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Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months

Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management

Pediatrics 2011;128;595; originally published online August 28, 2011;
DOI: 10.1542/peds.2011-1330

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CLINICAL PRACTICE GUIDELINE

Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months

SUBCOMMITTEE ON URINARY TRACT INFECTION, STEERING COMMITTEE ON QUALITY IMPROVEMENT AND MANAGEMENT

KEY WORDS
urinary tract infection, infants, children, vesicoureteral reflux, voiding cystourethrography

ABBREVIATIONS
SPA—suprapubic aspiration
AAP—American Academy of Pediatrics
UTI—urinary tract infection
RCT—randomized controlled trial
CFU—colony-forming unit
VUR—vesicoureteral reflux
WBC—white blood cell
RBUS—renal and bladder ultrasonography
VCUG—voiding cystourethrography

The recommendations in this report 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.

All clinical practice guidelines from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

www.pediatrics.org/cgi/doi/10.1542/peds.2011-1330

doi:10.1542/peds.2011-1330

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

COMPANION PAPERS: Companions to this article can be found on pages 572 and e749, and online at www.pediatrics.org/cgi/doi/10.1542/peds.2011-1818 and www.pediatrics.org/cgi/doi/10.1542/peds.2011-1332.

abstract

FREE

OBJECTIVE: To revise the American Academy of Pediatrics practice parameter regarding the diagnosis and management of initial urinary tract infections (UTIs) in febrile infants and young children.

METHODS: Analysis of the medical literature published since the last version of the guideline was supplemented by analysis of data provided by authors of recent publications. The strength of evidence supporting each recommendation and the strength of the recommendation were assessed and graded.

RESULTS: Diagnosis is made on the basis of the presence of both pyuria and at least 50 000 colonies per mL of a single uropathogenic organism in an appropriately collected specimen of urine. After 7 to 14 days of antimicrobial treatment, close clinical follow-up monitoring should be maintained to permit prompt diagnosis and treatment of recurrent infections. Ultrasonography of the kidneys and bladder should be performed to detect anatomic abnormalities. Data from the most recent 6 studies do not support the use of antimicrobial prophylaxis to prevent febrile recurrent UTI in infants without vesicoureteral reflux (VUR) or with grade I to IV VUR. Therefore, a voiding cystourethrography (VCUG) is not recommended routinely after the first UTI; VCUG is indicated if renal and bladder ultrasonography reveals hydronephrosis, scarring, or other findings that would suggest either high-grade VUR or obstructive uropathy and in other atypical or complex clinical circumstances. VCUG should also be performed if there is a recurrence of a febrile UTI. The recommendations in this guideline do not indicate an exclusive course of treatment or serve as a standard of care; variations may be appropriate. Recommendations about antimicrobial prophylaxis and implications for performance of VCUG are based on currently available evidence. As with all American Academy of Pediatrics clinical guidelines, the recommendations will be reviewed routinely and incorporate new evidence, such as data from the Randomized Intervention for Children With Vesicoureteral Reflux (RIVUR) study.

CONCLUSIONS: Changes in this revision include criteria for the diagnosis of UTI and recommendations for imaging. *Pediatrics* 2011;128:595–610

INTRODUCTION

Since the early 1970s, occult bacteremia has been the major focus of concern for clinicians evaluating febrile infants who have no recognizable source of infection. With the introduction of effective conjugate vaccines against *Haemophilus influenzae* type b and *Streptococcus pneumoniae* (which have resulted in dramatic decreases in bacteremia and meningitis), there has been increasing appreciation of the urinary tract as the most frequent site of occult and serious bacterial infections. Because the clinical presentation tends to be nonspecific in infants and reliable urine specimens for culture cannot be obtained without invasive methods (urethral catheterization or suprapubic aspiration [SPA]), diagnosis and treatment may be delayed. Most experimental and clinical data support the concept that delays in the institution of appropriate treatment of pyelonephritis increase the risk of renal damage.[1,2]

This clinical practice guideline is a revision of the practice parameter published by the American Academy of Pediatrics (AAP) in 1999.[3] It was developed by a subcommittee of the Steering Committee on Quality Improvement and Management that included physicians with expertise in the fields of academic general pediatrics, epidemiology and informatics, pediatric infectious diseases, pediatric nephrology, pediatric practice, pediatric radiology, and pediatric urology. The AAP funded the development of this guideline; none of the participants had any financial conflicts of interest. The guideline was reviewed by multiple groups within the AAP (7 committees, 1 council, and 9 sections) and 5 external organizations in the United States and Canada. The guideline will be reviewed and/or revised in 5 years, unless new evidence emerges that warrants revision sooner. The guideline is intended for use in a variety of clinical settings (eg, office, emergency department, or hospital) by clinicians who treat infants and young children. This text is a summary of the analysis. The data on which the recommendations are based are included in a companion technical report.[4]

Like the 1999 practice parameter, this revision focuses on the diagnosis and management of initial urinary tract infections (UTIs) in febrile infants and young children (2–24 months of age) who have no obvious neurologic or anatomic abnormalities known to be associated with recurrent UTI or renal damage. (For simplicity, in the remainder of this guideline the phrase "febrile infants" is used to indicate febrile infants and young children 2–24 months of age.) The lower and upper age limits were selected because studies on infants with unexplained fever generally have used these age limits and have documented that the prevalence of UTI is high (~5%) in this age group. In those studies, fever was defined as temperature of at least 38.0°C (≥100.4°F); accordingly, this definition of fever is used in this guideline. Neonates and infants less than 2 months of age are excluded, because there are special considerations in this age group that may limit the application of evidence derived from the studies of 2- to 24-month-old children. Data are insufficient to determine whether the evidence generated from studies of infants 2 to 24 months of age applies to children more than 24 months of age.

METHODS

To provide evidence for the guideline, 2 literature searches were conducted, that is, a surveillance of Medline-listed literature over the past 10 years for significant changes since the guideline was published and a systematic review of the literature on the effectiveness of prophylactic antimicrobial therapy to prevent recurrence of febrile UTI/pyelonephritis in children with vesicoureteral reflux (VUR). The latter was based on the new and growing body of evidence questioning the effectiveness of antimicrobial prophylaxis to prevent recurrent febrile UTI in children with VUR. To explore this particular issue, the literature search was expanded to include trials published since 1993 in which antimicrobial prophylaxis was compared with no treatment or placebo treatment for children with VUR. Because all except 1 of the recent randomized controlled trials (RCTs) of the effectiveness of prophylaxis included children more than 24 months of age and some did not provide specific data according to grade of VUR, the authors of the 6 RCTs were contacted; all provided raw data from their studies specifically addressing infants 2 to 24 months of age, according to grade of VUR. Meta-analysis of these data was performed.

Results from the literature searches and meta-analyses were provided to committee members. Issues were raised and discussed until consensus was reached regarding recommendations. The quality of evidence supporting each recommendation and the strength of the recommendation were assessed by the committee member most experienced in informatics and epidemiology and were graded according to AAP policy[5] (Fig 1).

The subcommittee formulated 7 recommendations, which are presented in the text in the order in which a clinician would use them when evaluating and treating a febrile infant, as well as in algorithm form in the Appendix. This clinical practice guideline is not intended to be a sole source of guidance for the treatment of febrile infants with UTIs. Rather, it is intended to assist clinicians in decision-making. It is not intended to replace clinical judgment or to

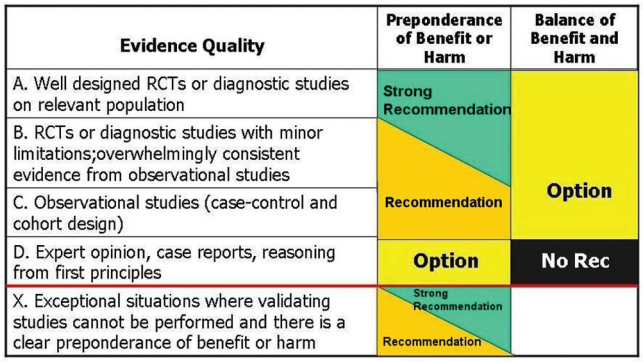

FIGURE 1
AAP evidence strengths.

establish an exclusive protocol for the care of all children with this condition.

DIAGNOSIS

Action Statement 1

If a clinician decides that a febrile infant with no apparent source for the fever requires antimicrobial therapy to be administered because of ill appearance or another pressing reason, the clinician should ensure that a urine specimen is obtained for both culture and urinalysis before an antimicrobial agent is administered; the specimen needs to be obtained through catheterization or SPA, because the diagnosis of UTI cannot be established reliably through culture of urine collected in a bag (evidence quality: A; strong recommendation).

When evaluating febrile infants, clinicians make a subjective assessment of the degree of illness or toxicity, in addition to seeking an explanation for the fever. This clinical assessment determines whether antimicrobial therapy should be initiated promptly and affects the diagnostic process regarding UTI. If the clinician determines that the degree of illness warrants immediate antimicrobial therapy, then a urine specimen suitable for culture should be obtained through catheterization or SPA before antimicrobial agents are administered, because the antimicrobial agents commonly prescribed in such situations would almost certainly obscure the diagnosis of UTI.

SPA has been considered the standard method for obtaining urine that is uncontaminated by perineal flora. Variable success rates for obtaining urine have been reported (23%–90%).[6–8] When ultrasonographic guidance is used, success rates improve.[9,10] The technique has limited risks, but technical expertise and experience are required, and many parents and physicians perceive the procedure as unacceptably invasive, compared with catheterization. However, there may be no acceptable alternative to SPA for boys with moderate or severe phimosis or girls with tight labial adhesions.

Urine obtained through catheterization for culture has a sensitivity of 95% and a specificity of 99%, compared with that obtained through SPA.[7,11,12] The techniques required for catheterization and SPA are well described.[13] When catheterization or SPA is being attempted, the clinician should have a sterile container ready to collect a urine specimen, because the preparation for the procedure may stimulate the child to void. Whether the urine is obtained through catheterization or is voided, the first few drops should be allowed to fall outside the sterile container, because they may be contaminated by bacteria in the distal urethra.

Cultures of urine specimens collected in a bag applied to the perineum have an unacceptably high false-positive rate and are valid only when they yield negative results.[6,14–16] With a prevalence of UTI of 5% and a high rate of false-positive results (specificity: ~63%), a "positive" culture result for urine collected in a bag would be a false-positive result 88% of the time. For febrile boys, with a prevalence of UTI of 2%, the rate of false-positive results is 95%; for circumcised boys, with a prevalence of UTI of 0.2%, the rate of false-positive results is 99%. Therefore, in cases in which antimicrobial therapy will be initiated, catheterization or SPA is required to establish the diagnosis of UTI.

- Aggregate quality of evidence: A (diagnostic studies on relevant populations).
- Benefits: A missed diagnosis of UTI can lead to renal scarring if left untreated; overdiagnosis of UTI can lead to overtreatment and unnecessary and expensive imaging. Once antimicrobial therapy is initiated, the opportunity to make a definitive diagnosis is lost; multiple studies of antimicrobial therapy have shown that the urine may be rapidly sterilized.
- Harms/risks/costs: Catheterization is invasive.
- Benefit-harms assessment: Preponderance of benefit over harm.
- Value judgments: Once antimicrobial therapy has begun, the opportunity to make a definitive diagnosis is lost. Therefore, it is important to have the most-accurate test for UTI performed initially.
- Role of patient preferences: There is no evidence regarding patient preferences for bag versus catheterized urine. However, bladder tap has

been shown to be more painful than urethral catheterization.

- Exclusions: None.
- Intentional vagueness: The basis of the determination that antimicrobial therapy is needed urgently is not specified, because variability in clinical judgment is expected; considerations for individual patients, such as availability of follow-up care, may enter into the decision, and the literature provides only general guidance.
- Policy level: Strong recommendation.

Individual Risk Factors: Girls
White race
Age < 12 mo
Temperature ≥ 39°C
Fever ≥ 2 d
Absence of another source of infection

Probability of UTI	No. of Factors Present
≤1%	No more than 1
≤2%	No more than 2

Individual Risk Factors: Boys
Nonblack race
Temperature ≥ 39°C
Fever > 24 h
Absence of another source of infection

Probability of UTI	No. of Factors Present	
	Uncircumcised	Circumcised
≤1%	[a]	No more than 2
≤2%	None	No more than 3

FIGURE 2
Probability of UTI Among Febrile Infant Girls[28] and Infant Boys[30] According to Number of Findings Present. [a]Probability of UTI exceeds 1% even with no risk factors other than being uncircumcised.

Action Statement 2

If a clinician assesses a febrile infant with no apparent source for the fever as not being so ill as to require immediate antimicrobial therapy, then the clinician should assess the likelihood of UTI (see below for how to assess likelihood).

Action Statement 2a

If the clinician determines the febrile infant to have a low likelihood of UTI (see text), then clinical follow-up monitoring without testing is sufficient (evidence quality: A; strong recommendation).

Action Statement 2b

If the clinician determines that the febrile infant is not in a low-risk group (see below), then there are 2 choices (evidence quality: A; strong recommendation). Option 1 is to obtain a urine specimen through catheterization or SPA for culture and urinalysis. Option 2 is to obtain a urine specimen through the most convenient means and to perform a urinalysis. If the urinalysis results suggest a UTI (positive leukocyte esterase test results or nitrite test or microscopic analysis results positive for leukocytes or bacteria), then a urine specimen should be obtained through catheterization or SPA and cultured; if urinalysis of fresh (<1 hour since void) urine yields negative leukocyte esterase and nitrite test results, then it is reasonable to monitor the clinical course without initiating antimicrobial therapy, recognizing that negative urinalysis results do not rule out a UTI with certainty.

If the clinician determines that the degree of illness does not require immediate antimicrobial therapy, then the likelihood of UTI should be assessed. As noted previously, the overall prevalence of UTI in febrile infants who have no source for their fever evident on the basis of history or physical examination results is approximately 5%,[17,18] but it is possible to identify groups with higher-than-average likelihood and some with lower-than-average likelihood. The prevalence of UTI among febrile infant girls is more than twice that among febrile infant boys (relative risk: 2.27). The rate for uncircumcised boys is 4 to 20 times higher than that for circumcised boys, whose rate of UTI is only 0.2% to 0.4%.[19–24] The presence of another, clinically obvious source of infection reduces the likelihood of UTI by one-half.[25]

In a survey asking, "What yield is required to warrant urine culture in febrile infants?," the threshold was less than 1% for 10.4% of academicians and 11.7% for practitioners[26]; when the threshold was increased to 1% to 3%, 67.5% of academicians and 45.7% of practitioners considered the yield sufficiently high to warrant urine culture. Therefore, attempting to operationalize "low likelihood" (ie, below a threshold that warrants a urine culture) does not produce an absolute percentage; clinicians will choose a threshold depending on factors such as their confidence that contact will be maintained through the illness (so that a specimen can be obtained at a later time) and comfort with diagnostic uncertainty. Fig 2 indicates the number of risk factors associated with threshold probabilities of UTI of at least 1% and at least 2%.

In a series of studies, Gorelick, Shaw, and colleagues[27–29] derived and validated a prediction rule for febrile infant girls on the basis of 5 risk factors, namely, white race, age less than 12 months, temperature of at least 39°C, fever for at least 2 days, and absence of another source of infection. This prediction rule, with sensitivity of 88% and specificity of 30%, permits some infant girls to be considered in a low-likelihood group (Fig 2). For example, of girls with no identifiable source of infection, those who are nonwhite and more than 12 months of age with a recent onset (<2 days) of low-

grade fever (<39°C) have less than a 1% probability of UTI; each additional risk factor increases the probability. It should be noted, however, that some of the factors (eg, duration of fever) may change during the course of the illness, excluding the infant from a low-likelihood designation and prompting testing as described in action statement 2a.

As demonstrated in Fig 2, the major risk factor for febrile infant boys is whether they are circumcised. The probability of UTI can be estimated on the basis of 4 risk factors, namely, nonblack race, temperature of at least 39°C, fever for more than 24 hours, and absence of another source of infection.[4,30]

If the clinician determines that the infant does not require immediate antimicrobial therapy and a urine specimen is desired, then often a urine collection bag affixed to the perineum is used. Many clinicians think 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. Even if contamination from the perineal skin is minimized, however, there may be significant contamination from the vagina in girls or the prepuce in uncircumcised boys, the 2 groups at highest risk of UTI. A "positive" culture result from a specimen collected in a bag cannot be used to document a UTI; confirmation requires culture of a specimen collected through catheterization or SPA. Because there may be substantial delay waiting for the infant to void and a second specimen, obtained through catheterization, may be necessary if the urinalysis suggests the possibility of UTI, many clinicians prefer to obtain a definitive urine specimen through catheterization initially.

- Aggregate quality of evidence: A (diagnostic studies on relevant populations).
- Benefits: Accurate diagnosis of UTI can prevent the spread of infection and renal scarring; avoiding overdiagnosis of UTI can prevent overtreatment and unnecessary and expensive imaging.
- Harms/risks/costs: A small proportion of febrile infants, considered at low likelihood of UTI, will not receive timely identification and treatment of their UTIs.
- Benefit-harms assessment: Preponderance of benefit over harm.
- Value judgments: There is a risk of UTI sufficiently low to forestall further evaluation.
- Role of patient preferences: The choice of option 1 or option 2 and the threshold risk of UTI warranting obtaining a urine specimen may be influenced by parents' preference to avoid urethral catheterization (if a bag urine sample yields negative urinalysis results) versus timely evaluation (obtaining a definitive specimen through catheterization).
- Exclusions: Because it depends on a range of patient- and physician-specific considerations, the precise threshold risk of UTI warranting obtaining a urine specimen is left to the clinician but is below 3%.
- Intentional vagueness: None.
- Policy level: Strong recommendation.

TABLE 1 Sensitivity and Specificity of Components of Urinalysis, Alone and in Combination

Test	Sensitivity (Range), %	Specificity (Range), %
Leukocyte esterase test	83 (67–94)	78 (64–92)
Nitrite test	53 (15–82)	98 (90–100)
Leukocyte esterase or nitrite test 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 test, nitrite test, or microscopy positive	99.8 (99–100)	70 (60–92)

Action Statement 3

To establish the diagnosis of UTI, clinicians should require *both* urinalysis results that suggest infection (pyuria and/or bacteriuria) *and* the presence of at least 50 000 colony-forming units (CFUs) per mL of a uropathogen cultured from a urine specimen obtained through catheterization or SPA (evidence quality: C; recommendation).

Urinalysis

General Considerations

Urinalysis cannot substitute for urine culture to document the presence of UTI but needs to be used in conjunction with culture. Because urine culture results are not available for at least 24 hours, there is considerable interest in tests that may predict the results of the urine culture and enable presumptive therapy to be initiated at the first encounter. Urinalysis can be performed on any specimen, including one collected from a bag applied to the perineum. However, the specimen must be fresh (<1 hour after voiding with maintenance at room temperature or <4 hours after voiding with refrigeration), to ensure sensitivity and specificity of the urinalysis. The tests that have received the most attention are biochemical analyses of leukocyte esterase and nitrite through a rapid dipstick method and urine microscopic examination for white blood cells (WBCs) and bacteria (Table 1).

Urine dipsticks are appealing, because they provide rapid results, do not require microscopy, and are eligible for a waiver under the Clinical Laboratory Improvement Amendments. They indicate the presence of leukocyte esterase (as a surrogate marker for pyuria) and urinary nitrite (which is converted from dietary nitrates in the presence of most Gram-negative enteric bacteria in the urine). The conversion of dietary nitrates to nitrites by bacteria requires approximately 4 hours in the bladder.[31] The performance characteristics of both leukocyte esterase and nitrite tests vary according to the definition used for positive urine culture results, the age and symptoms of the population being studied, and the method of urine collection.

Nitrite Test

A nitrite test is not a sensitive marker for children, particularly infants, who empty their bladders frequently. Therefore, negative nitrite test results have little value in ruling out UTI. Moreover, not all urinary pathogens reduce nitrate to nitrite. The test is helpful when the result is positive, however, because it is highly specific (ie, there are few false-positive results).[32]

Leukocyte Esterase Test

The sensitivity of the leukocyte esterase test is 94% when it used in the context of clinically suspected UTI. Overall, the reported sensitivity in various studies is lower (83%), because the results of leukocyte esterase tests were related to culture results without exclusion of individuals with asymptomatic bacteriuria. The absence of leukocyte esterase in the urine of individuals with asymptomatic bacteriuria is an advantage of the test, rather than a limitation, because it distinguishes individuals with asymptomatic bacteriuria from those with true UTI.

The specificity of the leukocyte esterase test (average: 72% [range: 64%–92%]) generally is not as good as the sensitivity, which reflects the nonspecificity of pyuria in general. Accordingly, positive leukocyte esterase test results should be interpreted with caution, because false-positive results are common. With numerous conditions other than UTI, including fever resulting from other conditions (eg, streptococcal infections or Kawasaki disease), and after vigorous exercise, WBCs may be found in the urine. Therefore, a finding of pyuria by no means confirms that an infection of the urinary tract is present.

The absence of pyuria in children with true UTIs is rare, however. It is theoretically possible if a febrile child is assessed before the inflammatory response has developed, but the inflammatory response to a UTI produces both fever and pyuria; therefore, children who are being evaluated because of fever should already have WBCs in their urine. More likely explanations for significant bacteriuria in culture in the absence of pyuria include contaminated specimens, insensitive criteria for pyuria, and asymptomatic bacteriuria. In most cases, when true UTI has been reported to occur in the absence of pyuria, the definition of pyuria has been at fault. The standard method of assessing pyuria has been centrifugation of the urine and microscopic analysis, with a threshold of 5 WBCs per high-power field (~25 WBCs per μL). If a counting chamber is used, however, the finding of at least 10 WBCs per μL in uncentrifuged urine has been demonstrated to be more sensitive[33] and performs well in clinical situations in which the standard method does not, such as with very young infants.[34]

An important cause of bacteriuria in the absence of pyuria is asymptomatic bacteriuria. Asymptomatic bacteriuria often is associated with school-aged and older girls,[35] but it can be present during infancy. In a study of infants 2 to 24 months of age, 0.7% of afebrile girls had 3 successive urine cultures with 10^5 CFUs per mL of a single uropathogen.[26] Asymptomatic bacteriuria can be easily confused with true UTI in a febrile infant but needs to be distinguished, because studies suggest that antimicrobial treatment may do more harm than good.[36] The key to distinguishing true UTI from asymptomatic bacteriuria is the presence of pyuria.

Microscopic Analysis for Bacteriuria

The presence of bacteria in a fresh, Gram-stained specimen of uncentrifuged urine correlates with 10^5 CFUs per mL in culture.[37] An "enhanced urinalysis," combining the counting chamber assessment of pyuria noted previously with Gram staining of drops of uncentrifuged urine, with a threshold of at least 1 Gram-negative rod in 10 oil immersion fields, has greater sensitivity, specificity, and positive predictive value than does the standard urinalysis[33] and is the preferred method of urinalysis when appropriate equipment and personnel are available.

Automated Urinalysis

Automated methods to perform urinalysis are now being used in many hospitals and laboratories. Image-based systems use flow imaging analysis technology and software to classify particles in uncentrifuged urine specimens rapidly.[38] Results correlate well with manual methods, especially for red blood cells, WBCs, and squamous epithelial cells. In the future, this may be the most common method by which urinalysis is performed in laboratories.

Culture

The diagnosis of UTI is made on the basis of quantitative urine culture results in addition to evidence of pyuria and/or bacteriuria. Urine specimens should be processed as expediently as

possible. If the specimen is not processed promptly, then it should be refrigerated to prevent the growth of organisms that can occur in urine at room temperature; for the same reason, specimens that require transportation to another site for processing should be transported on ice. A properly collected urine specimen should be inoculated on culture medium that will allow identification of urinary tract pathogens.

Urine culture results are considered positive or negative on the basis of the number of CFUs that grow on the culture medium.[36] Definition of significant colony counts with regard to the method of collection considers that the distal urethra and periurethral area are commonly colonized by the same bacteria that may cause UTI; therefore, a low colony count may be present in a specimen obtained through voiding or catheterization when bacteria are not present in bladder urine. Definitions of positive and negative culture results are operational and not absolute. The time the urine resides in the bladder (bladder incubation time) is an important determinant of the magnitude of the colony count. The concept that more than 100 000 CFUs per mL indicates a UTI was based on morning collections of urine from adult women, with comparison of specimens from women without symptoms and women considered clinically to have pyelonephritis; the transition range, in which the proportion of women with pyelonephritis exceeded the proportion of women without symptoms, was 10 000 to 100 000 CFUs per mL.[39] In most instances, an appropriate threshold to consider bacteriuria "significant" in infants and children is the presence of at least 50 000 CFUs per mL of a single urinary pathogen.[40] (Organisms such as *Lactobacillus* spp, coagulase-negative staphylococci, and *Corynebacterium* spp are not considered clinically relevant urine isolates for otherwise healthy, 2- to 24-month-old children.) Reducing the threshold from 100 000 CFUs per mL to 50 000 CFUs per mL would seem to increase the sensitivity of culture at the expense of decreased specificity; however, because the proposed criteria for UTI now include evidence of pyuria in addition to positive culture results, infants with "positive" culture results alone will be recognized as having asymptomatic bacteriuria rather than a true UTI. Some laboratories report growth only in the following categories: 0 to 1000, 1000 to 10 000, 10 000 to 100 000, and more than 100 000 CFUs per mL. In such cases, results in the 10 000 to 100 000 CFUs per mL range need to be evaluated in context, such as whether the urinalysis findings support the diagnosis of UTI and whether the organism is a recognized uropathogen.

Alternative culture methods, such as dipslides, may have a place in the office setting; sensitivity is reported to be in the range of 87% to 100%, and specificity is reported to be 92% to 98%, but dipslides cannot specify the organism or antimicrobial sensitivities.[41] Practices that use dipslides should do so in collaboration with a certified laboratory for identification and sensitivity testing or, in the absence of such results, may need to perform "test of cure" cultures after 24 hours of treatment.

- Aggregate quality of evidence: C (observational studies).
- Benefits: Accurate diagnosis of UTI can prevent the spread of infection and renal scarring; avoiding overdiagnosis of UTI can prevent overtreatment and unnecessary and expensive imaging. These criteria reduce the likelihood of overdiagnosis of UTI in infants with asymptomatic bacteriuria or contaminated specimens.
- Harms/risks/costs: Stringent diagnostic criteria may miss a small number of UTIs.
- Benefit-harms assessment: Preponderance of benefit over harm.
- Value judgments: Treatment of asymptomatic bacteriuria may be harmful.
- Role of patient preferences: We assume that parents prefer no action in the absence of a UTI (avoiding false-positive results) over a very small chance of missing a UTI.
- Exclusions: None.
- Intentional vagueness: None.
- Policy level: Recommendation.

MANAGEMENT

Action Statement 4

Action Statement 4a

When initiating treatment, the clinician should base the choice of route of administration on practical considerations. Initiating treatment orally or parenterally is equally efficacious. The clinician should base the choice of agent on local antimicrobial sensitivity patterns (if available) and should adjust the choice according to sensitivity testing of the isolated uropathogen (evidence quality: A; strong recommendation).

Action Statement 4b

The clinician should choose 7 to 14 days as the duration of antimicrobial therapy (evidence quality: B; recommendation).

The goals of treatment of acute UTI are to eliminate the acute infection, to prevent complications, and to reduce the likelihood of renal damage. Most children can be treated orally.[42–44] Patients whom clinicians judge to be "toxic" or who are unable to retain oral intake (including medications) should receive an antimicrobial agent parenter-

TABLE 2 Some Empiric Antimicrobial Agents for Parenteral Treatment of UTI

Antimicrobial Agent	Dosage
Ceftriaxone	75 mg/kg, every 24 h
Cefotaxime	150 mg/kg per d, divided every 6–8 h
Ceftazidime	100–150 mg/kg per d, divided every 8 h
Gentamicin	7.5 mg/kg per d, divided every 8 h
Tobramycin	5 mg/kg per d, divided every 8 h
Piperacillin	300 mg/kg per d, divided every 6–8 h

TABLE 3 Some Empiric Antimicrobial Agents for Oral Treatment of UTI

Antimicrobial Agent	Dosage
Amoxicillin-clavulanate	20–40 mg/kg per d in 3 doses
Sulfonamide	
Trimethoprim-sulfamethoxazole	6–12 mg/kg trimethoprim and 30-60 mg/kg sulfamethoxazole per d in 2 doses
Sulfisoxazole	120–150 mg/kg per d in 4 doses
Cephalosporin	
Cefixime	8 mg/kg per d in 1 dose
Cefpodoxime	10 mg/kg per d in 2 doses
Cefprozil	30 mg/kg per d in 2 doses
Cefuroxime axetil	20–30 mg/kg per d in 2 doses
Cephalexin	50–100 mg/kg per d in 4 doses

ally (Table 2) until they exhibit clinical improvement, generally within 24 to 48 hours, and are able to retain orally administered fluids and medications. In a study of 309 febrile infants with UTIs, only 3 (1%) were deemed too ill to be assigned randomly to either parenteral or oral treatment.[42] Parenteral administration of an antimicrobial agent also should be considered when compliance with obtaining an antimicrobial agent and/or administering it orally is uncertain. The usual choices for oral treatment of UTIs include a cephalosporin, amoxicillin plus clavulanic acid, or trimethoprim-sulfamethoxazole (Table 3). It is essential to know local patterns of susceptibility of coliforms to antimicrobial agents, particularly trimethoprim-sulfamethoxazole and cephalexin, because there is substantial geographic variability that needs to be taken into account during selection of an antimicrobial agent before sensitivity results are available. Agents that are excreted in the urine but do not achieve therapeutic concentrations in the bloodstream, such as nitrofurantoin, should not be used to treat febrile infants with UTIs, because parenchymal and serum antimicrobial concentrations may be insufficient to treat pyelonephritis or urosepsis.

Whether the initial route of administration of the antimicrobial agent is oral or parenteral (then changed to oral), the total course of therapy should be 7 to 14 days. The committee attempted to identify a single, preferred, evidence-based duration, rather than a range, but data comparing 7, 10, and 14 days directly were not found. There is evidence that 1- to 3-day courses for febrile UTIs are inferior to courses in the recommended range; therefore, the minimal duration selected should be 7 days.

- Aggregate quality of evidence: A/B (RCTs).
- Benefits: Adequate treatment of UTI can prevent the spread of infection and renal scarring. Outcomes of short courses (1–3 d) are inferior to those of 7- to 14-d courses.
- Harms/risks/costs: There are minimal harm and minor cost effects of antimicrobial choice and duration of therapy.
- Benefit-harms assessment: Preponderance of benefit over harm.
- Value judgments: Adjusting antimicrobial choice on the basis of available data and treating according to best evidence will minimize cost and consequences of failed or unnecessary treatment.
- Role of patient preferences: It is assumed that parents prefer the most-effective treatment and the least amount of medication that ensures effective treatment.
- Exclusions: None.
- Intentional vagueness: No evidence distinguishes the benefit of treating 7 vs 10 vs 14 days, and the range is allowable.
- Policy level: Strong recommendation/recommendation.

Action Statement 5

Febrile infants with UTIs should undergo renal and bladder ultrasonography (RBUS) (evidence quality: C; recommendation).

The purpose of RBUS is to detect anatomic abnormalities that require further evaluation, such as additional imaging or urologic consultation. RBUS also provides an evaluation of the renal parenchyma and an assessment of renal size that can be used to monitor renal growth. The yield of actionable findings is relatively low.[45,46] Widespread application of prenatal ultrasonography clearly has reduced the prevalence of previously unsuspected obstructive uropathy in infants, but the consequences of prenatal screening with respect to the risk of renal abnormalities in infants with UTIs have not yet been well defined. There is considerable variability in the timing and quality of prenatal ultrasonograms, and the report of "normal" ultrasonographic results cannot necessarily be relied on to dismiss completely the possibility of a structural abnormality unless the study was a detailed anatomic survey (with measurements), was performed during the third tri-

mester, and was performed and interpreted by qualified individuals.[47]

The timing of RBUS depends on the clinical situation. RBUS is recommended during the first 2 days of treatment to identify serious complications, such as renal or perirenal abscesses or pyonephrosis associated with obstructive uropathy when the clinical illness is unusually severe or substantial clinical improvement is not occurring. For febrile infants with UTIs who demonstrate substantial clinical improvement, however, imaging does not need to occur early during the acute infection and can even be misleading; animal studies demonstrate that *Escherichia coli* endotoxin can produce dilation during acute infection, which could be confused with hydronephrosis, pyonephrosis, or obstruction.[48] Changes in the size and shape of the kidneys and the echogenicity of renal parenchyma attributable to edema also are common during acute infection. The presence of these abnormalities makes it inappropriate to consider RBUS performed early during acute infection to be a true baseline study for later comparisons in the assessment of renal growth.

Nuclear scanning with technetium-labeled dimercaptosuccinic acid has greater sensitivity for detection of acute pyelonephritis and later scarring than does either RBUS or voiding cystourethrography (VCUG). The scanning is useful in research, because it ensures that all subjects in a study have pyelonephritis to start with and it permits assessment of later renal scarring as an outcome measure. The findings on nuclear scans rarely affect acute clinical management, however, and are not recommended as part of routine evaluation of infants with their first febrile UTI. The radiation dose to the patient during dimercaptosuccinic acid scanning is generally low (~1 mSv),[49] although it may be increased in children with reduced renal function. The radiation dose from dimercaptosuccinic acid is additive with that of VCUG when both studies are performed.[50] The radiation dose from VCUG depends on the equipment that is used (conventional versus pulsed digital fluoroscopy) and is related directly to the total fluoroscopy time. Moreover, the total exposure for the child will be increased when both acute and follow-up studies are obtained. The lack of exposure to radiation is a major advantage of RBUS, even with recognition of the limitations of this modality that were described previously.

- Aggregate quality of evidence: C (observational studies).
- Benefits: RBUS in this population will yield abnormal results in ~15% of cases, and 1% to 2% will have abnormalities that would lead to action (eg, additional evaluation, referral, or surgery).
- Harms/risks/costs: Between 2% and 3% will be false-positive results, leading to unnecessary and invasive evaluations.
- Benefit-harms assessment: Preponderance of benefit over harm.
- Value judgments: The seriousness of the potentially correctable abnormalities in 1% to 2%, coupled with the absence of physical harm, was judged sufficiently important to tip the scales in favor of testing.
- Role of patient preferences: Because ultrasonography is noninvasive and poses minimal risk, we assume that parents will prefer RBUS over taking even a small risk of missing a serious and correctable condition.
- Exclusions: None.
- Intentional vagueness: None.
- Policy level: Recommendation.

Action Statement 6

Action Statement 6a

VCUG should not be performed routinely after the first febrile UTI; VCUG is indicated if RBUS reveals hydronephrosis, scarring, or other findings that would suggest either high-grade VUR or obstructive uropathy, as well as in other atypical or complex clinical circumstances (evidence quality B; recommendation).

Action Statement 6b

Further evaluation should be conducted if there is a recurrence of febrile UTI (evidence quality: X; recommendation).

For the past 4 decades, the strategy to protect the kidneys from further damage after an initial UTI has been to detect childhood genitourinary abnormalities in which recurrent UTI could increase renal damage. The most common of these is VUR, and VCUG is used to detect this. Management included continuous antimicrobial administration as prophylaxis and surgical intervention if VUR was persistent or recurrences of infection were not prevented with an antimicrobial prophylaxis regimen; some have advocated surgical intervention to correct high-grade reflux even when infection has not recurred. However, it is clear that there are a significant number of infants who develop pyelonephritis in whom VUR cannot be demonstrated, and the effectiveness of antimicrobial prophylaxis for patients who have VUR has been challenged in the past decade. Several studies have suggested that prophylaxis does not confer the desired benefit of preventing recurrent febrile UTI.[51–55] If prophylaxis is, in fact, not beneficial and VUR is not required for development of pyelonephritis, then the rationale for performing VCUG routinely after an initial febrile UTI must be questioned.

RCTs of the effectiveness of prophylaxis performed to date generally included children more than 24 months of age, and some did not provide complete data according to grade of VUR. These 2 factors have compromised meta-analyses. To ensure direct comparisons, the committee contacted the 6 researchers who had conducted the most recent RCTs and requested raw data from their studies.[51–56] All complied, which permitted the creation of a data set with data for 1091 infants 2 to 24 months of age according to grade of VUR. A χ^2 analysis (2-tailed) and a formal meta-analysis did not detect a statistically significant benefit of prophylaxis in preventing recurrence of febrile UTI/pyelonephritis in infants without reflux or those with grades I, II, III, or IV VUR (Table 4 and Fig 3). Only 5 infants with grade V VUR were included in the RCTs; therefore, data for those infants are not included in Table 4 or Fig 3.

The proportion of infants with high-grade VUR among all infants with febrile UTIs is small. Data adapted from current studies (Table 5) indicate that, of a hypothetical cohort of 100 infants with febrile UTIs, only 1 has grade V VUR; 99 do not. With a practice of waiting for a second UTI to perform VCUG, only 10 of the 100 would need to undergo the procedure and the 1 with grade V VUR would be identified. (It also is possible that the 1 infant with grade V VUR might have been identified after the first UTI on the basis of abnormal RBUS results that prompted VCUG to be performed.) Data to quantify additional potential harm to an infant who is not revealed to have high-grade VUR until a second UTI are not precise but suggest that the increment is insufficient to justify routinely subjecting all infants with an initial febrile UTI to VCUG (Fig 4). To minimize any harm incurred by that infant, attempts have been made to identify, at the time of the initial UTI, those who have the greatest likelihood of having high-grade VUR. Unfortunately, there are no clinical or laboratory indicators that have been demonstrated to identify infants with high-grade VUR. Indications for VCUG have been proposed on the basis of consensus in the absence of data[57]; the predictive value of any of the indications for VCUG proposed in this manner is not known.

TABLE 4 Recurrences of Febrile UTI/Pyelonephritis in Infants 2 to 24 Months of Age With and Without Antimicrobial Prophylaxis, According to Grade of VUR

Reflux Grade	Prophylaxis		No Prophylaxis		*P*
	No. of Recurrences	Total *N*	No. of Recurrences	Total *N*	
None	7	210	11	163	.15
I	2	37	2	35	1.00
II	11	133	10	124	.95
III	31	140	40	145	.29
IV	16	55	21	49	.14

The level of evidence supporting routine imaging with VCUG was deemed insufficient at the time of the 1999 practice parameter to receive a recommendation, but the consensus of the subcommittee was to "strongly encourage" imaging studies. The position of the current subcommittee reflects the new evidence demonstrating antimicrobial prophylaxis not to be effective as presumed previously. Moreover, prompt diagnosis and effective treatment of a febrile UTI recurrence may be of greater importance regardless of whether VUR is present or the child is receiving antimicrobial prophylaxis. A national study (the Randomized Intervention for Children With Vesicoureteral Reflux study) is currently in progress to identify the effects of a prophylactic antimicrobial regimen for children 2 months to 6 years of age who have experienced a UTI, and it is anticipated to provide additional important data[58] (see Areas for Research).

Action Statement 6a

- Aggregate quality of evidence: B (RCTs).
- Benefits: This avoids, for the vast majority of febrile infants with UTIs, radiation exposure (of particular concern near the ovaries in girls), expense, and discomfort.
- Harms/risks/costs: Detection of a small number of cases of high-grade reflux and correctable abnormalities is delayed.
- Benefit-harms assessment: Preponderance of benefit over harm.
- Value judgments: The risks associated with radiation (plus the expense and discomfort of the procedure) for the vast majority of infants outweigh the risk of delaying the detection of the few with correctable abnormalities until their second UTI.
- Role of patient preferences: The judgment of parents may come into play, because VCUG is an uncomfortable procedure involving radiation exposure. In some cases, parents may prefer to subject their children to the procedure even when the chance of benefit is both small and uncertain. Antimicrobial prophylaxis seems to be ineffective in preventing recurrence of febrile UTI/pyelonephritis for the vast majority of infants. Some parents may want to avoid VCUG even after the second UTI. Because the benefit of identifying high-grade reflux is still in some doubt, these preferences should be considered. It is the judgment of the committee that VCUG is indicated after the second UTI.
- Exclusions: None.

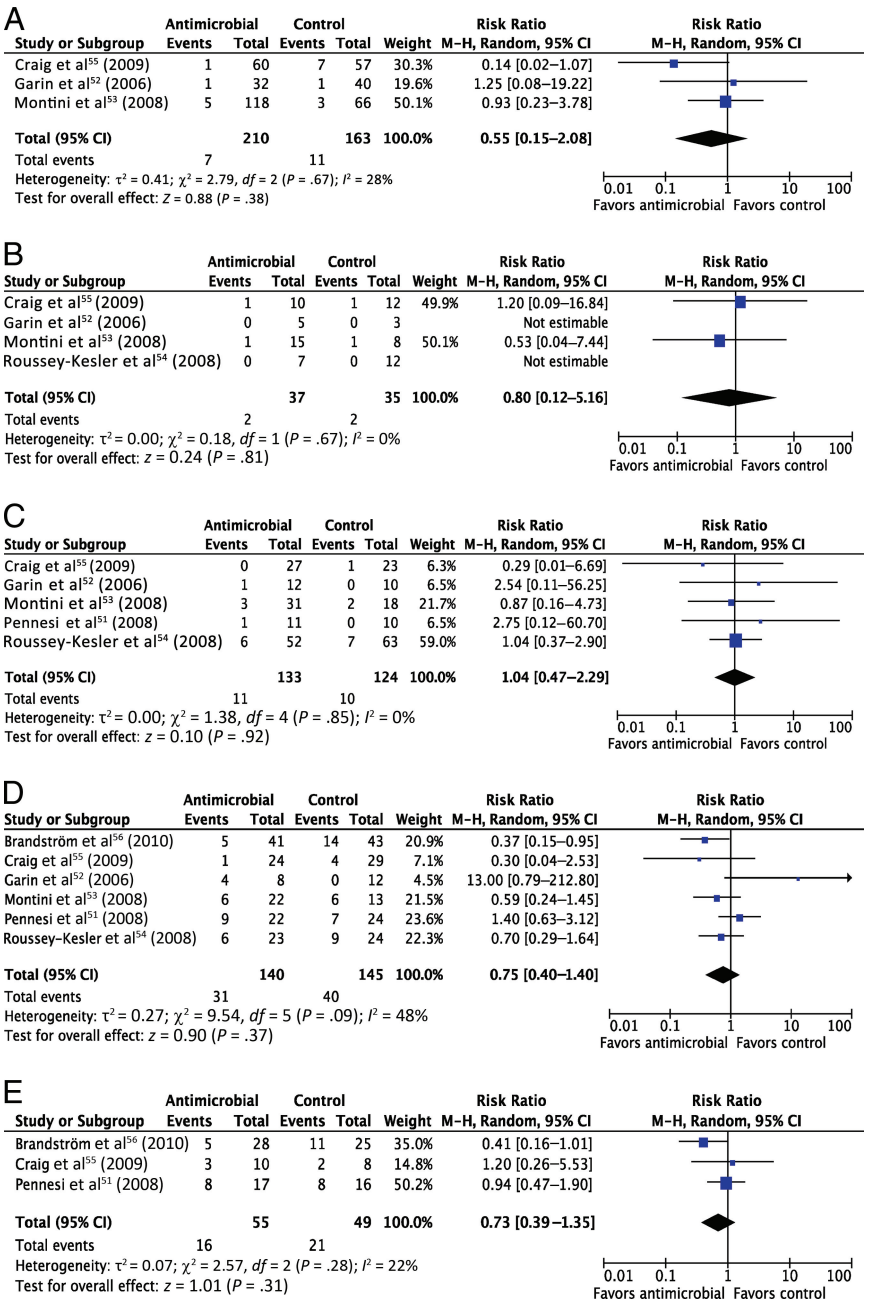

FIGURE 3

A, Recurrences of febrile UTI/pyelonephritis in 373 infants 2 to 24 months of age without VUR, with and without antimicrobial prophylaxis (based on 3 studies; data provided by Drs Craig, Garin, and Montini). B, Recurrences of febrile UTI/pyelonephritis in 72 infants 2 to 24 months of age with grade I VUR, with and without antimicrobial prophylaxis (based on 4 studies; data provided by Drs Craig, Garin, Montini, and Roussey-Kesler). C, Recurrences of febrile UTI/pyelonephritis in 257 infants 2 to 24 months of age with grade II VUR, with and without antimicrobial prophylaxis (based on 5 studies; data provided by Drs Craig, Garin, Montini, Pennesi, and Roussey-Kesler). D, Recurrences of febrile UTI/pyelonephritis in 285 infants 2 to 24 months of age with grade III VUR, with and without antimicrobial prophylaxis (based on 6 studies; data provided by Drs Brandström, Craig, Garin, Montini, Pennesi, and Roussey-Kesler). E, Recurrences of febrile UTI/pyelonephritis in 104 infants 2 to 24 months of age with grade IV VUR, with and without antimicrobial prophylaxis (based on 3 studies; data provided by Drs Brandström, Craig, and Pennesi). M-H indicates Mantel-Haenszel; CI, confidence interval.

TABLE 5 Rates of VUR According to Grade in Hypothetical Cohort of Infants After First UTI and After Recurrence

	Rate, %	
	After First UTI ($N = 100$)	After Recurrence ($N = 10$)
No VUR	65	26
Grades I–III VUR	29	56
Grade IV VUR	5	12
Grade V VUR	1	6

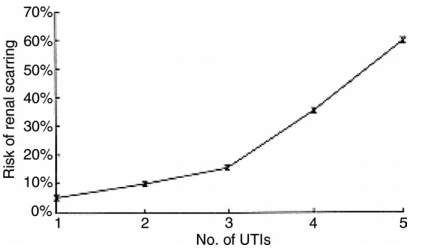

FIGURE 4

Relationship between renal scarring and number of bouts of pyelonephritis. Adapted from Jodal.[59]

- Intentional vagueness: None.
- Policy level: Recommendation.

Action Statement 6b

- Aggregate quality of evidence: X (exceptional situation).
- Benefits: VCUG after a second UTI should identify infants with very high-grade reflux.
- Harms/risks/costs: VCUG is an uncomfortable, costly procedure that involves radiation, including to the ovaries of girls.
- Benefit-harms assessment: Preponderance of benefit over harm.
- Value judgments: The committee judged that patients with high-grade reflux and other abnormalities may benefit from interventions to prevent further scarring. Further studies of treatment for grade V VUR are not underway and are unlikely in the near future, because the condition is uncommon and randomization of treatment in this group generally has been considered unethical.

- Role of patient preferences: As mentioned previously, the judgment of parents may come into play, because VCUG is an uncomfortable procedure involving radiation exposure. In some cases, parents may prefer to subject their children to the procedure even when the chance of benefit is both small and uncertain. The benefits of treatment of VUR remain unproven, but the point estimates suggest a small potential benefit. Similarly, parents may want to avoid VCUG even after the second UTI. Because the benefit of identifying high-grade reflux is still in some doubt, these preferences should be considered. It is the judgment of the committee that VCUG is indicated after the second UTI.
- Exclusions: None.
- Intentional vagueness: Further evaluation will likely start with VCUG but may entail additional studies depending on the findings. The details of further evaluation are beyond the scope of this guideline.
- Policy level: Recommendation.

Action Statement 7

After confirmation of UTI, the clinician should instruct parents or guardians to seek prompt medical evaluation (ideally within 48 hours) for future febrile illnesses, to ensure that recurrent infections can be detected and treated promptly (evidence quality: C; recommendation).

Early treatment limits renal damage better than late treatment,[1,2] and the risk of renal scarring increases as the number of recurrences increase (Fig 4).[59] For these reasons, all infants who have sustained a febrile UTI should have a urine specimen obtained at the onset of subsequent febrile illnesses, so that a UTI can be diagnosed and treated promptly.

- Aggregate quality of evidence: C (observational studies).
- Benefits: Studies suggest that early treatment of UTI reduces the risk of renal scarring.
- Harms/risks/costs: There may be additional costs and inconvenience to parents with more-frequent visits to the clinician for evaluation of fever.
- Benefit-harms assessment: Preponderance of benefit over harm.
- Value judgments: None.
- Role of patient preferences: Parents will ultimately make the judgment to seek medical care.
- Exclusions: None.
- Intentional vagueness: None.
- Policy level: Recommendation.

CONCLUSIONS

The committee formulated 7 key action statements for the diagnosis and treatment of infants and young children 2 to 24 months of age with UTI and unexplained fever. Strategies for diagnosis and treatment depend on whether the clinician determines that antimicrobial therapy is warranted immediately or can be delayed safely until urine culture and urinalysis results are available. Diagnosis is based on the presence of pyuria and at least 50 000 CFUs per mL of a single uropathogen in an appropriately collected specimen of urine; urinalysis alone does not provide a definitive diagnosis. After 7 to 14 days of antimicrobial treatment, close clinical follow-up monitoring should be maintained, with evaluation of the urine during subsequent febrile episodes to permit prompt diagnosis and treatment of recurrent infections. Ultrasonography of the kidneys and bladder should be performed to detect anatomic abnormalities that require further evaluation (eg, additional imaging or urologic consultation). Routine VCUG after the first UTI is not recommended; VCUG is indicated if RBUS reveals hydronephrosis, scarring, or other findings that would suggest either high-grade VUR or obstructive uropathy, as well as in other atypical or complex clinical circumstances. VCUG also should be performed if there is a recurrence of febrile UTI.

AREAS FOR RESEARCH

One of the major values of a comprehensive literature review is the identification of areas in which evidence is lacking. The following 8 areas are presented in an order that parallels the previous discussion.

1. The relationship between UTIs 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 40 to 50 years of age has not been conducted and is unlikely to be conducted. Therefore, 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 and thoughtful literature review have recognized the same limitations. Until recently, imaging tools available for assessment of the effects of UTIs have been insensitive. With the imaging techniques now available, it may be possible to identify the relationship of scarring to renal impairment and hypertension.
2. The development of techniques that would permit an alternative to invasive sampling and culture would be valuable for general use. Special attention should be given to infant girls and uncircumcised boys, because urethral catheterization may

be difficult and can produce contaminated specimens and SPA now is not commonly performed. Incubation time, which is inherent in the culture process, results in delayed treatment or presumptive treatment on the basis of tests that lack the desired sensitivity and specificity to replace culture.

3. The role of VUR (and therefore of VCUG) is incompletely understood. It is recognized that pyelonephritis (defined through cortical scintigraphy) can occur in the absence of VUR (defined through VCUG) and that progressive renal scarring (defined through cortical scintigraphy) can occur in the absence of demonstrated VUR.[52,53] The presumption that antimicrobial prophylaxis is of benefit for individuals with VUR to prevent recurrences of UTI or the development of renal scars is not supported by the aggregate of data from recent studies and currently is the subject of the Randomized Intervention for Children With Vesicoureteral Reflux study.[58]
4. Although the effectiveness of antimicrobial prophylaxis for the prevention of UTI has not been demonstrated, the concept has biological plausibility. Virtually all antimicrobial agents used to treat or to prevent infections of the urinary tract are excreted in the urine in high concentrations. Barriers to the effectiveness of antimicrobial prophylaxis are adherence to a daily regimen, adverse effects associated with the various agents, and the potential for emergence of antimicrobial resistance. To overcome these issues, evidence of effectiveness with a well-tolerated, safe product would be required, and parents would need sufficient education to understand the value and importance of adherence. A urinary antiseptic, rather than an antimicrobial agent, would be particularly desirable, because it could be taken indefinitely without concern that bacteria would develop resistance. Another possible strategy might be the use of probiotics.
5. Better understanding of the genome (human and bacterial) may provide insight into risk factors (VUR and others) that lead to increased scarring. Blood specimens will be retained from children enrolled in the Randomized Intervention for Children With Vesicoureteral Reflux study, for future examination of genetic determinants of VUR, recurrent UTI, and renal scarring.[58] VUR is recognized to "run in families,"[60,61] and multiple investigators are currently engaged in research to identify a genetic basis for VUR. Studies may also be able to distinguish the contribution of congenital dysplasia from acquired scarring attributable to UTI.
6. One of the factors used to assess the likelihood of UTI in febrile infants is race. Data regarding rates among Hispanic individuals are limited and would be useful for prediction rules.
7. This guideline is limited to the initial management of the first UTI in febrile infants 2 to 24 months of age. Some of the infants will have recurrent UTIs; some will be identified as having VUR or other abnormalities. Further research addressing the optimal course of management in specific situations would be valuable.
8. The optimal duration of antimicrobial treatment has not been determined. RCTs of head-to-head comparisons of various duration would be valuable, enabling clinicians to limit antimicrobial exposure to what is needed to eradicate the offending uropathogen.

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ACKNOWLEDGMENTS

The committee gratefully acknowledges the generosity of the researchers who graciously shared their data to permit the data set with data for 1091 infants aged 2 to 24 months according to grade of VUR to be compiled, that is, Drs Per Brandström, Jonathan Craig, Eduardo Garin, Giovanni Montini, Marco Pennesi, and Gwenaelle Roussey-Kesler.

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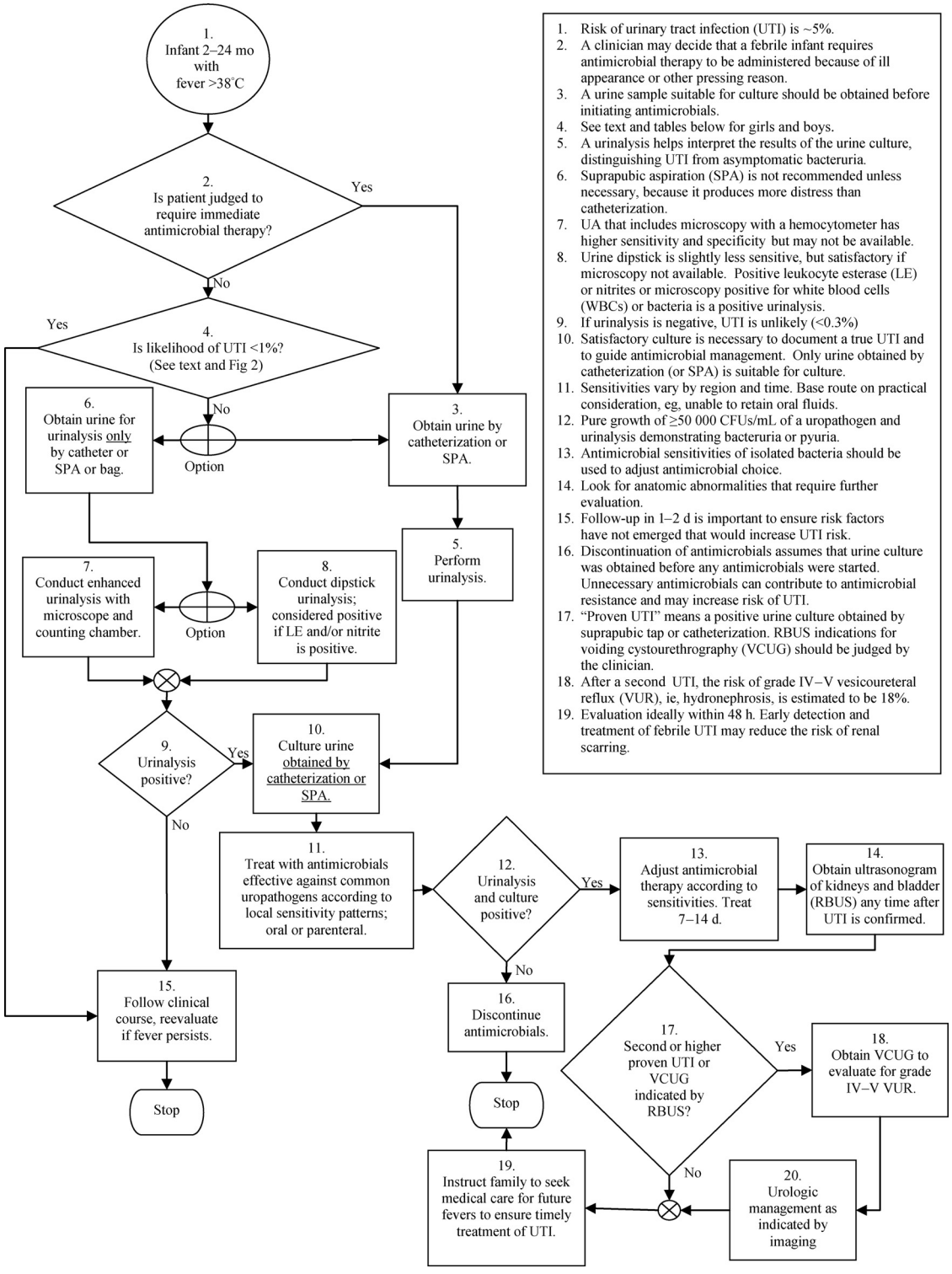

1. Risk of urinary tract infection (UTI) is ~5%.
2. A clinician may decide that a febrile infant requires antimicrobial therapy to be administered because of ill appearance or other pressing reason.
3. A urine sample suitable for culture should be obtained before initiating antimicrobials.
4. See text and tables below for girls and boys.
5. A urinalysis helps interpret the results of the urine culture, distinguishing UTI from asymptomatic bacteruria.
6. Suprapubic aspiration (SPA) is not recommended unless necessary, because it produces more distress than catheterization.
7. UA that includes microscopy with a hemocytometer has higher sensitivity and specificity but may not be available.
8. Urine dipstick is slightly less sensitive, but satisfactory if microscopy not available. Positive leukocyte esterase (LE) or nitrites or microscopy positive for white blood cells (WBCs) or bacteria is a positive urinalysis.
9. If urinalysis is negative, UTI is unlikely (<0.3%)
10. Satisfactory culture is necessary to document a true UTI and to guide antimicrobial management. Only urine obtained by catheterization (or SPA) is suitable for culture.
11. Sensitivities vary by region and time. Base route on practical consideration, eg, unable to retain oral fluids.
12. Pure growth of ≥50 000 CFUs/mL of a uropathogen and urinalysis demonstrating bacteruria or pyuria.
13. Antimicrobial sensitivities of isolated bacteria should be used to adjust antimicrobial choice.
14. Look for anatomic abnormalities that require further evaluation.
15. Follow-up in 1–2 d is important to ensure risk factors have not emerged that would increase UTI risk.
16. Discontinuation of antimicrobials assumes that urine culture was obtained before any antimicrobials were started. Unnecessary antimicrobials can contribute to antimicrobial resistance and may increase risk of UTI.
17. "Proven UTI" means a positive urine culture obtained by suprapubic tap or catheterization. RBUS indications for voiding cystourethrography (VCUG) should be judged by the clinician.
18. After a second UTI, the risk of grade IV–V vesicoureteral reflux (VUR), ie, hydronephrosis, is estimated to be 18%.
19. Evaluation ideally within 48 h. Early detection and treatment of febrile UTI may reduce the risk of renal scarring.

APPENDIX
Clinical practice guideline algorithm.

Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months

Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management

Pediatrics 2011;128;595; originally published online August 28, 2011;
DOI: 10.1542/peds.2011-1330