

Urinary tract infection(2+3)

PYELONEPHRITIS, NEPHROLITHIASIS AND CYSTITIS



Editing File

The content of the lecture is 7 pages only

“ All of us failed to match our dreams of perfection. So I rate us on the basis of our splendid failure to do the impossible” -William Faulkner

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.

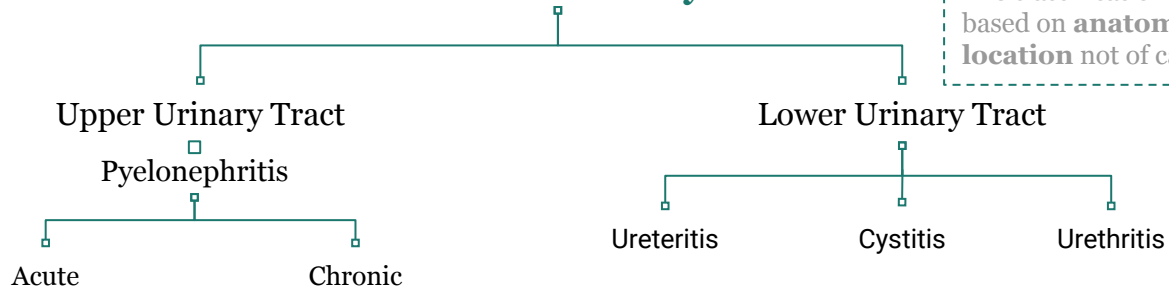
Describe the causes of urinary tract obstruction.

Recognize drug induced nephritis

Color Index :-

VERY IMPORTANT. Extra explanation **Examples** Diseases names: Underlined **Definitions**

Infections of Urinary Tract



❖ 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. $\geq 10^5$ cfu/ml**)

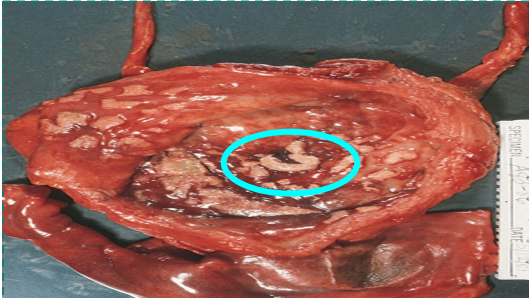
❖ Clinical features of UTI (Cystitis): from here we start lower tract infection

Frequency	Dysuria (painful voiding)	Cloudy or foul-smelling urine
Urgency	Suprapubic Pain	

Acute and Chronic Cystitis: Etiology

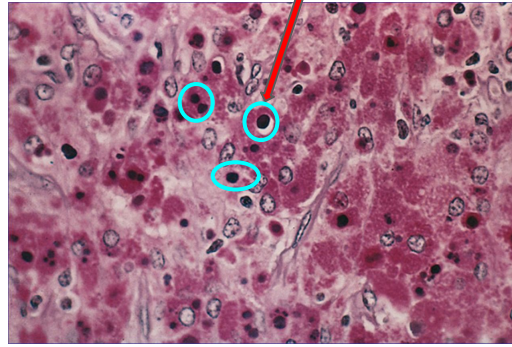
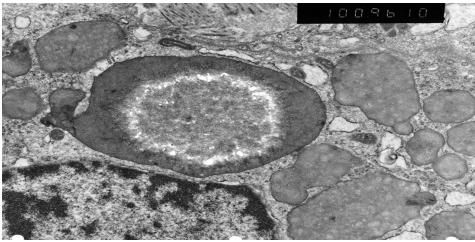
- ❑ **Women** are more likely to develop **cystitis**
- ❑ **Tuberculous cystitis** is always a sequel to **renal TB**
- ❑ **Candida albicans**
- ❑ **Schistosomiasis** (*Schistosoma haematobium*),
- ❑ **Chlamydia**, and **Mycoplasma** may also cause **cystitis**.
- ❑ Predisposing factors include **bladder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

Features of Cystitis



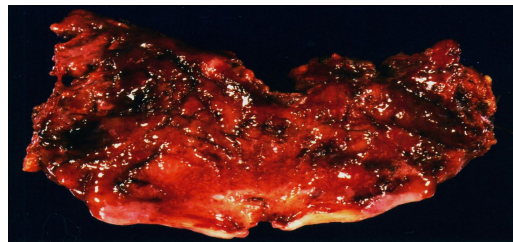
Cystitis with malakoplakia
Peculiar inflammatory reaction
 characterized by:
 soft, yellow, plaques 3-4 cm in diameter
Histologically by: foamy macrophages

M-G Body under EM



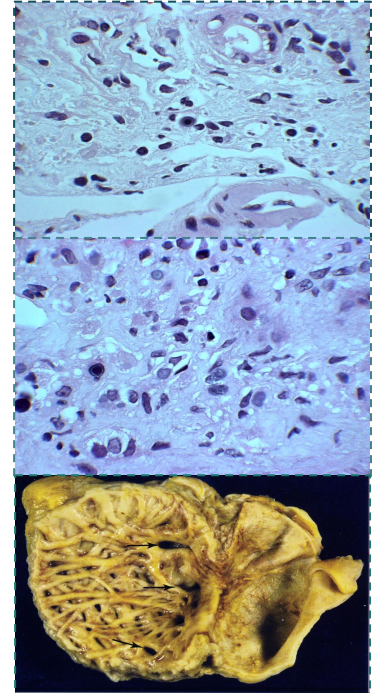
Michaelis Gutman

Cystitis with malakoplakia: **Michaelis Gutman¹** bodies
 1 M-G body: are thought to represent remnants of phagosomes mineralized by iron and calcium deposits.



Acute inflammation of the urinary bladder.

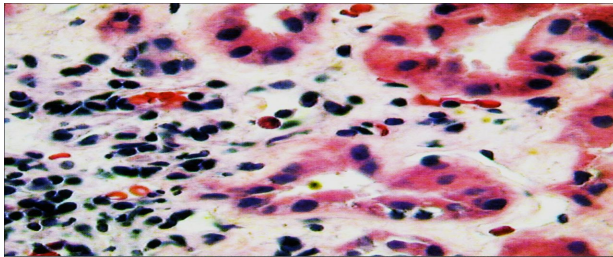
M-G Body under LM



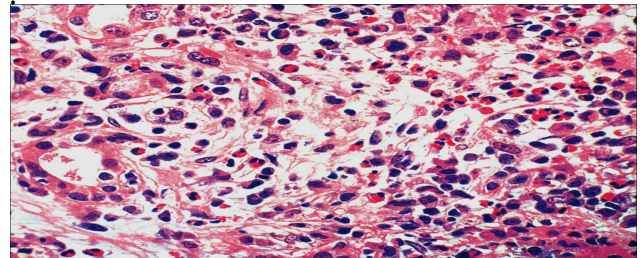
Fibrosis, scarring. -
 Thickened bladder wall. -
 Trabeculation.

◆ Tubulointerstitial Nephritis

-This group of renal diseases involves inflammatory injuries of the tubules and interstitium that are often insidious in onset and principally manifest by azotemia.



Acute Interstitial Nephritis (AIN). Higher power of tubulitis demonstrating interstitial edema and invasion of the tubular epithelium by lymphocytes.



AIN. The mononuclear infiltrate is accompanying by abundant **eosinophils** and may have a **granulomatous appearance**.

Pyelonephritis

upper urinary tract infection

Definition

Pyelonephritis: One of the **most common** diseases of the kidney and is defined as inflammation affecting the **tubules**¹, **interstitium**² and **renal pelvis**³.

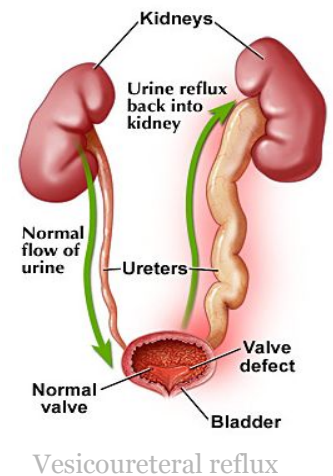
Route of Infection

- ❑ **Ascending infection**
 - ❑ **More than 85% of cases of urinary tract infection** are caused by the **gram-negative bacilli** that are normal inhabitants of the intestinal tract.
 - ❑ This is the **most common route of infection**

- ❑ Hematogenous infection “very rare”

Predisposing Conditions

- ❑ Urinary tract obstruction, either congenital or **acquired** “such as stones”
- ❑ Instrumentation⁴ of the urinary tract
- ❑ Vesicoureteral reflux⁵
- ❑ Pregnancy⁶
- ❑ Gender and age Females and old people are at greater risk due to decrease estrogen
- ❑ Pre Existing renal lesions, causing intrarenal scarring and obstruction
- ❑ Diabetes mellitus⁷
- ❑ Immunosuppression and immunodeficiency



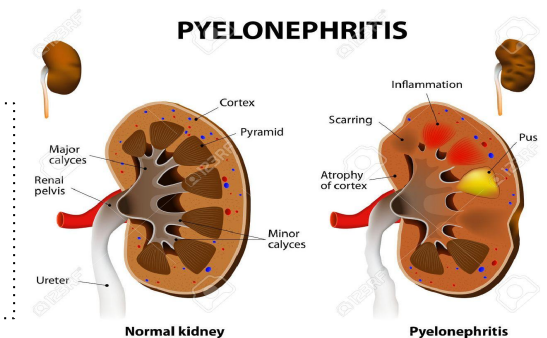
Complications -Acute Pyelonephritis

1/Papillary necrosis ,2/Pyonephrosis* 3/Perinephric abscess

*Pyonephrosis: pyo: pus, nephro: kidney so it's “pus inside the kidney”

Pathogenesis of acute pyelonephritis :

Adhesion of bacteria to mucosal surface is followed by colonization of the distal urethra (and the introitus in females) by growing of the colonies the organism reach the bladder ,by moving against the flow of urine ,When this could happen? This could happen during urethral instrumentation , including catheterization and cystoscopy



¹ More dangerous.

² Patient present with severe fever, vomiting and septicemia.

³ تحتاج علاج سريع

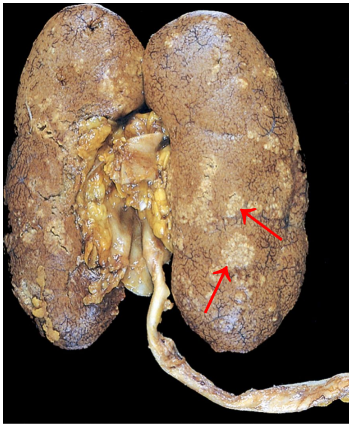
⁴ inducing Catheter

⁵ is an important cause of ascending infection, the reflux allows the bacteria to ascend the ureter into the pelvis, it's usually as a consequence of a defect congenital that results in incompetent of the ureterovesical valve, it can be acquired in person with flaccid bladder result from spinal cord injury or with neurogenic bladder dysfunction secondary to diabetes

⁶ during pregnancy the uterus push the bladder down more

⁷ because of presence of glucose in urine

Features of acute pyelonephritis



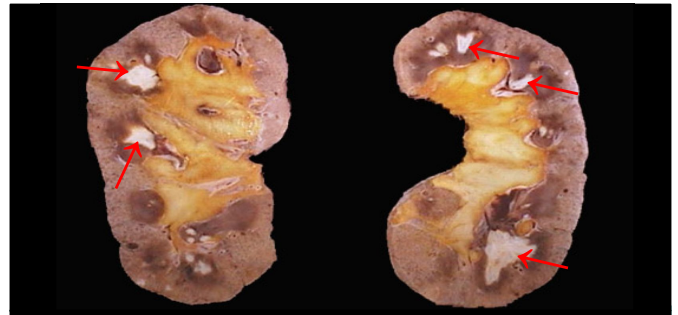
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Acute pyelonephritis.

Cortical surface shows grayish white areas of inflammation and **abscess formation**

Morphology: you see abscess all over.

Histologically: liquefactive necrosis+pus containing neutrophils. The neutrophils may extend to produce white cell cast seen in urine.



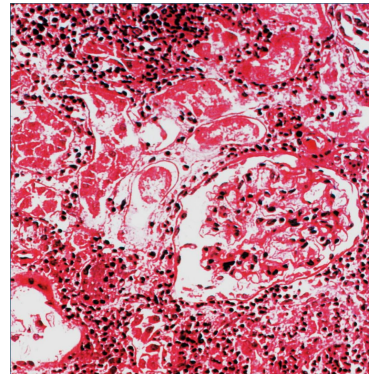
The pale white areas involving some or all of many renal papillae are areas of **papillary necrosis**



Acute on chronic pyelonephritis.

Acute Exacerbation of a chronic condition with numerous septic foci present in an **already scarred kidney.**

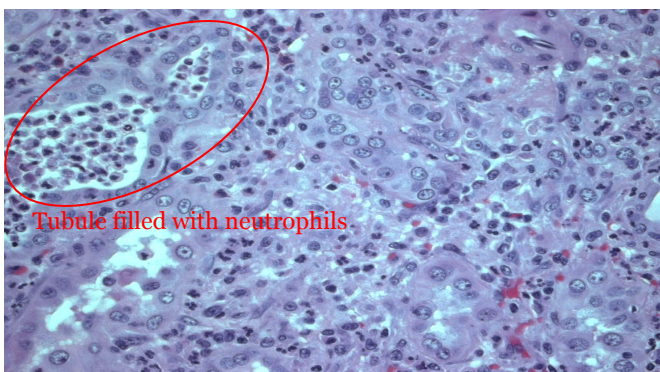
We can see pus and scar
polymorphonuclear leukocytes. + scar
=Acute in chronic



Acute pyelonephritis.

There is a diffuse interstitial infiltrate with **polymorphonuclear leukocytes.**

Tubule filled with neutrophils
It's called "white Blood cast"



Tubule filled with neutrophils



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Acute pyelonephritis :Common suppurative inflammation of the kidney and the renal pelvis caused by bacterial infection-negative rods,The great majority of cases of pyelonephritis are associated with infection of lower UTI,The infection, may remain localized or spreading.Bacteria can reach the kidney from lower UTI (ascending, hematogenous infections)



Chronic pyelonephritis

- ❑ Chronic pyelonephritis is a disorder in which chronic **tubulointerstitial inflammation** and **scarring involve** the calyces / pelvis or both
- ❑ is an important cause of chronic renal failure.
- ❑ It can be divided into two forms: obstructive , Reflux nephropathy


1-Chronic Obstructive Pyelonephritis

- ❑ Obstruction predisposes the kidney to infection. **Recurrent infections superimposed on diffuse or localized** obstructive lesions lead to recurrent bouts of renal inflammation and scarring, which eventually cause chronic pyelonephritis.
- ❑ The disease can be:
 1. **bilateral** as with congenital anomalies of the urethra (e.g., **posterior urethral valves**), resulting in fatal renal insufficiency unless the anomaly is corrected
 2. **unilateral**, such as occurs with **calculi** and **unilateral obstructive lesions of the ureter**.

2-Chronic Reflux–Associated Pyelonephritis (Reflux Nephropathy)

- ❑ **more common** form of chronic pyelonephritic scarring and results from superimposition of a UTI on congenital **vesicoureteral reflux and intrarenal reflux**.
- ❑ Reflux may be unilateral or bilateral; thus, the resultant renal damage either may cause **scarring** and **atrophy** of one kidney or may involve both, potentially leading to chronic renal insufficiency.

Chronic Pyelonephritis-gross

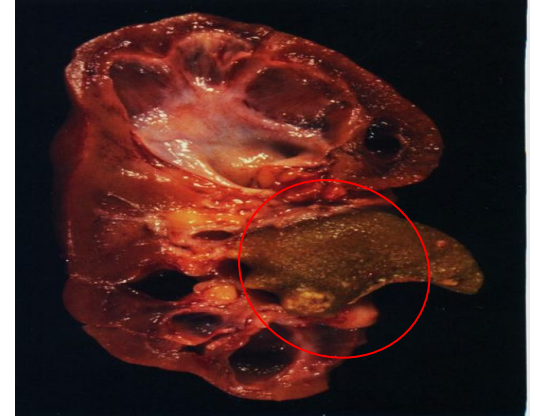
- ❑ The kidneys usually are **irregularly scarred**; **if bilateral, the involvement is asymmetric**.
 - ❑ The hallmarks of chronic pyelonephritis are **coarse, discrete, corticomedullary scars** overlying dilated, blunted, or deformed calyces, and **flattening of the papillae**.
- 

Special types of chronic pyelonephritis



Renal tuberculosis secondary to hematogenous spread of tubercle bacilli. grossly caseating necrosis (cheese-like appearance)
Microscopically: granuloma

- Caseating necrosis in the center.
- Giant cells.
- Lymphocytes.
- Necrotic material.
- Epithelioid Cells. (Bacilli are frequently seen in the edge between the necrosis + epithelioid cells.)



Staghorn calculus (large kidney stone with multiple irregular branches) in pelviureteric junction.

Other name

xanthogranulomatous pyelonephritis: Xantho= lipid.

grossly: staghorn stones.

- Microscopically: Foamy histiocytes.

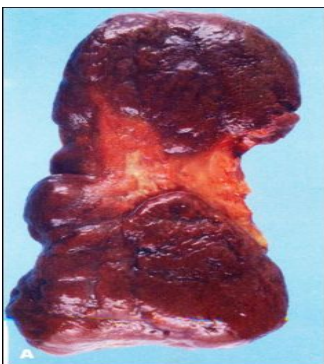
Note: the foamy histocytes are seen also in malakoplakia (Michaelis–gut man bodies) but **large numbers** are usually seen in xanthogranulomatous pyelonephritis



A. Bilateral **hydronephrosis** with acute on chronic pyelonephritis in a child due to urinary tract obstruction.



B. **Hydronephrosis** with thinned renal parenchyma in an adult kidney.
(Hydronephrosis is a swelling of renal pelvis and calyces due to a build-up of urine caused by obstruction)

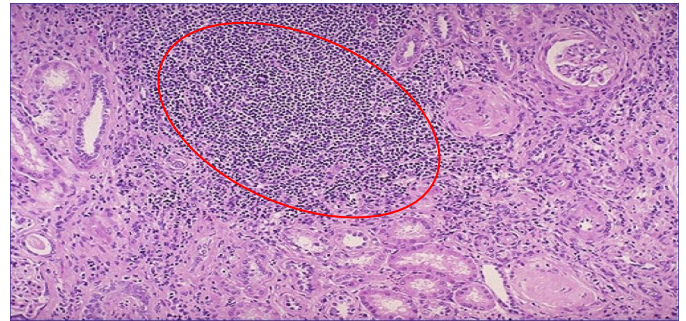
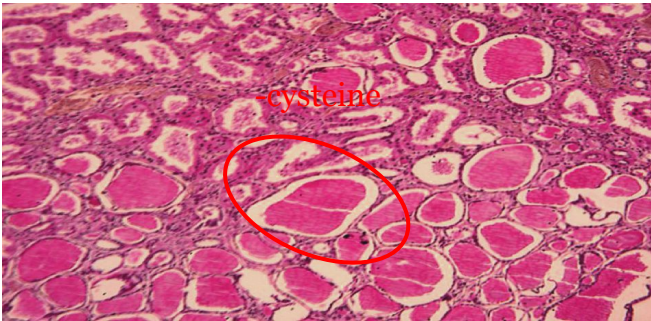


A. unshaped **scar** of healed **pyelonephritis**



B. 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.

chronic pyelonephritis



Thyroidization of the kidney occurs due to chronic pyelonephritis (Eosinophilic proteinaceous casts).
Thyroidization: the tubules become flattened epithelium + the casts are like hyaline

Chronic pyelonephritis: **collection of chronic inflammatory cells** here is a patient with a history of multiple recurrent urinary tract infections.
- collagen deposition in interstitial: fibrosis
Collagen deposition in glomerular : Glomerular sclerosis.
What type of chronic inflammatory cell we found here ?
Lymphocytes

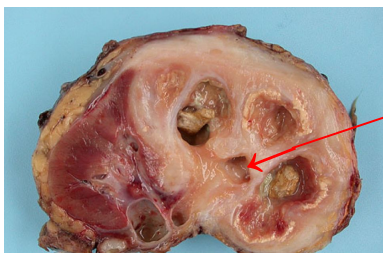
Urolithiasis (kidney stones)



Types of stones in urinary tract

1. CALCIUM OXALATE and PHOSPHATE (70%)
2. Magnesium ammonium phosphate (Struvite stone)(15-20%)
3. URIC ACID & URATE (5-10%)
4. CYSTINE (1-2%)

*Images from these studies may show faintly radiopaque calculi that become radiolucent with intravenous contrast



Stones in the calyces

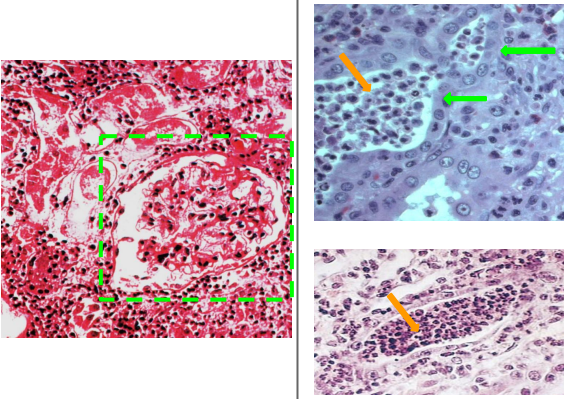
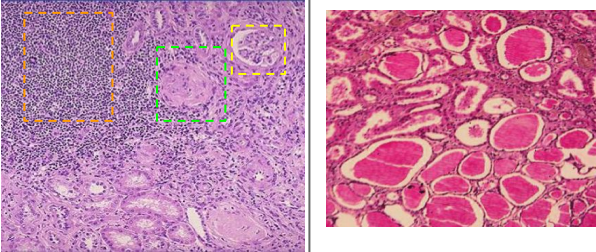
Destruction of approximately 70% of the kidney. Numerous dilated calyces with yellow-brown calculi. The central necrotic areas are surrounded by dense **Fibrosis.**

Radiopaque	Radiolucent
Ca - struvite stones - -cysteine*	Uric acid

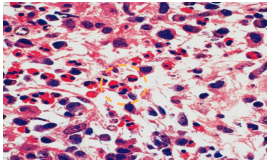
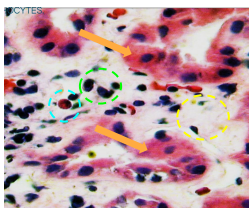
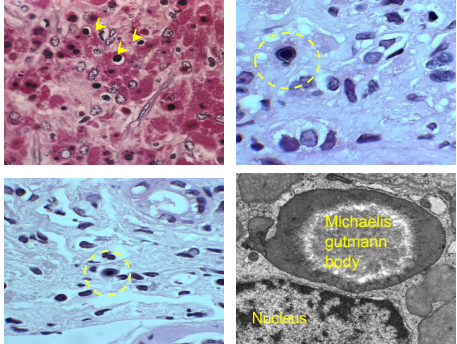
❖ Symptoms urolithiasis

- 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.

Histopathology Of Urinary Tract Infections

Disease	Acute pyelonephritis		Chronic pyelonephritis	
Picture				
Prominent Features	<p>There is a diffuse interstitial infiltrate with polymorphonuclear leukocytes.</p>		<p>Collection of chronic inflammatory cells here is in a patient with a history of multiple recurrent urinary tract infections.</p>	
Notes/ Comparisons	<p>First the glomeruli is resistant, but there is pus all around it with necrosis of the kidney</p>	<ul style="list-style-type: none"> ○ <u>Neutrophils</u> inside the <u>tubules</u> “polymorphs” ○ <u>Tubular epithelial cells</u> ○ Acute pyelonephritis ○ No fibrosis 	<ul style="list-style-type: none"> ○ Interstitial inflammation with <u>lymphocytes</u>¹ ○ <u>Interstitial fibrosis</u> ○ <u>Glomerular sclerosis</u> ○ <u>Periglomerular fibrosis</u>² <div style="border: 1px dashed gray; padding: 5px; margin-top: 10px;"> <p>-¹one round black dot, Chronic -²Fibrosis around the glomerulus</p> </div>	<ul style="list-style-type: none"> ○ Interstitial inflammation with lymphocytes ○ Thickened tubular basement membrane and ○ Tubular atrophy ○ Thyroidization¹ <div style="border: 1px dashed gray; padding: 5px; margin-top: 10px;"> <p>¹shrunken, flattened epithelium with a hyaline cast inside</p> </div>

Histopathology Of Urinary tract infection

Disease	Tubulointerstitial nephritis		Cystitis with malakoplakia
Picture		 <p data-bbox="743 832 911 948"> Tubules Fibrosis Lymphocytes eosinophils </p>	
Prominent Features	<p>The mononuclear infiltrate is accompanied by abundant eosinophils and may have a granulomatous appearance</p>	<p>Higher power of tubulitis demonstrating interstitial edema and invasion of the tubular epithelium by lymphocytes</p>	<p>foamy macrophages with Michaelis Gutmann bodies</p>
Notes/ Comparisons	<p>Presence of Eosinophils</p>	<p>The tubules are separated by edema not by fibrosis.</p> <p data-bbox="699 1547 946 1702"> When the tubules are not back to back, they are separated by either fibrosis or edema, if it was white edema, pink fibrosis </p>	<ul style="list-style-type: none"> - Specific infection that affects the mainly bladder and other site - Foamy macrophages with michaelis gutmann body “intra cellular bacteria - E.m central dense core, pericentral area



Summary-pathoma

URINARY TRACT INFECTION


I. BASIC PRINCIPLES

- A. Infection of **urethra, bladder, or kidney**
- B. Most commonly arises due to **ascending infection**; increased incidence in females
- C. **Risk factors include sexual intercourse, urinary stasis, and catheters.**

II. CYSTITIS (lower UTI)

- A. Infection of the **bladder**
- B. **Presents as dysuria, urinary frequency, urgency, and suprapubic pain; systemic signs (E.g. fever) are usually absent**
- . C. Laboratory findings:
 - 1. Urinalysis-**cloudy urine** with **> 10 WBCs/** high power field (hpf)
 - 2. **Dipstick-Positive leukocyte esterase** (due to pyuria) and **nitrites** (bacteria convert nitrates to nitrites)
 - 3. **Culture- greater than 100,000 colony forming units (goldstandard)**
- D. Etiology
 - 1. **E. coli (80%)**
 - 2. **Staphylococcus saprophyticus-increased incidence in young, sexually active women {but E coli is still more common in this population}**
 - 3. *Klebsiella pneumoniae*
 - 4. *Proteus mirabilis*-alkaline urine with ammonia scent
 - 5. *Enterococcus faecalis*
- E. Sterile pyuria is the presence of pyuria (> 10 WBCs/hpf and leukocyte esterase) with a negative urine culture.
 - I. Suggests **urethritis** due to **Chlamydia trachomatis** or *Neisseria gonorrhoeae* (Dominant presenting sign of urethritis is dysuria)

III. PYELONEPHRITIS (upper UTI)

- A. Infection of the **kidney**
 - I. Usually due to **ascending infection**; increased risk with **vesicoureteral reflux**
 - B. Presents with **fever, flank pain, WBC casts, and leukocytosis in addition to symptoms of cystitis**
 - C. Most common pathogens are
 - 1. **E coli (90%)**
 - 2. *Enterococcus faecalis*
 - 3. *Klebsiella* species
- 

URINARY TRACT INFECTION

IV. CHRONIC PYELONEPHRITIS

- A. **Interstitial fibrosis** and **atrophy of tubules** due to multiple bouts of acute pyelonephritis
- B. Due to vesicoureteral reflux (children) or obstruction (e.g., BPH or cervical carcinoma)
- C. **Leads to cortical scarring** with blunted calyces; scarring at upper and lower poles is characteristic of vesicoureteral reflux.
- D. **Atrophic tubules containing eosinophilic proteinaceous material** resemble thyroid follicles ('**thyroidization**' of the kidney); waxy casts may be seen in urine.

Kidney Stones

NEPHROLITHIASIS

I. BASIC PRINCIPLES

- A. **Precipitation** of a urinary solute as a stone (Table 12.2)
 - B. **Risk factors include high concentration of solute in the urinary filtrate and low urine volume.**
 - C. **Presents as colicky pain with hematuria and unilateral flank tenderness**
1. Stone is usually passed within hours; if not, surgical intervention may be required.

Table 12.2: Features of Nephrolithiasis

COMPOSITION	FREQUENCY	CAUSES	TREATMENT
Calcium oxalate and/or calcium phosphate	Most common type; usually seen in adults	Most common cause is idiopathic hypercalciuria; hypercalcemia and its related causes must be excluded. Also seen with Crohn disease	Treatment is hydrochlorothiazide (calcium-sparing diuretic).
Ammonium magnesium phosphate	Second most common type	Most common cause is infection with urease-positive organisms (e.g., <i>Proteus vulgaris</i> or <i>Klebsiella</i>); alkaline urine leads to formation of stone.	Classically, results in staghorn calculi in renal calyces (Fig. 12.18), which act as a nidus for urinary tract infections. Treatment involves surgical removal of stone (due to size) and eradication of pathogen (to prevent recurrence).
Uric acid	Third most common stone (5%); radiolucent (as opposed to other types of stones which are radiopaque)	Risk factors include hot, arid climates, low urine volume, and acidic pH. Most common stone seen in patients with gout; hyperuricemia (e.g., in leukemia or myeloproliferative disorders) increases risk.	Treatment involves hydration and alkalinization of urine (potassium bicarbonate); allopurinol is also administered in patients with gout.
Cysteine	Rare cause of nephrolithiasis; most commonly seen in children	Associated with cystinuria (a genetic defect of tubules that results in decreased reabsorption of cysteine)	May form staghorn calculi; treatment involves hydration and alkalinization of urine.

Summary- Robbins

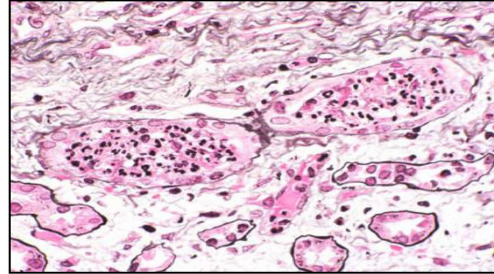
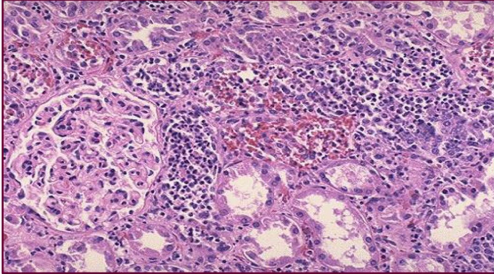
SUMMARY

Tubulointerstitial Nephritis

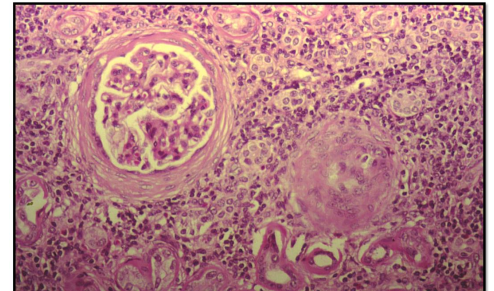
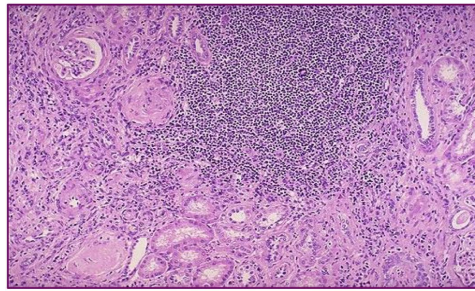
- TIN consists of inflammatory disease primarily involving the renal tubules and interstitium.
- *Acute pyelonephritis* is a bacterial infection caused either by ascending infection as a result of reflux, obstruction, or other abnormality of the urinary tract, or by hematogenous spread of bacteria; characterized 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.

*the term interstitial nephritis generally is reserved for cases of TIN that are nonbacterial in origin, this include tubular injury resulting from **drugs, metabolic disorder, such as hypokalemia, physical injury, such as irradiation, viral infection, and immune reaction.** 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.

Questions practical



- 1) patient suffering of **flank pain** and **fever**, he came to the ER after noticing that his **urine is cloudy**. A biopsy was taken from his kidney shown **interstitial inflammation** and **plasma cell polymorphonuclear neutrophils** are seen filling renal tubules and leukocytes may form into a **cast within the tubule**. What is the most likely diagnosis?
- A) Chronic pyelonephritis
 - B) Acute pyelonephritis
 - C) Cystitis
 - D) Urethritis



- 2) a women died after suffering of chronic renal failure. Her kidney gross shows **atrophic** and **deformity** with **cortical coarse scars**. Biopsy shows large **collection of chronic inflammatory cells, fibrosis, glomerular sclerosis** and **hyalinization** with marked **chronic interstitial inflammation**. What is the cause?
- A) Acute kidney injury
 - B) Acute pyelonephritis
 - C) Chronic pyelonephritis
 - D) Cystitis




1) A 46 year old male who has chronic **gouty** arthritis for the last 2 years. Recently has developed Urolithiasis what most likely it formed of ?

- A. Calcium oxalate stones
- B. Magnesium ammonium phosphate
- C. Cystine
- D. Uric acid

2) A 28-year-old woman has had **dysuria**, **frequency**, and **urgency** for the past 2 days. On physical examination, her temperature is 37.6°C. A urine culture grows greater than **100,000 colonies/mL** of **Escherichia coli**. She is treated with antibiotic therapy. If the problem **continues to recur**, the patient is likely to be at greatest risk for development of which of the following renal diseases?

- A. Diffuse glomerulosclerosis
- B. Chronic glomerulonephritis
- C. Membranous glomerulonephritis
- D. Chronic pyelonephritis

3) A 32-year-old man has developed a **fever** and **skin rash** over the past 3 days. Five days later, he has increasing malaise and visits his physician. On physical examination, the maculopapular erythematous rash on his trunk has nearly faded away. His temperature is 37.1°C, and blood pressure is 135/85 mm Hg. Urinalysis shows 2+ proteinuria; 1+ **hematuria**; and no glucose, ketones, or nitrite. The **leukocyte esterase result is positive**. Microscopic examination of urine shows RBCs and WBCs, some of which are **eosinophils**. What is the most likely cause of this patient's condition?

- A. Urinary tract infection
 - B. Antibiotic use
 - C. Congestive heart failure
 - D. Streptococcal pharyngitis
- 



4) A client complaining of dysuria, frequency, urgency, nocturia, pyuria, hematuria, and suprapubic discomfort is showing manifestations of :

- A. Cystitis
- B. Glomerulonephritis
- C. Urethritis
- D. Pyelonephritis

5) A 53-year-old woman has had dysuria and urinary **frequency** for the past week. On physical examination, her temperature is **38°C**, and she has pain on palpation over the left costovertebral angle. Microscopic examination of the urine shows numerous **neutrophils**, and a urine culture is **positive for Escherichia coli**. Which of the following complications is most likely to develop in this patient?

- A. Necrotizing papillitis
- B. Acute tubular necrosis
- C. Crescentic glomerulonephritis
- D. Cystitis

6) Which of the following is **not** a factor which predisposes an individual to urinary tract infections?

- A. High intake of fluids
- B. Pregnancy
- C. Kidney stones
- D. Benign prostatic hyperplasia

7)The most **prominent** feature of chronic pyelonephritis microscopically is :**(important)**

- 1- thyroidization of tubules
- 2- hyalinization of tubules
- 3- interstitial fibrosis
- 4- inflammatory infiltration

Answers:

1- D , 2- D , 3- B , 4- A , 5- A , 6- A ,7-1





« قُلْ هَلْ يَسْتَوِي الَّذِينَ يَعْلَمُونَ وَالَّذِينَ لَا يَعْلَمُونَ »

سورة الزمر الآية ٩

القادة

عبدالله العمر

فاطمة بالشرف

الأعضاء

عبدالجبار اليماني
عبدالله المعيزر
معن شكر
سيف المشاري
عبدالعزیز الجهني
محمد العمر
خالد المطيري
عبدالعزیز العبدالكريم
ماجد الجهني
منصور العبرة
أنس السيف
راكان الغنيم
فايز الدرسوني
خالد العقيلي
بندر الجماز
طارق العلوان
سلطان بن عبيد
تركي الشمري
محمد الأصقه
أحمد الصبي
سعد الفوزان

ريناد الغريبي
منيرة المسعد
شوق القحطاني
رزان الزهراني
بتول الرحيمي
فاطمة الديحان
الجوهرة الشنفي
نورة القاضي
غادة الحيدري
بلقيس الراجحي
غرام جليدان
آلاء الصويغ
ال فهدة السليم
شيرين حمادي
رناد الفر
نورة الحربي
ميعاد النفيعي
مجد البراك
رهام الحلبي

