

URINARY TRACT INFECTIONS

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ABSTRACT

Urinary tract infections are common clinical problems which result in significant morbidity and even mortality. UTI's can range from minimal disease to life-threatening sepsis and it is important to differentiate between the former which usually involves the lower urinary tract and the latter which invariably involves the upper urinary tract.

Diagnosis depends on an abnormal urine microscopy and demonstration of bacteria in the urine. Pre-therapy urine cultures are not mandatory in young women with uncomplicated UTI and many studies support the efficacy of short-course therapy in this group of patients.

For other patients, microbiological and radiological investigations are required and there is insufficient data to support short course therapy in these patients.

Treatment guidelines are different in special situations such as prostatitis, pregnancy, catheter-related infection and recurrent infections.

Keywords: urinary tract infection, short-course therapy, prostatitis, catheter-related bacteriuria, recurrent infections

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Urinary tract infections (UTI) are common clinical problems, resulting in substantial morbidity and mortality. It is estimated that 10-20% of all women will suffer acute infection of the urinary tract at some point in their lifetime.⁽¹⁾

The term "UTI" encompasses a whole range of different clinical syndromes ranging from life-threatening sepsis to an asymptomatic state where disease is not apparent.

UTI are usually divided into "upper" and "lower"⁽²⁾. This distinction is helpful not only in defining the anatomical site of infection but also in assessing severity and hence deciding on management.

Lower UTI results from infection of the bladder and/or the urethra. Dysuria is the symptom most often associated with lower UTI although it can also be caused by other conditions. (See Table I). Other symptoms include frequency, nocturia, urgency, pelvic or suprapubic pain and haematuria.

Upper UTI results from infection of the kidney or perinephric space, sometimes accompanied by bacteremia. Characteristic features would be that of flank pain, tenderness in the renal angle and systemic complaints of fever, chills, nausea and vomiting. Symptoms of lower UTI may also be present.

UTI are sometimes divided into "uncomplicated" and "complicated"^(3,4). "Uncomplicated" UTI occur in young women who do not have structural or functional urologic problems. "Complicated" UTI includes all infections in males and children, hospitalised patients or those with chronic indwelling catheters, and women who have recurrent infections. All children should be investigated even with a first episode of UTI to exclude congenital abnormalities. Patients with "complicated" UTI are at greater risk of persistence or recurrence of infection, as well as infection

Table I – Differential diagnosis of dysuria

Bacterial cystitis
Bacterial cystitis with "subclinical pyelonephritis"
Urethritis due to sexually transmitted disease
Vulvo-vaginitis
Sterile pyuria
Non-inflammatory causes

with more resistant organisms, and therapy for this group of patients is necessarily more prolonged than for the "uncomplicated" group.

INVESTIGATIONS

Investigations for UTI can be divided into those for establishing the diagnosis and others for eliciting underlying abnormalities. The diagnosis of UTI is supported by the presence of pyuria and haematuria, as well as documentation of bacteria in bladder urine. The presence of pyuria is sensitive but not specific of UTI. Other causes for pyuria should be sought in the absence of symptoms suggestive of UTI. (Table II).

Haematuria, either microscopic or gross, may be present in UTI. However, red blood cells can also be seen in calculi, tumours, glomerulonephritis, vasculitis and renal tuberculosis.

Demonstration of bacteria in a urine specimen would aid in diagnosis of UTI, with 1 bacterium per oil-immersion field from a clean-catch specimen equivalent to > 100,000 cfu/ml.

Rapid tests for detecting urinary leucocytes ("dip-stick" method) and bacteria (test for the presence of nitrite) are often used in the office management of UTI. However, they are generally less sensitive than conventional methods⁽⁵⁾.

Traditionally, the quantitative count of >100,000 cfu/ml

Table II – Causes of pyuria (other than bacterial UTI)

Calculi
Renal tuberculosis
Interstitial nephritis
Papillary necrosis

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of urine has been taken as the cut-off value differentiating between contaminated and infected urine. These criteria however apply only to *Enterobacteriaceae*, while Gram-positive organisms, fungi and bacteria with more fastidious growth requirements may not reach such titres even with infection. Recent studies have shown that a third of women with UTI caused by *E. coli*, *S. saprophyticus* and *Proteus* have colony counts between 100 and 1000 cfu/ml⁽⁶⁾. In men where contamination is less likely, >10,000 cfu/ml may be indicative of infection.

Although many authorities recommend that urine cultures be done to allow precise identification of infecting organism and testing of antibiotic susceptibility, in practice, treatment is often begun without the results of such cultures and a cost-effectiveness study has shown that routine pre-therapy culture would add 40% in costs while only reducing duration of symptoms by 10%⁽⁷⁾.

In a young woman with typical features of uncomplicated UTI and pyuria, pre-therapy urine cultures may not be necessary.

MICROBIOLOGY

The causative organisms in acute urinary tract infections are usually different from that seen in chronic or recurrent infections. *E. coli* is the most frequent bacteria isolated in cases of acute UTI. In contrast, the frequency of other Gram-negative bacteria such as *Proteus*, *Klebsiella* and *Enterobacter* as well as *Enterococci* and *Staphylococci* increases in patients who have obstructive lesions or congenital anomalies. In such circumstances infections may be polymicrobial. Anaerobes are, however, a rare cause of UTI.

Hospital-acquired UTI, especially with the presence of indwelling catheters would be different from community-acquired UTI in terms of bacterial flora and antibiotic resistance patterns.

Radiological investigations are required when the clinician suspects underlying structural abnormalities or when infection is complicated by development of abscess formation. Plain X-rays of the kidney, ureter and bladder may help to define the presence of stones, other calcifications, soft tissue masses or abnormal gas collections. Intravenous urograms remain useful for delineating abnormalities of the collecting system, though ultrasonography and CT scanning are better for defining changes in the parenchyma and surrounding retroperitoneum.

TREATMENT

"Uncomplicated" UTI

Various studies⁽⁸⁻¹⁰⁾ have shown the efficacy of short-course therapy for acute cystitis in women. Single-dose therapy with an appropriate antibiotic is cheaper and has fewer side effects than longer courses of therapy and is almost as effective⁽¹¹⁾. However, there are concerns regarding the use of single-dose therapy in special groups such as pregnant women, diabetics and patients with other immuno-suppressive conditions, all of whom are more likely to develop complications if infection is not eradicated⁽¹²⁾.

A three-day course of antibiotics has been shown to be as effective as 10 days, and yet have an incidence of side effects as low as single dose therapy^(13,14). Drugs used for short course therapy include

- a) Trimethoprim-sulfamethoxazole (4 normal strength

tablets as a single dose or 2 tablets bd for 3 days). Trimethoprim (400 mg single dose or 100 mg bd for 3 days) alone is just as efficacious as TMP-SMX and is associated with less side effects because of absence of the sulphur component.

- b) Nitrofurantoin (200 mg single dose or 100 mg 6 hourly for 3 days)
- c) 1st generation cephalosporin (2g single dose or 500 mg 6 hourly for 3 days)
- d) Quinolones such as ciprofloxacin and norfloxacin⁽¹⁵⁻¹⁷⁾.

Amoxycillin (3 gm single dose or 500 mg 8 hourly for 3 days) or ampicillin (3.5 gm single dose or 500 mg 6 hourly for 3 days) can be used in community-acquired UTI if the incidence of resistance of *E. coli* to ampicillin is low.

Upper UTI can be divided into 1) mild acute pyelonephritis which can be treated at home if the patient can take oral therapy, 2) more severe pyelonephritis where the patient requires hospitalisation for parenteral therapy, and 3) complicated cases where surgical procedures may be required in addition to antibiotics.

It is advisable to establish the infecting organism and its susceptibility profile so that therapy can be narrowed down from initial broad-spectrum antibiotics. Duration of therapy is usually 14 days for uncomplicated pyelonephritis.

Complicated upper UTI include pyonephrosis where infected hydronephrosis is associated with suppurative destruction of the kidney, renal carbuncle where there is collection of purulent material in the renal parenchyma, or perinephric abscess which usually results from rupture of a cortical abscess into the perinephric space⁽¹⁸⁾. In such situations, medical therapy is unlikely to be sufficient, and drainage may be required either through the percutaneous route or with open surgery.

SPECIAL SITUATIONS

Prostatitis

Prostatitis may be acute or chronic. Acute bacterial prostatitis presents with high fever, chills, low back or perineal pain, frequency, dysuria, urgency and varying degrees of bladder outlet obstruction. Rectal examination reveals a warm, swollen and tender prostate. Bacteria can be found in the urine as well as prostatic fluid but prostatic massage can precipitate bacteremia and should not be done unless the patient has had adequate serum levels of appropriate antibiotics. The usual organisms are Gram-negative enteric bacteria. Acute bacterial prostatitis usually responds dramatically to antibiotics which diffuse from the plasma into prostatic tissue with the intense inflammatory reaction, rather like in meningitis⁽¹⁹⁾.

Chronic prostatitis is a completely different syndrome from acute prostatitis. Acute prostatitis does not usually progress on to the chronic form, nor does chronic prostatitis arise from acute prostatitis. Chronic prostatitis may be caused by bacteria, usually Gram-negative enteric organisms or by agents such as Chlamydia.

Patients with chronic prostatitis may be relatively asymptomatic or have urinary frequency and urgency, perineal aching or low back pain. The prostate may have small calculi or abscesses which serve as the nidus of infection and give rise to relapses of UTI. As few antibiotics penetrate well into non-inflamed prostatic tissue, chronic prostatitis can be difficult to cure. Recent literature^(20,21) suggest that

fluoroquinolones though significantly more expensive than trimethoprim-sulphamethoxazole, may have better results in patients with chronic bacterial prostatitis, even in those who have failed prior therapy. Patients who fail prolonged courses of antimicrobial therapy may benefit from prostatectomy.

Pregnancy

During pregnancy physiologic alterations occurring in the urinary tract predispose the expecting female to UTI. There is dilatation of the ureters and renal pelvis, as well as reduction in ureteral peristalsis and bladder tone.

About a third of patients with bacteriuria early in pregnancy will develop acute pyelonephritis later in the antenatal course⁽²²⁾ and premature delivery has been found to be associated with pyelonephritis⁽²³⁾.

Because of this, evidence of bacteriuria should be sought from the first antenatal visit, even in the asymptomatic patient, and treated. Cultures should be repeated at regular intervals eg monthly, to monitor recurrences. The goal of therapy is to maintain sterile urine throughout pregnancy, using drugs that are non-toxic to the foetus such as ampicillin, cephalixin or nitrofurantoin.

Catheter-associated bacteriuria

The rate of acquiring bacteriuria after a single in-and-out catheterisation ranges from 1% to 20% depending on host factors and technique of catheterisation. In indwelling catheters, the risk of acquiring bacteriuria is between 3% to 6% per day⁽²⁴⁾.

The majority of hospitalised patients with indwelling catheters and bacteriuria are asymptomatic and need not be treated unless there are risk factors for bacteremia or ascending infection. Such risk factors would include neutropenia, immunosuppressive therapy, obstruction of the urinary tract and pregnancy.

Whenever possible, patients with neurogenic bladders should be managed with intermittent catheterisation rather than chronic catheterisation.

Bacteriuria occurs in essentially all patients with chronic indwelling catheters. Most of these bacteriuric episodes are asymptomatic but upper UTI with associated bacteremia can occur. Prevention of infection in such patients is difficult. Treatment of asymptomatic bacteriuria does not affect the frequency or natural history of infection, but may instead, lead to infection by resistant strains. Current recommendations would be to treat only clinically apparent infection.

RECURRENT INFECTIONS

Patients with recurrent infections should be investigated for structural lesions. There is a group of patients who continue to have relapses of infection even in the absence of urologic abnormalities. In the premenopausal women, sexual intercourse has been shown to have a direct temporal association with acute cystitis and studies have shown the effectiveness of post-coital voiding⁽²⁵⁾ and post-coital use of antibiotics in preventing UTI⁽²⁶⁾.

About 10% to 15% of women over 60 years suffer from frequent urinary tract infections⁽²⁷⁾. The pathogenesis in these patients is thought to be due to changes in the vaginal flora resulting from reduction in circulating oestrogens. *Lactobacilli* are replaced by organisms such as *E. coli* and such colonisation may be a source for subsequent UTI.

A few studies have shown that oestrogen replacement

either orally⁽²⁸⁾ or topically^(29,30) may reverse changes in vaginal pH and reduce the frequency of UTI.

ASYMPTOMATIC BACTERIURIA

Bacteriuria is common in the elderly. Various studies have failed to show that treatment of asymptomatic bacteriuria reduces the incidence of symptomatic UTI, bacteremia or death^(31,32). Repeated therapy with short courses of antibiotics predisposes to development of antibiotic resistance⁽³³⁾.

CONCLUSION

Urinary tract infections continue to be major causes of morbidity and mortality in both community-acquired and hospital-acquired infections. It is important to recognise the groups which do not benefit from therapy as well as situations where extensive investigations and aggressive therapy are required.

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