PATHOLOGY TEAM 439

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جامعة الملك سعود
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INFECTION OF THE UPPER & LOWER URINARY TRACT

UTI ,doctoon (helpful explanation)
UTI.USMLE (microbiology)
UTI,Armando(overview)

Objectives:

- At the end of the two lectures the students will be able to:
- 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.

Key Outlines:

- Urinary Tract Obstruction: causes and clinical manifestations in children and adults.
- Infections of the Urinary Tract: Predisposing Factors and Clinical Manifestations.
- Pathology of Acute and Chronic Pyelonephritis
- including causes and complications of urolithiasis.
- Drug induced interstitial nephritis and renal necrosis.

Index:
Important
NOTES
Extra Information

Infections of the upper urinary tract

Tubulointerstitial nephritis

Definition

Tubulointerstitial nephritis is inflammatory disease primarily involving the renal tubules and interstitium (inflammation or infection).

Types

It can be in the form of:

- Acute pyelonephritis
- Chronic pyelonephritis
- Drug induced tubulointerstitial nephritis

They are serious if untreated, and need biopsy to detect if there's kidney injury or renal failure

ACUTE PYELONEPHRITIS

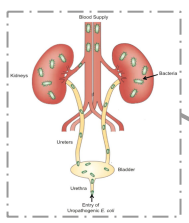
Definition

Acute pyelonephritis is an acute suppurative (neutrophilic) inflammation of the upper urinary tract (kidney & renal pelvis) caused by bacterial infection which typically follows infection of the lower urinary tract.

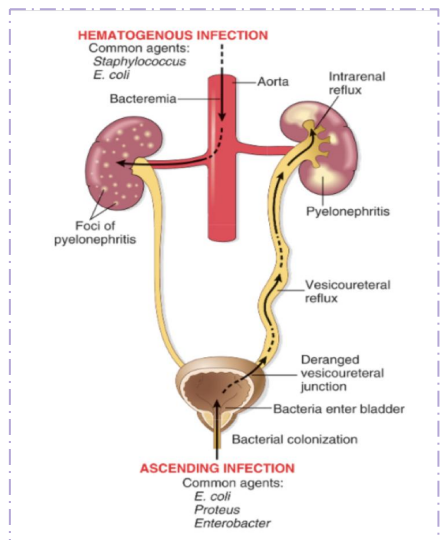
The most common causative organisms

- enteric gram-negative rods Escherichia coli
- Proteus spp.
- Klebsiella
- Enterobacter
- Pseudomonas

Routes of transmission



- Ascending infection (more common) from the lower urinary tract: bacteria ascends from the urethra into the urinary bladder and up the ureters to the kidneys.
- Through the bloodstream/ hematogenous (less common) e.g. from an infected heart valve in endocarditis, miliary tuberculosis etc.



Predisposing factors

Important because the will be repeated million times during the lecture

Obstruction

obstruction at the level of the urinary bladder (by stones, benign prostatic hypertrophy etc.) → incomplete emptying of bladder and increased residual urine → stasis of urine in bladder → allows bacteria to multiply → bacteria ascend up the ureters and infect the kidneys.

Gender

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

Pre-existing renal lesions

Immunosuppression & immunodeficiency

Urethral instrumentation
e.g. catheterization and cystoscopy.

Incompetence of the vesicoureteral orifice

→ allows reflux of bladder urine to ascend up into the ureter (normally ureteral insertion into the bladder is a competent one-way valve that prevents retrograde flow of urine). About 1/3rd of children with UTI have vesicoureteral reflux (due to a congenital defect of the valve).

Pregnancy

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

Diabetes mellitus

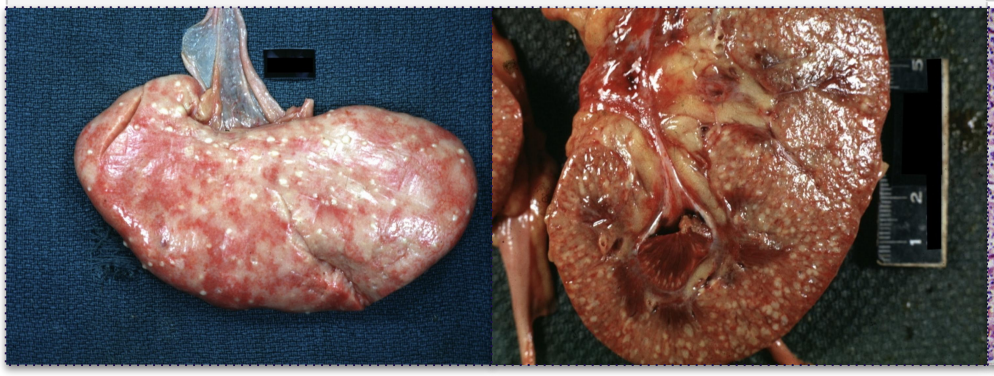
diabetic glycosuria predisposes to infection by providing a rich medium for bacterial growth. Diabetics also have increased risk of complications of pyelonephritis e.g. septicemia, necrotizing papillitis and recurrence of infection.

Infections of the upper urinary tract

Acute Pyelonephritis

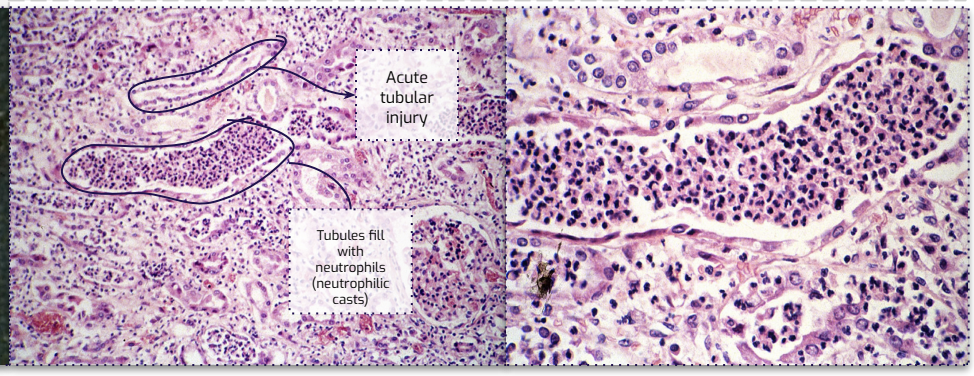
Morphology

Macroscopic



◦ The kidney may be enlarged and swollen and show small yellow/white subcapsular and **cortical microabscesses** (pus = suppurative necrosis).
◦ Rarely the kidney may become filled with large amounts of pus in the renal pelvis, calyces and ureter called pyonephrosis.

Microscopic



◦ There is a dense acute tubulointerstitial inflammation (neutrophils) with tubular destruction. The neutrophils fill the tubules and collecting ducts.
◦ The vessels and glomeruli often are preserved.
◦ There is possibility of regeneration .
◦ In severe cases → perinephric abscess The abscess can be inside the kidney or around it

Clinical features

- Fever with chills and sweats (those always with every bacterial infection)
- Flank pain with costovertebral angle tenderness.
- Dysuria, frequency and urgency.
- Pyuria (Pus in the urine), hematuria.
- Leukocytosis with neutrophilia.
- Positive urine culture and wbc casts in the urine.
- Differentiating upper from lower urinary tract infection is often clinically difficult.

Complications

- Papillary necrosis.
- Pyonephrosis. (pus collected in the renal pelvis)
- Perinephric abscess(.Pus around the kidney(renal parenchyma or perinephric space)
- Septicemia.
- Chronic pyelonephritis (If untreated).

Papillary necrosis (necrotizing papillitis)

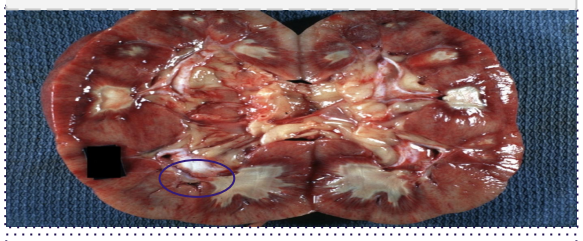
Definition

It is a type of pyelonephritis characterized by necrosis of the renal papillae (apex of renal pyramids).

Seen in: (Predisposing factors)

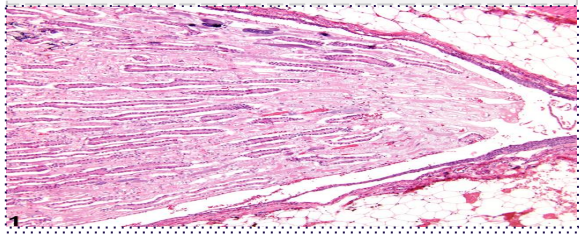
- **Diabetics with acute pyelonephritis.**
- Acute pyelonephritis with urinary tract obstruction.
- **Analgesic abuse** associated interstitial nephritis.
- **Chronic liver disease.**
- **Infections** e.g. tuberculosis.
- **Sickle cell disease.**
- **Renal transplant rejection.**

Macroscopic



Yellow white suppurative necrosis (pus) at the tips of renal papillae/pyramids.

Microscopic



coagulative necrosis & microabscess at the tips of renal papillae.

Infections of the upper urinary tract

Chronic Pyelonephritis

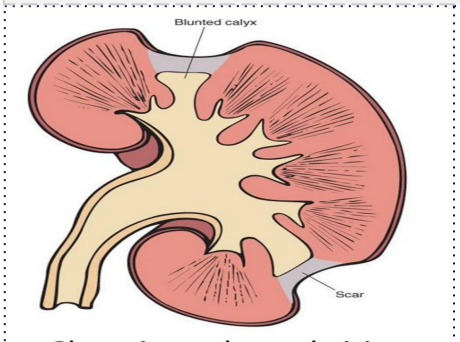
Definition

- It is a chronic tubulointerstitial inflammation of the kidney caused by repeated bouts of inflammation and healing.
- resulting in scarring of the involved kidney (so that part of kidney will be lost) with deformed renal pelvis & calyces and gradual renal insufficiency.

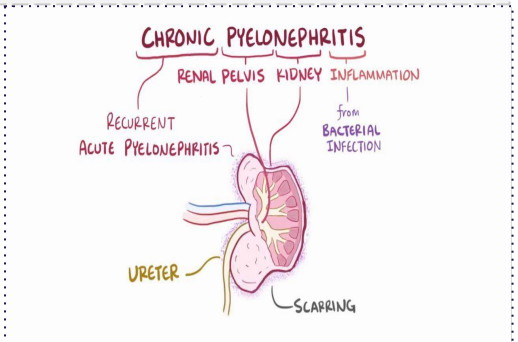
Caused by

- Recurrent chronic urinary tract infection.
- Chronic urinary obstruction (e.g. obstruction of the ureter by calculi **(stones)**, **tumor** within the ureter, or extrinsic compression etc.).
- Chronic reflux.

Macroscopic

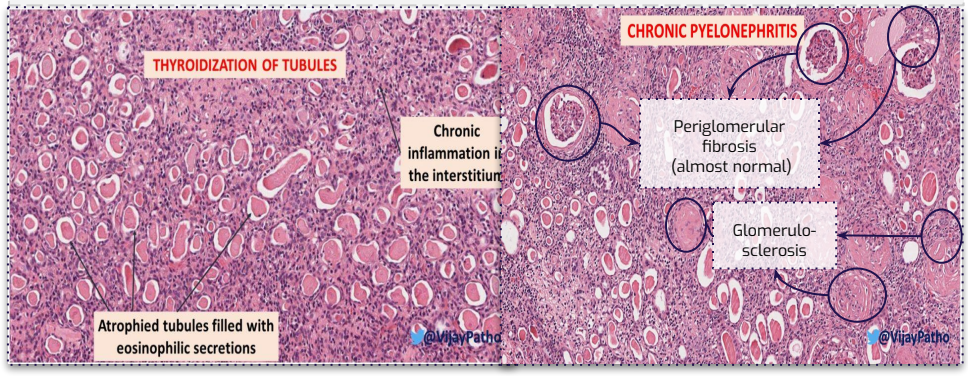


Chronic pyelonephritis



- The kidneys are **small** and **contracted** due to fibrosis.
- The surface of the kidney is irregularly scarred with areas of depression.
- The cortex in thinned out.
- There is deformity and blunting (dilating) of the pelvicalyceal system.

Microscopic



- Nonfunctioning kidney.
- Tubules →tubular atrophy with **thyroidization** of tubules (tubules are filled with eosinophilic hyaline casts resembling colloid of thyroid gland).
- Interstitium → interstitial **fibrosis** and chronic interstitial **inflammation** (**lymphocytes** and plasma cells)
- Glomeruli → periglomerular fibrosis and glomerulosclerosis

Chronic pyelonephritis can ultimately lead to renal failure (end stage renal disease)

Clinical Features

- Most patients have **episodic symptoms** of urinary tract infection or acute pyelonephritis.
- Hypertension.
- Some patients have a **silent** course until end-stage renal disease develops.
- Imaging studies show deformed pelvicalyceal system and cortical scarring.

Infections of the upper urinary tract

Drug induced tubulointerstitial nephritis

Drugs are an important cause of renal injury (also hepatic injury) for that it is important to check the renal function before giving the drug and during the course.

- It is characterized by interstitial inflammation with many eosinophils.
- It can be acute or chronic.

Drug-induced interstitial nephritis is an **IgE (hypersensitivity)** and **T cell–mediated immune reaction** to a drug.

Implicated therapeutic drugs: **penicillins** (e.g. ampicillin), **rifampicin**, diuretics (thiazides), nonsteroidal anti-inflammatory agents, etc.

Clinical Features

- Abnormal renal function test after few days or weeks after exposure to the drug.
- Urine: hematuria and eosinophils.
- Can present as acute kidney injury (rising serum creatinine and oliguria) + all the features of AKI.
- It is important to diagnose this condition, because if remove the offending drug on time the injury may be reversible.

Microscopic

- Interstitial infiltration by chronic inflammatory cells (lymphocytes and macrophages), typically with increased eosinophils.
- Interstitial **non-necrotizing granulomas** with multinucleated giant cells +/-.
- Tubular atrophy +/- due to healing with fibrosis.
- The glomeruli are usually normal until the patient rich the end stage renal disease.

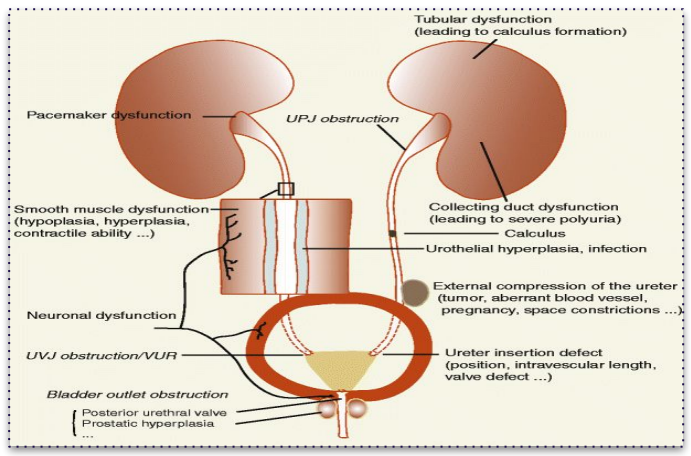
Urinary tract obstruction

Definition

Obstruction in the outflow of urine

Causes

- Congenital anomalies
- Urolithiasis (Stones)
- Benign prostate hyperplasia (In older men)
- Tumors (of prostate, cervix, urinary bladder etc.)
- Inflammations (prostatitis, urethritis etc.)
- Pregnancy due to compress on urinary tract.
- Others (paralysis of urinary bladder)



Infections of the upper urinary tract

Urolithiasis/nephrolithiasis

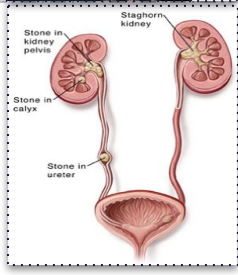
Definition

Formation of urinary calculi/stone along the urinary system e.g. kidney (inside the renal pelvis), bladder, ureters etc. Stones vary in composition.

Common sites for calculi formation

Renal pelvis and calyces (called nephrolithiasis), urinary bladder.

Predisposing factors



- **Metabolic factors**: **hypercalciuria**, **hyperphosphaturia**, **oxaluria**, gout etc.
- Persistently **alkaline urine** favors formation of calcium phosphate stones.
- Persistently **acidic urine** favors formation of oxalate or uric acid stones.
- **Stasis of urine** facilitates precipitation of salts and stone formation.
- **Chronic dehydration**: concentrates urine and favors stone formation
- For unknown reasons, renal stones are more common in **men** than in women.
- There may be a **familial** tendency toward stone formation.

Types of stones

Calcium stones

75% of kidney stones are calcium oxalate or phosphate (radio-opaque).

Infection stones

10% of stones are caused by infection → infection results in **alkaline urine** → leads to formation of **magnesium ammonium phosphate** stones. Infection stones can occasionally fill the pelvis and calyces to form large staghorn calculi.

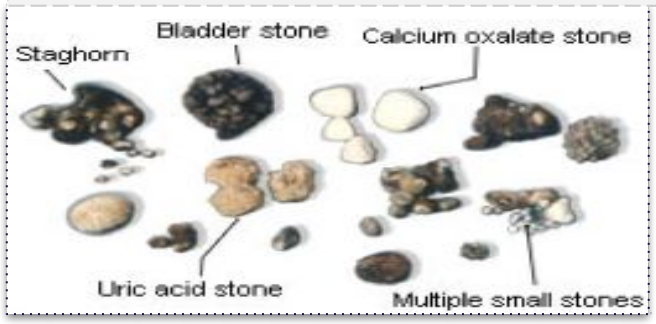
Uric acid stones

are formed in acidic pH. Patients with hyperuricemia and gout are predisposed to uric acid stones, but it can also be seen in people with no hyperuricemia or gout. Pure uric acid stones are radiolucent.

Cystine stones

are uncommon.

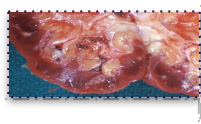
Morphology



- Majority (80%) of the stones are **unilateral**
- 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

Clinical features

(Depends on where the stones are located)

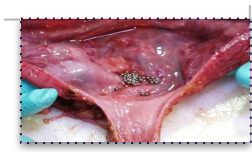


- May be asymptomatic if the stones are small esp. stones lodged in the renal pelvis
- Stone can erode the mucosa "epithelium" (ulceration) → hematuria.
- Smaller stones can pass into the **ureter**, where they cause obstruction → intense episodes of **flank pain radiating toward the** (thigh) **groin** known as renal or ureteral colic. They may pass out in urine → painful.
- Stones obstruct urine flow → predispose to bacterial infection

Complicitions

- Recurrent infection
- Hydronephrosis
- Pyelonephritis (Acute or chronic)
- Pyonephrosis
- Acute urinary retention
- Renal failure

Diagnosis & management



- Majority, the diagnosis → made **radiologically**.
- In the past most kidney stones required surgical removal, but now ultrasonic disintegration (lithotripsy) and endoscopic removal are now effective.

Infections of the upper urinary tract

Hydronephrosis

Definition

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

Caused by

- Complication of the obstruction to the outflow of urine.
- The obstruction can be acute or chronic and be at any level of the urinary tract.
- Obstruction below the level of ureters causes bilateral hydronephrosis e.g. in urethra.

The obstruction can be

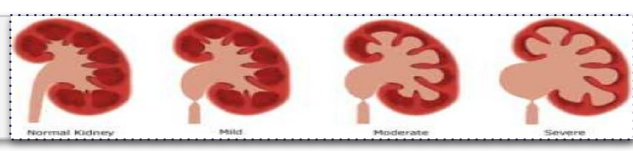
Congenital

atresia of urethra

Acquired

Calculi, Benign prostatic hyperplasia, Tumors (of prostate,bladder,cervix tumors etc.), Inflammation (Prostatitis, ureteritis, urethritis), Neurogenic (Spinal cord damage with bladder paralysis) , Pregnancy.

Pathogenesis

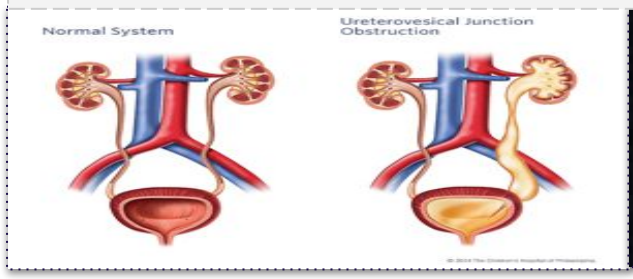


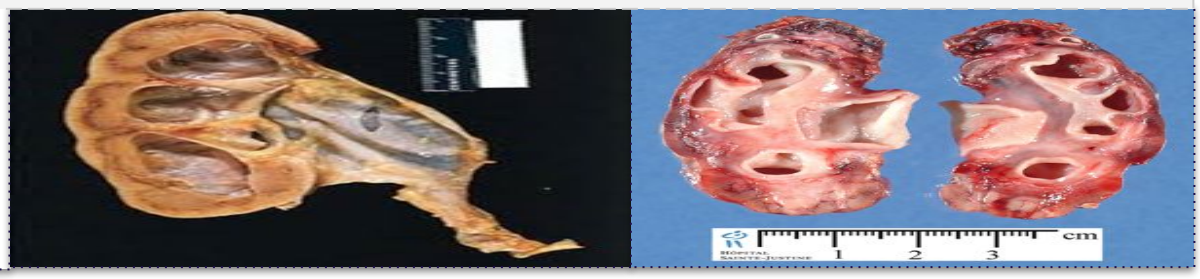
There is backflow of the urine into the kidney → The calyces and pelvis become markedly dilated → Back flow in collecting ducts of kidney → Ultimately back flow in renal cortex → Renal cortical atrophy

The obstruction also triggers an interstitial inflammatory reaction → Tubular atrophy and interstitial fibrosis.

Initially the glomeruli are spared but eventually (slowly) hey become sclerotic.

Morphology





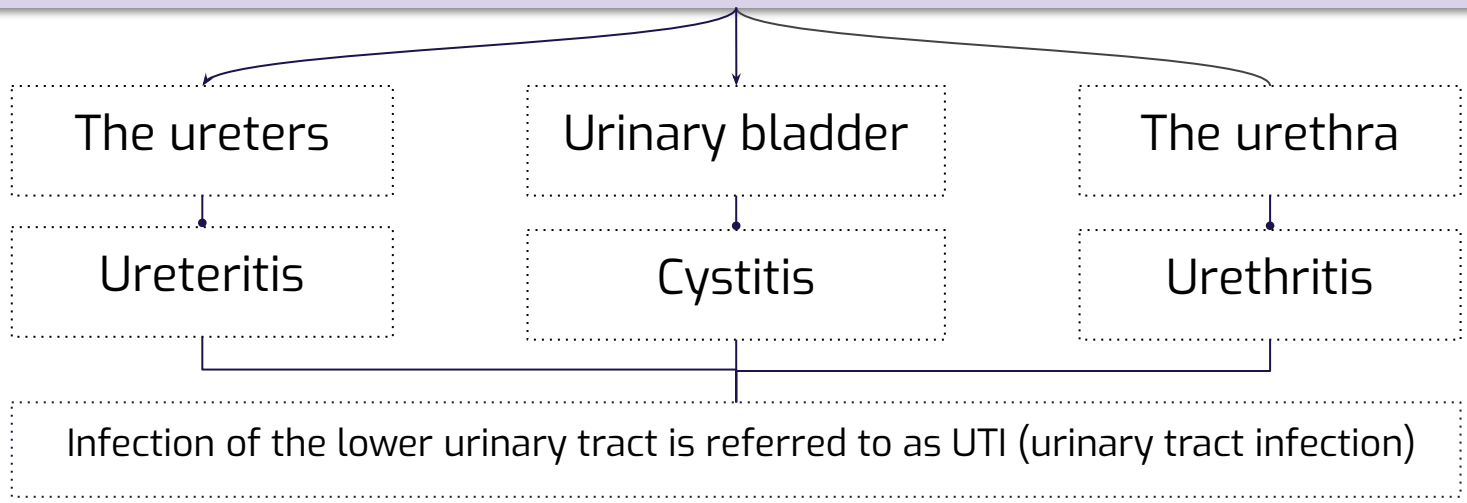
- Initially enlarged kidney due to **dilation of the renal pelvis and calyces**
- Followed by atrophy or compression of the renal parenchyma.
- Depending on the level of the obstruction, one or both ureters may also be dilated (hydroureter)

Clinical features

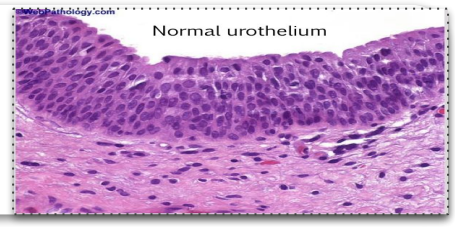
- **Unilateral** hydronephrosis may be **silent**/ asymptomatic for long periods (because the other kidney compensate)
- Bilateral hydronephrosis can leads to oliguria, anuria and acute renal failure
- In hydronephrosis, the kidney is more susceptible (predispose) to pyelonephritis, which causes additional injury
- With time the changes become irreversible even when we fix the obstruction.
- Early diagnosis and timely removal of obstruction within a few weeks usually permits full return of function

Infections of the Lower urinary tract

Lower urinary tract composed of



The ureters, urinary bladder and urethra
are lined by **transitional Normal urothelium epithelium** except the **terminal urethra** which is lined by stratified **squamous epithelium**.



Ureteritis

Ureteritis is an inflammation of the ureters. It is a complication of **descending** or **ascending** infections; ureteritis is often associated with ureteral obstruction (e.g. **calculi** in the ureter or extrinsic compression of ureter by an adjacent tumor/lymph node or pregnant uterus).

Cystitis

Overview	❖ It is inflammation of the urinary bladder. It may be acute or chronic. ❖ It is the most common site of urinary tract infection. ❖ The risk of cystitis is increased in **females** because of a short urethra, especially during pregnancy.
Causes	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.
Predisposing factors	bladder calculi, bladder outlet obstruction (e.g. prostatic hyperplasia), diabetes mellitus, immunodeficiency, radiation therapy, and chemotherapy, prior instrumentation or catheterization (often seen as a nosocomial infection in hospitalized patients, common in patients with indwelling catheters for prolonged periods).

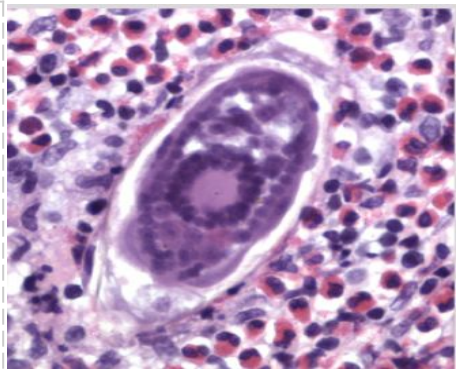
Comparison

Acute cystitis : edema, hemorrhage and a neutrophilic infiltrate.	lymphocytic, histiocytic and plasma cell infiltrate and fibrosis.

Infections of the Lower urinary tract

Special forms of cystitis

Follicular cystitis	chronic inflammation with many lymphoid follicles
Eosinophilic cystitis	Inflammation with prominent eosinophilic infiltrate (caused by parasites or allergy)
Tuberculous cystitis	shows granulomatous cystitis with or without caseous necrosis.
Hemorrhagic cystitis	shows mucosal hemorrhages. Seen in acute bacterial infection, adenovirus infection and bleeding diathesis (e.g., leukemia, treatment with cytotoxic drugs and disseminated intravascular coagulation).
Chronic interstitial cystitis	(chronic pelvic pain syndrome): persistent, painful chronic cystitis typically affects middle-aged women; characterized by intermittent, suprapubic pain, urinary frequency, urgency, hematuria and dysuria without evidence of bacterial infection. urine cultures are usually negative. cause is unknown. refractory to treatment. Eventually ➡ bladder fibrosis ➡ contracted bladder.
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 macrophages contain **laminated**, **rounded**, **basophilic calcified** bodies called **Michaelis-Gutmann bodies.**
Polypoid cystitis	bladder inflammation in which there is marked mucosal edema (resulting in polypoidal elevations).
Schistosomiasis	infection by parasitic flatworms called Schistosoma (Schistosoma haematobium) in which the worms may lay eggs in the wall of urinary bladder. These eggs elicit a granulomatous reaction (Because it is a foreign bodies) and an eosinophilic infiltrate. The ova can calcify and appear as grains of sand in bladder wall. Occasionally the entire urinary bladder becomes calcified ➡ known as calcific cystitis. Chronic Schistosomiasis can predispose to **squamous cell carcinoma of the urinary bladder.**



Schistosoma Egg and eosinophils

Acute and chronic cystitis

clinical features	• Fever with chills • 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.

Qulz

1- A 35-year-old man presents with fever and rash after beginning treatment with penicillin 2 weeks earlier for a sinus infection. Urinalysis shows 3+ hematuria, as well as mononuclear cells, neutrophils, and eosinophils. Which of the following is the most likely diagnosis?			
a-Acute tubulointerstitial nephritis	b-Crescentic glomerulonephritis	c-Chronic pyelonephritis	d-Focal segmental glomerulosclerosis
2- A 52-year-old woman who suffers from diabetes mellitus and frequent urinary tract infections presents with a 3-day history of flank pain, undulating fever, and general malaise. A CBC shows neutrophilic leukocytosis (16,000/μL). Urine cultures reveal more than 100,000 bacterial colonies, composed predominantly of Gram-negative microorganisms. Blood pressure is 170/100 mm Hg, BUN is 30 mg/dL, and creatinine is 2.0 mg/dL. Fasting serum glucose is 190 mg/dL. Urinalysis shows 2+ sugar and 1+ protein. Microscopic examination of the urine sediment reveals neutrophils and occasional leukocyte casts. Which of the following is the most likely diagnosis?			
A-Postinfectious glomerulonephritis	B-Acute tubular necrosis	C-Acute pyelonephritis	D-Nephrolithiasis
3- 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?			
A-Postinfectious glomerulonephritis	B-Acute cystitis	C-Acute pyelonephritis	D-Bladder calculi
4- A 52-year-old woman complains of dysuria, frequency, and urgency. She has a long history of urinary tract infections. Urine cultures are positive for E. coli. Cystoscopy reveals soft yellow plaques on the mucosal surface. Histologic examination shows mucosal chronic inflammatory cells with numerous macrophages a biopsy shows calcium-rich spherical structures (Michaelis-Gutmann bodies). Which of the following is the appropriate diagnosis?			
A-malakoplakia	B-Cystitis cystica	C-Polypoid cystitis	D-Urothelial cell carcinoma
5-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?			
A-Acute vasculitis	B-Hydronephrosis	C-Polycystic kidney disease	D-Staghorn calculi

1-A , 2-C , 3-B , 4-A,5-B

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	- **Macroscopic** • 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** • Neutrophils with tubular destruction. • The vessels and glomeruli often are preserved. • Perinephric abscess	- **Macroscopic** • 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** • Tubular atrophy with thyroidization. • Interstitial fibrosis & chronic inflammation. • Periglomerular fibrosis and glomerulosclerosis.
Clinical features	— Fever, chills, sweats, malaise, flank pain. — Costovertebral angle tenderness. — Dysuria, frequency and urgency. — Leukocytosis with neutrophilia. — Pyuria, hematuria and WBC casts. — Positive urine culture.	— 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...

Drug induced tubulointerstitial nephritis	• 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.
Urolithiasis	• 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.
Hydronephrosis	• The dilation of the renal pelvicalyceal system with resultant renal parenchymal atrophy. • Caused mainly by **obstruction** to the outflow of urine.
Cystitis	• 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:** - Tuberculous cystitis - hemorrhagic cystitis - chronic interstitial cystitis - Malakoplakia - polypoid cystitis - schistosomiasis

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