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Urinary tract infections in young febrile children

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The evaluation and management of infants and young children who have fever without an apparent source is controversial. The disappearance of disease caused by *Haemophilus influenzae* type b after the introduction of universal immunization with polysaccharide conjugate vaccines has substantially reduced the frequency of invasive bacterial infections in early childhood. Urinary tract infection (UTI), however, is the most common serious bacterial illness among febrile infants and young children and can contribute to permanent renal damage. This article reviews the studies conducted at Children's Hospital of Pittsburgh during the past 6 years in which the prevalence, diagnostic methods, evaluation and management strategies for young febrile children with UTI were investigated.

PREVALENCE

Our initial study attempted to determine the prevalence of UTI in febrile infants, with and without an apparent source of fever, presenting to the Emergency Department. A catheterized urine culture was routinely obtained as part of the diagnostic evaluation of all febrile infants ≤60 days old. For infants who were >60 days old, a urine culture was obtained at the discretion of the examining resident physician. When a urine culture had not been obtained as part of an infant's evaluation, parental permission was requested to obtain a urine specimen by catheterization. Infants were classified as having: (1) an unequivocal source of fever (meningitis, pneumonia or septic arthritis); (2) a possible source of fever (acute otitis media, upper respiratory infection or gastroenteritis); and (3) no source. A positive urine culture was defined as the presence of at least 10 000 colony-forming units (CFU) per ml of a single pathogen in a catheterized urine specimen.

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The prevalence of UTI in relation to five variables, age, sex, race, temperature and the presence or absence of an apparent source of fever, is summarized in Table 1. Urine cultures were positive in 14 of the 306 infants ≤2 months old evaluated for fever without source (4.6%; 95% confidence interval (CI)), 2.2 to 6.9%); in 26 of the 443 infants aged >2 months in whom UTI was suspected (5.9%; 95% CI, 3.7 to 8.1%) and in 10 of the 196 infants in whom cultures had not been ordered but whose parents consented to participate in the study (5.1%; 95% CI, 2.0 to 8.2%). Overall of the 945 febrile infants in whom catheterized urine cultures were obtained, results were positive in 50 (5.3%; 95% CI, 3.9 to 6.7%). The prevalence did not vary with age but was higher in girls than in boys, and in white *vs.* African-American infants. No association was apparent between the prevalence of UTI and infants' temperature as recorded in the Emergency Department. However, when the highest temperature either in the Emergency Department or at home within

TABLE 1. Prevalence of UTI according to age, sex, race, height of temperature and source of fever in 945 infants presenting to the Emergency Department for evaluation

Characteristic	*n*	Positive Culture			*N*
		No.	%	95% CI	
Age (days)					
≤60	306	14	4.6	2.2–6.9	0.5
61–365	639	36	5.6	3.8–7.4	
Sex					
Male	526	13	2.5	1.1–3.8	<0.0001
Female	419	37	8.8	6.1–11.5	
Race					
White	533	35	6.6	4.5–8.7	0.04*
Black	392	14	3.6	1.7–5.4	
Other	20	1	5.0	−4.6–14.6	
Temperature at presentation					
<38.3°C	233	11	4.7	2.0–7.4	
38.3–38.9°C	287	12	4.2	1.9–6.5	0.22†
≥39°C	424	27	6.4	4.0–8.7	
Not available	1	0	0	0–0	
Highest temperature by history					
<38.3°C	41	2	4.9	−1.7–11.5	
38.3–38.9°C	363	13	3.6	1.7–5.5	0.08†
≥39°C	541	35	6.5	4.4–8.5	
Source of fever					
Unequivocal	62	1	1.6	−1.5–10.5	
Possible	429	15	3.5	1.8–5.2	0.02‡
No source	454	34	7.5	5.1–9.9	
Total	945	50	5.3	3.9–6.7	

* White *vs.* black infants.
† Rectal temperature <39°C *vs.* ≥39°C.
‡ Possible source *vs.* no source of fever.

the previous 24 h was considered, infants with temperatures of ≥39°C were more likely to have UTI. When sex, race and elevation of temperature were combined, white females whose highest temperature had been at least 39°C were found to be at particularly high risk (prevalence, 17%). Urinary tract infection was more prevalent among infants with no identified source of fever than among infants with a condition identified as a possible source of fever and least prevalent among those with an unequivocal source of fever.[1]

If we extrapolate these findings to the 4 000 000 infants born in the US each year and assume that each child has at least three febrile illnesses during the first 2 years of life (of which at least one may not have a definite source for fever), the number of UTIs is substantially higher than has been previously reported. Of 2 000 000 females 85% (1.7 million) are white and 15% (300 000) are African-American. Assuming a prevalence of UTI of 17% among white girls (289 000), 3.5% among African-American girls (11 000) and 2.5% among all boys (50 000), the total prevalence in a 1-year cohort will be in the range of 300 000 to 400 000 children.

MICROSCOPIC URINALYSES

In our initial study we evaluated standard criteria frequently recommended by others to define an abnormal urinalysis (UA). Pyuria was defined as at least 5 white blood cells (WBC) per high power field (hpf) in a centrifuged specimen, and bacteriuria was defined as any bacteria per hpf seen on an unstained specimen of urinary sediment. According to these definitions pyuria identified only 54% of infants with at least 10 000 CFU/ml of a single pathogen, and bacteriuria identified 86% of infants with positive cultures. However, bacteriuria had a positive predictive value of only 11%.[1] The poor predictability of the standard UA prompted consideration of a new protocol for the performance of a UA we have termed as enhanced UA. Borrowing from a protocol developed for adult women with dysuria,[2] an uncentrifuged urine specimen is evaluated and WBC are enumerated per mm^3 with a Neubauer hemocytometer. The use of an uncentrifuged specimen: (1) reduces variability in results caused by centrifugation and resuspension; (2) enables evaluation of a fixed volume of urine; and (3) facilitates accurate counting by providing a marked visual field with uniform illumination. The uncentrifuged specimen is also Gram-stained under conditions that standardize the number of drops of urine, the diameter of the smear and the number of microscopic fields observed.

Results of the standard *vs.* enhanced UA were compared for 698 catheterized urine specimens obtained from young febrile children. For the standard UA, performed on a centrifuged specimen, pyuria was defined as the presence of at least 5 WBC per hpf, and bacteriuria was defined as the presence of any bacteria per hpf on an unstained specimen. For the enhanced UA, performed on an uncentrifuged specimen, pyuria was defined as at least 10 WBC/mm^3, and bacteriuria was defined as the presence of any bacteria/10 oil immersion fields on a Gram-stained smear. Standard and enhanced urinalyses were considered positive when both pyuria and bacteriuria were present. In this study a positive culture was defined as the presence of at least 50 000 CFU/ml of a single pathogen. This definition was selected because in the initial study most patients with UTI had urine cultures with growth of $>10^5$ CFU/ml. The sensitivity of the enhanced UA for identifying positive urine cultures was 84.5%, compared with 65.6% for the standard UA (test for differences between proportions; $P < 0.05$). The positive predictive value of the enhanced UA was 93.1% compared with 80.8% for the standard UA ($P < 0.05$).[3]

DEFINITION OF URINARY TRACT INFECTION

Bacteria grown from a urine culture may arise from (1) contamination outside of the urinary tract, (2) colonization of the distal urethra (contamination from within the urinary tract), (3) asymptomatic colonization of the bladder urine or (4) true urinary tract infection. Figure 1 shows the frequency distribution of bacterial colony counts in 3257 cultures of catheterized urine obtained from young febrile children. Most cultures (2983 of the 3257) showed no growth. Specimens with bacterial counts between 1 and 49 000 CFU/ml were more likely to yield nonpathogens or mixed organisms than single pathogens. Specimens with counts of ≥50 000 were most likely to yield single pathogens. Accordingly significant bacteriuria is defined as ≥50 000 CFU/ml. Figure 2 shows relationships between the number of WBC per mm^3 and bacterial colony counts. Of all the specimens in which there was a sterile culture (2894), 97% had <10 WBC/mm^3, and only 89 or 3% had ≥10 WBC/mm^3. In contrast 90% of urine specimens with >50 000 CFU/ml had at least 10 WBC/mm.[3] Therefore UTI is best defined by the pres-

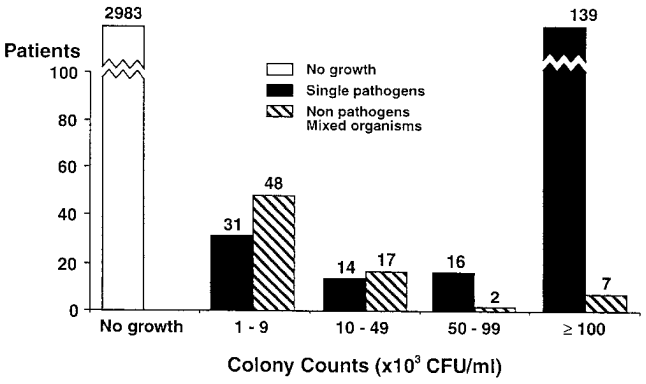


FIG. 1. Bacterial colony counts in 3257 urine specimens obtained by catheter from febrile children 1 to 24 months old.

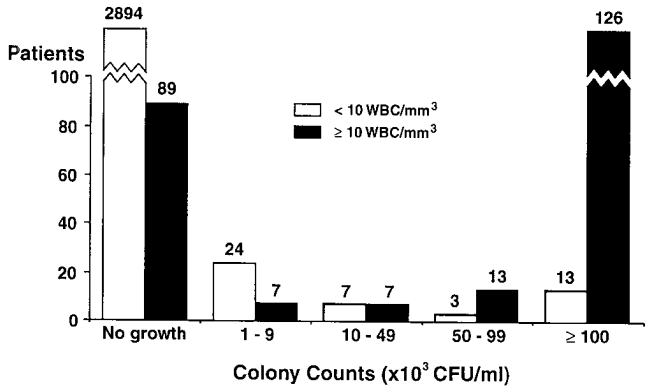


FIG. 2. Amount of pyuria according to bacterial colony counts in 3257 urine specimens obtained by catheter from febrile children 1 to 24 months old.

ence of at least 10 WBC/mm^3 and cultures with growth of at least 50 000 CFU/ml on the UA of catheterized specimens obtained from febrile children. This definition will almost always discriminate true UTI from bacteriuria associated with contamination or colonization of the urinary tract. It is important to recognize that occasionally low colony counts of bacteria in urine may be significant. This is especially true when suprapubic aspiration is the method of specimen retrieval. However, even with catheterized specimens, the repeated recovery of a single bacterial species in colony counts of <50 000 CFU/ml (especially in a symptomatic patient) should be regarded as representative of true infection. Bacterial colony counts may fall below the range that is characteristic of infections when: (1) a bacteriostatic agent is present in the urine; (2) when there is rapid rate of urine flow with reduced incubation time; (3) when there is obstruction of the ureter that interferes with discharge of bacteria into the bladder; or (4) when the infection is limited to areas of the kidney not directly accessible to renal tubules.[4]

SCREENING FOR URINARY TRACT INFECTION

Is urine culture necessary? The high positive predictive value of the enhanced UA prompted the adoption of this method for examining catheterized urine specimens in the Emergency Department at Children's Hospital of Pittsburgh. The diagnostic validity of pyuria combined with bacteriuria compared with pyuria alone on 4253 catheterized specimens is shown in Table 2. The positive predictive value of the combination of pyuria and bacteriuria (84.6%) justifies prompt institution of antimicrobial therapy before culture results are available, whereas the lower positive predictive value of pyuria alone (48.0%) dictates delaying treatment decisions until culture results are available.

Although accurate enumeration of the WBC per mm^3 in an uncentrifuged urine specimen is a simple technical procedure, which can be performed easily in the office setting, interpretation of a Gram-stained smear is a more difficult task for the less experienced individual. Accordingly we analyzed the false negative results and achievable cost savings incurred if pyuria alone was used as the sole criterion for performing urine cultures. In the screening method we have used during the past 3 years, a urine culture was performed on all specimens (4253) at a reimbursable cost of $276 500. Two hundred twelve cultures were positive. In contrast if only the 396 specimens with pyuria had been cultured, 190 patients would have been identified at a reimbursable cost of $25 750. Of 22 patients who would not have been cultured, 14 were presumed to have asymptomatic bacteriuria as suggested by results of acute phase reactants and ^{99}Tc-dimercaptosuccinic acid (DMSA) renal scans (shown below), and 8 were presumed to have an early stage of UTI based on pyuria observed on a subsequent UA. Review of records of 500 febrile children <2 years of age seen in the Emergency Department who did not have pyuria at presentation showed that 1257 (38%) were managed

TABLE 2. Sensitivity, specificity and predictive values of pyuria* and bacteriuria† compared with pyuria alone for identifying positive urine cultures‡

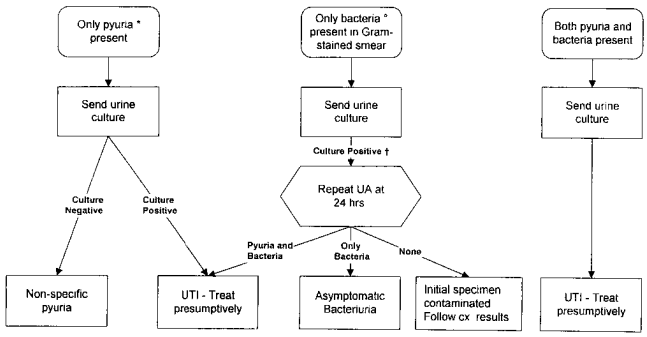
Analysis	Culture-positive*	Culture-negative	Analysis	Culture-positive	Culture-negative
Pyuria and bacteriuria +	186	34	Pyuria +	190	206
Pyuria and bacteriuria −	26	4007	Pyuria −	22	3835
	%			%	
Sensitivity	87.7 (83.3–92.2)§			89.6 (85.5–93.7)	
Specificity	99.2 (98.9–99.4)			94.9 (94.2–95.6)	
Positive predictive value	84.6 (79.8–89.3)			48.0 (43.1–52.9)	
Negative predictive value	99.4 (99.1–99.6)			99.4 (99.2–99.7)	
Prevalence	4.98			4.98	

* ≥10 white blood cells/mm^3.
† Any bacteria on any of 10 oil immersion fields in a Gram-stained smear.
‡ Growth of a single pathogen at a concentration of ≥50 000 CFU/ml.
§ Numbers in parentheses, 95% confidence interval.

presumptively with antimicrobials. For patients treated at the outset with antimicrobials, a baseline urine culture is necessary because treatment obscures the results of subsequent cultures. Accordingly, culturing urine specimens only in patients with pyuria or those presumptively treated with antimicrobials would have resulted in expenditures of approximately $107 500 (25 750 plus 81 705), thereby saving nearly $170 000 by not culturing all specimens.

Figure 3 shows an algorithm for the use of the enhanced urinalysis. There are several circumstances in which a urine culture should always be obtained regardless of urinalysis findings. These include children who (1) have had a previous UTI, (2) have abnormalities of the urinary tract or (3) will be presumptively treated with antibiotics. To detect a false negative urinalysis (one in which the absence of pyuria has been misleading), the enhanced urinalysis should be repeated within 24 to 48 h if there is persistence of fever without an identified source. This practice will identify the patient from whom a specimen may have been obtained so early in the illness that a local inflammatory response had not yet developed. For other children, whose treatment may be guided by results of the enhanced urinalysis, Figure 3 provides guidelines.[5]

Dipstick urinalysis. Although we have been intent on developing accurate methods for diagnosis of UTI based on microscopic analysis, others have relied on the dipstick UA. The leukocyte esterase component detects esterases released from leukocytes that have broken down. It is therefore an indirect test for the presence of WBC. The nitrite component detects nitrites that have been produced by the reduction of dietary nitrates by bacteria within the urinary tract. Nitrates must be exposed to nitrate-reducing bacteria for hours before this reaction can take place. Accordingly the test has its greatest utility in the analysis of first morning voided specimens, as usually obtained in adults, rather than randomly obtained catheterized specimens. Table 3 shows the sensitivity, specificity and positive and negative predictive values of: (1) the leukocyte esterase component for detecting the presence of at least 10 WBC/mm^3; and (2) the nitrite component alone; or (3) either the leukocyte esterase or nitrite components for identifying urine cultures with growth of at least 50 000 CFU/ml. The finding of low sensitivity of dipstick nitrite testing among young febrile children, contrary to findings in adults, may be the result of the use of random urine specimens obtained by catheter, rather than specimens obtained from a first morning void. The low sensitivity of the dipstick leukocyte esterase and nitrite tests in identifying young febrile children with pyuria or positive urine cultures underscores the need to perform the more labor-intensive but significantly more accurate microscopic urinalysis and urine culture to diagnose UTI.



* Pyuria defined as ≥10 white blood cells/mm^3
° Bacteriuria defined as any bacteria per 10 oil immersion fields in a Gram-stained smear
† Culture-positive defined as growth of a single pathogen at a concentration of ≥ 50,000 colony forming units / milliliter

FIG. 3. Algorithm for interpretation of enhanced urinalysis results.

UTI WITHOUT PYURIA

A frequently debated issue is whether UTI can occur in the absence of pyuria. Most UTIs are characterized by the presence of both pyuria and bacteriuria. Pyuria represents the usual inflammatory response of a normal host to the presence of infection in the urinary tract. Pyuria may be absent under three conditions: (1) when there is bacterial contamination of a urine specimen; (2) early in a urinary tract infection before a local inflammatory response develops; and (3) during colonization of the urinary tract (asymptomatic bacteriuria). If a repeat urinalysis performed within 24 h shows persistent bacteriuria without pyuria, contamination and early infection are excluded, leaving asymptomatic bacteriuria (ABU) as the most likely explanation. To determine whether pyuria alone could be used to discriminate true UTI (acute pyelonephritis or cystitis) from colonization (ABU), we evaluated a group of febrile children who had been admitted to the Emergency Department and found to have a positive urine culture. As part of an ongoing study of the treatment of UTI, blood specimens from 153 patients with their first diagnosed UTI were drawn for acute phase reactants (peripheral white blood cell count, erythrocyte sedimentation rate and C-reactive protein) as well as DMSA scans performed at study entry (to ascertain the presence of acute pyelonephritis) and again 6 months after diagnosis (to determine the presence of renal scarring). According to these results patients could be classified in three clinical categories, ABU, acute pyelonephritis and cystitis (Table 4). Eleven patients had no pyuria and normal DMSA scans at entry (presumed ABU). Of the remaining 142 patients 114 had an abnormal initial DMSA (acute pyelonephritis) scan and 28 had a normal scan (presumed cystitis). The acute phase reactants of the 11 patients without pyuria were significantly lower than those of the 114 patients in the

TABLE 3. Sensitivity, specificity and positive and negative predictive values of dipstick leukocyte esterase and nitrites in detecting ≥10 WBC/mm^3 and cultures with growth of ≥50 000 CFU/ml of a single pathogen in 5549 urine specimens obtained by catheter from febrile children 1 to 24 months old

Dipstick Test	Validating Standard	%			
		Sensitivity	Specificity	PPV	NPV
Leukocyte esterase	≥10 WBC/mm^3	48.2	99.4	89.2	94.6
Nitrates	≥50 000 CFU/ml	30.4	99.9	94.6	96.4
Leukocyte esterase or nitrates	≥50 000 CFU/ml	78.7	98.3	71.9	98.8

PPV, positive predictive value; NPV, negative predictive value.

trial who had pyuria and DMSA scan evidence of acute pyelonephritis, and the 28 patients with pyuria but normal scans (presumed cystitis), supporting the hypothesis that these 11 patients had ABU. The absence or low level of pyuria is consistent with the absence of an inflammatory response in colonized (rather than infected) individuals. The source of their fever is likely outside of the urinary tract. Five patients had a source of fever identified: two with acute otitis media; two with roseola; and one with gastroenteritis caused by rotavirus. Initially we managed patients with ABU with antimicrobials. However, two of the eight patients who received antimicrobials developed acute pyelonephritis within 6 months. Swedish studies have noted that in girls with ABU, pyelonephritis occurred only among those who had received antimicrobials for respiratory infections.[6, 7] It is possible that colonization of the urinary tract with nonpathogenic strains, which do not induce inflammation, may provide biologic protection against UTI by inhibiting more virulent bacteria or by inducing a local immunologic response. Accordingly we now avoid antimicrobials for children with ABU and no other indication for therapy. The three most recent patients without pyuria were not treated with antimicrobials and cleared their bacteriuria spontaneously within 2 weeks; none developed a UTI in the subsequent 6 months. All completed follow-up and had a normal DMSA scan at 6 months. Consequently febrile children with a positive urine culture, in whom pyuria is not observed on at least two urine samples, are considered to have ABU with fever from another source.[5] The occurrence of bacteriuria without pyuria in 0.5% of urine specimens during the past years is consistent with the 0.6% point prevalence of ABU reported by Wettergren et al.[8] among 3581 infants. Therefore failure to identify patients with ABU may be of no consequence.

TREATMENT

Although we are confident that we can correctly identify young febrile children with UTI and are aware that prevention of renal scarring constitutes the most important goal of therapy, other treatment issues are still unsettled. Specifically the optimum route of administration of antibiotics in febrile infants with UTI has not been evaluated. Most pediatric textbooks and review articles recommend that young children with UTI, especially those younger than 1 year of age, be hospitalized, at least initially, to receive intravenous antibiotics.[9–11] This recommendation is probably based on a presumed advantage of intravenous therapy in terms of clinical effectiveness when compared with oral antimicrobials. However, oral therapy, if effective in treating the acute infection and preventing the development of scars, has definite advantages. Outpatient management may be less traumatic psychologically to the child, less disruptive to the family and less likely to be associated with nosocomial infection. In addition outpatient management is substantially less costly than hospitalization. The current availability of well-absorbed antimicrobials with excellent activity against enteric Gram-negative organisms prompted consideration of this therapeutic trial. The third generation cephalosporin, cefixime, is an attractive oral agent for treating UTIs in children. Its advantages include: (1) achievement of high peak serum concentrations; (2) long elimination half-life; (3) effectiveness against 98% of common UTI pathogens; (4) acceptance by children because of its pleasant smell and taste[12]; (5) once daily dosing; and (6) fewer potential serious side effects than sulfonamides.

A study has been initiated to compare the effectiveness of oral *vs.* intravenous antimicrobial treatment of UTI in febrile children ages 1 to 24 months. Patients are randomized to receive treatment either entirely by the oral route or initially intravenously followed by oral therapy. Oral therapy consists of 14 days of cefixime given at home. Intravenous therapy consists of 3 days of cefotaxime therapy while the patient is hospitalized, followed by oral cefixime given at home for 11 days. A DMSA renal scan is performed at 24 h of entry into the study. After the 14-day treatment course, patients are maintained on a prophylactic dose of cefixime or trimethoprim-sulfamethoxazole (which is given in one-half of the therapeutic dose once daily) for 2 additional weeks until a voiding cystourethrogram is performed. At 6 months after study entry, a repeat DMSA scan is performed to determine the incidence and extent of

TABLE 4. Mean acute phase reactants in patients with positive urine cultures (N = 153)*

Clinical Category	N	PWBC ($\times 10^3/mm^3$)	ESR (mm/h)	CRP ($\mu g/ml$)
Asymptomatic bacteriuria	11	11.7	15.3	1.3
Acute pyelonephritis	114	22.4	44.9	10.1
Cystitis	28	14.6	26.8	2.7
Total	153			

* All comparisons $P < 0.05$ by Wilcoxon rank sum test.

PWBC, peripheral white blood cells; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

renal scarring, the main measure of long term outcome. Results on 179 patients enrolled to date suggest that the two treatment modalities are equivalent. During 1994 the National Association of Children's Hospitals and Related Institutions reported that for children younger than 17 years of age with acute kidney and urinary tract infection (DRG 322), the average length of stay was 4.08 days and the average adjusted charges were $5706. Because UTI is the most frequently occurring serious bacterial infection in young febrile children large savings in health care expenditures are possible.[13]

IMAGING STUDIES

Imaging studies are part of standard care after diagnosis of a first UTI in young children. Indications for radiologic evaluation of a child with UTI are: (1) pyelonephritis; (2) first UTI in a boy (of any age); (3) first UTI in a girl younger than 3 years of age; (4) second UTI in a girl 3 years of age or older; (5) first UTI in a child (of any age) with a family history of UTIs, abnormalities of the urinary tract, an abnormal voiding pattern, hypertension or poor growth. Renal ultrasound, voiding cystourethrogram and DMSA scans are performed to identify unsuspected urinary tract anomalies or obstruction, vesicoureteral reflux, renal parenchymal inflammation and renal scarring. As part of the ongoing clinical trial evaluating oral *vs.* intravenous therapy for first time UTI, 179 children aged 1 to 24 months with fever (≥38.3°C) received a renal ultrasound and a DMSA scan within 48 h of diagnosis, a voiding cystourethrogram 1 month after diagnosis and a repeat scan 6 months later. Results of renal ultrasound and DMSA scan at the time of presentation with UTI have not modified management in any patient. Current widespread use of prenatal ultrasound leads to identification of obstructions of the urinary tract *in utero*. Accordingly, selective (in patients with persistent fever or abdominal findings and in those who did not have a prenatal ultrasound) rather than routine performance of ultrasound is recommended. A voiding cystourethrogram at 1 month and a DMSA scan 6 months later were useful for identifying (1) patients with vesicoureteral reflux who require prophylactic antimicrobial therapy and (2) patients with renal scarring. The latter group may benefit from the early performance of urine culture in subsequent febrile episodes.[14]

LONG TERM SEQUELAE

Although we are currently able to identify accurately young febrile children with UTI and successfully manage their infections, the long term implications of identifying small renal scars with highly sensitive renal scintigraphy are unknown. Studies that reported the association of renal scarring early in life with the development of hypertension, preeclampsia, renal insufficiency and end stage renal disease decades later, used intravenous pyelograms, a method substantially less sensitive than DMSA scanning.[15] Almost certainly previous reports of renal scarring represented examples of extensive parenchymal damage.

The demographic composition of patients in our ongoing treatment trial has been almost identical with that reported in the initial prevalence study; most (72%) patients identified and enrolled have been white females with high fever. This distribution of patients is not representative of the population of children evaluated at the Emergency Department of Children's Hospital of Pittsburgh (~50% white, 50% African-American, 50% males). If UTI and acute pyelonephritis are more prevalent among white females, this group would be most likely to have long term sequelae. During 1995 the North American Pediatric Renal Transplant Cooperative Study, which includes ~70% of pediatric renal transplants conducted in the US and Canada, provided us with data on 2066 children younger than 20 years of age receiving dialysis and on 4029 children who had already had transplants. Table 5 shows that a significantly higher proportion of whites as well as of females were transplanted with a primary diagnosis of pyelonephritis or reflux nephropathy when compared with all other conditions (chi square, $P < 0.0001$). Almost identical proportions were seen for patients receiving dialysis ($P < 0.0001$).

TABLE 5. Demographic characteristics of 4029 children 0 to 20 years of age who are recipients of renal transplants according to primary diagnosis*

Characteristic	Pyelonephritis	Reflux Nephropathy	Other Conditions
Sex			
Male	39 (44.8)†‡	94 (41.2)†	2261 (60.9)†
Female	48 (55.2)†	134 (58.8)†	1453 (39.1)†
Race			
White	61 (70.1)†	167 (73.2)†	2374 (63.9)†
Black	11 (12.6)†	7 (3.1)†	611 (16.5)†
Other	15 (17.2)	54 (23.7)	729 (19.6)

* North American Pediatric Renal Transplant Cooperative Study; personal communication.

† Comparisons between pyelonephritis and/or reflux nephropathy *vs.* other conditions; chi square $P < 0.0001$.

‡ Number in parentheses, percent.

SUMMARY

UTI is a common and important clinical problem in infants and young children, with a prevalence of 5.3% among febrile infants seen in our Emergency Department. White females with rectal temperature ≥39°C are at particularly high risk (prevalence, 17%). Several studies have highlighted the limitations of the standard urinalysis for identifying UTI in infants and young children and have recommended performance of both urinalysis and urine culture.[1, 16, 17] Alternative methods such as dipstick urinalysis, although attractive because of ease of performance, are inadequate as a screen for UTI. Hemocytometer WBC counts of an uncentrifuged urine specimen can be performed in an office or hospital-based laboratory with minimal training. Performance of Gram-stained smears, however, is most appropriate for the hospital-based laboratory. In the hospital setting where both tests can readily be performed, the positive predictive value of the combination of pyuria and bacteriuria (85%) allows prompt institution of antimicrobial therapy before culture results are available, whereas the lower positive predictive value of the single finding of either pyuria or bacteriuria (40%) justifies delaying treatment decisions until culture results are available. In the office setting where hemocytometer counts can easily be performed, culturing only specimens with pyuria and those of children presumptively treated with antimicrobials will result in the identification of almost all patients with true UTI, sparing large health care expenditures. Although the urine culture is traditionally regarded as the gold standard of UTI, positive urine cultures may occur secondary to contamination or in cases of ABU, leading to a false diagnosis of UTI. In contrast we found pyuria to be a reliable marker to discriminate infection from colonization of the urinary tract. The sustained absence of an inflammatory response, on repeat UA within 24 h, constitutes strong evidence that infection is absent. Management of ABU is controversial; many experts recommend withholding antibiotics because eradication of low virulence organisms may be followed by colonization with more virulent species that cause pyelonephritis.

Preliminary results of our ongoing treatment trial suggest that management of young febrile children with UTI as outpatients receiving oral cefixime is as efficacious as inpatient management with intravenous cefotaxime. Results of renal ultrasound and DMSA scan at the time of infection have not modified management in any patient. Accordingly selective rather than routine performance of ultrasound is recommended. A voiding cystourethrogram at 1 month and a DMSA scan 6 months later have been valuable in identifying patients with vesicoureteral reflux and renal scarring, respectively. Among patients initially identified as having acute pyelonephritis, the incidence of renal scarring at 6 months has been substantially more frequent (~40%) than we had expected. However, the long term implications of small scars identified with renal scintigraphy remain to be determined.

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