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GENITOURINARY EMERGENCIES

PEDIATRIC URINARY TRACT INFECTION

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Urinary tract infections (UTIs) are common in children, however, they are "sneaky and sly" because they frequently do not

manifest as dysuria, as is common in adults.[30] [2] The diagnosis of UTI should be considered in all infants and children who present to the emergency department (ED) with classic symptoms of UTI, as well as in those with nonspecific symptoms, including fever, vomiting, abdominal, or flank pain. The goal of early diagnosis and treatment of UTIs in the pediatric population is the prevention of the complications of bacteremia and renal scarring. Although the most severe complication of pyelonephritis, renal scarring with progression to end stage renal disease is rare, aggressive treatment and work-up of pediatric urinary tract infection is preventive.

UTI is a nonspecific phrase used to define an inflammatory response to bacterial invasion anywhere within the renal system. Bacteria is present within the urine, as well as other signs of infection (nitrates, pyuria), and the patient may have local (dysuria, frequency, urgency) or systemic symptoms (fever, myalgias, rigors, nausea, vomiting, abdominal, or flank pain). Asymptomatic bacteriuria is defined as bacterial growth in the urine without signs or symptoms of infection. UTIs are divided into two overlapping categories--uncomplicated lower tract infection of cystitis and urethritis and upper tract infections of ureteritis, pyelitis (upper collecting system), and pyelonephritis (renal parenchyma). In general, the presence of fever, systemic symptoms, or back pain with infected urine indicates the presence of upper tract infection. Reliance upon the presence of fever alone to indicate the presence of an upper tract infection is problematic because renal scanning fails to show that fever is a reliable marker for pyelonephritis.[36] As well, studies that have analyzed fever as a marker for upper tract infection have shown a wide range of sensitivities (53%-84%) and specificities (44%-92%).[9] Also complicating the diagnosis of upper tract infection is the fact that there is no "gold standard" test for pyelonephritis. In the past, antibody-coated bacteria, and more recently, renal nuclear scanning have been used as indicators of pyelonephritis. However, the utility of these tests is still limited.

This chapter will discuss the spectrum of infections that fall under the heading of UTI. The diagnostic approach and management of the pediatric patient will be addressed. Infection in adults is addressed elsewhere.

EPIDEMIOLOGY

The prevalence of UTIs varies with age and gender but is a relatively common occurrence in the first year of life. The

prevalence of UTI in the neonatal period is about 1% for full-term infants and 3% for premature infants.[32] [2] Population- based studies in Sweden found the risk of UTI from age 0 to 10 years to be 3.5% in girls and 1.1% in boys. Some studies have shown

that infant males have a higher risk for UTI than age-matched females.[37] Other physicians believe there is an equal incidence of disease in this early period.[32] After the first year of life, UTI is clearly more common in females.

When faced with a febrile neonate, the likelihood of a UTI increases from 1% in all neonates to 4.6% in the presence of fever (for neonates less than 2 months old).[21] [22] [23] For febrile children presenting in the first year of life the incidence of UTI is approximately 5.6%.[22] [23] Although this number is helpful as a general guideline, a study by Hoberman considers UTI in greater detail. This study noted that febrile infants less than 1 year old who had urinalysis performed, 5.3% had UTIs. The rate was 2.5% for boys and 8.8% for girls. During the evaluation, if a definite source of fever was present (meningitis or pneumonia), the rate of UTI was only 1.6%. However, if there was only a probable source (otitis media or upper respiratory infection), the rate of UTI was 3.5%. If no source of the fever was identified, the rate was 7.5%.[22] The rate of UTI was higher in children with a fever greater than 39°C (6.4% compared with 4%). Among white girls with fever >39°, there was a 17% rate of UTI.[22] Similar results were found in a study of febrile children less than 24 months of age with and without bronchiolitis (1.9% UTIs in infants with bronchiolitis and 13.6% of controls).[24] Therefore, the risk of a UTI in a febrile infant is significant, especially if there is no source of fever or only a presumptive source of fever.

Girls have a trimodal age distribution for UTI. The rate is highest in the first year, then again at 2 to 3 years at the time of toilet training, and finally in adolescence when sexual activity begins. During the first year, infection is most commonly pyelonephritis. The second peak is caused primarily by cystitis because of dysfunctional voiding around the toilet training years.

Once treated it is not uncommon for children to develop additional UTIs. These infections can be caused by a persistent or partially treated UTI. On the other hand, infection may result from a recurrent infection within 6 months or a year of the previous UTI. During the first year, 18% of boys will have a recurrence, as will 26% of girls. The recurrence rate decreases with age.[39]

RISK FACTORS FOR UTI

Conditions that cause urinary stasis such as vesicoureteral reflux (VUR), and other anatomic abnormalities such as renal calculi

and voiding disorders, may all predispose children to the development of infections. The most common risk is VUR, which is present in 31% of children with UTIs.[29] Urine refluxing up the ureters places children at increased risk both for UTI as well as for scarring that results from the repeated infections. VUR is graded from I to V depending on the level of ureteral reflux and the degree of dilation of the collecting system. By

dimercaptosuccinie acid (DMSA) scan, scarring from recurrent pyelonephritis occurs in 42% of kidneys, especially those with high-grade reflux.[4]

In girls with culture-proven UTI, VUR is present in approximately 30% to 40%. Fortunately, this number decreases with age. In boys with UTIs, who are less than 1 year old, the rate of VUR is even higher (68%). Likewise, the rate decreases as boys become older to 25% in boys age 1-3 years old. The decrease in prevalence as children age is primarily due to resolution of the lesser grades of reflux (grades I-III), and less frequently due to the operative treatment of the more severe reflux (grades IV-V).

Additional risk factors for UTI include previous UTI, or a history of UTI or reflux in a parent or sibling.[39] Race may also play a role as noted in a study that found white children to be approximately 2 times more likely to have UTIs than black children.[8] As mentioned, an increased incidence of UTI is witnessed during the toilet training period because of dysfunctional voiding habits. Frequent voiding flushes bacteria from the bladder, and, therefore, children who void infrequently or incompletely are at increased risk for infection. Constipation or encopresis often accompanies voiding dysfunction and therefore UTIs.[10] In addition, the urinary stasis of dysfunctional voiding may contribute to lesser degrees of VUR. Some studies have found that normalizing voiding patterns leads to resolution of VUR.[43]

Other risks for UTI are prematurity and systemic or immunologic diseases. Anatomic abnormalities such as ureterovesical junction (UVJ) obstruction, congenital megaureter, ectopic ureter, ureterocele, and ureteral polyps also increase the risk for infection. Urinary stasis caused by extrinsic compression (neoplasms, inflammatory bowel disease, hematoma) or bladder outlet syndromes (posterior urethral valves, bladder diverticula, urethral stricture, urethral atresia, phimosis, meatal stenosis, urethral foreign bodies) all increase the risk of UTI.[2]

Inconclusive studies have shown an increase in UTIs in uncircumcised infants less than 6 to 12 months of age.[18] [46] [39] [45] Infection is thought to be a result of bacterial colonization of the foreskin. A Canadian-based UTI study documented increased rates of hospital admissions in uncircumcised compared to circumcised infants. There was a 3.7-fold increased risk of UTI in uncircumcised boys in the first year of life and 4.5-fold increase in the first month of life. This increased risk for uncircumcised males may persist up until age 5.[39]

In adolescent females, sexual activity becomes the most significant risk for UTI. The reader is referred to the chapter on UTI in adults.

PATHOGENESIS

Pediatric UTI is a spectrum of disease that includes urethritis, asymptomatic bacteruria, cystitis, and pyleonephritis. Most

UTIs are caused by ascent of bacteria from the prepuce and perineum up the urethra. In girls, the proximity of the rectum and a short urethra contribute to the increased incidence of UTIs. In boys with UTI, colonization of the prepuce by uropathic bacteria is disproportionately found. Not all strains of fecal flora will cause UTIs or pyelonephritis. There is a selection for those organisms with uropathic virulence factors such as those that permit adhesion to the epithelium, thus allowing ascent into the urinary system.[37] In neonates and premature infants, pyelonephritis may also be caused by hematogenous spread of bacteria.

Asymptomatic bacteriuria (ASB) is defined as the growth of bacteria in culture without symptoms of infection or abnormalities on urinalysis such as pyuria or nitrites. There is debate about both the importance and treatment of ASB. Positive urine cultures may be caused by contaminated collection of urine, low infectivity, or colonization of a less-virulent strain. Escherichia coli from children with ASB is frequently from nontypable strains and differs from those causing infections. However, asymptomatic bacteriuria may be related to the presence of urinary tract abnormalities,[16] [37] and some children will go on to develop symptomatic infection. Despite these facts, most physicians do not feel that treatment is warranted except in the neonate and perhaps in children with known urologic anomalies. In general, asymptomatic bactiuria is not relevant to ED practice because the urinalysis is typically performed in the presence of symptoms such as fever or abdominal pain. Findings that suggest ASB may be referred to the primary care provider.

Most uncomplicated UTIs are caused by gram negative organisms, predominantly Escherichia coli (80%), but other enterobacteraciae such as Proteus mirabilis, Klebsiella pneumonia, and Pseudomonas aeruginosa may be seen. Gram positive organisms such as Streptococcus faecalis (enterococcus), Staphylococcus epidermidis, and Streptococcus viridans are less common causes of UTI. Unusual causes of infection are candida in immunocompromised children and coagulase negative staphylococcus in teens. Adenovirus is associated with hemorrhagic cystitis with hematuria, intense dysuria, and fever. This is usually seen in young male children.

During the past years, there has been increasing resistance of organisms to the usual antimicrobials, especially amoxicillin and more recently to trimethoprim-sulfamethoxazole (TMP/SMX). In Hoberman's study on UTI caused by gram negative organisms, 97% were from E. coli, and the rest were K. pneumoniae, proteus mirabilis, and others. Forty percent were resistant to ampicillin/amoxicillin, 5% were resistant to TMP/SMX, and 17% were resistant to cephalexin.[20]

Urethritis causes symptoms similar to cystitis but is usually caused by organisms with a predilection for the urethra such as Chlamydia trachomatous, Neisseria gonorrhea, ureaplasm urealyticum, and Herpes simplex virus. Male patients with these organisms may have urethral discharge and history of new sexual contact. Differentiating these causes in women is more difficult, and may be missed at the initial exam. The urinalysis may have white cells without bacteria. Standard cultures will be sterile. Women with

these findings and symptoms consistent with a UTI should have an evaluation for the above organisms.

CLINICAL PRESENTATION

Symptoms of UTI are nonspecific and overlap with common benign childhood illnesses. Although it is temping to diagnosis a

upper respiratory infection in an infant with a fever and mild congestion, there may be an underlying UTI. Missing this diagnosis has serious implications. The clinical presentation of UTI depends on the age of the child. Neonates may present with poor feeding, vomiting, jaundice, irritability, sepsis, lethargy, or failure to gain weight, and may not always have fever.[37] Infants most commonly present with fever, diarrhea, vomiting, irritability, foul smelling diapers, or other symptoms that overlap with neonates. Older infants may appear completely healthy but present with a fever and lack of other symptoms. With this in mind, all infants without an obvious source for their fever, especially girls and uncircumcised males to 6 months, should have a urinalysis as part of their work-up. The rate of UTI in this group may be as high as 17%.[22]

As children become verbal and toilet trained, the symptoms of cystitis are more easily noted such as dysuria, abdominal pain, hematuria, cloudy urine, incontinence, enuresis, frequency, or hesitancy.[16] Young children may present with new bed wetting or loss of bladder training. Dysfunctional voiding, daytime urgency-frequency syndrome, and constipation may be the equivalent of frequency or pain on urination. The young child may simply not be able to explain these symptoms. In older children with pyelonephritis, fever is the predominant symptom, often without symptoms of dysuria. In children older than 2 years with febrile UTIs, only 32% of boys and 40% of girls had dysuria. Flank pain was even more uncommon.[16] Nausea, vomiting, and abdominal pain may be present, but ultimately a high index of suspicion must be maintained to make the diagnosis of pyelonephritis even in older children.

The differential for cystitis includes vulvitis, vulvovaginitis, and urethritis. These may be caused by candida, herpes, pinworms, or may be irritant rather than infectious from bubble bath or swim suits. Urethral or vaginal foreign bodies may also give symptoms of cystitis. Urethral discharge is unusual in small children, and when present, sexual abuse and sexually transmitted organisms must be considered. The discomfort of pyleonephritis must be differentiated from gastroenteritis, glomerulonephritis, appendicitis and other more benign abdominal processes. In children with fever, other causes of fever such as pneumonia and meningitis should also be considered.

A careful history should include history of trauma, behavioral changes (bed wetting, loss of bladder control), poor hygiene, possible foreign bodies, bubble bath, or other irritants. Note voiding habits of infrequent voiding, squirming, incomplete bladder emptying,

urinary frequency, daytime enuresis, or constipation.[39] [2] Family history is important because reflux is more common if there is a history in parents or siblings.

Physical exam includes the standard exam as well as a careful examination of the abdomen for masses (bladder, constipation, renal, or pelvic masses). The back should be percussed for costovertebral tenderness. A close exam of the perineum and genitalia should be performed to look for evidence of foreign bodies or irritation. In girls, look for labial adhesions, vulvovaginitis, or foreign bodies. In boys, note the presence and condition of the foreskin and whether there is stricture at the urethral meatus. The testicles should be palpated for evidence of torsion. Note the presence of hernias. If incontinence has been present, check for evidence of spinal cord or cauda equina injury by testing perineal sensation, rectal tone, and lower extremity strength and sensation. A rectal exam may be helpful if there is a question of constipation or neurologic injury. When examining a child, keep in mind that sexual abuse can cause voiding dysfunction as well as urethritis and UTI symptoms.

LABORATORY EVALUATION

To make the diagnosis of a UTI, one must first suspect the diagnosis. A urine culture is the gold standard for the diagnosis of

UTI, but the ED physician must rely on chemical and microscopic urinalysis. There is debate and inconsistent practices over which well-appearing febrile children should have a urinalysis and culture. However, there is little argument that a UTI should be suspected in all septic or ill-appearing children, especially those without another source of fever. In addition, neonates less than 28 days with fever, vomiting, poor feeding or irritability should have urinalysis and urine culture sent.

The approach to the diagnosis and management of pediatric UTIs may be separated by age groups: 0 to 3 months, 3 months to 2 years, and older. In neonates less than 3 months old, a catheterized urinalysis or suprapubic bladder aspiration is part of the standard work-up for fever. UTI should also be considered in the afebrile child who has poor feeding, irritability, or other symptoms without a source.

Controversy about candidates for urinalysis focuses on the child from ages 2 to 3 months to 2 to 3 years. In 1993 Baraff et al published practice guidelines for children with fever in both Pediatrics and Annals of Emergency Medicine. They recommended urine culture for girls less than 2 years old and boys less than 6 months old (no differentiation made between circumcised and uncircumcised males) with a fever greater than 39°C.[6] The American Academy of Pediatrics guidelines recommend that "the presence of UTI should be considered in all infants and young children 2 months to 2 years with unexplained fever."[9] Girls less than 2 years and boys less than 6 months with a fever and a probable source of fever (otitis media, URI) have a significant rate of UTI (about 5%). Therefore, a UTI should still be considered. However, some clinicians prefer close follow-up for the

group of children with a probable source of infection and a fever. Urine may be checked if the child fails to improve at the follow-up visit. This approach may be complicated if the child is given antibiotics for the "ear infection" before being seen by their pediatrician.

Older children may be less complicated because they can sometimes provide both clear symptoms of UTI and a clean specimen for analysis. However, as previously noted, it is not uncommon for children with pyelonephritis to have a fever in the absence of flank pain or dysuria. As well, behavioral changes may be present rather than a clear complaint of dysuria. Therefore, this diagnosis should always be entertained in the febrile child who has no other clear source to explain the fever. Children on prophylactic antibiotics for reflux or with a history of reflux should have a urinalysis and culture checked with each febrile episode regardless of the height of fever or other probable source.

The urinalysis is best obtained by a catheterized specimen in infants using a small feeding tube (8-10F) sterilely inserted in the bladder. Although it is tempting to obtain specimens by placing a bag on the perineum, these specimens have an unacceptably high rate of contamination. Bagged urine specimens are only acceptable for a screening urinalysis. The urinalysis is reliable if negative, but if positive needs to be confirmed with a catheterized specimen.[9] All specimens should be plated immediately to prevent growth of bacterial contaminates.

Suprapubic aspiration, although not usually necessary, is considered the gold standard method for obtaining urine. It is performed after cleaning the suprapubic area with antiseptic solution. A 21- to 25- gauge needle is inserted one finger breadth above the symphysis pubis perpendicularly while aspirating until urine is obtained.[3] Although suprapubic aspiration is popular in some EDs, it is both invasive and has variable success rates for obtaining urine because of the lack of urine in the bladder. Physical examination to palpate for a full bladder is sometimes limited if the child is very upset. Ultrasound, if available, may be useful to check bladder fullness before aspiration. For males with phimosis, tight foreskin, or stricture, and for girls with severe labial adhesions, suprapubic aspiration may be only method for obtaining clean urine.

Older children can usually provide a clean catch specimen after careful instruction. Having girls sit backwards on the toilet seat (facing the wall) favors labial retraction, exposure of the urethral meatus and may provide a cleaner specimen.[2] However, the presence of epithelial cells indicates perineal contamination, and another specimen should be obtained if there is evidence of infection.

Many methods have been used to determine the presence of a UTI from dipstick to microscopy to culture. The gold standard is a urine culture growing a single organism. However, in the ED it is not practical to wait for the culture result before initiating treatment. Therefore, most ED physicians use a combination of chemical and microscopic analysis to arrive at a presumptive diagnosis of a UTI.

Numerous studies examining the various urine tests show a wide range of sensitivity and specificity depending on the method of urine collection and the threshold value of colony-forming units on culture.[34] [27] [25] [21] [26] [11] [23] Markers for the presence of urinary infection such as leukocyte esterase and nitrites can be rapidly measured on urine chemical strips. Leukocyte esterase is released by the breakdown of white blood cells in the urine. Dietary nitrates in the urine are converted to nitrites by bacteria during period of hours. Both of these tests provide indirect evidence for the presence of infection. The sensitivity of LE alone is 50%-85%, with a positive predictive value (PPV) of 89%. The PPV increases to 94% when the prevalence of disease increases (i.e., when the child has urinary symptoms). The specificity ranges from 63% to 92%. Nitrites alone have higher specificity (90%-100%) and lower sensitivity (16%-82%, 90% PPV). When either nitrite or LE is positive, the sensitivity and specificity ranges from 70 to 90% respectively, and PPV 72%.[22]

The presence of pyuria (>5 white blood cell (WBC)/HPF) and bacteria on a spun specimen is 54% to 85% sensitive and 70% to 81% specific.[22] [9] The microscopic notation of the presence of bacteria in the urine has a sensitivity of 60% to 90% and specificity of 80% to 90%. The results are dependent on the volume of urine, force and duration of centrifugation, and observer error. Occasionally, there is not enough volume to spin; in this case, the presence of any WBC is suggestive of a UTI. Rarely, the urine cultures of specimens with pyuria have no growth. This may occur in children on antibiotics or the presence of betadine in the specimen. Likewise, it is possible to have a completely negative urinalysis and still have a positive culture. Neonates, in particular, should have a culture sent, even when the urinalysis is negative. These positive cultures are theorized to occur because of early infection before local inflammatory response occurs, asymptomatic colonization of urinary tract, or contaminated specimens. There is debate whether children without pyuria but with positive cultures should be treated. In the absence of urinary symptoms, a reasonable course is to repeat the urinalysis and culture if antibiotics have not been started. If the child has symptoms, then it is appropriate to treat the child.

One can use the tests in parallel (positive if any part is positive), which increases the sensitivity to about 99% but decreases the specificity, or require all parts to be positive, which decreases sensitivity but increases specificity. Enhanced urinalysis is a special technique of counting WBC in unspun urine along with a gram stain of the urine. This test is recommended by Hoberman and has increased sensitivity and specificity for positive urine cultures.[22] [42]

In all cases that the urinalysis is positive, a urine culture should be sent to make a definitive diagnosis.[9] This is to increase the specificity of the diagnosis and prevent unnecessary work-up in children who had a falsely positive urinalysis. In addition, bacterial antibiotic resistances are changing; therefore, cultures are necessary to ensure that the patient receives adequate coverage.

Some physicians recommend always sending a culture despite a negative urinalysis because the consequence of missing a UTI is significant in both the short and long term

(urosepsis, missed urinary tract abnormality, renal scarring that may later contribute to hypertension, and end stage renal disease).[20] [21] [22] [6] [46] Other physicians point out that a urinalysis is 80% sensitive and with a 5% prevalence of UTI, the rate of UTI in a negative urinalysis is about 1.3%.[33] Reasonable guidelines for sending urine culture include all febrile infants (up to 2 years of age), children with history of previous UTI, children who are on suppressive antibiotic therapy, and in children in whom empiric antibiotic therapy is started.[22]

Growth of a single organism on urine culture is considered positive depending on the method of sampling and the colony count as follows: suprapubic aspiration growth of 2-3 × 103 CFU/mL except coagulase negative staphylococci; by catheterization of 5 × 104 CFU/mL; and by clean catch 100,000 or 105 CFU/mL of single pathogen in symptomatic children. Some physicians use 104 in a male in a clean catch. Bacterial counts may be lower than expected when there is a bacteriostatic agent in the urine (betadine), rapid urine flow, obstruction of a ureter, or in the presence of a localized renal parenchymal infection that has not yet involved the renal tubules.[23] Bacterial concentrations may also be effected by volume of urine, use of antibiotics, duration of symptoms, and the storage of urine. Urine cultures with low colony counts should be repeated if possible.

Although urinalysis and urine cultures provide the diagnosis of UTI, blood tests are frequently requested as part of the evaluation of the febrile infant. In pyelonephritis, the WBC count may be elevated, along with the sedimentation rate and C- reactive protein level. Blood cultures may be sent, although they are not generally helpful even when positive. In Hoberman's study of UTI in children aged 2 months to 2 years, only 4% had positive blood cultures and the mean WBC count was 20.[20]

Tests of renal function (blood urea nitrogin [BUN] creatinine) and electrolytes are appropriate in ill-appearing children and infants. Elevated levels may suggest obstruction or dehydration. In children in whom obstruction is suspected, elevated potassium may rarely be present.

In special circumstances, other tests may be indicated for the ED patient with pyelonephritis. Children with UTI and kidney stone should be admitted for intravenous antibiotics. Therefore, an intravenous pyelography or helical computerized tomography scan should be considered in children with severe pain inconsistent with a diagnosis of pyelonephritis and/or pain with significant numbers of red blood cells in the urine.

DMSA renal scans are used to localize the site of infection and to determine if renal scarring is present.[36] This test is rarely indicated in an acute infection. However, a child that has failed outpatient treatment should have an imaging study (renal scan or ultrasound) performed early in their hospitalization.[9]

TREATMENT

In the ED, UTI should have empiric antibiotic therapy started without waiting 24 to 48 hours for the urine culture result.

Cystitis may be treated with a variety of antibiotics such as TMP-SMX, nitrofurantion, or a cephalosporin (Table 1) .[9] [2] Once the results of urine cultures are available, therapy should be tailored to the microbial sensitivities. Unfortunately, many bacteria are resistant to amoxicillin and ampicillin, so these agents should not be chosen as first-line unless the sensitivities are known. The duration of treatment for uncomplicated cystitis is debated, in both children and adults. Reasoning that 1-3 days is not sufficiently effective, the AAP consensus recommended 7 days of treatment for children.[44] [28] [12]

TABLE 1 -- OUTPATIENT TREATMENT OF UTI (ORAL)[2] [19]

TMP/SMX
6-12 mg/kg/d TMP 30-60 mg/kg/d SMX bida

Augmentin
50 mg/kg/d tid

Cephalexin
50-100 mg/kg/d qid

Cefixime
8 mg/kg/d bid

Cefpodixime
10 mg/kg/d bid

Cefprozil
30 mg/kg/d bid

Loracarbef
30 mg/kg/d bid

Nitrofurantoin
5-7 mg/kg/d qidb

Sulfisoxazole
120-150 mg/kg/d qid

Amoxicillin
20-40 mg/kg/d tidc

Phenazopyridine

10 mg/kg/d tidd

a Should not be used in children less than 2 months.

b Concentrated in the urine so adequate for cystitis but poor for pyelonephritis, should not be used in neonates.
c High resistance to E. coli.
d May be given for 3 days only to older children for relief of bladder spasm. Inform parents that this will turn the urine orange.

Pyelonephritis or febrile UTIs should be aggressively treated with antibiotics. Mirroring the pattern seen in adults, the threshold

age of mandatory hospitalization for pyelonephritis in children has steadily decreased. Most physicians feel that hospitalization is indicated for children less than 3 months as well as for children with dehydration, toxicity, vomiting, or failure to respond to outpatient treatment.[37] [36] In addition, younger children in whom compliance may be a problem may need to be treated as inpatients.

Neonates should receive ampicillin and gentamicin to cover hematogenously spread pathogens. Some hospitals are moving to single daily dosing of gentamicin in children to decrease the cost as well as toxicity.[7] [41] Older infants may receive a third- generation cephalosporin instead, although enterococcus is not well covered by these agents. Additional antibiotic regimens are listed in Table 2 .[9] [2] If gram staining is done, the antibiotic treatment can be tailored to the organisms found (double coverage of ampicillin and gentamicin for gram positive bacteria that is most commonly enterococcus, and cephalosporins for gram negative bacteria that is most likely E. coli). Neonates are usually treated parenterally for the duration of the 10 to 14 days, whereas infants older than 28 days may be discharged on an outpatient regimen once they defervese.

TABLE 2 -- PARENTERAL TREATMENT OF UTI*

Ceftriaxone
75 mg/kg IV or IM q 24

Cefotaxime
150 mg/kg/d q 6

Ceftazidime
150 mg/kg/d q 6

Cefazoline
50-100 mg/kg/d q 8

Gentamicin
7.5 mg/kg/d q 8 for infants >1 week of age

5 mg/kg/d q 12 for infants <1 week of age

Tobramycin
5 mg/kg/d q 8

Ticarcillin
300 mg/kg/d q 8

Ampicillin
100 mg/kg/d divided q12h if <1 wk or q 6-8 if >1 wk§

*Cannot use quinolones in children less than age 17.

Discuss frequency of dosing with your hospital's pediatric pharmacist or infectious disease specialist.
Adjust the dose in neonates.
§Use ampicillin in conjunction with another antibiotic due to high resistance.

For children older than 3 months without contraindications, outpatient treatment of pyelonephritis or febrile UTIs is

appropriate.[20] [37] [17] Conservative management of the febrile infant is to give the first dose of antibiotics parenterally (third- generation cephalosporin or gentamicin) followed by outpatient oral treatment.[37] A recent article attempted to demonstrated the safety of outpatient management of UTI in young children with oral cefixime.[20] The study included infants age 4 to 7 weeks, but there were insufficient numbers (four infants) treated as outpatients to make meaningful conclusions in this age group. The majority of the children in the study were 8 weeks to 11 months old and only one infant was unable to tolerate oral antibiotic (treatment failure). Although the older group did

well, the small number of infants in the 4- to 7-week group does not yet allow an outpatient management plan to be applied to this group.

Although the above study goes further than other studies in treating very young infants as outpatients, it agrees with other studies that infants older than 3 months (and maybe younger) may safely be treated as outpatients.[20] [37] [17] The optimal outpatient regiment has yet to be proven. Some physicians may chose to give a parenteral dose of ceftriaxone or gentamicin before discharge in infants less than 12 months of age with high fevers or high WBC counts.[37] Other pediatricians prefer to treat young infants with daily outpatient parenteral antibiotics such as ceftriaxone. This is done until the fever resolves, and then therapy may be completed with oral antibiotics. Mildly dehydrated children may be rehydrated, given parenteral antibiotics, and treated as outpatients once they are able to tolerate liquids. Well-appearing older children may do well with oral agents alone as long as they are tolerating fluids. For outpatient treatment, there are several choices of antibiotics (Table 1) , but total treatment should last for 10 to 14 days regardless of antibiotic.[39] We recommend the use of a second- or third-generation cephalosporins until the urine cultures can direct therapy. These agents are used because our institution has noted the development of significant E. coli resistance to standard antibiotics during the 3 years (ampicillin 56%, TMP/SMX 17%, nitrofurantoin 4%, amox/sulbactam 11%). [47] With this in mind, it is important to know the regional antibiotic resistance patterns to better tailor antibiotic use. In addition, children with urinary tract abnormalities, older children (2-6 years old), two or more hospitalizations in the past year, or more than 4 weeks of antibiotics in the past 6 months are more likely to have resistant organisms.[1]

Some physicians recommend treatment of uncomplicated cystitis for 1, 3, or 5 days.[37] However, the practice of treating the pediatric patient with cystitis for less than 7 days creates problems in terms of antibiotic resistance and treatment failure. Studies comparing standard treatment of 7 to 14 days to short-course treatments of 1 to 3 days continue to show that longer treatment regimens are better than or equivalent to the shorter regimens. However, the sample sizes used in these studies are generally too small to show whether a small difference exists.[31] In the consensus statement, the AAP recommends 7- to 14- day treatment in children ages 2 months to 2 years. In children older than 2 years, the recommendation is still to treat for a minimum of 7 days.

Regardless of the duration of treatment, after completion most urologists recommend suppressive antimicrobial therapy until urologic evaluation is completed.[15] [9] Children with known reflux or children with recurrent UTIs may need suppressive treatment for longer periods.

FOLLOW-UP AND IMAGING STUDIES

For those children treated for pyelonephritis or febrile UTI as outpatients, carefully arranged follow-up must take place within

24 to 48 hours. This visit serves to determine response to antibiotics, adjustment of antibiotics from the results of urine cultures, and to arrange to further imaging if needed. Therefore, before discharge from the ED, it is important to notify the child's pediatrician of the diagnosis and treatment plan. For children without follow-up, it may be necessary to have the child return to the ED in 24 to 48 hours for a recheck. Cultures should be repeated if the child remains febrile or ill in 48 hours. At this point, the child should be admitted as a treatment failure.[9]

Discharge instructions should include direction to return to the ED for persistent vomiting, dehydration, lethargy, persistent fever after 48 hours, or worsening symptoms. Parents should be instructed to use antipyretics and to increase the child's fluid intake.

Although most ED physicians are not responsible for the work-up after a UTI, the ED physician may want to educate the parents and stress the importance of follow-up and further work-up. Forty to fifty percent of infants and 30% of older children with a UTI will have anatomic abnormality (reflux is most common).[20] [39] There are three methods to image the urinary tract. Sonography, which images renal anomalies or ureteral duplication; voiding cystourethrogram, which shows the function of the ureters, bladder, and urethra thus diagnosing and grading reflux, and radionucleotide imaging may be used. Renal cortical scintigraphy uses technetium-labeled dimercaptosucciinic acid, which is taken up by non injured renal tubular cells and is about 90% sensitive and 100% specific for acute pyelonephritis, as well as for renal scarring. Radionucleotide cystogram detects mild, moderate, or severe reflux of the ureters. However, the bladder is incompletely imaged, and the urethra is not imaged at all. Most imaging is performed after the resolution of the UTI. However, children failing treatment should be imaged by ultrasound or renal cortical scan with DMSA to rule out obstruction and to determine the extent of renal involvement.[38]

With several choices of imaging modality, debate exists about both the best method of testing, as well as exactly which children should have imaging studies performed. The AAP guidelines recommend voiding cytourethrogram and sonography in all children age 2 months to 2 years with their first culture-proven UTI.[9] In addition, imaging may be appropriate for boys, regardless of age, after their first UTI, girls with UTI occurring at less than 3 to 5 years old, and children with pyelonephritis or febrile UTIs.[8] [36]

Children with high-grade reflux (grade V, most with grade IV) need operative repair, whereas children with less severe reflux may be managed on prophylactic antibiotics.[15] [38] [39] A fever in children with these abnormalities always warrants a urinalysis and urine culture.

COMPLICATIONS AND MORBIDITY

The immediate complications of UTIs are abscess formation, sepsis, and death. Sepsis is more common in neonates,

premature infants, and infants with urinary obstruction. The prognosis is good for children with UTIs with prompt diagnosis and rapid treatment. The long-term complication of pyelonephritis is renal scar formation, end stage renal disease, and hypertension. Although it is possible to have scar formation with the first infection, the risk increases with each subsequent infection. It is estimated that 15% of end stage renal disease in children is caused by the combination of reflux and renal scarring.[2]

SUMMARY

UTIs are common in children. They may present with a range of severity from cystitis to febrile UTI or pyelonephritis. The

presentation may be vague and have nonspecific symptoms. Therefore, a UTI should be considered in all children with a fever in whom other sources have been excluded. Treatment depends on the age, location of infection, and degree of illness in the child. Sick children and infants less than 3 months should be treated as inpatients, and healthy children and older infants may be treated as outpatients. Urinalysis provides presumptive evidence of infection, whereas urine culture is definitive. Close follow-up and outpatient evaluations are needed to prevent long-term consequences of infection.

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