

AMERICAN ACADEMY OF PEDIATRICS

Practice Parameter: The Diagnosis, Treatment, and Evaluation of the Initial Urinary Tract Infection in Febrile Infants and Young Children. American Academy of Pediatrics. Committee on Quality Improvement. Subcommittee on Urinary Tract Infection.

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Comments also were solicited and received from the American Academy of Family Physicians, the American College of Emergency Physicians, and the American Urological Association.

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Objective. To formulate recommendations for health care professionals about the diagnosis, treatment, and evaluation of an initial urinary

tract infection (UTI) in febrile infants and young children (ages 2 months to 2 years).

Design. Comprehensive search and analysis of the medical literature, supplemented with consensus opinion of Subcommittee members.

Participants. The American Academy of Pediatrics (AAP) Committee on Quality Improvement selected a Subcommittee composed of pediatricians with expertise in the fields of epidemiology and informatics, infectious diseases, nephrology, pediatric practice, radiology, and urology to draft the parameter. The Subcommittee, the AAP Committee on Quality Improvement, a review panel of office-based practitioners, and other groups within and outside the AAP reviewed and revised the parameter.

Methods. The Subcommittee identified the population at highest risk of incurring renal damage from UTI--infants and young children with UTI and fever. A comprehensive bibliography on UTI in infants and young children was compiled. Literature was abstracted in a formal manner, and evidence tables were constructed. Decision analysis and cost-effectiveness analyses were performed to assess various strategies for diagnosis, treatment, and evaluation.

Technical Report. The overall problem of managing UTI in children between 2 months and 2 years of age was conceptualized as an evidence model. The model depicts the relationship between the steps in diagnosis and management of UTI. The steps are divided into the following four phases: 1) recognizing the child at risk for UTI, 2) making the diagnosis of UTI, 3) short-term treatment of UTI, and 4) evaluation of the child with UTI for possible urinary tract abnormality.

Phase 1 represents the recognition of the child at risk for UTI. Age and other clinical features define a prevalence or a prior probability of UTI, determining whether the diagnosis should be pursued.

Phase 2 depicts the diagnosis of UTI. Alternative diagnostic strategies may be characterized by their cost, sensitivity, and specificity. The result of testing is the division of patients into groups according to a relatively higher or lower probability of having a UTI. The probability of UTI in each of these groups depends not only on the sensitivity and specificity of the test, but also on the prior probability of the UTI among the children being tested. In this way, the usefulness of a diagnostic test depends on the prior probability of UTI established in Phase 1.

Phase 3 represents the short-term treatment of UTI. Alternatives for treatment of UTI may be compared, based on their likelihood of clearing the initial UTI.

Phase 4 depicts the imaging evaluation of infants with the diagnosis of UTI to identify those with urinary tract abnormalities such as vesicoureteral reflux (VUR). Children with VUR are believed to be at risk for ongoing renal damage with subsequent infections, resulting in hypertension and renal failure. Prophylactic antibiotic therapy or surgical procedures such as ureteral reimplantation may prevent progressive renal damage. Therefore, identifying urinary abnormalities may offer the benefit of preventing hypertension and renal failure.

Because the consequences of detection and early management of UTI are affected by subsequent evaluation and long-term management and, likewise, long-term management of patients with UTI depends on how they are detected at the outset, the Subcommittee elected to analyze the entire process from detection of UTI to the evaluation for, and consequences of, urinary tract abnormalities. The full analysis of these data can be found in the technical report. History of the literature review along with evidence-tables and a comprehensive bibliography also are available in the report. This report is published in Pediatrics electronic pages and can be accessed at the following URL: <http://www.pediatrics.org/cgi/content/full/103/4/e54>.

Results. Eleven recommendations are proposed for the diagnosis, management, and follow-up evaluation of infants and young children with unexplained fever who are later found to have a diagnosed UTI. Infants and young children are of particular concern because UTI in this age group (approximately 5%) may cause few recognizable signs or symptoms other than fever and has a higher potential for renal damage than in older children. Strategies for diagnosis and treatment depend on the clinician's assessment of the illness in the infant or

The recommendations in this statement do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

Practice Parameter: The Diagnosis, Treatment, and Evaluation of the Initial Urinary Tract Infection in Febrile Infants and Young Children" was reviewed by the appropriate committees and sections of the American Academy of Pediatrics (AAP), including the Committee on Infectious Diseases, the Committee on Medical Liability, and the Committee on Practice and Ambulatory Medicine; the Sections on Infectious Diseases, Nephrology, Radiology, and Urology; and the Chapter Review Group, a focus group of office-based pediatricians representing each AAP District: Gene R. Adams, MD; Charles S. Ball, MD; Robert M. Corwin, MD; Diane Fuquay, MD; Barbara M. Harley, MD; Michael J. Heimerl, MD; Thomas J. Herr, MD; Kenneth E. Matthews, MD; Robert D. Mines, MD; Lawrence C. Pakula, MD; Howard B. Weinblatt, MD; and Delosa A. Young, MD. The COQI and Subcommittee on UTI greatly appreciate the expertise of Richard N. Shiffman, MD, Center for Medical Informatics, Yale School of Medicine, for his input and analysis in the development of this practice guideline.

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young child. Diagnosis is based on the culture of a properly collected specimen of urine; urinalysis can only suggest the diagnosis. A sonogram should be performed on all infants and young children with fever and their first documented UTI; voiding cystourethrography or radionuclide cystography should be strongly considered.

ABBREVIATIONS.

UTI

urinary tract infections

SPA

suprapubic aspiration

VUR

vesicoureteral reflux

WBC

white blood cell

TMP-

SMX

trimethoprim-

sulfamethoxazole

VCUG

voiding cystourethrography

RNC

radionuclide cystography.

The urinary tract is a relatively common site of infection in infants and young children. Urinary tract infections (UTIs) are important because

they cause acute morbidity and may result in long-term medical problems, including hypertension and reduced renal function. Management of children with UTI involves repeated patient visits, use of antimicrobials, exposure to radiation, and cost. Accurate diagnosis is extremely important for two reasons: to permit identification, treatment, and evaluation of the children who are at risk for kidney damage and to avoid unnecessary treatment and evaluation of children who are not at risk, for whom interventions are costly and potentially harmful but provide no benefit. Infants and young children with UTI are of particular concern because the risk of renal damage is greatest in this age group and because the diagnosis is frequently challenging: the clinical presentation tends to be nonspecific and valid urine specimens cannot be obtained without invasive methods (suprapubic aspiration [SPA], transurethral catheterization).

Considerable variation in the methods of diagnosis, treatment, and evaluation of children with UTI was documented more than 2 decades ago. [1] Since then, various changes have been proposed to aid in diagnosis, treatment, and evaluation, but no data are available to suggest that such innovations have resulted in reduced variation in practice. This practice parameter focuses on the diagnosis, treatment, and evaluation of febrile infants and young children (2 months to 2 years of age). Excluded are those with obvious neurologic or anatomic abnormalities known to be associated with recurrent UTI and renal damage. Neonates and infants younger than 2 months have been excluded from consideration in this practice parameter. Children older than 2 years experiencing their first UTI also are excluded because they are more likely than younger children to have symptoms referable to the urinary tract, are less likely to have factors predisposing them to renal damage, and are at lower risk of developing renal damage.

This parameter is intended for use by clinicians who treat infants and young children in a variety of clinical settings (eg, office, emergency department, hospital).

METHODS

A comprehensive literature review was conducted to provide data for evidence tables that could be used to generate a decision tree. More

than 2000 titles were identified from MEDLINE and bibliographies of current review articles from 1966 to 1996, and the authors' files. Of these, 402 articles contained relevant original data that were abstracted in a formal, standardized manner. An evidence-based model was developed using quantitative outcomes derived from the literature and cost data from the University of North Carolina. Decision analysis was used to perform risk analyses and cost-effectiveness analyses of alternative strategies for the diagnosis, management, and evaluation of UTI, using hypertension and end-stage renal disease as the undesirable outcomes. The calculated probability of undesirable outcome is the

product of the probabilities of several steps (diagnosis, treatment, evaluation) and therefore is an estimate, influenced by approximations at each step. Cost-effectiveness of various strategies was assessed using the methods of Rice and associates [2] in which the break-even cost to prevent a chronic condition, such as hypertension or end-stage renal disease, is considered to be \$700 000, an amount based on the estimated lifetime productivity of a healthy, young adult. Once this cost is assigned to the untoward clinical outcome (ie, hypertension or end-stage renal disease), it is possible to use the threshold method of decision-making. [3] The threshold approach to decision-making involves changing the value of a variable in the decision analysis to determine the value at which one strategy of diagnosis, treatment, and evaluation exceeds the break-even cost and an alternative strategy is preferred. Based on the results of these analyses and consensus, when necessary, an Algorithm was developed representing the strategies with the greatest benefit-risk characteristics. The strength of evidence on which recommendations were based was rated by the Subcommittee methodologist as strong, good, fair, or opinion/consensus. A detailed description of the methods by which the parameter was derived is available in a technical report from the American Academy of Pediatrics.

DIAGNOSIS

Recommendation 1

The presence of UTI should be considered in infants and young children 2 months to 2 years of age with unexplained fever (strength of

evidence: strong).

The prevalence of UTI in infants and young children 2 months to 2 years of age who have no fever source evident from history or physical examination is high, 5%. [4] [5] [6] [7] [8] The genders are not affected equally, however. The prevalence of UTI in febrile girls age 2 months to 2 years is more than twice that in boys (relative risk, 2.27). The prevalence of UTI in girls younger than 1 year of age is 6.5%; in boys, it is 3.3%. The prevalence of UTI in girls between 1 and 2 years of age is 8.1%; in boys it is 1.9%. The rate in circumcised boys is low, 0.2% to 0.4%. [9] [10] [11] [12] [13] The literature suggests that the rate in uncircumcised boys is 5 to 20 times higher than in circumcised boys.

Infants and young children are at higher risk than are older children for incurring acute renal injury with UTI. The incidence of vesicoureteral reflux (VUR) is higher in this age group than in older children (Fig 1) , and the severity of VUR is greater, with the most severe form (with intrarenal reflux or pyelotubular backflow) virtually limited to infants.

Infants and young children with UTI warrant special attention because of the opportunity to prevent kidney damage. First, the UTI may bring to attention a child with an obstructive anomaly or severe VUR. Second, because infants and young children with

UTI may have a febrile illness and no localizing findings, there may be a delay in diagnosis and treatment of the UTI. Clinical and experimental data support the concept that delay in instituting appropriate

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Figure 1. Prevalence of VUR by age. Plotted are the prevalences reported in 54 studies of urinary tract infections in children (references in Technical Report). The studies are weighted by sample size. The line is a third order polynomial fit to the data.

treatment of acute pyelonephritis increases the risk of kidney damage. [14] [15] Third, the risk of renal damage increases as the number of recurrences increases [16] (Fig 2) .

The presence of fever has long been considered a finding of special importance in infants and young children with UTI, because it has been accepted as a clinical marker of renal parenchymal involvement (pyelonephritis). The concept that otherwise unexplained fever in a child with UTI indicates that renal parenchymal involvement is based on comparison of children with high fever (39°C) and the clinical diagnosis of acute pyelonephritis with those with no fever (38°C) and a clinical diagnosis of cystitis. [17] Indirect tests for localization of the site of UTI, such as the presence of a reversible defect in renal concentrating ability and high levels of antibody titer to the infecting strains of *Escherichia coli*, and nonspecific tests of inflammation, such as elevated white blood cell (WBC) count, C-reactive protein, or sedimentation rate, are encountered more frequently in children with clinical pyelonephritis than in those with clinical cystitis. However, the indirect tests for localization of the site of infection and the nonspecific indicators of inflammation do not provide confirmatory evidence that the febrile infant or young child

Figure 2. Relationship between renal scarring and number of urinary tract infections. [16]

with UTI has pyelonephritis. Cortical imaging studies using technetium 99 m Tc-dimercaptosuccinic acid (DMSA) or 99 m Tc-glucoheptonate may prove useful in determining whether the presence of high fever does identify children with pyelonephritis and distinguish them from those with cystitis; currently available studies with data that can be used to assess fever as a marker of pyelonephritis (defined by a positive scan) provide a wide range of sensitivity (53% to 84%) and specificity (44% to 92%). [18] [19] [20]

The likelihood that UTI is the cause of the fever may be increased if there is a history of crying on urination or of foul-smelling urine. An altered voiding pattern may be

recognized as a symptom of UTI as early as the second year after birth in some children. Dysuria, urgency, frequency, or hesitancy may be present but are difficult to discern in this age group. Nonspecific signs and symptoms, such as irritability, vomiting, diarrhea, and failure to thrive, also may reflect the presence of UTI, but data are not available to assess the sensitivity, specificity, and predictive value of these clinical manifestations.

Decision analysis and cost-effectiveness analyses were performed, considering the different prevalences for age, gender, and circumcision status, and the prevalence of VUR by age. For girls and uncircumcised boys, it is cost-effective to pursue the diagnosis of UTI by invasive means and to perform imaging studies of the urinary tract. For circumcised boys younger than 1 year, the cost-benefit analysis is equivocal, but the Subcommittee supports the same diagnostic and evaluation measures as for girls and uncircumcised boys. Circumcised boys older than 1 year have a lower prevalence of UTI, and the prevalence of reflux is lower than that in those younger than 1 year. As a result, the cost-effectiveness analysis does not support invasive diagnostic procedures for all circumcised boys older than 1 year with unexplained fever. Analysis of a bag-collected specimen is a reasonable screening test in these boys, as long as they do not appear so ill as to warrant the initiation of antimicrobial therapy. Those who will be given antimicrobials on clinical grounds should have a specimen obtained for culture that is unlikely to be contaminated.

Recommendation 2

In infants and young children 2 months to 2 years of age with unexplained fever, the degree of toxicity, dehydration, and ability to retain oral intake must be carefully assessed (strength of evidence: strong).

In addition to seeking an explanation for fever, such as a source of infection, clinicians make a subjective assessment of the degree of illness or toxicity. Attempts have been made to objectify this assessment, using the prediction of bacteremia or serious bacterial infection as the outcome measure. [21] This clinical assessment, operationalized as whether antimicrobial therapy will be initiated, affects the diagnostic and therapeutic process regarding UTI as follows. If the clinician determines that the degree of illness warrants antimicrobial therapy, a valid urine

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specimen should be obtained before antimicrobials are administered, because the antimicrobials commonly prescribed in such situations will be effective against the usual urinary pathogens; invasive means are required to obtain such a specimen. If the clinician determines that the degree of illness does not require antimicrobial therapy, a urine culture is not essential immediately. In this situation, some clinicians may choose to obtain a specimen by noninvasive means (eg, in a collection bag attached to the

perineum). The false-positive rate with such specimens dictates that before diagnosing UTI, all positive results be confirmed with culture of a urine specimen unlikely to be contaminated (see below).

Recommendation 3

If an infant or young child 2 months to 2 years of age with unexplained fever is assessed as being sufficiently ill to warrant immediate antimicrobial therapy, a urine specimen should be obtained by SPA or transurethral bladder catheterization; the diagnosis of UTI cannot be established by a culture of urine collected in a bag (strength of evidence: good).

Urine obtained by SPA or transurethral catheterization is unlikely to be contaminated and therefore is the preferred specimen for documenting UTI. In a clinical setting in which the physician has determined that immediate antimicrobial therapy is appropriate, the use of a bag-collected urine specimen is insufficient to document the presence of UTI.

Establishing a diagnosis of UTI requires a strategy that minimizes false-negative and false-positive results. Urine obtained by SPA is the least likely to be contaminated; urine obtained by transurethral bladder catheterization is next best. Either SPA or transurethral bladder catheterization should be used to establish the diagnosis of UTI. Cultures of urine specimens collected in a bag applied to the perineum have an unacceptably high false-positive rate; the combination of a 5% prevalence of UTI and a high rate of false-positive results (specificity, 70%) results in a positive culture of urine collected in a bag to be a false-positive result 85% of the time. If antimicrobial therapy is initiated before obtaining a specimen of urine for culture that is unlikely to be contaminated, the opportunity may be lost to confirm the presence or establish the absence of UTI. Therefore, in the situation in which antimicrobial therapy will be initiated, SPA or catheterization is required to establish the diagnosis of UTI.

SPA has been considered the "gold standard" for obtaining urine for detecting bacteria in bladder urine accurately. The technique has limited risks. However, variable success rates for obtaining urine have been reported (23% to 90%), [16] [22] [23] [24] technical expertise and experience are required, and many parents and physicians perceive the procedure as unacceptably invasive compared with catheterization. There may be no acceptable alternative in the boy with moderate or severe phimosis, however.

Urine obtained by transurethral catheterization of the urinary bladder for urine culture has a sensitivity of 95% and a specificity of 99% compared with that obtained by SPA. [23] [25] Catheterization requires some skill and experience to obtain uncontaminated specimens, particularly in small infants, girls, and uncircumcised boys. Early studies in adults provided widely varying estimates of risk of introducing infection by a single, in-out catheterization. Turck and colleagues [26] demonstrated that the rate of bacteriuria secondary to transurethral catheterization in healthy young adults was considerably lower than that in hospitalized, older adults. Of the 200 healthy young adults studied, 100 men and 100 women, bacteriuria ultimately developed in only 1 woman--2 weeks after catheterization; bacteriuria was documented not to be present during the first 1 to 2 weeks

after her catheterization. The risk of introducing infection in infants by transurethral catheterization has not been determined precisely, but it is the consensus of the Subcommittee that the risk is sufficiently low to recommend the procedure when UTI is suspected.

The techniques required for transurethral bladder catheterization and SPA are well described. [27] When SPA or transurethral catheterization is being attempted, the clinician should have a sterile container ready to collect a urine specimen voided because of the stimulus of the patient by manipulation in preparation for or during the procedure.

Recommendation 4

If an infant or young child 2 months to 2 years of age with unexplained fever is assessed as not being so ill as to require immediate antimicrobial therapy, there are two options (strength of evidence: good).

Option 1

Obtain and culture a urine specimen collected by SPA or transurethral bladder catheterization.

Option 2

Obtain a urine specimen by the most convenient means and perform a urinalysis. If the urinalysis suggests a UTI, obtain and culture a urine specimen collected by SPA or transurethral bladder catheterization; if urinalysis does not suggest a UTI, it is reasonable to follow the clinical course without initiating antimicrobial therapy, recognizing that a negative urinalysis does not rule out a UTI.

The option with the highest sensitivity is to obtain and culture a urine specimen collected by SPA or transurethral bladder catheterization; however, this approach may be resisted by some families and clinicians. In infants and young children assessed as not being so ill as to require immediate antimicrobial therapy, a urinalysis may help distinguish those with higher and lower likelihood of UTI. The urinalysis can be performed on any specimen, including one collected from a bag applied to the perineum, and has the advantage of convenience. The major disadvantage of collecting a specimen in a bag is that it is unsuitable for quantitative culture. In addition, there may be a delay of 1 hour or longer for the infant or young child to void; then, if the urinalysis suggests

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UTI, a second specimen is required. The sensitivity of the bag method for detecting UTI is essentially 100%, but the false-positive rate of this method is also high, as

demonstrated in several studies. [23] [25] [28] If the prevalence of UTI is 5%, 85% of positive cultures will be false-positive results; if the prevalence of UTI is 2% (febrile boys), the rate of false-positive results is 93%; if the prevalence of UTI is 0.2% (circumcised boys), the rate of false-positive results is 99%. The use of bag-collected urine specimens persists because collection of urine by this method is noninvasive and requires limited personnel time and expertise. Moreover, a negative (sterile) culture of a bag-collected urine specimen effectively eliminates the diagnosis of UTI, provided that the child is not receiving antimicrobials and that the urine is not contaminated with an antibacterial skin cleansing agent. Based on their experience, many clinicians believe that this collection technique has a low contamination rate under the following circumstances: the patient's perineum is properly cleansed and rinsed before application of the collection bag; the urine bag is removed promptly after urine is voided into the bag; and the specimen is refrigerated or processed immediately. Nevertheless, even if contamination from the perineal skin is minimized, there may be significant contamination from the vagina in girls or the prepuce in uncircumcised boys. Published results demonstrate that although a negative culture of a bag-collected specimen effectively rules out UTI, a positive culture does not document UTI. Confirmation requires culture of a specimen collected by transurethral bladder catheterization or SPA. Transurethral catheterization does not eliminate completely the possibility of contamination in girls and uncircumcised boys.

Of the components of urinalysis, the three most useful in the evaluation of possible UTI are leukocyte esterase test, nitrite test, and microscopy. A positive result on a leukocyte esterase test seems to be as sensitive as the identification of WBCs microscopically, but the sensitivity of either test is so low that the risk of missing UTI by either test alone is unacceptably high (Table 1) . The nitrite test has a very high specificity and positive predictive value when urine specimens are processed promptly after collection. Using either a positive leukocyte esterase or nitrite test improves sensitivity at the expense of specificity; that is, there are many false-positive results. The wide range of reported test characteristics for microscopy indicates the difficulty in ensuring quality performance; the best results are achieved

TABLE 1 -- Sensitivity and Specificity of Components of the Urinalysis, Alone and in Combination (References in Text)

Test
Sensitivity %

(Range)
Specificity %
(Range)

Leukocyte esterase
83 (67-94)
78 (64-92)

Nitrite
53 (15-82)
98 (90-100)

Leukocyte esterase or nitrite positive
93 (90-100)
72 (58-91)

Microscopy: WBCs
73 (32-100)
81 (45-98)

Microscopy: bacteria
81 (16-99)
83 (11-100)

Leukocyte esterase or nitrite or microscopy positive
99.8 (99-100)
70 (60-92)

with skilled technicians processing fresh urine specimens.

The urinalysis cannot substitute for a urine culture to document the presence of UTI, but the urinalysis can be valuable in selecting individuals for prompt initiation of treatment while waiting for the results of the urine culture. Any of the following are suggestive (although not diagnostic) of UTI: positive result of a leukocyte esterase or nitrite test, more than 5 white blood cells per high-power field of a properly spun specimen, or bacteria present on an unspun Gram-stained specimen.

In circumcised boys, whose low a priori rate of UTI (0.2% to 0.4%) does not routinely justify an invasive, potentially traumatic procedure, a normal urinalysis reduces the likelihood of UTI as the cause of the fever still further, to the order of 0.1%.

Recommendation 5

Diagnosis of UTI requires a culture of the urine (strength of evidence: strong).

All urine specimens should be processed as expeditiously as possible. If the specimen is not processed promptly, it should be refrigerated to prevent the growth of organisms that can occur in urine at room temperature. For the same reason, specimens requiring transportation to another site for processing should be transported on ice.

The standard test for the diagnosis of UTI is a quantitative urine culture; no element of the urinalysis or combination of elements is as sensitive and specific. A properly

collected urine specimen should be inoculated on culture media that will allow identification of urinary tract pathogens.

UTI is confirmed or excluded based on the number of colony-forming units that grow on the culture media. Defining significant colony counts with regard to the method of collection considers that the distal urethra is commonly colonized by the same bacteria that may cause UTI; thus, a low colony count may be present in a specimen obtained by voiding or by transurethral catheterization when bacteria are not present in bladder urine. As noted in Table 2 , what constitutes a significant colony count depends on the collection method and the clinical status of the patient; definitions of positive and negative cultures are operational and not absolute. Significance also depends on the identification of the isolated organism as a pathogen. Organisms such as Lactobacillus species, coagulase-negative staphylococci, and Corynebacterium species are not considered clinically relevant urine isolates in the otherwise healthy 2-month to 2-year-old. Alternative culture methods such as the dipslide may have a place in the office setting; sensitivity is reported in the range of 87% to 100%, and specificity, 92% to 98%.

TREATMENT

Recommendation 6

If the infant or young child 2 months to 2 years of age with suspected UTI is assessed as toxic, dehydrated, or unable to retain oral intake,

initial antimicrobial

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TABLE 2 -- Criteria for the Diagnosis of UTI⁵³

Method of Collection
Colony Count (Pure Culture)
Probability of Infection (%)

SPA
Gram-negative bacilli: any number
>99%

Gram-positive cocci: more than a few
thousand

Transurethral catheterization
>10⁵
95%; Infection likely suspicious; repeat
infection unlikely
10⁴ - 10⁵

10³ - 10⁴

<10³

Clean void

Boy
>10⁴
Infection likely

Girl
3 Specimens 10⁵
95%

2 Specimens 10⁵
90%

1 Specimen 10⁵
80%

5 × 10⁴ - 10⁵
Suspicious, repeat

10⁴ - 5 × 10⁴
Symptomatic: suspicious, repeat

Asymptomatic: infection unlikely

<104
infection unlikely

therapy should be administered parenterally and hospitalization should be considered (strength of evidence: opinion/consensus).

The goals of treatment of acute UTI are to eliminate the acute infection, to prevent urosepsis, and to reduce the likelihood of renal damage. Patients who are toxic-appearing, dehydrated, or unable to retain oral intake (including medications) should receive an antimicrobial parenterally (Table 3) until they are improved clinically and are able to retain oral fluids and medications. The parenteral route is recommended because it ensures optimal antimicrobial levels in these high-risk patients. Parenteral administration of an antimicrobial also should be considered when compliance with obtaining and/or administering an antimicrobial orally cannot be ensured. In patients with compromised renal function, the use of potentially nephrotoxic antimicrobials (eg, aminoglycosides) requires caution, and serum creatinine and peak and trough antimicrobial concentrations need to be monitored. The clinical conditions of most patients improve within 24 to 48 hours; the route of antimicrobial administration then can be changed to oral (Table 4) to complete a 7- to 14-day course of therapy.

Hospitalization is necessary if patients have clinical urosepsis or are considered likely to have bacteremia based on clinical or laboratory evaluation. These patients need careful monitoring and repeated clinical examinations.

For children who do not appear toxic but who are vomiting, or when noncompliance is a concern, options include beginning therapy in the hospital or administering an antimicrobial parenterally on an

TABLE 3 -- Some Antimicrobials for Parenteral Treatment of UTI

Antimicrobial
Daily Dosage

Ceftriaxone
75 mg/kg every 24 h

Cefotaxime
150 mg/kg/d divided every 6 h

Ceftazidime
150 mg/kg/d divided every 6 h

Cefazolin
50 mg/kg/d divided every 8 h

Gentamicin
7.5 mg/kg/d divided every 8 h

Tobramycin
5 mg/kg/d divided every 8 h

Ticarcillin
300 mg/kg/d divided every 6 h

Ampicillin
100 mg/kg/d divided every 6 h

outpatient basis. The route of administration is changed to oral when the child is no longer vomiting, and compliance appears to be ensured.

Recommendation 7

In the infant or young child 2 months to 2 years of age who may not appear ill but who has a culture confirming the presence of UTI, antimicrobial therapy should be initiated, parenterally or orally (strength of evidence: good).

The usual choices for treatment of UTI orally include amoxicillin, a sulfonamide-containing antimicrobial (sulfisoxazole or trimethoprim- sulfamethoxazole [TMP-SMX]), or a cephalosporin (Table 4) . Emerging resistance of E coli to ampicillin appears to have rendered ampicillin and amoxicillin less effective than alternative agents. Studies comparing amoxicillin with TMP-SMX have demonstrated consistently higher cure rates with TMP-SMX (4% to 42%), regardless of the duration of therapy (1 dose, 3 to 4 days, or 10 days). [29] [30] [31] [32] [33] [34] [35] [36] [37] [38] [39] [40] [41] [42] [43] [44] [45]

Agents that are excreted in the urine but do not achieve therapeutic concentrations in the bloodstream, such as nalidixic acid or nitrofurantoin, should not be used to treat UTI in febrile infants and young children in whom renal involvement is likely.

Recommendation 8

Infants and young children 2 months to 2 years of age with UTI who have not had the expected clinical response with 2 days of antimicrobial therapy

TABLE 4 -- Some Antimicrobials for Oral Treatment of UTI

Antimicrobial
Dosage

Amoxicillin
20-40 mg/kg/d in 3 doses

Sulfonamide

TMP in combination with SMX
6-12 mg TMP, 30-60 mg SMX per kg per d in 2 doses

Sulfisoxazole
120-150 mg/kg/d in 4 doses

Cephalosporin

Cefixime
8 mg/kg/d in 2 doses

Cefpodixime
10 mg/kg/d in 2 doses

Cefprozil
30 mg/kg/d in 2 doses

Cephalexin
50-100 mg/kg/d in 4 doses

Loracarbef
15-30 mg/kg/d in 2 doses

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should be reevaluated and another urine specimen should be cultured (strength of evidence: good).

Routine reculturing of the urine after 2 days of antimicrobial therapy is generally not necessary if the infant or young child has had the

expected clinical response and the uropathogen is determined to be sensitive to the antimicrobial being administered. Antimicrobial sensitivity testing is determined most commonly by the application of disks containing the usual serum concentration of the antimicrobial to the culture plate. Because many antimicrobial agents are excreted in the urine in extremely high concentrations, an intermediately sensitive organism may be fully eradicated. Studies of minimal inhibitory concentration may be required to clarify the appropriateness of a given antimicrobial. If the sensitivity of the organism to the chosen antimicrobial is determined to be intermediate or resistant, or if sensitivity testing is not performed, a "proof-of-bacteriologic cure" culture should be performed after 48 hours of treatment. Data are not available to determine that clinical response alone ensures bacteriologic cure.

Recommendation 9

Infants and young children 2 months to 2 years of age, including those whose treatment initially was administered parenterally, should complete a 7- to 14-day antimicrobial course orally (strength of evidence: strong).

In 8 of 10 comparisons of long treatment duration (7 to 10 days) and short duration (1 dose or up to 3 days), results were better with long duration, with an attributable improvement in outcome of 5% to 21%. [33] [38] [41] [44] [45] [46] [47] [48] Most uncomplicated UTIs are eliminated with a 7- to 10-day antimicrobial course, but many experts prefer 14 days for ill-appearing children with clinical evidence of pyelonephritis. Data comparing 10 days and 14 days are not available.

Recommendation 10

After a 7- to 14-day course of antimicrobial therapy and sterilization of the urine, infants and young children 2 months to 2 years of age with UTI should receive antimicrobials in therapeutic or prophylactic dosages until the imaging studies are completed (strength of evidence: good).

Although this practice parameter deals with the acute UTI, it is important to recognize the significance of recurrent infections. The association between recurrent bouts of febrile UTI and renal scarring follows an exponential curve [16] (Fig 2) . Because the risk of recurrence is highest during the first months after UTI, children treated for UTI should continue antimicrobial treatment or prophylaxis (Table 5) until the imaging studies are completed and assessed. Additional treatment is based on the imaging findings assuming sterilization of the urine.

EVALUATION: IMAGING

Recommendation 11

Infants and young children 2 months to 2 years of age with UTI who do not demonstrate the expected clinical response within 2 days of

antimicrobial therapy should undergo ultrasonography promptly, and either voiding cystourethrography (VCUG) or radionuclide cystography (RNC) should be performed at the earliest convenient time. Infants and young children who have the expected response to antimicrobials should have a sonogram and either VCUG or RNC performed at the earliest convenient time (strength of evidence: fair).

UTI in young children serve as a marker for abnormalities of the urinary tract. Imaging of the urinary tract is recommended in every febrile infant or young child with a first UTI to identify those with abnormalities that predispose to renal damage. Imaging should consist of urinary tract ultrasonography to detect dilatation secondary to obstruction and a study to detect VUR.

Ultrasonography

Urinary tract ultrasonography consists of examination of the kidneys to identify hydronephrosis and examination of the bladder to identify dilatation of the distal ureters, hypertrophy of the bladder wall, and the presence of ureterocele. Previously, excretory urography (commonly called intravenous pyelography) was used to reveal these abnormalities, but now ultrasonography shows them more safely, less invasively, and often less expensively. Ultrasonography does have limitations, however. A normal ultrasound does not exclude VUR. Ultrasonography may show signs of acute renal inflammation and established renal scars, but it is not as sensitive as other renal imaging techniques.

Usually the timing of the ultrasound is not crucial, but when the rate of clinical improvement is slower than anticipated during treatment, ultrasonography should be performed promptly to look for a cause such as obstruction or abscess.

VUR

The most common abnormality detected in imaging studies is VUR (Fig 1) . The rate of VUR among children younger than 1 year of age with UTI exceeds 50%. VUR is not an all-or-none phenomenon; grades of severity are recognized, designated I to V in the

TABLE 5 -- Some Antimicrobials for Prophylaxis of UTI

Antimicrobial
Dosage

TMP in combination with SMX
2 mg of TMP, 10 mg of SMX per kg as single bedtime dose or 5 mg of
TMP, 25 mg of SMX per kg twice per week

Nitrofurantoin
1-2 mg/kg as single daily dose

Sulfisoxazole
10-20 mg/kg divided every 12 h

Nalidixic acid
30 mg/kg divided every 12 h

Methenamine mandelate
75 mg/kg divided every 12 h

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International Study Classification (International Reflux Study Committee, 1981), based on the extent of the reflux and associated dilatation of the ureter and pelvis. The grading of VUR is important because the natural history differs by grade, as does the risk of renal damage. Patients with high-grade VUR are 4 to 6 times more likely to have scarring than those with low-grade VUR and 8 to 10 times more likely than those without VUR. [16] [49] VCUG; RNC

Either traditional contrast VCUG or RNC is recommended for detecting reflux. Although children may have pyelonephritis without reflux, the child with reflux is at increased risk of pyelonephritis and of scarring from UTI. With VCUG and RNC, a voiding phase is important because some reflux occurs only during voiding. If the predicted bladder capacity is not reached, the study may underestimate the presence or degree of reflux.

VCUG with fluoroscopy characterizes reflux better than does RNC. In addition, RNC does not show urethral or bladder abnormalities; for this reason, boys, whose urethra must be examined for posterior urethral valves, or girls, who have symptoms of voiding dysfunction when not infected, should have a standard fluoroscopic contrast VCUG as part of their initial studies. RNC has a lower radiation dose and therefore may be preferred in follow-up examinations of children with reflux. However, the introduction of low-dose radiographic equipment has narrowed the gap in radiation between the VCUG and RNC. [50]

There is no benefit in delaying performance of these studies as long as the child is free of infection and bladder irritability is absent. While waiting for reflux study results, the child should be receiving an antimicrobial, either as part of the initial treatment or as posttreatment prophylaxis (Table 5).

Radionuclide Renal Scans

Renal cortical scintigraphy (with ^{99m}Tc -DMSA or ^{99m}Tc -glucoheptonate) and enhanced computed tomography are very sensitive means of identifying acute changes from pyelonephritis or renal scarring. However, the role of these imaging modalities in the clinical management of the child with UTI still is unclear.

CONCLUSIONS

Eleven recommendations are proposed for the diagnosis, management, and evaluation of infants and young children with UTI and

unexplained fever. Infants and children younger than 2 years of age with unexplained fever are identified for particular concern because UTI has a high prevalence in this group (5%), may cause few recognizable signs or symptoms other than fever, and has a greater potential for renal damage than in older children. Strategies of diagnosis and treatment depend on how ill the clinician assesses the infant or young child to be, ie, whether antimicrobial therapy is warranted immediately or can be delayed safely until the results of urine culture are available. Diagnosis is based on the culture of an appropriately collected specimen of urine; urinalysis can only suggest the diagnosis. Imaging studies should be performed on all infants and young children with a documented initial UTI.

AREAS FOR FUTURE RESEARCH

The relationship between UTI in infants and young children and reduced renal function in adults has been established but is not well

characterized in quantitative terms. The ideal prospective cohort study from birth to age 40 to 50 years has not been conducted and is unlikely to be conducted. Thus, estimates of undesirable outcomes in adulthood, such as hypertension and end-stage renal disease, are based on the mathematical product of probabilities at several steps, each of which is subject to bias and error. Other attempts at decision analysis [51] and thoughtful literature review [52] have recognized the same limitations. Until recently, imaging tools available to assess the effect of UTI have been insensitive. With the imaging techniques available now, it may be possible to follow a cohort of infants and young children who present with fever and UTI to assess the development of scars and functional impairment. Research is underway in this area.

The development of noninvasive methods of obtaining a urine specimen or of techniques that obviate the need for invasive sampling would be valuable for general use. One component of the urinalysis that merits particular attention is the assessment of WBCs in the urine. Bacteriuria can occur without pyuria, but it is not clear whether pyuria is a specific marker for renal inflammation, obviating the need for culture if WBCs are not present in the urine. Research is underway in this area under conditions that optimize the detection of WBCs in the urine by microscopy. If studies continue to demonstrate usefulness of microscopy, the general applicability of the test will need to be studied, particularly in offices without on-site laboratories or trained laboratory staff. Special attention will need to be given to specimens from girls and from uncircumcised boys, particularly infants, because transurethral catheterization may be difficult and produce a contaminated specimen. An alternative to SPA, which is not commonly performed anymore, would be welcome in clinical practice and in research to clarify such issues as the true prevalence of UTI in young uncircumcised boys.

There is consensus about the antimicrobial treatment of infants and young children with acute UTI, but questions remain relating to the specific duration and route of therapy. Currently, the efficacy of orally administered treatment is being compared with parenterally administered treatment under controlled conditions. If orally administered therapy is as efficacious as that administered parenterally, concern about variable adherence to a prescribed regimen will remain and influence the decision of whether to hospitalize

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and whether to administer the antimicrobial(s) parenterally or orally.

As noted in the section "Evaluation: Imaging," ultrasonography is recommended to detect dilatation associated with obstruction and is preferred over other modalities because it is noninvasive and does not expose the child to radiation. Data defining the yield of positive findings were generated before the widespread use of fetal ultrasonography, and it is not clear that they are applicable today. The absence of extensive data from modern studies

and variations in the frequency and quality of fetal ultrasonography do not permit a determination of whether ultrasonography can reasonably be omitted. Further complicating the assessment is the changing utilization of fetal ultrasonography under the financial pressures of managed care. Studies in this area will need to be defined carefully so that the generalizability and applicability to individual patients can be assessed.

A study to determine the presence and severity of VUR also is recommended. It is recognized, however, that pyelonephritis (defined by cortical scintigraphy) can occur in the absence of VUR (defined by VCUG or RNC) and that progressive renal scarring (defined by cortical scintigraphy) can occur in the absence of demonstrated VUR. Whether children with pyelonephritis (defined clinically or by cortical scintigraphy) who have normal results on VCUG or RNC benefit from antimicrobial prophylaxis is unknown but is being studied.

The role of cortical scintigraphy in the imaging examination of infants and young children with initial UTI is unclear and requires additional study. The demonstration by cortical scintigraphy of "cold" areas of decreased perfusion has led to the development of alternative imaging techniques, such as enhanced computed tomography and power Doppler ultrasonography. These modalities also can demonstrate hypoperfusion and have advantages, particularly power Doppler ultrasonography, which is noninvasive and does not expose the child to radiation. Studies are now in progress.

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