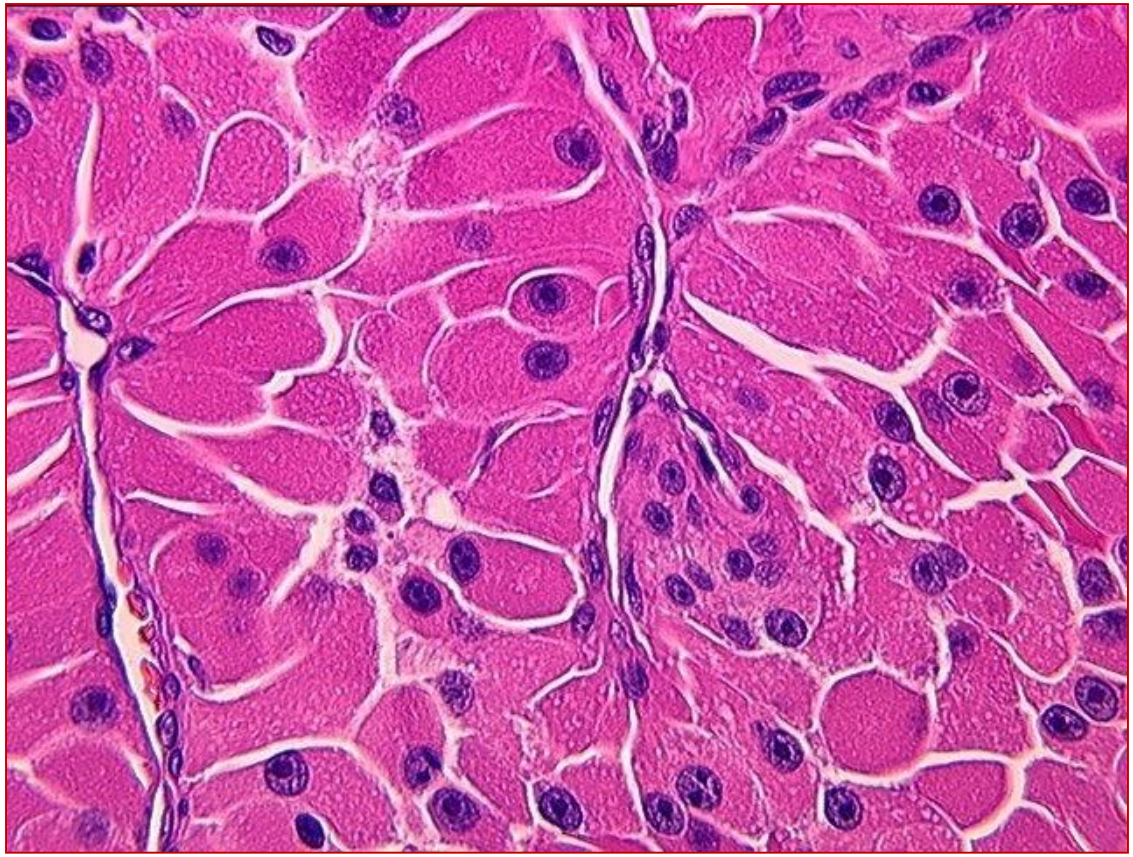
Oncocytoma

Oncocytoma - Gross



Gross: well-circumscribed mahogany (reddish-brown) ***colored renal mass with a central pale stellate scar.***

Oncocytoma



- *Oncocytoma is a benign tumor of the kidney arising from the intercalated cells of collecting ducts.*
- *It is made up of oncocytic cells called oncocytes. Oncocytes are uniform round polygonal cells with abundant, intensely eosinophilic and granular cytoplasm with uniform round and central nuclei and prominent nucleoli.*

Oncocytoma

Numerous mitochondria in the cytoplasm of neoplastic cells (Red arrows).

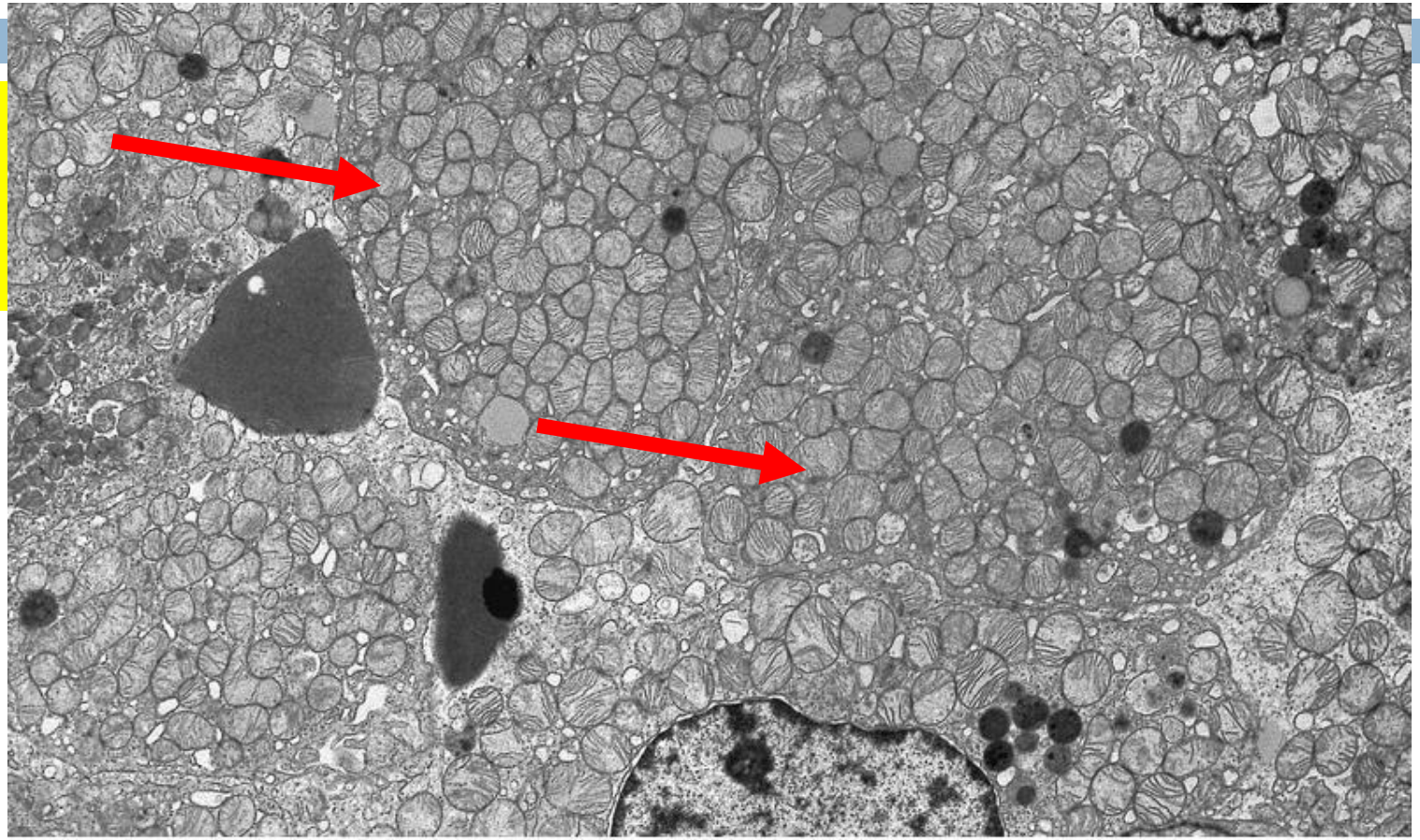
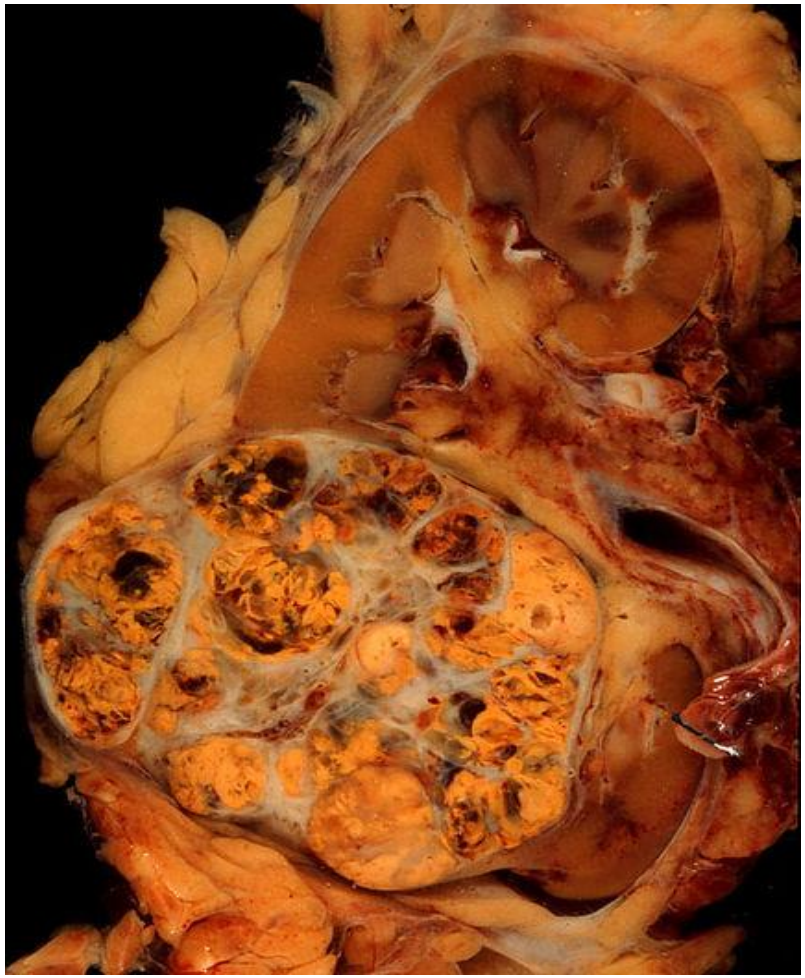


Fig. 1-220 AFIP 3rd Series, Vol. 11
RENAL ONCOCYTOMA
The cytoplasm of the oncocyte is packed with large mitochondria (X3000).

Electron microscopy study of oncocytoma: the cytoplasm of the neoplastic cells are filled with numerous mitochondria [red arrows(the circles)]. It is because of the numerous mitochondria that the oncocytic cell is granular and eosinophilic.

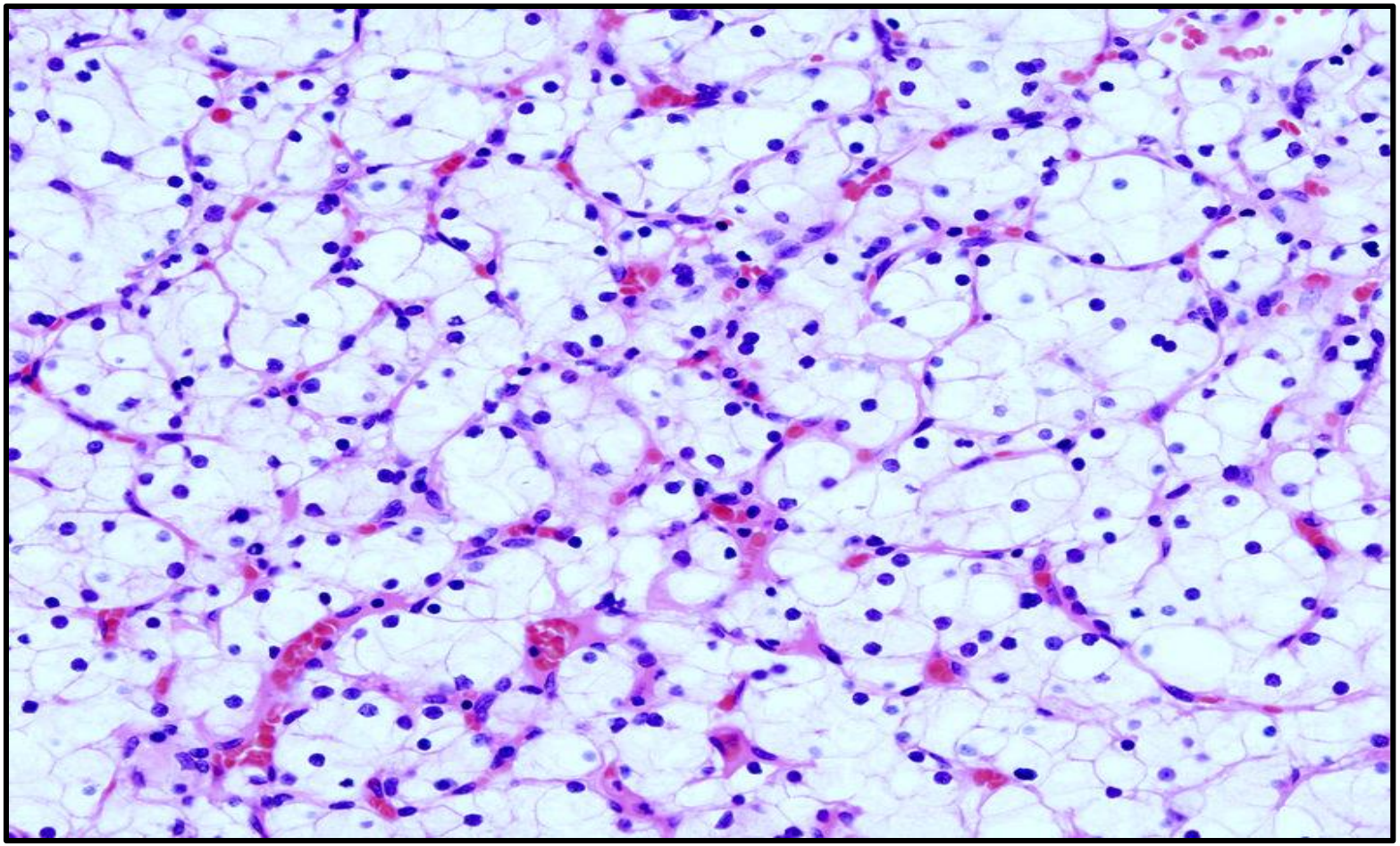
Renal Cell Carcinoma, clear cell type

Renal Clear Cell Carcinoma – Gross pathology



A well circumscribed renal cortical heterogenous lobulated mass which is partly yellow and partly hemorrhagic.

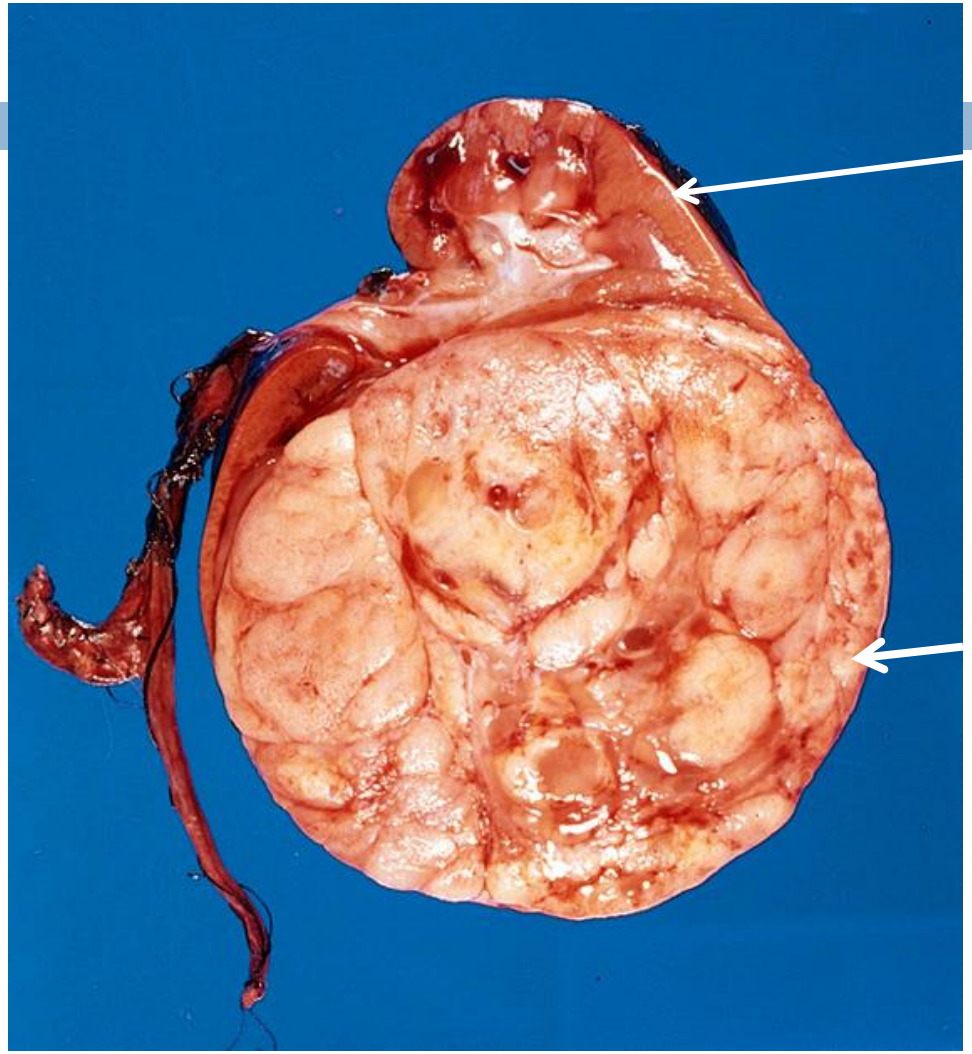
Renal Clear Cell Carcinoma - Histopathology



Tumor is made up of large polygonal cells with clear cytoplasm and sharp cell membrane. The cells are often arranged in sheets or nests. The stroma is highly vascularized.

WILM'S TUMOR

Wilm's Tumor – Gross Pathology



Gross: a well circumscribed tumor occupying most of the kidney. Cut section shows uniform, pale gray, soft (fish flesh like) tumor with foci of hemorrhage. Necrosis can also be present.

Wilms tumor:

Microscopy:

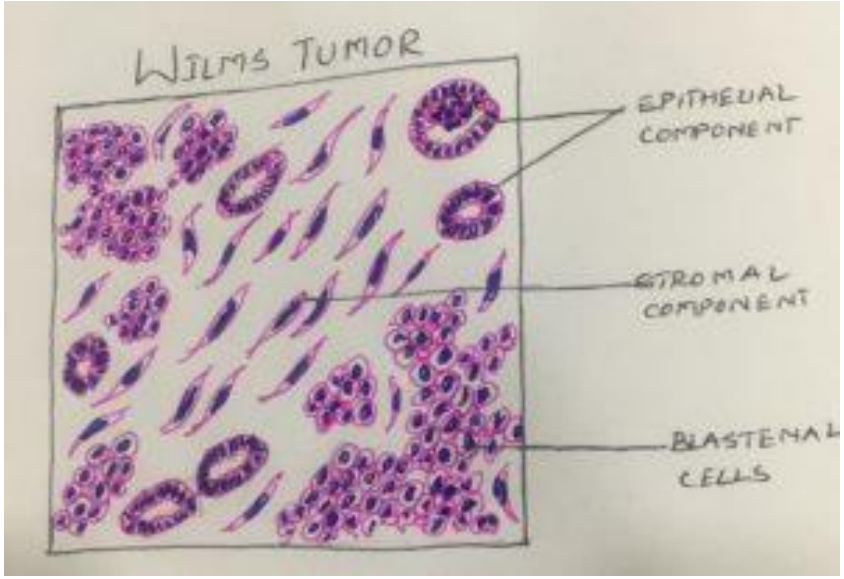
It is malignant neoplasm arising from embryonic nephrogenic elements composed of triphasic mixtures of blastemal, stromal and epithelial tissue.

The classical triphasic combination of:

1. Blastemal component: composed of densely packed small round blue cells with scanty cytoplasm and brisk mitosis
2. Epithelial component: composed of immature primitive tubular structures (rosettes) and immature glomeruli.
3. Stromal component: composed of loose immature stroma of undifferentiated mesenchymal cells (immature spindle cells and myxoid material).

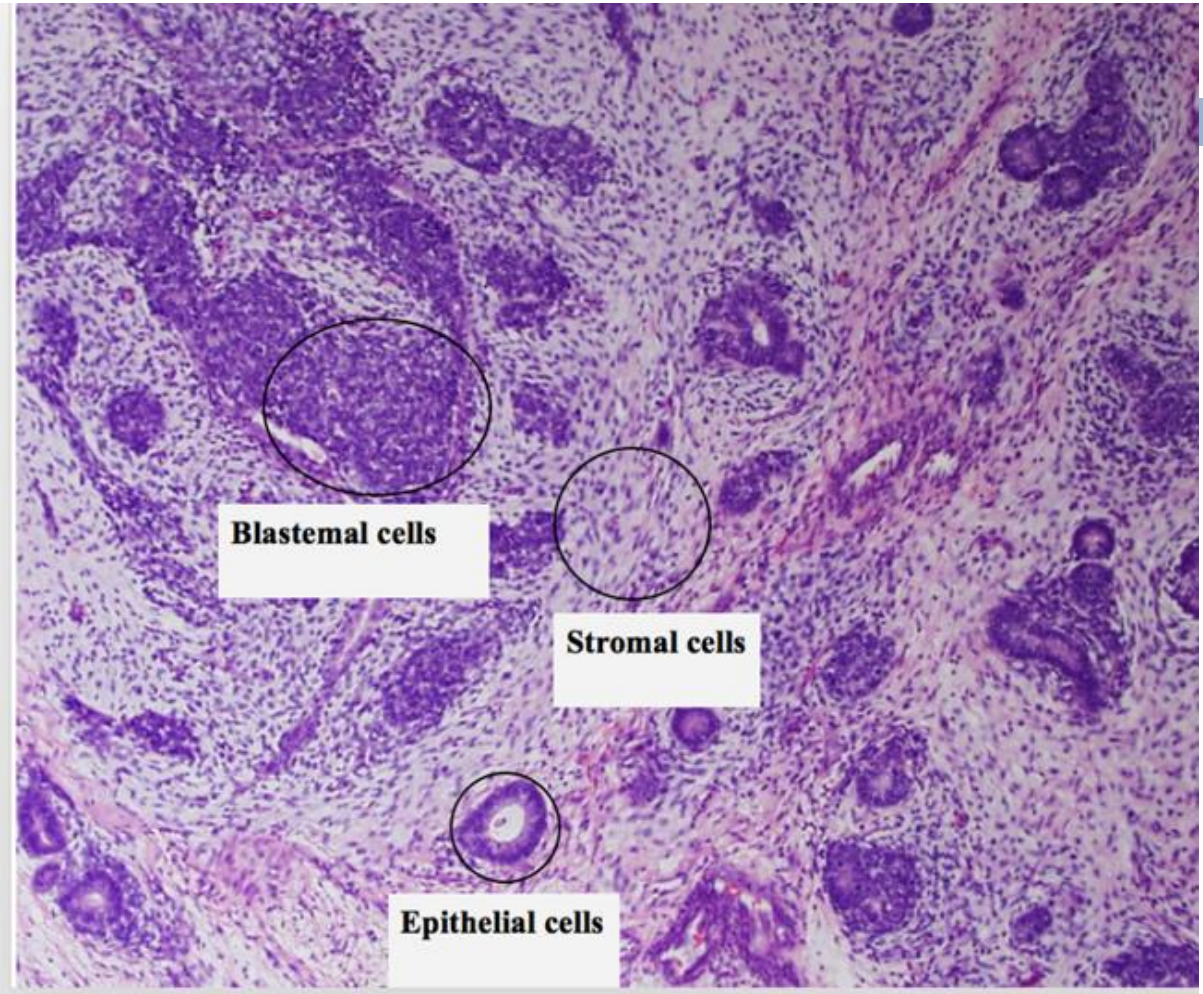
Biphasic and monophasic patterns can also occur.

5% of tumors contain foci of anaplasia. Anaplasia is an indication of poor prognosis.



http://www.histopathology.guru/wp-content/uploads/2018/06/wilms-tumor-300x207.jpg

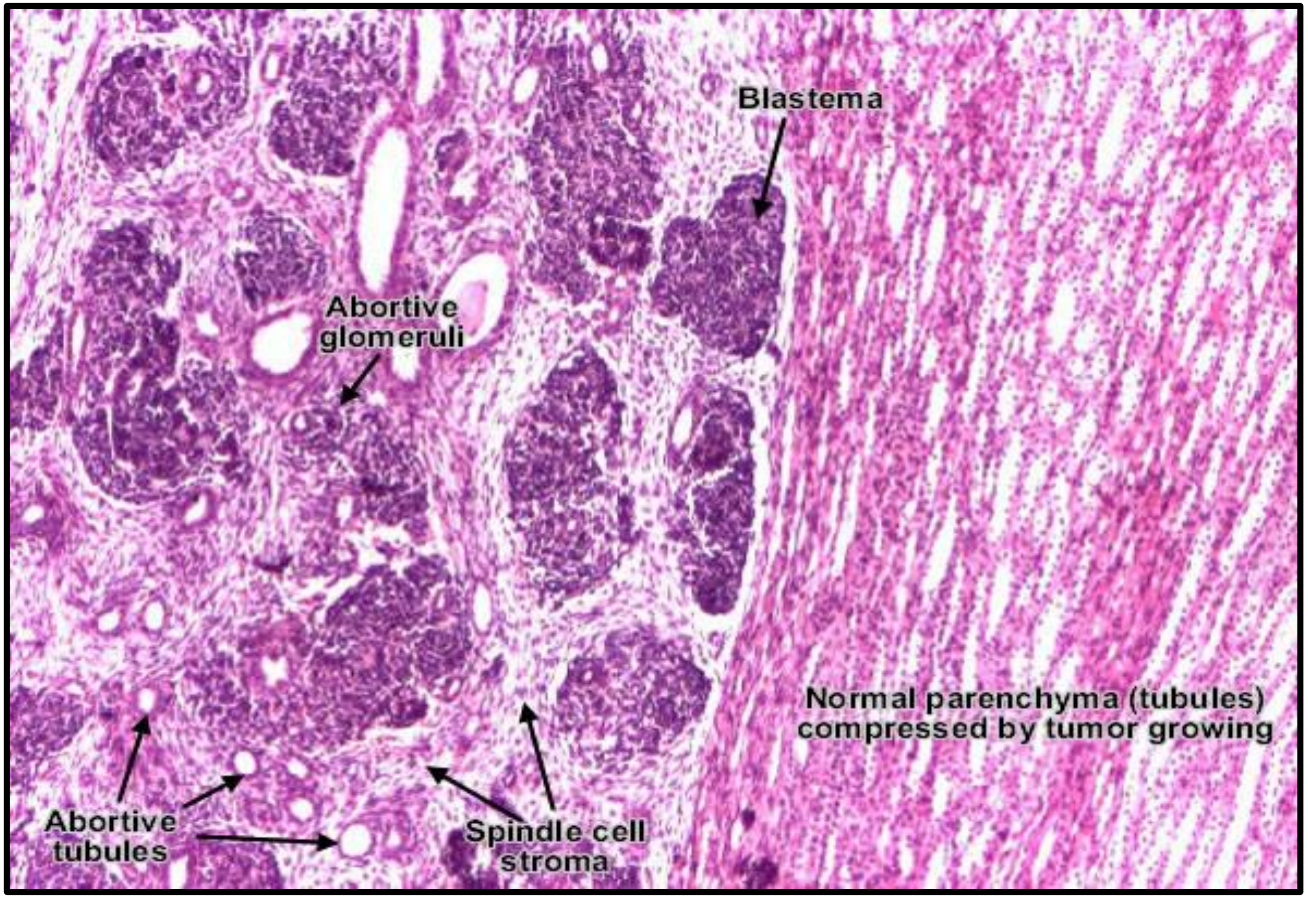
Wilm's Tumor – Histopathology



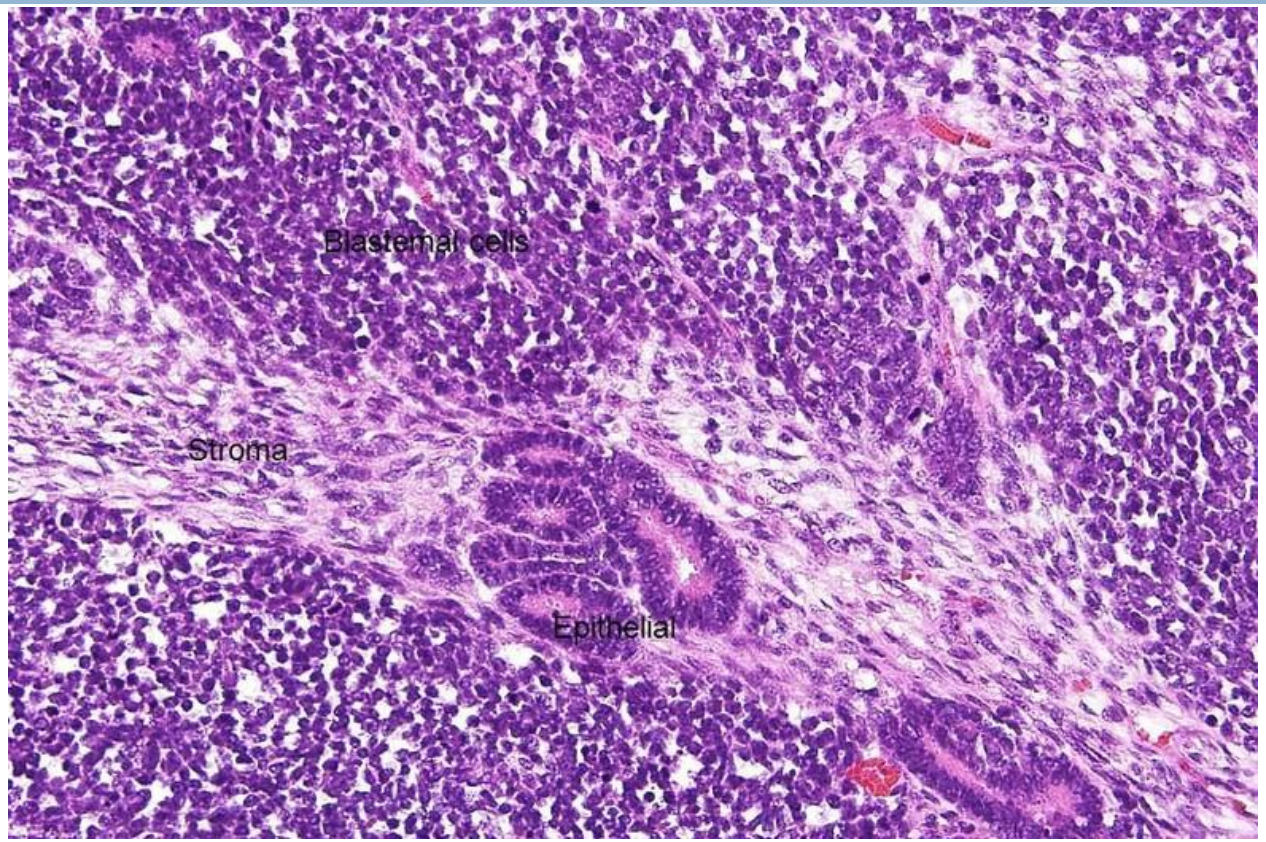
Three major components:

1. *Blastema cells: densely packed small round blue cells*
2. *Epithelial tissue: primitive glomerular & tubular structures (rosettes)*
3. *Stromal component : immature mesenchymal stromal tissue*

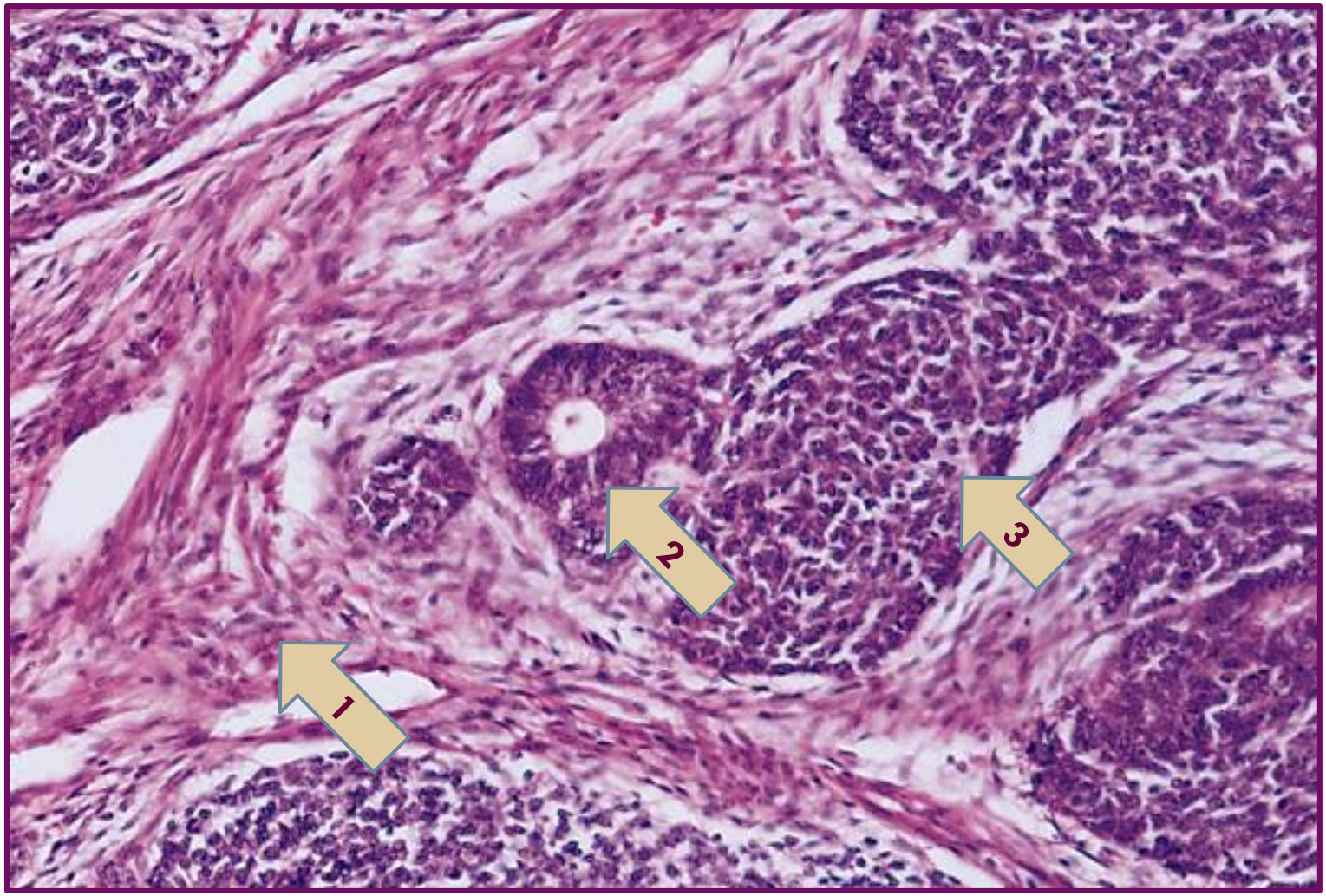
Wilm's Tumor – Histopathology



Wilm's Tumor – Histopathology



Wilm's Tumor – Histopathology



1. Spindle cell stroma.
2. Abortive glomeruli.
3. Blastema.

CARCINOMA OF THE URINARY BLADDER

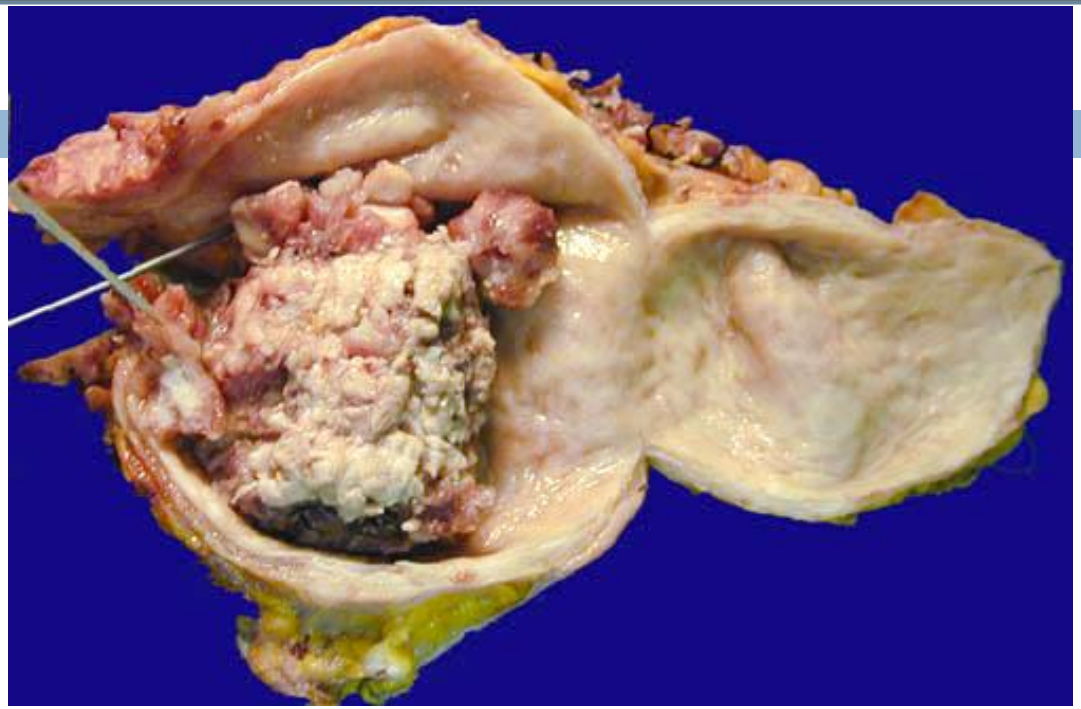
Urothelial carcinomas

Predisposing factors:

- Bladder tumors are more common in people exposed to chemicals called aromatic amines (arylamines) such as benzidine and beta-naphthylamine, which are sometimes used in the dye industry (aniline and Azo dyes).
- Cigarette smoking and chronic cystitis
- Chronic bladder irritation (from stones or long term bladder catheters)
- Chemotherapy (long-term use of cyclophosphamide) and
- Radiotherapy (previous exposure of the bladder to irradiation)

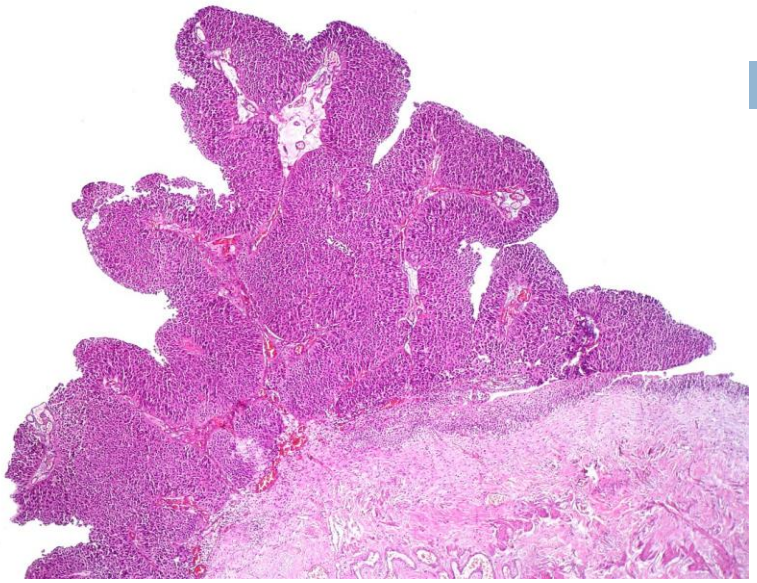
Note: long standing Schistosoma haematobium infections in endemic areas can predispose to squamous cell carcinoma of the urinary bladder.

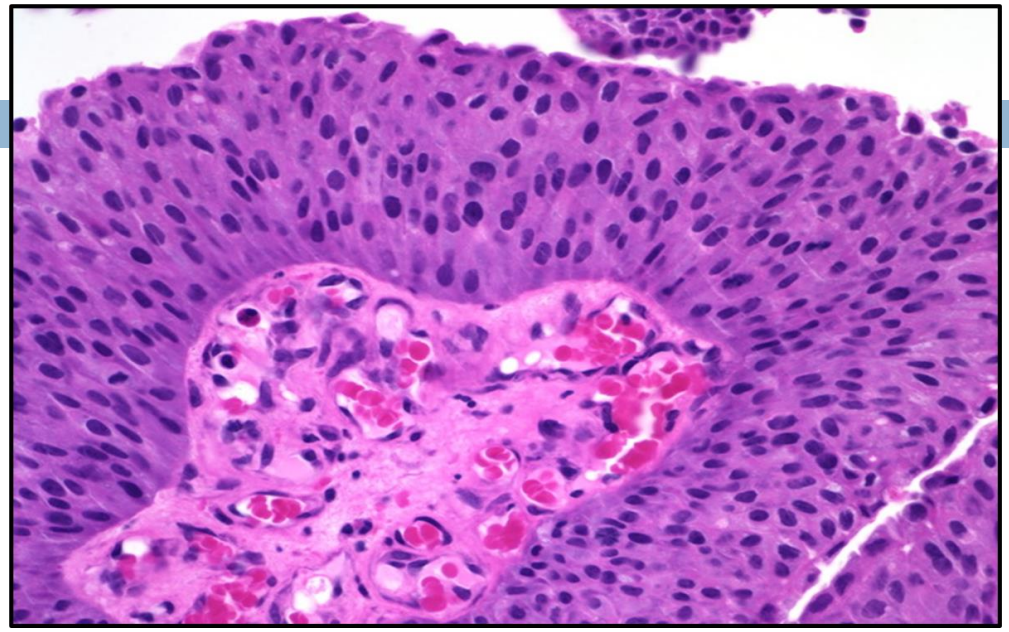
Urinary Bladder Carcinoma - Urothelial (Transitional cell) papillary Carcinoma - Gross



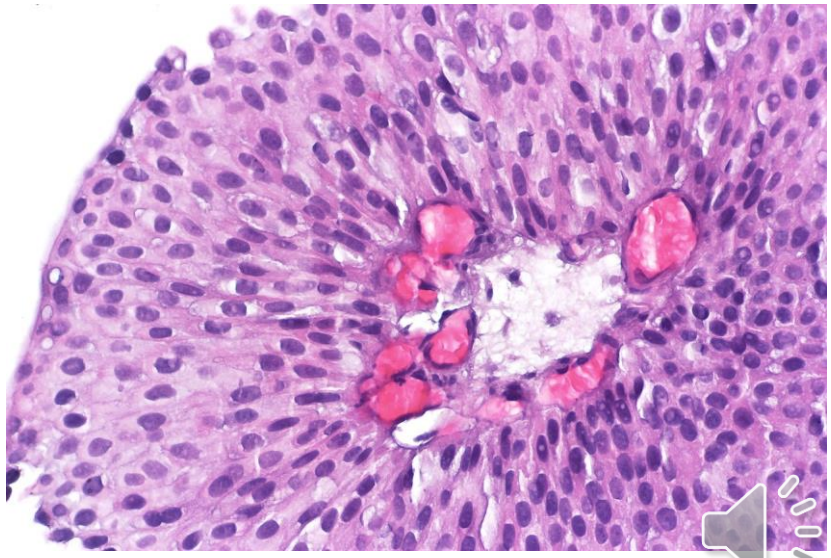
- *Cystectomy specimen shows a large friable grey white tumor mass with focal necrosis. It is occupying most of the bladder cavity.*
- *Common presentation is hematuria.*
- *Urine cytologic examination: shows malignant cells that are shed from the surface of the neoplasm. For diagnosis cystoscopy and biopsy is done.*
- *Other types of malignant tumors seen in the urinary bladder: squamous cell carcinoma, adenocarcinoma, sarcomas, small cell neuroendocrine carcinoma and metastatic (from cervix, prostate etc).*

Papillary Urothelial carcinoma – Low Grade

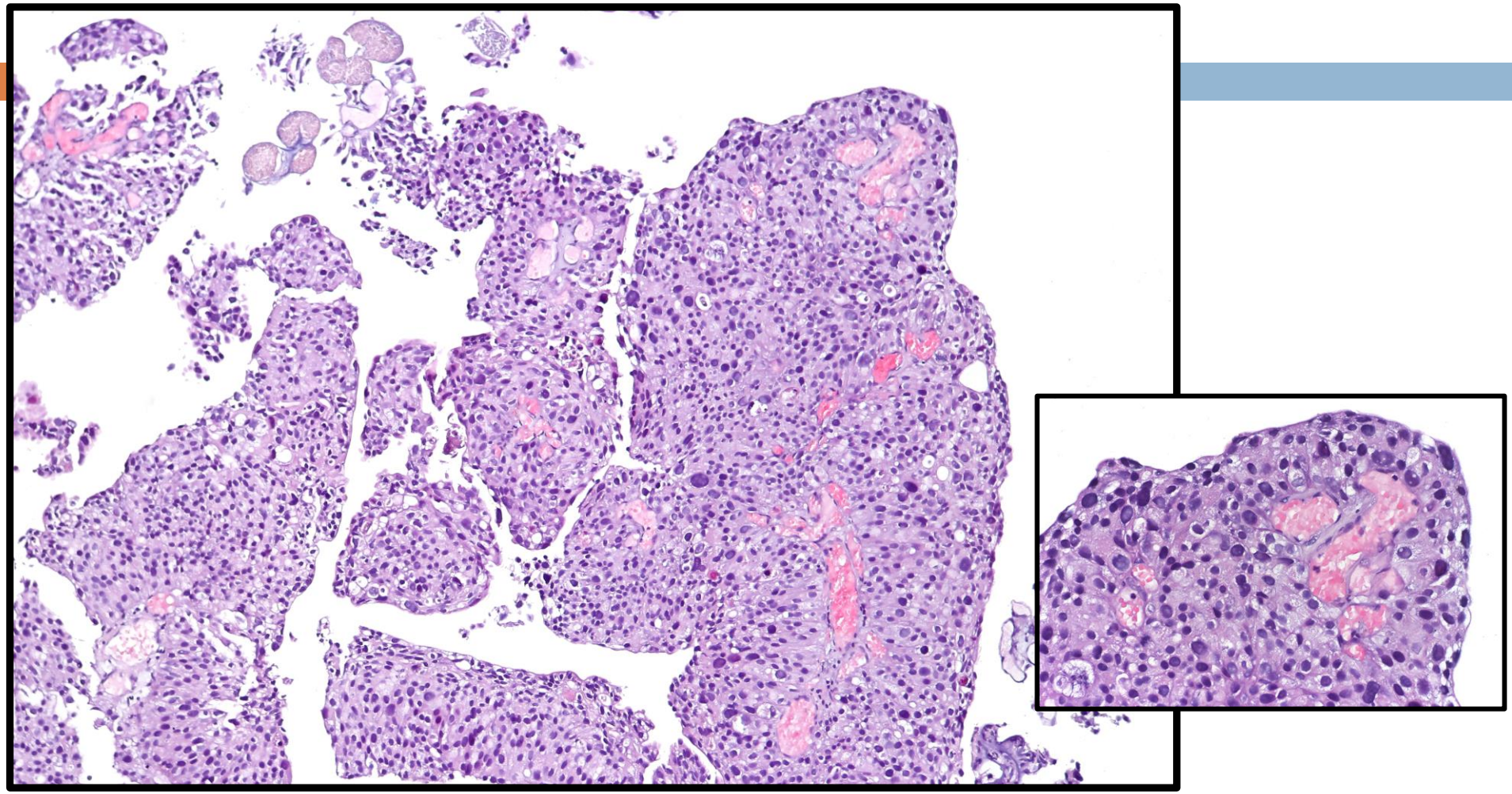




- *Picture show a* ***low grade*** *exophytic papillary tumor with overall preservation of cell polarity, and lack of marked atypia or pleomorphism.*
- *This exophytic papillary tumor has multiple finger-like projections with fibrovascular cores lined by multiple layers of urothelium. Urothelial cells show mild pleomorphism of nuclei and few mitoses.*

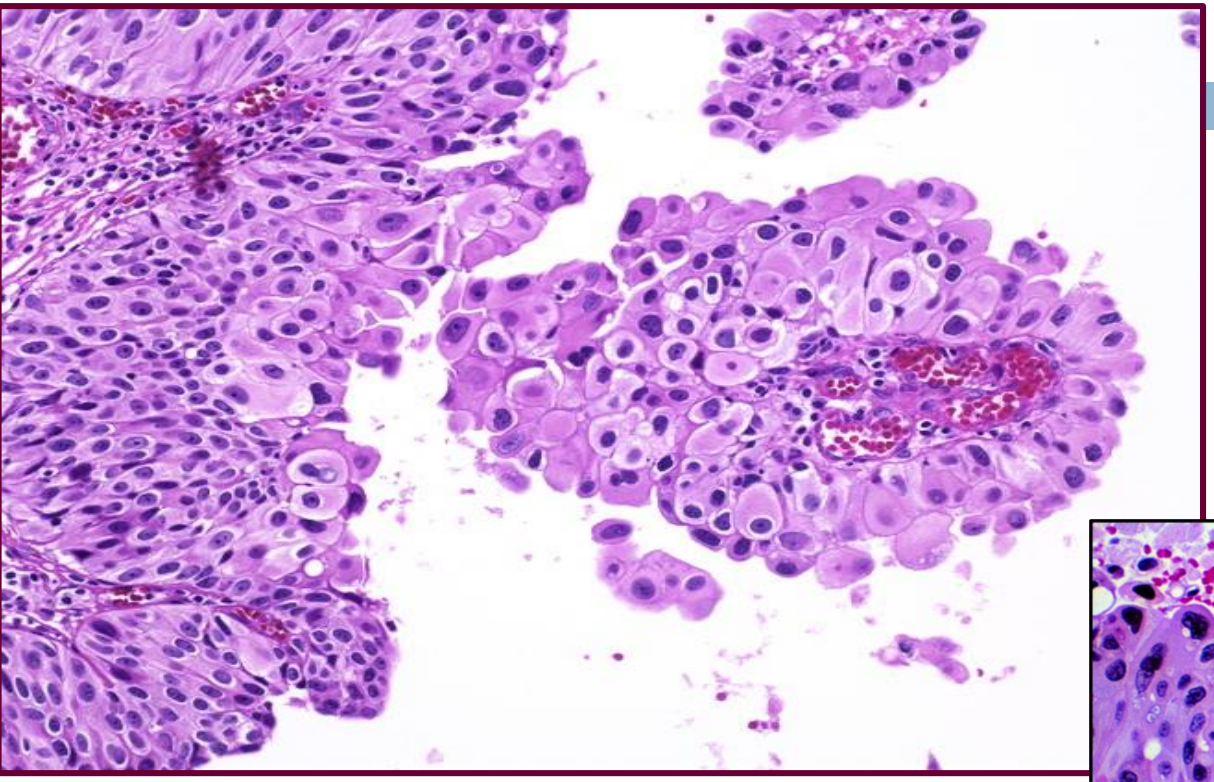


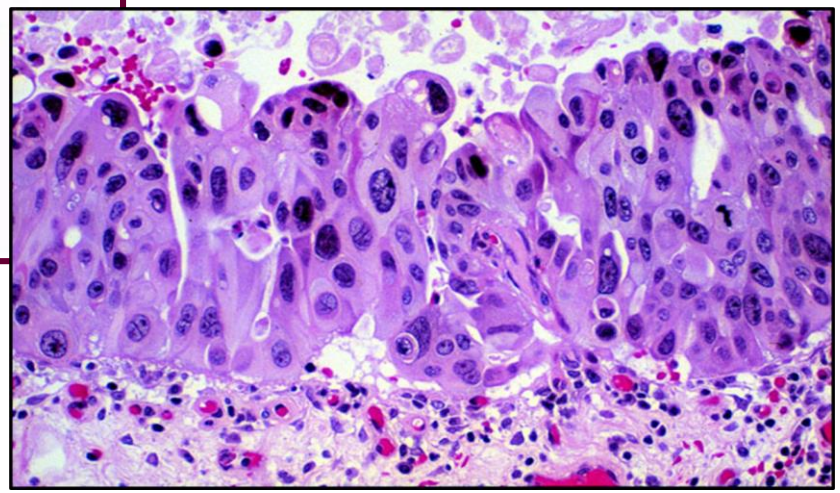
Papillary Urothelial carcinoma – High Grade



papillary projections with fibrovascular cores.
Tumor cells are pleomorphic with high grade nuclear changes.

Papillary Urothelial carcinoma – High Grade

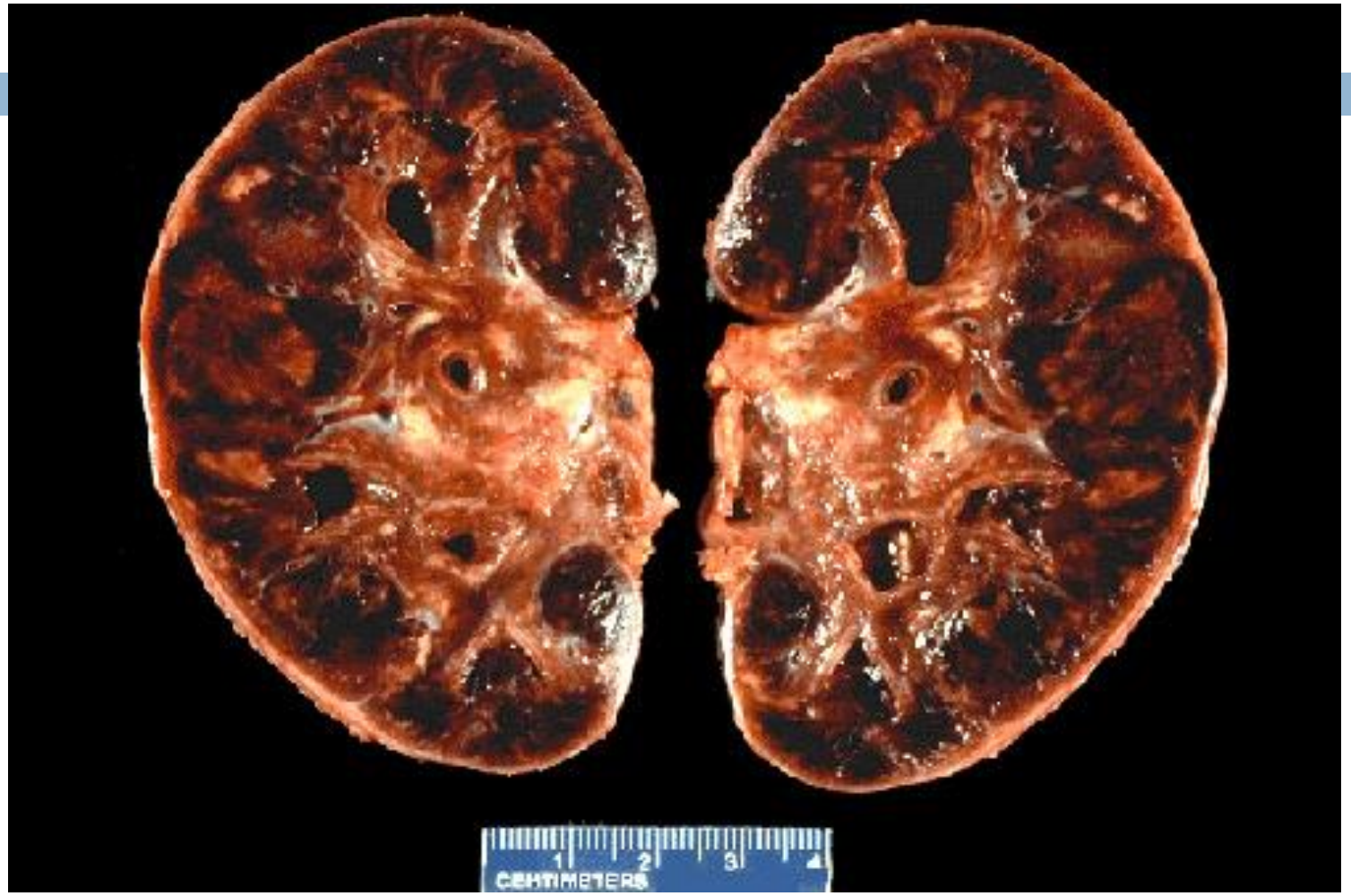




The tumor is made up of papillary projections with fibrovascular cores.
Tumor cells are pleomorphic with high grade nuclear changes.

Transplanted kidney (allograft kidney): acute cellular rejection

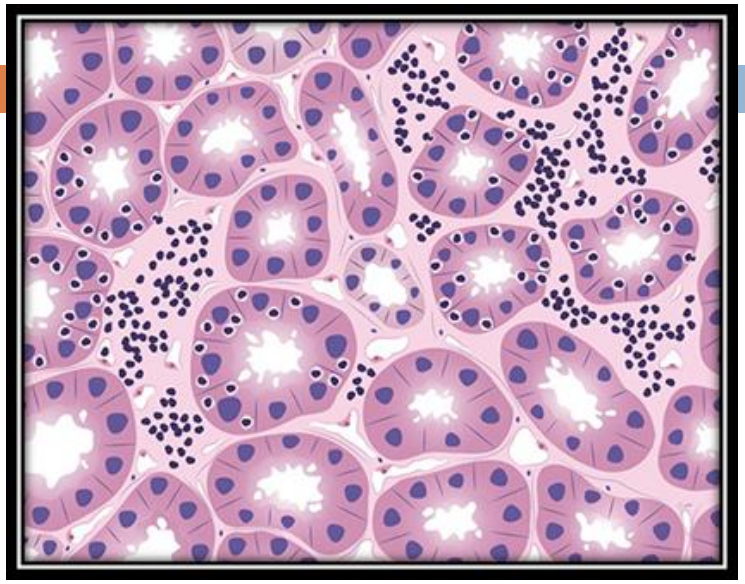
Acute Allograft Rejection

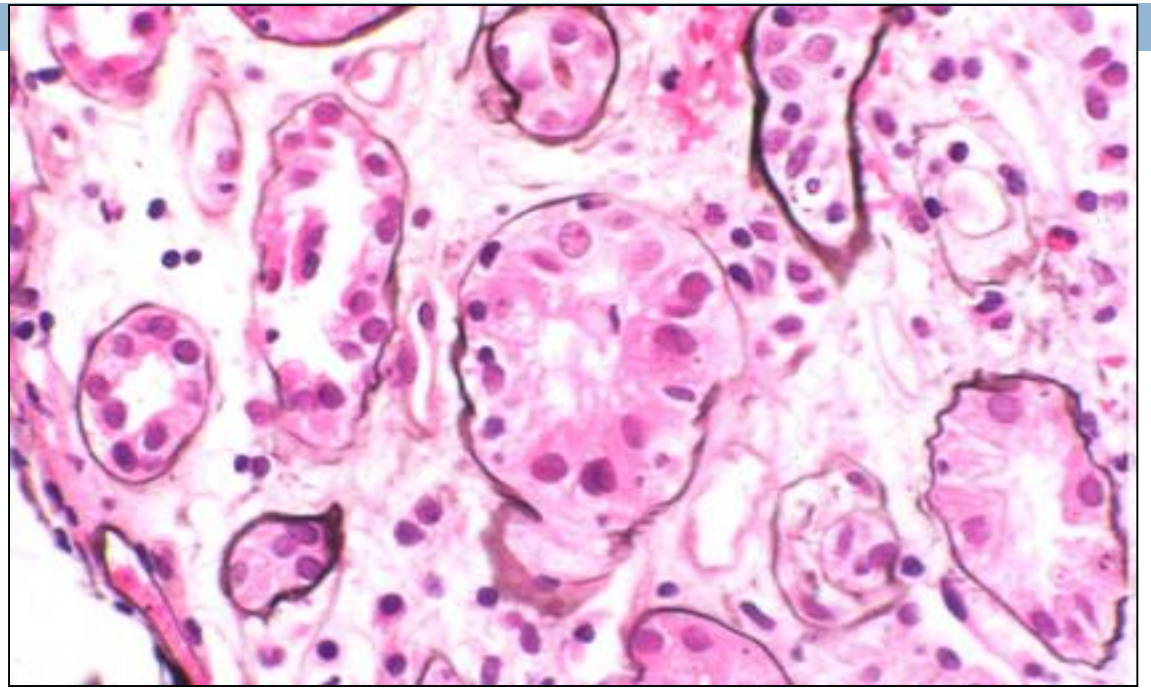


This kidney was removed because of acute transplant rejection. Note the swollen and hemorrhagic appearance of this entire kidney.

- The transplanted kidney is called the allograft.
- Acute Rejection is the most common type of rejection in the newly transplanted kidney patient. Developing in a short time span. It can occur within days or the first few months after surgery. Sometimes it can occur after years.
- 2 types
  - **Acute T-cell mediated (cellular) rejection.**
  - **Acute antibody-mediated rejection.**

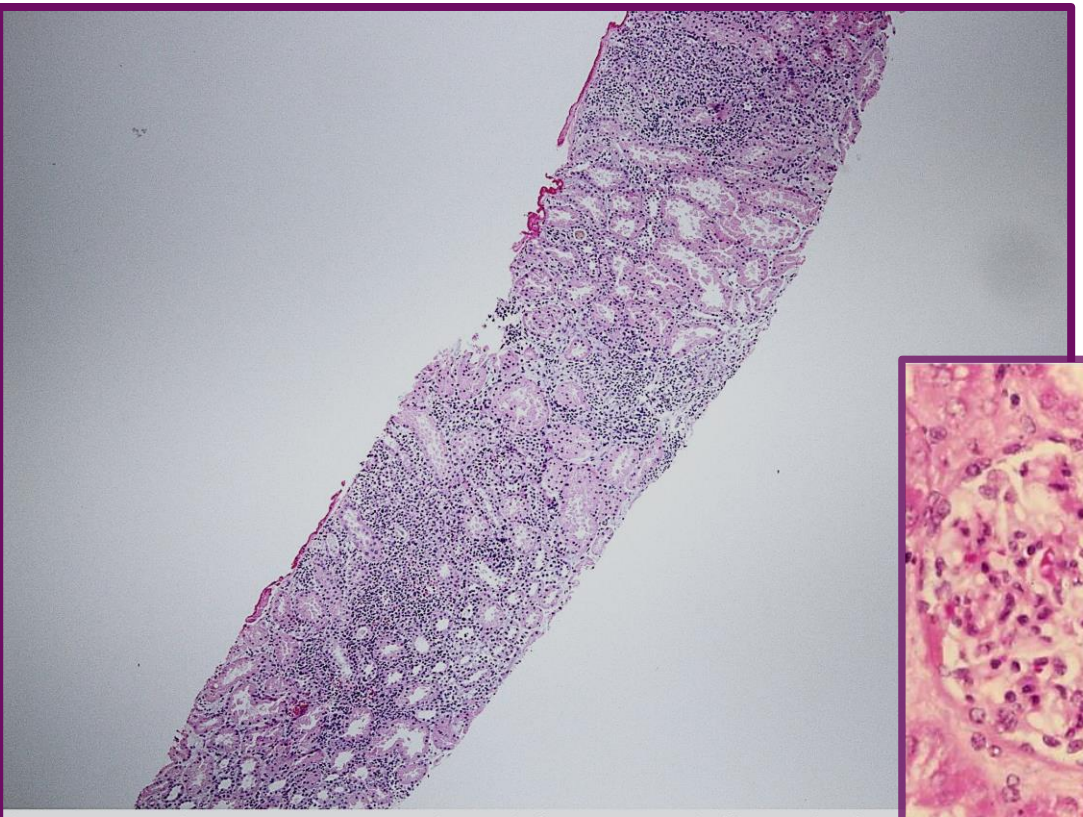
Acute T-Cell Mediated (Cellular) Rejection



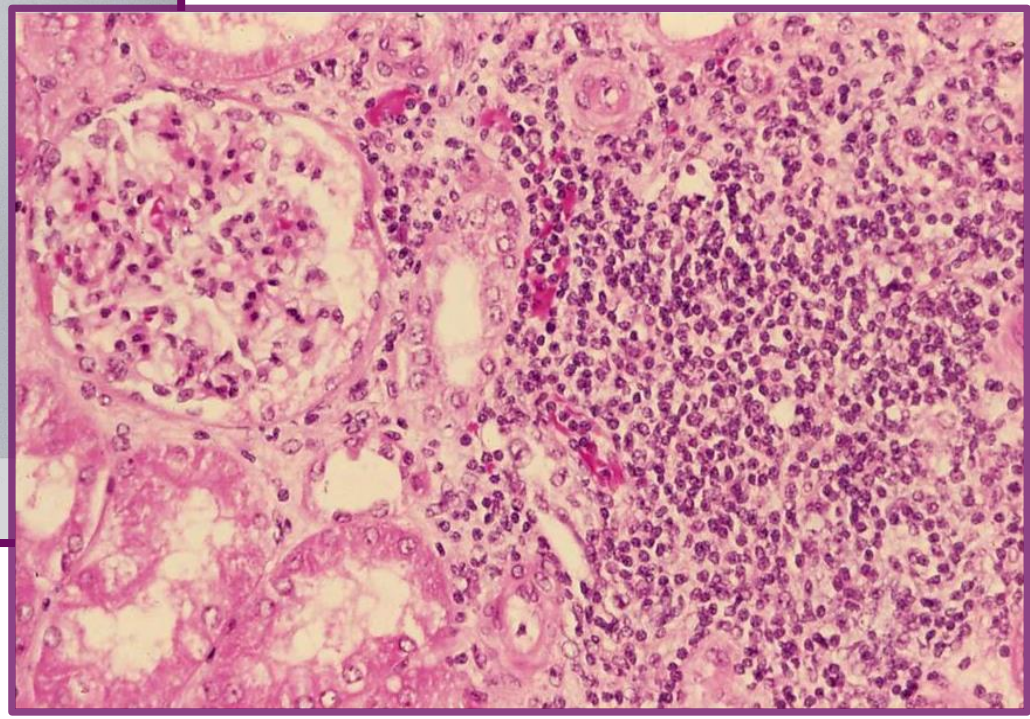


- *There is tubulointerstitial infiltration (interstitial inflammation & tubulitis) of the allograft kidney by lymphocytes and other inflammatory cells with or without arteritis.*
- *Tubulitis = infiltration of tubular epithelium by lymphocytes, is the hallmark of acute cellular rejection*
- *Arteritis = inflammation of the arteries in the allograft (+/- fibrinoid necrosis of arteries).*
- *Note: glomerular usually not involved*

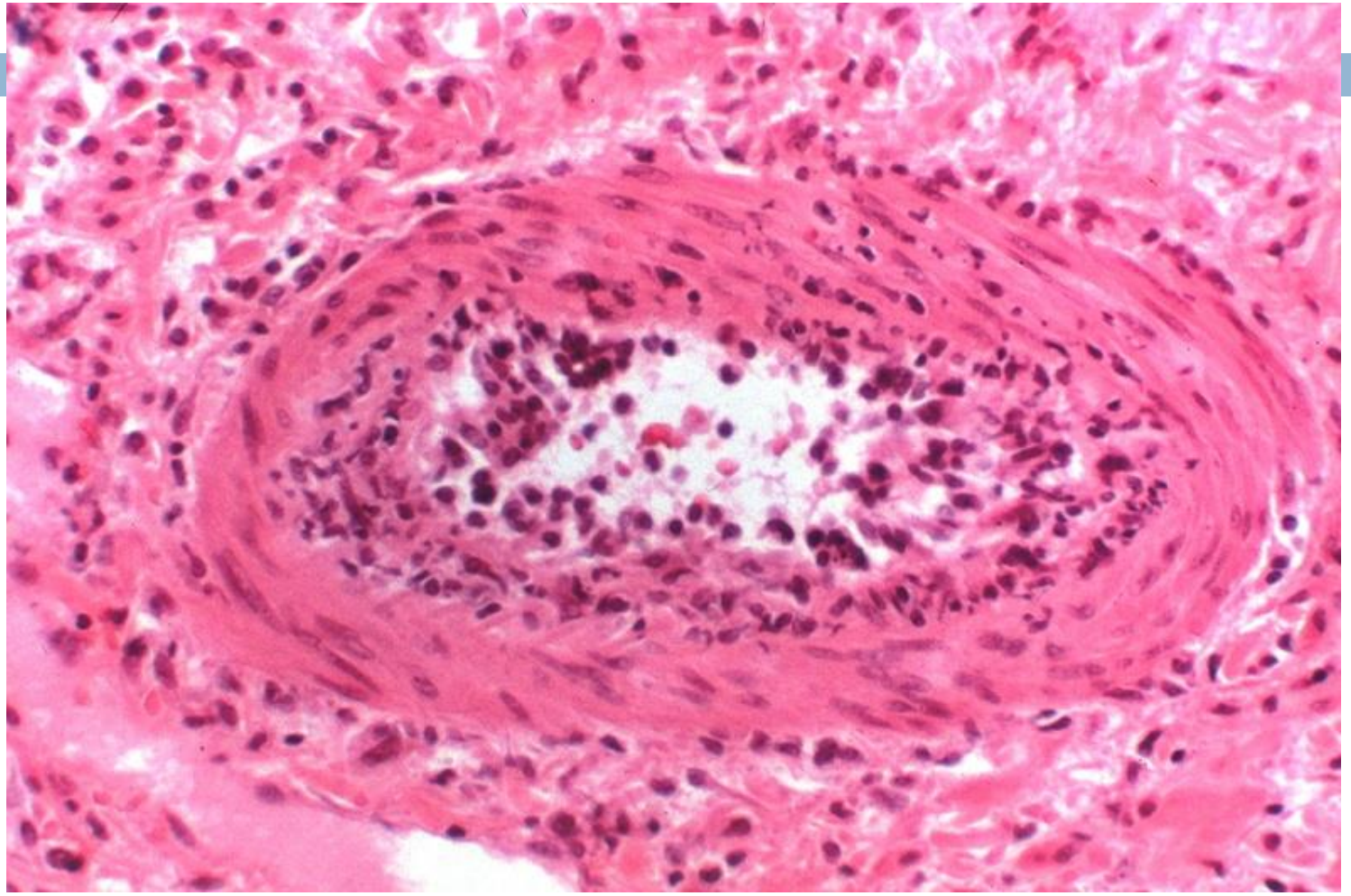
Acute Cellular Allograft Rejection



Low power demonstrates prominent inflammatory infiltrate in the tubulointerstitial space



Acute Rejection - vasculitis



Infiltration of the arterial wall by inflammatory cells with endothelial cell swelling and narrowing of the vascular lumina = vasculitis/arteritis.

Vasculitis/arteritis can be seen in both acute cellular rejection & acute antibody mediated rejection.

THE END