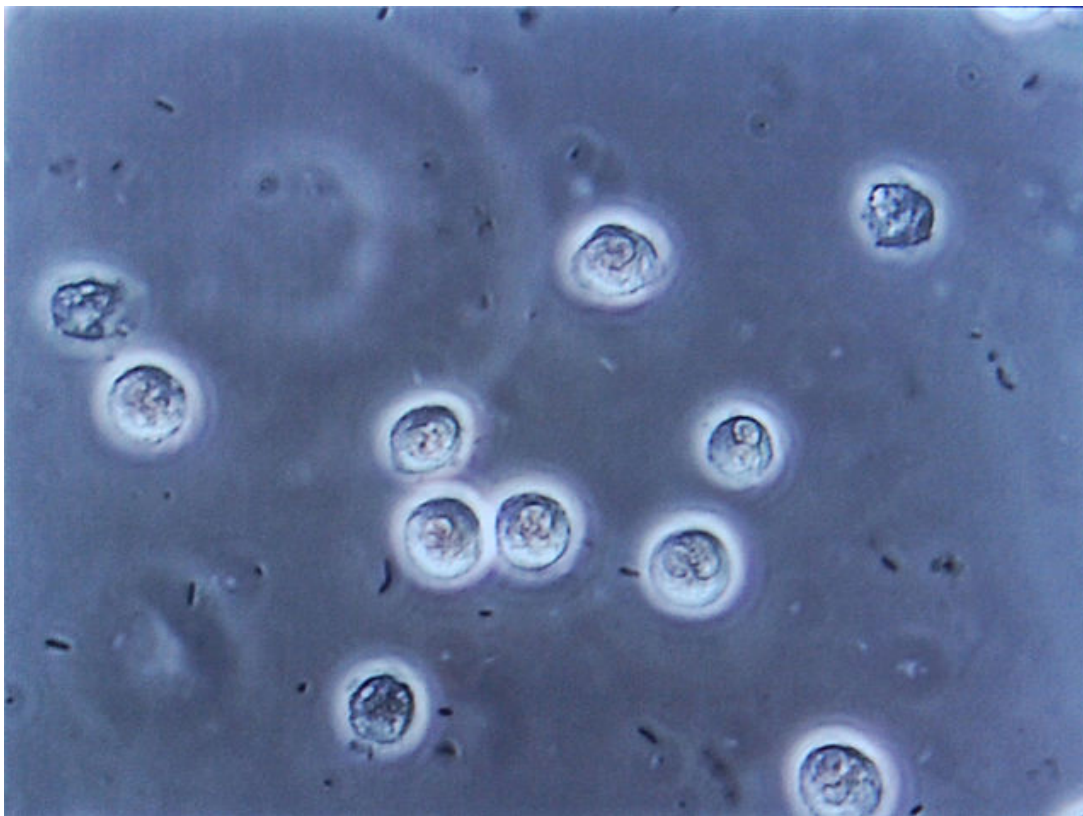


Urinary Tract Infection (UTI; Bladder Infection)

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Urinary tract infections (UTI) are an inflammatory condition of an infectious etiology that involves the urinary tract. Anatomically, it can be divided into upper and lower urinary tract infections. Most common symptoms are fever, chills and rigor, foul smelling urine and other constitutional symptoms. Different risk factors include vesico-ureteric reflux, neurogenic bladder, calculi in the urinary tract, strictures and female gender. Culture and sensitivity testing is the gold standard for the diagnosis of a UTI. Antibiotics are the treatment of choice depending on the causative organisms, drug resistance, and pharmacokinetic of the drug.



Definition of Urinary Tract Infections

Urinary tract infections (UTIs) are quite common. A UTI is defined as a condition in which bacteria invades, persists, and multiplies within the urinary tract. UTIs are most commonly caused by **gram-negative organisms**.

Epidemiology of Urinary Tract Infections

In the United States alone, there were an estimated 10.5 million office visits for UTI symptoms. Approximately, 3 million visits to the emergency departments in the United States are due to UTI symptoms. Females are more likely to develop a UTI than males. Extremes of age are also more likely to develop a UTI. Patients with indwelling catheters, immunosuppression, urinary tract abnormalities, and previous antibiotic exposure are at risk of developing a complicated UTI.

UTIs can be anatomically classified into **lower tract infection** (including urethritis, prostatitis and cystitis) and **upper tract infections** (pyelonephritis and perinephric abscess).

According to clinical pictures, it can be classified as:

Asymptomatic bacteriuria: it is the presence of bacteriuria, i.e., more than 10⁵ organisms per ml on two occasions in women and one occasion in men. It indicates UTI without the symptoms. It is **commonly seen during pregnancy**.

Symptomatic bacteriuria: it includes acute urethritis, acute cystitis, acute prostatitis, acute pyelonephritis and septicemia with septic shock.

Pathophysiology of Urinary Tract Infections

The most recent literature has agreed on the following suggested step-wise pathogenesis of UTIs:

1. Contamination of the peri-urethral area with a uropathogens from the gut. The most common organism is *Escherichia coli*.
2. Colonization of the urethra and migration of the causative organism to the bladder. By then, the patient would have developed urethritis.
3. Colonization of the urinary bladder, invasion of the bladder wall, inflammation of the bladder and the accumulation of fibrinogen. At this stage, the patient would present with cystitis.
4. Neutrophil infiltration of the urinary bladder happens at a later stage.
5. Once neutrophils infiltrate the urinary bladder, and bacteria start multiplying, a systemic immune reaction happens. Patients at this stage start to show leukocytosis and systemic symptoms and signs.
6. A biofilm is formed and the uroepithelial surface of the ureters is extensively damaged by bacterial toxins and proteases.
7. Finally, the bacterial organisms ascend to the kidneys and the patient develops pyelonephritis.

Etiology of Urinary Tract Infections

More than 75% of uncomplicated UTIs are due to *Escherichia Coli*. *K. pneumoniae* and *S. saprophyticus* are responsible for up to 6% of uncomplicated UTI cases each.

Enterococcus spp. are encountered as causative pathogens in 5% of uncomplicated UTI cases. Other microorganisms such as *P. mirabilis*, *P. aeruginosa*, *S. aureus*, and *Candida spp.* account for the remainder of the cases of UTIs.

There are two important differences between complicated and uncomplicated UTIs in

terms of etiology. *Candida* spp. and *Enterococcus* spp. are responsible for 7% and 11% respectively for complicated UTI cases.

Risk factors associated with UTIs

The following risk factors have been implicated with a higher risk of developing a UTI:

Anatomical factors

- Posterior urethral valve
- Vesicoureteric reflux
- Urethral stricture
- Benign prostatic hypertrophy

Functional factors like neurogenic bladder

Familial susceptibility

Disease conditions

- Diabetes
- Immunosuppression
- Calculi
- Congenital abnormalities
- Urinary foreign bodies like a stent or a catheter

Factors associated with a higher risk of UTIs in females

- Voiding habits
- Post-menopausal state
- Perineal hygiene
- Spermicidal jelly use
- Vaginal douching

Factors associated with a higher risk of UTIs in males

- Phimosis
- Chronic prostatitis
- Seminal vesiculitis
- Epididymorchitis

Causes of sterile pyuria

- Partially treated UTI
- Bladder tumors
- Chemical cystitis
- Interstitial nephritis
- Appendicitis
- Urinary tuberculosis
- Infection of other organisms like chlamydia or *Corynebacterium*

Clinical Features of Urinary Tract Infections

The **common symptoms** of UTI are:

1. Fever with chills and rigor
2. Increased frequency of micturition
3. Dysuria

4. Urgency
5. Haematuria
6. Suprapubic pain resulting from cystitis
7. Strangury resulting from cystitis. After the bladder has been emptied, there may be an intense desire to pass more urine due to detrusor spasm.
8. Urine is cloudy
9. Foul smelling urine

Clinical features **depend on the site of infection** of the urinary tract. For example, symptoms pertaining to voiding are more common in lower urinary tract infections, while pain and constitutional symptoms are more common in upper urinary tract infections. The following are the description of infection according to the site:

Cystitis and urethritis

Cystitis or urethritis **may be asymptomatic or may present with urgency, dysuria, frequency, nocturia, incontinence, and pain in the supra-pubic region.** An offensive smell of urine may be a major sign. 30% of cases present with haematuria. **Interstitial cystitis** is characterized by symptoms suggestive of cystitis with a negative urine culture. The diagnosis is confirmed by biopsy and cystoscopy.

Prostatitis and seminal vesiculitis

These conditions mainly present with **dysuria, perineal pain, frequency, voiding difficulties and painful ejaculations.** Fever with chill and rigor and other constitutional symptoms are major presenting symptoms in acute bacterial prostatitis. In these cases, a per-rectal digital examination should be avoided due to the chance of inducing bacteremia. Chronic bacterial prostatitis may be asymptomatic. These conditions are important causes of recurrent UTI in male patients. **Culture result of expressed prostatic secretion** may confirm the diagnosis in this case.

Pyelonephritis

It is the **infection of renal parenchyma.** **Myalgia, nausea, vomiting, pain in the loin region, fever with chills and rigor** are the presenting features in acute pyelonephritis. Renal angle tenderness during a physical examination is a prominent finding. Significant leucocytosis with leukocyte casts may be found in the urine. Micro- or macroscopic haematuria may be found. Blood culture may be positive in a quarter of the patients.

Fulminant emphysematous pyelonephritis can be seen as an acute condition in diabetic patients. In this condition, there is an **accumulation of fermentative gases in collecting tubules, kidney and parenchyma.** Chronic pyelonephritis is **difficult to diagnose.** It is mostly diagnosed by clubbed calyces with focal and diffuse renal scarring on radiograph. This usually develops in patients with vesicoureteral reflux in early childhood.

Renal Abscess

Staphylococcus aureus is the most common bacteria causing renal abscess. It is mostly due to the spread of infection from another site through the bloodstream. Since it is a systemic infection in the majority of cases, **fever, constitutional symptoms, and loin pain** are the presenting symptoms. Renal cortex shows hypoechoic lesions on

radiograph. The symptoms resemble acute pyelonephritis. Diagnosis is confirmed by aspiration and culture from the suspected area under ultrasound guidance.

A perinephric abscess is the abscess formation in the perinephric space. It is insidious in origin as compared to a renal abscess, so it remains **undiagnosed for a long period of time**. Flank or abdominal mass may be an initial presentation.

Investigations of Urinary Tract Infection

- **Dipstick tests** are often used to detect nitrite which is a metabolic product of typical pathogens of the urinary tract.
- Leucocyte esterase, which is marker of inflammation, can be found in a dipstick test. The presence of nitrite and leucocyte esterase increases the possibilities of UTIs.
- **Clean catch technique** is used to collect the clean freshly voided midstream specimen of urine. It should be examined for leukocytes, leukocyte casts, and red cells etc. If these cells are found, it increases the suspicion of UTI.
- **Suprapubic aspiration of urine from the bladder** can be used to collect an uncontaminated urine sample, but now it is rarely required.
- **Gram staining and bacterial colony count** can be done to identify the causative organism.
- **Culture and sensitivity testing** can confirm the diagnosis.
- **Prostatic massage** followed by urine culture is done if prostatitis is suspected.
- Bladder lesion can be diagnosed by **cystoscopy**.
- Obstruction, stricture, cysts and calculi can be diagnosed by **ultrasonography**.
- **Intravenous urography (IVU)** with a post void film of bladder can be a diagnostic modality for physiological and anatomical abnormalities of the urinary tract.
- **Micturating cystourethrography (MCU)** is useful in diagnosing vesicoureteric reflux and disturbed bladder emptying.
- Pyelonephritis can be diagnosed by a **DMSA scan**.
- **Rectal examination** can be done in prostatitis, but with antibiotic cover.
- In females with recurrent UTI, a **pelvic examination** is mandatory to exclude cystocele, rectocele and uterovaginal prolapse.

Treatment of Urinary Tract Infection

Antibiotics are the treatment of choice in the cases of UTI. The choice of antibiotic depends on the culture sensitivity testing, pharmacokinetics of the drug, and the pH of urine. Uncomplicated and symptomatic UTIs can be treated with a **3 to 5 days course of antibiotics**. Clotrimazole or fluoroquinolones are the treatment of choice in these cases.

Such short course treatment also **eradicates vaginal colonization** which could be the cause of recurrent UTIs in a female patient. Azithromycine or doxycycline is used in the cases of acute urethritis due to chlamydia infection. If a patient presents with an uncomplicated UTI with upper gastrointestinal symptoms, then a single dose of parenteral antibiotics on the first day, followed by oral antibiotic, is preferred (single dose of 2 gm ceftriaxone, 80 mg of gentamycine or 750 mg of amikacin can be given in this case).

Prostatitis is usually treated with a 6-week course of antibiotics like quinolones and cotrimoxazole. Macrolide antibiotics or doxycycline are the second-line drug in case of prostatitis. In some cases, the treatment's course can be prolonged to 12 weeks. The following table shows the recommended antibiotics in some common case scenarios of UTIs:

Condition	Common pathogens	Associated condition	Treatment schedule	Duration
Uncomplicated acute cystitis in women	<i>E. coli</i> , <i>Staphylococcus aureus</i> , <i>Proteus mirabilis</i> , <i>Klebsiella pneumoniae</i>	Nil	Trimethoprim plus sulphamethoxazole or fluoroquinolones	3 days
Uncomplicated acute pyelonephritis in women	<i>E. coli</i> , <i>Klebsiella pneumoniae</i> , <i>Staphylococcus</i>	Nil	Amoxicillin, nitrofurantoin, cephalosporin	7 days
Complicated acute cystitis in women	<i>E. coli</i> , <i>Staphylococcus aureus</i> , <i>Proteus mirabilis</i> , <i>Klebsiella pneumoniae</i>	Diabetes mellitus, Symptoms more than 7 days, recurrent form of UTI	Trimethoprim plus sulphamethoxazole or fluoroquinolones	7 days
Complicated acute cystitis in pregnant women	<i>E. coli</i> , <i>Staphylococcus aureus</i> , <i>Proteus mirabilis</i> , <i>Klebsiella pneumoniae</i>	Pregnancy	Amoxicillin, nitrofurantoin, cephalosporin	7 days
Complicated UTI	<i>E. coli</i> , <i>Proteus mirabilis</i> , <i>Pseudomonas</i>		Amoxicillin, nitrofurantoin, cephalosporin	14 days
Complicated UTI	<i>E. coli</i> , <i>Proteus mirabilis</i> , <i>Pseudomonas</i>	Severe infection in pregnancy	Amoxicillin, nitrofurantoin, cephalosporin	14 days
Acute urethral syndrome	<i>Ureaplasma urealyticum</i> , <i>Mycoplasma hominis</i>	Sexual activity, dysuria, pyuria, Non-gonococcal urethritis	Doxycycline	5 days

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