Pathology of the Infections of the urinary tract Students 211

Pathology of Infections of the Urinary Tract

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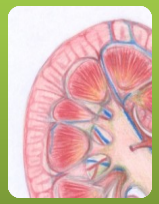


Objectives

- Definition
- Distinguish types of infections of urinary tract- pyelonephritis urethritis, cystitis, ureteritis
- Recognize the pathophysiology of the most common infections of the kidney and urinary tract
- Complications of infections of the urinary tract

Infections of Urinary Tract

Upper Urinary tract

Pyelonephritis-

Acute

Chronic,

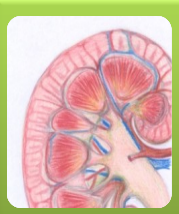
Xanthomatous

Lower Urinary tract

ureteritis

cystitis

urethritis

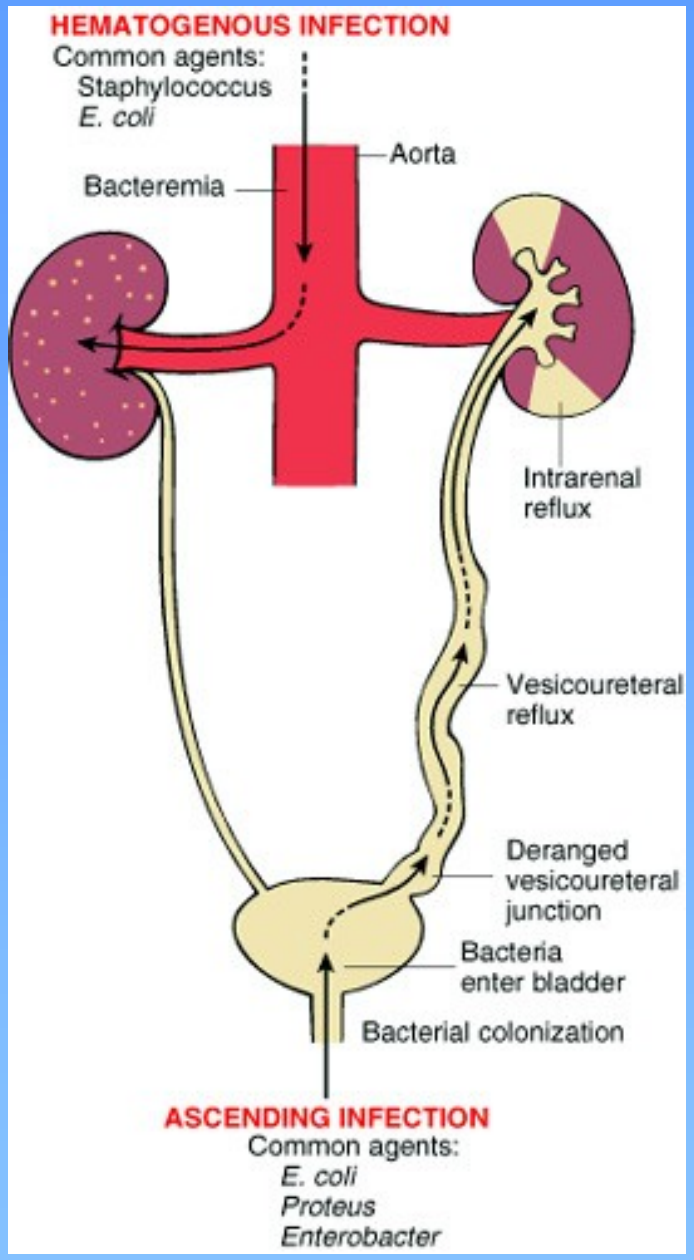


Route of infection

- Ascending infection
  - Bacteria in perineal area ascends through the urethra, enters the urinary bladder and multiplies
  - This is the most common route of infection
  - e.g. E.coli to the bladder
- Hematogenous infection
  - In a patient with bacteremia, bacteria may be “seeded” into the kidneys from the blood
  - e.g. staph .aureus , T.B

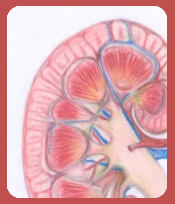
ROUTES OF INVASION TO KIDNEY

upward spread - common
blood-borne - rare
lymphatic - unlikely


HEMATOGENOUS INFECTION
Common agents:
Staphylococcus
E. coli
Aorta
Bacteremia
Intrarenal reflux
Vesicoureteral reflux
Deranged vesicoureteral junction
Bacteria enter bladder
Bacterial colonization
ASCENDING INFECTION
Common agents:
E. coli
Proteus
Enterobacter

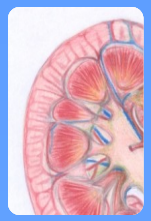
Pyelonephritis

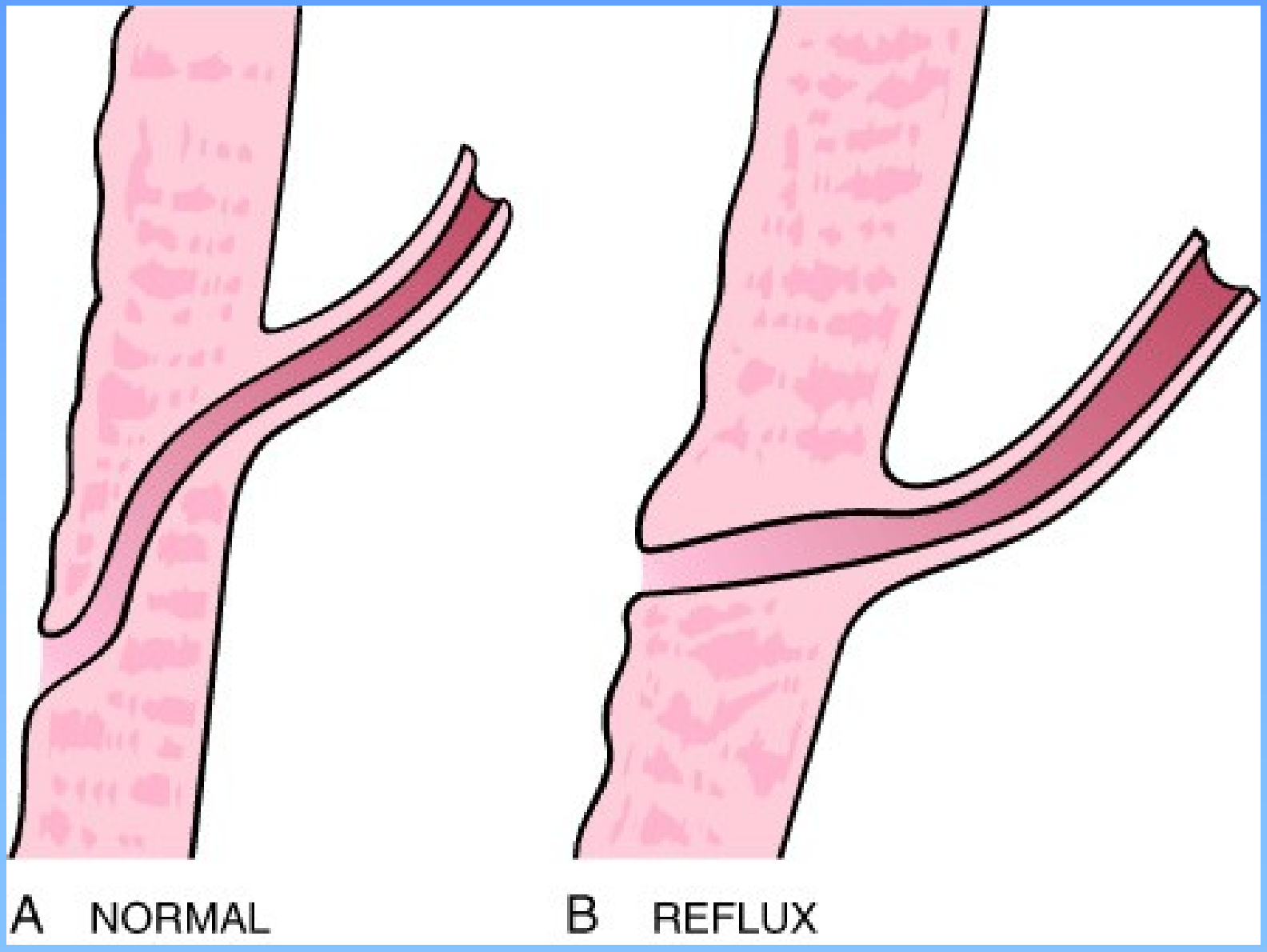
- **ACUTE**-*Acute pyelonephritis* is caused by bacterial infection and is the renal lesion associated with urinary tract infection
- **CHRONIC**-*Chronic pyelonephritis* is a more complex disorder; bacterial infection plays a dominant role, but other factors (vesicoureteral reflux, obstruction) are involved in its pathogenesis



Predisposing conditions- acute pyelonephritis

- *Urinary tract obstruction,* either congenital or acquired
- *Instrumentation* of the urinary tract
- *Vesicoureteral reflux*
- *Pregnancy..*
- *Gender and age..*
- *Preexisting renal lesions,* causing intrarenal scarring and obstruction
- *Diabetes mellitus*
- *Immunosuppression and immunodeficiency*



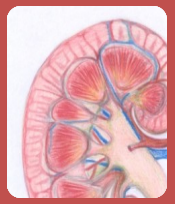

A NORMAL
B REFLUX

Etiology and pathogenesis of urinary tract infection

- **gram-negative bacilli** : *Escherichia coli*, *Proteus*, *Klebsiella*, and *Enterobacter.*
- **Ascending infection**: is the most common cause of clinical pyelonephritis.

  Predisposing factors:

  * *Vesicoureteral reflux*
  * *Intrarenal reflux*
  * *Urinary tract obstruction and stasis of urine*
- **Descending infection**



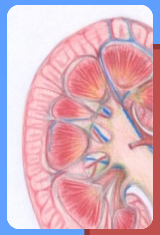
Acute Pyelonephritis

- Acute suppurative inflammation of the kidney caused by bacterial and sometimes viral
- The hallmarks of acute pyelonephritis are:

  ***Patchy interstitial suppurative inflammation**

  ***Intratubular aggregates of neutrophils,**

  ***Tubular necrosis**

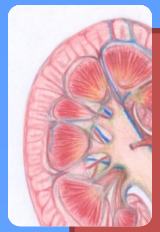


Complications -acute pyelonephritis

1 Papillary necrosis , seen mainly in diabetics and in those with urinary tract obstruction

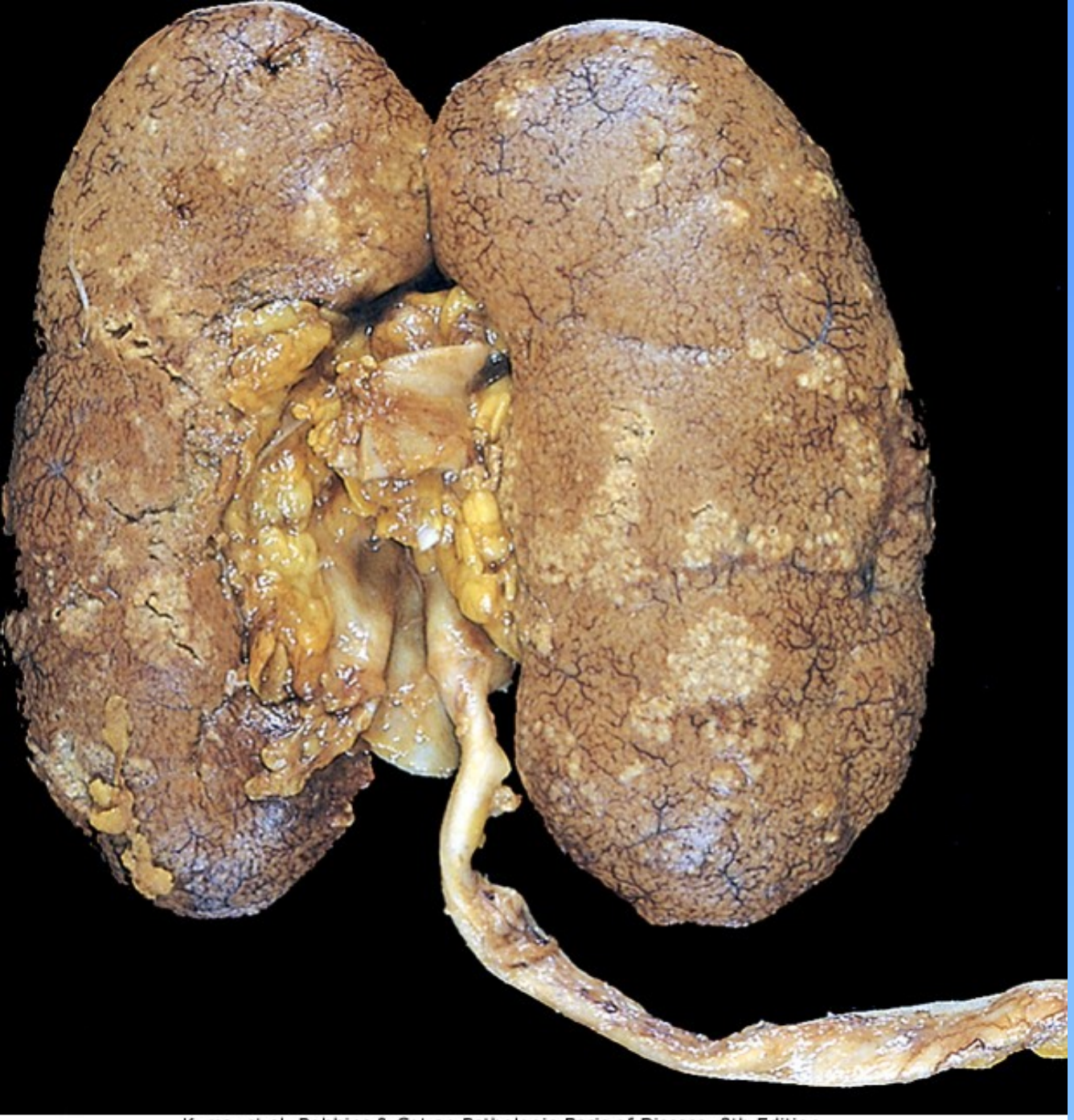
2 Pyonephrosis is seen when there is total or almost complete obstruction

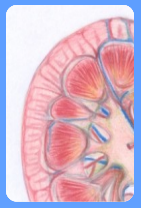
3 Perinephric abscess extension of suppurative inflammation through the renal capsule into the perinephric tissue



Outcome- acute pyelonephritis

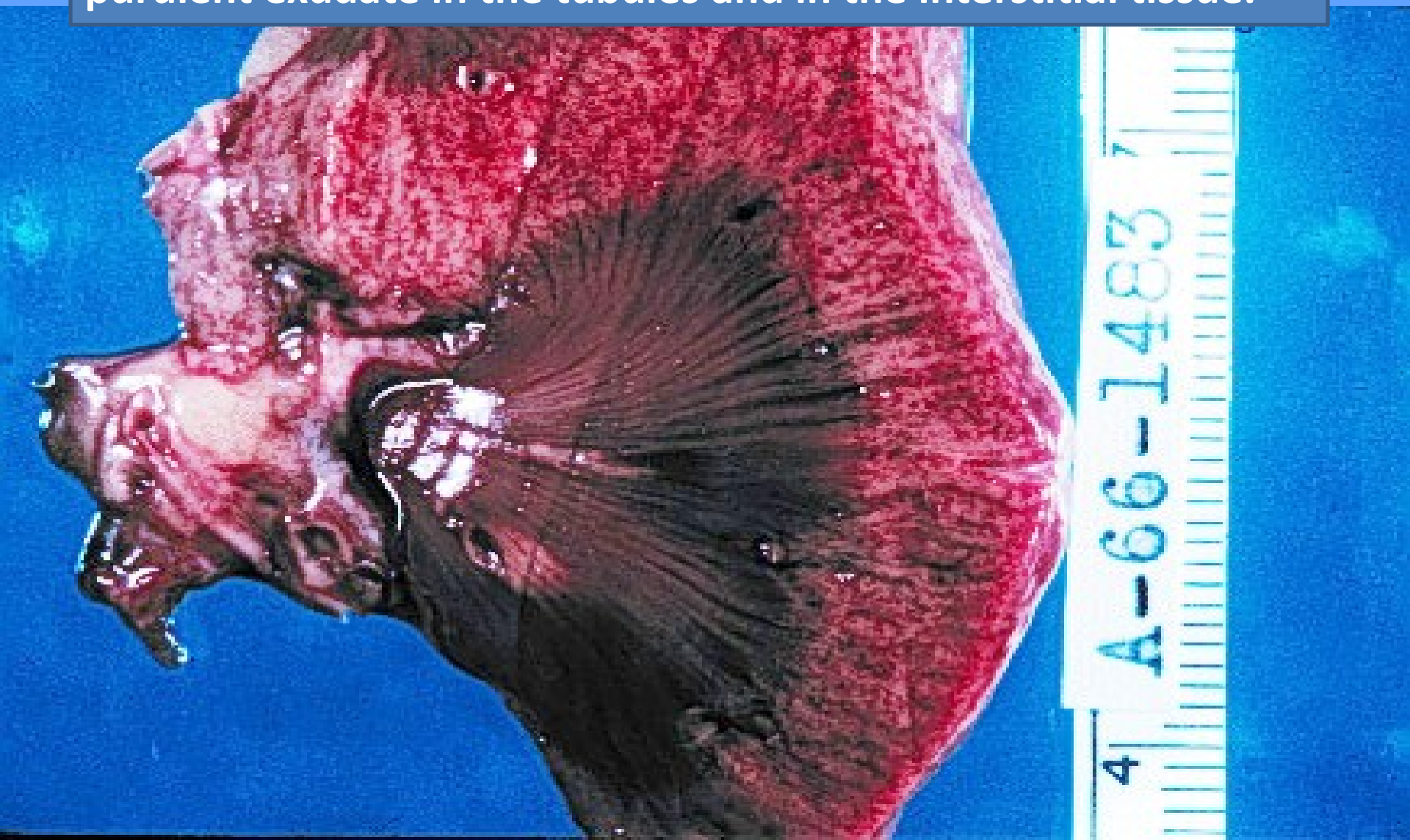
- After the acute phase of pyelonephritis, healing occurs.
- The neutrophilic infiltrate is replaced by one that is predominantly composed of macrophages, plasma cells, and (later) lymphocytes.
- The inflammatory foci are eventually replaced by irregular scars that can be seen on the cortical surface as fibrous depressions.
- Such scars are characterized microscopically by tubular atrophy, interstitial fibrosis, and a lymphocytic infiltrate in a characteristic patchy, jigsaw pattern with intervening preserved parenchyma



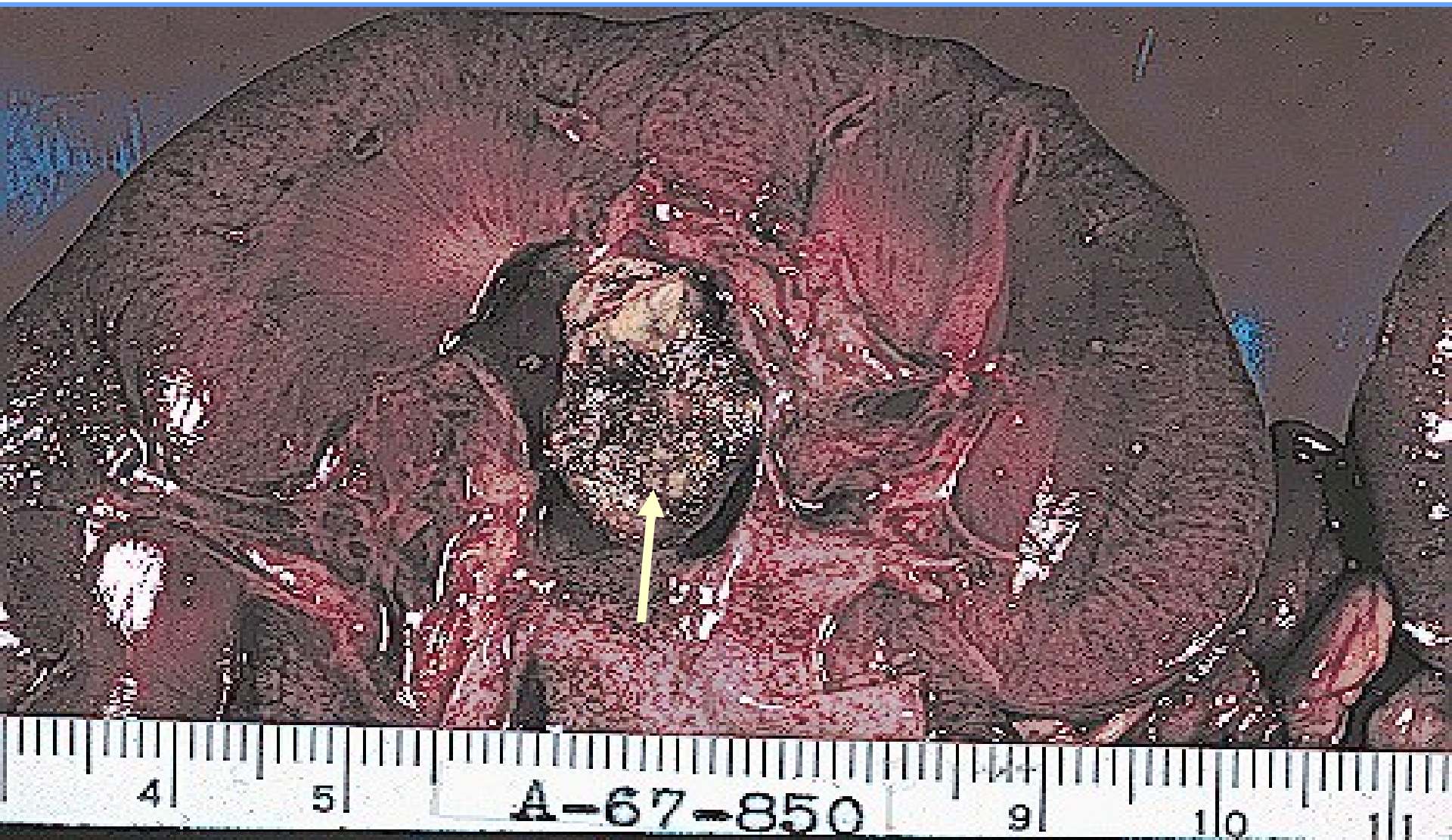


Acute pyelonephritis. Cortical surface shows grayish white areas of inflammation and abscess formation

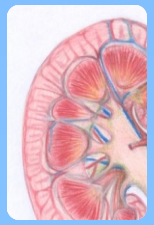
This is a cross-section of a piece of a kidney showing acute suppurative pyelonephritis. The white streaks running through the medulla and the white blotches in the cortex represent purulent exudate in the tubules and in the interstitial tissue.



Section of a kidney with acute suppurative pyelonephritis. The parenchyma is congested and swollen - a calculus in the calyx.

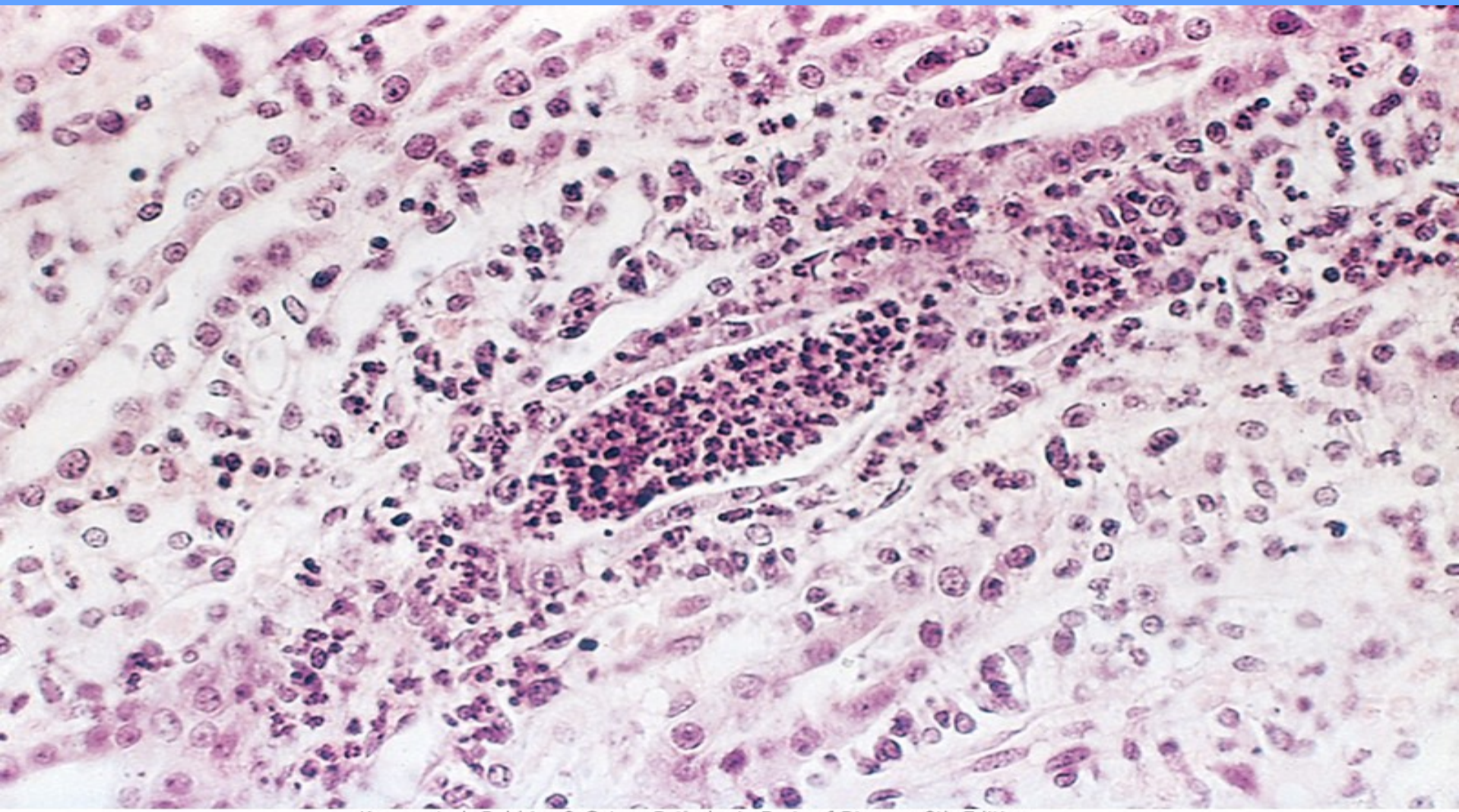


One pole of a kidney showing metastatic pyelonephritis. The small white specks on the surface are actually metastatic abscesses in an individual with streptococcal septicemia. The large scars on the surface represent the healed remnants of chronic pyelonephritis.

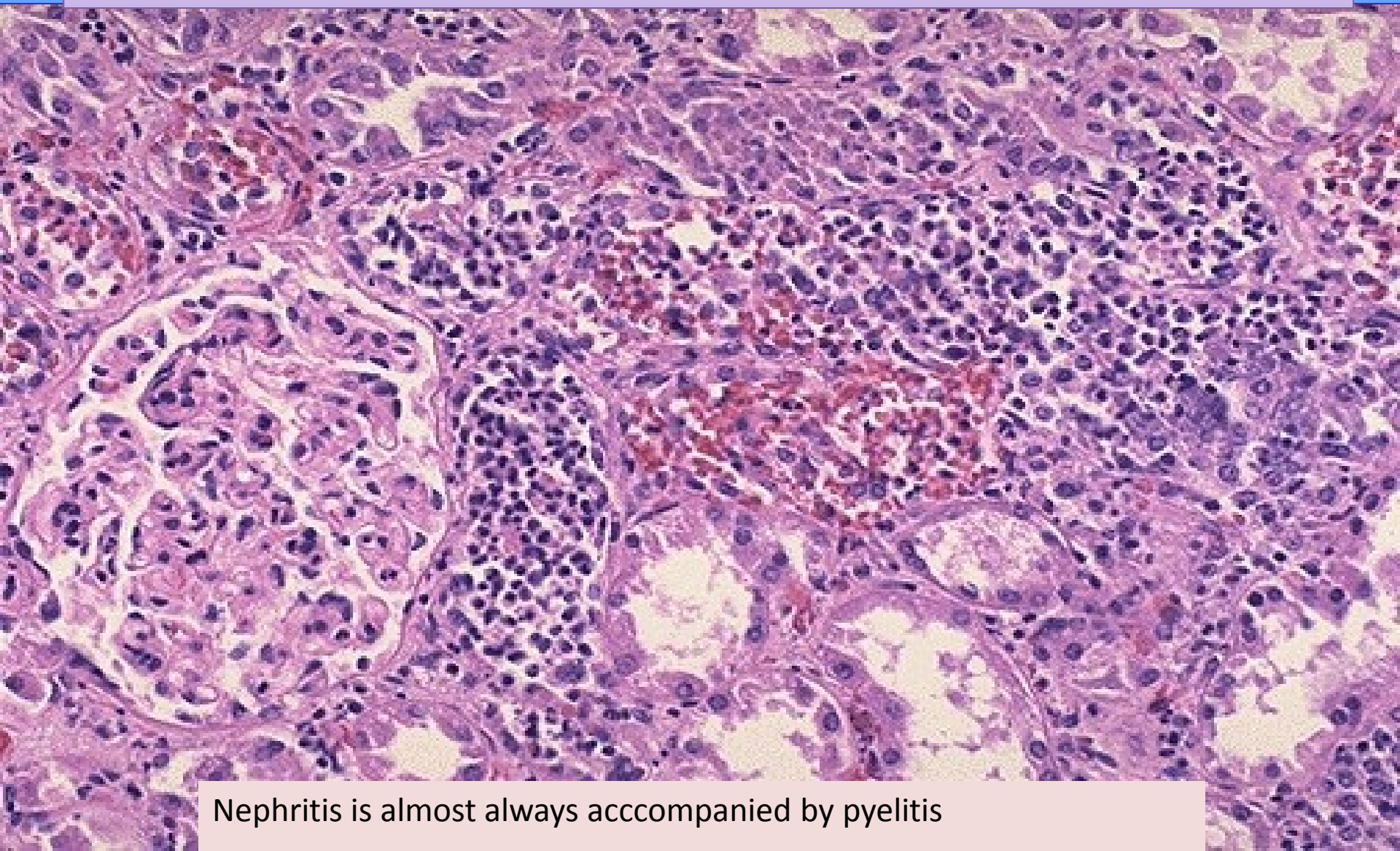


Cut surface of this kidney demonstrates many small yellowish microabscesses.

Acute pyelonephritis marked by an acute neutrophilic exudate within tubules and interstitial inflammation

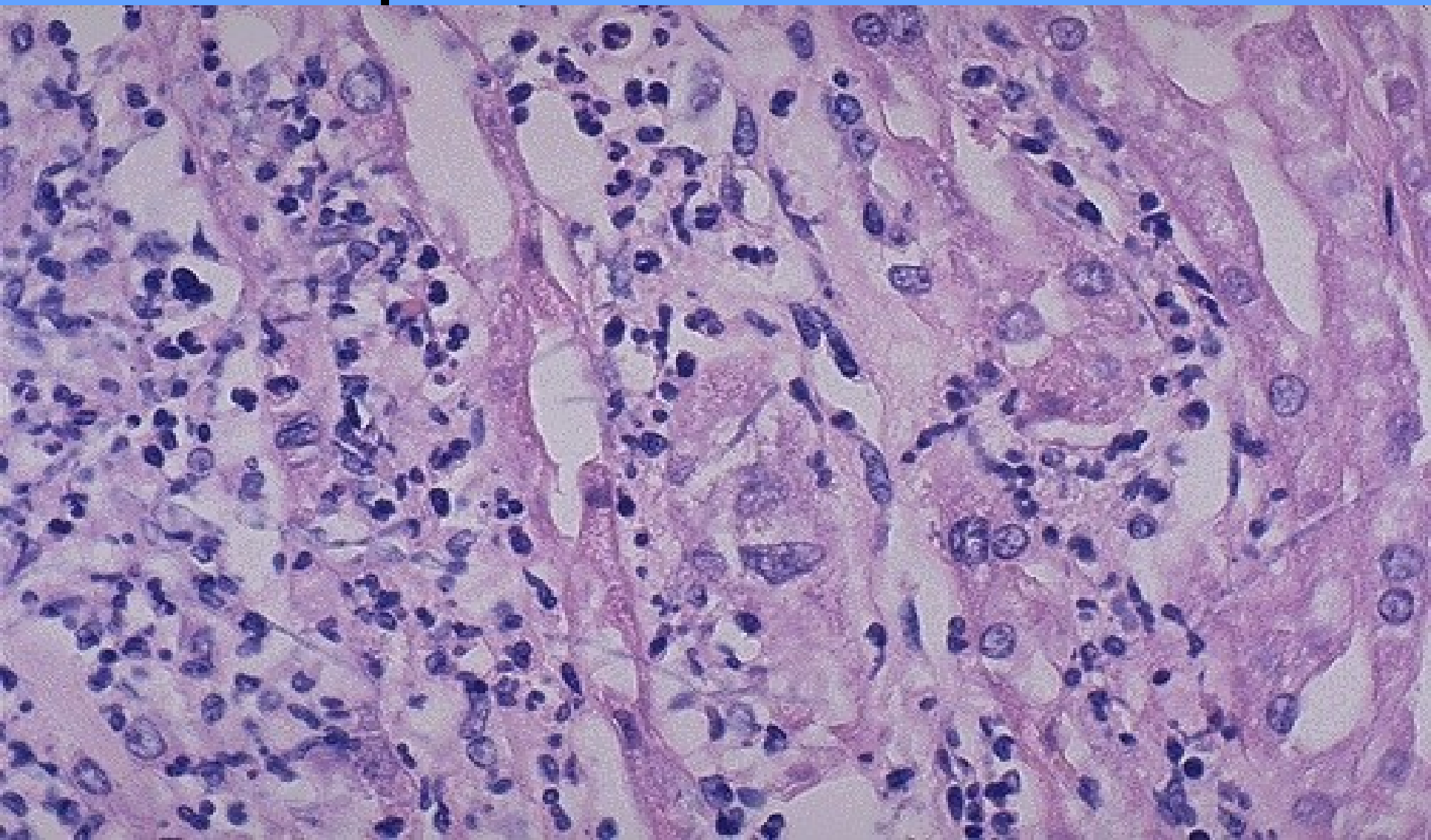


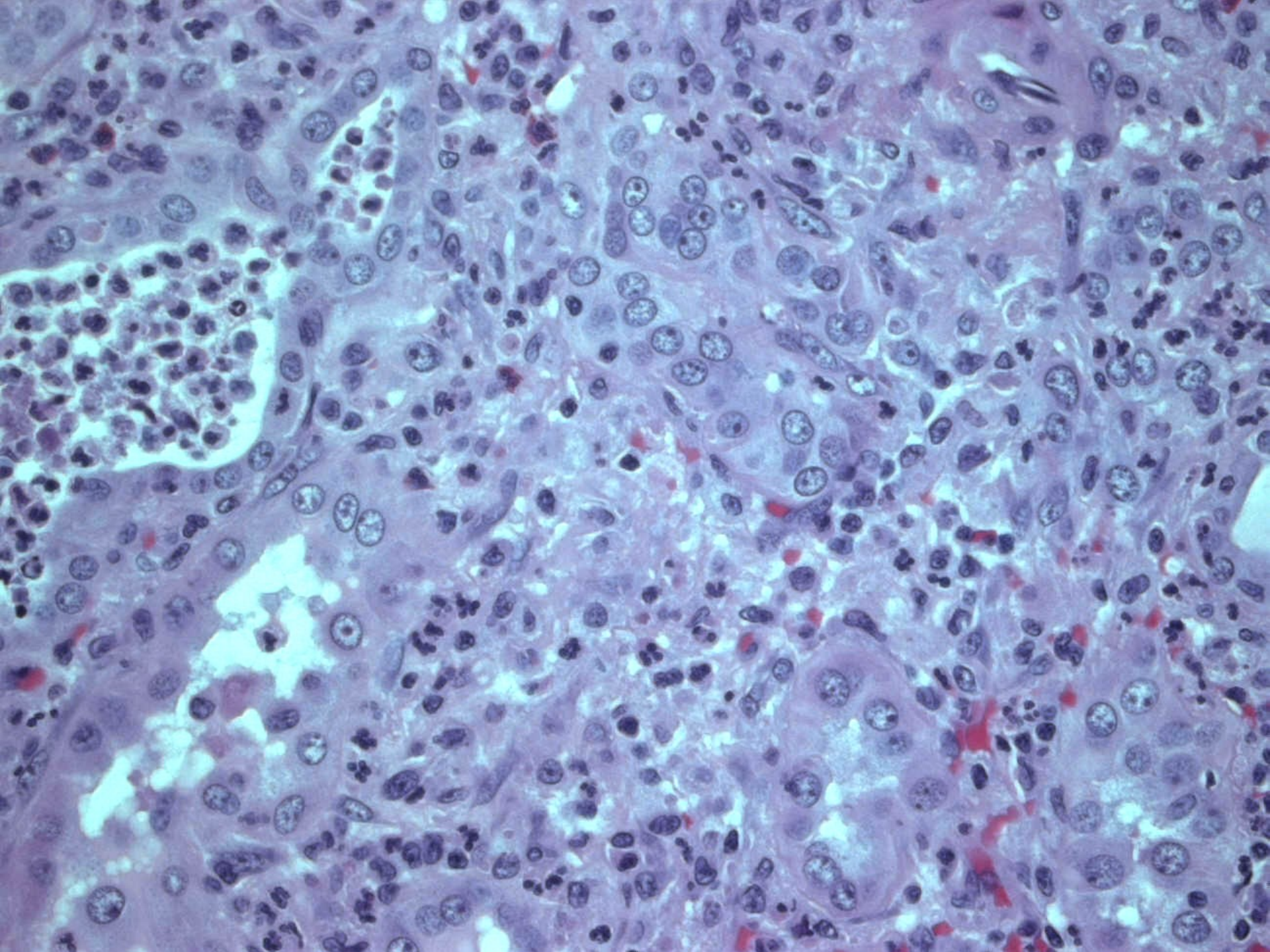
An ascending bacterial infection leading to acute pyelonephritis. Numerous PMN's are seen filling renal tubules.



Nephritis is almost always acccompanied by pyelitis

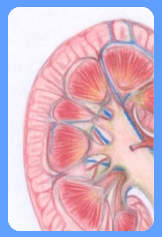
Acute pyelonephritis, high power. The neutrophils can collect in the distal tubules and be passed in urine as WBC casts





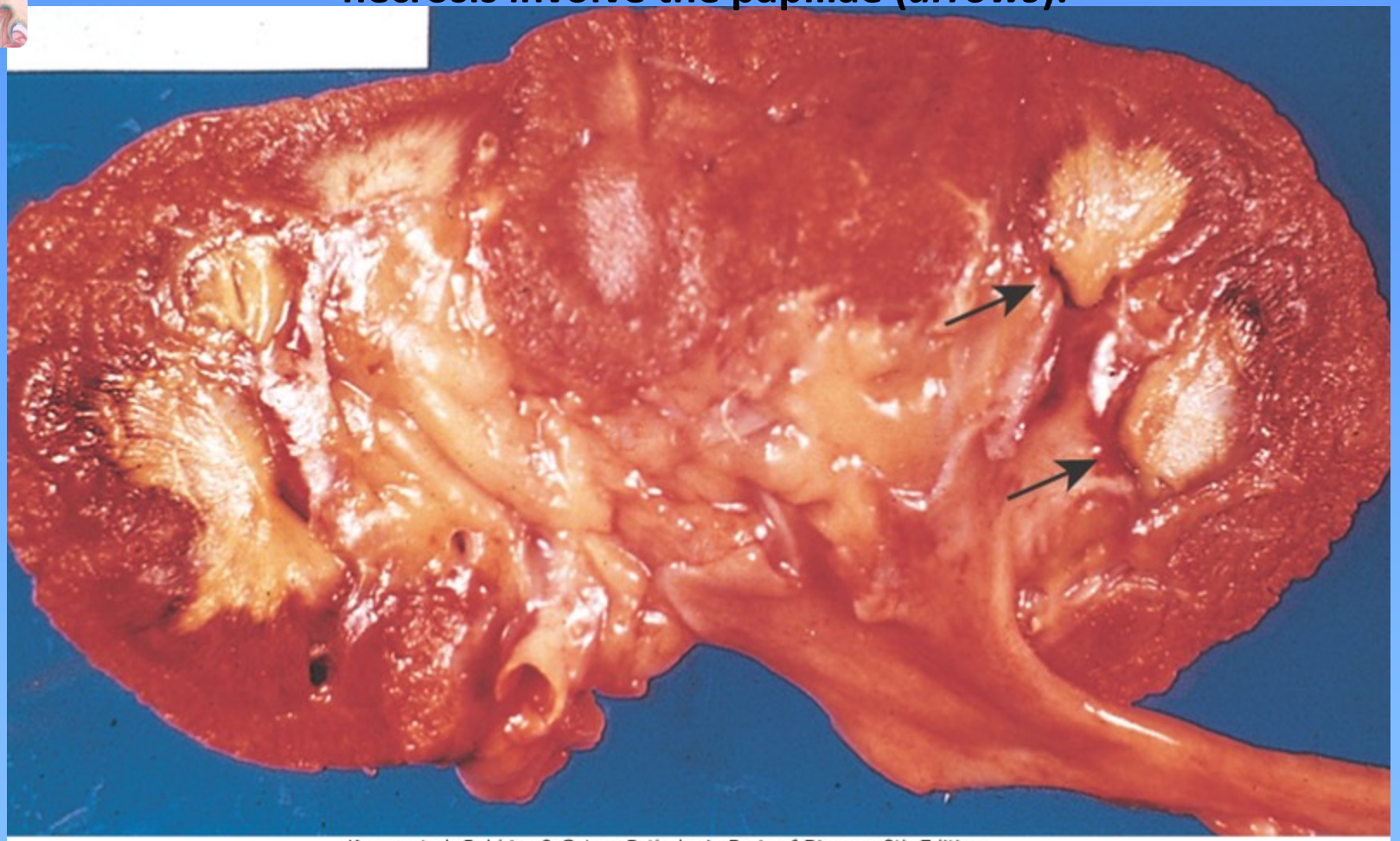
Papillary necrosis

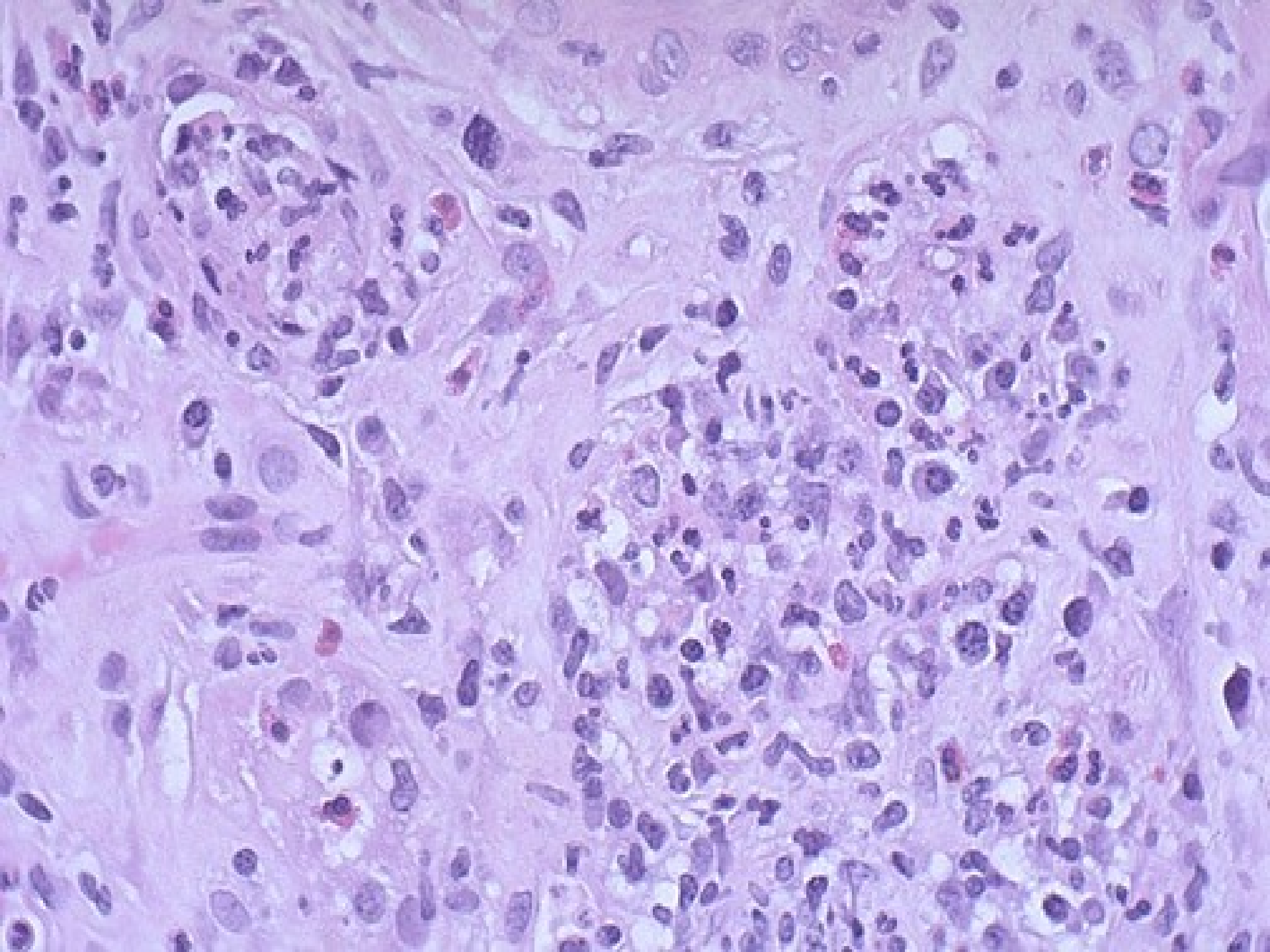
- Seen mainly in diabetics and in those with urinary tract obstruction.
- Usually bilateral but may be unilateral.
- One or all of the pyramids of the affected kidney may be involved.
- On cut section, the tips or distal two thirds of the pyramids have areas of gray-white to yellow necrosis
- On microscopic examination the necrotic tissue shows characteristic coagulative necrosis, with preservation of outlines of tubules.
- The leukocytic response is limited to the junctions between preserved and destroyed tissue

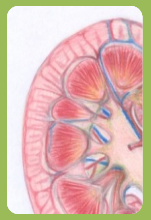


The pale white areas involving some or all of many renal papillae are areas of papillary necrosis

Papillary necrosis. Areas of pale-gray necrosis involve the papillae (*arrows*).

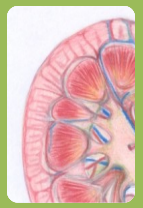






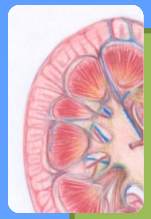
Chronic Pyelonephritis

- It is chronic tubulo-interstitial inflammation and renal scarring associated with pathologic involvem.ent of the calyces and pelvis.
- It is an important cause of end-stage kidney disease.
- It is divided into two forms:
  - * chronic reflux-associated and
  - * chronic obstructive pyelonephritis.



Chronic Pyelonephritis-gross

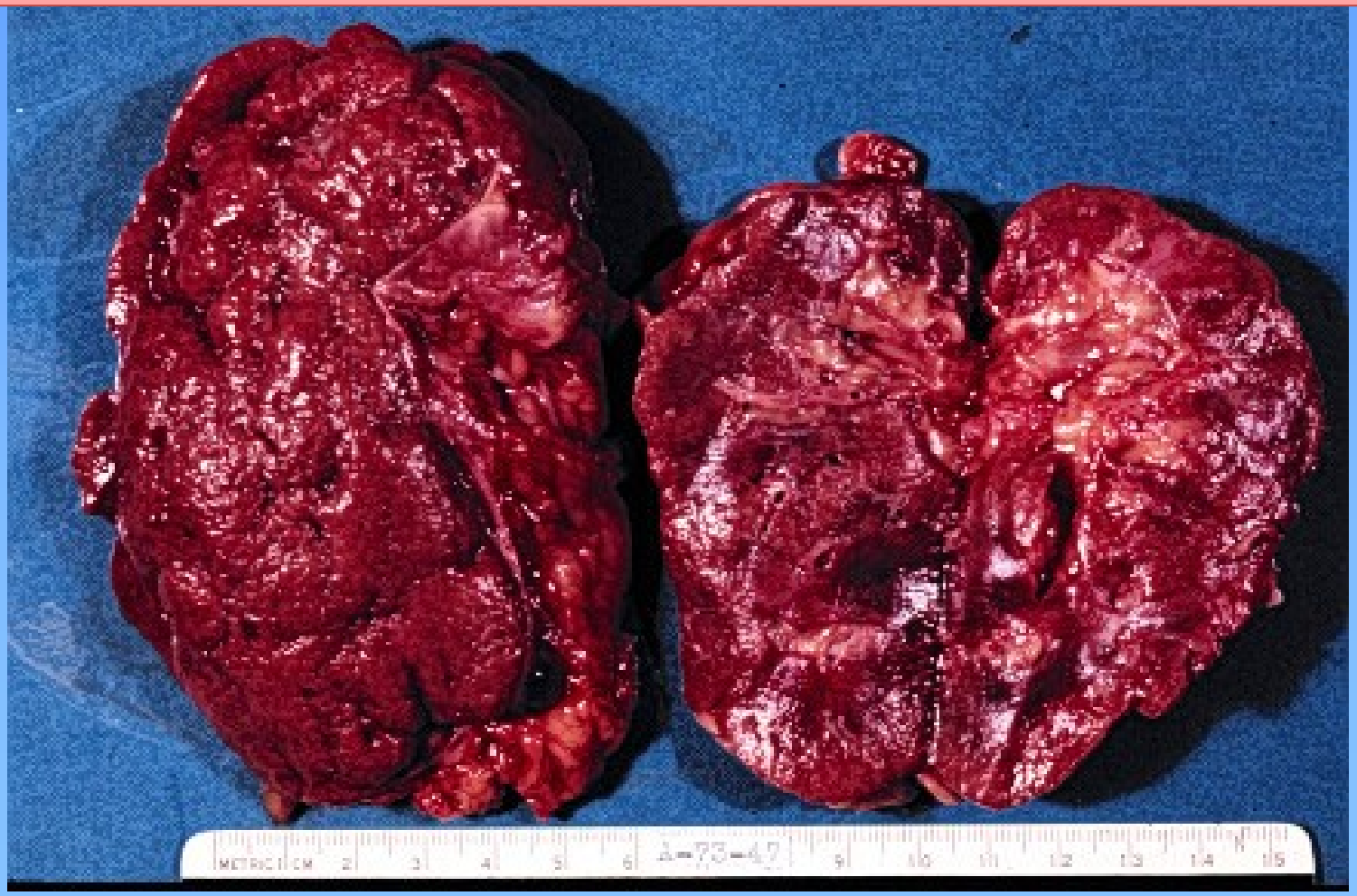
- The kidneys usually are irregularly scarred; if bilateral, the involvement is asymmetric.
- The hallmarks of chronic pyelonephritis are **coarse, discrete, corticomedullary scars** overlying dilated, blunted, or deformed calyces, and **flattening of the papillae .**



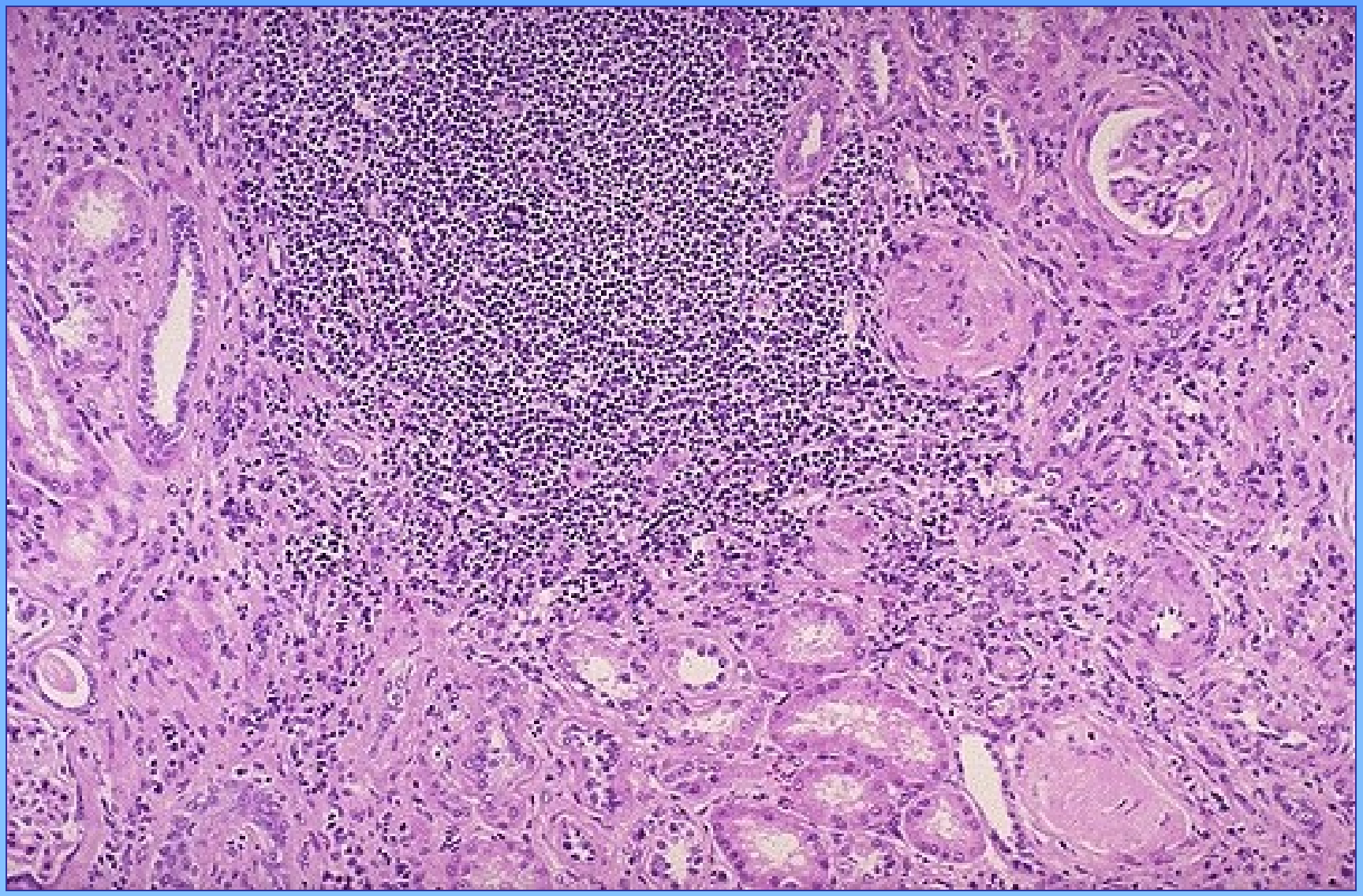
Chronic Pyelonephritis-Microscopic

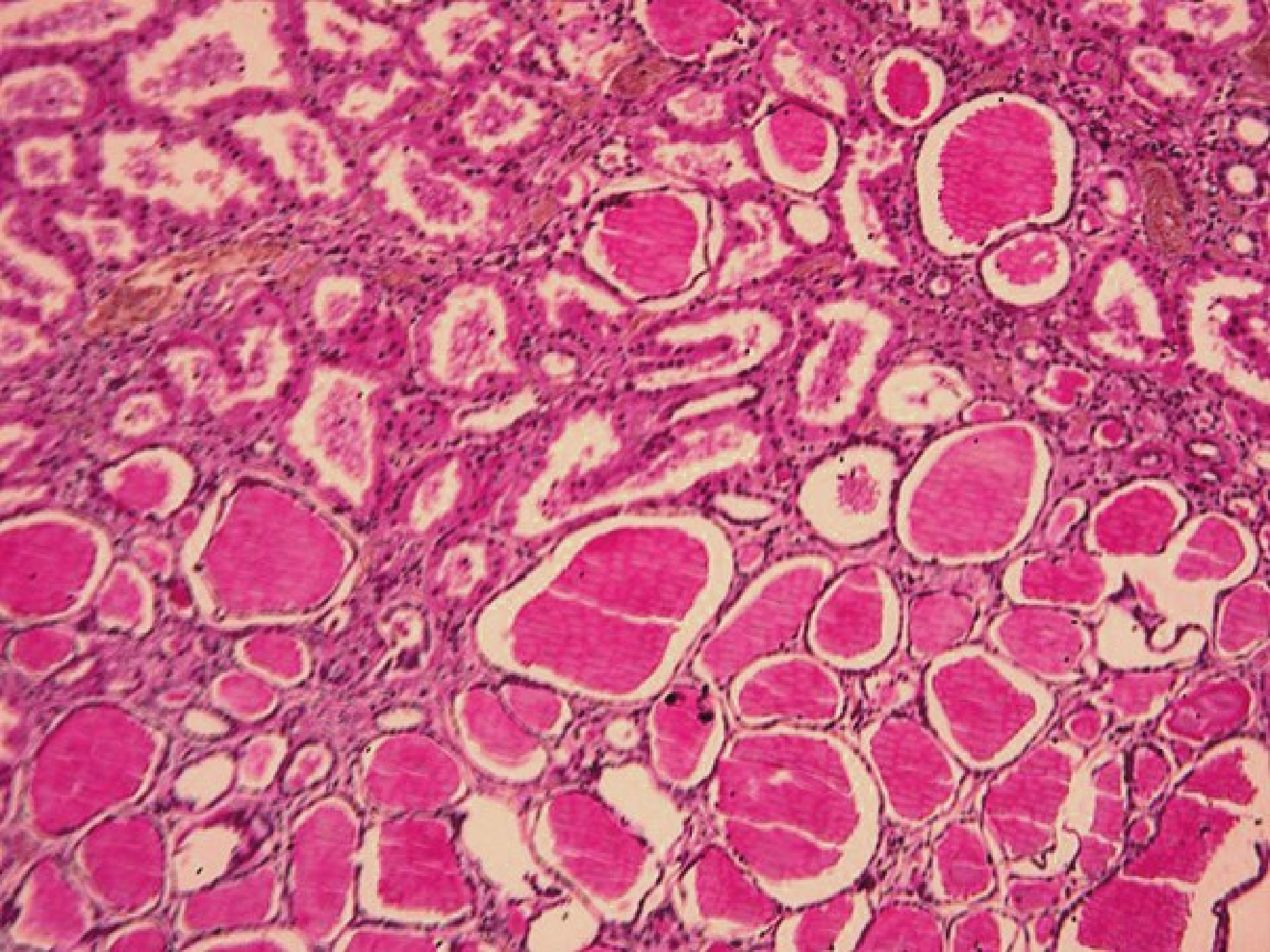
- Involve predominantly tubules and interstitium.
- The tubules show atrophy in some areas and hypertrophy or dilation in others.
- Dilated tubules with flattened epithelium may be filled with colloid casts **(thyroidization).**
- Varying degrees of chronic interstitial inflammation and fibrosis in the cortex and medulla.
- Neutrophils in the interstitium and pus casts in the tubules.

An example of chronic pyelonephritis. Repeated bouts of suppurative inflammation in the cortex have resulted in widespread scarring as seen on the left, and a diminution in the overall cortical mass as seen on the right.



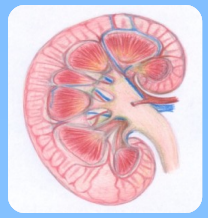
Chronic pyelonephritis: collection of chronic inflammatory cells here is in a patient with a history of multiple recurrent urinary tract infections.

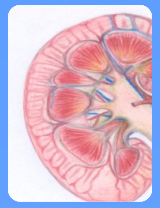




Drug -induced interstitial nephritis

- The classic example of this occurs occasionally with methicillin, but can occur with a variety of drugs such as rifampin, NSAIDS, thiazide diuretics and the H2 blocker cimetidine.
- Develops 3-7 days after exposure
- The immune mechanism may be either type I or type IV hypersensitivity



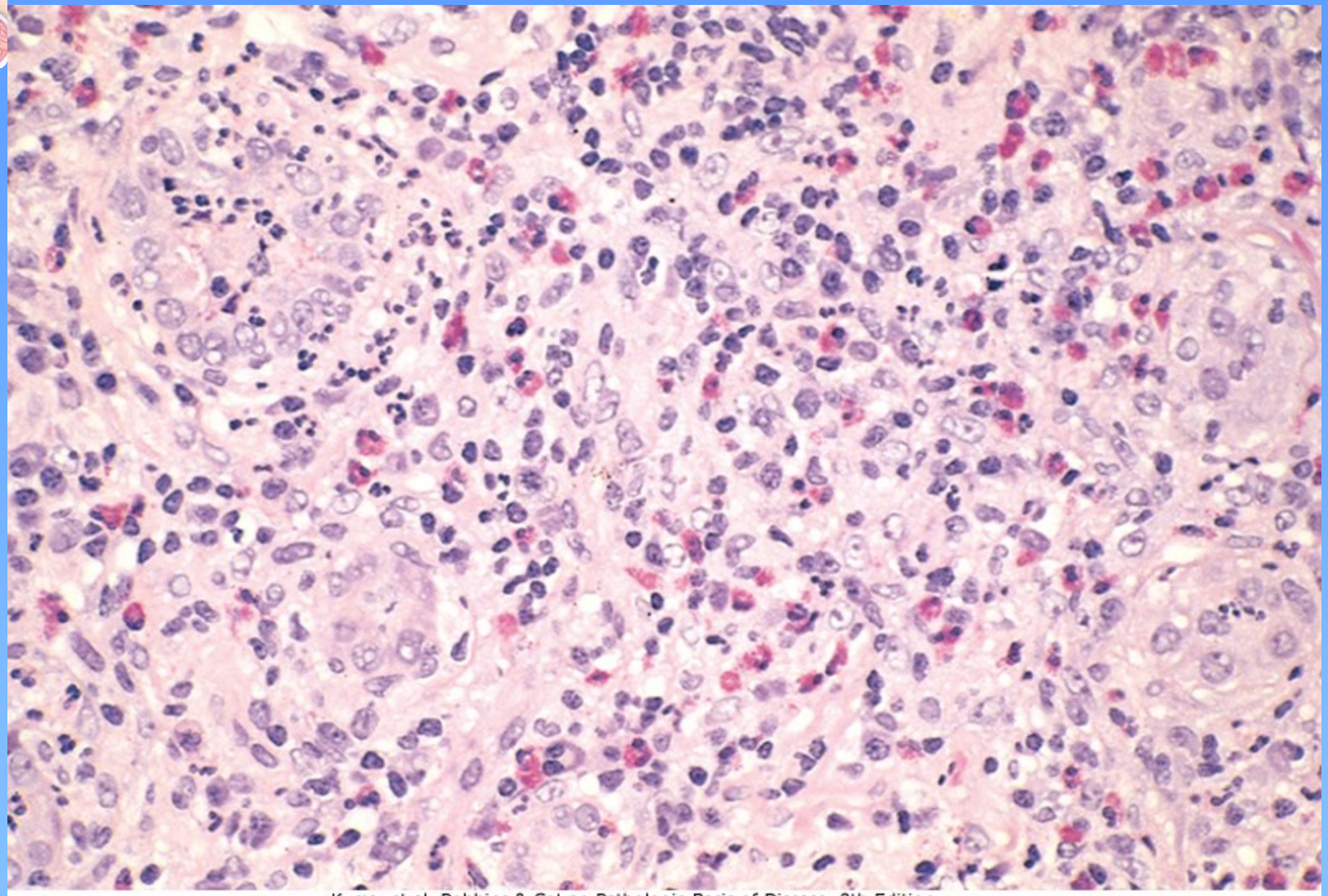


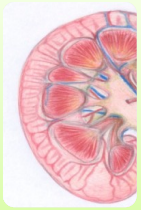
Drug -induced interstitial nephritis

Morphology

- On histologic examination the abnormalities are in the interstitium, which shows variable but frequently pronounced edema and infiltration by mononuclear cells, principally lymphocytes and macrophages.
- Eosinophils and neutrophils may be present often in clusters and large numbers, and plasma cells and basophils are sometimes found in small numbers.
- With some drugs (e.g., methicillin, thiazides), interstitial non-necrotizing granulomas containing giant cells may be seen.
- "Tubulitis," the infiltration of tubules by lymphocytes, is common.
- The glomeruli are normal except

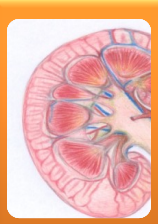
Drug-induced interstitial nephritis





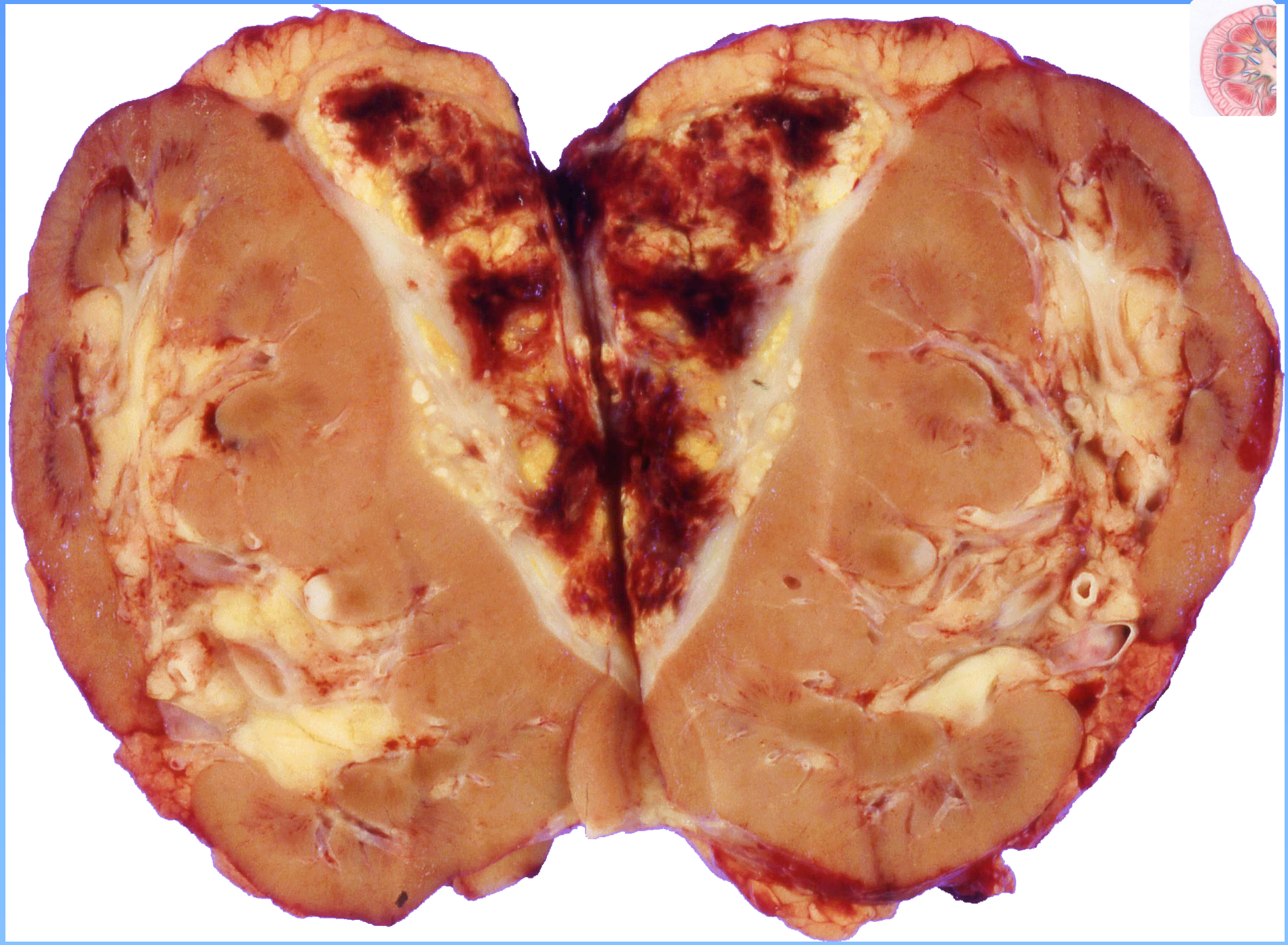
Infections of the Kidney

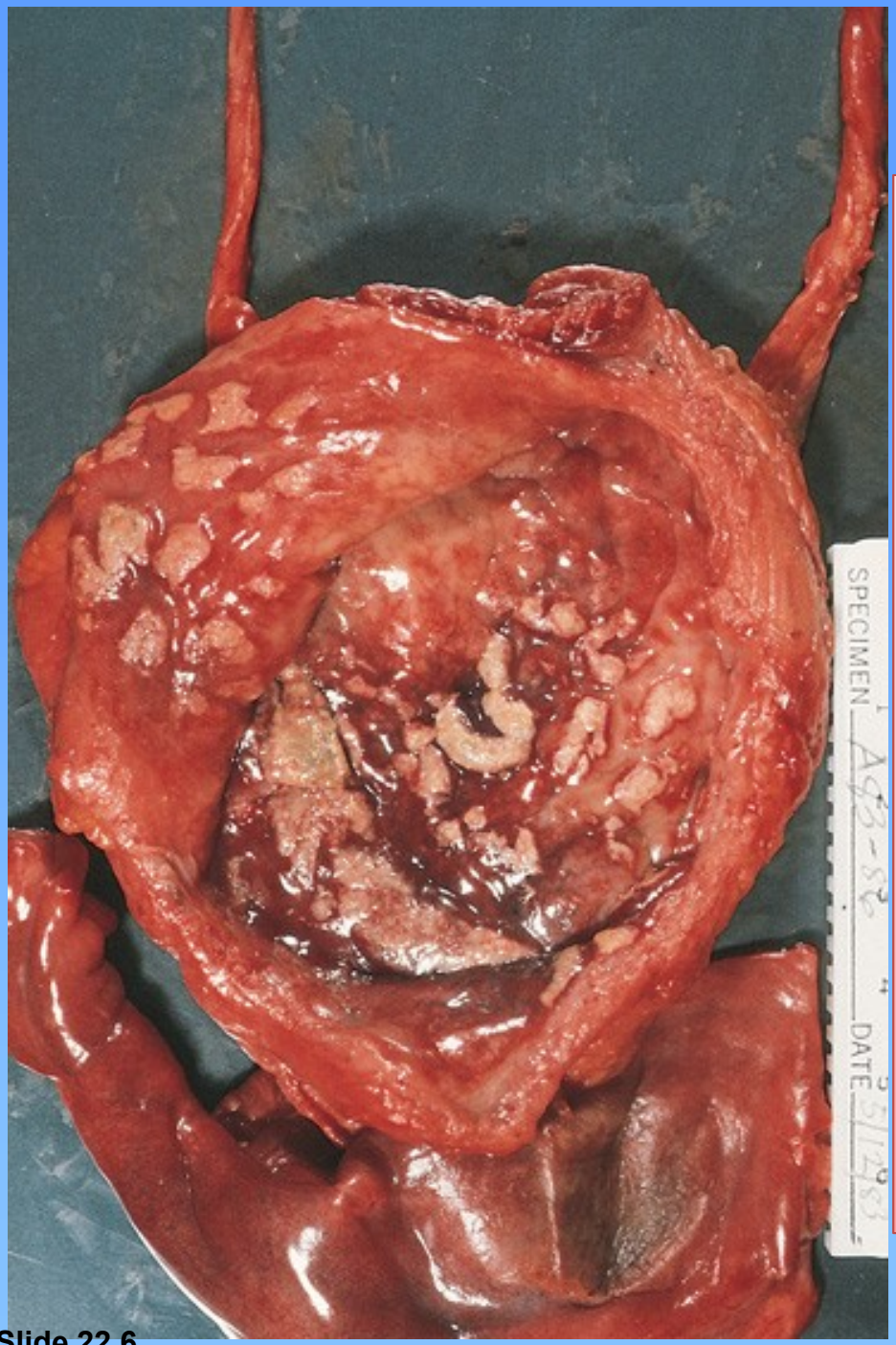
- MALAKOPLAKIA
- XANTHOGRANULOMATOUS PYELONEPHRITIS
- TB
- Fungal infection
- CMV

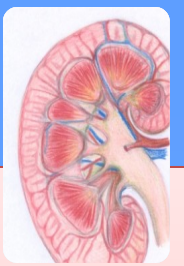


Malakoplakia

- This designation refers to a *peculiar pattern of vesical inflammatory reaction characterized macroscopically by soft, yellow, slightly raised mucosal plaques 3 to 4 cm in diameter* .
- *Microscopically there is infiltration with large, foamy macrophages mixed with occasional multinucleate giant cells and interspersed lymphocytes*.
- In addition, laminated mineralized concretions resulting from deposition of calcium in enlarged lysosomes, known as Michaelis-Gutmann bodies, are typically present within the macrophages .



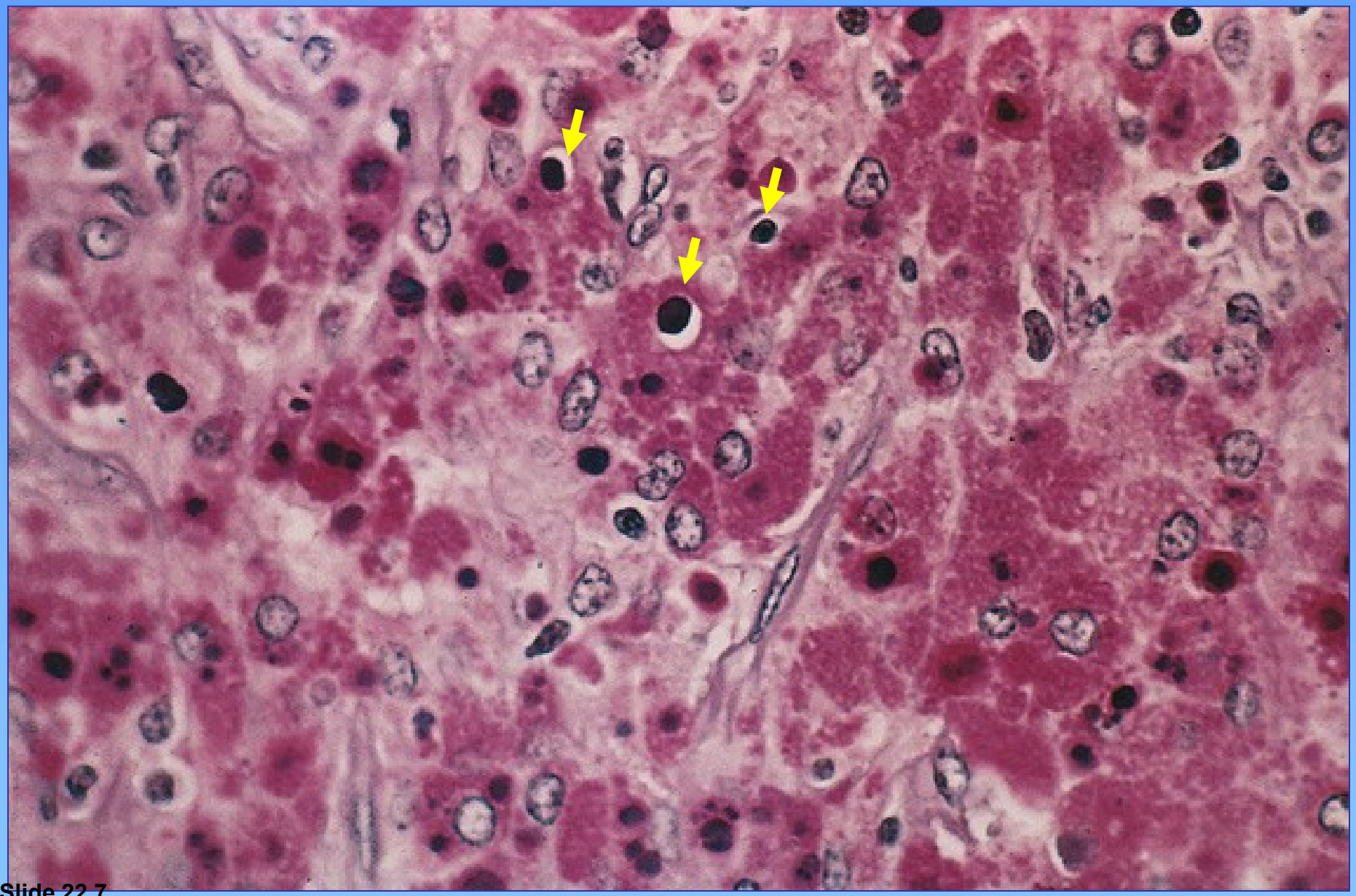


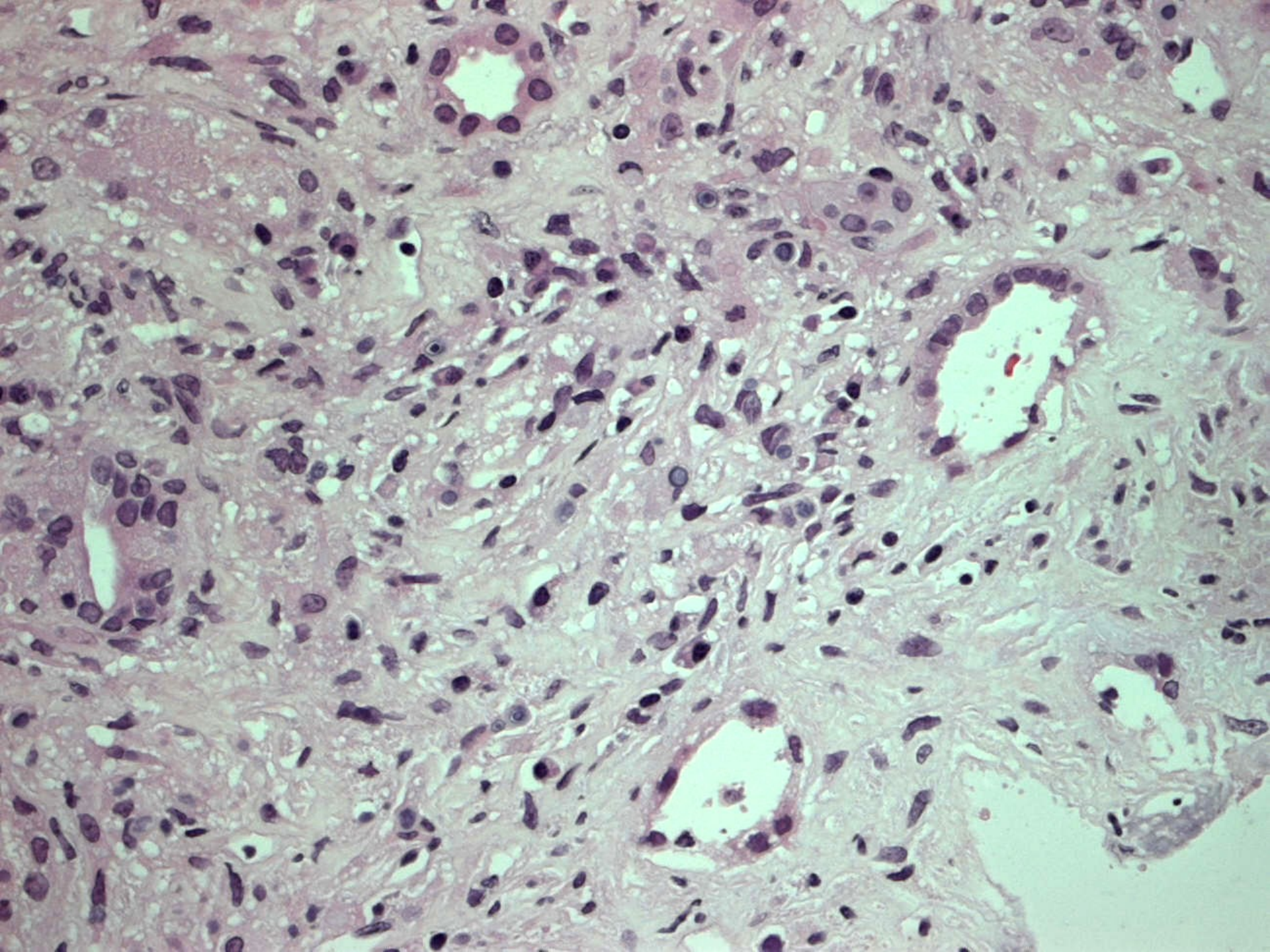


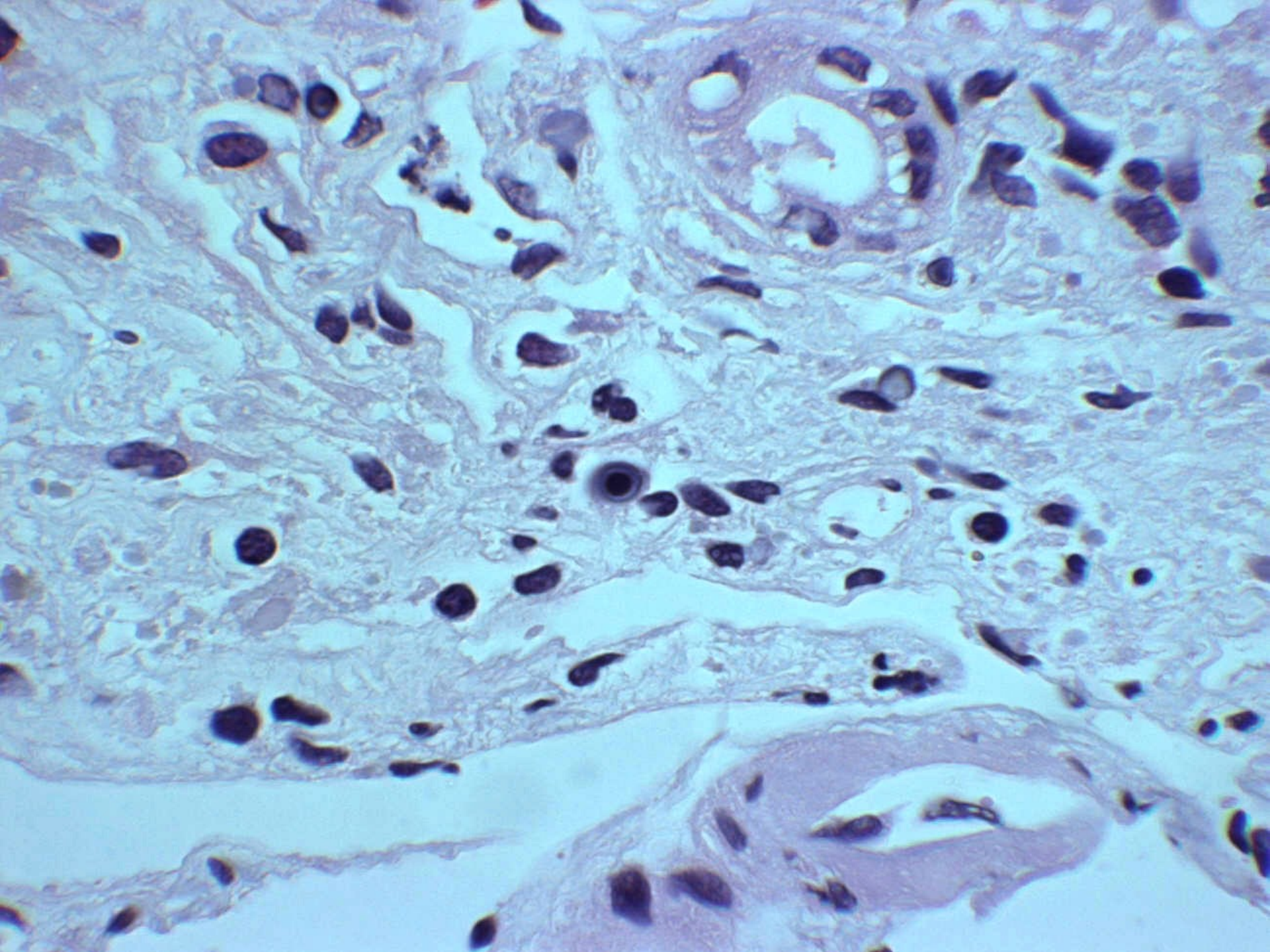
Cystitis with malakoplakia

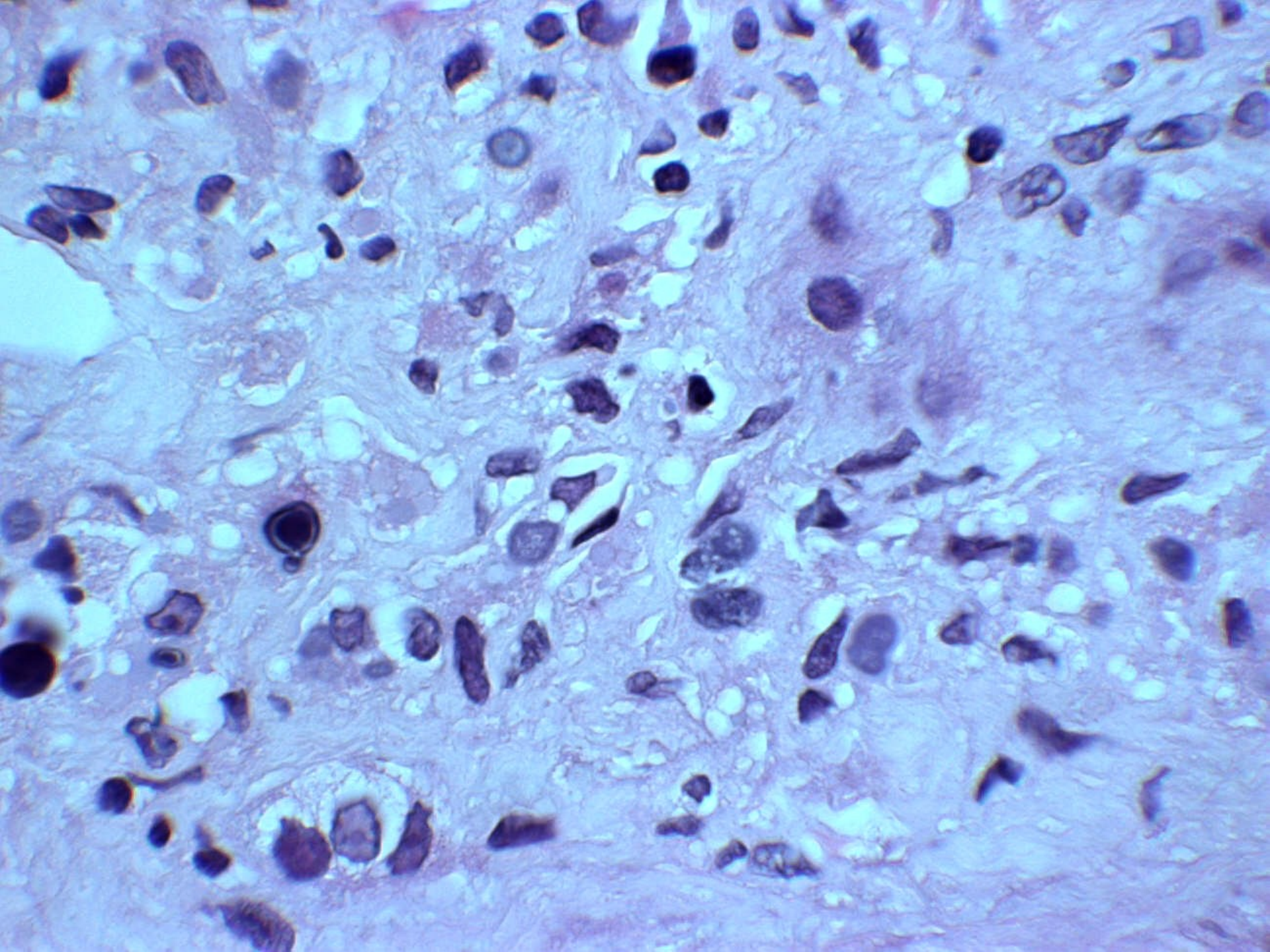
Peculial inflammatory reaction chacakterized by soft, yellow, plaques 3-4 cm in diameter and histologically by foamy macrophages

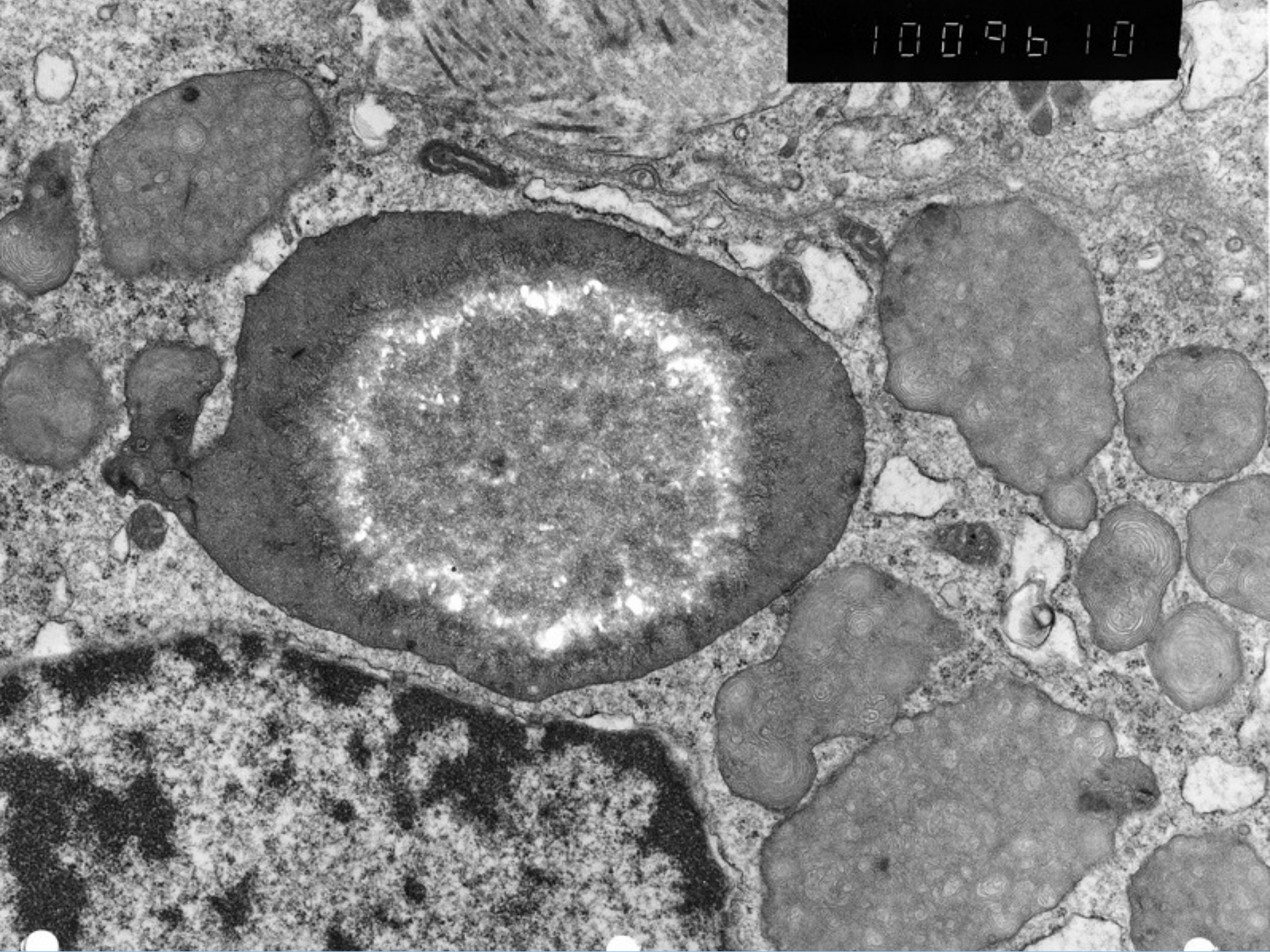
Cystitis with malakoplakia: Michaelis Gutman bodies







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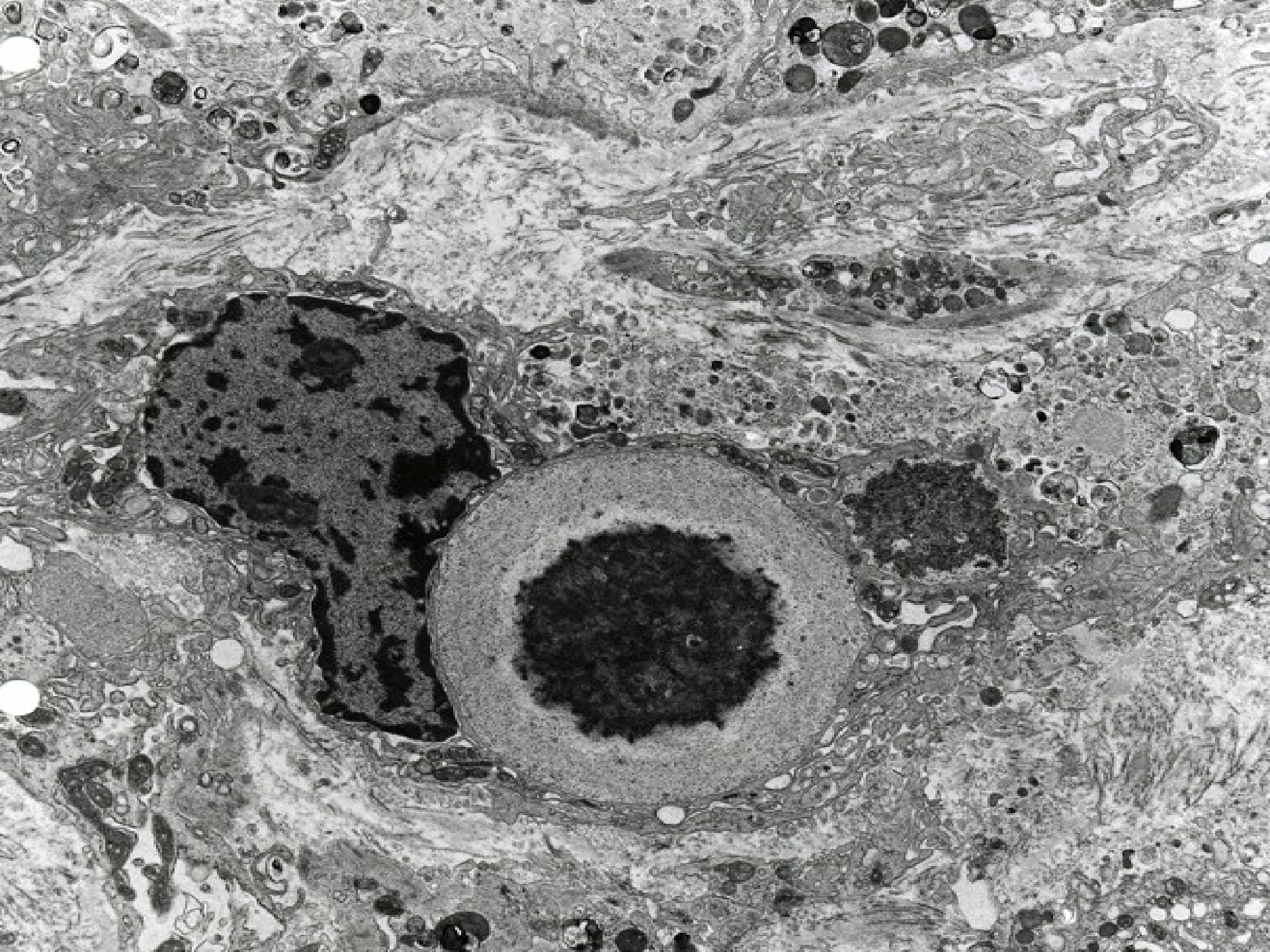
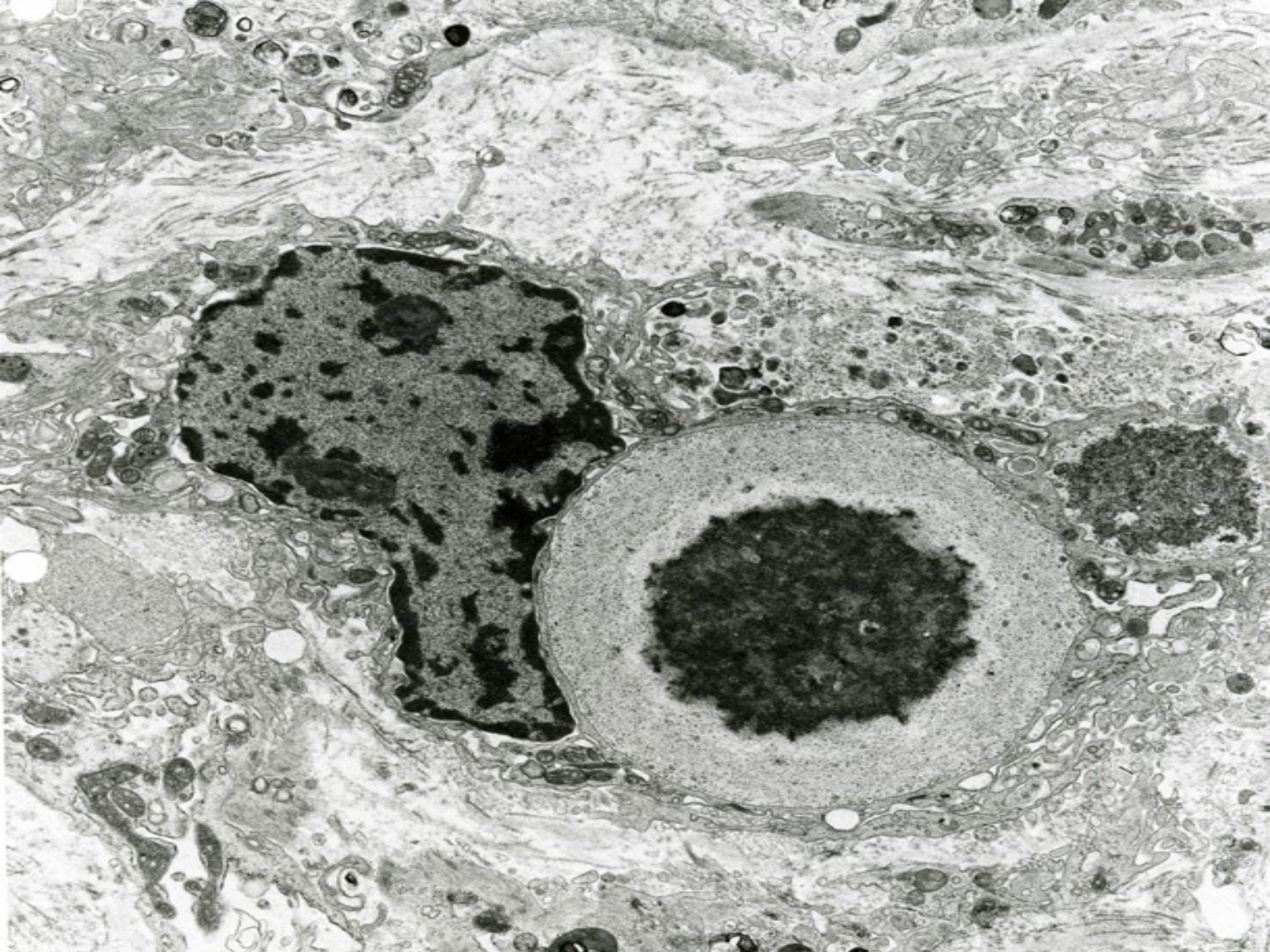
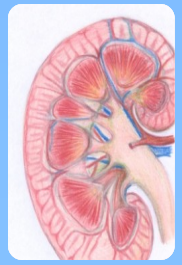
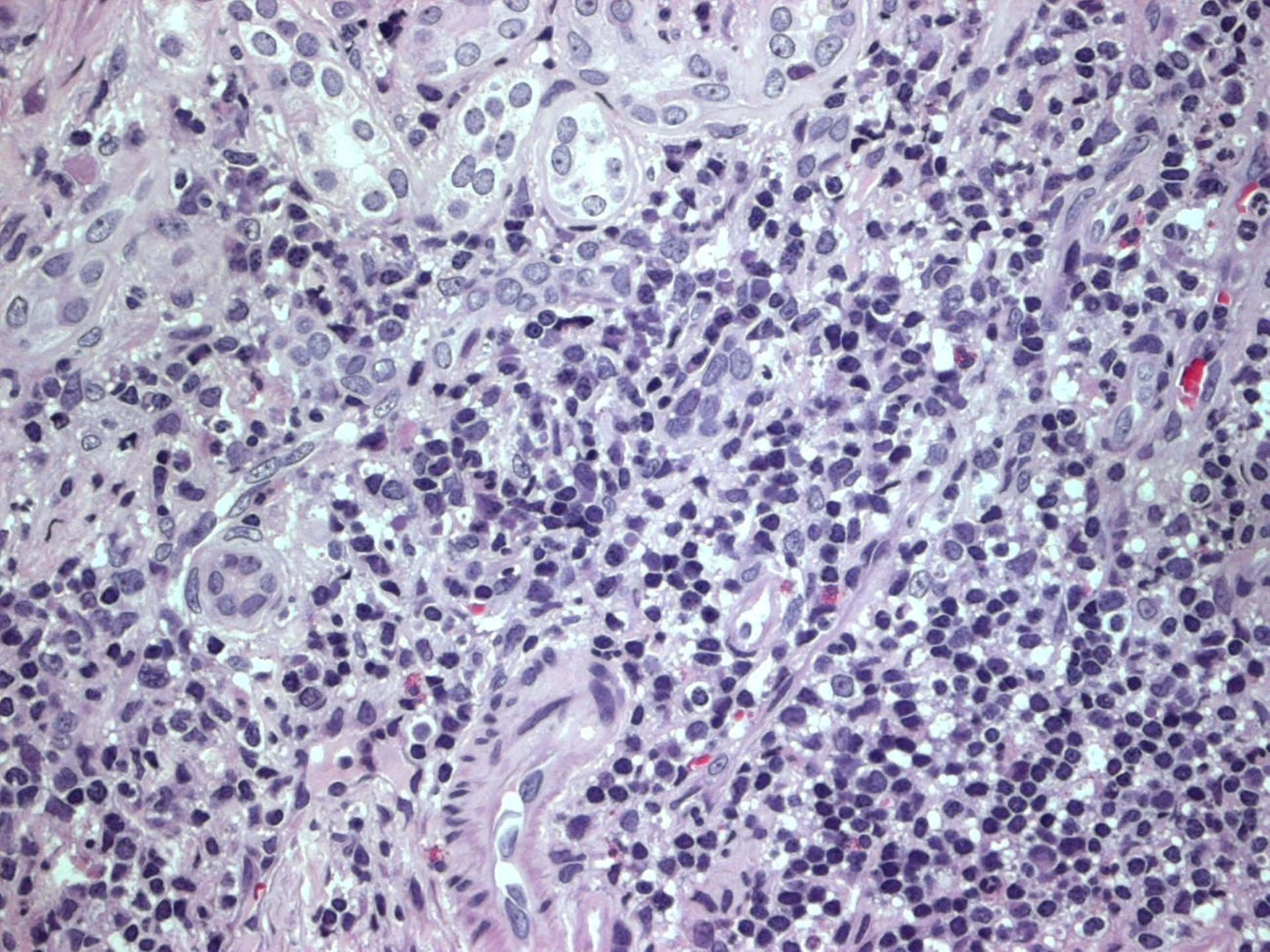


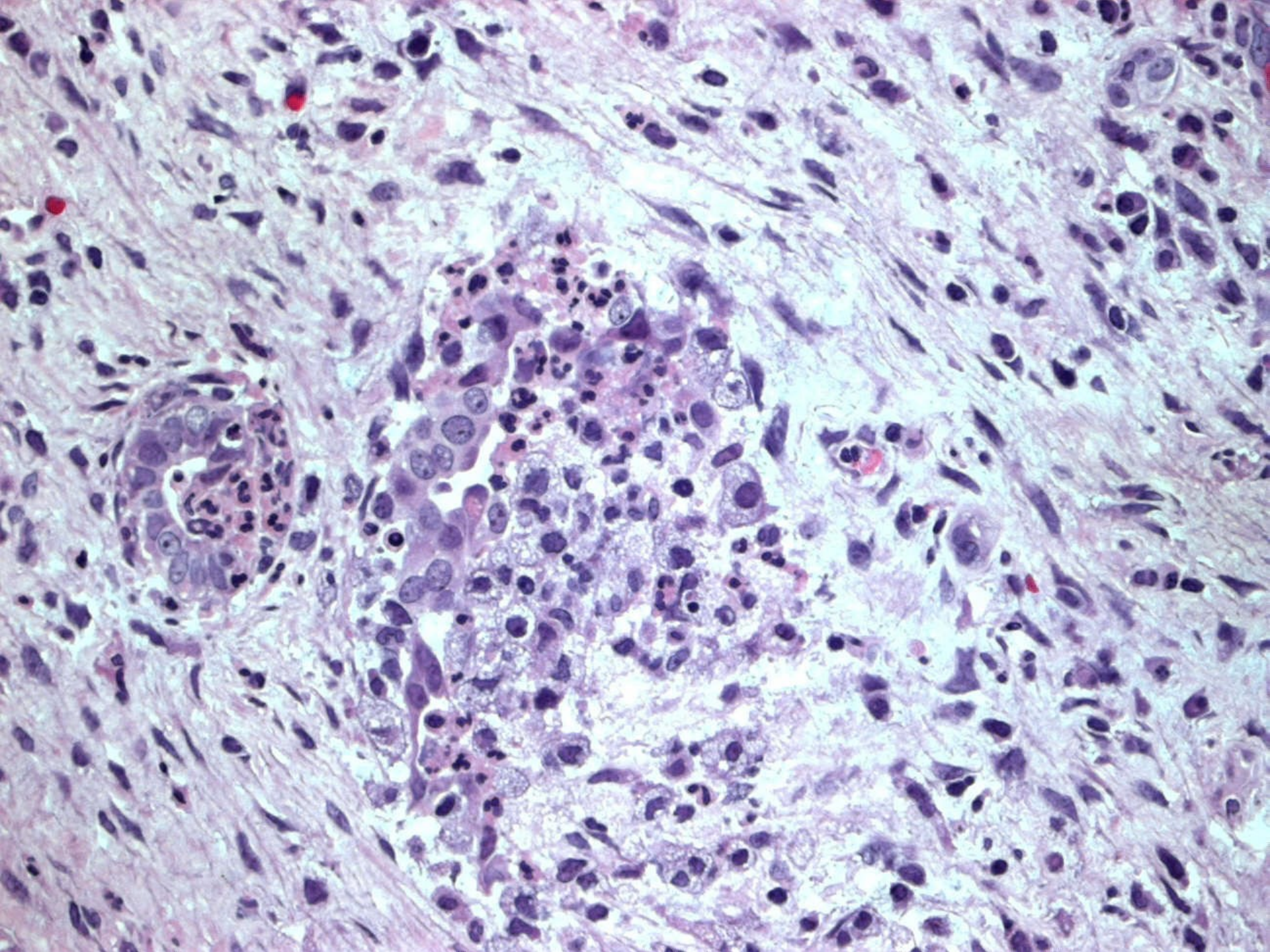


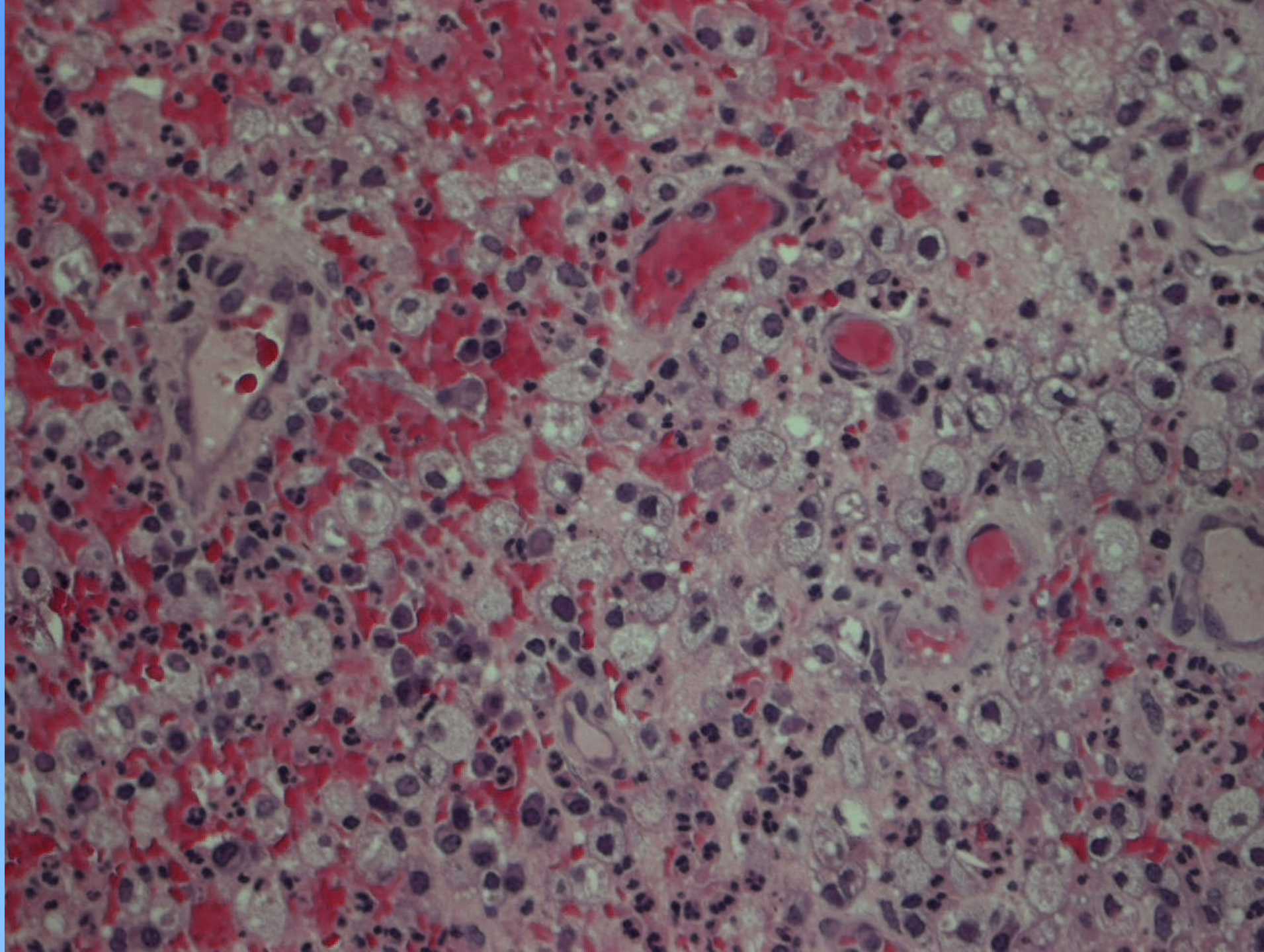
Xanthogranulomatous pyelonephritis

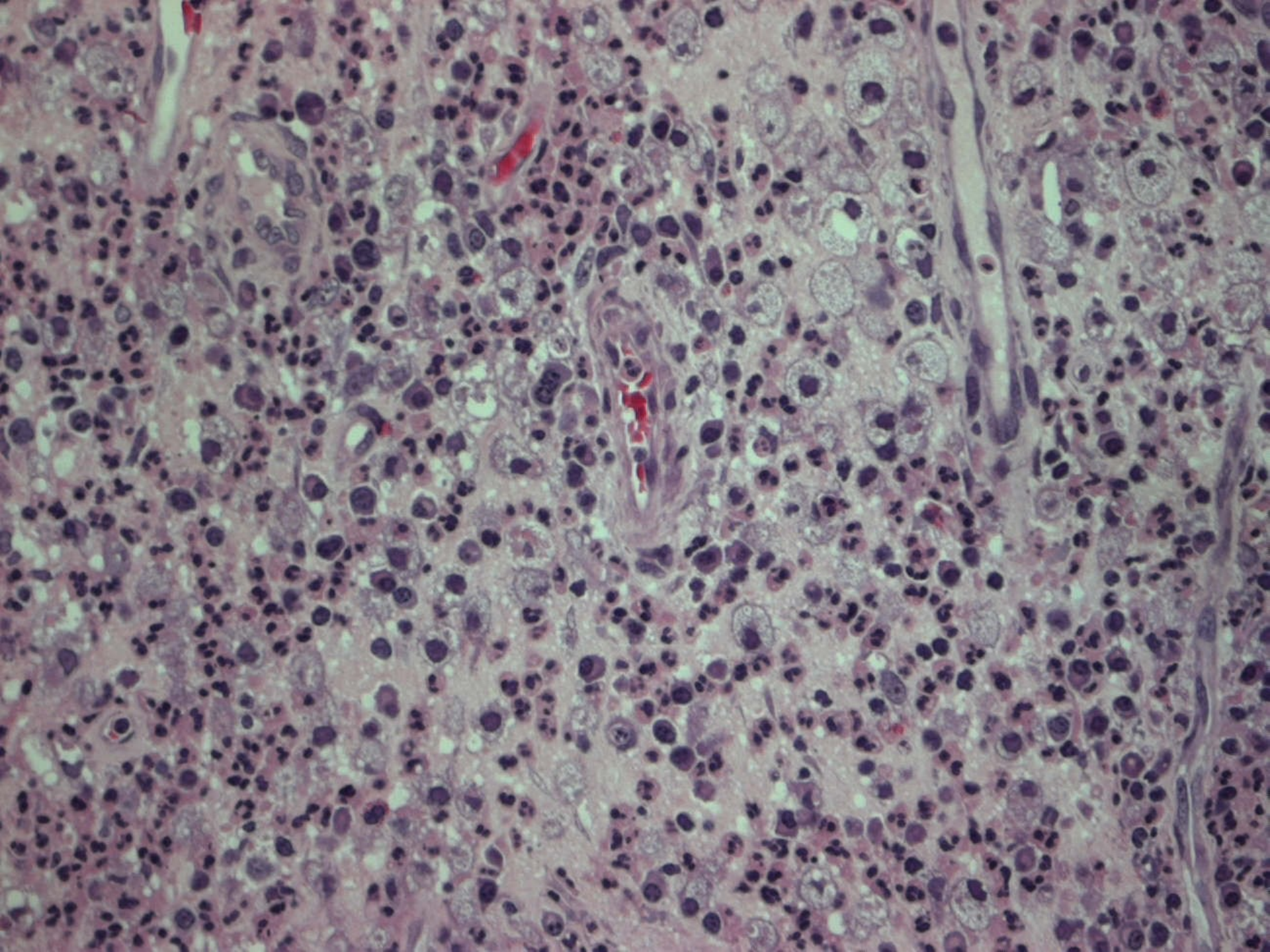
- It is an unusual and relatively rare form of chronic pyelonephritis characterized by accumulation of foamy macrophages intermingled with plasma cells, lymphocytes, polymorphonuclear leukocytes, and occasional giant cells.
- Often associated with *Proteus* infections and obstruction, the lesions sometimes produce large, yellowish orange nodules that may be grossly confused with renal cell carcinoma.

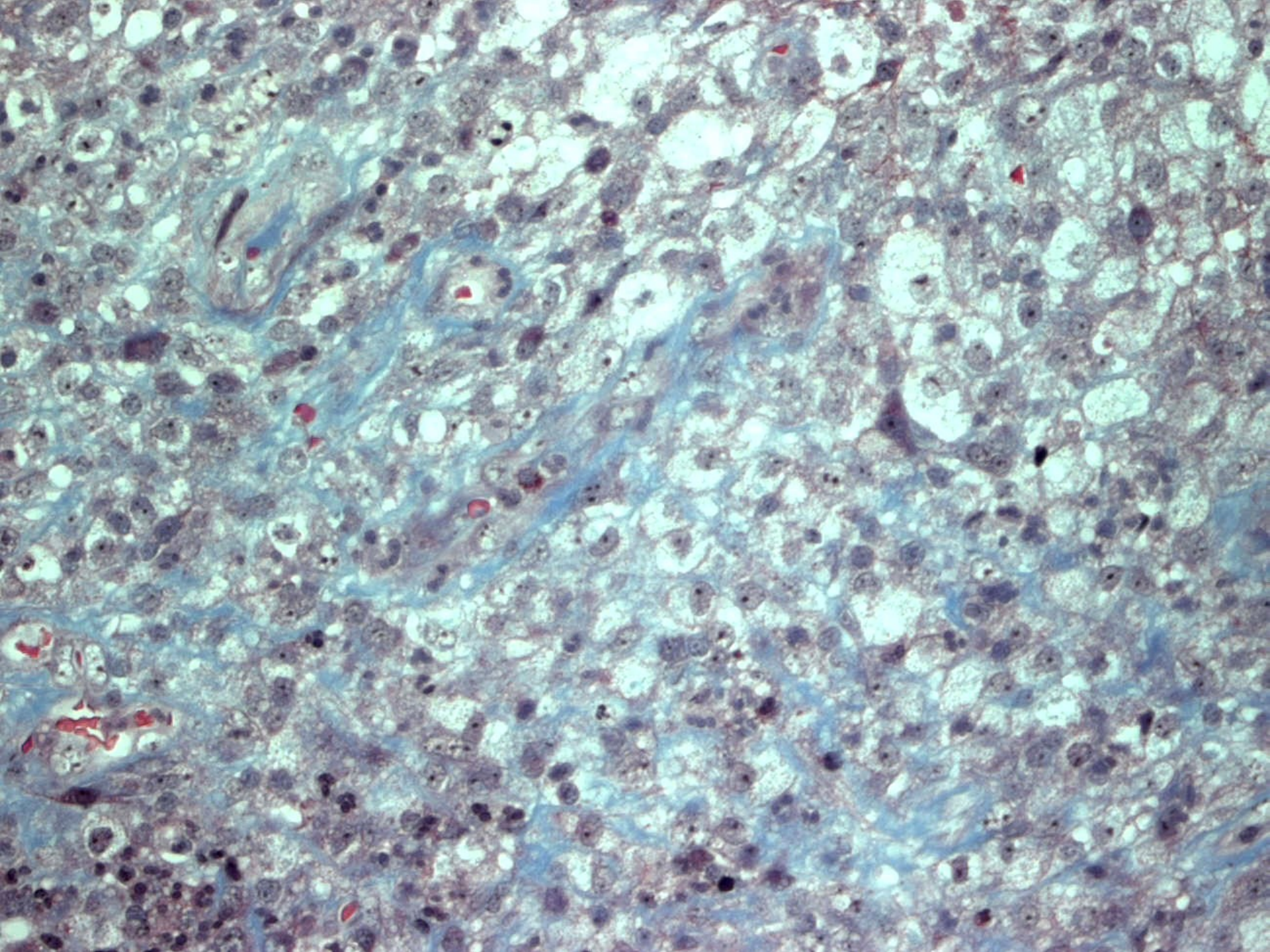


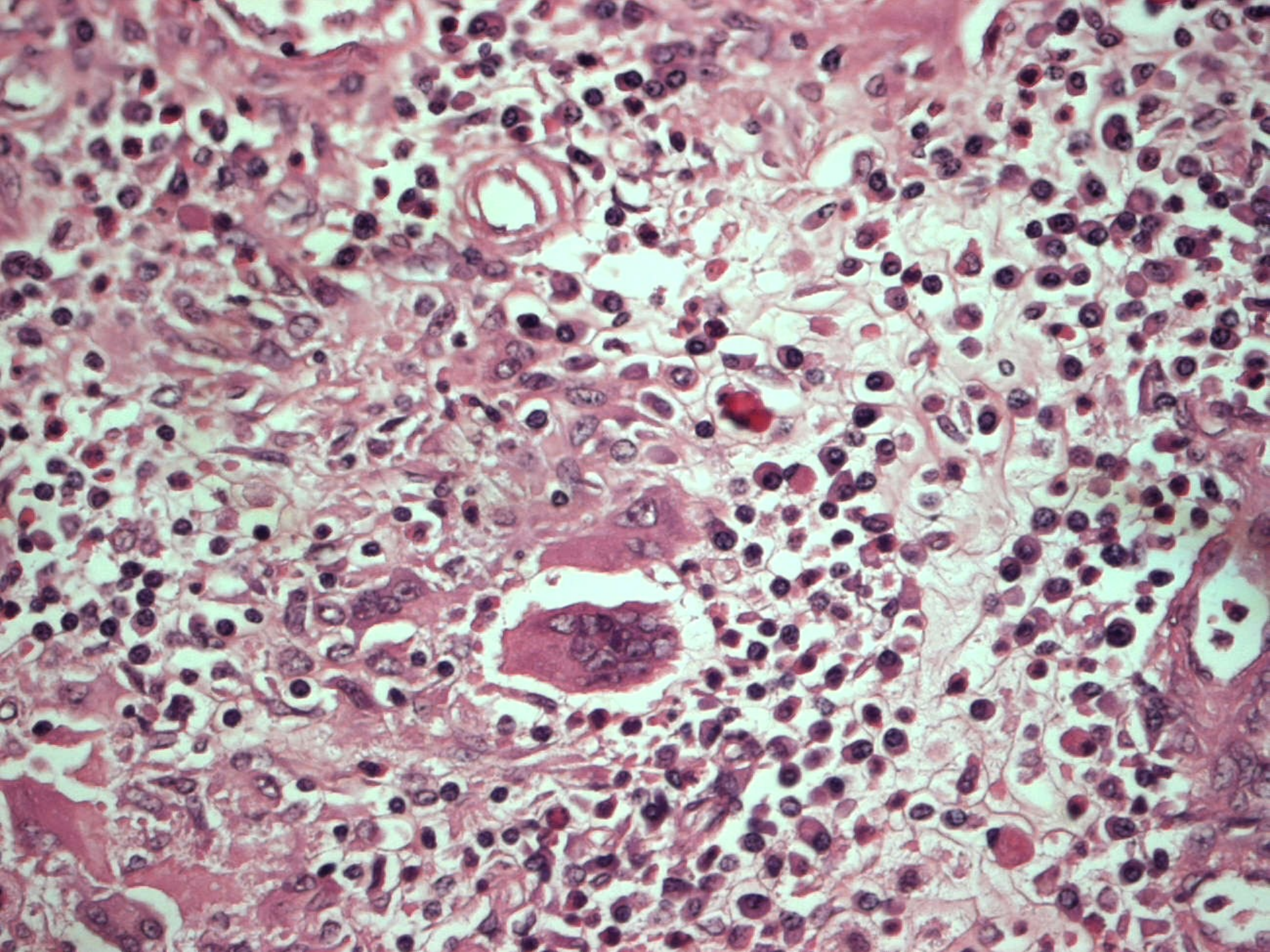


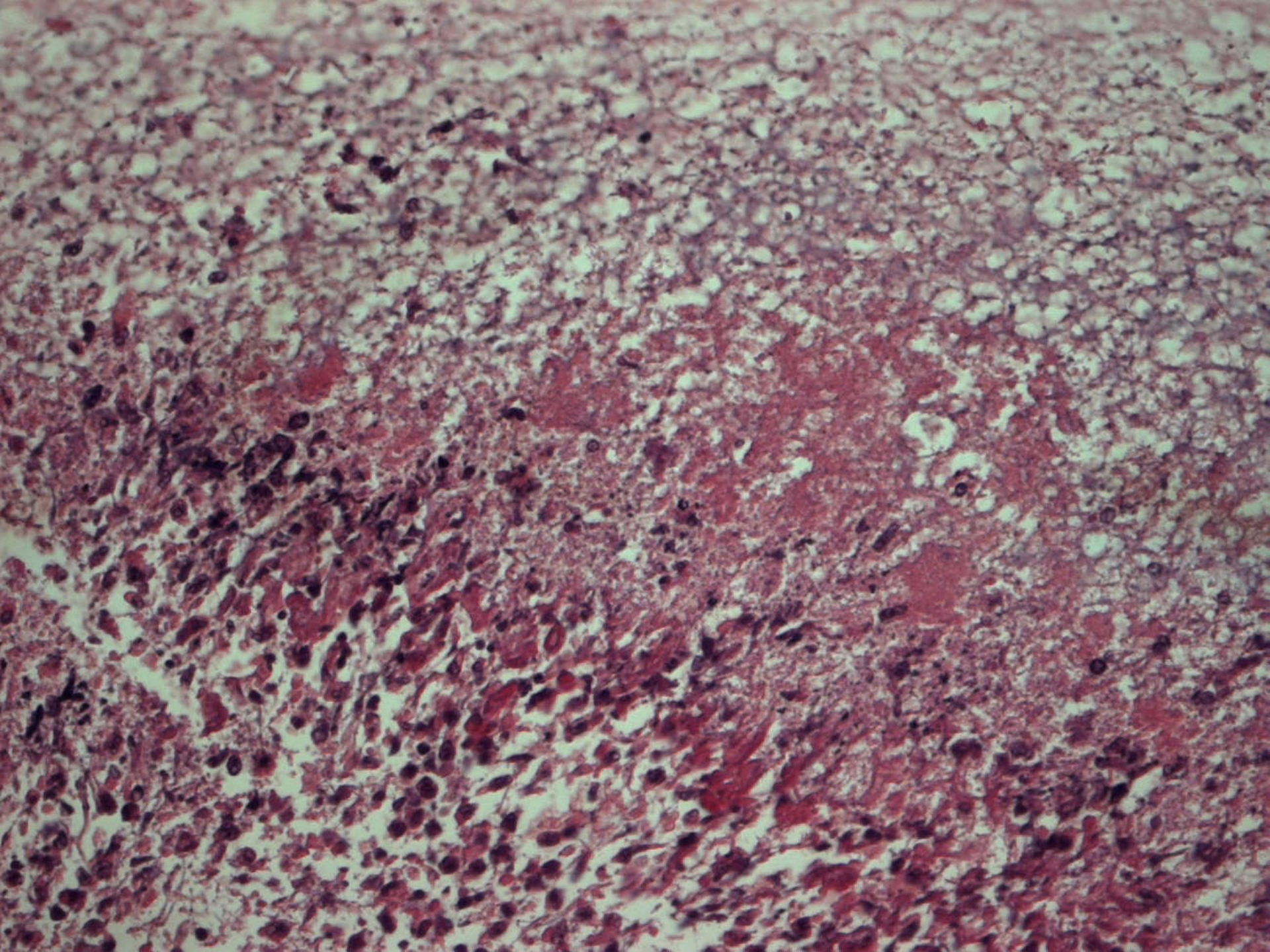


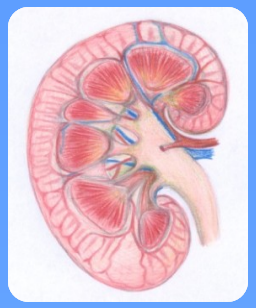










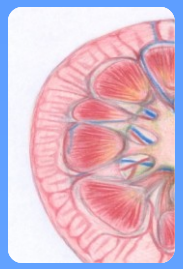


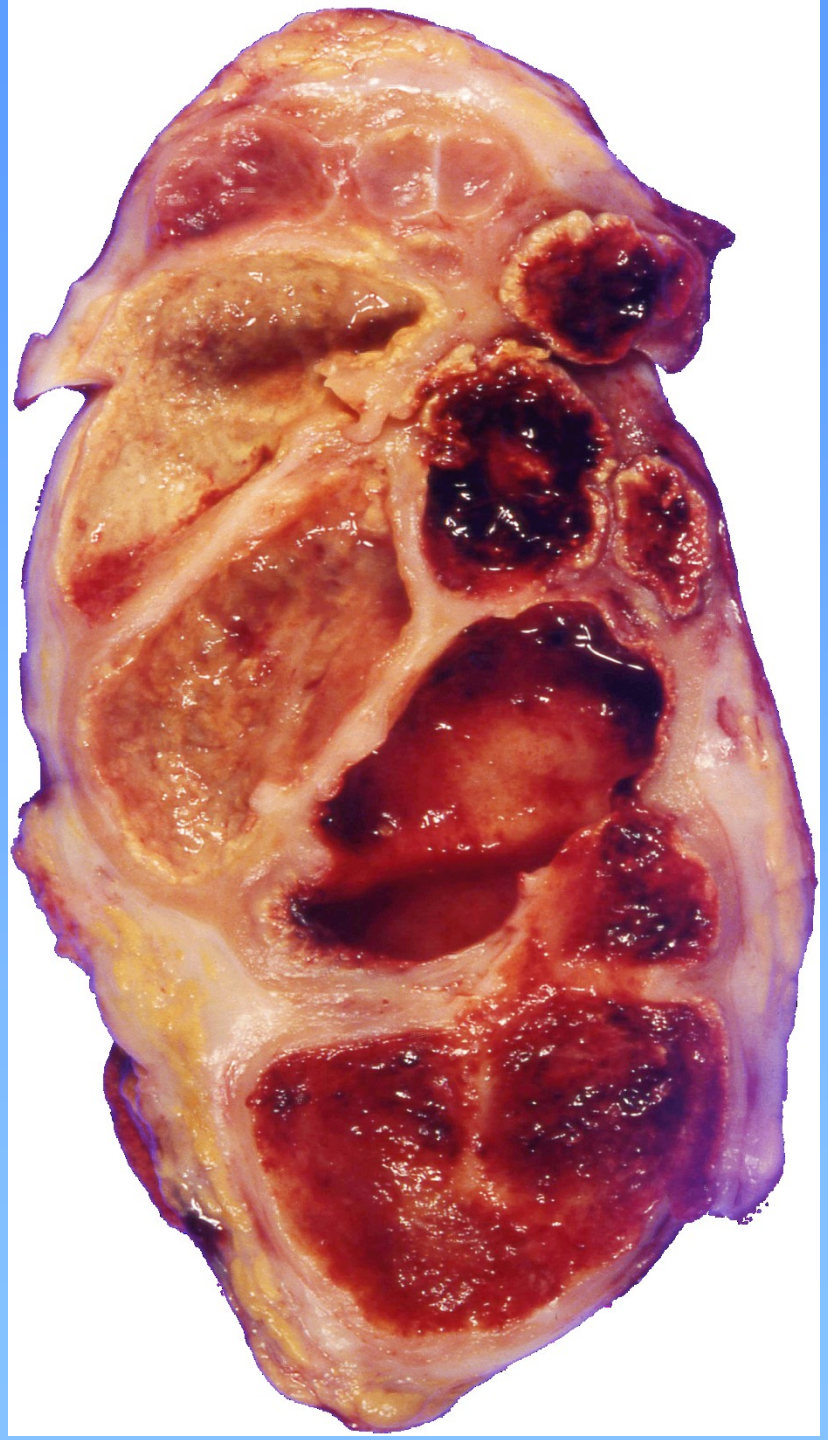
Other infections of kidney

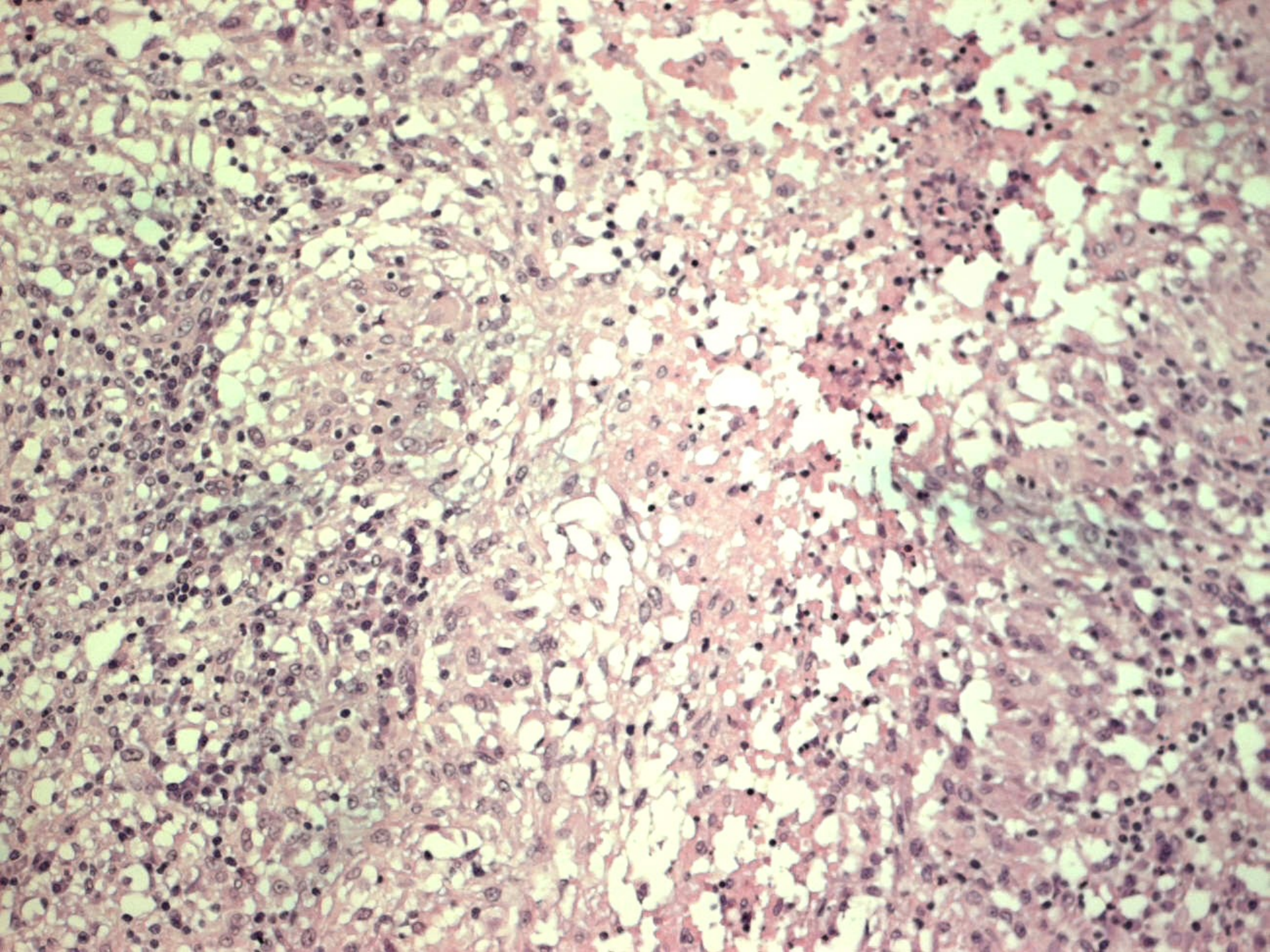
TB

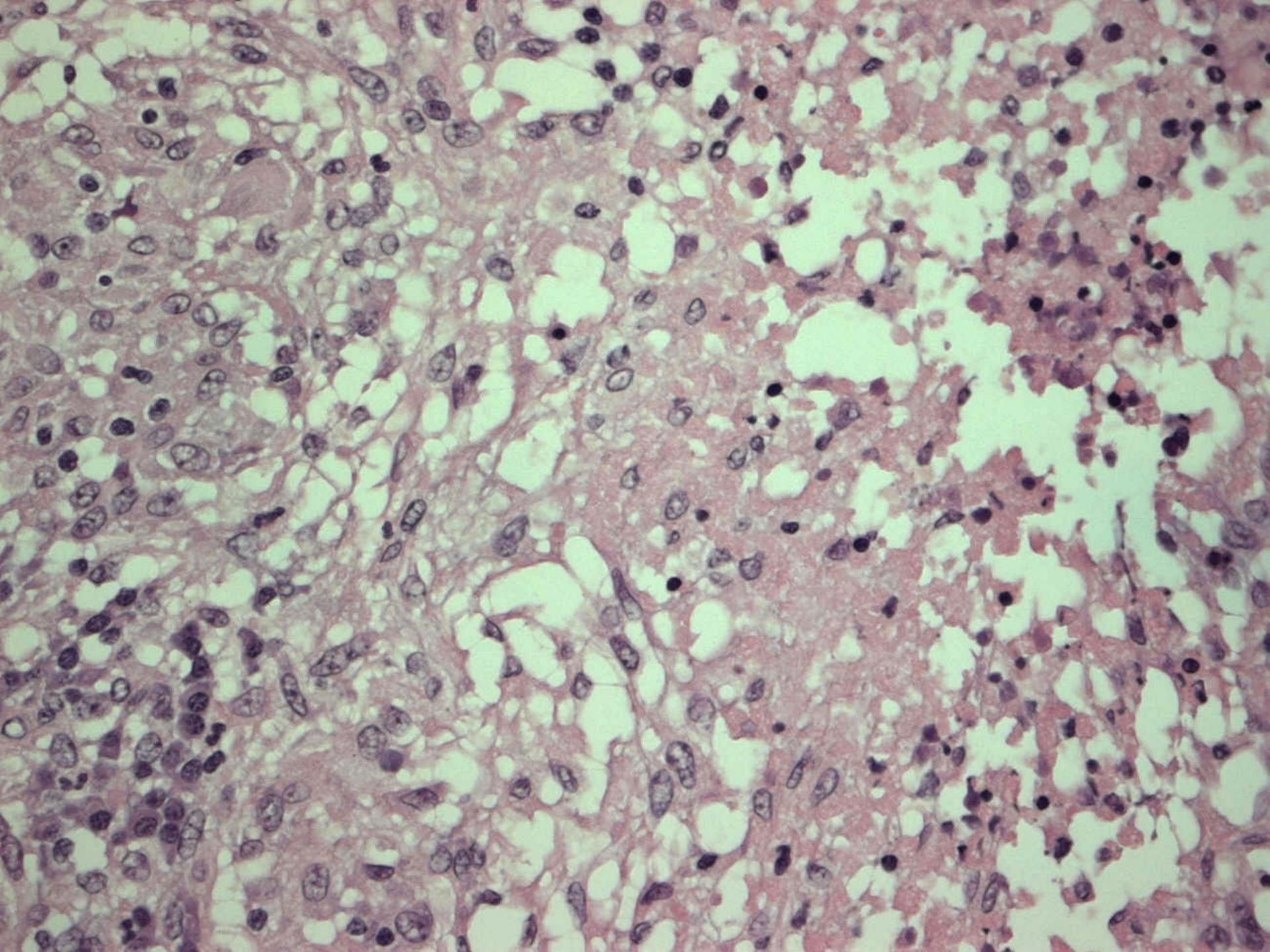
Fungal infection

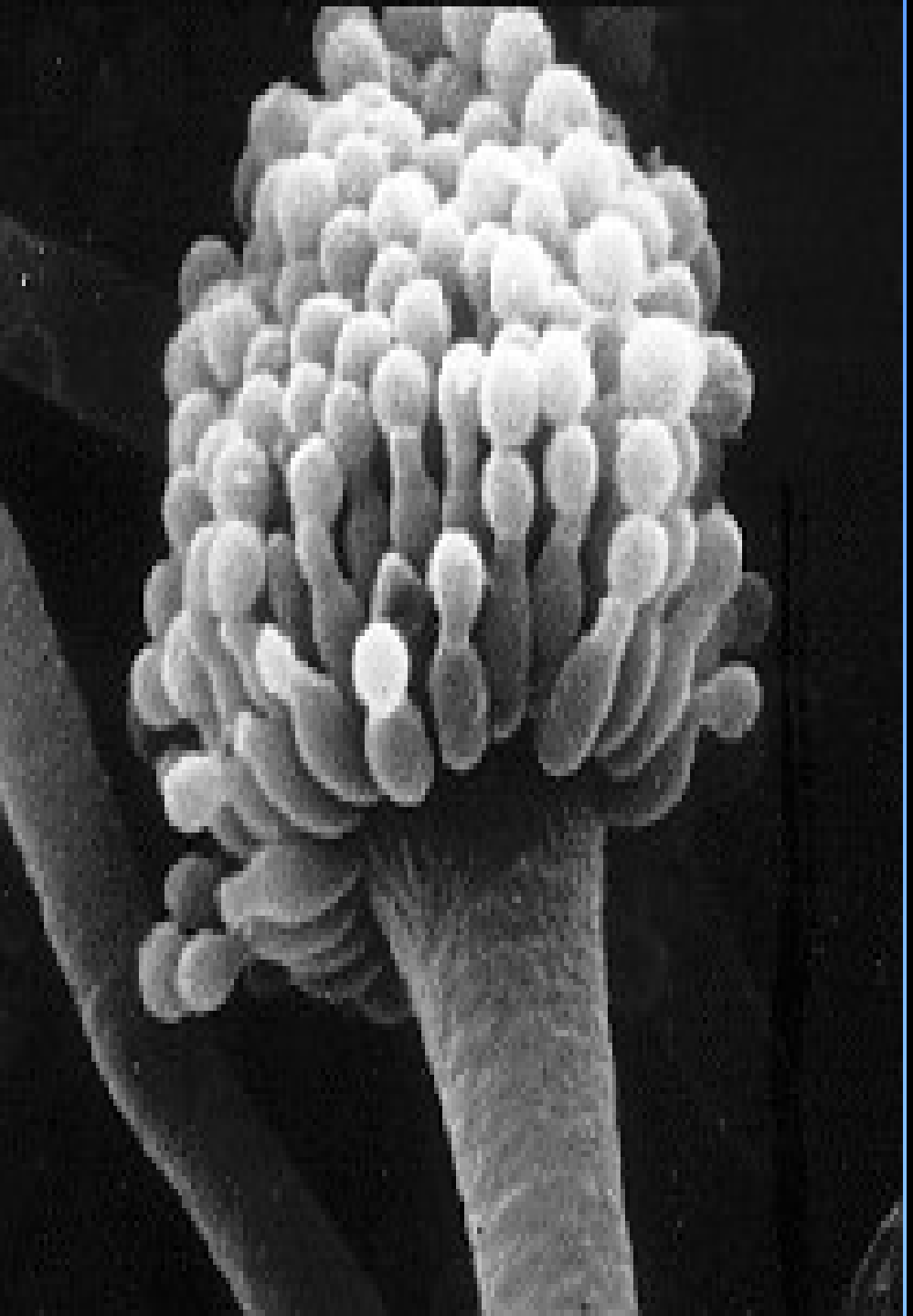
CMV

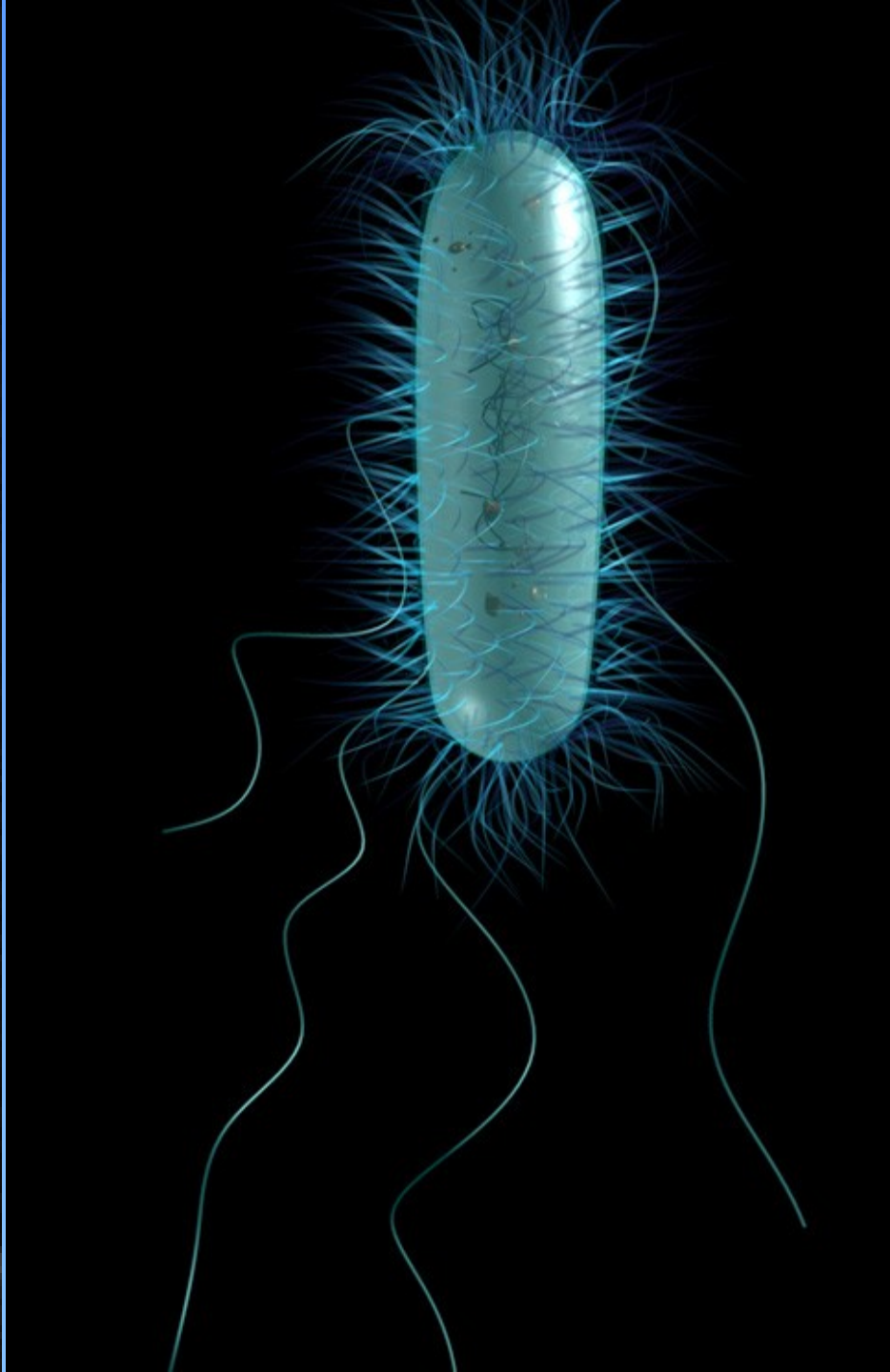


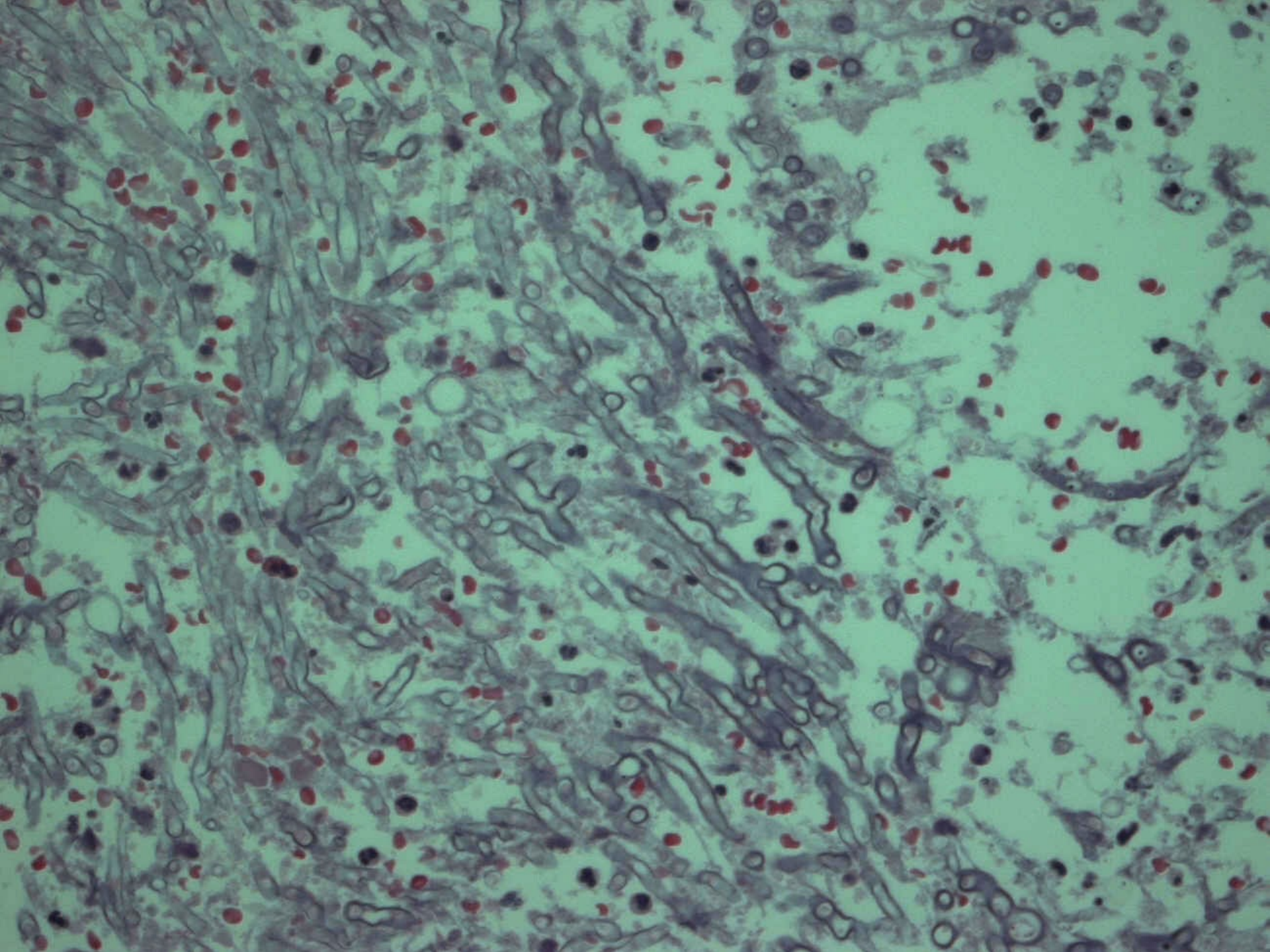


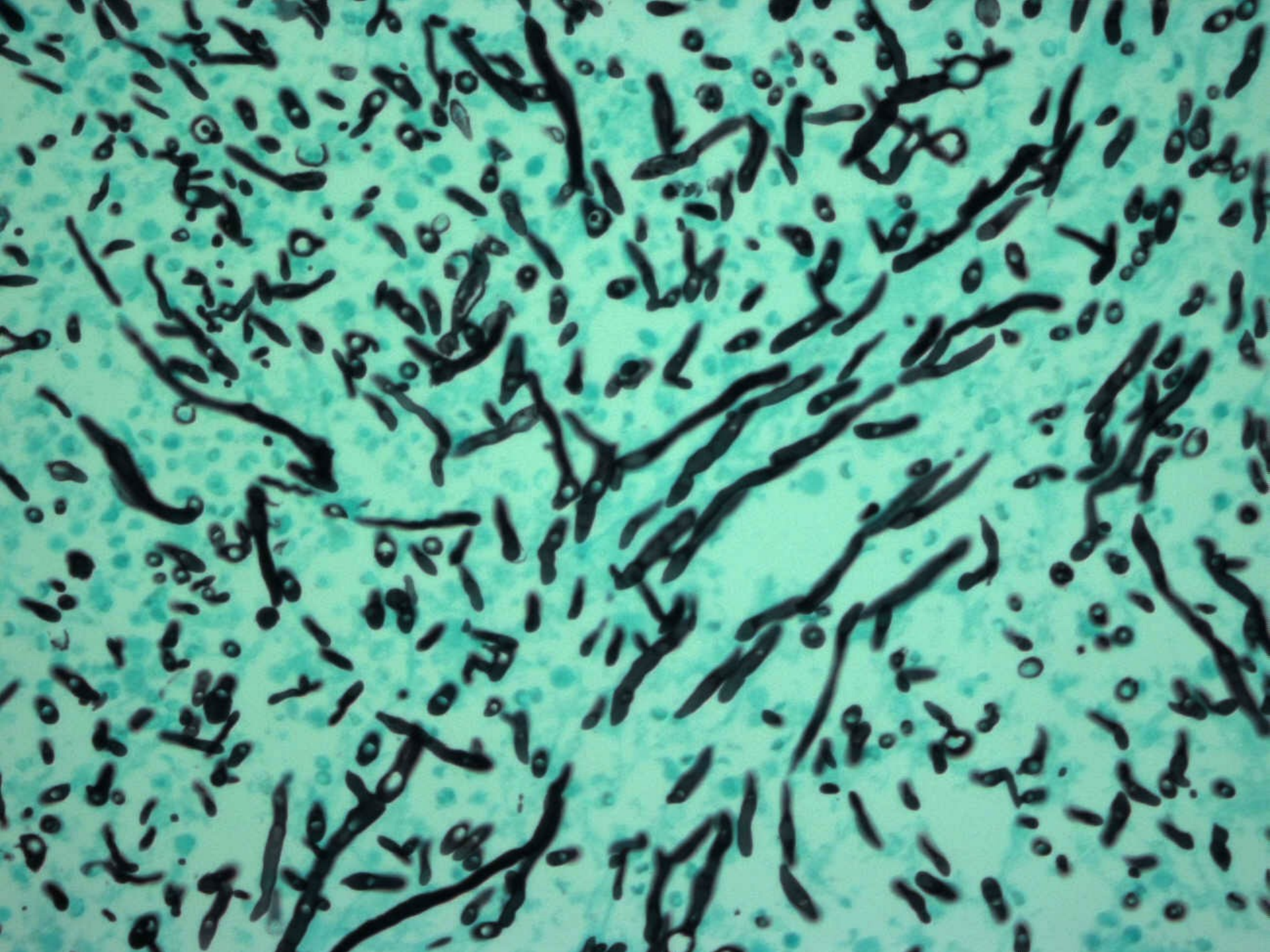


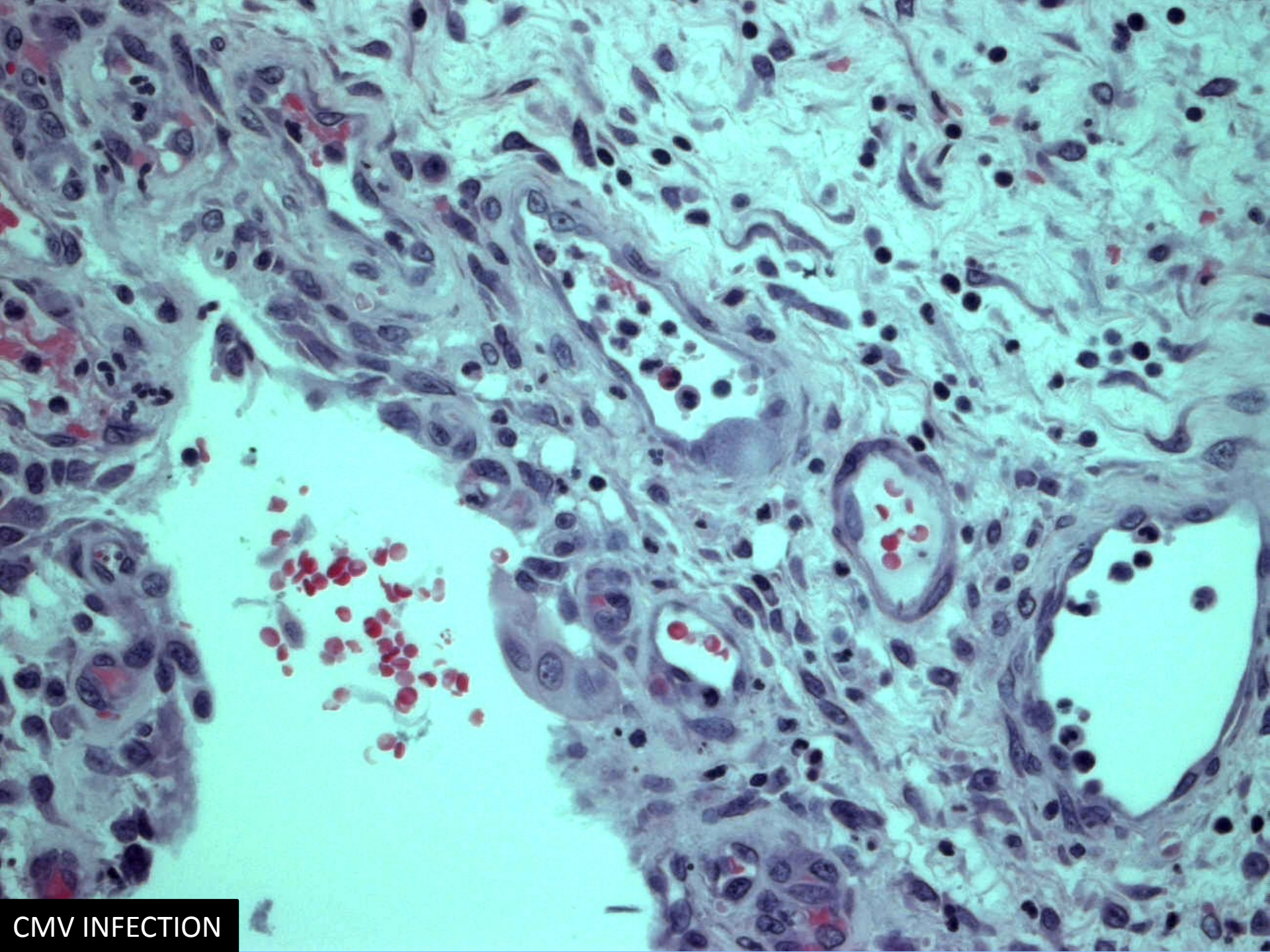


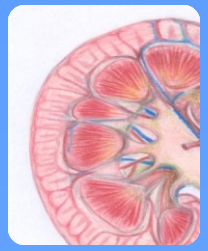









CMV INFECTION

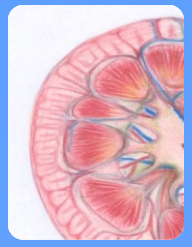


Urolithiasias

Types of stones in urinary tract

- CALCIUM OXALATE and PHOSPHATE (70%)
- Magnesium ammonium phosphate (15-20%)

  (Struvite stone)
- URIC ACID & URATE (5-10%)
- CYSTINE (1-2%)



Etiology, stone formation

- Supersaturation of urine is the key to stone formation
- Intermittent supersaturation - Dehydration
- Crystal aggregation
- Anatomic Abnormailities – PUJ , MSK
- Bacterial Infection
- Defects in transport of Calcium and Oxalate by Renal epithelia

Inhibitors & Promoters of Stone Formation in Urine

INHIBITORS

Inhibits crystal Growth -

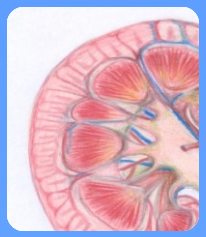
- Citrate – complexes with Ca
- Magnesium – complexes with oxalates
- Pyrphosphate - complexes with Ca
- Zinc

Inhibits crystal Aggregation

- Glycosaminoglycans
- Nephrocalcin
- Tamm- Horsfall Protein

PROMOTERS

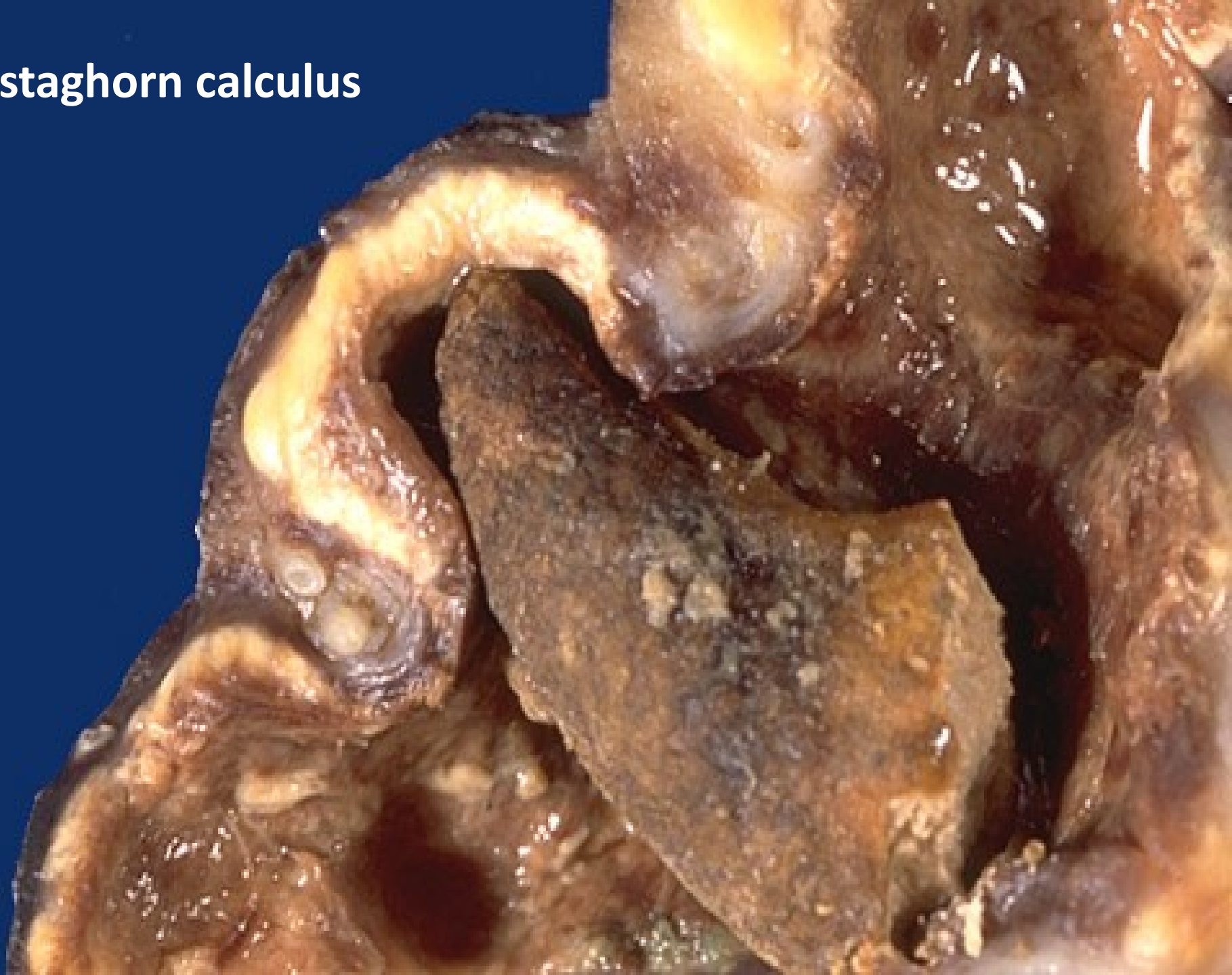
- Bacterial Infection
- Matrix
- Anatomic Abnormalities – PUJ obst., MSK
- Altered Ca and oxalate transport in renal epithelia
- Prolonged immobilisation
- Increased uric acid levels I.e taking increased purine subs– promotes crystalisation of Ca and oxalate
- ?? Nanobacteria – seen in 97% of renal stones



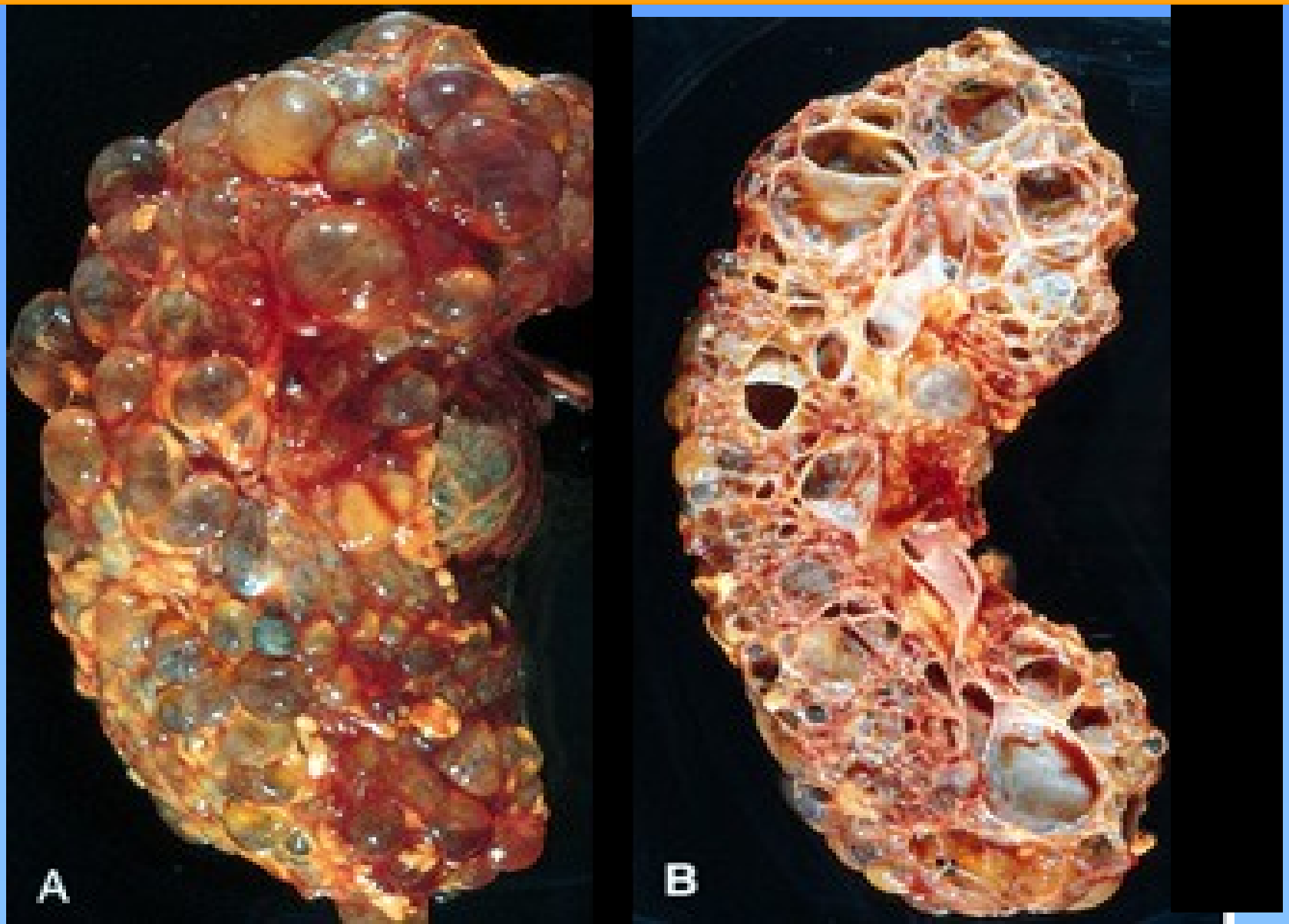
Symptoms urolithiasis

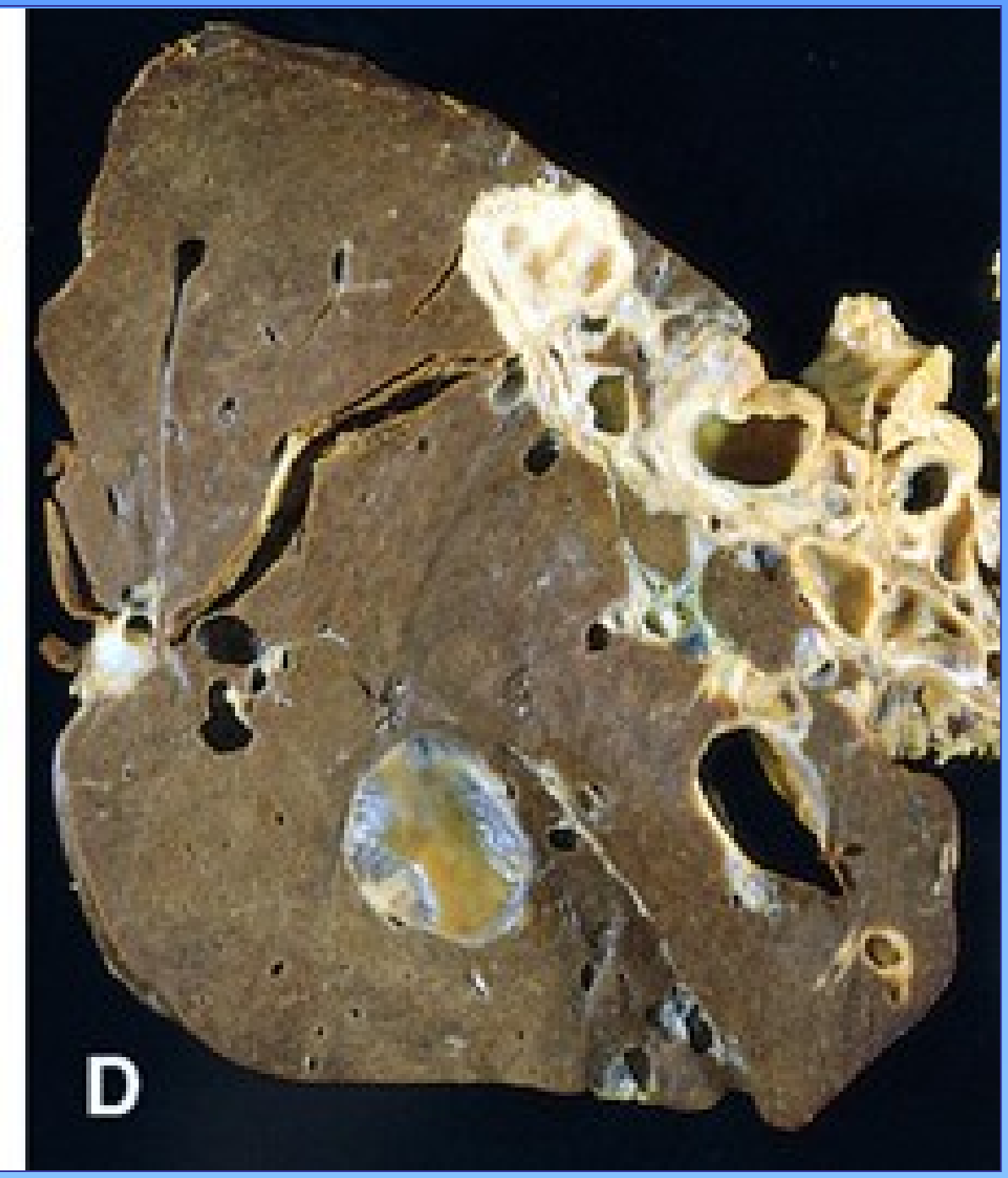
- Pain in the lower back part or in the lower abdomen, which might move to the groin. Pain may last from hours to minutes.
- Nausea, vomiting
- Blood in urine
- Burning during urination, foul smell in urine, chills, weakness and fevers for urinary tract infection.

staghorn calculus



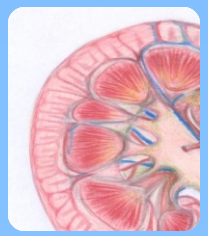
Adult polycystic renal disease





"Polycystic" liver

in
adult polycystic kidney disease disease



Childhood polycystic renal disease

Manifestation at birth or in infantile period, associated with "congenital" hepatic fibrosis

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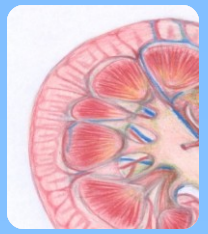
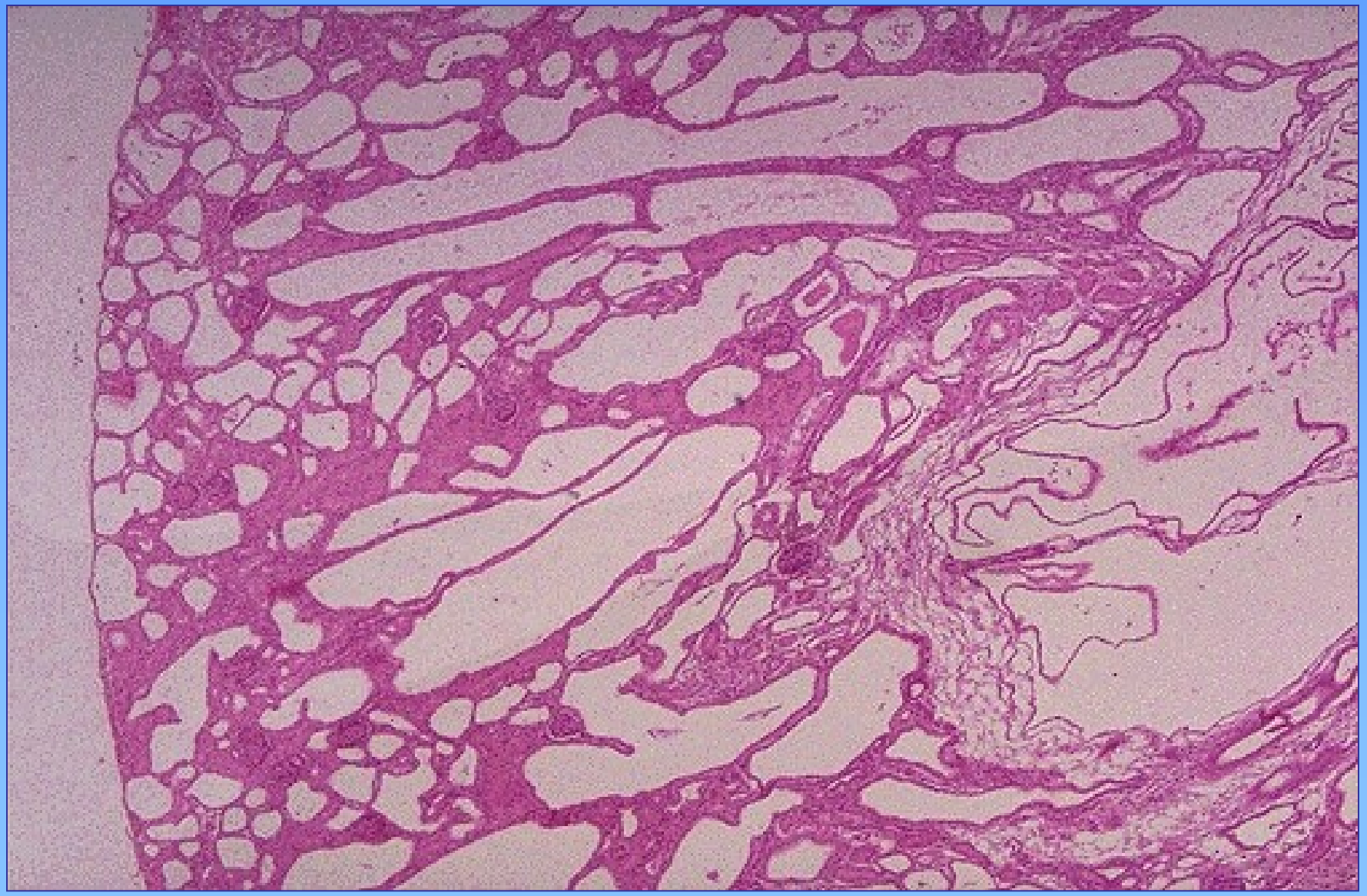
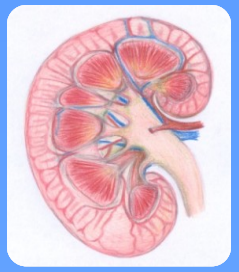
Autosomal recessive (congenital) polycystic kidney disease (RPKD).

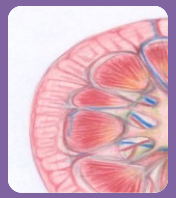


Microscopic appearance of recessive polycystic kidney disease (RPKD). The cysts fill most of the parenchyma, and it is hard to find glomeruli.





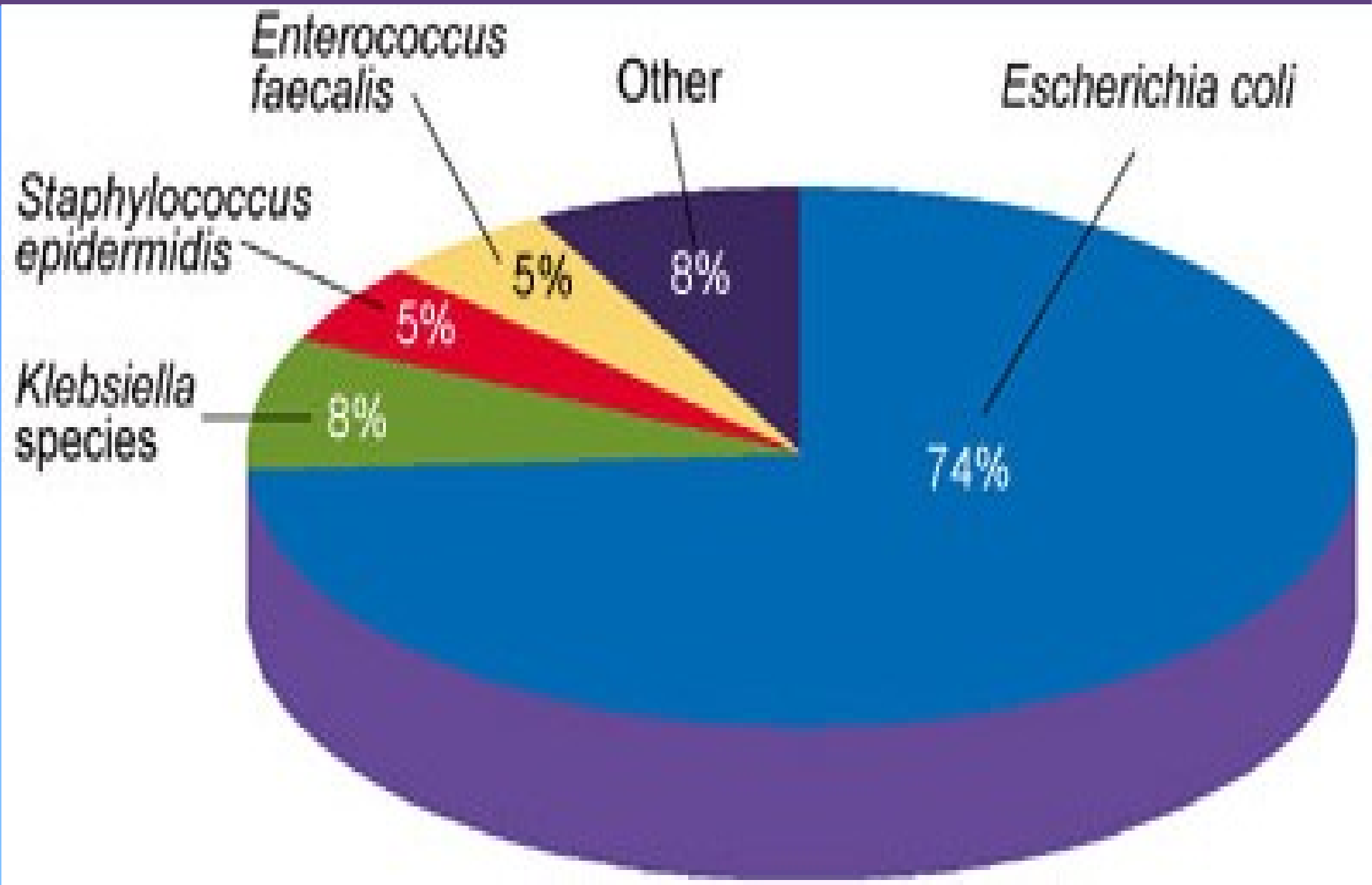
Infections lower urinary system

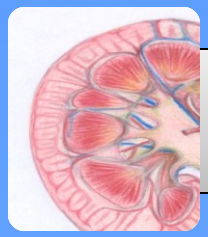


Definition-UTI

- UTI: the finding of microorganisms in bladder urine with or without clinical symptoms and with or without renal disease
- Significant bacteriuria: the number of bacteria in the voided urine exceeds the number that can be expected from contamination (i.e. ≥ 10^5 cfu/ml)

Causative agents of UTIs





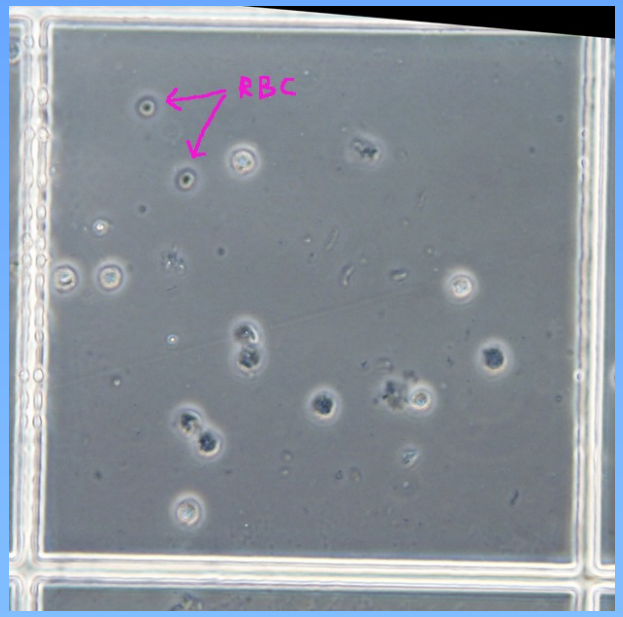
Clinical features of UTI

- **Cystitis**
  - Frequency
  - Urgency
  - Dysuria – painful voiding
  - suprapubic Pain
  - Cloudy or foul-smelling urine

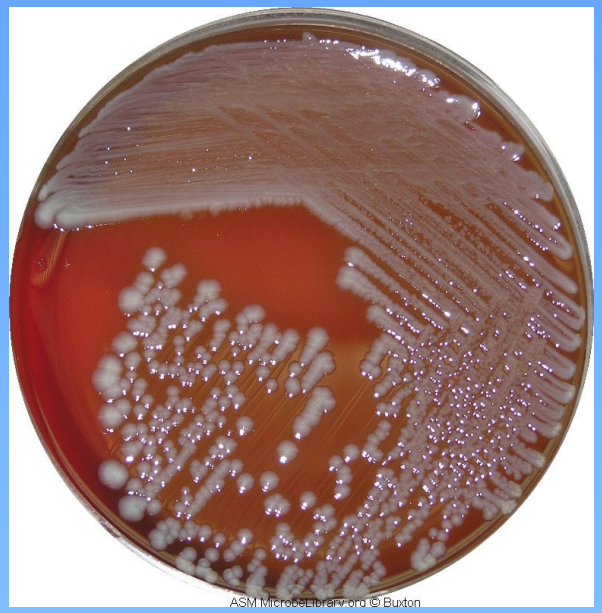
INVESTIGATION OF UTI

- Midstream urine (MSU) for:

dipstick for nitrite

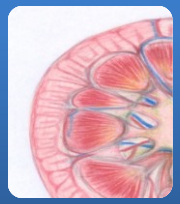


microscopy for WBCs & RBCs



urine culture

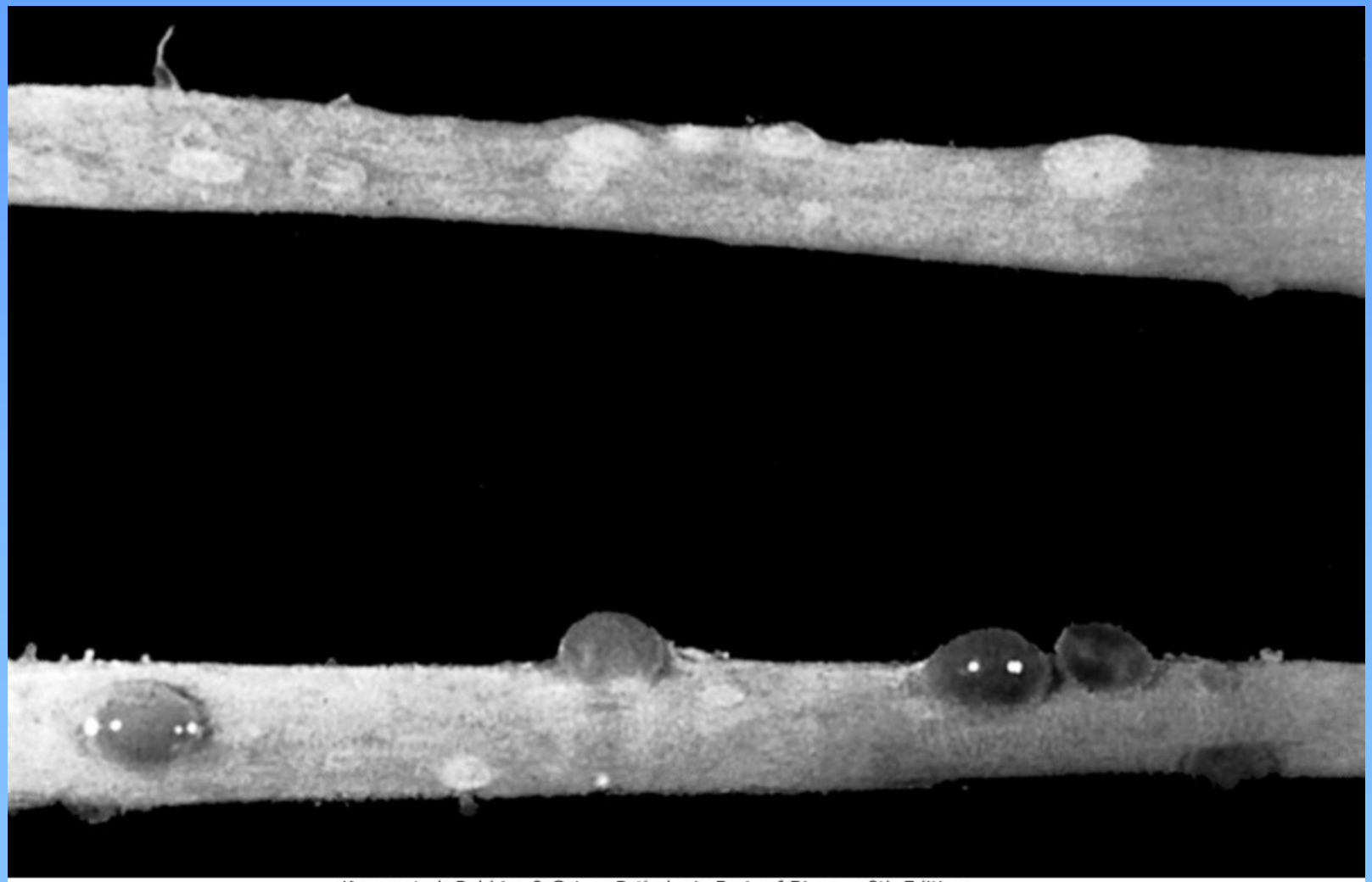
If sterile pyuria is detected then T.B has to be considered in the differential diagnosis

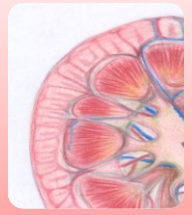


Ureteritis

- Though associated with inflammation, is typically not associated with infection and is of little clinical consequence.
- **Morphology.** The accumulation or aggregation of lymphocytes forming germinal centers in the subepithelial region may cause slight elevations of the mucosa and produce a fine granular mucosal surface **(ureteritis follicularis).**
- At other times the mucosa may become sprinkled with fine cysts varying in diameter from 1 to 5 mm lined by flattened urothelium **(ureteritis cystica)**

Ureteritis: Opened ureters showing ureteritis cystica. Note smooth cysts projecting from the mucosa.

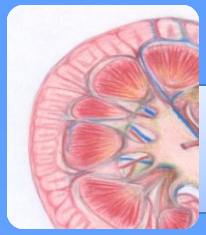




Urethritis

- It is the urethral inflammation
- Classically divided into gonococcal and nongonococcal. *Gonococcal urethritis* is one of the earliest manifestations of this venereal infection.
- *Nongonococcal urethritis* is common and can be caused by a variety of bacteria, among which *E. coli* and other enteric organisms predominate.
- *Mycoplasma (Ureaplasma urealyticum)* also accounts for the symptoms of urethritis in many cases.
- Urethritis is also one component of *Reiter syndrome*, which comprises the clinical triad of arthritis, conjunctivitis, and urethritis

Urinary bladder



Bladder

- Transitional epithelium: some cells binucleated, thickened membrane to protect tissues from urine
- Smooth muscle runs in random directions except at neck where 3 layers may be detected: inner longitudinal, middle circular and outer longitudinal layers
- Outer adventitia
- Urethra covered in reproductive system lectures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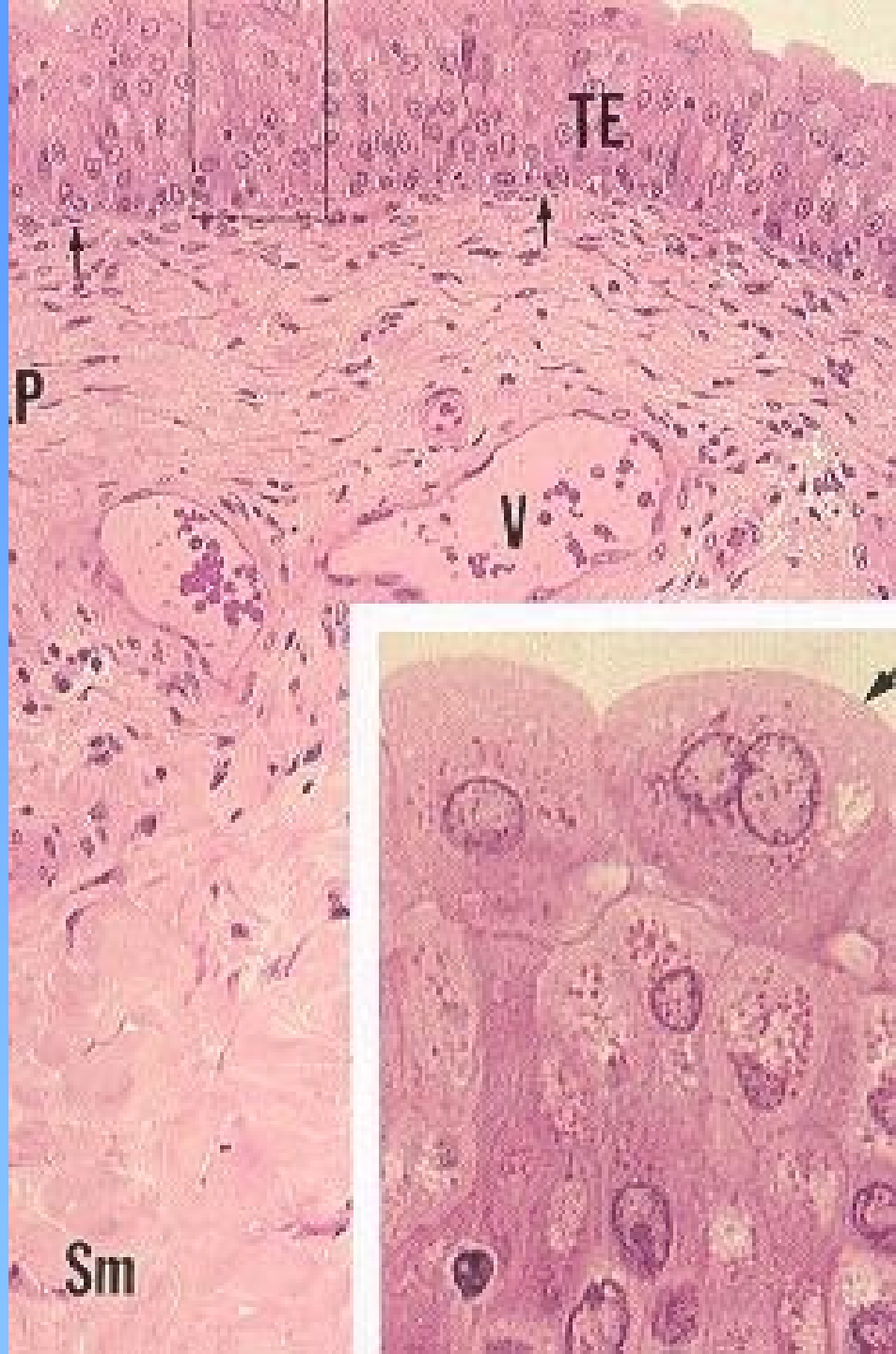
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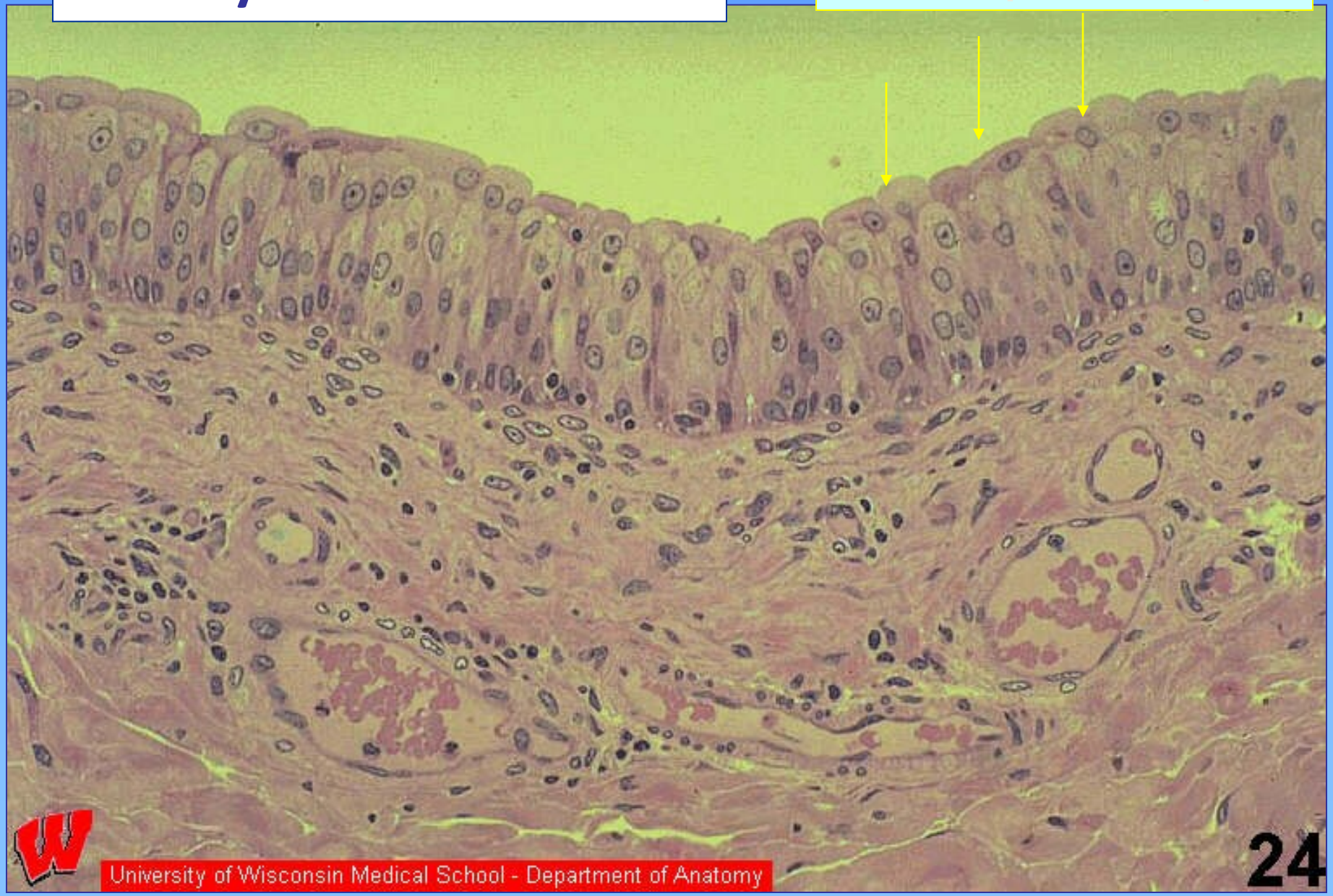
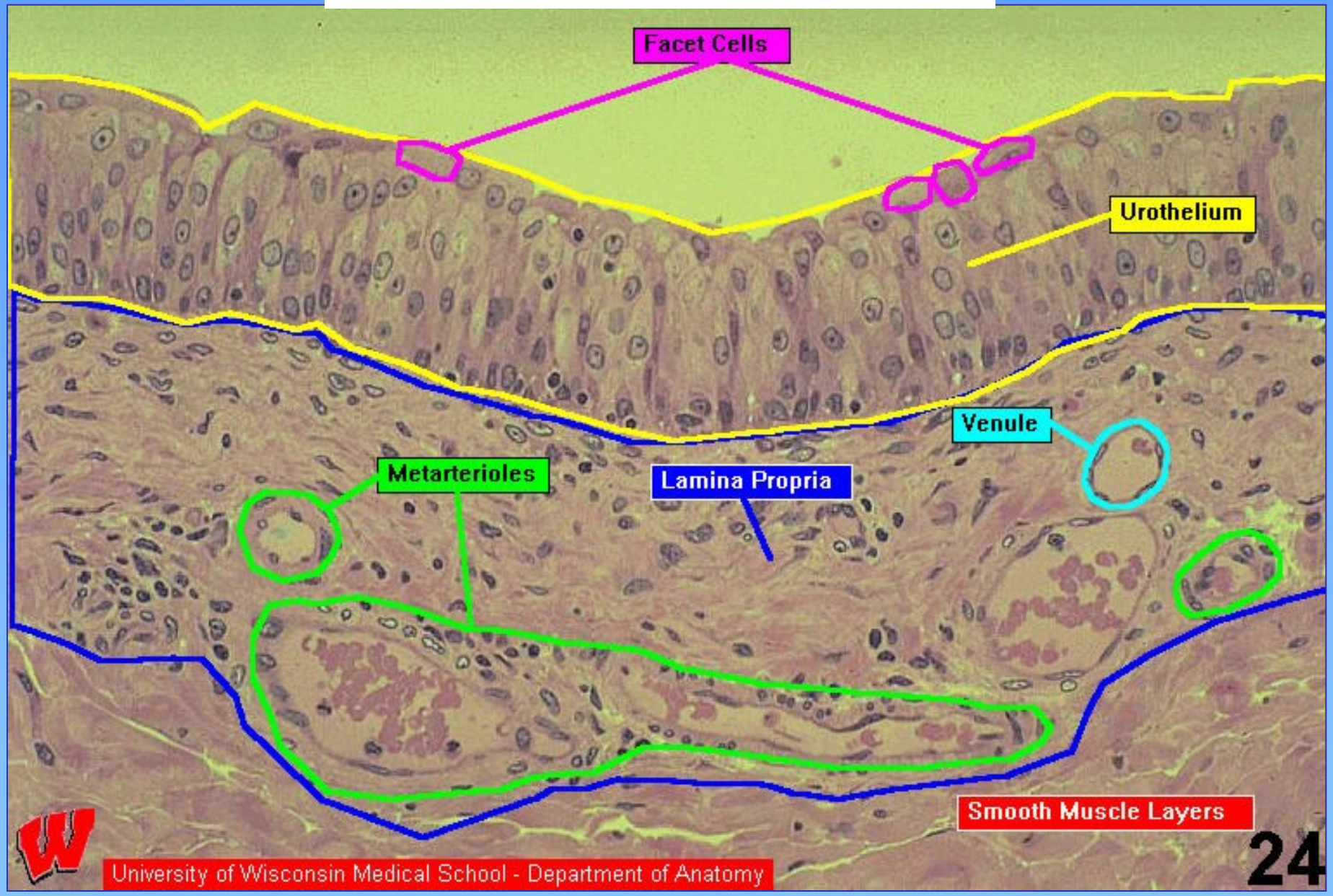
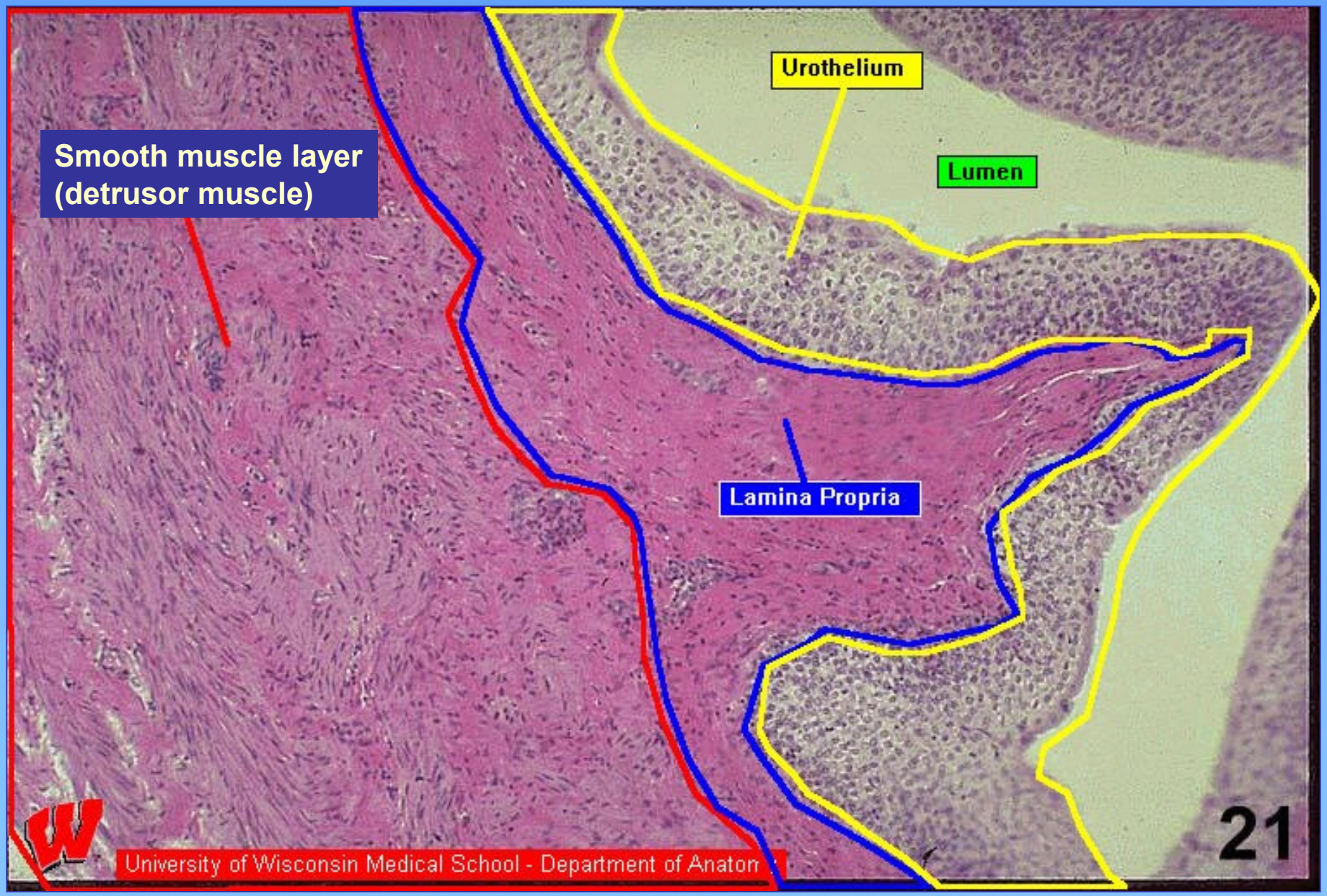
Urinary bladder musosa



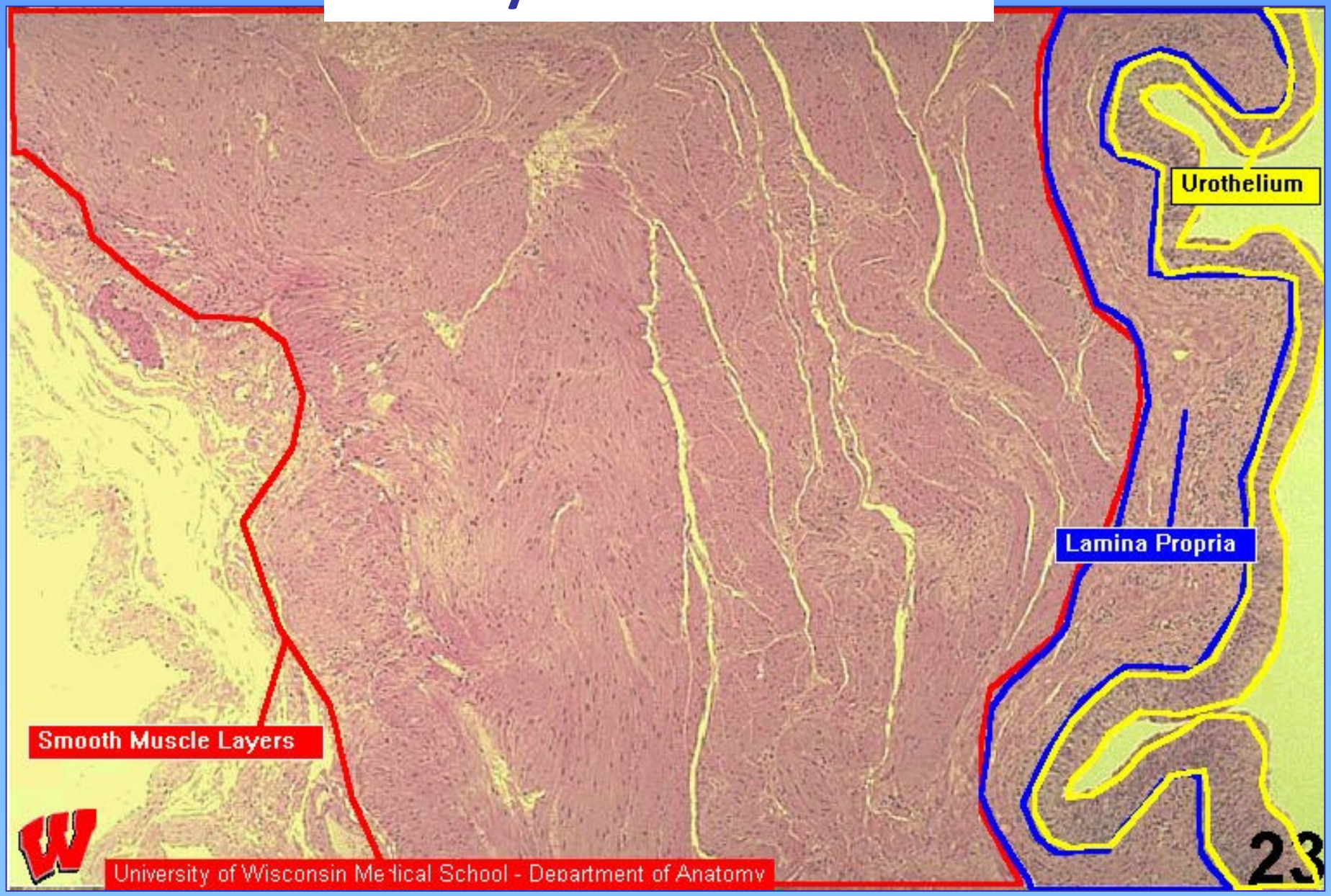
Urinary bladder musosa



Urinary bladder musosa

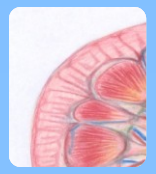


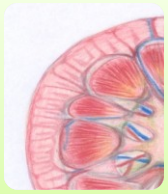
Urinary bladder musosa



Acute and Chronic Cystitis: Etiology

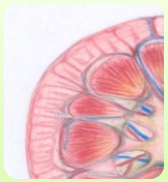
- Women are more likely to develop cystitis
- *Tuberculous cystitis* is always a sequel to renal TB
- *Candida albicans*
- Schistosomiasis *(Schistosoma haematobium)*),
- *Chlamydia*, and *Mycoplasma* may also cause cystitis.
- Predisposing factors include bladder calculi, urinary obstruction, diabetes mellitus, instrumentation, and immune deficiency.
- Finally, irradiation of the bladder region gives rise to *radiation cystitis.*





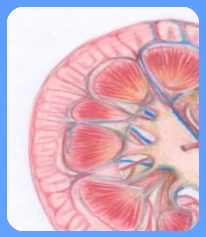
Acute and Chronic Cystitis: Morphology

- Most cases of cystitis take the form of nonspecific acute or chronic inflammation of the bladder.
- In gross appearance there is hyperemia of the mucosa, sometimes associated with exudate.
- Persistence of the infection leads to **chronic cystitis**, which differs from the acute form only in the character of the inflammatory infiltrate

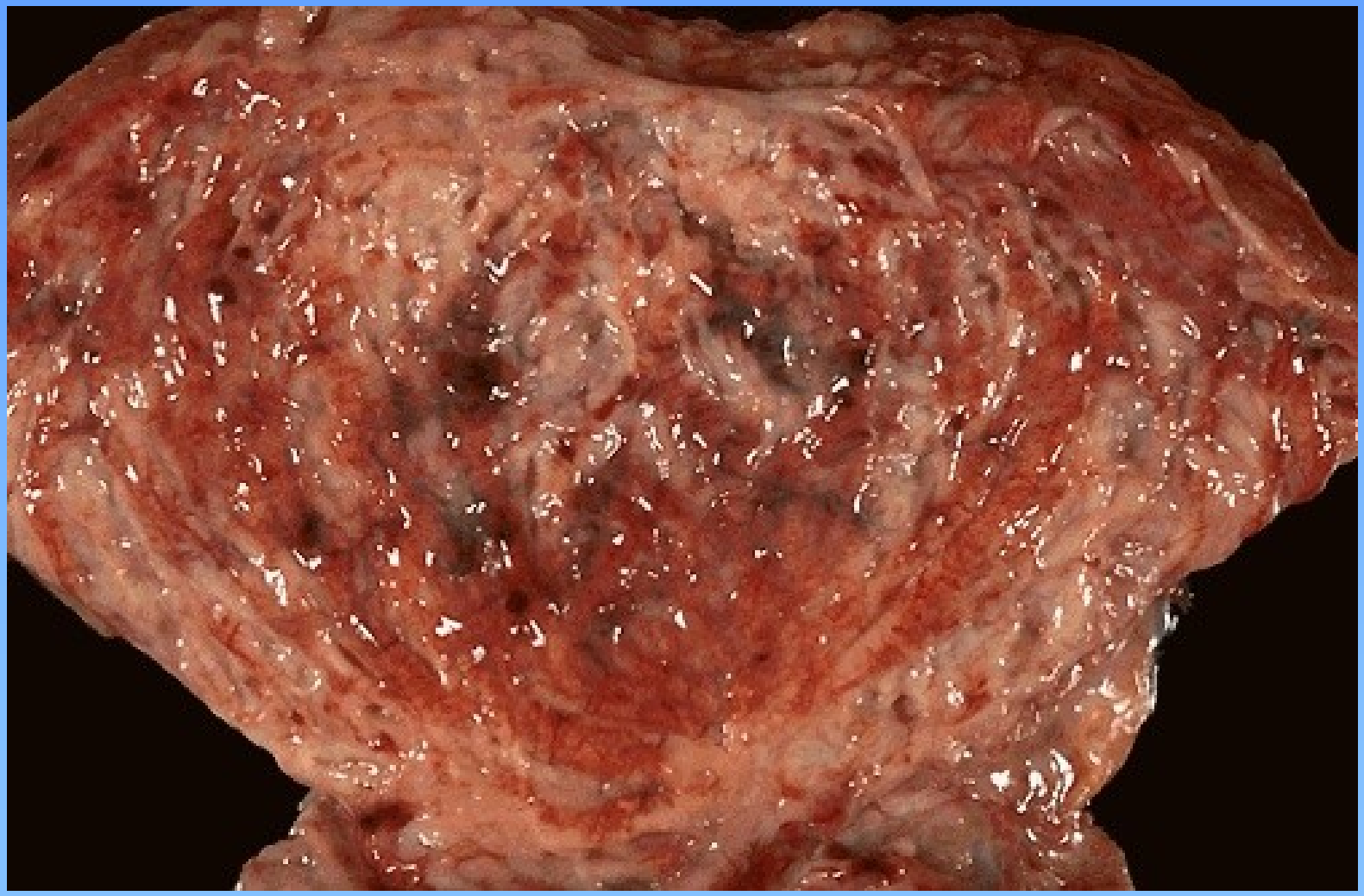


Cystitis

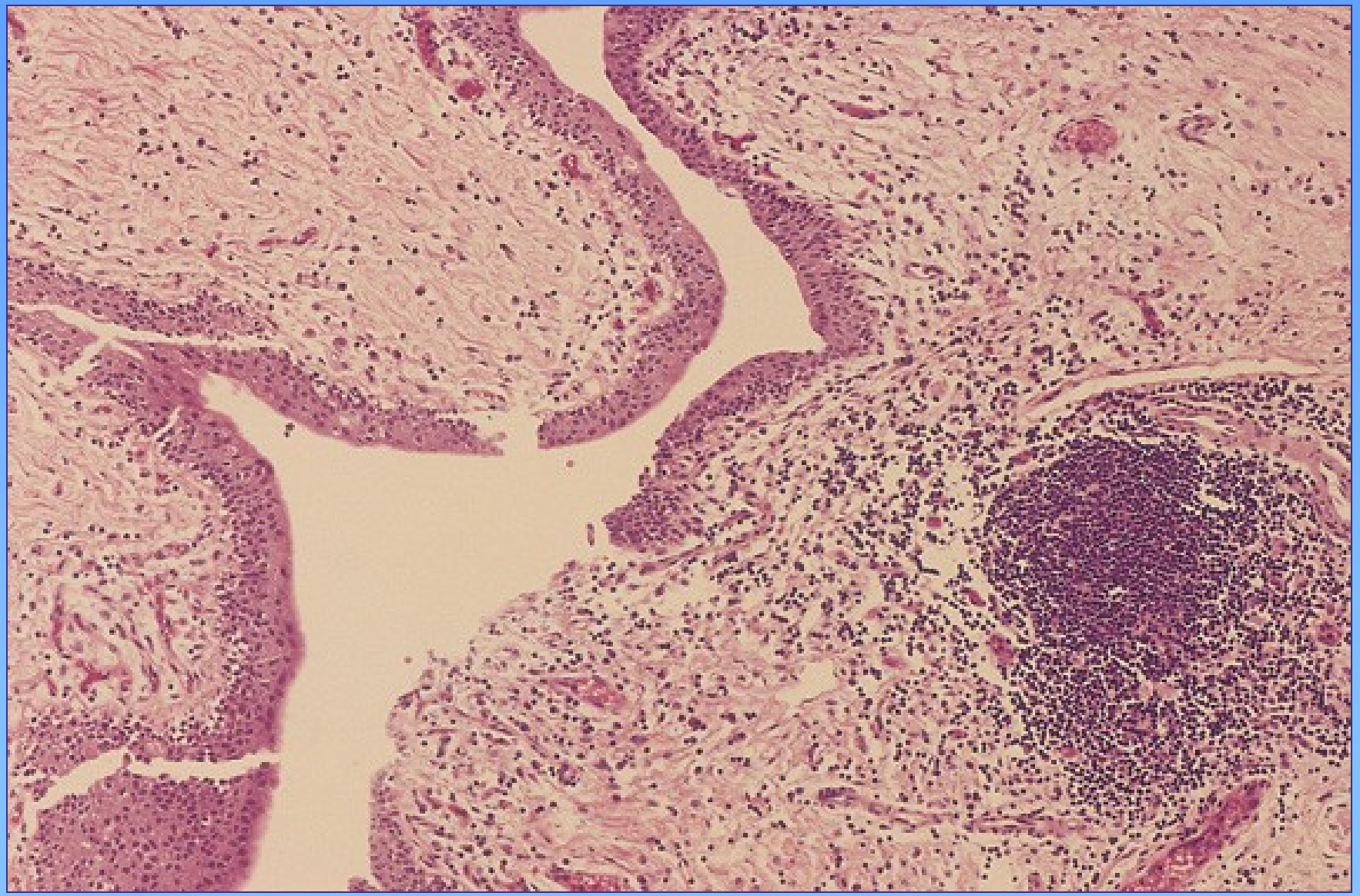
- **Follicular cystitis**, characterized by the aggregation of lymphocytes into lymphoid follicles within the bladder mucosa and underlying wall, is not necessarily associated with infection.
- **Eosinophilic cystitis**, manifested by infiltration with submucosal eosinophils, typically also represents nonspecific subacute inflammation, although rarely it is a manifestation of a systemic allergic disorder

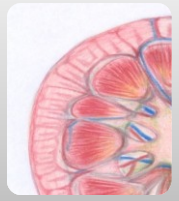


Hyperemia of the mucosa seen in acute cystitis.



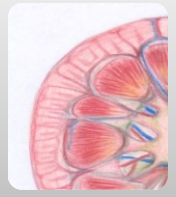
Urinary bladder cystitis





Interstitial Cystitis (Chronic Pelvic Pain Syndrome)

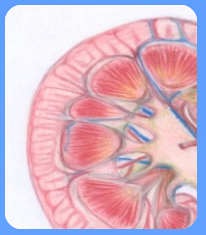
- This is a *persistent, painful form of chronic cystitis occurring most frequently in women.*
- It is characterized clinically by intermittent, often severe supra-pubic pain, urinary frequency, urgency, hematuria and dysuria without evidence of bacterial infection.
- Although mast cells are characteristic of this disease, there is no uniformity in the literature about their specificity and diagnostic utility.
- Late in the disease, transmural fibrosis may ensue, leading to a contracted bladder.

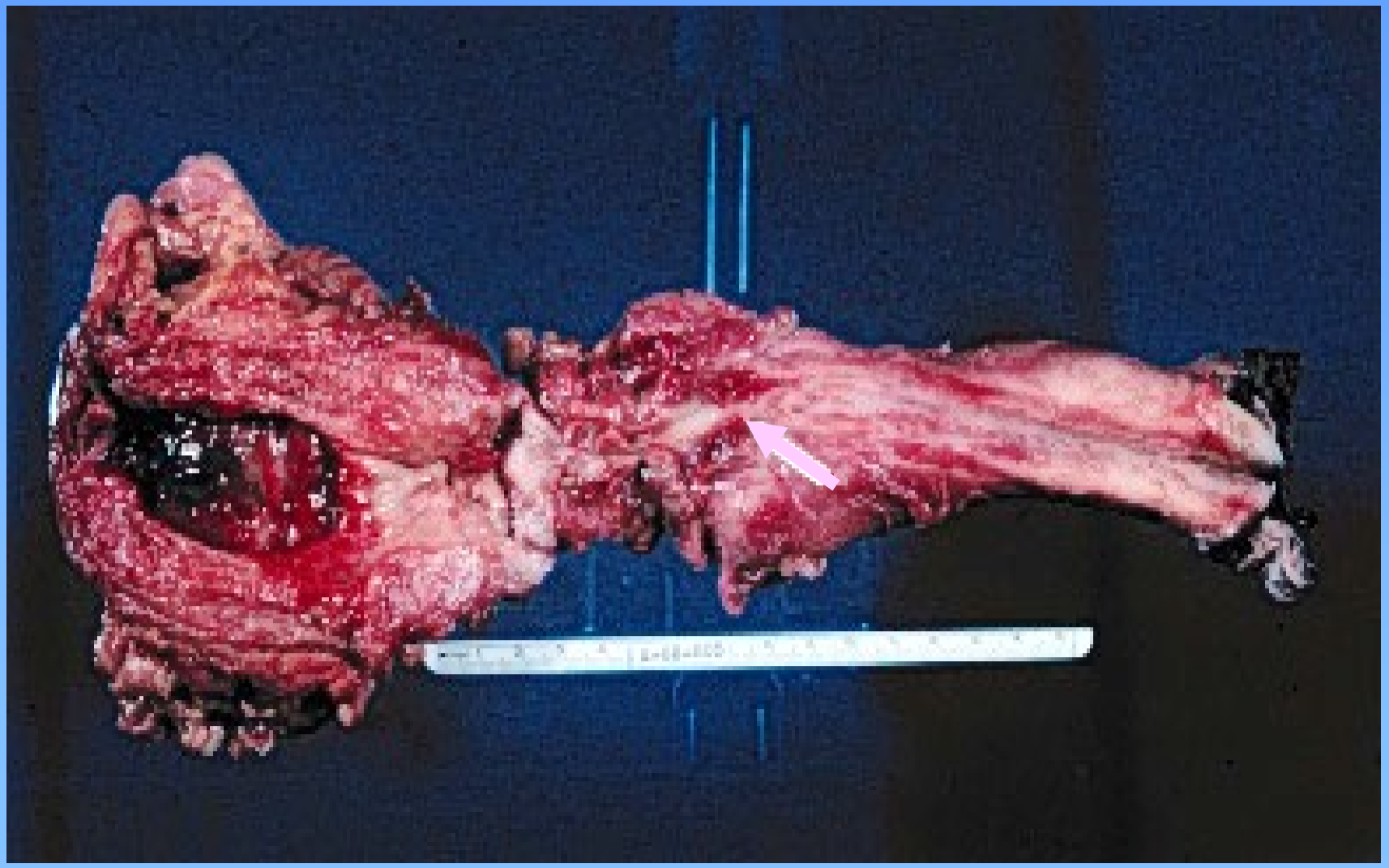


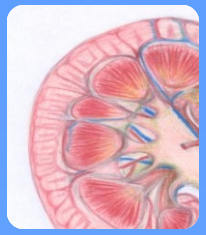
Polypoid cystitis

- It is an inflammatory condition resulting from irritation to the bladder mucosa.
- Although indwelling catheters are the most commonly cited culprits, any injurious agent may give rise to this lesion.
- The urothelium is thrown into broad bulbous polypoid projections as a result of marked submucosal edema.
- Polypoid cystitis may be confused with papillary urothelial carcinoma both clinically and histologically.

Urinary tract obstruction - an obstruction of the urethra at the base of the penis.







CONCLUSION