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Detection of Bacteriuria and Pyuria Within Two Minutes

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A study was performed to evaluate two rapid urine screening methods, Bac-T-Screen (Marion Laboratories, Inc., Kansas City, Mo.) and Chemstrip LN (Boehringer Mannheim Diagnostics, BioDynamics, Indianapolis, Ind.), for their ability to screen for bacteriuria and pyuria within 2 min. A total of 1,000 urine specimens were tested with the Bac-T-Screen and the Chemstrip LN and compared with a semiquantitative plate culture method. Of the 1,000 specimens tested, 249 had colony counts of $\geq 10^5$ CFU/ml by the culture method. Of these, the Bac-T-Screen detected 94.8% (236 of 249) and the Chemstrip LN detected 84.7% (210 of 249). There were 120 pure cultures of probable pathogens of which the Bac-T-Screen detected 97.5% (117 of 120) and the Chemstrip LN detected 91.7% (110 of 120). Leukocyte counts were performed on all specimens, and both methods have the ability to detect >10 leukocytes per mm^3 in a majority (>93%) of the specimens. The cost per test for a negative screen is approximately $1.30 for the Bac-T-Screen and $0.40 for the Chemstrip LN. Overall there is a similar negative predictive value with both methods for bacteriuria and pyuria.

Screening methods for bacteriuria have gained increased recognition in recent years. As a result, many methods have been developed for use in the clinical microbiology laboratory. These methods provide results rapidly (2 min to 13 h) compared with the most widely used plate culture method and allow the microbiologist more time to spend on positive specimens.

Most screening methods have the ability to detect bacteriuria, but not pyuria; they employ multistep procedures that encourage batching of specimens and require at least 30 min for detection of negative specimens. Recently, two rapid (2-min) methods, the Bac-T-Screen (Marion Laboratories, Inc., Kansas City, Mo.) and the Chemstrip LN (Boehringer Mannheim Diagnostics, Bio-Dynamics, Indianapolis, Ind.), have been described which detect bacteriuria (3, 4, 7, 9, 10, 12, 17, 18). In this investigation the ability of both systems to detect bacteriuria within 2 min was compared with that of a standard semiquantitative plate culture method.

It has been reported that the presence of pyuria is a significant finding and should be considered when evaluating a urinary tract infection (13–16). The Chemstrip LN has been reported to detect pyuria (1, 4, 5, 12, 18). In this study, we also evaluated the ability of the Bac-T-Screen to detect significant pyuria as well as bacteriuria. White blood cell (WBC) chamber counts were performed on each specimen, and results from both the Bac-T-Screen and the Chemstrip LN were compared with the chamber counts. Additionally, the cost of each method was determined and compared with that of the reference method.

MATERIALS AND METHODS

Specimens. A total of 1,000 clean-voided and catheterized urine specimens from both inpatients and outpatients submitted to the Medical Microbiology Laboratory at the University of California Irvine Medical Center, Orange, were included in the study. Patients receiving antimicrobial therapy were not excluded. Collected urine was placed in a sterile tube, refrigerated (4°C), and processed within 4 h of collection.

Semiquantitative culture. A semiquantitative plate count as described by Barry et al. (2) was used as the reference method. By using calibrated platinum loops, 0.01- and 0.001-ml samples of a well-mixed urine specimen were inoculated onto a 5% sheep blood agar plate and a biplate consisting of MacConkey agar and polymyxin B-nalidixic acid blood agar (CalScott, Carson, Calif.). Cultures were incubated at 35°C aerobically and examined for the number and types of organisms present.

A positive culture was defined as a urine specimen containing $\geq 10^5$ CFU/ml. This category was further divided into significant positives and contaminants. Significant positives were defined as urine specimens with a single potential pathogen, and contaminants were defined as mixed cultures or those containing a pure culture of diphtheroids, lactobacilli, or viridans streptococci other than group D.

All urine cultures were divided into the following five categories based on the CFU per milliliter obtained by the reference culture method: group 1, $\geq 10^5$ CFU/ml; group 2, $\geq 10^4$ and $< 10^5$ CFU/ml; group 3, $\geq 10^3$ and $< 10^4$ CFU/ml; group 4, $\geq 10^2$ and $< 10^3$ CFU/ml; and group 5, $< 10^2$ CFU/ml.

Bac-T-Screen. Urine specimens were processed with the Bac-T-Screen according to the manufacturer's instructions and as previously described (3, 9, 10, 17). One milliliter of well-mixed urine and 3 ml of urine diluent (14.5% acetic acid) were suctioned through a filter card, followed by the addition and filtration of 3 ml of safranin O dye and 3 ml of 2.4% acetic acid decolorizer. A second rinse of 3.0 ml of 2.4% acetic acid decolorizer was added manually. The color intensity remaining was coded (0 to 4+) with a color guide on the filter card. A positive test was one that gave a pink residual color on the filter card of $\geq$1+. Results were available within 2 min. An uninterpretable test was one that gave a color other than pink on the filter card or one that clogged the filter. In this study, uninterpretable specimens were considered positive since they required cultures for interpretation.

Chemstrip LN. The Chemstrip LN is a plastic strip to which are attached reagent papers for indicating the presence of leukocyte esterase and nitrite in urine. The plastic strip was dipped into the urine specimen for 1 s, and the strip was withdrawn over the specimen container rim to remove

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TABLE 1. Distribution of specimens

Reference method		No. positive	
Concn (CFU/ml)	No. of specimens	Bac-T-Screen	Chemstrip LN
$\geq 10^5$ (all specimens)	249	236	210
$\geq 10^5$ (pure pathogens)	120	117[a]	110[b]
$\geq 10^4 < 10^5$	142	94	74
$\geq 10^3 < 10^4$	121	57	46
$\geq 10^2 < 10^3$	23	10	9
$< 10^2$	465	146	135

[a] False-negatives included one *E. coli* and two enterococci.
[b] False-negatives included four *E. coli*, four enterococci, one *K. pneumoniae*, and one *Citrobacter* sp.

the excess urine. Results were read after 1 and 2 min. The color intensities remaining were coded with a color guide provided by the manufacturer. A positive leukocyte esterase was one that gave a purple color ranging from a trace to a 2+ intensity. For nitrite, any pink color was considered positive.

Chamber counts. Ten milliliters of urine was centrifuged (600 × *g*, 10 min) at room temperature. Nine milliliters of the supernatant was decanted, and the sediment was suspended in the remaining 1 ml of urine. The number of WBC present in each specimen was counted in a hemacytometer.

Predictive value. Predictive values were calculated by the method of Ransohoff and Feinstein (11). The sensitivity, specificity, and positive and negative predictive values were calculated as follows: sensitivity = TP/(TP + FN); specificity = TN/(TN + FP); positive predictive value = TP/(TP + FP); and negative predictive value = TN/(TN + FN), where TP is true positive, TN is true negative, FP is false-positive, and FN is false-negative.

Time and cost analysis. The time required to perform each method was determined. An analysis of cost per test was done by calculating the cost of materials and technical time. These costs were based on actual costs for our laboratory.

RESULTS

Detection of bacteriuria. A total of 1,000 clean-voided and catheterized specimens were evaluated. Of these, 249 were positive with colony counts of $\geq 10^5$ CFU/ml by the standard semiquantitative plate culture reference method. Of the culture-positive specimens, 48.2% (120 of 249) had pure cultures of probable pathogens. The remaining 751 specimens were considered negative by culture and were divided into four additional groups based on CFU per milliliter (Table 1). Of the 1,000 urine specimens tested, 543 were positive by Bac-T-Screen, and 457 were negative (Table 1). Of the 249 specimens positive by the reference method, the Bac-T-Screen detected 236. The detection rate for Bac-T-Screen was 94.8% when all organisms were evaluated and 97.5% (117 of 120) for pure pathogens.

Of the 1,000 urine specimens tested, 474 were positive by leukocyte esterase, nitrite, or both, and 526 were negative (Table 1). Of the 249 specimens positive by the reference method, 210 were positive by either leukocyte esterase, nitrite, or both, and 39 were negative. The detection rate for all organisms was 84.3% (210 of 249) for the Chemstrip LN. The Chemstrip LN detected 91.7% (110 of 120) of the pure pathogens.

The readings for the Chemstrip LN were taken at 1 and 2 min. Of the positive cultures, 77.5% (193 of 249) were positive for leukocyte esterase. Of the 193 positive leukocyte esterase reactions, 80.0% (154 of 193) were positive after 1 min, and the remaining 20.0% required the additional minute before they could be interpreted as positive. Of the positive specimens, 37.3% (93 of 249) had positive nitrite reactions after 1 min, which increased to 43.4% (108 of 249) at 2 min. Overall, the detection rate of the Chemstrip LN for all organisms $\geq 10^5$ CFU/ml at 1 min was 70.0% compared with 84.3% at 2 min. The detection rate for pure pathogens was 68.5% after 1 min, which increased to 91.7% after 2 min.

Detection of pyuria. There were 292 specimens with >10 WBC/mm^3 (Table 2). Of these, the Bac-T-Screen detected 93.1% (272 of 292), and the Chemstrip LN detected 94.2% (275 of 292). Considering all organisms $\geq 10^5$ CFU/ml and >10 WBC/mm^3, the detection rates for both the Bac-T-Screen and the Chemstrip LN were 97.3% (143 of 147) and 100% (86 of 86), respectively, for pure pathogens. There were 145 specimens that had colony counts of $< 10^5$ CFU/ml and WBC counts of >10 WBC/mm^3. The Bac-T-Screen detected 90.0% (129 of 145) of these compared with 91.0% (132 of 145) for the Chemstrip LN.

Of the pure pathogens with $\geq 10^5$ CFU/ml, *Escherichia coli* represented 55% (66 of 120) of the isolates. The remaining pathogens were *Klebsiella pneumoniae* (17 isolates), enterococci (13 isolates), *Pseudomonas aeruginosa* (8 isolates), *Citrobacter* spp. (4 isolates), *Candida albicans* (3 isolates), and one or two isolates each of other gram-negative rods and gram-positive cocci. Of these, 71.7% (86 of 120) had >10 WBC/mm^3. Of the specimens with $\geq 10^5$ CFU/ml and >10 WBC/mm^3, there were 74.2% (49 of 66) of the *E. coli* isolates and 94.1% (16 of 17) of the *K. pneumoniae* isolates within this group compared with 53.8% (7 of 13) and 50% (4 of 8) of the enterococci and *P. aeruginosa* isolates, respectively. Three of the four isolates of *Citrobacter* spp. fell within this group, and all three isolates of *Candida albicans* had >400 WBC/mm^3. The remaining pure pathogens had counts ranging from 1 to 72 WBC/mm^3.

Of the 708 specimens with ≤10 WBC/mm^3, 38.3% (271 of 708) were positive by the Bac-T-Screen, and 28.1% (199 of 708) were positive by the Chemstrip LN (Table 3). Approximately one-third of these false-positive results for WBCs were specimens with $\geq 10^5$ CFU/ml. This represented 33.4%

TABLE 2. Distribution of WBC/mm^3 and positive urine screens

Colony count (CFU/ml)	No. of specimens	No. of specimens					
		0 to 10 WBC/mm^3 (708)			>10 WBC/mm^3 (292)		
		Total specimens	Bac-T-Screen	Chemstrip LN	Total specimens	Bac-T-Screen	Chemstrip LN
$\geq 10^5$ (all organisms)	249	102	93	67	147	143	143
$\geq 10^5$ (pure pathogens)	120	34	31	24	86	86	86
$\geq 10^2 < 10^5$	286	207	83	53	79	78	76
$< 10^2$	465	399	95	79	66	51	56

TABLE 3. Predictive values for Bac-T-Screen and Chemstrip LN

Determination	Colony count ($\geq 10^5$ CFU/ml)				WBC count (>10 WBC/mm^3)	
	Bac-T-Screen		Chemstrip LN		Bac-T-Screen	Chemstrip LN
	All organisms	Pure pathogens	All organisms	Pure pathogens		
Sensitivity	94.8	97.5	84.3	91.7	93.1	94.2
Specificity	59.1	51.9	64.8	59.7	61.4	71.9
Predictive value						
Positive	43.4	21.6	44.3	23.7	50.1	58.0
Negative	97.1	99.3	92.6	98.1	95.6	96.8

(93 of 271) positive by the Bac-T-Screen and 33.7% (67 of 199) positive by the Chemstrip LN. Of those specimens with ≤ 10 WBC/mm^3 and $<10^2$ CFU/ml, there were 95 positive by the Bac-T-Screen compared with 79 positive by the Chemstrip LN.

Predictive value. Table 3 shows the positive and negative predictive values for the Bac-T-Screen and the Chemstrip LN for both colony count and WBC count. The Bac-T-Screen was more sensitive than the Chemstrip LN when all organisms or pure pathogens alone with colony counts of $\geq 10^5$ CFU/ml were analyzed. The ability of the Bac-T-Screen to detect a negative specimen was greater (97.1%) than that of the Chemstrip LN (92.6%) when all organisms were considered; however, for pure pathogens alone, the two methods were comparable (99.3% versus 98.1%).

The sensitivities and negative predictive values for both the Bac-T-Screen and the Chemstrip LN were similar when >10 WBC/mm^3 were used for determining predictive values. The sensitivity for Bac-T-Screen was 93.1% compared with 94.2% for Chemstrip LN, and the negative predictive values were 95.6 and 96.8%, respectively.

Cost analysis. The total cost of screening by each method was determined. Although salaries differ from laboratory to laboratory, we estimated the cost per test based on the average salary of medical technologists and laboratory assistants in our institution ($10.00/h) and 4.0, 1.5, and 1.0 min for the reference method, Bac-T-Screen, and Chemstrip LN, respectively. Our supply cost was $0.67 for the reference method, $0.90 for the Bac-T-Screen, and $0.17 for the Chemstrip LN. The cost per test for a negative screen was $1.34 for the reference method, $1.15 for the Bac-T-Screen, and $0.34 for the Chemstrip LN. For a positive screen, the cost was increased by $1.34 for the Bac-T-Screen and the Chemstrip LN since each positive result required a culture. The average cost per specimen, including both positive and negative specimens, was calculated at $1.34, $1.88, and $0.97 for the reference method, Bac-T-Screen, and Chemstrip LN, respectively. At the time of the study, the Bac-T-Screen supply cost included the instrument.

DISCUSSION

The main purpose of urine screening is to rapidly detect the majority (70 to 80%) of urine specimens that do not have significant bacteriuria. Previously described methods have the ability to accomplish this accurately; however the major difference from the two methods described here is the time required to obtain results. Both urine screening methods evaluated in this study provide results within 2 min, compared with 30 min to 13 h for other methods. In addition to being a 2-min test, their sensitivities and negative predictive values compare favorably to those of other screening methods (8).

The overall sensitivity for the Bac-T-Screen was 94.8%, which increased to 97.5% for pure pathogens. This is comparable to other reported studies (3, 9, 10). The sensitivity and negative predictive value for the Chemstrip LN in our study were 84.3% and 92.6%, respectively, for all organisms at $\geq 10^5$ CFU/ml which increased to 91.7% and 98.1%, respectively, for pure pathogens. These results are also similar to those reported in two other studies (12, 18).

Using $\geq 10^5$ CFU/ml as the definition of a positive specimen may not always be acceptable. We now know that as few as 10^2 CFU/ml may be significant for symptomatic patients. However, many screening tests, especially the automated methods, do not have an acceptable sensitivity below 10^5 CFU/ml. In addition to bacteriuria, the presence of pyuria may suggest infection (6, 12–16, 19). In this study, we found that both screening methods detected significant pyuria and had increased sensitivities when both bacteriuria and pyuria were considered.

It has been reported that pyuria in the presence of low-count or negative bacteriuria is a significant finding when considering a urinary tract infection (13, 15, 16). Stamm et al. showed that 70% of symptomatic, nonbacteriuric women have pyuria and mostly likely will have infection with low counts of *E. coli* or other pathogens (12, 16). Other studies have reported that the presence of >10 WBC/mm^3 in asymptomatic, bacteriuric patients may indicate infection rather than colonization (6, 19). Therefore, it may be important for the clinical microbiology laboratory to consider pyuria along with bacteriuria when screening urine specimens (15). The presence of >10 WBC/mm^3 and $<10^5$ CFU/ml of bacteria, especially gram-negative rods, may alert the laboratorian regarding significant low-level bacteriuria.

To determine the correlation between pyuria and bacteriuria, well-controlled chamber counts were performed in this study. These conditions included the volume of urine centrifuged, the speed and time of centrifugation, and the volume suspended and examined in the hemacytometer. Using this method for performing chamber counts can be a tedious and time-consuming task. However, Stamm also reported a correlation between pyuria and bacteriuria using fresh, uncentrifuged urine in a hemacytometer chamber (13). This method might be a viable alternative in a busy clinical laboratory.

Our study and another by Kusumi et al. (5) demonstrate a correlation between the chamber count and leukocyte esterase activity. Their studies reported an 87.9% sensitivity for leukocyte esterase with a cutoff of >10 WBC/mm^3 compared with 93.8% in this study.

Until now, reports of the Bac-T-Screen have shown its ability to detect bacteriuria alone. Our study shows that the Bac-T-Screen could be used for detection of pyuria. The predictive values for both the Bac-T-Screen and the Chem-

strip LN were similar when the data were analyzed with >10 WBC/mm^3. The sensitivity and negative predictive value for each method were >93% and >95%, respectively. Each method detected all of the significant pure pathogens with >10 WBC/mm^3.

The major difference between the two systems is cost. When used for the screening of negative specimens, the reference plate culture method was the most expensive method, and the Chemstrip LN was the least expensive method. The Chemstrip LN remained the least expensive method when both positive and negative specimens were included. Both systems provide a cost savings compared with the reference method when considering negative specimens. However, the Bac-T-Screen is more costly when both positive and negative specimens are included.

In conclusion, the most important contribution of these rapid screening methods to patient care is in their ability to obtain results within 2 min. In addition to eliminating negative urine specimens within 2 min, they have the ability to detect significant pyuria as well as bacteriuria. A positive test for pyuria with $<10^5$ CFU/ml should alert the laboratorian to identify common urinary pathogens as well as investigate other organisms such as *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Mycobacterium tuberculosis*.

The Bac-T-Screen is more sensitive in its ability to detect positive and negative specimens for significant bacteriuria; however, each system has a >98% probability of detecting negative specimens. For significant pyuria, the sensitivity and negative predictive values are similar for both systems. The cost for screening negative specimens with these rapid methods is less than that the reference method; however, it is considerably less with the Chemstrip LN. Use of either the Bac-T-Screen or the Chemstrip LN to screen urine specimens will provide an overall time savings to the clinical microbiology laboratory and an advantage to both the physician and the patient.

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