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# Unsatisfactory Performance of Flow Cytometer UF-100 and Urine Strips in Predicting Outcome of Urine Cultures

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**UF-100 flow cytometer and urine strip results were cross-interpreted to predict culture outcomes. The best negative predictive value was obtained with bacteria at ≥1,000/μl, white blood cells at ≥20/μl, or leukocyte esterase positivity. Nine of 24 false negatives were clinically significant. Thus, UF-100 and urine strip results do not accurately predict the outcome of cultures.**

Urinary tract infection (UTI) is a common cause of human illness, and failure to diagnose and treat it properly can lead to further chronic morbidity. Quantitative urine culture and identification are still the standard laboratory procedures for definitive diagnosis of UTI. In our laboratory, 70% of the urine culture requests are negative.

We were interested in eliminating the costs and time expended in examinations of these negative cultures. We investigated the feasibility of achieving our aim by combining the results obtained with the UF-100 urine flow cytometer and those obtained with urine sticks to predict the outcome of urine cultures.

Fresh midstream clean-catch urine samples (10 ml, $n = 554$) collected in accordance with standard guidelines (4) and transported by a pneumatic tube system (Aerocom GmbH &Co., Kernen, Germany) were randomly selected for the study.

The specimens came from 284 females (mean age, 52 years; age range, 1 month to 95 years) and 270 males (mean age, 56 years; age range, 1 week to 93 years) who belonged to the following general groups: intensive care unit ($n = 157$), internal medicine ($n = 69$; 41 of these had received renal transplants), emergency department ($n = 66$), surgery ($n = 50$), obstetrics-gynecology ($n = 40$), outpatients ($n = 33$), pediatrics ($n = 14$), geriatrics ($n = 11$), oncology ($n = 5$), and others ($n = 17$).

Urine cultures were performed by inoculating 10 μl of uncentrifuged and well-mixed urine on blood agar and MacConkey agar plates (Oxoid, Hampshire, United Kingdom) and incubating them aerobically at 36°C for 24 h. Growth of <10,000 CFU/ml was considered negative unless the patient was symptomatic, pregnant, or undergoing treatment with antibiotics. In these cases, the threshold for the diagnosis of UTI was $10^3$ CFU/ml in the presence of concomitant pyuria. If more than two organisms were isolated, the total amount of bacteria was quantitated and reported as "mixed urethral flora." Identification of pathogens was accomplished by routine biochemical tests.

After inoculation for cultures, urine samples were first analyzed on a Super Aution (A. Menarini Diagnostics, Florence, Italy) automated urinalysis analyzer using Uriflet S9 UB urine strips (A. Menarini Diagnostics). This analysis was followed by identification and quantification of the formed elements on a Sysmex UF-100 (Merck Eurolab) flow cytometer for urine. The principles of analysis and evaluation of this analyzer have already been published (1, 2, 5–7). The reference cutoffs for white blood cells (WBC) and bacteria on the UF-100 cytometer were 20/μl and 2,750/μl.

With $10^4$ CFU/ml as the diagnostic criterion for UTI, 159

TABLE 1. Organisms isolated from 152 positive urine cultures

| Organism(s) | No. |
|---|---|
| *Escherichia coli* | 39 |
| *Proteus mirabilis* | 13 |
| *Pseudomonas aeruginosa* | 13 |
| *Klebiella pneumoniae* | 3 |
| *Klebsiella oxytoca* | 2 |
| *Enterobacter aerogenes* | 2 |
| *Morganella morganii* | 2 |
| *Proteus vulgaris* | 1 |
| *Enterococcus* sp. | 22 |
| *Citrobacter freundii* + *Klebsiella pneumoniae* | 1 |
| *Escherichia coli* + *Enterococcus* sp. | 2 |
| *Escherichia coli* + *Pseudomonas aeruginosa* | 1 |
| *Escherichia coli* + *Streptococcus agalactiae* | 1 |
| *Escherichia coli* + *Corynebacterium* species | 1 |
| *Escherichia coli* + CNS | 2 |
| *Proteus mirabilis* + *Escherichia coli* | 1 |
| *Proteus mirabilis* + *Klebsiella oxytoca* | 1 |
| *Pseudomonas aeruginosa* + *Enterococcus* sp. | 1 |
| *Pseudomonas aeruginosa* + *Staphylococcus aureus* | 1 |
| *Pseudomonas aeruginosa* + *Candida albicans* | 1 |
| *Klebsiella oxytoca* + *Streptococcus viridans* | 2 |
| *Klebsiella oxytoca* + *Proteus mirabilis* | 2 |
| *Morganella morganii* + *Klebsiella pneumoniae* | 1 |
| *Proteus vulgaris* + *Escherichia coli* | 1 |
| *Enterococcus* sp. + *Escherichia coli* | 1 |
| CNS | 17 |
| *Staphylococcus aureus* | 4 |
| *Streptococcus agalactiae* | 3 |
| *Streptococcus viridans* | 2 |
| *Lactobacillus* sp. | 2 |
| *Candida albicans* | 5 |
| *Non-albicans Candida* sp. | 1 |
| *Candida tropicalis* | 1 |
| Mixed flora | 22 |

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TABLE 2. Diagnostic performance of UF-100 and urine strip results in comparison with urine cultures [a]

| Positive screening test(s) | | Reference cutoff for culture | No. of samples | % FP | % FN | % Sen | % Sp | % PPV | % NPV |
|---|---|---|---|---|---|---|---|---|---|
| UF-100 | Urine strip | | | | | | | | |
| Bacteria[a] | And LE | $10^4$ (CFU/ml) | 185 | 18.2 (101)[d] | 12.3 (68) | 55.3 | 74.9 | 45.4 | 81.6 |
| Bacteria[a] | Or LE | $10^4$ | 321 | 38.1 (211) | 7.6 (42) | 72.4 | 47.5 | 34.3 | 82.6 |
| WBC and bacteria[c] | And LE | $10^4$ | 139 | 11.2 (62) | 13.5 (75) | 50.7 | 84.6 | 55.4 | 81.9 |
| WBC or bacteria[a] | Or LE | $10^4$ | 362 | 42.2 (234) | 4.3 (24) | 84.2 | 41.9 | 35.4 | 87.5 |
| Bacteria[a] | And LE and $NO_2$ | $10^4$ | 27 | 0.5 (3) | 23.1 (128) | 15.8 | 99.3 | 88.9 | 75.7 |
| Bacteria[a] | Or LE or $NO_2$ | $10^4$ | 309 | 33.8 (187) | 5.4 (30) | 80.3 | 53.5 | 39.5 | 87.5 |
| WBC and bacteria[a] | And LE and $NO_2$ | $10^4$ | 27 | 0.5 (3) | 23.1 (128) | 15.8 | 99.3 | 88.9 | 75.7 |
| WBC or bacteria[a] | Or LE or $NO_2$ | $10^4$ | 362 | 43.2 (234) | 4.3 (24) | 84.2 | 41.8 | 35.4 | 87.5 |
| WBC and bacteria[b] | And LE | $10^4$ | 96 | 6.7 (37) | 26.8 (93) | 38.8 | 90.8 | 61.5 | 79.7 |
| WBC or bacteria[b] | Or LE | $10^4$ | 333 | 38.8 (215) | 6.1 (34) | 77.6 | 46.5 | 35.4 | 84.6 |

[a] LE, leukocyte esterase; $NO_2$, nitrite; FP, false positive; FN, false negative; Sen, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value.
[b] UF-100 cutoff for bacteria, 1,000/μl.
[c] UF-100 cutoff for bacteria, 2,750/μl, as suggested by the manufacturer.
[d] The values in parentheses are numbers of specimens (from a total of 554).

(28.7%, $n = 554$) specimens yielded positive cultures. However, seven cases of mixed growth consisting of *Escherichia coli* and coagulase-negative staphylococci (CNS) ($n = 2$); *Enterococcus* spp. and *Acinetobacter lwoffii* ($n = 2$); *Klebsiella pneumoniae*, an *Enterococcus* sp., and CNS ($n = 1$); CNS and *Streptococcus viridans* ($n = 1$); and *Citrobacter freundii*, *Klebsiella oxytoca*, and an *Enterococcus* sp. ($n = 1$) were considered contaminations. Therefore, the number of true-positive cultures was reduced to 152 (27.4%). The organisms isolated from these cultures are shown in Table 1.

The diagnostic performance of the UF-100 results for bacteria and WBC and urine strip results for leukocyte esterase and nitrite in comparison with the urine culture data is shown in Table 2. Inclusion or omission of nitrite as one of the variables made no difference to the diagnostic performance of the UF-100 and urine strip results. The best specificity (99.3%) and positive predictive value (88.9%) were obtained with bacteria at ≥1,000/μl, WBC at ≥20/μl, and positivity for leukocyte esterase (and nitrite), but this combination of variables produced a high number of false negatives ($n = 128$).

The best negative predictive value (87.5%) and the lowest percentage of false negatives (4.3%, representing 24 patient samples) were achieved with bacteria at ≥1,000/μl, WBC at ≥20/μl, or leukocyte esterase positivity. The false-negative cases were further examined for clinical significance by determining if the preceding and/or following specimens were also positive for the same organism. Nine of the 24 false-negative cases, consisting of three renal transplant patients, each with an enterococcus infection; three ambulatory patients with UTI symptoms, one with an *E. coli* infection, another with a *Proteus mirabilis* infection, and the third with a *Pseudomonas aeruginosa* infection; two leukemic patients on chemotherapy, both with CNS infections; and one intensive care patient with an enterococcus infection, were found to be clinically significant. With the UF-100 cutoff set at 2,750 bacteria/μl, as suggested by the manufacturer, the best negative predictive value was found with WBC at ≥20/μl or leukocyte esterase positivity, but this increased the percentage of false negatives (Table 2).

In the present study, the primary purpose of screening urine specimens was to find out if it is possible to predict positive urine cultures and thereby eliminate the negative ones rapidly and safely. If this were feasible, it would offer the advantages of reducing the time required for the diagnosis of bacteriuria, prompt institution of clinical treatment, cost containment, and allowing time for laboratories to investigate the positive specimens more thoroughly.

We have used different variables of the UF-100 flow cytometer and urine strips pertaining to UTI in "and/or" combinations to see if they could predict urine culture outcome. The "and" combination of bacteria, WBC, and leukocyte esterase yielded high specificity and positive predictive values, but the false-negativity rate was also high (Table 2). The highest negative predictive value (87.5%) and the lowest false-negativity rate (4.3%) were obtained with the following variables: WBC at ≥20/μl (on UF-100), bacteria at ≥1,000/μl (on UF-100), or leukocyte esterase positivity. Inclusion of nitrite as an additional variable made no difference to our results (Table 2). A closer examination of the 24 false negatives revealed that 9 (37.5%) were clinically significant in that in each case the preceding and/or the following culture was also positive for the same organism. Bearing in mind the possible impact of missing these nine cases on patient morbidity (9), we consider that the use of UF-100 and urine strip results to screen urine samples for UTI is not advisable. Although they did not state it clearly, Okada et al. (8) came to the same conclusion with regard to screening for UTI by using UF-50. Kellogg et al. (3) have proposed that a screening test should have sensitivity and negative predictive values of ≥95%. The tests used in this study do not meet this criterion either.

In conclusion, we find that the use of UF-100 cytometer and urine strip results, separately or in combination, does not accurately predict the outcome of urine cultures and that these tests are therefore unsuitable for the safe screening of urine samples for UTI.

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