

# Management of recurrent urinary tract infections in adults

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## Abstract

Many women will experience one or more urinary tract infection (UTI) during their life. The most unfortunate will have numerous. They can occur at all ages, and bring significant morbidity and disruption to daily activities. Men presenting with infections, and women with recurrent episodes require further investigation. A diagnosis of a UTI is often based on a typical spectrum of symptoms, with confirmatory urine cultures lagging a few days behind. Unfortunately, symptoms of a UTI may not be typical, and other conditions can manifest similarly. Treatment of UTI with antibiotics is usually required, but there is an increasing awareness of the need for antimicrobial stewardship to avoid the misuse and overuse of antibiotics, even as patients are increasingly reluctant to take them. For patients experiencing recurrent UTI, each recurring infection can be very burdensome yet investigations rarely demonstrate a reversible cause. There are a host of different interventions, both antibiotic and non-antibiotic that aim to reduce the likelihood of further infections, however these are not reliably effective, bring side effects of their own and are often proposed to this desperate population of patients on the back of weak evidence of efficacy.

**Keywords** Antibiotics; D-mannose; immunomodulators; prophylaxis; recurrent UTI; uropathogenic; vaginal oestrogens

## Introduction

Urinary tract infections (UTIs) are the most commonly encountered bacterial infections in healthcare with a spectrum of presentation ranging from benign symptoms of dysuria to life-threatening pyelonephritis. The majority of infections occur in women (80%) and approximately 30% of 20–40 year old females report at least one episode of UTI requiring treatment. Six percent of all GP consults relate to urine infections and culture of a mid-stream urine sample is the most common microbiological test. Thus they are burdensome to patients and the healthcare system alike. Between 30% and 44% of women who have one infection will have a recurrence, often within 3 months. Multiple recurrences will tend to cluster around an initial infection. Observational studies have found an average recurrence rate of 2.6 infections per year.<sup>1</sup>

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## Diagnosis and definitions

Lower urinary tract infection typically presents with dysuria, urinary frequency and suprapubic pain. Other features can include nocturia, urgency, urge incontinence, strangury (further pain after voiding), offensive urine, a 'bearing down' heaviness in the pelvis, the constant sensation of needing to pass urine, generalized malaise and/or visible haematuria. A history of fever, rigours and loin pain (which can be unilateral) should raise the suspicion of infection that has ascended to the kidneys. The presentation may be atypical in the elderly, with confusion, worsening mobility and more systemic malaise. In men, a UTI can precipitate acute urinary retention.

Women presenting with classical symptoms are 90% likely to have a urine infection, and can be treated empirically without requiring a urine dipstick. In a study where women with frequency and dysuria but negative urine dipsticks for nitrites and leucocytes, were given antibiotics regardless, 75% had a faster resolution of symptoms. If treatment is withheld until urine culture results are available, each UTI episode is associated with on average 6.1 days of symptoms, 2.4 days of restricted activity, 1.2 days of not attending work or school, and 0.4 days of bed rest.<sup>2</sup>

When symptoms are less typical urine can be tested. This should be a clean catch of the urine from the middle of the void to avoid contamination from urethral and peri-urethral flora. There is no need to clean the vulva/penis prior to urine collection. If the dipstick is positive to either nitrites or leukocytes this increases the probability of UTI to about 80% while a dipstick negative to both nitrites and leukocytes reduces the probability of UTI to about 20%.

Urine culture identifies the causative organism and local resistance trends, A threshold of  $10^4$  colony forming units (cfu)/ml is generally accepted as indicative of UTI, so samples with fewer cfu may be reported as 'no significant growth'. However symptomatic women with  $10^2$  cfu/ml and symptomatic men with  $10^3$  are also likely to have a UTI. The most common responsible organism is *Escherichia coli* in up to 85% of cases and the majority of these are uropathogenic *E. coli* (UPEC). This is a group of *E. coli* strains, distinct from faecal commensal *E. coli* found in the gastrointestinal tract, with additional genes and virulence factors encoded in their genomes that facilitate infection of the host urinary tract.<sup>3</sup> Other frequently identified pathogens are listed in Table 1 which are often found as part of the vaginal and bowel flora and retrograde passage of organisms up the urethra is thought to precede infection. In 2007, however, intracellular bacterial communities were first reported in human urothelium suggesting a potential intravesical reservoir of bacteria though the clinical significance of these and how to eradicate them is not known.

Urine should be cultured in men, pregnant women, and in women with recurrent UTIs or those with a rapid return of symptoms after antibiotics. It is also necessary when pyelonephritis or prostatitis is suspected and in complicated patients (see Table 2).

In women with recurrent UTI it is important to find out what they interpret as a new infection and the response of symptoms to antibiotics (which should resolve acute symptoms within 1–2 days if appropriate for the organism). Also, to clarify the number

### Typical pathogens causing UTI

Acute community acquired uncomplicated UTIs	Acute hospital acquired complicated UTIs
<i>E. coli</i> and coliforms (85% of cystitis, 60% of recurrent infections)	<i>E. coli</i> and coliforms (majority)
<i>Staphylococcus saprophyticus</i> (10%)	Gram positive organisms more common
<i>Klebsiella</i> sp.	Polymicrobial (33% of elderly women)
<i>Enterobacter</i> sp.	<i>Klebsiella</i> sp.
<i>Proteus</i> sp.	Group B streptococci
<i>Enterococci</i> sp. (8% recurrent UTI)	<i>Enterococci</i> sp.

Table 1

### Definitions of terms describing urinary infections

Recurrent UTI	At least two episodes in 6 months or 3 in 12 months
Relapsing UTI	Repeat UTI within 2 weeks of previous UTI with same pathogen
Re-infection UTI	UTI occurring more than 4 weeks after previous UTI with a different pathogen
Asymptomatic bacteriuria	Presence of bacteriuria in urine revealed by culture or microscopy in the absence of typical symptoms of lower or upper UTI. Increasingly common in those over 65 and in catheterized patients. Treatment contributes to resistant strains so only treat in pregnancy, pre-instrumentation and complex patients
Uncomplicated UTI	Typical lower urinary tract symptoms in women with a normal, unobstructed genitourinary tract, no recent instrumentation, and symptoms confined to the lower urinary tract
Complicated UTI	Structural or functional genitourinary tract abnormality e.g. catheterization, stones, vesico-ureteric reflux, incomplete emptying Impaired host defences e.g. pregnancy, diabetes, immune-suppression, impaired renal function

Table 2

and timings of infections to distinguish between a single relapsing infection and a re-infection. Scrutiny of all past urine culture results is useful.

The history must include their urinary symptoms between infections, menopausal status, duration of antibiotic courses, sexual history, relevant co-morbidities such as diabetes, medication (for drugs that cause immunosuppression or impair emptying such as psychotropics) and allergies. Examination must exclude renal angle tenderness and a palpable bladder. In women a pelvic exam allows assessment for post-menopausal vulvovaginal atrophy, pelvic organ prolapse and the presence

of a urethral diverticulum or peri-urethral cysts. In men the genitalia must be examined for phimosis and epididymo-orchitis and the prostate to assess size and tenderness.

### Differential diagnoses

In younger patients, especially those under 50 consider sexually transmitted diseases such as gonococcal and non-gonococcal urethritis, trichomonas and chlamydia. Genital candidiasis and bacterial vaginosis can also cause dysuria and are more likely after antibiotic use. Other conditions with overlapping symptoms are acute pyelonephrosis, overactive bladder, bladder pain conditions, bladder cancer, bladder stones, urethral diverticulum, genital herpes and vulval skin conditions such as lichen sclerosis or vulvovaginal atrophy. Prostatitis can occur at any age and requires 4–6 weeks of antibiotics to clear the soft tissue infection which can act as a reservoir for relapsing infections. Culture of expressed prostatic secretions obtained at prostate massage can help identify an organism.

### Treatment strategy for managing a recurrent UTI

The first priority for the patient attending clinic is to exclude or treat any current symptomatic infection to achieve a sterile urinary tract. Secondly to investigate for any risk factors for UTI, and thirdly to prevent subsequent infection. There are a number of strategies for this, both antibiotic and non-antibiotic based that can help. It is not always clear which will be of most benefit to the individual, and often a trial period using any one preventative measure is required. The length of the trial period will depend on the frequency of infections.

### Antibiotics for symptomatic UTI

Choice of antibiotic should be guided by knowledge of local microbial sensitivities, urine culture results and patient allergies and contraindications. The same antibiotic protocols can be used for the initial and recurrent episodes. The duration will depend on the site of the infection being treated and the response of symptoms to treatment. For uncomplicated UTI in women, 1 day of antibiotics is insufficient, and 3 days of treatment is similar to 5–10 days for resolution of symptoms, though the longer courses more reliably achieve bacteriological cure.<sup>4</sup> Longer 10–14 day courses are required in pyelonephritis. Suggested antibiotics are given in Table 3. Women on the contraceptive pill can be reassured that there is no interaction with antibiotics, and they need take no extra precautions. Where uncertainty exists, it is useful to send a repeat urine culture 1–2 weeks after stopping a course of antibiotics.

### Investigations

Patients often ask why they keep getting infections, and for the majority, there is no obvious cause. Investigations look for risk factors that predispose to infection, which can be divided into host factors and pathogen factors. The healthy young woman with post-coital UTI is unlikely to have positive findings, but men and those with accompanying haematuria, loin pain and renal insufficiency merit further assessment.

Host factors may not always be modifiable – such as immunosuppression or incomplete emptying – but should be

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