Urinary tract infections

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UTIs are considered to be one of the most common bacterial infections. Diagnosis depends on the symptoms, urinalysis, and urine culture.

- UTIs occur more frequently in women than in men. Half of all women will have a UTI during their lifetime.
- Others at risk for UTI include the elderly, pregnant women, patients who have had renal transplantation, patients with spinal cord injuries, patients with catheters, and patients with genitourinary (GU) tract abnormalities.
- It is practical to separate UTIs into upper and lower UTIs.
  - Upper UTIs involve the renal parenchyma (pyelonephritis) or the ureters (ureteritis).
  - Lower UTIs involve the bladder (cystitis), the urethra (urethritis) and, in males, the prostate (prostatitis).

<table>
<thead>
<tr>
<th>Lower UTI (Cystitis)</th>
<th>Upper UTI (Pyelonephritis)</th>
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<tbody>
<tr>
<td>Predominantly a benign illness</td>
<td>Often a serious illness</td>
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<tr>
<td>No systemic signs of infection</td>
<td>Systemic signs of infection such as fever, nausea and vomiting</td>
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<td>Physical exam generally normal, may have suprapubic tenderness</td>
<td>Flank pain (up to 25% may have bilateral pyelonephritis)</td>
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There are two clinical schemas for classifying UTIs:
1. single episode versus recurrent
2. complicated versus uncomplicated.

A single-episode UTI occurs once and does not recur. Patients with chronic or recurrent UTIs have repeated episodes of bacteriuria with or without clinical manifestations.

These episodes are divided into relapse and reinfection. The former involves the same organism and implies a focus of infection in the renal or prostatic
parenchyma; the latter implies a different organism and usually is limited to the bladder.

**ETIOLOGIC AGENTS**

**Community-Acquired**
- *Escherichia coli* is by far the most frequent cause of uncomplicated community-acquired UTIs.
- *E. coli*, designated uropathogenic *E. coli* (UPEC), that causes UTIs is sufficiently different from other types of *E. coli*.
- Other bacteria frequently isolated from patients with UTIs are *Klebsiella* spp., other *Enterobacteriaceae*, *Staphylococcus saprophyticus*, and *Enterococci*.
- In more complicated UTIs, particularly in recurrent infections, the relative frequency of infection caused by *Proteus*, *Pseudomonas*, *Klebsiella*, and *Enterobacter* spp. increases.

**Hospital-Acquired**
- The hospital environment plays an important role in determining the organisms involved in UTIs. Hospitalized patients are most likely to be infected by *E. coli*, *Klebsiella* spp., *Proteus* spp., *Staphylococci*, other *Enterobacteriaceae*, *Pseudomonas aeruginosa*, *Enterococci*, and *Candida* spp.
- The introduction of a foreign body into the urinary tract (e.g., catheter), carries a substantial risk of infection, particularly if obstruction is present.
- 35% of all hospital-acquired infections are urinary tract infections, 80% of those infections are associated with the use of an indwelling catheter.
Miscellaneous

- Other less frequently isolated agents are other gram negative bacilli, such as *Acinetobacter* and *Alcaligenes* spp., other *Pseudomonas* spp., *Citrobacter* spp., *Gardnerella vaginalis*, *Aerococcus urinae*, and beta-hemolytic Streptococci.

- Bacteria such as Mycobacteria, *Chlamydia trachomatis*, *Ureaplasma urealyticum*, *Campylobacter* spp., *Haemophilus influenzae*, *Leptospira*, and certain *Corynebacterium* spp. (e.g., *C. renale*) are rarely recovered from urine.

- Because renal transplant recipients are immunosuppressed, these patients not only suffer from common uropathogens but are also susceptible to opportunistic infections with unusual pathogens.

- In general, viruses and parasites are not usually considered urinary tract pathogens. *Trichomonas vaginalis* may occasionally be observed in urinary sediment, and *Schistosoma haematobium* can lodge in the urinary tract and release eggs into the urine.

- *Chlamydia trachomatis* and *Mycoplasma genitalium* can infect the urethra but not the bladder. These infections are usually classified as a *urethritis* rather than urinary tract infection.

Routes of Infection

Bacteria can invade and cause a UTI via three major routes:

1. Ascending
2. Hematogenous (Descending)
3. Lymphatic pathways.

Although the ascending route is the most common course of infection in females, ascent in association with instrumentation (e.g., urinary catheterization, cystoscopy) is the most common cause of hospital-acquired UTIs in both sexes.
For UTIs to occur by the ascending pathway, enteric gram-negative bacteria and other microorganisms that originate in the gastrointestinal tract must be able to colonize the vaginal cavity or the periurethral area. Once these organisms gain access to the bladder, they may multiply and then pass up the ureters to the kidneys.

UTIs occur more often in women than men, at least partially because of
- the short female urethra and its proximity to the anus
- sexual activity can increase chances of bacterial contamination of the female urethra.

**Examples of Probable Virulence Factors of Uropathogenic *E. coli***
- Type 1 fimbriae that bind to uroepithelial cells
- Type P fimbriae that recognize kidney glycosphingolipids
- Siderophores that help gather iron from the host
- Alpha and beta hemolysins that lyse host erythrocytes
- Capsules
- Sat protein that acts as a proteolytic toxin
Types of infection and their clinical manifestations

Urethritis

- Symptoms associated with urethritis include: dysuria (painful or difficult urination), and frequency are similar to those associated with lower UTIs.
- Urethritis is a common infection.

There are two main categories of bacterial urethritis:

1. Gonorrheal urethritis
2. Nongonococcal urethritis

Gonorrheal urethritis is caused by *Neisseria gonorrhoeae* and is associated with gonorrhea, a common STI.

The term Nongonococcal urethritis (NGU) refers to inflammation of the urethra that is unrelated to *N. gonorrhoeae*. In women, NGU is often asymptomatic. In men, NGU is typically a mild disease, but can lead to purulent discharge and dysuria.

Untreated NGU can spread to the reproductive organs, causing pelvic inflammatory disease and salpingitis in women and epididymitis and prostatitis in men. Important bacterial pathogens that cause nongonococcal urethritis
include *Chlamydia trachomatis, Mycoplasma genitalium, Ureaplasma urealyticum, and Mycoplasma hominis.*

**Cystitis**
- Typically, patients with cystitis complain of dysuria, frequency, and urgency (need to urinate).
- Often, there is tenderness and pain over the area of the bladder. In some individuals, the urine is grossly bloody. The patient may note urine cloudiness and a bad odor.
- Because cystitis is a localized infection, fever and other signs of a systemic (affecting the body as a whole) illness are usually not present.

**Ureteritis**
- Inflammation or infection within the ureters is considered in combination with kidney infections.
- UTI within the ureters indicates that organisms have begun or are in the process of ascending into the kidneys and should be treated similarly to prevent further infection.

**Pyelonephritis**
- Pyelonephritis refers to inflammation of the kidney parenchyma, calices (cup-shaped division of the renal pelvis), and pelvis (upper end of the ureter that is located inside the kidney) and is usually caused by bacterial infection.
- The typical clinical presentation of an upper urinary tract infection includes fever and flank (lower back) pain and, frequently, lower tract symptoms (frequency, urgency, and dysuria).
- Patients can also exhibit systemic signs of infection such as vomiting, diarrhea, chills, increased heart rate, and lower abdominal pain. Of significance, 40% of patients with acute pyelonephritis are bacteremic.
Urosepsis
- Approximately 25% of sepsis cases (severe blood infection) are a result of urosepsis, a systemic infection that may develop from community- or hospital-acquired urinary tract infections.
- Early diagnosis and treatment of urinary tract infections are essential in preventing urosepsis.

Asymptomatic bacteriuria
Asymptomatic bacteriuria is absence of UTI signs or symptoms in a patient whose urine culture satisfies criteria for UTI. Pyuria may or may not be present. Because it is asymptomatic, such bacteriuria is found mainly when high-risk patients are screened or when urine culture is done for other reasons.

Screening patients for asymptomatic bacteriuria is indicated for those at risk of complications if the bacteriuria is untreated. Such patients include

- Pregnant women at 12 to 16 wks' gestation
- Patients who have had a kidney transplant within the previous 6 months
- Young children with gross VUR (Vesicoureteral reflux).
- Before certain invasive GU procedures that can cause mucosal bleeding (eg, transurethral resection of the prostate)
- Certain patients (eg, postmenopausal women; patients with ongoing use of urinary tract foreign objects such as nephrostomy tubes, and indwelling catheters) often have persistent asymptomatic bacteriuria and sometimes pyuria.
**Bacterial Infections of the Urinary Tract**

Urinary tract infections can cause inflammation of the urethra (urethritis), bladder (cystitis), and kidneys (pyelonephritis), and can sometimes spread to other body systems through the bloodstream. Table 1 captures the most important features of various types of UTIs.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pathogen</th>
<th>Signs and Symptoms</th>
<th>Transmission</th>
<th>Diagnostic Tests</th>
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<tbody>
<tr>
<td>Cystitis</td>
<td><em>Escherichia coli</em>, <em>E. faecalis</em>, <em>St. agalactiae</em>, <em>K. pneumoniae</em>, <em>S. saprophyticus</em>, others</td>
<td>Dysuria, pyuria, hematuria, and bladder pain; most common in females due to the shorter urethra and abundant normal vaginal microbiota</td>
<td>Nontransmissible; opportunistic infections occur when fecal bacteria are introduced to urinary tract or when normal urination or immune function is impaired</td>
<td>Urine dipstick, urine culture for confirmation</td>
</tr>
<tr>
<td>Nongonococcal urethritis (NGU)</td>
<td><em>Chlamydia trachomatis</em>, <em>Mycoplasma genitalium</em>, <em>Mycoplasma hominis</em>, <em>Ureaplasma urealyticum</em></td>
<td>Mild or asymptomatic; may cause purulent discharge and dysuria</td>
<td>Transmitted sexually or from mother to neonate during birth</td>
<td>Urethral swabs and urine culture, PCR</td>
</tr>
<tr>
<td>Pyelonephritis, Glomerulonephritis</td>
<td><em>E. coli</em>, <em>Proteus spp.</em>, <em>Klebsiella spp.</em>, <em>Streptococcus pyogenes</em>, others</td>
<td>Back pain, fever, nausea, vomiting, blood in urine; possible scarring of the kidneys and impaired kidney function</td>
<td>Nontransmissible; infection spreads to kidneys from urinary tract or through bloodstream</td>
<td>Urinalysis, urine culture, radioimaging of kidneys</td>
</tr>
</tbody>
</table>

**Laboratory diagnosis of urinary tract infections**

As previously mentioned, because noninvasive methods for collecting urine must rely on a specimen that has passed through a contaminated sites, quantitative cultures for the diagnosis of UTI are used to discriminate between contamination, colonization, and infection.
SPECIMEN COLLECTION
1. Clean-catch midstream urine: Clean external genitalia; begin voiding and after several mL have passed; collect midstream without stopping flow of urine. 2-3 mL must be collect (The first portion of the urine flow washes contaminants from the urethra, and the midstream portion is more representative of that in the bladder).

2. Catheter Clean urethral area, insert catheter, and allow first 15 mL to pass; then collect remainder Sterile urine using screw-cap container.

3. Indwelling catheter, Disinfect catheter collection port, aspirate 5-10 mL with a syringe using urine container

4. Suprapubic aspirate, Disinfect skin, aspirate with needle and syringe through abdominal wall into full bladder

SCREENING PROCEDURES

Gram Stain
A Gram stain of urine is an easy, inexpensive means to provide immediate information as to the nature of the infecting organism (bacteria or yeast) to guide empiric therapy.
The Gram stain should not be relied on for detecting PMN in urine because leukocytes deteriorate quickly in urine that is not fresh or not adequately preserved.

Pyuria: the hallmark of inflammation, and the presence of PMN can be enumerated in uncentrifuged urine sample. This method of screening urine is the best indicator of the host’s state. Patients with more than 400,000 PMNs excreted into the urine per hour are likely to be infected

Multiple white cells seen in the urine of a person with a urinary tract infection
**Indirect Indices**

**Nitrate Reductase Test.** This screening procedure looks for the presence of urinary nitrite, an indicator of UTI. Nitrate-reducing enzymes that are produced by the most common urinary tract pathogens reduce nitrate to nitrite.

**Leukocyte Esterase Test.** As previously mentioned, evidence of a host response to infection is the presence of PMNs in the urine. Because inflammatory cells produce leukocyte esterase, a simple, inexpensive, and rapid method that measures this enzyme has been developed.

**Cultures** are recommended in patients whose characteristics and symptoms suggest complicated UTI or an indication for treatment of bacteriuria. Common examples of culture media include the following: MacConkey, EMB, XLD, BA

**INTERPRETATION OF RESULTS**

- Specimens with multiple uropathogens (i.e., three or more) indicate probable contamination.
- One or two significant uropathogens present (i.e., $10^5$ CFU/mL or more) should routinely be identified. Susceptibility tests should be performed for inpatients.
- One or two uropathogens present in small numbers (i.e., $10^2$ CFU/mL or more to less than $10^5$ CFU/mL) should be routinely identified if the clinical situation warrants, such as in acute urethral syndrome or cases of previous antibiotic therapy.