Pediatric Urinary Tract Infections

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KEYWORDS

• Urinary tract infections • Urine culture • Urinalysis
• *Escherichia coli* • Pediatric

Urinary tract infections (UTIs) in children are commonly seen in the emergency department (ED) and pose several challenges to establishing the proper diagnosis and determining management. The emergency medicine provider cannot ignore the possibility of UTI when evaluating a neonate (<1 month), infant (1 month to 1 year), or child (≥1 year) with fever without a significant, definite source. Accurate and timely diagnosis of pediatric UTI can prevent short-term complications, such as severe pyelonephritis or sepsis, and long-term sequelae including scarring of the kidneys, hypertension, and ultimately chronic renal insufficiency and need for transplant.[1,2] This article reviews pediatric UTI and addresses epidemiology, diagnosis, treatment, and imaging, and their importance to the practicing emergency medicine provider. The term "febrile UTI" is used to describe upper tract UTI, which typically refers to progression of infection beyond the confines of the bladder with associated systemic symptoms. The term "lower UTI" is used to describe UTI without fever or other systemic symptoms, which is typically diagnosed only in children who can specifically verbalize urinary or other associated complaints.

ETIOLOGY

Bacterial Pathogens

Escherichia coli are responsible for over 80% of pediatric UTIs.[3–8] Other common gram-negative organisms include *Klebsiella, Proteus, Enterobacter*, and occasionally *Pseudomonas*.[6] Gram-positive pathogens include group B *Streptococcus* and *Enterococcus* in neonates and infants, and *Staphylococcus saprophyticus* in adolescent girls.[2,9] Fungal infections are much less common and are usually seen in patients who

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are diabetic, immunocompromised, or have bladder catheters, particularly those also on long-term antibiotic therapy.[10] Common contaminants include *Lactobacillus* spp, *Corynebacterium* spp, coagulase-negative staphylococci, and α-hemolytic streptococci.[11]

Pathogenesis

As with all infectious processes, UTI represents a battle between host defenses and bacterial virulence factors.[3,12] Host defenses, such as frequent voiding and unidirectional urine flow, work to prevent bacteriuria and urinary stasis, whereas Tamm-Horsfall glycoprotein inhibits bacterial adherence to the urinary mucosa.[13]

Epidemiology

There have been hundreds of heterogeneous studies over the decades examining numerous cohorts that all differ in terms of age range, inclusion criteria, racial composition, circumcision status, and location of enrollment. One of the greatest limitations is that beyond the neonatal period, most studies are observational and inclusion rates (eg, for febrile infants) are at the discretion of the clinician and are well below 100%. However, consistently observed is an increased prevalence of febrile UTI in uncircumcised male neonates and girls under the age of 2 years.[14] A 2007 community-based, multicenter study demonstrated that the cumulative risk of UTI in children under the age of 6 years was 4.2%.[15] The highest prevalence of UTI is consistently found to be in uncircumcised boys less than 3 months of age, followed by girls under 12 months of age.[3,4,14,16] In the ED setting, UTIs are the most common serious bacterial illness encountered in febrile children between 0 and 24 months, with a prevalence ranging from 1.9% to 21%, depending on the population studied.[4,5,14–21]

HOST RISK FACTORS

Gender and Circumcision Status

Interestingly, girls are less likely than uncircumcised boys to present with a febrile UTI in the first few months of life based on the available data.[14] In a representative study by Zorc and coworkers,[4] uncircumcised, febrile boys less than 60 days of age had the greatest incidence of UTI, with a rate of 21% compared with 5% in female infants and only 2.3% in circumcised boys. Beyond the first 6 months of age, however, girls have a significantly greater risk of UTI than boys.[14,16,20] Most authorities recommend routine examination and culture of the urine in febrile girls 0 to 24 months of age.[16,20,22]

Uncircumcised males have a significantly higher rate of UTI than any other population, particularly in early infancy.[4,16,23,24] Most studies have consistently confirmed a 10- to 20-fold increase in the risk of UTI in uncircumcised males.[4,5,16,21,23,24] Uncircumcised males experience a higher rate of UTI through several mechanisms, including heavy periurethral colonization by uropathogens, and an inability to fully retract the foreskin.[24–26] When evaluating a febrile, uncircumcised infant in the ED, the best available evidence suggests that a significant risk of UTI persists up until 12 months of age, and work-up should include urinalysis and culture.[22] Febrile circumcised boys over 6 months of age have a statistically lower risk of UTI and generally do not require a work-up with urinalysis and culture.[22]

Race

White race, as compared with African American and Hispanic ethnicities, has consistently been found to be a significant risk factor for febrile UTIs.[14,16,19,27,28] A meta-analysis of four separate studies found that white children had about twice the rate

of UTI compared with black children (8% vs 4.7%).[21] In particular, febrile white girls under the age of 2 years with a temperature greater than or equal to 39°C are at greatest risk, with reported rates as high as 16%.[16,19]

Behavioral

In older children, parents often ask why their child has developed a UTI and whether it has anything to do with hygienic habits. Bubble baths and direction of wiping after defecation have little support as independent risk factors for the development of UTI.[3,29] Urgency–frequency syndrome (excessively frequent voiding) and primary nocturnal enuresis (nighttime bedwetting) likewise have not been definitively linked to increased risk of UTI.[3] Dysfunctional elimination syndrome (incomplete or infrequent voiding, often caused by overly active urinary sphincter tone) may increase the risk of febrile UTI,[30–32] although this association has recently been questioned.[33] UTI has also been linked to the presence of severe constipation, and successful treatment of constipation has been shown to reduce the risk of recurrent UTI.[34,35]

Anatomic Issues

Any abnormality resulting in obstruction to flow of urine can lead to an increased risk of UTI by promoting urinary stasis. These obstructions can be anatomic (urethral stricture, posterior urethral valves) or neurogenic, generally from congenital or acquired abnormalities of the spinal cord.

Vesicoureteral reflux (VUR) is an abnormality of urine flow, with reflux of urine from the bladder proximally into the ureters. Normally, the distal ureter courses obliquely through the bladder wall and intramural pressure of the bladder wall compresses this segment, preventing retrograde flow.[36] Children with VUR typically have a shorter, less oblique intramural segment, resulting in an ineffectual vesicoureteral junction. As the grade of reflux increases (on a five-point scale), the risk of renal scarring increases.[36] It is unclear whether this scarring is the result of a higher rate of febrile UTI or caused by the hydrostatic pressures alone.[37]

DIAGNOSIS

History and Physical Examination

The evaluation of UTI is generally dependent on the age of the child. The presentation generally shifts from quite nonspecific to more focused complaints as the child grows older. However, signs and symptoms may continue to be subtle even in older children, and one should maintain a reasonable index of suspicion, particularly in highly febrile (>39°C) children. Young infants in particular may present with vague and nonspecific symptoms, such as poor feeding, decreased urinary output, lethargy, increased sleeping, vomiting, failure to thrive, and jaundice.[5,12,38–40] Fever is not necessary to raise the suspicion of UTI in neonates. Occult UTI has been significantly associated with the presence of jaundice, particularly if the onset of jaundice was after 8 days of age and an elevated conjugated bilirubin fraction is present.[39]

Beyond the neonatal period, fever is generally the primary symptom that leads to the diagnosis of UTI, and most ED-based studies explicitly identify fever as inclusion criteria for pediatric UTI.[4,5,16,19,41,42] The duration and height of the fever at presentation are clearly identified risk factors.[43] In a 2007 meta-analysis, more than 2 days of fever greater than or equal to 38°C without a source carried a positive likelihood ratio of 3.6 (95% confidence interval [CI], 1.4–8.8), whereas temperatures greater than or equal to 39°C had a positive likelihood ratio of 4 (95% CI, 1.2–13).[43] This association between higher fevers and occult UTI has been confirmed in other large studies.[4,5,16]

Other nonspecific features commonly reported in children with occult UTI include vomiting; loose stools (often mistaken for diarrhea); and abdominal discomfort.[40] However, other investigators have found that these associations lack statistical significance.[16,19]

It is important to note that in children under the age of 2 years, the presence of another possible source of fever, such as gastroenteritis, bronchiolitis, upper respiratory infection, or otitis media, does not entirely exclude UTI.[16,19] Positive viral antigen studies (eg, respiratory syncytial virus or influenza) have been associated with a significant decrease in UTI risk.[4,11,44,45] However, the risk is not insignificant in young infants; respiratory syncytial virus–positive infants less than 60 days of age have a 5.4% risk of UTI, compared with 10% in respiratory syncytial virus–negative infants.[45]

Likewise, presence of an unequivocal source for the fever (eg, varicella, pneumonia, croup, herpangina, or stomatitis) has been associated with only a modest decrease in the risk of UTI from 5.9% to 3.3%.[16] Hoberman and colleagues[19] found that children with a "possible" source still had an intermediate risk of occult UTI (3.5%) compared with children with an unequivocal source (1.6%) and no clear source (7.5%). Shaw and colleagues[16] studied 2411 febrile children 12 to 24 months of age and found that the prevalence of UTI in children without a source was 5.9%, compared with 2.7% in those with a potential source. Fully 64% of children with UTI were thought to have another source for their fever by the examining clinician.[16] In febrile infants, no single sign or symptom maintains a sufficiently low negative likelihood ratio to exclude UTI.[43]

In older, verbal children, the classic symptoms of dysuria, frequency, abdominal or flank pain, new-onset (often nocturnal) incontinence, and fever all carry significant and useful positive likelihood ratios.[40,43] However, these findings are not adequately specific to diagnose UTI and mandate laboratory evaluation. Adolescent girls with urethritis from an unrecognized sexually transmitted disease (often chlamydia or gonorrhea) are at high risk of misdiagnosis and inappropriate therapy.[46] Many young children experience a brief period in which any urge to void is manifested as urgency or frequency, yet do not have an infectious etiology. Additionally, dysuria is frequently the presenting complaint for nonspecific vaginitis in young girls and occasionally dysuria and hematuria may be the presenting symptoms of urethral prolapse.[47,48] This emphasizes the value of genitourinary examination in all ages, along with a detailed history in children with suspected UTI.

Children with a history of documented UTI are at significant risk of recurrence and should be evaluated aggressively. A recent, large, community-based study found that children with documented UTI under the age of 6 have a 12% risk of recurrence per year.[15]

Laboratory Assessment

The gold standard for the diagnosis of UTI is the urine culture. However, culture results are not typically available until 24 to 48 hours after the initial patient evaluation.[20,40,49,50] Rapid screening tests (ie, dipstick and urinalysis) have long been used to identify children likely to have a positive urine culture.[51] Early identification is particularly important in attempting to avoid renal involvement.[20,51] However, rapid screening tests suffer significant problems with sensitivity and specificity in young children. As such, although they can be used to select children for immediate treatment, they should never be a substitute for obtaining a urine culture.[20,40,50,52]

Urine dipstick

Rapid screening performed by a urine dipstick test primarily looks for the presence of leukocyte esterase (LE) or nitrites in the urine sample. LE is released when leukocytes

are broken down with the subsequent release of esterases from lysed urine granulocytes. Nitrites are a byproduct of dietary nitrate metabolism by uropathogenic bacteria.[53] In a 2010 meta-analysis evaluating the accuracy of rapid urine tests in children, Williams and colleagues[54] examined the data from 95 studies with a total of 95,703 children. Summary estimates for the sensitivity and specificity for LE were 79% (95% CI, 73–84) and 87% (95% CI, 79–91), respectively. To emphasize the great variability within the published literature, they noted that across 30 different studies, the sensitivities of LE ranged from 47% to 95%. These results are quite consistent with other published estimates for LE.[14,20,52] Importantly, LE misses more than 20% of children with UTI and inappropriately suggests the presence of UTI in more than 10% of tested patients. Nitrites are far more specific than LE in identifying likely UTI; however, sensitivity is quite poor. The meta-analysis by Williams and colleagues[54] produced sensitivity and specificity estimates of 49% (95% CI, 41%–57%) and 98% (95% CI, 96%–99%), respectively. Again, the range of reported sensitivities across 46 different studies was extreme: 8.3%–95.2%. Nitrites have such a high false-negative rate because not all organisms produce nitrites (eg, gram-positive and *Acinetobacter* spp) or the urine is too dilute. More frequent voiding in non–toilet-trained infants reduces the time available for nitrite conversion.[52,53,55] Thus, although the absence of nitrites in the urine has little diagnostic meaning, their presence virtually guarantees that the child has bacteria in the urine.

Using an either/or strategy to define a positive dipstick has been shown to significantly improve the sensitivity of the urine dipstick without greatly reducing the specificity of the test.[20,52,54] Williams and colleagues[54] found that the presence of either nitrites or LE was more accurate than LE alone, with a sensitivity and specificity of 88% (95% CI, 82%–91%) and 79% (95% CI, 69%–87%), respectively.

Urine microscopy

The presence of pyuria (leukocytes in the urine) has been used for decades to identify patients likely to have a UTI.[56] The definition of pyuria, however, varies widely in the literature.[20] Researchers have traditionally determined a cutoff for pyuria of greater than or equal to five white blood cells per high power field (WBC/hpf) or 10 WBC/hpf, with each study arriving at a different area under the curve and each investigator choosing a different cutoff point for optimal sensitivity or specificity.[52,57] Other investigators have simply chosen one of these values before conducting the study.[18,52,57–60] This lack of standardization is further reflected in the different cutoffs used in nationally published practice guidelines. The most widely disseminated guideline for fever-without-a-source, published by Baraff and colleagues[61] in 1993, recommends using a cutoff of 10 WBC/hpf, whereas the 1999 American Academy of Pediatrics (AAP) UTI Practice Parameter considers a cutoff of 5 WBC/hpf.[20] The question of which cutoff should be used is not a trivial one because positive and negative likelihood ratios can vary significantly (**Table 1**).[40]

Two large meta-analyses in the past decade have tried to address the sensitivity and specificity of microscopic urinalysis, recognizing the extensive heterogeneity in the literature.[54,62] Gorelick and Shaw[52] evaluated five studies using 5 WBC/hpf as a cutoff and nine studies using 10 WBC/hpf. They produced a summary true-positive rate of 67% for 5 WBC/hpf (range, 55%–88%) and 77% using 10 WBC/hpf (range, 57%–92%). False-positive rates were 21% and 11%, respectively. Similarly, Williams and colleagues[54] evaluated 49 studies with 66,937 children and calculated a sensitivity for urine microscopy WBC of 74% (95% CI, 67%–80%) and specificity of 86% (95% CI, 82%–90%) using a cutoff of greater than 5 WBC/hpf in most of the included studies analyzed.

Table 1
Likelihood Ratios of Diagnosing UTI by Age Group

	Microscopy (>5 WBC/hpf for Pyuria and Few Bacteria for Bacteriuria)		Microscopy (>10 WBC/hpf for Byuria and Moderate Bacteria for Bacteriuria)		Dipstick Urine Testing (Both Leukocyte Esterase and Nitrite)	
Children	Younger than 2 years	2 years or older	Younger than 2 years	2 years or older	Younger than 2 years	2 years or older
LR+ (95% CI)	1.63 (1.24–2.13)	1.69 (1.52–1.87)	15.6 (4.16–58.44)	10.84 (5.95–19.75)	6.24 (1.14–34.22)	27.1 (11.44–64.21)
LR– (95% CI)	0.27 (0.07–0.99)	0.04 (0.00–0.59)	0.66 (0.44–0.97)	0.51 (0.35–0.73	0.31 (0.13–0.71)	0.17 (0.07–0.41)

Abbreviation: LR, likelihood ratio.
From National Collaborating Centre for Women's and Children's Health. Urinary tract infection in children: diagnosis, treatment and long-term management. Clinical Guideline. London (UK): RCOG Press; 2007; with the permission of the Royal College of Obstetricians and Gynaecologists.

Both Gorelick and Shaw[52] and Williams and colleagues[54] also examined the accuracy of bacteria noted on microscopic examination. Each investigator reported excellent sensitivity and specificity for the presence of bacteria noted on gram-stained and unstained samples, outperforming both dipstick analysis and microscopy for WBCs. Williams and colleagues[54] reported sensitivities of 91% (95% CI, 80%–96%) in gram-stained samples and 88% (95% CI, 75%–94%) in unstained samples. Specificities were also quite high at 96% and 92%, respectively.

Urine dipstick versus microscopic urinalysis

When the accuracy of dipstick analysis is compared with that of urine microscopy, it is not clear that microscopy, at least for WBCs, provides significant added value.[14,52,54] Gorelick and Shaw[52] and Williams and colleagues[54] both concluded that urine microscopy for white cells should not be used in the diagnostic work-up of UTI, noting comparable sensitivity and specificity to dipstick, along with delay in diagnosis and added cost.[52,54] However, this issue remains unsettled because other investigators have concluded that microscopy outperforms urine dipstick results, particularly in younger children, using higher cutoffs (ie, 10 WBC/hpf) when combined with presence of bacteria.[40,63,64] The real question that remains to be answered is the added value of urine microscopy after dipstick results have already been reported.[40] To date, there has not been a well-designed study that addresses this question.

Urine culture: defining UTI

A positive urine culture is necessary for the diagnosis of a UTI, although actually defining what constitutes a "positive" culture has proved to be difficult and somewhat imprecise.[50,65] It has been known for almost a century that because of the ubiquitous problem of contamination, the mere presence of microorganisms in a urine culture is not enough to prove infection.[50,66] A positive urine culture may be the result of pathogenic bacteriuria (UTI), collection contamination, or asymptomatic bacteriuria.[62] Since the 1950s, a positive urine culture has generally been defined as greater than 10^5 (100,000 or 100K) colony forming units per milliliter (CFU/mL) of urine.[66] This cutoff was initially established by Kass[66] with adults, and later confirmed by Pryles[50] in children, and was based on the bimodal distribution between true bacteriuria and contamination. However, even Kass recognized that some UTIs probably resulted in colony counts less than 10^5, and since then variable cutoffs (often 10K, 50K, or 100K) have been used in various

studies to define a positive urine culture, depending on the investigator and the method of collection.[11,19,67] The traditional cutoff for urine obtained by noninvasive collection methods (clean-catch or clean bag) has remained 10^5 (100K) CFU/mL for decades.[5,11,14,15,40,42,67,68] Most investigators use a cutoff of 10^4 (10K) CFU/mL to define infection with specimens obtained by catheterization.[11,16,18,19,69] Because it was recognized very early on that urine obtained by suprapubic aspiration (SPA) in noninfected children is almost invariably sterile, most authorities use 10^2 (0.1K) CFU/mL as the cutoff for defining a positive culture in an SPA sample.[5,18,27] Other published thresholds include 50,000 CFU/mL from a catheterized specimen,[4,44,70,71] 10,000 CFU/mL from a catheterized specimen with a positive urinalysis,[4,44] or any growth from SPA.[64]

A high suspicion for contamination should be maintained for cultures with low colony counts, heavy mixed growth of bacteria, or growth of a pure organism not known to cause infection.[72] Examples of nonpathogenic organisms include *Lactobacillus*, *Corynebacterium*, α-hemolytic streptococci, *Micrococcus*, *Candida*, and coagulase-negative staphylococci.[11,14,67] Investigators often consider the presence of more than one organism to signify contamination; however, mixed growth may represent primary bacteriuria with secondary contamination and clinical judgment should be applied in this scenario.[14,40,45,67] The bottom line is that decisions in the ED setting are often made well before availability of urine culture results. With this said, in evaluating recent urine culture results available at the time of the ED visit, or when interpreting culture results after the ED visit, the important things to remember include the following: more than 100K of a single organism is essentially diagnostic of UTI, more than 50K is suggestive, more than 10K is highly suspicious in a catheterized specimen, and any bacterial growth after SPA should be considered a UTI.

Asymptomatic bacteriuria

A small but defined number of normal, healthy, asymptomatic children have bacteriuria if cultured.[73,74] It is unclear whether these patients will go on to have symptomatic UTIs in the future or would benefit from immediate treatment. Because there is no way to differentiate symptomatic UTI from asymptomatic bacteriuria in the ED setting, patients with positive urine cultures, as defined in the prior section, must be assumed to have symptomatic UTI and treated as such.

Methods of Collection

It has long been recognized that the reliability of urine culture for the diagnosis of UTI depends on the method of collection.[69,75–78] Although urethral catheterization largely eliminated problems with contamination, concerns about invasiveness and the introduction of infection by the procedure itself led to the development of SPA as an alternative, initially considered no more invasive than "an intramuscular injection, and the required skill is no greater."[78,79] In practice, however, convincing a parent to allow this invasive procedure to be performed on their child may not be so straightforward.

Bagged specimens

Medical personnel and parents alike often prefer the use of noninvasive clean bag urine collection, and a negative urine culture collected by this method can effectively exclude UTI.[20] However, even with meticulous cleaning, bagged specimens produce an unacceptably high rate of contaminated cultures, generally around 63%.[20,56,73,75,78] In one representative study, of the 3440 contaminated cultures evaluated in the study, 132 (1.7%) resulted in one or more adverse clinical outcomes, including unnecessary treatment, admission, or radiologic investigation.[75]

Other investigators have tried to suggest that clean-bag specimens may be more reliable than once believed.[42,80] A large Pediatric Research in Office Setting study of 1646 febrile infants published in 2005 suggested that bagged specimens may have a role in the office setting.[42] Bagged specimens produced more ambiguous cultures compared with catheterization (7.4% vs 2.7%). However, one would need to catheterize 21 children to avoid one ambiguous culture by bag method. Catheterized specimens were more accurate in this study, although the magnitude of the difference was small. In the acute care setting, published guidelines by the AAP, the National Institute for Health and Clinical Excellence, and the World Health Organization clearly discourage the use of bagged specimens, because most studies suggest an unacceptably high culture contamination rate.[20,64,81] A positive culture obtained by bag specimen cannot be used to reliably diagnose UTI.[20] Additionally, because urine dipstick and microscopy (using any method of collection) are not sufficiently sensitive to rule out a UTI, a urine culture is essential. As a result, the urine must be obtained by catheter or SPA in non–toilet-trained children.

Suprapubic aspiration

To distinguish true bacteriuria from contamination, Pryles and several subsequent investigators successfully demonstrated that with proper technique, SPA consistently provides an uncontaminated specimen (**Fig. 1**).[76–79] However, the perception and demonstration of increased discomfort and procedural failure rate has led to a precipitous decline in its use, particularly outside of the neonatal intensive care unit.[82–84] Nevertheless, SPA continues to be considered the gold standard method of urine collection.[12,20,77] Despite the lack of experience by most currently practicing clinicians, the procedure may still be necessary in girls with labial adhesions and boys with phimosis. The relatively recent introduction of ultrasound technology has led to a significant improvement in success rates, and likely in the comfort of the clinician performing the procedure.[82,85–87]

Transurethral bladder catheterization

Despite initial concerns regarding the potential to introduce infection, urinary catheterization has become the standard of practice for febrile children under the age of 2 years.[12,20,40,50,61,78] Early studies demonstrated dramatically reduced contamination

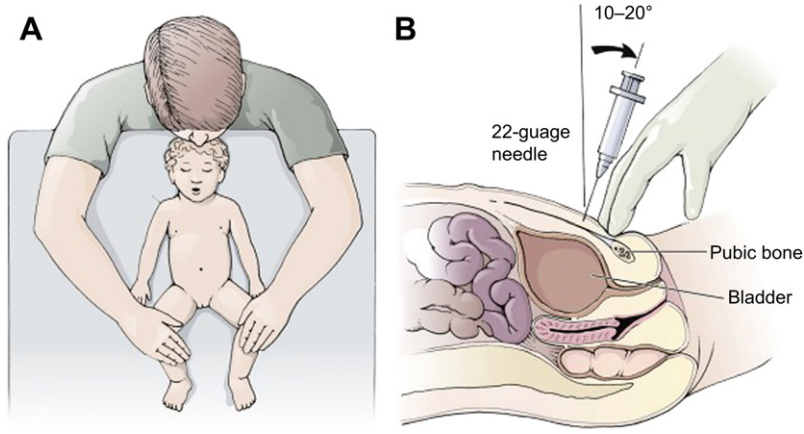

Fig. 1. (*A, B*) SPA procedure. (*From* Silverman MA, Schneider RE. Urologic Procedures. In: Roberts JR, Hedges JR, editors. Clinical procedures in emergency medicine. 5th edition. Philadelphia; Saunders; 2009. Figure 55-24; with permission.)

rates over previous methods, without the discomfort of SPA.[69,79,84] Nevertheless, compared with SPA, catheterized specimens still demonstrate a higher rate of contamination, particularly in the ambiguous range between 1000 and 10,000 colony counts.[69,79] If antibiotics have not been given, a repeat urine culture usually clarifies the issue of contamination.[68,79] To reduce discomfort with bladder catheterization, intraurethral or topical lidocaine have been shown to be effective in several studies.[88–90] Ultrasound may be strategically useful just before transurethral bladder catheterization in determining the likelihood of a successful catheterization based on bladder volume (**Fig. 2**).[91,92]

Clean-catch urine collection

Midstream clean-catch urine collection has been shown to obviate the need for catheterization in older, toilet-trained children.[69,78] With proper technique, contamination rates are within acceptable limits.[67,69,93–95] Even clean-catch midstream urine culture from infants has been shown to be accurate when collected properly.[96] The importance of proper cleaning and the limitations of clean-catch urine collection are both emphasized by Vaillancourt and coworkers[67] in a study of 350 randomized, toilet-trained children presenting to a pediatric ED. The rate of contamination for the non-cleaning group far exceeded that of the group that received cleansing instructions (24% vs 8%).

Additional Testing

Both procalcitonin and C-reactive protein, along with the peripheral WBC count, have been studied for their ability to accurately differentiate upper from lower UTI.[97] Although C-reactive protein and procalcitonin have demonstrated reasonable sensitivity, the specificity of C-reactive protein for upper tract infection is low, limiting its usefulness.[98–100] Similarly, peripheral WBC count does not reliably differentiate upper from lower UTI.[99,100] The use of procalcitonin testing seems promising but more investigation is necessary before moving beyond the research stage.[101,102]

Blood cultures are frequently drawn as part of the standard evaluation for fever-without-a-source for infants, or in the older febrile child who looks moderately or severely ill. Positive blood cultures associated with UTI may occur at all ages but rates tend to be significantly higher in younger infants (>10%), particularly those under 6 months of age.[5,18,41,103,104] Most children with bacteremia are clinically indistinguishable from those without bacteremia, and bacteremia is cleared within 24 hours with

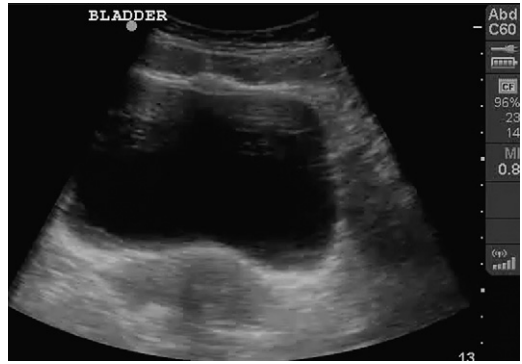

Fig. 2. Full bladder as visualized with transabdominal (suprapubic) ultrasound. (*Courtesy of* Medstar Health, Washington, DC.)

appropriate therapy, regardless of the route of antibiotic delivery.[6,38] Regardless of age, the presence of bacteremia rarely impacts management because the organism is invariably the same as the urine culture, and antibiotic treatment is also the same.[5,6,38,103,104] The usefulness of obtaining blood cultures in the context of febrile UTI is likely to be minimal.[6,38]

Frequently, the question arises whether one still needs to perform a lumbar puncture on young infants (<60 days) who have been diagnosed with a febrile UTI. Many authorities recommend a lumbar puncture to exclude meningitis caused by hematogenous dissemination before initiation of antibiotic therapy. Meningitis concomitant with UTI in young infants does not seem to be common; however, sterile cerebrospinal fluid pleocytosis may be noted.[105] However, the authors recommend sending cerebrospinal fluid for culture before starting intravenous antibiotics in infants younger than 8 weeks of age because of a lack of definitive evidence that it is safe to omit this procedure.[103]

DISPOSITION AND INITIAL MANAGEMENT

Most children, including young infants, with febrile UTI can be managed as outpatients.[3,6,41] The availability of highly effective oral third-generation cephalosporins has also allowed the shift toward increased outpatient management. As resistance patterns evolve, however, the wisdom of this approach may change.[6]

Children younger than 2 to 3 months of age, or children of any age who are toxic, dehydrated, unable to tolerate oral fluids or medications, or those who are at high risk for missed follow-up, are generally best managed with admission for parenteral antimicrobial therapy.[20,40] Admitted children should be treated with an intravenous third-generation cephalosporin or an aminoglycoside.[20]

For children discharged with febrile UTIs, choice of antimicrobial is largely driven by local resistance patterns and previous antimicrobial exposure, which currently favor third-generation cephalosporins.[6,8,20,106] Nitrofurantoin should never be used for febrile UTI because it does not achieve therapeutic serum or renal concentrations, and quinolones should be reserved for resistant organisms in the pediatric patient.[12,20] An initial parenteral dose of ceftriaxone has not been proved to improve outcome, but this may be advisable in younger infants because of their increased risk of sepsis.[41,107]

Significant improvement should not be expected for 24 to 48 hours; in one study, the mean time to defervescence was 24 hours for both the intravenous and oral therapy arms.[6,108] The AAP recommends prompt ultrasonography (to exclude abscess, obstruction, pyonephrosis, and so forth) in children who fail to respond within 48 hours, although a recent study suggests that the likelihood of finding significant abnormalities is extremely small.[20,108] Antimicrobial treatment should be for 7 to 14 days depending on the appearance of the child.[20,109] Shorter courses of therapy may be associated with treatment failure in the pediatric population, even for lower tract infection.[109]

FOLLOW-UP IMAGING

The diagnosis of UTI in a young child often triggers further diagnostic evaluation for genitourinary tract abnormalities that is time-consuming, uncomfortable, and expensive.[110,111] Even though follow-up imaging studies are outside the scope of routine ED practice, it is important to understand the patient's subsequent evaluation and cascade of testing that may follow. The traditional approach, currently advocated by the AAP and many other experts, is to obtain a renal ultrasound followed by voiding cystourethrography or radionuclide cystography in all infants under 2 years of age diagnosed with UTI.[3,20] This approach has been questioned and is not as aggressively

recommended in the recent United Kingdom National Institute for Health and Clinical Excellence guidelines, with imaging only recommended for infants under 6 months of age or children with an "atypical" presentation, including severely ill, poor urine flow, elevated creatinine, abdominal mass, sepsis, failure to respond to antibiotic therapy in 48 hours, or infection with organisms other than *E coli*.[40]

Renal ultrasound can describe static anatomic abnormalities, such as abnormal kidney size, hydroureter, duplicated collecting system, or bladder diverticuli.[36,63,101] It is not accurate in identifying renal scarring from prior UTIs or parenchymal involvement with current UTI, and in the modern era of prenatal ultrasound, the yield for this test is quite low.[71,112] The primary purpose of the voiding cystourethrography is to identify the presence of VUR or posterior urethral valves. VUR is graded on a 1 to 5 scale, with grades 4 and 5 representing moderate to severe dilation of the ureters and renal pelvis.[36,101] For a long time, VUR has been considered to be a risk factor for recurrent UTI and renal scarring. This time-honored assumption is based on flawed studies and more recent studies question this association.[111,112] Radionuclide studies (eg, technetium-99 dimercaptosuccinic acid) are useful for the detection of renal scarring.[112,113]

The goal of radiographic evaluation is to identify patients with functional or anatomic abnormalities that might place them at risk for recurrent UTI and subsequent renal scarring and possibly chronic renal failure.[81] This approach (and these underlying assumptions) has recently received great scrutiny and has been questioned.[67,114] These radiographic studies are only useful if subsequent intervention can be shown to change a patient's risk and outcome (ie, if surgical intervention or prophylactic antimicrobials reduces further risk of infection and subsequent renal damage).[71,81] However, prophylaxis has not been shown to effectively prevent recurrent infection, even in children with documented VUR.[15,40,115,116] Surgical intervention also has not been proven to improve outcome compared with watchful waiting and early identification and treatment of recurrent UTIs.[111]

SUMMARY

The general approach to pediatric UTI is relatively straightforward: a child presents with fever (typically without a definite source), the clinician decides to obtain a urinalysis and urine culture, evaluates the urinalysis results, initiates antibiotics if indicated, and follows-up on the urine culture result in 24 to 48 hours. However, the decision on who to obtain a urine sample from can be particularly difficult in febrile infants and toddlers who look well and present in the context of a likely viral process. This is particularly true in younger children who typically require urinary catheterization to obtain an appropriate specimen for culture. Statistically speaking, most febrile children do not have a UTI, and the process of urine collection can be invasive and unpleasant. However, children without fever may have certain nonspecific complaints that should also trigger the clinician to think about the possibility of UTI. Significant limitations in the sensitivity and specificity of rapid urine screening tests make interpretation of the urinalysis results challenging. Therefore, concomitant sterile acquisition of urine for culture is critical. Finally, evaluation of ambiguous urine culture results must be approached with caution. The implications of initial decision-making are significant for the patient and family, and can drive a potentially uncomfortable and costly follow-up process. This, in turn, potentially labels a child as at risk for recurrent UTI, lowering the threshold for future invasive tests, thereby reinitiating a viscous cycle. Although there is the potential for treachery and diagnostic dilemma when approaching pediatric UTI, most patients can be safely and effectively managed in the ED and referred for close outpatient follow-up by a primary care provider.

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