

# URINARY TRACT INFECTIONS: CURRENT MANAGEMENT

R N Srivastava

Division of Nephrology, Department of Pediatrics, Indraprastha Apollo Hospital, New Delhi 110076, India

**Abstract :** Urinary tract infections (UTI) are common in infants and children and recur in 10-30%. UTI are often associated with a structural or functional abnormality of kidney and urinary tract. Vesico ureteric reflux may be detected in about 30% cases with the first UTI. *Escherichia coli* is the most commonly isolated urinary pathogen. Patients with malformations or dysfunction of urinary tract may become infected with other bacterial species that normally have low virulence for urinary tract such as enterococci, *Staphylococcus aureus* or *epidermidis*, *proteus*, *pseudomonas*, and *serratia* spp. UTI occurs when virulent bacteria gain access to the normally sterile urinary tract mostly by the ascending route. Incomplete bladder emptying with residual urine is a major factor in acquiring UTI. Some of the bacterial strains causing such infection may show wide antibiotic resistance. The symptoms of UTI depend on the intensity of inflammation, site of infection and age of the patient. Laboratory evaluation: careful urine analysis and urine culture are crucial. Children with symptomatic UTI should be given antibiotics without delay but after obtaining a proper urine sample. Second and third generation cephalosporins (such as cefixime) given orally or intravenously or amoxicillin + clavam are adequate for empiric therapy For confirmed or suspected pyelonephritis treatment is given for 10- 14 days. Children without symptoms of pyelonephritis are treated for 7-10 days. Further observation and imaging are considered in every case.

Urinary tract infections (UTI) are common (5-10%) in infants and children and recur in 10-30%<sup>1</sup>. The prevalence of UTI in young children having unexplained fever is between 3 to 5% (higher in premature infants than in term infants). After one year of age, the prevalence of UTI in boys decreases to about 2%, whereas in girls it increases to 8%. UTI are often associated with a structural or functional abnormality of kidney and urinary tract. Obstructive anomalies of urinary tract may be present in 2% of girls and 10% of boys with UTI. Vesicoureteric reflux may be detected in about 30% cases with the first UTI<sup>1</sup>. Eradication of UTI is difficult in such situations and recurrence is common. Serious sequelae such as renal scarring, hypertension and chronic renal failure may follow. Urine examination is often neglected in infants and young children with nonspecific symptoms and UTI go undetected. On the other hand, presumed UTIs are inappropriately treated on the basis of wrong interpretation of "routine" urine examination report (showing a few "pus cells" on microscopy).

## CAUSATIVE ORGANISMS

In acute, uncomplicated UTI, the most commonly isolated urinary pathogens are enteric Gram-negative bacteria, especially *Escherichia coli*. Patients with malformations or dysfunction of urinary tract may become infected by other bacterial species that normally have low virulence for urinary tract such as Enterococci, *Staphylococcus aureus* or *epidermidis*, *Proteus*, *Pseudomonas*, and *Serratia* spp. Fungal infection of the urinary tract may occur in pre-term babies and older immunosuppressed patients with an indwelling bladder catheter and those receiving broad spectrum antibiotics. Uropathogens are derived from the fecal flora.

## MECHANISMS OF INFECTION

UTI occurs when virulent bacteria gain access to the normally sterile urinary tract, mostly by the ascending route. Hematogenous spread may occur in neonates who have yet to develop a mature immune system and in children who are immunocompromised. Bacteria reaching the bladder multiply readily unless eliminated by defense mechanisms. Effective voiding washes out the bacteria, but some may be left in the film of urine lining the bladder epithelium. *Incomplete bladder emptying with residual urine is a major factor in recurring UTI*. In the hospital setting, urinary catheters are a major risk factor for acquisition of nosocomial infection, which increases with prolonged duration of catheterization. Some of the bacterial strains causing such infection may show wide antibiotic resistance.

## RECURRENCE OF UTI<sup>3</sup>

Recurrence of UTI is common when underlying anatomical or functional

abnormalities of kidney and urinary tract are present, most common being obstruction and vesicoureteric reflux. Voiding dysfunction is increasingly being recognized as an important cause of recurrent UTI.

### Obstruction

Children with obstructive abnormalities, whether anatomic (posterior urethral valves, ureteropelvic junction obstruction, constipation), neurologic (e.g., myelomeningocele with neurogenic bladder), or functional, are at increased risk of developing UTIs. Stagnant urine is an excellent culture medium for most uropathogens.

### Vesicoureteric reflux.

VUR is very often associated with UTI. Higher grades of VUR constitute the major risk factor for pyelonephritis and renal scarring in infants and young children.

### Uncircumcised infant.

The risk for UTI in uncircumcised boys is 5- 20-fold higher than in those circumcised, with the greatest risk being in boys below 1 year. The presence of preputial folds in uncircumcised boys encourages a high density of bacterial growth and contamination of the urethral opening. Circumcision reduces meatal contamination, thereby decreasing the ascent of bacteria into the bladder. Lack of circumcision puts the infant at a higher risk for having recurrent UTI<sup>2</sup>.

### Dysfunctional voiding.

This term refers to a lack of coordination between the detrusor and the urethral sphincter at the onset of voiding. Ordinarily, the sphincter must relax as the detrusor contracts. Failure of the sphincter to relax causes an obstruction to the outflow of urine (as does the distended rectum in constipated children). These conditions are associated with incomplete emptying of the bladder and significant amounts of residual urine.

## CLINICAL FEATURES

The symptoms of UTI depend not only on the intensity of the inflammatory reaction but also on the site of infection and the age of the patient. During the first year of life pyelonephritis is the most common presentation of UTI. Symptomatic UTI may chiefly involve the upper tract or the lower tract. Infection in a normal urinary tract with no prior instrumentation is considered "uncomplicated," whereas "complicated" infections occur in urinary tracts that have a structural or functional abnormality<sup>1</sup>.

## LOWER URINARY TRACT INFECTION

Majority of children with cystitis present with urgency, frequency and dysuria. Children who have the urge to urinate may have a history of difficulty in initiating the urinary stream. Acute voiding problems are not

synonymous with acute bacterial cystitis as they can occur with vulvitis or balanitis. Occasionally the child may complain of abdominal or suprapubic pain. Fever, if associated, is of low grade. Suprapubic tenderness may be present. Urine may be foul smelling and cloudy. It is important to note that symptoms such as urgency, frequency and dysuria can be caused by any factor or process that gives rise to inflammation in the lower urinary tract. Examples include mechanical irritation (that might result from insertion of foreign bodies, migration of pinworms) and chemical irritation (disinfectants, shampoos).

## **PYELONEPHRITIS**

During the first month of life, the symptoms are non-specific such as vomiting, poor feeding and jaundice, failure to thrive with little or no fever in about 50% cases. Beyond infancy, fever often is the only symptom of acute pyelonephritis. The characteristic features include high fever with chills and rigors, abdominal pain, vomiting and toxic appearance. A neutrophilic leucocytosis is usually present. Children usually cannot complain of loin pain until 4 to 5 years or older.

### **Clinical evaluation**

The height and duration of fever, urinary symptoms, vomiting, recent illnesses, antibiotic intake should be recorded. The following should be carefully evaluated: (1) colour, clarity and smell of urine; (2) age of toilet training; (3) characteristics and frequency of voiding (voiding frequency, urgency, squatting or other holding maneuvers, day time wetting, poor or interrupted stream, dribbling, prolonged voiding, straining during voiding); (4) presence of constipation / soiling; (5) previous UTIs; (6) previous undiagnosed febrile illnesses; (7) family history of frequent UTIs, VUR and other genitourinary abnormalities.

Physical examination includes evaluation of physical development, accurate record of blood pressure and temperature, assessment of suprapubic and costovertebral tenderness, and a search for other sources of fever. External genitalia should be examined for signs of vulvovaginitis, vaginal foreign body and anatomic abnormalities. Lower back should be examined for sinus, pigmentation, lipoma or tufts of hair and if there is suspicion of a neurological abnormality, anal sphincter tone should also be evaluated. UTI and occult bacteremia is a common cause of fever in a "well-appearing infant."

### **Laboratory evaluation**

Careful urinalysis and urine culture are crucial. Urine in the normal bladder is sterile, but may get contaminated by bacteria during the passage from bladder to the sampling container, especially in infants and small children. This often leads to a false diagnosis of UTI and the child is subjected to unnecessary treatment, investigations and follow-up. On the other hand, failure to identify the child with UTI carries a risk of progressive renal damage.

### **Collection of urine specimen**

#### **Clean Voided Bag Samples.**

Culture of a urine specimen obtained by bag is often "false positive". An infant or young child should not receive antibiotics on such a result. If urinalysis from the bag sample suggests UTI, or M/E shows > 5 white blood cells per high-power field (centrifuged specimen), or bacteria on Gram stain of uncentrifuged urine, a fresh urine sample for urinalysis and culture should be collected by invasive means.

#### **Clean catch samples**

Older children can provide clean voided urine mid-stream samples after careful cleansing and minimizing contact with skin.

#### **Suprapubic bladder aspiration**

This procedure is a safe and effective method for obtaining urine specimens in infants and young children. Ultrasound guidance improves the yield.

#### **Bladder Catheterization.**

Bladder catheterization may occasionally be resorted to. The complications

are minimal (urethral trauma and microscopic hematuria) and the risk of introducing infection is very low.

### **Dipstick tests**

Dipstick tests are useful for screening. The strip detects urinary nitrite, which is formed by bacterial reduction of nitrate, (the colour change being proportional to the number of bacteria in urine) and leucocyte esterase. If positive, treatment for UTI can be initiated while awaiting the culture result.

### **Urine microscopy**

A centrifuged sample of unstained urine is examined for the presence of bacteria and leucocytes. WBCs are measured more precisely by microscopy of uncentrifuged urine using a counting chamber; more than 10 leucocytes/ $\mu$ l in a boy and 50 in a girl are abnormal. Neutrophils are present in 80-90% of symptomatic UTI, but a urine sample without WBCs does not exclude UTI. WBCs may also be found in febrile children with infections outside the urinary tract, in inflammatory diseases other than UTI in or near the urinary tract, or due to contamination from the vagina. Phase contrast microscopic examination is greatly superior to characterize cells and formed elements in the urine and is being adopted by modern laboratories.

### **Urine culture**

Urine should be immediately refrigerated at 4°C (and not left at room temperature) until cultured, to prevent growth of contaminating bacteria. This temperature must be maintained during transport. However, the urinary leukocyte count may be altered by refrigeration, possibly affecting interpretation of the urinalysis. The interpretation of culture results depends on the method of urine collection and the clinical background. In urine obtained by suprapubic aspiration, any growth is considered significant. In urine obtained by catheterization, the level of significance is 1000 to 10,000 CFU/ml. Children with 100 to 50,000 organisms should have a fresh urine culture examination. For voided specimens, the cutoff level is 100,000 CFU/ml. In combination with acute localizing symptoms such as marked dysuria and frequency together with pyuria, one positive urine culture can be considered adequate for a diagnosis. For all patients lacking symptoms, a second sample should be obtained before antibacterial treatment is started except when suprapubic aspiration is used.

## **LOCALIZATION OF THE SITE OF INFECTION**

In a typical case of acute pyelonephritis there is little reason to attempt to localize the site of infection. High fever, chills and rigors, vomiting, neutrophilic leucocytosis, and elevated levels of C-reactive protein suggest renal parenchymal involvement. In infants and young children localization is very difficult and unnecessary. When in doubt it is more prudent to regard the UTI as pyelonephritis and manage accordingly. In pyelonephritis DMSA scan shows diminished tracer uptake, which is indicative of parenchymal involvement. The procedure may be employed to determine the site of infection in older children with absent or equivocal features of renal involvement. DMSA scan is not routinely carried out to localize the site of infection.

## **TREATMENT**

The management of children with presumed UTI depends upon a number of factors, including age of the patient, degree of toxicity, presence of vomiting, duration of fever prior to presentation, and the antimicrobial resistance patterns in the community. Children with symptomatic UTI should be given antibiotics without delay, but after obtaining a proper urine sample. Neonates and infants should be hospitalized and provided appropriate supportive care (control of fever, IV fluids).

The choice of antimicrobial therapy is based upon the severity of UTI as assessed clinically. Second- and third-generation cephalosporins (such as cefixime), given orally or intravenously, or amoxicillin+clavum are adequate for empiric therapy. Aminoglycosides are used in inpatients.

Quinolones are effective and bacterial resistance is uncommon but these are not recommended as initial agents. First generation cephalosporins and trimethoprim-sulfamethoxazole may be used in older children with lower UTI. For confirmed or suspected pyelonephritis, treatment is given for 10 to 14 days. Children without symptoms of pyelonephritis are treated for 7-10 days. Shorter courses of therapy are not recommended in children. A repeat urine culture is obtained if fever does not abate within 48 hours. Further observation UTI with urinary tract abnormalities and imaging are considered in every case.

## IMAGING MODALITIES<sup>6,7</sup>

Imaging of kidney and urinary tract is necessary to exclude any anomaly of the kidney and urinary tract, exclude obstruction and detect VUR<sup>1,5</sup>. Plain X-ray film of abdomen and I.V.P. are rarely performed.

### Ultrasonography

Renal ultrasonography detects the location, and size of the kidney, dilatation of the upper urinary tract, severe loss of renal parenchyma, and any major bladder anomaly. The procedure is inadequate for detecting VUR.

### Voiding cystourethrogram

VCUG is required to look for VUR and any abnormality of bladder and urethra. The initial procedure is the contrast VCUG, which provides clear anatomic resolution and is necessary for grading VUR. Strict aseptic precautions are necessary and an antibiotic cover is provided.

### Renal scintigraphy

DMSA or Mercurioacetylglucine (MAG3) are the agents commonly used for scanning to detect parenchymal involvement. DMSA is injected intravenously, and uptake by the kidney is measured two to four hours later. An area of decreased uptake represents an area of pyelonephritis or scarring. In children with UTI and VU reflux, the kidney having reflux is most at risk of both congenital and acquired renal damage, and this risk increases with the severity of reflux.

### Recommendations for imaging<sup>5</sup>

1. Ultrasonography should be performed in infants and young children and whenever pyelonephritis is suspected. Documenting the absence of an anomaly is also important.
2. VCUG is indicated in all children with UTI who are less than two years of age and in any child with recurrent episodes of UTI regardless of sonographic findings. In older children with a first febrile UTI, VCUG should be obtained if the ultrasound demonstrates significant abnormality.
3. DMSA scanning should be carried out in children below 2 years and preferably below 5 years to detect renal scarring. In occasional instances DMSA scanning may be performed if the diagnosis of pyelonephritis is uncertain due to equivocal urinalysis or culture results.

## MANAGEMENT: SPECIAL CONSIDERATIONS

Obstructive abnormalities are appropriately treated. Grade 1 – 4 VUR is managed conservatively with antibacterial prophylaxis (using nitrofurantoin or cotrimoxazole) and UTI surveillance. Careful evaluation of various problems is made before deciding to undertake a surgical procedure (ureteric reimplantation or intravesical injection of Deflux) for grade 5 VUR or bilateral VUR. The benefits of chemoprophylaxis or surgical intervention are unproven. However, until clear evidence is available existing recommendations should be followed<sup>8</sup>.

### Recurrent UTI in the absence of structural anomaly and VUR

Recurrent UTI in the absence of demonstrable anatomic abnormality of kidney and urinary tract raise the suspicion of an underlying voiding dysfunction<sup>9</sup>. A detailed history of voiding pattern is obtained particularly about frequency, urgency, dribbling, holding maneuvers and constipation. Frequency, urgency and urge incontinence suggest dysfunctional voiding as occurs with idiopathic detrusor instability or urge syndrome. A voiding diary over a 3-4 day-period, noting the volume of urine output, fluid intake and involuntary wetting is very useful in evaluation. A careful neurological examination is done and perianal sensations tested. Any evidence of spinal and sacral anomalies (lipoma, dimple, tuft of hair) is

looked for and perineum is examined for ectopic ureter, epispadias, vaginal pooling and labial adhesion in girls. Ultrasonographic evaluation is done and the bladder capacity and volume of post void residual urine (more than 2 ml/kg or 25 ml is abnormal) recorded. The presence of neurogenic bladder is carefully excluded. Clinical and ultrasound evaluation is sufficient in a majority of cases but occasionally uroflowmetry and urodynamic studies are required.

### Voiding disorders<sup>10,11,12</sup>

Voiding disorders involve an abnormality during the *bladder filling or evacuation*. These are distinguished on urodynamic studies. A small capacity, hypertonic bladder or detrusor instability characterise filling phase defect. In evacuation defect detrusor sphincter dyssynergia may be a prominent feature.

### Symptomatic Management

Treatment of constipation, a liberal fluid intake and regular complete voiding are most important. In children with detrusor instability anticholinergic agents such as oxybutynin or tolterodine may be useful. Patients with dysfunctional voiding and having large post residual volumes, it is important to lower intravesical pressures with clean intermittent catheterisation. Motivational therapy and behaviour modification measures are undertaken as necessary.

### Recurrent UTI with no obvious abnormality<sup>13</sup>

In some children with recurrent UTI no structural or functional abnormality appears to be present. It is important to appreciate that asymptomatic bacteriuria does not require antibiotic therapy. For symptomatic recurrent UTI, prophylactic antibiotic administration has been employed, using a single dose of nitrofurantoin or cotrimoxazole given at bedtime. Nonspecific measures including use of vitamin A, probiotics and cranberry juice have been tried and may be beneficial in individual cases. Lactobacilli adhere to mucus and form a biosurfactant barrier that could prevent attachment of uropathogens to epithelial receptors and may modulate the host immune system<sup>14</sup>. Their usefulness is currently being examined. UTI surveillance is, however, important since UTI may occur despite instituting non specific measures.

## CONCLUSIONS

Urinary tract infections are common in infants and children and may lead to serious complications. UTI must be suspected, confirmed by careful urine examination and adequately treated. Imaging procedures of kidney and urinary tract should be considered in every case of UTI. Besides structural abnormalities and vesicoureteric reflux, voiding dysfunction should be looked for and appropriately managed.

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