ARTICLE

Urine Testing and Urinary Tract Infections in Febrile Infants Seen in Office Settings

The Pediatric Research in Office Settings' Febrile Infant Study

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Objective: To determine the predictors and results of urine testing of young febrile infants seen in office settings.

Design: Prospective cohort study.

Setting: Offices of 573 pediatric practitioners from 219 practices in the American Academy of Pediatrics Pediatric Research in Office Settings' research network.

Subjects: A total of 3066 infants 3 months or younger with temperatures of 38°C or higher were evaluated and treated according to the judgment of their practitioners.

Main Outcome Measures: Urine testing results, early and late urinary tract infections (UTIs), and UTIs with bacteremia.

Results: Fifty-four percent of the infants initially had urine tested, of whom 10% had a UTI. The height of the fever was associated with urine testing and a UTI among those tested (adjusted odds ratio per degree Celsius, 2.2 for both). Younger age, ill appearance, and lack of a fever source were associated with urine testing but not with a UTI, whereas lack of circumcision (adjusted odds ratio, 11.6), female sex (adjusted odds ratio, 5.4), and longer duration of fever (adjusted odds ratio, 1.8 for fever lasting ≥24 hours) were not associated with urine testing but were associated with a UTI. Bacteremia accompanied the UTI in 10% of the patients, including 17% of those younger than 1 month. Among 807 infants not initially tested or treated with antibiotics, only 2 had a subsequent documented UTI; both did well.

Conclusions: Practitioners order urine tests selectively, focusing on younger and more ill-appearing infants and on those without an apparent fever source. Such selective urine testing, with close follow-up, was associated with few late UTIs in this large study. Urine testing should focus particularly on uncircumcised boys, girls, the youngest and sickest infants, and those with persistent fever.

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URINARY TRACT infection (UTI) is the most commonly identified serious bacterial infection among febrile infants younger than 2 to 3 months, occurring in 3% to 10% of such infants.[1-6] Because the signs and symptoms of UTI in this age group are nonspecific, urinalysis and urine culture generally are recommended to determine the source of the fever.[1,5,7-10] Is the recommendation for universal urine testing of febrile infants younger than 3 months being followed by practitioners? Should it be?

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The Pediatric Research in Office Settings' (PROS) Febrile Infant Study was a prospective study of 3066 febrile infants 3 months or younger who were seen by pediatric practitioners in their offices. Unlike previous large series of febrile infants in this age group, urine testing was done at the discretion of the study practitioners rather than routinely. This provided the opportunity to determine the frequency of urine testing and the prevalence of UTIs among those tested. In addition, the predictors of UTI could be compared with the factors associated with urine testing. Because many febrile infants were managed without initial urine testing, we could also investigate how often lack of initial testing resulted in subsequent problems. This report from the PROS Febrile Infant Study addresses the following questions: (1) What are the frequency and clinical predictors of urine testing of young febrile infants seen in office settings? (2) What are the frequency and clinical predictors of UTI and of UTI with bacteremia among those tested? (3) What are the frequencies of late diagnosis of UTI and of UTI with bacteremia among patients who did not have an initial urine specimen tested?

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SUBJECTS AND METHODS

PROS NETWORK AND PRACTITIONERS

This prospective cohort study was conducted in practices participating in the American Academy of Pediatrics' practice-based research network, PROS.[11] The PROS network currently includes more than 1600 practitioners from 50 states, Puerto Rico, and Canada; 573 practitioners from 219 practices enrolled eligible patients in this study between February 28, 1995, and April 25, 1998. Pediatric Research in Office Settings' practitioners for this study came from 44 states, the District of Columbia, and Puerto Rico. When compared with American Academy of Pediatrics' members who listed patient care as their primary activity in a 1995 American Academy of Pediatrics' periodic survey,[12] PROS practitioners were comparable for age, sex, and practice arrangement, but were less likely to practice in inner-city locations (7% vs 12%).

STUDY SUBJECTS

Infants were eligible for inclusion in the study if they (1) were no older than 3 months; (2) had axillary, rectal, or tympanic temperatures of at least 38°C in the office or in the previous 24 hours at home; and (3) were initially examined by a PROS practitioner. Because practitioners ordered diagnostic tests and treatments according to their usual clinical judgment, informed consent from the subjects was not required. The study was approved by the University of California, San Francisco, Committee on Human Research.

PREDICTOR VARIABLES

Clinical and Demographic Data

The PROS practitioners and their office staffs recorded clinical and demographic data on standard forms. The study protocol required that the initial physical examination results, diagnostic impression, and assessment of overall severity of illness be recorded before the results of any laboratory tests were available.

The temperature variable used for these analyses was created by adding 0.5°C to axillary temperatures, then taking the higher of the temperatures taken in the office or at home.[13] Results for many components of the history and physical examination (eg, duration of fever, general appearance, degree of respiratory distress, and quality of cry) could be indicated by checking appropriate boxes on the data collection form. Practitioners recorded other significant findings as free text; these were grouped and coded by the study staff without knowledge of the child's ultimate diagnosis or outcome.

Laboratory Data

To facilitate comparisons of urinalysis results across practices, all practices were supplied with dipsticks (Ames-Multistix; Miles, Inc, Elkhart, Ind), which include tests for leukocyte esterase and nitrite. All other laboratory tests, including urine cultures, were done in the laboratories normally used by the practitioners.

Missing Data

For the most important data items (initial temperature, age, sex, and final outcome), most missing, ambiguous, or suspicious data items were obtained or verified through inquiries to individual PROS practitioners. The data collection form included the dates of urine cultures but not of urinalyses. We considered urine testing to have been done on the date of the urine culture, if available. For the 240 infants for whom no urine culture date was provided (14% of the 1775 whose urine was tested), we used the date of the initial examination. Many other items existed on the data collection form as boxes to check if the finding was present; for these items, we assumed the finding was absent if the box was not checked. For categorical variables describing aspects of the infant's overall appearance (eg, level of alertness), we dichotomized the variables and grouped infants with missing data (about 1%) with those who did not have worrisome values. We also coded the variable regarding ill family members as none in the 160 infants (5% of the total 3066 infants) in whom it was missing. For other variables, missing values were either explicitly grouped with other values or analyzed separately.

OUTCOME VARIABLES

Laboratory Data

We considered urine testing to have been done if results of either a urinalysis or a urine culture were recorded. We

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RESULTS

CHARACTERISTICS OF PROS PRACTITIONERS

Characteristics of the 573 PROS practitioners who enrolled 1 or more infants in the study are shown in **Table 1**. Most were physicians, white, and in group practice. Slightly more than half were men and younger than 45 years. The median number of infants enrolled per practitioner was 3 (range, 1-78 infants).

URINE TESTING

Pediatric Research in Office Settings' practitioners obtained a urinalysis on 1652 (54%) of the 3066 infants and urine cultures on 1608 (52%) of the infants. At least 1 of the 2 tests was performed on 1775 infants (58%). In 1666 infants (54% of all infants and 94% of those tested), either a urinalysis or a urine culture was performed on the day the infant was first examined. Of the cultured urine specimens, 70% were obtained by urethral catheterization, 25% by urine bag, 3% by suprapubic aspiration, and 2% by clean catch.

Numerous demographic and clinical predictors were statistically significantly associated with urine testing on the day of the initial visit (**Table 2**). The highest rate of initial urine testing (44 [88%] of 50 patients) occurred among those whose initial appearance was "very ill"; all 6 of the very ill–appearing infants whose urine was not tested had respiratory distress. On multiple logistic regression analyses, the strongest independent predictors

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chose to look at predictors of urine testing rather than predictors of urine culture, because a major obstacle to urine culture is obtaining the sample and because some of the decisions to perform urine cultures might have been made based on the results of the urinalysis.

The diagnosis of a UTI was based on urine culture results; a positive urinalysis result was not required. A pediatric infectious disease consultant who was blinded to data on individual subjects classified organisms identified in the urine as pathogenic, sometimes pathogenic, and nonpathogenic. Organisms that were either pathogenic or sometimes pathogenic were considered pathogenic for this study. Infants whose urine was obtained by suprapubic aspiration were considered to have a UTI if the urine culture grew at least 100 colony-forming units per milliliter of 1 or more pathogenic organisms. Infants whose urine was obtained by urethral catheterization were considered to have a UTI if urine cultures grew at least 20 000 colony-forming units per milliliter of a single pathogenic organism. For bag- and clean-voided specimens, at least 100 000 colony-forming units per milliliter of a single pathogenic organism were required. Three additional infants were considered to have a UTI: 1 whose urine culture was lost in the laboratory, but who had pyuria and was diagnosed as having a renal abscess, and 2 whose urine colony counts were missing but who had *Escherichia coli* isolated from blood and urine.

Follow-up

Practitioners followed up all infants and recorded each interaction until the infants had recovered from the acute illness. No follow-up data could be obtained for 119 (4%) of the 3066 infants. Compared with infants for whom follow-up data were available, these infants were similar in age (average, 3 days older; $P=.22$), but their mean temperature was 0.1°C lower ($P=.003$) and they were more likely to have a diagnosis of upper respiratory tract infection (49% vs 34%; $P=.001$).

STATISTICAL ANALYSES

We used a spreadsheet program (Excel, version 5.0; Microsoft Corporation, Redmond, Wash) to calculate odds ratios and statistical software (Stata, releases 5 and 6; Stata Corp, College Station, Tex) for all other statistical analyses. For analyses of predictors of urine testing and of UTI, we considered only variables available and urinalyses and urine cultures done on the date of the initial examination. We began with simple bivariate analyses relating these outcomes to clinical and demographic predictors (in their original form) to screen for associations that might be missed if predictor variables were dichotomized. We then dichotomized variables as appropriate and entered significant predictors based on bivariate analyses into backward stepwise multiple logistic regression analyses to identify significant independent predictors of urine testing and of UTI. All logistic regression analyses were done using the "cluster" option in the statistical software (Stata) to account for the nonindependence of infants enrolled by the same practitioner. Goodness of fit of the logistic model was assessed using the method of Hosmer-Lemeshow with 10 groups.[14] Discrimination was assessed using the *c* statistic, equal to the area under the receiver-operating characteristic curve.[14]

For multiple logistic analyses in which the outcome variable was initial urine testing, because of the many infants whose urine was tested, we included only variables significant at $P=.03$ to avoid identifying too many statistically but not clinically significant predictors. For analyses in which the outcome variable was a UTI, because of the much smaller sample size (of UTIs), we used $P=.05$. In addition to variables associated with a UTI at $P<.05$ on bivariate analyses, we also included race, ethnicity, and all variables that were significantly associated with urine testing in the logistic analyses previously described.

The multiple logistic model provides a predicted probability of a UTI for each infant, based on that infant's values for the various variables that were predictive of a UTI.[15] We used these predicted probabilities of UTI to estimate the number of infants whose urine was not tested at the first visit who would be expected to have a UTI if their urine were cultured initially. For these analyses, we restricted attention to infants with complete follow-up data who were not initially treated with antibiotics. By multiplying the average predicted probability of a UTI for these infants by the number of infants at risk, we arrived at an approximate number of infants expected to have a UTI at the initial visit whose UTIs were not initially diagnosed or treated. We then determined how many infants were later diagnosed as having a UTI, based on positive urine culture results with dates after the initial examination date.

of testing were younger age, higher fever, initial ill appearance, and absence of findings suggesting an alternative source for the fever, such as otitis media, upper respiratory tract symptoms, or ill family members (**Table 3**). Several potential signs of serious illness, such as sleepiness, inconsolability, and not smiling, were associated with increased urine testing, but vomiting was not. Overall, the discrimination of the logistic model for urine testing was good ($c=0.77$), with a good fit (Hosmer-Lemeshow $\chi^2_8=12.7$; $P=.12$).

URINARY TRACT INFECTION

One hundred sixty-seven infants (5% of the entire cohort and 9% of those ever tested) met our criteria for a UTI. Of these 167 infants, 161 underwent urine testing on the initial examination date; the UTI rate among those initially tested was 10% (161/1666). The infections were predominantly due to *E coli* (**Table 4**). Bivariate analyses of predictors of a UTI on the day of the initial examination (Table 2) and results of stepwise multiple logistic regression (**Table 5**) demonstrate considerable overlap between predictors of urine testing and predictors of a UTI among those tested. The ability of the logistic model to predict a UTI was similar to the ability to predict testing ($c=0.77$); the goodness of fit was excellent (Hosmer-Lemeshow $\chi^2_8=4.0$, $P=.85$). The height of the fever was a strong predictor of urine testing and a UTI. A history of ill family members or physical findings suggesting a different source for the fever, especially respiratory dis-

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tress, were associated with less testing and a lower risk of a UTI.

On the other hand, several variables associated with testing were not associated with a UTI. The infant's age and overall appearance were strong predictors of urine testing but poor predictors of a UTI. In fact, infants with more findings generally associated with serious illness were less likely to have a UTI. On multivariate analysis, the finding that the infant was inconsolable was associated with a statistically significant decrease in the odds of having a UTI (Table 5).

The predictors of a UTI that were not predictors of testing are of particular interest. The strongest of these were female sex and lack of circumcision. In multiple logistic regression analyses with circumcised boys as the comparison group, the odds of a UTI were 5.4 times higher in girls and 11.6 times higher in uncircumcised boys. However, circumcision status ($P=.06$) and sex ($P=.20$) were not significantly associate with urine testing. Infants whose fever had lasted more than 24 hours had an 80% higher odds of having a UTI, but were no more likely to be tested. Hispanic infants were less likely to have a UTI on multivariate analysis (adjusted odds ratio, 0.5), but no less likely to be tested. Because Hispanic boys were much more likely to be uncircumcised (66% compared with 12% in non-Hispanic white boys), their decreased risk of a UTI was not apparent until confounding by circumcision status was controlled. A lower risk for African Americans was not statistically significant in either bivariate ($P=.22$) or multivariate ($P=.10$) analyses; if included in the final logistic model, the adjusted odds ratio for African Americans was 0.54 (95% confidence interval [CI], 0.3-1.1).

UTI WITH BACTEREMIA OR MENINGITIS

Of the 167 infants with a UTI, 17 (10%) had bacteremia caused by the same organism that was isolated from the urine (**Table 6**). The proportion of UTIs accompanied by bacteremia was similar in uncircumcised boys, girls, and circumcised boys. The risk of bacteremia with a UTI seemed to decline with age, but this difference did not reach statistical significance. Although about half of the infants with a UTI and bacteremia looked only minimally ill and about half had temperatures lower than 39°C, all but 3 had a positive urinalysis result (the dipstick was positive for leukocyte esterase or there were >10 white blood cells per high-power field) and all but 2 were initially hospitalized. Rates of bacteremia were similar among infants whose diagnoses of UTI were based on urine collected by bag and by urethral catheterization. Of the 167 infants with a UTI, 98 (59%) underwent a lumbar puncture. None had bacterial meningitis. Three were diagnosed as having viral meningitis.

DIAGNOSES OF UTI IN INFANTS NOT INITIALLY TESTED

We applied the logistic model derived from infants whose urine was tested on the date of their initial examination to the remainder of the infants to estimate how many additional UTIs might be observed if all infants were tested on the first day (**Figure**). The logistic model allows us to take into account that infants not initially tested were at lower risk of a UTI than those tested, as illustrated by their lower average temperature, 38.5°C compared with 38.8°C. Based on their temperature, sex, circumcision status, and other variables, the predicted probability of a UTI in the group that was not tested was about 8%. This means that if the model is not missing any key variables, about 8% of the 1400 infants not tested on day 1 (111 infants) would have been diagnosed as having a UTI had they been tested.

Our study design permitted us to investigate the natural history of UTIs in low-risk infants (those judged by their practitioners to be at sufficiently low risk not to need a urine test or antibiotics on day 1). There were 807 infants not initially tested, not unavailable for follow-up, and not initially treated with antibiotics. In this group, the average predicted probability of a UTI was 7.6%, suggesting that about 61 of the 807 infants would have had positive urine culture results at their initial visit, had a culture been performed. Only 2 (0.25%) of the 807

Table 1. Characteristics of the 573 PROS Practitioners Participating in the Febrile Infant Study*

Characteristic	No. (%) of Practitioners†
Sex	
Male	300 (52)
Female	273 (48)
Race‡	
White	519 (91)
Asian or Pacific Islander	36 (6)
African American	3 (1)
Other or missing	15 (3)
Age, y	
<45	307 (54)
≥45	266 (46)
Practice type	
Solo	46 (8)
Group	386 (67)
HMO	22 (4)
Medical school	32 (6)
Other	87 (15)
Practice setting	
Urban	
Not inner city	133 (23)
Inner city	42 (7)
Suburban	259 (45)
Rural	131 (23)
Other or missing	8 (1)
Region	
Northeast	197 (34)
West	144 (25)
South	141 (25)
North-central	91 (16)
Practitioner type	
Physician	524 (91)
Physician assistant	8 (1)
Nurse practitioner	41 (7)
No. of infants enrolled per practitioner	
1-3	305 (53)
4-9	169 (29)
≥10	99 (17)

*PROS indicates Pediatric Research in Office Settings; HMO, health maintenance organization.
†Percentages may not total 100 because of rounding.
‡Eighteen Hispanic practitioners (3%) were included within these categories.

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Table 2. Selected Clinical and Demographic Predictors of Urine Testing on the Day of the Initial Examination and of a UTI Among Those Tested*

Variable	Total No. of Infants	No. (%) of Infants in Whom Urine Was Tested	*P* Value for Urine Testing†	Infants in Whom Urine Was Tested: No. (%) With a UTI	OR for a UTI‡	*P* Value for a UTI§
Total group	**3066**	**1666** (54)	. . .	**161** (10)	. . .	. . .
Demographics and history						
Sex						
Girls	1436	798 (56)	. . .	102 (13)	2.0	<.001
Boys	1630	868 (53)	.20	59 (7)	1.0‖	. . .
Circumcised	1173	608 (52)	. . .	15 (2)	1.0‖	. . .
Uncircumcised	356	209 (59)	. . .	40 (19)	9.0	<.001
Circumcision status missing	101	51 (50)	.06	4 (8)	3.4	.03
Age, d						
0-30	775	527 (68)	. . .	51 (10)	0.8	.30
31-60	1220	723 (59)	. . .	61 (8)	0.7	.07
61-93	1071	416 (39)	<.001	49 (12)	1.0‖	. . .
Race/ethnicity						
White	2150	1160 (54)	. . .	116 (10)	1.0‖	. . .
African American	246	134 (54)	. . .	9 (7)	0.6	.22
Asian or Pacific Islander	67	36 (54)	. . .	6 (17)	1.8	.19
Hispanic (any race)	453	251 (55)	. . .	20 (8)	0.8	.32
Other, unknown, or missing	150	85 (57)	.90	10 (12)	1.2	.54
Payer						
HMO or PPO	1054	548 (52)	. . .	54 (10)	1.0	.67
Private	641	324 (51)	. . .	38 (12)	1.3	.30
Medicaid	1074	618 (58)	. . .	59 (10)	1.0‖	. . .
Champus	77	52 (68)	. . .	4 (8)	0.8	.66
Self-pay	91	51 (56)	. . .	2 (4)	0.4	.18
Other, unknown, or missing	129	73 (57)	.006	4 (5)	0.5	.25
Time of the visit						
Daytime (8 AM-8 PM)	2677	1398 (52)	. . .	136 (10)	1.0‖	. . .
Nighttime (8 PM-8 AM)	301	214 (71)	. . .	23 (11)	1.1	.64
Missing	88	54 (61)	<.001	2 (4)	0.4	.14
History items checked						
Increased sleepiness	784	504 (64)	<.001	54 (11)	1.2	.34
Decreased urination	318	233 (73)	<.001	27 (12)	1.3	.28
Decreased social interaction	637	434 (68)	<.001	38 (9)	0.9	.46
Decreased feeding	1067	622 (58)	.001	59 (9)	1.0	.85
Decreased activity	468	305 (65)	<.001	28 (9)	0.9	.75
Increased vomiting	526	290 (55)	.69	24 (8)	0.8	.38
Ill family members	1512	772 (51)	<.001	53 (7)	0.5	<.001
Duration of the fever, h						
<24	2712	1487 (55)	. . .	131 (9)	1.0‖	. . .
≥24	354	179 (51)	.13	30 (17)	2.1	.001
Physical examination results						
Maximum temperature, °C¶						
38.0-38.4	1361	607 (45)	. . .	37 (6)	1.0‖	. . .
38.5-38.9	1049	608 (58)	. . .	60 (10)	1.7	.01
39.0-39.4	458	305 (67)	. . .	33 (11)	1.9	.01
≥39.5	198	146 (74)	<.001	31 (21)	4.2	<.001
Initial appearance						
Well or minimally ill	2206	1053 (48)	. . .	97 (9)	1.0‖	. . .
Moderately ill	767	547 (71)	. . .	55 (10)	1.1	.58
Very ill	50	44 (88)	. . .	6 (14)	1.6	.32
Missing	43	22 (51)	<.001	3 (14)	1.6	.48
Physical findings noted suggesting another source for the fever						
URI or runny nose	455	163 (36)	<.001	8 (5)	0.5	.03
Otitis media or abnormal TMs	437	133 (30)	<.001	7 (5)	0.5	.07
Respiratory distress	400	218 (54)	.94	10 (5)	0.4	.007
Chest findings	183	78 (43)	.001	3 (4)	0.4	.08
Cough	85	26 (31)	<.001	1 (4)	0.4	.31
Conjunctivitis	40	14 (35)	.01	1 (7)	0.7	.75
Infant findings suggesting serious illness						
Color pale, mottled, or cyanotic	183	142 (78)	<.001	15 (11)	1.1	.70
Not alert	524	404 (77)	<.001	31 (8)	0.7	.12

(continued)

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Table 2. Selected Clinical and Demographic Predictors of Urine Testing on the Day of the Initial Examination and of a UTI Among Those Tested* (cont)

Variable	Total No. of Infants	No. (%) of Infants in Whom Urine Was Tested	*P* Value for Urine Testing†	Infants in Whom Urine Was Tested: No. (%) With a UTI	OR for a UTI‡	*P* Value for a UTI§
Infant findings suggesting serious illness (cont)						
Dehydrated	189	139 (74)	<.001	9 (6)	0.6	.18
Weak or high-pitched cry	251	199 (79)	<.001	17 (9)	0.9	.57
Inconsolable	638	473 (74)	<.001	32 (7)	0.6	.01
No smile	820	595 (73)	<.001	49 (8)	0.8	.14
No. of findings suggesting a serious illness						
0	1721	728 (42)	. . .	82 (11)	1.0‖	. . .
1	636	381 (60)	. . .	38 (10)	0.9	.51
2	361	271 (75)	. . .	21 (8)	0.7	.10
≥3	348	286 (82)	<.001	20 (7)	0.6	.04
Method of obtaining urine						
Bag	. . .	356	. . .	36 (10)	0.9	.65
Urethral catheterization	. . .	1038	. . .	114 (11)	1.0‖	. . .
Suprapubic aspiration	. . .	50	. . .	5 (10)	0.9	.83
Clean catch	. . .	27	. . .	5 (19)	1.8	.22
Not indicated	. . .	195	. . .	1 (0.5)	0.04	<.001

*UTI indicates urinary tract infection; OR, odds ratio; HMO, health maintenance organization; PPO, preferred provider organization; URI, upper respiratory tract infection; TM, tympanic membrane; and ellipses, not applicable.

†For dichotomous and nonordered categorical variables, values are derived from χ^2 tests comparing the frequency of testing across categories. For ordered variables (such as age and temperature), values are derived from the Kruskal-Wallis test using individual values of the variables.

‡Unadjusted value comparing the odds of a UTI at a given level of a predictor variable with the odds of a UTI among those in the indicated comparison group, including only infants whose urine was tested on the day of the initial examination. When no comparison group is listed, the comparison group is the infants in whom a particular characteristic (eg, "increased sleepiness") was not noted to be present.

§By χ^2 test (compared with the comparison group).

‖Comparison group.

¶See "Clinical and Demographic Data" subsection of the "Subjects and Methods" section of the text for a definition.

Table 3. Multivariate Predictors of Urine Testing on the Date of the Initial Visit

Variable*	Odds Ratio (95% Confidence Interval)	*P* Value
Age (per week)	0.9 (0.8-0.9)	<.001
Maximum temperature (per degree Celsius)	2.1 (1.8-2.6)	<.001
Any PE source for the fever	0.4 (0.3-0.6)	<.001
Decreased urination	2.0 (1.5-2.6)	<.001
Appearance moderately or very ill	1.6 (1.3-2.1)	<.001
Inconsolable	1.6 (1.3-2.1)	<.001
No smile	1.6 (1.2-2.0)	.001
Urban inner-city practice	2.3 (1.4-4.0)	.002
Increased sleepiness	1.4 (1.1-1.7)	.008
Otitis media or abnormal TMs	0.6 (0.5-0.9)	.01
Ill family members	0.8 (0.7-1.0)	.02
Decreased social interaction	1.4 (1.0-1.9)	.03

*Listed in order of decreasing statistical significance. PE indicates physical examination; TM, tympanic membrane.

Table 4. Causative Organisms for UTI and UTI With Bacteremia*

Organism	UTI: Alone	UTI: With Bacteremia
Escherichia coli	134 (80)	15 (88)
Klebsiella	8 (5)	1 (6)
Enterobacter	8 (5)	1 (6)
Enterococcus	3 (2)	0
Staphylococcus aureus	3 (2)	0
Group B streptococci	2 (1)	0
Others	9 (5)	0
Total	**167 (100)**	**17 (100)**

*Data are given as number (percentage) of infants affected. UTI indicates urinary tract infection.

untested and untreated infants (95% CI, 0.03%-0.90%) subsequently were diagnosed as having a UTI, based on cultures done on the day following the initial examination. Neither had bacteremia, and both were treated and recovered uneventfully.

COMMENT

In this study, we found that office-based pediatric practitioners obtained urine for urinalysis or culture in about 58% of febrile infants aged 3 months and younger, most often on the date of the initial examination. This contrasts with many published recommendations[1,7-10] that suggest urine testing in all febrile infants this young. However, it is consistent with results from other studies[16-19] that indicate that many practitioners order fewer tests in febrile infants than recommended in published guidelines.

In selecting which infants to test, practitioners seemed to rely on 2 groups of factors: those associated with the potential severity of illness, such as age and ill appearance, and those associated with the probability of a UTI, such as a medical history or physical findings suggesting another cause for the fever. This is consistent with a survey[17] of Utah primary care pediatric practitioners,

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in which 91% responded that they would order a urinalysis for a 3-week-old infant with a temperature of 38.5°C, but only 24% would order a urinalysis for a 2-month-old infant with a temperature of 38.7°C and bilateral otitis media. Infants with respiratory distress often did not undergo urine testing; this is consistent with reports[20,21] that the yield of urine cultures in infants with bronchiolitis is low.

We documented that 10% (95% CI, 8%-11%) of those whose urine was initially tested had a UTI, including 19% of uncircumcised boys and 13% of girls. Ten percent of those with a UTI had bacteremia caused by the same organism that was found in their urine. As found in previous studies,[1,2,22,23] almost all UTIs were due to *E coli* or other enteric gram-negative rods. The rate of UTI among those whose urine was cultured in the present study is higher than the 3% to 7% reported in most previous studies,[1-3,5,6] in which all febrile infants had their urine cultured. Some of this discrepancy is because of selective urine testing in the present study. As shown in the Figure, those whose urine was not initially tested had a lower projected risk of a UTI (8%) than those whose urine was initially tested (10%) because of differences like lower temperatures. The projected UTI rate for the entire cohort of infants, 9%, is closer to results from other studies[1-3,5,6] and is probably still a bit inflated because of residual selection bias by predictors of UTI that were not included in our logistic model.

Table 5. Multivariate Predictors of UTI Among Infants Whose Urine Was Tested on the Date of the Initial Visit*

Variable	Odds Ratio (95% Confidence Interval)	*P* Value
Uncircumcised boys	11.6 (5.9-22.6)	<.001
Girls	5.4 (3.1-9.4)	<.001
Maximum temperature (per degree Celsius)	2.2 (1.7-2.9)	<.001
Ill family members	0.5 (0.4-0.8)	<.001
Fever duration ≥24 h	1.8 (1.2-2.8)	.004
Inconsolable	0.6 (0.4-0.9)	.006
Hispanic ethnicity	0.5 (0.3-0.8)	.009
Respiratory distress	0.4 (0.2-0.9)	.02
Circumcision status missing	3.5 (1.0-11.5)	.04

*Listed in order of decreasing statistical significance. UTI indicates urinary tract infection.

Table 6. Infants With a UTI and Bacteremia*

Variable	No. of Infants: In Whom Urine Was Cultured	No. of Infants: With a UTI	Infants With a UTI and Bacteremia: Total No.	Infants With a UTI and Bacteremia: % of Those in Whom Urine Was Cultured	Infants With a UTI and Bacteremia: % of Those With a UTI	*P* Value (for Bacteremia Given a UTI)
Total group	**1608**	**167**	**17**	1	10	. . .
Sex						
Girls	795	107	11	1	10	.95†
Boys	813	60	6	0.7	10	
Circumcised	572	15	2	0.3	13	.73†
Uncircumcised	197	41	4	2	10	
Circumcision status missing	44	4	0	0	0	
Age, d						
0-30	516	52	9	2	17	.11‡
31-60	693	64	5	0.7	8	
61-93	399	51	3	0.8	6	
Maximum temperature, °C						
38.0-38.4	585	39	0	0	0	.13‡
38.5-38.9	586	62	9	2	15	
39.0-39.4	293	35	4	1	11	
≥39.5	144	31	4	3	13	
Initial appearance						
Well or minimally ill	1029	102	9	0.9	9	.57‡
Moderately ill	517	56	8	2	14	
Very ill	41	6	0	0	0	
Missing	21	3	0	0	0	
No. of physical findings suggesting serious illness						
0	710	87	7	1	8	.37‡
1	369	38	3	0.8	8	
2	253	21	4	2	19	
3	276	21	3	1	14	
Method of obtaining urine for culture						
Bag	391	36	4	1	11	.72†
Catheter	1102	120	12	1	10	
Suprapubic aspiration	54	5	0	0	0	
Clean catch	29	5	1	3	20	
Missing	32	1	0	0	0	

*Includes 6 UTIs in infants whose urine was not initially tested. UTI indicates urinary tract infection; ellipses, data not applicable.
†χ^2 Test (missing data included).
‡Kruskal-Wallis test (missing data excluded).

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On the other hand, the method of urine collection cannot explain the observed higher rates. Only 22% of the UTIs in the present study were diagnosed based on bag urine samples, and the frequency of UTIs among infants whose urine was obtained by bag was the same as the frequency in those whose urine was obtained by urethral catheterization. This finding suggests that bag urine collection, although not recommended in guidelines, performs reasonably well in practice settings and may be preferable to no urine collection at all.

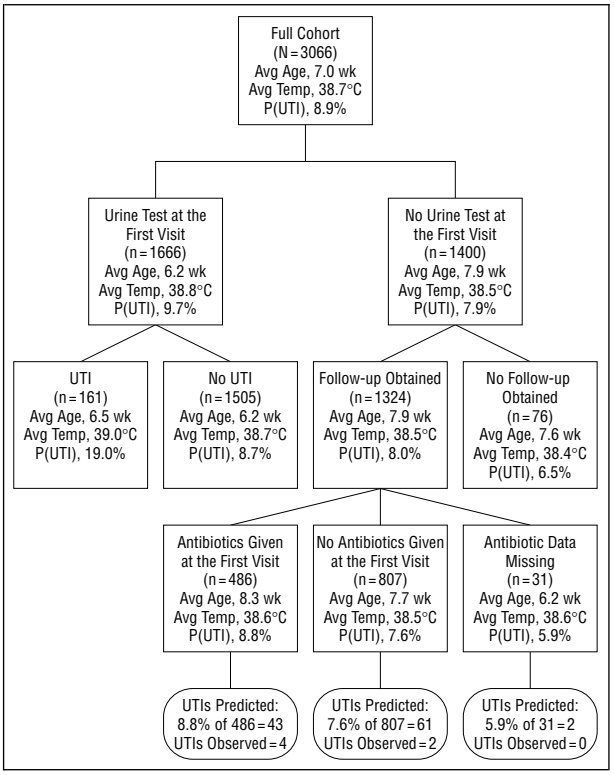
The bacteremia rates among infants with a UTI in the present study, ranging from 6% in 2- to 3-month-old infants to 17% in infants younger than 1 month, are consistent with previous studies[24-27] that found a much higher risk of bacteremia among the youngest infants with UTIs. In fact, these figures underestimate the age gradient for bacteremia, because urine and blood cultures were done more selectively in older than in younger infants in the present study. Unlike some previous studies,[25,28] we observed no deaths and no cases of bacterial meningitis among the infants with UTIs. However, the nearly 20% rate of bacteremia with UTI in infants younger than 1 month suggests that younger infants should be especially considered for urine testing.

The discrepancies between factors associated with urine testing and those predictive of a UTI suggest strategies for improving the way practitioners select infants for urine testing. In particular, female sex and lack of circumcision were strongly associated with a UTI, but not with urine testing. The nearly 12-fold increase in the odds of a UTI in uncircumcised boys in the present study is similar to that observed in other studies.[29,30] The risk of bacteremia in uncircumcised boys with a UTI was similar to that of girls and circumcised boys, suggesting that these UTIs are real, as opposed to an artifact of difficulty obtaining clean urine specimens for culture in uncircumcised boys. We, therefore, recommend urine testing in most uncircumcised boys.

Two additional discrepancies are worth noting. Infants whose fever was present for 24 hours or longer had an 80% higher odds of a UTI than those whose fever was of shorter duration, but were not more likely to have their urine tested. Thus, prolonged duration of fever seems to be an indication for urine testing. In addition, we found that after adjusting for other variables, particularly circumcision status, Hispanic infants were at lower risk than non-Hispanic infants, but were tested at the same rate.

The possibility that race or ethnicity might predict a UTI is supported by previous studies[31,32] of older infants that found a significantly lower risk for UTIs among African Americans. African American infants seemed to be at lower risk in the present study, but the numbers were too small to be statistically significant. We are unaware of previous studies indicating a lower risk in Hispanic infants. Thus, we believe that, based on the present study only, it would be premature to use a much different threshold for obtaining urine culture samples from Hispanic infants than from infants of other ethnicities.

The variation in urine testing practices among different practitioners allowed us to compare short-term outcomes among infants who did and did not undergo initial urine tests. Among the 807 infants not initially tested or treated with antibiotics, we would have expected about 61 to have had a UTI, based on their sex, circumcision status, temperature, and other predictors of UTIs. Yet, in only 2 infants was that diagnosis subsequently made, suggesting that in most infants at least the acute symptoms of UTI subside spontaneously. This conclusion is not sensitive to the accuracy of the logistic model for predicting a UTI, because even if the risk of a UTI in those not tested were only a third as high as our estimate (ie, 20 predicted UTIs rather than 61), we would still conclude that the acute symptoms resolved spontaneously in most (18 [90%] of 20) infants. Furthermore, the observed low rates of late UTI (2/807; 95% CI, 0.03%-0.89%) and of catastrophic events because of a missed UTI (0/807; 95% CI, 0%-0.37%) in those not initially tested or treated with antibiotics are not dependent on the projection of the number of missed UTIs.



Predicted and observed urinary tract infections (UTIs) by initial urine testing, follow-up, and antibiotic treatment. The predicted probability of a UTI in each box (P[UTI]) is derived from the logistic model based on infants whose urine was tested on the day of their first visit. Avg indicates average; Temp, temperature.

On the other hand, the absence of catastrophic events does not imply the absence of harm. This study was not designed to address renal damage or other potential late sequelae of UTIs. These might differ in frequency between those whose UTIs were diagnosed and treated and those whose UTIs spontaneously resolved.

Some additional limitations of the PROS Febrile Infant Study should be addressed. By design, this study included only those young febrile infants who had their initial clinical assessment with a PROS practitioner. Therefore, any infants presenting or referred directly to an emergency department were not included in the study. The frequency and outcomes of urine testing and UTIs

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Participants in the Pediatric Research in Office Settings' Febrile Infant Study

The pediatric practices or individual practitioners who enrolled subjects in this study are listed here by American Academy of Pediatrics chapter.

Alabama, Birmingham: Drs Heilpern & Reynolds, PC; Growing Up Pediatrics, PC; and University of Alabama.

Alaska: Anchorage Neighborhood Health Center, Anchorage Pediatric Group, and Pediatrics (*Anchorage*), and Eielson Clinic (*Eielson*).

Arizona: Mesa Pediatrics Professional Associates, and Orange Grove Pediatrics, Tanque Verde Pediatrics, and Cigna HealthCare (*Tucson*).

California-1: Palo Alto Medical Clinic, University of California–San Francisco, Palo Alto Medical Foundation (*Los Altos*), Palo Alto Medical Clinic (*Fremont*), Shasta Community Health Center (*Redding*), Healthy Trails Pediatric Medical Group (*Freedom*), Anita Tolentino-Macaraeg, MD (*Hollister*), Eureka Pediatrics (*Eureka*), Cantor, Giedt, & Kamachi (*Salinas*), and Marin Community Clinic (*Greenbrae*).

California-2: Clinic Sierra Vista (*Lamont*), Pediatric Associates of Pasadena, Touraj Shafai, MD (*Riverside*), and Facey Medical Group (*Canyon Country*).

California-4: Edinger Medical Group, Inc (*Fountain Valley*) and Southern Orange County Pediatric Associates (*Lake Forest*).

Colorado, Denver: Rocky Mountain Youth.

Connecticut: St Francis Pediatric Primary Care Center (*Hartford*), Hemant Panchal, MD (*Enfield*), and Uwe Koepke, MD (*Danbury*).

Delaware, Newark: Pediatric Associates.

District of Columbia, Washington: George Washington University Health Plan.

Florida: Sawgrass Pediatrics, PA (*Coral Springs*), Jonathan Rubin, MD, PA (*Margate*), MacKoul Pediatrics (*Cape Coral*), SW Florida Pediatric Network and Emilio DelValle, MD (*Fort Myers*), Atlantic Coast Pediatrics (*Merritt Island*), Orlando Health Care Group and Arnold Palmer Women & Children's Hospital (*Orlando*), Sacred Heart Pediatric Care Center (*Pensacola*), and Giangreco & Scarano Pediatrics (*Bradenton*).

Georgia: The Pediatric Center (*Stone Mountain*) and Children's Hospital at Memorial (*Savannah*).

Hawaii, Honolulu: Jeffrey Lim, MD, Melinda Ashton, MD, and Pediatrics Department, Kapiʻolani Medical Center for Women and Children.

Illinois: Southwest Pediatrics (*Palos Park*), SIU Physicians & Surgeons–Auburn, LaGrange Pediatrics (*Western Springs*), Sidney Smith, MD (*Carbondale*), and Signature Medical Associates (*Elgin*).

Indiana: Georgetown Medical Care and Northpoint Pediatrics (*Indianapolis*), Pediatric Advocates (*Peru*), George Sorrells, MD (*Bedford*), Bloomington Pediatric Associates, PC, and Southern Indiana Pediatrics, LLC (*Bloomington*), Lynn Ryan, MD (*Lawrenceburg*), Marshall County Pediatrics (*Plymouth*), Jeffersonville Pediatrics (*Jeffersonville*), and Children's Health Care (*Batesville*).

Iowa: David Kelly, MD (*Marshalltown*), and West Des Moines Family Physicians (*West Des Moines*).

Kansas: Bethel Pediatrics (*Newton*) and Ashley Clinic (*Chanute*).

Kentucky, Lexington: Michael Simon, MD.

Maine: John Salvato, MD (*Waterville*), and Intermed Pediatrics (*Yarmouth*).

Maryland: Clinical Associates, PA (*Towson*); Andorsky, Finkelstein and Cardin (*Owings Mills*); Children's Medical Group (*Cumberland*); Steven Caplan, MD, and O'Donovan & Ahluwalia, MD, PA (*Baltimore*); Shore Pediatrics (*Easton*); Drs Wiczer, Korengold, Mayol, and D'Albora & Osha, MD, PA (*Bethesda*); Shady Side Medical Associates (*Shady Side*); The Children's Doctors (*Westminster*); Coleman, Coleman, & Sachs (*Rockville*); and Potomac Physicians (*Severna Park*).

Massachusetts: Framingham Pediatric, PC, Garden City Pediatrics (*Beverly*), Burlington Pediatrics (*Burlington*), Medical West Associates (*Chicopee*), Holyoke Pediatric Associates (*Holyoke*), John Mulqueen, MD (*Gardner*), Pediatric Associates of Norwood (*Norwood*), Cape Cod Pediatrics (*Forestdale*), and Winthrop Community Health Center (*Winthrop*).

Michigan: Botsford Pediatrics (*Farmington*), H. M. Hildebrandt, MD (*Ypsilanti*), Essexville Medical Clinic (*Bay City*), Downriver Pediatric Associates, PC (*Lincoln Park*), Child Health Associates (*Ann Arbor*), Pediatric & Family Care of Rochester Hills, PC (*Rochester Hills*), Lee & Kim Associates (*Warren*), and Orchard Pediatrics (*West Bloomfield*).

Minnesota, Minnetonka: South Lake Pediatrics.

Missouri: Pediatric Associates of SW Missouri (*Joplin*), Children's Clinic (*Springfield*), and Doctor's Clinic (*Carruthersville*).

Montana, Stevensville: Stevensville Pediatrics.

New Hampshire: Exeter Pediatric Associates (*Exeter*), Lahey-Hitchcock Clinic, Concord, Dartmouth-Hitchcock Clinic (*Lebanon*), Laconia Clinic (*Laconia*), Pediatric & Adolescent Medicine (*Kingston*), and Dartmouth-Hitchcock Clinic, Keene.

New Jersey: Kids Care Pediatrics (*Egg Harbor Township*), Salem Road Pediatrics (*Burlington*), and Coventry Family Practice (*Phillipsburg*).

New Mexico, Albuquerque: Albuquerque Pediatric Associates, Ltd, and University of New Mexico Hospital.

Nevada: Physician's Center West (*Fallon*), and Job's Peak Primary Care Specialists (*Gardnerville*).

New York-1: Panorama Pediatric Group, Elmwood Pediatric Group, Park Medical Group, Edward Lewis, MD, and Genesee Health Service (*Rochester*); Albany Medical College Pediatric Group; Southern Tier Health Associates (*Wayland*); Gayle Buckley, MD (*Ballston Lake*); Pine Street Pediatric Associates, PC (*Kingston*); North Country Children's Clinic (*Watertown*); and Springville Pediatrics (*Springville*).

New York-2: Women & Children's Health Center (*Long Island City*), Gary Mirkin, MD (*Great Neck*), Southampton Pediatric Associates (*Southampton*), and Sonia Vinas, MD (*Brooklyn*).

New York-3, New York: Saint Vincent's Pediatric Associates.

(*continued*)

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North Carolina: Eastover Pediatrics (*Charlotte*), Triangle Pediatric Center (*Cary*), and Peace Haven Family Health Center (*Winston-Salem*).

North Dakota: Medical Arts Clinic (*Minot*), Altru Clinic (*Grand Forks*), Dakota Clinic, Ltd–Jamestown.

Ohio: Bryan Medical Group (*Bryan*), South Dayton Pediatrics, Inc (*Dayton*), Oxford Pediatrics & Adolescents (*Oxford*), Pediatrics (*Portsmouth*), Family Health Center (*Idaho*), Oberlin Clinic (*Oberlin*), Children's Hospital Physicians Associates (*Twinsburg*), North Central Ohio Family Care (*Galion*), Drs Harris & Rhodes (*Lancaster*).

Oklahoma: Pediatric & Adolescent Care and OU Pediatric Clinic (*Tulsa*), and Eastern Oklahoma Medical Plaza (*Poteau*).

Oregon: Eugene Clinic (*Eugene*), North Bend Medical Center (*Coos Bay*).

Pennsylvania: Pennridge Pediatric Associates (*Sellersville*), Praful Bhatt, MD (*Lock Haven*), Reading Pediatrics, Inc (*Wyomissing*), Children's Health Care (*Allentown*), Erdenheim Pediatrics (*Flourtown*), Yoon-Taek Chun, MD (*East Stroudsburg*), Pediatric Associates of Plymouth (*Norristown*), Plum Pediatrics (*Pittsburgh*), Einstein Community Health Associates and Pediatric Group Services (*Philadelphia*), Cevallos and Moise Pediatric (*Quakertown*), VNA KidsCare (*Bethlehem*), Laurel Health Center (*Blossburg*).

Puerto Rico, San Juan: Edna Zayas, MD, and Pediatric Ambulatory Clinic.

Rhode Island, Cranston: Marvin Wasser, MD.

South Carolina: Anderson Pediatric Group (*Anderson*), Grand Strand Pediatrics & Adolescent Medicine (*Surfside Beach*), and Barnwell Pediatrics, PA (*Barnwell*).

Tennessee, Johnson City: Johnson City Pediatrics, PC.

Texas: The Pediatric Clinic (*Greenville*), Winnsboro Pediatrics (*Winnsboro*), Pediatrics (*Sherman*), Sarah Helfand, MD, and White Rock Pediatrics, PA (*Dallas*), Cleveland Pediatric & Adolescent Clinic (*Cleveland*), University of Texas Health Center at Tyler–Pediatrics, Pediatric Clinic (*Mineral Wells*), UNTHSC at Fort Worth Pediatric Clinic, and Family Medical Center (*Big Spring*).

Utah: Gordon Glade, MD, and John Weipert, MD (*American Fork*); Mountain View Pediatrics (*Sandy*); and Granger Medical Center, Willow Creek Pediatrics, and University of Utah Health Sciences Center (*Salt Lake City*).

Vermont: University Pediatrics (*Burlington*); Practitioners of Pediatric Medicine, CHP Timber Lane Pediatrics, and Joseph Hagan, Jr, MD (*South Burlington*); CHP Brattleboro Pediatrics (*Brattleboro*); University Pediatrics (*Williston*); Rebecca Collman, MD (*Colchester*); Mousetrap Pediatrics (*Milton*); Judy Orton, MD (*Bennington*); and St Johnsbury Pediatrics (*St Johnsbury*).

Virginia: Pediatric Associates of Richmond, Inc; Alexandria Lakeridge Pediatrics; Drs Casey, Goldman, Lischwe, Garrett & Kim and Pediatric Clinic (*Arlington*); Fishing Bay Family Practice (*Deltaville*); and Stafford Pediatrics, PC (*Stafford*).

Washington: Valley Children's Clinic (*Renton*), Rockwood Clinic (*Spokane*), Yakima Valley Farm Workers Clinic (*Toppenish*), Paulouse Pediatrics (*Pullman*), Columbia Health Center (*Seattle*).

West Military, Lackland Air Force Base: Department of Pediatrics/PSP.

West Virginia: Grant Memorial Pediatrics (*Petersburg*), and Tess Alejo, MD (*Martinsburg*).

Wisconsin: Beloit Clinic SC, Gundersen Clinic (La Crosse); Waukesha Pediatric Associates and Aurora Health Center–Waukesha (*Waukesha*); and Children's Hospital of Wisconsin Downtown Health Center (*Milwaukee*).

Wyoming: Jackson Pediatrics (*Jackson*), and Cheyenne Children's Clinic (*Cheyenne*).

What This Study Adds

It is known that 3% to 10% of young febrile infants have UTIs and that uncircumcised boys are at highest risk. It is not known whether pediatric practitioners follow guidelines and order urine tests for all febrile infants or whether they order urine tests selectively. To our knowledge, no previous studies have reported the short-term follow-up results of untreated febrile infants whose urine was not initially tested.

We found that many pediatric practitioners ordered initial urine tests selectively. They were more likely to test younger and sicker infants and those with no apparent fever source, but not uncircumcised boys, girls, and those with a fever for more than 24 hours, although these infants are at higher risk of a UTI. Only 2 of 807 infants not initially tested or treated with antibiotics were subsequently diagnosed as having a UTI, and both did well, suggesting that, with close follow-up, short-term adverse outcomes from selective urine testing are uncommon.

might differ in these infants. Similarly, some eligible infants who presented to PROS practitioners were not enrolled. However, whether such infants were more, equally, or less ill than infants in the study, the main conclusions of the study would not be affected.

CONCLUSIONS

Many pediatric practitioners test the urine of young febrile infants according to their clinical judgment rather than routinely. Although this approach differs from usual recommendations, we found few late diagnoses of UTIs and no cases of UTIs with bacteremia among more than 800 infants whose urine was not initially tested. This suggests that a selective approach to urine testing is likely to be safe in the hands of experienced practitioners who closely follow up their patients, as was the case in the present study. However, when using a selective approach to testing for UTIs, some factors placing infants at high risk for a UTI, including female sex, lack of circumcision, and longer duration of fever, should be more

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heavily weighted in deciding which infants should undergo urine testing.

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