

# Urinary tract infection

Neil S Sheerin

## Abstract

Urinary tract infection is one of the most common infections to affect humans. Uncomplicated infections occur most commonly in otherwise healthy women when uropathogenic bacteria, usually *Escherichia coli*, enter the bladder and overcome host innate immunity. Complicated infections occur in patients with an anatomical or functional abnormality of the urinary tract. Diagnosis is made on the basis of symptoms and diagnostic precision is improved by urinalysis. Urine culture is important in patients with severe, recurrent or complicated infection and when diagnosis is uncertain, for example children and the elderly. Most women with symptoms that resolve quickly do not require further investigation, but imaging of the renal tract, functional testing and cystoscopy should be considered in children, men and patients with recurrent or severe infection. Empirical antibiotic treatment started on the basis of symptoms and directed by urinalysis is suitable for uncomplicated cystitis but should be altered based on culture results for more severe infections. Three days of antibiotic treatment is usually sufficient for uncomplicated cystitis in women. Long-term or post-coital antibiotics are effective treatments for patients with recurrent infection.

**Keywords** Antibiotics; cystitis; host defence; pyelonephritis; urinary tract infection

## Introduction

Urinary tract infection (UTI) is one of the most common bacterial infections, affecting 40% of women at some point in their life. UTI can cause life-threatening sepsis but most infections are less severe. Nevertheless, UTI causes significant distress to the individual and is associated with high healthcare and social costs. In the USA UTIs are responsible for 7 million clinic visits annually, with a cost exceeding \$1.6 billion.

UTI is most commonly bacterial, but fungal, viral and parasitic infections can occur. Cystitis is the most common UTI but infection can occur throughout the urinary tract causing pyelonephritis, urethritis and prostatitis. Asymptomatic bacterial colonization of the urinary tract is a common finding in women and the elderly.

UTI can be classified as complicated or uncomplicated. Uncomplicated UTI occurs in the absence of any anatomical or functional abnormality within the urinary tract and is the most common type of infection. Complicated UTI occurs in the presence of an abnormal urinary tract or any other factor that

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## What's new?

- Three days of antibiotics is sufficient to treat uncomplicated cystitis in women. Men should be treated for 7 days with an antibiotic that penetrates into the prostate
- Extended-spectrum beta-lactamase-producing uropathogens are an emerging problem
- UTI is a common hospital-acquired infection. Reducing the duration of catheterization is critical in reducing infection rates

increases susceptibility to infection. The common causes of complicated UTI are listed in [Table 1](#).

## Epidemiology

Asymptomatic bacteriuria is found in 1–2% of school-age girls and 5% of women but is rare in males. The prevalence increases with age and bacteriuria is found in 21% of women and 12% of men over the age of 65 years and over 40% of people living in institutions.<sup>1</sup> Acute uncomplicated cystitis is the most common form of symptomatic UTI, affecting 40% of women at some point in their life. One-third of patients who develop a UTI will go on to have recurrent infections. Symptomatic infection is less common in men.

Nosocomial UTI is the most common hospital-acquired infection, the majority being catheter associated. UTI develops in 25% of patients who require a catheter for over 7 days, with a 5% daily risk. UTI adds to the duration and cost of hospitalization and nosocomial uropathogens form a reservoir of antibiotic-resistant bacteria.

## Aetiology

Under normal circumstances the urinary tract is sterile and infection develops only when bacterial virulence overcomes normal host defence mechanisms. *Escherichia coli* is the most common uropathogen in both the community and hospitals with *Proteus mirabilis*, *Staphylococcus saprophyticus*, *Enterococcus faecalis*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* each causing <10% of cases.

## Host factors

Sterility is maintained by physical factors, including the unidirectional flow of urine, frequent and complete emptying of the bladder, separation of the bladder from a source of pathogens and reduced bacterial growth in urine. Contact between the urinary tract epithelium and bacteria induces an inflammatory response, activation of the innate immune system (in particular neutrophils) and synthesis of antibacterial peptides (defensins and cathelicidins). The secretion of the P blood group antigen and Tamm–Horsfall protein (uromodulin) interferes with bacterial adhesion to epithelial cells and colonized epithelial cells are shed into the urine. Although there is evidence of an adaptive immune response in UTI (pathogen-specific IgA in the urine following infection) it is unclear whether it is important in the defence against further infection.

### Common causes of complicated urinary tract infection

Bladder outflow obstruction  
*Prostatic disease*  
*Urethral stricture*  
*Bladder neck obstruction*  
 Neuropathic bladder  
*Multiple sclerosis*  
*Diabetes mellitus*  
*Spina bifida*  
*Spinal cord trauma*  
 Catheterization or stent  
 Renal tract stone disease  
 Instrumentation of the renal tract  
 Renal or urinary tract malignancy  
 Reflux  
 Duplex system  
 Ileal conduit  
 Pregnancy  
 Glycosuria  
 Kidney transplant  
 Immunosuppression

**Table 1**

### Bacterial virulence factors

To overcome the flow of urine, uropathogenic bacteria express a series of fimbrial adhesions. Fimbriae are filamentous structures that project from the surface of the bacteria and are responsible for binding to the host epithelium. Uropathogens also produce toxins, haemolysin and colony-necrotizing factor, which disrupt epithelial integrity and permit bacterial invasion.

### Pathogenesis of infection

In most cases the uropathogens originate in the rectal flora and colonization of the perineum and periurethral area precedes the development of infection. Colonization is inhibited by the normal bacterial flora, including *Staph. epidermidis*, lactobacilli and corynebacteria, which are disrupted by antibiotics and post-menopausal oestrogen deficiency. Uropathogens then use their fimbrial adhesions to ascend through the urethra to the bladder and kidney. The shorter length of the urethra and the proximity of the urethral meatus to the perineum explain the higher rate of infection in women.

Several factors are associated with risk of infection, including sexual activity, the use of a diaphragm and spermicide-based contraception, and a history of previous or recurrent UTI (Table 2).<sup>2</sup> Fifty per cent of women presenting with UTI will have a maternal history of UTI. Although associations between UTI and some genes (blood group secretor status and interleukin 8 receptor) have been reported, genetic factors influencing UTI risk are not fully understood.

### Complicated UTI

Complicated UTI occurs if there is an anatomical or functional abnormality of the renal tract (Table 1). The normal host defence is disturbed, so the requirement for virulence factors is reduced

### Risk factors for urinary tract infection

Female > male  
 Complicated urinary tract anatomy  
 Incomplete bladder emptying  
 Recent or recurrent UTI  
 Sexual intercourse  
 Diaphragm and spermicidal contraception  
 Disruption of normal bacterial flora  
*Recent antibiotic use*  
*Post-menopausal alteration in vaginal flora*  
 Pregnancy  
 Family history of UTI  
 Non-secretor status (P blood group antigen)

**Table 2**

and the spectrum of pathogens increases. Disruption of the normal flow of urine or a foreign body within the urinary tract are the most frequent associations. Management should include treatment of the acute infection and, when possible, reversal of the underlying pathology.

### Clinical features of UTI

Colonization of the urinary tract, usually defined as  $>10^5$  bacteria/ml in freshly voided urine, causes a spectrum of clinical presentations. UTI, particularly in children and the elderly, may not present with typical symptoms and the diagnosis can easily be missed.

*Asymptomatic bacteriuria* is the presence of  $>10^5$  bacteria/ml of urine on two occasions in the absence of other features of infection. Asymptomatic bacteriuria increases the risk of developing symptomatic UTI; 8% of women with asymptomatic bacteriuria develop a symptomatic UTI within 1 week. In most circumstances asymptomatic bacteriuria does not require treatment. As it has limited prognostic significance, antibiotic use is unnecessary and the recurrence rate is high. However, in pregnant women<sup>3</sup> asymptomatic bacteriuria is associated with an increased risk of pyelonephritis and low birth weight, so screening and treatment are indicated.<sup>3</sup> Screening is also often performed before urological intervention.

**Cystitis.** Bladder infection is the most common form of UTI. It typically presents with dysuria, frequency, urgency, suprapubic pain, haematuria and offensive or cloudy urine. Typical symptoms, when present, are sufficient to diagnose cystitis. Systemic symptoms such as fever, nausea and vomiting can occur.

**Pyelonephritis.** Infection involving the renal parenchyma is usually due to ascending infection from the bladder. In addition to local symptoms (loin pain, haematuria and possibly symptoms of cystitis (50% of cases)), systemic symptoms and signs are common and frequently severe, with fever, rigors, vomiting and septic shock. CRP and ESR are often raised and blood cultures are positive in 20% of cases.

Although infection is normally focal, diffuse infection causing renal failure can occur. Severe infection can cause papillary necrosis, particularly in patients with diabetes mellitus, who are also especially susceptible to emphysematous pyelonephritis if infection is with a gas-forming organism (often *E. coli*, a

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