

Urinary Tract Infection

Urinary tract infections (UTIs) are a major cause of morbidity in the United States. They are the second most common infection, after respiratory infections, and largely affect women (1). Sixty percent of women will have at least one UTI in their lifetime, of which twenty-five percent will recur after an initial infection (2). Although UTIs are not sexually transmitted, they frequently occur in young, sexually active women, though they are by no means confined to this population.

Healthy females may have an occasional isolated episode of uncomplicated UTI, but some suffer from highly recurrent infections. In approximately one-third to one-half of cases, the same strain is reintroduced from an extraurinary tract reservoir. Recurrent infection within a week or two after treatment is usually due to persistence of the same pathogen; whereas, recurrence after two weeks is more often a result of reinfection, especially in women.

The urinary tract is ordinarily sterile except at the distal end of the urethra. Although, in females prone to recurrent infections, the urethra and vaginal introitus are more likely to be colonized with gram-negative bacteria which grow well in urine. UTIs occur when a pathogen invades the bladder. The high rate of urinary infections in females appears to be due to their shorter urethras. Infections that remain confined to the bladder are called cystitis.

More severe infections that spread to the kidneys are called pyelonephritis. There are 250,000 cases of pyelonephritis in the US each year, 10,000 of which require hospitalization (3). Complications of pyelonephritis can include sepsis, and in some cases, death.

Patients suffering from UTIs usually experience painful, frequent, and urgent urination. Their urine is often cloudy or malodorous and has white blood cells present (pyuria). In addition, patients with pyelonephritis often have flank pain, fever, nausea, and vomiting. A presumptive diagnosis of UTI is often made based on these signs and symptoms and empiric antibiotic therapy is prescribed.

The necessity of urine culture for UTIs is an area of debate among experts. However, there is a consensus

that laboratory testing should be performed in cystitis cases where symptoms do not improve in 24 hours or if there is a recurrent infection. In addition, laboratory testing should be performed for any patient suspected of pyelonephritis (4). In these cases, laboratory testing can confirm the diagnosis and determine antibiotic susceptibility of the pathogen. The physician can then modify the antibiotic therapy appropriately.

The recommended first-line antibiotic therapy for cystitis is a 3-day course of trimethoprim-sulfamethoxazole (TMP-SMX). In geographic areas where resistance to TMP-SMX exceeds 15% to 20%, a 3-day course of a fluoroquinolone, such as ciprofloxacin, is recommended. Treatment with fluoroquinolones is the first line therapy for pyelonephritis patients. β -lactam antibiotics are not recommended for treatment, since resistance is prevalent among Gram-negative uropathogens and their use is associated with a high risk of recurrence.

However, if Gram staining reveals a Gram-positive bacterium in the urine, amoxicillin, possibly in combination with clavulanic acid, can be used for treatment (4). Relapses in diabetics, transplant recipients, and elderly men should be treated for up to 4 to 6 weeks.

The traditional culture standard is that $>10^5$ bacteria/milliliter of urine indicates an acute UTI. However, lower counts can still be clinically relevant, as excessive rehydration, frequent urination, and/or changes in urine pH can reduce the number of cultured bacteria present in a urine sample from an infected patient (4). Each UTI is caused by invasion of the bladder by a single pathogenic species. Therefore, a urine culture containing multiple species is often considered to be contaminated. *Escherichia coli* is the cause of the majority of UTIs, with the remainder due to a variety of bacterial pathogens including *Proteus mirabilis*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Staphylococcus saprophyticus*.

Medical Diagnostic Laboratories (MDL) has developed sensitive and specific Real-Time PCR tests to detect these pathogens in **UroSwab**[®] specimens from patients to assist the physician in the diagnosis of a UTI.

Escherichia coli

Escherichia coli is a rod-shaped, Gram-negative facultative anaerobe. Most *E. coli* strains are non-pathogenic. Although *E. coli* lives in the human gut as a commensal organism, certain pathogenic strains can exit the human gut and cause disease at other anatomical sites. One example of this phenomenon is uropathogenic *E. coli* (UPEC), which causes 70% of UTIs (5). UPEC strains are thought to originate in the patient's fecal flora and be spread via fecal contamination to the periurethral area. The bacteria can then ascend the urethra into the bladder and cause a UTI. UPEC strains express a variety of virulence factors including adhesive appendages, known as pili, and toxins that allow them to infect the bladder.

Proteus mirabilis

Proteus mirabilis is a rod-shaped, Gram-negative facultative anaerobe that causes 4% of UTIs (5). *P. mirabilis* expresses the enzyme urease that hydrolyzes urea to ammonia, leading to alkaline urine and the formation of kidney stones. These stones can cause obstruction and renal failure, and bacteria can persist within them to survive antibiotic therapy. *P. mirabilis* also exhibits swarming motility. Although this ability does not play a role in UTI, it gives a distinctive colony phenotype that allows rapid identification after urine culture.

Klebsiella pneumoniae

Klebsiella pneumoniae is a rod-shaped, Gram-negative facultative anaerobe that is part of the normal flora of the mouth, skin, and intestines. *K. pneumoniae* is an opportunistic pathogen that can cause respiratory, wound, and urinary tract infections. It is increasingly found as a nosocomial infection and is commonly implicated in hospital-acquired urinary tract and wound infections, particularly in immunocompromised individuals. Feces are the most significant source of patient infection, followed by contact with contaminated instruments. *Klebsiella* species cause 5% of UTIs and rank second to *E. coli* as a cause of urinary tract infections in older persons (5).

Klebsiella oxytoca

Klebsiella oxytoca is primarily a health care-associated pathogen acquired from environmental sources. *K. oxytoca* is emerging as an important bacterial isolate causing hospital-acquired infection in adults, most often involving immunocompromised patients or those requiring intensive care, and having multiple drug resistance to commonly used antibiotics. They may cause infection of the skin, blood, respiratory, urinary, and gastrointestinal tracts.

Staphylococcus saprophyticus

Staphylococcus saprophyticus is a coccid Gram-positive facultative anaerobe. It possesses surface structures known as fimbriae or pili responsible for allowing the adherence to uroepithelial cells which facilitates the colonization of urinary tracts. It accounts for 4% of UTIs, and is the second leading cause of UTI among women aged 16-25 (5, 6). Patients suffering from *S. saprophyticus* UTI often exhibit lower levels of bacteriuria (<10⁵ bacteria/milliliter of urine) than those infected with other uropathogens.

The **UroSwab**[®] platform allows for the detection of the four aforementioned urinary tract pathogens from a single specimen. Benefits of this system include:

- One vial, multiple pathogens
- DNA amplification via PCR technology
- Microbial drug resistance profiling
- High precision robotic accuracy
- High diagnostic sensitivity & specificity
- 24 - 72 hour turnaround time
- Specimen viability up to 5 days after collection
- Test additions available up to 30 days after collection
- No refrigeration required before or after collection

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