

URINARY TRACT INFECTIONS

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Urinary Tract Infection Mohammad Abufaraj

OUTLINES

- Definition
- Epidemiology
- Pathogenesis
- Causative pathogens
- Diagnosis
- Antibiotics
- Clinical presentation in kidneys, bladder, and urethral, prostatic and specific situations infections

DEFINITION

- Urinary tract infection (UTI) is a term that is applied to a variety of clinical conditions ranging from the asymptomatic presence of bacteria in the urine to severe infection of the kidney with resultant sepsis.
- Accurate diagnosis and treatment of a UTI is essential to **limit its associated morbidity and mortality** and avoid prolonged or unnecessary use of antibiotics.

EPIDEMIOLOGY

Incidence (%)			
Age (y)	Female	Male	Risk Factors
<1	0.7	27	Foreskin, anatomic GU ab- normalities
1-5	4.5	0.5	Anatomic GU abnormalities
6-15	4.5	0.5	Functional GU abnormalities
16-35	20	0.5	Sexual intercourse, diaphragm use
36-65	35	20	Surgery, prostate obstruc- tion, catheterization
>65	40	35	Incontinence, catheteriza- tion, prostate obstruction

GU, genitourinary.

- The incidence of UTI in uncircumcised males is higher than in circumcised males (1.12% compared with 0.11%) during the first 6 months of life.
- 1-5 : VUR
- 6-15 : Dysfunctional voiding
- 16-35 : increase in female, but stay constant in males.
- 36-65: increase for both, gynecological problems and bladder prolapse in women, in men ,catheterization and prostatic obstruction

EPIDEMIOLOGY

- Approximately 7 million cases of acute cystitis are diagnosed yearly in young women; this likely is an underestimate of the true incidence of UTI because at least 50% of all UTIs do not come to medical attention.
- In those younger than 1 year and those older than 65 years the morbidity and mortality are the greatest.

Pathogenesis

- Understanding the mode of **bacterial entry**, **host susceptibility factors**, and **bacterial pathogenic factors** is essential to tailoring appropriate treatment for the diverse clinical manifestations of UTI.
- There are four possible modes of bacterial entry into the genitourinary tract.

BACTERIAL ENTRY :

1- **Periurethral ascending into the urinary tract** (the most common), example: short female urethra combined with its close proximity to vagina and rectum predispose women to more frequent UTI than males.

2- Hematogenous (in immunocompromised pts and neonates) (*Staphylococcus aureus, Candida* species, and *Mycobacterium tuberculosis*)

3- Lymphatogenous spread through the rectal, colonic, and periuterine lymphatics has been postulated as a cause for UTI

4- Direct extension from adjacent organs (like intraperitonial abcess and fistulas)

OR Relapsing infection from an inadequately treated focus in the prostate or kidney may seed other parts of the urinary tracts.

HOST DEFENSES :

1- Unobstructed urinary flow>>>washout of ascending bacteria.

2- **Specific characteristic of urine** (osmolality, urea, organic acid, and pH) that inhibit bacterial growth, colonization, and adherence.

** factors that inhibit bacterial adherence, such as Tamm–Horsfall glycoprotein

** So any anatomic or functional abnormalities (like obstruction and neurologic disease) of the urinary tract OR foreign bodies that impede urinary flow can increase susceptibility to UTI.

3- The epithelium lining of urinary tract provides physical barrier and has ability to recognize bacteria.
 **Bacteria induce innate immunity.

4-Normal flora of the periurethral area or the prostate and the presence of vesicoureteral reflux.

5- Aging is associated with an increased susceptibility to UTI, in part because of the increased incidence of obstructive uropathy in men, and alteration in the vaginal and periurethral flora from menopause in women.

6-Other causes include soiling of the perineum from fecal incontinence, neuromuscular diseases, increased instrumentation, and bladder catheterization.

FACTORS:

- Not all bacteria are capable of adhering to and infecting the urinary tract.
- E.Coli as an example:

1- E.coli has increased adherence properties to uroepithelial cells.

2- Resistance to the bactericidal activity of human serum and production of hemolysin.

3- The ability of E. coli to adhere to epithelial cells is **mediated by ligands** located on the tips of the bacterial fimbriae .

4- The presence of K antigen on the invading bacteria protects them from phagocytosis by neutrophils

5- E. coli have the ability to invade into the host cells, acting as **opportunistic intracellular pathogens**.

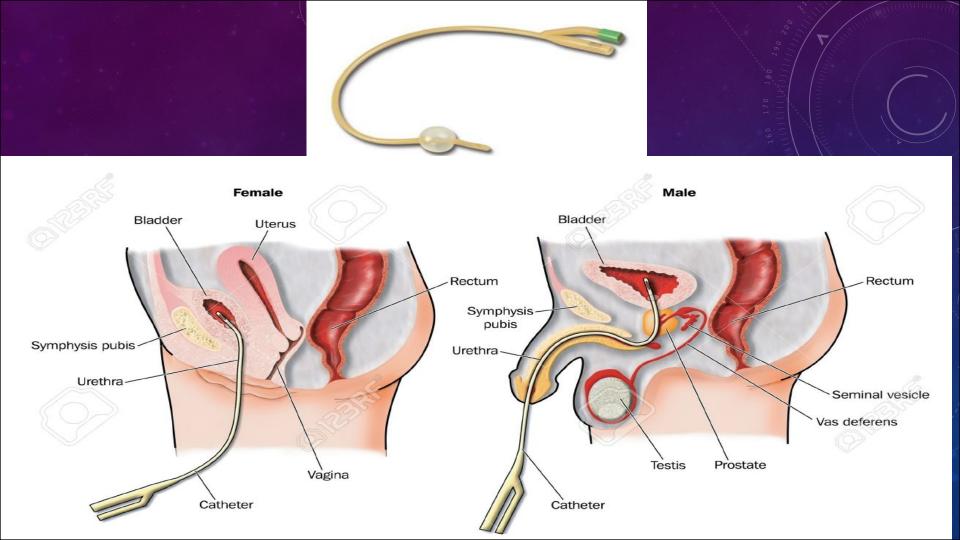
CAUSATIVE PATHOGENS

- Most UTIs are caused by a single bacterial species.
- At least 80% of the uncomplicated cystitis and pyelonephritis are due to E. coli, with most of pathogenic strains belonging to the O serogroups
- Less common uropathogens include Klebsiella, Proteus, and Enterobacter spp
- In hospital-acquired UTIs, a wider variety of causative organisms is found, including Pseudomonas and Staphylococcus spp
- S. aureus often result from hematogenous dissemination.
- Group B beta-hemolytic streptococci can cause UTIs in pregnant women

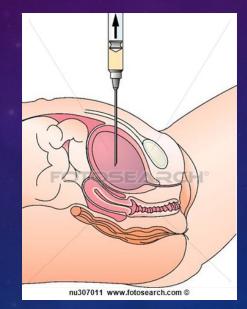
 Anaerobic bacteria, lactobacilli, corynebacteria, streptococci (not including enterococci), and Staphylococcus epidermidis are found in normal periurethral flora. They do not commonly cause UTIs in healthy individuals and are considered common urinary contaminants.

DIAGNOSIS

- Urine collection
- Voided specimen (m.c) but there is a high false-positive rate due to potential contamination from the vagina and perirectal area.
- Suprapubic aspiration (Invasive)
- Urinary catheter is less invasive than a suprapubic aspiration and is less likely to be contaminated than that obtained from a voided specimen



SUPRAPUBIC ASPIRATION



URINALYSIS

- The urine can be immediately evaluated for leukocyte esterase and urinary nitrate
- Can be detected by a urine dipstick and are more reliable when the bacterial count is >100,000 (CFUs) per milliliter.
- Microscopic examination :bacteria counts are >100,000 CFU/mL, bacteria can be detected microscopically.
 More than three WBCs per high-power field suggest a possible infection

Table 14–2. Sensitivity and specificity of urinalysis.

Tests	Sensitivity (%)	Specificity (%)	
Esterase (E)	79 (73-84)	87 (80-92)	
Nitrite (N)	49 (41-57)	98 (96-99)	
E or N	88 (82-91)	79 (69-87)	
E + N	45 (30-61)	98 (96-99)	
WBC	74 (67-80)	86 (82-90)	
Bacteria	88 (75-94)	92 (83-96)	

WBC, white blood cell.

THE SENSITIVITY OF 4 VARIABLES TOGETHER IS 98%

URINE CULTURE

- The gold standard for identification of UTI is the quantitative culture of urine for specific bacteria.
- The urine should be collected in a sterile container and cultured immediately after collection.
- Traditionally, >100,000 CFU/mL is used to exclude contamination. However, studies have clearly demonstrated that clinically significant UTI can occur with <100,000 CFU/mL bacteria.
- Defining the CFU/mL that represents clinically significant infection can be difficult. It is dependent on the method of collection, the sex of the patient, and the type of bacteria isolated

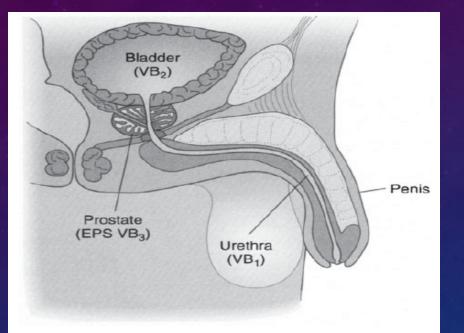
Table 14-3. Probability of UTIs based upon urine culture.

Collection	CFU	Probability of infection (%)
Suprapubic	Gram negative any Gram positive >1000	>99
Catheterization	>10 ⁵ 10 ⁴⁻⁵ 10 ³⁻⁴ <10 ³	95 Likely Repeat Unlikely
Clean catch		
Male	>10 ⁴	Likely
Female	3 specimens: >10 ⁵ 2 specimens: >10 ⁵ 1 specimen: >10 ⁵ 5×10^{4} -10 ⁵ 1-5 × 10 ⁴ symptomatic 1-5 × 10 ⁴ nonsymptomatic <10 ⁴	95 90 80 Repeat Repeat Unlikely Unlikely

UTIs, urinary tract infections; CFU, colony-forming unit.

LOCALIZATION STUDIES

- Occasionally, it is necessary to localize the site of infection.
- For upper urinary tract localization the bladder is irrigated with sterile water and a ureteral catheter is placed into each ureter. A specimen is collected from the renal pelvis.
- Specimen from renal pelvis. Culture of this specimen will indicate whether infection in the upper urinary tract is present.
- In men, infection in the lower urinary tract can be differentiated, A specimen is collected at the beginning of the void and represents possible infection in the urethra. A midstream specimen is next collected and represents possible infection. The prostate is then massaged and the patient is asked to void again. This specimen represents possible infection of the prostate.



▲ Figure 14–1. Localization of lower urinary tract infection. A positive culture in the voided bladder urine specimen VB₁ suggests infection of the urethra, while in VB₂, an infection of the bladder, and in EPS or VB₃, an infection of the prostate.

ANTIBIOTICS

- The goal in treatment is to eradicate the infection by selecting the appropriate antibiotics that would target specific bacterial susceptibility.
- The general principles for selecting the appropriate antibiotics include consideration of:
- The infecting pathogen (antibiotic susceptibility, single-organism vs poly-organism infection, pathogen vs normal flora, community vs hospital-acquired infection);
- The patient (allergies, underlying diseases, age, previous antibiotic therapy, other medications currently taken, outpatient vs inpatient status, pregnancy)
- The site of infection (kidney vs bladder vs prostate)

• Trimethoprim–Sulfamethoxazole

Commonly used to treat many UTIs, **except those caused by Enterococcus and Pseudomonas spp**. It is the most frequently prescribed antibiotic for uncomplicated UTI

• Fluoroquinolones

Have a broad spectrum of activity, especially against gram-negative bacteria , Although they are highly effective in the treatment of UTI, they are relatively expensive.

Nitrofurantoin

Good activity against most gram-negative bacteria (except for Pseudomonas and Proteus spp.), Staphylococci, and Enterococci species. Its usage in the treatment of uncomplicated UTIs has increased from 14% to 30% in the past 5 years.

Aminoglycosides

Commonly used in the treatment of complicated UTI. They are highly effective against most gram-negative bacteria.

The principal adverse effects of aminoglycosides are nephrotoxicity and ototoxicity

Cephalosporins

Oral cephalosporins have been used effectively in the empiric treatment of uncomplicated UTIs , **First generation** cephalosporins have good activity against gram-positive bacteria, E. coli, and Proteus and Klebsiella spp.

Second-generation cephalosporins have increased activity against anaerobes and Haemophilus influenzae.

<u>Third-generation</u> cephalosporins have broader coverage against gram-negative bacteria but less against grampositive bacteria.

• Penicillins

1st generation is ineffective against most uropathogens and are not commonly used in the treatment of UTI unless they are combined with beta-lactamase inhibitors.

Adverse reactions include hypersensitivity (which can be immediate or delayed), gastrointestinal upset, and diarrhea.

ANTIBIOTIC RESISTANCE

 Drug resistance among uropathogens has increased steadily during the past several years and has much, geographical variability.

• The **use of broad-spectrum antibiotics** has long been associated with the development of methicillin-resistant Staphylococcus aureus (MRSA) and Clostridium difficile superinfection.

CLINICAL PRESENTATION

KIDNEYS DISEASES

1. ACUTE PYELONEPHRITIS

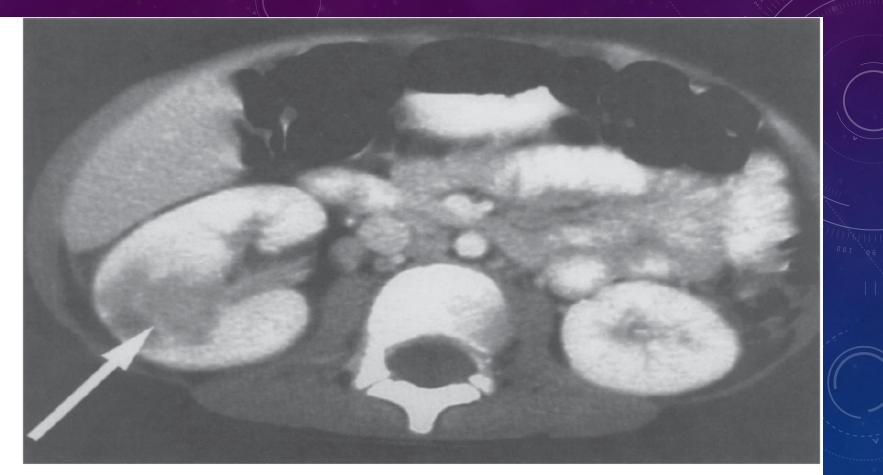
Inflammation of the kidney and renal pelvis, and its diagnosis is made clinically.

c/p :chills, fever, and CVA tenderness. They often have accompanying **lower-tract symptoms** such as dysuria, frequency, and urgency, **Sepsis may occur.**

Lab tests : Leukocytosis, increased ESR, and elevated levels of C-RP are commonly seen on blood analysis

Culture : Bacteria are cultured from the urine when the culture is obtained before antibiotic treatment is instituted. **E. coli is the most common causative organism, accounting for 80% of the cases**

Imaging: (CT) scans >> constriction of peripheral arterioles and reduces perfusion of the affected renal segments Renal enlargement, attenuated parenchyma, and a compressed collecting system.



▲ Figure 14–2. Acute pyelonephritis. Computed tomography scan with intravenous contrast demonstrates a perfusic defect (*white arrow*) and enlargement of the affected kidney.

Management of acute pyelonephritis depends on the severity of the infection. In patients who have toxicity because of associated septicemia hospitalization is warranted. Empiric therapy with intravenous ampicillin and aminoglycosides is effective against a broad range of uropathogens. Therapy should be continued for an additional 7–10 days and then the patient should be switched to oral treatment for 10–14 days

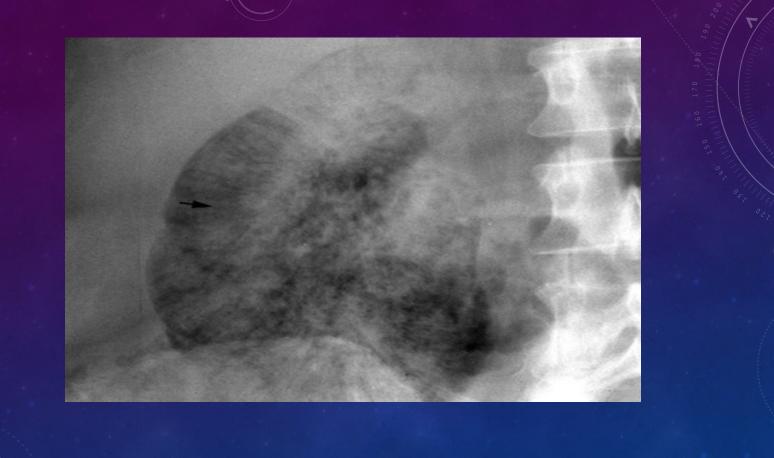
2.EMPHYSEMATOUS PYELONEPHRITIS

**Necrotizing infection characterized by the presence of gas within the renal parenchyma or perinephric tissue. About 80–90% of patients have diabetes.

/p: same as pyelonephritis but fails to respond to initial management with parenteral antibiotics.

Imaging :Gas overlying the affected kidney may be seen on a plain abdominal radiograph [kidneys, ureters, bladder (KUB**)]. CT scan is more sensitive**

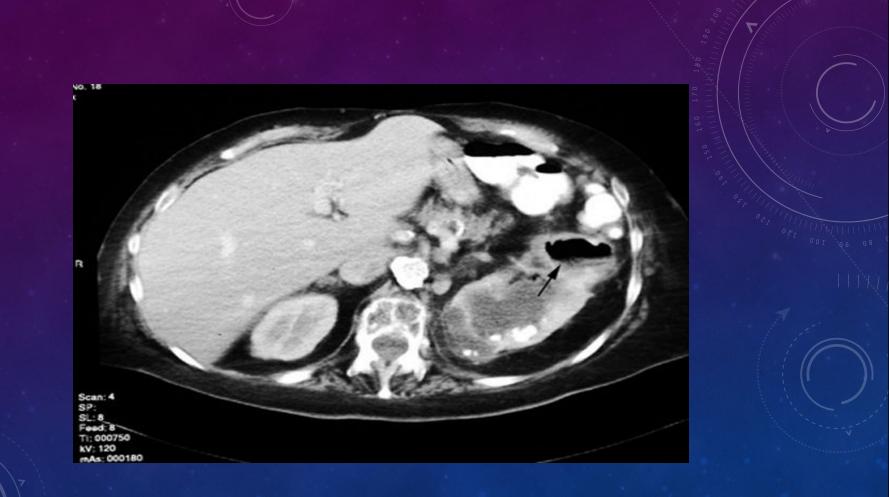
Management prompt control of blood glucose is essential, in addition to fluid resuscitation and parenteral antibiotics 3-4wks. The mortality rate is 11–54%

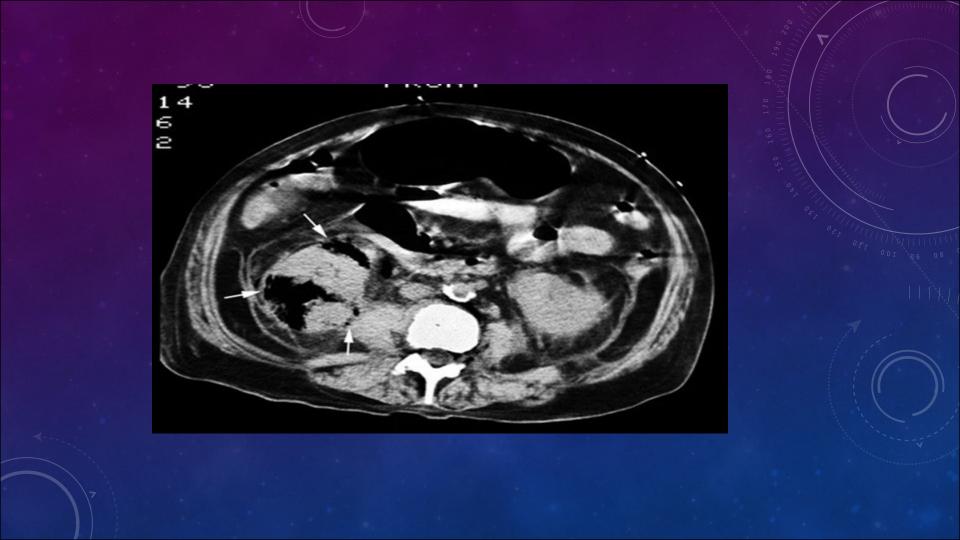


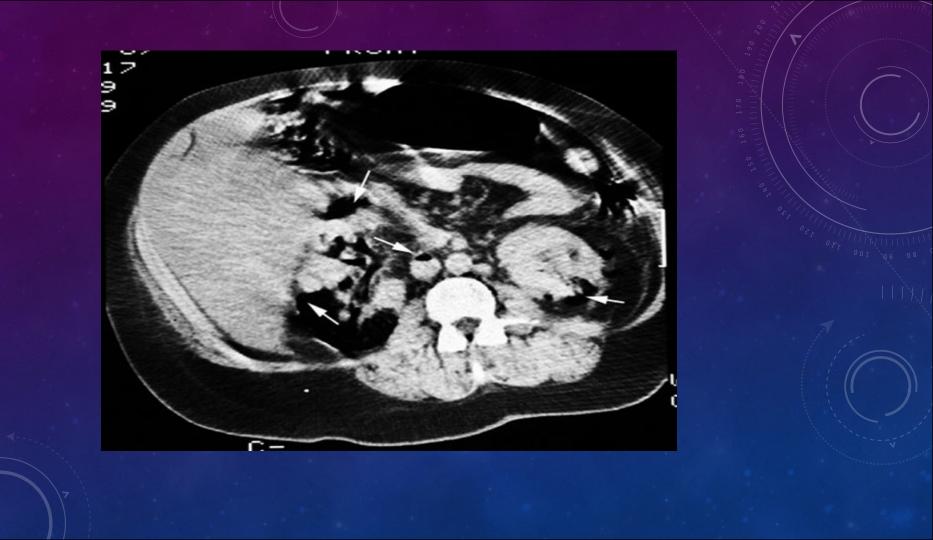




Emphysematous pyelonephritis. Renal sonogram showing hyperechoic shadows suggestive of gas along the lower pole of the kidney.







CHRONIC PYELONEPHRITIS

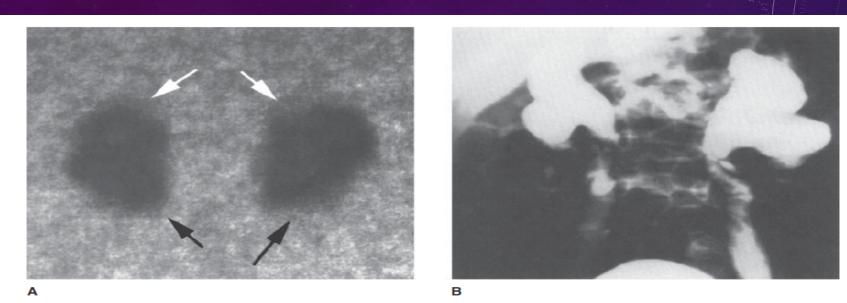
Results from **repeated renal infection**, which leads to **scarring**, atrophy of the kidney, and subsequent renal insufficiency.

c/p: Many individuals have **no symptoms**, but they may have a history **of frequent UTIs**.

Diagnosis : is made incidentally when radiologic investigation is initiated to evaluate for the complications associated with renal insufficiency. (it's a disease of children)

Imaging :Intravenous pyelogram or CT scan can readily demonstrate a small and atrophic kidney on the affected side **Dimercaptosuccinic acid (DMSA) is the best imaging modality to look for renal scarring**

 Management of chronic pyelonephritis is somewhat limited because renal damage incurred by chronic pyelonephritis is not reversible. Correcting any underlying anatomic or functional urinary problems to prevent further renal damage



▲ Figure 14–3. Chronic pyelonephritis. Multiple parenchymal defects (*white and black arrows*) are seen on DMSA scan (*A*), suggestive of scarring from recurrent infection. Voiding cystourethrogram (*B*) revealed high-grade reflux in this patient.



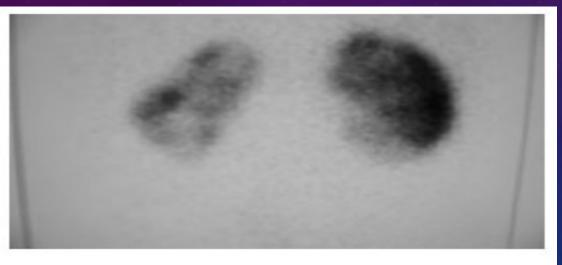


FIGURE 3D. Major right kidney parenchymal damage on the anterior view of a Tc99 DMSA scan.

RENAL ABSCESSES

A severe infection that leads to liquefaction of renal tissue; this area is subsequently sequestered, forming an abscess.

They can rupture out into the perinephric space, forming **perinephric abscesses**. When the abscesses extend beyond the Gerota's fascia, **paranephric abscesses** develop

Most renal/perinephric abscesses result from hematogenous spread of staphylococci, in particular from infected skin lesions.

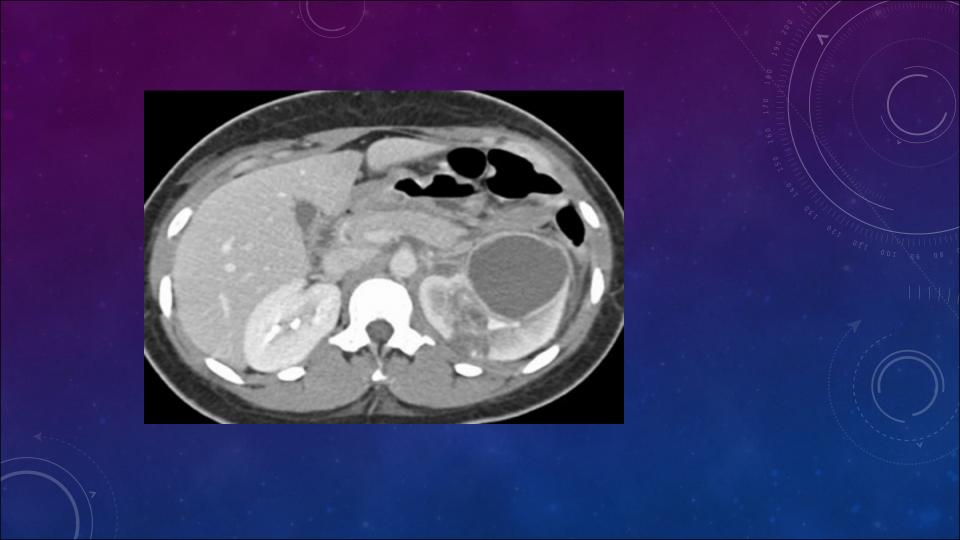
Most commonly in **diabetics**, hemodialysis and IV abusers.

c/p :like pyelonephritis , >2 wks and palpable abdominal mass

naging: Renal abscesses can be accurately detected using ultrasonography or CT scans



Figure 14–4. Renal abscess. CT scan with intravenous contrast demonstrates a large perinephric fluid collection with rim enhancement (*white arrow*). The parenchyma defect in the right kidney is suggestive of pyelonephritis.





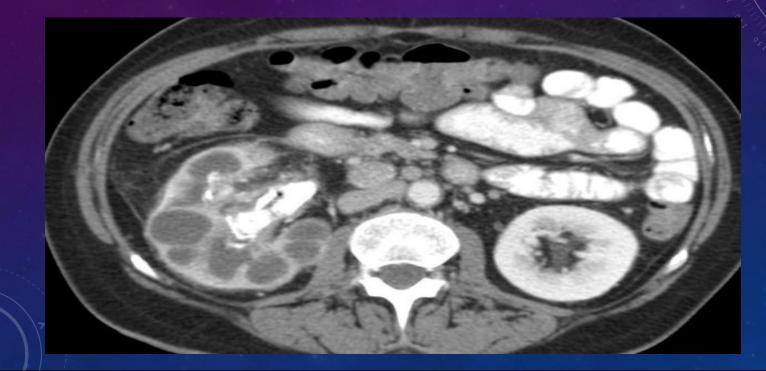
XANTHOGRANULOMATOUS PYELONEPHRITIS

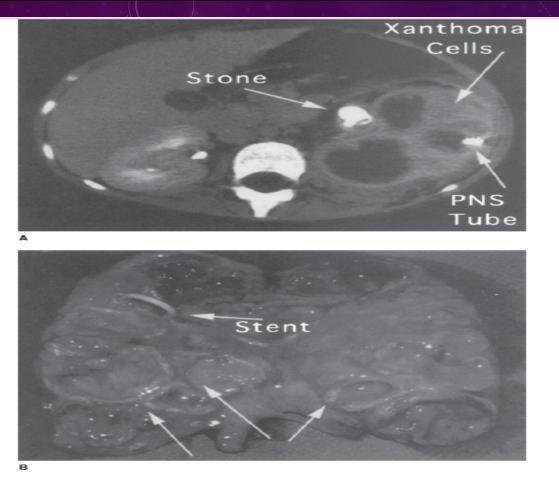
A form of chronic bacterial infection of the kidney. The affected kidney is almost always hydronephrotic and obstructed, Characteristically, foamy lipid-laden histiocytes (xanthoma cells)

c/p : like pyelonephritis , **urolithiasis** in 35% and a **flank mass** can often be palpated ,it **primarily occurs unilaterally**, azotemia or renal failure is not often seen.

Imaging : CT scan is the most reliable method in imaging patients suspected of having XGP. It usually demonstrates a large heterogeneous mass.

 Management : In some cases, XGP is misdiagnosed as a renal tumor. A <u>nephrectomy is performed and a</u> <u>diagnosis is made pathologically</u>. In those in whom a diagnosis of XGP is suspected, kidney-sparing surgery such as a partial nephrectomy is indicated.





▲ Figure 14–5. Xanthogranulomatous pyelonephritis. A: CT scan demonstrates a large heterogeneous left kidney, with dilated calyces and areas filled with lipid-laden macrophages. Xanthogranulomatous pyelonephritis is often associated with the presence of renal stones. B: Pathology specimen better demonstrated the pockets of intraparenchymal abscesses and deposition of macrophages (arrows). PNS, percutaneous nephrostomy.

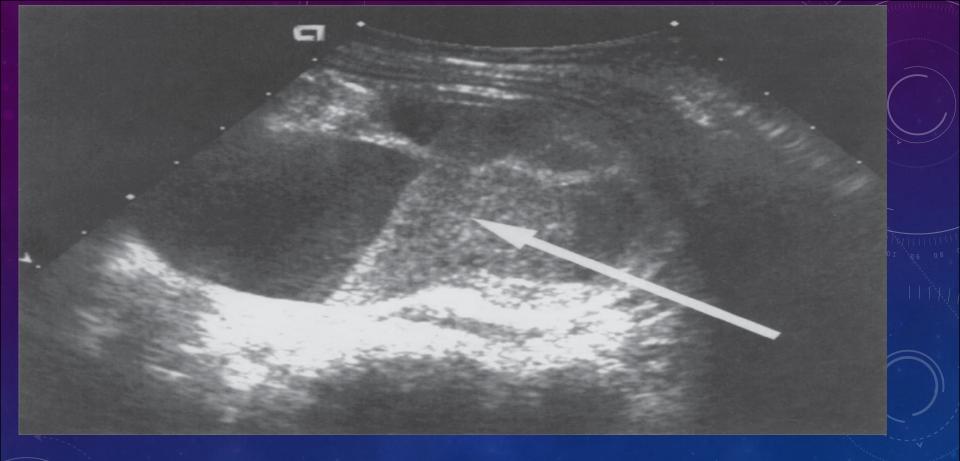
PYONEPHROSIS

Bacterial infection of a hydronephrotic, obstructed kidney, which leads to suppurative destruction of the renal parenchyma and potential loss of renal function.

/p: very ill, with high fever, chills, and flank pain. Lower tract symptoms are not usually present.

maging: renal ultrasonography can be performed to rapidly diagnose pyonephrosis.

Management : immediate institution of antibiotic therapy and drainage of the infected collecting system.



Pyonephrosis. Ultrasonography demonstrates fluid–debris level (*white arrow*) within the dilated renal pelvis.

BLADDER INFECTIONS

ACUTE CYSTITIS

- Urinary infection of the lower urinary tract, principally the bladder.
- More commonly affects women (short urethra) than men.
- The primary mode of infection is ascending from the periurethral/vaginal and fecal flora
- c/p: irritative voiding symptoms such as dysuria, frequency, and urgency. Low back and suprapubic pain, hematuria, and cloudy/foul-smelling urine are also common symptoms. Fever and systemic symptoms are rare.
- . E. coli causes most of the acute cystitis by urinalysis and culture.

- Imaging :In uncomplicated infection of the bladder, radiologic evaluation is often not necessary.
- Management for acute cystitis consists of a short course of oral antibiotics.
 TMP–SMX, nitrofurantoin, and fluoroquinolones have excellent activity against most pathogens that cause cystitis.
 In adults and children, the duration of treatment is usually limited to 3–5 days.

RECURRENT CYSTITIS/UTI

- Is caused either by bacterial persistence or reinfection with another organism.
- Identification of the cause of the recurrent infection is important, because the management of bacterial persistence and reinfection are distinct.
- Persistance of infection >>>removal of source is curative
- Reinfection >>preventative therapy

- Imaging :Ultrasonography can be obtained to provide a screening evaluation of the genitourinary tract. More
 detailed assessment with intravenous pyelogram, cystoscopy, and CT scans may occasionally be necessary.
- Management :depends on its cause. Surgical removal of the infected source (such as urinary calculi) is needed to treat bacterial persistence. Similarly, fistulas need to be repaired surgically to prevent bacterial reinfection.
- In most cases of bacterial reinfection, medical management with prophylactic antibiotics is indicated. Lowdose continuous prophylactic antibiotic has been shown to reduce the recurrences of UTI by 95%

Table 14–7. Prophylactic antibiotics regimen.

- Nitrofurantoin, 50 or 100 mg daily
- Nitrofurantoin macrocrystals, 100 mg daily
- TMP-SMX, 40/200 mg daily
- Cephalexin, 250 mg daily
- Ciprofloxacin, 250 mg daily
- Trimethoprim, 100 mg daily

URETHRITIS

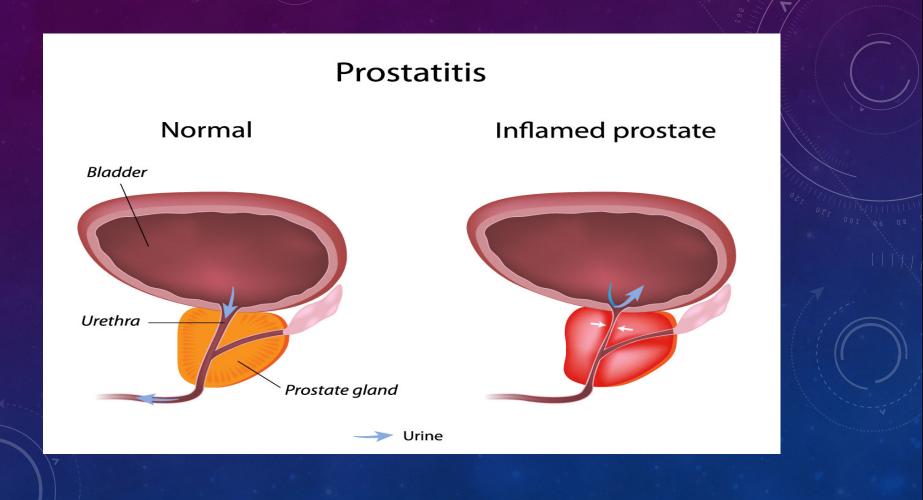
- Infection/inflammation of the urethra can be categorized into those types caused by Neisseria gonorrhoeae and by other organisms (Chlamydia trachomatis, Trichomonas vaginalis, and herpes simplex virus) most of them are STD.
- c/p: urethral discharge and dysuria. The amount of discharge may vary significantly, from profuse to scant amounts. Obstructive voiding symptoms are primarily present in patients with recurrent infection, in whom urethral strictures subsequently develop
- Imaging: Most patients with uncomplicated urethritis do not require any radiologic imaging unless they have recurrent infection and obstructive voiding symptoms.
- Management: Pathogen-directed antibiotic therapy is required.

PROSTATE INFECTION

ACUTE BACTERIAL PROSTATITIS

- Inflammation of the prostate associated with a UTI.
- It is thought that infection results from ascending urethral infection or reflux of infected urine from the bladder into the prostatic ducts.
- It frequently affects adult men. It is the most common urologic diagnosis in men younger than 50 years
- **c/p**: **abrupt onset of constitutional** (fever, chills, malaise, arthralgia, myalgia, lower back/rectal/perineal pain) and **urinary symptoms** (frequency, urgency, dysuria).

- They may also present with **urinary retention** due to swelling of the prostate.
- Digital rectal examination reveals tender, enlarged glands that are irregular .
- Prostate-specific antigen levels are often elevated.
- The diagnosis of prostatitis is made with microscopic examination and culture of the prostatic expressate and culture of urine obtained, E. coll is the most common causative organism in patients with acute prostatitis
- Imaging: is rarely indicated in patients with acute prostatitis.
- Management : with antibiotics is essential in the management of acute prostatitis. Empiric therapy is indicated , Trimethoprim and fluoroquinolones have high drug penetration into prostatic tissue and are recommended for 4–6 weeks.



CHRONIC BACTERIAL PROSTATITIS

- More insidious onset, characterized by relapsing, recurrent UTI caused by the persistence of pathogen in the prostatic fluid despite antibiotic therapy.
- c/p: dysuria, urgency, frequency, nocturia, and low back/perineal pain. History of recurrent or relapsing UTI, urethritis.

Others are asymptomatic .

- Digital rectal examination of the prostate is often normal; Prostate-specific antigen levels may be elevated.
- Diagnosis is made after identification of bacteria from prostate expressate or urine specimen after prostatic massage

• Imaging: is rarely indicated in patients with chronic prostatitis.

Transrectal ultrasonography is only indicated if a prostatic abscess is suspected.

• Management : Antibiotic therapy is similar to that for acute bacterial prostatitis

The duration of antibiotic therapy may be 3–4 months. Using **fluoroquinolones**, some patients may respond after 4–6 weeks of treatment, **alpha-blocker** and **anti-inflammatory** agents to antibiotic therapy has been shown to reduce symptom recurrences

Prostatic abscess. Transrectal ultrasonography demonstrates hypoechoic lesions (*black and whitearrows*) in the prostate consistent with abscesses

SPECIAL CIRCUMSTANCES

UTI RELATED TO PREGNANCY

- Changes in pregnancy:
- **1. Renal length increases** approximately by 1 cm during normal pregnancy as a result of increased vascular and interstitial volume
- 2. The glomerular filtration rate increases by 30–50%, most likely secondary to the increase in cardiac output
- **3.** Significant ureteral dilation with resultant urinary stasis during the second and third trimesters of gestation
- 4. The **enlarged uterus displaces the bladder superiorly and anteriorly**. The bladder becomes hyperemic, and its **capacity is increased**.

- Because of these changes in the urinary tract during normal pregnancy, bacteriuria is a clinically relevant finding in pregnant women. It is estimated that the prevalence of bacteriuria is 4–6%.
- 30% of those who have bacteriuria on screening evaluation later have pyelonephritis, compared with only 1–2% in those who do not have bacteriuria.
- In 10–20%, recurrent episodes of pyelonephritis develop before delivery.
- When left untreated, pyelonephritis during pregnancy is associated with a high rate of infant prematurity and its associated perinatal mortality.

- It is recommended that women be screened for bacteriuria during pregnancy to prevent the development of pyelonephritis at the first prenatal visit and at 16 weeks of gestation. (Increased risk of prematurity)
- For asymptomatic individuals, <u>significant bacteriuria</u> is defined as two voided urine cultures with >10^5 CFU/mL of a single organism. For symptomatic pregnant women, >10^3CFU/mL is considered to be significant.

Table 14–9. Antibiotics a	nd their effects	on pregnancy.
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Drugs	Side effects on the developing fetus
Sulfonamides	Kernicterus
Trimethoprim	Interferes with neural tube development
Tetracyclines	Dysplasia and discoloration of teeth and bones
Nitrofurantoin	Hemolysis and G6PD deficiency
Aminoglycosides	Nerve damage
Fluoroquinolones	Interferes with cartilage formation
Penicillins	Safe
Cephalosporins	Safe
Beta-lactamase inhibitors	Safe
Monobactams	Safe
Fosfomycin trometamol	Safe

 HOWEVER, AMOXICILLIN IS NOT RECOMMENDED BECAUSE OF THE RATE OF BACTERIAL RESISTANCE .
 A 3-DAY COURSE IS SUGGESTED.

UTIS IN PATIENTS WITH DM

- UTIs are more common and tend to have more complicated course in patients with diabetes mellitus.
- There is a two- to five fold increase in the incidence of acute pyelonephritis in diabetic patients.
- <u>Complications</u> such as emphysematous pyelonephritis and renal and perirenal abscesses are more frequently seen in the diabetic patients
- Asymptomatic bacteriuria occurs in diabetic women more commonly than in nondiabetics.

THE RISK FOR UTI CORRELATED WITH

- The degree of glycemia as measured by HBA1c.
- Autonomic neuropathy resulting in <u>dysfunctional voiding and urinary retention</u> can prevent bacterial clearance through micturition and thereby promoting bacterial growth.
- Increased adherence of the microorganisms to the uroepithelial cells
- No relationship between specific uropathogen prevalence and diabetes status have been found.
- Treatment with TMP–SMX should be avoided if possible, because it can potentiate the hypoglycemic effects of the oral hypoglycemic drugs.
- Fluoroquinolones are safe and effective

THANK YOU

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