

CONFERENCE REPORT

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Urinary Tract Infection

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(Chairman of the Symposium)

In this article, important and practical points regarding the pathogenesis, diagnosis and management of urinary tract infections (UTI) in adults and children will be discussed. This report is mostly a consensus statement based on the subjects presented at the symposium supplemented by the author's preferences and opinion where specific points were not covered during the meeting. The speakers and their respective topics were:

Microbiology:	Dr Paul Cuschieri
Imaging:	Dr Anthony Samuel
UTI in children:	Dr Simon Attard-Montalto
UTI in women:	Dr Isabelle Saliba
UTI in the elderly:	Dr Stephen Abela
UTI in general practice:	Dr Philip Sciortino
Surgical aspects of UTI:	Mr Steve Mattocks

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UTIs can be classified as uncomplicated or complicated. Due to their very different aetiology, pathogenesis and management, uncomplicated and complicated UTIs will be discussed separately.

Uncomplicated urinary tract infections aetiopathogenesis

Uncomplicated UTI occurs in patients without physiologic or anatomic abnormalities of the urinary tract and in the absence of recent urological surgery or instrumentation. There is no evidence that this type of UTI causes any long-term detrimental effect on renal function. Acute uncomplicated lower tract infection (cystitis) and/or upper tract infection (pyelonephritis) are community-acquired. UTI has been reported to account for 1-3% of general practice consultations and almost all occur in women between the ages of 18 and 40. Nearly 50% of all women will have symptoms of UTI at some stage during their lives. Uncomplicated UTIs are rare in males, although recent studies suggest that uncircumcised infants and adult homosexual males may be at increased risk. In young males, uncomplicated UTI may occasionally spread from the bladder to the prostate (acute prostatitis) or to the epididymis (acute epididymitis), but such cases are also infrequent.

80% of UTIs are due to *Escherichia coli*, and the rest due to *Staphylococcus saprophyticus*, *Proteus* and *Klebsiella*. Both bacterial and host factors are important in predisposing to acute uncomplicated UTI. By possessing specific virulence factors such as fimbriae or production of haemolysin, certain strains of *E. coli* are rendered more uropathogenic. Some women may be predisposed to recurrent UTI because their uroepithelium has an increased number of receptors for *E. coli*, a trait that may be genetically determined. Behavioural factors

such as sexual intercourse, not voiding after intercourse, postponing voiding, and diaphragm and/or spermicide use increase the risk of acute UTI.

Clinical manifestations and differential diagnosis

Typical symptoms of cystitis include dysuria, frequency, urgency, voiding of small volumes, and suprapubic pain. Foul-smelling or cloudy urine is frequently described and gross haematuria may develop in up to one-third of patients. Besides acute cystitis, acute dysuria can be secondary to either acute vulvovaginitis (caused by candidal, trichomonal or bacterial infection) or acute urethritis (due to *Chlamydia trachomatis*, gonococcus or herpes simplex virus). Pointers to bacterial cystitis include a sudden onset of symptoms, absence of vaginal discharge or odour, absence of cervical tenderness, and the presence of gross or microscopic haematuria. Acute urethral syndrome refers to a syndrome in females characterised by frequency, dysuria and usually, a sterile culture. Most of these cases are acute cystitis with a low bacterial count; others represent *Chlamydia urethritis*, but in a significant minority, no cause can be found.

Acute pyelonephritis characteristically presents with localised flank pain accompanied by fever, chills, sweats, headache, nausea, vomiting and malaise. Symptoms of lower UTI may or may not be present. Approximately 20% of patients with uncomplicated UTI have positive blood cultures. Acute pyelonephritis must be differentiated from other intra-abdominal conditions such as pelvic inflammatory disease, appendicitis, ectopic pregnancy or ruptured ovarian cyst.

Asymptomatic bacteriuria is common in sexually active women, in whom the prevalence is approximately 5%. The prevalence of asymptomatic bacteriuria in the

elderly population rises to 30% in both sexes.

Diagnosis

Careful microscopy of fresh unspun urine, collected by the 'clean catch' method, shows pyuria (more than 10 neutrophils per high power field) in essentially all cases of acute cystitis. Additionally, up to 50% may have microscopic hematuria. The leucocyte esterase dipstick can also be used to rapidly screen a urine specimen for pyuria but is less sensitive than a microscopic examination. Culture of midstream urine, either by the loop-method in hospital or the dip-slide in general practice, will generally demonstrate the aetiological bacterial agent in concentrations greater than 100,000 colony forming units (CFU)/ml. However, bacteriuria may be low (e.g. 10,000 CFU/ml) yet significant, especially when the patient is drinking copiously or was already treated with antibiotics.

Treatment

Women with acute uncomplicated cystitis should, generally, be empirically treated with a 3-day course of trimethoprim or trimethoprim-sulphamethoxazole. Nitrofurantoin and beta-lactam drugs are also effective but do not eliminate *E. coli* from the vaginal introitus and urethra. Fluoroquinolones such as norfloxacin or ciprofloxacin are more expensive and should be reserved for patients with recurrent infections, treatment failures, drug allergies or drug resistance. Single-dose therapy results in higher recurrence rates and is thus not recommended. In non-pregnant women, asymptomatic bacteriuria is not treated.

Seven-day regimens and a pre-treatment urine culture can be reserved for patients with factors that may result in lower rates of cure with shorter regimens. These factors include: pregnancy (amoxicillin and macrocrystalline nitrofurantoin are the drugs of choice), diabetes mellitus, age more than 65 years, symptoms for more than a week, use of diaphragm and recent UTI.

Patients with uncomplicated pyelonephritis can be safely treated outside hospital provided they have no vomiting, no evidence of septicaemia, are reliable, are not pregnant and have a clear-cut diagnosis. High fluid intake, antipyretics and analgesics are used as required. Fourteen days of a fluoroquinolone is a suggested antimicrobial regimen. For inpatients, a suitable regimen includes an intravenous third generation cephalosporin until the fever is gone, then oral fluoroquinolone for 14 days. If fever and flank pain persist after 72 hours of therapy, cultures should be repeated and ultrasonography or CT scan should be performed to seek perinephric or intrarenal abscesses, unrecognised urologic abnormalities, or obstruction.

Acute uncomplicated cystitis responds to effective initial treatment in over 90% of cases. The remainder respond either to a second course of treatment or to more prolonged therapy. Twenty percent of women develop a pattern of frequent recurrences, characterised by episodes occurring as often as once per month. A high fluid intake, frequent and complete voiding, including double micturition and voiding immediately after intercourse, should be encouraged in all women. Three antibiotic strategies exist to treat this subset of patients.

Firstly, women with infrequent infection (e.g. 3 UTI or less per annum) could initiate 3-day therapy themselves. Women with frequent episodes of cystitis should be given low-dose antimicrobial prophylaxis, such as trimethoprim (100mg/day), trimethoprim-sulphamethoxazole (1/2 single strength tablet/day), nitrofurantoin (50mg/day), or cephalexin (250mg/day). If the women can temporally relate their recurrent UTI to intercourse, the antibiotic could be taken only after sexual intercourse. If, however, the UTIs are not related to coitus, daily or thrice weekly prophylaxis is recommended. In postmenopausal women, topically applied oestrogen may also be an effective means of prevention.

Complicated urinary tract infections aetiopathogenesis

The vast majority of complicated UTIs occur in older men and women. Obstruction to urine flow, for example due to prostate hypertrophy and urinary calculi, or other functional abnormalities of the urinary tract impair the normally efficient ability of the bladder to eliminate bacteria. Instrumentation of the urinary tract, particularly catheterization, provides a portal of entry for bacteria and also makes it more difficult to eradicate bacteria with antibiotics. Vesico-ureteric reflux may facilitate the ease with which bladder bacteria can ascend to the kidney, producing pyelonephritis. Pregnancy induces hydroureter, bladder enlargement and urinary stasis. These, and other broad spectrum clinical conditions encompassed by the terms complicated and hospital-acquired UTIs are caused by a much broader spectrum of bacterial species than that seen in uncomplicated UTIs. These organisms generally exhibit more antimicrobial resistance than those causing uncomplicated UTIs, and include *E. coli* (still the most common), *Proteus*, *Providencia*, *Serratia*, *Klebsiella*, *Pseudomonas*, *Enterococci*, and *Staphylococcus aureus*. *Candida* infections can be seen in catheter-associated infections, in diabetics and in immunosuppressed patients.

Clinical manifestations and differential diagnosis

Manifestations range widely from asymptomatic bacteriuria (common in catheter-associated infections and in the elderly, especially in nursing homes) to gram-negative septicaemia. The hallmark of acute cystitis or pyelonephritis in the complicated setting is their lesser responsiveness to antibiotic treatment and their tendency to recur after therapy. In hospitalised patients who develop fever and hypotension, the urinary tract should be suspected as a possible source despite the absence of urinary symptoms, especially in patients with recent instrumentation or catheterization.

Diagnosis

In symptomatic patients, urinary microscopy and culture should be used to confirm the presence of infection as described for uncomplicated UTI. In asymptomatic bacteriuria, at least two cultures growing the same organism (>100,000 CFU/ml) should be obtained to confirm the diagnosis. Depending on the clinical circumstance, CT scanning, ultrasound, or

intravenous urography may be useful in demonstrating the nature of the urologic abnormality or obstruction.

Treatment

Asymptomatic bacteriuria in the patient with a urinary catheter, as well as in the elderly non-catheterised patient, should ordinarily not be treated. Treatment in such patients should be instituted if clinically apparent infection arises or in special circumstances such as pregnant women, patients who are undergoing prostatic surgery or other urologic procedures, are neutropenic or have a renal transplant. All pregnant women should be screened for bacteriuria in the first trimester, and if present, bacteriuria should always be treated to reduce their markedly increased risk of acute pyelonephritis and premature labour. Screening for asymptomatic bacteriuria is unnecessary in adults, except in the selected circumstances listed immediately above.

For septicaemia in hospitalised patients, empirical therapy with a broad-spectrum antibiotic, such as ceftazidime (third generation cephalosporin with antipseudomonas activity) is given until the offending organism is identified; alternatives are iminipenem-cilastin/meropenem, given for at least 10 to 14 days. In patients who can be managed outside hospital, oral fluoroquinolones can be given for 7 to 21 days, depending on the clinical circumstance. Post-treatment urine cultures are mandatory.

Underlying anatomic, functional or metabolic defects need to be corrected whenever possible. Calculi are removed by extracorporeal or percutaneous lithotripsy or open surgery. As the prevalence of infection increases with the duration of catheterization, indwelling catheters should always be removed as soon as possible.

Urinary tract infection in infancy and childhood

UTI in infancy and childhood merits special consideration as it can interfere with kidney function and growth. Prompt diagnosis and treatment of infections in this age group have been shown to diminish the incidence of reflux nephropathy (formerly called chronic pyelonephritis), hypertension and end-stage renal failure later on in life.

Clinical presentation is variable, ranging from life-threatening septicaemic shock through a variety of symptoms, frequently unrelated to the urinary tract, to asymptomatic infection which may be detected incidentally or on screening. Infants may present with failure to thrive, feeding problems, fever, convulsions, diarrhoea, screaming attacks and offensive urine. Given the non-specific symptoms, it is important not to overlook UTI by culturing the urine of every sick infant or toddler if illness or fever persists for more than 24 hours. Above two years of age, children often have frequency, dysuria, haematuria, cloudy urine, enuresis, abdominal pain and fever.

Swift and accurate diagnosis of UTI, particularly in infancy, is extremely important. Ideally, the urine should be cultured as soon as the specimen has been passed or, alternatively, cooled to 4°C to prevent bacteria multiplying prior to being plated on culture media. The child's perineum should be washed with soap and water and dried with a clean paper towel, but antiseptic solutions should be avoided. Urine samples can be collected clean-catch (infants often micturate after having their clothes removed and during examination of the abdomen), via adhesive plastic bag or suprapubic aspiration, preferably under ultrasound control.

Children with UTI should be investigated in order to identify or exclude cases of vesico-ureteric reflux, obstruction, calculi, neurogenic bladder, or conditions which benefit unequivocally from intervention. It is important that tests should be used judiciously and only undertaken after appropriate guidance and counselling. All too often, children with recurrent infection consequent on host factors, or due to simple problems such as constipation and incomplete bladder emptying, are subjected to a series of ever more invasive tests in a vain quest for the elusive radiological abnormality.

Following the first UTI in childhood, investigation starts with an ultrasound of the kidneys and bladder pre- and post-micturition and a plain abdominal radiograph. In sick infants, ultrasound should be performed immediately to exclude obstruction needing urgent drainage. If the ultrasound is normal and the child is aged 7 or over, no further tests are indicated. If, however, the child is under 7 years old, a dimercaptosuccinic acid (DMSA) scan is recommended to rule out vesico-ureteric reflux or renal scarring. In infants, a micturating cystogram should also be undertaken. A cystogram is also indicated in a child over 12 months of age with recurrent breakthrough infection, clinically severe illness or established scarring. Abnormal ultrasounds should be further investigated with micturating cystography, radionuclide imaging and/or intravenous urography. Early consultation with a radiologist and paediatric surgeon is mandatory at this stage.

Treatment of acute UTI in children consists of a broad-spectrum antibiotic: an oral 5-day course for mild infection and a parenteral / oral 14-day course for severe infection. Prophylactic antibiotics (trimethoprim and nitrofurantoin, both used in a dose of 1 to 2 mg/kg/day) should then immediately be started but may be discontinued in children who have completed their investigations and no significant abnormalities have been detected. In children with vesico-ureteric reflux, dilatation and/or renal scarring, prophylactic antibiotics should be continued until the reflux resolves spontaneously. This is to reduce the risk of progressive infection and renal scarring. Reimplantation of the ureter or the suburoepithelial injection of Teflon are alternatives to prophylactic antibiotics if vesico-ureteric reflux is persistent.

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