

Infection of the Upper & Lower Urinary Tract

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 acute and chronic pyelonephritis.
- Describe the causes of urinary tract obstruction.
- Recognize drug induced nephritis.

Color index:

Black: original content.
Red: Important.
Light Purple: From Robbin's.
Blue: only found in boys slides.

Green: Boy's doctor notes .
Dark orange: Girl's Doctor notes.
Grey: Explanation.
Pink: Only found in girls slides.



Tubulointerstitial nephritis

- Refers to a group of inflammatory kidney diseases that primarily involve the interstitium and tubules.
- The glomeruli and vessels may be spared altogether or affected only late in the course.

Acute pyelonephritis

Chronic pyelonephritis

Drug induced pyelonephritis

Acute Pyelonephritis

Definition

is an acute suppurative inflammation of the upper urinary tract (the kidney and the renal pelvis) caused by bacterial infection. It typically follows infection of the lower urinary tract.

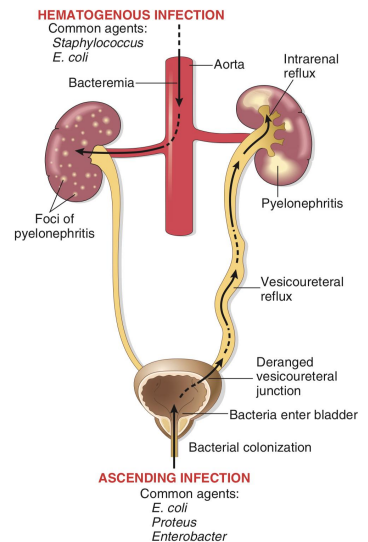
The most common causative organism is enteric gram-negative rods **Escherichia coli (E. coli)**

Etiology

Other organisms are species of **Proteus, Klebsiella, Enterobacter, and Pseudomonas**¹.

There are **two routes** by which bacteria can reach the kidneys:

Ascending infection from the lower urinary tract	Hematogenous through the bloodstream
most important and common route by which bacteria reach the kidney	less common
Bacteria ascends from urethra to urinary bladder to ureters to kidneys.	e.g. from an infected heart valve in endocarditis, miliary tuberculosis, etc.



1/ especially in individuals who undergo urinary tract manipulations or have congenital or acquired anomalies. *S. faecalis* also might cause pyelonephritis, but uncommon.

In cases of TIN caused by bacterial infection, the renal pelvis is prominently involved—hence the more descriptive term pyelonephritis (from *pyelo*, "pelvis"). While the term interstitial nephritis generally is reserved for cases of TIN that are nonbacterial in origin.

Acute Pyelonephritis

Predisposing Factors

01

Urethral instrumentation

catheterization and cystoscopy

That's why we do aseptic precautions.

02

Gender

UTI most commonly affects **females** (predisposed because of the close proximity of the urethra to the rectum and short urethra).

03

Pre-existing renal lesions

04

Immunosuppression & immunodeficiency

05

Pregnancy

Asymptomatic bacteriuria occurs in 10% of pregnant women, out of which some develop acute pyelonephritis.

06

Obstruction

Obstruction at the level of the urinary bladder (ex: stones and benign prostatic hypertrophy) → incomplete emptying and increased residual urine → stasis which allows bacteria to colonize and multiply → bacteria ascends along the ureters to infect kidneys.

07

Diabetes mellitus

- *diabetic glycosuria* predisposes to infection by providing a rich medium for bacterial growth.
- Diabetics also have an increased risk of complications of pyelonephritis e.g. septicemia, necrotizing papillitis and recurrence of infection.

08

Incompetence of the vesicoureteral orifice

leads to increased residual urine → favor bacterial growth and allows reflux of bladder urine with bacteria to **ascend** to the ureter (normally ureteral insertion into the bladder is a competent **one-way** valve that prevent retrograde flow of urine).

Vesicoureteral reflux is seen in 30% of young children with UTI and it is usually due to a congenital defect of the valve ¹.

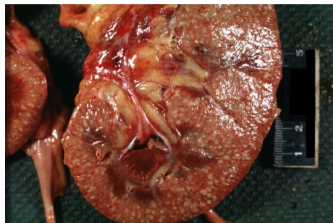
^{1/} its also can be acquired in individuals with a flaccid bladder resulting from spinal cord injury or with bladder dysfunction secondary to DM.

Acute Pyelonephritis

Morphology

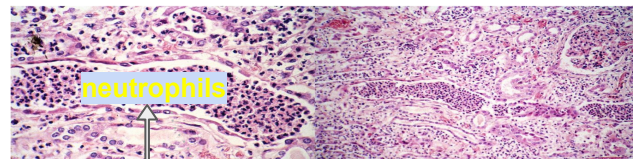
Macroscopic

- **Kidney:** enlarged, swollen with a bulging cut surface.
- **Cut surface:** small yellowish white subcapsular microabscesses (**suppurative necrosis**)
- **Renal papillae:** diffusely blunt
- **Pelvicalyceal mucosa:** hyperemic & covered by purulent exudate
- **Pyonephrosis** (rare): large amounts of pus filling the renal pelvis, calyces & ureter



Microscopic

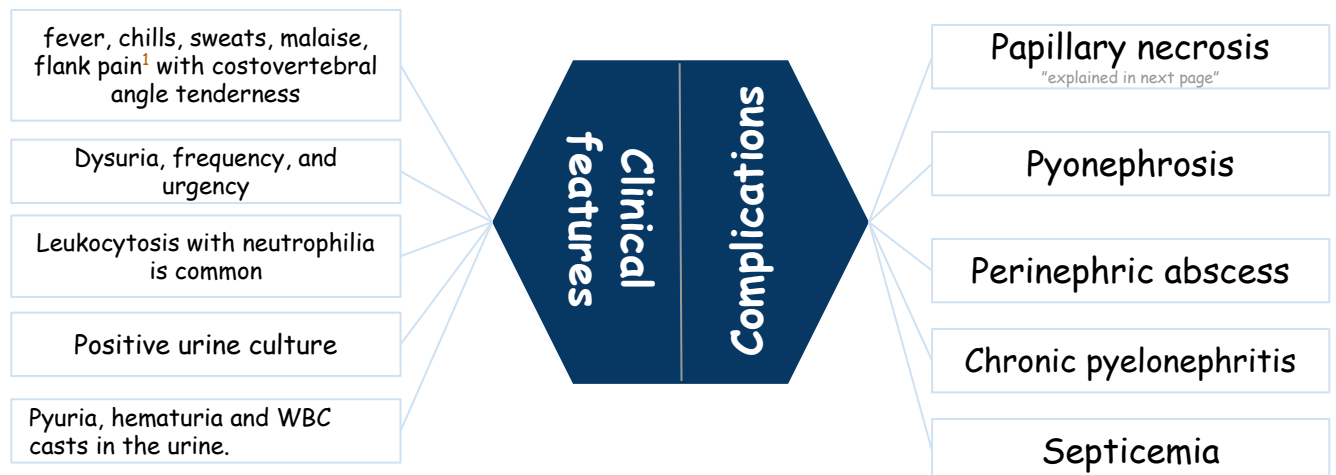
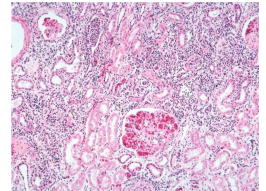
- **Tubules & interstitium:** dense acute tubulointerstitial inflammation (**neutrophils** fill the tubules and collecting ducts) with tubular destruction.
- **Vessels and glomeruli:** often are **preserved**
- **perinephric abscess:** presents in severe cases of acute pyelonephritis where inflammation extends beyond the renal capsule
- **Liquifactive necrosis**



neutrophils

Fully dilated and distended tubule with neutrophils

1st Stage: Flattened Epithelium
2nd Stage: Loss of brush border
3rd Stage: Necrosis



- Differentiating upper from lower UTIs is often clinically difficult.

(1): Flank pain can be related to disease of the kidneys, pancreas and liver e.g.:liver abscess.
Lymphocytes: indicate viral infection.
Neutrophils:indicate bacterial infection
Eosinophils:indicate allergy and parasitic infection

Papillary necrosis (necrotizing papillitis)

Definition

It is a type of pyelonephritis characterized by the necrosis of the renal papillae (the apex of the renal pyramids). It can spread to the rest of the renal pyramid and the rest of the kidney

It is
seen in

Diabetics with acute pyelonephritis

In acute pyelonephritis with significant urinary tract obstruction

Interstitial nephritis associated with analgesic abuse

Chronic liver disease

Renal transplant rejection

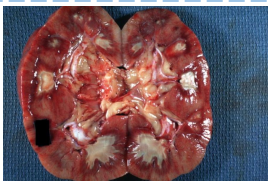
Infection e.g. tuberculosis

Sickle cell disease

Morphology

• Macroscopic

yellow white suppurative necrosis of the tips of some or all renal papillae (renal pyramids)



• Microscopic

coagulative necrosis at the tips of renal papillae with surrounding neutrophilic infiltrate

Chronic Pyelonephritis

Definition

A chronic tubulointerstitial inflammation of the kidney caused by **repeated bouts of inflammation and healing**. Results a **scarred kidney** with deformed renal pelvis and calyces.

Chronic obstruction (≥ 6 months) associated pyelonephritis

e.g. obstruction of the ureter by calculi (stones), tumor within the ureter, or extrinsic compression etc.

Can be divided into two forms:

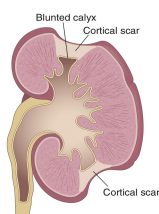
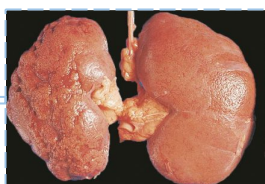
chronic reflux associated pyelonephritis.¹

Chronic pyelonephritis usually is associated with urinary obstruction or reflux; results in **scarring of the involved kidney** and gradual renal insufficiency

Morphology

Macroscopic

- The cortex is thinned out and there is deformity and blunting of the pelvicalyceal system
- The kidneys are small and contracted
- The surface of the kidney is irregularly scarred with areas of depression



Microscopic

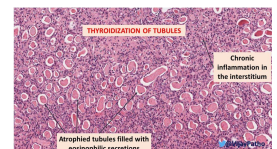
VS

Tubules:

- tubular atrophy with thyroidization of tubules

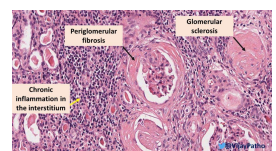
Interstitium:

- interstitial fibrosis and chronic interstitial inflammation,



Glomeruli:

- periglomerular fibrosis and glomerulosclerosis



¹/ its most common cause. Results from superimposition of a UTI on congenital vesicoureteral reflux and intrarenal reflux. Intrarenal reflux is when the infected bladder urine can be propelled up to the renal pelvis and further into the renal parenchyma through open ducts at the tips of the papillae.

Chronic Pyelonephritis

Clinical features

Symptoms:

- 1| recurrent fever
- 2| flank pain
- 3| chronic renal failure (slowly developing)
- 4| hypertension

1

Most patients have episodic symptoms of urinary tract infection or acute pyelonephritis

2

3

Some patients have a silent course until end-stage renal disease develops.
Ex: Diabetic patients

4

Imaging studies show abnormalities of the pelvicalyceal system and cortical scarring.

Drug induced tubulointerstitial nephritis

01

Drugs are an important cause of renal injury.

02

Drug-induced interstitial nephritis is an IgE (hypersensitivity) and T cell-mediated immune reaction

characterized by interstitial inflammation, often with abundant eosinophils, and edema

Acute drug-induced tubulointerstitial nephritis (TIN) occurs as an adverse reaction to various therapeutic drugs: ¹

- penicillins (methicillin, ampicillin)
- ² diuretics (thiazides)
- rifampin
- nonsteroidal anti-inflammatory agents

Morphology:

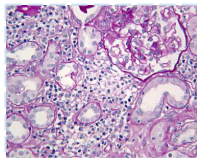
What can I see histologically in the Interstitium ?

A infiltration by chronic inflammatory cells (lymphocytes and macrophages).

C edema

B Eosinophils are usually present in large numbers

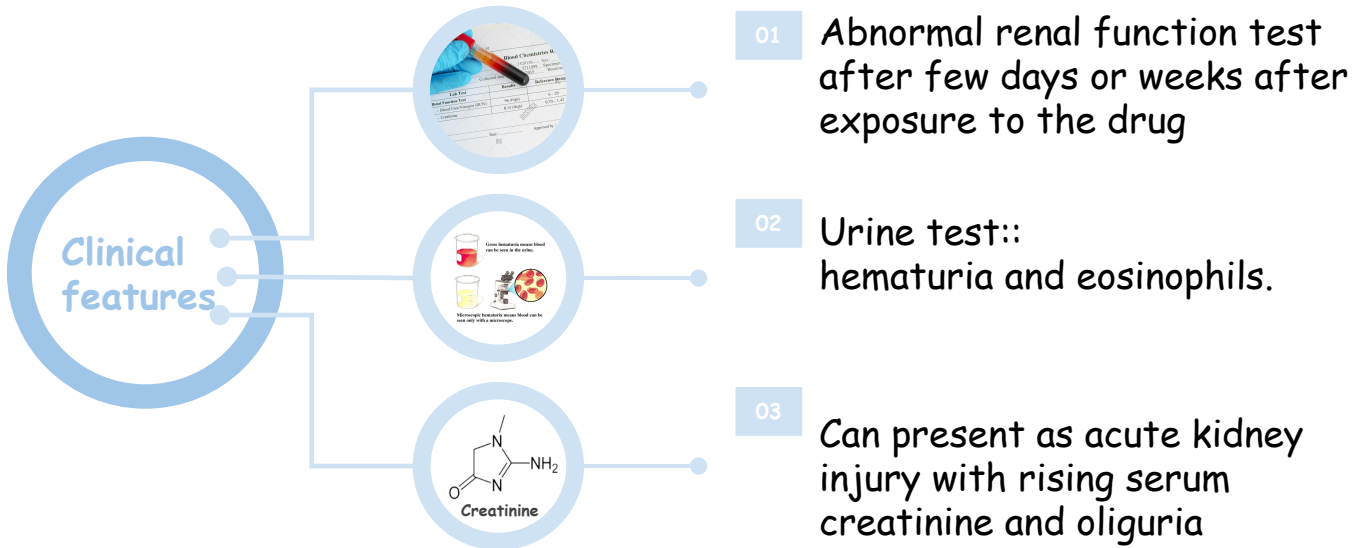
D Sometimes there are non-necrotizing granulomas and multinucleated giant cells



The glomeruli are usually normal

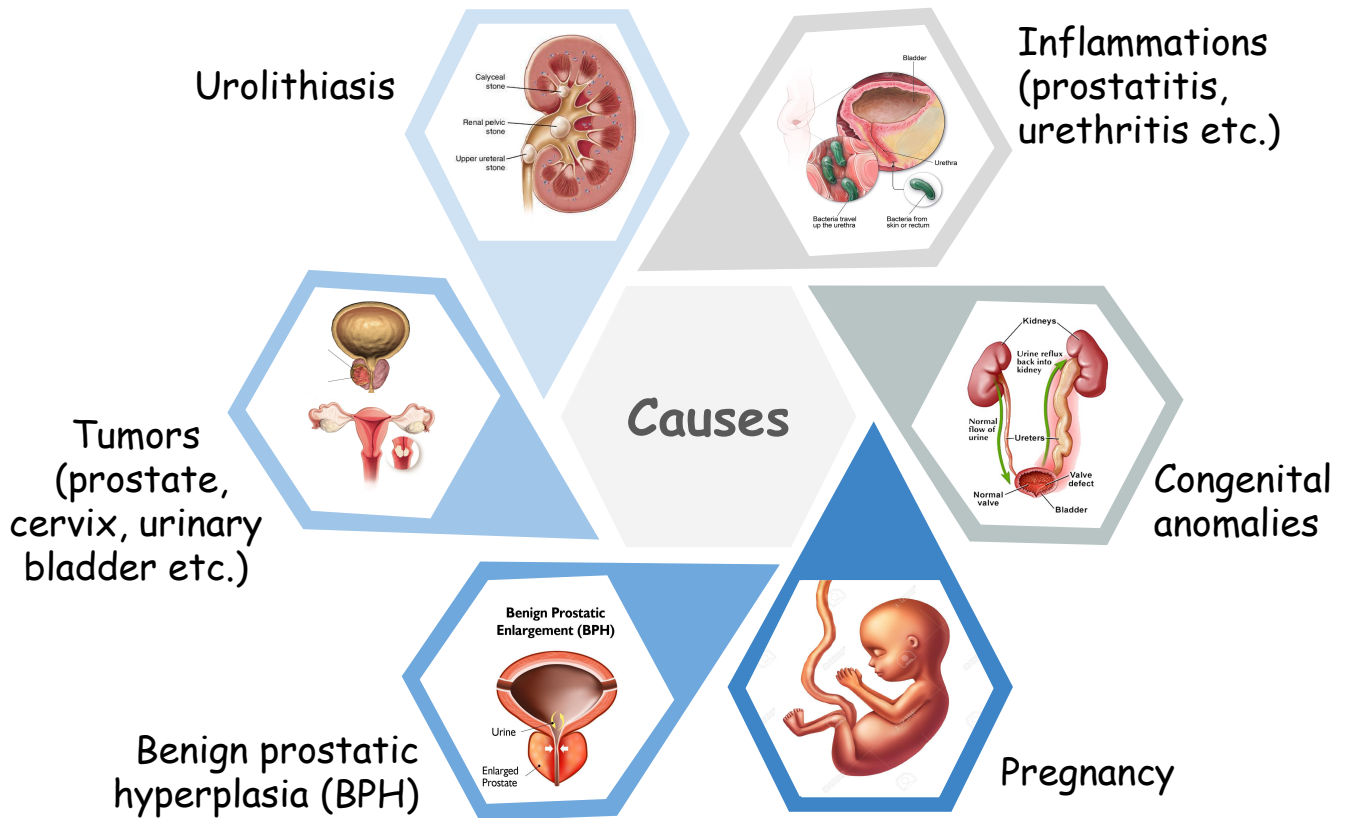
^{1/} proton pump inhibitors (omeprazole), phenindione cimetidine and immune checkpoint inhibitors
^{2/} ex. Furosemide

Drug induced tubulointerstitial nephritis



It is important to diagnose because if remove the offending drug on time the injury may be reversible

Urinary Tract Obstruction (urinary outflow obstruction)



- Others (paralysis of urinary bladder)

UROLITHIASIS

Urolithiasis

is the condition where urinary calculi are formed or located anywhere in the urinary system e.g. kidney, bladder, ureters etc.

(location of stone decides symptoms)

Renal pelvis and calyces are common sites for calculi formation.

Predisposing factors

Chronic dehydration:
concentrates urine and
favors stone formation

There may be a **familial**
tendency toward stone
formation

A persistently **acidic** urine
favors formation of
oxalate or uric acid stones

Stasis facilitates
precipitation of salts and
stone formation

Metabolic factors:
hypercalciuria (does not
necessarily come with
hypercalcemia),
hyperphosphaturia, oxaluria,
gout (uric acid) ,
Hyperparathyroidism etc.

For unknown reasons, renal
stones are **more common in**
men than in women

A persistently **alkaline**
urine favors formation of
calcium phosphate stones

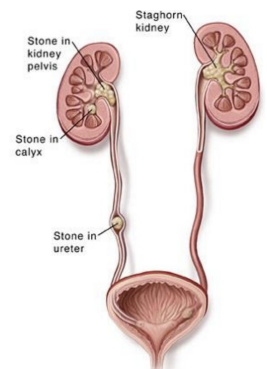
UROLITHIASIS

- Stones vary in composition, depending on various factors.
- Types of stones seen are:

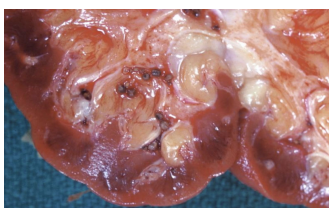
Type	Characteristics
Calcium stones	<ul style="list-style-type: none"> • 75% of kidney stones are calcium oxalate or phosphate (<u>radio-opaque</u>).
Infection stones	<ul style="list-style-type: none"> • 10% of stones are caused by infection ¹ results in alkaline urine leads to formation of magnesium ammonium phosphate stones (AKA: triple phosphate stones/ struvite stones). • Infection stones can occasionally fill the pelvis and calyces to form large <u>staghorn calculi</u>.
Uric acid stones	<ul style="list-style-type: none"> • Formed in acidic pH. Patients with hyperuricemia and gout are predisposed to uric acid stones, however it can be seen in people with no hyperuricemia and gout. Pure uric acid stones are <u>radiolucent</u>.
Cystine stones	<ul style="list-style-type: none"> • uncommon. • Associated with a genetically determined defect in renal transport of certain amino acids, most specifically cystine (Cystinuria).They are more likely to form when the urine is relatively acidic

Morphology

- Majority (80%) of the stones are unilateral.
- Common sites of formation are renal pelvis and calyces and the bladder.
- Commonly multiple stones are found in one kidney.
- Stones vary in size from few mm to large stones that dilate the entire renal pelvis.
- They range from hard to soft , from smooth to rough.
- The staghorn calculi take the shape of the pelvicalyceal system. They are large stones are usually composed of magnesium ammonium phosphate.



Rough stones can cause injury and ulceration of mucosa leading to hematuria.



Staghorn calculi



Staghorn calculi

Cause symptoms if they leave into the ureter reaching a constriction.



Staghorn calculi

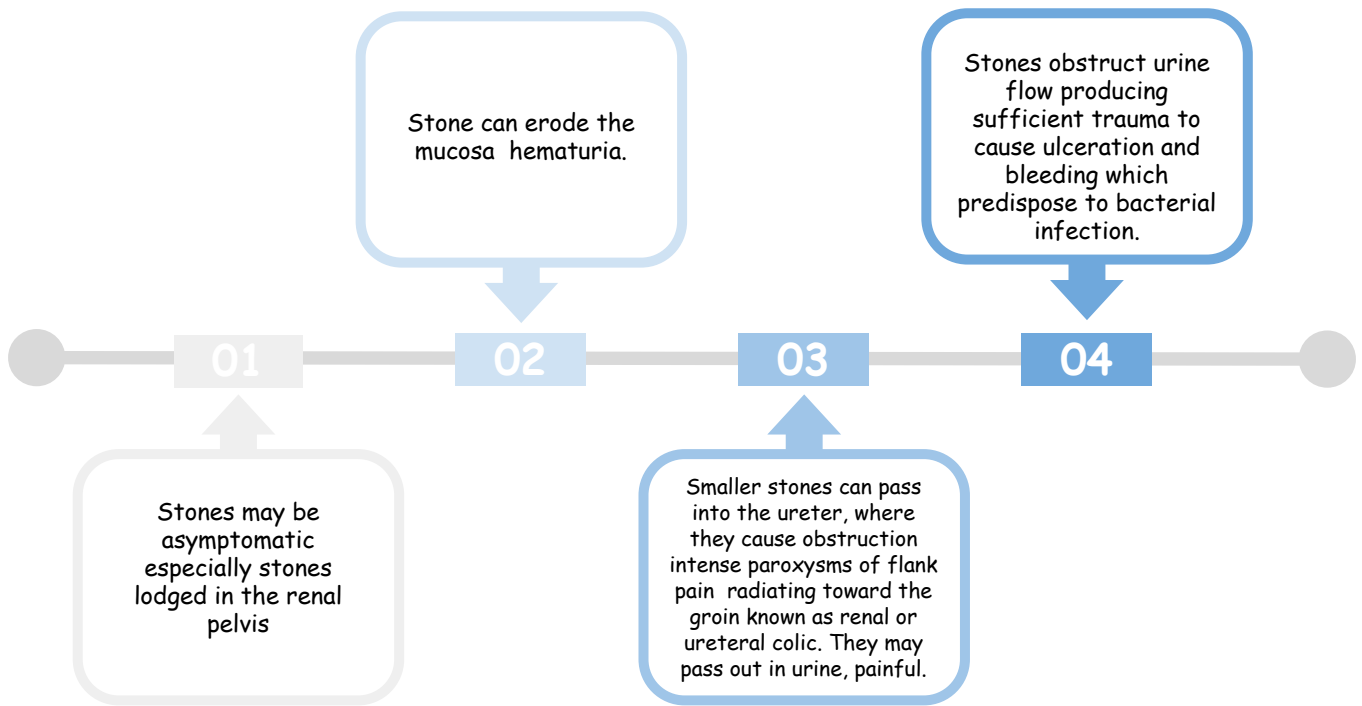


Staghorn calculi

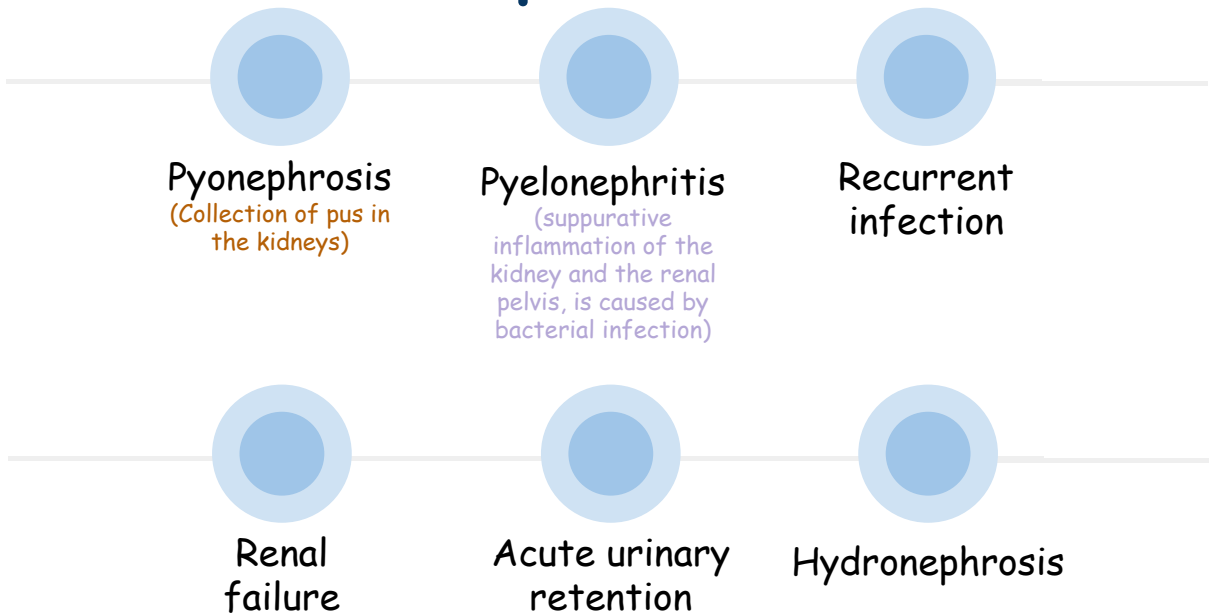
causes symptoms and chronic infection.

1/ with urea-splitting bacteria (proteus vulgaris and staphylococci).

UROLITHIASIS



Complications



Diagnosis and management

Diagnosis: is mostly readily made radiologically

management:

- In the past: most kidney stones required surgical removal.
- now: **ultrasonic disintegration** (lithotripsy) that breaks the stones to pieces and endoscopic removal are now effective.

HYDRONEPHROSIS

Definition

It is the dilation of the renal pelvicalyceal system with resultant renal parenchymal atrophy.

It is caused mainly by **obstruction** to the outflow of urine.

The obstruction can be:

acute or chronic

at any level

Obstruction below the level of ureters causes **bilateral hydronephrosis** (when bladder or urethra are involved)

Congenital

- e.g:
 - atresia of urethra
 - abnormal compression of ureter by renal artery etc.

Acquired

Foreign bodies: Calculi or sloughed necrotic papillae

Tumors: Benign prostatic hyperplasia, prostate, bladder or cervix tumors or contiguous malignant disease, ex: retroperitoneal lymphoma etc.

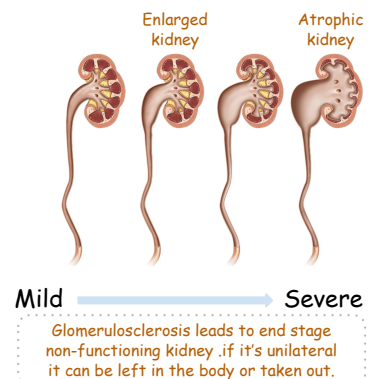
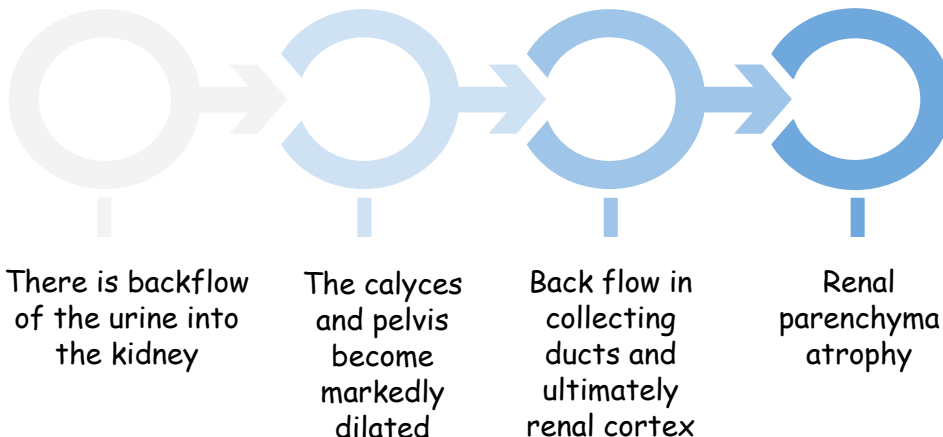
Inflammation: Prostatitis, ureteritis, urethritis

Neurogenic: Spinal cord damage with bladder paralysis

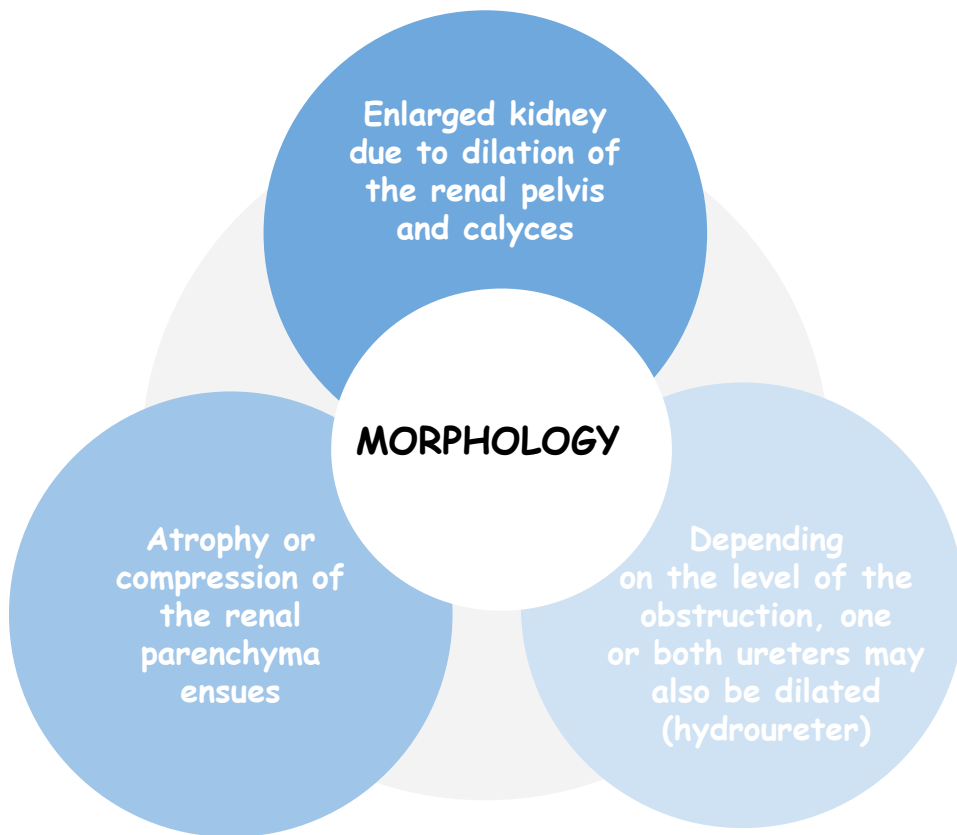
Pregnancy

Pathogenesis:

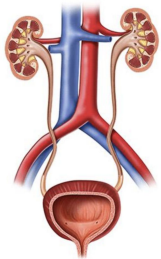
- The obstruction also triggers an interstitial inflammatory reaction leading eventually to **tubular atrophy** and **interstitial fibrosis**.
- Initially the glomeruli are spared but eventually they become sclerotic (glomerulosclerosis).



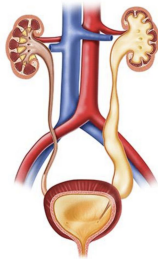
HYDRONEPHROSIS



Normal System



Ureterovesical Junction Obstruction



Clinical features

- Unilateral hydronephrosis: may remain **completely silent** for long periods (**usually incidentally found**).
- Bilateral hydronephrosis can lead to oliguria to anuria and **renal failure**.
- With time the changes become irreversible.
- In the presence of hydronephrosis, the kidney is **more susceptible to pyelonephritis**, which causes additional injury.
- Early diagnosis and timely removal of obstruction within a few weeks usually permits full return of function

INFECTIONS OF THE LOWER URINARY TRACT

The Lower urinary tract			
	Ureter	Urinary bladder	Urethra
Transitional epithelium (urothelium)	✓		posterior urethra except the terminal urethra which is lined by squamous epithelium.
Inflammation	Ureteritis	Cystitis	Urethritis

Ureteritis

- It is a complication of descending infections of kidneys or ascending infections if there is vesicoureteral reflux.
- often associated with ureteral obstruction (e.g. calculi, intraluminal blood clots, or extrinsic compression of ureter by an adjacent tumors, or lymph nodes and the pregnant uterus can compress the ureters).

Prostatitis: inflammation of the prostate and sometimes the areas around the prostate.

Cystitis

- Inflammation of the urinary bladder
- May be acute or chronic.
- The most common urinary tract infection and is often seen as a nosocomial infection in hospitalized patients.

Predisposing factors include:

1 bladder calculi

3 diabetes mellitus

5 prior instrumentation or catheterization

2 bladder outlet obstruction (e.g. prostatic hyperplasia)

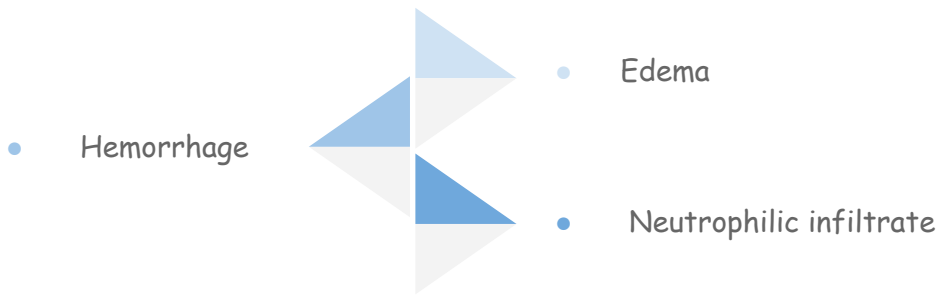
4 immunodeficiency

6 radiation therapy or chemotherapy.

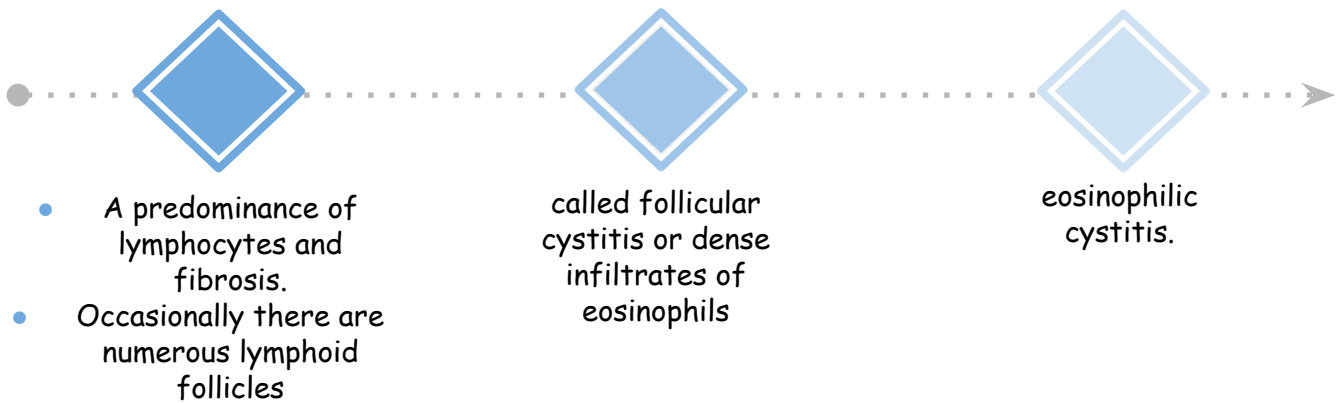
- The risk of cystitis is increased in **females** because of a **short urethra**, especially during pregnancy.
- Common in patients in whom indwelling catheters remain for prolonged periods.
- **Bacterial cystitis is most common form of cystitis.** It is caused mainly by coliform bacteria e.g. **E. coli**, Proteus vulgaris, Pseudomonas and Enterobacter spp.

INFECTIONS OF THE LOWER URINARY TRACT

Acute cystitis



Chronic cystitis



Special forms of cystitis:

Tuberculous cystitis	<ul style="list-style-type: none"> • there is granulomatous cystitis with or without necrosis.
Hemorrhagic cystitis	<ul style="list-style-type: none"> • shows mucosal hemorrhages. • Is often seen in acute bacterial infection, adenovirus infection, bleeding diathesis (e.g., leukemia, treatment with cytotoxic drugs and disseminated intravascular coagulation).
Polypoid cystitis	<ul style="list-style-type: none"> • is an inflammatory condition resulting from irritation to the bladder mucosa in which there is marked submucosal edema resulting in polypoidal (polyp-like) projections.

INFECTIONS OF THE LOWER URINARY TRACT

Special forms of cystitis:

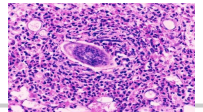
Malakoplakia

- uncommon inflammatory disorder of unknown etiology.
- Seen in the bladder and other sites within and outside the urinary tract; characterized by plaques on the mucosal surface of the bladder.
- Histology shows a chronic inflammation with numerous macrophages.
- Some of these macrophages contain laminated, mineralized concretions of basophilic calcium called **Michaelis-Gutmann bodies**.

Schistosomiasis

- in it the *S. haematobium* eggs (picture) can be seen and they elicit a **granulomatous reaction with an eosinophilic infiltrate**. The ova can calcify ova and appear as grains of sand in bladder wall.
- Occasionally the entire urinary bladder become calcified (**dystrophic calcification**) → known as **calcific cystitis**.

-Long term Schistosomiasis predisposes to squamous cell neoplasia of the bladder.
- schistosomiasis affects liver, colon and urinary bladder



Chronic interstitial cystitis (chronic pelvic pain syndrome)

- is a persistent, painful form of chronic cystitis typically affects middle-aged women.
- It is characterized by intermittent, suprapubic pain, urinary frequency, urgency, hematuria and dysuria without evidence of bacterial infection; cause is unknown; urine **cultures are usually negative**.
- The disease is refractory to all forms of therapy → Eventually bladder fibrosis → contracted bladder.

Acute and chronic cystitis: clinical features

Excessive urinary frequency, painful burning urination (dysuria) and lower abdominal or pelvic discomfort.

Examination of urine usually reveals inflammatory cells and causative organism can be identified by urine culture.

Most cases of cystitis respond well to treatment with antimicrobial agents.

Summary

	Acute Pyelonephritis	Chronic Pyelonephritis
Definition	Acute suppurative inflammation of the upper urinary tract (kidney and renal pelvis) Caused by; bacterial infection (E.coli). Affects: tubules and interstitium	Repeated bouts of inflammation & healing, scarred kidney & deformed renal pelvis and calyces.
Morphology	<ul style="list-style-type: none"> - Macroscopic <ul style="list-style-type: none"> • Enlarged, Swollen kidney. • small yellowish white subcapsular microabscesses. • renal papillae are diffusely blunted. • hyperemic Pelvi-calyceal mucosa & covered by purulent exudate. • kidney may be filled with large amounts of pus. - Microscopic <ul style="list-style-type: none"> • Neutrophils with tubular destruction. • The vessels and glomeruli often are preserved. • Perinephric abscess 	<ul style="list-style-type: none"> - Macroscopic <ul style="list-style-type: none"> • Small & contracted kidneys. • The surface of the kidney is irregularly scarred with areas of depression. • Thinned cortex. • Deformity and blunting of the pelvicalyceal system - Microscopic <ul style="list-style-type: none"> • Tubular atrophy with thyroidization. • Interstitial fibrosis & chronic inflammation. • Periglomerular fibrosis and glomerulosclerosis.
Clinical features	<ul style="list-style-type: none"> - Fever, chills, sweats, malaise, flank pain. - Costovertebral angle tenderness. - Dysuria, frequency and urgency. - Leukocytosis with neutrophilia. - Pyuria, hematuria and WBC casts. - Positive urine culture. 	<ul style="list-style-type: none"> - Symptoms of urinary tract infection such as recurrent fever and flank pain. - chronic renal failure. - Hypertension. - Abnormalities of the pelvicalyceal system and cortical scarring. - Some patients have a silent course until end-stage renal disease develops.
Complications	Papillary necrosis Pyonephrosis Perinephric abscess Chronic pyelonephritis Septicemia	

Summary (cont.)

<p>Drug induced tubulointerstitial nephritis</p>	<ul style="list-style-type: none"> • Drugs are an important cause of renal injury. • Drug-induced interstitial nephritis is an IgE and T cell-mediated immune reaction to a drug. • Acute drug-induced tubulointerstitial nephritis (TIN) occurs as an adverse reaction to various therapeutic drugs e.g. penicillins, diuretic.
<p>Urolithiasis</p>	<ul style="list-style-type: none"> • Renal pelvis and calyces are common sites for calculi formation. • Types of stones seen are: Calcium stones, Infection stones, Uric acid stones, Cystine stones. • Complications: Recurrent infection, Hydronephrosis, Pyelonephritis, Pyonephrosis, Acute urinary retention, Renal failure.
<p>Hydronephrosis</p>	<ul style="list-style-type: none"> • The dilation of the renal pelvicalyceal system with resultant renal parenchymal atrophy. • Caused mainly by obstruction to the outflow of urine.
<p>Cystitis</p>	<ul style="list-style-type: none"> • The most common urinary tract infection (E.coli). • The risk of cystitis is increased in females because of a short urethra and is especially apparent during pregnancy. • Special forms of cystitis: <ul style="list-style-type: none"> - Tuberculous cystitis - hemorrhagic cystitis - chronic interstitial cystitis - Malakoplakia - polypoid cystitis - schistosomiasis

Quiz

<p>1) A 22-year-old woman in the second trimester of pregnancy presents with flank pain, fever of 38.7°C (103°F), and chills. Hemoglobin is 13.4 g/dL, WBCs are elevated (13,500/μL with 78% neutrophils), and there are 265,000 platelets/μL. Physical examination reveals costovertebral angle tenderness. The urine shows numerous WBCs and WBC casts. Which of the following is the most likely diagnosis?</p>		<p>2) A 70-year-old diabetic woman presents with sudden onset of excruciating groin and flank pain. Physical examination shows pitting edema of the lower extremities. Laboratory studies reveal decreased serum albumin and increased serum lipids. Urine cultures reveal more than 100,000 bacterial colonies composed predominantly of Gram-negative microorganisms. Which of the following is the most likely diagnosis?</p>		
A	Cystitis	A	Acute tubular necrosis	
B	Endometritis	B	Crescentic glomerulonephritis	
C	Glomerulonephritis	C	Diabetic glomerulosclerosis	
D	Pyelonephritis	D	Renal papillary necrosis	
E	Urethritis	E	Renal vein thrombosis	
<p>3) A 50-year-old woman complains of severe headaches and dizziness. The patient has a history of repeated urinary tract infections. The blood pressure is 180/110 mmHg. Laboratory studies show elevated levels of BUN (38 mg/dL) and creatinine (2.8mg/dL). A CT scan of the lower abdomen reveals small, irregularly shaped kidneys with deep coarse scars. A percutaneous renal biopsy is shown. Which of the following is the appropriate diagnosis?</p>		<p>4) A 20-year-old pregnant woman (gravida II, para I) complains of lower pelvic discomfort, fever, and pain during urination for the past 2 days. She also reports seeing blood in her urine. Which of the following is the most likely cause of hematuria in this patient?</p>		
A	Acute pyelonephritis		A	Acute cystitis
B	Acute tubular necrosis		B	Acute pyelonephritis
C	Chronic pyelonephritis		C	Bladder calculi
D	Nephrosclerosis		D	Postinfectious glomerulonephritis
E	Tubulointerstitial nephritis		E	Urothelial cell carcinoma of the bladder
<p>5) A 50-year-old woman presents with acute right flank pain of 72 hours in duration. Physical examination is unremarkable. Her temperature is 37°C (98.6°F), blood pressure 140/85 mm Hg, and pulse 85 per minute. A CBC is normal. Urinalysis reveals hematuria and urine cultures are negative. Imaging studies show stones in the right renal pelvis and ureter. This patient's condition may be associated with which of the following endocrine disorders?</p>		<p>6) A 36-year-old woman presents with advanced cervical carcinoma, and a CT scan shows widespread pelvic spread. If this condition is not surgically corrected, the patient's kidneys will most likely develop which of the following conditions?</p>		
A	Conn Syndrome	A	Acute vasculitis	
B	Cushing syndrome	B	Hydronephrosis	
C	Hyperparathyroidism	C	Polycystic kidney disease	
D	Hyperthyroidism	D	Staghorn Calculi	
E	Hypoparathyroidism	E	Tubulointerstitial nephritis	



Thank you

Team leaders:

Raghad AlKhashan & Mashal Abaalkhail

Team members:

- Alhanouf Alhaluli
- Amirah Alzahrani
- Danah Alhalees
- Deana Awartani
- Elaf AlMusahel
- Joud AlJebreen
- Lama Alassiri
- Lama Alzamil
- Leena Alhassar
- Leen Almazroa
- Njoud Alali
- Noura Alturki
- Reema Alserhani
- Rema Almutawa
- Taibah Alzaid
- Abdulaziz Alghamdi
- Alwaleed Alarabi
- Alwaleed Alsaleh
- Faisal Almuhid
- Jihad Alorainy
- Khalid Alkhani
- Mohammad Alhamoud
- Mohammad Aljumah
- Mohanad makkawi
- Muaath Aljehani
- Nawaf AlBhijan
- Suhail Basuhail
- Abdulla Alhawamdeh
- Tariq Aloqail
- Mohammed Alqahtani