Renal Block

Lecture Two & Three

UTIs

Objectives:

- Recognize the predisposing factors for infections of the kidney and urinary tract.
- Describe the different types of infections in the kidney and urinary tract.
- Recognize the clinicopathological features of acute and chronic pyelonephritis.
- Describe the causes of urinary tract obstruction.
- Recognize drug induced nephritis

Introduction: Urinary Tract Obstruction:

This obstruction may occur anywhere in the urinary system.

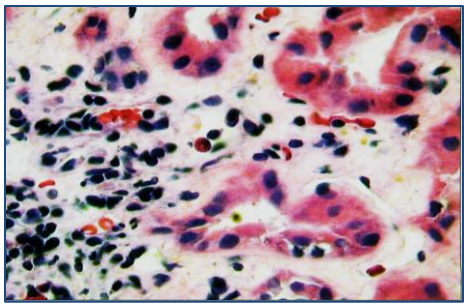
In children	In adults
Most often due to congenital malformations (associated with reflux or other causes).	Most often acquired and usually occurring as a consequence of renal stones or benign prostatic hyperplasia.

Clinical manifestation include:

1. Renal colic, which is an excruciating pain caused by acute distention of the ureter, usually due to the transit (movement) of a stone.
2. Hydronephrosis, which is a progressive dilation of the renal pelvis and calyces.
3. Infection, which is localized proximal to the site of obstruction and may lead to infection of the renal parenchyma.

Tubulointerstitial nephritis: (Robbins pg. 533)

- This group of diseases generally involve inflammatory injuries of the tubules and/or the interstitium of the kidney resulting in decreased renal function.
- It is often insidious in onset and principally manifest by azotemia
- Common causes include infection and drugs (analgesics such as NSAID or antimicrobials such as penicillin and methicillin)



Higher power of tubulitis demonstrating interstitial edema and invasion of the tubular epithelium by lymphocytes.

Renal papillary necrosis:

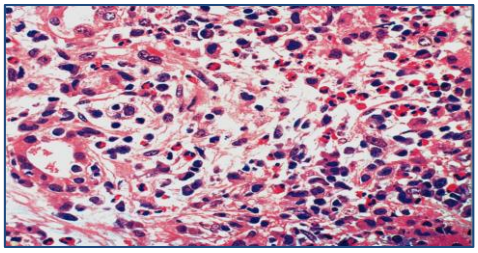
a) Ischemic necrosis of the tips of the renal papillae.

b) Chronic form

c) Usually associated with long term persistent abuse of phenacetin (pain-relieving and fever-reducing drug)

This can lead to chronic analgesic nephritis, a chronic inflammatory change characterized by loss and atrophy of tubules and interstitial fibrosis and inflammation.

d) Usually associated with diabetes mellitus



The mononuclear infiltrate is accompanied by abundant eosinophils and may have a granulomatous appearance.

Acute drug included interstitial nephritis:

Acute drug-induced tubulointerstitial nephritis (TIN) occurs as an adverse reaction to any of an increasing number of drugs. Acute drug-induced TIN is associated most frequently with synthetic penicillins (methicillin, ampicillin), rifampin, diuretics, NSAIDs, and numerous other drugs (phenindione, cimetidine).

a) Acute form, of immune etiology.
b) Usually triggered by penicillin derivatives or NSAIDs & diuretics.
c) Eosinophils are characteristic.
d) Resolves on cessation of the inciting drug.

Pathogenesis:

* Serum IgE levels are increased in some persons, suggesting type I hypersensitivity.
* In other cases the nature of the inflammatory infiltrate and the presence of positive skin tests to drugs suggest a T cell–mediated (type IV) hypersensitivity reaction.

Morphology:

* The abnormalities in acute drug-induced nephritis are in the interstitium.
* With some drugs (e.g., methicillin, thiazides, rifampin), interstitial non-necrotizing granulomas with giant cells may be seen.
* The glomeruli are normal except in some cases caused by nonsteroidal anti-inflammatory agents, in which the hypersensitivity reaction also leads to podocyte foot process effacement and the nephrotic syndrome.

Pyelonephritis: (Robbins pg. 533)

One of the most common diseases of the kidney and is defined as inflammation affecting the tubules, interstitium, and renal pelvis. (Pyelo- means pelvis. nephritis- inflammation in nephron).

Routes of infection (Pathogenesis):

1- Ascending infection: (most common)

More than 85% of cases of urinary tract infection are caused by the gram-negative bacilli (E. coli is by far the most common) that are normal inhabitants of the intestinal tract.

2- Hematogenous infection: e.g. TB

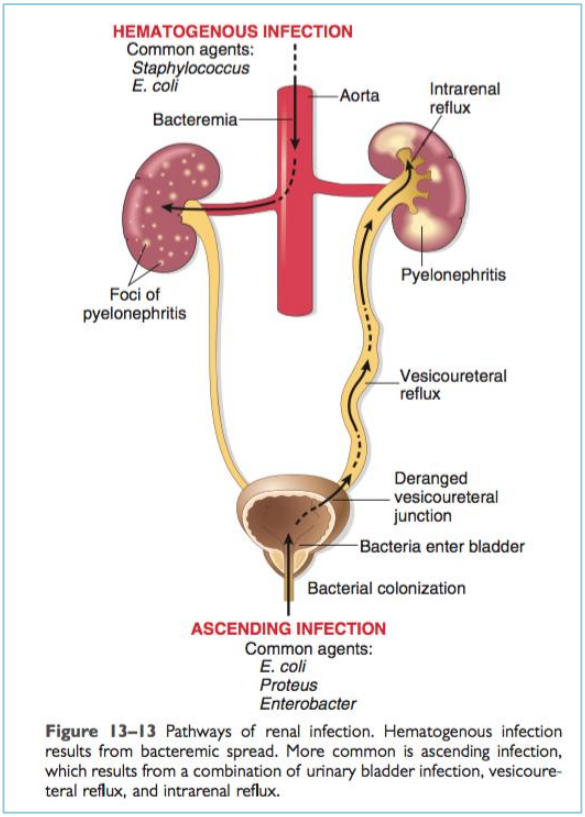


Figure 13–13 Pathways of renal infection. Hematogenous infection results from bacteremic spread. More common is ascending infection, which results from a combination of urinary bladder infection, vesicoureteral reflux, and intrarenal reflux.

What happens?

- Adhesion of bacteria to mucosal surfaces is followed by colonization of the distal urethra.
- The organisms then reach the bladder, moving against the flow of urine.
- Outflow obstruction or bladder dysfunction setts the stage for UTI.
- Bacteria then multiply undisturbed, without being flushed out or destroyed by the bladder wall.
- From the contaminated bladder urine, the bacteria ascend along the ureters to infect the renal pelvis and parenchyma.

Predisposing factors of acute pyelonephritis:

- Urinary tract obstruction, either congenital or acquired (stasis allowing bacteria to multiply a lot easier)
- Instrumentation of the urinary tract (e.g. catheterization)
- Vesicoureteral reflux (Youtube):
  - Young children with UTI, usually as a consequence of a **congenital defect**
  - Acquired in persons with a **flaccid bladder** resulting from spinal cord injury or with neurogenic bladder dysfunction secondary to diabetes.
- Pregnancy (hormonal and mechanical changes increase the risk of urinary stasis and vesicoureteral reflux.)
- Gender and age (Females are commonly infected due to short urethra)
  With increasing age the incidence in males rises as a result of prostatic hypertrophy and instrumentation.
- Preexisting renal lesions, causing intrarenal scarring and obstruction
- Diabetes mellitus (predisposing factor for infection and bladder dysfunction)
- Immunosuppression and immunodeficiency

Clinical features: (Robbins pg. 535)

The onset of uncomplicated acute pyelonephritis usually is sudden, with:

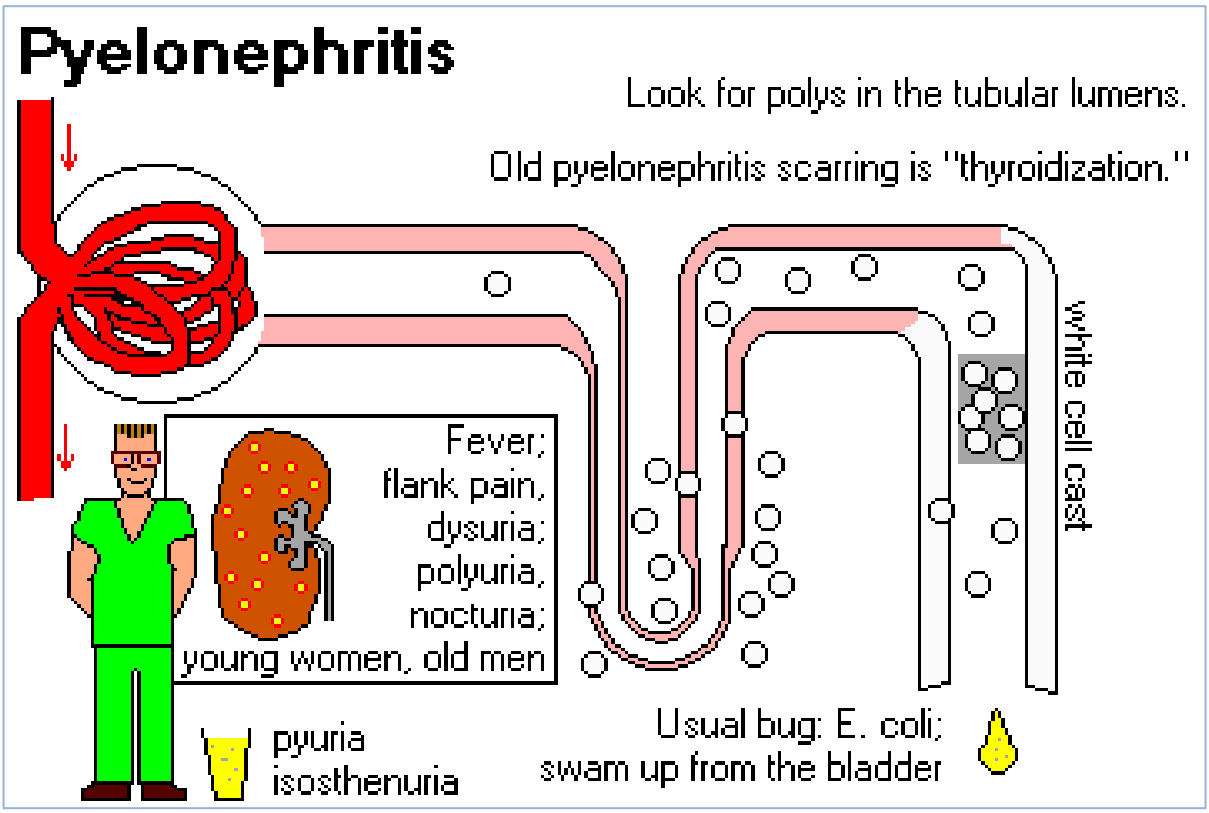
- Flank pain
- Systemic evidence of infection: fever, chills and malaise
- Dysuria, frequency and urgency
- Pyuria, the urine appears cloudy due to the appearance of pus
- Leukocytosis, urinary white cells, and white cells casts in the urine (this latter finder is pathognomonic of acute pyelonephritis).
- Usually unilateral.

Complications of acute Pyelonephritis:

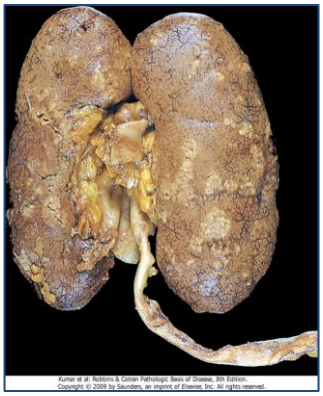
1- Papillary necrosis.

2- Pyonephrosis (pus inside the kidney)

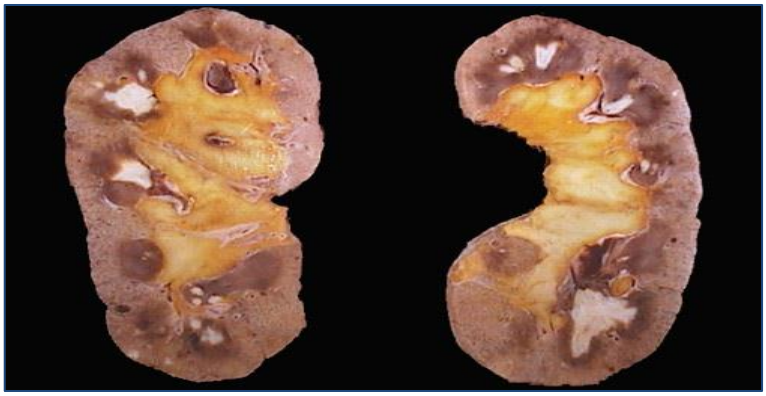
3- Perinephric abscess (pus around the kidney "retroperitoneal cavity"



Morphology: (Robbins pg. 534)

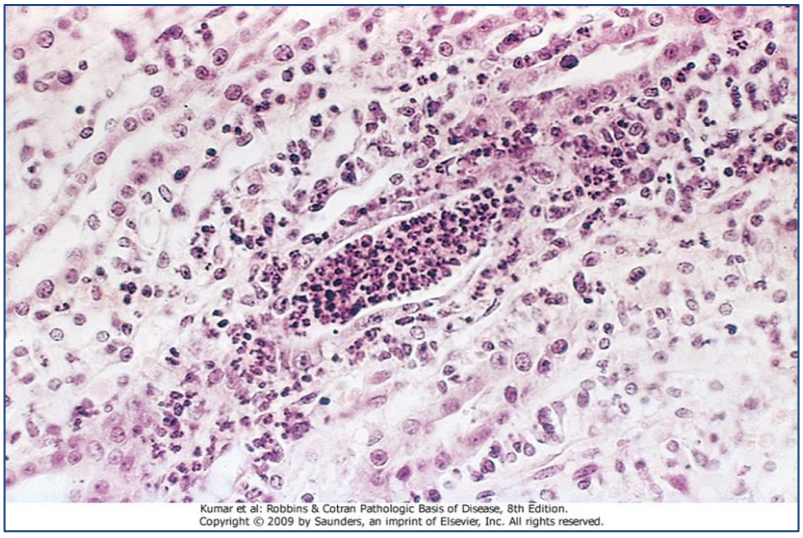


Acute pyelonephritis. Cortical surface shows grayish white areas of inflammation and abscess formation

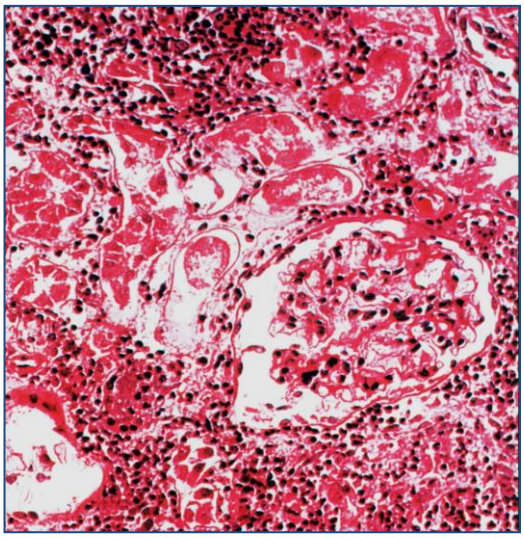


The pale white areas involving some or all of many renal papillae are areas of papillary necrosis.
This is an uncommon but severe complication of acute pyelonephritis, particularly in persons with diabetes mellitus. Papillary necrosis may also accompany analgesic nephropathy

Acute on chronic pyelonephritis
With numerous septic foci present in an already scarred kidney.



Acute neutrophilic exudate within tubules and interstitium inflammation (showing the characteristic white cell casts)



Acute pyelonephritis. There is a diffuse interstitial infiltrate with polymorphonuclear leukocytes.

Chronic pyelonephritis: (Robbins pg. 535)

- Chronic pyelonephritis is a disorder in which interstitial inflammation (at the beginning) and scarring (later) involve in the calyces and pelvis.

- Patients may have an underlying cause that predisposes them to having repeated bouts of acute pyelonephritis; which may progress to chronic pyelonephritis.

- It is an important cause of *chronic renal failure.*

- Causes almost always include chronic urinary tract obstruction and repeated bouts (attacks) of acute inflammation. Consequences include renal hypertension and end-stage renal disease.

It is divided into two forms:

1) **Chronic Reflux-Associated pyelonephritis (reflux nephropathy):**
   - When the chronic pyelonephritis is caused by a **vesicoureteric reflux** (flow of urine from the bladder back into the ureters can cause kidney infection) or **intrarenal reflux**, it is called reflux nephropathy.
   - It's the most common form of chronic pyelonephritis. It could be *unilateral* or *bilateral*, & it may result in one kidney scarring and atrophy or both, leading to renal insufficiency.
2) **Chronic Obstructive pyelonephritis:**

   Pathogenesis:

   1. Obstruction → leads to stagnation→ predispose infection.
   2. Recurrent infection → leads to recurrent bouts of renal inflammation and scarring.

   The disease can be *bilateral*, as with congenital anomalies of the urethra or *unilateral* ex: calculi (stones), obstructive lesions of ureter.

Chronic Pyelonephritis - gross:

- ***Scarring*** & ***fibrosis*** of the kidney.
- The fibrosis involves the capillaries of the glomeruli → ***glomerular sclerosis***.
- If bilateral, the involvement is ***asymmetric*** (the areas involved in both kidneys are not identical).

The hallmarks of chronic pyelonephritis are **coarse, discrete, corticomedullary scars** overlying dilated, blunted, or deformed calyces, and **flattening of the papillae.**

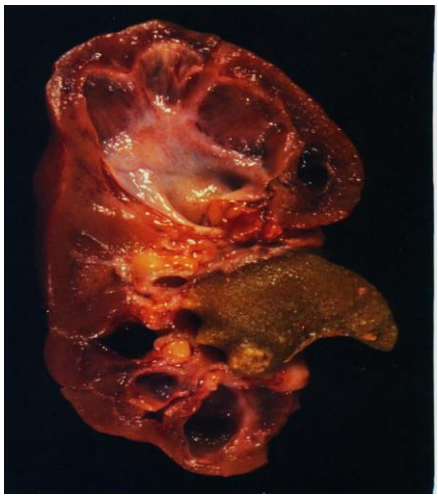
This contrasts with chronic glomerulonephritis, in which both kidneys are diffusely and symmetrically scarred.

Renal tuberculosis

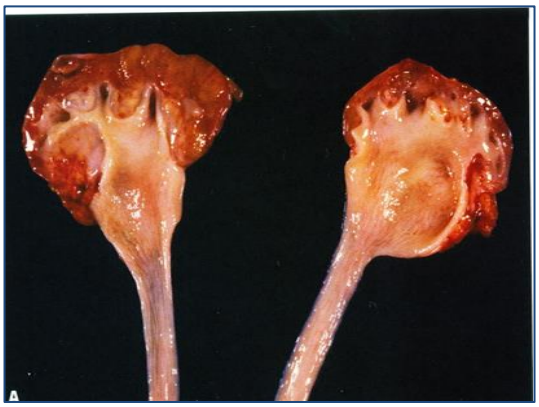
Renal tuberculosis secondary to hematogenous spread of tubercle bacilli.

- Caseating necrosis.

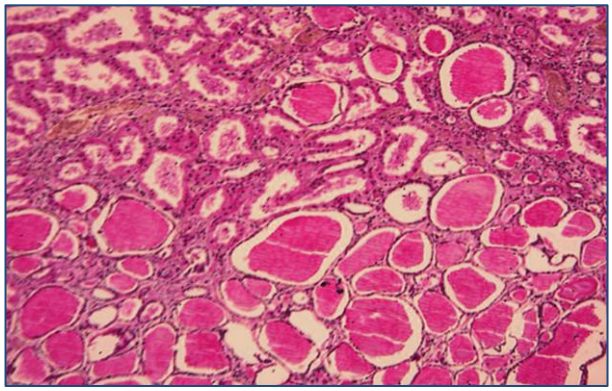
Staghorn calculus



- Staghorn calculus in pelviureteric junction.
- obstruction which causes stagnation then infection.



A. Bilateral hydronephrosis : its pressing and causing dilatation of pelvis and calyces due to
Obstruction with acute on chronic pyelonephritis in a child due to urinary tract obstruction.

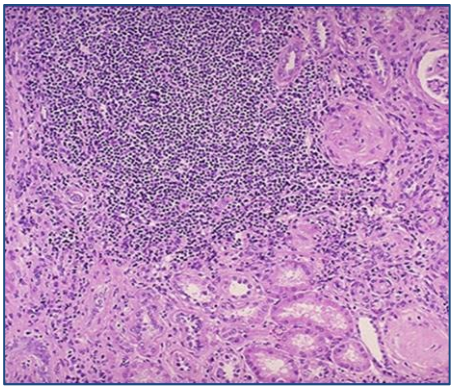


Thyroidization of the kidney occurs due to chronic pyelonephritis (Eosinophilic proteinaceous casts)

B. Hydronephrosis with thinned renal parenchyma in an adult kidney.

C. Scar of healed pyelonephritis

D. Healed pyelonephritis associated with vesicoureteral reflux has produced scarring of both poles of the kidney with calyceal distortion due to infection of the peripheral compound papillae.



Collection of chronic inflammatory cells here is in a patient with a history of multiple recurrent UTI. Both lymphocytes and plasma cells are seen in this case. However, the plasma cells are most characteristic

Hydronephrosis: (Robbins Pg. 546), what is it?

Hydronephrosis refers to dilation of the renal pelvis and calyces, with accompanying atrophy of the parenchyma, caused by obstruction to the outflow of urine. The obstruction may be sudden or insidious, and it may occur at any level of the urinary tract, from the urethra to the renal pelvis.

Could be congenital or acquired for example:

- *Foreign bodies*: calculi, sloughed necrotic papillae
- *Proliferative lesions*: benign prostatic hyperplasia,
- *Inflammation*
- *Normal pregnancy*

Summary:

- TIN consists of inflammatory disease primarily involving the renal tubules and interstitium.
- *Acute pyelonephritis* is a bacterial infection caused either by ascending infection as a result of reflux, obstruction, or other abnormality of the urinary tract, or by hematogenous spread of bacteria; characterized by abscess formation in the kidneys, sometimes with papillary necrosis.
- *Chronic pyelonephritis* usually is associated with urinary obstruction or reflux; results in scarring of the involved kidney, and gradual renal insufficiency.
- *Drug-induced interstitial nephritis* is an IgE- and T cell– mediated immune reaction to a drug; characterized by interstitial inflammation, often with abundant eosinophils, and edema.

Urolithiasis: (Robbins pg. 545)

This condition is characterized by the formation of calculi (stones) in the urinary tract.
The incidence is increased in men.
Mostly unilateral.

Symptoms urolithiasis:

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

Destruction of approximately 70% of the kidney. Numerous dilated calyces with yellow-brown calculi. The central necrotic

Types of stones in urinary tract

- **Calcium stones:**
  - CALCIUM OXALATE and PHOSPHATE (70%). (Either one or both)
  - They are radiopaque (can be seen by using x-rays).
  - They are associated with hypercalciuria, which is caused by:
    A) Increased intestinal absorption of calcium.
    B) Increased primary renal excretion of calcium.
    C) Hypercalcemia, which may be caused by:
      (1) Hyperparathyroidism leads to nephrocalcinosis (calcification of the kidney), as well as urolithiasis.
      (2) Malignancy leads to hypercalcemia because of osteolytic metastases or ectopic production of parathyroid hormone (often by squamous cell carcinoma of the lung).
      (3) Other causes include sarcoidosis, Vitamin D intoxication, and the milk-alkali syndrome[1].
- **Ammonium magnesium phosphate stones are the second most common form of urinary stones.**
  - Magnesium ammonium phosphate (15-20%) - (Struvite stone).
  - These stones are formed in alkaline urine, which is caused most often by ammonia producing or "splitting" (urease-positive) organisms, such as proteus vulgaris or staphylococcus.
  - They are radiolucent. But if they were mixed with calcium phosphate, they become radiopaque.
  - They can form large staghorn (struvite) calculi (casts of renal pelvis and calyces).
- **URIC ACID & URATE (5-10%).**
  - Uric acid stones are associated with hyperuricemia in approximately half of the patients; hyperuricemia can be secondary to gout or to increased cellular turnover, as in the leukemias or myeloproliferative syndromes.
- **Cysteine stone:**

  They are almost always associated with cystinuria or genetically determined aminoaciduria.

[1] Characterized by high blood calcium caused by taking in too much calcium and absorbable **alkali**

Cystitis:

It's the finding of microorganism in the bladder 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)

Clinical features:

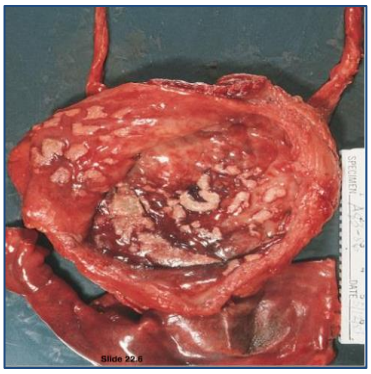
- Frequency compelling necessity to void a small amount of urine at frequent interval
- Urgency
- Dysuria painful voiding
- Suprapubic pain
- Cloudy or foul-smelling urine
- Characteristic include pyuria large number of neutrophils in urine and often hematuria blood in the urine (non-specific finding of UTI) but urinary white cell cast are not found

Etiology:

- Women are more likely to develop cystitis due to short urethral distance.
- 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.

Cystitis with Malakoplakia:

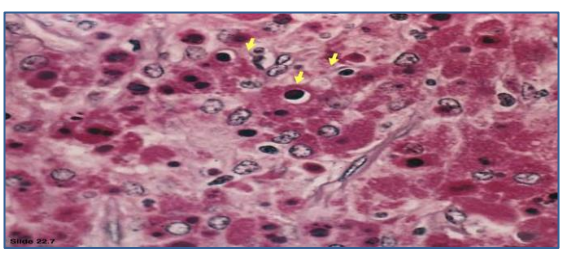
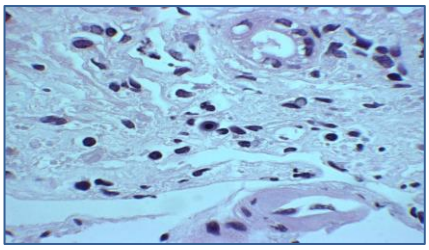
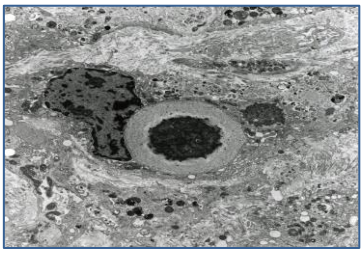
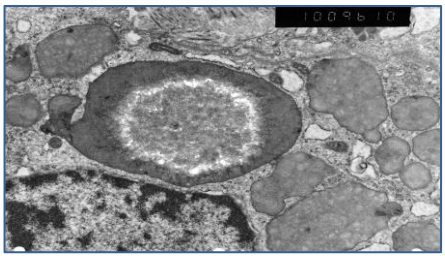
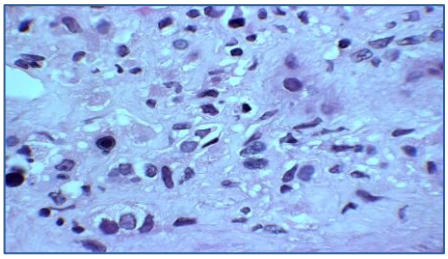
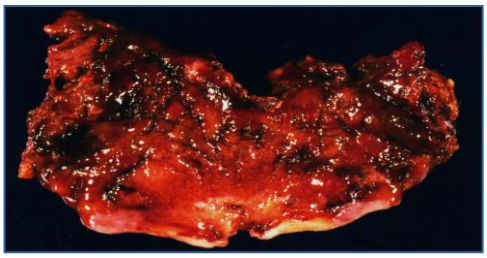
Peculiar[2] inflammatory reaction characterized by soft, yellow, plaques 3-4 cm in diameter. Most commonly occurs in the bladder and results from defects in phagocytic or degradative function of macrophages, such that phagosomes become overloaded with undigested bacterial products (foamy macrophages)



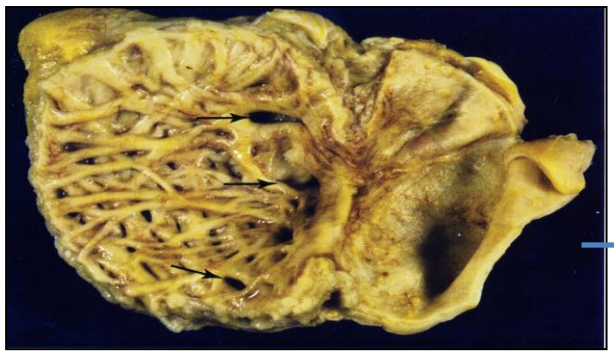
[2] Strange

Michaelis-Gutmann bodies:

A pathognomonic feature of malakoplakia found within the macrophages.

Acute inflammation of the urinary bladder.

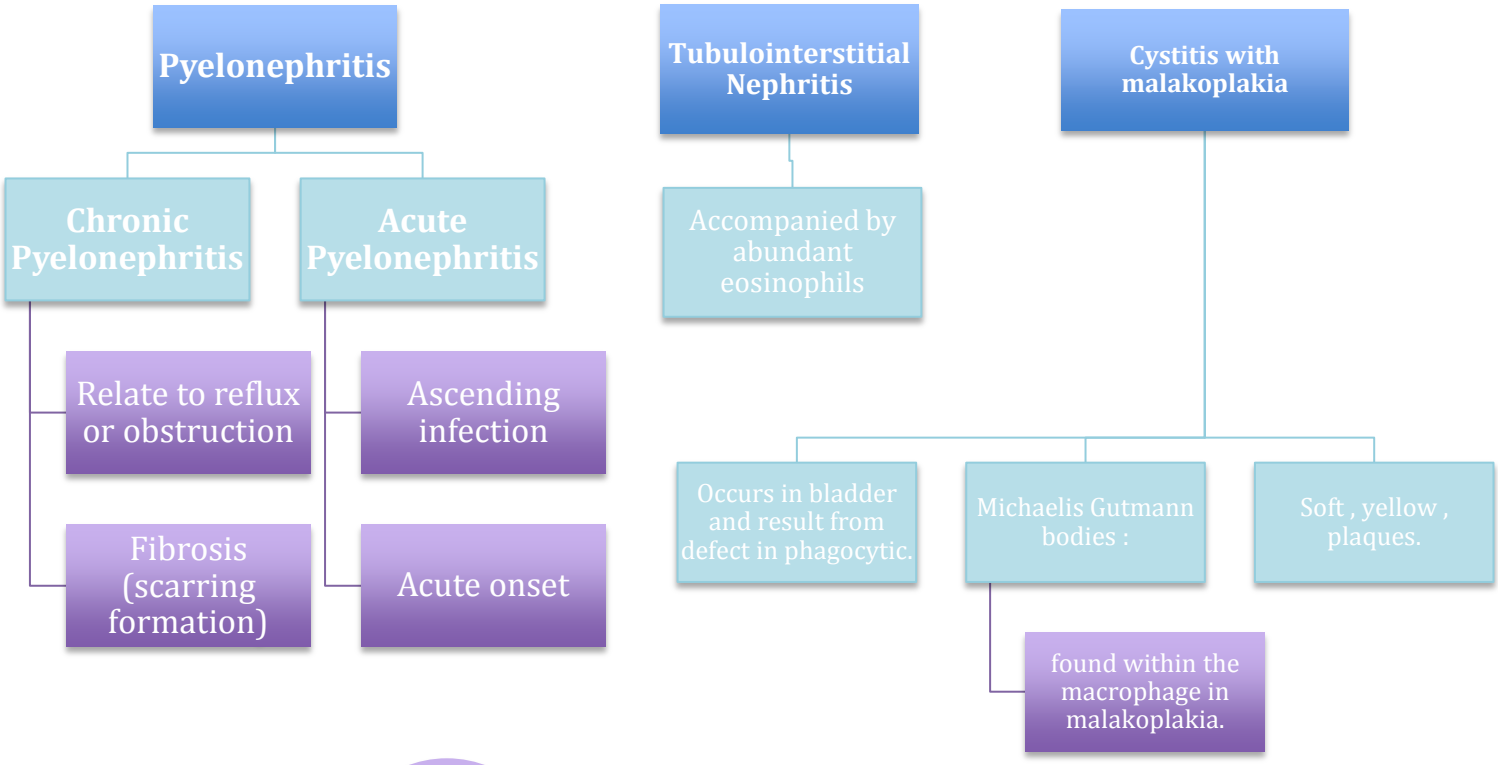


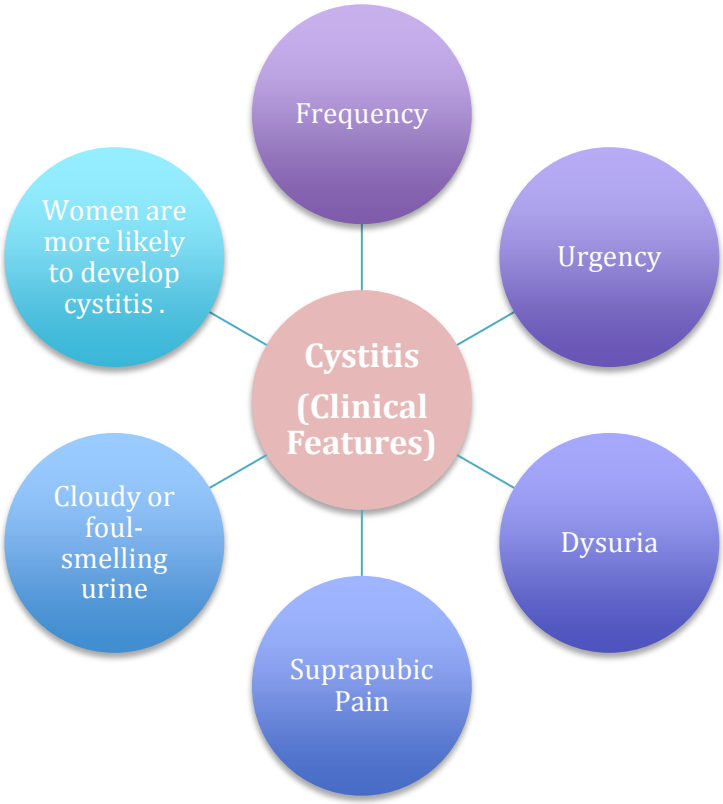
Multiple acquired diverticula (arrows) lie between hypertrophied muscular bundles in a hypertrophied bladder of the patient who had severe prostatic hyperplasia

Radiodensity: (Homework)

Radiopaque calculi	Radiolucent calculi
Referring to a material or tissue that blocks passage of X-rays, and has a bone or near-bone density; radiopaque structures are white or nearly white on conventional X-rays.	**(lucere,to shine) pertaining to materials that allow x-rays to penetrate with a minimum of absorption.**
Shows: **1- Ca 75-85 %** **2- struvite 10-15%**	**Shows:** **1- uric acid 5-8%** **2- cystine: 1%**

Summary


Pyelonephritis
Chronic Pyelonephritis
Acute Pyelonephritis
Relate to reflux or obstruction
Fibrosis (scarring formation)
Ascending infection
Acute onset
Tubulointerstitial Nephritis
Accompanied by abundant eosinophils
Cystitis with malakoplakia
Occurs in bladder and result from defect in phagocytic.
Michaelis Gutmann bodies :
found within the macrophage in malakoplakia.
Soft , yellow , plaques.


Cystitis (Clinical Features)
Frequency
Urgency
Dysuria
Suprapubic Pain
Cloudy or foul-smelling urine
Women are more likely to develop cystitis .

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قال ﷺ: (من سلك طريقًا يلتمس فيه علمًا سهّل الله له به طريقًا إلى الجنة).

دعواتنا لكم بالتوفيق.