



Overview of the Evaluation, Diagnosis, and Management of Urinary Tract Infections in Infants And Children

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Although urinary tract infection (UTI) may appear straightforward, it can be a diagnostic challenge to pediatricians, nurse practitioners, and pediatric urologists. While there has been significant progress with regard to our understanding of the pathogenesis and host factors related to a UTI, the diagnosis remains complicated by nonspecific symptoms and the difficulty in obtaining an uncontaminated urine specimen. Prompt diagnosis and treatment of a UTI in infants and children is critical especially in children with renal anomalies because delay in diagnosis can result in preventable morbidity and long-term complications associated with renal damage.

Definition

A UTI in infants and children is defined as the detection of sig-

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Note: CE Objectives and Evaluation Form appear on page 192.

Urinary tract infection (UTI) is the most common serious bacterial infection in infants and children. UTI is an infection of the lower urinary tract, the upper urinary tract, or both. The diagnosis is dependent on the collection and analysis of an uncontaminated urine specimen. It is the combination of bacterial virulence, and host factors that are closely interrelated, which lead to the development of a UTI. Management of UTI in infants and children requires prompt diagnosis, treatment, and resolution of symptoms followed by appropriate radiologic evaluation. The ultimate goal is the preservation of kidney function.

nificant bacteria in the urine (quantitative culture) with associated specific and nonspecific signs and symptoms. The established definition for a bacterial UTI is greater than 100,000 colony-forming units (cfu) of a single bacteria when obtained from a midstream collection of urine or 50,000 cfu or greater of a single organism collected by transurethral catheterization from a child with fever (Hoberman & Wald, 1998). Current evidence is that lower colony counts may be of importance in young children, especially those not yet toilet trained (Poole, 2002). The American Academy of Pediatrics (AAP, 1999) guidelines suggest that any colony count with a single organism collected from a suprapubic bladder aspirate is indicative of infection. Hoberman and Wald (1998) agree except in those instances where a colony count of 20,000 to 30,000 cfu of coagulase negative staphylococcus is obtained.

A UTI can occur in the bladder or lower tract (cystitis), kidneys or upper urinary tract (pyelonephritis), or both. Infection of the lower tract or cystitis may be painful but normally does not cause significant or long-term morbidity. On the other hand, bacterial infection of the upper tract or pyelonephritis is considered serious with potential morbidity (Wald, 2004).

Asymptomatic Bacteriuria

It is important to distinguish between infection and covert or asymptomatic bacteriuria. Asymptomatic bacteriuria is a transient colonization of the bladder, which if left untreated will usually resolve without sequelae (Smith, 1994). Asymptomatic bacteriuria is defined by a specific colony count usually greater than 100,000 cfu in an infant or child without symptoms of a UTI (Smith, 1994). Asymptomatic bacteriuria is detected through



routine urinary screening. The significance with regard to a UTI is clearly stated by Hoberman and Wald (1998) who showed that treating asymptomatic bacteriuria increases the risk for a symptomatic UTI. Furthermore, a study conducted by the Canadian Task Force on Preventative Health Care concluded that "a screening urinalysis should not be performed on healthy infants and children for the purpose of detecting bacteriuria" (Smith, 1994). Thus, most experts agree and do not recommend routine screening of asymptomatic children for bacteriuria.

Cystitis vs. Pyelonephritis

Understanding and appropriately differentiating cystitis from pyelonephritis is crucial. The AAP states that an appropriate diagnosis is imperative for two reasons: (a) to permit identification, treatment, and evaluation of the children who are at risk for kidney damage; and (b) to avoid unnecessarily evaluating and treating children who are not at risk. To make an accurate diagnosis, the difference between pyelonephritis and cystitis must be understood. Classically, the presence of a fever has separated the diagnosis of pyelonephritis from cystitis. Cystitis is an inflammatory condition of the urinary bladder. General signs and symptoms of cystitis include dysuria, frequency, urgency, malodorous urine, enuresis, hematuria, and suprapubic pain (Anderson, Anderson, & Glanze, 1994). Pyelonephritis is a diffuse pyogenic infection of the pelvis and parenchyma of the kidney. The onset of pyelonephritis is generally abrupt. Clinical signs and symptoms include fever (100 F or greater), chills, along with costovertebral angle or flank pain and tenderness (Gillenwater, Grayhack, Howards, & Duckett, 1996). Older children may report cystitis symptoms, such as strong

smelling urine, dysuria, urgency, and frequency along with the fever and flank pain. Infants and children may have nonspecific signs such as poor appetite, failure to thrive, lethargy, irritability, vomiting, or diarrhea. It is important to consider the presence of a UTI in any young infant and child with an unexplained fever (AAP, 1999).

Incidence

A UTI is among the most common serious bacterial infections in infants and children (Wald, 2004). The incidence in children is surpassed only by upper respiratory infections (Plachter, Schulman, & Canning, 1999). UTIs occur throughout childhood, but with highest frequency during infancy. Uncircumcised males have a 10-fold increase of developing a UTI than circumcised males (Rushton & Pohl, 2002). Children who have had one UTI have an increased risk of developing another UTI within the subsequent 6 months following acute pyelonephritis (Hellerstein, 2002). The male to female ratio is greater in infants with the prevalence of bacteriuria; in males 3.7% and for females 2% (Plachter et al., 1999). In preschool and school age children the prevalence of UTI is about 1% to 5% for females and rare in males. Following puberty the incidence increases for females and remains uncommon for males (Landau, 2002).

Etiology

Normal bladder function is a complex process between urine storage and emptying. It requires the bladder to be compliant and hold an adequate volume of urine. Sphincter and detrusor muscles must appropriately coordinate between contraction and relaxation for the bladder to completely empty (Fisher & Frank, 2000). Both anatomic and physiologic factors that interfere with this process put infants and children at risk for developing UTI.

Anatomic abnormalities such as vesicoureteral reflux (VUR), neurogenic bladder, and an uncircumcised male all increase risk for UTI. VUR is a condition in which urine travels backward from the bladder toward the kidney and may affect one or both ureters and/or kidneys. General dogma holds that if bacteria grow in the bladder the refluxing, infected urine can infect the kidneys, and lead to significant renal scarring and loss of function.

In children with a neurogenic bladder, the most frequent medical complication is urinary tract infections (Matsumoto, Takahashik, Manabe, Iwatsubo, & Kawakami, 2001). This increased risk is due to improper storage, incomplete bladder emptying, and potential high-pressure systems. The treatment goal in this population is to restore the normal low-pressure reservoir function of the bladder (Sauerwein, 2002).

Uncircumcised males are thought to be at an increased risk for developing a urinary tract infection. Boys with a prepuce have a tendency to harbor organisms in the foreskin likely due to the warm, moist mucosal environment. The bacteria can migrate up the urethra and colonize in the bladder (Poole, 2002). The AAP acknowledges that there is an increased risk of UTIs in uncircumcised boys in the first 6 months of life; however, there is not sufficient risk to recommend routine neonatal circumcision. Other authors believe that their findings confirm the protective effect of newborn circumcision. For example, one study examined the incidence of UTI in all infants (female and male) over a 1-year period. Of the 154 males that became infected, 132 (86%) were not circumcised (Schoen, Colby, & Ray, 2000). A second study concluded that during the first 6 months of an infant's life, uncircumcised males had an increased chance of



having periurethral bacteria. This was discovered following a study in which the bacterial flora in the urethra were compared between circumcised and uncircumcised infants at 2 days, 2 months, 4 months, and 6 months (Wiswell, Miller, Gelston, Jones, & Clemings, 1988).

Physiologic factors such as dysfunctional voiding and constipation place children at risk for developing urinary tract infections. Infrequent voiding and incomplete bladder emptying could lead to the development of a UTI. In these cases, urine may be sitting in the bladder for prolonged periods of time. Urine is an ideal medium for bacterial growth. To defend against this infection, regular and complete bladder emptying should be achieved (Poole, 2002). Constipation is also an associated factor in the development of a UTI. If stool is chronically in the rectum, more bacteria tend to colonize in the perineum, increasing the risk of UTI. Loening-Baucke (1997) found that treating constipation decreases the risk of recurrence of UTI.

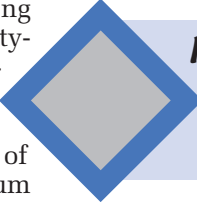
Sexual intercourse is a known risk factor for developing urinary tract infections. The increased risk of infection is likely due to the movement of bacteria from the vagina to the urethra and the friction trauma to the urethral meatus. This allows the ascent of bacteria into the urethra. Only a small percentage of teenage girls and women appear to be at risk for intercourse-associated infection, presumably those already prone to UTIs (Hellerstein, 2002).

Pathogenesis

The bladder and upper urinary tracts are considered sterile but the distal urethra and the peri-urethral area are colonized by bacteria from the GI tract that act as a normal defense to invasive pathogens (Hellerstein,

2002). When this “normal defense” is disrupted it increases the risk for a UTI. The bacteria gain entrance to the urinary system via the urethra and ascend into the bladder and/or kidneys (McCracken, 1989). The susceptibility of the infant or child to a UTI is a combination of bacterial virulence, as well as a breakdown in the host factor defense mechanisms (Hellerstein, 1995).

Escherichia coli is the



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most frequent bacteria to cause UTIs in infants and children. *E. coli* accounts for about 85% to 90% of all UTIs in this age group (Jantunen et al., 2001). *P. fimbriatae*, organelles on strains of *E. coli*, are particularly virulent in that they may attach or adhere on specific receptors of uroepithelial cells and interfere with the washout of bacteria (Hellerstein, 2002). Other organisms causing UTIs include *Klebsiella*, *Enterobacter*, *Enterococci*, *Staphylococcus*, *Proteus*, *Pseudomonas aeruginosa*, *Staphylococcus*, and *Saphrophyticus* (usually recovered in sexually active females) (McCracken, 1989). Adenoviruses can also affect the urinary tract and cause infection. Fungi are not common but are seen in infants and children who are on long-term antibiotics or patients who are immunocompromised (Shapiro, 1992).

The host factors that contribute or increase the risk of a UTI include urine holding, unstable bladder, frequent UTIs, constipation, sexual intercourse, chronic illness, and prolonged use of antibiotics (Hellerstein, 2002). Anatomic host factors are a short urethra in females, foreskin in uncircumcised males, VUR, and urinary obstruction (Schaeffer, 2001).

Diagnosis

Making the diagnosis of UTI is of critical importance. Health care providers should have an index of suspicion in infants and children with fever and no other obvious source of infection. This also is true in children with diurnal or nocturnal enuresis that were previously toilet trained, infants and children with poor growth, or infants and children with previously diagnosed and

treated renal disease. Factors that complicate the diagnosis of a UTI in infants and children include the nonspecific nature of symptoms like fever, vomiting, and pain that are associated with many childhood illnesses. The most recent guidelines issued by the AAP (1999) suggest that a UTI should be considered in infants and young children with unexplained fever, and warrants the collection of specimens for urinalysis and urine culture. Afebrile children older than 2 years of age, who present without fever but with symptoms of dysuria, urgency/frequency, hematuria, flank pain, or new onset of enuresis, should also be evaluated with a urinalysis and urine culture (Johnson, 1999).

The urinalysis and urine culture are the two diagnostic tests that will assist with making the diagnosis. The urinalysis is a helpful screening and diagnostic tool, while the urine culture is considered the “gold standard” and the only absolute way to make the diagnosis of a UTI (Wald, 2004).

The urinalysis is used to provide quick information to support the diagnosis of a UTI. In most office settings, urinalysis is performed using a dipstick method. When using a urine dip-



stick one must be careful to ensure that the dipsticks have not expired. When interpreting the results it is important to check the urine dipstick at the appropriate time intervals as indicated on the dipstick bottle. The urine dipstick test checks for the presence of leukocyte esterase and nitrites. Leukocyte esterase is a biochemical that is released from white blood cells (WBCs) secondary to bacterial invasion, which causes the release of esterase. Urinary nitrites are produced by the bacterial breakdown of dietary nitrate. Leukocyte esterase, nitrites, and microscopy are the components of the urinalysis that are most useful in the evaluation of a UTI (Poole, 2002). The sensitivity of both esterase and nitrites is low and therefore there is a high risk of missing a UTI (Wald, 2003). The specificity or accuracy for leukocyte esterase is in the range of 78% while the specificity for urine nitrite is about 98% (Rushton & Long, 2002). When either the leukocyte esterase or the nitrite tests are positive, the likelihood of a UTI increases but the number of false positives also increases (Ahmed & Swedlund, 1998).

The enhanced urinalysis is a newer technique developed to predict UTI in low-risk infants and children. It utilizes uncentrifuged urine and a Neubauer hemocytometer to evaluate the number of WBC/mm³ (cell count). This method is far superior to the standard urinalysis in successfully distinguishing between colonization, contamination, and asymptomatic bacteriuria, thus providing health care providers with the ability to detect a true UTI, especially in the febrile infant (Herr, Wald, Pitetti, & Sylvia, 2001).

To make a definitive diagnosis of UTI, a quantitative urine culture must be performed. This requires that urine be properly collected and the specimen transmitted to a lab for inocula-

tion on culture media within 1 hour of collection. Urine specimens that cannot be processed within 1 hour of collection should be refrigerated to prevent the growth of organisms that occur with prolonged exposure to room temperature.

The challenge in obtaining a reliable urine culture is related directly to the difficulty in collecting uncontaminated urine from infants and young children. Methods to obtain a urine specimen include the suprapubic aspiration (SPA), transurethral catheterization, midstream collection, and bagged collection. The method of collection least likely to result in contaminated urine is the SPA because collection bypasses the distal urethra. Transurethral catheterization is considered the next best approach for obtaining uncontaminated urine.

In the infant or child aged 2 months to 2 years, the most effective and reliable way of obtaining a urine specimen is to perform either a SPA or transurethral catheterization (AAP, 1999). It is important to keep in mind, however, that parents may resist the recommendation to obtain urine by SPA, in which case the health care provider should be prepared to acquire the urine specimen through another method of collection. For older children a midstream urine collection is adequate when obtained correctly. In our experience a good way to obtain the clean catch urine is to have the child sit facing the back of the toilet (straddle). The nurse or parent should be positioned behind the child holding a sterile container for urine collection. Cleansing is not helpful or necessary because the first few drops of urine are discarded into the toilet to allow for collection of the midstream specimen.

A bagged specimen is useful for urinalysis, but unsuitable for urine culture. If urinalysis of a bagged specimen suggests the

presence of a UTI, then a second specimen (preferably obtained by transurethral catheterization) is needed to verify the diagnosis. To increase the likelihood of obtaining an uncontaminated bag specimen, the child's perineum should be cleansed with soap and rinsed thoroughly with water before the bag is applied. As soon as the child has voided the bag should be removed. If voiding does not occur within 15 minutes after applying the bag, the bag must be removed and reapplied following the same cleaning routine. The bag must be checked every 15 minutes until the child voids. According to the AAP (1999), most pediatricians believe that the analysis of urine obtained through bag collection is an effective means of eliminating the diagnosis of UTI in children not receiving antimicrobial therapy. Moreover, the procedure is noninvasive, requires limited staff training or involvement, and is reliable so long as the urine is not contaminated by antibacterial agents used for perineal skin cleansing.

Treatment

Treatment of UTI should begin only after the proper collection of a urine specimen for culture, and is based on the age of the child at diagnosis, the presenting signs and symptoms, evidence of underlying renal pathology, and presence or absence of immunologic problems (Nelson, Gurr, & Schunk, 1998). Parenteral antibiotics and hospitalization are recommended for the young infant under 3 months of age with pyelonephritis. Hospitalization is also recommended for the infant or child with pyelonephritis and who appears ill, or "toxic," and the child who does not appear "toxic" but is vomiting (Landau, 2002). Parenteral antibiotics are initiated and continued until the child is afebrile for at least 24 hours. Oral antibiotics are continued for at least 10 to 14 days



(Wald, 2003). For the febrile child who does not appear ill and is able to drink fluids without vomiting, it is appropriate to treat as an outpatient with oral antibiotics for 10 days (AAP, 1999). Antibiotic prophylaxis is continued until after the necessary diagnostic tests are completed (AAP, 1999).

The treatment of cystitis is often managed as an outpatient. Oral antimicrobial therapy varies from one dose to 3 days, to the conventional 7 to 10 days (McCracken, 1989). While short course therapy is effective for adult women, a 7 to 10 day course of antibiotics is recommended by the AAP (1999) for infants and children up to 2 years of age. For older children the recommended therapy for cystitis is 3 to 7 days (McCracken, 1989). Appropriate followup is required regardless of the duration of treatment.

The selection of an appropriate antimicrobial for treating pediatric UTI is dependent upon the age of the child, presenting signs and symptoms, the sensitivity of the organism causing the infection, and resistance patterns in the community. Among the antimicrobials that may be used for oral treatment of UTI are sulfamethoxazole-trimethoprim, amoxicillin with or without potassium-clavulanate acid, cephalosporins, and aminoglycosides. However, the preferred antibiotic for oral administration is sulfamethoxazole-trimethoprim, but only in children over 2 months of age. Agents such as nalidixic acid and nitrofurantoin should not be used to treat infants with febrile UTI, or young children with UTI and accompanying renal problems because these drugs do not achieve therapeutic concentrations in the bloodstream, but instead are concentrated and excreted through the urine only (AAP, 1999).

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used to protect the kidneys from further renal damage. The best approach to achieve this goal remains controversial. Antibiotic prophylaxis is recommended for all children following acute pyelonephritis until the appropriate radiologic tests are performed, and it is confirmed that the child does not have a structural renal anomaly (Hellerstein, 2002). The highest risk of developing a second urinary tract infection is within the first 6 months of the initial pyelonephritis. Therefore, antibiotic prophylaxis is recommended in children without vesicoureteral reflux for that period of time (Hellerstein, 1995).

[Editor's note: The reader is referred to the AAP's "Practice Parameters: The Diagnosis, Treatment and Management of UTI in Febrile Infants and Young Children" for specific recommendations on antimicrobial therapy choices and dosages.]

Radiologic Diagnosis of UTI

Determining what radiologic studies to obtain following the diagnosis of a UTI is an area of medicine that is still not agreed upon, nor is there a gold standard. However, the presentation of a fever with a UTI should trigger a strong suspicion of an underlying urologic abnormality (Gillenwater et al., 1996). Thus, infants and young children should undergo radiologic imaging as soon as possible to examine the urinary tract for structural abnormalities if there is no significant improvement of symptoms after 2 days of antimicrobial therapy. Other children with a diagnosis of UTI should be scheduled for radiologic studies at a convenient time after documented resolution of the infec-

tion (AAP, 1999).

A renal and bladder ultrasound is the least invasive method to visualize the kidneys and bladder, and should be used primarily to screen for an obstruction or abscess when resolution of UTI symptoms is slower than expected, despite treatment (AAP, 1999). Structural abnormalities such as hydronephrosis, renal calculi, ureteroceles, and a thickened bladder wall can be detected through ultrasonography. Ultrasounds do not detect or diagnose vesicoureteral reflux. In fact, one study done by Hoberman et al. (2003) revealed that only three out of five children with high-volume vesicoureteral reflux had dilation on their ultrasound. Additionally, decreased echogenicity seen on an ultrasound can be indicative for scarring, but should be verified using other radiologic procedures.

A voiding cystourethrogram (VCUG) is recommended for all infants and young children with a febrile UTI to rule out vesicoureteral reflux. VUR is the retrograde flow of urine from the bladder to the kidneys, which occurs in 30% to 40% of infants and young children with UTI (Hoberman et al., 2003). Additionally, the degree of reflux is generally much higher in this population putting them at the greatest risk for developing pyelonephritis and renal scarring. The AAP reports that the rate of VUR seen in children with a UTI less than 1 year of age can exceed 50%.

Detecting VUR is done through either a conventional VCUG or a nuclear voiding cystourethrogram (NVCUG). The difference between the two procedures is the medium and methods used to visualize the urinary system. A VCUG uses a radiopaque contrast medium instilled into the bladder to highlight the lower urinary tract,



which is captured on film using traditional radiographic techniques. The NVCUG requires the instillation of a radionuclide into the bladder and a gamma camera to capture the images of the lower urinary tract. While the NVCUG delivers less radiation and is considered equally sensitive as the VCUG in identifying structural abnormalities, it is less precise in grading of VUR compared to the VCUG. Regardless of the technique used, the anatomic images of the bladder and urethra must be carefully highlighted and examined to exclude the diagnosis of posterior urethral valves in males as a contributing factor to UTI.

Technetium-99m-labeled dimercaptosuccinic acid (DMSA) scans are a very sensitive method to identify acute changes in the kidney associated with pyelonephritis. DMSA scans are considered normal if homogenous uptake of the radioisotope is evident throughout the kidneys and the renal contour is preserved (Hoberman et al., 2003). In acute pyelonephritis the DMSA scan will show focal or diffuse areas of decreased uptake by the dimercaptosuccinic acid without evidence of cortical thinning. Evidence of renal scarring will show decreased uptake of labeled dimercaptosuccinic acid with cortical thinning. The scan will also allow visualization of the collecting system and estimation of the percentage of renal function of each kidney (Hoberman et al., 2003).

Lavocat and colleagues (1997) examined the importance of DMSA screening in patients with pyelonephritis. In their study, 55 children with a febrile urinary tract infection were screened with both an ultrasound and a DMSA scan. Ultrasound abnormalities were seen in 25 children (45%) and 51 patients (93%) showed findings of parenchymal changes on their

DMSA scan; however, the finding of a normal ultrasound did not rule out renal parenchymal involvement. It is also suggested to repeat the DMSA scan following the resolution of the infection. In this same study DMSA scans were repeated in 45 children 7.5 months after the initial study with 19 children showing

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resolution of parenchymal changes, 16 children showing improvement, 8 children with persistent symptoms, and 2 children showing further parenchymal deterioration.

Patient and Family Education

Encouraging parents to be proactive with their pediatricians in their child's care is essential in preventing and treating UTI. Education should begin with teaching related to the signs and symptoms of UTI. It is especially important to emphasize to parents and other health care providers that infants generally have nonspecific signs that often mimic other illnesses. If an infant or young child presents with a fever and no obvious source for an infection, the urine should be cultured. More detailed education will depend on the predisposing factors such as VUR, neurogenic bladder, and dysfunctional elimination.

Conclusion

Pediatric UTI in the 21st century continues to generate discussion. The controversies surrounding UTI include recognizing the diagnosis, obtaining an accurate urine specimen, length of treatment, delivery of antibiotics, and use of prophylaxis. The management of underlying pathology along with the appro-

priate radiology studies to diagnose those children who could potentially have renal scarring from UTI is an area that needs further investigation.

In summary, UTIs are a common bacterial illness in infants and children (Honikinen, Jahnukainen, Mertsola, Eskola, & Ruuskanen, 2000). Proper urine collection, prompt diagnosis, effective antimicrobial treatment, and followup evaluation are necessary to successfully treat UTI with low morbidity. The ultimate goal

of treatment is to decrease the incidence of infection in order to protect the kidneys. The principals of treatment include the proper collection of uncontaminated urine, identifying the infecting microorganism(s), choosing among appropriate antimicrobials to eradicate bacteria and minimize drug toxicity, resolving symptoms, and preventing reinfection. ■

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