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Screening for Urinary Tract Infection in Infants in the Emergency Department: Which Test Is Best?

Kathy N. Shaw, MD*; Karin L. McGowan, PhD*; Marc H. Gorelick, MD*; and J. Sanford Schwartz, MD†

ABSTRACT. *Objective.* Comparison of rapid tests and screening strategies for detecting urinary tract infection (UTI) in infants.

Methods. Cross-sectional study conducted in an urban tertiary care children's hospital emergency department and clinical laboratories of 3873 infants <2 years of age who had a urine culture obtained in the emergency department by urethral catheterization; results of urine dipstick tests for leukocyte esterase or nitrites, enhanced urinalysis (UA) (urine white blood cell count/mm³ plus Gram stain), Gram stain alone, and dipstick plus microscopic UA (white blood cells and bacteria per high-powered field) compared with urine culture results (positive urine results defined as $\geq 10^4$ colony-forming units per milliliter of urinary tract pathogen) for each sample. Cost comparison of 1) dipstick plus culture of all urine specimens versus 2) cell count \pm Gram stain of urine, culture only those with positive results.

Results. The enhanced UA was most sensitive at detecting UTI (94%; 95% confidence interval: 83,99), but had more false-positive results (16%) than the urine dipstick or Gram stain (3%). The most cost-effective strategy was to perform cultures on all infants and begin presumptive treatment on those whose dipstick had at least moderate (+2) leukocyte esterase or positive nitrite at a cost of \$3.70 per child. With this strategy, all infants with UTI were detected. If the enhanced UA was used to screen for when to send the urine for culture, 82% of cultures would be eliminated, but 4% to 6% of infants with UTI would be missed and the cost would be higher (\$6.66 per child).

Conclusion. No rapid test can detect all infants with UTI. Physicians should send urine for culture from all infants and begin presumptive treatment only on those with a significantly positive dipstick result. The enhanced UA is most sensitive for detecting UTI, but is less specific and more costly, and should be reserved for the neonate for whom a UTI should not be missed at first visit. *Pediatrics* 1998;101(6). URL: <http://www.pediatrics.org/cgi/content/full/101/6/e1>; *urinalysis, Gram stain, dipstick, UTI, rapid screening, febrile infants.*

ABBREVIATIONS. UTI, urinary tract infection; ED, emergency department; WBC, white blood cells; UA, urinalysis; LE, leukocyte esterase; CFU/mL, colony forming units per milliliter; CI, confidence interval.

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Recent research has indicated that the prevalence of urinary tract infection (UTI) in febrile young children in the emergency department (ED) is ~3% to 5%, and in some groups, as high as 30%.^{1,2} Additionally, recent use of nuclear renal scans has indicated that the majority of febrile young children with UTI have pyelonephritis, putting them at risk for renal scarring and the possible long-term sequelae of hypertension and chronic renal failure.³⁻⁵ It is imperative that physicians identify these children to institute early treatment, work-up of their urinary tracts, and provide follow-up.

Although there are several screening tests for UTI, there has been no prospective clinical comparison of these tests in the same sample of children in the ED. Test results reported in the literature vary by the definition of UTI and sample population.⁶⁻¹³ Recently, the enhanced urinalysis (UA), white blood cell (WBC) count per cubic millimeter plus Gram stain, has been proposed as being a more sensitive method for detecting UTI in young children and as a screen to eliminate cultures.⁶⁻⁸ This test, however, is not used routinely in most hospitals. The aims of this study were to 1) provide a prospective comparison of the rapid screening tests' abilities (urine dipstick, a combination of dipstick and microscopy, enhanced UA, and Gram stain alone) to detect UTI in a sample of young children in our ED; and 2) compare the test costs and outcomes of three possible screening strategies for UTI (bedside dipstick and culture for all⁹; enhanced UA for all, culture positive results only⁷; and urine cell count for all, culture \pm Gram stain positive results only).⁷

METHODS

Clinical Information

This was a cross-sectional study conducted prospectively in an urban children's hospital ED and its clinical laboratories. The clinical practice in our ED is to obtain urine cultures on boys <1 year of age and girls <2 years of age by urethral catheterization, if they do not have a definite source for their fever ($\geq 38.3^\circ\text{C}$) or do have UTI symptoms. As part of a study monitoring UTI prevalence in these children, the bedside nurse labeled the urine specimens to identify them for an additional laboratory test (enhanced UA). Demographic data, temperature, and results of tests and cultures were recorded by research nurses. Culture analyses were obtained for all urine specimens.

Laboratory Methods

As per routine clinical practice, the urine specimens were sent to the hospital laboratories in sterile containers by pneumatic tube, and trained laboratory technologists performed the tests using standard laboratory procedures. Urine for culture was refrigerated if not plated within 10 minutes of receipt. The urine dipstick and

UA tests were performed immediately on fresh urine. Extra urine was saved by each laboratory and stored at 2°C to 6°C, and the two nonstandard tests (cell count and Gram stain) were performed daily at no cost to the patient until study funds were depleted.

Technologists in the hematology laboratory performed the dipstick, microscopic UA, and cell count tests. Results of the dipstick test (Multistix 10SG 228, Bayer Diagnostics, Elkhart, IN) were interpreted visually according to standard color charts. The leukocyte esterase (LE) measurement was read after 2 minutes and recorded as negative, trace, small (+1), moderate (+2), or large (+3). The nitrite measurement was read at 60 seconds and recorded as negative or positive. The current clinical practice at our institution, based on previous study,¹⁰ is to use the urine dipstick on all specimens. If the dipstick indicates a positive finding for any component (including LE, nitrite, ketones, protein, glucose, or blood), a microscopic UA is performed. Urine was centrifuged for 5 minutes at low speed (2200 rpm), and the number of leukocytes and bacteria per average high-powered field (40 × magnification) recorded. For the WBC count, uncentrifuged urine was drawn into a Neubauer (Reichert, Buffalo, NY) hemocytometer by capillary action. Leukocytes were counted on one side of the chamber and multiplied by 1.1 to obtain a total cell count per cubic millimeter (Fig 1).

Quantitative urine cultures and Gram stain were performed in the hospital microbiology laboratory. Urine received in sterile containers was inoculated onto blood and MacConkey agar plates with a 0.01 mL calibrated loop, incubated at 35°C, and examined daily for growth for 2 days. Smears were prepared using 2 drops of uncentrifuged urine on a slide within the standardized marked area (1.5 cm in diameter), air-dried, fixed, and Gram-stained. The average number of bacteria per 10 oil immersion fields, morphology, and Gram stain were recorded.

Definitions and Costs

A positive urine culture was defined as growth of a urinary tract pathogen at $\geq 10^4$ colony-forming units per milliliter (CFU/mL).¹⁴ Urinary tract pathogens in this age group were considered *Escherichia coli*, *Proteus sp*, *Klebsiella sp*, *Enterococcus sp*, *Enterobacter sp*, *Pseudomonas sp*, group β streptococci, *Serratia sp*, and *Staphylococcus aureus*. Nonpathogens included *Lactobacillus sp*, *Corynebacterium sp*, coagulase-negative staphylococci, and β -hemolytic streptococci, not group A or B. Cultures with growth of ≥ 500 CFU/mL of mixed organisms or nonpathogens were considered contaminated. No growth (< 100 CFU/mL) or growth of < 500 CFU/mL was considered negative.

The cost, not charges or reimbursement rates, of urine cultures and screening tests was calculated using the Labtrak cost analysis software (Allied/Fisher Scientific, Pittsburgh, PA). This program takes into account the basic reagent and control costs; technologist salaries; and benefits, cost of kits, and time to perform tests and instrument costs (initial and maintenance). The cost of urine cultures was \$1.15 for negative results, \$15.05 for contaminants, and \$23.05 for positive results with antibiotic sensitivities. The urine cell count cost \$2.60, the Gram stain \$3.04, and both (the enhanced UA) \$5.64. The combination of dipstick and microscopic UA per-

formed by the hematology laboratory costs \$5.20, whereas the urine dipstick costs \$0.32 when performed at bedside.

Statistical Analysis

The sensitivity, specificity, and predictive values for the dipstick, cell count, Gram stain, enhanced UA, and combination dipstick plus microscopic UA were calculated at various definitions, with a positive urine culture as the standard. Cost analyses of three screening strategies were calculated using the prevalence of positive cultures and contaminants in the study, performance of the tests, and calculated costs as above. Descriptive statistics included frequencies of categorical data and mean \pm SD for continuous data.

RESULTS

Description of the Study Sample

During the study period (December 12, 1994, through February 2, 1996), 3873 cultures were sent from the ED on boys < 1 year and girls < 2 years of age. The majority of the children were African-American (83%) and female (61%), with an average age of 9.2 ± 5.7 months and temperature of $39.2^\circ\text{C} \pm 2.3^\circ\text{C}$. Urine was obtained by urethral catheterization except in 1% of patients, for whom urine was obtained by sterile preparation with a specimen caught mid-stream in a sterile container. No specimens were obtained by urine bag.

Of the 3873 total cultures, 105 (2.7%) were positive for UTI and 454 (11.7%) were contaminated. The majority of children with positive urine cultures were white (57%), female (74%), and had fever $\geq 38.3^\circ\text{C}$ (87%). Three quarters (81) of the positive cultures grew $\geq 100\,000$ CFU/mL, whereas 13% (13) had growth between 50 000 and 100 000 CFU/mL and 10%¹¹ had growth $< 50\,000$ CFU/mL. Overall, 91% (92 of 101 tested) had evidence of pyuria by cell count (≥ 10 WBC/mm³), dipstick (at least trace LE), or microscopy (≥ 5 WBC/high-powered field). Of those positive cultures with $< 50\,000$ CFU/mL, 64% (7/11) had pyuria, whereas 90% of those with $\geq 50\,000$ CFU/mL had pyuria. The vast majority grew *E coli* (89%), with 3% *Enterobacter cloacae*, 2% *Enterococcus*, and 2% *Pseudomonas*. The remainder grew *Klebsiella*, group B β hemolytic strep, or *S aureus*.

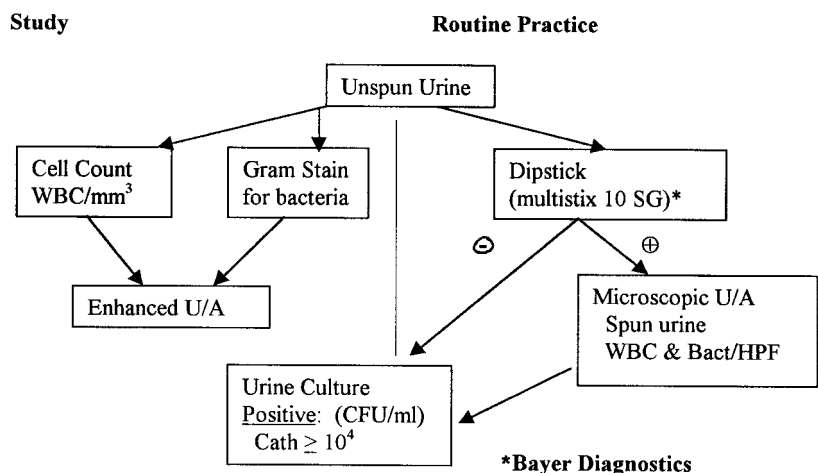


Fig 1. Methods: clinical laboratories.

Performance of Rapid Screening Tests

Table 1 lists the number of specimens and positive cultures, sensitivity, specificity, and positive and negative predictive values with 95% confidence interval (CI) values for each individual test. In the first section ("Most Sensitive Definitions"), the test parameters are defined at their most sensitive for detecting UTI, whereas in the second section ("Most Specific Definitions"), the test parameters are defined at their most specific to try to reduce the number of false-positive results. The enhanced UA was the most sensitive (94%), with the dipstick, cell count, combination dipstick and microscopy, and Gram stain each having sensitivities of ~80% (79% to 83%). The dipstick and Gram stain had much better specificity or fewer false-positive results, and therefore, a higher positive predictive value than either the combination of dipstick and microscopy or the enhanced UA at these definitions. A positive dipstick or Gram stain result in our sample of children where the prevalence is 3% indicated UTI in almost half of children. As expected in a sample with a low prevalence of UTI, all tests had very high ($\geq 99\%$) negative predictive values.

When the definition of the test results are changed to their most specific (Table 1), the sensitivity or ability to detect UTI is lowered for all tests. This is expected because a more rigorous definition of a positive result is used. The specificity improved remarkably, especially for the enhanced UA and the combination dipstick and microscopy. Both the dipstick LE or nitrate and the enhanced UA had $<1\%$ false-positive results. Negative predictive values remained at $\geq 99\%$.

If a positive urine culture were to be defined at $\geq 50\,000$ CFU/mL as suggested by Hoberman et al, the findings are similar. At the more sensitive definitions of a positive test result, the enhanced UA remains more sensitive (96%; 95% CI: 84,99), whereas the Gram stain and dipstick had lower sensitivity (89% and 81%, respectively) but significantly higher specificity (97% for both; 95% CI: 96,98). At the more rigorous and specific test definitions, the dipstick and enhanced UA had $<1\%$ false-positive results.

Although four of the nine specimens without pyuria are eliminated with this definition, seven infants with fever and significant pyuria would be considered to have contaminated urine.

Costs and Outcomes of Screening Strategies

Using both the performance (Table 1) and the cost of the tests, we compared three proposed screening strategies for a hypothetical cohort of 1000 children (Table 2). In the first, all children have a dipstick performed and all urine is sent for culture. The cost would be \$3.70 per child. No children with UTIs would be missed because all would have cultures performed. If the more rigorous definition of a positive dipstick result is used to determine when to treat presumptively, only 14 children would be treated unnecessarily, and 7 of the 27 children with UTI would have a delay in treatment until their urine culture results were known.

In the second strategy, all children would have enhanced UA, and only those with a positive enhanced UA would have urine cultured. The cost would be \$6.66 per child despite the fact that only 180 were cultured because the cost of an enhanced UA is much higher than that of a negative culture. Two children with UTI would have been missed because no culture would have been performed. If only those with a more rigorous definition for positive enhanced UA are treated, there would be fewer treated unnecessarily, and only 5 with delayed start in treatment when their urine culture results were known.

Finally, if only the cell count is performed initially to determine who should have urine obtained for culture and Gram stain, the cost decreases to \$4.80 per child; however, 5 children (18%) with UTI would be missed if no culture was performed. Using a more rigorous definition of a positive enhanced UA to determine treatment would reduce the number of children who have unnecessary treatment to 5 and those with delayed treatment to 2. Using only the cell count to determine whom to treat would not be ideal, even with a cost of \$3.48 per child, because 124 children who did not have UTI would be treated.

TABLE 1. Comparison of Rapid Screening Tests for UTI

Test	N	Positive Cultures	Sensitivity	Specificity % (95% CI)	PPV
Most sensitive definitions					
Dipstick (\geq trace LE or \oplus nitrite)	3394	95	79 (69,86)	97 (97,98)	46 (38,54)
Enhanced UA (≥ 10 WBC/mm ³ or \oplus Gram stain)	2016	52	94 (83,99)	84 (82,86)	13 (10,17)
Cell count (≥ 10 WBC/mm ³)	2193	57	82 (70,91)	87 (86,89)	15 (11,19)
Gram stain (any bacteria)	2305	62	81 (68,89)	97 (96,98)	43 (34,52)
Dipstick + UA*					
Dipstick \oplus or UA (≥ 5 WBC/HPF or any bacteria/HPF)	3394	95	83 (74,90)	87 (86,88)	16 (12,19)
Most specific definitions					
Dipstick (\geq moderate LE or nitrite)	3394	95	73 (62,81)	99 (98,99)	61 (52,70)
Enhanced UA (≥ 10 WBC/mm ³ plus \oplus Gram stain)	2016	52	75 (61,86)	99 (99,100)	80 (66,90)
Gram stain (single organism on Gram stain)	2305	62	79 (67,88)	98 (97,98)	49 (39,59)
Dipstick + UA*					
Dipstick \oplus plus UA \oplus (≥ 5 WBC plus bacteremia/HPF)	3394	95	73 (62,81)	98 (98,99)	57 (47,65)

* UA performed only if any component is positive on dipstick multistrip 10SG test including protein, blood, glucose, LE, NI, ketones. \oplus , positive.

TABLE 2. Comparison of Screening Strategies for UTI per 1000 Patients

Screening Strategy	Test Cost* Per Patient	Number of Patients With UTI Missed	Number of False- Positive Results	Number With Delayed Treatment
Dipstick and culture all				
<u>Treat if</u>				
≥Trace LE or nitrite ⊕	\$3.70	None	27	6
≥Moderate LE or nitrate	\$3.70	None	14	7
Enhanced UA all				
<u>Culture if</u> ≥10 WBC/mm ³ or ⊕ Gram stain				
<u>Treat if</u>				
≥10 WBC/mm ³ or ⊕ Gram stain	\$6.66	2	159	0
≥10 WBC/mm ³ and ⊕ Gram stain	\$6.66	2	5	5
Cell count all				
<u>Culture if</u> ≥10 WBC/mm ³				
<u>Treat if</u>				
≥10 WBC/mm ³	\$3.48	5	124	0
≥10 WBC/mm ³ and ⊕ Gram stain	\$4.80	5	5	2

* Costs of tests: dipstick by MR/RN, \$0.32; cell count, \$2.60; Gram stain, \$3.04; enhanced UA, \$5.64; dipstick and microscopic UA, \$5.20 per hospital laboratories.

Cost of urine cultures: negative, \$1.15; contaminant, \$15.05; positive with sensitivities to antibiotics, \$23.05.

⊕, positive.

In our study sample, there were 3 children who had a negative enhanced UA with a positive culture result. One 14-month-old child probably did not have a UTI because he also had a negative dipstick result, growth of only 15 000 CFU/mL of *Pseudomonas* on culture and was diagnosed with otitis media. The other 2 children were 7- and 10-month-old girls with pyuria by dipstick LE or microscopic UA with fevers $\geq 39.5^{\circ}\text{C}$ who grew $\geq 100\,000$ CFU/mL of *E coli* and did not have another source for fever on examination.

DISCUSSION

The enhanced UA, a combination of the urine cell count described in 1927 by Dukes¹⁵ and the urine Gram stain, has been proposed both as a more sensitive and specific method for identifying children with UTI^{6,7} and as a means of screening for when to have a urine culture performed.⁷ Indeed, the enhanced UA does appear to be most sensitive for detecting UTI in young children. Hoberman and co-workers⁷ also found 96% sensitivity for the enhanced UA in a similar sample of 4253 children <24 months of age, with a positive urine culture defined as $\geq 50\,000$ CFU/mL. The enhanced UA, however, was less specific (84% vs 93%) in our sample. Although the test was performed by trained personnel at both hospitals using the same procedure, our enhanced UA was performed by the hospital clinical laboratories, as would occur in routine clinical practice. The higher specificity by Hoberman and colleagues may be attributable to performing the test at an on-site study laboratory by a limited number of technicians.

Use of the enhanced UA to determine when to send a urine culture for tests or to begin presumptive treatment would eliminate the culturing of many samples, but it would be more expensive and miss 4% to 6% of children with UTI. Because renal scans, enhanced UA, and repeat microscopic UA are not routine practice at our institution, this is our best assessment based on the data obtained. Hoberman et al⁷ also found that the enhanced UA would miss 10% of positive cultures, of which 4% were determined to

have true UTI as determined by nuclear scan, repeat UA for pyuria, and acute phase reactants, whereas the remainder were presumed to have asymptomatic bacteriuria. The cost of this screening method is higher than that of performing dipstick and culturing of all specimens, misses some infants with UTI, and is not a test run routinely at most hospitals. Thus, urine cultures should be sent on all infants. The enhanced UA may be best reserved for neonates in whom both very high sensitivity is important for identification of a bacterial illness and early treatment may be more important.

The urine dipstick test for LE and nitrite continues to be a low-cost excellent screening test for UTI in children.⁹⁻¹¹ Of all the tests studied, it is the only one not requiring Clinical Laboratory Improvement Amendments certification and can be performed by the bedside nurse or physician. The strategy of urine dipstick and culture tests for all children for whom a UTI is considered is less costly, identifies all infants with UTI, and allows one to screen which children should begin presumptive treatment.

The urine Gram stain is comparable with the urine dipstick test in both sensitivity and specificity. A study by Lockhart and colleagues¹² of 207 infants <6 months of age with fever found the Gram stain to have a sensitivity of 94% (95% CI: 73,100) and specificity of 92% (95% CI: 8,95), which are comparable with our findings. Because its cost and difficulty of performance are much greater than the for the dipstick test, it is not as attractive as the dipstick test in clinical practice. In combination with the cell count, it comprises the enhanced UA. The cell count alone shows no advantage over dipstick tests or Gram stain because it had comparable sensitivity and is less specific. As a less expensive screen for when to send a urine culture and perform a Gram stain, it would miss 18% of the children with UTI.

Our study did not examine the use of the microscopic UA alone. Previous studies^{9,10,12} of young children have found it to have sensitivity in the 57% to 87% range, with lower specificity of 53% to 79%. It may perform better in older, symptomatic chil-

dren.^{9,13} Our practice of performing a microscopic UA on all urine specimens that are positive on dipstick study not appear to have any advantage over dipstick alone for screening for UTI in our ED.

This study was run at one urban children's hospital ED; therefore, prevalence, predictive values of the tests, and costs may not be generalized to other settings. Different definitions of UTI, study populations, and type and location of laboratories may alter test results.⁶⁻¹³ We believe a more conservative definition of $\geq 10^4$ CFU/mL of growth should be used because one would not want to miss 64% of infants with growth in the 10 000 to 50 000 CFU/mL range who had pyuria and pure growth of a urinary tract pathogen. Even at this definition, some children with $< 10^4$ CFU/mL growth of urinary tract pathogens or with growth of both contaminants and a pathogen may have been categorized incorrectly as not having infection. Although we are most concerned about children with pyelonephritis, which is best determined by nuclear scan,³⁻⁵ the standard in this study was a positive urine culture because nuclear renal scan is not performed routinely at our hospital. Thus, asymptomatic bacteriuria is difficult to distinguish, but is thought to have a prevalence of $< 1\%$.^{7,16}

No test can screen accurately for UTI in young children. The urine dipstick plus culture tests appear to be the most cost-effective strategy for screening and beginning presumptive treatment for UTI in febrile young children in the ED. In subsets of children who are particularly at high risk for UTI or its sequelae, one should consider performing the enhanced UA to identify more infants with possible UTI and to begin early presumptive treatment. However, additional cost-effectiveness analysis, which includes clinical predictors and long-term outcomes, is needed to determine the best and most effective screening strategy.

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