URINARY TRACT INFECTIONS IN CHILDREN II. INVESTIGATIONS, TREATMENT AND PROGNOSIS

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Urinary tract infections (UTI) in children are of serious concern because they may indicate underlying abnormalities like vesico-ureteral reflux (VUR), posterior uretheral valves (PUV), ureteroceles and other defects. Unless UTI is promptly and adequately managed, long-term complications like renal scarring, chronic renal failure (CRF), end stage renal disease (ESRD), hypertension and renal stones may develop. The importance of childhood UTI is evident from the fact, that in the European Dialysis and Transplant Registry, UTI and related problems are responsible for 20% of children with ESRD(1). The aims thus in the management of children with UTI include: (*a*) early diagnosis and prompt treatment, (*b*) diagnosis and management of underlying abnormalities, (*c*) prevention of recurrences, and (*d*) to ensure adequate renal growth.

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Radiological Evaluation

Almost all children with UTI require some kind of radiological evaluation. The importance of radiological evaluation becomes clear if one realises that between 18 to 50% of children with symptomatic UTI will have some degree of VUR. An additional 5-10% of boys and 1-2% of girls will have some underlying congenital malformation that predisposes to UTI(2).

The modes of radiological evaluation available are: ultrasound, intravenous urography (IVU), micturating cysto-urethrography (MCU), radio-nuclide cysto-urethrography (direct and indirect) and radio-nuclide renal scans (static and dynamic). Static scans (done with ^{99}Tc-Dimercapto-succinic acid, DMSA) is the best method available for the detection of renal cortical scars. As compared to IVU, DMSA scans have the advantage of being more sensitive in the detection of renal cortical scars. The radiation exposure is also a fraction as compared to IVU; thus for serial evaluation, DMSA scans are ideal. However, availability is the limiting factor. Dynamic scans, (done with ^{99}Tc-diamino-tetraethyl-penta-acetic acid, DTPA) give an excellent idea of the functional status of the kidneys.

The aims of radiological evaluation are: (*a*) to identify defects that may predispose to UTI, *i.e.*, congenital or acquired defects of urine flow like VUR, PUV, ureteroceles, duplex system, calculi, *etc.*, (*b*) to detect renal scarring at the earliest, and (*c*) to monitor the rate of renal growth. Diagnostic radiology (except plan *X*-ray abdomen and ultrasound) should be delayed till 4-6 weeks after a UTI, because functional defects caused by the UTI may last till this period.

Indications

For children with UTI a working protocol should be developed for a sequential and logical work-up. The kidneys of young children below the age of 5 years and especially those below 1 year are particularly vulnerable to damage. After the age of 5 years, UTI rarely leads to scarring, even in the presence of VUR. Thus, resources for diagnostic radiology should be concentrated for the younger age groups.

A working protocol for sequential work-up is suggested in *Fig. 1.* With the first documented UTI, a plain *X*-ray of the abdomen (to exclude calculi) and an ultrasound (for kidney size and to demonstrate any dilatation of the collecting system) are the preliminary investigations. If any abnormalities are detected in these, further investigations are done as indicated. Even if the preliminary investigations are normal, all children below the age of 5 years will require in addition an MCU to demonstrate VUR and to diagnose PUV. If the MCU is normal, no further investigations are required unless recurrences occur, in which case a DMSA scan (or an IVU if DMSA not available) is indicated to demonstrate renal scars. If PUV is

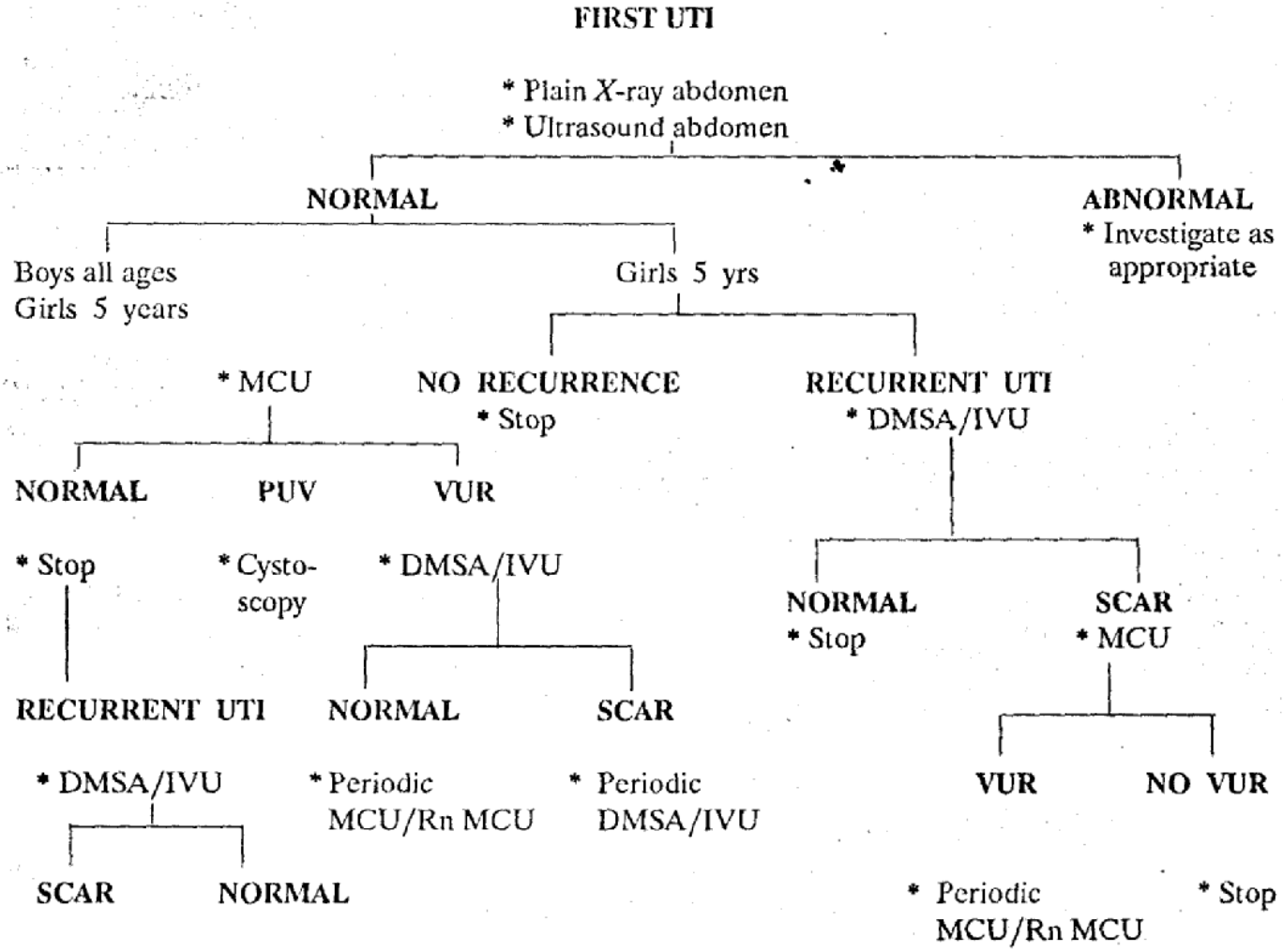

Fig. 1. Working protocol for radiological work-up of children with a first attack of UTI. MCU: Micturating cystourethrography, PUV: Posterior uretheral valves, VUR: Vesicoureteral reflux, IVU: Intravenous urography, DMSA: Radionuclide DMSA Scan, Rn DMSA: Radionuclide micturating cystourethrography.

detected on MCU, cystoscopy should be done. If primary VUR is diagnosed, it should be radiologically graded (preferably by the International Classification) and DMSA scan/IVU done to look for scars. In the absence of scars, periodic MCU/ radionuclide MCU and DMSA scan/IVU should be done to monitor reflux and renal growth.

In children above 5 years of age, boys will require an MCU (to rule out PUV) in addition to plain *X*-ray abdomen and ultrasound. Girls require further evaluation only in the presence of some gross abnormalities on the preliminary investigations. Recurrent UTI in this age group, however, will require DMSA scan/IVU to detect renal scars. If a scar is detected, an MCU is suggested.

For all children demonstrated to have VUR and are undergoing conservative treatment, a periodic MCU (preferably a radionuclide MCU) is required to evaluate the extent of the reflux with increasing age. The advantage of radionuclide MCU is that the radiation exposure is 1/100 of a conventional MCU.

TABLE I –*Clinical Classification of Childhood UTI*

A. Symptomatic (first) Infection	
1. Uncomplicated infection	
2. Complicated Infection	
	Age less than 3 months
	Systemic symptoms
	Fever (more than 39°C)
	Flank pain/mass
	Leucocytosis
	Raised ESR, Raised CRP
	Azotemia
	Unusual pathogen
	Clinical evidence of obstructive uropathy
B. Recurrent infection	
C. Urinary tract infection with VUR	
D. Asymptomatic bacteriuria	

Treatment

From the treatment point of view, children with UTI can conveniently be classified as shown in *Table I.*

Symptomatic Infections

Children with symptomatic but uncomplicated infections are to be treated on an outpatient basis with oral antibacterial drugs, depending on the sensitivity pattern of the infecting organism. Children with symptomatic complicated infections need hospitalization, with due attention paid to fluid electrolytes and renal status. Parenteral antibiotics are required for this group of patients. The drugs, and doses of antibiotics commonly used in UTI is given in *Table II.* In all instances, treatment is required for a period of 7-10 days. 'Short' and 'Ultra short' therapy with only a single dose, though well established in the treatment of adults with non-obstructive UTI, has no place in the treatment of childhood UTI. Follow-up urine cultures should be done 2-3 days after discontinuation of therapy, 2-3 weeks later and 3-4 monthly for the next 1 year.

Recurrent Infections

All recurrent infections are initially treated as described above, with a full course of the appropriate antibiotic. All children who have recurrent infections, will require some form of prophylaxis. The alternatives available are nitrofurantoin 1-2 mg/kg/day, trimethoprim sulfa-

TABLE II—*Drugs Commonly Used in UTI*

Drug	Dose (mg/kg/day)	No. of doses	Remarks
Ampicillin	50-100	4	
Amoxycillin	25-50	3	
Trimethoprim sulfamethoxazole	6	2	Not to be used before 6 weeks of age.
Nalidixic acid	55	3-4	Not to be used in newborns. Dose at 1-4 mo, 30 mg/kg/day.
Nitrofurantoin	3-5	4	Not to be used in newborns. Not effective if GFR <50%.
Cephalexin	50-100	4	
Cephadroxil	40-60	2	
Gentamicin	7.5	3	Dose adjustment needed in renal failure.
Amikacin	15-22.5	3	-do-
Cefotaxime	50	3	
Ciprofloxacin	10-15	2	Experience very limited in children. Not to be used in routine UTI. Reserved for use in resistant complicated UTI.

methaxozole 2-3 mg/kg/day and nalidixic acid 20 mg/kg/day. All these are given in a single dose at bed time. The duration of prophylaxis is by trial and error and the initial period is for 2-4 months. If reinfection follows prophylaxis, the duration of prophylaxis should be increased to 6 months, and so on. Some children may require prophylaxis for many years(2). During prophylaxis, urine cultures should be obtained every 2-3 months.

Infection with VUR

When VUR is diagnosed on MCU, it should be graded, preferably by the International Classification(3) which classifies reflux from I to V. The corner-stone of therapy is to keep the urine sterile at all times. All children with reflux of grades I-III should undergo medical management with prophylactic antibiotics on a long term basis. Since reflux disappears at the rate of 20 to 30% per every 2 years, the antibiotics are continued till such time when VUR has been demonstrated to have disappeared(4). During the period of prophylactic treatment, periodic MCU (preferably radionucide MCU) needs to be done: The indications of surgery are relative, since controlled studies tend to show that surgery though effectively controls VUR, does not influence the overall prognosis(5). Surgery should be contemplated in the following circumstances: (*a*) Grade V and possibly Grade IV VUR, (*b*) failure to keep the urine sterile on antibiotic prophylaxis, (*c*) VUR persisting till late childhood or

adolescence, (*d*) development of renal scars while on medical treatment, and (*e*) non-compliance with the long-term prophyactic treatment.

Asymptomatic Bacteriuria (ABU)

ABU is typically discovered in 'healthy' school girls during routine screening. The bacterial isolates from these children are qualitatively different from those with symptomatic infection in that the bacteria are often cell-wall deficient and have low virulence. Though a short course of antibiotics will eliminate infection in a majority of cases, about 80% will be reinfected within 1-2 years. Though VUR is seen in 20-35% and renal scars in 10-25% children with ABU, treated and untreated children fare equally, even in the presence of VUR(6). These figures tend to suggest that ABU is the result of neglected UTI during infancy and early childhood, and the damage is already done by the time ABU is discovered. Treatment of ABU with antibiotics may, by eliminating the organisms of low virulence, lead to infection by more virulent strains. However, treated children 'feel better' even if they did not have any symptoms to begin with. The current practice is to reserve treatment for those patients of ABU with even minimal symptoms, or with foul smelling urine.

Prognosis

The prognosis of an acute infection is excellent, but it is the long term outcome that determines the success of therapy. The chance of a renal scar in a young girl falling ill with her first symptomatic UTI is 5% and that in a boy is 10-15%(7). These are the figures in children given optimal treatment; with delayed or inadequate treatment, the figures would be higher. Untreated, girls often go on to develop ABU, and in these children, as many as 25% may develop scars, indicating indirectly that a quarter of untreated children may develop scars. Scars usually develop during the earliest infections though they may manifest or be detected many years later. New scars rarely develop after the age of 5 years. It has been conclusively shown that delay (even a few days) in therapy in symptomatic UTI enhances the chance of scar formation. Thus early detection and adequate and prompt treatment of acute infection in infancy and early childhood will go a long way in the prevention of long term sequele of UTI.

Conclusions

UTI in childhood is often associated with structural or functional defects of the genito-urinary tract; this is more commonly seen in males. All children with UTI thus should be systematically investigated. Obstructive conditions need appropriate surgical intervention. Prompt and adequate treatment of acute infections is of paramount importance. The ultimate prognosis of UTI is determined to a large extent by the way the infection is managed during the earliest years.

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