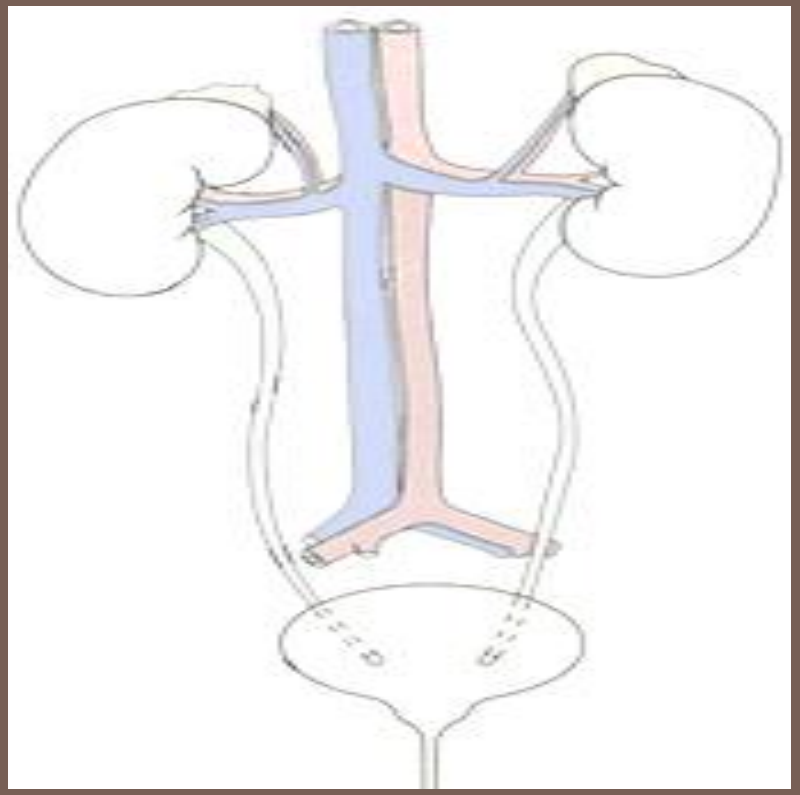
RENAL BLOCK



PATHOLOGY PRACTICAL

Prepared by:

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

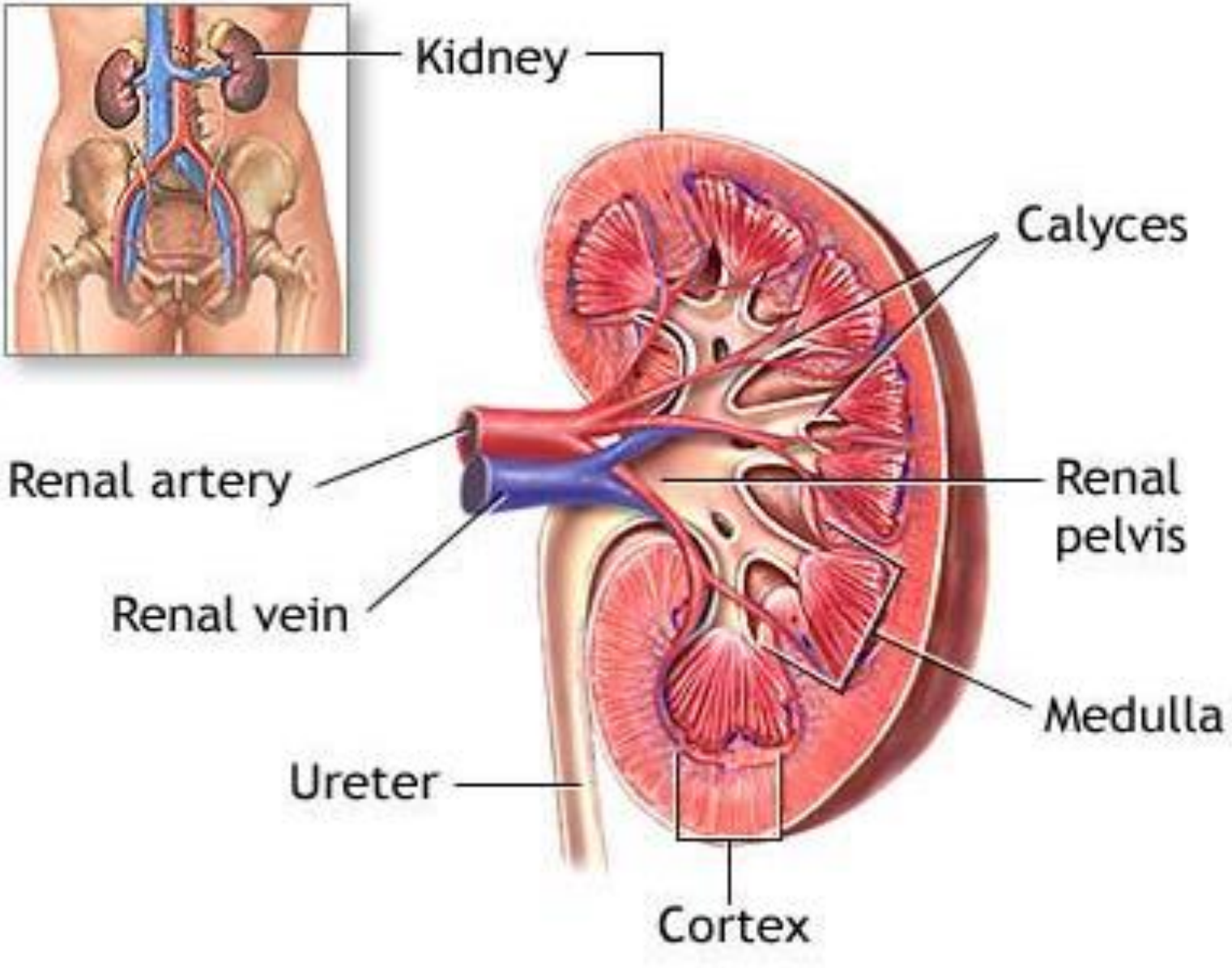
NORMAL ANATOMY AND HISTOLOGY

Objectives:

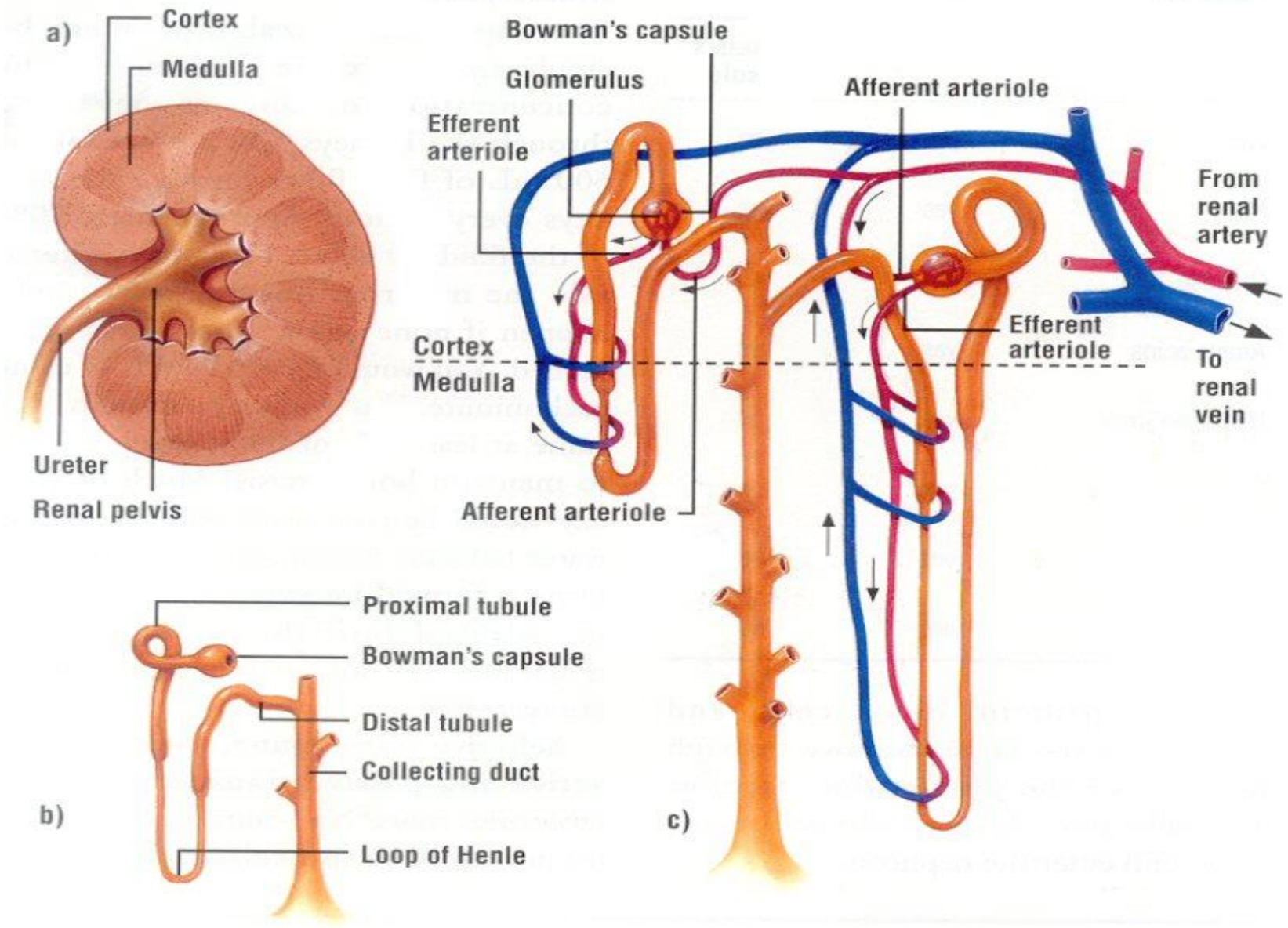
At the end of the practical sessions for the renal block, the students will be able to:

- Describe the normal constituents of the nephron, renal glomeruli and tubules.
- Identify the gross and microscopic features of:
  - Post-streptococcal glomerulonephritis.
  - Renal hydronephrosis, pyonephrosis & polycystic kidney.
  - Acute & chronic pyelonephritis.
  - Nephrotic and nephritic Syndrome.
  - Wilm's tumor.
  - Renal cell carcinoma, urothelial carcinoma of the urinary bladder.
  - Clear cell carcinoma of the kidney.
  - Pathology of renal allograft.

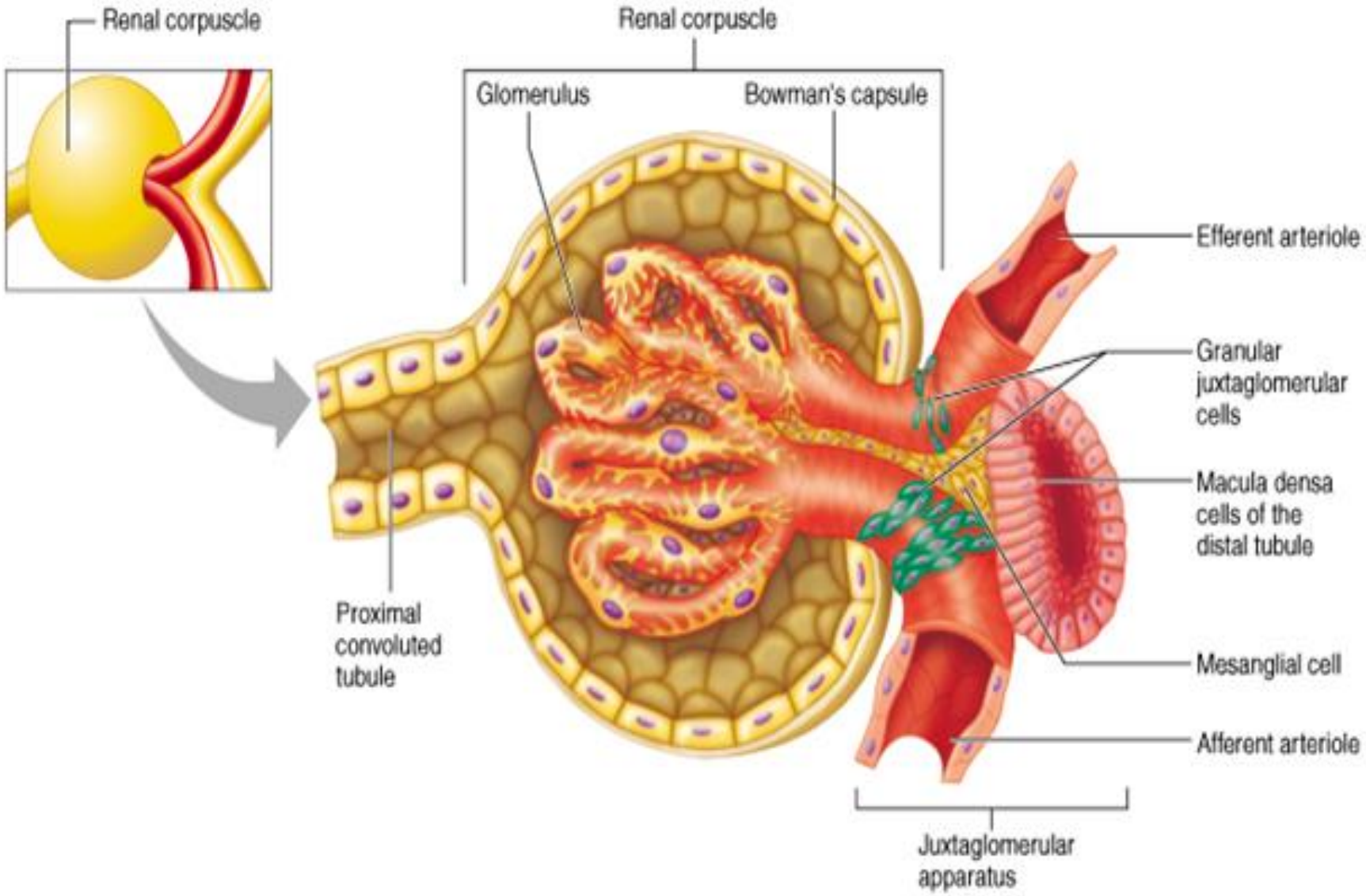
Anatomy of the Kidney



NEPHRON STRUCTURE



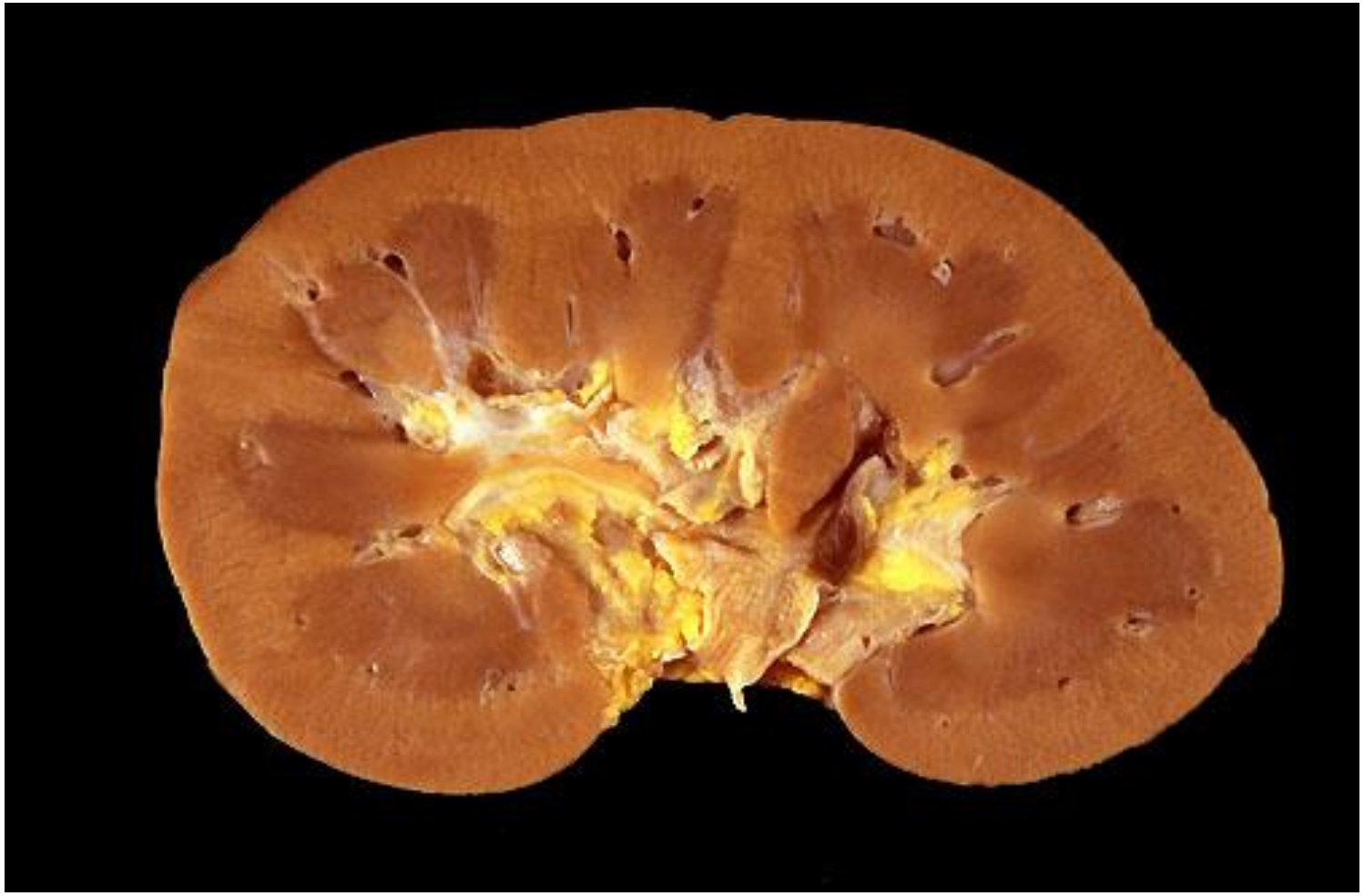
Renal Corpuscle



KIDNEY ANATOMY : NEPHRONS

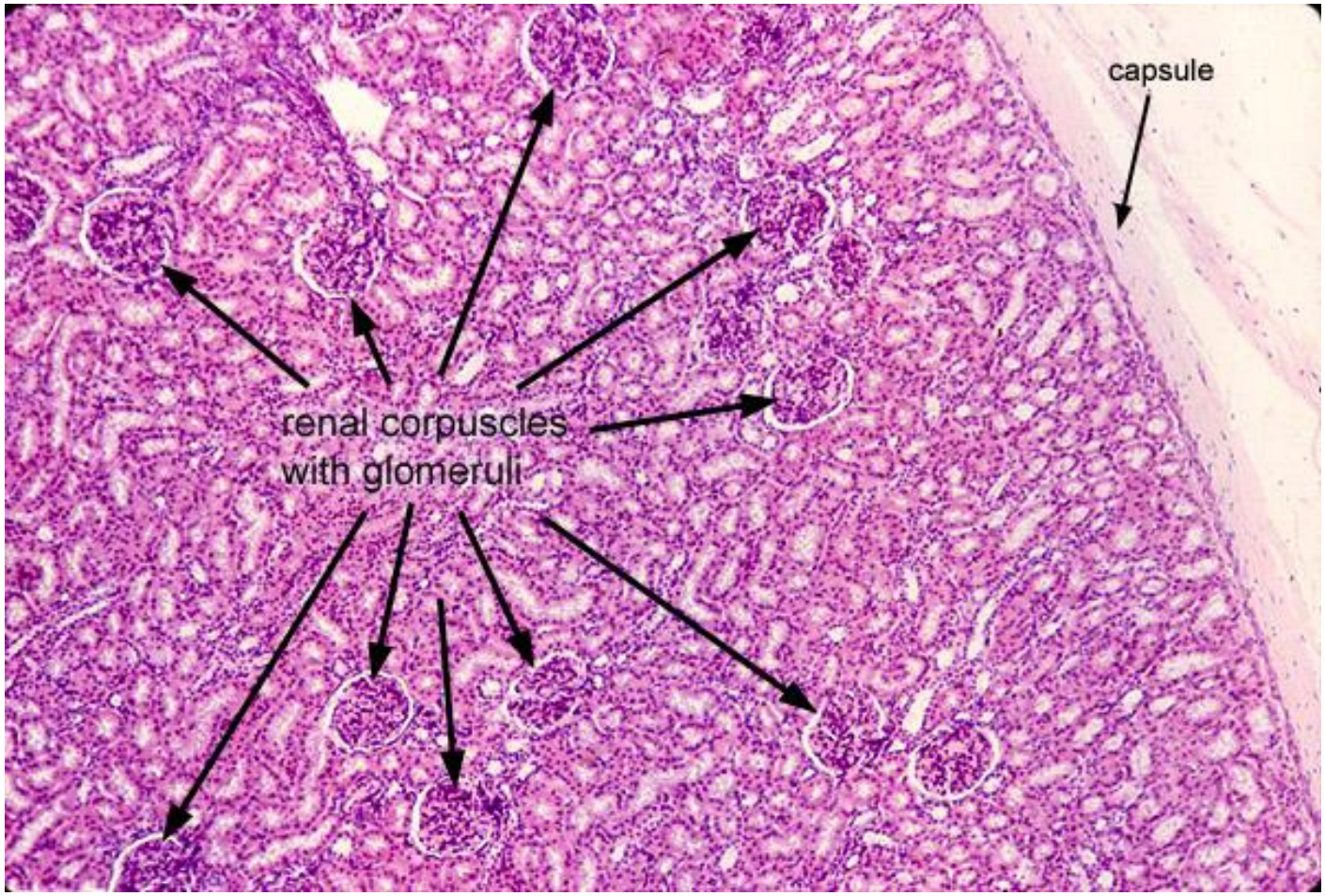
- *Nephron is the functional unit of the kidney.*
- *Each kidney contains about 1,000,000 to 1,300,000 nephrons.*
- *The nephron is composed of glomerulus and renal tubules .*
- *The nephron performs its function by ultra filtration at glomerulus and secretion and reabsorption at renal tubules.*

Normal Kidney - Gross

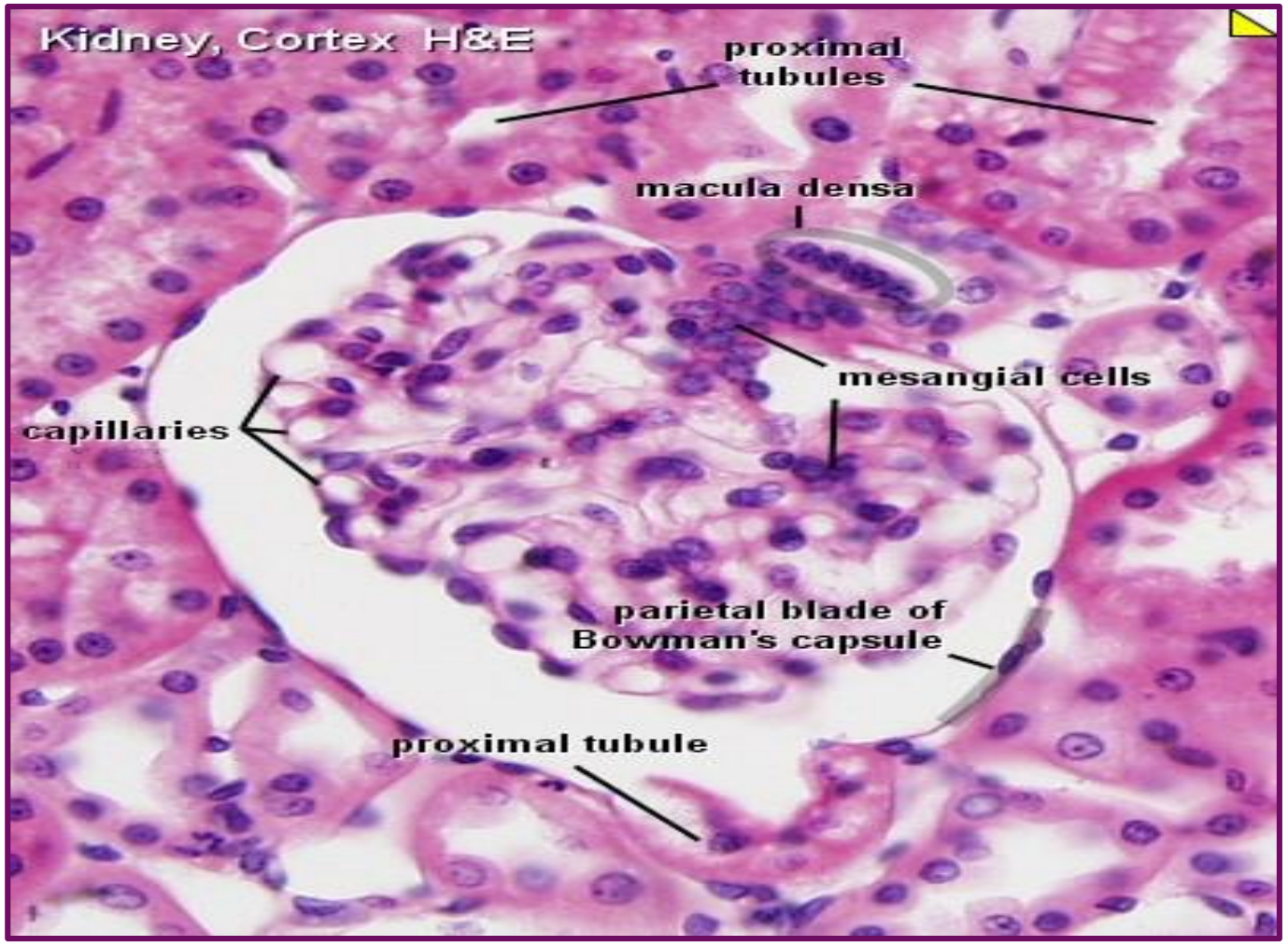


In cross section, this normal adult kidney demonstrates the lighter outer cortex and the darker medulla, with the renal pyramids into which the collecting ducts coalesce and drain into the calyces and central pelvis.

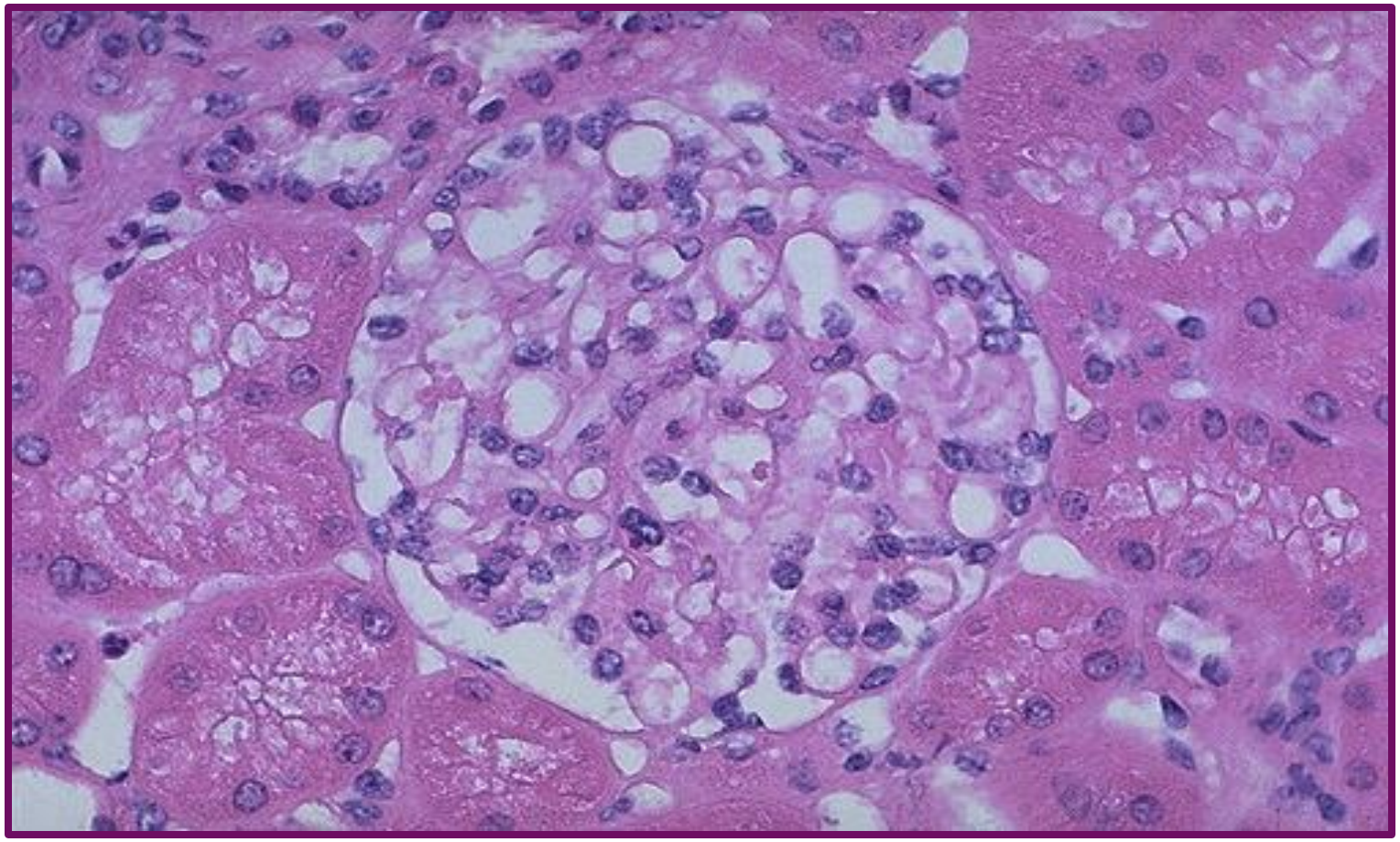
Kidney – Normal Histology



Renal Corpuscle – Normal Histology

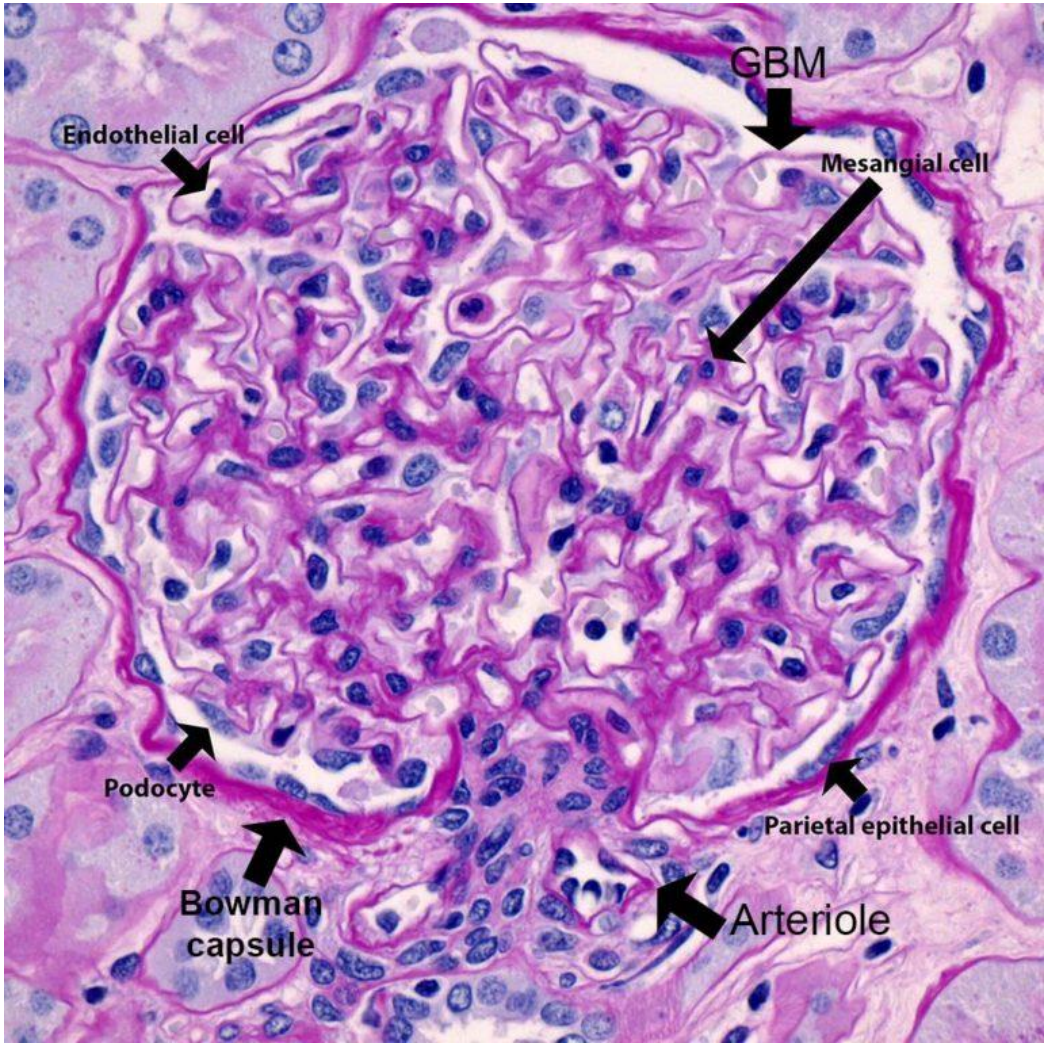


Renal Corpuscle – Normal Histology



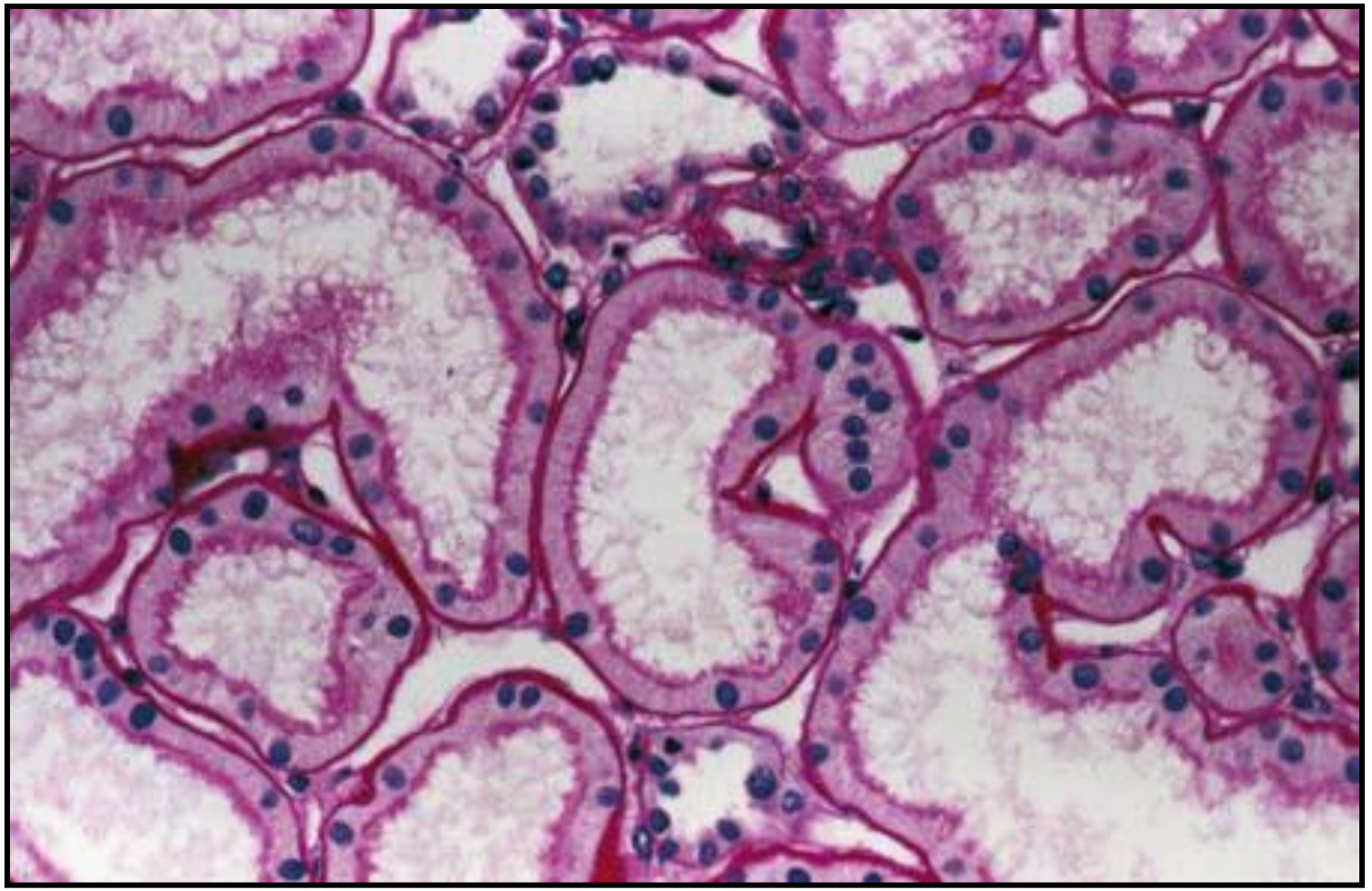
Normal glomerulus by light microscopy. The glomerular capillary loops are thin and delicate. Endothelial and mesangial cells are normal in number. The surrounding tubules are normal

Renal Corpuscle – Normal Histology



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

Normal Cortical Tubules



Normal cortical tubules, interstitium, and peritubular capillaries; most of the tubules are proximal, with well-defined brush borders (PAS stain).

PRACTICAL SESSION : 1

ACUTE KIDNEY INJURY

Acute Kidney Injury

Causes:

Pre-renal

(All those that decrease effective blood flow to the kidney)

- *Low blood volume, low blood pressure, and heart failure.*
- *Renal artery stenosis, and renal vein thrombosis.*
- *Renal ischemia.*

Renal:

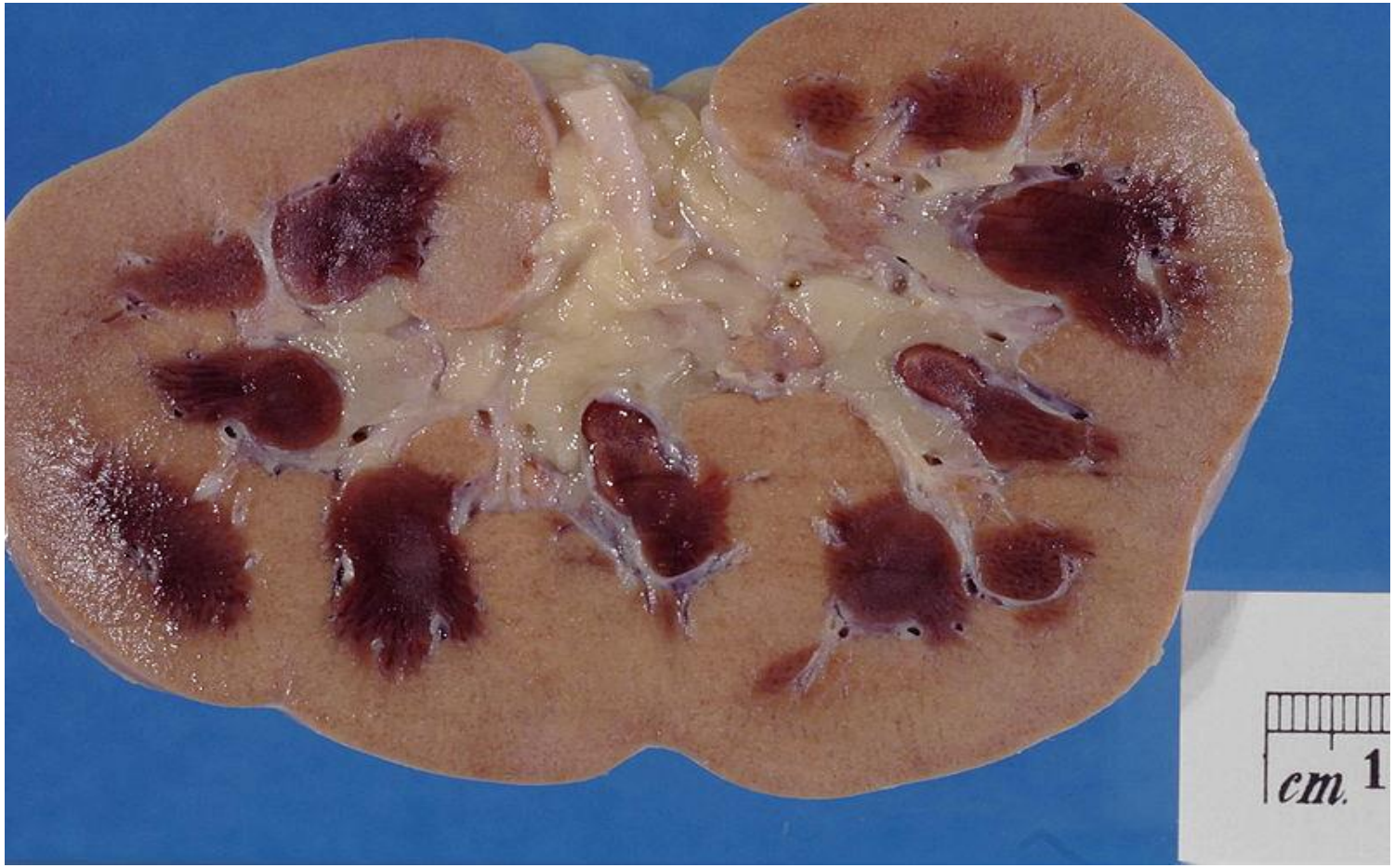
- *Glomerulonephritis (GN).*
- *Acute tubular necrosis (ATN).*
- *Acute interstitial nephritis (AIN).*

Post-renal:

(is a consequence of urinary tract obstruction)

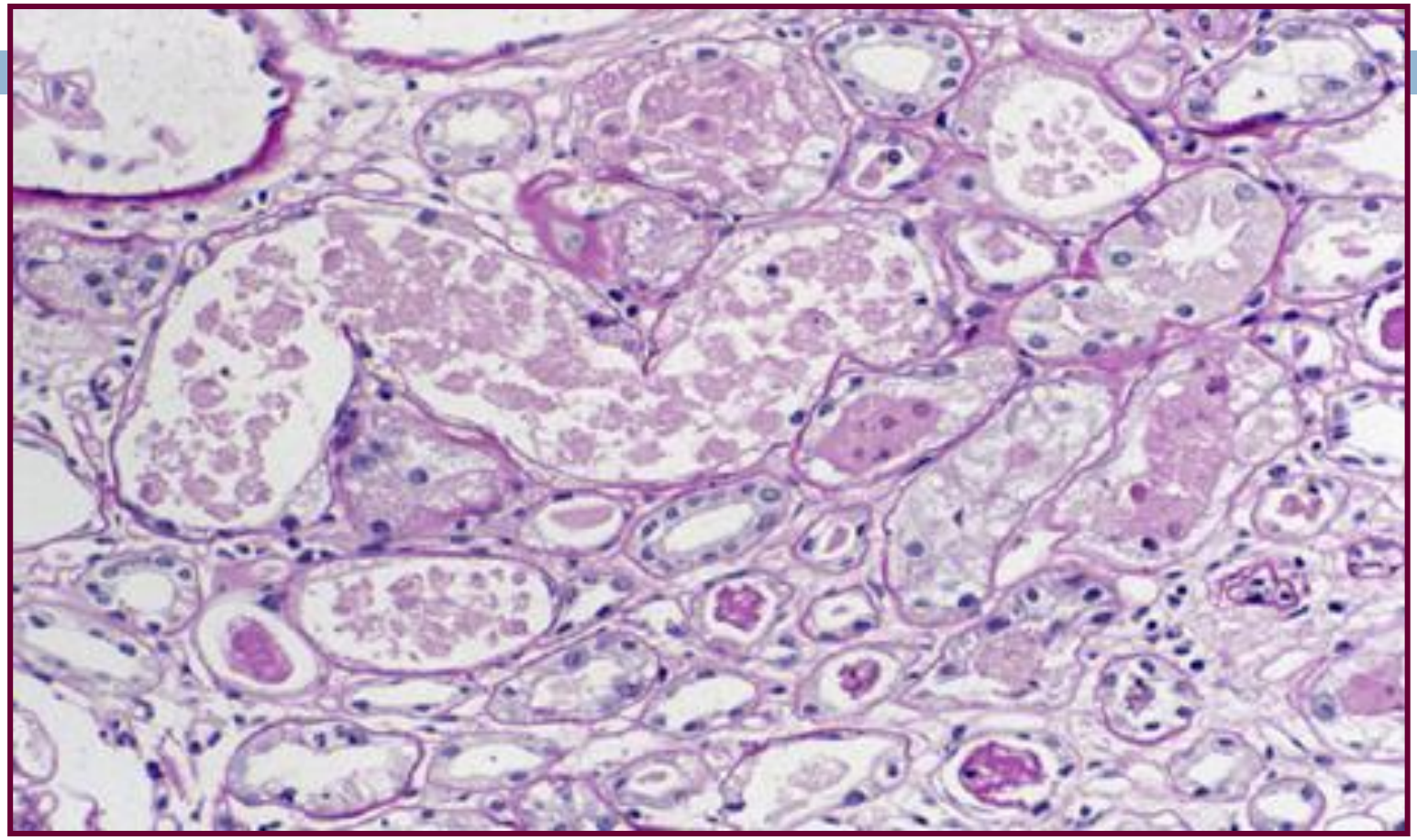
- *Benign prostatic hyperplasia.*
- *Kidney stones.*
- *Obstructed urinary catheter.*
- *Bladder stone .*
- *Bladder, ureteral or renal malignancy.*

Acute Kidney Injury



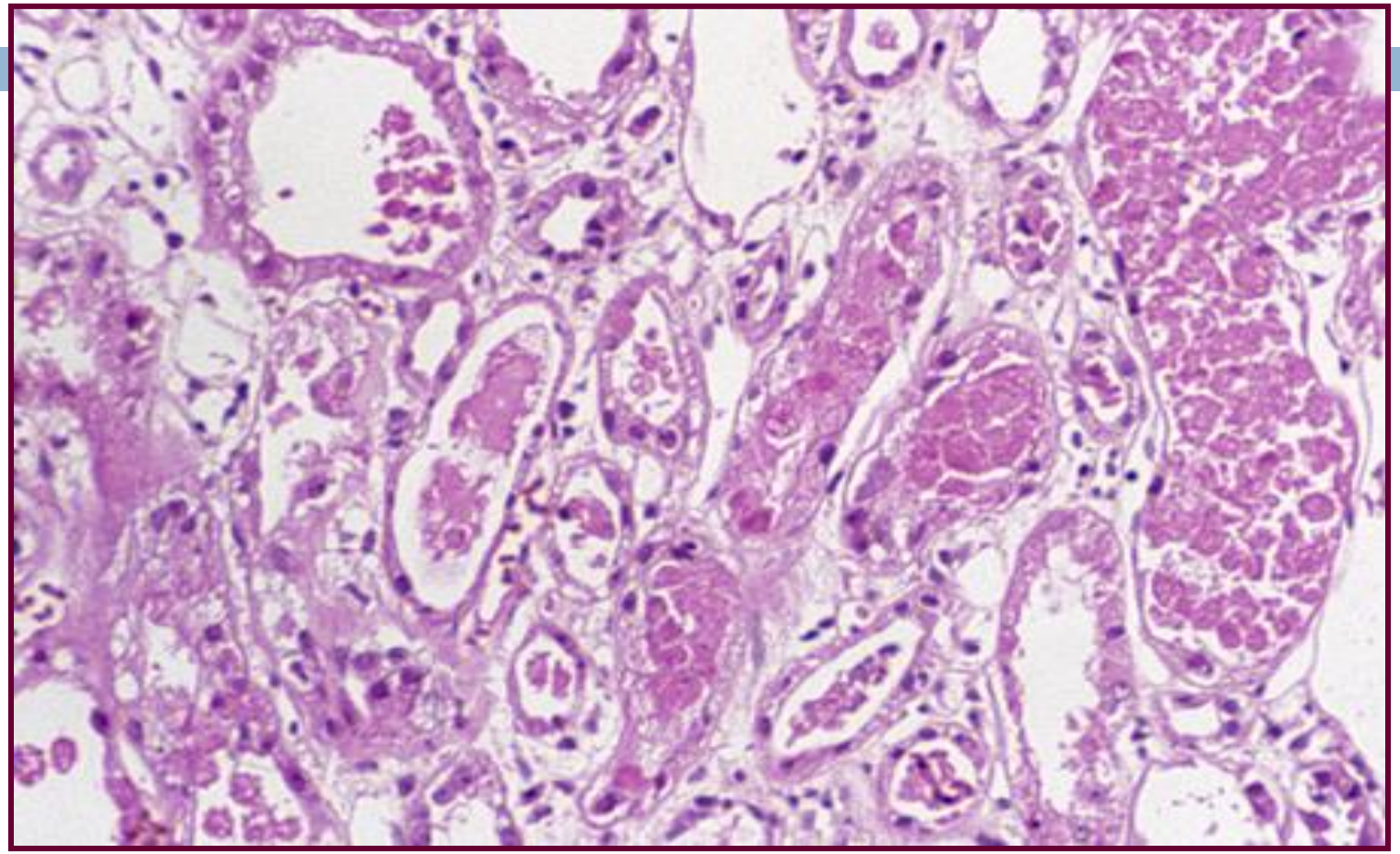
Kidney showing marked pallor of the cortex, contrasting to the darker areas of surviving medullary tissue.

Acute Tubular Necrosis



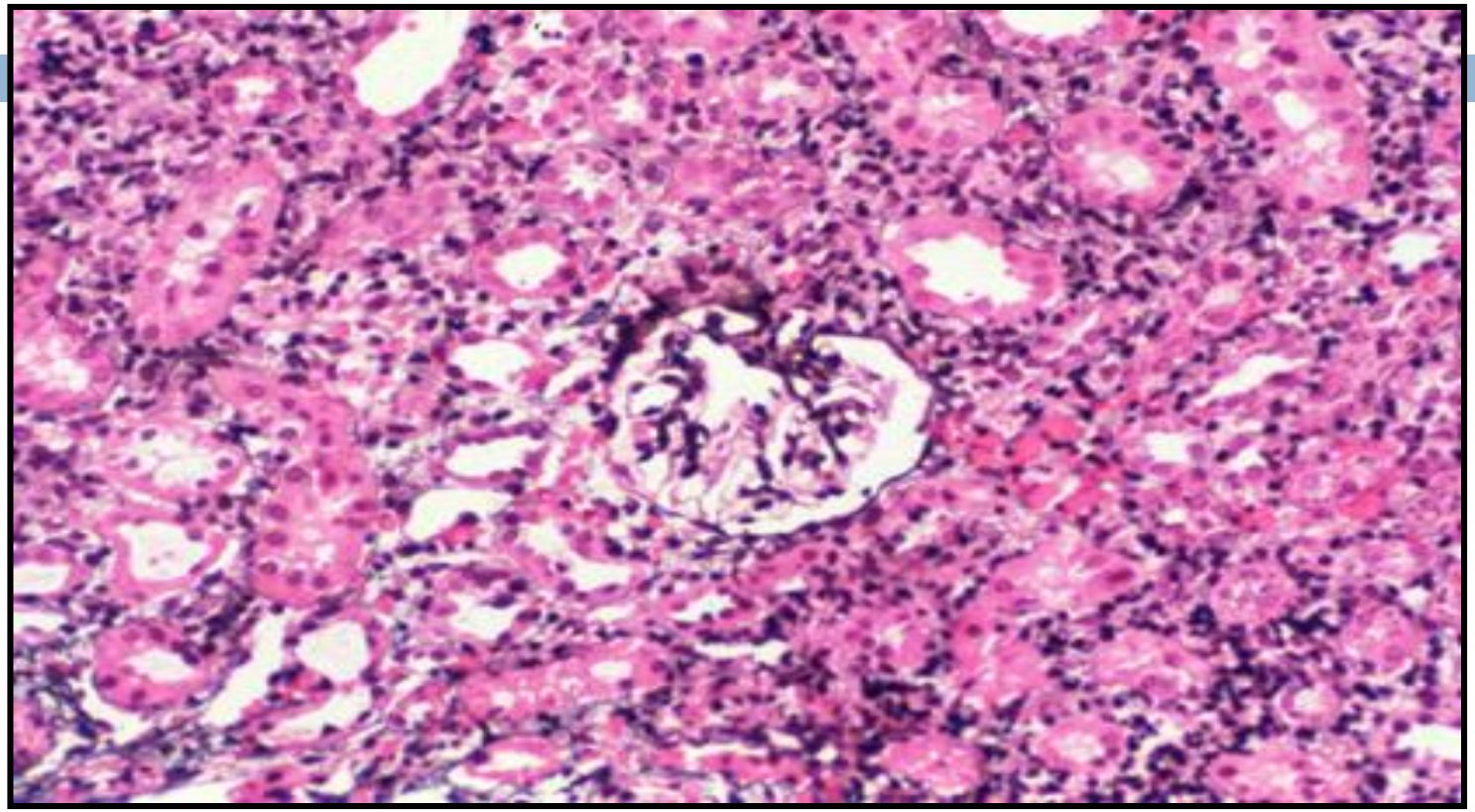
Acute tubular necrosis is manifest by vacuolated cells and sloughed, necrotic cells in tubular lumina, with some tubules lined by flattened epithelium and some showing frank necrosis (PAS stain, x 400).

Acute Tubular Necrosis



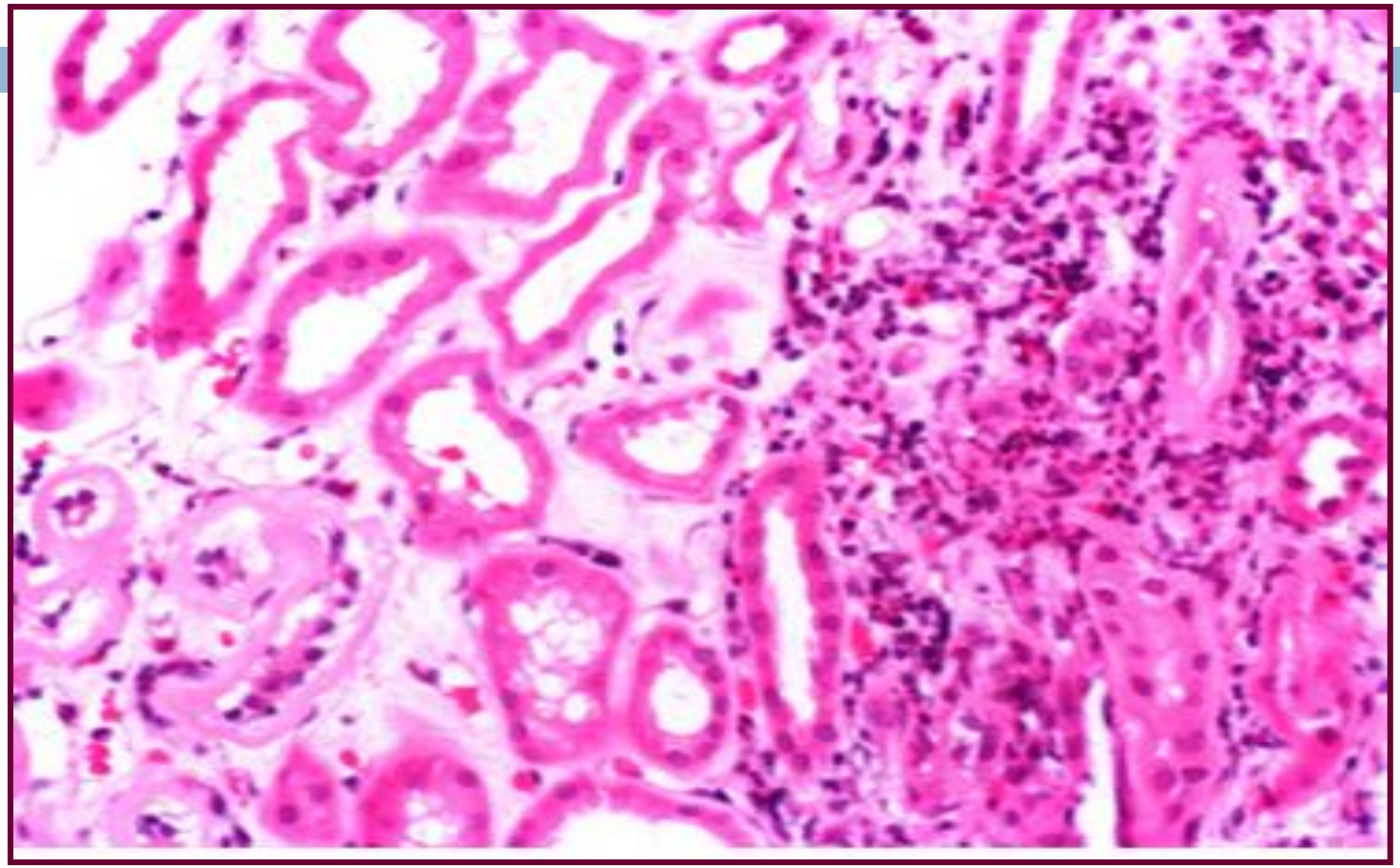
There may also be degeneration and frank necrosis of individual cells or tubular segments in acute tubular necrosis, or flattened, regenerating type epithelium with degenerated cells in the lumen (middle left) (H&E x 200).

Acute Interstitial Nephritis



There is edema associated with an interstitial lymphoplasmocytic infiltrate. There are numerous causes for acute interstitial nephritis, including toxins, viral infections and drug-induced hypersensitivity reactions. The glomeruli are uninvolved, unless there is an associated minimal change disease-type injury caused by non steroidal anti-inflammatory drugs

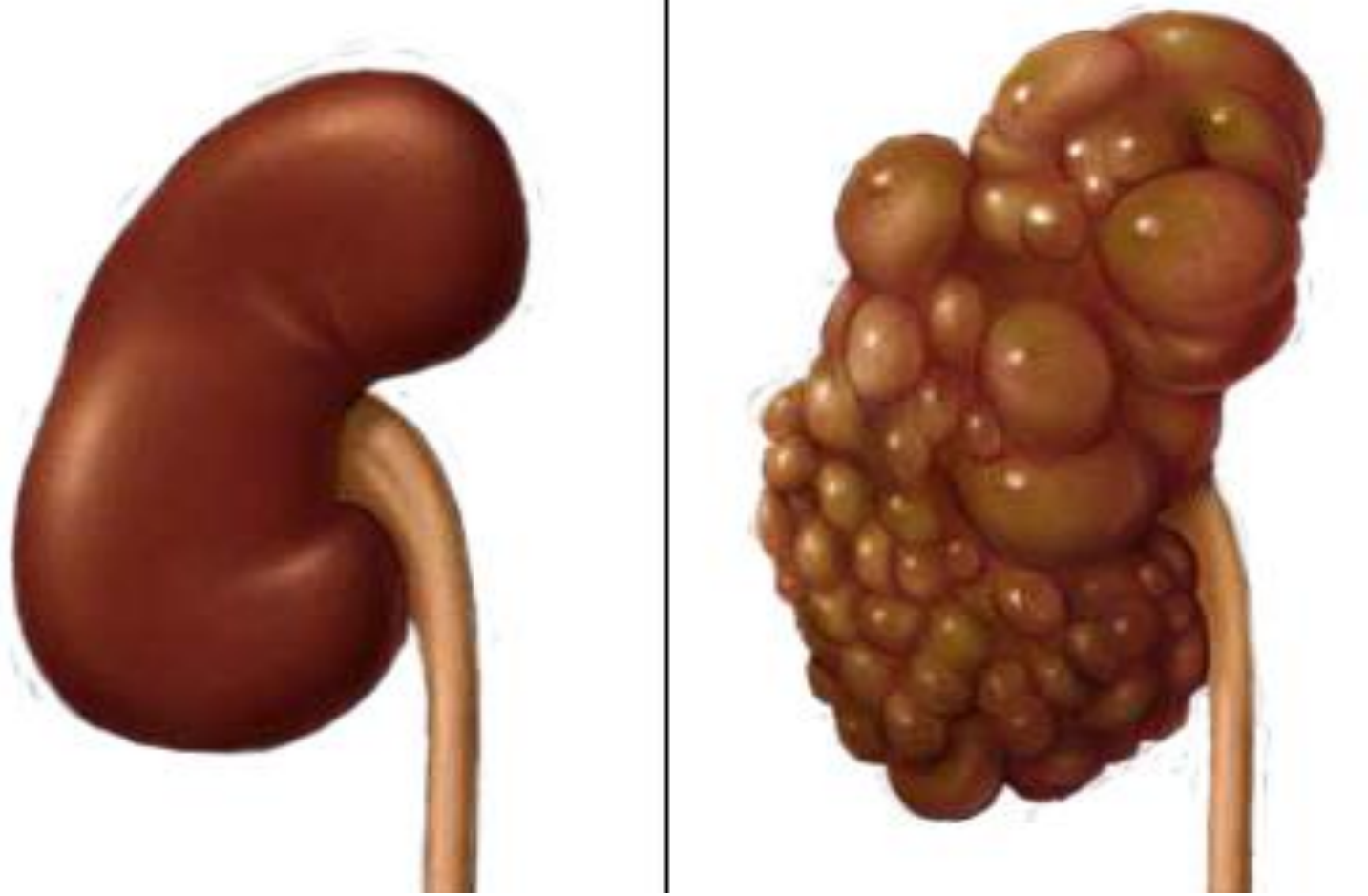
Acute Interstitial Nephritis (Drug-Induced Interstitial Nephritis)



- *Eosinophils in interstitium.*
- *Interstitial oedema.*

POLYCYSTIC KIDNEY

Normal vs Polycystic Kidney



Polycystic kidney

- Autosomal Dominant (Adult) Polycystic Kidney Disease is a disease of autosomal dominant inheritance caused by mutations in the genes encoding polycystin-1 or -2. It accounts for about 10% of cases of chronic renal failure; kidneys may be very large and contain many large cysts.
- *Autosomal recessive (childhood) polycystic kidney disease* is caused by mutations in the gene encoding fibrocystin. It is less common than the adult form and strongly associated with liver abnormalities like fibrosis; the kidneys contain numerous small cysts.

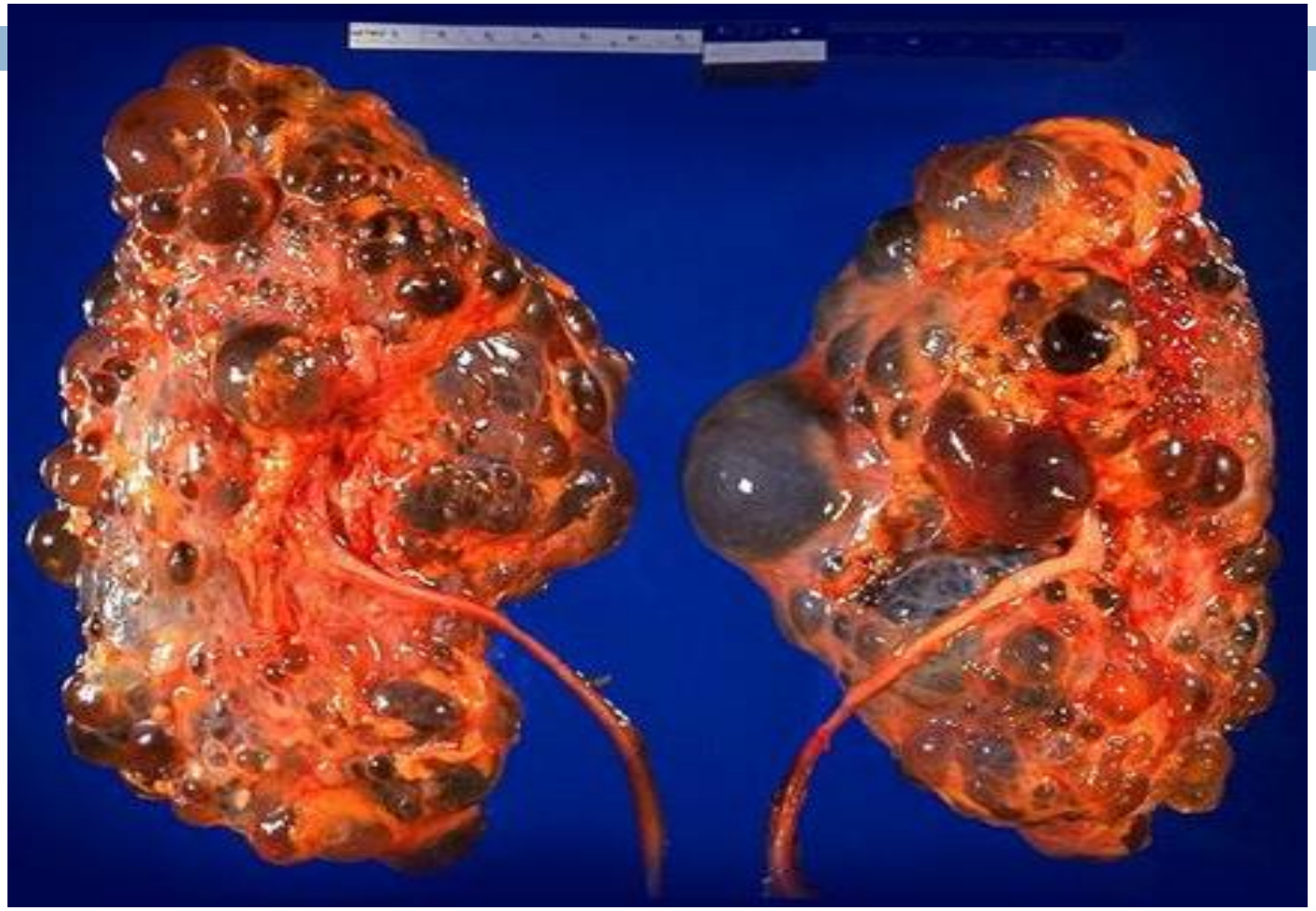
Autosomal Dominant (Adult) Polycystic Kidney Disease

- Polycystic kidney disease in adults usually *produces symptoms by the fourth decade of life,* by which time the kidneys are quite large (the cysts start to develop in adolescence).
- Common clinical features
  - *flank pain* or a heavy, dragging sensation
  - *Intermittent gross hematuria*
  - palpable abdominal mass.
- Complications of adult polycystic kidney
  - acute distention of a cyst, either by intracystic hemorrhage or by obstruction, may cause excruciating pain.
  - *urinary infection*.
  - Hypertension of variable severity develops in about 75% of persons with this disorder.
  - Saccular aneurysms of the circle of Willis are present in 10% to 30% of patients and they can rupture → subarachnoid hemorrhage.
  - Renal failure/uremia (end-stage kidney disease) usually occurs by age 50.
- Patients in whom the disease progresses to renal failure are treated by renal transplantation.
- Death usually results from uremia or hypertensive complications.

Autosomal Dominant (Adult) Polycystic Kidney Disease – *Gross Anatomy*

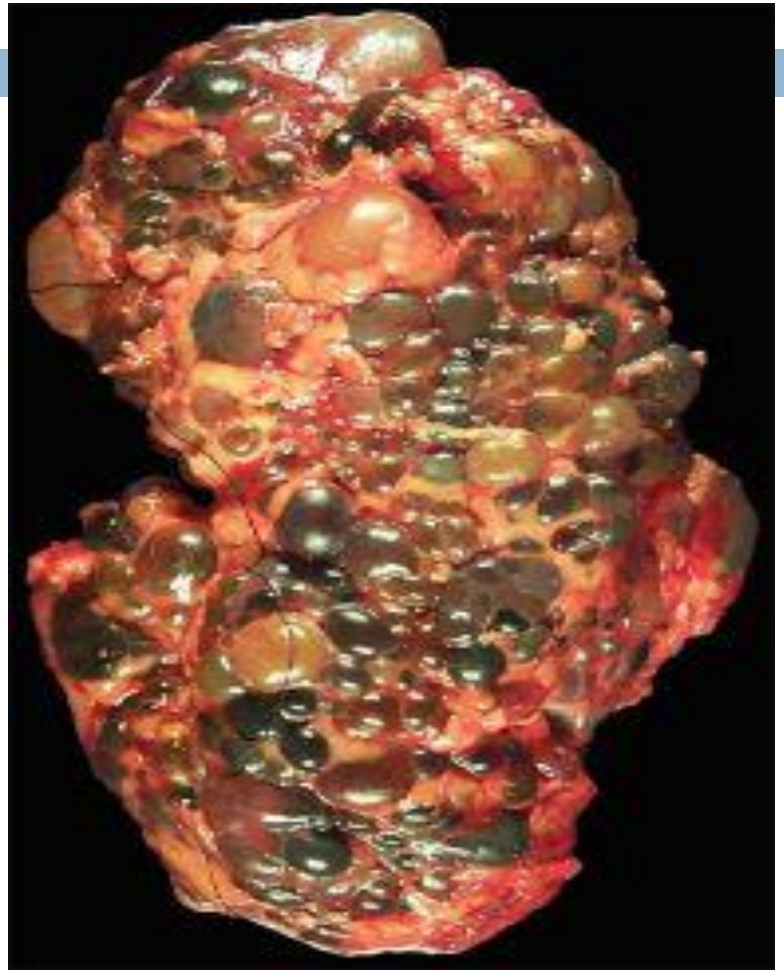
Markedly enlarged kidney and replacement of the renal parenchyma by numerous cysts of variable sizes

Autosomal Dominant (Adult) Polycystic Kidney Disease – *Gross Anatomy*

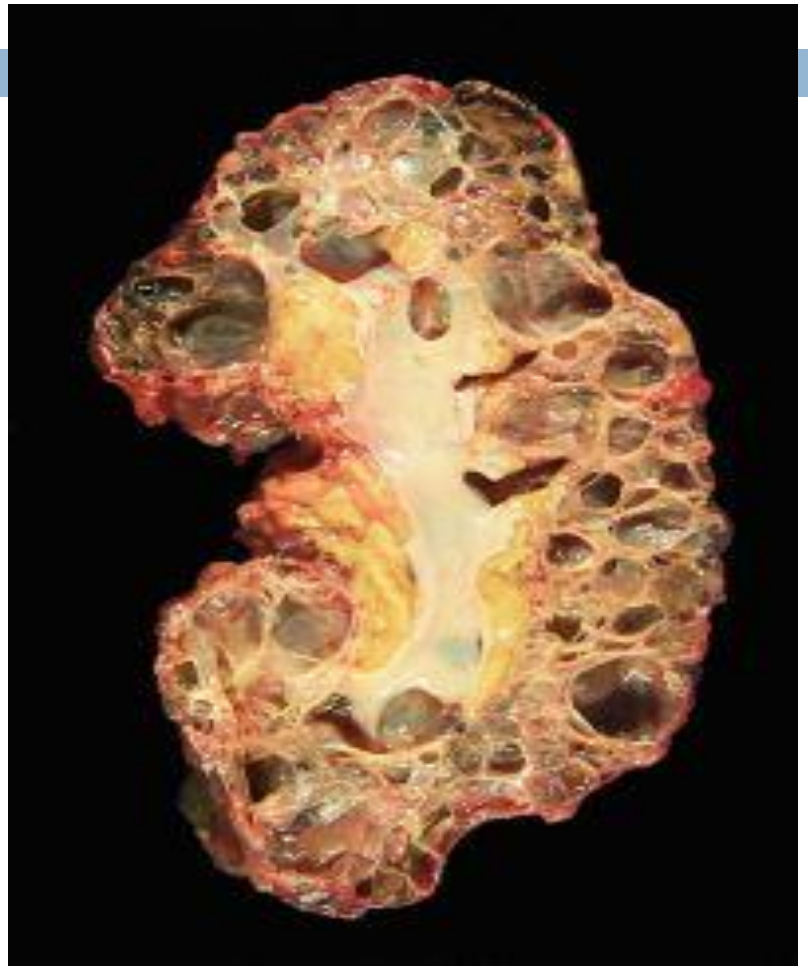


Bilateral autosomal dominant polycystic kidney disease

Gross Autosomal Dominant (Adult) Polycystic Kidney Disease *and its Cut Section*

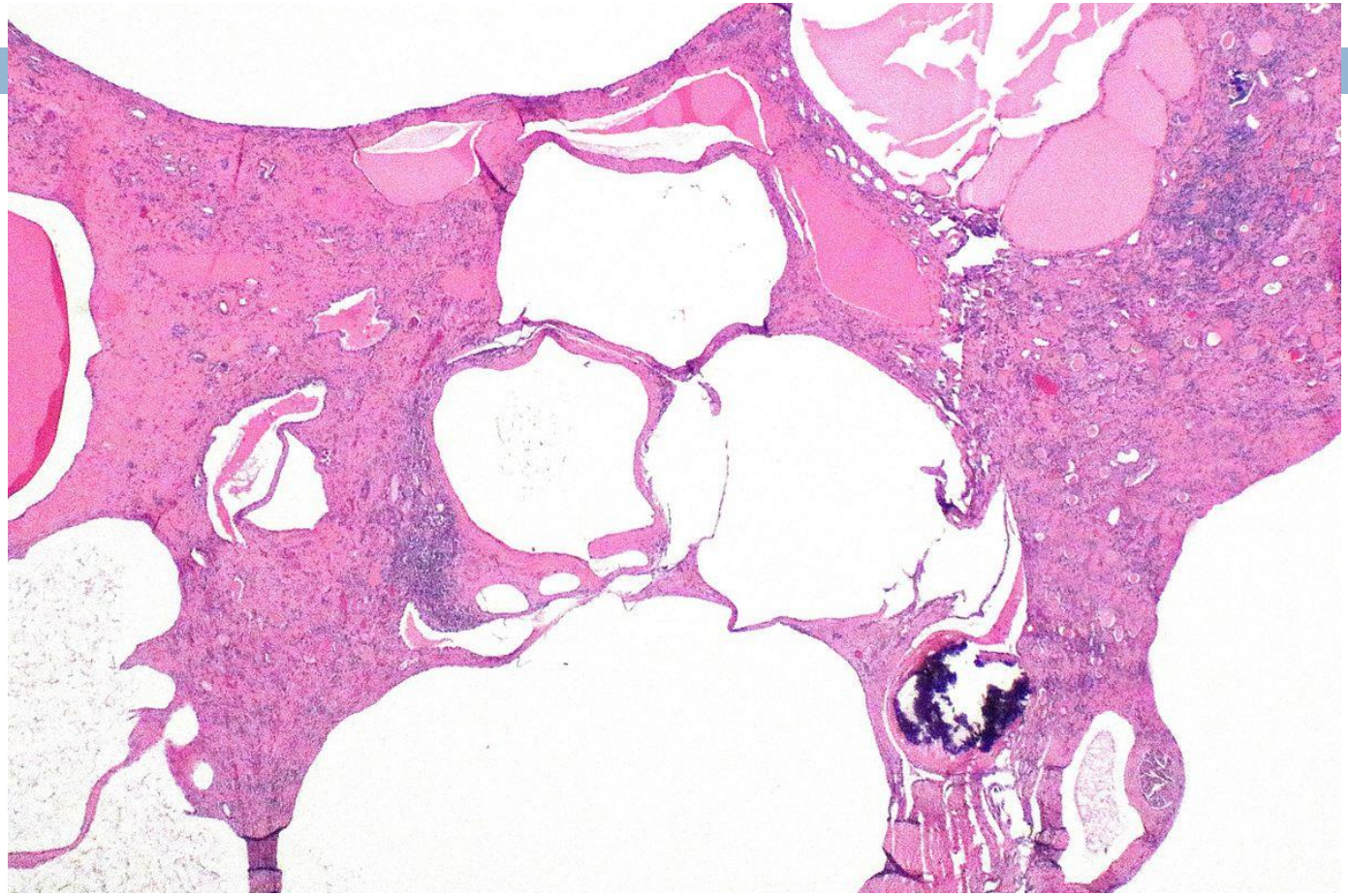


Massively enlarged kidney disrupted by numerous cysts



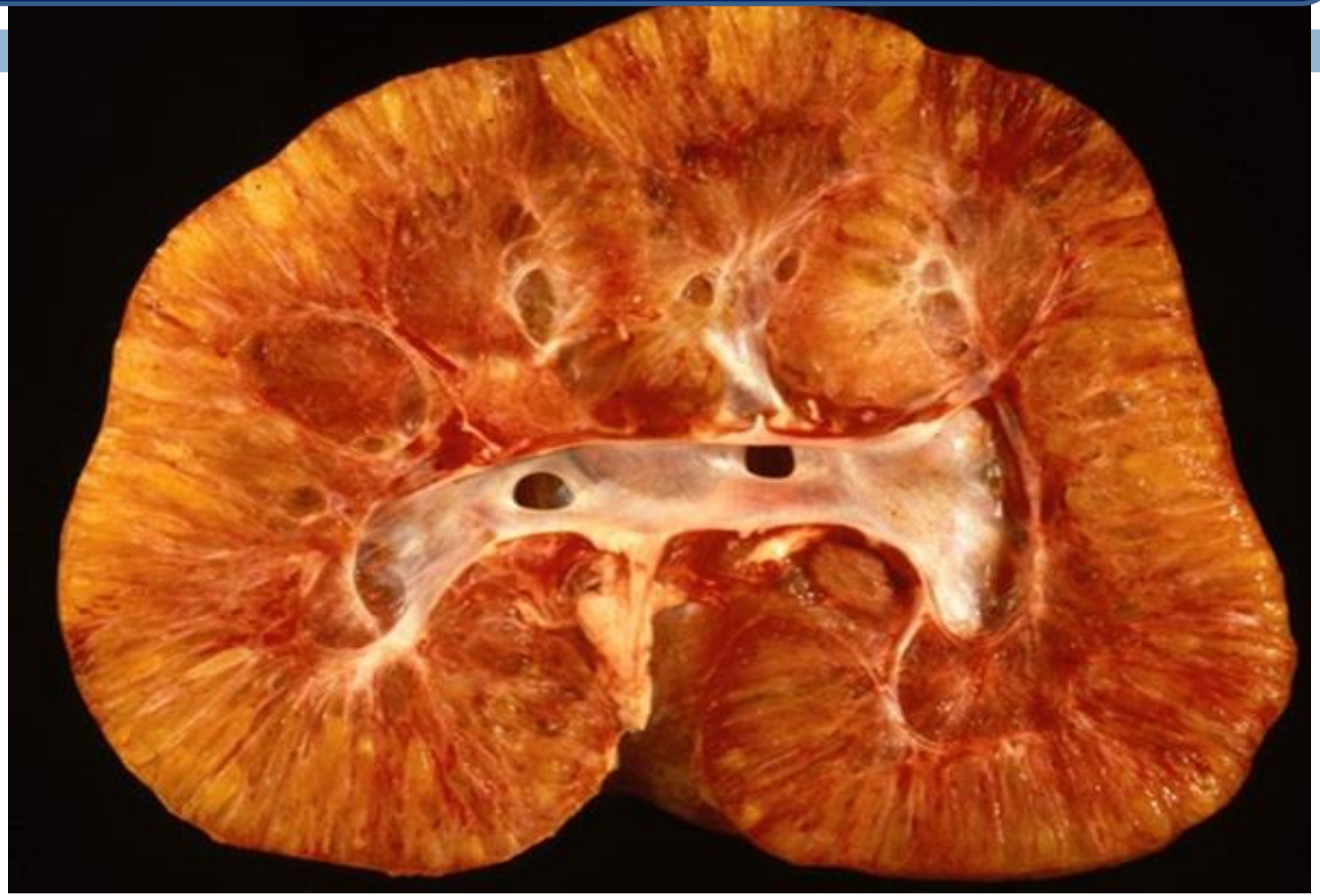
Cut surface of the kidney, showing extensive cortical destruction by cysts

Autosomal dominant polycystic kidney – histopathology



Sections show cortical cysts lined by simple flattened epithelium, with interspersed atrophic tubules, interstitial fibrosis and calcifications.

*Autosomal recessive (childhood) polycystic kidney disease – **Gross***

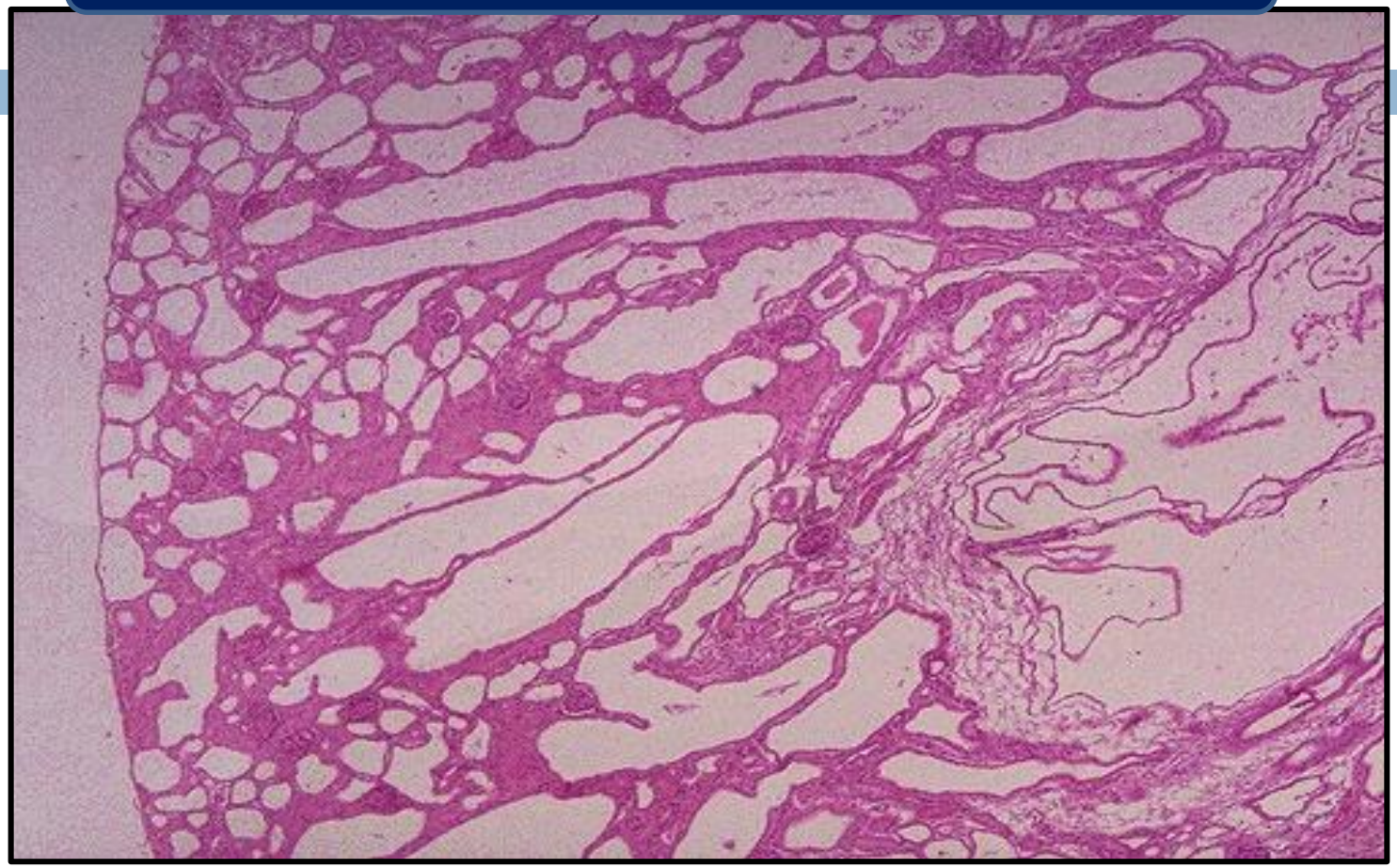


Coronal section of an infantile polycystic kidney

*Autosomal recessive (childhood) polycystic kidney disease – **Gross***

- Markedly enlarged kidneys with smooth surface
- Small cysts in cortex and medulla
- Dilated channels are perpendicular to cortical surface
- Cysts are present in medulla (collecting ducts)

Polycystic kidney – Histopathology



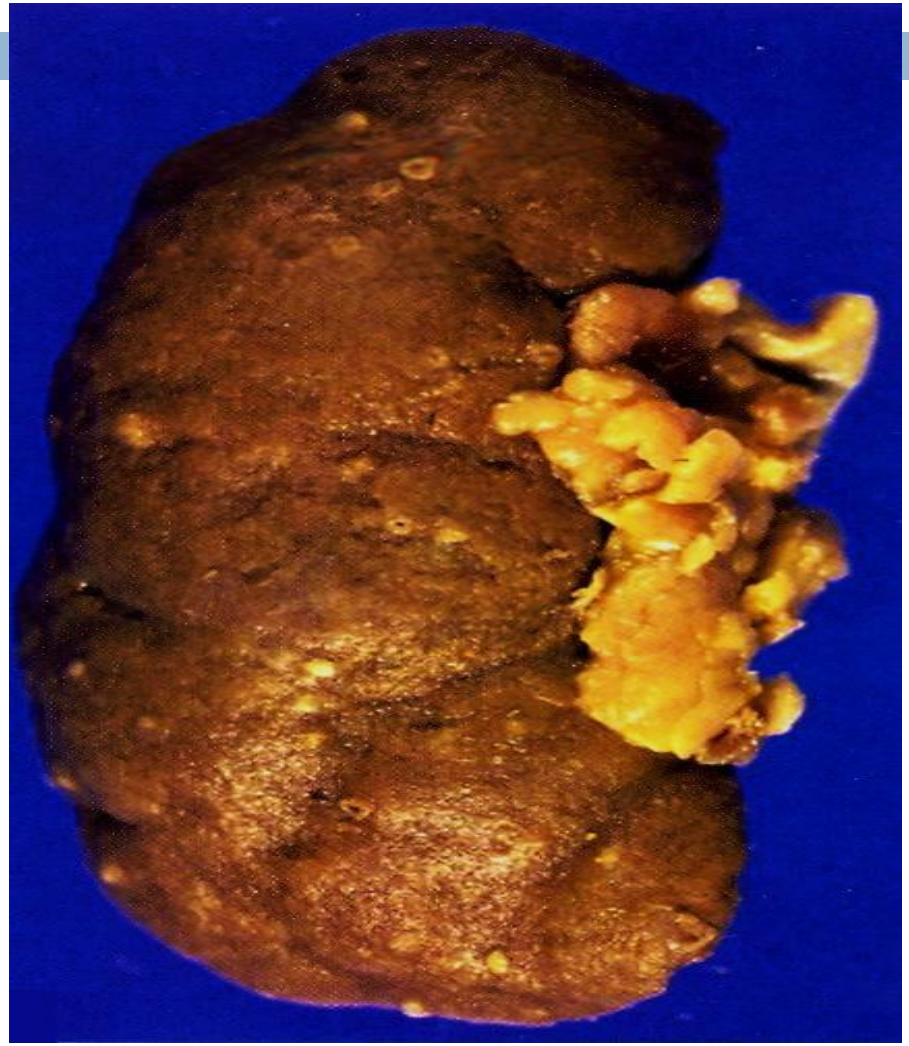
The childhood form of polycystic kidney disease is a rare autosomal recessive disorder that is genetically distinct from adult polycystic kidney disease. In autosomal recessive polycystic kidney disease (ARPCKD), **numerous small cysts** in the cortex and medulla give the kidney a sponge like appearance. Dilated, elongated channels at right angles to the cortical surface completely replace the medulla and cortex. The cysts are lined by cuboidal cells. The disease is bilateral. In almost all cases, findings include multiple epithelium-lined **cysts in the liver** and proliferation of portal bile ducts. ***Note that the cysts fill most of the parenchyma, and it is hard to find glomeruli.***

PRACTICAL SESSION : 2

INFECTION OF THE URINARY TRACT

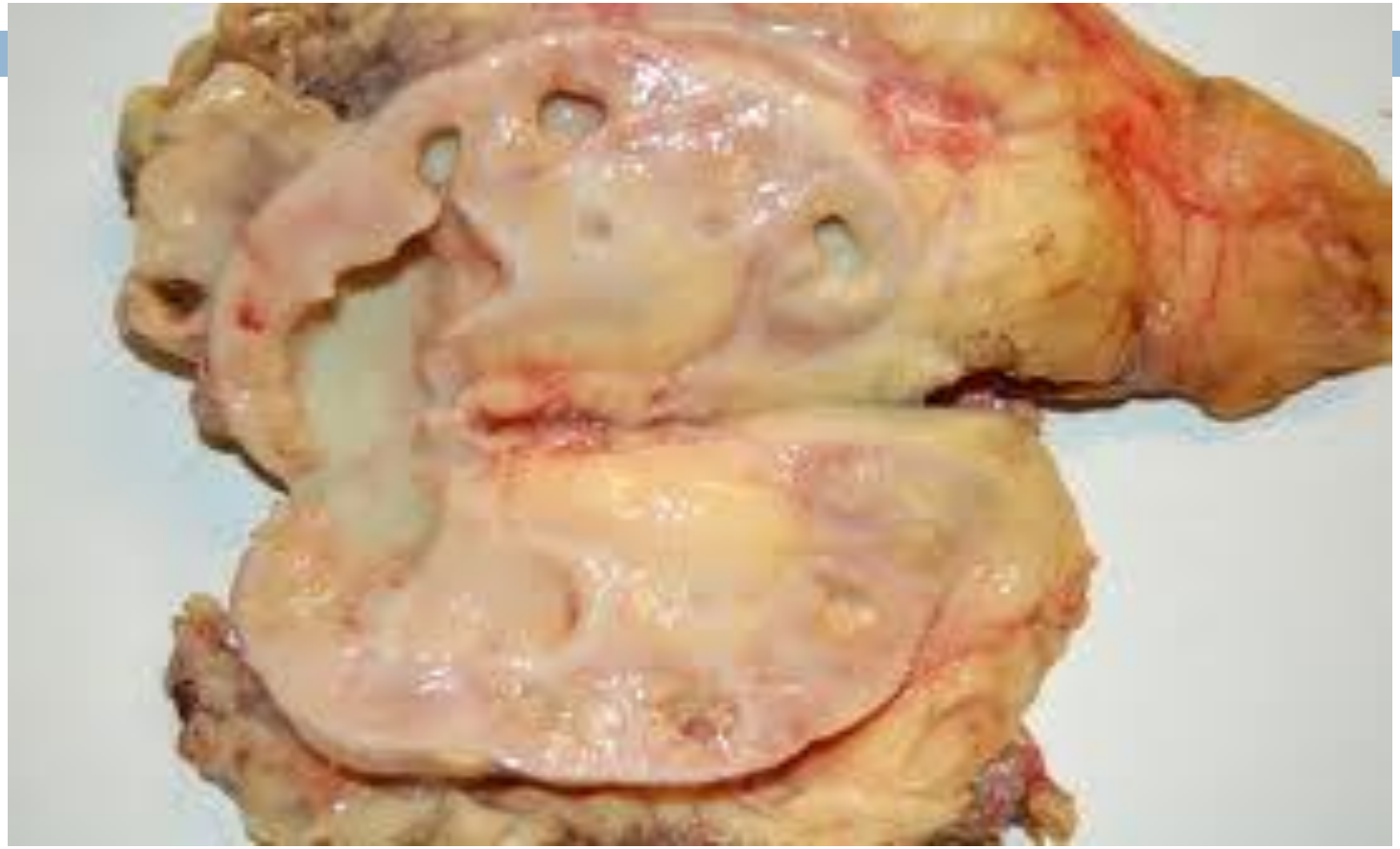
ACUTE & CHRONIC PYELONEPHRITIS

Acute Pyelonephritis with small cortical abscesses



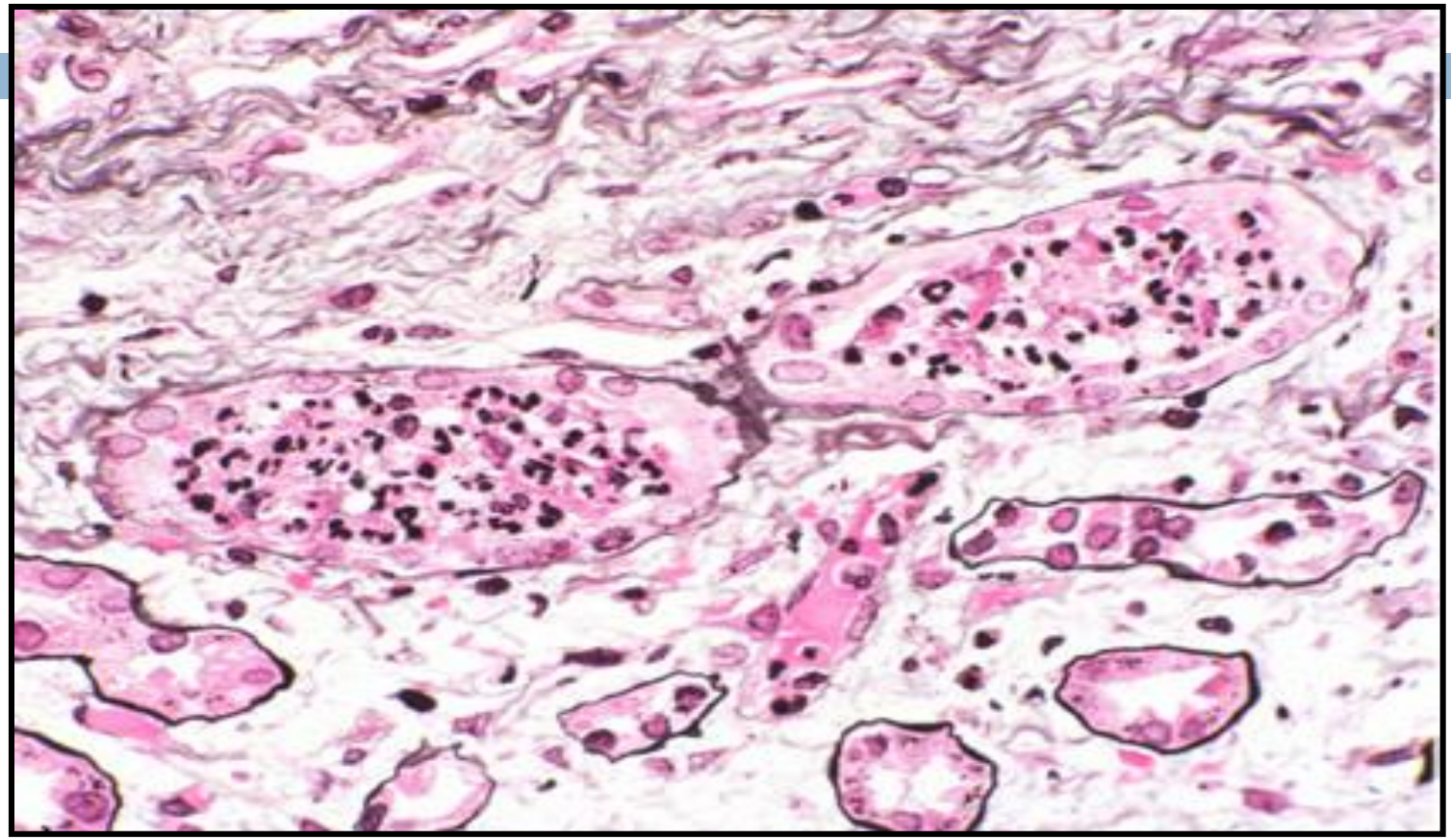
Acute Pyelonephritis with small cortical abscesses

Classic picture of Acute Pyelonephritis



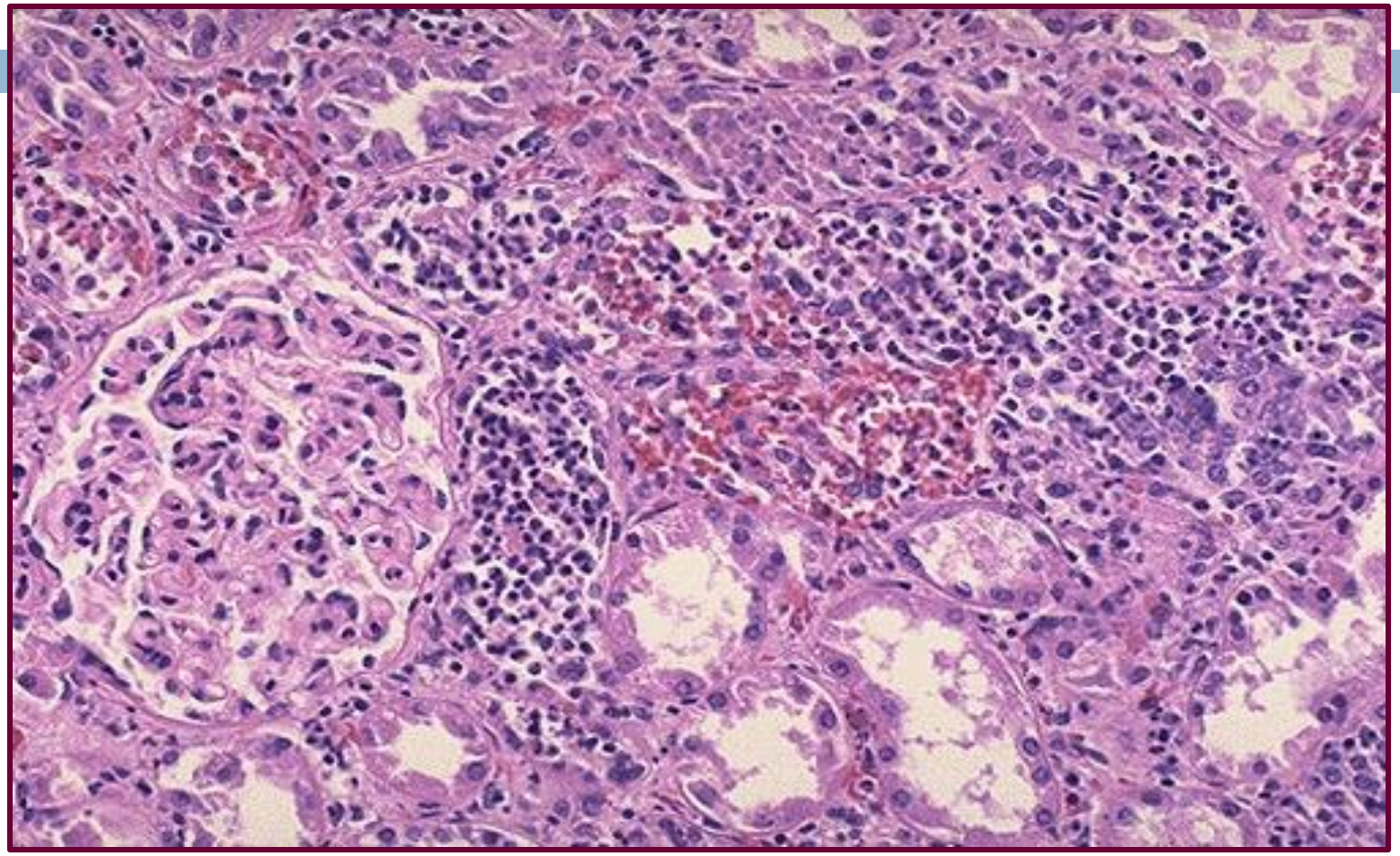
This kidney is bisected to reveal a dilated pelvis and calyxes filled with a yellow-green purulent pus which is consistent with a pyelonephritis. The cortex and medulla are pale and the corticomedullary junction is ill-defined.
No tumors are seen.

Acute Pyelonephritis - Histopathology



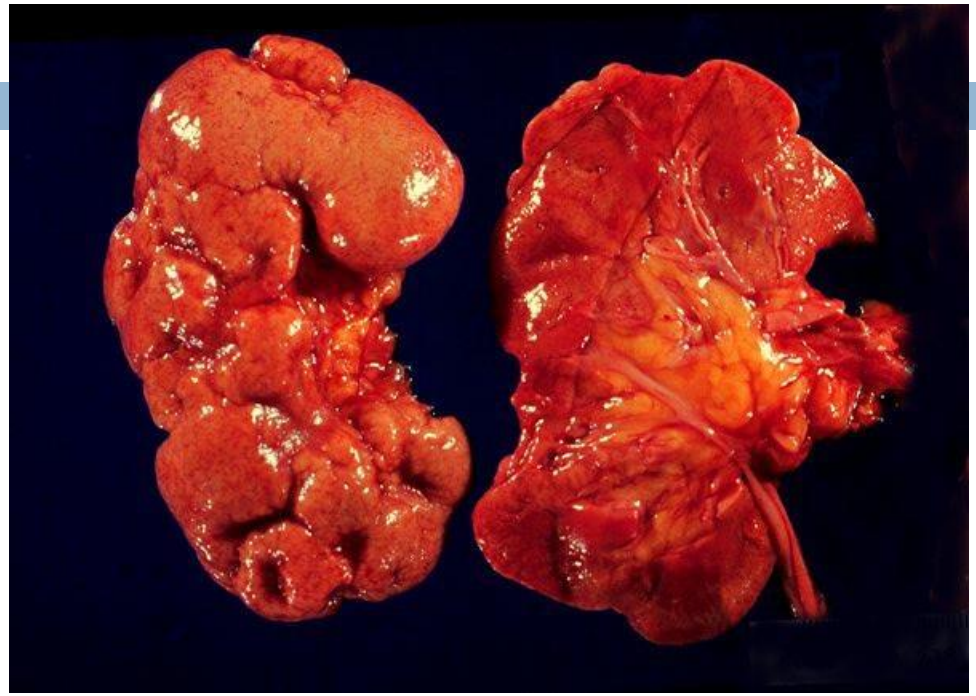
Acute pyelonephritis is diagnosed by intratubular aggregations of polymorphonuclear neutrophils (PMNs). There may be surrounding interstitial inflammation with a mixture of PMNs, lymphocytes, and plasma cells, but the predominant inflammation is within the tubule

Acute Pyelonephritis - Histopathology



Numerous PMN's are seen filling renal tubules across the center and right of this picture. These leukocytes may form into a cast within the tubule. Casts appearing in the urine originate in the distal renal tubules and collecting ducts

Chronic Pyelonephritis - Gross Pathology

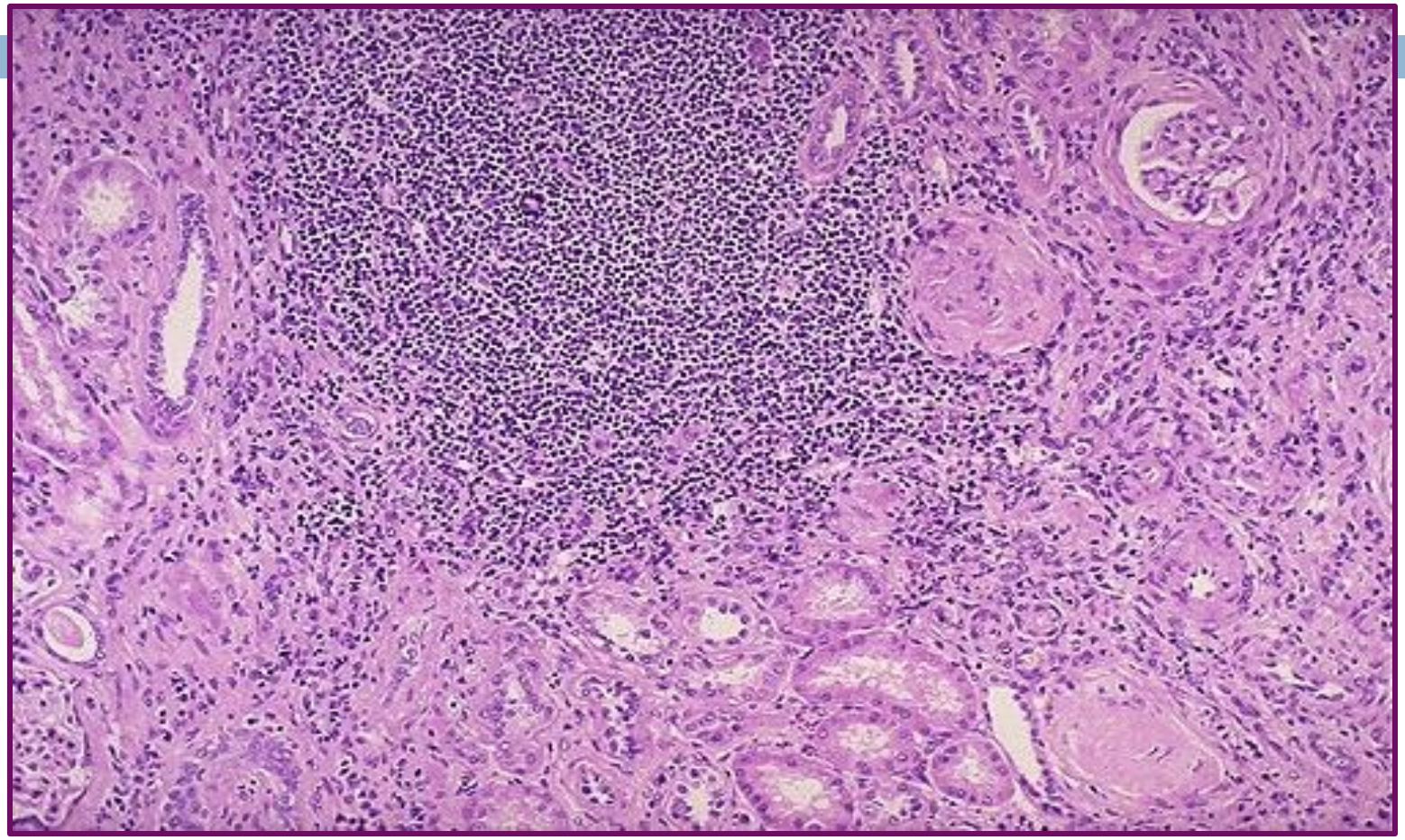


The picture shows slightly atrophic and deformed kidneys with cortical coarse scars .

The most common causes are:

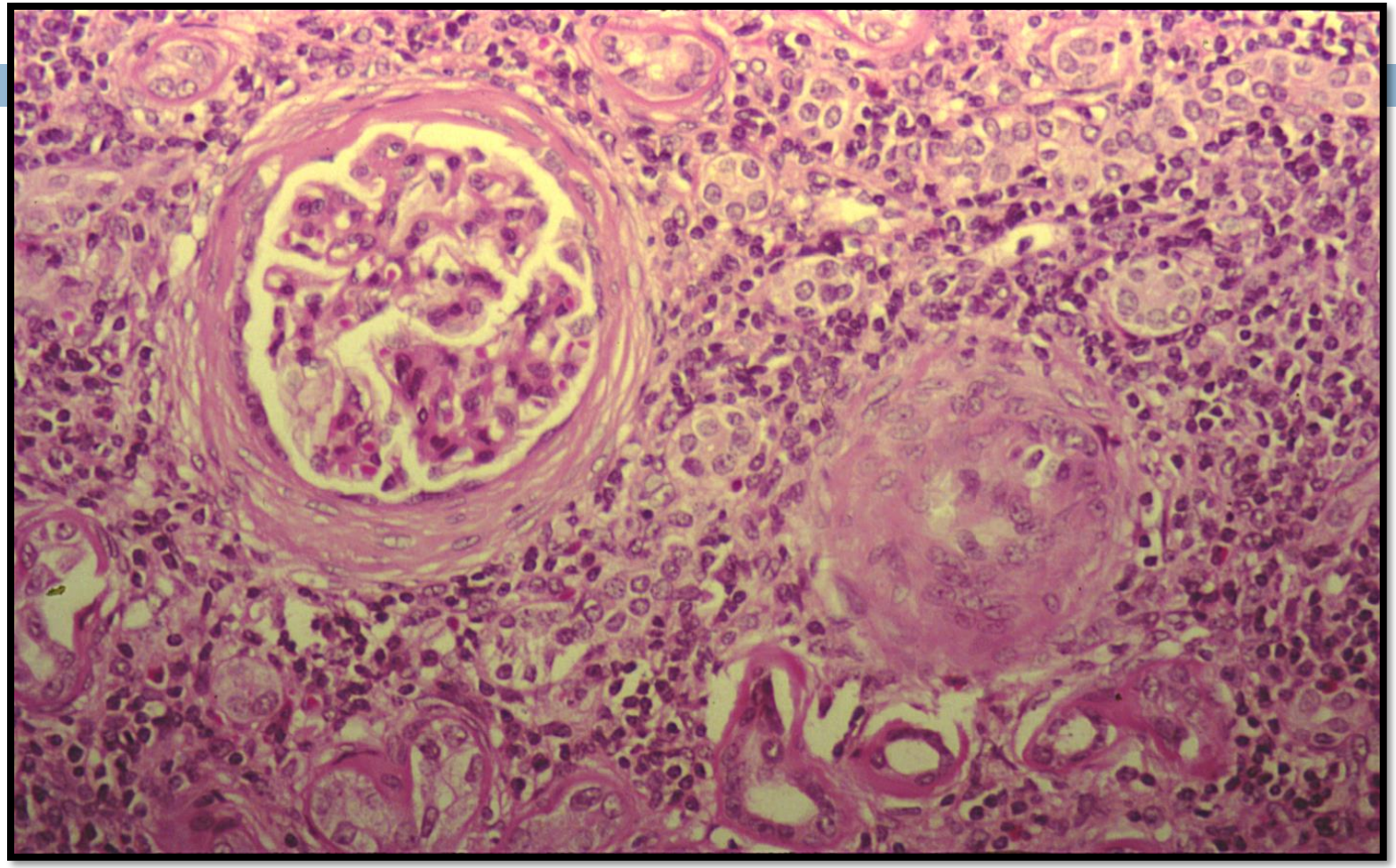
- ***Obstruction by renal stones and others.***
- ***Reflux uropathy – urinary reflux.***
- ***Drugs like NSAID's, methicillin etc.***
- ***Recurrent urinary tract infections.***

Chronic Pyelonephritis - Histopathology



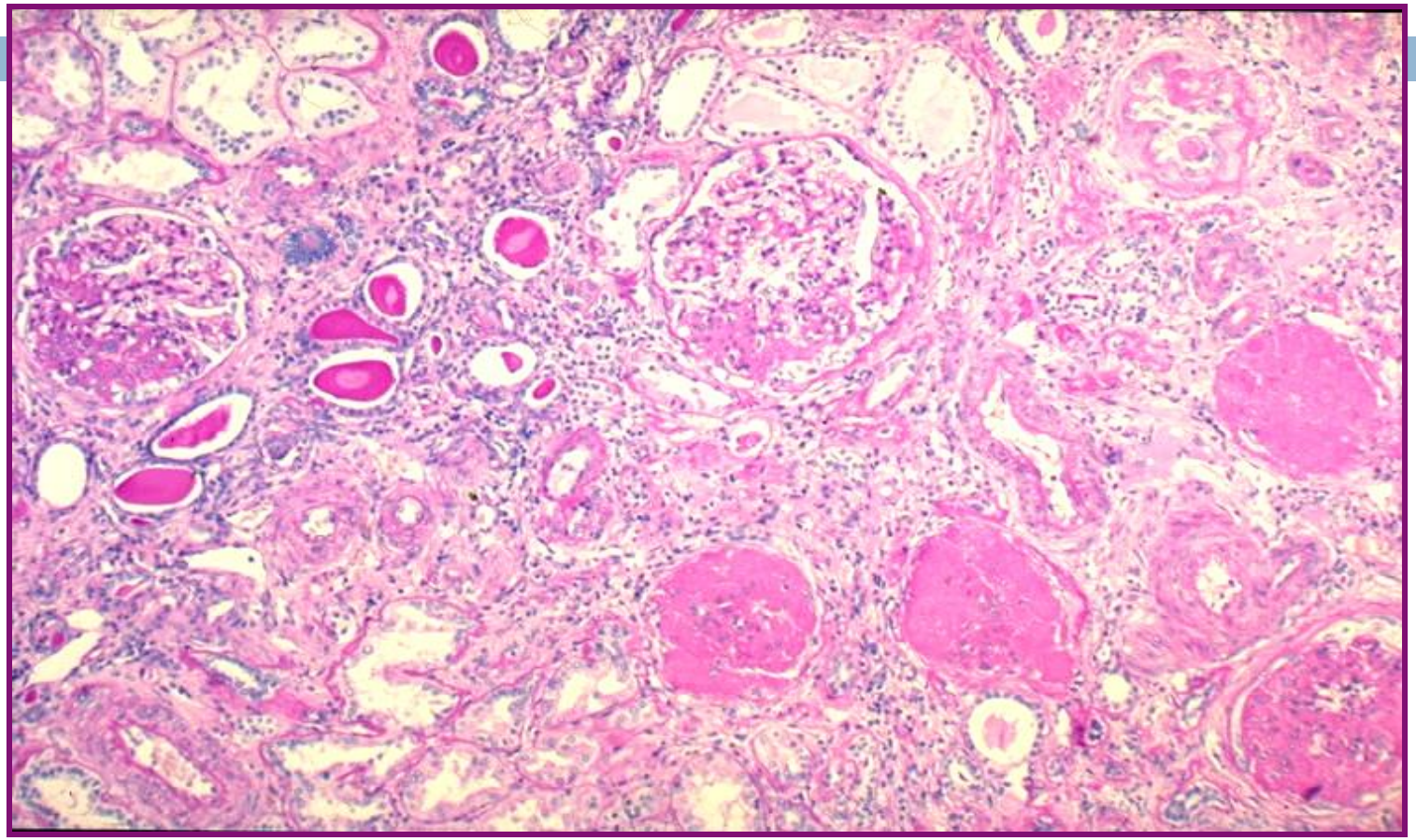
This is chronic pyelonephritis where a large collection of chronic inflammatory cells . The severity of disease depends upon the amount of remaining functional renal parenchyma **(Renal failure – insufficiency or end – stage renal disease)**.

Chronic Pyelonephritis - Histopathology



- Periglomerular fibrosis.
- Glomerulosclerosis.
- Marked chronic interstitial inflammation.
- Hyalinization and atrophy of renal tubules.

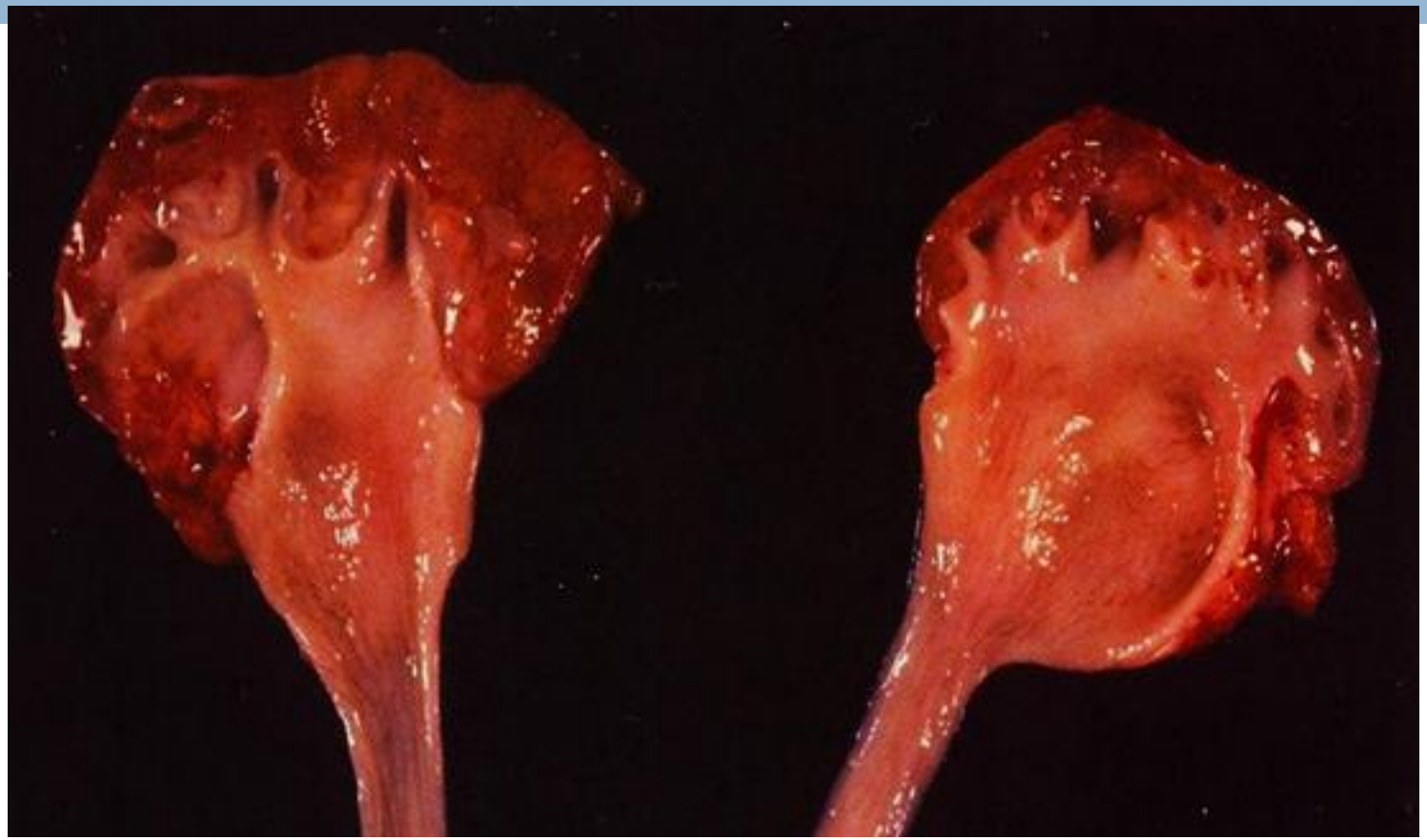
Chronic Pyelonephritis - Histopathology



- ***Glomeruli*** *show varying degrees of sclerosis & periglomerular fibrosis.*
- ***Tubules*** *show varying degrees of atrophy, Some tubules are dilated and filled with Eosinophilic hyaline casts resembling colloid (thyroidization).*
- ***Interstitial tissue*** *shows chronic inflammatory cells infiltrate and fibrosis.*

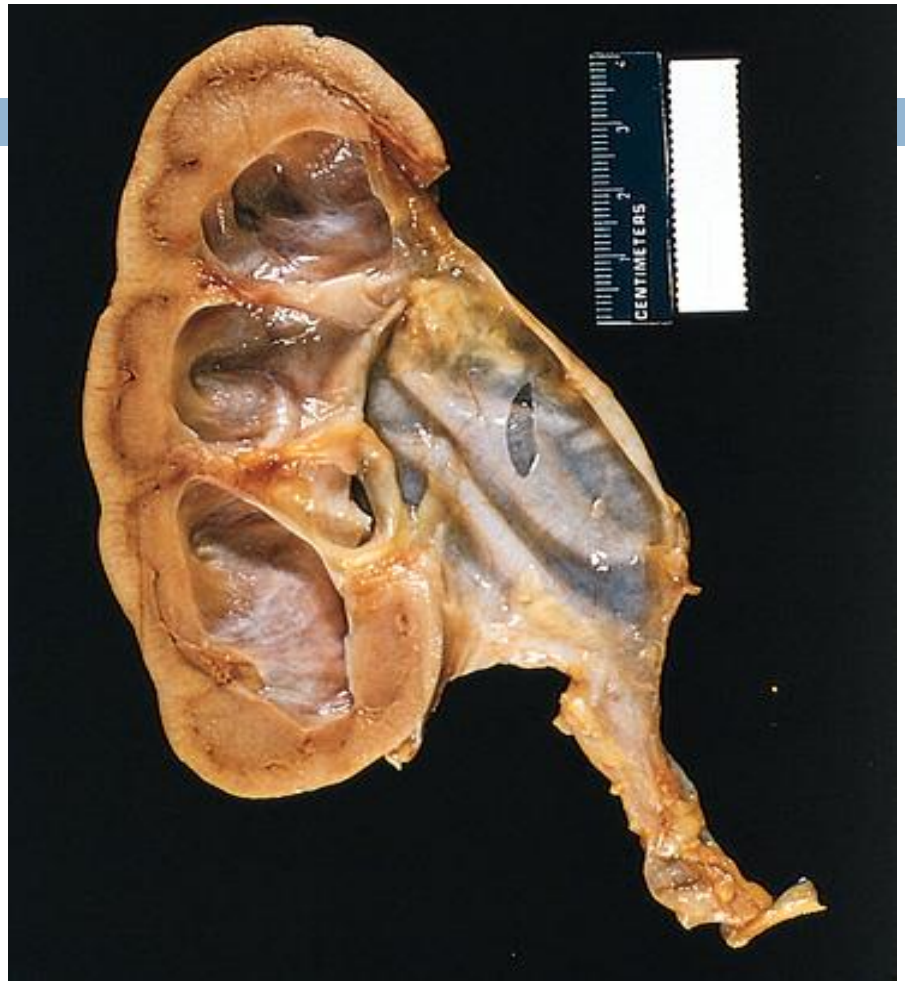
HYDRONEPHROSIS

Hydronephrosis



Bisected kidney shows markedly dilated renal pelvis and calyces with atrophic and thin renal cortex /parenchyma

Hydronephrosis

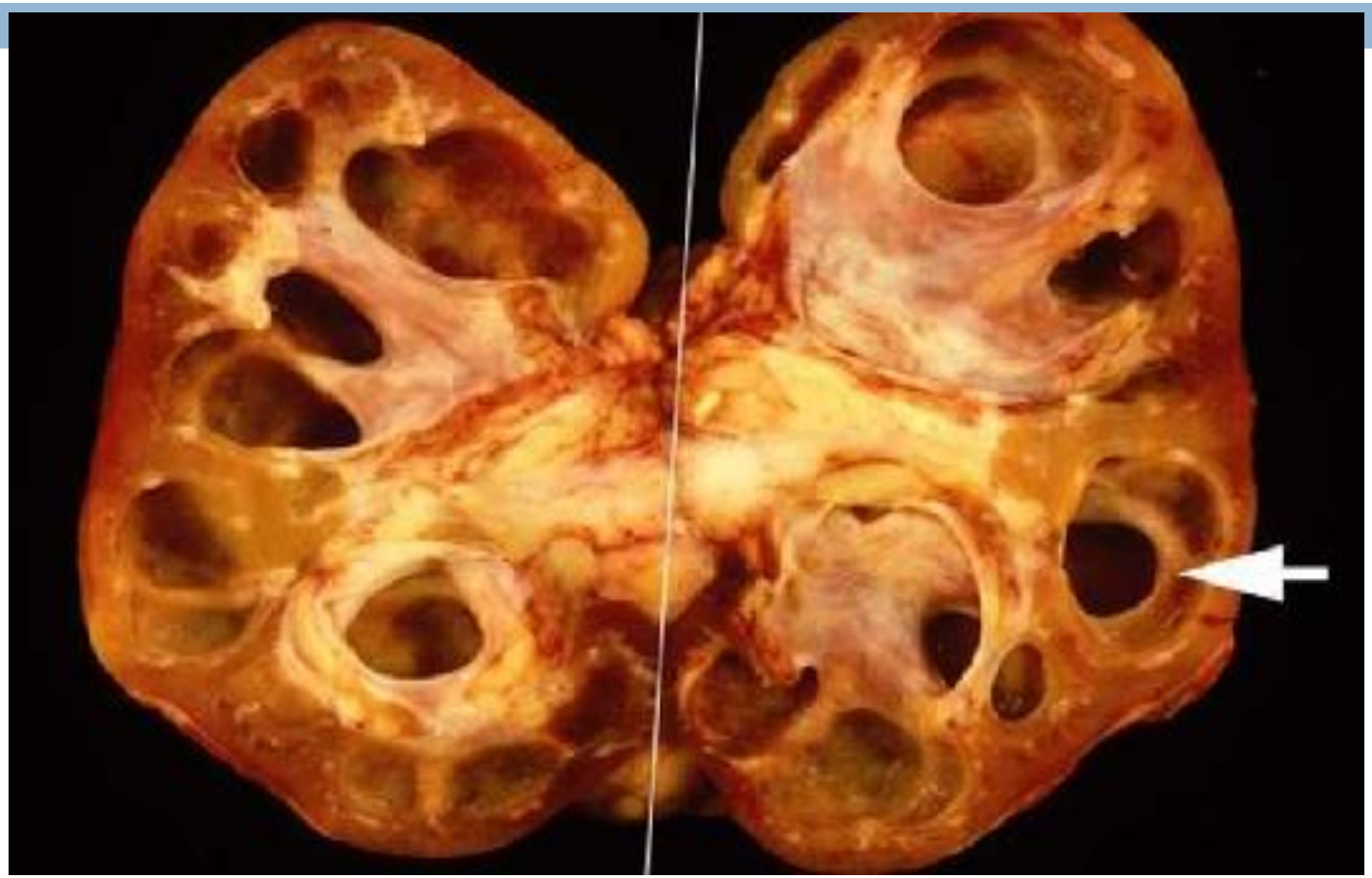


The picture shows markedly dilated renal pelvis and calyces with atrophic and thin renal cortex /parenchyma

The most common causes are:

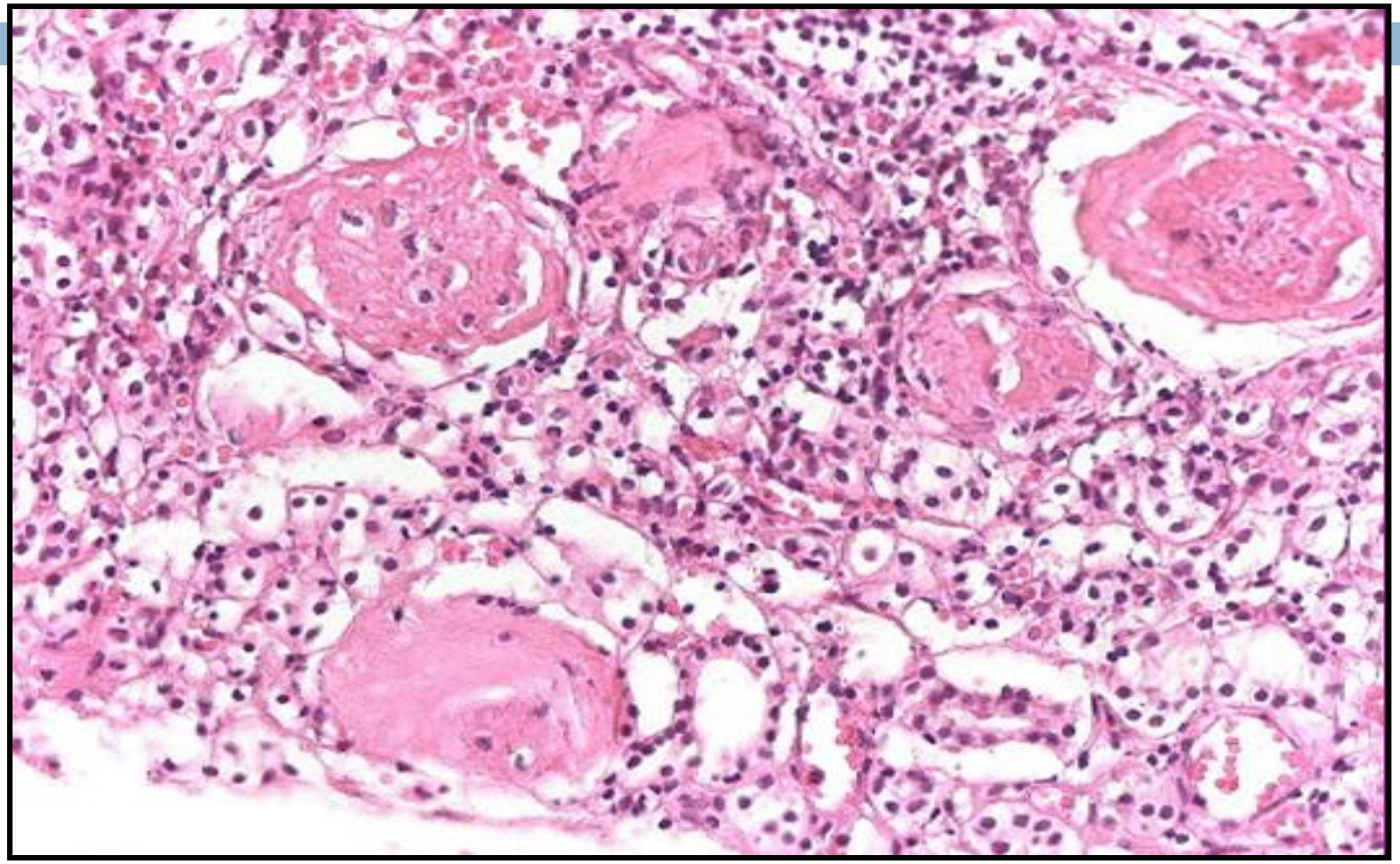
- *Foreign bodies like calculi with obstruction,*
- *Atresia of the urethra,*
- *Benign prostatic hyperplasia ,*
- *Neoplasia of the prostate and bladder*
- *Spinal cord damage with paralysis of the bladder .*

Hydronephrosis



Markedly dilated renal pelvis and calyces with atrophic and thin renal cortex

Chronic Pyelonephritis presenting as complication to Hydronephrosis



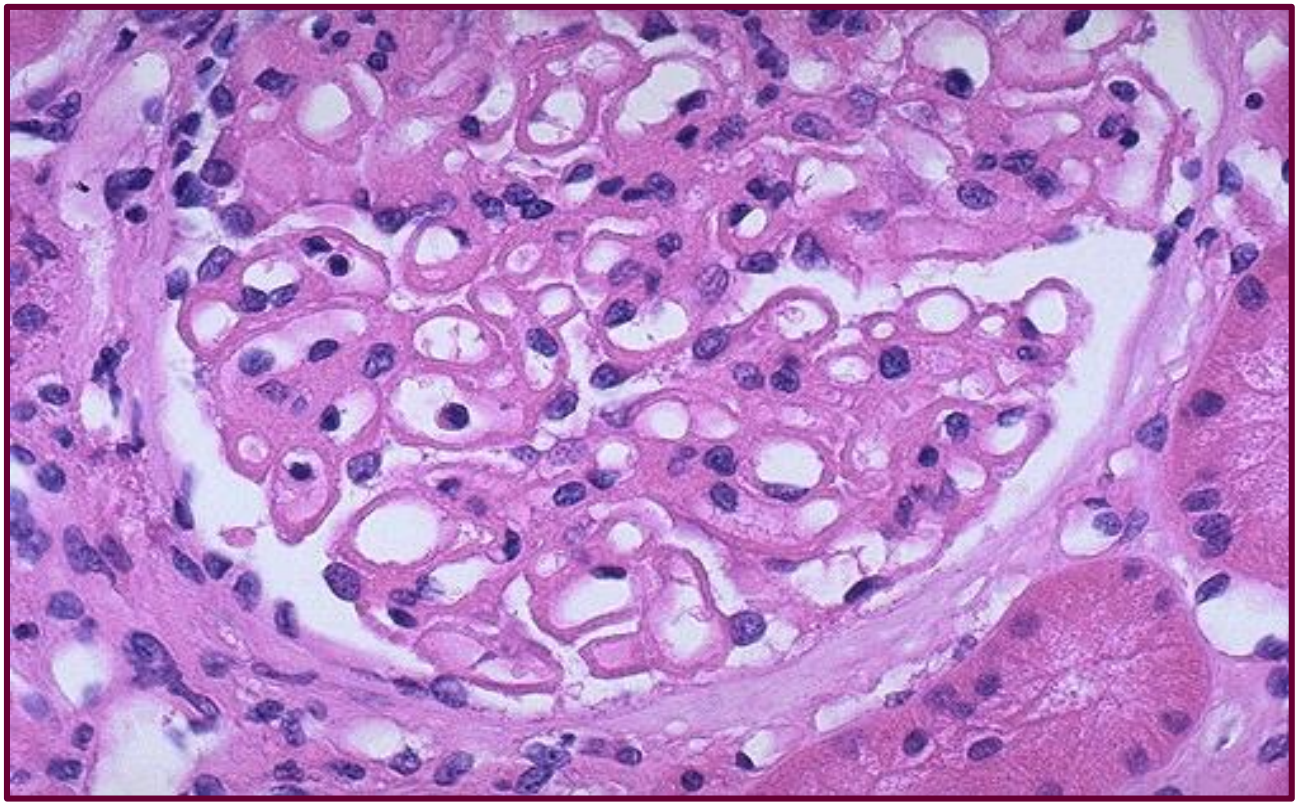
Thinning renal parenchyma with residual large renal vessels in the hilum. Sclerosis of glomeruli with atrophic tubules

PRACTICAL SESSION : 3

NEPHROTIC SYNDROME

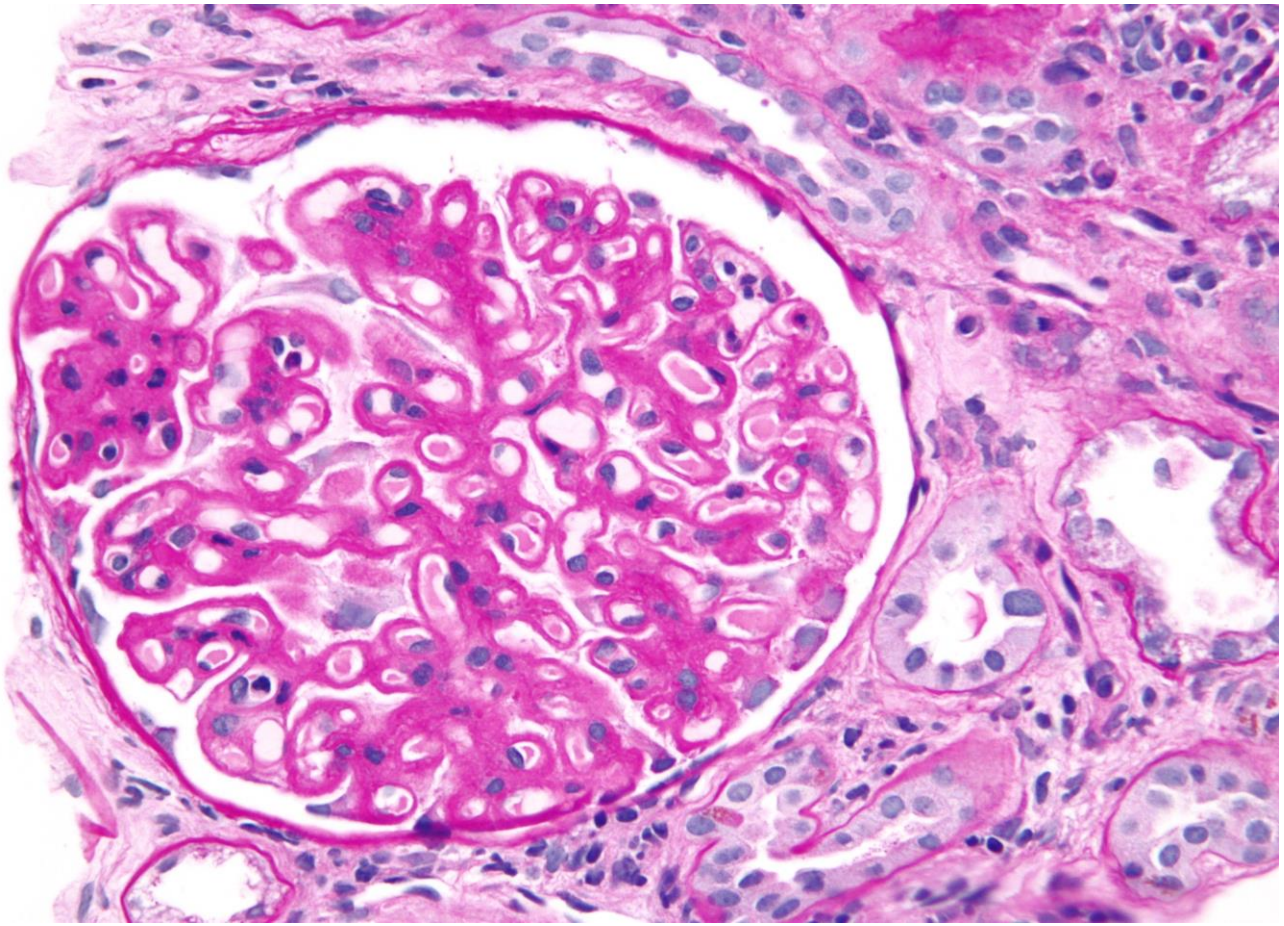
Membranous Glomerulonephritis

Membranous glomerulonephritis (The common cause of Nephrotic syndrome in adults): the capillary loops are thickened and prominent, but the cellularity is not increased.



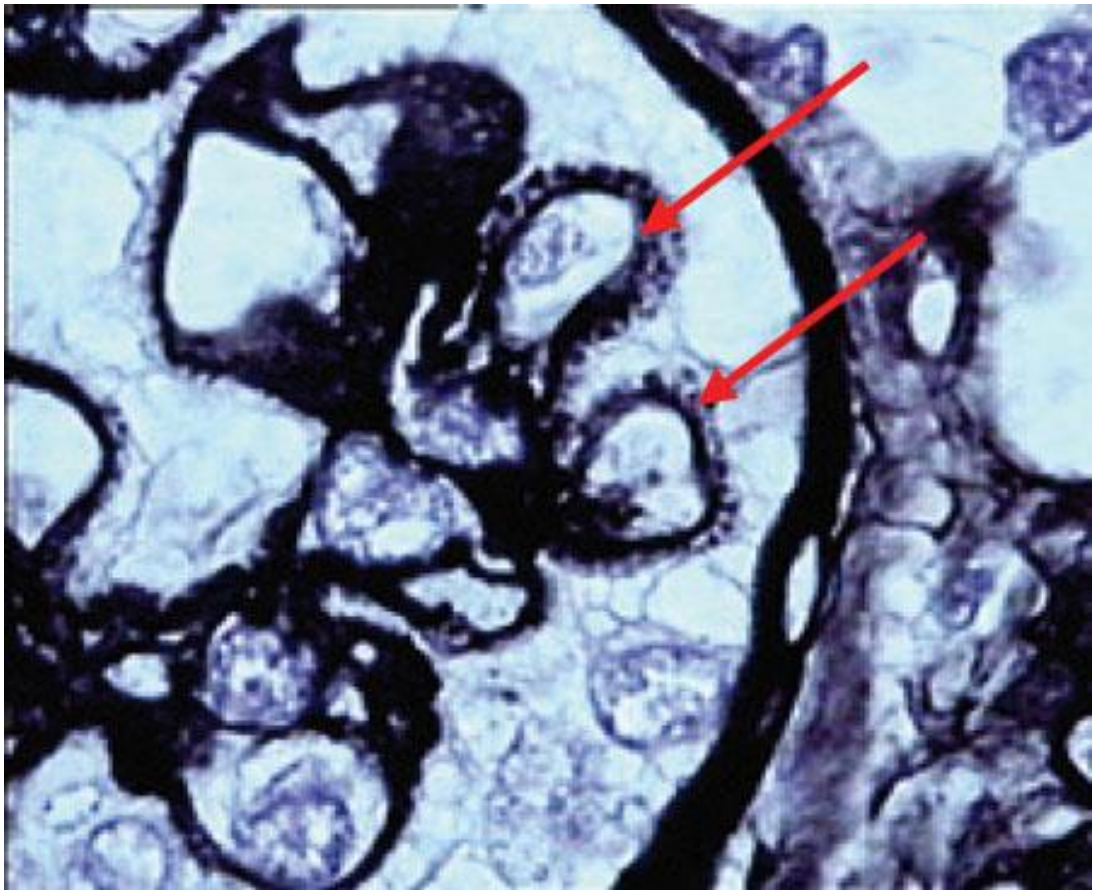
Thickened capillary loops and walls.

Membranous Glomerulonephritis



Close-up of glomerulus illustrating rigid, uniformly-thickened capillary walls (H&E stain, 400x original magnification).

Membranous Glomerulonephritis



Early stage II membranous glomerulonephritis: The thickened capillary wall shows numerous "holes" in tangential sections, indicating deposits. (Deposits do not take up the silver stain.) Well-developed spikes around the deposits are not present here.

Membranous Glomerulonephritis

Causes:

- **Idiopathic/primary**
- **Secondary**
  - **Carcinoma (malignancy).**
  - **Therapeutic drugs (penicillamine).**
  - **Infections: Hepatitis B, Malaria.**
  - **Autoimmune disease e.g. Systemic lupus erythematosus.**
  - **Neoplasms (lung cancer**

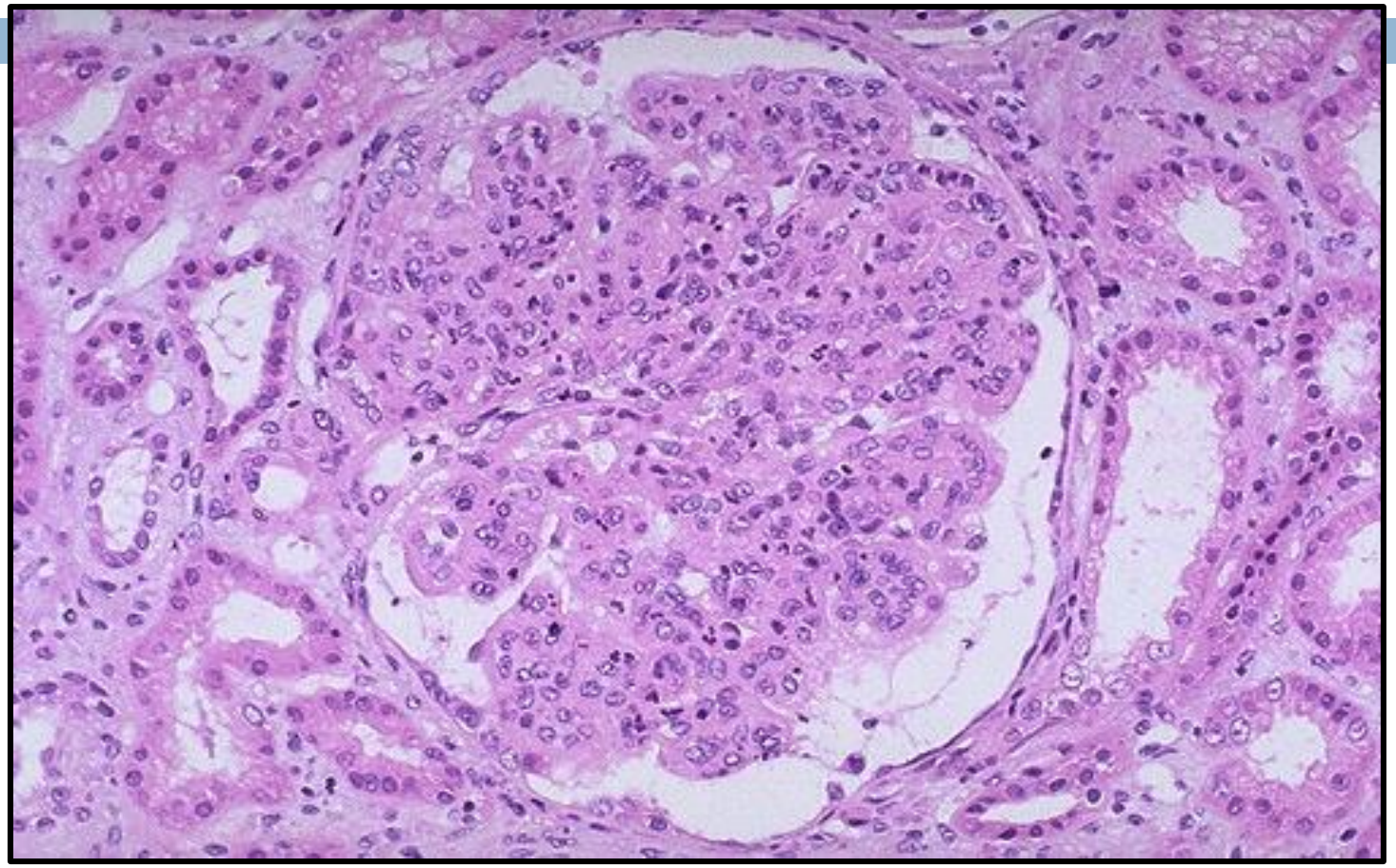
NEPHRITIC SYNDROME

Acute (Post-streptococcal) Post infectious Glomerulonephritis

Section of the kidney shows:

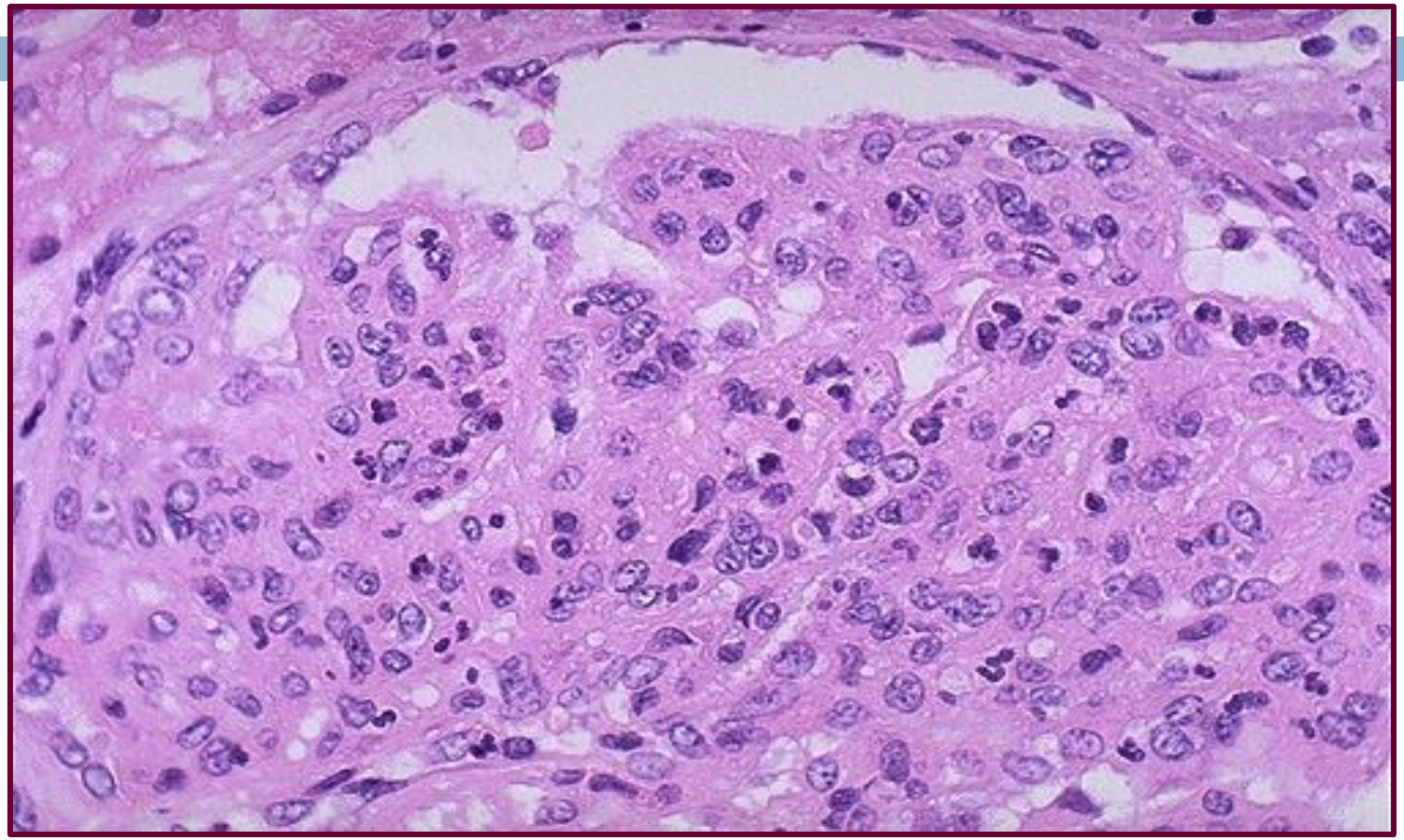
- **The glomeruli are enlarged, lobulated and hypercellular.**
- **Cellularity is due to proliferation of endothelial and mesangial cells with migration of some neutrophils and monocytes.**

Acute (Post-streptococcal) Glomerulonephritis



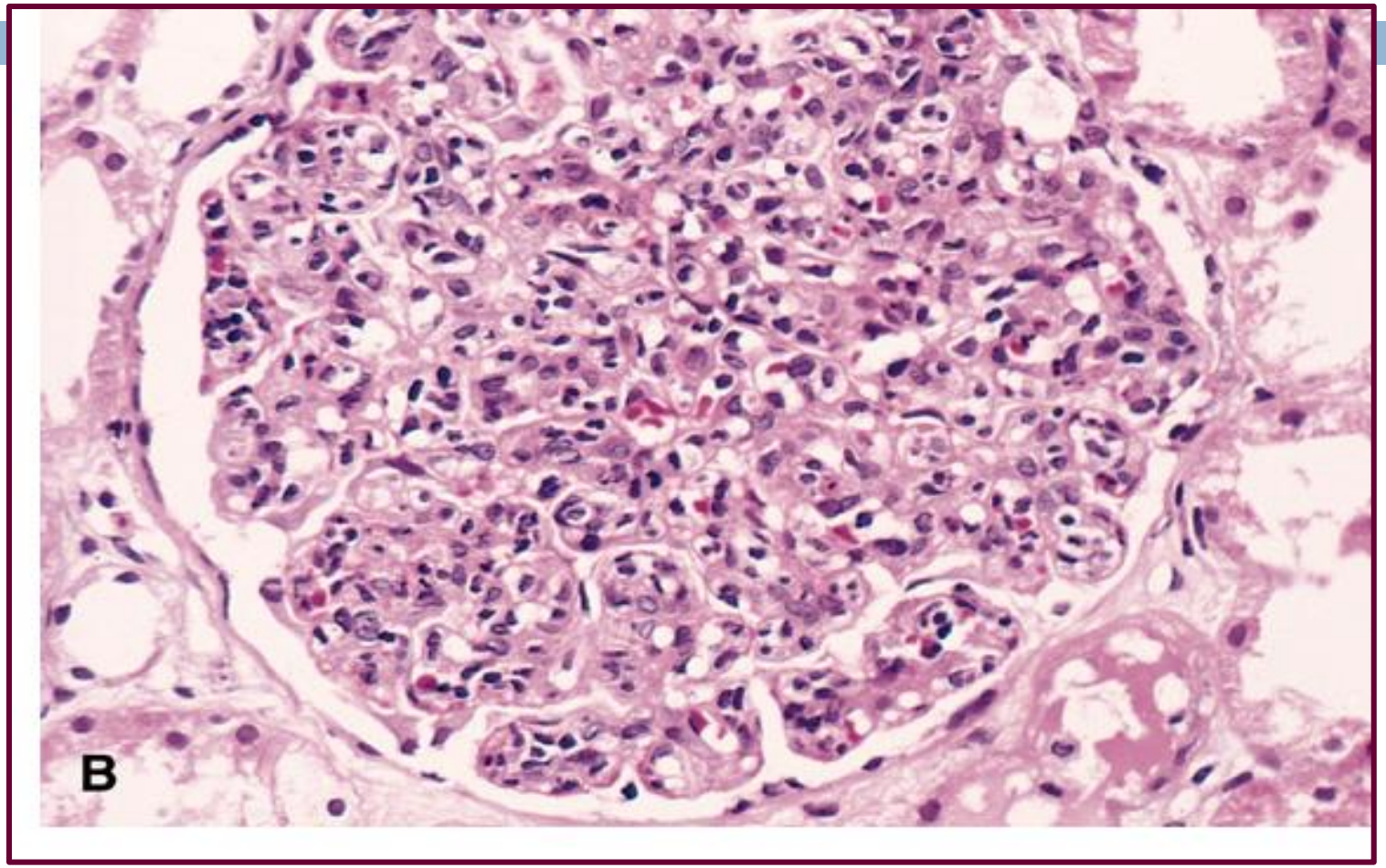
There is glomerular injury. It is hypercellular and lobulated. This is a type of proliferative glomerulonephritis known as post-infectious glomerulonephritis

Acute (Post-streptococcal) Glomerulonephritis



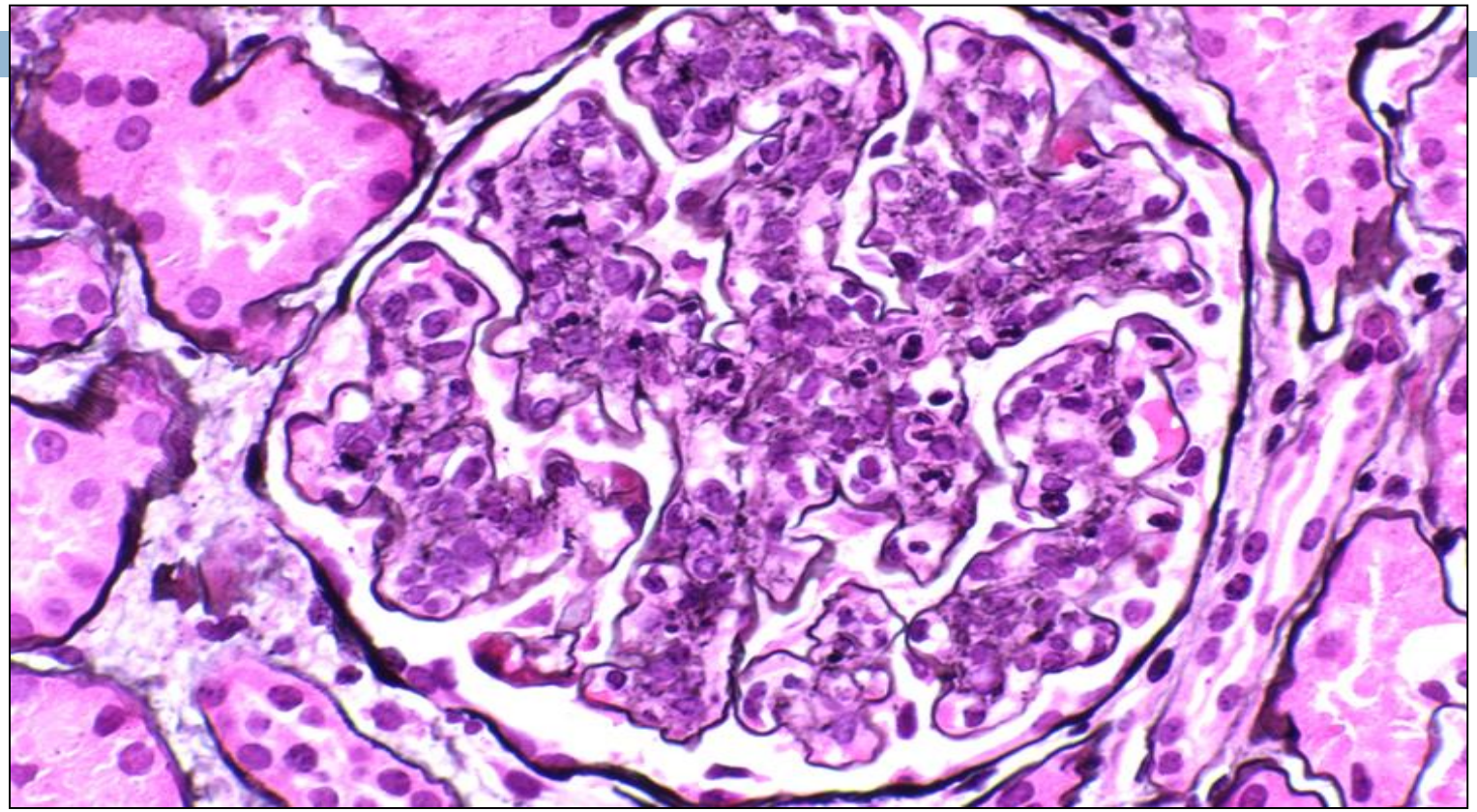
The hypercellularity of post-infectious glomerulonephritis is due to increased numbers of endothelial, and mesangial cells as well migration of neutrophils and monocyte in and around the glomerular capillary loops

Acute (Post-streptococcal) Glomerulonephritis



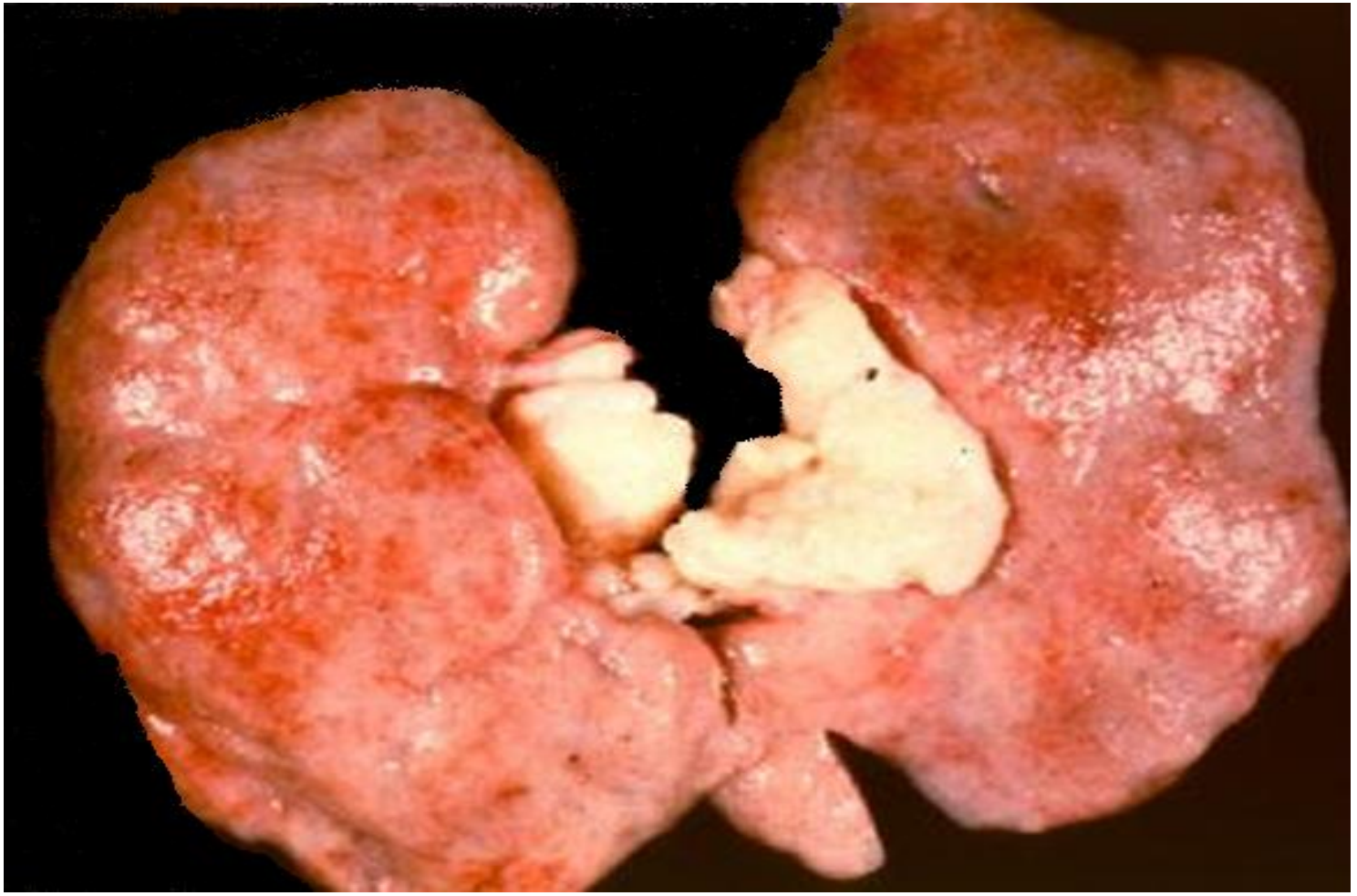
High power LM of a hypercellular glomerulus; numerous capillaries contain inflammatory cells, mostly neutrophils

Acute Post-streptococcal Glomerulonephritis



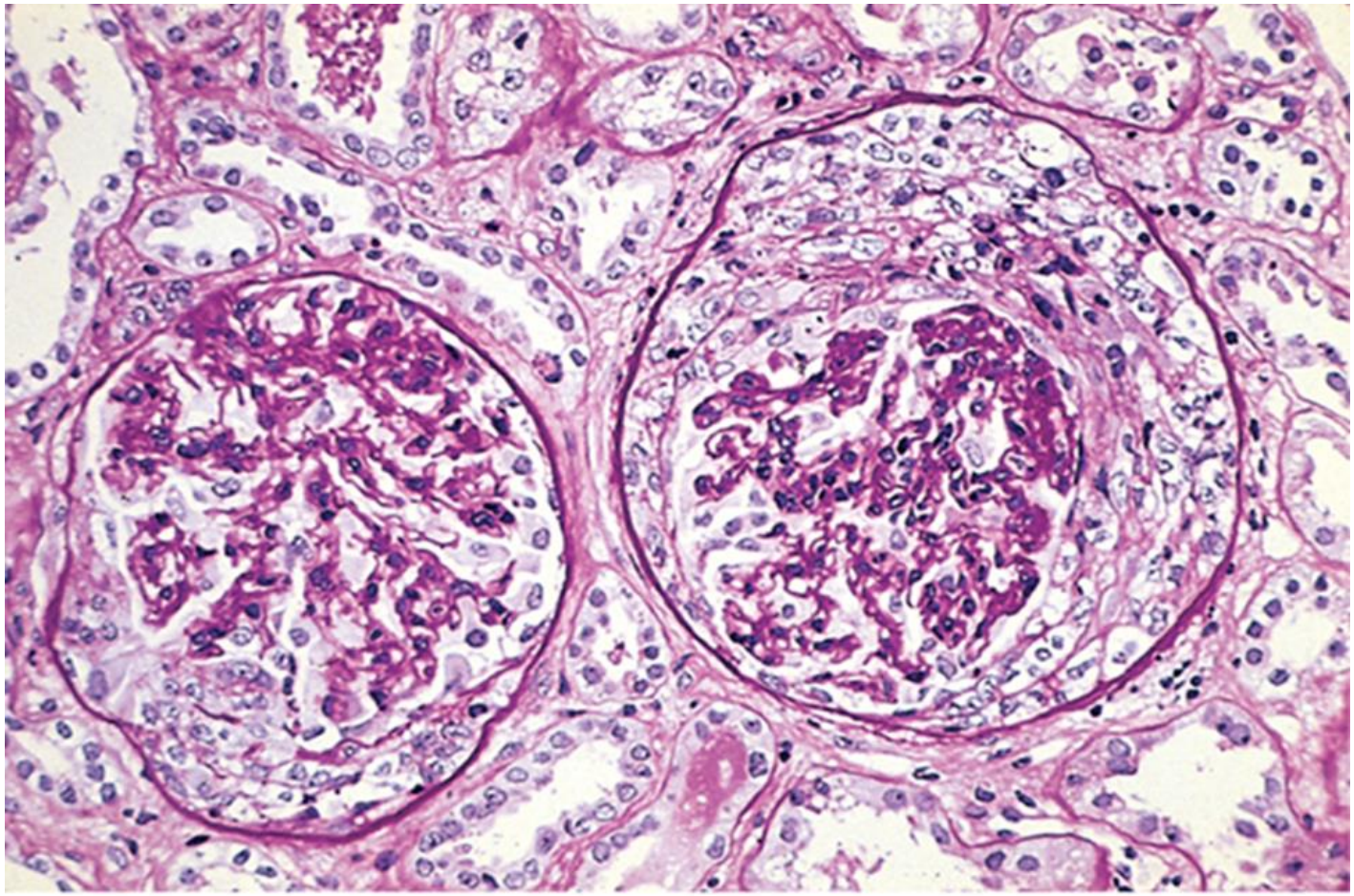
Acute Poststreptococcal Glomerulonephritis is evident in this high-power silver stain with large number of PMNs. The glomerular basement membrane does not show splitting or spikes. There is proliferation of endothelial and mesangial cells and infiltrating cells filling and distending capillary loops.

Rapid Progressive Glomerulonephritis (RPGN)



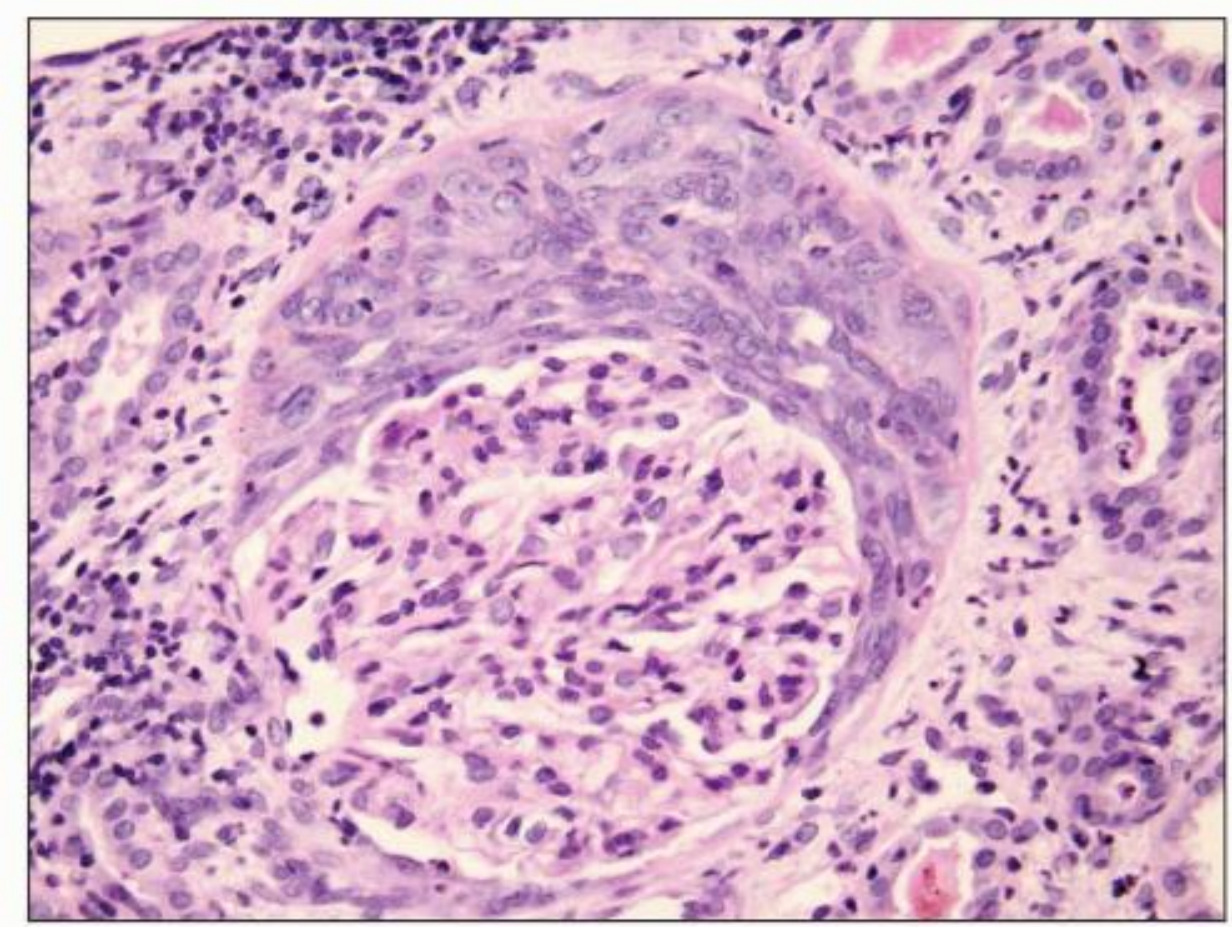
Gross appearance of RPGN - note the flea beaten appearance

Rapid Progressive Glomerulonephritis (RPGN)



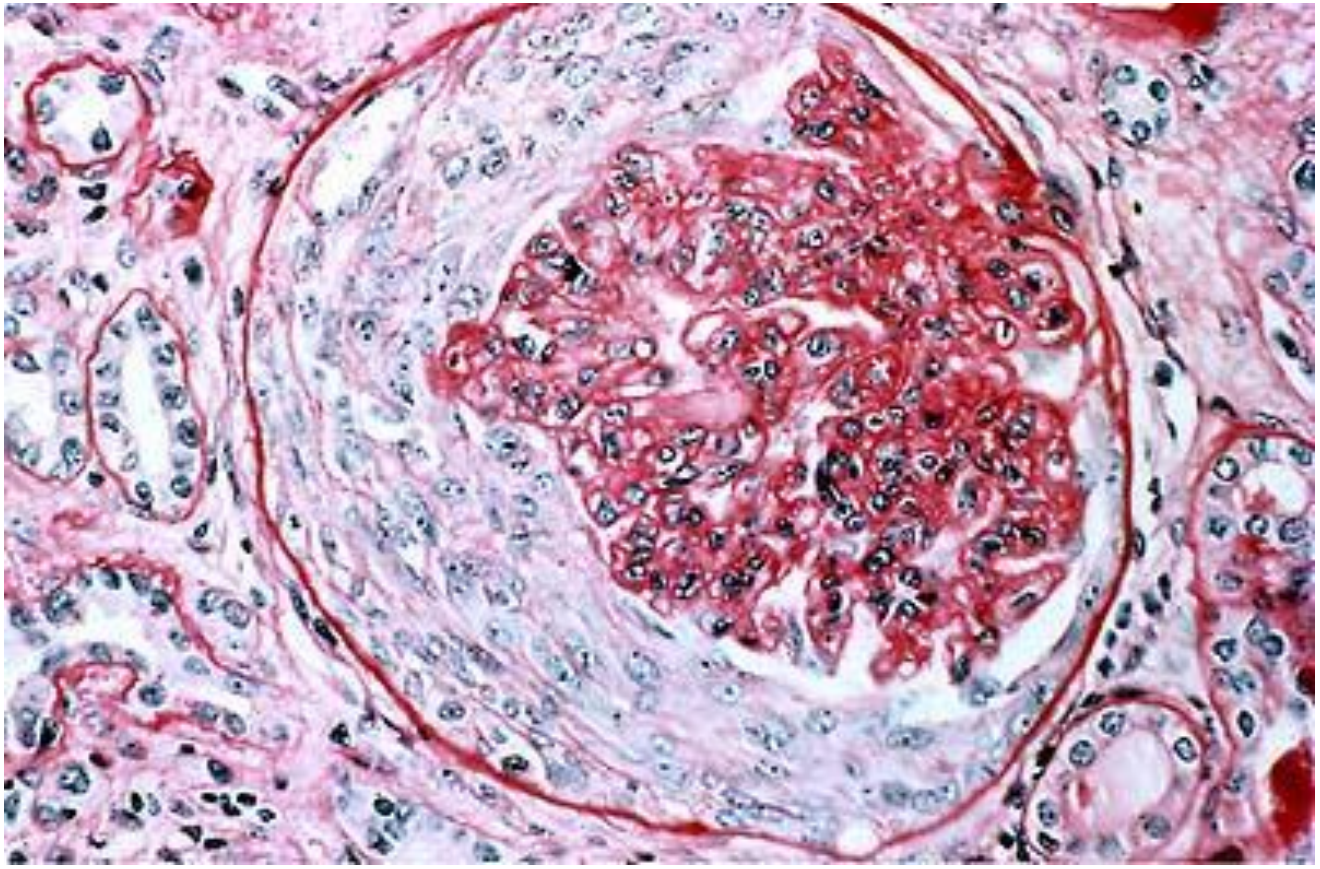
Seen here within the glomeruli are crescents composed of proliferating epithelial cells. Crescentic glomerulonephritis is known as rapidly progressive glomerulonephritis (RPGN) because this disease is very progressive

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.

Rapid Progressive Glomerulonephritis (RPGN)



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

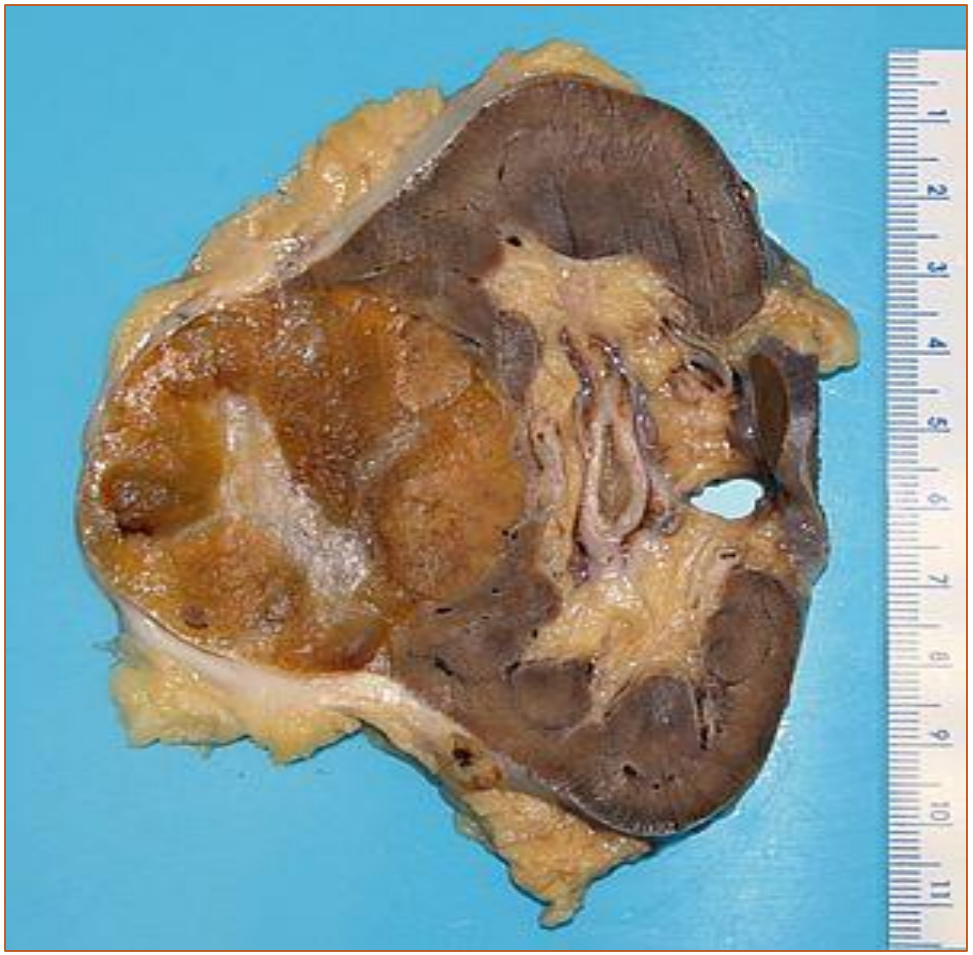
RENAL TUMORS

BENIGN RENAL TUMORS

RARE Tumors

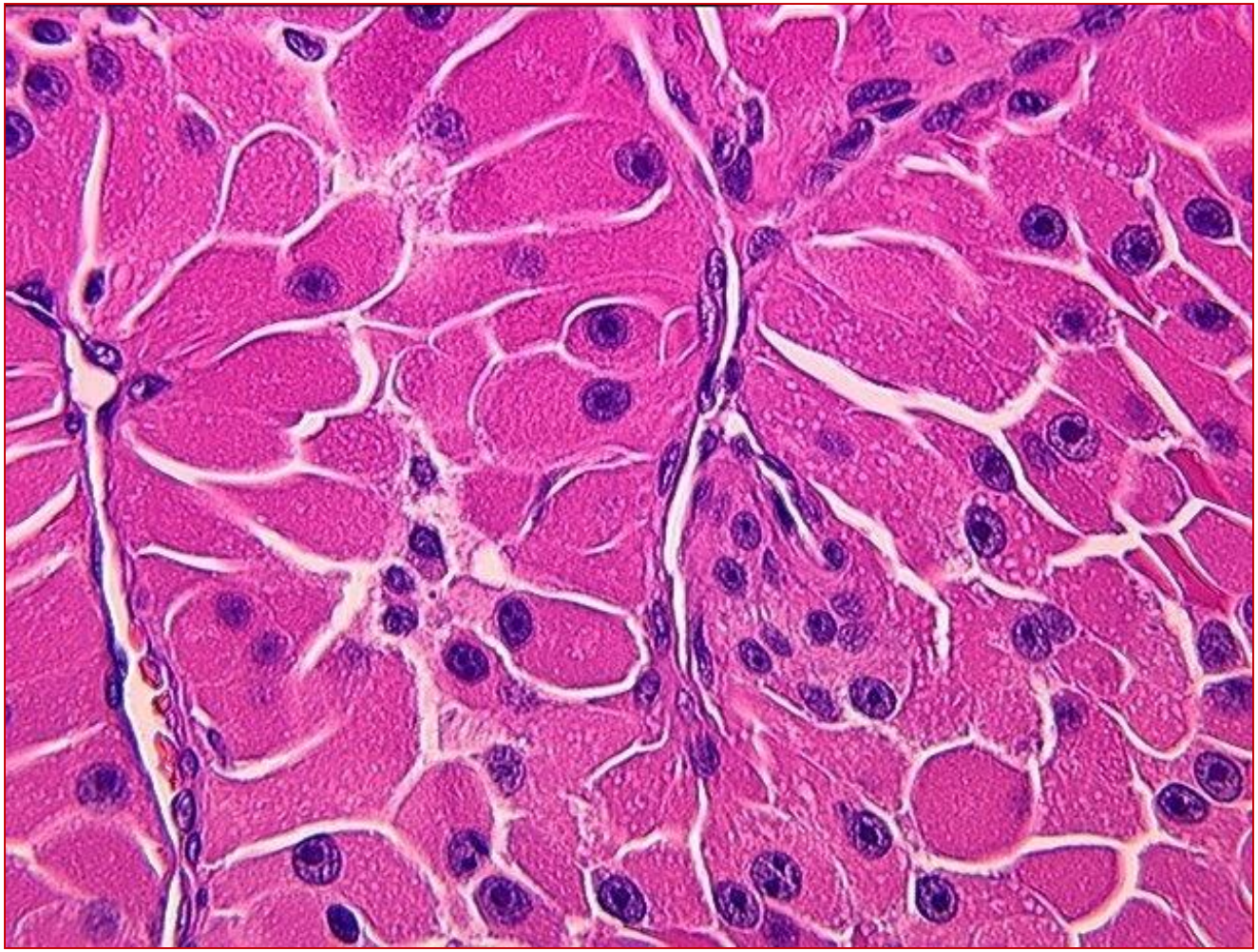
- ***Angiomyolipoma***
- ***Oncocytoma (very red, granular, mitochondria)***

Oncocytoma - Gross



- *Well-circumscribed mahogany colored renal mass.*
- *Central pale scar.*

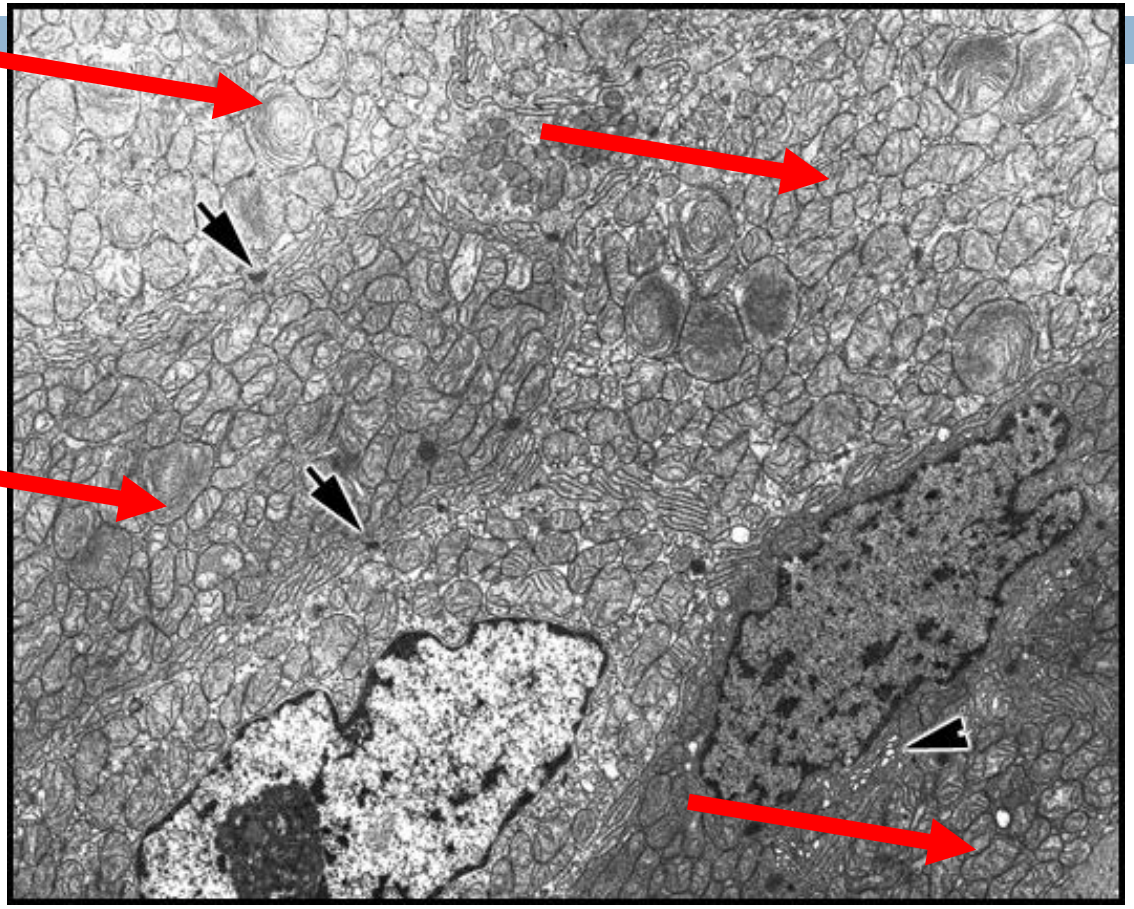
Oncocytoma



Oncocytes showing red and granular cytoplasm with vesicular nuclei and prominent nucleoli.

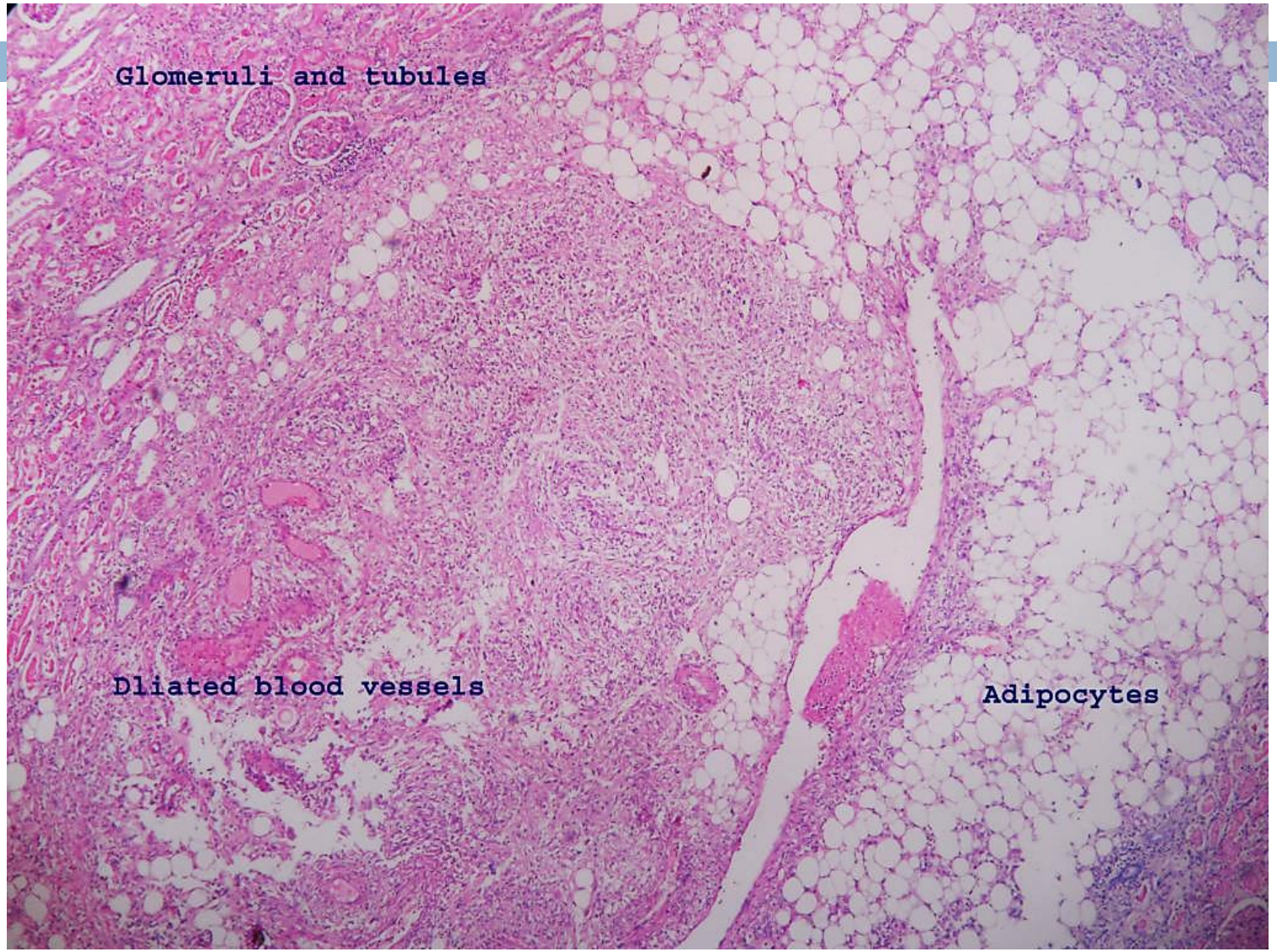
Oncocytoma

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



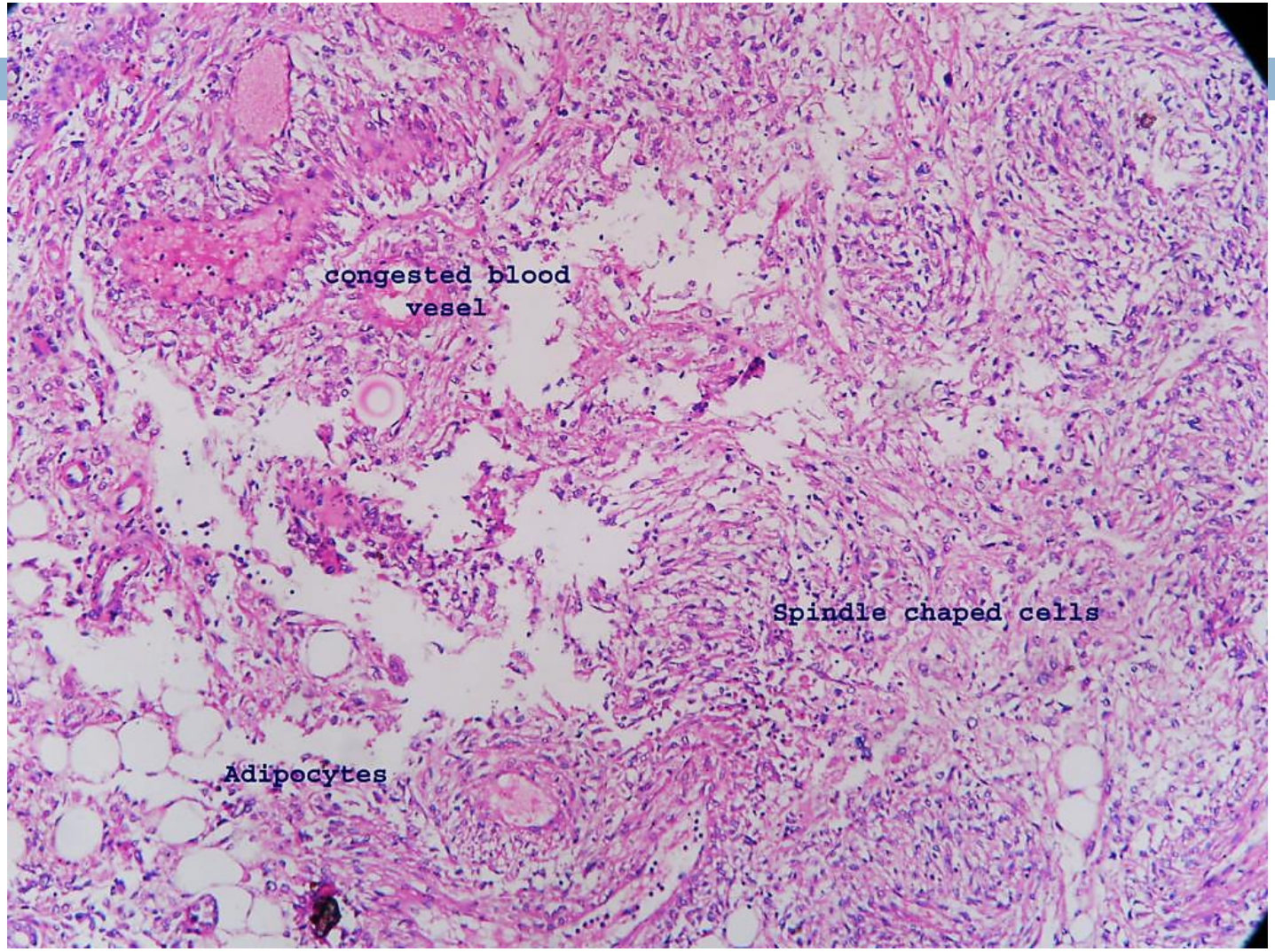
In oncocytoma, the neoplastic cells are filled with mitochondria (red arrows) to the exclusion of almost all other organelles. These correspond to the oncocytoma cells with abundant granular, eosinophilic cytoplasm seen by light microscopy.

Angiomyolipoma



Benign tumor composed of vessels, smooth muscle and fat.

Angiomyolipoma



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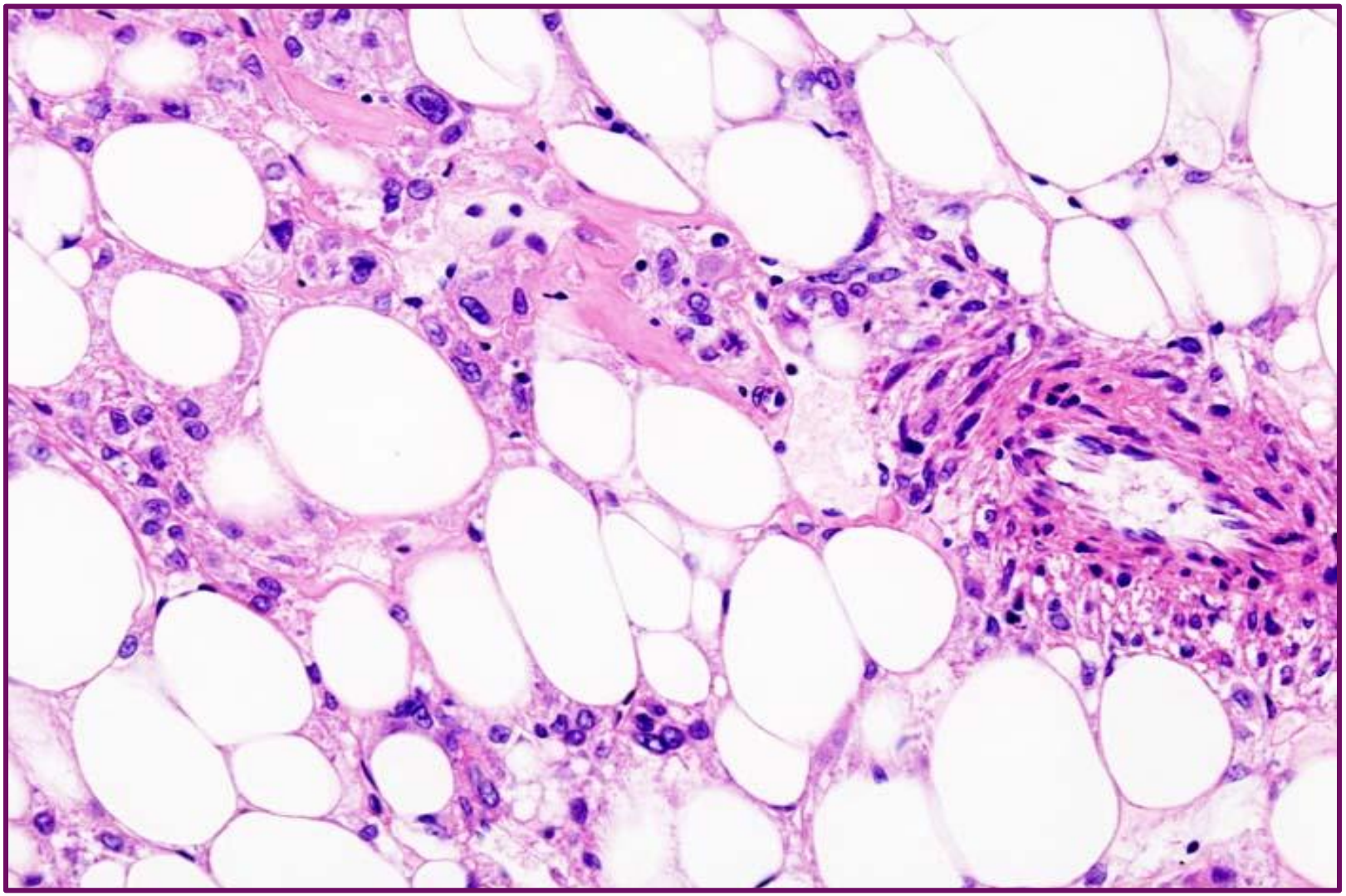
Angiomyolipoma



Benign tumor composed of vessels, smooth muscle and fat.

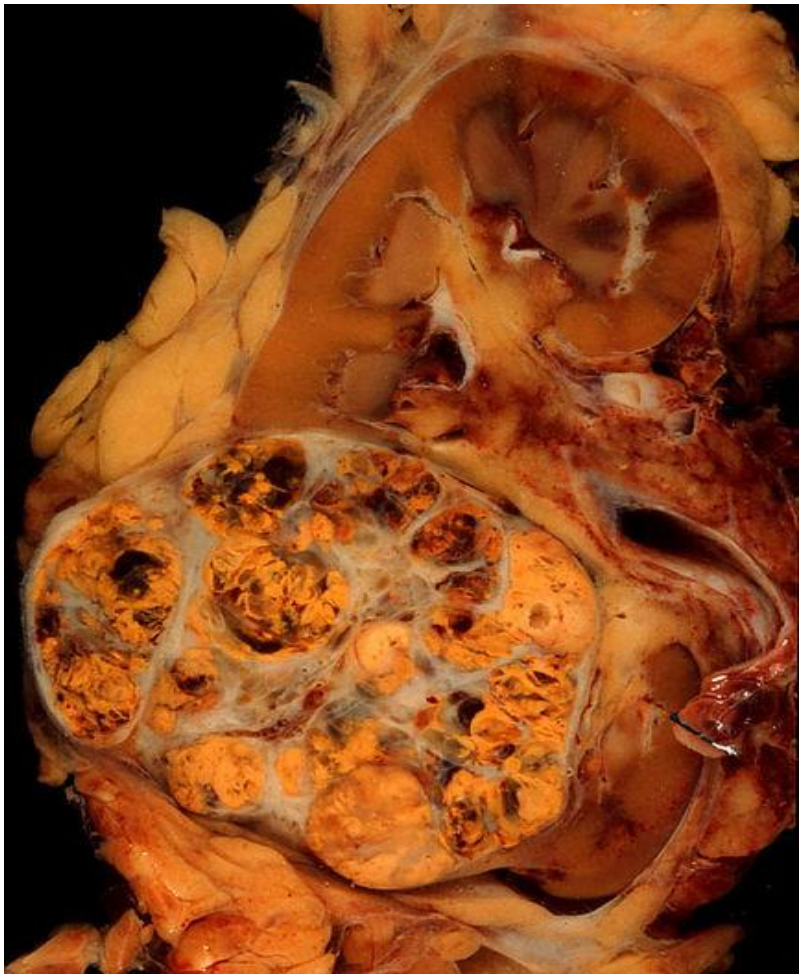
Angiomyolipoma

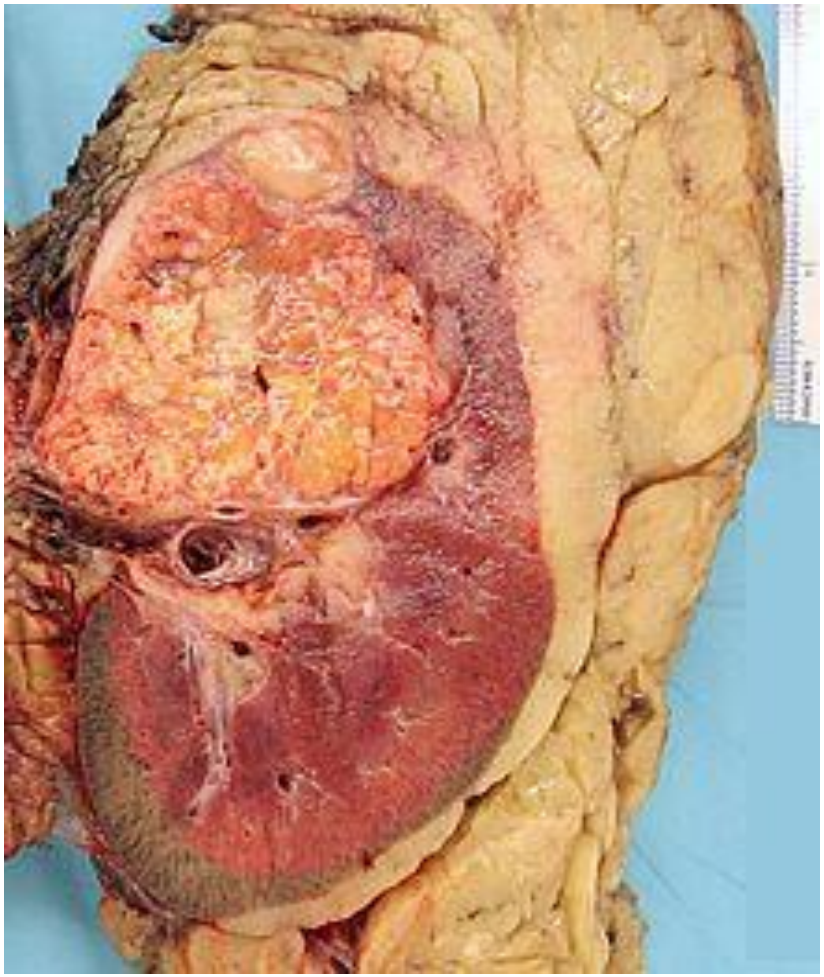
This is a benign neoplasm consisting of vessels, smooth muscle, and fat. Angiomyolipomas are present in 25% to 50% of patients with tuberous sclerosis. Tuberous sclerosis is characterized by lesions of the cerebral cortex that produce epilepsy and mental retardation, a variety of skin abnormalities, and unusual benign tumors at other sites, such as the heart. The clinical importance of angiomyolipoma is due largely to their susceptibility to spontaneous hemorrhage.

MALIGNANT RENAL TUMORS

- *Renal Cell Carcinoma → Clear Cell Carcinoma*
- *Wilm's Tumor*

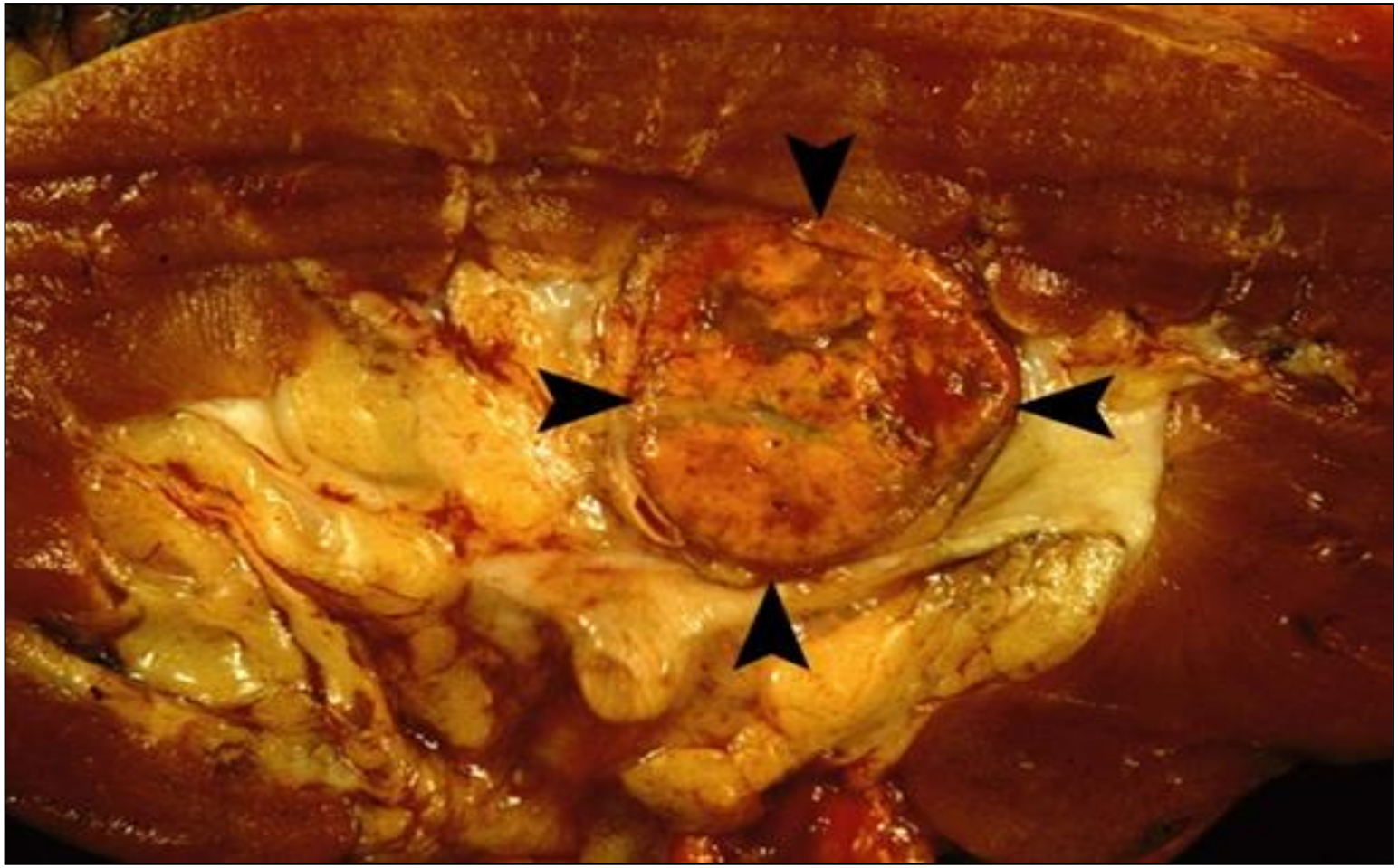
Renal Clear Cell Carcinoma – Gross pathology





A well circumscribed renal cortical mass which is partly yellow due to presence of fat and partly hemorrhagic with lobulated cut surface .

Renal Clear Cell Carcinoma – Gross

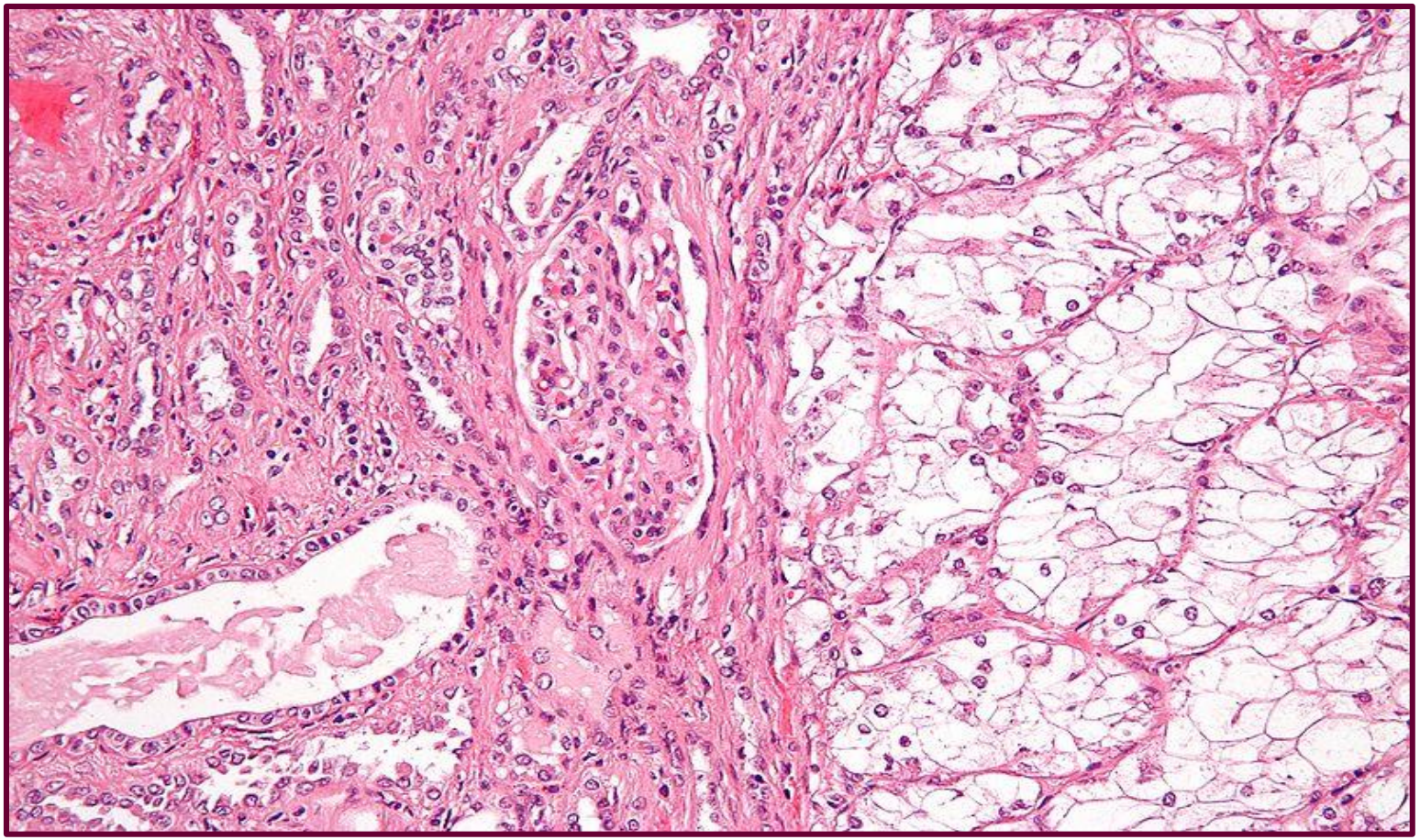


Renal clear cell carcinoma. *The tumor is well demarcated from the surrounding non-neoplastic renal parenchyma by a pseudocapsule*

Renal Clear Cell Carcinoma - Histopathology

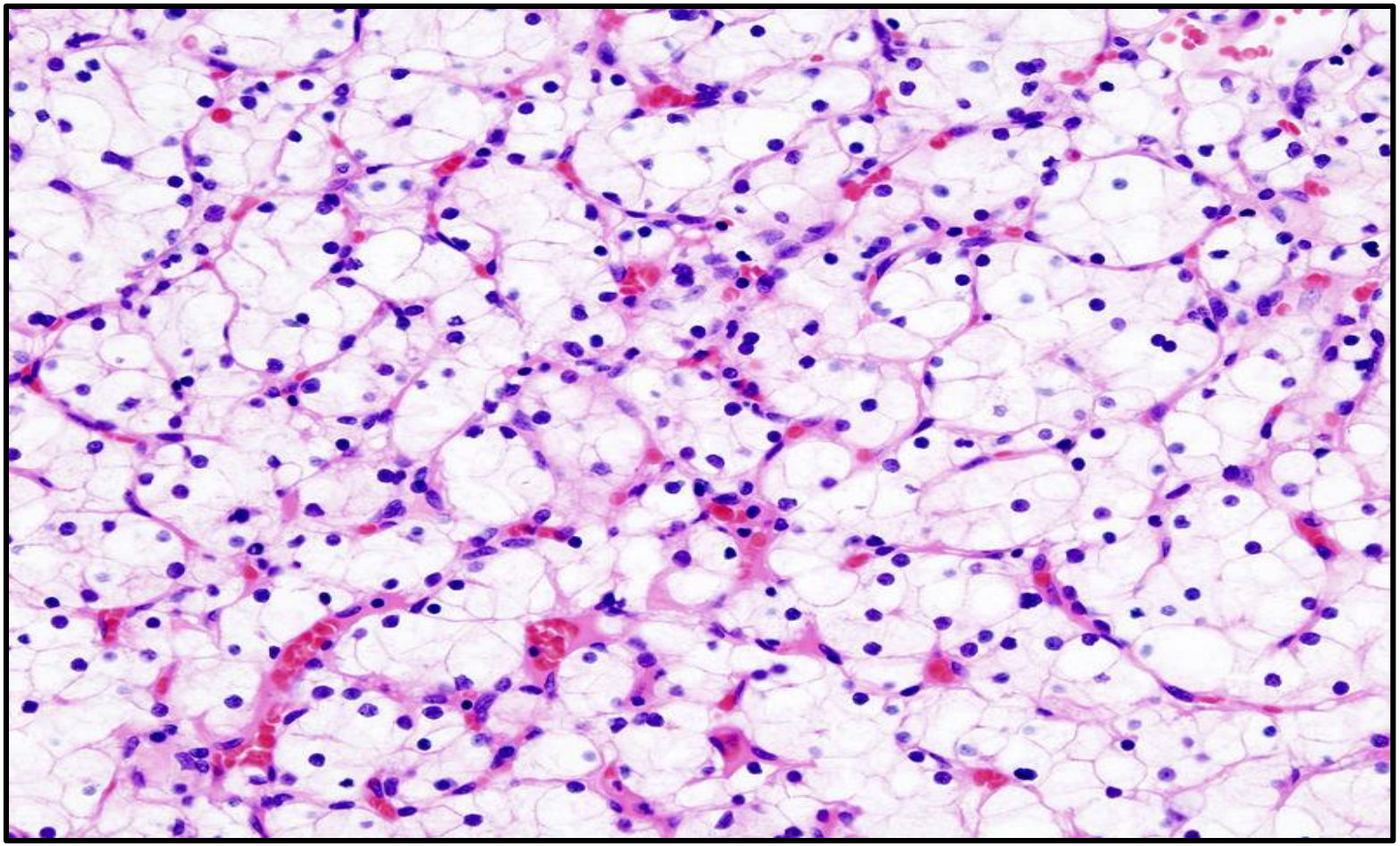
- *Tumor cells are large polygonal with clear cytoplasm (dissolved glycogen and lipid) and piknotic nuclei.*
- *Cells are arranged as alveolar groups or tubules with papillary formations separated by thin fibrovascular septae.*
- *Cells show pleomorphism and mitosis.*
- *Areas of haemorrhage and necrosis are present.*
- *Commonly associated with Von Hippel-Lindau disease that shows alterations in a gene localized on chromosome 3*

Renal Clear Cell Carcinoma - Histopathology



The most common type of renal cell carcinoma (clear cell) - on right of the image : Cells with clear cytoplasm, typically arranged in nests and Nuclear atypia is common. Non-tumour kidney is on the left of the image

Renal Clear Cell Carcinoma - Histopathology



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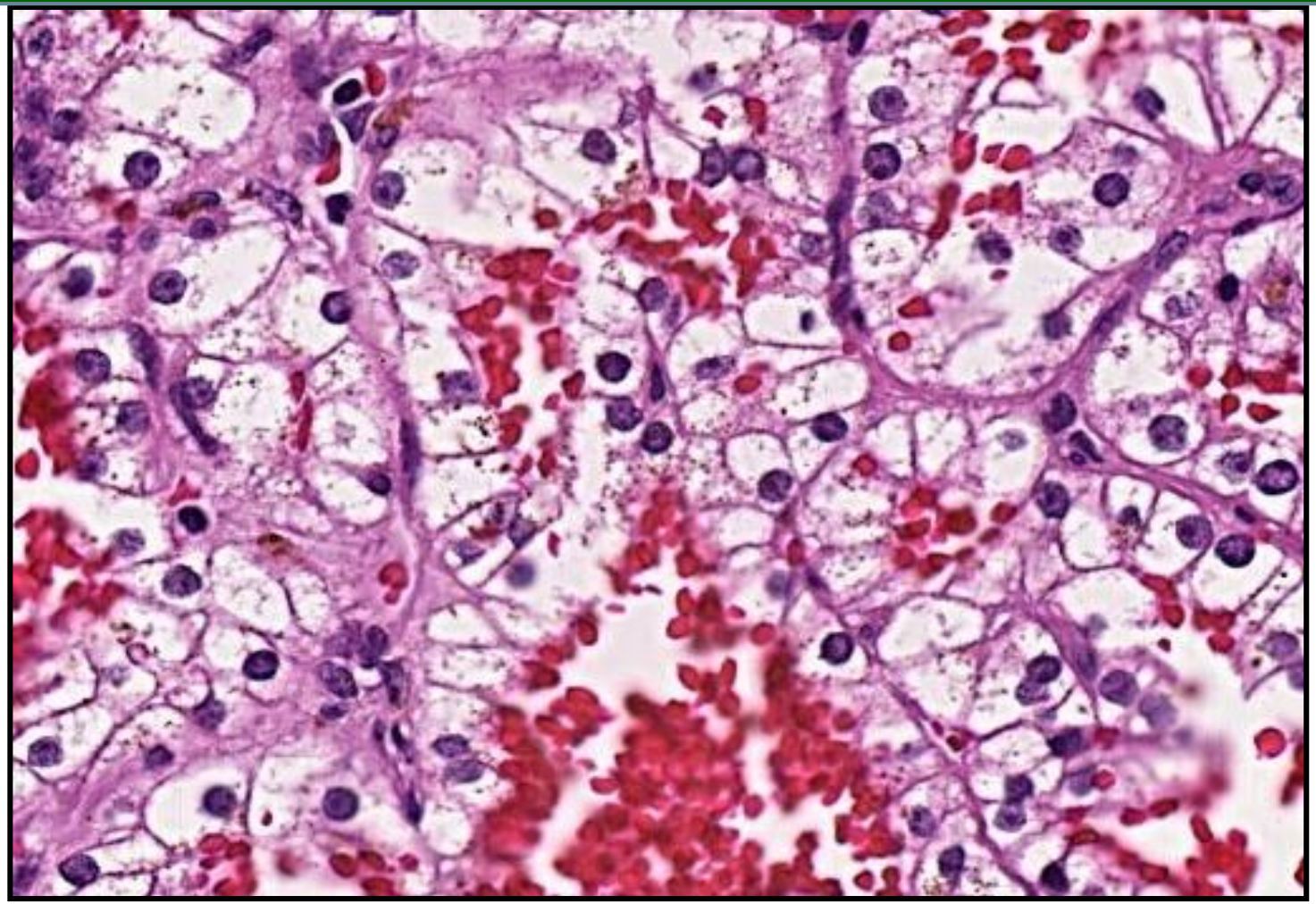
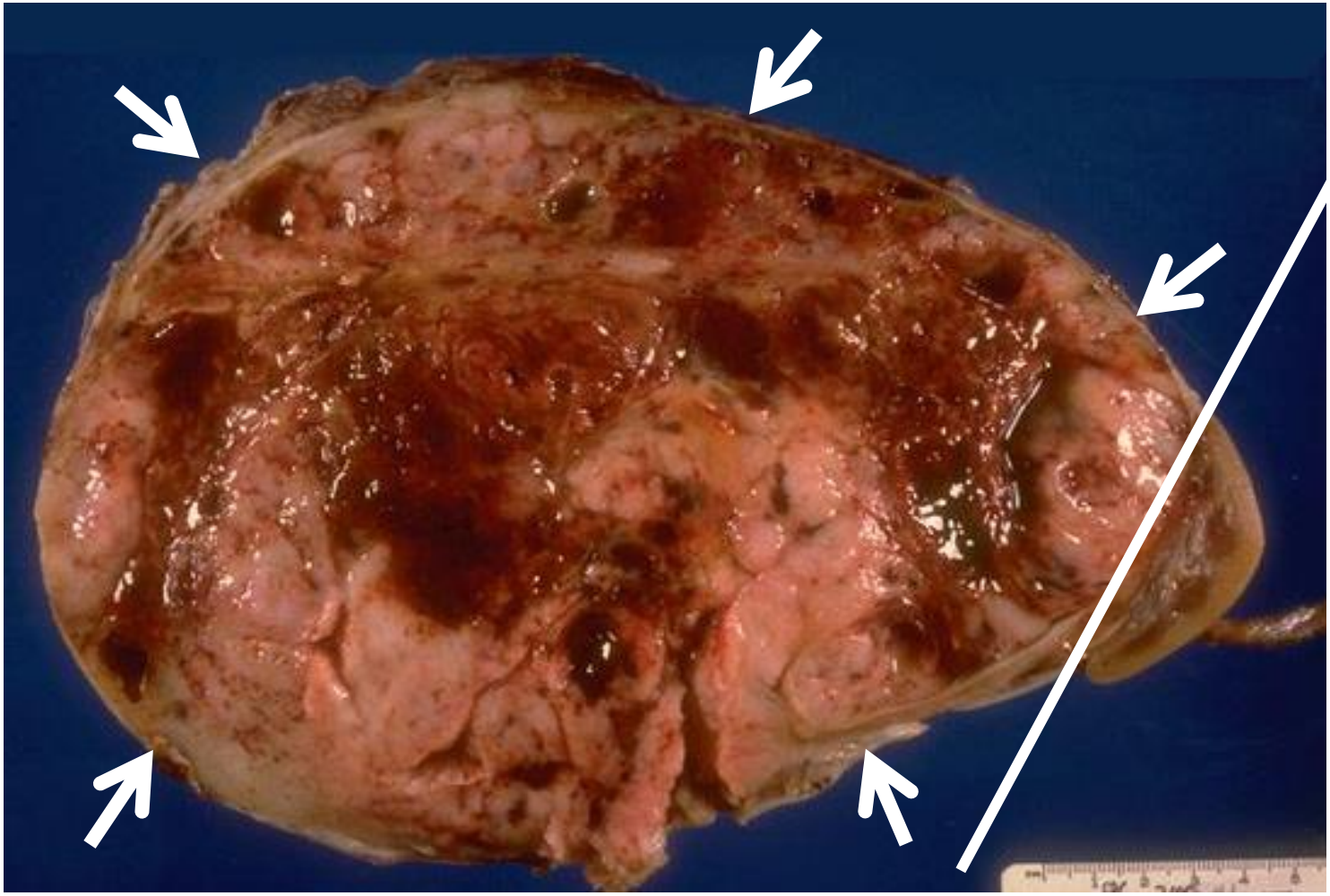
Renal Clear Cell Carcinoma - Histopathology



Section shows clear tumor cells arranged in nests. The tumor cells have a clear cytoplasm with central nuclei and areas of hemorrhage .

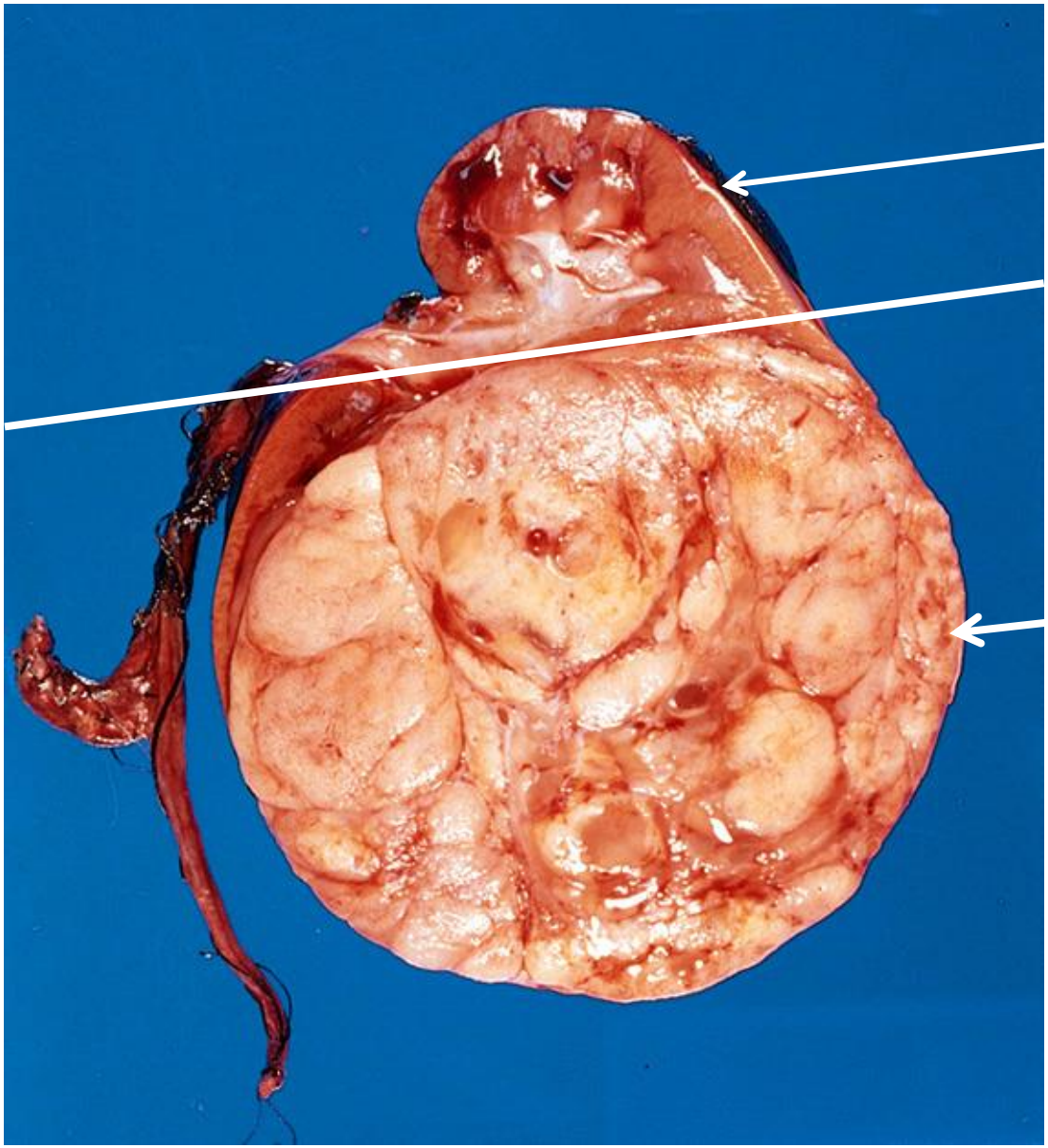
WILM'S TUMOR

Wilm's Tumor – Gross Pathology

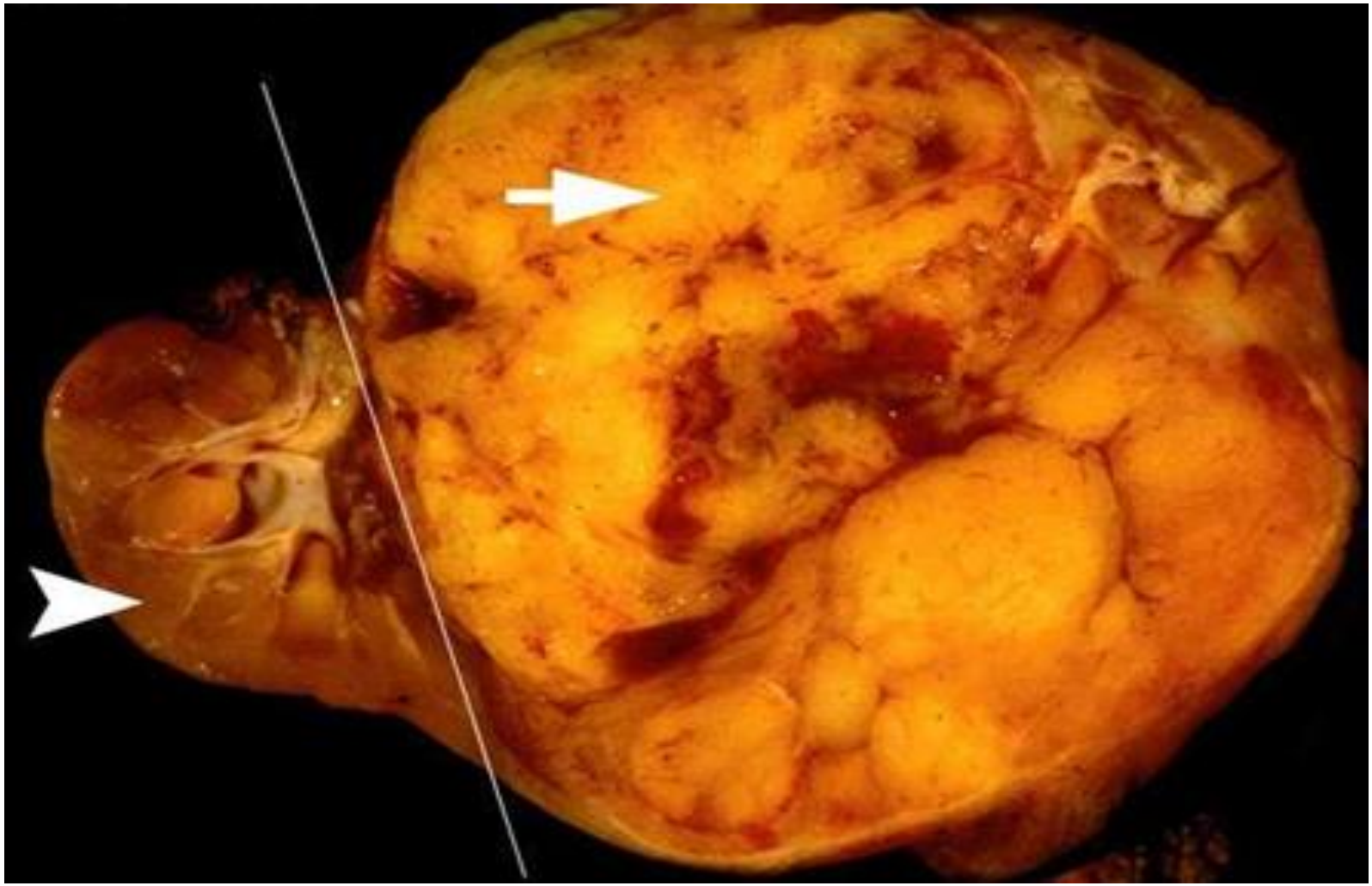


Gross picture shows partly pale and partly hemorrhagic solid tumor replacing almost the entire renal parenchyma and areas of necrosis also seen .

Wilm's Tumor – Gross Pathology



Wilm's Tumor – Gross Pathology



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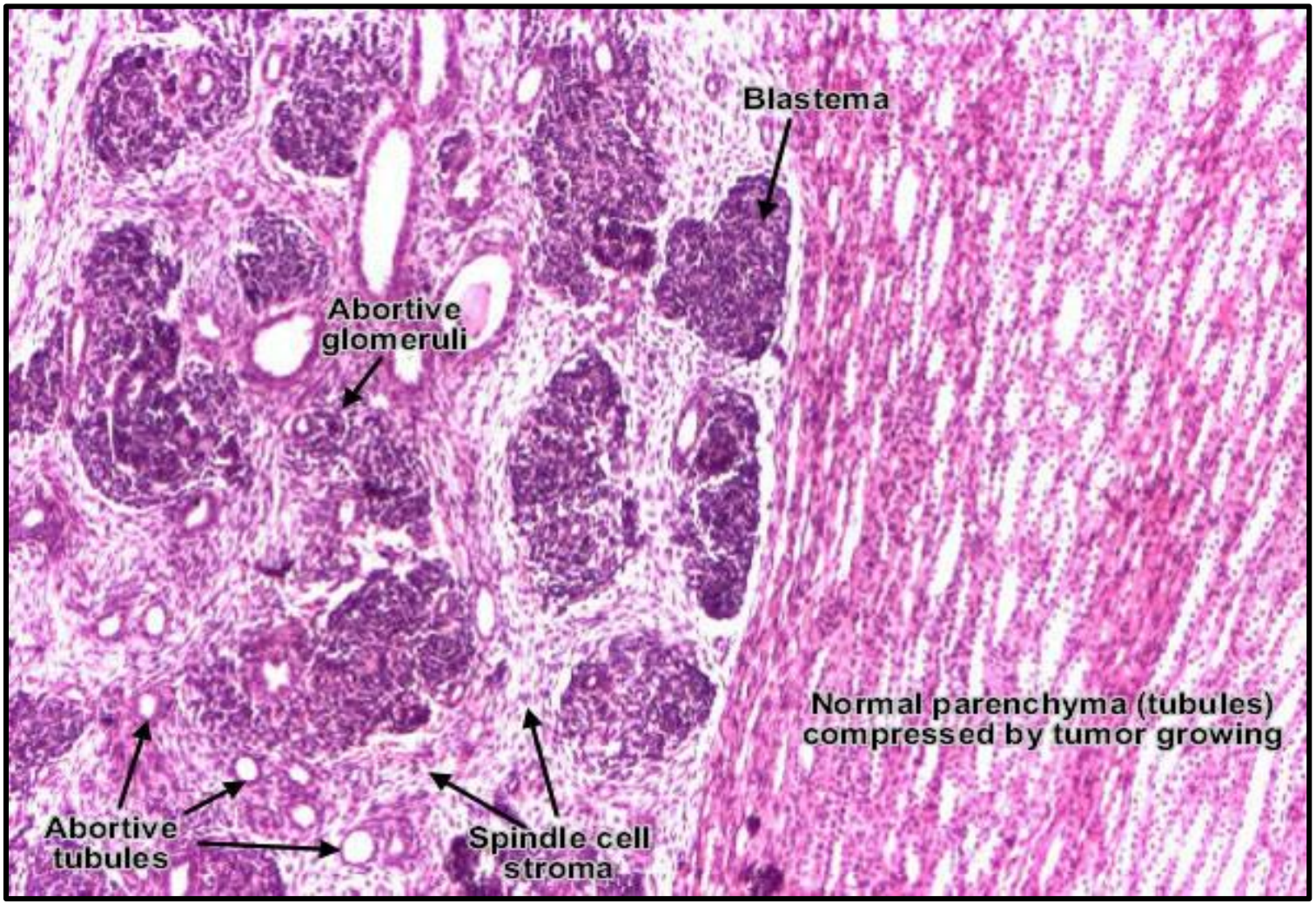
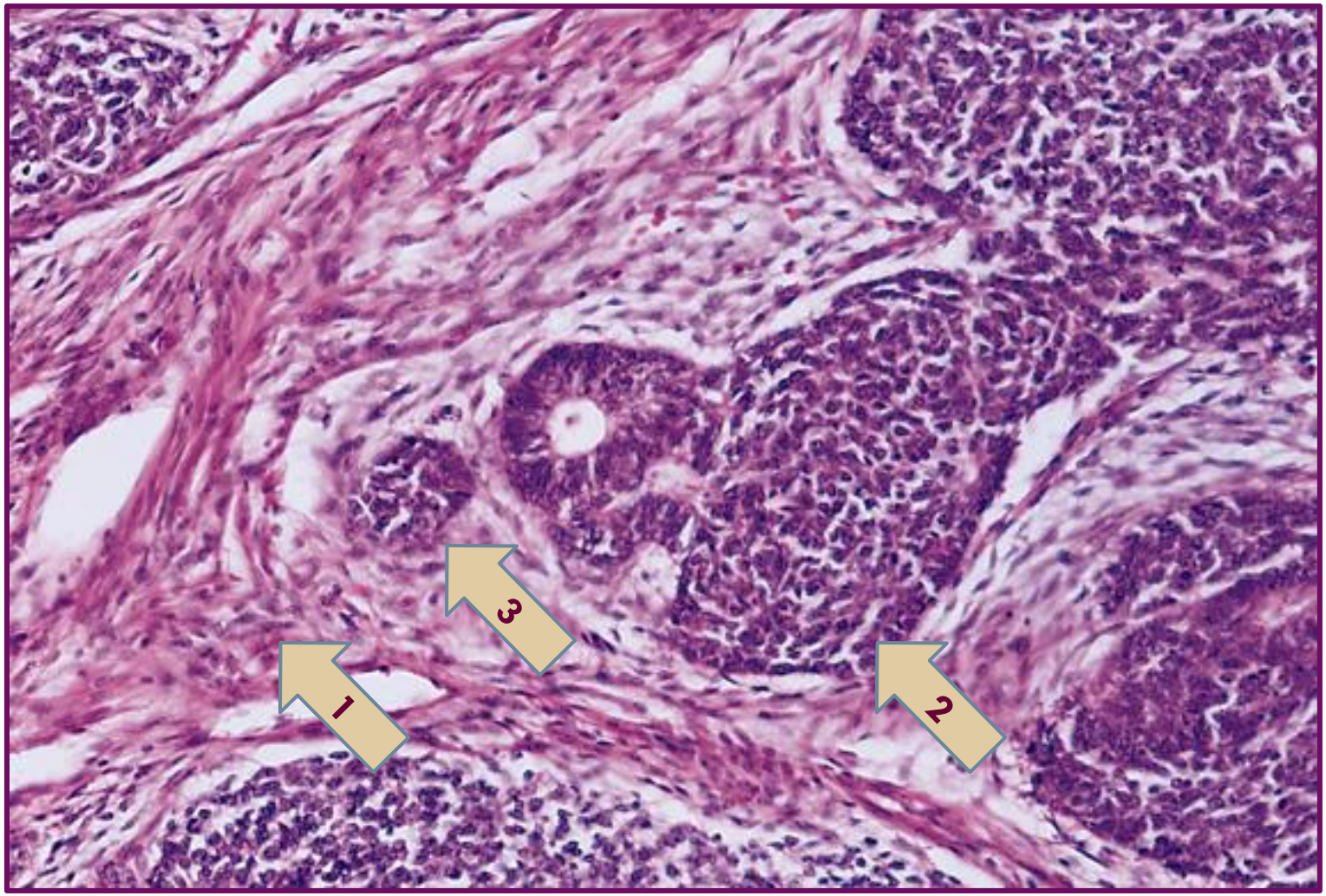
Wilm's Tumor – Histopathology



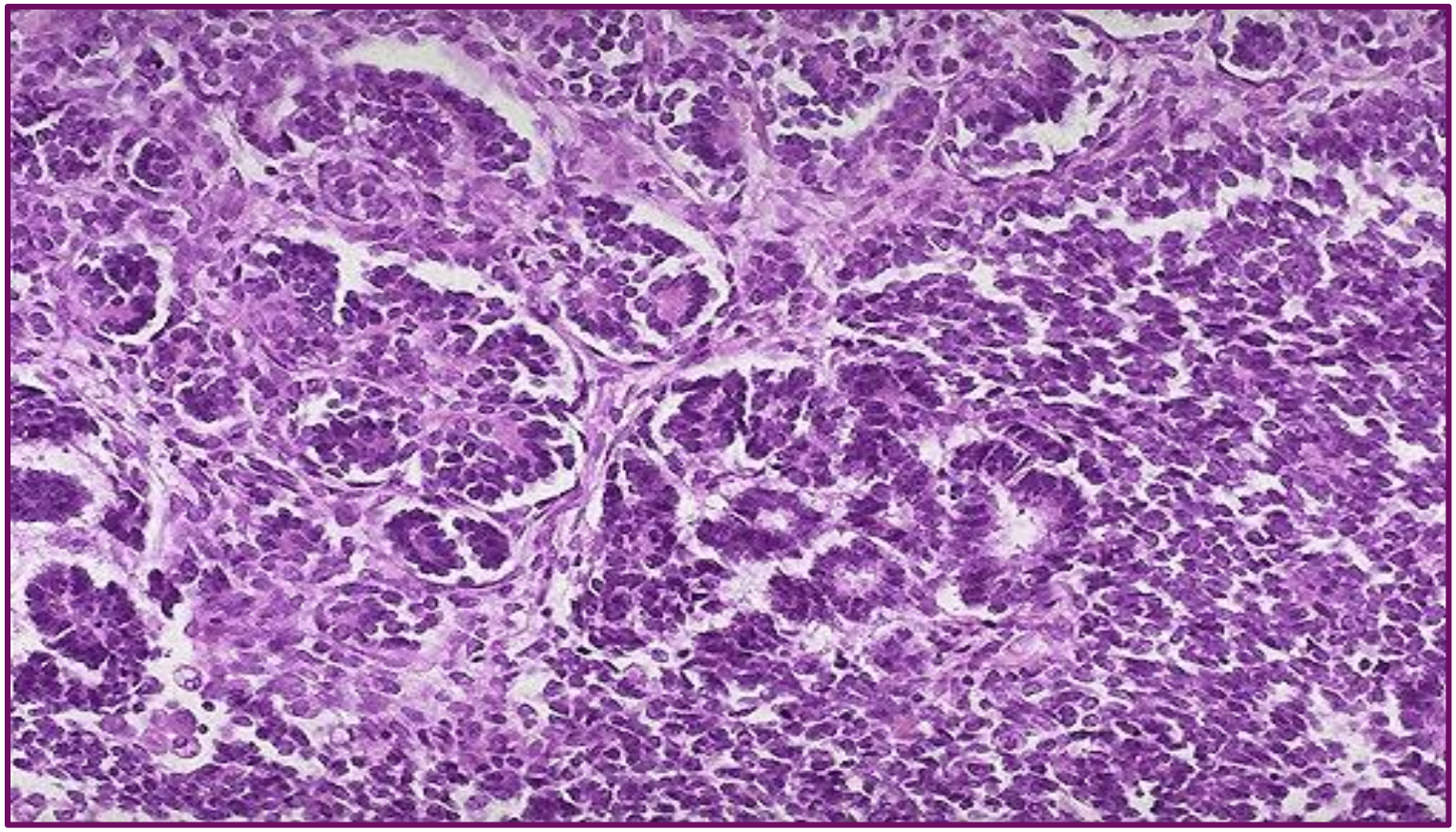
Blastema in WT consists of sheets of densely packed small blue cells with hyperchromatic nuclei, little cytoplasm and conspicuous mitotic activity.

Wilm's Tumor – Histopathology



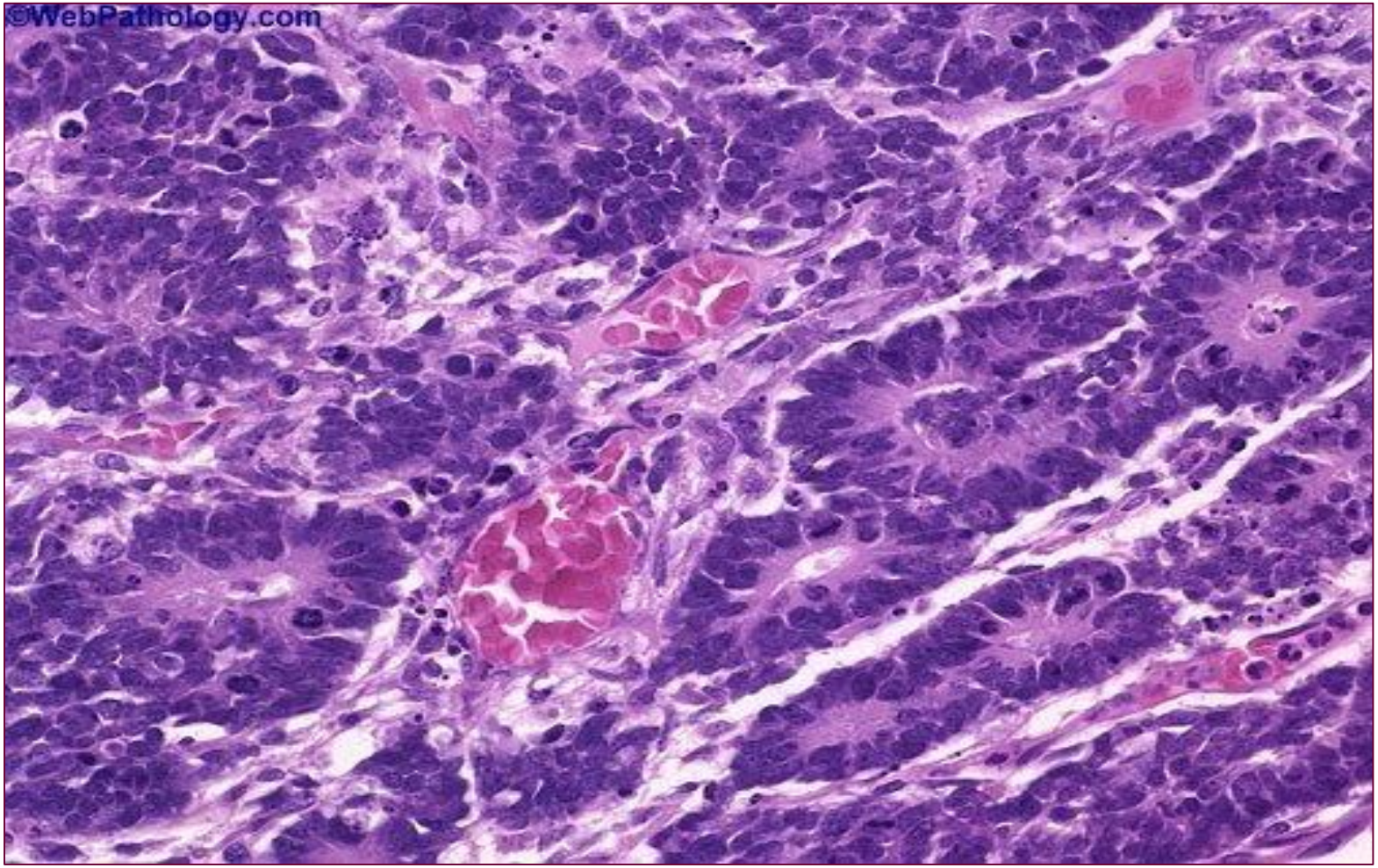
1. Spindle cell stroma.
2. Blastema.
3. Abortive glomeruli.

Wilm's Tumor – Histopathology



Wilm's tumor resembles the fetal nephrogenic zone of the kidney.
Three major components: Undifferentiated blastema cells , epithelial tissue which shows attempts to form primitive glomerular & tubular structures and mesenchymal (stromal) tissue

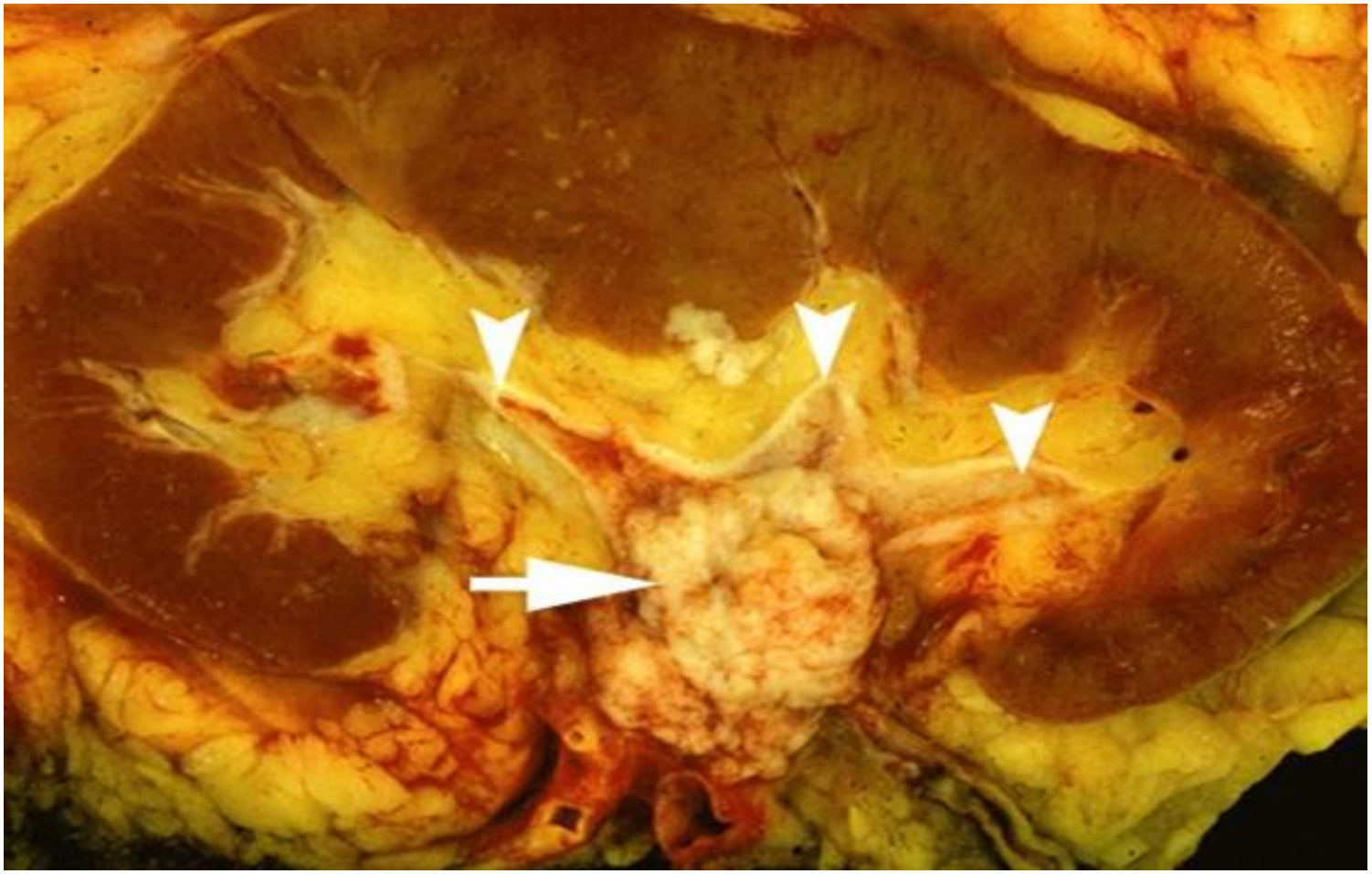
Wilm's Tumor – Histopathology



The epithelial component in this Wilm's tumor consists of primitive tubular structures and rosettes.

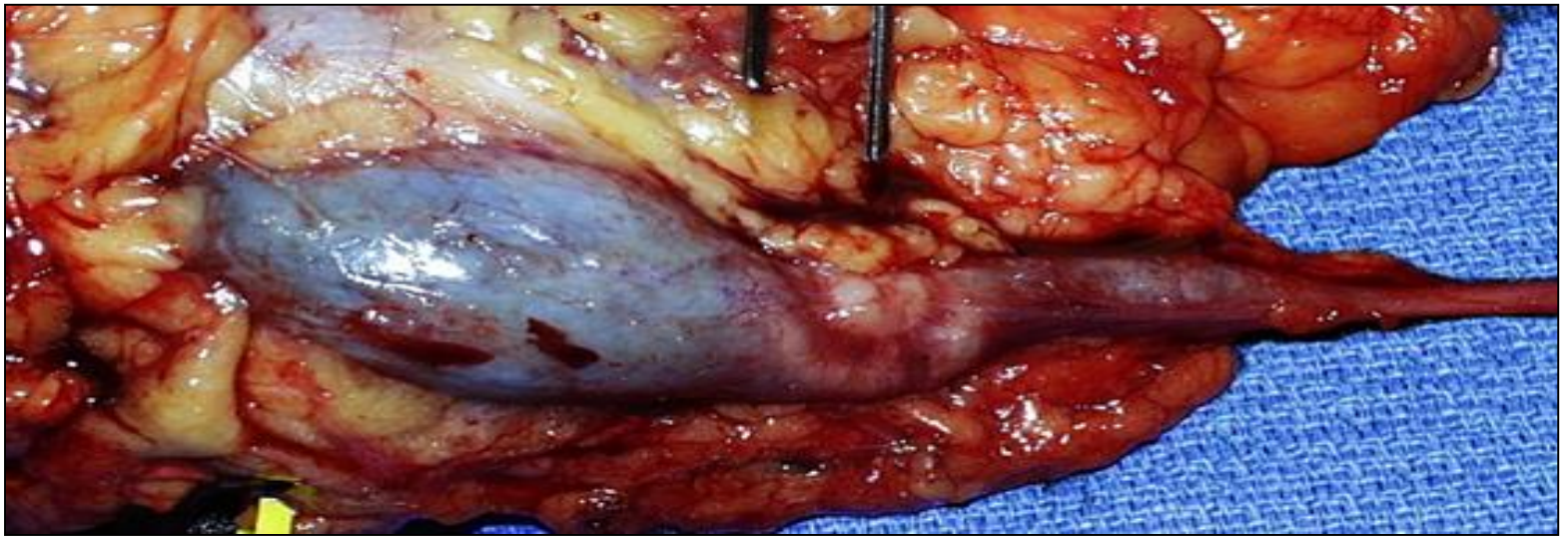
CARCINOMA OF RENAL PELVIS AND URETER

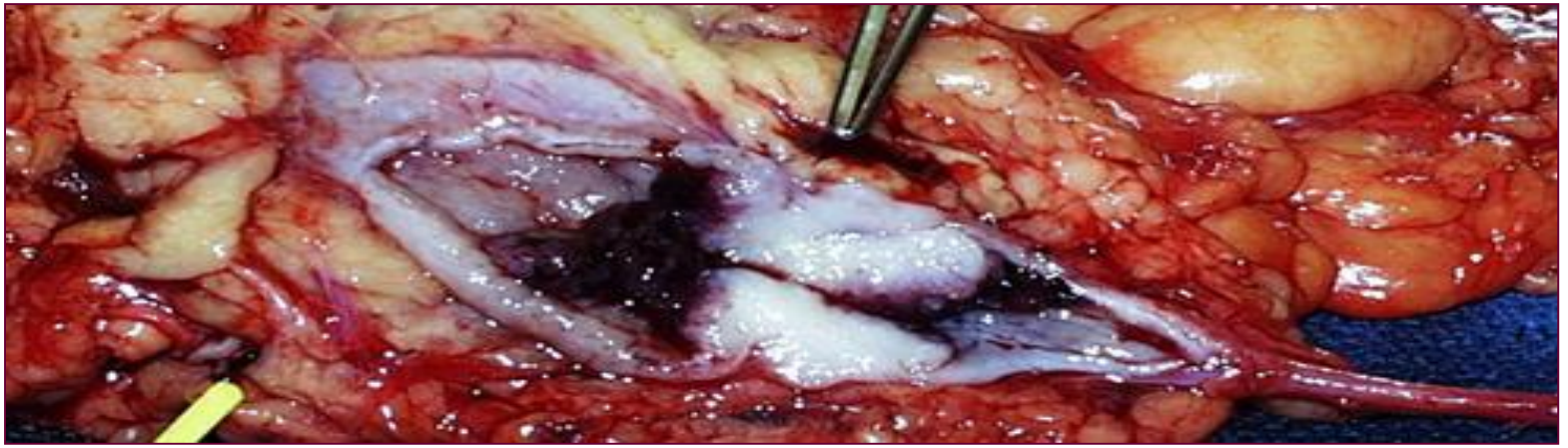
Urothelial (Transitional) Carcinoma of Renal Pelvis



More commonly infiltrative and prognosis is worse than urothelial carcinoma of the bladder

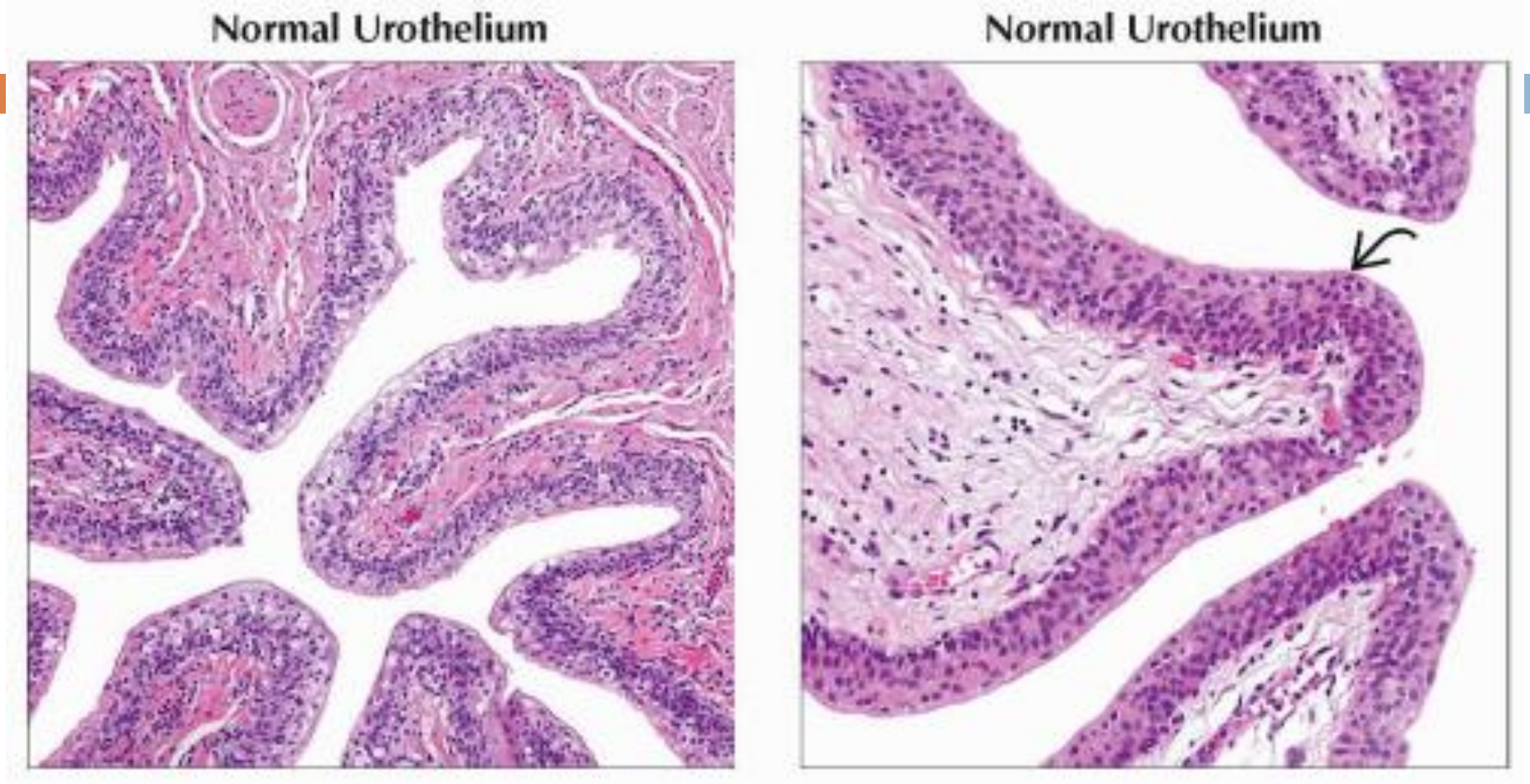
Urothelial Carcinoma involving Ureter - Gross





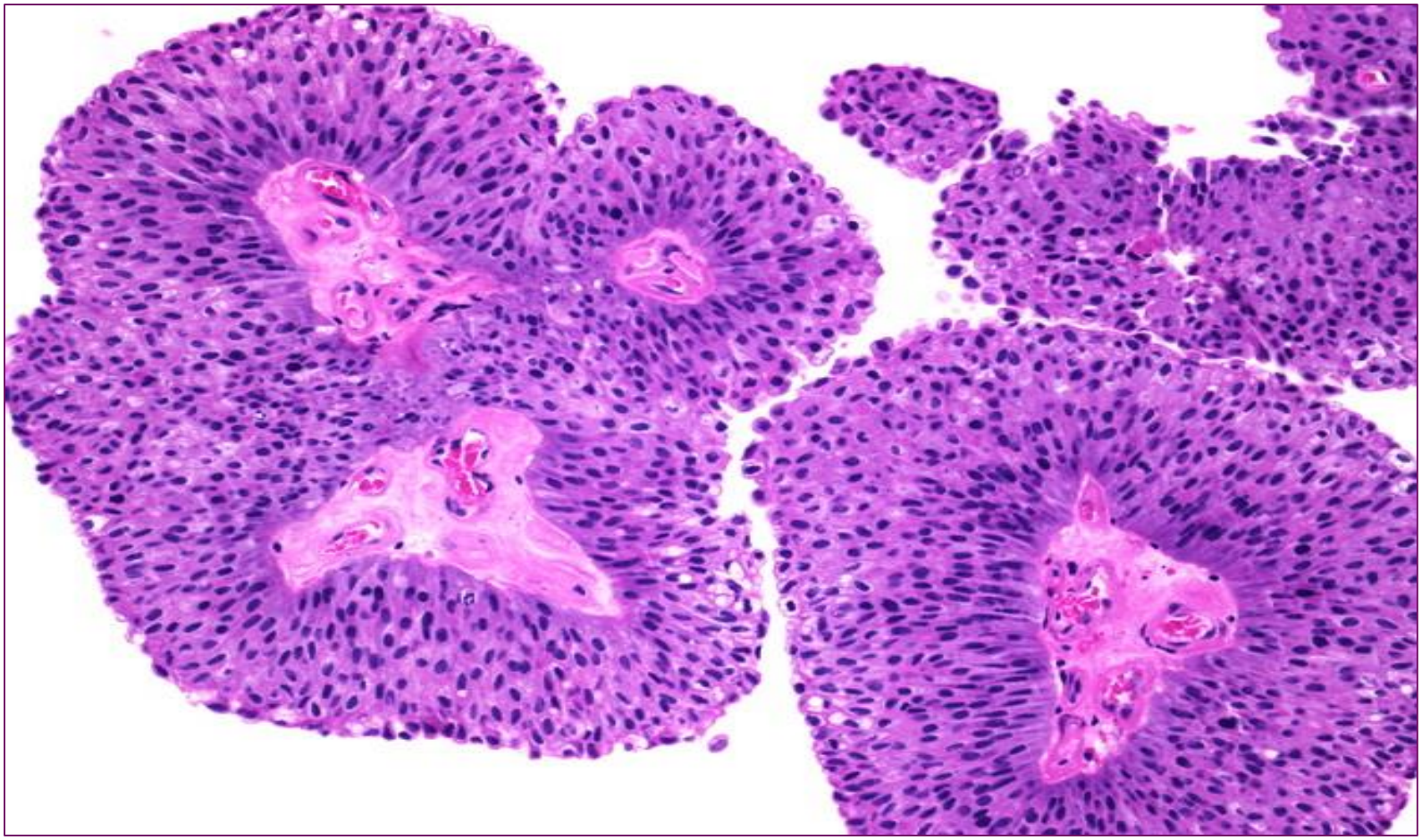
A nephroureterectomy specimen showing bulbous expansion of proximal ureter near the renal pelvis caused by papillary urothelial carcinoma

Normal Urothelium



Adopted from: Gakis G et al: Sequential resection of malignant ureteral margins at radical cystectomy: a critical assessment of the value of frozen section analysis. World J Urol. 29(4):451-6, 2011

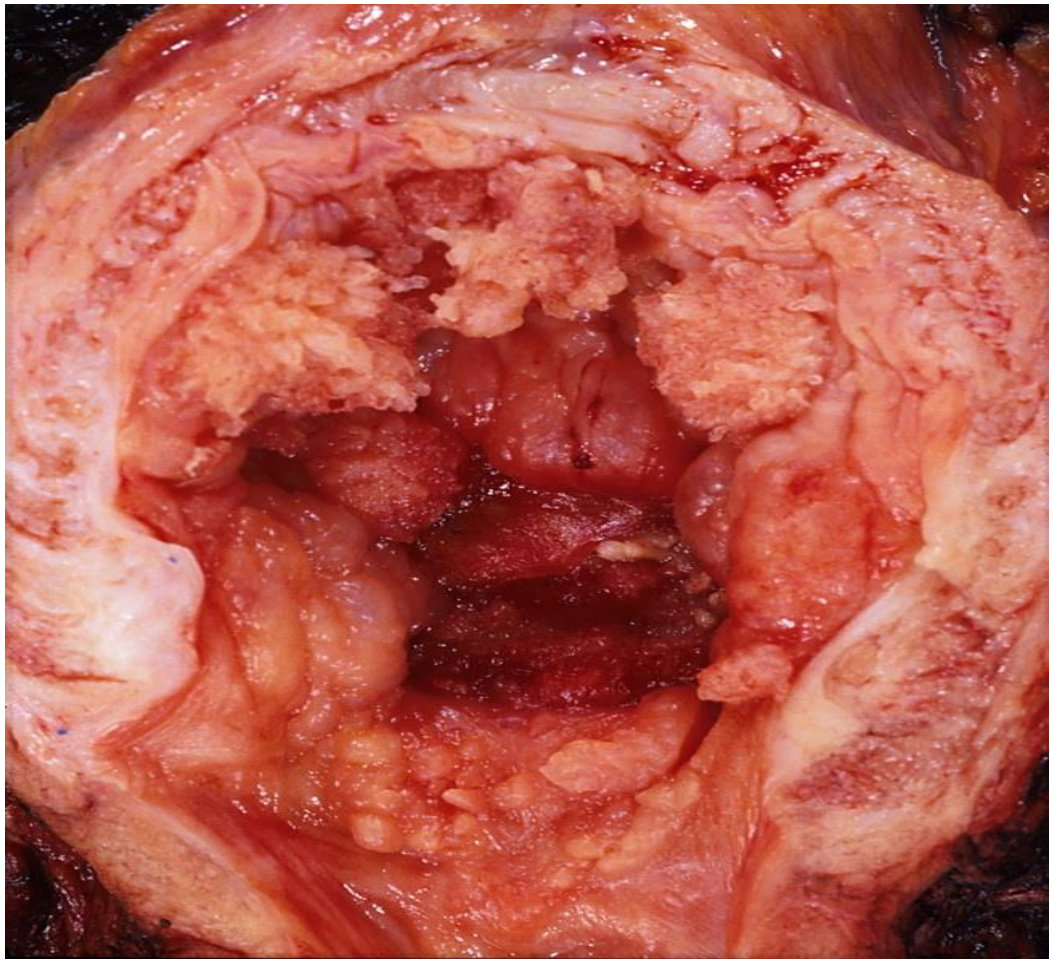
Papillary Urothelial carcinoma of the renal pelvis – Low Grade



Low-grade papillary urothelial carcinoma shows minimal cytologic and architectural atypia. Adjacent papillary fronds may fuse, as seen in this image

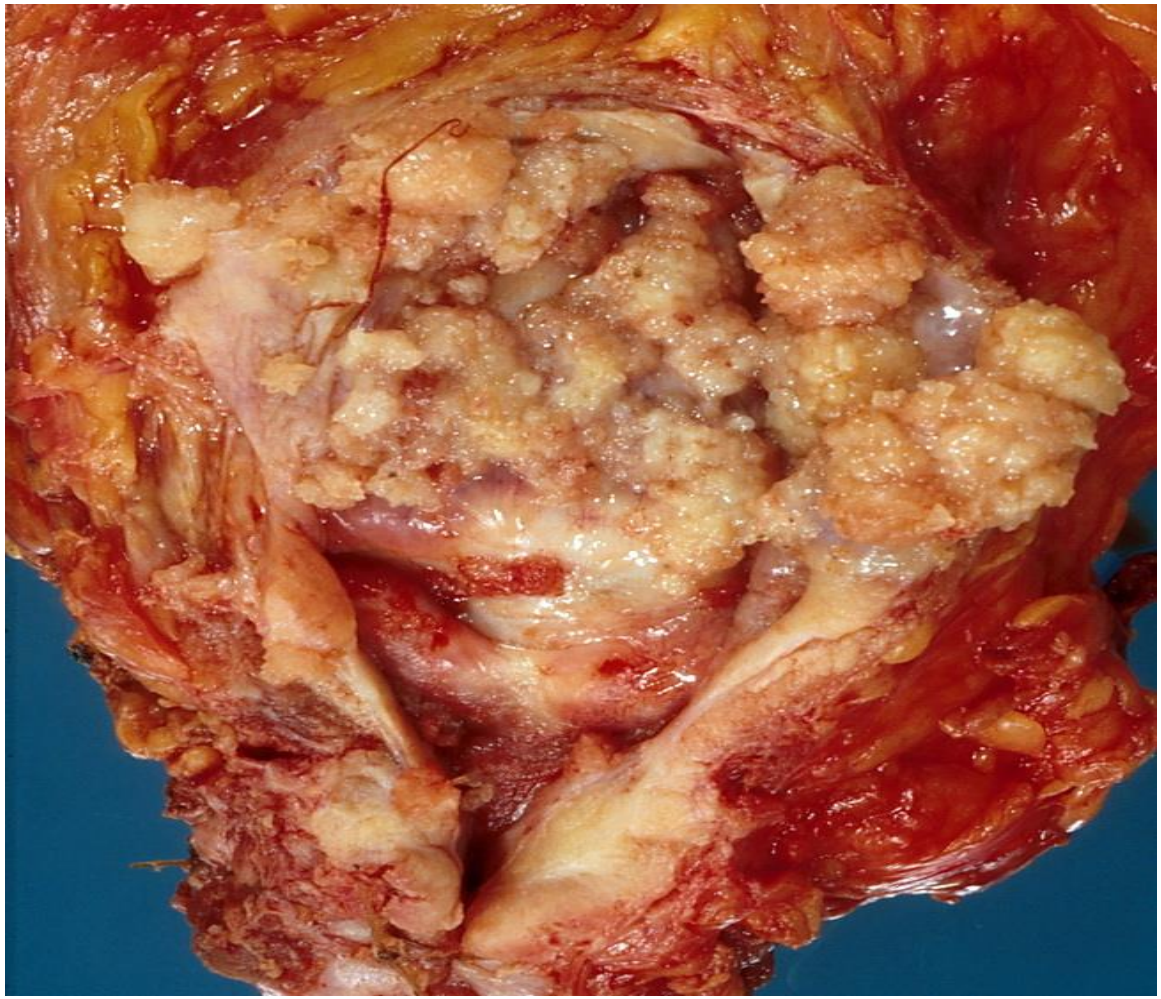
CARCINOMA OF THE URINARY BLADDER

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



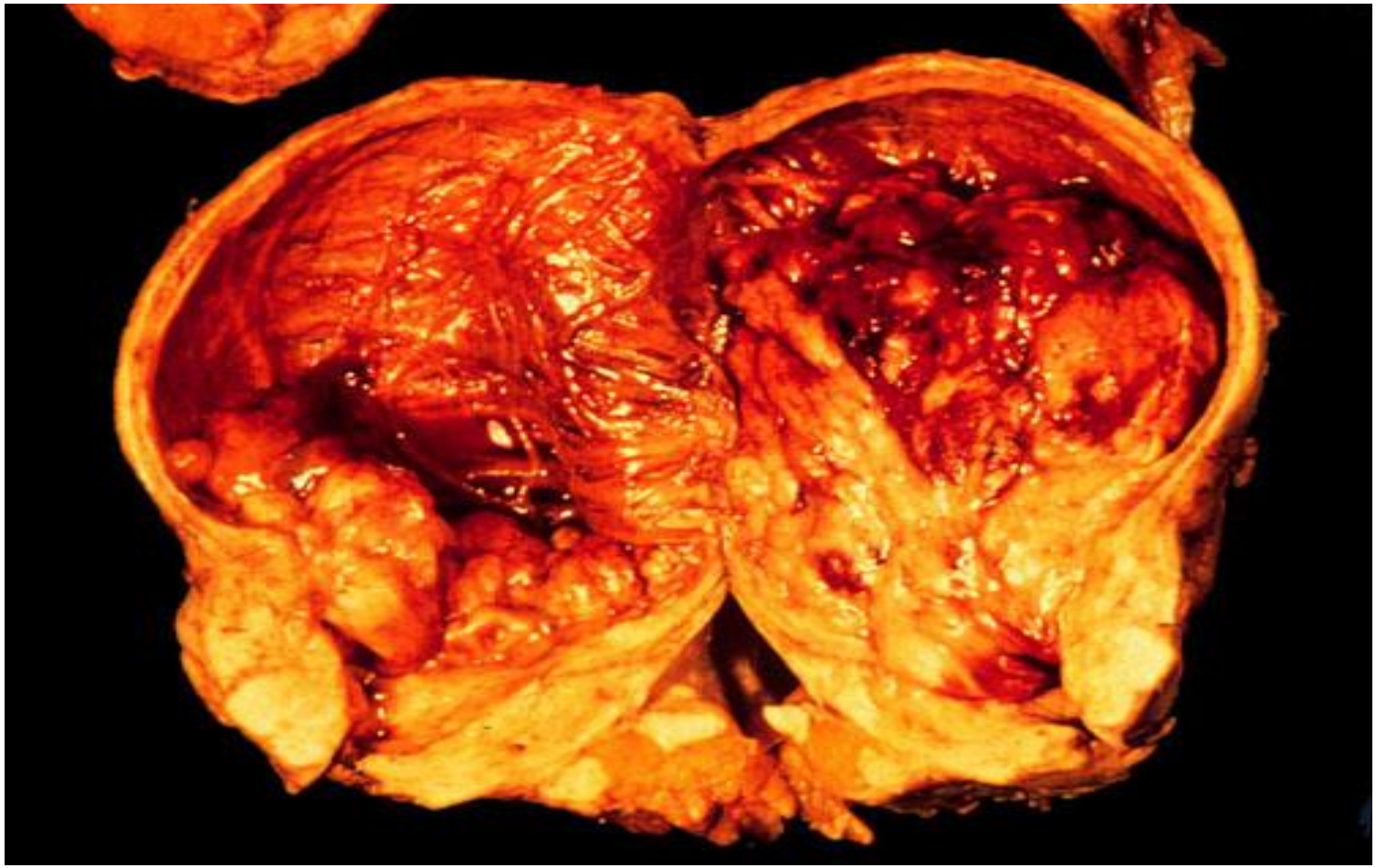
90% of bladder cancers are transitional cell carcinoma. The other 10% are squamous cell carcinoma, adenocarcinoma, sarcoma, small cell carcinoma, and secondary metastases

Papillary Urothelial Carcinoma of Bladder - Gross



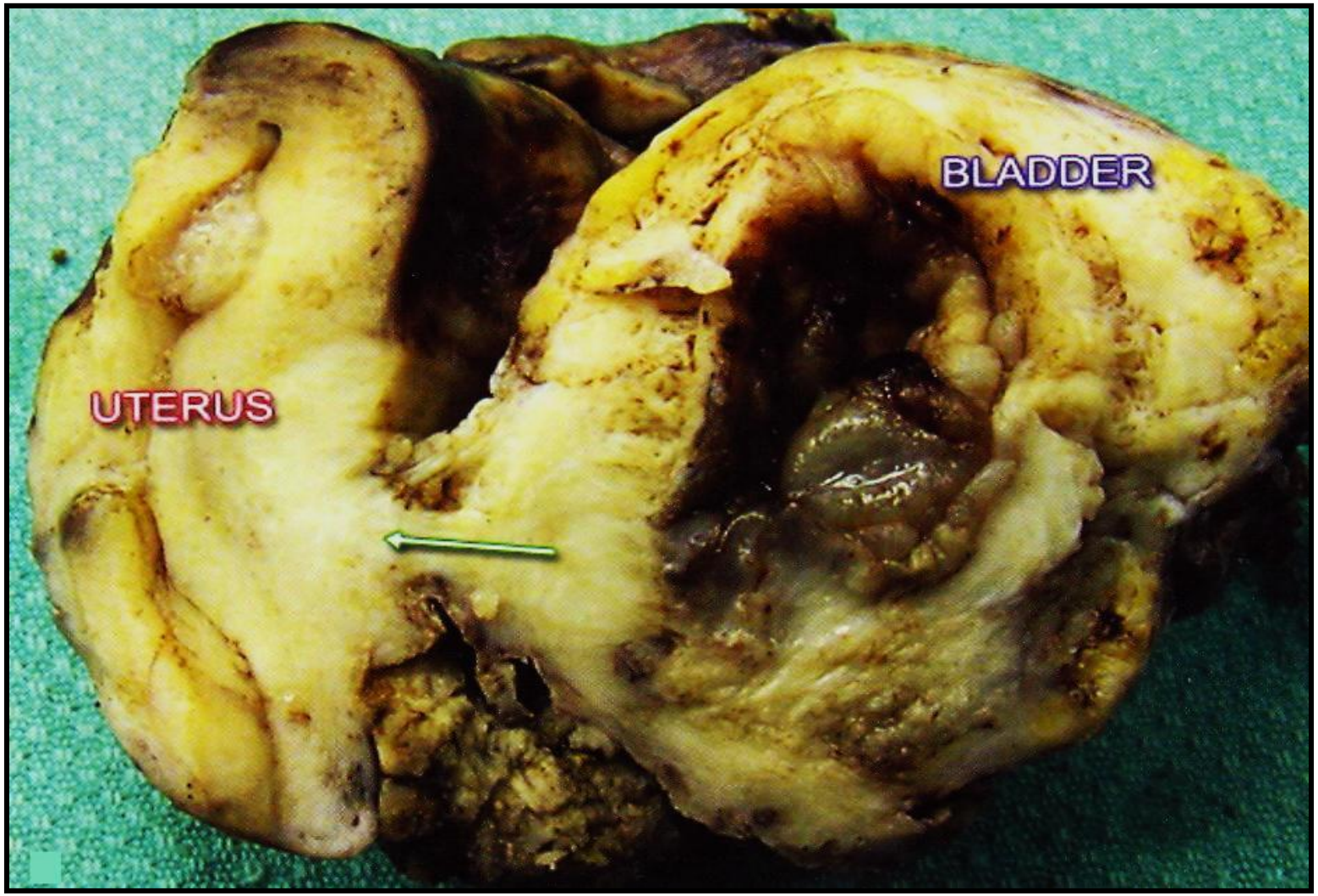
Radical cystectomy specimen showing multifocal papillary urothelial carcinoma..

Transitional Carcinoma of Bladder - Gross



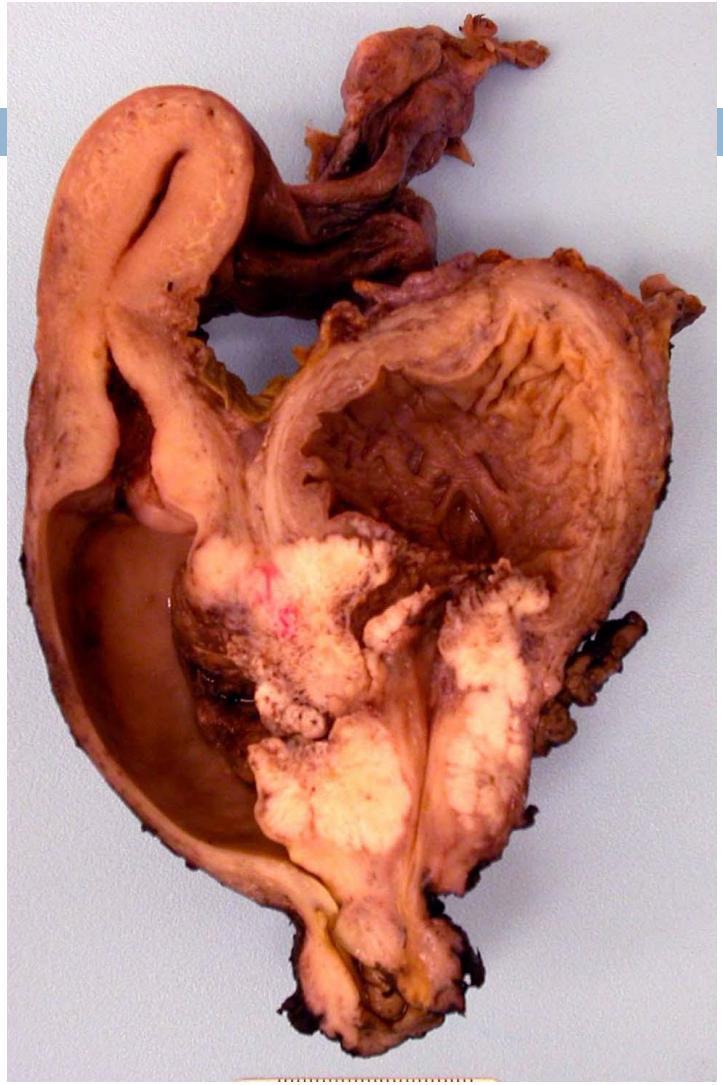
The mucosa of the open urinary bladder appears edematous. There are several whitish or red nodules and patches indicative of a multi-focal nature of this tumor

Bladder Tumor invading the Uterus – Gross



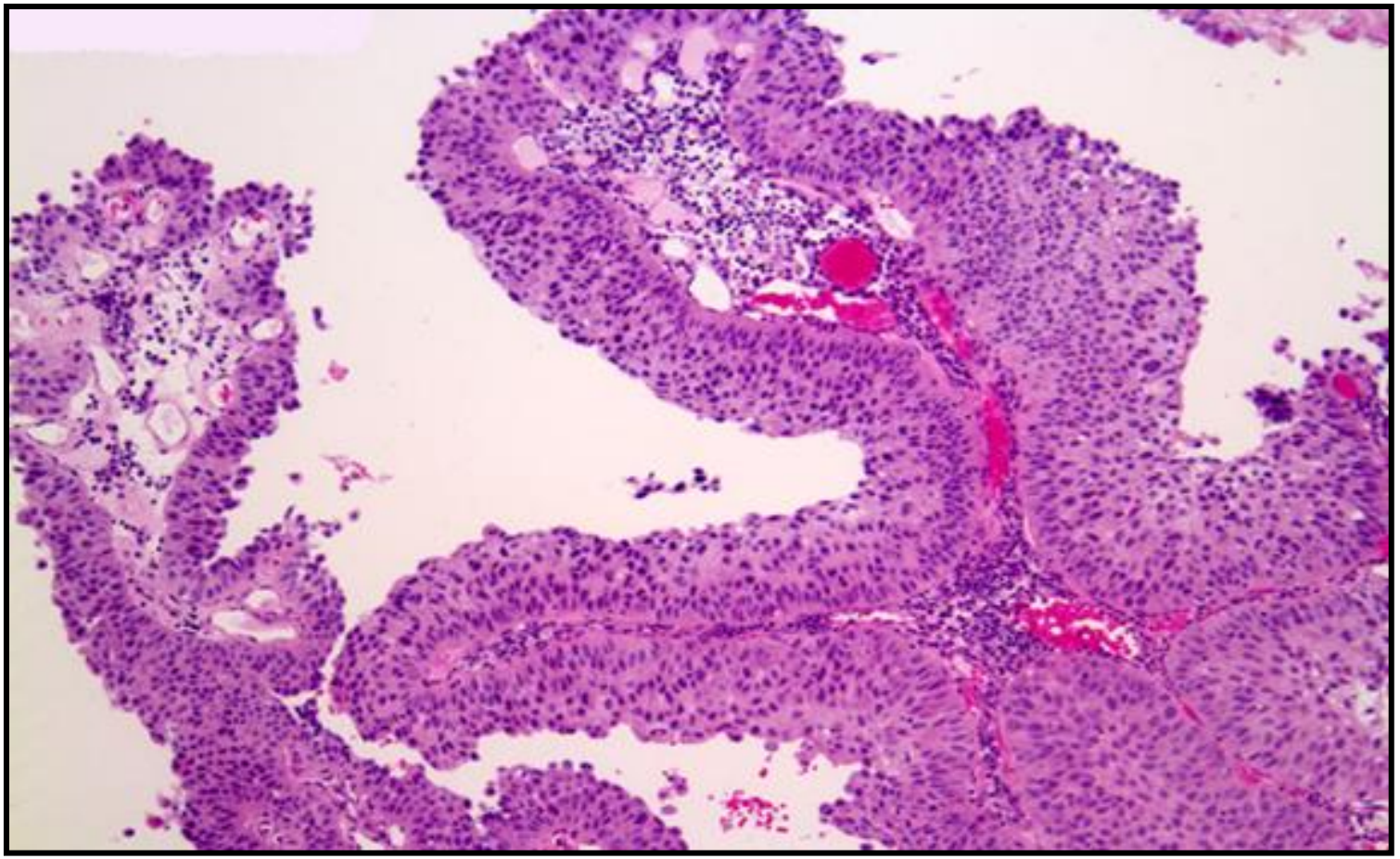
Urinary bladder carcinoma infiltrating the urinary bladder wall with extension to the uterus .

Bladder Tumor invading the Uterus – Gross



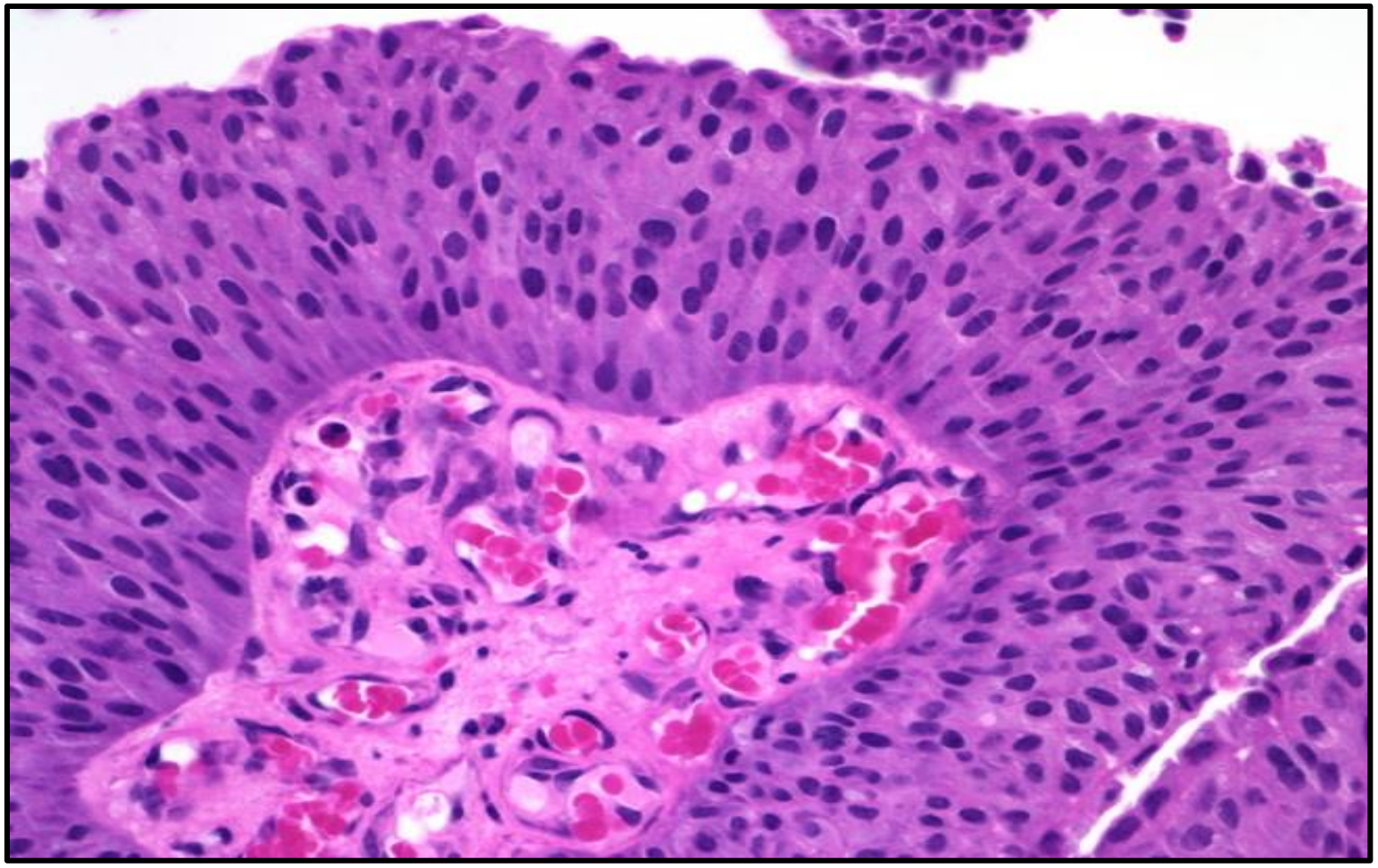
Urinary bladder carcinoma infiltrating the urinary bladder wall with extension to the uterine cervix and vagina.

Papillary Urothelial carcinoma – Low Grade



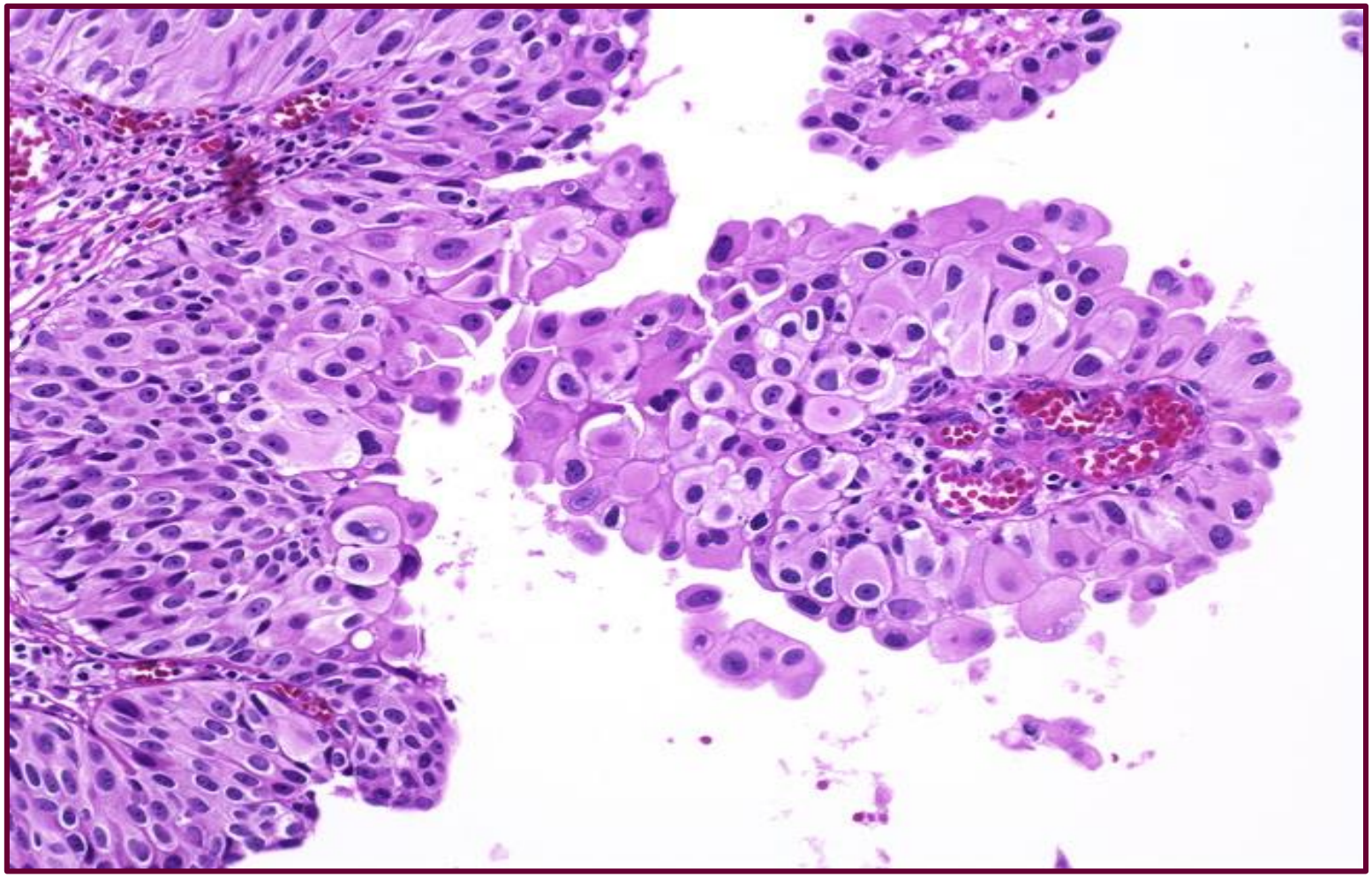
The low grade tumors show overall preservation of cell polarity, few mitoses, and lack of significant morphologic atypia. This exophytic papillary tumor shows multiple finger-like projections lined by multiple layers of urothelium (transitional epithelium)

Papillary Urothelial Carcinoma – Low Grade



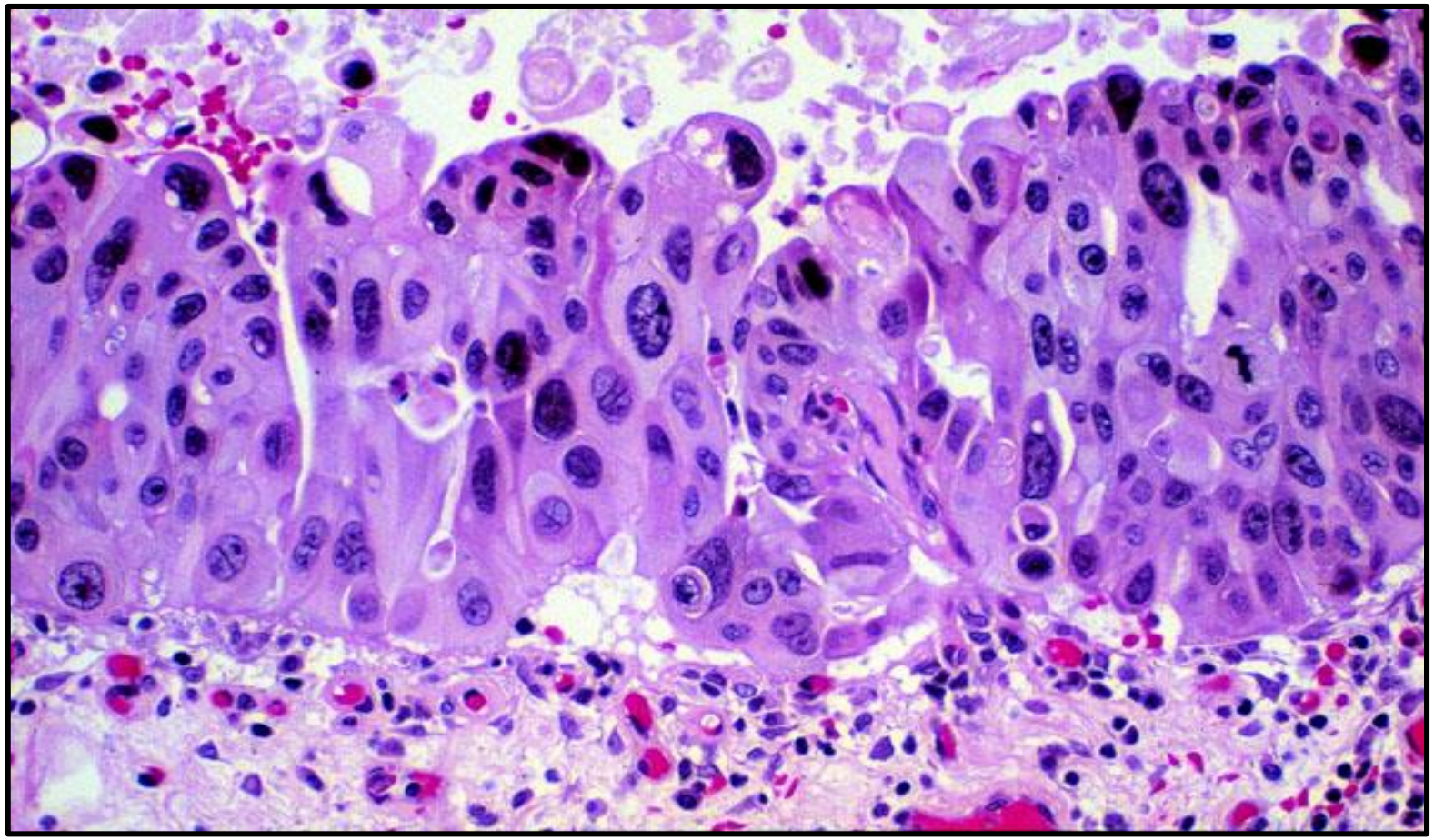
Urothelial cells forming papillae and showing hyperchromatic nuclei with some typical mitoses.

Papillary Urothelial carcinoma – High Grade



This high-grade papillary urothelial carcinoma shows highly pleomorphic cells with voluminous cytoplasm

Urothelial (Transitional) carcinoma – HPF



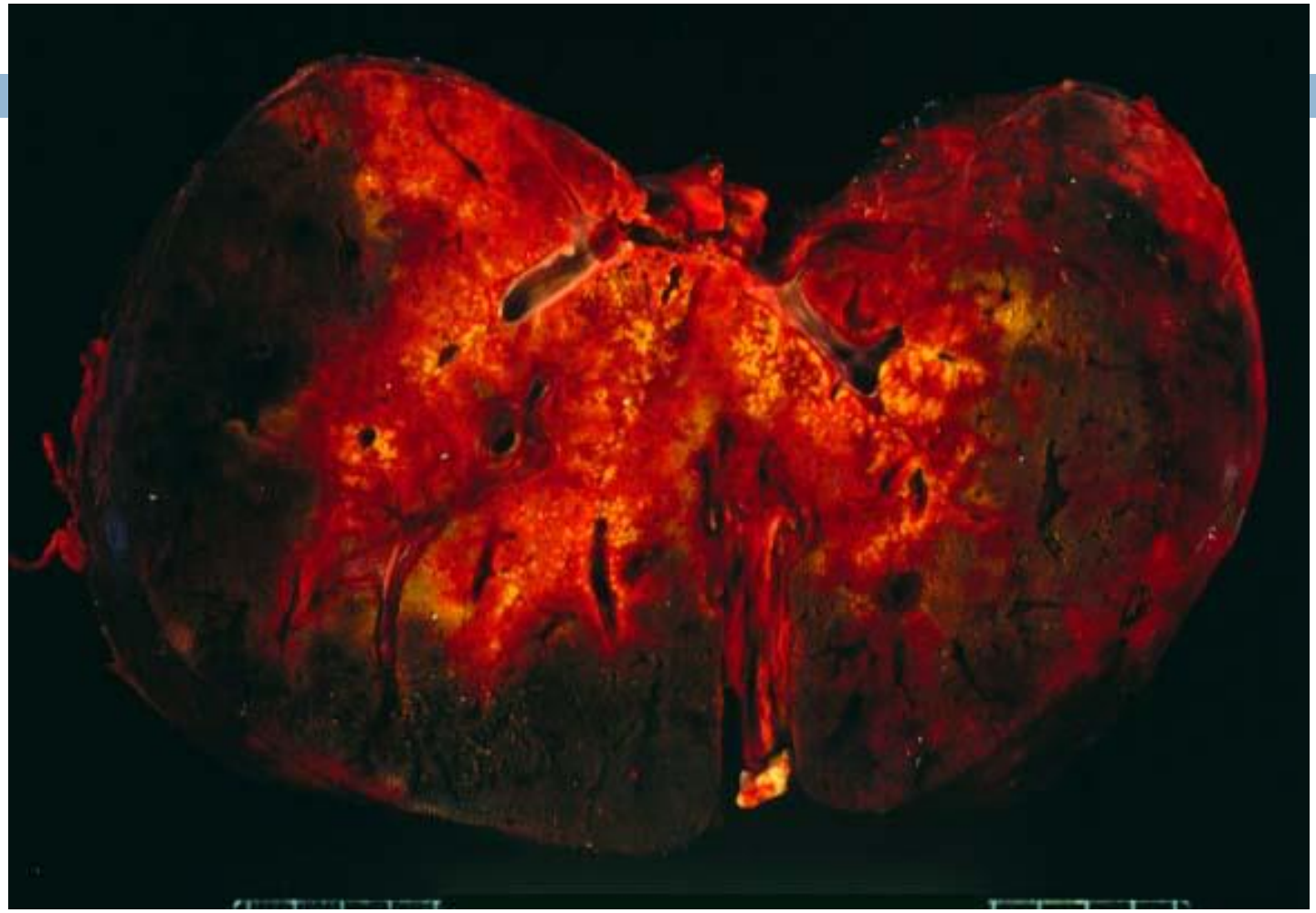
Almost all cases of Bladder carcinomas originate from the transitional epithelium. Bladder carcinoma might be squamous cell in nature (infection with Schistosoma haematobium) . Rarely, it presents as adenocarcinoma.

Predisposing conditions and exposures that can lead to Urothelial (Transitional) carcinoma :

- *Exposure to aniline and Azo dyes.*
- *Cigarette smoking.*
- *Cyclophosphamide.*

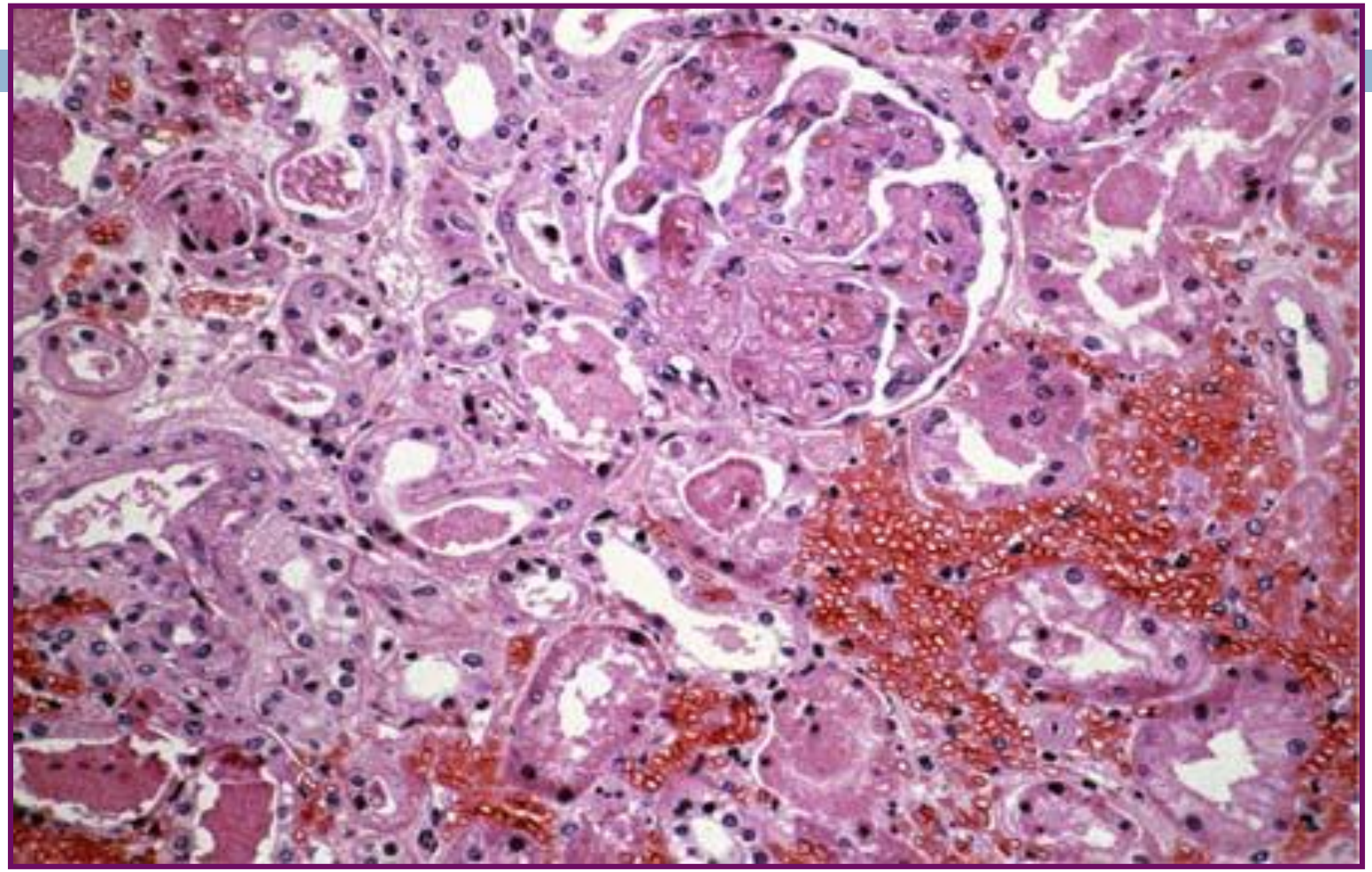
PATHOLOGY OF RENAL ALLOGRAFT

Hyperacute Rejection



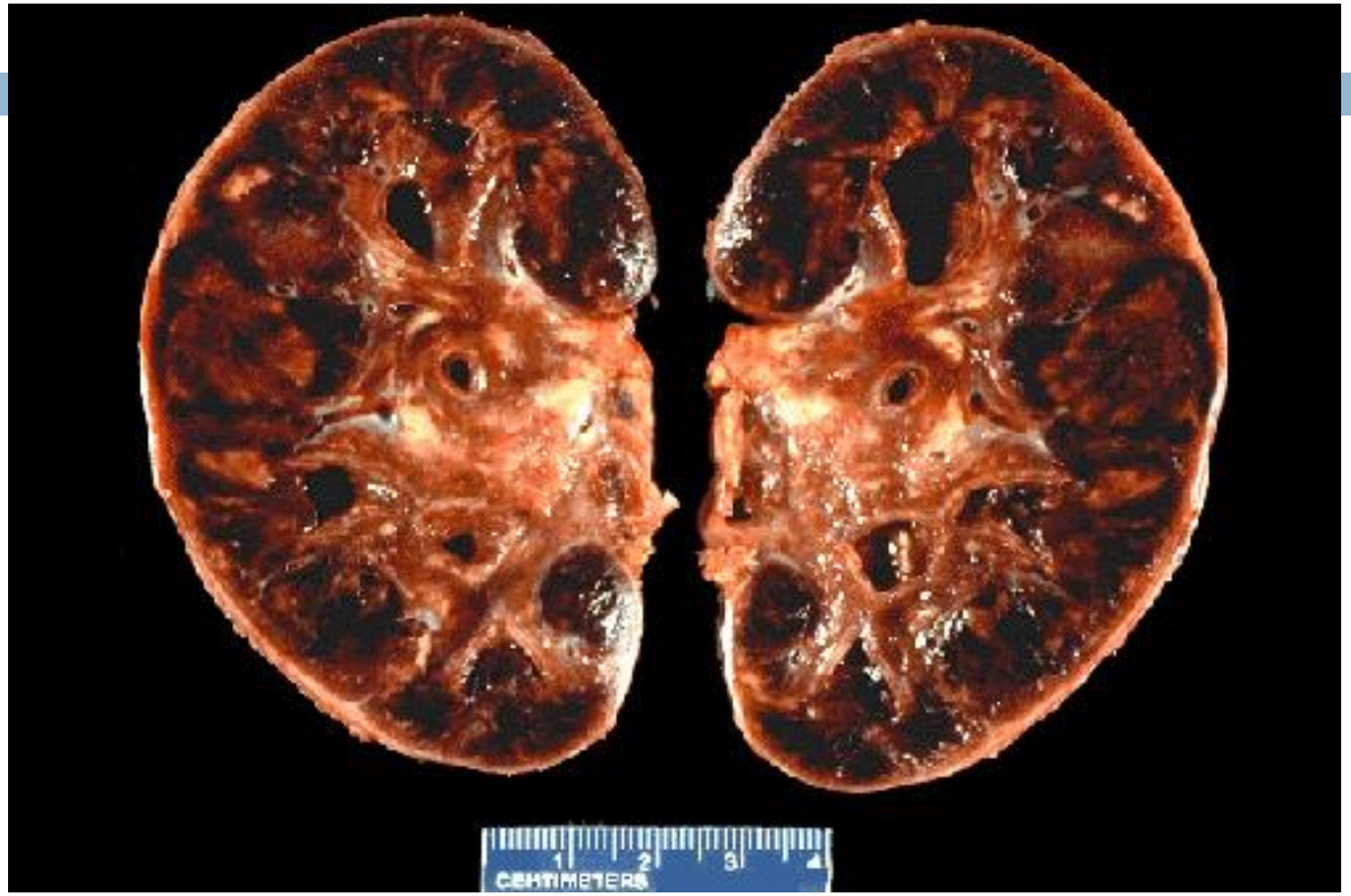
This kidney was removed because of hyperacute transplant rejection. The kidney is markedly enlarged, swollen with widespread hemorrhagic infarct/necrosis.

Hyperacute Allograft Rejection



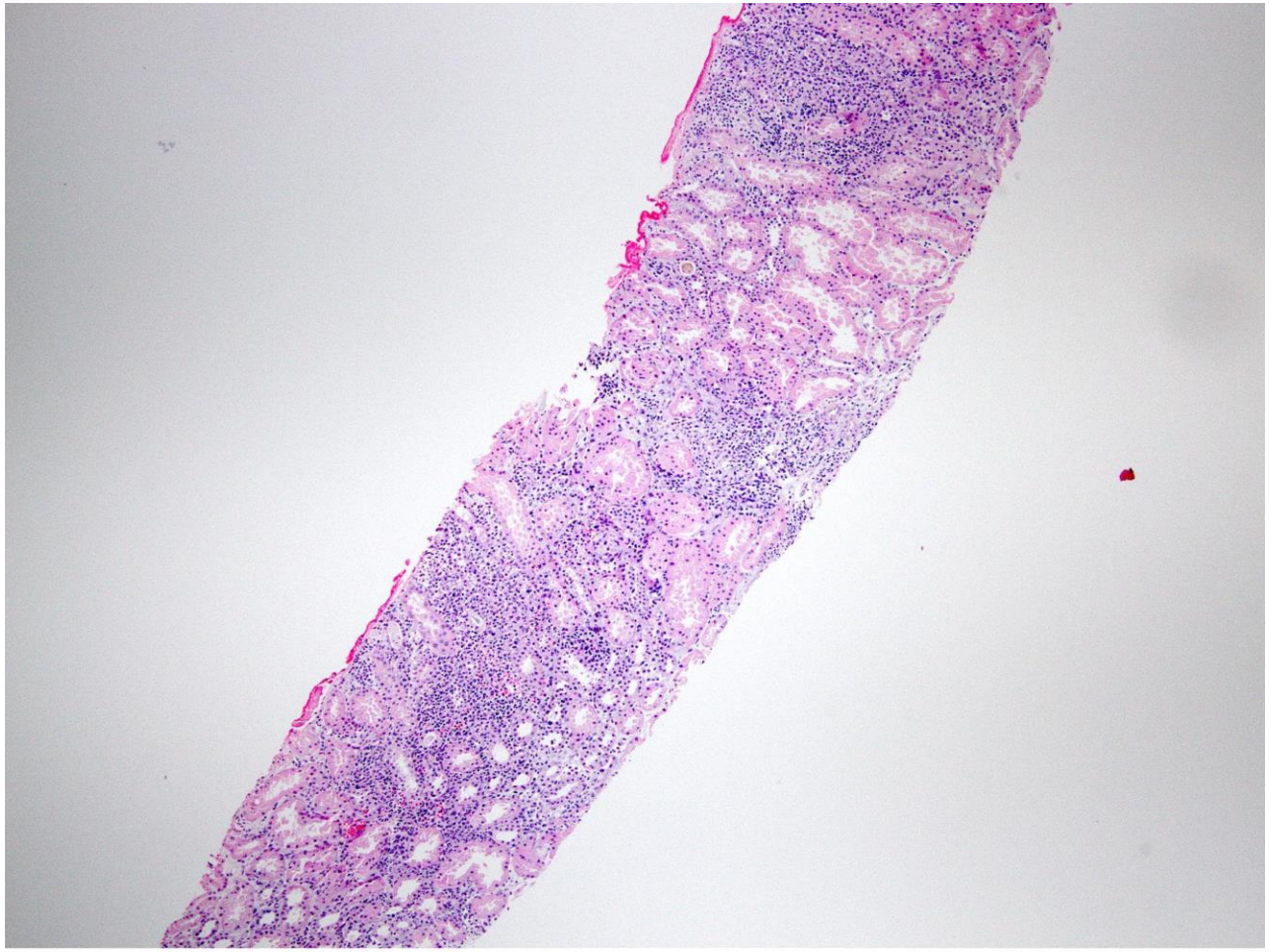
Hyperacute rejection → the glomerulus shows severe ischemic injury and fibrin thrombi. The interstitum shows edema and hemorrhage.

Acute Allograft Rejection



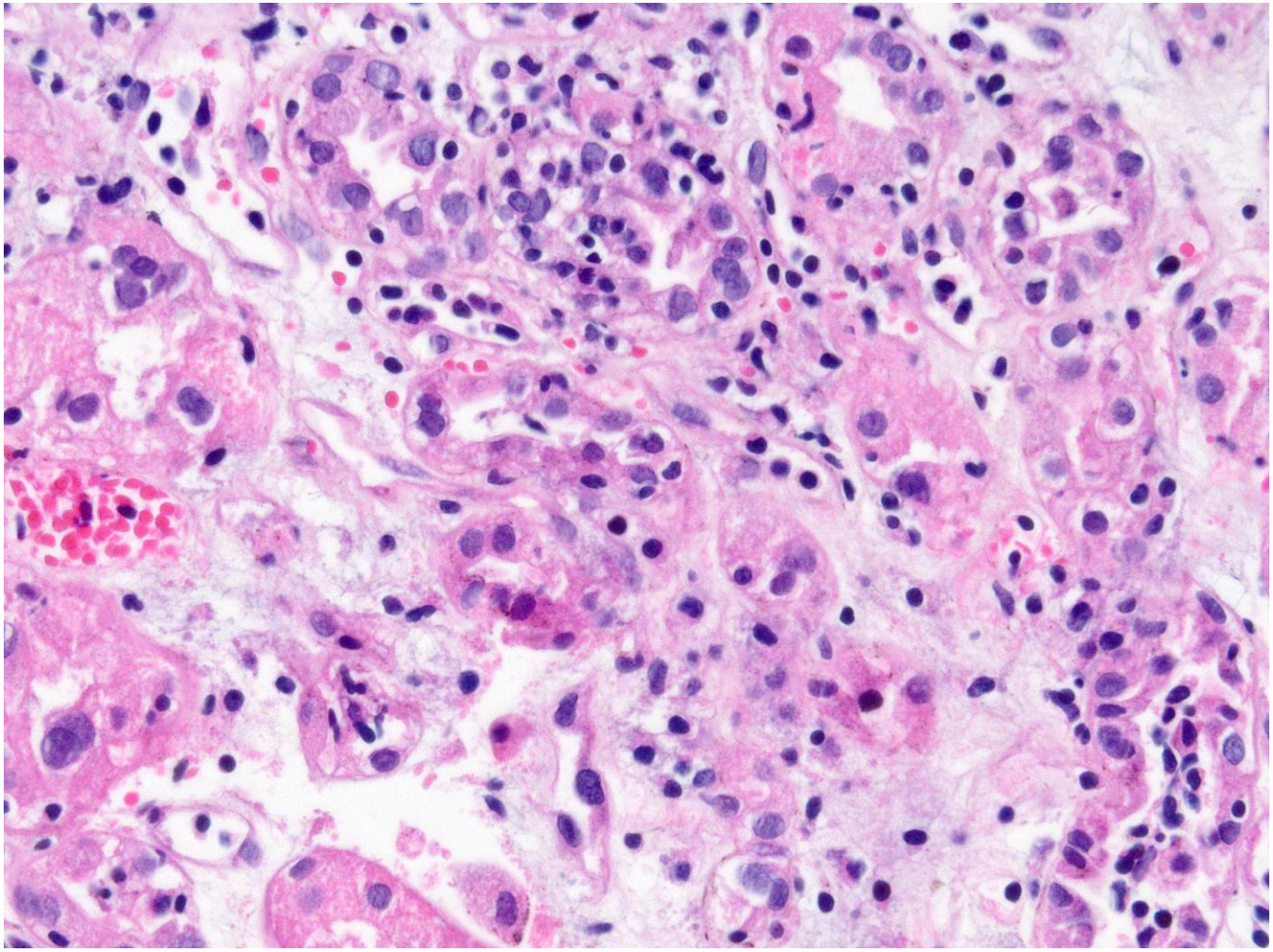
This kidney was removed because of acute transplant rejection. Note the swollen and hemorrhagic appearance of this entire kidney.

Acute Cellular Allograft Rejection



Low power demonstrates prominent inflammatory infiltrate in the tubulointerstitial space

Acute Cellular Allograft Rejection



There is infiltration of tubules by lymphocytes = tubulitis → hallmark of acute cellular rejection

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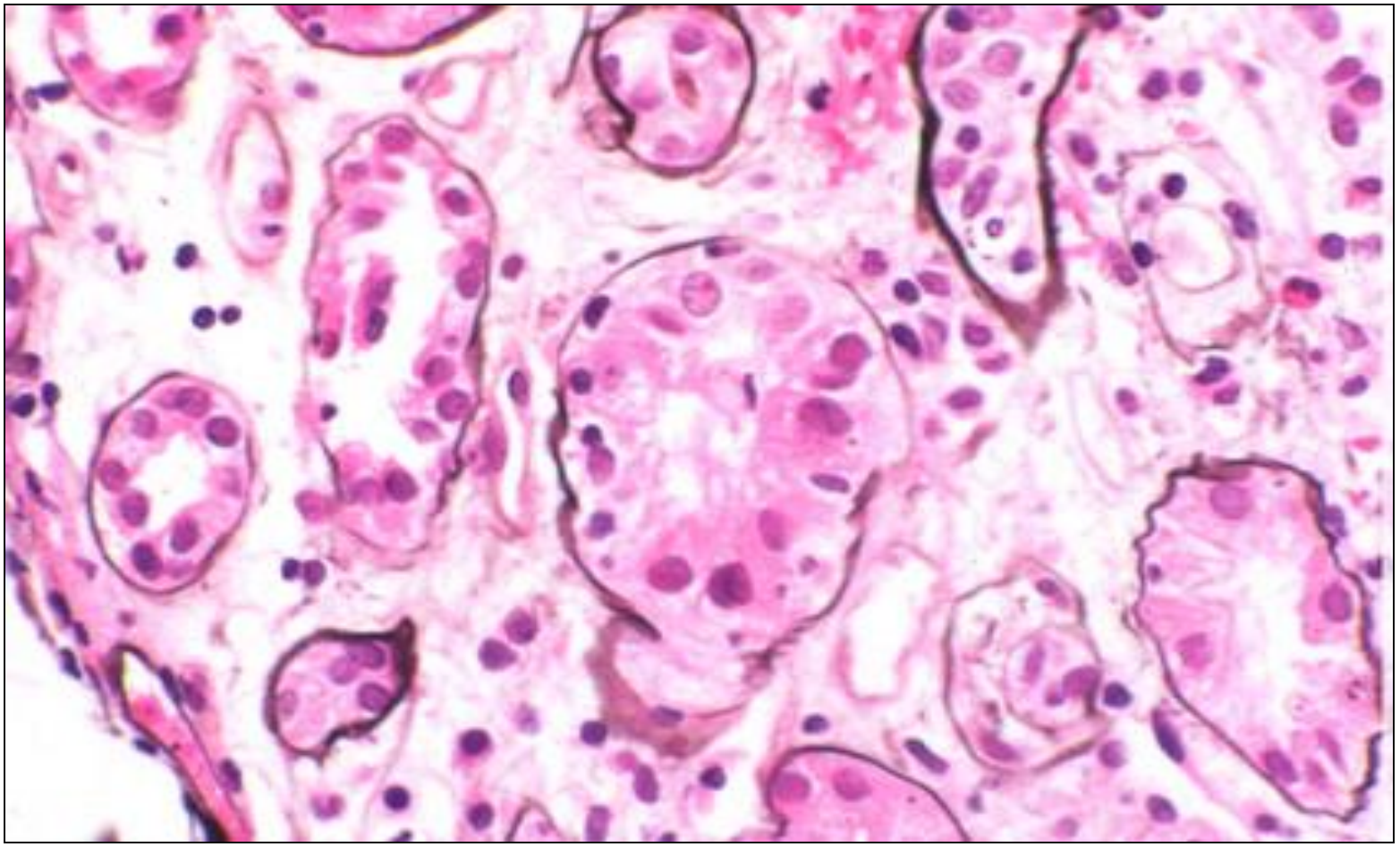
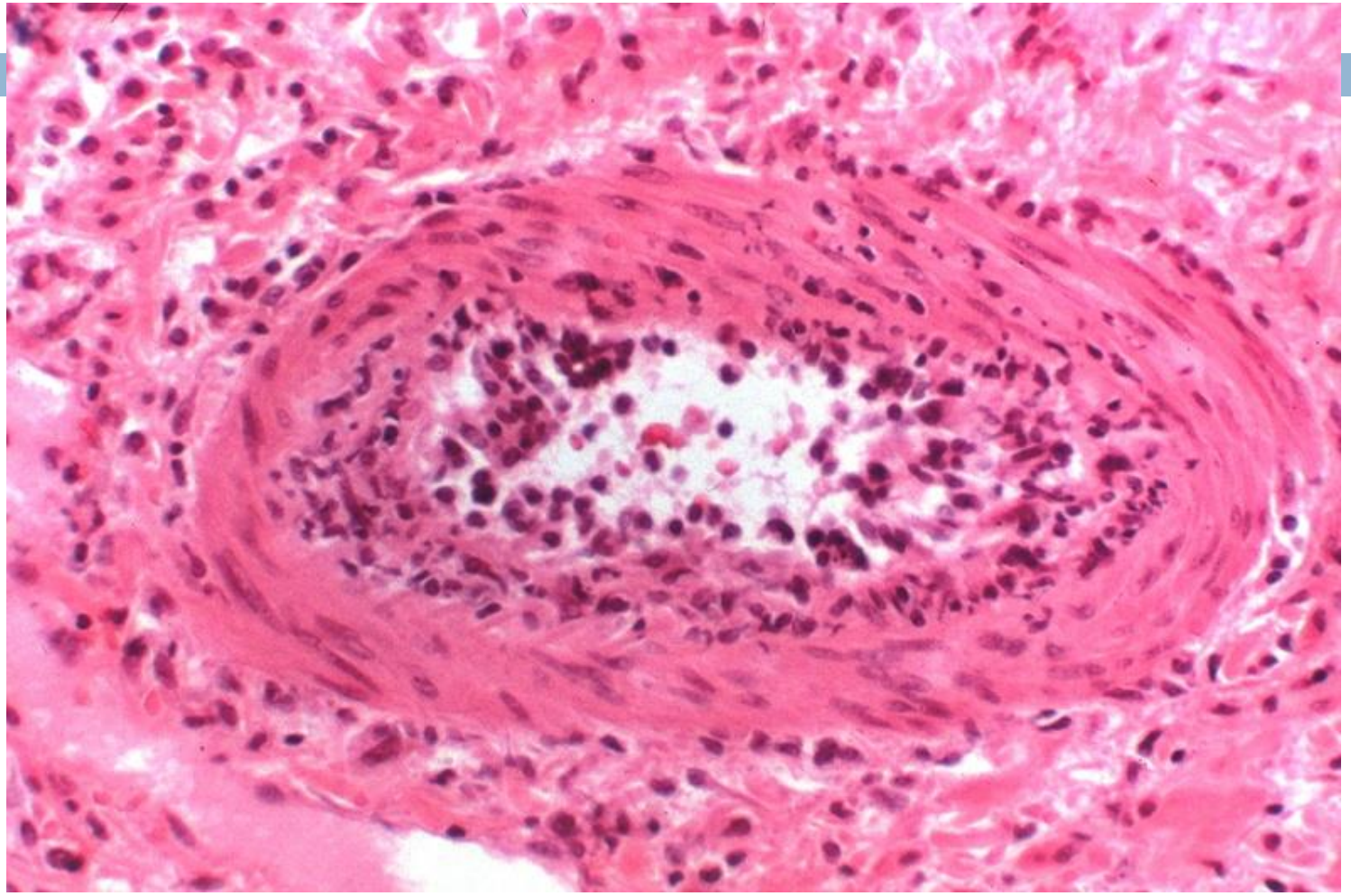


Tubulitis = infiltration of tubular epithelium by lymphocytes, is the hallmark of acute cellular rejection

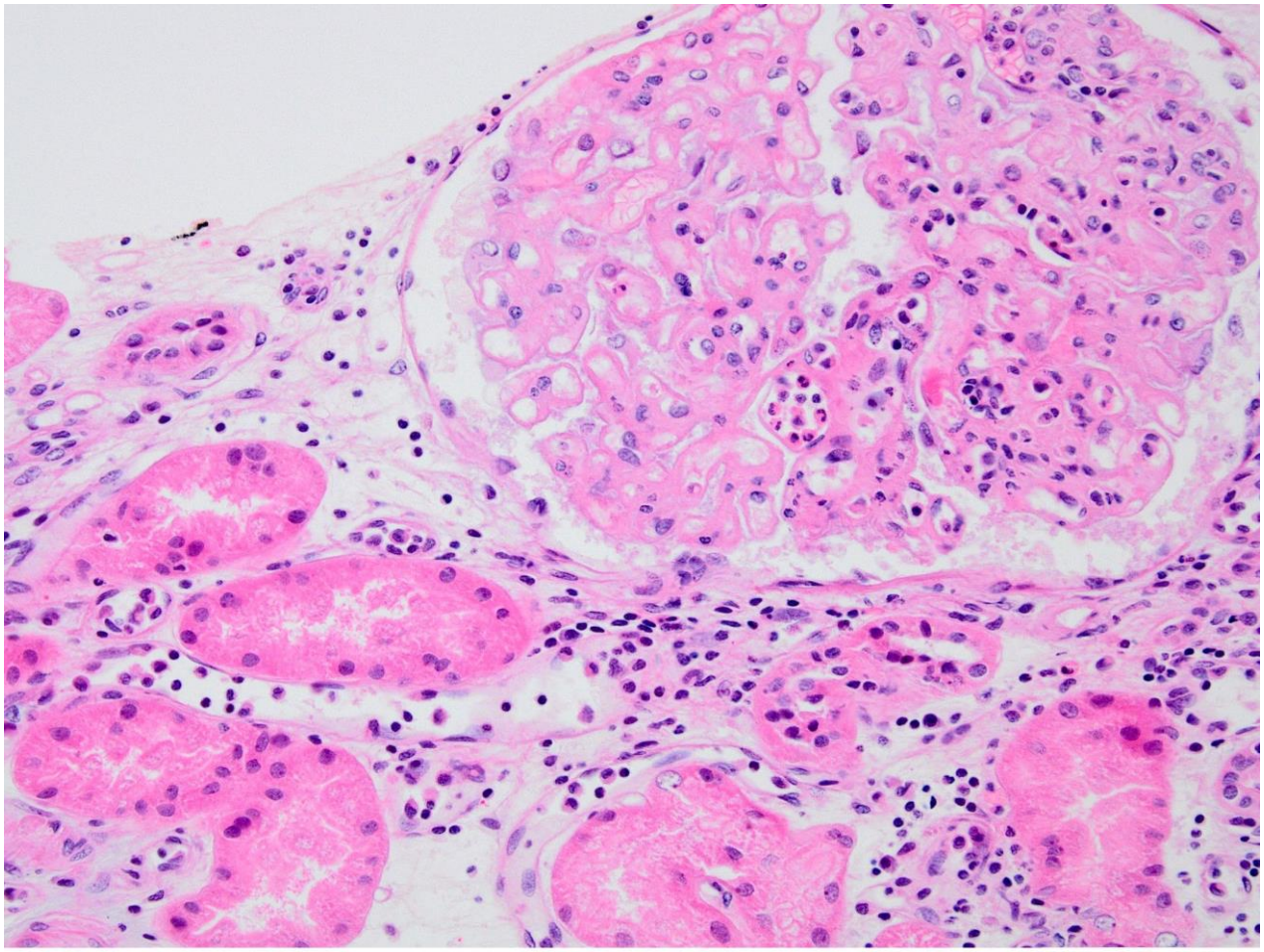
Acute Rejection - vasculitis



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

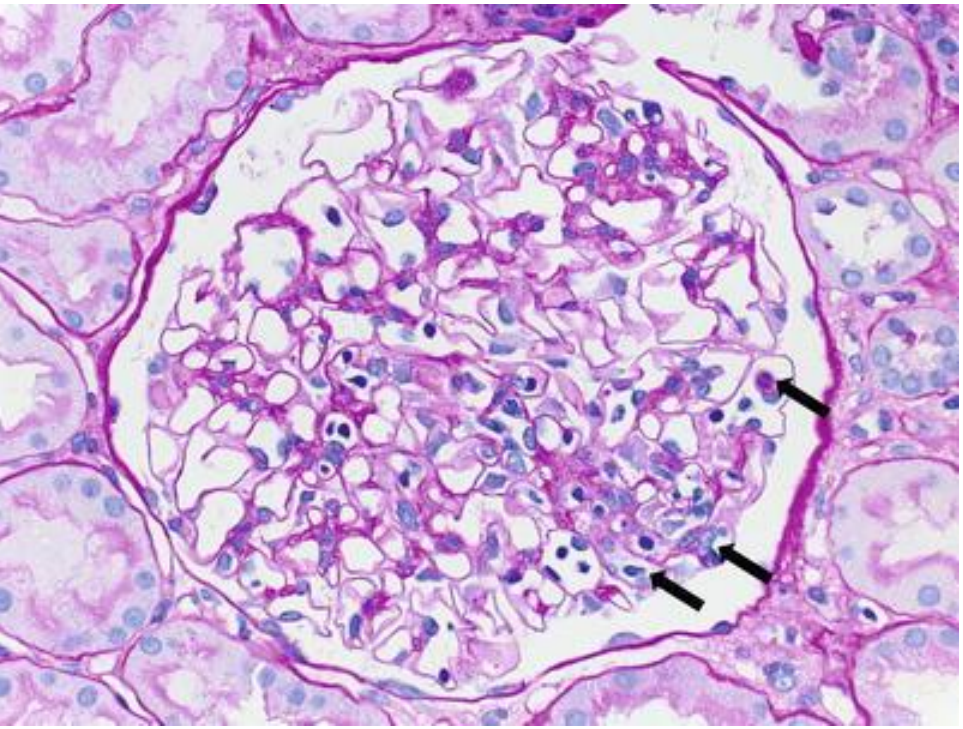
Vasculitis/arteritis can be seen in both acute cellular rejection & acute antibody mediated rejection.

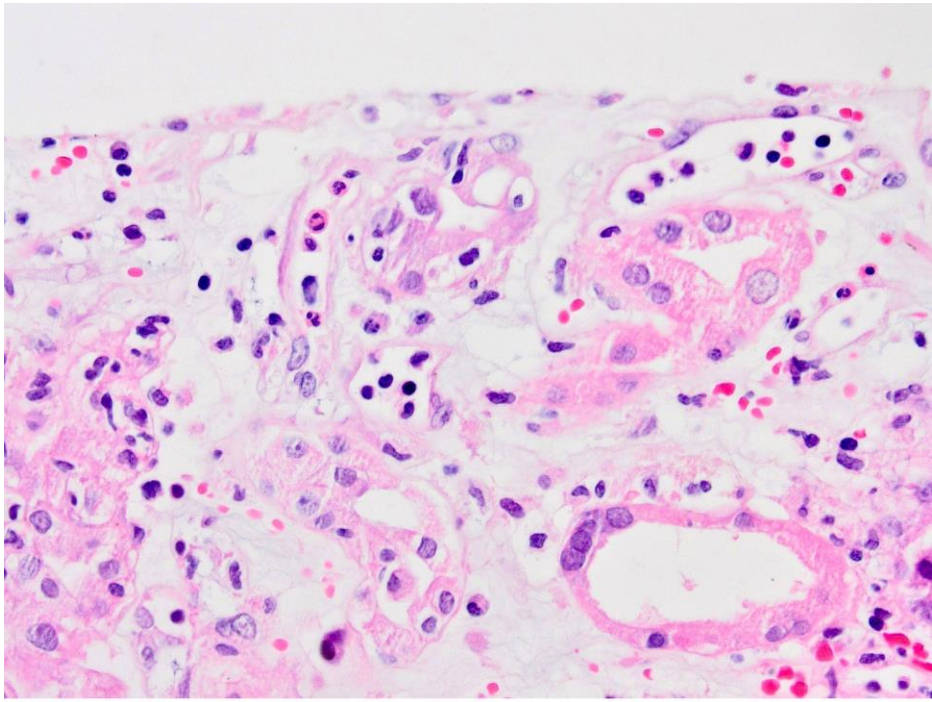
Acute antibody mediated Rejection



Acute antibody-mediated rejection. There is neutrophilic infiltrate in the glomerular capillaries (glomerulitis) and peritubular capillaries (capillaritis). Also there is interstitial edema.

Acute antibody mediated Rejection





Both neutrophils and mononuclear cells are seen within the capillary lumina

Acute antibody-mediated rejection. There is neutrophilic infiltrate in the glomerular capillaries (glomerulitis) and peritubular capillaries (capillaritis). Also there is interstitial edema.

THE END