

Follow-up Urine Cultures and Fever in Children With Urinary Tract Infection

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Background: The American Academy of Pediatrics practice parameter for urinary tract infection suggests a repeat urine culture if the expected clinical response is not achieved within the first 48 hours of therapy. The utility of repeat urine cultures and clinical significance of fever at 48 hours is unclear.

Objectives: To determine the frequency of positive repeat urine cultures in children admitted to the hospital with urinary tract infection, and to describe the fever curves of children admitted to the hospital with urinary tract infection.

Design and Methods: We reviewed all cases of urinary tract infection in children 18 years and younger who were admitted during a 5-year period to Children's Hospital of Wisconsin (Milwaukee). We recorded temperatures from hospital admission to discharge, age, sex, initial and follow-up culture results, antibiotics received, imaging performed, and medical history.

Results: Urinary tract infection was identified in 364 patients, and 291 (79.9%) had follow-up urine cultures. None were positive. Follow-up cultures produced \$21 388.50 in patient charges. Fever lasted beyond 48 hours in 32% of patients. Older children were more likely to have fever beyond 48 hours.

Conclusions: Follow-up urine cultures were of no utility in children hospitalized for urinary tract infection, including those with fever lasting beyond 48 hours or those with an underlying urologic disease. Fever beyond 48 hours is common and should not be used as a criterion for obtaining a repeat urine culture. These conclusions are valid for children with vesicoureteral reflux. Such an approach would result in significant cost savings.

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URINARY TRACT infection (UTI) is a common reason for hospital admission for children.¹⁻³ The American Academy of Pediatrics (AAP) practice parameter for children aged 2 months to 2 years with first-time febrile UTI suggests a repeat urine culture if the expected clinical response (usually defined as fever) is not achieved within the first 48 hours of therapy.⁴

*For editorial comment
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Many articles on UTI in children recommend routine repeat cultures to ensure sterility of urine at some point after beginning treatment.^{2,3,5-10} The AAP practice parameter assumes that a repeat urine culture will provide useful information that will change clinical management. However, there is no evidence to support this recommendation when there is an identified organism with antibiotic sensitivities from the initial culture. In addition,

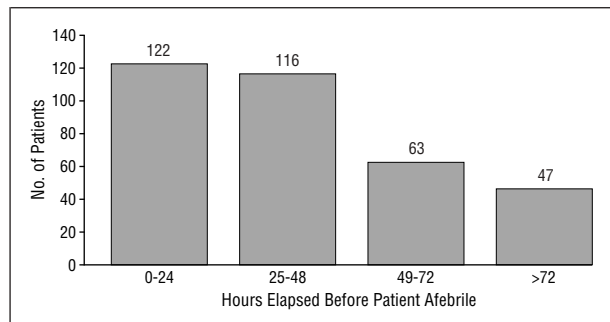
the AAP practice parameter implies that fever beyond 48 hours is abnormal and should prompt investigation. A previous study indicated that 11% of children 2 years and younger hospitalized for UTI were still febrile at 48 hours.¹¹

There are no previous studies defining the utility of follow-up urine cultures and the fever curves of all patients younger than 19 years hospitalized for UTI. The objectives of this study are to determine the frequency of positive repeat urine cultures in children with UTI and to describe the fever curves of children admitted to the hospital with UTI.

METHODS

The Children's Hospital of Wisconsin (Milwaukee) institutional review board approved this study. We retrospectively reviewed hospital records for all patients 18 years and younger who were discharged from Children's Hospital of Wisconsin with a principal diagnosis of UTI or pyelonephritis (using *International Classification of Diseases, Ninth Re-*

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Number of patients who became afebrile on each day of hospitalization (N=348).

Table 1. Effect of Vesicoureteral Reflux and History of Urinary Tract Infection on Fever Duration

	All Patients	VUR		History of UTI	
		Yes	No	Yes	No
Had fever beyond 48 h, %	32	35	27	42	30
Median time to fever resolution, h	40	40	32	48	32

Abbreviations: UTI, urinary tract infection; VUR, vesicoureteral reflux.

Table 2. Effect of Age on Fever Duration*

	Patient Age		
	0-12 mo	1-8 y	9-18 y
Had fever beyond 48 h, %	27	41	34
Median time to fever resolution, h	32	48	40

* $P=.02$ for 0 to 12 months vs 1 to 8 years; $P=.47$ for 0 to 12 months vs 9 to 18 years; $P=.59$ for 1 to 8 years vs 9 to 18 years.

vision [ICD-9] codes) for 5 consecutive years, 1997 to 2001. A UTI was defined as $\geq 10,000$ pure colony-forming units (CFUs) per milliliter on a catheterized specimen or $\geq 100,000$ CFUs per milliliter on a clean-catch specimen. There were 73 and 286 cultures obtained by clean-catch and catheterization, respectively (the method was not documented in 5 patients). No patients had urine obtained by suprapubic aspiration. There were 3 patients who had 2 different organisms isolated; an additional 2 patients had 2 different strains of *Escherichia coli* isolated. Patients were excluded if they had received outpatient antibiotics prior to admission, if they performed regular self-catheterization for spina bifida or other causes of neurogenic bladder, if they had urologic stents in place, or if they had a bladder ostomy requiring self-catheterization.

We recorded pertinent medical history, including vesicoureteral reflux (VUR), prior UTI, history of renal transplantation, sickle cell disease, or posterior urethral valves. These disorders were among the most common comorbid conditions noted in our population. In addition, they are frequently thought either to contribute to the pathogenesis of UTI (owing to mechanical or immunological factors) or to require special treatment if UTI is diagnosed. We recorded VUR that was identified within 1 month of hospital admission. We recorded the maximum temperature in each 8-hour time block after hospital admission, with time zero defined as the time of admission. Fever was defined as a body temperature of $\geq 38.0^\circ\text{C}$ for rectal or oral temperatures and $\geq 37.0^\circ\text{C}$ for axillary temperatures.¹¹⁻¹³ Since temperatures

are not recorded continuously in the hospital, time to defervescence was divided into 12 categories, each representing an 8-hour time block. Some patients were discharged at less than 88 hours while still febrile: they were categorized separately, as were patients who were never febrile. We also recorded the organism and sensitivities with number of CFUs on initial culture, antibiotic(s) given in the hospital, organism and sensitivities with number of CFUs on any repeat culture, presence or absence of urine leukocyte esterase or nitrite on any repeat urine dipstick, and any imaging performed and its result. Categorical data were analyzed using the χ^2 test.

RESULTS

Among the medical records reviewed, 364 patients met all inclusion criteria. Their ages ranged from 1 week to 18 years, with a median age of 7 months and a mean age of 31 months. Two hundred twenty-two patients (61%) were younger than 1 year, 103 (28%) were aged 1 to 8 years, and 39 (11%) were aged 9 to 18 years. Seventy-six percent were girls. This varied from 72% in children younger than 1 year, 86% in children aged 1 to 8 years, and 74% in children aged 9 to 18 years. Preexisting diagnoses in the study population included 84 patients with VUR (36 of those had grades III, IV, or V), 54 with previous UTI, 16 with sickle cell disease, 6 with a history of renal transplantation, and 2 with posterior urethral valves. The most common organism was *E coli* (87%), followed by *Klebsiella pneumoniae* (3.5%), *Pseudomonas aeruginosa* (1.92%), and *Enterococcus* species (1.64%).

Of the 364 patients identified, 291 (79.9%) had follow-up urine cultures done within 72 hours of hospital admission. None met positive culture criteria, and therefore none resulted in a change in management.

The **Figure** shows the fever characteristics for the total population. Thirty-two percent of patients had fever beyond 48 hours. The median time for fever resolution was 40 hours, with 75% of patients afebrile by 64 hours (2½ days). **Table 1** compares the fever characteristics of patients based on the presence or absence of VUR or a history of UTI. There was no significant difference in the percentage of patients afebrile at 48 hours between patients with and without VUR ($P=.28$). Fever after 48 hours occurred in 42% of the children with a history of UTI and in 30% of those without a history of UTI ($P=.13$).

Table 2 compares fever characteristics by age. A fever beyond 48 hours was present in 27% of the children younger than 1 year and in 39% of the children older than 1 year ($P=.03$).

Of the 291 patients with follow-up cultures, 256 (88%) had follow-up urine dipsticks. Two were positive for nitrites, and 172 (59%) were positive for leukocyte esterase.

The percentage of children who had repeat urine cultures during each year of the study is presented in **Table 3**. Repeat urine cultures were performed in 86% of the patients who were febrile beyond 48 hours and 79% who were afebrile at 48 hours ($P=.14$).

At our institution, the charge for a urine culture is \$73.50. The total charges for repeat urine cultures in these patients were \$21 388.50.

The AAP practice parameter for the diagnosis, treatment, and evaluation of the initial UTI in febrile infants and young children recommends repeat urine culture when the child does not achieve the expected clinical response in the first 2 days of antimicrobial therapy.⁴ While the strength of evidence is classified as “good,” there is little published data supporting this recommendation. Although “expected clinical response” is not explicitly defined in the AAP parameter, it is generally accepted in the medical community to represent the resolution of fever. One can raise 2 questions from this statement. First, what is the typical length of fever for children admitted to the hospital with UTI? In other words, is it reasonable to expect resolution of fever within 48 hours of therapy? Second, what additional information does a repeat culture add, given that organism and sensitivities are available from the initial culture?

The study by Bachur¹¹ provided us with some of these answers. He showed that of 288 children 2 years and younger, 11% were still febrile beyond 48 hours of therapy. Among the 93% of his patients that had repeat urine cultures, all were negative.

In our study, 32% of children had fever beyond 48 hours. There are a number of possible explanations for the higher percentage of patients in our study who were still febrile at 48 hours when compared with the study by Bachur (11%).¹¹ That study only included patients younger than 2 years and excluded patients with a history of UTI. We found that older age was a risk factor for fever beyond 48 hours. In addition, we did not exclude children with other medical problems, including a diagnosis of VUR, sickle cell disease, posterior urethral valves, or a history of renal transplantation. While our definition of fever was the same as that of Bachur, it is possible that there are variations in measuring or recording temperatures between the 2 hospitals.

The majority of our patients were girls and more than 80% of the infections were due to *E coli*, as has been observed in other studies of children with UTI.^{1,14}

In our study, children with fever beyond 48 hours were slightly more likely to have a repeat urine culture. Nevertheless, all cultures were negative, arguing against the utility of using prolonged fever as a criterion for obtaining a follow-up culture. This is especially relevant given the high percentage of children with fever beyond 48 hours.

Repeat urine cultures were performed on 79% of patients despite fever resolution less than 48 hours after hospitalization. While it is possible that the repeat cultures were performed because of the persistence of clinical symptoms other than fever, it is likely these were done as a matter of routine, since there was no prolonged fever to prompt a repeat culture. None of those cultures added additional useful information. It is common practice to repeat urine cultures on children with UTI to prove sterility.^{2,3,5-10,15} However, there is no clear evidence in support of this practice. In fact, routine repeat culture (in the absence of lack of expected clinical response) is not recommended in the AAP practice parameter.⁴ It is commonly assumed that a repeat culture might theoretically

Table 3. Percentage of Children With Repeat Urine Culture by Year

Year	Percentage
1997	83
1998	84
1999	77
2000	81
2001	80

detect a complication of UTI, such as a renal abscess. None of our patients developed a renal abscess or other complication that might have been detected by a repeat urine culture. Furthermore, studies have shown that only about 50% of children with a renal abscess have a positive urinalysis or urine culture.¹⁶⁻¹⁸

Also common in the study population was the repeat urine dipstick. Among those with repeat urine dipsticks (performed at least 24 hours after initiation of therapy), the majority (59%) were still positive for leukocyte esterase. Nevertheless, all cultures were negative, arguing that a persistently positive urine dipstick has no predictive value. There is no rationale for a follow-up urine dipstick; it appears to be a reflex order when obtaining the follow-up urine culture. Elimination of follow-up urine dipsticks would result in cost savings without affecting patient care.

Our patients were admitted to the hospital during a 5-year period, 1997 to 2001. In 1999, the AAP practice parameters were published, recommending against routine follow-up urine cultures unless the expected clinical response did not occur within 48 hours.⁴ Yet, in our medical record review, we observed no change in physician behavior regarding obtaining follow-up urine cultures in 2000 or 2001. Almost all of the physicians caring for patients at Children’s Hospital of Wisconsin are pediatricians and the majority are members of the AAP. This emphasizes that practice parameters do not necessarily change physician behavior.^{19,20} One obstacle to acceptance of the AAP recommendation is the presence of numerous review articles that advocate routine repeat urine cultures in children with UTI.⁶⁻¹⁰ A second difficulty with the AAP practice parameter is that it is restricted to children aged 2 months to 2 years. Similarly, the study by Bachur¹¹ only includes children younger than 2 years and excludes many patients who are commonly admitted for UTI (ie, patients with known VUR or a history of UTI). Our study, by including all patients younger than 19 years, argues for the universality of the recommendation that follow-up urine cultures are not needed, even in the child who is still febrile at 48 hours.

Another obstacle to acceptance of the AAP practice parameter is the recommendation that a culture is necessary if the expected clinical response does not occur within 48 hours. Waiting 48 hours before obtaining the repeat culture may commit the patient to an additional 24 to 48 hours in the hospital before the culture is negative. This may lead to obtaining the repeat culture prior to 48 hours so that an early “proof of cure” can be documented, permitting more expeditious discharge from the

What This Study Adds

The AAP practice parameter for the diagnosis, treatment, and evaluation of the initial UTI in febrile infants and young children recommends repeat urine culture when the child does not achieve the expected clinical response within the first 2 days of antimicrobial therapy. Although repeat urine cultures, both routine and owing to prolonged fever, are commonly performed, there are no previous studies defining the utility of follow-up urine cultures and the fever curves of patients younger than 19 years hospitalized with a UTI.

We found that most children admitted to the hospital with a UTI had a repeat urine culture, but none were positive. Moreover, fever beyond 48 hours was common. This argues that routine follow-up urine cultures are unnecessary and that fever beyond 48 hours is not an appropriate criterion for obtaining a repeat urine culture.

hospital. Our study does not deal with why physicians order follow-up urine cultures. Future studies should address this issue and determine what educational interventions can result in wider acceptance of practice parameters. In addition, our study does not address the issue of repeat urine cultures once the patient has completed therapy. While children are at an increased risk for a UTI after finishing therapy, the role of routine follow-up cultures has not been defined. The current AAP guidelines do not advocate routine follow-up cultures.⁴

Limitations of this study include the inability to draw any conclusions about fever curve or expected clinical response among certain subpopulations that were present in small numbers (eg, renal transplant recipients and patients with posterior urethral valves). Also, in 16 of our patients (4%), true duration of fever could not be determined because they were sent home before becoming afebrile, although it is unlikely that this small population would have changed our results significantly. We excluded these patients when reporting fever duration.

Our study focused on hospitalized patients receiving intravenous antibiotics. It does not address the utility of repeat urine cultures in the outpatient setting. Oral antibiotics may be less effective owing to poor patient compliance or decreased efficacy. Yet, even in the outpatient setting, the frequency of a positive follow-up urine culture was only 1% in a highly compliant patient population.²¹

In our study population, 80% of patients had repeat urine cultures. Along with the direct cost of the urine culture, there are potentially significant hidden costs due to a delay in hospital discharge caused by waiting to obtain the specimen for a repeat culture or waiting for culture results. This is especially important given the evidence that intravenous and oral antibiotics produce equivalent outcomes in children with UTI.²² In addition, repeat urine cultures in infants and toddlers are often obtained by catheterization. This may produce physical pain and emotional distress.²³ Moreover, there is a small risk of complications with urethral catheterization.²⁴

Based on our findings, the routine use of repeat urine culture in hospitalized children younger than 19 years with UTI when an initial positive culture with sensitivities is available is not justified. There is no evidence that the procedure provides any additional useful information (in patients with or without prolonged fever). Fever beyond 48 hours is common and is therefore not an appropriate criterion for justifying either repeat culture or prolonging hospitalization.

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