Automated Urinalysis and Urine Dipstick in the Emergency Evaluation of Young Febrile Children

**WHAT’S KNOWN ON THIS SUBJECT:** Urinary tract infection is the most common serious bacterial illness among febrile infants and young children. Automated urine cytometry may supplant traditional urinalysis, but diagnostic performance at unique pediatric cutpoints has not been described for this labor-saving technique.

**WHAT THIS STUDY ADDS:** We describe new, clinically useful cutpoints for automated leukocyte and bacterial counts. The sensitivity and specificity of bacterial counts $\geq 250$ cells/μL exceed those of other methods. However, point-of-care dipstick tests for leukocyte esterase or nitrite have acceptable performance.

**abstract**

**OBJECTIVE:** The performance of automated flow cytometric urinalysis is not well described in pediatric urinary tract infection. We sought to determine the diagnostic performance of automated cell counts and emergency department point-of-care (POC) dipstick urinalyses in the evaluation of young febrile children.

**METHODS:** We prospectively identified a convenience sample of febrile pediatric emergency department patients $\leq 48$ months of age who underwent urethral catheterization to obtain POC and automated urinalyses and urine culture. Receiver operating characteristic analyses were performed and diagnostic indices were calculated for POC dipstick and automated cell counts at different cutpoints.

**RESULTS:** Of 342 eligible children, 42 (12%) had urinary bacterial growth $\geq 50,000$/mL. The areas under the receiver operating characteristic curves were: automated white blood cell count, 0.97; automated bacterial count, 0.998; POC leukocyte esterase, 0.94; and POC nitrite, 0.76. Sensitivities and specificities were 86% and 98% for automated leukocyte counts $\geq 100$/μL and 98% and 98% for bacterial counts $\geq 250$/μL. POC urine dipstick with $1+$ leukocyte esterase or positive nitrite had a sensitivity of 95% and a specificity of 98%. Combinations of white blood cell and bacterial counts did not outperform bacterial counts alone.

**CONCLUSIONS:** Automated leukocyte and bacterial counts performed well in the diagnosis of urinary tract infection in these febrile pediatric patients, but POC dipstick may be an acceptable alternative in clinical settings that require rapid decision-making. Pediatrics 2014;134:523–529
Febrile illness is the most common reason for pediatric emergency department (ED) visits. The most common bacterial source of fever is urinary tract infection (UTI), with a prevalence of 3% to 7% among febrile ED patients <1 to 2 years of age and 8% to 14% among febrile infants <8 weeks of age. Rapid and accurate identification or exclusion of UTI may improve efficiency of the ED and acute care for febrile infants, particularly when the diagnostic strategy requires no blood sampling. Furthermore, upper tract infection is less frequent with early identification and treatment of UTI.

Flow cytometry quantifies the formed elements in urine and has variable sensitivity and specificity in the diagnosis of adult UTI. Only a small minority (15%) of hospital laboratories use automated cytometry to reduce reliance on labor-intensive manual microscopic urinalyses, but the 2011 American Academy of Pediatrics clinical practice guideline for UTI predicts that automated methods will become the most common laboratory-based method of diagnosis. Pediatric reference ranges for automated white blood cell (WBC) and bacterial counts, established without culture confirmation, may not define a clinically meaningful risk of pediatric UTI. Children comprised only 4% to 9% of populations that defined cutoffs for flow cytometric urinalysis against a culture standard. One pediatric study that evaluated automated cell counts with a culture standard applied adult reference values to an older (median age: 10 years), unselected subspecialty cohort. A recent comparison of automated digital microscopy and enhanced urinalysis among pediatric ED patients used cutoffs derived from manual microscopy. Because test performance varies with threshold, we sought to determine performance of urine flow cytometry over a range of WBC and bacterial count cutoffs and to describe the performance of point-of-care (POC) dipstick urinalyses in the diagnosis of UTI in young febrile ED patients <48 months of age.

METHODS

This prospective, observational study was performed from May 15, 2009, to May 15, 2010 in the ED and clinical laboratory of a freestanding tertiary children’s hospital. The ED, with a yearly census of ~65 000, serves as the principal pediatric emergency facility for a population of ~3 million. The institutional review board of the University of California San Diego approved this study and granted a waiver of informed consent.

We assembled a convenience sample of children <48 months old who presented to the ED with fever and a clinical need to evaluate for UTI. Attending physicians ordered laboratory analysis and prescribed treatment at their discretion. Patients were included who had temperatures ≥38°C in the ED or tactile or documented fevers at home within 24 hours and who underwent urethral catheterization to obtain samples for POC dipstick testing, automated urinalyses, and urine cultures. Patients were excluded who had incomplete data or urine testing, who had received systemic antibiotics in the previous 24 hours, who were immunocompromised or at risk for neutropenia, or who had conditions that predispose to asymptomatic genitourinary bacterial colonization (including neurogenic bladder, chronic or intermittent bladder instrumentation, or surgical diversion of the urinary tract). Patients with risk factors for acute symptomatic UTI who generally had acellular, sterile urine between infections and whose initial evaluation and treatment are similar to those of other febrile patients were included.

Competency-verified ED nurses performed POC dipstick testing (Siemens Multistix 10 SG, Siemens Corporation, Diagnostics Division, Elkhart, IN), and they visually interpreted reagent strips according to standard color charts. Urinary nitrite was recorded as positive or negative and leukocyte esterase (LE) as negative, trace, 1+ (small), 2+ (moderate), or 3+ (large). The specimens were then transported by pneumatic tube to the clinical laboratory, where technologists interpreted urine test strips with the Siemens Clinitek 500 Urine Chemistry Analyzer (Bayer Corporation, Elkhart, IN) and performed cell counts with the Sysmex UF-1000i Automated Urine Particle Analyzer (Sysmex America, Inc, Lincolnshire, IL). The UF-1000i quantifies to the nearest 0.1 cell/μL the formed elements in 0.8 to 1.2 mL of uncentrifuged urine based on size, shape, and staining characteristics. Technologists verified automated WBC counts >20/μL manually by using hemocytometer slides. Using standard quantitative culture methods, a positive urine culture result was defined as growth of ≥50 000 CFU/mL of a urinary pathogen. Urine cultures with growth of normal flora, mixed organisms, or <50 000 CFU/mL of a pathogen were considered negative.

Data collected during the ED visit included age, gender, medical history, maximum home and ED temperatures, and results of POC and automated dipstick testing and automated WBC counts. We obtained culture results from the electronic medical record and reviewed all UF-1000i printouts to confirm the reported automated WBC counts and to obtain manual WBC and automated bacterial counts not reported in the medical record.

Primary outcome measures included the POC LE and nitrite results, automated urine WBC and bacterial counts, and urine culture results. Our sample size was determined by using precision of calculated sensitivity. Based on a previously observed 13% prevalence of...
UTIs in febrile children in our ED, we calculated that a sample size of 375 patients would yield 95% confidence intervals (CIs) ± 10% around a point estimate for a sensitivity of 85%. A receiver operating characteristic (ROC) analysis was performed of the ability of POC LE and nitrite measurements and automated WBC and bacterial counts to predict urine cultures yielding ≥50,000 CFU/mL. For analysis of test performance at different thresholds, WBC and bacterial counts were rounded to whole numbers, and we calculated sensitivity, specificity, and negative and positive likelihood ratios (LRs). To inform clinicians who must integrate multiple test results, we calculated the same indices for combinations of POC LE and nitrites and combinations of WBC and bacterial counts. Because reported sensitivity varies widely for patients <3 months of age,15,6,21 and because current teaching commonly cites increased false-negative rates for young infants and children,22,23 indices were calculated for the subset of patients 0 to 90 days of age.

RESULTS

Of 476 eligible patients, 134 (28%) were excluded because urine testing was incomplete or the printout containing bacterial counts was not available. Of the 342 remaining patients, 42 (12.3%) had cultures positive for *Escherichia coli* (*n* = 37), *Klebsiella pneumoniae* (*n* = 3), *Klebsiella oxytoca* (*n* = 1), and *Enterococcus faecium* (*n* = 1). The urinary analysis for the ampicillin-sensitive *Enterococcus* isolate was negative for LE and nitrite and had 19 WBC/μL and 337 bacterial/μL. Four patients had single urinary pathogens in concentrations <50,000 CFU/mL, and 1 had >4 organisms at a concentration ≥80,000 CFU/mL. All 5 had positive POC nitrite or LE, 4 had high WBC or bacterial counts, and all received antibiotic therapy for UTI. Twenty-seven cultures yielded mixed organisms or low growth, and none resulted in antibiotic treatment of UTI. Except for characteristics known to influence the risk of UTI,24 patients with and without UTI had similar pretest clinical features (Table 1).

POC and laboratory results agreed in 98.5% of nitrite and 98.0% of LE determinations. Of the 5 patients with POC-positive, laboratory-negative nitrite results, 4 had growth of pathogens ≥10^5 CFU/mL, and the fifth received antibiotics after the culture yielded 30,000 CFU/mL of *E. coli*. For the 10 POC-LE-positive, culture-negative specimens, 6 corresponding laboratory LE test results were positive, including all 4 with POC LE ≥1+ and 2 of 6 trace positive tests. Three laboratory trace-LE-positive, culture-negative specimens had corresponding negative POC results. All 4 POC-LE-negative, culture-positive specimens were LE-negative according to the laboratory. Automated cytometry counts ranged from 0 to 39,374/μL for WBC and 0 to 54,445/μL for bacteria (Table 1). Concurrent manual hemocytometer WBC counts on 323 samples (94%) differed from the automated counts by ≥10% in 58 (18%). However, the differences exceeded 10 cells/μL in only 33 samples (10%) (Fig 1). In only 2 culture-negative cases did manual and automated WBC counts lie on opposite sides of the cutoff of 100 cells/μL; for 92% of differences, automated counts were higher than manual counts.

In the ROC analysis, all urine test results except nitrite had areas under the curve (AUCs) ≥0.94, and the AUC for the bacterial count was highest. AUCs (with 95% CIs) were as follows: WBC, 0.97 (0.95–0.99); bacteria, 0.998 (0.996–0.999); POCSLE, 0.94 (0.89–0.996); and POC nitrite, 0.76 (0.66–0.86).

Favorable sensitivity and specificity pairs resulted from selected thresholds for POC dipstick and automated cell counts in the diagnosis of UTI (Table 2). POC dipsticks with ≥1+ LE or positive nitrite yielded a sensitivity of 0.95 and a specificity of 0.98. Clinically practical cytometric thresholds were 100 cells/μL for automated WBC counts (sensitivity: 0.68; specificity: 0.88) and 250 cells/μL for automated bacterial counts (sensitivity: 0.98; specificity: 0.98). Higher bacterial count thresholds improved specificities and LRs minimally with a substantial decrease in sensitivity. Among the 72 patients aged 0 to 90 days with 11 UTIs, comparable performance occurred.

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**TABLE 1 Characteristics of the 342 Study Patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>UTI (N = 42)</th>
<th>No UTI (N = 300)</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mo, median (IQR)</td>
<td>6.2 (3.1–12.1)</td>
<td>8.2 (3.7–14.3)</td>
<td>8.1 (3.6–14.3)</td>
</tr>
<tr>
<td>Female gender, n (%)</td>
<td>24 (57)</td>
<td>178 (59)</td>
<td>202 (59)</td>
</tr>
<tr>
<td>Circumcised males, n/N (%)</td>
<td>2/18 (11)</td>
<td>36/111 (32)</td>
<td>38/129 (29)</td>
</tr>
<tr>
<td>Maximum home temperature, °C, mean ± SD</td>
<td>39.1 ± 0.7</td>
<td>39.0 ± 0.6</td>
<td>39.0 ± 0.8</td>
</tr>
<tr>
<td>Maximum ED temperature, °C, mean ± SD</td>
<td>38.8 ± 0.9</td>
<td>38.7 ± 1.1</td>
<td>38.8 ± 1.1</td>
</tr>
<tr>
<td>Previous UTI, n (%)</td>
<td>3 (19)</td>
<td>15 (5)</td>
<td>23 (7)</td>
</tr>
<tr>
<td>Genitourinary abnormalities, n (%)</td>
<td>4 (10)</td>
<td>6 (2)</td>
<td>10 (3)</td>
</tr>
<tr>
<td>Automated WBC count, cells/μL</td>
<td>1433 (393–5894)</td>
<td>12 (6–28)</td>
<td>13 (6–28)</td>
</tr>
<tr>
<td>Range</td>
<td>18–39,374</td>
<td>0–881</td>
<td>0–39,374</td>
</tr>
<tr>
<td>Automated bacterial count, cells/μL</td>
<td>7138 (2074–14,055)</td>
<td>18 (11–38)</td>
<td>20 (11–60)</td>
</tr>
<tr>
<td>Range</td>
<td>140–54,445</td>
<td>1–1905</td>
<td>1–54,445</td>
</tr>
<tr>
<td>ED diagnosis of UTI, n (%)</td>
<td>40 (95)</td>
<td>7 (2)</td>
<td>47 (14)</td>
</tr>
</tbody>
</table>

IQR, interquartile range.

a Male circumcision status presented as number circumcised per number of male patients. Data were missing for 11 patients in the non-UTI group. UTI rate among uncircumcised boys was 16 (18%) of 91 patients; among circumcised boys, it was 2 (5%) of 38.

b Home temperature measurements were available in 21 patients in the UTI group and in 255 patients in the non-UTI group.

c Abnormalities among UTI group: vesicoureteral reflex, history of nephrolithiasis, dysplastic kidney, and hydrenephrosis; among non-UTI group: duplex collecting system (2), vesicoureteral reflex, dysplastic kidney (2), hypospadias repair.
at thresholds of POC LE $\geq 1+$ (sensitivity: 1.0 [95% CI: 0.74–1.0]; specificity: 0.93 [95% CI: 0.84–0.97]), $\geq 100$ WBC/$\mu$L (sensitivity: 0.91 [95% CI: 0.62–0.98]; specificity: 0.95 [95% CI: 0.87–0.98]), and $\geq 250$ bacteria/$\mu$L (sensitivity: 1.0 [95% CI: 0.74–1.0]; and specificity: 0.95 [95% CI: 0.87–0.98]). At the threshold of 10 WBC/$\mu$L used for the enhanced urinalysis,25,26 sensitivity of the automated WBC count increased to 1.0, but specificity decreased to 0.40 (Table 3). No combination of WBC count $\geq 10/\mu$L and bacteria at any concentration outperformed the automated bacterial count alone. Combinations of high WBC and bacterial counts achieved specificities as high as 0.993 with sensitivities ranging from 0.79 to 0.83.

**DISCUSSION**

In this study, we report the excellent diagnostic performances of automated cytometry and POC dipstick among young febrile children evaluated for UTI in a pediatric ED. Automated bacterial counts exhibited the best ability to diagnose UTI. A bacterial cutoff point of 100/$\mu$L had a sensitivity of 1.0 and a specificity of 0.95, and a cutoff point of 250/$\mu$L produced a clinically useful high-sensitivity, high-specificity combination (0.98 for both). Automated WBCs began to have useful LRs at counts $\geq 100/\mu$L. However, the combination of POC dipstick LE and nitrites, although slightly less sensitive, had acceptable diagnostic performance and may be an attractive alternative option when manual or automated microscopic urinalysis is not available or practical. POC and automated tests performed well in the subset of patients 0 to 90 days of age.

Most studies of automated urinalysis predominantly involve adults and often include hospitalized, elderly, or uncharacterized patients.10,16,19 Children <16 years of age comprised 9% of a combined adult and pediatric study population for which a combination of $\geq 15$ WBC/$\mu$L or $\geq 500$ bacteria/$\mu$L yielded a sensitivity of 0.98 and a specificity of 0.25 for urine bacterial growth $\geq 10^5$/mL.15 Patients <3 years of age

**TABLE 2** Test Characteristics of POC Dipstick and Automated Cell Count Urinalyses

<table>
<thead>
<tr>
<th>Test and Threshold</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR +</th>
<th>LR -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrites</td>
<td>22/42 (0.52), 0.38–0.67</td>
<td>298/300 (0.99), 0.98–0.998</td>
<td>78.6, 18.2–322.2</td>
<td>0.48, 0.35–0.86</td>
</tr>
<tr>
<td>LE $\geq$ trace</td>
<td>38/42 (0.91), 0.78–0.96</td>
<td>290/300 (0.97), 0.84–0.98</td>
<td>27.1, 14.6–50.3</td>
<td>0.10, 0.04–0.25</td>
</tr>
<tr>
<td>LE $\geq$ trace OR nitrite positive</td>
<td>40/42 (0.95), 0.84–0.99</td>
<td>289/300 (0.96), 0.84–0.98</td>
<td>26.0, 14.5–46.6</td>
<td>0.05, 0.01–0.19</td>
</tr>
<tr>
<td>LE $\geq$1+</td>
<td>37/42 (0.88), 0.75–0.95</td>
<td>296/300 (0.99), 0.97–0.995</td>
<td>66.1, 24.8–176.0</td>
<td>0.12, 0.05–0.27</td>
</tr>
<tr>
<td>LE $\geq$1+ OR nitrite positive</td>
<td>40/42 (0.95), 0.84–0.99</td>
<td>295/300 (0.98), 0.96–0.99</td>
<td>57.1, 23.9–136.6</td>
<td>0.05, 0.01–0.19</td>
</tr>
<tr>
<td>LE $\geq$2+</td>
<td>35/42 (0.83), 0.89–0.92</td>
<td>297/300 (0.99), 0.97–0.997</td>
<td>83.3, 26.8–259.0</td>
<td>0.17, 0.09–0.33</td>
</tr>
<tr>
<td>LE $\geq$2+ OR nitrite positive</td>
<td>39/42 (0.93), 0.81–0.98</td>
<td>296/300 (0.99), 0.97–0.995</td>
<td>69.6, 26.2–185.0</td>
<td>0.07 0.02–0.22</td>
</tr>
</tbody>
</table>

**Automated counts**

| WBC $\geq 10$ cells/$\mu$L | 42/42 (1.0), 0.92–1.0 | 120/300 (0.40), 0.35–0.46 | 1.7, 1.5–1.8 | 0.0 — |
| WBC $\geq 25$ cells/$\mu$L | 39/42 (0.93), 0.81–0.98 | 246/300 (0.82), 0.77–0.86 | 5.2, 4.0–6.7 | 0.08, 0.03–0.26 |
| WBC $\geq 50$ cells/$\mu$L | 35/42 (0.88), 0.72–0.85 | 285/300 (0.95), 0.92–0.97 | 17.1, 10.3–28.5 | 0.15, 0.07–0.32 |
| WBC $\geq 100$ cells/$\mu$L | 36/42 (0.89), 0.72–0.85 | 294/300 (0.98), 0.96–0.99 | 42.9, 19.2–95.5 | 0.15, 0.07–0.31 |
| WBC $\geq 200$ cells/$\mu$L | 34/42 (0.81), 0.87–0.90 | 295/300 (0.98), 0.96–0.99 | 48.6, 20.1–117.3 | 0.19, 0.10–0.36 |
| Bacteria $\geq 50$ cells/$\mu$L | 42/42 (1.0), 0.92–1.0 | 244/300 (0.81), 0.77–0.85 | 5.4, 4.2–8.8 | 0.0 — |
| Bacteria $\geq 100$ cells/$\mu$L | 42/42 (1.0), 0.92–1.0 | 285/300 (0.95), 0.92–0.97 | 20.0, 12.2–32.8 | 0.0 — |
| Bacteria $\geq 250$ cells/$\mu$L | 41/42 (0.98), 0.88–0.996 | 294/300 (0.98), 0.96–0.99 | 48.8, 22.1–107.9 | 0.02, 0.0–0.17 |
| Bacteria $\geq 500$ cells/$\mu$L | 39/42 (0.93), 0.81–0.98 | 295/300 (0.98), 0.96–0.99 | 55.7, 23.3–133.4 | 0.07, 0.02–0.22 |

Sensitivity presented as true-positives per number with UTI and specificity as true-negatives per number without UTI with point estimates and 95% CIs for proportions. LRs presented with 95% CIs, except when a zero term appears in a denominator. LR +, LR of positive test result; LR −, LR of negative test result.

**FIGURE 1** Scatter plot of manual microscopic WBC counts against automated WBC counts ($r = 0.999$).
TABLE 3 Test Characteristics of Combinations of Automated WBC and Bacterial Counts

<table>
<thead>
<tr>
<th>Test and Threshold</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR +</th>
<th>LR –</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC ≥10 cells/μL</td>
<td>42/42 (1.0), 0.92–1.0</td>
<td>527/500 (0.88), 0.78–0.86</td>
<td>473.3, 0.22, 0.12–0.38</td>
<td>0.98–0.99, 0.96–0.98, 0.95–0.99</td>
</tr>
<tr>
<td>WBC ≥10 cells/μL and bacteria ≥50 cells/μL</td>
<td>42/42 (1.0), 0.92–1.0</td>
<td>247/300 (0.82), 0.78–0.86</td>
<td>5.7, 4.4–7.2</td>
<td>0.0–0.0</td>
</tr>
<tr>
<td>WBC ≥10 cells/μL and bacteria ≥100 cells/μL</td>
<td>42/42 (1.0), 0.92–1.0</td>
<td>286/300 (0.95), 0.92–0.97</td>
<td>21.4, 12.9–35.7</td>
<td>0.0–0.0</td>
</tr>
<tr>
<td>WBC ≥100 cells/μL and bacteria ≥250 cells/μL</td>
<td>41/42 (0.98), 0.88–0.99</td>
<td>294/500 (0.98), 0.96–0.99</td>
<td>48.8, 22.1–107.9</td>
<td>0.02, 0.0–0.17</td>
</tr>
<tr>
<td>WBC ≥100 cells/μL and bacteria ≥500 cells/μL</td>
<td>39/42 (0.93), 0.81–0.98</td>
<td>295/500 (0.98), 0.96–0.99</td>
<td>55.7, 23.5–135.3</td>
<td>0.07, 0.02–0.22</td>
</tr>
<tr>
<td>WBC ≥25 cells/μL and bacteria ≥100 cells/μL</td>
<td>39/42 (0.93), 0.81–0.98</td>
<td>293/500 (0.98), 0.95–0.99</td>
<td>39.8, 19.1–83.2</td>
<td>0.07, 0.02–0.22</td>
</tr>
<tr>
<td>WBC ≥25 cells/μL and bacteria ≥250 cells/μL</td>
<td>38/42 (0.91), 0.78–0.96</td>
<td>297/500 (0.99), 0.97–0.99</td>
<td>90.5, 29.2–280.1</td>
<td>0.10, 0.04–0.24</td>
</tr>
<tr>
<td>WBC ≥50 cells/μL and bacteria ≥100 cells/μL</td>
<td>38/42 (0.91), 0.78–0.96</td>
<td>294/500 (0.98), 0.96–0.99</td>
<td>42.9, 19.2–95.5</td>
<td>0.15, 0.07–0.31</td>
</tr>
<tr>
<td>WBC ≥50 cells/μL and bacteria ≥250 cells/μL</td>
<td>35/42 (0.83), 0.69–0.92</td>
<td>297/500 (0.99), 0.97–0.99</td>
<td>83.3, 26.8–259.0</td>
<td>0.17, 0.09–0.33</td>
</tr>
<tr>
<td>WBC ≥100 cells/μL and bacteria ≥100 cells/μL</td>
<td>36/42 (0.88), 0.72–0.93</td>
<td>295/500 (0.98), 0.96–0.99</td>
<td>51.4, 21.4–123.7</td>
<td>0.15, 0.07–0.30</td>
</tr>
<tr>
<td>WBC ≥100 cells/μL and bacteria ≥250 cells/μL</td>
<td>35/42 (0.83), 0.69–0.92</td>
<td>298/500 (0.99), 0.98–0.99</td>
<td>125.0, 31.2–500.8</td>
<td>0.17, 0.09–0.33</td>
</tr>
<tr>
<td>WBC ≥200 cells/μL and bacteria ≥250 cells/μL</td>
<td>34/42 (0.81), 0.67–0.90</td>
<td>298/500 (0.99), 0.98–0.99</td>
<td>121.4, 30.3–471.7</td>
<td>0.19, 0.10–0.36</td>
</tr>
<tr>
<td>WBC ≥250 cells/μL and bacteria ≥250 cells/μL</td>
<td>33/42 (0.79), 0.64–0.88</td>
<td>298/500 (0.99), 0.98–0.99</td>
<td>117.9, 29.4–473.3</td>
<td>0.22, 0.12–0.38</td>
</tr>
</tbody>
</table>

Sensitivity presented as true-positives per number with UTI and specificity as true-negatives per number without UTI with point estimates and 95% CIs for proportions. LRs presented with 95% CIs, except when a zero term appears in a denominator. LR +, LR of positive test result; LR –, LR of negative test result.

Comprised 4% of a population that produced sensitivities and specificities of 0.99 and 0.77, respectively, for WBC counts ≥150/μL and 0.97 and 0.80, respectively, for bacterial counts ≥150/μL. However, neither study reported the clinical features or results of the pediatric subsets. Automated urinalyses performed on noncatheterized samples from pediatric nephrology and urology patients predominantly ≥3 years of age yielded a sensitivity of 0.89 and a specificity of 0.85 with the use of an adult bacterial cutpoint and an unclear WBC cutpoint. Patients’ symptoms were not described, and 37% of those with positive urine culture results did not receive treatment for a UTI. Automated digital microscopy diagnosed nonenterococcal pediatric UTI with sensitivities and specificities of 0.89 and 0.9, respectively, at a WBC cutpoint of 2/high-power field and 0.79 and 0.85, respectively, for detection of any bacteria. We expanded on previous work by using catheter collection and a culture standard to determine unique optimal cutpoints for automated cytomteric WBC and bacterial counts among young febrile outpatients at risk for UTI. POC dipstick testing may be preferable in clinical settings in which rapid decision-making is required or where microscopic or automated techniques are not practical. An ED POC dipstick cutpoint of ≥1+ LE or positive nitrite had moderately high sensitivity (0.85) but low specificity (0.53) in a high-prevalence population of symptomatic adult women. Even with sensitivity as low as 79%, urine dipstick paired with culture may be an adequate, cost-effective screen for UTI in young children. Laboratory-based determinations of LE28 and combinations of LE and nitrite29,30 performed similarly to microscopic urinalysis in detection of UTI in infants and young children. Automated dipstick heme and LE measurements have statistically significant correlations with automated erythrocyte and WBC counts.18 Our findings similarly demonstrate that the sensitivity and specificity of POC dipstick urinalysis approach those of automated cytomteric urinalysis and may provide an adequate screen for UTI among febrile children in the ED, urgent care, or primary care setting. Positive POC test results justify antibiotic therapy without formal urinalysis, and negative POC or automated test results may allow clinicians to withhold antibiotic therapy pending culture results. In addition, negative POC urine results may obviate the need for laboratory-based tests or cultures in well-appearing children at low risk for complications of UTI, especially with specimens obtained by using less invasive methods.

We reasoned that automated cytometry would be similar to manual hemocytemeter counts as measures of particle concentration in uncentrifuged urine. Strong correlations have been reported between cell counts performed by using UF-1000i and those by microscopy performed by using a counting chamber.20 Leukocyte counts by hemocytometer had better sensitivity and specificity25,32 and ROC AUCs6,32 than those according to standard urinalysis in the detection of UTI in febrile infants. The continuous and precise WBC counts provided by using automated methods will likely prove less labor intensive and more versatile and will provide more useful risk stratification than single cutpoints of 10 WBC/μL25,26,32 or 5 WBC/high-power field12,26,28 for uncentrifuged and centrifuged samples, respectively. We did not examine centrifuged urine or perform Gram-stain analysis and could not compare automated cytometry with enhanced urinalyses or the more familiar standard urinalysis. However, unblinded manual hemocytometer counts were within 10 cell/μL of 90% of our automated WBC counts, and automated bacterial counts may provide a highly precise substitute for the inspection of Gram-stained urine for bacteria.
Our study design likely contributed to its favorable results. We enrolled a narrowly defined population of young febrile patients whose prospectively identified clinical characteristics constituted a reasonable suspicion for acute untreated UTI and who uniformly underwent bladder catheterization. Previous studies have lacked clinical exclusion criteria,\textsuperscript{13} obtained clinical data or exclusion criteria by using retrospective chart review,\textsuperscript{1,18} or did not specifically exclude patients with antibiotic pretreatment.\textsuperscript{1,3,25,26,33} Non-catheter collection methods contributed some\textsuperscript{5} or nearly all\textsuperscript{15,14,17} specimens in previous studies. Technologists tested our specimens upon receipt rather than storing them for batch-testing.\textsuperscript{18,26} We recognize several limitations to our study, which was conducted in a high-volume, tertiary pediatric ED in which clinical staff were experienced in POC testing. Other clinical settings with lower patient volumes or less experienced clinical staff were experienced in POC testing by ED nurses or pediatric trainees\textsuperscript{5,27} is subject to operator variability; however, all ED nurses performing our POC tests underwent competency verification. Through inconsistent performance of urinalyses in patients ≤3 months of age\textsuperscript{1,5,6,21} has caused concern for lower sensitivity,\textsuperscript{22,23} our uniform study conditions resulted in excellent performance in the subset of patients aged 0 to 90 days.

We recognize several limitations to our study, which was conducted in a high-volume, tertiary pediatric ED in which clinical staff were experienced in POC testing. Other clinical settings with lower patient volumes or less experience using POC urine dipstick or cytometry may be unable to replicate our results. Because clinicians ordered tests based on clinical risk factors, such as age, gender, circumcision status, and height and duration of fever,\textsuperscript{24} our data cannot be used to estimate prevalence or identify clinical predictors. Non-consecutive enrollment and the exclusion of patients with incomplete urine testing or data could have led to nonrepresentative sampling but were unlikely to have systematically selected urine specimens with altered test performance characteristics. Because our POC data result from routine clinical testing, we did not measure interrater reliability or the accuracy of individual nurses. However, the observed agreement between POC and laboratory determinations suggests excellent reliability. The unexpected differences between automated and microscopic WBC counts likely reflect improved precision due to the 10\textsuperscript{3}- to 10\textsuperscript{4}-fold greater sampling volumes of automated analyzers (0.8–1.2 mL) over counting chambers (0.1–0.9 μL) and caused no loss of sensitivity. Although we used a well-established definition of UTI as ≥50 000 CFU/mL of a single urinary pathogen for specimens obtained according to catheter,\textsuperscript{5,25} other definitions use bacterial concentrations ≥10 000 CFU/mL,\textsuperscript{1,2,5,26,25} or combinations of growth at 10 000 to <50 000 CFU/mL\textsuperscript{35,36} ≥50 000 CFU/mL\textsuperscript{12} or ≥100 000 CFU/mL\textsuperscript{17} with positive urinalyses. Because we used a moderately stringent bacteriologic criterion and excluded the tests under evaluation from the definition of UTI, our results may be less helpful to clinicians who wish to treat at lower levels of bacterial growth or who wish to incorporate urinalysis into the interpretation of positive urine culture results. Our flow cytometric data cannot be generalized directly to WBC counts obtained by enhanced urinalysis or digital imaging,\textsuperscript{18} but our experience suggests that alternate thresholds exist for those methods. In addition, we cannot predict the ability of POC or automated methods to identify enterococcal infections, which provoke a less pyogenic response.\textsuperscript{18} Unlike other authors,\textsuperscript{9,33,38} we did not attempt to identify asymptomatic bacteriuria or to differentiate pyelonephritis from cystitis. However, some clinicians using highly sensitive and specific rapid urine tests would discontinue therapy if scintigraphic studies reveal no renal involvement.

CONCLUSIONS

Using automated flow cytometry on catheterized urine samples from febrile young ED patients at risk for UTI, bacterial counts ≥250 cells/μL have the best combination of sensitivity and specificity. However, a POC dipstick with ≥1+ LE or positive nitrite produced a favorable performance and may be an acceptable screen for UTI in the ED and other outpatient settings in which pediatric patients are evaluated for febrile illnesses.

ACKNOWLEDGMENTS

The authors thank Erin M. Fletcher, BS, for management of the database and Robert H. Riffenburgh, PhD, for assistance in planning the statistical analysis.

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John T. Kanegaye, Jennifer M. Jacob and Denise Malicki

Pediatrics 2014;134;523; originally published online August 18, 2014;
DOI: 10.1542/peds.2013-4222

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*Pediatrics* 2014;134:523; originally published online August 18, 2014;
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