

Urinary Tract Infections

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INTRODUCTION

Urinary tract infections are a group of common diseases that occur predominantly by the ascension of normal enteric flora through the urethra into the bladder. These infections more frequently affect women due to anatomic differences including a shorter urethra.

Diagnosis is made by identifying related clinical symptoms in combination with an abnormal urinalysis and growth on urine culture. Antibiotics are often effective therapy, although antibiotic resistance is increasing.

Bacterial virulence

How well an organism adheres to urothelium determines its virulence.

The presence of flagella (for motility), aerobactin (used to acquire iron), hemolysin (to form pores), and, above all, the presence of fimbriae (adhesins that attach organisms to the perineum and urothelium) on the bacterial cell surface make *E. coli* such a common pathogen.

Innate host defence

Innate host defense

Innate host defense prevents UTIs in the following ways:

1. **Neutrophil.** Bacterial adhesins activate receptors, e.g. Toll receptor 4, on the mucosal surface, resulting in IL-8 production and expression of its receptor, CXCR1, on neutrophil surfaces. Activation of neutrophils is essential for bacterial killing.
2. **Urine osmolality and pH.** Urinary osmolality >800 mOsm/kg and low or high pH reduce bacterial survival.
3. **Complement.** Complement activation with mucosal IgA production by uroepithelium (acquired immunity) plays a major role in defense against UTI.

4. Commensal organisms. Eradication of commensal organisms such as lactobacilli, corynebacteria, streptococci, and Bacteroides by spermicidal jelly or antibiotics results in the overgrowth of E. coli.

5. Urine flow. Good urine flow and normal micturition wash out bacteria. Urine stasis promotes UTI.

6. Uroepithelium. Mannosylated Tamm-Horsfall proteins (THPs), present in the mucus and glycocalyx covering uroepithelium, have antibacterial properties and interfere with bacterial binding to uroepithelium. Cranberry juice and blueberry juice contain a large-molecular-weight factor (pro-anthocyanidins) that prevents the binding of E. coli to the uroepithelium.





DIAGNOSTIC TESTING FOR URINARY TRACT INFECTIONS

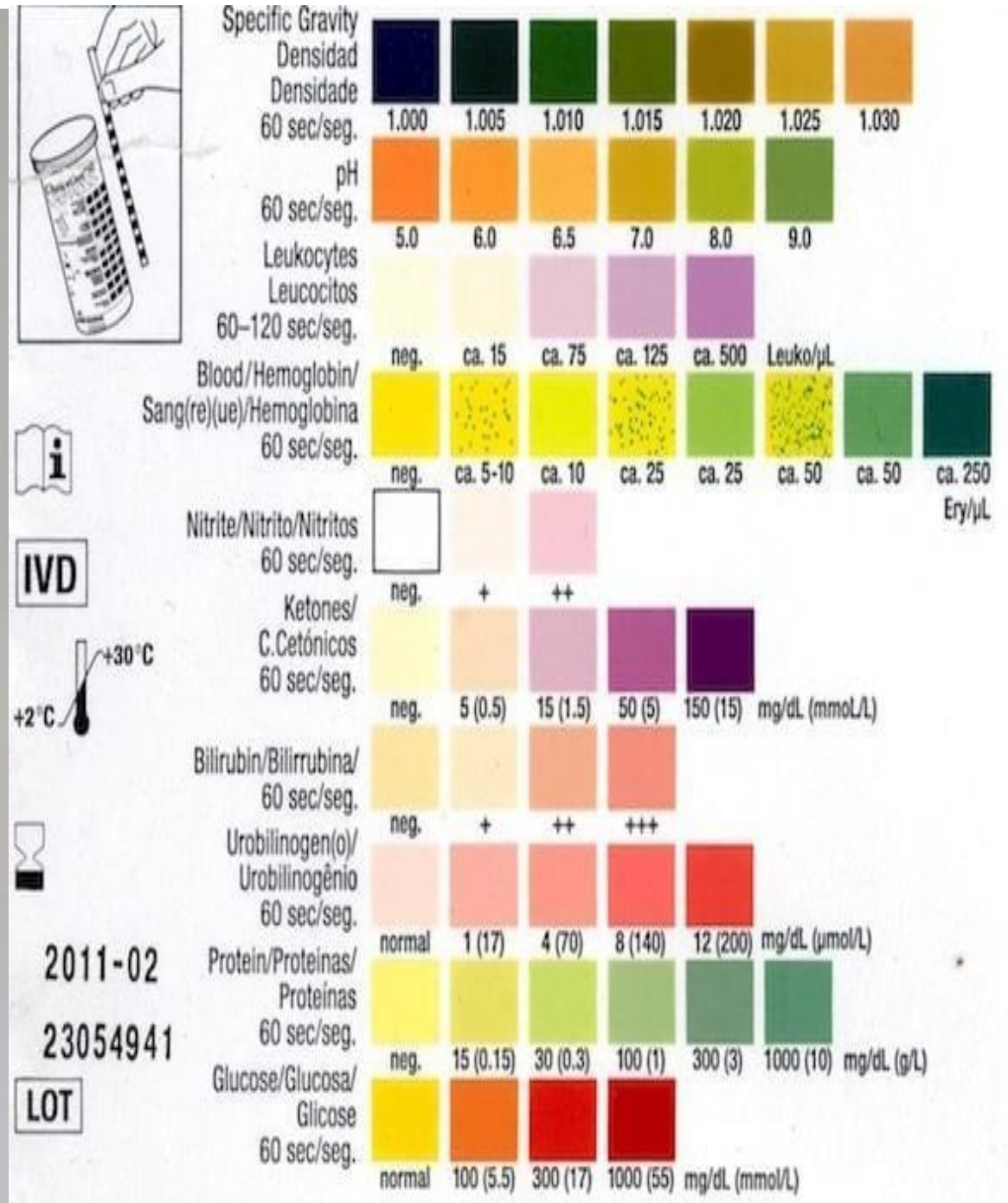
Urine microscopy is the use of a microscope to look at urine. In patients with urinary tract infections, one can often find pyuria (elevated white blood cells [WBCs] in urine) and hematuria (red blood cells in urine), and sometimes bacteria can be seen. The presence of WBC casts indicates pyelonephritis rather than cystitis. A urine sample that has abundant squamous epithelial cells suggests that it is contaminated and the results of the culture are not reliable.

Urine dipsticks use different chemicals reagents on a strip that is dipped in urine to diagnose urinary tract diseases.

Certain dipstick test results are suggestive of infection, namely positive leukocyte esterase, positive nitrite, and positive hemoglobin. **The positive nitrite occurs from the conversion of nitrate to nitrite by Enterobacteriaceae.**

Urine culture allows identification of the organism causing infection. Urine in the bladder is normally sterile.

In samples obtained from a **midstream void**, $\geq 1 \times 10^5$ CFU/mL is consistent with infection. In samples collected via **catheterization**, $\geq 1 \times 10^2$ CFU/mL is consistent with infection. Either a voided midstream urine specimen or a specimen obtained by bladder catheterization can be used for urine culture.



The criteria for the diagnosis of UTI, particularly in symptomatic women,



Box 20.23 Criteria for the diagnosis of bacteriuria

Symptomatic young women

- $\geq 10^2$ coliform organisms/mL urine plus pyuria (>10 white blood cells/ mm^3)
or
- $\geq 10^5$ any pathogenic organism/mL urine
or
- Any growth of pathogenic organisms in urine by suprapubic aspiration

Symptomatic men

- $\geq 10^3$ pathogenic organisms/mL urine

Asymptomatic patients

- $\geq 10^5$ pathogenic organisms/mL urine on two occasions

Most Gram-negative organisms reduce nitrates to nitrites and produce a red color in the reagent square.

False-negative results are common. Dipsticks that detect significant pyuria depend on the release of an esterase from leucocytes.

Dipstick tests positive for **both nitrite and leucocyte esterase** are highly predictive of acute infection (sensitivity of 75% and specificity of 82%).



Box 20.22 Organisms causing urinary tract infection in domiciliary practice

Organism	Approximate frequency (%)
<i>Escherichia coli</i> and other 'coliforms'	70
<i>Proteus</i> spp.	12
<i>Staphylococcus saprophyticus</i> or <i>epidermidis</i> ^a	10
<i>Enterococcus faecalis</i> ^b	6
<i>Pseudomonas</i> spp.	5
<i>Klebsiella</i> spp.	4
^a More common in young women (20–30%). ^b More common in hospital practice.	

CYSTITIS

Definition

Cystitis is an infection of the bladder. The term “cysto” refers to the bladder, and “itis” refers to inflammation. Uncomplicated cystitis is defined as cystitis in otherwise healthy women, whereas complicated cystitis is defined as cystitis in all other groups such as men, pregnant women, diabetics, those with anatomic and neurologic problems, and those with recurrent urinary tract infections.

Pathophysiology

Bacteria (rarely fungi) reach the bladder via ascension through the urethra. This is much more common in women due to the short urethra and close approximation of the urethra to the vagina and anus.

Preceding infection, the vagina, which is normally colonized by *Lactobacillus* species, will become colonized by enteric organisms such as *Escherichia coli* instead. *Escherichia coli* are able to adhere to the urethral and bladder mucosa via pili. Once bacteria enter the bladder, they are able to reproduce and cause an inflammatory response, resulting in the symptoms of infection.

Medical conditions that cause abnormal emptying of bladder increase risk for urinary tract infections.

These include anatomic abnormalities such as **cystoceles, neurologic disorders such as spinal cord injuries and multiple sclerosis, and the presence of foreign bodies such as indwelling Foley catheters.**

In infants less than 3 months of age, uncircumcised boys are at higher risk for urinary tract infections than girls. However, after infancy, girls are at higher risk for infection than all boys.

Clinical Manifestations

The most common clinical manifestations of cystitis include dysuria (pain with urination); frequent, low-volume urination; suprapubic tenderness; and gross hematuria.

Most patients with cystitis do not have a fever or other systemic symptoms of infection, and when they are present, an upper urinary tract infection (pyelonephritis) should be considered.

Pathogens

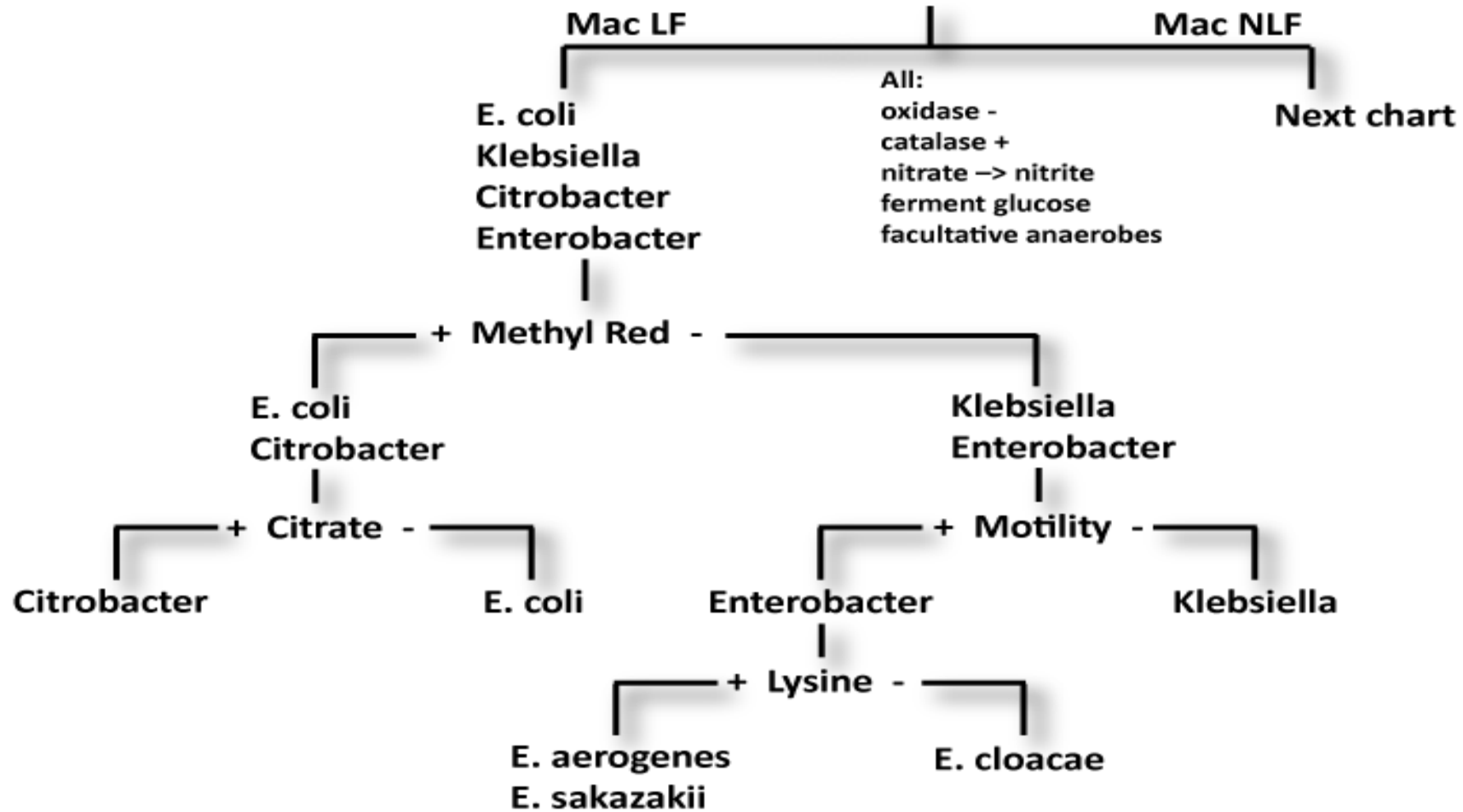
Escherichia coli is by far the most common cause of urinary tract infections, especially cystitis . Other enteric gram-negative rods such as *Klebsiella* species and *Proteus* species are regular culprits.

Pseudomonas aeruginosa can cause urinary tract infection, but this is most common in health care–associated infections, patients with anatomic/ neurologic abnormalities afflicting their urinary tract, or heavily antibiotic-experienced patients.

Gram-positive pathogens include *Enterococcus* species and *Staphylococcus saprophyticus*. *Staphylococcus saprophyticus* is common in young women. *Candida* species can cause infection in patients who have extensive prior antibiotic use and indwelling Foley catheters.

Rarely, viruses such as adenovirus, BK virus, and cytomegalovirus can cause hemorrhagic cystitis. These viruses almost exclusively cause cystitis in immunocompromised hosts.

Enterobacteriaceae
Gram negative G(-) bacilli



Diagnosis

The diagnosis of cystitis requires identifying a combination of pyuria (by seeing WBCs on microscopy or positive leukocyte esterase on urine dipstick) often accompanied by a positive nitrite test and evidence of red blood cells in the urine, plus positive urine cultures plus clinical symptoms consistent with infection.

Treatment

Treatment of cystitis requires antibiotic therapy. Empiric therapy is directed against *E. coli* in cases of uncomplicated cystitis and is accomplished with either trimethoprim-sulfamethoxazole or nitrofurantoin.

Empiric therapy for complicated cystitis is usually with fluoroquinolone (ciprofloxacin or levofloxacin). Symptomatic relief of the dysuria can be accomplished using phenazopyridine.

PYELONEPHRITIS

Definition

Pyelonephritis is an infection of the kidney(s). “Pyelo” refers to the renal pelvis, and “nephritis” means inflammation of the kidney. Uncomplicated pyelonephritis is defined as pyelonephritis in otherwise healthy women, whereas complicated pyelonephritis is pyelonephritis in all other patients.

Pathophysiology

Pyelonephritis may occur either by **ascension of bacteria from the urethra** to the bladder and then to the kidney(s) or, less commonly, through hematogenous spread from other sites of infection such **as endocarditis**. **Kidney stones** predispose to pyelonephritis . **Urinary tract infections** in children can be associated with anatomic abnormalities, and additional workup for diseases such as **vesicoureteral reflex** should be considered.

Reflux nephropathy

This was called chronic pyelonephritis or atrophic pyelonephritis, resulting from a combination of:

- vesicoureteral reflux
- infection acquired in infancy or early childhood.

Normally, the vesicoureteral junction acts as a one-way valve, with urine entering the bladder from above; the ureter is shut off during bladder contraction, thus preventing the reflux of urine. In some infants and children - possibly even in utero - this valve mechanism is incompetent, bladder voiding being associated with variable reflux of a jet of urine up the ureter.

A secondary consequence is incomplete bladder emptying, as refluxed urine returns to the bladder after voiding. This latter event predisposes to infection, and the reflux of infected urine leads to kidney damage.

Typically, there is papillary damage, tubulointerstitial nephritis and cortical scarring in areas adjacent to 'clubbed calyces'.

Normal

Smooth renal
outline

Cupped calyces

No loss of cortex

Competent
vesicoureteric valve

Reflux nephropathy

Irregular
renal outline

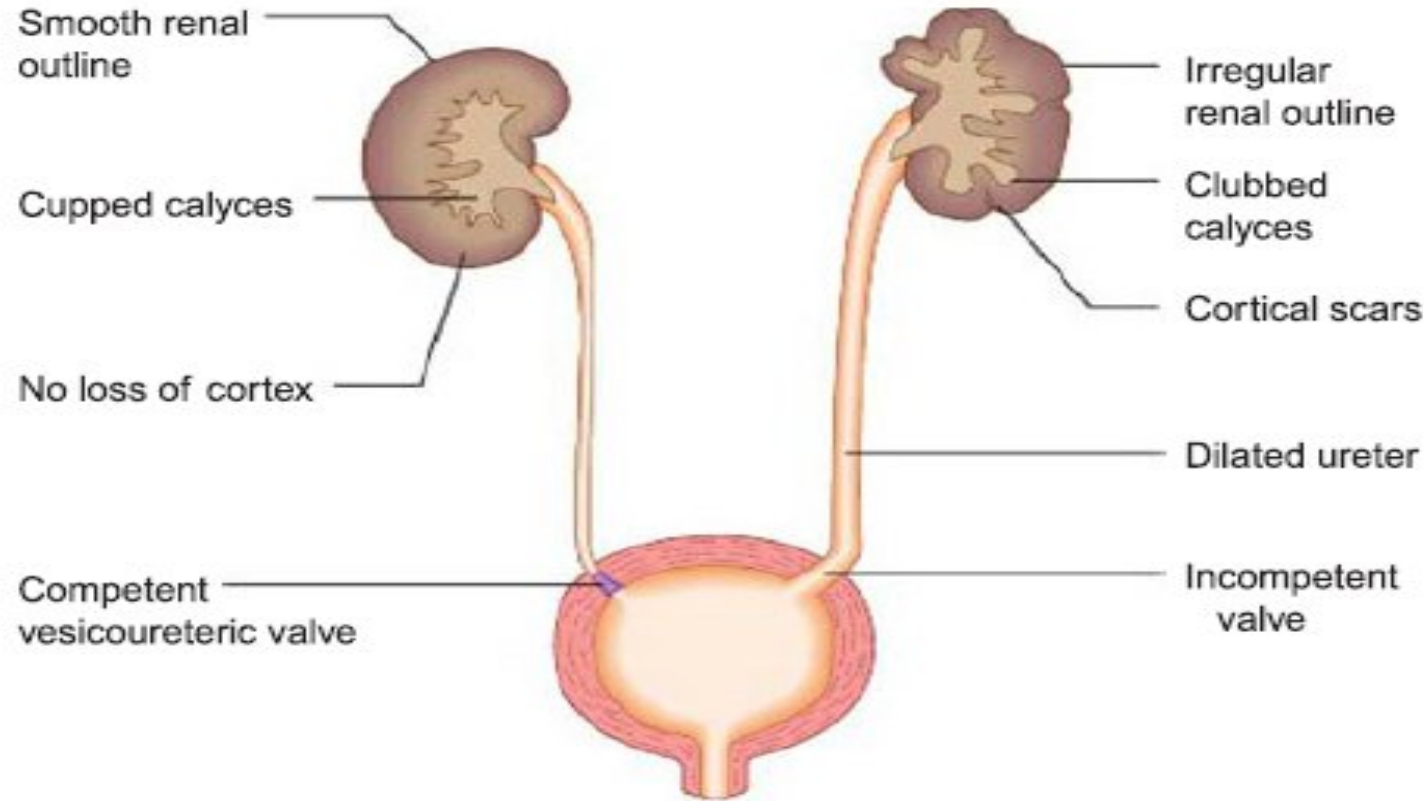
Clubbed
calyces

Cortical scars

Dilated ureter

Incompetent
valve

Figure 20.39 Findings in patients with reflux nephropathy compared with normal individuals.



Clinical Manifestations

Patients with pyelonephritis typically present with fever, flank pain, nausea, and vomiting. They may or may not have signs and symptoms of lower tract infection (dysuria, frequency, hematuria, suprapubic tenderness).

Pathogens

Escherichia coli is the most common pathogen causing pyelonephritis. Other enteric gram-negative rods such as Klebsiella and Proteus species are also involved. *Pseudomonas aeruginosa* can cause pyelonephritis, but this typically occurs in health care–associated infections, patients with anatomic/neurologic abnormalities afflicting their urinary tract, or heavily antibiotic-experienced patients.

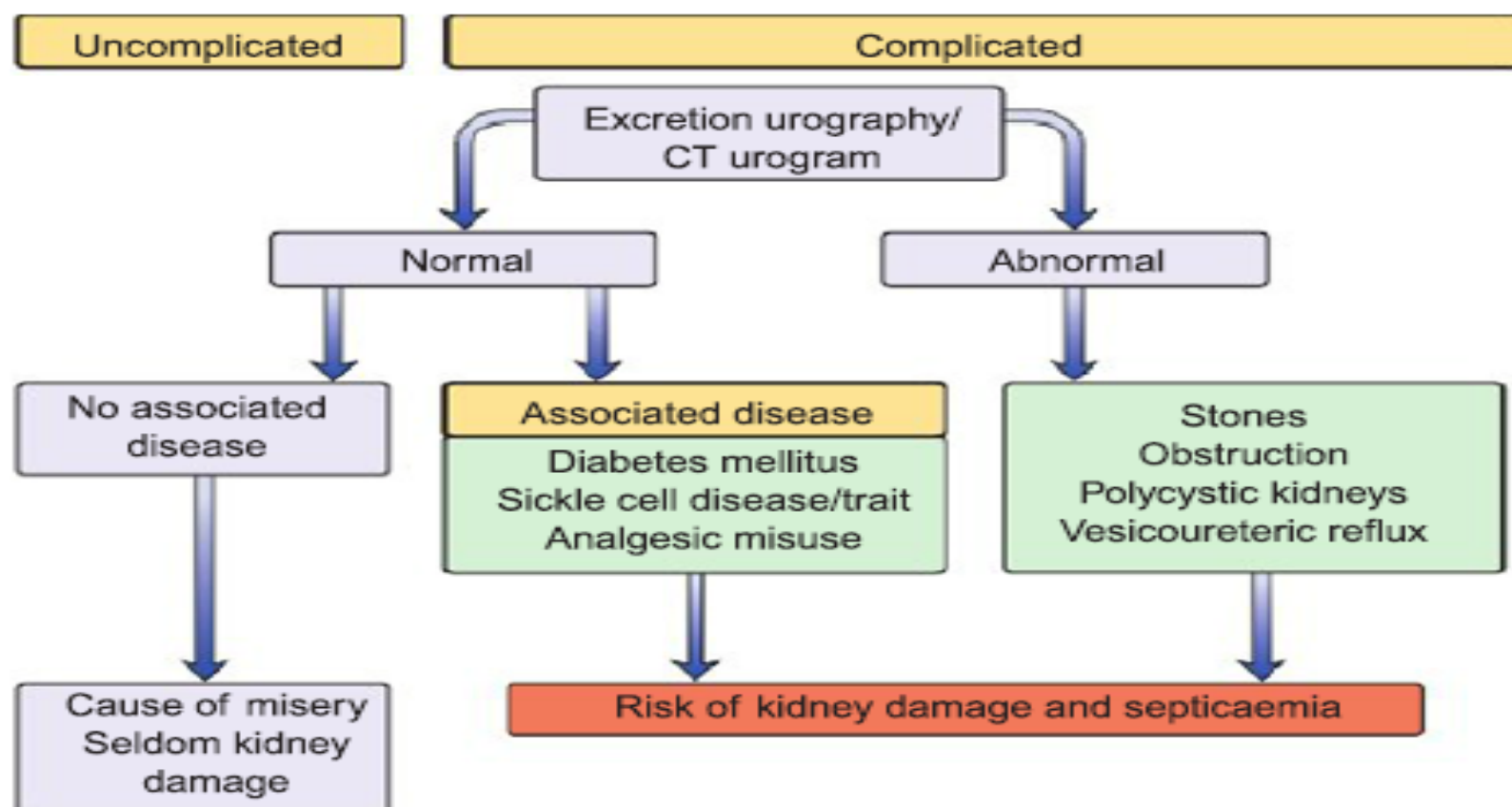


Figure 20.37 Complicated versus uncomplicated urinary tract infection.



FIGURE 78-1 Pyelonephritis. Note enlarged right kidney (left side of image) caused by a stone at the ureteropelvic junction. (Reproduced with permission from McKean SC et al. *Principles and Practice of Hospital Medicine*. New York: McGraw-Hill, 2012. Copyright © 2012 by The McGraw-Hill Companies, Inc.)

Patients with recurrent *Proteus* pyelonephritis should be evaluated for struvite stones.

Infection of the kidney following the hematogenous spread of infection can occur with essentially any organism but is seen most commonly with *Staphylococcus aureus*. Hematogenous spread also occurs with *Mycobacterium tuberculosis* and has been seen in disseminated fungal infections as well.

Diagnosis

Urine test findings are similar to those seen in cystitis, but urinary WBC casts can be seen. Blood WBC counts are frequently elevated, and occasionally blood cultures can be positive. Ultrasound and computed tomography scans can reveal inflammation and can occasionally reveal obstruction or perinephric abscess. Radiographic imaging is not routinely recommended in patients who respond quickly to antibiotics and in whom there is no clinical concern for associated nephrolithiasis or obstruction. Patients with renal tuberculosis may have pyuria in the absence of positive cultures (sterile pyuria) because *M. tuberculosis* does not grow in routine culture media.

Treatment

Antibiotics that are able to obtain high concentrations in the renal parenchyma and have activity against common pathogens are required to treat pyelonephritis. Empiric regimens for community-onset infection include fluoroquinolone (ciprofloxacin or levofloxacin) or a third-generation cephalosporin such as ceftriaxone.

Patients with heavy exposure to prior antibiotics, anatomic abnormalities, or exposure to the health care setting should be treated with antibiotics with reliable activity against *Pseudomonas*, such as cefepime, piperacillin, or meropenem.

Prevention

Patients who have bladder dysfunction that predisposes them to pyelonephritis may require frequent catheterization to allow proper urinary tract drainage. Pregnant women with asymptomatic bacteriuria may benefit from antibiotic therapy to prevent pyelonephritis.

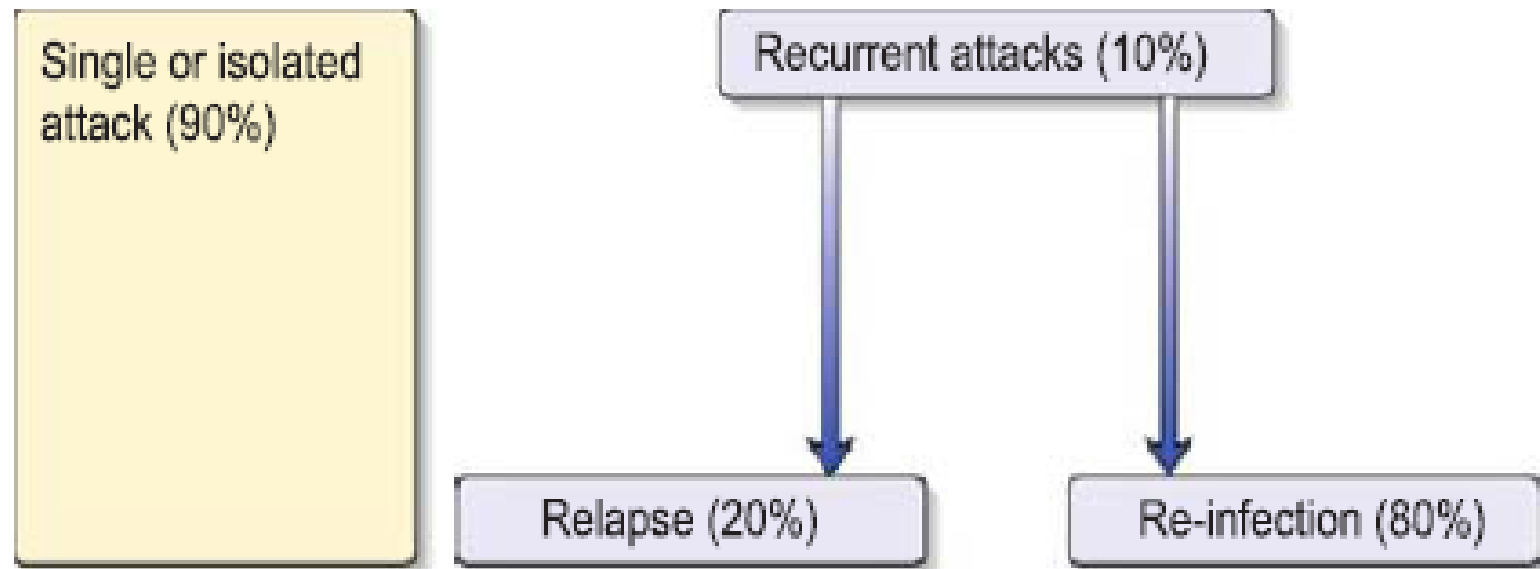


Figure 20.35 The natural history of urinary tract infection.

Re-infection versus relapsing infection may be distinguished as follows:

Relapse is diagnosed by the recurrence of bacteriuria with the same organism within 7 days of completion of antibacterial treatment. Treatment failure may suggest associated stones, scarred kidneys, polycystic disease, or bacterial prostatitis.

Re-infection is when bacteriuria is absent after treatment for at least 14 days, usually longer, followed by a recurrence of infection with the same or different organisms. This is not due to failure to eradicate infection but is the result of the re-invasion of a susceptible tract with new organisms. Approximately 80% of recurrent infections are due to re-infection.

Recurrent UTI

Relapse :- •

- Recurrence of bacteriuria with the same organism within 7 days •
of completion of antibacterial treatment
- Implies failure to eradicate infection, •
- Usually in conditions such as stones, scarred kidneys, PKD •
or bacterial prostatitis.

Reinfection;- •

- When bacteriuria is absent after treatment for at least 14 days, •
- Followed by recurrence of infection with the same or different •
organisms.
- the result of reinvasion of a susceptible tract with new •
organisms.

Pseudomonas

- Pip-tazo (first choice)
- Cefepime (first choice)
- Fluoroquinolones (cipro and levo, not moxi) -- only oral option
- Carbapenems (not ertapenem)
- Ticarcillin-clavulanate [no longer available in US]
- Ceftazidime (ceftazidime-avibactam generally has same pseudo coverage)
- Ceftolozane-tazobactam (MDR infection)
- Aztreonam
- Aminoglycosides: amikacin, tobramycin
- Colistin/Polymixin B
- [azithromycin in CF prevents proliferation of mucoid strain]

ASYMPTOMATIC BACTERIURIA

Definition

Asymptomatic bacteriuria is when bacteria colonize the urinary bladder in the absence of signs or symptoms of upper or lower urinary tract infection. It is defined as the presence of $\geq 1 \times 10^5$ CFU/mL of a single bacterial species on two successive urine cultures in a patient without urinary tract symptoms.

Pathophysiology

Asymptomatic bacteriuria is common in many populations including persons with diabetes, patients with anatomic and neurologic abnormalities of the urinary tract, patients with indwelling Foley catheters, and elderly patients. The bacteria reach the bladder via ascension through the urethra, not from hematogenous dissemination.

Treatment

Treatment of asymptomatic bacteriuria is indicated in select populations who have been identified to be at risk for subsequent severe infection from presence of bacteriuria. These high-risk groups include (1) pregnant women, (2) adults scheduled to undergo urinary tract procedures that could cause mucosal bleeding and translocation of bacteria into the blood, and (3) neutropenic patients.

PROSTATITIS

Definition

Prostatitis is inflammation of the prostate, most often caused by bacterial infection.

Pathophysiology

Infection most frequently occurs via the urethra and then into the prostatic ducts. However, hematogenous seeding of the prostate can occur as well. Micro abscesses may develop within the prostate.

Clinical Manifestations

Acute prostatitis may present with acute onset of fever, dysuria, urinary frequency, and severe pain with palpation of the prostate. Patients may be very ill and can present with severe sepsis. In contrast, chronic prostatitis presents with more subacute onset of dysuria, frequency, urinary hesitancy, and pelvic discomfort

Pathogens

In younger patients, *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are the most common causes of prostatitis.

However, in older patients, enteric bacteria, such as *E. coli*, are the predominant pathogens. When hematologic seeding occurs, *S. aureus* is a common cause.

Treatment

Antimicrobial therapy with excellent penetration to the prostatic tissues is recommended for the treatment of prostatitis.

Fluoroquinolones (e.g., ciprofloxacin or levofloxacin) and trimethoprim-sulfamethoxazole both achieve high Levels in the prostate and are good options. Antibiotic susceptibility testing should be used to guide the treatment of infecting pathogens.