Urinary Tract Infections

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Urinary tract infection (UTI) is the collective term used to describe infections involving any part of the urinary tract, which includes the kidneys, ureters, bladder and urethra. Infections of the bladder (cystitis) and urethra (urethritis) are known as lower UTIs and infections of the kidneys (pyelonephritis) or ureters are classed as upper UTIs.[1, 4] The urinary tract is the second most common site of bacterial infection and a significant cause of morbidity both in terms of the number of people affected and potential complications. UTI's are classified as complicated or uncomplicated. An infection is considered complicated if it affects pregnant women, children, men and the elderly orif it affects the upper urinary tract. Uncomplicated UTI's involve the lower urinary tract and cause acute dysuria and frequency in otherwise healthy, non-pregnant women.[4]

The urinary tract is a common source of infection in paediatrics and is the most common bacterial infection in children under 2 years of age, both in community and hospital settings. Approximately 8% of girls and 2% of boys will have a symptomatic UTI in childhood. During the first six months of life however, UTIs are more common in boys than girls and especially in uncircumcised males. E. coli is the causative organism in 90% of cases. 30% of children with UTI have vesicoureteric reflux. Accurate diagnosis via urine culture is essential.[2, 10] The incidence of UTIs in adult males under age 50 years is low. Up to 40% of women develop a UTI at some point in their life compared to 12% in men. In men, cystitis is often associated with infection and inflammation of the prostate gland (prostatitis). Anatomically the female urethra is shorter and located closer to the anus than in males, which makes it easier for bacteria to reach the female urethra and bladder. Adult women are 30 times more likely than men to develop a UTI, with almost half of them experiencing at least one episode during their lifetime and one in three women experiencing their first episode by the age of 24 years. UTIs are most commonly seen in sexually active young women. Sex can irritate and weaken the urethra, making it easier for bacteria to enter. Certain contraceptives can increase a woman's risk of developing UTIs. These include the diaphragm and spermicide coated condoms. Keeping hydrated, urinating as soon as possible after sex, and avoiding synthetic underwear can help prevent UTIs in females. Other susceptible adults include the elderly and patients requiring urethral catheterisation.[3] Urinary tract symptoms are not always obvious in the elderly. Presentation may be vague with incontinence, change in mental status or fatigue as the only symptoms, while some present with sepsis as the first symptoms. Diagnosis can be complicated by the fact that many elderly people have pre-existing incontinence or dementia. 5 Other risk factors for developing UTIs include conditions that prevents fully emptying the bladder, kidney stones, a weakened immune system, undergoing chemotherapy, diabetes, and an enlarged prostate gland in males.[1]

Symptoms of a lower urinary tract infection include dysuria, frequency, and the urge to urinate despite having an empty bladder. Symptoms may also include cloudy and unpleasant smelling urine, haematuria, abdominal pain, pelvic tenderness, back pain and a general sense of feeling unwell.[1] Symptoms of a kidney infection include fever of 38ºC (100.4ºF) or above, shivering, nausea, vomiting, diarrhoea and flank pain. In addition frequency, dysuria, urgency and haematuria may also be present because the infection can spread from the kidneys to the lower urinary tract.[1]

The presence of bacteria in urine does not necessarily depict a urinary tract infection. Many people, especially the elderly, have bacteria in their urine without having any ill effects. This is known as asymptomatic bacteriuria. E. coli bacteria from the gut is the cause of 80–85% of community-acquired urinary tract infections, with Staphylococcus saprophyticus the cause in 5–10%. Occasionally they may be caused by viral or fungal infections.[6] Healthcare-associated urinary tract infections mostly related to urinary catheterisation involve a much broader range of pathogens including: E. coli (27%), Klebsiella (11%), Pseudomonas (11%), Candida albicans (9%), and Enterococcus (7%) among others. Urinary tract infections due to Staphylococcus aureus typically occur secondary to blood-borne infections. 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.[7]

Diagnosis

Urinalysis reagent strips are the most frequently used instruments for diagnostic testing if there is clinical evidence that a patient has a UTI. A high number of leucocytes in the urine points to the presence of white blood cells indicating inflammation or infection along the urinary tract, often in the bladder or kidney. The presence of nitrites in the urine is highly specific to certain bacterial infections but nitrites do not occur with all types of bacteria. E. coli bacteria are most commonly associated with nitrites in the urine. An infection may occur in the presence of leucocytes with no nitrites, however, leucocytes in the urine without nitrites can also lead to a false-positive result that points to a bacterial infection when there is none. Negative nitrite and negative leucocyte has a 95% negative predictive value. A positive nitrite test is more indicative than a positive leucocyte test, although the presence of both increase the possibility of a UTI diagnosis.[16]

For most woman who have the typical symptoms of a lower UTI, further testing is not usually required to confirm the diagnosis. Circumstances where laboratory testing is recommended are:[1]

- All cases of UTI in men. UTIs are uncommon in men, so it is important to rule out other possible causes of the symptoms.
- Cases of a suspected upper UTI. These infections have a higher risk of complications, so a careful assessment of the state of the urinary tract needs to be made.
- UTIs that occur in pregnant women due to the higher risk of developing complications.
- In cases where a person has blood in their urine. Although unlikely, this could be a symptom of bladder cancer so it is important to rule out or confirm the diagnosis.
- In cases where a person has a risk factor that makes them more vulnerable to developing serious complications, such as having a weakened immune system. Other diagnostic tests required may include ultrasound, computerized tomography (CT) scan, magnetic resonance imaging (MRI) or cystoscopy.

Treatment: Adult Uncomplicated UTI (no fever or flank pain)[8]

Treatment	Dose	TX Duration
nitrofurantoin [A-]	50mg QDS	3 days, (7 days in men)
OR trimethoprim [A-]	200mg BD	3 days, (7 days in men)
OR fosfomycin*	3g	STAT (Females only)

Choice of empirical therapy should be governed by local resistance rates as patterns vary significantly across the country. For first presentations, with low risk of resistant organisms in uncomplicated UTI, narrow-spectrum antibiotics such as fosfomycin, nitrofurantoin or trimethoprim should be considered. For uncomplicated UTIs, quinolones should be reserved for resistant infections with limited options and confirmed by culture and sensitivity.[8]

Community multi-resistant E. coli with extended-spectrum betalactamase (ESBL) enzymes are increasing so cultures should be carried out in all treatment failures. ESBLs are multi-resistant but often remain sensitive to nitrofurantoin and fosfomycin. There is less relapse with trimethoprim than cephalosporins. To preserve the efficacy of fosfomycin, its use should be limited where possible to uncomplicated UTI in women, or in specific situations on advice of an infection specialist. Fosfomycin is not recommended for use in treatment of UTI in patients over 65 years in long term care facilities except in specific situations on advice of an infection specialist. Fosfomycin should be avoided in the elderly and in patients with renal impairment due to diminished urinary concentrations. Recommendation for use in pregnancy remains under review pending further evidence and safety data.[8]

Treatment (Acute Pyelonephritis)[9]

Treatment	Dose	TX Duration
ciprofloxacin	500 mg BD	7 days [A-]
co-amoxiclav	625 mg TDS	14 days
If susceptible, trimethoprim	200 mg BD	14 days

An MSU must be sent for culture. In acute Pyelonephritis, 7 days of treatment with ciprofloxacin is considered as effective a treatment as 14 days of trimethoprim (co-trimoxazole). If there is no response within 24 hours the patient should be admitted to hospital.[1, 9]

Treatment: Paediatrics

Children less than 3 months old who present with UTIs will be referred to a specialist and treated in hospital. Children over three months old, with a UTI where there is a risk of serious complications will also be referred to hospital for treatment. For children over 3 years old with a low risk of complications, the infection can be treated at home using oral antibiotics, and paracetamol. For lower UTIs, a three-day course of antibiotics (cefalexin, nitrofurantoin or trimethoprim) is usually commenced and for upper UTIs, a seven-day course (cefalexin or co-amixoclav) is usually recommended. Positive nitrites must be present in the urine to commence antibiotic therapy.[11]

Treatment: Recurrent UTI in Women[12]

Treatment	Dose	TX Duration
nitrofurantoin	50 mg	Stat post-coital (off-label)
OR trimethoprim	100 mg	OD at night

If more than 3 UTIs occur per year, continuous or post-coital prophylaxis with antibiotics can be effective in women. However, both are associated with antibiotic side effects. There is no evidence that standby antibiotics are effective.[12]

Treatment: UTI in Pregnancy[13]

Treatment		Dose	TX Duration
First line	nitrofurantoin	50-100mg QDS	7 days
OR	amoxicillin (if known to be susceptible)	500mg TDS	7 days
Second line	cephalexin	500mg BD	7 days

For UTIs in pregnancy an MSU must be sent for culture and any empirical treatment reviewed when results of the MSU culture and susceptibility are available. Amoxicillin resistance is common and should be used only if susceptibility data is available. Nitrofurantion should be avoided after 36 weeks gestation due to the risk of neonatal haemolysis. Fosfomycin use in pregnancy remains under review pending further evidence and safety data.[13]

Diagnosis & Management of UTI in Long Term Care Residents > 65 years[14]

A positive urinalysis reagent strip (dipstick) result in an asymptomatic patient should not be treated. Residents in long term care facilities have high rates of positive dipstick urinalysis results without infection necessarily being present. Antibiotic therapy in these cases does not reduce mortality or prevent symptomatic episodes, rather it increases side effects and leads to antibiotic resistance. Empiric treatment may be considered in a symptomatic patient with a positive dipstick. A urine sample should be sent to the microbiology laboratory for culture and antimicrobial susceptibility testing in these cases. Symptoms suggestive of a UTI include dysuria, frequency, urgency, new onset incontinence, fever >38°C, suprapubic tenderness and haematuria. Diagnosis of UTIs in long term care residents over 65 years should be based on a full clinical assessment. In patients with a urinary catheter, loin pain and fever >38°C are significant indicators of a UTI.[14]

Empirical Treatment of UTI in Long Term Care Residents > 65 years[14]

Empiric antibiotic therapy should only be considered in symptomatic patients pending urine culture result. Choice of empirical therapy should be guided by local resistance rates and treatment modified according to culture result when available.

Uncomplicated UTI i.e. no fever or flank pain, first presentations / low risk of resistant organisms	Acute pyelonephritis
Trimethoprim 200mg BD OR Nitrofurantoin* 50mg QDS for 7 days (*Avoid in renal impairment)	Co-amoxiclav 625mg TDS for 14 days OR Ciprofloxacin 500mg BD for 7 days
Use of Cephalexin 500mg BD or Co-amoxiclav 625mg TDS may also be considered - based on local resistance rates	If no response within 24 hours consider hospital referral

Empirical Treatment of UTI in Residents with a Urinary Catheter[14]

First presentations / low risk of resistant organisms	Previous resistance to, or risk of, trimethoprim or nitrofurantoin resistance
Trimethoprim 200mg BD OR Nitrofurantoin* 50-100mg QDS (*Avoid in renal impairment)	Cephalexin 500mg BD OR Co-amoxiclav 625mg TDS (Consider based on local resistance rates)

Duration of therapy is usually 7 days. Delayed response regardless of whether the patient remains catheterised or not is 10-14 days. If an indwelling catheter has been in place for more than 2 weeks at the onset of UTI and is still indicated, the catheter should be replaced. Antibiotic prophylaxis is not recommended for the prevention of symptomatic UTI in catheterised patients or for urinary catheter changes unless there is a definite history of symptomatic UTIs due to catheter change. Antimicrobial prophylaxis may however be considered in patients for whom urinary infections are of such frequency or severity that they chronically impinge on function and well-being.[14] Although UTIs are often considered to be easily managed infections, they remain an economic burden for the healthcare system. In 2014 the annual estimated primary care costs were approximately €19.2 million compared to the low annual cost of UTIs in secondary care at approximately €155,000. Health care costs were estimated on the basis of GP consultation costs, antibiotic costs, laboratory costs and secondary inpatient and outpatient costs. The latter was acquired from national clinical data on discharges in acute hospitals.[15] Suspected UTIs are a common reason to attend primary care services in Ireland. From the health service perspective, the overall economic cost of UTIs is mainly driven by primary care costs with comparatively low secondary care costs.[15] The increasing prevalence of antibiotic resistance among uropathogens presents a major challenge to the clinical management of UTIs. Although in most situations antibiotics are required, inappropriate treatment contributes to the growing problem of antibiotic resistance in UTIs. Appropriate empirical treatment of urinary tract infections (UTIs) is important for successful treatment and prevention of complications. However, with the increasing prevalence of antibiotic-resistant urinary pathogens, the selection of an appropriate empirical agent is increasingly difficult.[17] Resistance to co-trimoxazole and other antimicrobials used in the treatment of UTIs, particularly fluoroquinolones, is increasing, as is the prevalence of extended-spectrum-beta-lactamase (ESBL) producing Enterobacteriaceae and multidrug-resistant (MDR) Pseudomonas aeruginosa. The problem is particularly prominent in the hospital setting, where UTIs can present as severe infections and MDR organisms are frequent.[17] Understanding the key criteria for antibiotic selection, pathology of UTI and therapeutic profile of commonly prescribed agents is vital for practitioners to ensure rational, safe and cost-effective treatment. Judicious use of antibiotics in common clinical situations is crucial for minimising antibiotic resistance and the effective treatment of patients.

Article was previously published in the Medical Independent. References on request