Personal Practice

Urinary Tract Infection

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Urinary tract infection (UTI) is a common problem in day to day practice with prevalence probably second only to respiratory tract infections. UTI remains a major cause of hospitalization and morbidity and accounts for a majority of causes of unexplained fever in children below 3 years of age (l). Even though urine is readily accessible for examination, diagnosis and management of UTI may not always be easy.

Magnitude of the Problem

It is estimated that approximately 1% of boys and 3% of girls will experience UTT before the eleventh year of life, the risk being greatest in the first year(2). Asymptomatic bacteriuria occurs more frequently than symptomatic UTI at all ages during childhood(3). Further, recurrence of UTI is common in childhood. About 25% of neonates will have a recurrence. In older children, the recurrence rate is 30% after one episode and increases to 60% and 75% after second and third episodes, respectively.

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Definition of Terms

Bacteriuria is defined as the presence in urine of $>10^{s}$ organisms per ml in apparently healthy children, usually detected as a result of screening programmes. Distinguishing between asymptomatic infection and prolonged colonization is a matter of definition, often determined by the presence or absence of pyuria. *Simple uncomplicated UTI (cystitis)* implies restriction of infection to the bladder only, without upper tract involvement. *Acute pyelonephritis* is defined as infection involving the pelvis, calyces and parenchyma of kidney and is characterized by fever and flank pain with or without symptoms of lower tract infection. *Complicated UTI* includes all infections when they occur in the setting of catheterization, outflow obstruction, urinary calculus, abnormal post void residual bladder urine, vesicoureteral reflux or renal insufficiency.

Natural History

The natural history of UTI in children is determined by a complex relationship of agent factors and host defense factors.

Agent Factors

The important agent factors include: (z) *Etiologic agents,* majority of whom are Gram negative bacteria, the commonest being *E. coli.* Non *E. coli* infections are more common in children with anatomic or functional defects and in recurrences *[Table I);* and *(it) Virulence factors* including specific serotypes, adhesins, aerobactin and hemolysin production. These are

TABLE I- *Distribution of Bacterial Species Recovered (%) from Children During First UTI and Recurrences*

Bacterial	Total (n=4176)	First infections (n=1428)	Recurrences (n=2748)
Escherichia coli	79.5	88.6	74.7
Klebsiella	3.5	2.0	3.2
Proteus	3.3	3.4	3.2
Pseudomonas	0.5	0.1	0.6
Enterococcus	2.6	2.9	2.5
Staphylococcus	2.6	0.6	3.6
Others and unknown	8.0	2.4	11.1

Source: Swanbory-Eden C and de Man P (4).

important in mediating adherence of the organism to the host mucosa, acquisition of nutrients and induction of inflammation.

Host Factors

These include: *(i) Route of Infection:* The gastrointestinal tract provides the reservoir for bacteria producing UTI by the ascending route. The short length of the female urethra is the possible reason for the greater incidence of UTI in girls, *(ii) Circumcision:* Most studies suggest that there is a higher incidence of UTI in uncircumcised male infants as compared to circumcised ones(5); *(iii) Vesicoureteral reflux* is a congenital disorder that may predispose young children to UTI; it may be present among 20-30% of children of all ages with UTI. Other structural anomalies of the urinary tract and renal calculi also increase the risk of UTI; *(iv) Functional bladder abnormalities* either due to major disease as in neurogenic bladder or because of minor functional disorders associated with psychosocial stress, improper toilet training and abnormal behavior as in non-neurogenic bladder are also associated with increased frequency of UTI; and *[v) Nephrotic syndrome:* There is an increased incidence of UTI in children due to the disease *per se* as well as a result of immunosuppressive therapy(6).

Clinical Presentation

There is a wide spectrum of clinical features associated with UTI in children. Infants and younger children often have no localizing symptoms and hence a high index of suspicion is required. Infants may show signs and symptoms of sepsis as UTI is often a consequence of bacteriuria. Young children may just present as failure to thrive(7).

History

Besides obvious clues like dysuria, frequency and urgency, unusual patterns of voiding and stooling are important in identifying patients who may have bladder and bowel dysfunction as a basis for recurrent infections. Feeding intolerance and poor weight gain may be clues to UTI in the very young. Older children may present with vague abdominal complaints.

Physical Examination

Particular attention needs to be directed towards children with anatomic abnormalities of the urinary tract as they are more likely to develop renal parenchymal damage, hypertension and renal failure(8). Fever and hypotension or hypertension may be signs of upper UTI. Growth failure may indicate presence of renal insufficiency. Genital and rectal examination in uncooperative male infants may be the best approach for detecting a firm enlarged bladder, typical of posterior urethral valves. Occasionally a ureterocele may be the only physical finding(9). Other major associated abnormalities may signal structural problems in the urinary tract including preauricular pits, cardiac defects, abdominal musculature defects, cryptorchidism, severe hypospadias and skeletal abnormalities.

Diagnosis

1. Urine Culture

This remains the gold standard for the diagnosis of UTI. The method of collection is often a major problem, especially in infants and young children *(Table II).* Studies in children show that urine specimens containing $<10^3$ colonies/ml are indicative of contamination, 10^3-10^5/ml are suggestive of infection, especially in the presence of associated symptoms and $>10^5$/ml are definitive indicators of infection, even in asymptomatic patients(l0). Patients with UTI may have a colony count $<10^5$/ml in the following conditions; *(i)* partial treatment; *(ii)* very dilute or concentrated urine; (*iii)* frequent bladder emptying, as is often seen in infants; and *(iv)* methenamine therapy. Signs of contamination include low colony counts, multiple agents, different organisms obtained in serial samples or isolation of uncommon bacteria. In catheterized samples, colony counts of $>10^3$ are suggestive of UTI. The growth of any number of Gram negative bacteria from suprapubic aspirates is indicative of UTI(IO). Scanty growth of Gram positive organisms indicates contamination (if sterile technique is not adhered to).

2. Pyuria

Pyuria (>5 WBC/HPF in a centrifuged specimen) is a hall mark of pyelonephritis with sensitivity and specificity of 30-50%. However, pyuria alone is not satisfactory for making a diagnosis, as a number of conditions are associated with sterile pyuria including dehydration, instrumentation, chemical inflammation, oral polio vaccine administration non specific gastroenteritis and respiratory tract infections. Pyuria is strong supportive evidence of UTI in the presence of positive culture. Many (30-50%) patients with bacteriuria with UTI do not demonstrate significant pyuria(7). The most accurate method of measuring

TABLE II–*Comparative Utility of Various Methods of Collections of Urine for Culture*

Method of collection	Reliability of the specimen	
	<4 yrs	>4 yrs
Clean catch midstream	Unreliable because of difficulty of collection	Reliable when collection is properly obtained. Method of choice
Catheterization	Reliable with proper technique; relatively easy in girls; requires care in males to avoid urethral trauma; counts $>10^3$ significant	Reliable with proper technique; helpful if adequacy of midstream specimen is questioable
Suprapubic aspiration	Very reliable, simple to perform gold standard for diagnosis in infants	Very reliable, simple to perform
Collection bag	Most prone to contamination; culture has value	Not recommended.

measuring pyuria is to quantitate the urinary leukocyte excretion rate. However, this is a cumbersome procedure and on measuring pyuria by hemocytometer, counts >10 leukocytes/mm^3 have a good correlation with UTI(ll).

3. Bacteriuria

The most consistent and reliable method of microscopically assessing bacteriuria is the examination of Gram stained un-centrifuged urine. Gram stained urine that reveal at least one organism per oil immersion field correlates with $>10^5$ CFU/ml of urine with a sensitivity and specificity of almost 90%. An additional finding of 5 or more organisms per oil immersion field increases the specificity to 99%(12). However, lower count UTIs are difficult to assess by these methods.

4. Rapid Screening Tests

Recently nitrate and leukocyte esterase tests have been introduced but none yet appears to be adequate to replace the urine culture and quantitative counts. These tests may have the advantage of relatively high specificity (80-95%) but sensitivity is rather low (30-50%)(13).

5. Diagnostic Imaging

The aims of investigating children with UTI are: *(i)* to identify abnormalities of the urinary tract that may have predisposed to infection and require treatment to reduce the risk of further infections and of progressive renal damage; *(ii)* to identify renal scarring; and *(iii)* to identify vesicoureteral reflux. Diagnostic imaging is ideally recommended in all boys with UTI, girls under the age of 5 years, all children with physical findings suggestive of genitourinary abnormality and older girls with recurrent symptomatic bacteriuria(7). The modality used depends upon the availability of the technique and skill of the radiologist. A simple algorithm is depicted in *Fig. 1.* Ultrasound, an effective non invasive modality, is often the first investigation in child with UTI. However, it is highly operator dependent and hence must be performed by an experienced sonographer with real time equipment. Unless these conditions are satisfied, an IVP should be preferred. IVP is useful in detecting obstruction and assessing the renal size and contour and lower urinary tract abnormalities and stones. It cannot be relied upon to detect or exclude scars and milder grades of vesico-ureteral reflux (VUR). Hence an additional dimercaptosuccinic acid (DMSA) scan with a voiding cystourethrogram (VCUG) is essential(14). Technetium labelled dimercaptosuccinc acid (Tc 99m DMSA) scan is a highly sensitive technique for detection of children at risk of renal cortical scarring after UTI. Besides it provides information on renal function and structure, Tc 99 m (diethylene tetramine pentacetic acid; DTP A) cystography can be used as a substitute for VCUG in following up children with UTI with VUR. Once a child is diagnosed to have VUR with or without reflux nephropathy, he needs to be referred to a pediatric nephrologist. VCUG is recommended for diagnosis and exclusion of VUR in all infants and older children (15 years) with recurrent infections, acute pyelonephritis, family history of reflux and chronic pyelonephritis

Treatment

Treatment can be broadly considered in two categories, namely, antimicrobial and surgical.

Antimicrobial Therapy

It is unacceptable to wait 48 hours for the results of culture and sensitivity before starting treatment in an infant or acutely symptomatic child with pyelonephritis as

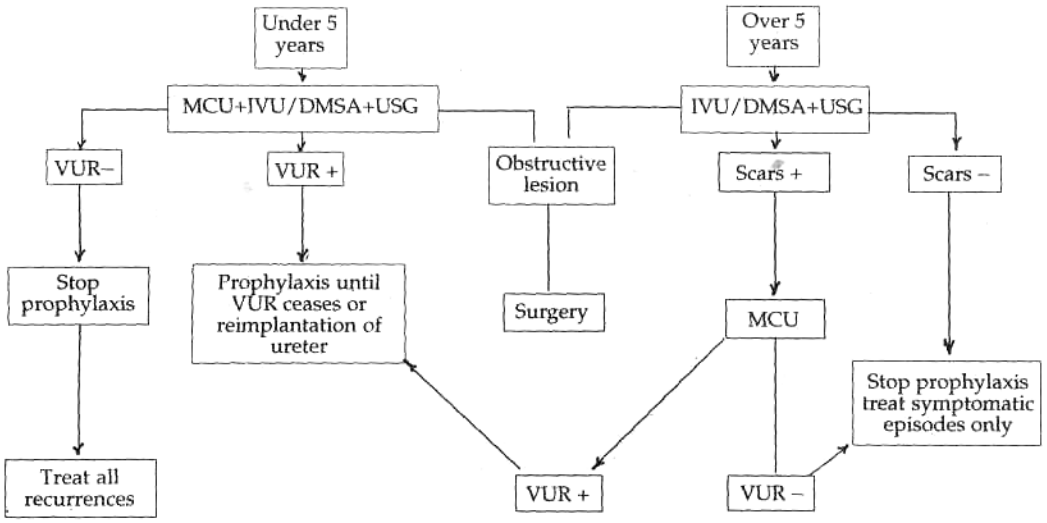

Fig. 1. Algorithm for management of children following successful treatment of first proven urinary tract infection. MCU - Micturating cystourethrogram; VUR-Vesicoureteric reflux; IVU - Intravenous urogram. DMSA - Dimercaptosuccinic acid scan.

delay in treatment can result in permanent renal damage(15). Diagnosis in these cases should be based on the presence of white cells and organisms on direct microscopy of the unspun urine.

1. Infants with UTI

Since UTI is usually a result of hematogenous spread in this age group, they are at risk for developing serious sequelae including sepsis, shock and life threatening metabolic abnormalities. They should be treated with intravenous ampicillin and aminoglycosides or cephalosporines for the initial 5-7 days *(Table HI).* A repeat urine culture should be obtained after 48 hours. Once urine is sterile and the patient apyrexic for 3 days, oral antibiotics can be started to complete 14 days therapy(7).

2. *Simple (Uncomplicated) UTI*

These children should be initially treated with amoxydllin, cotrimoxazole or cephalexin, with modifications, once the sensitivity report is available. A total of 7-10 days therapy is recommended. If there is no clinical improvement in 48 h, mode of therapy may be made parenteral and a repeat urine culture and ultrasound abdomen performed to rule out obstruction. Patients treated with shorter courses have a higher recurrence rate(16). Single dose treatment is reserved for girls over 5 years of age with grossly normal urinary tracts.

3. Complicated UTI

Patients with acute bacterial pyelonephritis who present with fever, chills, costovertebral angle tenderness or severe GIT upset as well as those with structural abnormalities of the urinary tract should be treated promptly with intravenous ampicillin and aminoglycoside and dose adjustments should be made for renal failure. Third generation cephalosporins may be particularly beneficial in sick hospitalized children with infections due to resistant organisms. The longer the delay in starting antibiotics, the more severe is the

TABLE III–*Antibiotic Agents for UTI*

Drug	Dosage	Side effects
Parenteral		
Ampicillin	50-100 mg/kg/day q 6 h	Diarrhea, rash
Cefotaxime	100-150 mg/kg/day q 6 h	Allergic reactions
Gentamicin	5-7.5 mg/kg/day q 8 h	Ototoxicity, nephrotoxicity
Tobramycin	5-7.5 mg/kg/day q 8 h	Ototoxicity, nephrotoxicity
Oral		
Amoxicillin	30-50 mg/kg/day q 8 h	Diarrhea, rash
Cephalexin	25-100 mg/kg/day q 6 h	Allergic reactions
Trimethoprim-sulfamethazole	8-10 mg/kg/day TMP and 40-50 mg/kg/day SMX q 12 h	Skin rash, hemolysis in G6PD deficiency
Nalidixic acid	55 mg/kg/day q h	Allergy, benign intracranial hypertension
Nitrofurantoin	3-8 mg/kg/day q 6 h	Nausea, vomiting

renal damage. Sometimes, one may have to resort to the use of short courses of flouroquinolones (ciprofloxacin or norfloxacin). The safety of this group of drugs in children is not firmly established. Failure of defervescence after 48 h requires prompt urological assessment as surgical intervention may be required. Intravenous therapy should be continued till 3-5 days afebrile period with subsequent oral antibiotics determined by the sensitivity pattern for the next 2-3 weeks.

4. *Recurrent Infection*

The approach is guided by the presence or absence of structural abnormalities. Patients with normal urinary tracts are treated with low dose antibiotics (trimethoprim 2 mg/kg/day or nitrofurantoin 2 mg/kg/day) as a single nighttime dose for 3-6 months. Amoxycillin, cephalosporines and nalidixic acid are less effective as prophylactic agents probably because the bowel soon becomes colonized with *E. coli* resistant to the ingested drug(17). Patients with structural abnormalities especially VUR require continuous use of prophylactic antibiotics to prevent upper UTI and possible renal damage secondary to reflux.

5. Prophylactic Therapy

There is a significant risk of producing bacteriuria during catheterization, urological instrumentation or surgery of the genitourinary tract. This risk can be significantly reduced by the use of a short course of antibiotics in full doses for 48 h *(Table III).* Children undergoing urological instrumentation or MCU can be given a single intramuscular dosing of aminoglycosides in full dosage, whatever their level of renal function.

6. *Covert Bacteriuria*

A number of long term studies have documented good long term prognosis even in untreated children(18,19). However, many patients with covert bacteruria on close questioning have symptoms of UTI while others have intermittent episodes. This subgroup of patients should be treated like any simple UTI.

Surgical Intervention

This is mandatory for obstructed systems. Ureteral reimplantation is recommended in patients with VUR in the following conditions: *(i)* Grade V reflux in an infant; *(ii)* Breakthrough infections despite antimicrobial therapy; *(iii)* Non compliance; and *(iv)* When regular follow up can't be ensured(20).

In conclusion UTI is a major challenge in pediatric practice because of its frequent occurrence and tendency to relapse and its propensity for causing long term sequelae like hypertension and reflux nephropathy.

REFERENCES

1. Bidor TA, Resnick MI. Urinary tract infection in children. Pediatr Clin North Am 1983, 30: 323-332.

2. Winberg J, Anderson H, Bergstorm T, *et al.* Epidemiology of symptomatic urinary tract infection in childhood. Acta Pediatr Scand 1974, 252: 2-20.

3. Ogran P, Faden H. Urinary tract infections in childhood: An update. Pediatr 1985, 106: 1023-1029.

4. Swanbory-Eden C, deMan P. Bacterial virulence in urinary tract infection. Infect Dis Clin North Am 1987,1: 737-738.

5. American Academy of Pediatrics. Report of the Task Force on Circumcision. J Pediatr 1989,1023-1029.

6. Gulati S, Kher V, Gupta A, Arora P, Rai P, Sharma RK. Spectrum of infection in Indian children with nephrotic syndrome. Pediatr Nephrol 1995, 9: 431-434.

7. Sherbotie JR, Cornfeld D. Management of urinary tract infections in children. Med Clin North Am 1991, 75: 327-338.

8. Winberg J, Bollgren I, Kallenius G, *et al.* Clinical pyelonephritis and focal renal scarring. Pediatr Clin North Am 1982, 29: 801-805.

9. Milner CS, Kaplan BS. Urinary tract infection and reflux in the child. Medicine 1985, 27: 3680-3682.

10. Pyles CV, Lustik B. Laboratory diagnosis of urinary tract infection in children. Pediatr Clin North Am 1971,18: 233-243.

11. Pappas PG. Laboratory in the diagnosis and management of urinary tract infection. Med Clin North Am 1991, 75: 313-325.

12. Jenkins RD, Fenn JP, Matsen JM. Review of urine microscopy for bacteriuria. JAMA 1986, 225: 3397-3399.

13. Blaufox MD. Current concepts in the diagnosis of urinary tract infection. Curr Opinion Nephrol Hypertension 1994, 316: 652-655.

14. Haycock GB. A practical approach in evaluating urinary tract infection in children. Pediatr Nephrol 1991, 5: 401-402.

15. Ransley PG, Risdon RA. Reflux nephropathy: Effect of antimicrobial therapy on the evaluation of the early pyelonephritic scan. Kidney Int 1981, 20: 733-742.

16. McCracken GH. Diagnosis and manage ment of acute urinary tract infection in infants and children. Pediatr Infect Dis J 1987, 6: 107-112.

17. Verrier Jones K. Antimicrobial treatment for urinary tract infections. Arch Dis Child 1990, 65: 327-330.

18. Kincaid Smith P. Reflux nephropathy. Br Med J1983, 280: 2002-2004.

19. Newcastle Covert Bacteriuria Research Group. Covert bacteriuria in school girls in Newcastle upon Tyne. A 5 years follow up. Arch Dis Child 1981, 56: 585-585.

20. International Reflux Study in Children European Group. Five year study of medical and surgical treatment in children with severe reflux: Radiological and renal findings. Pediatr Nephrol 1992, 6: 223-230.