



Reaffirmation of AAP Clinical Practice Guideline: The Diagnosis and Management of the Initial Urinary Tract Infection in Febrile Infants and Young Children 2–24 Months of Age

SUBCOMMITTEE ON URINARY TRACT INFECTION

It is the policy of the American Academy of Pediatrics to reassess clinical practice guidelines (CPGs) every 5 years and retire, revise, or reaffirm them. The members of the urinary tract infection (UTI) subcommittee who developed the 2011 UTI CPG¹ have reviewed the literature published since 2011 along with unpublished manuscripts and the status of some clinical trials still in progress. With this article, we reaffirm the 2011 UTI CPG and provide an updated review of the supporting evidence. For the convenience of the reader, we reiterate the 7 Key Action Statements here to obviate the need to consult the 2011 UTI CPG, although interested readers may want to review the text of the guideline¹ and/or its accompanying technical report.²

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 is administered; the specimen needs to be obtained through catheterization or suprapubic aspiration (SPA), because the diagnosis of UTI cannot be established reliably through culture of urine collected in a bag (evidence quality: A; strong recommendation).

Comment

A key to an accurate diagnosis of UTI is obtaining a sample of urine for culture with minimal contamination before starting antimicrobial

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The recommendations in this practice 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.

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

DOI: 10.1542/peds.2016-3026

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

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FINANCIAL DISCLOSURE: The authors have indicated they do not have a financial relationship relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: AAP SUBCOMMITTEE ON URINARY TRACT INFECTION. Reaffirmation of AAP Clinical Practice Guideline: The Diagnosis and Management of the Initial Urinary Tract Infection in Febrile Infants and Young Children 2–24 Months of Age. *Pediatrics*. 2016;138(6):e20163026

agents. Urine collected in a bag or via a clean catch method is suitable for urinalysis (see Action Statement 2, Option 2), but such specimens (especially urine collected in a bag) are less appropriate for culture. If a culture obtained by bag is positive, the likelihood of a false positive is extremely high, so the result must be confirmed by culturing urine obtained by a more reliable method; if an antimicrobial agent is present in the urine, the opportunity for confirmation is likely to be lost.

Although samples of urine obtained by transurethral catheterization may be contaminated by urethral flora, meticulous technique can reduce this possibility. To avoid contamination, 2 practical steps should be implemented: (1) the first few milliliters obtained by catheter should be discarded (allowed to fall outside of the sterile collecting vessel) and only the subsequent urine cultured; and (2) if the attempt at catheterization is unsuccessful, a new, clean catheter should be used (aided, in girls, by leaving the initial catheter in place as a marker).

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.

Action Statement 2a. If the clinician determines the febrile infant to have a low likelihood of UTI (see text), then clinical follow-up monitoring without testing is sufficient (evidence quality: A; strong recommendation).

Action Statement 2b. If the clinician determines that the febrile infant is not in a low-risk group (see below), then there are 2 choices (evidence quality: A; strong recommendation).

Option 1 is to obtain a urine specimen through catheterization or SPA for culture and urinalysis.

Option 2 is to obtain a urine specimen through the most convenient means and to perform a urinalysis. If the urinalysis results suggest a UTI (positive leukocyte esterase test results or nitrite test or microscopic analysis results for leukocytes or bacteria), then a urine specimen should be obtained through catheterization or SPA and cultured; if urinalysis of fresh (less than 1 hour since void) urine yields negative leukocyte esterase and nitrite results, then it is reasonable to monitor the clinical course without initiating antimicrobial therapy, recognizing that a negative urinalysis does not rule out a UTI with certainty.

Comment

When the patient's degree of illness does not warrant immediate antimicrobial treatment and the risk of UTI is extremely low, the patient may be observed without assessing the urine. (The risk assessment tables in the 2011 UTI CPG have been simplified into algorithm form.³) If there is a low but real risk of infection, then either the best possible specimen should be obtained for urinalysis and culture, or a sample of urine obtained by a convenient method and a judgment made about culturing the urine dependent on the findings of the urinalysis or dipstick. A positive urinalysis provides sufficient concern to mandate a properly obtained urine specimen. This 2-step process (Option 2) is not only suitable for office practice but has been demonstrated to be feasible and beneficial in a busy pediatric emergency department, with the catheterization rate decreasing from

63% to fewer than 30% without increasing length of stay or missing UTIs.⁴

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 (cfu) per milliliter of a uropathogen cultured from a urine specimen obtained through transurethral catheterization or SPA (evidence quality: C; recommendation).

Comment

The thrust of this key action statement is that the diagnosis of UTI in febrile infants is signaled by the presence of both bacteriuria and pyuria. In general, pyuria without bacteriuria is insufficient to make a diagnosis of UTI because it is nonspecific and occurs in the absence of infection (eg, Kawasaki disease, chemical urethritis, streptococcal infections). Likewise, bacteriuria, without pyuria is attributable to external contamination, asymptomatic bacteriuria, or, rarely, very early infection (before the onset of inflammation). Non-*Escherichia coli* isolates are less frequently associated with pyuria than *E coli*,⁵ but the significance of this association is not clear at present. Non-*E coli* uropathogens are of concern because they are more likely to result in scarring than *E coli*,⁶ but animal studies demonstrate the host inflammatory response to be what causes scarring rather than the presence of organisms.⁷ Moreover, the rate of asymptomatic bacteriuria is sufficient to account for the lack of association with pyuria.

The remaining question is what constitutes "significant" bacteriuria and "significant" pyuria. In 1994,

by using single versus multiple organisms to distinguish true UTI from contamination, 50 000 cfu/mL was proposed as the appropriate threshold for specimens obtained by catheterization,⁸ recommended in the 2011 UTI CPG and implemented in the Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) trial.⁹ Lower colony counts are sufficient if the urine specimen is obtained by SPA and, thus, less likely to be contaminated, but most (80%) cases of UTI documented with urine obtained by SPA have 10⁵ cfu/mL or more. Colony counts lower than 50 000 cfu/mL are currently being considered for the diagnosis of UTI.¹⁰ If 10 000 cfu/mL coupled with symptoms (eg, fever) and evidence of inflammation (pyuria) proves both sensitive and specific, this threshold would be of particular assistance to clinicians who use laboratories that do not specify colony counts between 10 000 and 100 000 cfu/mL and, thereby, make the criterion of 50 000 cfu/mL difficult to use.

Significant pyuria is ≥ 10 white blood cells/mm³ on an "enhanced urinalysis" or ≥ 5 white blood cells per high power field on a centrifuged specimen of urine or any leukocyte esterase on a dipstick.

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).

Comment

Basing the choice of an initial antimicrobial agent on local sensitivity patterns can be difficult because applicable information may not be available. Whether the child has received antimicrobial therapy in the recent past should be considered. This exposure constitutes a risk factor for resistance to the recently prescribed antimicrobial. Further delineation of treatment duration has not been forthcoming, but a randomized controlled trial is currently under way comparing the effectiveness of 5 days versus 10 days of treatment.¹¹

Note: The dose of ceftriaxone in Table 2 should be 50 mg/kg, every 24 h.

ACTION STATEMENT 5

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

Comment

As noted in the 2011 CPG, it is important that the study be a renal and bladder ultrasonogram, not a limited renal ultrasonogram. Ideally, the patient should be well-hydrated for the examination and the bladder should be evaluated while distended. Concern has been raised that RBUS is not effective to detect vesicoureteral reflux (VUR), as it is frequently normal in infants with low-grade VUR and even in some who have high-grade VUR. Moreover, nonspecific RBUS findings, such as mild renal pelvic or ureteral distention, are common and are not necessarily associated with reflux. However, low-grade VUR is generally not considered of concern for renal damage, and most studies (other than the RIVUR trial⁹) have demonstrated continuous antimicrobial prophylaxis

(CAP) to lack benefit in this group.^{1,2} Although RBUS is not invariably abnormal in infants with grades IV and V VUR, it does identify most, and, of particular importance, an abnormal RBUS is a major risk factor for scarring.⁶

ACTION STATEMENT 6

Action Statement 6a. Voiding cystourethrography (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).

Comment

For decades, UTIs in infants were considered harbingers of underlying anatomic and/or physiologic abnormalities, so RBUS and VCUG were recommended to be performed routinely. VUR was a particular concern; CAP was assumed to be effective in preventing UTI and became standard practice when VUR was discovered. In the years leading up to the 2011 guideline, randomized controlled trials of CAP were performed. Authors of the 6 studies published in 2006-2010 graciously provided data to the guideline committee, permitting a meta-analysis of data specifically targeting febrile infants 2 to 24 months of age. CAP was not demonstrated to be effective, so the need to identify VUR by routine voiding cystourethrography was discouraged.^{1,2} A recent large trial in the United States, the RIVUR trial,

concluded that CAP was of benefit, but, to prevent 1 UTI recurrence required 5840 doses of antimicrobial and did not reduce the rate of renal scarring.⁹

Since the publication of the 2011 guideline, multiple studies have demonstrated that abnormalities are missed by the selective imaging recommended in the guideline; however, there is no evidence that identifying these missed abnormalities is of sufficient clinical benefit to offset the cost, discomfort, and radiation.¹² Compared with performing the full array of imaging tests, the radiation burden incurred with the application of the guideline has been calculated to be reduced by 93%.¹³ Moreover, in population studies, the significance of VUR and the value of treating VUR have been questioned.^{14,15}

The authors of the RIVUR trial and its companion study, Careful Urinary Tract Infection Evaluation, have called attention to bowel/bladder dysfunction (BBD) as a major risk factor for UTI recurrences and recognize that, in children who have a UTI recurrence, evaluation for BBD (ie, constipation), rather than for VUR, can be performed by nonspecialists and does not incur high cost, cause discomfort, or require radiation.¹⁶ BBD has long been underappreciated and deserves greater consideration.

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).

Comment

Prompt treatment is of clinical benefit to the child with the acute infection. What has been controversial is the definition of “prompt” and the relationship to renal scarring. A recent study identified that the median time to treatment was shorter in infants who did not incur a scar than in those who did (48 vs 72 hours). The study also noted that the rate of scarring increased minimally between days 1 and 2 and between days 2 and 3 but was much higher thereafter.¹⁷

SUBCOMMITTEE ON URINARY TRACT INFECTION, 2009-2011

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ABBREVIATIONS

BBD: bowel/bladder dysfunction
CAP: continuous antimicrobial prophylaxis
cfu: colony-forming units
CPG: clinical practice guideline
RBUS: renal and bladder ultrasonography
RIVUR: Randomized Intervention for Children with Vesicoureteral Reflux
SPA: suprapubic aspiration
UTI: urinary tract infection
VCUG: voiding cystourethrography
VUR: vesicoureteral reflux

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SUBCOMMITTEE ON URINARY TRACT INFECTION

Pediatrics 2016;138;; originally published online November 28, 2016;

DOI: 10.1542/peds.2016-3026

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OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

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SUBCOMMITTEE ON URINARY TRACT INFECTION

Pediatrics 2016;138;; originally published online November 28, 2016;

DOI: 10.1542/peds.2016-3026

The online version of this article, along with updated information and services, is located on the World Wide Web at:
</content/138/6/e20163026.full.html>

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