

Laboratory Evaluation of Urinary Tract Infections in an Ambulatory Clinic

KAREN C. CARROLL, MD,¹ DEVON C. HALE, MD,² DONALD H. VON BOERUM, BS,¹
GLENN C. REICH, MT(ASCP),² LESLIE T. HAMILTON, MT(ASCP),³
AND JOHN M. MATSEN, MD¹

A 4-month evaluation of ambulatory patients with a suspicion of a urinary tract infection was performed. Specific objectives included assessment of five urinary screening methods, reevaluation of the necessity of the phenylethyl alcohol plate (PEA), and cost-effectiveness of screening for low colony count bacteriuria.

Urine samples were collected as midstream, clean-caught specimens. A total of 142 samples, 87 from 79 symptomatic patients and 55 negative controls, were evaluated. All urine specimens were cultured using a 0.01 mL loop and a 0.001 mL loop onto Columbia sheep blood agar, MacConkey agar, and PEA agar. Twenty-four specimens (17%) were sterile, 64 (45%) were contaminated, and 54 (38%) were infected. Five

urine screening methods were performed. These tests and their associated sensitivity and specificity are as follows. The Chemstrip 9 (Behring, Inc., Somerville, NJ) for leukocyte esterase and nitrate, 67%, 98%; microscopic analysis on spun urine, 79%, 93%; methylene blue stain for pyuria, 60%, 99%; Gram stain for pyuria, 45%, 93%; Gram stain for bacteriuria, 65%, 75%; and the URISCREEN (Analytab Products, Plainview, NY), 92%, 89%. Inclusion of a PEA plate for isolation of gram-positive organisms provided no additional information. Routine culture of urine samples at 10^{-2} mL increased the contamination rate by 19%. (Key words: Urinary tract infections; Urine screening tests) *Am J Clin Pathol* 1994;101:100-103.

The diagnosis of urinary tract infection (UTI) remains problematic despite many available systems for the detection of pyuria and bacteriuria. The patient with dysuria may have several clinical conditions, each of which may require a different management strategy.¹ These conditions include acute pyelonephritis, urethritis, vaginitis, cystitis, and noninfectious conditions.

Several reports in the literature indicate varying sensitivities for a variety of urine screening methods.²⁻⁶ Most of these appear to be comparable in infections with $\geq 10^4$ colony forming units (cfu)/mL, but fall short in patients with acute urethral syndrome. In addition, many of the studies reported have been performed under research conditions and may not accurately simulate what occurs in the typically busy, outpatient clinic.

A 4-month study was performed at the Wasatch Clinics, an ambulatory care facility associated with the University of Utah Medical Center, Salt Lake City. The study had several objectives: to evaluate five screening methods in the diagnosis of UTI; to evaluate the necessity for a phenylethyl alcohol plate (PEA) for the recovery of gram-positive bacteria; to evaluate the cost-effectiveness of routine quantitative culture for low

colony count bacteriuria (10^2 cfu/mL); and to evaluate the adequacy of urine collection in a busy practice setting.

METHODS

Patients

The study was conducted at the Wasatch Clinics, from July through October, 1991. Patients with a suspicion of UTI were instructed by the nursing staff to obtain a midstream, clean-caught urine sample. Fifty-five other patients without urinary complaints were evaluated as a control group. Eighty-nine patients were women and 45 were men. No children under 17 years of age were included in the study. Patients thought to have a suspicion of a sexually transmitted disease or vaginitis were excluded from the study. The physician evaluating each patient was asked to complete a brief survey indicating the following: the age and sex of the patient; symptoms (back pain, suprapubic pain, dysuria, urgency, hematuria, fever, nausea, vomiting, or vaginal discharge); method of contraception; history of previous UTI; antibiotic usage; and suspicion of UTI as not likely, somewhat likely, or very likely. A total of 142 specimens from 134 patients were evaluated.

Laboratory Methods

Each urine sample was split into two aliquots. The urine Chemstrip 9 (Behring, Inc.) microscopic analysis and URISCREEN (API Analytab Products, Plainview, NY) were performed on site at the clinic within 1 hour of collection. The

From the ¹Department of Pathology, University of Utah Medical Center; the ²University of Utah Wasatch Clinics; and ³the Associated Regional and University Pathologists, Microbiology Laboratory, Salt Lake City, Utah.

Manuscript received July 15, 1992; revision accepted December 14, 1992.

Address reprint requests to Dr. Carroll: Department of Pathology, University of Utah Medical Center, 5C130 SOM, 50 North Medical Drive, Salt Lake City, UT 84143.

Diagnosis of Urinary Tract Infections

second aliquot was refrigerated for < 2 hours and then sent to the Associated Regional and University Pathologists Laboratory, Salt Lake City, UT, for Gram stain, methylene blue stain, and culture.

The following procedures were performed. For the Chemstrip and the API URISCREEN, manufacturers instructions were followed. The URISCREEN is a 2-minute test that detects both pyuria and bacteriuria. The microscopic analysis was performed on the sediment of 9 mL of urine spun for 5 minutes at 2160 rpm. The number of red blood cells, white blood cells, and epithelial cells were recorded per high power field. Significant pyuria was considered ≥ 5 white blood cells per high power field. Bacteria and yeasts were quantitated as negative, 1+, 2+, and 3+. Standard protocols were followed for the methylene blue and Gram stains on unspun urine.⁷ The streakplate method culture was performed using sterile 0.01 mL and 0.001 mL loops. The urine was inoculated to Columbia sheep blood agar (SBA) plates (0.01 mL and 0.001 mL), MacConkey Agar (MAC) plates (0.001 mL), and phenylethyl alcohol (PEA) plates (0.001 mL). All plates were incubated at 35 °C without carbon dioxide. Colony counts were determined by counting the number of colonies and multiplying by a factor of 100 (0.01 mL) or 1000 (0.001 mL).

Definitions

Patients were said to have a UTI if they had symptoms and a positive urine culture for any organism not considered skin or urogenital normal flora regardless of cfu/mL. Samples were said to be contaminated if any quantity of normal skin or urogenital flora was present in the absence of a significant pathogen. Organisms considered normal flora included viridans streptococci, diphtheroids, coagulase negative staphylococci (except *Staphylococcus saprophyticus*), and *Lactobacillus* species. Fecal contamination was defined as the presence of any quantity of three different species of enteric gram-negative bacilli.

Asymptomatic bacteriuria was defined as a positive urine culture with $\geq 10^3$ cfu/mL of a single pathogen in the absence of symptoms.

Statistics

The sensitivity, specificity, positive, and negative predictive values for the five screening methods were calculated against the urine culture as the "gold standard." Significance was determined by the chi-square method.⁸

RESULTS

Eighty-seven specimens from patients suspected of having a UTI and 55 control specimens were submitted for analysis. Table 1 lists the number of specimens in each group that were sterile, contaminated, or infected. Twenty-four specimens were sterile (17%) and 64 (45%) were contaminated. Fifty-four specimens were infected, 31 (57%) with gram-negative bacilli and 23 (43%) with gram-positive cocci. Twenty-six (48%) of the in-

TABLE 1. NUMBER OF STERILE, CONTAMINATED, AND INFECTED URINE SAMPLES IN EACH PATIENT GROUP

	Control	Suspected UTI	Total
Sterile	15	9	24 (17)
Contaminated	34	30	64 (45)
Infected	6*	48	54 (38)
Total	55	87	142

Values are no. (%).

* Six patients had asymptomatic bacteriuria.

fectured specimens contained $\leq 10^3$ cfu/mL, whereas 28 (52%) specimens contained $\geq 10^4$ cfu/mL.

Patients with low colony count bacteriuria more frequently had completed antibiotics within three days of culture ($P < 0.005$). Although the numbers were too small to reach statistical significance, patients with low colony count bacteriuria also tended to be sexually active women less than 55 years of age, whereas patients with colony counts $\geq 10^4$ cfu/mL tended to be older and more frequently had an anatomic abnormality (Fig. 1).

Table 2 summarizes the overall reliability of five urine screening tests. The methylene blue and Gram stains were relatively poor predictors of UTI. The URISCREEN was the most sensitive screening test (92% overall), followed by the microscopic exam (79%). The Chemstrip 9, Methylene blue, and the Gram stain all had very poor sensitivity, especially in patients with low colony count bacteriuria.

Pyuria was present or the URISCREEN was positive in all of the patients with $\geq 10^4$ cfu/mL. Three patients (11%) with low colony count bacteriuria did not have significant pyuria by our screening methods. Screening for pyuria in the 39 patients suspected of having a UTI who had a contaminated or sterile urine culture would have eliminated the need to culture 34 sterile or contaminated samples (87%).

The overall contamination rate was 45%. Culturing at 10^{-2} mL increased the contamination rate by 19%. In our laboratory, this would lead to processing an additional 2400 samples yearly. If we assume that complete identification would ensue, the total annual cost for the increase would be \$5232.00.

The PEA plate was positive for gram-positive organisms not detected by the SBA plate in 11 of 54 infected specimens. In only one specimen was the result considered significant. That specimen contained $\geq 10^3$ cfu/mL of *Escherichia coli* and 50,000 *Enterococcus*. The remaining specimens contained a single pathogen and were contaminated with gram-positive bacteria usually considered normal flora, in quantities of $\leq 10^3$ cfu/mL.⁴

CONCLUSIONS

The evaluation of the five urine screen methods revealed that the URISCREEN was the most sensitive screening method. This observation is supported by a larger study by Pezzlo and coworkers.⁹ This kit has the advantage of being less time consuming than the Gram stain. Both the Gram stain and methylene blue stain had relatively poor sensitivity, related to poor performance with samples containing low numbers of bacteria and white blood cells. Surprisingly, the urine dipstick and mi-

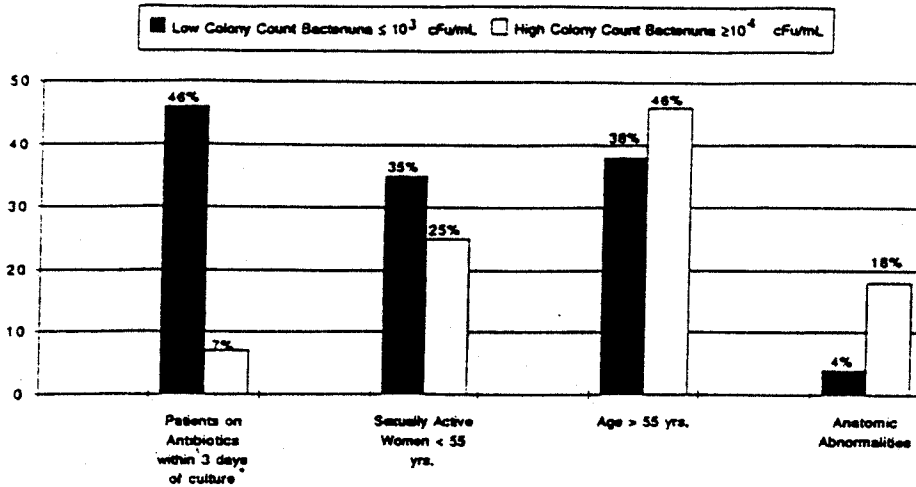


FIG. 1. Characteristics of patients with low-colony count bacteriuria versus high-colony counts. $P < 0.005$ by chi-square.

croscopic exam had lower overall sensitivity than has been previously reported.⁴

A contamination rate of 45% indicates that in a busy ambulatory care clinic, there is poor patient instruction and compliance regarding the appropriate collection of a midstream, clean-caught urine sample. Such a high contamination rate was also due in part to routinely culturing all specimens for low colony counts. Although we likely would have incorrectly diagnosed a large number of patients without the inclusion of the 10^{-2} mL plate, these persons predictably fell into one of several categories: patients on antibiotics within 3 days of urine culture; sexually active women less than 55 years of age with dysuria; males with chronic prostatitis. We agree with others who emphasize the importance of a thorough clinical history and examination in the evaluation of patients with genitourinary symptoms.⁹⁻¹¹ We feel strongly that this information must be communicated to the laboratory so that appropriate processing can be performed.

Performance of a sensitive screening test for pyuria, or a method that detects both, such as the URISCREEN, is useful for stratification of patients. Cultures would be done on those patients with a positive test for pyuria or bacteriuria and symp-

oms. We have demonstrated that routine plating for low colony counts without screening adds considerable expense to the laboratory evaluation of UTIs. In addition, we propose that requisition slips include categories of suspected diagnoses that the physician can simply check, indicating the type of syndrome and whether the patient is receiving antibiotics. The laboratory would subsequently use this information to process the sample. Patients recently taking antibiotics, patients with symptoms of acute urethral syndrome, males with chronic prostatitis, and patients with indwelling catheters, would have urine samples processed for low colony counts routinely. Patients under evaluation for asymptomatic bacteriuria and acute pyelonephritis would be evaluated only for larger colony counts. These findings support the conclusions of Latham and coworkers.²

More difficult is the symptomatic patient who is screen-negative. Although this situation occurred infrequently, such patients usually had chronic prostatitis or had recently received antibiotics. Under the strategy proposed above, these patients would receive a full culture.

Finally, the addition of a PEA plate was not essential to the recovery of clinically significant gram-positive isolates.

TABLE 2. SUMMARY OF TEST RELIABILITY OF FIVE URINE SCREENING METHODS

Test	Sensitivity (%)			Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
	Overall	$>10^4$	$<10^3$			
Chemstrip-9*	67	93	38	98	95	84
Microscopic†	79	96	58	93	87	89
URISCREEN‡	92	100	83	89	83	95
Methylene blue						
Pyuria	60	75	44	99	97	80
Gram stain						
Bacteriuria	65	86	32	75	59	80
Pyuria	45	68	12	93	76	75

* Positive nitrate and/or leukocyte esterase.

† Presence of either bacteriuria or pyuria.

‡ Detects both pyuria and bacteriuria.

Diagnosis of Urinary Tract Infections

REFERENCES

1. Komaroff AL. Acute dysuria in women. *N Engl J Med* 1984;310:368-375.
2. Latham RH, Wong ES, Larson A, et al. Laboratory diagnosis of urinary tract infection in ambulatory women. *JAMA* 1985;254:3333-3336.
3. Komaroff AL. Urinalysis and urine culture in women with dysuria. *Ann Intern Med* 1986;104:212-218.
4. Pezzlo M. Detection of urinary tract infections by rapid methods. *Clin Microbiol Rev* 1988;1:268-280.
5. Murray PR, Smith TB, McKinney TC. Clinical evaluation of three urine screening tests. *J Clin Microbiol* 1987;25:467-470.
6. Lipsky BA, Plorde JJ, Tenover FC, Brancato FB. Comparison of the automicrobic system, acridine orange stained smears and gram stained smears in detecting bacteriuria. *J Clin Microbiol* 1985;22:176-181.
7. Balows A, Hausler WJ, Herrmann, HD, et al., eds. *ASM Manual of Clinical Microbiology*. 5th ed. Washington, DC: American Society for Microbiology, 1991, pp. 1306, 1308.
8. Shott S. *Statistics for Health Professionals*. Philadelphia, Pa: WB Saunders, 1990, pp. 65-75.
9. Pezzlo MT, Amsterdam D, Anhalt JP, et al. Detection of bacteriuria and pyuria by URISCREEN, a rapid enzymatic screening test. *J Clin Microbiol* 1992;30:680-684.
10. Johnson JR, Stamm WE. Diagnosis and treatment of acute urinary tract infections. *Infect Dis Clin North Am* 1987;1:773-791.
11. Stamm WE. Protocol for the diagnosis of urinary tract infection: Reconsidering the criterion for significant bacteriuria. *Urology* 1988(suppl 2):6-10.