Quality Improvement for the Management of Children Hospitalized with Urinary Tract Infection (Q-UTI)

Change Package
(Quality Improvement Toolkit)
OVERVIEW OF Q-UTI CHANGE PACKAGE

This Change Package (Quality Improvement Toolkit) is designed to provide your quality improvement team with ready-made material that your team can use to initiate improvement efforts as part of the Quality Improvement for the Management of Children Hospitalized with Urinary Tract Infection (Q-UTI) Project. Over the course of the project, your team and the other teams in the collaborative will be encouraged to refine and repurpose the tools and resources in this toolkit based on further review of the evidence and your own experiences testing and implementing the changes.

This Change Package is based on evidence-based research focused on diagnosis and treatment of UTI, 2011 AAP clinical practice guidelines on urinary tract infections, and the local experience of the UTI Expert Group members. The Expert Group has chosen a subset of recommendations from the guidelines and other relevant literature, for which we have set specific goals in order to offer a framework for your local project. Depending on the particular circumstances in your hospital, you may also need to implement other practices or modify your goals in order to successfully improve outcomes.

The aims and measures in this collection are not necessarily the only ones required to achieve the improved outcomes you are targeting. This project is not exhaustive, exclusive, or all-inclusive. Changes in practice will require testing and adaptation to your particular circumstances and context in order to achieve measured improvements in outcomes. As you test and implement new processes, you will monitor the results closely to ensure that you are obtaining the desired outcome, that no harm is being done, and that no unanticipated results or consequences emerge. In addition to the evidence-based measures, we have also provided some balancing measures to assess in order to help with the process of avoiding unanticipated consequences. Establishing sustainability efforts in order to promote continuous quality improvement (CQI) will be crucial for success as well.

Model for Improvement
One theoretical basis for promoting change in healthcare is the Model for Improvement. We recommend the Model for Improvement\(^1\) as a framework for your efforts. The three key questions of the Model for Improvement are:

\[
\begin{align*}
\text{Model for Improvement} & \\
\text{3 Key Questions for Improvement} & \\
\text{What are we trying to accomplish?} & \text{How will we know that a change is an improvement?} & \text{What changes can we make that will result in an improvement?}
\end{align*}
\]

\(\text{Act} \quad \text{Plan} \quad \text{Study} \quad \text{Do}\)

Quality Improvement Elements
For the Q-UTI project, the following four items will be quality improvement elements which we will support: 1) clearly identified aims; 2) targeted measures; 3) planned changes; and 4) cycles of action - Plan-Do-Study-Act (PDSA)

\[
\begin{align*}
\text{Test Ideas & Changes in} & \\
\text{Cycles for Learning & Improvement} & \\
\text{Act} & \quad \text{Plan} & \quad \text{Study} & \quad \text{Do}
\end{align*}
\]

- What refinements or modifications need to be made?
- What is the next cycle?
- Plan
- Do
- Study
- Act
- Complete action
- Compare to predictions
- What did you learn?
- What conclusions can you draw from this?
- Objective
- Questions & predictions
- What will happen & why
- Plan to carry out the cycle
- Who, what, where, when
- Outcomes
- Document experience, problems, surprises
- Collect data to plan, begin analysis

Thank you for your participation in this important systemic change to improve the treatment of UTI in the pediatric hospital setting.

Richard Engel, MD, FAAP  
Co-Chair, Q-UTI Expert Group  
Phoenix Children’s Hospital

Brian Pate, MD, FAAP  
Co-Chair, Q-UTI Expert Group  
University of Kansas School of Medicine - Wichita

Matthew Garber, MD, FAAP  
QI Advisor, Q-UTI Expert Group  
USC-SOM

---

ABOUT CHANGE PACKAGE (QUALITY IMPROVEMENT TOOLKIT)

The specific aim of the project is to improve the care of children with urinary tract infection (UTI) by increasing compliance with evidence-based practices for UTI diagnosis and treatment, including the AAP UTI clinical practice guideline as well as other key evidence-based UTI research.

A change package or quality improvement toolkit is meant to be a source of ideas that may help your quality improvement team progress towards your goals. Local adaptation of ideas will always be necessary to ensure the success of changes selected from the quality improvement toolkit.

The elements from evidence-based research and the guidelines that the UTI project will address, as well as the specific aims of the project, are incorporated in the quality improvement resources that follows.

A collection of a few key references related to quality improvement tools for UTI are included.
Quality Improvement for the Management of Children Hospitalized with Urinary Tract Infection (Q-UTI) Project Change Package

**Table of Contents**

- **Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months**
  This clinical practice guideline is a systematically developed statement to assist practitioners and patient decisions about appropriate health care for specific circumstances.

- **AAP Technical Report: Diagnosis and Management of an Initial UTI in Febrile Infants and Young Children**
  This report was developed to inform the revised, evidence-based, clinical guideline regarding the diagnosis and management of initial UTIs in febrile infants and young children, 2 to 24 months of age, from the American Academy of Pediatrics Subcommittee on Urinary Tract Infection.

- **Clinical Pathway**
  A clinical pathway is used to remind providers of the current state of the evidence and are intended to reduce variability in clinical practice.

- **ICD-10 Codes**
  The International Classification of Diseases (ICD) is the standard diagnostic tool for epidemiology, health management and clinical purposes. This includes the analysis of the general health situation of population groups. It is used to monitor the incidence and prevalence of diseases and other health problems, proving a picture of the general health situation of countries and populations.

  A listing of the ICD-10 inclusion/exclusion codes that are equivalent to the ICD-9 codes previously provided by the project in the measures grid.

- **Order set**
  An order set is a standardized list of orders for a specific diagnosis based on current evidence.
  - Sample Order set 1
  - Sample Order set 2

- **UTI Algorithm**
  The clinical algorithm (flow chart) is a text format that is especially suited for representing a sequence of clinical decisions, for teaching clinical decision making, and for guiding patient care.

- **UTI Management beyond the AAP Guideline: New Evidence, Current Controversies, and Quality Improvement** *(Power Point Presentation)*
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

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/128/3/595.full.html
Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months

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 medical care. Variations, taking into account individual circumstances, may be appropriate.

CONCLUSIONS: Changes in this revision include criteria for the diagnosis of UTI and recommendations for imaging.
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 infected infants (eg, SPA), diagnosis and treatment may be delayed. Most experimental and clinical data support the concept that bacteriuria 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.) 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 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 urological 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 (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...
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 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%). When ultrasonographic guidance is used, success rates improve. 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. The techniques required for catheterization and SPA are well described. 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. 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.

**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 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 practitioners26; 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 colleagues27–29 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.

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

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (Range), %</th>
<th>Specificity (Range), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte esterase test</td>
<td>83 (67–94)</td>
<td>78 (64–82)</td>
</tr>
<tr>
<td>Nitrite test</td>
<td>53 (15–82)</td>
<td>98 (80–100)</td>
</tr>
<tr>
<td>Leukocyte esterase or nitrite test positive</td>
<td>93 (90–100)</td>
<td>72 (58–81)</td>
</tr>
<tr>
<td>Microscopy, WBCs</td>
<td>73 (52–100)</td>
<td>81 (45–88)</td>
</tr>
<tr>
<td>Microscopy, bacteria</td>
<td>81 (18–99)</td>
<td>83 (11–100)</td>
</tr>
<tr>
<td>Leukocyte esterase test, nitrite test, or microscopy positive</td>
<td>99.8 (99–100)</td>
<td>70 (60–92)</td>
</tr>
</tbody>
</table>

### 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 is 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 (\(\sim 25 \text{ WBCs per } \mu \text{L}\)). If a counting chamber is used, however, the finding of at least 10 WBCs per \(\mu\)L 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.\(^{36}\) 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\(^{35}\) 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 number of CFUs that grow on the culture medium will allow identification of urinary tract pathogens.

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.31 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-
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. 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 cephalaxin, 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.

### TABLE 2 Some Empiric Antimicrobial Agents for Parenteral Treatment of UTI

<table>
<thead>
<tr>
<th>Antimicrobial Agent</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
<td>75 mg/kg per d, every 24 h</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>150 mg/kg per d, divided every 6–8 h</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>100–150 mg/kg per d, divided every 8 h</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>7.5 mg/kg per d, divided every 8 h</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>5 mg/kg per d, divided every 8 h</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>300 mg/kg per d, divided every 6–8 h</td>
</tr>
</tbody>
</table>

### TABLE 3 Some Empiric Antimicrobial Agents for Oral Treatment of UTI

<table>
<thead>
<tr>
<th>Antimicrobial Agent</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>20–40 mg/kg per d in 3 doses</td>
</tr>
<tr>
<td>Sulphonamide</td>
<td></td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>6–12 mg/kg trimethoprim and 30–60 mg/kg sulfamethoxazole per d in 2 doses</td>
</tr>
<tr>
<td>Sulfoxazole</td>
<td>120–150 mg/kg per d in 4 doses</td>
</tr>
<tr>
<td>Cephalosporin</td>
<td></td>
</tr>
<tr>
<td>Cefixime</td>
<td>8 mg/kg per d in 1 dose</td>
</tr>
<tr>
<td>Cefpodoxime</td>
<td>10 mg/kg per d in 2 doses</td>
</tr>
<tr>
<td>Cefprozil</td>
<td>30 mg/kg per d in 2 doses</td>
</tr>
<tr>
<td>Cefuroxime axetil</td>
<td>20–30 mg/kg per d in 2 doses</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>50–100 mg/kg per d in 4 doses</td>
</tr>
</tbody>
</table>

### 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. Wide-spread 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. 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. 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), 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. 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. 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.\textsuperscript{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 \textit{χ}\textsuperscript{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\textsuperscript{57}; the predictive value of any of the indications for VCUG proposed in this manner is not known.

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\textsuperscript{58} (see Areas for Research).

\textbf{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.

\textbf{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

<table>
<thead>
<tr>
<th>Reflux Grade</th>
<th>Prophylaxis</th>
<th></th>
<th>No Prophylaxis</th>
<th></th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Recurrences</td>
<td>Total N</td>
<td>No. of Recurrences</td>
<td>Total N</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>7</td>
<td>210</td>
<td>11</td>
<td>163</td>
<td>.15</td>
</tr>
<tr>
<td>I</td>
<td>2</td>
<td>37</td>
<td>2</td>
<td>35</td>
<td>1.00</td>
</tr>
<tr>
<td>II</td>
<td>11</td>
<td>133</td>
<td>10</td>
<td>124</td>
<td>.95</td>
</tr>
<tr>
<td>III</td>
<td>31</td>
<td>140</td>
<td>40</td>
<td>145</td>
<td>.29</td>
</tr>
<tr>
<td>IV</td>
<td>16</td>
<td>55</td>
<td>21</td>
<td>49</td>
<td>.14</td>
</tr>
</tbody>
</table>
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 aged 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. 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. The role of VUR (defined through VCUG) and that progressive renal scarring can occur in the absence of demonstrated VUR. 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. Another possible strategy might be the use of probiotics.

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.

REFERENCES

FROM THE AMERICAN ACADEMY OF PEDIATRICS

Lead Author
Kenneth B. Roberts, MD

Subcommittee on Urinary Tract Infection, 2009–2011
Kenneth B. Roberts, MD, Chair
Stephen M. Downs, MD, MS
S. Maria E. Finnell, MD, MS
Stanley Hellerstein, MD
Linda D. Shorttleife, MD
Ellen R. Wald, MD
J. Michael Zerin, MD

Oversight by the Steering Committee on Quality Improvement and Management, 2009–2011

Staff
Caryn Davidson, MA

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.


5. American Academy of Pediatrics, Steering Committee on Quality Improvement and Management. Classifying recommenda-
tions for clinical practice guidelines. *Pedia-
trics.* 2004;114(3):874–877

6. Leong YY, Tan KW. Bladder aspiration for
diagnosis of urinary tract infection in in-
fants and young children. *J Singapore Paed-

7. Pryles CV, Atkin MD, Morse TS, Welch KJ.
Comparative bacteriologic study of urine
obtained from children by percutaneous
suprapubic aspiration of the bladder and

8. Djojohadiprin-ggo S, Abdul Hamid RH, Thahir
S, Karim A, Darsono I. Bladder puncture in
newborns: a bacteriologic study. *Paediatr
Indones.* 1976;16(11–12):527–534

9. Gochman RF, Karasic RB, Heller MB. Use of
portable ultrasound to assist urine collect-
ion by suprapubic aspiration. *Ann Emerg

10. Buys H, Peal L, Hallett R, Maskell R. Supra-
pubic aspiration under ultrasound guid-
ance in children with fever of undiagnosed

11. Kramer MS, Tange SM, Drummond KN, Mills
EL. Urine testing in young febrile children: a
6–13

12. Bonadio WA. Urine culturing technique in fe-
75–78


14. Taylor CM, White RH. The feasibility of
screening preschool children for urinary tract
infection using dipsticks. *Int J Pedia-triatr

15. Sørensen K, Lose G, Nathan E. Urinary tract
infections and diurnal incontinence in girls.

16. Shannon F, Sepp E, Rose G. The diagnosis of
bacteriuria by bladder puncture in infancy
97–100

17. Hoberman A, Chao HP, Keller DM, Hickey R,
Davis HW, Ellis D. Prevalence of urinary tract
infection in febrile infants. *J Pedia-triatr.* 1993;
123(1):17–23

18. Haddon YY, Barnett PL, Grimwood K, Hogg
GG. Bacteriemia in febrile children present-
19. Wiswell TE, Roscelli JD. Corroboration ev-
dence for the decreased incidence of ur-
inary tract infections in circumcised male infants.
*Pedia-triatrics.* 1986;78(1):96–99

20. To T, Agha M, Dick PT, Feldman W. Cohort
study on circumcision of newborn boys and
subsequent risk of urinary-tract infection.

21. Wiswell TE, Hachey WE. Urinary tract infec-
tions and the uncircumcised state: an up-
date. *Clin Pedia-triatr (Phila).* 1993;32(3):
130–134

22. Wiswell TE, Smith FR, Bass JW. Decreased
incidence of urinary tract infections in cir-
cumcised male infants. *Pedia-triatrics.* 1985;
75(5):901–903

23. Ginsburg CM, McCracken GH Jr. Urinary
tract infections in young infants. *Pedia-triatrics.*
1982;69(4):409–412

24. Craig JC, Knight JF, Sureshkumar P, Mantz
E, Roy LP. Effect of circumcision on inci-
dence of urinary tract infection in pre-

25. Levine DA, Platt SL, Dayan PS, et al. Risk of
serious bacterial infection in young fe-
brile infants with respiratory syncytial vi-
rus infections. *Pedia-triatrics.* 2004;113(6):
1728–1734

Urinary tract infection in infants with unex-
plained fever: a collaborative study. *J Pedia-
atriat.* 1983;103(6):864–867

27. Gorelick MH, Hoberman A, Kearney D, Wald
E, Shaw KN. Validation of a decision rule
identifying febrile young girls at high risk for
urinary tract infection. *Pediatr Emerg Care.*
2003;19(3):162–164

28. Gorelick MH, Shaw KN. Clinical decision rule
to identify febrile young girls at risk for ur-
inary tract infection. *Arch Pedia-triatr Adolesc

29. Shaw KN, Gorelick M, McGowan KL, Yakcsoc
NM, Schwartz JS. Prevalence of urinary tract
infection in febrile young children in the
emergency department. *Pedia-triatrics.*
1998;102(2). Available at: www.pediatrics.
org/cgi/content/full/102/2/e16

30. Shaikh N, Morone NE, Lopez J, et al. Does this
child have a urinary tract infection? *JAMA.*
2007;298(4):2895–2904

31. Powell HR, McCredie DA, Ritchie MA. Urinary
nitrile in symptomatic and asymptomatic
urinary infection. *Arch Dis Child.* 1987;62(2):
138–140

32. Kunin CM, DeGroot JE. Sensitivity of a nitrile
indicator strip method in detecting bacteri-
uria in preschool girls. *Pedia-triatrics.* 1977;
60(2):244–245

33. Hoberman A, Wald ER, Reynolds EA, Pen-
chansky L, Charron M. Pyuria and bacteri-
uria in urine specimens obtained by cathe-
ter from young children with fever. *J Pedia-

34. Downs SM. Technical report: urinary tract infec-
tions in febrile infants and young children.
org/cgi/content/full/103/4/e64

35. Hoberman A, Wald ER, Reynolds EA, Pen-
chansky L, Charron M. Pyuria and bacteri-
uria in young febrile children. *Ann Emerg
Care.* 2004;113(6):262–270

36. Kemper K, Avner E. The case against screen-
ing urinalyses for asymptomatic bacteri-
343–346

37. Wald E. Genitourinary tract infections: cysti-
tis and pyelonephritis. In: Feigin R, Cherry
JD, Demmler GJ, Kaplan SL, eds. *Textbook of
Pediatriat Infectious Diseases.* 5th ed. Phila-
delphia, PA: Saunders; 2004:541–555

38. Mayo S, Acevedo D, Quiñones-Torrelo C,
Canós I, Sancho M. Clinical laboratory auto-
mated urinalysis: comparison among auto-
mated microscopy, flow cytometry, two test
strips analyzers, and manual microscopic
examination of the urine sediments. *J Clin
Lab Anal.* 2008;22(4):262–270

39. Kass E. Asymptomatic infections of the uri-
nary tract. *Trans Assoc Am Phys.* 1956;69:
56–64

40. Hoberman A, Wald ER, Reynolds EA, Pen-
chansky L, Charron M. Pyuria and bacteri-
uria in urine specimens obtained by cathe-
ter from young children with fever. *J Pedia-

41. Kass E. Asymptomatic infections of the uri-
nary tract. *Trans Assoc Am Phys.* 1956;69:
56–64

versus initial intravenous therapy for uri-
nary tract infections in young febrile chil-


43. Hodson EM, Willis NS, Craig JC. Antibiotics
for acute pyelonephritis in children.
*Cochrane Database Syst Rev.* 2007;4(4):
CD003772

44. Bloomfield P, Hodson EM, Craig JC. Antibiot-
ics for acute pyelonephritis in children.
CD003772

45. Hoberman A, Charron M, Hickey RW, Baskin
M, Kearney DH, Wald ER. Imaging studies af-
ter a first febrile urinary tract infection in young
195–202

46. Jahnukainen T, Honkinen O, Ruuskanen O,
Mertsola J. Ultrasonography after the first
febrile urinary tract infection in children.
*Eur J Pedia-triatr.* 2006;165(8):556–559

47. Economou G, Egginton J, Brookfield D. The
importance of late pregnancy scans for re-
14(3):177–180

48. Roberts J. Experimental pyelonephritis in the
monkey, part III: pathophysiology of ure-

FROM THE AMERICAN ACADEMY OF PEDIATRICS

Downloaded from pediatrics.aappublications.org by guest on July 2, 2013
teral malfunction induced by bacteria. Invest Urol. 1975;13(2):117–120
APPENDIX
Clinical practice guideline algorithm.

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 bacteriuria.
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.

1. Infant 2–24 mo with fever >38°C
2. Is patient judged to require immediate antimicrobial therapy?
3. Obtain urine by catheterization or SPA.
4. Is likelihood of UTI <1%? (See text and Fig 2)
5. Perform urinalysis.
6. Obtain urine for urinalysis only by catheter or SPA or bag.
7. Conduct enhanced urinalysis with microscope and counting chamber.
8. Conduct dipstick urinalysis, considered positive if LE and/or nitrite is positive.
9. Urinalysis positive?
10. Culture urine obtained by catheterization or SPA.
11. Treat with antimicrobials effective against common uropathogens according to local sensitivity patterns; oral or parenteral.
12. Urinalysis and culture positive?
13. Adjust antimicrobial therapy according to sensitivities. Treat 7–14 d.
14. Obtain ultrasonogram of kidneys and bladder (RBUS) any time after UTI is confirmed.
15. Follow clinical course; reevaluate if fever persists.
17. Second or higher proven UTI or VCUG indicated by RBUS?
18. Obtain VCUG to evaluate for grade IV–V VUR.
19. Instruct family to seek medical care for future fevers to ensure timely treatment of UTI.
20. Urologic management as indicated by imaging.
Diagnosis and Management of an Initial UTI in Febrile Infants and Young Children
the Subcommittee on Urinary Tract Infection

*Pediatrics* 2011;128;e749; originally published online August 28, 2011;
DOI: 10.1542/peds.2011-1332

The online version of this article, along with updated information and services, is located on the World Wide Web at:

[http://pediatrics.aappublications.org/content/128/3/e749.full.html](http://pediatrics.aappublications.org/content/128/3/e749.full.html)
Technical Report—Diagnosis and Management of an Initial UTI in Febrile Infants and Young Children

S. Maria E. Finnell, MD, MS, Aaron E. Carroll, MD, MS, Stephen M. Downs, MD, MS, and the Subcommittee on Urinary Tract Infection

OBJECTIVES: The diagnosis and management of urinary tract infections (UTIs) in young children are clinically challenging. This report was developed to inform the revised, evidence-based, clinical guideline regarding the diagnosis and management of initial UTIs in febrile infants and young children, 2 to 24 months of age, from the American Academy of Pediatrics Subcommittee on Urinary Tract Infection.

METHODS: The conceptual model presented in the 1999 technical report was updated after a comprehensive review of published literature. Studies with potentially new information or with evidence that reinforced the 1999 technical report were retained. Meta-analyses on the effectiveness of antimicrobial prophylaxis to prevent recurrent UTI were performed.

RESULTS: Review of recent literature revealed new evidence in the following areas. Certain clinical findings and new urinalysis methods can help clinicians identify febrile children at very low risk of UTI. Oral antimicrobial therapy is as effective as parenteral therapy in treating UTI. Data from published, randomized controlled trials do not support antimicrobial prophylaxis to prevent febrile UTI when vesicoureteral reflux is found through voiding cystourethrography. Ultrasonography of the urinary tract after the first UTI has poor sensitivity. Early antimicrobial treatment may decrease the risk of renal damage from UTI.

CONCLUSIONS: Recent literature agrees with most of the evidence presented in the 1999 technical report, but meta-analyses of data from recent, randomized controlled trials do not support antimicrobial prophylaxis to prevent febrile UTI. This finding argues against voiding cystourethrography after the first UTI. Pediatrics 2011;128:e749–e770
In 1999, the Subcommittee on Urinary Tract Infection of the American Academy of Pediatrics released its guideline on detection, diagnosis, and management for children between 2 and 24 months of age with febrile urinary tract infections (UTIs). The guideline was supported by a technical report that included a critical review of the relevant literature and a cost-effectiveness analysis. Consistent with the policies of the American Academy of Pediatrics, the subcommittee has undertaken a revision of the guideline. This technical report was developed to support the guideline.

The revised technical report was to be based on a selective review of the literature, focusing on changes in the evidence regarding detection, diagnosis, and management of UTIs in these children. The original technical report was designed around an evidence model (Fig 1). Each cell (numbered 1–4) corresponded to a stage in the recognition, diagnosis, or management of UTI. The boxes represented steps the clinician must follow, and the arrows represented the process of moving from one step to the next. Downward arrows represented undesirable consequences in management.

In cell 1, the clinician must combine patient demographic data and other presenting clinical data to arrive at an assessment of the risk of UTI. Failure to do so results in a missed opportunity to make the diagnosis. In cell 2, the clinician must undertake a diagnostic strategy, primarily involving laboratory testing, to arrive at a posterior (posttest) probability of UTI, ruling the diagnosis in or out. Poor test choices or interpretation of results can lead to misdiagnosis. In cell 3, the clinician must choose a treatment for acute UTI; in cell 4, the clinician must consider the possibility of structural or functional anomalies of the urinary tract and diagnose them appropriately to avoid ongoing renal damage.

Implicit in cell 4 is the idea that anomalies of the urinary tract, such as vesicoureteral reflux (VUR) and obstructions, may, if left untreated, lead to significant renal damage, resulting in hypertension or end-stage renal disease. Furthermore, it is assumed that treatment with medical or surgical therapies can prevent these consequences successfully.

The conclusions of the 1999 technical report were that there were high-quality data regarding the prevalence of UTI among febrile infants, the performance of standard diagnostic tests for UTI, and the prevalence of urinary tract abnormalities among children with UTI. The evidence indicating that certain patient characteristics (age, gender, and circumcision status) affected the probability of UTI was weaker. The evidence supporting the relationship between urinary tract abnormalities and future complications, such as hypertension or renal failure, was considered very poor, and the effectiveness of treatments to prevent these complications was not addressed directly but was assumed.

The cost-effectiveness analysis using these data led to the conclusion that diagnosis and treatment of UTI and evaluation for urinary tract anomalies had borderline cost-effectiveness, costing approximately $700,000 per case of hypertension or end-stage renal disease prevented. On the basis of these results, the subcommittee recommended testing all children between 2 and 24 months of age with fever with no obvious source for UTI, by culturing urine obtained through bladder tap or catheterization. As an option for children who were not going to receive immediate antimicrobial treatment, the committee recommended ruling out UTI through urinalysis of urine obtained with any convenient method. The committee concluded that children found to have a UTI should undergo renal ultrasonography and voiding cystourethrography (VCUG) for evaluation for urinary tract abnormalities, most frequently VUR.

Ten years later, the subcommittee has undertaken a review of the technical analysis for a revised guideline. The strategy for this technical report was to survey the medical literature published in the past 10 years for studies of UTIs in young children. The literature was examined for any data that varied significantly from those analyzed in the original report.
first technical report. This survey found an emerging body of literature addressing the effectiveness of antimicrobial agents to prevent recurrent UTI. Therefore, the authors conducted a critical literature review and meta-analysis focused on that specific issue.

METHODS

Surveillance of Recent Literature

The authors searched Medline for articles published in the past 10 years with the medical subject headings “urinary tract infection” and “child (all).” The original search was conducted in 2007, but searches were repeated at intervals (approximately every 3 months) to identify new reports as the guideline was being developed. Titles were reviewed by 2 authors (Drs Downs and Carroll) to identify all articles that were potentially relevant and seemed to contain original data. All titles that were considered potentially relevant by either reviewer were retained. Abstracts of selected articles were reviewed, again to identify articles that were relevant to the guideline and that seemed to contain original data. Review articles that were relevant also were retained for review. Again, all abstracts that were considered potentially relevant by either reviewer were retained. In addition, members of the subcommittee submitted articles that they thought were relevant to be included in the review. Selected articles were reviewed and summarized by 2 reviewers (Drs Finnell and Downs). The summaries were reviewed, and articles presenting potentially new information were retained. In addition, representative articles reinforcing evidence in the 1999 technical report were retained.

The most significant area of change in the UTI landscape was a new and growing body of evidence regarding the effectiveness of antimicrobial prophylaxis to prevent recurrent infections in children with VUR. To explore this particular issue, a second, systematic, targeted literature search and formal meta-analysis were conducted to estimate the effectiveness of antimicrobial prophylaxis to prevent renal damage in children with VUR. In addition, 1 author (Dr Finnell) and the chairperson of the guideline committee (Dr Roberts) contacted the authors of those studies to obtain original data permitting subgroup analyses.

Targeted Literature Search and Meta-analysis

To examine specifically the effectiveness of antimicrobial prophylaxis to prevent recurrent UTI and pyelonephritis in children with VUR, a formal meta-analysis of randomized controlled trials (RCTs) was conducted. First, a systematic literature review focused on RCTs, including studies in press, was performed.

Inclusion Criteria

RCTs published in the past 15 years (1993–2009) that compared antimicrobial treatment versus no treatment or placebo treatment for the prevention of recurrent UTI and included a minimum of 6 months of follow-up monitoring were included. Published articles, articles in press, and published abstracts were included. There were no language restrictions. To be included, studies needed to enroll children who had undergone VCUG for determination of the presence and grade of VUR. Studies that examined antibiotic prophylaxis versus no treatment or placebo treatment were included.

Outcome Measures

The primary outcome was the number of episodes of pyelonephritis or febrile UTI diagnosed on the basis of the presence of fever and bacterial growth in urine cultures. A secondary outcome was an episode of any type of UTI, including cystitis, nonfebrile UTI, and asymptomatic bacteriuria in addition to the cases of pyelonephritis or febrile UTI.

Search Methods

The initial literature search was conducted on June 24, 2008, and the search was repeated on April 14, 2009. Studies were obtained from the following databases: Medline (1993 to June 2008), Embase (1993 to June 2008), Cochrane Central Register for Controlled Trials, bibliographies of identified relevant articles and reviews, and the Web site www.ClinicalTrials.gov. The search terms “vesico-ureteral reflux,” “VUR,” “vesicouret*r,” “vesicoureter*,” “vesicourethral,” or “vesico urethral” and “antibiotic,” “anti biotic,” “antibacterial,” “anti bacterial,” “anti microbial,” “anti microbial,” “anti infective,” or “anti infective” were used. The asterisk represents the truncation or wild card symbol, which indicates that all suffixes and variants were included. The search was limited to the publication types and subject headings for all clinical trials and included all key word variants for “random” in Medline and Embase.5 In addition, the Web site www.ClinicalTrials.gov was searched on May 20, 2010.

The search strategy and the screening of the titles for selection of potentially relevant abstracts were completed by 1 reviewer (Dr Finnell). Two reviewers (Drs Finnell and Downs) screened selected abstracts to identify appropriate articles. Published articles and abstracts that met the inclusion criteria were included in the meta-analysis. Additional information was sought from authors whose articles or abstracts did not contain the information needed for a decision regarding inclusion. The selection process is summarized in Fig 2.

Assessment of Studies

The quality of selected articles and abstracts was assessed with the scoring
system described by Downs and Black in 1998.6 Each study received scores (from 2 assessors) on a scale from 0 to 32. Six of the articles and abstracts were included in a first meta-analysis, which evaluated febrile UTI or pyelonephritis as the outcome. A second meta-analysis, which included all studies with the outcome “all UTI,” also was conducted.

### Meta-analyses

All statistical tests were performed by using Review Manager 5.1 (Nordic Cochrane Centre, Copenhagen, Denmark). The following settings were used for the analyses: dichotomous outcome and Mantel-Haenszel statistical method. Data were analyzed with a random-effects model. When no statistically significant effect and no statistical heterogeneity were detected, data also were analyzed with a fixed-effects model, because that type of analysis is more likely to detect a difference. The effect measure was presented as a risk ratio (RR). The results for the primary outcome (pyelonephritis or febrile UTI) and the secondary outcome (any type of UTI, including cystitis, nonfebrile UTI, and asymptomatic bacteriuria) were calculated as point estimates with corresponding 95% confidence intervals (CIs). Heterogeneity was analyzed by using the Q statistic with a threshold of $P < .05$. The number of studies was insufficient for assessment of publication bias with a funnel plot.

### Meta-analyses of Data According to VUR Grade and for Children 2 to 24 Months of Age

The published data on which the meta-analyses were based did not contain subgroup data relevant to the practice guideline. Specifically, some studies did not report outcomes according to the severity of VUR, and some did not report outcomes specific to the age range of interest (2–24 months). Therefore, the committee chairperson contacted the authors of the reports included in the meta-analysis, to obtain original data. Data on recurrence according to VUR grade and for the subgroup of children 2 to 24 months of age were received from the authors, and these data were analyzed in separate meta-analyses.

![FIGURE 2](https://example.com/figure2.png)

**FIGURE 2**

Study selection for meta-analyses.
RESULTS

Surveillance of Recent Literature

The surveillance of recent literature yielded 1308 titles. Of those, 297 abstracts were selected for review. From among the abstracts, 159 articles were selected for full review. The results of this surveillance, as well as the full review and meta-analyses, are organized according to the evidence diagram in Fig 1.

Box 1: Prevalence and Risk Factors for UTI

The Presence of UTI Should Be Considered for Any Child 2 Months to 2 Years of Age With Unexplained Fever

The previous technical report described a very consistent UTI prevalence of 5% among children 2 to 24 months of age with a fever without obvious source. In 1996, Hoberman et al conducted a study of urine diagnostic tests with a cohort of 4253 infants with fever and found a prevalence of 5%. Similarly, in a 1999 cohort study of 534 children 3 to 36 months of age with a temperature of more than 39°C and no apparent source of fever, UTI prevalence was determined to be 5%. In a 1998 cohort study of 2411 children (boys and girls 12–24 months of age) seen in the emergency department with a temperature of more than 39°C, Shaw et al determined the prevalence of UTI to be 3.3%. Because 84% of those children were black, this estimate may be low for the general population (see below).

In a meta-analysis of 14 studies, the pooled prevalence of UTI was 7% (95% CI: 5.5%–8.4%) among febrile children 0 to 24 months of age, of both genders, with or without additional symptoms of UTI. In the 6- to 12-month age group, however, the prevalence was 5.4%; in the 12- to 24-month age group, the prevalence was 4.5%. Taken together, these estimates are consistent with a pooled prevalence of 5% determined in earlier studies.

The previous technical report examined the effects of age, gender, and circumcision status on the prevalence of UTI. The conclusion was that boys more than 1 year of age who had been circumcised were at sufficiently low risk of UTI (<1%) that evaluation of this subpopulation would not be cost-effective. New work confirms an approximately threefold to fourfold decreased risk of UTI among circumcised boys. The difference seems to be greater for younger children. Additional clinical characteristics were shown more recently to affect the risk of UTI among febrile infants and children. From a study by Shaikh et al, a set of likelihood ratios (LRs) for various risk factors for UTI was derived (Table 1).

A simplified way to examine the data on boys from Shaikh et al is to first exclude boys with a history of UTI, because the guideline addresses only first-time UTIs, and to exclude those with ill appearance, because they are likely to require antimicrobial agents, in which case a urine specimen would be required. Finally, boys with and without circumcision should be considered separately. This leaves 4 risk factors for boys who present with fever, namely, temperature above 39°C, fever for more than 24 hours, no apparent fever source, and nonblack race. All 4 have similar LRs. If 2 assumptions are made, then the decision rule can be simplified. The first assumption is that, as a first approximation, each risk factor has a positive LR of 1.4 and a negative LR of 0.7. The second assumption is that the presence of each risk factor is conditionally independent of the others, given the presence or absence of UTI. With these reasonable assumptions, Table 2 applies to boys with no previous history of UTI.

### Table 1: LRs and Posttest Probabilities of UTI for Infant Boys According to Number of Findings Present

<table>
<thead>
<tr>
<th>Finding</th>
<th>LR (Positive)</th>
<th>LR (Negative)</th>
<th>Posttest Probability, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
<td>After Positive Results</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>After</td>
<td>After Positive Results</td>
</tr>
<tr>
<td></td>
<td>Results</td>
<td>Results</td>
<td>Results</td>
</tr>
<tr>
<td>Uncircumcised</td>
<td>2.8</td>
<td>0.33</td>
<td>5.9</td>
</tr>
<tr>
<td>History of UTI</td>
<td>2.6</td>
<td>0.96</td>
<td>5.5</td>
</tr>
<tr>
<td>Temperature of &gt;39°C</td>
<td>1.4</td>
<td>0.76</td>
<td>3.1</td>
</tr>
<tr>
<td>Fever without apparent</td>
<td>1.4</td>
<td>0.69</td>
<td>3.1</td>
</tr>
<tr>
<td>source</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ill appearance</td>
<td>1.9</td>
<td>0.68</td>
<td>4.1</td>
</tr>
<tr>
<td>Fever for &gt;24 h</td>
<td>2.0</td>
<td>0.9</td>
<td>4.3</td>
</tr>
<tr>
<td>Nonblack race</td>
<td>1.4</td>
<td>0.52</td>
<td>3.1</td>
</tr>
</tbody>
</table>

### Table 2: LRs and Posttest Probabilities of UTI for Infant Boys According to Number of Findings Present

<table>
<thead>
<tr>
<th>No. of Risk Factors</th>
<th>LR (Positive)</th>
<th>LR (Negative)</th>
<th>Posttest Probability, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Boys</td>
<td>Circumcised</td>
<td>Uncircumcised</td>
</tr>
<tr>
<td>0</td>
<td>0.34</td>
<td>0.8</td>
<td>0.2</td>
</tr>
<tr>
<td>1</td>
<td>0.69</td>
<td>1.5</td>
<td>4.1</td>
</tr>
<tr>
<td>2</td>
<td>1.37</td>
<td>3.0</td>
<td>7.9</td>
</tr>
<tr>
<td>3</td>
<td>2.74</td>
<td>5.8</td>
<td>14.7</td>
</tr>
<tr>
<td>4</td>
<td>5.49</td>
<td>11.0</td>
<td>25.6</td>
</tr>
</tbody>
</table>

Risk factors: temperature above 39°C, fever for more than 24 hours, no apparent fever source, and nonblack race.
and do not appear ill. The LR is calculated as \( \text{LR} = (1.4)^p \times (0.7)^n \), where \( p \) is the number of positive findings and \( n \) is the number of negative findings. This assumes that the clinician has assessed all 4 risk factors. It should be noted that, for uncircumcised boys, the risk of UTI never decreases below 2%. For circumcised boys, the probability exceeds 1% if there are 2 or more risk factors.

Other studies have shown that the presence of another, clinically obvious source of infection, particularly documented viral infections, such as respiratory syncytial virus infections, reduces the risk of UTI by one-half. In a series of studies conducted by Gorelick, Shaw, and others, male gender, black race, and no history of UTI were all found to reduce the risk. The authors derived a prediction rule specifically for girls, with 95% sensitivity and 31% specificity. In a subsequent validation study, they confirmed that these findings had predictive power, but the validation study used a weaker, retrospective, case-control design, compared with the more-robust, prospective, cohort design of the original derivation study. On the basis of these estimated negative LRs and the positive LRs provided in the article, it was possible to approximate them through extrapolation from the receiver operating characteristic curve presented. On the basis of these estimated negative LRs and the positive LRs provided in the article, Table 3 was derived. For each cutoff value in the number of risk factors, Table 3 shows the posterior probability for children with fewer than that number of risk factors (below the cutoff value) and for those with that number of risk factors or more. Therefore, the posttest probability is not the risk of UTI for children with exactly that number of risk factors. Similar results could be derived from the validation study and are shown in Table 4. However, because the second study had a weaker design, the values in Table 3 are more reliable.

These studies provide criteria for practical decision rules that clinicians can use to select patients who need urine samples for analysis and/or culture. They do not establish a threshold or maximal risk of UTI above which a urine sample is needed. However, in surveys of pediatricians, Roberts et al found that only 10% of clinicians thought that a urine culture is indicated if the probability of UTI is less than 1%. In addition, the cost-effectiveness analysis published in the 1999 technical report set a threshold of 1%. However, circumstances such as risk of loss to follow-up monitoring or other clinician concerns may shift this threshold up or down.

### Table 3: LRs and Posttest Probabilities of UTI for Febrile Infant Girls According to Number of Findings Present (Prospective Original Study)

<table>
<thead>
<tr>
<th>Cutoff Value, No. of Factors</th>
<th>LR Positive (Approximate)</th>
<th>LR Negative</th>
<th>Below Cutoff Value</th>
<th>At or Above Cutoff Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.04</td>
<td>0.20</td>
<td>0.8</td>
<td>5.1</td>
</tr>
<tr>
<td>2</td>
<td>1.35</td>
<td>0.17</td>
<td>0.8</td>
<td>6.3</td>
</tr>
<tr>
<td>3</td>
<td>2.5</td>
<td>0.42</td>
<td>2.1</td>
<td>11.4</td>
</tr>
<tr>
<td>4</td>
<td>9.4</td>
<td>0.79</td>
<td>3.9</td>
<td>53.0</td>
</tr>
<tr>
<td>5</td>
<td>15.8</td>
<td>0.95</td>
<td>4.7</td>
<td>45.0</td>
</tr>
</tbody>
</table>

Risk factors: less than 12 months of age, white race, temperature > 39°C, fever for at least 2 days, and absence of another source of infection.

### Table 4: LRs and Posttest Probabilities of UTI for Febrile Infant Girls According to Number of Findings Present (Retrospective Validation Study)

<table>
<thead>
<tr>
<th>No. of Findings</th>
<th>LR</th>
<th>Posttest Probability, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 or 1</td>
<td>1.02</td>
<td>0.8</td>
</tr>
<tr>
<td>2</td>
<td>1.10</td>
<td>0.9</td>
</tr>
<tr>
<td>3</td>
<td>1.26</td>
<td>1.0</td>
</tr>
<tr>
<td>4</td>
<td>3.04</td>
<td>2.4</td>
</tr>
<tr>
<td>5</td>
<td>2.13</td>
<td>1.7</td>
</tr>
</tbody>
</table>

Risk factors: less than 12 months of age, white race, temperature > 39°C, fever for at least 2 days, and absence of another source of infection.

### Table 5: List of Test Characteristics of Diagnostic Tests for UTI Reported in 1999 Technical Report

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte esterase test</td>
<td>67–94</td>
<td>64–92</td>
</tr>
<tr>
<td>Nitrite test</td>
<td>15–82</td>
<td>90–100</td>
</tr>
<tr>
<td>Blood assessment</td>
<td>25–64</td>
<td>60–88</td>
</tr>
<tr>
<td>Protein assessment</td>
<td>40–55</td>
<td>67–84</td>
</tr>
<tr>
<td>Microscopy, leukocytes</td>
<td>32–100</td>
<td>45–99</td>
</tr>
<tr>
<td>Microscopy, bacteria</td>
<td>16–99</td>
<td>11–100</td>
</tr>
<tr>
<td>Leukocyte esterase or nitrite test</td>
<td>90–100</td>
<td>58–91</td>
</tr>
<tr>
<td>Any positive test results in urinalysis</td>
<td>99–100</td>
<td>60–92</td>
</tr>
</tbody>
</table>
The 1999 technical report reviewed a large number of studies that described diagnostic tests for UTI. The results are summarized in Table 5. This updated review of the literature largely reinforced the findings of the original technical report.

More-recent work compared microscopy, including the use of hemocytometers and counting chambers (enhanced urinalysis), with routine urinalysis or dipslide reagents (Table 6). Lockhart et al\textsuperscript{19} found that the observation of any visible bacteria in an uncentrifuged, Gram-stained, urine sample had better sensitivity and specificity than did combined dipslide results are summarized in Table 5. This updated review of the literature largely reinforced the findings of the original technical report.

More-recent work compared microscopy, including the use of hemocytometers and counting chambers (enhanced urinalysis), with routine urinalysis or dipslide reagents (Table 6). Lockhart et al\textsuperscript{19} found that the observation of any visible bacteria in an uncentrifuged, Gram-stained, urine sample had better sensitivity and specificity than did combined dipslide leukocyte esterase and nitrite test results. Hoberman et al\textsuperscript{7} in 1996 and Shaw et al\textsuperscript{9} in 1998 both evaluated enhanced urinalysis, consisting of more than 10 white blood cells in a counting chamber or any bacteria seen in 10 oil emersion fields; they found sensitivity of 94% to 96% and specificity of 84% to 83%. In 2000, Lin et al\textsuperscript{21} found that a count of at least 10 white blood cells per \( \mu L \) in a hemocytometer was less sensitive (83%) but quite specific (89%). Given the sensitivity of enhanced urinalysis, the probability of UTI for a typical febrile infant with a previous likelihood of UTI of 5% would be reduced to 0.2% to 0.4% with negative enhanced urinalysis results.

Obtaining a Urine Sample

In the UTI practice parameters from 1999, the subcommittee defined the gold standard of a UTI to be growth of bacteria on a culture of urine obtained through suprapubic aspiration (SPA). In the previous technical report, SPA was reported to have success rates ranging from 23% to 90%,\textsuperscript{22–24} although higher success rates have been achieved when SPA is conducted under ultrasonographic guidance.\textsuperscript{25,26} SPA is considered more invasive than catheterization and, in RCTs from 2006\textsuperscript{27} and 2010,\textsuperscript{28} pain scores associated with SPA were significantly higher than those associated with catheterization. This result was found for both boys and girls. Similar to previous studies, these RCTs also revealed lower success rates for SPA (66% and 60%), compared with catheterization (83% and 78%).\textsuperscript{27,28} In comparison with SPA results, cultures of urine specimens obtained through catheterization are 95% sensitive and 99% specific.\textsuperscript{7,11,12}

Cultures of bag specimens are difficult to interpret. In the original technical report, sensitivity was assumed to be 100% but the specificity of bag cultures was shown to range between 14% and 84%.\textsuperscript{2} Our updated surveillance of the literature did not show that these numbers have improved.\textsuperscript{29–35} One article suggested that a new type of collection bag may result in improved specificity,\textsuperscript{34} but that study was not controlled. With a prevalence of 5% and specificity of 70%, the positive predictive value of a positive culture result for urine obtained in a bag would be 15%. This means that, of all positive culture results for urine obtained in a bag, 85% would be false-positive results.

Box 2: Diagnostic Tests for UTI

The 1999 technical report reviewed a large number of studies that described diagnostic tests for UTI. The results are summarized in Table 5. This updated review of the literature largely reinforced the findings of the original technical report.

<table>
<thead>
<tr>
<th>Study</th>
<th>Test Description</th>
<th>Population</th>
<th>n</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lockhart et al\textsuperscript{19} (1995)</td>
<td>Leukocyte esterase or nitrite test results positive Any bacteria with Gram-staining</td>
<td>Prospective sample, &lt;6 mo of age, ED</td>
<td>207</td>
<td>67</td>
<td>79</td>
</tr>
<tr>
<td>Hoberman et al\textsuperscript{7} (1996)</td>
<td>&gt; 10 white blood cells per counting chamber or any bacteria per 10 oil emersion fields</td>
<td>&lt;2 y of age, 95% febrile, ED</td>
<td>4253</td>
<td>96</td>
<td>93</td>
</tr>
<tr>
<td>Shaw et al\textsuperscript{9} (1998)</td>
<td>Enhanced urinalysis Dipslide or standard urinalysis</td>
<td>Infants &lt;12 mo of age and girls &lt;2 y of age, =38.5°C, ED</td>
<td>3873</td>
<td>94</td>
<td>84</td>
</tr>
<tr>
<td>Lin et al\textsuperscript{21} (2000)</td>
<td>Hemocytometer, ≥10 cells per ( \mu L )</td>
<td>Systematic review, febrile infants hospitalized, febrile UTI</td>
<td>NA</td>
<td>83</td>
<td>88</td>
</tr>
</tbody>
</table>

ED indicates emergency department; NA, not applicable.

Box 3: Short-term Treatment of UTIs

General Principles of Treatment

Published evidence regarding the short-term treatment of UTIs supports 4 main points. First, complications, such as bacteremia or renal scarring, are sufficiently common to necessitate early, thorough treatment of febrile UTIs in infants.\textsuperscript{35} Second, treatment with orally administered antimicrobial agents is as effective as parenteral therapy.\textsuperscript{36,37} Third, bacterial sensitivity to antimicrobial agents is highly variable across time and geographic areas, which suggests that therapy should be guided initially by local sensitivity patterns and should be adjusted on the basis of sensitivities of isolated pathogens.\textsuperscript{38,39} Fourth, meta-analyses have suggested that shorter durations of oral therapy may not have a disadvantage over longer courses for UTIs. However, those studies largely excluded febrile UTI and pyelonephritis.\textsuperscript{40}

Experimental and Clinical Data Support the Concept That Delays in the Institution of Appropriate Treatment for Pyelonephritis Increase the Risk of Renal Damage

The 1999 technical report cited evidence that febrile UTIs in children less

TABLE 6: Test Characteristics of Laboratory Tests for UTI in Children

<table>
<thead>
<tr>
<th>Study</th>
<th>Test Description</th>
<th>Population</th>
<th>n</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lockhart et al\textsuperscript{19} (1995)</td>
<td>Leukocyte esterase or nitrite test results positive Any bacteria with Gram-staining</td>
<td>Prospective sample, &lt;6 mo of age, ED</td>
<td>207</td>
<td>67</td>
<td>79</td>
</tr>
<tr>
<td>Hoberman et al\textsuperscript{7} (1996)</td>
<td>&gt; 10 white blood cells per counting chamber or any bacteria per 10 oil emersion fields</td>
<td>&lt;2 y of age, 95% febrile, ED</td>
<td>4253</td>
<td>96</td>
<td>93</td>
</tr>
<tr>
<td>Shaw et al\textsuperscript{9} (1998)</td>
<td>Enhanced urinalysis Dipslide or standard urinalysis</td>
<td>Infants &lt;12 mo of age and girls &lt;2 y of age, =38.5°C, ED</td>
<td>3873</td>
<td>94</td>
<td>84</td>
</tr>
<tr>
<td>Lin et al\textsuperscript{21} (2000)</td>
<td>Hemocytometer, ≥10 cells per ( \mu L )</td>
<td>Systematic review, febrile infants hospitalized, febrile UTI</td>
<td>NA</td>
<td>83</td>
<td>88</td>
</tr>
</tbody>
</table>
than 2 years of age are associated with bacterial sepsis in 10% of cases. Furthermore, renal scarring is common among children who have febrile UTIs. The risk is higher among those with higher grades of VUR but occurs with all grades, even when there is no VUR. Although it was not confirmed in all studies, older work and newer studies demonstrated an increased risk of scarring with delayed treatment. Children whose treatment is delayed more than 48 hours after onset of fever may have a more than 50% higher risk of acquiring a renal scar.

**Oral Versus Intravenous Therapy**

In a RCT from 1999, Hoberman et al studied children 1 to 24 months of age with febrile UTIs. They compared 14 days of oral cefixime treatment with 3 days of intravenous cefotaxime treatment followed by oral cefixime treatment to complete a 14-day course. The investigators found no difference in outcomes between children who were treated with an orally administered, third-generation cephalosporin alone and those who received intravenous treatment.

In a Cochrane review, Hodson et al evaluated studies with children 0 to 18 years of age, examining oral versus intravenous therapy. No significant differences were found in duration of fever (2 studies; mean difference: 2.05 hours [95% CI: −0.84 to 4.94 hours]) or renal parenchymal damage at 6 to 12 months (3 studies; RR: 0.80 [95% CI: 0.50−1.26]) between oral antimicrobial therapy (10−14 days) and intravenous antimicrobial treatment (3 days) followed by oral antimicrobial treatment (11 days).

**Duration of Therapy**

In the 1999 technical report, data slightly favoring longer-duration (7−10 days) over shorter-duration (1 dose to 3 days) antimicrobial therapy for pediatric patients with UTIs were presented. Since then, several meta-analyses with different conclusions have been published on this topic. A 2003 Cochrane review addressing the question analyzed studies that examined the difference in rates of recurrence for positive urine cultures after treatment. It compared short (2−4 days) and standard (7−14 days) duration of treatment for UTIs and found no significant difference in the frequency of bacteriuria after completion of treatment (8 studies; RR: 1.06 [95% CI: 0.64−1.76]). Although the authors of the review did not exclude studies of children with febrile UTIs or pyelonephritis, each individual study included in the meta-analysis had already excluded such children. To date, there are no conclusive data on the duration of therapy for children with febrile UTIs or pyelonephritis.

**Proof of Cure**

Data supporting routine repeat cultures of urine during or after completion of antimicrobial therapy were not available for the 1999 technical report. Retrospective studies did not show "proof of bacteriologic cure" cultures to be beneficial. Studies demonstrating that clinical response alone ensures bacteriologic cure are not available.

**Box 4: Evaluation and Management of Urinary Tract Abnormalities**

**Prevalence of VUR**

Several cohort studies published since the 1999 technical report provide estimates of the prevalence of VUR of various grades among infants and children with UTIs (Table 7). Overall, these estimates are reasonably consistent with those reported in earlier studies, although the grades of reflux are now reported more consistently, by using the international system of radiographic grading of VUR.

The prevalence of VUR among children in these studies varies between 18% and 35%. The weighted average prevalence is 34%, but this is largely driven by the enormous retrospective study by Chand et al. Most studies report a rate of 24% or less, which is less than the estimate of VUR prevalence in the 1999 technical report.

Data on the prevalence of VUR among children without a history of UTI do not
exist. Using a retrospective approach and existing urine culture data, Hannula and Ventola and colleagues, in 2 separate publications, found similar rates of prevalence of any grade of VUR among children with proven (37.4%) or certain (36%) UTI versus false (34.8%) or improbable (36%) UTI. These results suggest that VUR is prevalent even among children without a history of UTI.

The prevalence of VUR decreases with age. This was approximated by analysis across studies in the 1999 technical report. Since then, Chand et al reported the prevalence VUR within age substrata of their cohort. Figure 3 shows the prevalence of VUR plotted as a function of the midpoint of each age stratum.

Seven studies reported the prevalence of different grades of reflux, by using the international grading system. The distributions of different reflux grades among children who had VUR are shown in Fig 4. There is significant variability in the relative predominance of each reflux grade, but grades II and III consistently are the most common. With the exception of the study by Camacho et al, all studies showed grades IV and V to be the least frequent, and grade V accounted for 0% to 5% (weighted average: 3%) of reflux. With that value multiplied by the prevalence of VUR among young children with a first UTI, we would expect grade V reflux to be present in <1% of children with a first UTI.

It has been suggested that the risk of VUR and, more specifically, high-grade VUR may be higher for children with recurrent UTI than for children with a first UTI. Although it was not tested directly in the studies reviewed, this idea can be tested and the magnitude of the effect can be estimated from the data found in the literature search for this meta-analysis. These data clearly demonstrate that the risk of UTI recurrence is associated with VUR (Fig 5). Furthermore, this relationship allows the likelihood of each grade of reflux (given that a UTI recurrence has occurred) to be estimated by using Bayes’ theorem, as follows:

\[
p(VUR|UTI) = \frac{p(UTI|VUR) \times p(VUR)}{\sum_{i=0}^{V} p(UTI|VUR_i) \times p(VUR_i)},
\]

where \(p(UTI|VUR_i)\) refers to the probability of VUR of grade \(i\) given the recurrence of UTI. If it is assumed that the conditional probabilities remain the same with second or third UTIs, then Bayes’ theorem can be reapplied for a third UTI as well. By using estimates of \(p(UTI|VUR)\) (Fig 5) and the previously determined distri-
butions of VUR grades (Fig 4), a very approximate estimate of the distribution of VUR grades after the first, second, and third UTI can be made (Fig 6). The likelihood that there is no VUR decreases rapidly. Conversely, the likelihood of VUR grades III to V increases rapidly. The risk of grades I and II changes little.

Ultrasonography

Ultrasonography is used as a noninvasive technique to identify renal abnormalities in children after UTI. The sensitivity of the test varies greatly and has been reported to be as low as 5% for detection of renal scarring and 10% for detection of VUR. However, most studies report moderate specificity. One possible reason for a decrease in specificity is that, in animal models, *Escherichia coli* endotoxin has been shown to produce temporary dilation of the urinary tract during acute infection. Therefore, use of routine ultrasonography for children with UTIs during acute infection may increase the false-positive rate. However, no human data are available to confirm this hypothesis.

Ultrasonography is used during acute infection to identify renal or perirenal abscesses, pyonephrosis, or posterior urethral valves in children who fail to experience clinical improvement despite antimicrobial therapy. The sensitivity of ultrasonography for such complications is thought to be very high, approaching 100%. Therefore, ultrasonography in the case of a child with a UTI who is not responding to therapy as expected can be very helpful in ruling out these infectious complications.

Ultrasonography also is advocated for screening for renal abnormalities such as hydronephrosis, suggesting posterior urethral valves, ureteropelvic junction obstruction, or ureteroceles. The evidence model illustrates the expected outcomes from routine ultrasonography of the kidneys, ureters, and bladder after the first febrile UTI in infants and young children (Fig 7). The model is based on the study results documented in Tables 8 and 9 and a strategy of performing kidney and bladder ultrasonography for all infants with UTIs. The numbers are not exact for 2 reasons, namely, (1) study populations vary and do not always precisely meet the definitions of 2 to 24 months of age and febrile without another fever source and, (2) even within similar populations, reported rates vary widely.

Ultrasonography yields ~15% positive results. However, it has a ~70% false-negative rate for reflux, scarring, and other abnormalities. Limited data exist regarding the false-negative rate for high-grade VUR (grade IV and V), but the studies reviewed presented 0% to 40% false-negative rates for detection of grade IV reflux through ultrasonography. Among the 15% of results that are positive, between 1% and 24% are false-positive results. Of the true-positive results, ~40% represent some dilation of the collecting system, such as would be found on a VCUG; 10% represent abnormalities that are potentially surgically correctable (eg, ureteroceles or ureteropelvic junction obstruction). Approximately one-half represent findings such as horseshoe kidneys or renal scarring, for which there is no intervention but which might lead to further evaluations, such as technetium-99m–labeled dimercaptosuccinic acid renal scintigraphy. The 40% with dilation of the collecting system are problematic. This represents only a small fraction of children (15% × 88% × 40% = 5%) with first UTIs who would be expected to have VUR before ultrasonography. Ultrasonography does not seem to be enriching for this population (although ultrasonography might identify a population with higher-grade VUR).

---

**FIGURE 6**
Distribution of VUR grades after different numbers of UTIs.

**FIGURE 7**
Evidence model for ultrasonography after a first UTI.
Prenatal Ultrasonography

Urinary tract abnormalities also may be identified during prenatal ultrasonography, which theoretically would decrease the number of new abnormalities found through later ultrasonography. However, the extent to which normal prenatal ultrasonographic findings decrease the need for later studies remains in doubt.

Miron et al studied 209 children who underwent ultrasonography prenatally and again after a UTI. They found that, among 9 children with abnormal ultrasonographic results after UTI, 7 had normal prenatal ultrasonographic results. These cases included 3 cases of hydronephrosis, 3 cases of moderate dilation, and 1 case of double collecting system. Similarly, in a study by Lakho et al in 1996, 22 of 39 children with UTIs had normal prenatal ultrasonographic results but “abnormal” post-UTI ultrasonographic results; the abnormalities were not described. These studies suggest that normal prenatal ultrasonographic findings may not be sufficient to obviate the need for additional studies if a UTI occurs in infancy.

Results of Targeted Literature Review and Meta-analysis on Prophylaxis to Prevent Recurrent UTI

Study Identification

For the meta-analysis of studies on the effectiveness of antimicrobial agents to prevent recurrent UTI in children with VUR, we reviewed a total of 213 titles from our primary literature search. Of those, 45 were retained for abstract review on the basis of the title, of which 7 were selected for full review. Six of the studies met the inclusion criteria. Figure 2 summarizes the selection process. Thirty-eight abstracts were excluded before full review (Fig 2). Eight of those studies were RCTs comparing prophylactic antimicrobial agent use with some type of surgical intervention. None of those studies included a placebo arm. One study compared different lengths of antimicrobial prophylaxis. Another study compared different antimicrobial regimens but did not include a placebo arm. Sixteen studies were determined, on closer inspection, to be not clinical trials but prospective cohort studies, reviews, systematic reviews, or meta-analyses. Twelve studies were found twice, either in Medline or Embase and the Cochrane Clinical Trials Registry.

One article was excluded after full review (Fig 2). That study compared prophylactic antimicrobial agent use with probiotic use. The study was not included in the meta-analysis, but the results are described separately.

There are RCTs of antimicrobial prophylaxis that are older than 15 years. In 4 studies from the 1970s, a total of 179 children were enrolled. Less than 20% of those children had VUR. Because of limited reporting of results in that subgroup, those older studies were not included in the analyses.

Two additional RCTs comparing antimicrobial prophylaxis and placebo treatment for children were published in October 2009. The first trial enrolled children 0 to 18 years of age after a first UTI, with 2% of enrolled children (12 of 576 children) being more than 10 years of age. The second trial enrolled children diagnosed as having VUR after a first UTI (194 [96%] of 203 children) or after prenatal ultrasonography (9 [4%] of 203 children), who were then assigned randomly to receive antimicrobial prophylaxis, surveillance, or endoscopic therapy, at 1 to 2 years of age. The majority of these children (132 children [65%]) had been diagnosed as having VUR before 1

<table>
<thead>
<tr>
<th>Table 8</th>
<th>Summary of Ultrasonography Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>n/N (%)</td>
</tr>
<tr>
<td>False-negative rate</td>
<td></td>
</tr>
<tr>
<td>Scarring</td>
<td></td>
</tr>
<tr>
<td>Sinha et al (2007)</td>
<td>61/79 (77)</td>
</tr>
<tr>
<td>Montini et al (2009)</td>
<td>33/45 (73)</td>
</tr>
<tr>
<td>VUR</td>
<td></td>
</tr>
<tr>
<td>Mahant et al (2002)</td>
<td>14/35 (40)</td>
</tr>
<tr>
<td>Hoberman et al (2003)</td>
<td>104/117 (90)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>False-positive rate</td>
<td></td>
</tr>
<tr>
<td>Scarring</td>
<td></td>
</tr>
<tr>
<td>Sinha et al (2007)</td>
<td>9/870 (1)</td>
</tr>
<tr>
<td>VUR</td>
<td></td>
</tr>
<tr>
<td>Smellie et al (1995)</td>
<td>2/12 (17)</td>
</tr>
<tr>
<td>Hoberman et al (2003)</td>
<td>17/185 (10)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>Giorgi et al (2005)</td>
<td>21/203 (10)</td>
</tr>
</tbody>
</table>

IVU indicates intravenous urography; DMSA, dimercaptosuccinic acid.
year of age and thus had been receiving prophylaxis before random assignment. These studies were included in the meta-analysis.

Description of Included Studies

Table 10 presents characteristics of the 8 included studies.4,66–70,104,105 Four studies enrolled children after diagnosis of a first episode of pyelonephritis.4,66–68 In those 4 studies, pyelonephritis was described as fever of more than 38°C or 38.5°C and positive urine culture results. In 1 of those studies,67 dimercaptosuccinic acid scanning results consistent with acute pyelonephritis represented an additional requirement for inclusion. The remaining studies had slightly different inclusion criteria. In the study by Craig et al71 from 2009, symptoms consistent with UTI and positive urine culture results were required for inclusion. Fever was documented for 79% of enrolled children (454 of 576 children). In the study by Brandström et al,70 96% of enrolled children (194 of 203 children) had pyelonephritis, defined in a similar manner as in the 6 initial studies. The remaining patients were enrolled after prenatal diagnosis of VUR. The 2 included abstracts described studies that enrolled any child with VUR and not only children who had had pyelonephritis.79,105 Seven of the 8 studies (all except the study by Reddy et al108) reported a gender ratio. Among those studies, there were 67% girls and 33% boys. Six studies compared antimicrobial treatment with no treatment. Only 2 studies were placebo controlled, and those 2 were the only blinded studies.69,105 The grade of VUR among the enrolled children varied from 0 to V, but few of the children had grade V VUR.

The ages of children included in the initial meta-analyses were 0 to 18 years; therefore, some children were included who were outside the target age range. The ages of children enrolled in the initial meta-analyses were 0 to 18 years; therefore, some children were included who were outside the target age range.

Table 9 presents characteristics of the 8 included studies.64,66–70,104,105 Four studies enrolled children after diagnosis of a first episode of pyelonephritis.64,66–68 In those 4 studies, pyelonephritis was described as fever of more than 38°C or 38.5°C and positive urine culture results. In 1 of those studies,67 dimercaptosuccinic acid scanning results consistent with acute pyelonephritis represented an additional requirement for inclusion. The remaining studies had slightly different inclusion criteria. In the study by Craig et al71 from 2009, symptoms consistent with UTI and positive urine culture results were required for inclusion. Fever was documented for 79% of enrolled children (454 of 576 children). In the study by Brandström et al,70 96% of enrolled children (194 of 203 children) had pyelonephritis, defined in a similar manner as in the 6 initial studies. The remaining patients were enrolled after prenatal diagnosis of VUR. The 2 included abstracts described studies that enrolled any child with VUR and not only children who had had pyelonephritis.79,105 Seven of the 8 studies (all except the study by Reddy et al108) reported a gender ratio. Among those studies, there were 67% girls and 33% boys. Six studies compared antimicrobial treatment with no treatment. Only 2 studies were placebo controlled, and those 2 were the only blinded studies.69,105 The grade of VUR among the enrolled children varied from 0 to V, but few of the children had grade V VUR.

The ages of children included in the initial meta-analyses were 0 to 18 years; therefore, some children were included who were outside the target age range.

Table 9 Distribution of Positive Ultrasonographic Findings

| Study | n/N (%)
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Alon and Ganapathy62 (1999)</td>
<td>19/124 (15)</td>
</tr>
<tr>
<td>Minimal unilateral changes</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>VUR</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Normal VCUG findings</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Resolved on repeat study</td>
<td>3 (2.4)</td>
</tr>
<tr>
<td>Not monitored further</td>
<td>8 (6.5)</td>
</tr>
<tr>
<td>Major changes</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Normal findings</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Posterior urethral valve</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Gelfand et al64 (2000)</td>
<td>141/844 (16.7)</td>
</tr>
<tr>
<td>Bladder wall thickening</td>
<td>31 (3.7)</td>
</tr>
<tr>
<td>Hydroureter</td>
<td>6 (0.7)</td>
</tr>
<tr>
<td>Parenchymal abnormalities</td>
<td>42 (5.0)</td>
</tr>
<tr>
<td>Pelvocalyceal dilation</td>
<td>27 (3.2)</td>
</tr>
<tr>
<td>Renal calculus</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Simple renal cyst</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Ureteral thickening</td>
<td>31 (3.7)</td>
</tr>
<tr>
<td>Jothilakshmi et al65 (2001)</td>
<td>42/262 (16)</td>
</tr>
<tr>
<td>Duplex kidney</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Crossed renal ectopia</td>
<td>1 (0.38)</td>
</tr>
<tr>
<td>Horseshoe kidney</td>
<td>1 (0.38)</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>5 (1.9)</td>
</tr>
<tr>
<td>Megaurter</td>
<td>6 (2.3)</td>
</tr>
<tr>
<td>Polycystic kidney</td>
<td>1 (0.38)</td>
</tr>
<tr>
<td>Pelviureteric junction obstruction</td>
<td>1 (0.38)</td>
</tr>
<tr>
<td>Posterior urethral valve</td>
<td>2 (0.76)</td>
</tr>
<tr>
<td>Renal calculus</td>
<td>3 (0.01)</td>
</tr>
<tr>
<td>Rotated kidney</td>
<td>2 (0.76)</td>
</tr>
<tr>
<td>Ureterocele</td>
<td>2 (0.76)</td>
</tr>
<tr>
<td>VUR</td>
<td>7 (2.7)</td>
</tr>
<tr>
<td>Dilated pelvis</td>
<td>13 (4.2)</td>
</tr>
<tr>
<td>Pelvocalyceal dilation</td>
<td>12 (3.9)</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>2 (0.6)</td>
</tr>
<tr>
<td>Dilated ureter</td>
<td>9 (2.9)</td>
</tr>
<tr>
<td>Double collecting system</td>
<td>3 (1.0)</td>
</tr>
<tr>
<td>Extrarenal pelvis</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Calculus</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Mild unilateral pelvis dilation</td>
<td>32 (12.5)</td>
</tr>
<tr>
<td>Moderate unilateral pelvis dilation</td>
<td>1 (0.04)</td>
</tr>
<tr>
<td>Enlargement kidney</td>
<td>1 (0.04)</td>
</tr>
<tr>
<td>Small renal cyst</td>
<td>1 (0.04)</td>
</tr>
<tr>
<td>Double collecting system and severe hydronephrosis</td>
<td>1 (0.04)</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>8 (3)</td>
</tr>
<tr>
<td>Double collecting system</td>
<td>11 (7)</td>
</tr>
<tr>
<td>Multicystic dysplasia</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Renal hypoplasia</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Solitary kidney</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Horseshoe kidney</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Huang et al69 (2008)</td>
<td>112/390 (28.7)</td>
</tr>
<tr>
<td>Nephromegaly</td>
<td>46 (11.8)</td>
</tr>
<tr>
<td>Isolated hydronephrosis</td>
<td>20 (5.1)</td>
</tr>
<tr>
<td>Intermediated hydronephrosis</td>
<td>3 (0.8)</td>
</tr>
<tr>
<td>Hydroureter</td>
<td>8 (2.1)</td>
</tr>
<tr>
<td>Hydroureter and hydronephrosis</td>
<td>3 (0.8)</td>
</tr>
<tr>
<td>Thickened bladder wall</td>
<td>11 (2.8)</td>
</tr>
<tr>
<td>Small kidneys</td>
<td>8 (2.1)</td>
</tr>
<tr>
<td>Simple ureterocele</td>
<td>5 (1.3)</td>
</tr>
<tr>
<td>Double collecting systems</td>
<td>4 (1.0)</td>
</tr>
<tr>
<td>Increased echogenicity</td>
<td>3 (0.8)</td>
</tr>
<tr>
<td>Horseshoe kidney</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Montini et al70 (2009)</td>
<td>58/300 (13)</td>
</tr>
<tr>
<td>Dilated pelvis, ureter, or pelvis and calyces</td>
<td>12 (4)</td>
</tr>
<tr>
<td>Renal swelling or local parenchymal changes</td>
<td>10 (3.3)</td>
</tr>
<tr>
<td>Increased bladder wall or pelvic mucosa, thickness</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Other</td>
<td>10 (3.3)</td>
</tr>
</tbody>
</table>

* Hospitalized children with UTI.
age range for this report and for whom other factors (eg, voiding and bowel habits) might have played a role. The median age of the included children, however, was not above 3 years in any of the included studies in which it was reported. Separate meta-analyses were subsequently performed for the subgroup of children who were 2 to 24 months of age. The duration of antimicrobial treatment and follow-up monitoring ranged from 12 to 48 months. The antimicrobial agents used were trimethoprim-sulfamethoxazole (1–2 or 5–10 mg/kg),64,68,69,105 trimethoprim-sulfamethoxazole or amoxicillin-clavulanic acid (15 mg/kg),66 trimethoprim-sulfamethoxazole or nitrofurantoin,67,104 or trimethoprim-sulfamethoxazole, cefadroxil, or nitrofurantoin.70 Urine collection methods differed among studies. Bag specimens were reported for 3 studies.64,66,70 In an additional 4 studies, the description of the urine collection methods did not exclude the use of bag specimens.67,68,104,105 Recurrent UTI was described as (1) asymptomatic bacteriuria (diagnosed through screening cultures), (2) cystitis, (3) febrile UTI, and (4) pyelonephritis (diagnosed on the basis of focal or diffuse uptake on di-mercaptosuccinic acid scans) in the different articles.

**Quality Assessment**

The included studies received scores (from 2 assessors) from 7 to 26 (scale range: 0–32) with the scoring system described by Downs and Black,6 with a median score of 16. Score deductions resulted from lack of blinding of patients (all except 2 studies69,105), lack of blinding of assessors (all except 2 studies69,105), limited or no information about patients lost to follow-up monitoring (3 studies64,67,104), lack of reporting of adverse effects (all except 2 studies66,69), and small sample sizes. The lowest scores, 7 and 12, were received by the 2 abstracts because of lack of details in the descriptions of the methods.104,105

**Antimicrobial Therapy Versus No Treatment**

**Overview of Findings**

Described here are the results of several meta-analyses, subdivided according to type of recurrence (pyelonephritis versus UTI), degree of VUR (none to grade V), and patient age. In summary, antimicrobial prophylaxis does not seem to reduce significantly the rates of recurrence of pyelonephritis, regardless of age or degree of reflux. Although prophylaxis seems to reduce significantly but only slightly the risk of UTI when all forms are included, most of this effect is attributable to reductions in rates of cystitis or asymptomatic bacteriuria, which would not be expected to lead to ongoing renal damage.

**Recurrence of Pyelonephritis/Febrile UTI Among All Studied Children With VUR of Any Grade**

Recurrence of pyelonephritis was reported in 6 of the 8 studies. The study by Pennesi et al68 presented the results as recurrence of pyelonephritis, but recurrence was defined as episodes of fever or “symptoms of UTI.” When contacted, this author confirmed that all reported recurrences were characterized by fever above 38.5°C. Therefore, the article was included in the meta-analysis. With a random-effects model, there was no significant difference in rates of recurrence of pyelonephritis for children who received antimicrobial therapy and those who did not. This meta-analysis yielded a RR of 0.77 (95% CI: 0.47–1.24) (Fig 8). Heterogeneity test-

---

**TABLE 10**  Studies Included in Meta-analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Sites</th>
<th>n</th>
<th>Age VUR Grade</th>
<th>Antimicrobial Agents</th>
<th>Control</th>
<th>Follow-up Period, mo</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Australia</td>
<td>48</td>
<td>0</td>
<td>I–V</td>
<td>TMP-SMX Placebo</td>
<td>36</td>
<td>UTI and renal damage</td>
</tr>
<tr>
<td>Craig et al105</td>
<td>Australia</td>
<td>243</td>
<td>0–18 y</td>
<td>I–V</td>
<td>TMP-SMX Placebo</td>
<td>12</td>
<td>Symptomatic UTI, febrile UTI, hospitalization, and renal scarring</td>
</tr>
<tr>
<td>Garin et al67</td>
<td>Chile, Spain, United States</td>
<td>113</td>
<td>0</td>
<td>0–III</td>
<td>TMP-SMX/ nitrofurantoin No treatment</td>
<td>12</td>
<td>Asymptomatic UTI, cystitis, pyelonephritis, and renal scarring</td>
</tr>
<tr>
<td>Montini et al66 (2008)</td>
<td>Italy</td>
<td>128</td>
<td>2 mo to 7 y</td>
<td>0–III</td>
<td>TMP-SMX/amoxicillin-clavulanate No treatment</td>
<td>12</td>
<td>Febrile UTI and renal scarring</td>
</tr>
<tr>
<td>Pennesi et al68 (2008)</td>
<td>Italy</td>
<td>100</td>
<td>0</td>
<td>0–30 mo</td>
<td>II–IV</td>
<td>TMP-SMX No treatment</td>
<td>48 UTI and renal scarring</td>
</tr>
</tbody>
</table>

**TMP-SMX indicates trimethoprim-sulfamethoxazole.**
ing results were significant (P = .04), which indicated statistical heterogeneity between studies.

Recurrence of Pyelonephritis/Febrile UTI Among Children of All Ages Without VUR

There was no significant difference in rates of recurrence of pyelonephritis for children without VUR who received antimicrobial therapy and those who did not. With random-effects modeling, the meta-analysis yielded a RR of 0.62 (95% CI: 0.30–1.27) (Fig 9). Heterogeneity testing results were not significant (P = .39). Because no difference was detected with a random-effects model and there was no statistical heterogeneity in this analysis, analysis also was conducted with a fixed-effects model. With fixed-effects modeling, the meta-analysis yielded a RR of 0.61 (95% CI: 0.31–1.23).

Recurrence of Pyelonephritis/Febrile UTI Among Children of All Ages With VUR

Table 11 summarizes the results of separate meta-analyses of subpopulations from each study with different grades of VUR. None of those analyses showed a statistically significant difference in rates of recurrence with random- or fixed-effects modeling. Random-effects modeling results are presented.

Recurrence of Pyelonephritis/Febrile UTI Among Children 2 to 24 Months of Age With VUR of Any Grade

There was no significant difference in rates of recurrence of pyelonephritis for children 2 to 24 months of age with VUR who received antimicrobial agents and those who did not. With random-effects modeling, the meta-analysis yielded a RR of 0.78 (95% CI: 0.48–1.26) (Fig 10). Heterogeneity testing results were not significant (P = .07). With fixed-effects modeling, the meta-analysis yielded a RR of 0.79 (95% CI: 0.58–1.07). Heterogeneity testing results were not significant (P = .07).

Recurrence of Pyelonephritis/Febrile UTI Among Children 2 to 24 Months of Age With No VUR

There was no significant difference in rates of recurrence of pyelonephritis for children 2 to 24 months of age without VUR who received antimicrobial agents and those who did not. With random-effects modeling, the meta-analysis yielded a RR of 0.55 (95% CI: 0.32–0.94).
Recurrence of Pyelonephritis/Febrile UTI Among Children 2 to 24 Months of Age According to Grade of VUR

When results were analyzed according to VUR grade, there was no significant difference in rates of recurrence of pyelonephritis for children 2 to 24 months of age who received antimicrobial agents and those who did not in any of the analyses, with random- or fixed-effects modeling. Results of random-effects modeling are presented in Figs 12 through 16. Heterogeneity testing results were not significant in any of the analyses.

Recurrence of Any Type of UTI Among Children of All Ages With VUR of Any Grade

In this meta-analysis, in which the 2 published abstracts that never resulted in published articles were included, there was a statistically significant difference in rates of recurrence of any type of UTI for children with VUR who received antimicrobial agents and those who did not. With random-effects modeling, the meta-analysis yielded a RR of 0.70 (95% CI: 0.51–0.98) (Fig 17). Heterogeneity testing results were not significant (P = .20).

The inclusion of the published abstracts in these meta-analyses can be criticized, because the investigators in those studies enrolled all children with VUR and not just those who had been diagnosed as having UTI; therefore, recurrent UTIs were not measured. With exclusion of the 2 abstracts from the meta-analyses for prevention of any UTI, the RR with random-effects modeling would be 0.73 (95% CI: 0.53–1.01). Heterogeneity testing results were not significant (P = .16).
Recurrence of Any Type of UTI Among Children of All Ages Without VUR

There was no significant difference in rates of recurrence of any type of UTI for children without VUR who received antimicrobial agents and those who did not. With random-effects modeling, the meta-analysis yielded a RR of 0.72 (95% CI: 0.43–1.20) (Fig 18). Heterogeneity testing results were not significant ($P = .37$).

Effect on Studies of Inclusion of Bag Specimens

With the exception of the study by Craig et al., no studies reported that bag urine specimens were excluded. The inclusion of such specimens might...
have resulted in increased numbers of false-positive urine culture results in both the antimicrobial prophylaxis and control groups, yielding a bias toward the null hypothesis in those studies.

Results of Excluded Study
The study by Lee et al[65] was excluded from the meta-analysis because it compared antimicrobial prophylaxis with probiotic treatment. A total of 120 children 13 to 36 months of age with a history of UTI and VUR of grade I to V who had been receiving trimethoprim-sulfamethoxazole once daily for 1 year were again assessed for VUR; if VUR persisted, then children were assigned randomly either to continue to receive trimethoprim-sulfamethoxazole or to receive Lactobacillus acidophilus twice daily for 1 additional year. The study showed no statistical difference in recurrent UTI rates between the 2 groups during the second year of follow-up monitoring.

Antimicrobial Prophylaxis and Antimicrobial Resistance
The antimicrobial resistance patterns of the pathogens isolated during UTI recurrences were assessed in 5 of the RCTs included in the meta-analyses.[64,66,68–70] All authors concluded that UTI recurrences with antimicrobial-resistant bacteria were more common in the groups of children assigned randomly to receive antimicrobial prophylaxis. In the placebo/surveillance groups, the proportions of resistant bacteria ranged from 0% to 39%; in the antimicrobial prophylaxis groups, the proportions of resistant bacteria ranged from 53% to 100%. These results are supported by other studies in which antimicrobial prophylaxis has been shown to promote resistant organisms.[106,107]

Surgical Intervention Versus Antimicrobial Prophylaxis
Data on the effectiveness of surgical interventions for VUR are quite limited. To date, only 1 RCT has compared surgical intervention (only endoscopic therapy) for VUR with placebo treatment.[70] In that study, there was a statistically significant difference in the rates of recurrence of febrile UTI for girls treated with endoscopic therapy and those under surveillance (10 of 43 vs 24 of 42 girls; \( P = 0.004 \)). No such difference was noted among boys, for whom the results trended in the opposite direction (4 of 23 vs 1 of 26 boys). A meta-analysis examined the outcomes of UTIs and febrile UTIs in children assigned randomly to either reflux correction plus antimicrobial therapy or antimicrobial therapy alone.[108] By 2 years, the authors found no significant reduction in the risk of UTI in the surgery plus antimicrobial therapy group, compared with the antimicrobial therapy-only group (4 studies; RR: 1.07 [95% CI: 0.55–2.09]). The frequency of febrile UTIs was reported in only 2 studies. Children in the surgery plus group...
antimicrobial therapy group had significantly fewer febrile UTIs than did children in the antimicrobial therapy-only group between 0 and 5 years after intervention (RR: 0.43 [95% CI: 0.27–0.70]). Although there may be some promise in endoscopic interventions for children with VUR, to date there are insufficient data to show whether and for whom such interventions may be helpful.

Long-term Consequences of VUR
The link between VUR discovered after the first UTI and subsequent hypertension and end-stage renal disease remains tenuous at best. There have been no longitudinal studies monitoring children long enough to quantify these outcomes. Retrospective studies evaluated highly selected populations, and their findings might not apply to otherwise healthy children with a first UTI. Ecologic data from Australia demonstrated no changes in the rates of hypertension and renal failure since the widespread introduction of antimicrobial prophylaxis and ureteric reimplantation surgery for VUR in the 1960s.113

DISCUSSION
Review of the evidence regarding diagnosis and management of UTIs in 2- to 24-month-old children yields the following. First, the prevalence of UTI in febrile infants remains about the same, at ~5%. Studies have provided demographic features (age, race, and gender) and clinical characteristics (height and duration of fever, other causes of fever, and circumcision) that can help clinicians identify febrile infants whose low risk of UTI obviates the need for further evaluation.

Among children who do not receive immediate antimicrobial therapy, UTI can be ruled out on the basis of completely negative urinalysis results. For this purpose, enhanced urinalysis is preferable. However, facilities for urine microscopy with counting chambers and Gram staining may not be available in all settings. A urine reagent strip with negative nitrite and leukocyte esterase reaction results is sufficient to rule out UTI if the pretest risk is moderate (~5%). Diagnosis of UTI is best achieved with a combination of culture and urinalysis. Cultures of urine collected through catheterization, compared with SPA, are nearly as sensitive and specific but have higher success rates and the process is less painful. Cultures of urine collected in bags have unacceptably high false-positive rates.

The previous guideline recommended VCUG after the first UTI for children between 2 and 24 months of age. The rationale for this recommendation was that antimicrobial prophylaxis among children with VUR could reduce subsequent episodes of pyelonephritis and additional renal scarring. However, evidence does not support antimicrobial prophylaxis to prevent UTI when VUR is found through VCUG. The only statistically significant effect of antimicrobial prophylaxis was in preventing UTI that included cystitis and asymptomatic bacteriuria. Statistically significant differences in the rates of febrile UTI or pyelonephritis were not seen. Moreover, VCUG is one of the most uncomfortable radiologic procedures performed with children. Even if additional studies were to show a statistically significant effect of prophylaxis in preventing pyelonephritis, our point estimates suggest that the RR would be ~0.80, corresponding to a reduction in RR of 20%. If we take into account the prevalence of VUR, the risk of recurrent UTI in those children, and this modest potential effect, we can determine that ~100 children would need to undergo VCUG for prevention of 1 UTI in the first year. Even more striking is the fact that the evidence of benefit is the same (or better) for children with no VUR, which makes the benefit of VCUG more dubious. Taken in light of the marginal cost-effectiveness of the procedure found under the more-optimistic assumptions in the 1999 technical report, these data argue against VCUG after the first UTI. VCUG after a second or third UTI would have a higher yield of higher grades of reflux, but the optimal care for infants with higher-grade reflux is still not clear. Ultrasonography of the kidneys, ureters, and bladder after a first UTI has poor sensitivity and only a modest yield of “actionable” findings. However, the procedure is less invasive, less uncomfortable, and less risky (in terms of radiation) than is VCUG.

There is a significant risk of renal scarring among children with febrile UTI, and some evidence suggests that early antimicrobial treatment mitigates that risk. It seems prudent to recommend early evaluation (in the 24- to 48-hour time frame) of subsequent fevers and prompt treatment of UTI to minimize subsequent renal scarring.

LEAD AUTHORS
S. Maria E. Finnell, MD, MS
Aaron E. Carroll, MD, MS
Stephen M. Downs, MD, MS

SUBCOMMITTEE ON URINARY TRACT INFECTION, 2009–2011
Kenneth B. Roberts, MD, Chair
Stephen M. Downs, MD, MS
S. Maria E. Finnell, MD, MS
Stanley Hellerstein, MD
Linda D. Shortliffe, MD
Ellen R. Wald, MD
J. Michael Zerin, MD

OVERTSIGHT BY THE STEERING COMMITTEE ON QUALITY IMPROVEMENT AND MANAGEMENT, 2009–2011
Caryn Davidson, MA

STAFF

ACKNOWLEDGMENTS
The committee gratefully acknowledges the generosity of the researchers who graciously shared their data to permit the data set with data for 1096 infants 2 to 24 months of age 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.
REFERENCES


27. Kozer E, Rosenbloom E, Goldman D, Levy G, Rosenfeld N, Goldman M. Pain in infants who are younger than 2 months during suprapubic aspiration and transurethral bladder catheterization: a randomized, controlled study. Pediatrics. 2006;118(1). Available at: www.pediatrics.org/cgi/content/full/118/1/e51


73. Smellie JM, Ridden SP, Prescod NP. Urinary tract infection: a comparison of four


Diagnosis and Management of an Initial UTI in Febrile Infants and Young Children

the Subcommittee on Urinary Tract Infection

*Pediatrics* 2011;128:e749; originally published online August 28, 2011;
DOI: 10.1542/peds.2011-1332

Updated Information & Services
including high resolution figures, can be found at:
http://pediatrics.aappublications.org/content/128/3/e749.full.html

References
This article cites 103 articles, 34 of which can be accessed free at:
http://pediatrics.aappublications.org/content/128/3/e749.full.html#ref-list-1

Citations
This article has been cited by 2 HighWire-hosted articles:
http://pediatrics.aappublications.org/content/128/3/e749.full.html#related-urls

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Genitourinary Tract
http://pediatrics.aappublications.org/cgi/collection/genitourinary_tract

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
http://pediatrics.aappublications.org/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
http://pediatrics.aappublications.org/site/misc/reprints.xhtml

PEDiATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDiATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2011 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.
Urinary Tract Infection (UTI)
Phoenix Children’s Hospital Inpatient Pathway

**SCOPE:**

**Inclusion Criteria:**
- Diagnosis of UTI in a patient with suggestive signs and symptoms of UTI as well as supporting urinalysis and positive culture
- Hospitalized children, including admission and observation status, ages 2 months through 18 years.
- Consider also for infants less than 2 months of age who meet no other exclusion criteria.

**Exclusion Criteria:**
- History of renal disease
- Known anatomic abnormalities of the urogenital tract
- Neurogenic bladder including the need for catheterization
- Previous urologic surgery
- Presence of catheters, stents, drains or other equipment
- Presence of sepsis or meningitis
- Severe co-morbid condition such as immunodeficiency
- Suspicion of Sexually Transmitted Infection

**KEY CLINICAL RECOMMENDATIONS:**

- **Diagnosis**
  1. In the appropriate clinical context, urine should be checked using catheterization, or clean catch if the patient is toilet-trained.
  2. To establish the diagnosis of UTI in the appropriate clinical setting, clinicians should require both a urinalysis suggesting infection (i.e. presence of pyuria and/or bacteriuria, +/- leukocyte esterase, nitrite) as well as a positive urine culture with $\geq 50,000$ CFUs of a uropathogen via catheterized specimen. Positive urine cultures with less than 50,000 CFUs of a uropathogen should be interpreted in the proper clinical context. The diagnosis of UTI may be considered in these cases, particularly with positive urinalysis, clear clinical symptoms, or in other specific clinical circumstances.
Treatment:

1. Oral and parenteral antibiotic treatment is equally efficacious. Thus practical considerations (i.e. whether patient is tolerating PO, etc) should be used to decide whether to use parenteral vs. oral antibiotic therapy. However, if signs of severe illness/sepsis are present, IV antibiotics are recommended.\textsuperscript{v}

2. A patient with uncomplicated UTI, without signs of severe illness/sepsis, who was started on parenteral therapy, should be changed to oral as soon as the patient is able to tolerate oral therapy.

3. First-line empiric antibiotic choices include:
   - Oral: Cephalexin or Cefdinir (FDA approved for ages over 6 months).
     - For cephalosporin allergic patients, Trimethoprim-Sulfamethoxazole should be considered
   - IV: Ceftriaxone
     - For cephalosporin allergic patients, Gentamicin should be considered
   - Adjust regimen when culture susceptibilities are available\textsuperscript{vi}

4. It is recommended that UTI be treated for a total of 7-10 days regardless of the route of therapy.

5. It is recommended that if the urine culture is negative, antibiotics be discontinued.

Imaging/Ongoing Management:

1. Patients less than 2 years of age with their first febrile UTI should undergo renal and bladder ultrasonography (RUS), ideally prior to discharge.\textsuperscript{vii} Consider RUS, as well, in older children depending on clinical circumstances to include:
   - Recurrent febrile UTIs
   - Severe UTI
   - Presence of family history of VUR
   - Presence of elevated blood pressure unrelated to pain or discomfort
   - Significant proteinuria on urinalysis
   - Abnormal renal function
   - Unusual uropathogen identified (i.e. Pseudomonas species)

2. Voiding cystourethrogram (VCUG) is not indicated \textit{routinely} after first febrile UTI. VCUG is indicated if renal ultrasound reveals hydronephrosis or other findings that would suggest high-grade (VUR) or obstructive uropathy. VCUG is also indicated for a recurrence of febrile UTI. Consider also in other complex clinical circumstances to include:
   - Severe UTI
   - Presence of family history of VUR

Updated 10/10/2013
- Presence of elevated blood pressure unrelated to pain or discomfort
- Significant proteinuria on urinalysis
- Abnormal renal function
- Unusual uropathogen identified (i.e. Pseudomonas species)

**ADMISSION CRITERIA:**
1. Dehydration with inability to take oral fluids
2. Signs of severe illness/sepsis
3. Failed outpatient appropriate antibiotic treatment
4. Social concerns making treatment outside the hospital unsafe or unfeasible
5. Status assignment (observation vs. inpatient) to be determined in consultation with the admitting service/ case management department using Milliman Care Guidelines

**DISCHARGE CRITERIA:**
1. Ability to maintain adequate oral hydration
2. Pain control, if needed, with oral medications only
3. Afebrile or trending towards afebrile
4. Expect outpatient oral antibiotic therapy to be tolerated and effective with organism (antibiotic susceptibility results preferably available)
5. Indicated imaging studies performed or arranged
6. Discharge education complete
7. Responsible and capable parent(s) or guardian(s) and follow-up to care for the child as an outpatient

**ORDER SET**
“UTI – Urinary Tract Infection Clinical Pathway”

**PATHWAY FLOW DIAGRAM**
Urinary Tract Infection (UTI)
PCH Inpatient Clinical Pathway

START
Hx/PE suggestive of UTI

Signs and Symptoms:
- Fever
- Abdominal or flank pain
- Vomiting
- Dysuria, frequency, urgency

Urinalysis and urine culture confirms UTI

Diagnosis of UTI:
- Cath/clean catch (if age appropriate) ≥ 50,000 CFUs of uropathogen
- Urinalysis with pyuria, bacteriuria, +/- LE/nitrite

Meets Inpatient/Observation criteria for UTI without exclusion criteria?

Admission Criteria:
- Dehydration with inability to take PO
- Ill, toxic or septic appearing
- Failed outpatient appropriate antibiotics
- Inability to be cared for or f/u as outpatient

Exclusion Criteria:
- History of renal disease
- Known anatomic abnormalities of urogenital tract
- Neurogenic bladder including need for catheterization
- Previous urologic surgery
- Presence of catheters, stents, drains or other equipment
- Presence of sepsis or meningitis
- Severe co-morbid condition such as immunodeficiency
- Suspicion of sexually transmitted infection

Antibiotics:
1. IV Ceftriaxone or PO Cefdinir (> 6 mo) or Cephalexin
   - IV/PO ATB equally efficacious if tolerating PO without severe illness/sepsis or failed outpatient PO ATB

Imaging:
1. < 2 yo = Renal and bladder ultrasonography (RUS)
2. Abnormal RUS → Voiding cystourethrogram (VCUG)

Clinical improvement meeting discharge criteria in 12-48h?

Discharge Criteria:
- Maintaining oral hydration
- Pain control, if needed, with PO meds
- Afebrile or trending towards afebrile
- Indicated imaging studies performed or arranged
- D/C education complete
- Follow-up and PO ATB arranged with susceptibility results preferably available

Discharge Outpatient Oral Antibiotics:
Cefdinir (>6 mo) or Cephalexin to complete 7-10 days
Adjust based on culture results and available sensitivities

Expected Length of Stay 12-48h
PATIENT AND FAMILY EDUCATION / DISCHARGE PLANNING:

- Begin discharge education upon presentation to the ED and subsequent admission/observation
  - Review UTI education material with parent(s) or guardian(s) and teach signs of worsening infection and dehydration
  - Review whom to contact for questions or problems and reasons to call physician and return to ED
- Educate families that the expected length of stay is 12-48 hours and that their child will be discharged when they meet the discharge criteria
- Involve case management and social work upon admission if special needs exist that may be expected to delay discharge
- Review antibiotic administration including dosage, frequency, length of therapy, taste, pharmacy availability and cost
- Review follow-up recommendations with primary care provider and any recommendations for further testing or specialty care

EVIDENCE BASED SUPPORTING MATERIALS:

Background:
Urinary tract infections are the most common serious bacterial infections in infants and young children affecting 2-5% of all children\textsuperscript{x}. Although common, certain aspects of UTI management have remained controversial. In September of 2011, the American Academy of Pediatrics (AAP) developed a Clinical Practice Guideline to aid in the accurate diagnosis and appropriate treatment of UTI.\textsuperscript{x} The AAP also suggests appropriate screening measures to diagnose underlying risk factors that may lead to recurrent UTI and possible long-term sequelae. The AAP Section on Urology supports many aspects of the AAP Guideline but takes issue with some recommendations regarding imaging and antibiotic prophylaxis.\textsuperscript{xi, xii} In light of the above, this guideline is intended to aid physicians in properly incorporating the best available evidence in the management of UTI.

Risk factors for UTI include girls (relative risk 2.27), uncircumcised boys, and absence of another source of infection.\textsuperscript{xiii, xiv}

Organisms:
1. \textit{Escherichia coli} is the most common organism and the causative agent in >80% of first UTIs
2. \textit{Klebsiella} species is the second most common organism in UTIs

Antibiotic Therapy

Updated 10/10/2013
When initiating empiric treatment the clinician should consider the likely uropathogens and their resistance patterns according to the PCH antibiogram. In 2012, *E. coli* isolates at PCH showed a sensitivity pattern of 90% to Cefazolin and 96% to Ceftriaxone, respectively. An individual patient’s characteristics should be taken into account such as history of allergies or co-morbid conditions.

**Antimicrobial prophylaxis** has not been proven to reduce the likelihood of recurrent UTI in patients with low-grade vesicoureteral reflux (VUR), nor has it been proven to reduce the likelihood of renal scarring or chronic kidney disease in these patients. Controversy remains regarding its utility in the context of high-grade VUR and in patients with anatomical abnormalities of the urogenital tract.

**Imaging**
Since no link has been proven between low-grade VUR and chronic kidney disease and no specific prophylactic or definitive therapy for VUR has been proven useful, there is no proven utility of finding low-grade VUR. As very few patients have high-grade VUR, and evidence for high grade VUR will usually be seen on ultrasonography, the cost of *routine* VCUG after first UTI (i.e. radiation, cost, and discomfort) are not outweighed by this unclear benefit. In the event that high-grade VUR is not detected on ultrasound or screened for with a VCUG, presumably recurrent UTIs will ensue, a VCUG will be indicated and the high grade VUR discovered and addressed appropriately.

**Consultation** should be considered but not limited to the following clinical scenarios:
- Management is uncertain in the face of high grade (> grade 3) VUR
- Renal scarring or structural abnormality
- Presence of renal or bladder stone
- Unusual organism isolated on urine culture
- Presence of elevated blood pressure unrelated to pain or discomfort, significant proteinuria on urinalysis or abnormal renal function

Such cases may benefit from consultation with Pediatric Urology, Pediatric Nephrology and/or Pediatric Infectious Disease as deemed appropriate.

**Special Considerations for Patients less than 2 months of Age:**
Although the AAP Clinical Practice Guideline does not specifically address treatment of UTI in this age group, significant evidence exists to suggest that it is reasonable to use the same general approach. Assuming other infections (such as meningitis or bacteremia) have been ruled-out, there is data to suggest early transition to oral antibiotics is appropriate. There has been no risk proven to occur to infants of this age group when transitioned early to oral antibiotics, however, risks of complications from PICC lines and other interventions associated with prolonged IV antibiotic use have been clearly demonstrated.

**Disclaimer:**
This guideline is not intended to replace clinical judgment. It is meant to assist physicians and other health care providers in clinical decision-making by describing a range of generally acceptable approaches to the diagnosis and management of UTIs. A particular patient’s circumstances should always be taken into account when a practitioner is deciding on a course of
management. Phoenix Children’s Hospital shall not be liable for direct, indirect, special, incidental or consequential damages related to the user’s decision to use the guideline.

REFERENCES:


**DEVELOPMENT AND APPROVAL, AND IMPLEMENTATION PROCESS**

Guideline Champions: Richard Engel, M.D. Ryan S. Bode, M.D., Hospitalist Division, Michael Ritchey, M.D., Urology

Approved by Medical Staff Hospitalist Section: September 2012, October 2013

Approved by Clinical Effectiveness Committee: October 2012, October 2013

Updated Literature Review and Revisions: September 2013

Updated 10/10/2013
Inclusions:

<table>
<thead>
<tr>
<th>ICD-9-CM Diagnosis</th>
<th>ICD-10-CM Translation Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>59010  Acute pyelonephritis without lesion of renal medullary necrosis</td>
<td>N10  Acute tubulo-interstitial nephritis</td>
</tr>
<tr>
<td>59080  Pyelonephritis, unspecified</td>
<td>N119  Chronic tubulo-interstitial nephritis, unspecified</td>
</tr>
<tr>
<td>5909   Kidney infection, unspecified</td>
<td>N12  Tubulo-interstitial nephritis, not specified as acute or chronic</td>
</tr>
<tr>
<td>5990   Urinary tract infection, site not specified</td>
<td>N135  Pyonephrosis</td>
</tr>
<tr>
<td>77182  Urinary tract infection of newborn</td>
<td>N159  Renal tubulo-interstitial disease, unspecified</td>
</tr>
<tr>
<td></td>
<td>N390  Urinary tract infection, site not specified</td>
</tr>
<tr>
<td></td>
<td>P393  Neonatal urinary tract infection</td>
</tr>
</tbody>
</table>
### Exclusions:

<table>
<thead>
<tr>
<th>ICD-9-CM Diagnosis</th>
<th>ICD-10-CM Translation Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>5935 Neplroplasia</td>
<td>N2003 Neplroplasia</td>
</tr>
<tr>
<td>5931 Hypeptrophy of kidney</td>
<td>N2881 Hypeptrophy of kidney</td>
</tr>
<tr>
<td>5932 Cyst of kidney, acquired</td>
<td>N281 Cyst of kidney, acquired</td>
</tr>
<tr>
<td>5933 Stricture/kinking of ureter</td>
<td>N136 Crossing vessel and stricture of ureter without hydronephrosis</td>
</tr>
<tr>
<td>5934 Ureter obstruction</td>
<td>N138 Other obstructive and reflux urethropy</td>
</tr>
<tr>
<td>5936 Hydronephrotex</td>
<td>N134 Hydronephrotex</td>
</tr>
<tr>
<td>5936 Postural proteinuria</td>
<td>R602 Orthostatic proteinuria, unspecified</td>
</tr>
<tr>
<td>59376 Vesicoureteral reflux unspecified or without reflux nphropathy</td>
<td>N1170 Vesicoureteral reflux, unspecified</td>
</tr>
<tr>
<td></td>
<td>N1171 Vesicoureteral reflux without reflux nphropathy</td>
</tr>
<tr>
<td>59371 Vesicoureteral reflux with reflux nphropathy, unilateral</td>
<td>N11721 Vesicoureteral reflux with reflux nphropathy without hydronephrotex, unilateral</td>
</tr>
<tr>
<td></td>
<td>N11731 Vesicoureteral reflux with reflux nphropathy with hydronephrotex, unilateral</td>
</tr>
<tr>
<td>59372 Vesicoureteral reflux with reflux nphropathy, bilateral</td>
<td>N11722 Vesicoureteral reflux with reflux nphropathy without hydronephrotex, bilateral</td>
</tr>
<tr>
<td></td>
<td>N11732 Vesicoureteral reflux with reflux nphropathy with hydronephrotex, bilateral</td>
</tr>
<tr>
<td>59373 Vesicoureteral reflux with reflux nphropathy, NOS</td>
<td>N11729 Vesicoureteral reflux with reflux nphropathy without hydronephrotex, unspecified</td>
</tr>
<tr>
<td></td>
<td>N11739 Vesicoureteral reflux with reflux nphropathy with hydronephrotex, unspecified</td>
</tr>
<tr>
<td></td>
<td>N139 Obstructive and reflux urethropy, unspecified</td>
</tr>
<tr>
<td>59351 Vascular disorder of kidney</td>
<td>N280 Ischemia and infarction of kidney</td>
</tr>
<tr>
<td>59382 Ureteral reflux</td>
<td>N2883 Other specified disorders of kidney and ureter</td>
</tr>
<tr>
<td></td>
<td>N2882 Megoureter</td>
</tr>
<tr>
<td></td>
<td>N2889 Other specified disorders of kidney and ureter</td>
</tr>
<tr>
<td>5938 Disorder of kidney and ureter, specified type</td>
<td>N2889 Disorder of kidney and ureter, unspecified</td>
</tr>
<tr>
<td></td>
<td>N29 Other disorders of kidney and ureter in diseases classified elsewhere</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>75310</td>
<td>Renal agenesis/dysgenesis</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>75311</td>
<td>Cystic kidney disease, unspecified</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>75312</td>
<td>Congenital single renal cyst</td>
</tr>
<tr>
<td>75313</td>
<td>Polycystic kidney, unspecified type</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>75314</td>
<td>Polycystic kidney, autosomal dominant</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>75315</td>
<td>Renal dysplasia</td>
</tr>
<tr>
<td>75316</td>
<td>Medullary cystic kidney</td>
</tr>
<tr>
<td>75317</td>
<td>Medullary sponge kidney</td>
</tr>
<tr>
<td>75319</td>
<td>Cystic kidney disease</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>75320</td>
<td>Unspecified obstructive defect of renal pelvis and ureter</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>75321</td>
<td>Congenital obstruction of uretero pelvic junction</td>
</tr>
<tr>
<td>75322</td>
<td>Congenital obstruction of uretero vesical junction</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>75323</td>
<td>Congenital ureterocele</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>75329</td>
<td>Obstructive defect of renal pelvis and ureter</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>7533</td>
<td>Congenital anomaly of kidney</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>7534</td>
<td>Congenital anomaly of ureter</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>------</td>
<td>-----------------------------------------------------------------</td>
</tr>
<tr>
<td>7535</td>
<td>Extrophy of urinary bladder</td>
</tr>
<tr>
<td>7536</td>
<td>Congenital atresia &amp; stenosis of urethra &amp; bladder neck</td>
</tr>
<tr>
<td>7537</td>
<td>Congenital anomaly of urachus</td>
</tr>
<tr>
<td>7538</td>
<td>Congenital anomaly of bladder/urethra</td>
</tr>
<tr>
<td>7539</td>
<td>Congenital anomaly of urinary system</td>
</tr>
<tr>
<td></td>
<td>*</td>
</tr>
<tr>
<td></td>
<td>Q6410 Extrophy of urinary bladder, unspecified</td>
</tr>
<tr>
<td></td>
<td>Q6411 Supravesical fissure of urinary bladder</td>
</tr>
<tr>
<td></td>
<td>Q6412 Clinical extrophy of urinary bladder</td>
</tr>
<tr>
<td></td>
<td>Q6419 Other extrophy of urinary bladder</td>
</tr>
<tr>
<td></td>
<td>Q642 Congenital posterior urethral valves</td>
</tr>
<tr>
<td></td>
<td>Q6431 Congenital bladder neck obstruction</td>
</tr>
<tr>
<td></td>
<td>Q6432 Congenital stricture of urethra</td>
</tr>
<tr>
<td></td>
<td>Q6433 Congenital stricture of urinary meatus</td>
</tr>
<tr>
<td></td>
<td>Q6439 Other atresia and stenosis of urethra and bladder neck</td>
</tr>
<tr>
<td></td>
<td>Q644 Malformation of urachus</td>
</tr>
<tr>
<td></td>
<td>Q6441 Renovesical fissure of urinary bladder</td>
</tr>
<tr>
<td></td>
<td>Q645 Congenital absence of bladder and urethra</td>
</tr>
<tr>
<td></td>
<td>Q646 Congenital diverticulum of bladder</td>
</tr>
<tr>
<td></td>
<td>Q647 Congenital malformation of bladder and urethra</td>
</tr>
<tr>
<td></td>
<td>Q6471 Congenital prolapse of urethra</td>
</tr>
<tr>
<td></td>
<td>Q6472 Congenital prolapse of urinary meatus</td>
</tr>
<tr>
<td></td>
<td>Q6473 Congenital urethronocal fistula</td>
</tr>
<tr>
<td></td>
<td>Q6474 Double urethra</td>
</tr>
<tr>
<td></td>
<td>Q6475 Double urinary meatus</td>
</tr>
<tr>
<td></td>
<td>Q6479 Other congenital malformations of bladder and urethra</td>
</tr>
<tr>
<td></td>
<td>Q648 Other specified congenital malformations of urinary system</td>
</tr>
<tr>
<td></td>
<td>Q649 Congenital malformation of urinary system, unspecified</td>
</tr>
<tr>
<td>ICD-9-CM Diagnosis</td>
<td>ICD-10-CM Translation Options</td>
</tr>
<tr>
<td>---------------------------------------------------------</td>
<td>-------------------------------------------------------------------</td>
</tr>
<tr>
<td>74100 Spina bifida, with hydrocephalus, unspecified region</td>
<td>G054 Unspecified spina bifida with hydrocephalus</td>
</tr>
<tr>
<td></td>
<td>G056 Spina bifida, unspecified</td>
</tr>
<tr>
<td></td>
<td>G0761 Arnold-Chiari syndrome with spina bifida</td>
</tr>
<tr>
<td></td>
<td>G0762 Arnold-Chiari syndrome with hydrocephalus</td>
</tr>
<tr>
<td></td>
<td>G0763 Arnold-Chiari syndrome with spina bifida and hydrocephalus</td>
</tr>
<tr>
<td>74101 Spina bifida, with hydrocephalus, cervical region</td>
<td>G056 Cervical spina bifida with hydrocephalus</td>
</tr>
<tr>
<td>74102 Spina bifida, with hydrocephalus, dorsal (thoracic) region</td>
<td>G051 Thoracic spina bifida with hydrocephalus</td>
</tr>
<tr>
<td>74103 Spina bifida, with hydrocephalus, lumbar region</td>
<td>G052 Lumbar spina bifida with hydrocephalus</td>
</tr>
<tr>
<td></td>
<td>G053 Sacral spina bifida with hydrocephalus</td>
</tr>
<tr>
<td>74198 Spina bifida, without mention of hydrocephalus</td>
<td>G054 Sacral spina bifida without hydrocephalus</td>
</tr>
<tr>
<td>74190 Spina bifida, without mention of hydrocephalus, unspecified region</td>
<td>G056 Spina bifida without hydrocephalus</td>
</tr>
<tr>
<td></td>
<td>G0761 Arnold-Chiari syndrome without spina bifida or hydrocephalus</td>
</tr>
<tr>
<td>74191 Spina bifida, without mention of hydrocephalus, cervical region</td>
<td>G055 Cervical spina bifida without hydrocephalus</td>
</tr>
<tr>
<td>74192 Spina bifida, without mention of hydrocephalus, dorsal (thoracic) region</td>
<td>G056 Thoracic spina bifida without hydrocephalus</td>
</tr>
<tr>
<td>74193 Spina bifida, without mention of hydrocephalus, lumbar region</td>
<td>G057 Lumbar spina bifida without hydrocephalus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-9-CM Diagnosis</th>
<th>ICD-10-CM Translation Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>V4451 Cutaneous-vesicostomy status</td>
<td>Z9351 Cutaneous-vesicostomy status</td>
</tr>
<tr>
<td>V4452 Appendice-vesicostomy status</td>
<td>Z9352 Appendice-vesicostomy status</td>
</tr>
<tr>
<td>V4459 Cystostomy status</td>
<td>Z9359 Other cystostomy status</td>
</tr>
<tr>
<td>V446 Status of artificial opening of urinary tract</td>
<td>Z936 Other artificial openings of urinary tract status</td>
</tr>
</tbody>
</table>
Fever Codes:

<table>
<thead>
<tr>
<th>ICD-9-CM Diagnosis</th>
<th>ICD-10-CM Translation Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>7784</td>
<td>P812 Environmental hyperthermia of newborn</td>
</tr>
<tr>
<td></td>
<td>P816 Other specified disturbances of temperature regulation of newborn</td>
</tr>
<tr>
<td></td>
<td>P912 Disturbance of temperature regulation of newborn, unspecified</td>
</tr>
<tr>
<td>78060</td>
<td>R502 Drug induced fever</td>
</tr>
<tr>
<td></td>
<td>R503 Fever, unspecified</td>
</tr>
<tr>
<td>78081</td>
<td>R501 Fever presenting with conditions classified elsewhere</td>
</tr>
</tbody>
</table>
### N Ped UTI SS

#### Nursing
- In And Out Straight Cath (PCS)
  - Today Now As Directed (See Comments)

#### Imaging
- US Renal Cmp (US)
  - Today Now
  - Bilateral Kidney

#### Medication
**Parenteral**
- Cefotaxime Inj (ped) (Claforan Inj (ped))
  - MC IVPB q8h
    - Sodium Chloride 0.9%(Normal Saline) 25 ML
  - DOSE INSTRUCTIONS:
    - 50 mg/kg/dose
  - COMMENTS:
    - Infuse over 30 min

- Cefotaxime Inj (ped) (Claforan Inj (ped))
  - 1000 MG IVPB q8h
    - Sodium Chloride 0.9%(Normal Saline) 50 ML
  - DOSE INSTRUCTIONS:
    - 50 mg/kg/dose, max 1000 mg
  - COMMENTS:
    - Dilute the 1000 mg vial with 2.1 mL of NS or 1% Lidocaine solution to a final concentration of 350 mg/mL

- ceTriaxone Inj (ped) (Rocephin Inj (ped))
  - MG IVPB q24h
    - Sodium Chloride 0.9%(Normal Saline) 0 ML
  - DOSE INSTRUCTIONS:
    - 50 mg/kg/dose, max 1000 mg
    - COMMENTS:
      - 50 mg/kg/dose, max 1000 mg

#### Link to Problem List
- Problem List (PROB)
  - Today Now

#### Order Set Tracking - No Action Needed
- ZTAG-N-Ped-UTI (TAG)
  - Today Now
Known Allergies: __________________________

Admission (check all that apply and complete)
- Notify H.O. of patient’s arrival to floor to obtain additional orders, including maintenance medications
- Notify attending physician of patient’s location: □ in a.m. □ upon arrival to floor
- FIS patient (call ext. 4-5455 for room notification)
- Inpatient admit to ______ floor/unit to Dr. ______ Service ________
- Place in observation ______ floor/unit to Dr. ______________________ Service __________________
- Patient’s PCP

Condition: □ Guarded □ Fair □ Stable
Reason for admission: □ Fever □ Vomiting □ Flank Pain □ Other, specify: _________________

Diagnosis (check all that apply and complete)
- Urinary tract infection
- Other, specify: __________________________

Isolation Precautions (check all that apply and complete)
- Contact isolation
- Other, specify: __________________________

Activity (check all that apply and complete)
- Crib with side rails
- Bed rest
- Ad lib
- Other, specify: __________________________

Diet/Nutrition (check all that apply and complete)
- NPO
- Breastfeeding
- Age-appropriate diet
- Breastmilk/Formula (complete Breastmilk/Formula Order Form DTY 1581)
- Other, specify: __________________________

Vital Signs (check all that apply and complete)
- Routine vital signs
- Other, specify: __________________________

Nursing (check all that apply and complete)
- I & O every shift
- Weigh daily
- Start peripheral IV

Laboratory Tests (check all that apply if not already completed)
- Urinalysis with micro
- Urine culture (Risk factors: Males < 6 months; 6-12 months & uncircumcised; Females < 24 months)
  □ Cath □ Clean catch
  NOTE: Non-toilet trained children via catheter; toilet trained children via midstream clean catch.
- Gentamicin peak and trough levels with the third dose of gentamicin (generally ordered for therapy > 48 h and for patients with renal dysfunction)

Diagnostic Imaging (check all that apply)
- Renal ultrasound (RUS)
- Voiding cystourethrogram 24-48 h post fever if indicated
  NOTE: Indicated for with positive RUS or the following risk factors: sibling with reflux, decreased renal function, proteinuria, or hypertension.
Date/Time: 

Patient Wt: 

Age: 

First Febrile Urinary Tract Infection 

IP Order Set 

Page 2/2 

Medications (check all that apply and complete) 

Per Protocol 

☐ Procedural Pain Protocol 
☐ Acetaminophen per Protocol 
☐ PO 
☐ PR 
☐ Flush per Protocol- Complete Order Form PHM 3098 

Intravenous Fluids 

☐ D5 - 1/4 NS IV at _____ mL/h 
☐ D5 - 1/4 NS + 2 mEq KCl/100 mL IV at _____ mL/h 

NOTE: 2 mEq KCl/100 mL should only be added after first void. 
☐ Other, specify: 

Empiric Parenteral Therapy 

☐ CefOTAXime______ mg IV every _____ h 

(Usual dose: Infants > 2 months: 50-75 mg/kg/dose every 8 h; 
1-12 years and ≤ 50 kg: 50-75 mg/kg/dose every 8 h; 
> 50 kg: 1-2 grams/dose every 8 h; MAX: 2 grams/dose) 
☐ Gentamicin Sulfate*______ mg IV every _____ h 

(Usual dose: 2.5 mg/kg/dose every 8 h; MAX: 3 mg/kg/dose, not to exceed 120 mg/dose) 

*NOTE: Not typically first line monotherapy; peak and trough levels generally ordered for therapy > 48 h and for patients with renal dysfunction. 

Directed Parenteral Therapy (based on lab results) 

☐ CefOTAXime______ mg IV every _____ h 

(Usual dose: Infants > 2 months: 50-75 mg/kg/dose every 8 h; 
1-12 years and < 50 kg: 50-75 mg/kg/dose every 8 h; 
> 50 kg: 1-2 grams/dose every 8 h; MAX: 2 grams/dose) 
☐ Ampicillin______ mg IV every _____ h 

(Usual dose: 50 mg/kg/dose every 6 h; MAX: 100 mg/kg/dose, not to exceed 2 grams/dose or 2 grams/DAY) 
☐ Gentamicin Sulfate†______ mg IV every _____ h 

(Usual dose: 2.5 mg/kg/dose every 8 h; MAX: 3 mg/kg/dose, not to exceed 120 mg/dose) 
†Check peak and trough levels with the third dose – see laboratory section to order tests (generally ordered for therapy > 48 h and for patients with renal dysfunction) 

Other Medications 

☐ Ibuprofen______ mg PO every _____ h PRN temp greater than ______ 

(Usual dose: 5-10 mg/kg/dose every 6-8 h; MAX: 40 mg/kg/DAY, not to exceed 600 mg/dose) 

NOTE: Avoid if abnormal renal function. 

1. 
2. 
3. 

Other Orders (check all that apply and complete) 

☐ Other, specify: 

Discharge Planning (check all that apply and complete) 

☐ Confirm transportation home 
☐ Assess for discharge criteria: 
  - Oral feedings tolerated at a level to maintain hydration 
  - Fever defervescing or afebrile 

☐ Other, specify: 

Other, specify: 

Other, specify: 

Other, specify: 

Other, specify:
Clinical Algorithm for Children with First Febrile Urinary Tract Infection (UTI)

Begin

History and physical indicative of UTI

Yes

Obtain specimen for analysis (dipstick or urinalysis) & urine culture by cath or clean catch

UA + for LE or nitrates

OR microscopy + for WBC or bacteria

Initiate empiric antimicrobial therapy

(See antibiotic table)

Well-appearing and tolerating oral fluids

Yes

Urine culture +

RUS abnormal

OR

the following risk factors present:

- sibling with reflux (VUR)
- decreased renal function
- proteinuria
- hypertension

Schedule VCUG†

(see antimicrobial susceptibility results to choose the most appropriate, narrow spectrum agent)

NOTE: Antibiotics should be discontinued if the culture is negative and the child has NOT been treated with antibiotics prior to obtaining the urine culture.

OFF algorithm

Search for alternate source of infection and follow up appropriately

- Consider 23 hour observation or admission
- Continue antimicrobial therapy
- Follow culture and adjust therapy based on antimicrobial susceptibility results to choose the most appropriate, narrow spectrum agent

NOTE: Antibiotics should be discontinued if the culture is negative and the child has NOT been treated with antibiotics prior to obtaining the urine culture.

**Discharge Criteria

- tolerating oral intake
- patient/caregiver discharge teaching complete on:
  - discharge care
  - s/sx of concern
  - risk of recurrence
  - proper perineal care
  - documentation of scheduled PCP follow-up
  - if admitted, decreasing trend in daily maximal temperatures combined with physician discretion

Schedule VCUG†

(possible as outpatient)

- PCP to follow up VCUG results for VUR
- Consult Urology if surgical intervention is being considered
- Consult Nephrology for children with Grade IV and V VUR

Meets discharge criteria**

OFF algorithm

Consider additional antibiotics and search for alternate source of infection; follow up appropriately

Discharge home on appropriate antibiotics

Abbreviations:

- UA – urinalysis
- LE – leukocyte esterase
- Cath – transurethral catheterization
- IV – intravenous
- RUS – renal ultrasound
- VCU – voiding cystourethrogram

†VCUG may be performed as soon as fever is decreasing and culture specific antibiotics are in use. There is no need to perform an additional urinalysis if the patient is on antibiotics.

**Discharge Criteria

- tolerating oral intake
- patient/caregiver discharge teaching complete on:
  - discharge care
  - s/sx of concern
  - risk of recurrence
  - proper perineal care
  - documentation of scheduled PCP follow-up
  - if admitted, decreasing trend in daily maximal temperatures combined with physician discretion

Abbreviations:

- UA – urinalysis
- LE – leukocyte esterase
- Cath – transurethral catheterization
- IV – intravenous
- RUS – renal ultrasound
- VCU – voiding cystourethrogram

†VCUG may be performed as soon as fever is decreasing and culture specific antibiotics are in use. There is no need to perform an additional urinalysis if the patient is on antibiotics.

Inclusion Criteria

- 2 months - 12 years
- prepubertal
- first episode of UTI
- febrile

Exclusion Criteria

- afebrile
- conditions in which immunity may be compromised (transplant recipient or chronic renal insufficiency/kidney disease)
- known major genitourinary anomalies
- toxic- appearing
- sepsis with shock or meningitis
- ICU admission
- other severe comorbid conditions

Abbreviations:

- UA – urinalysis
- LE – leukocyte esterase
- Cath – transurethral catheterization
- IV – intravenous
- RUS – renal ultrasound
- VCU – voiding cystourethrogram

\*Admission Criteria

- unable to tolerate oral fluids (requires IV fluids for hydration)
- failed outpatient therapy (requires IV antibiotics)

Abbreviations:

- UA – urinalysis
- LE – leukocyte esterase
- Cath – transurethral catheterization
- IV – intravenous
- RUS – renal ultrasound
- VCU – voiding cystourethrogram
UTI Management Beyond the AAP Guideline: New Evidence, Current Controversies, and Quality Improvement

Richard Engel, MD
VIP Q-UTI Project Co-Chair
Hospitalist, Phoenix Childrens Hospital
Clinical Assistant Professor
University of Arizona College of Medicine – Phoenix

Brian Pate, MD
VIP Q-UTI Project Co-Chair
Chair, Department of Pediatrics
Associate Professor of Pediatrics
Kansas University School of Medicine-Wichita
The mission of the VIP Network is to be a healthcare stewardship organization which improves the value of care delivered to any pediatric patient in a hospital bed by helping providers implement clinical practice guidelines and other best practices, with a special focus on eliminating harm and waste caused by overutilization.

VIP Provides:
- Network
- Measures
- Strategies
- Tools
- Resources
• 43 States
• 3 other countries
• 160 hospital settings
• 215 members

U.S Virgin Islands

New Zealand

Pakistan
AAP UTI Guideline 2011

- Developed by subcommittee that included experts in:
  - academic general pediatrics
  - epidemiology and informatics
  - pediatric ID
  - pediatric nephrology
  - pediatric radiology
  - pediatric urology

- Reviewed by 7 committees, 1 council, 9 sections in AAP, and 5 external organizations

- As with all guidelines, they are to be used to assist the clinician in decision-making, not to replace clinical judgment

- Apply only to children 2-24 months of age
AAP UTI Guidelines 2011

- Action Statement 4
  - Oral and Parenteral antibiotics are equally efficacious. Practical considerations should be the basis of choice (i.e. tolerating PO, etc.)
    - Evidence Quality A

- Duration 7-14 days
  - Evidence Quality B
AAP UTI Guidelines 2011

Action Statement 3

- to establish diagnosis there should be BOTH
  - 1. Positive UA (pyuria +/- nitrites/L.E.) AND
  - 2. $\geq 50,000$ CFU’s of uropathogen in culture from cath or suprapubic specimen

  - Evidence Quality C (observational studies)

- Presence of pyuria in UA is key (along with clinical picture) to distinguishing true UTI from asymptomatic bacteriuria
AAP UTI Guidelines 2011

- Action Statement 5
  - Febrile infants with UTIs should undergo Renal US
    - Evidence Quality C
  - 2-3% false-positive results worth it given RUS is non-invasive and has potential for finding correctable abnormalities in 1-2% of patients
Action Statement 6

VCUG should not be performed *routinely* after first febrile UTI unless RUS abnormal or in other ‘atypical or complex clinical circumstances’
- Evidence Quality B

VCUG should be done with 2\textsuperscript{nd} episode febrile UTI
- Evidence Quality X
Evidence Update post AAP CPG

- **Methods:**
  - Lit searches with the help of PCH Librarian, Kathy Zeblisky
  - **Resources:** Medline, Cochrane Database, Web of Science, National Guidelines Clearinghouse
  - **Search:** UTI in children, post September 2011
  - **Results:** 123 total articles, 19 reviewed in depth

- **Themes/Controversies**
  - Imaging/Prophylaxis
  - Risk stratification using inflammatory markers, etc
  - Compare AAP CPG with other Guidelines
  - Bacteremia
  - How to manage infants <2mos
Controversies: Imaging/prophylaxis

The Evidence Against Prophylaxis pre AAP CPG

- The use of prophylaxis began in 1950’s based on little data.
  - No studies had proven a benefit for low-grade reflux
  - Swedish Reflux Trial did show benefit, but study only included high-grade (and Pt’s w/ duplications not excluded)

- Several studies called into question benefits of prophylaxis

- AAP committee combined data from 6 RCT—that meta-analysis (with 1091 infants) did not detect benefit of ppx for Grades 1-4 VUR. Grade V—too few to be statistically significant.
Controversies: Imaging/prophylaxis
Section on Urology response

SOU: VCUG after first febrile UTI should still be an accepted option

- Studies cited have confounders
  - some use data from bag specimens
  - circumcision status not accounted for
  - no mention of bowel/bladder habits
  - no mention of compliance

- Some literature shows surgical options can prevent recurrent UTIs in grade III and grade IV VUR

- New Guideline will result in missing VUR and/or scarring
AAP response to SOU:

- Diminish importance of confounding factors identified by SOU
- Goal is “to provide proven clinical benefit while keeping harm at a minimum”
  - Benefit of finding VUR after first episode UTI not clear
  - Small harm (radiation, discomfort, cost) to lots of children vs. possible but unclear benefit to a few
Controversies: Imaging/prophylaxis

  - Reviewed 1576 cases in literature of CKD—None where childhood UTIs could be identified as main cause
  - Monitored 366 patients with CKD at Oulu University Hospital in Finland
    - 308 had specific noninfectious etiology
    - Of remaining, 13 had history of childhood UTIs—all of which had abnormalities detectable by RUS
    - 3 patients had recurrent UTIs in childhood which may have contributed to CKD but all had dysplasia already on first imaging (hard to determine which came first)
  - In the absence of structural kidney abnormalities (i.e. normal RUS), recurrent UTI’s cause, at most, 0.3% of CKD
Controversies: Imaging/prophylaxis

  - Retrospective Lit Review 1980-2011, including 20 cohorts of children
  - No clear data to establish long-term consequences following UTI’s in Childhood
    - Only 0.4% of children who presented with normal renal function went on to have decreased renal function later
    - Low risk HTN
    - Little data available seems to exclude growth problems or pregnancy problems such as eclampsia
Controversies: Imaging/prophylaxis

- Hoberman, et al. NEJM. May 2014. Randomized Intervention for Children with VUR. “RIVUR Trial”

  **Methods:**
  
  - 2yr, multi-site (19 sites), randomized, placebo-controlled trial
  - 607 children with VUR dx after 1st or 2nd febrile or symptomatic UTI
  - Evaluated efficacy of bactrim ppx in preventing recurrences, effect on renal scarring and antimicrobial resistance
Controversies: Imaging/prophylaxis

- Results:
  - Prophylaxis decreased recurrence rate by about half
    - 39/302 in ppx group vs. 72/305 in placebo
  - Renal scarring did not differ between the 2 groups
  - Treatment group had significantly higher rate of resistant organisms
    - 63% in ppx group vs. 19% in placebo
Controversies: Imaging/prophylaxis

- **Conclusion**
  - "As long as evidence supporting the benefit of ppx was dubious, the recommendation of a watchful waiting approach, without performing a VCUG, seemed reasonable because the imaging findings would not affect the nature of the treatment. However, our findings that antimicrobial ppx was associated with a reduced risk of recurrence may warrant reconsideration."
  - **Alternative view:**
    - Need ppx for 9 children with VUR X 2yrs to prevent 1 UTI
      - Or…6570 days of antibiotic to prevent one 7-14 day course!
Controversies: Imaging/prophylaxis

- Other Post-RIVUR Guidelines:
  - Canadian Paediatric Society
    - Ppx not routinely recommended. May consider for grades IV or V VUR or with significant urological anomaly. “An increasing risk for antibiotic resistance may soon negate the benefits even in these cases”
    - Change or stop ppx if pt has recurrent UTI with resistant organism

Controversies: Imaging/prophylaxis

- Other Post-RIVUR Guidelines:
  - Asian Pacific Society of Nephrology (Australia)
    - Recommend more restrictive imaging than AAP
    - RUS after 1st UTI only if no pre-natal US in 2nd or 3rd trimester or if bacteremia, <3mos age, atypical organism, or other atypical/severe circumstances
    - VCUG with recurrent UTI only or in boys with abnormal RUS after first UTI

Controversies: Concurrent bacteremia

- Not directly addressed by AAP CGP

- Roman, H; Chang, P; Schroeder, A. Diagnosis and Management of Bacteremic UTI in infants
  - Hospital Pediatrics. 2015;5:1
  - Retrospective cross sectional design to determine prevalence and characteristics of pts with UTI with concurrent bacteremia
  - Reviewed 1379 cases of UTI at Santa Clara Valley Medical Center 1998-2012 in pts <1yr old. Blood Cx’s obtained in 52% of cases
Controversies: Concurrent bacteremia

- Roman, et. al. results:
  - Prevalence of concurrent bacteremia was 8% (among cases where blood Cx obtained)
  - No significant differences in clinical presentation between those with bacteremia and those in paired cohort without bacteremia
  - Bacteremic infants received longer parenteral courses (mean 6.7 days vs 2.4 days)
  - Treatment highly variable but outcomes excellent regardless of length of course of abx or whether IV
Controversies: Infants <2mo

- Accuracy of Urinalysis in infants <3mos:
  - Collected data from 276 infants with bacteremic UTI
    - Sensitivity of L.E. was 97.6%; pyuria: 96%
  - Spectrum bias (since these patients all had bacteremia)?
  - Or inclusion of faulty gold standards in previous studies (contaminants or asymptomatic bacteriuria)?
    - Editorial, Roberts, K. Liquid Gold and the Problem of Gold Standards
Controversies: Infants <2mo

VIP Q-UTI includes these metrics <2mo:

- Positive urinalysis: Goal 90%
- Catheterized specimen used for diagnosis: Goal 95%
- Renal Ultrasound obtained after first febrile UTI: Goal 90%
- Other data to be collected as benchmarking in this age group
Controversies: Risk Stratification with inflammatory markers, etc.

- The Procalcitonin (PCT) Issue
  - Several recent studies exploring its ability to predict VUR or scarring
      - 272 children <2yrs underwent RUS, DMSA, VCUG, PCT.
      - Sensitivity for PCT >1 to predict scarring was 94% with negative predictive value 95%
Controversies: Risk Stratification with inflammatory markers, etc.


  **Method:** Review and meta-analysis of individual patient data cohorting all patients who had DMSA and PCT

  **Results:**
  - 1011 patients from 18 studies
  - PCT >0.5 predicted scarring with 79% sensitivity; 50% specificity
  - More robust predictor than CRP, WBC

**Methods:**

- Performed meta-analysis extracting individual patient data from cohort studies, creating a cohort of 1280 infants and children
- Examined association between predictor variables and the development of renal scarring
- Assessed 3 models:
  1. Fever, non e.coli organism, RUS
  2. Model 1 + inflammatory markers (including PCT)
  3. Model 2 + VCUG
Controversies: Risk Stratification with inflammatory markers, etc.

Results:

- 15.5% (199/1280) had renal scarring
- Model 1 predicted 45% of patients with scarring (2 or more features)
- Model 2 only slightly more predictive
- Model 3:
  - Presence of Grade III or IV VUR highly predictive of scarring (69%) but only occurred in 4% of children
We can improve...

  - **Objective:** to decrease those with normal RUS from undergoing VCUG from 92% of in-patients and 100% in ED to 5% for both
  - **Results:**
    - 1st UTI with normal RUS, **VCUG rate decreased from 92% to 0% in 1 month!**
      - 100% to 40% within 4mo in ED
    - Rates sustained for 12mo
    - EHR was most impactful intervention
**Q-UTI Project Metrics**

**Antibiotic Treatment Duration**
- Total antibiotic treatment duration (7-14 days)
  - Goal (patients 7 – 59 days): Benchmarking only
  - Goal (patients 2 – 24 months): ≥95%

**IV antibiotics prescribed at discharge**
- Number of patients prescribed IV antibiotics after discharge
  - Goal (patients 7 – 59 days): Benchmarking only
  - Goal (patients 2 – 24 months): ≤5%
Q-UTI Metrics Cont...

**Urine Collection Method**
- Percent of diagnostic urine cultures obtained via cath/SPA and documented for all patients
  - Goal: ≥95%

**Blood Culture Utilization**
- Percentage of patients with blood cultures obtained during admission for all patients
  - Goal: Benchmarking only

**Concordant Blood Cultures**
- Percentage of obtained blood cultures positive with same pathogen as urine culture for all patients
  - Goal: Benchmarking only

**Diagnostic Urinalysis**
- Percent of abnormal UAs used for diagnosis
  - Goal: ≥90% (patients 7 – 59 days)
  - Goal: ≥95% (patients 2-24 months)
Q-UTI Metrics Cont...

50K CFU Criteria on Culture
- Percent diagnostic urine cultures made using a culture of ≥50K CFU with a single uropathogen
  - Goal (patients 7 – 59 days): Benchmarking only
  - Goal (patients 2 – 24 months): ≥95%

Voiding Cystourethrogram (VCUGs)
- Rate of VCUGs in patients without abnormal ultrasound
  - Goal (patients 7 – 59 days): Benchmarking only
  - Goal (patients 2 – 24 months): ≤5%

Renal Ultrasound (RUS)
- Rate of RUS in patients diagnosed with first time UTI for all patients
  - Goal: ≥90%

Prophylactic Antibiotics
- Patients prescribed prophylactic antibiotics at discharge
  - Goal (patients 7 – 59 days): Benchmarking only
  - Goal (patients 2 – 24 months): ≤5%