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Inability of the Chemstrip LN Compared with Quantitative Urine Culture to Predict Significant Bacteriuria

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The Chemstrip LN (Boehringer Mannheim Biochemicals, Indianapolis, Ind.), designed to detect pyuria and bacteriuria, was compared with culture of 1,020 unselected, consecutive midstream urine specimens and evaluated on its ability to predict colony counts at three levels. At the level of $\geq 10^5$ CFU/ml, the combined test (detection of leukocyte esterase and nitrite) had sensitivity of 82.3%, specificity of 67.9%, positive predictive value of 41.3%, and negative predictive value of 93.3% at prevalence rate of 21.6%. The test would have rejected 9.4% of the specimens with significant bacteriuria if the Chemstrip alone had been used.

The enumeration of bacteria in midstream urine specimens has been the basis for laboratory diagnosis of urinary tract infections. The culture of $\geq 10^5$ CFU/ml of a single bacterial species, so-called significant bacteriuria correlates with infection in asymptomatic patients and patients with acute pyelonephritis (5, 6). In patients with the anterior urethral syndrome and pyuria, fewer than 10^5 CFU/ml of a coliform organism may be present even in mixed culture in association with bladder bacteriuria (13). Bacteria present in these lower counts may be difficult to distinguish from bacteria present due to contamination by commensal flora.

In these circumstances, a laboratory faced with a large number of urine specimens for processing may take the view that urine specimens with certain colony counts should be selected by screening and that the investigation of other specimens be done on request when indicated by pyuria and symptoms of urinary tract infection.

Rapid screening methods for the detection of bacteriuria would reduce the time taken for a laboratory diagnosis and lower the cost of processing urine specimens. The Chemstrip LN (Boehringer Mannheim Biochemicals, Indianapolis, Ind.) is a dipstick designed to detect leukocytes and to determine nitrites in urine and is said to be useful for the detection of significant bacteriuria (2, 12). This study examines the value of the LN strip in screening urine specimens at different levels of bacteriuria.

MATERIALS AND METHODS

Midstream urine specimens from 1,020 patients submitted to the Microbiology Department, St. Joseph's Hospital, Hamilton, Ontario, from Monday to Friday during a 5-week period were examined. Of the specimens, 71% were processed within 6 h of collection and designated fresh specimens, and the remainder was processed within 12 h of voiding and designated overnight specimens. All urine specimens were refrigerated at 4°C until they were processed.

TABLE 1. Results of the Chemstrip LN test and colony counts

Colony count (CFU/ml)	No. of bacterial species isolated by quantitative culture	Total no. of specimens classified by culture	No. of specimens classified by Chemstrip[a]					
			L strip		N strip		L or N strip	
			+	−	+	−	Either or both +	Both −
$\geq 10^5$	1	127	111	16	54	73	115	12
	2	17	13	4	5	12	13	4
	≥3	76	51	25	13	63	53	23
$\geq 10^4$ to $<10^5$	1	38	23	15	2	36	25	13
	≥2	186	80	106	2	184	81	105
≥1 to $<10^4$		272	83	189	4	268	85	187
No growth		304	63	241	3	301	66	238

[a] L, Leukocyte esterase; N, nitrite.

The bacteria were enumerated by spreading 0.01 ml of urine on a 5% horse blood agar plate with a calibrated bacteriological loop (4). After overnight incubation in air at 35°C, colonies were counted and expressed as CFU per milliliter. The specimen was also inoculated onto one-half of a MacConkey plate. Up to two bacterial species isolated from specimens with CFU $\geq 10^5$/ml and a single species isolated from specimens with CFU of 10^4 to 10^5/ml were identified by established methods (8).

The Chemstrip LN (Boehringer Mannheim, lot 210959) consisted of an inert plastic strip to which two reagent strips for the detection of nitrite and leukocyte esterase, respectively, were attached. The strip was used according to the instructions of the manufacturer (2).

Data analysis. The following values were calculated (3) for

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TABLE 2. Bacterial species isolated in pure culture from midstream urine specimens

Species	No. of specimens with colony count (CFU/ml) of:		Total no. of isolates (%)
	$\geq 10^4$ to $<10^5$	$\geq 10^5$	
Escherichia coli	8	87	95 (57.6)
Klebsiella pneumoniae	2	8	10 (6.1)
Staphylococcus epidermidis	9	6	15 (9.1)
Streptococcus faecalis	7	7	14 (8.5)
Beta-hemolytic streptococcus	5	4	9 (5.5)
Staphylococcus saprophyticus	0	4	4 (2.4)
Proteus mirabilis	2	4	6 (3.6)
Others	5	7	12 (7.3)

the performance of the test in screening for bacteriuria at $\geq 10^5$CFU/ml, $\geq 10^4$ CFU/ml, and $\geq 10^3$ CFU/ml. Sensitivity = (true positives [TP] × 100)/(TP + false-negatives [FN]). Specificity = (true negatives [TN] × 100)/(TN + false-positives [FP]). Positive predictive value = (TP)/(TP + FP) × 100. Negative predictive value = (TN)/(TN + FN) × 100.

A true positive was a positive Chemstrip test result in specimens with a specified level of bacteriuria. Negative Chemstrip test results in specimens with CFU below these predetermined levels were true negatives.

RESULTS

There was no difference in the findings between the fresh and overnight specimens, so the results were combined. Results of the quantitative culture and the Chemstrip LN are presented in Table 1.

Quantitative culture. There were 220 midstream urine specimens with a colony count $\geq 10^5$ CFU/ml, accounting for 21.6% of all specimens. Of these, 127 yielded a single isolate, representing 12.5% of total specimens. Of the specimens, 22% had counts of 10^4 to 10^5 CFU/ml, and 57% had $<10^4$ CFU/ml, including 30% showing no growth. The bacterial species isolated in pure culture are shown in Table 2.

Chemstrip LN test results. The leukocyte esterase test and the nitrite test results were recorded separately and in combination (either one or both positive and both negative). Positive leukocyte esterase activity was present in 424 (41.6%) of specimens tested. Of these, only 111 yielded a single bacterial species at $\geq 10^5$ CFU/ml, and 146 yielded $<10^4$ CFU/ml or showed no growth.

The majority of specimens gave a negative nitrite test, with only 83 (8.1%) giving a positive test. Among the negative specimens were 73 of the 127 specimens with $\geq 10^5$ CFU/ml and a single bacterial isolate.

The results of the combination of the leukocyte esterase and the nitrite tests were very little different from those of the leukocyte esterase test alone.

Data analysis. The sensitivity, specificity, and predictive values of the Chemstrip LN test at three levels of bacteriuria are shown in Table 3.

DISCUSSION

The ideal screening test for the selection of urine specimens for culture in the laboratory should satisfy two requirements: firstly, the identification of midstream urine specimens containing bacteria at levels considered likely to indicate specimens from infected patients, and secondly, the exclusion of urine specimens with counts below these previously determined levels, which could reduce the number that are cultured and also permit the early reporting of negative results to the referring physician. The importance of these requirements relative to each other depends on the consequences of failure of the laboratory to diagnose a patient with urinary tract infection on the one hand and the costs of processing urine specimens on the other (1).

Our data analysis shows that the Chemstrip LN does not fulfill either of these requirements at the levels of bacteriuria selected. The enumeration of bacteria by quantitative culture has its greatest value in sorting specimens with bacterial counts $\geq 10^5$ CFU/ml that have been shown to be associated with infection. At this level, our findings show the nonutility of the LN strip in the quantitative culture of urine. These findings are similar to previously reported studies on the use of the Chemstrip LN as a predictive assay of significant bacteriuria (10, 11). The sensitivity of the combined leukocyte esterase and nitrite test, a measure of its ability to recognize true positives, was 82.3% at the $\geq 10^5$-CFU/ml level of bacteriuria. Of 127 specimens, 12 (9.4%) with a single bacterial species isolated would have been missed if only the Chemstrip test was used. In symptomatic patients who have a false-negative test, there are other diagnostic criteria to alert the physician. However, the asymptomatic patient with a false-negative test would not be recognized, and this may have a serious outcome (9). The combined leukocyte esterase, and nitrite did not perform well in excluding the true negatives. The specificity was 67.9%, an indication that screening would not be useful in reducing work load because of a high number of false-positives. False-positive results in this study may indeed be indicative of true infection since the diagnostic relevance of colony counts $<10^5$ CFU/ml is unclear, as counts as low as 10^2

TABLE 3. Analysis of Chemstrip LN results and correlation with quantitative culture results

Colony count (CFU/ml)	Chemstrip indicator	Value (%)			
		Sensitivity	Specificity	Predictive	
				Positive	Negative
$\geq 10^5$	Leukocyte$^+$	79.5	68.9	41.3	92.5
	Nitrite$^+$	32.7	98.6	86.7	84.2
	Leukocyte$^+$ or nitrite$^+$ or both positive	82.3	67.9	41.3	93.3
$\geq 10^4$	Leukocyte$^+$	62.6	74.7	65.6	72.1
	Nitrite$^+$	17.1	98.8	91.6	60.7
	Leukocyte$^+$ or nitrite$^+$ or both positive	64.6	73.8	65.5	73.0
$\geq 10^3$	Leukocyte$^+$	50.4	79.3	85.1	40.4
	Nitrite$^+$	11.2	99.0	96.4	32.1
	Leukocyte$^+$ or nitrite$^+$ or both positive	52.0	78.3	84.9	40.9

CFU/ml, well below the statistical accuracy of the calibrated loop method (7), may be associated with infection.

Predictive values vary with prevalence rates (3). In this study, specimens with $\geq 10^5$ CFU/ml had a prevalence rate of 21.6%. The negative predictive value, a measure of the ability of the test to determine that a negative test is truly negative, was 93.3%. The positive predictive value was low (only 41.3% identified as positive would be truly positive), thus reducing the cost-effectiveness of the test.

It is interesting that the leukocyte esterase test performed almost as well as the combined leukocyte esterase and nitrite test. This implies that pyuria is a better indicator of significant bacteriuria than nitrituria. Additional work is required to define the use of screening methods for routine specimen culturing in the diagnosis of urinary tract infection.

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