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Do Clinical Microbiology Laboratories Report Complete Bacteriology in Urine from Patients with Long-Term Urinary Catheters?

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Bacteriuria associated with long-term urinary catheters (those in place for ≥30 days) appears to be the most common nosocomial infection in U.S. medical care facilities. This bacteriuria is polymicrobial and dynamic and accompanied by fevers, catheter obstructions, bacteremias, and deaths. We compared the reporting by our research laboratory of bacteria present in urine from long-term-catheterized nursing home patients with that by two commercial laboratories. The commercial laboratories isolated significantly fewer bacterial species at 10^5 CFU/ml of urine specimen. Organisms well recognized as causes of urinary tract infections in noncatheterized patients (*Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae*) were isolated in comparable frequencies by both the research and commercial laboratories. However, other organisms, including uncommon uropathogens like *Providencia stuartii* and *Morganella morganii*, which were actually among the most frequent bacteriuric species in these long-term-catheterized patients, were isolated significantly less frequently by the commercial laboratories. Reasons for the discrepancies are unclear but may involve use of different techniques. More complete reporting may lead to better understanding of the polymicrobial bacteriuria of long-term catheters and its associated complications. This, in turn, may result in improved patient care and infection control in nursing homes.

In recent years, the number of nursing home beds has grown to exceed the number of hospital beds, a reflection of the aging of the U.S. population (1, 4). Chronic urinary incontinence is a problem in up to 50% of nursing home patients and is commonly managed by long-term indwelling urethral catheterization (4, 12). Over weeks and months of catheterization, bacteriuria develops and generally is polymicrobial and dynamic (22). The large number of patients and the high incidence of new episodes of bacteriuria indicate that bacteriuria associated with long-term catheterization is the most frequent nosocomial infection in the United States (18).

Although usually asymptomatic, long-term-catheterization-associated bacteriuria may be complicated by morbidity and mortality (16, 18, 20). Bacteriuria appears to be the most common cause of fever in long-term-catheterized patients in nursing homes. Bacteremia can be present during some such fevers. The risk of death during fevers which appear to be of urinary tract origin may be 60 times greater than the risk of death when the patients are afebrile (J. W. Warren, D. J. Damron, J. H. Tenney, J. M. Hoopes, B. Deforge, and H. J. Muncie, IVth Int. Symp. Pyelonephritis, Goteborg, Sweden, 1986, p. 39). These complications of bacteriuria associated with long-term catheterization may be difficult to manage because many causative bacteria are resistant to commonly used antibiotics (3, 19).

During a prospective study of the complications associated with long-term indwelling urethral catheters in two Baltimore nursing homes, we noted that reports on urine cultures performed by commercial laboratories appeared to identify fewer species per urine specimen than did our research laboratory. This prompted a retrospective comparison of the microbiologic findings of the research laboratory and the commercial laboratories. We corroborated these retrospective findings by a prospective comparison of samples of the same urine specimens.

MATERIALS AND METHODS

A total of 51 patients (47 women and 4 men) 65 years of age or older residing in two Baltimore nursing homes and who had indwelling catheters in place for 30 or more consecutive days participated in the ongoing study.

Urine bacteriology. As part of the study, urine specimens for culture were routinely obtained weekly, as well as during febrile episodes of 100.0°F (37.8°C) or more. All specimens were collected aseptically from a collection port in the distal catheter, placed immediately into an iced box at the bedside, and transported to the Division of Infectious Diseases Laboratory (our research laboratory) for culture. The urine was diluted 1:100 in sterile saline (0.85%) and inoculated with a calibrated 0.001-ml loop upon Trypticase soy agar with 5% sheep blood and Levine eosin methylene blue agar (both from BBL Microbiology Systems, Baltimore, Md.). Organisms present at $\geq 10^5$ CFU/ml were isolated and identified by standard methods; gram-negative bacilli were characterized by the Minitek system Enterobacteriaceae II (BBL). Using this methodology in split specimens, we have shown that 85% of facultative and aerobic organisms are identified in a single specimen (J. H. Tenney and J. W. Warren, IVth Int. Symp. Pyelonephritis, Goteborg, Sweden, 1986, p. 40).

During the study, the patients' attending physicians occasionally and independently ordered urine cultures. The specimens were obtained from the distal catheter in the same manner as described above. However, they were carried to a refrigerator in a central location and stored there until the commercial laboratory picked them up, a process which occurred 3 to 4 times per day. Both commercial laboratories used a standard clinical set-up procedure for their urine specimens. Undiluted urine was inoculated with a calibrated 0.001-ml loop upon agar plates. The media used were Tryp-

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TABLE 1. Retrospective and prospective comparisons of microbiologic findings of a research laboratory and commercial laboratories

Species category	No. of isolates identified/total no. of isolates (% identified) by the following comparison:							
	Retrospective (different specimens, same day [n = 17])		Retrospective (different specimens, same week [n = 19])		Prospective (same specimen [n = 10])		All comparisons (n = 46)	
	Research laboratory	Commercial laboratory	Research laboratory	Commercial laboratory	Research laboratory	Commercial laboratory	Research laboratory	Commercial laboratory
Gram-negative bacilli								
P. stuartii	16/16 (100)	10/16 (63)[a]	10/11 (91)	8/11 (73)	8/8 (100)	5/8 (63)	34/35 (97)	23/35 (66)[a]
P. mirabilis	11/11 (100)	10/11 (91)	12/12 (100)	12/12 (100)	4/4 (100)	1/4 (25)	27/27 (100)	23/27 (85)
P. aeruginosa	10/12 (83)	4/12 (33)	5/6 (83)	3/6 (50)	5/5 (100)	4/5 (80)	20/23 (87)	11/23 (48)[a]
M. morganii	9/9 (100)	4/9 (44)	5/5 (100)	2/5 (40)	7/7 (100)	3/7 (43)	21/21 (100)	9/21 (43)[b]
E. coli	5/5 (100)	5/5 (100)	6/8 (75)	8/8 (100)	5/7 (71)	6/7 (86)	16/20 (80)	19/20 (95)
K. pneumoniae	3/4 (75)	4/4 (100)			3/3 (100)	1/3 (33)	6/7 (86)	5/7 (71)
Other	11/14 (79)	5/14 (36)	8/8 (100)	4/8 (50)	4/4 (100)	3/4 (75)	23/26 (88)	12/26 (46)[a]
Gram-positive organisms								
Enterococci	9/9 (100)	5/9 (56)	6/6 (100)	2/6 (33)	6/7 (86)	7/7 (100)	21/22 (95)	14/22 (64)[a]
Other	9/10 (90)	4/10 (40)	4/4 (100)	0/4 (0)	5/7 (71)	6/7 (86)	18/21 (86)	10/21 (48)

[a] $P < 0.05$.
[b] $P < 0.001$.

ticase soy agar with 5% sheep blood for colony counts and MacConkey agar for differentiation of gram-negative bacilli. The identification systems used by the commercial laboratories were API 20E (Analytab Products, Plainview, N.Y.) in one and MicroScan (American Scientific Products, McGaw Park, Ill.) in the other. Reports of bacterial species present at $\geq 10^5$ CFU/ml were compared with reports from the research laboratory.

Retrospective comparison: different specimens, same day. The first set of comparisons was of cultures of urine specimens which coincidentally were obtained on the same day by both the research laboratory and the commercial laboratory.

Retrospective comparison: different specimens, same week. The comparison of urine specimens obtained in the same week was somewhat more complex and required that cultures be performed by the research laboratory both before and after a commercial laboratory culture, all within a 7-day period. An organism was considered to be identified by the research laboratory only if it was isolated from both the culture taken before and that taken after the commercial laboratory culture (Table 1).

In this example, although the research laboratory identified a total of five different bacterial species in its cultures (cultures taken on 27 March and 3 April), we would consider only two species to be appropriate for comparison with the interim commercial laboratory culture (taken on 30 March). These were the two species that appeared in both the previous and subsequent research laboratory specimens, *Providencia stuartii* and *Pseudomonas aeruginosa*. Thus, we did not consider enterococci, *Klebsiella pneumoniae*, and *Escherichia coli* to be appropriate for comparison because each appeared in only one of the two research laboratory cultures. Therefore, in this example, our interpretation would be that both the research laboratory and the commercial laboratory identified the *P. stuartii* and *P. aeruginosa* but that only the commercial laboratory identified *E. coli*. This method, then, tended to bias the comparison against finding the research laboratory more efficient than the commercial laboratory. We did not compare specimens from patients who had received antibiotics within the 2 weeks before or the 7 days during the collection period or who had a new catheter inserted during the collection period.

Prospective comparison: same specimen. The third comparison was a prospective one to determine corroboration of the two retrospective comparisons. Urine specimens from 10 different patients were obtained, and samples of each were delivered to the research laboratory and to one of the commercial laboratories. The procedures at the research laboratory were as described above, except that additional dilutions of urine (1:10, 1:1,000, and 1:10,000) were inoculated upon the agar plates. The commercial laboratory procedure was unchanged; MicroScan was the identification system used. All specimens were collected from patients who had not received antibiotics within the preceding 2 weeks.

Analysis. For each comparison, we calculated the mean number of bacterial species present at concentrations $\geq 10^5$ CFU/ml which were isolated and identified by the research and commercial laboratories; these means were compared by paired t tests. We also calculated the percentage of the total organisms which was isolated by each laboratory. For these proportions, all bacterial species identified by the research laboratory, the commercial laboratory, or both were included in the denominator. Thus, the denominator represents the best estimate of the actual bacterial population of the urine. These proportions were compared by two-tailed Fisher exact tests.

RESULTS

Retrospective comparison: different specimens, same day. A total of 17 urine cultures were performed on the same days by both our laboratory and one of the commercial laboratories. Of these 17 cultures, 13 were done by commercial laboratory A and 4 were done by commercial laboratory B. These laboratories were similar in the number of species isolated per specimen (3.1 and 2.8, respectively) and in the types of species isolated. Therefore, we have combined their data for this report.

The research laboratory identified a mean of 4.9 species per specimen from the 17 urine specimens, a figure significantly higher than that of the commercial laboratories ($P <$ 0.001). These isolates were 92% of all of those identified by either the research laboratory or the commercial laboratories. In comparison, the commercial laboratories identified 57% of the total isolates ($P < 0.001$). *E. coli*, *Proteus*

TABLE 2. Typical example of identification of isolates by the research laboratory and a commercial laboratory

Date of culture	Laboratory	Isolates identified
27 March 1985	Research	*P. stuartii* *P. aeruginosa* Enterococci
30 March 1985	Commercial	*P. stuartii* *P. aeruginosa* *E. coli*
3 April 1985	Research	*P. stuartii* *P. aeruginosa* *E. coli* *K. pneumoniae*

mirabilis, and *K. pneumoniae* were isolated in equivalent frequencies by the research laboratory and the commercial laboratories. However, the research laboratory identified *P. stuartii* significantly more often than did the commercial laboratories ($P < 0.05$). Furthermore, substantially more *P. aeruginosa*, *Morganella morganii*, and enterococci were isolated by the research laboratory. Of the nine species categories of organisms noted in Table 2, the research laboratory identified more isolates in eight, the commercial laboratory identified more isolates in one, and both laboratories isolated the same number in one.

Retrospective comparison: different specimens, same week. There were 38 urine specimens submitted to the commercial laboratories on days that were bracketed by two urine cultures performed by the research laboratory, all within a 7-day period. However, 19 of these comparison sets were excluded because of catheter changes during the 7-day period (9), antibiotics used within the preceding 2 weeks or within the 7-day collection period or both (7), or because of catheter changes and use of antibiotics (3). For the remaining 19 comparisons, the research laboratory reported a total of 56 isolates present in both the culture before and the culture after the commercial laboratory culture. The commercial laboratories reported only 39 species from their interval cultures (Table 1). The research laboratory identified 93% of all isolates, whereas the commercial laboratories identified 65% ($P < 0.001$). Virtually all *E. coli* and *P. mirabilis* isolates were identified by both laboratories. Of the eight categories of organisms summarized in Table 2, the research laboratory identified more isolates in six, the commercial laboratory identified more isolates in one, and both laboratories identified the same number in one.

Prospective comparison: same specimen. The prospective study comparing samples of the same 10 urine specimens yielded results similar to those of the retrospective studies. The mean number of organisms identified by the commercial laboratory was 3.6; our research laboratory identified an average of 4.7 organisms per specimen ($P < 0.001$). Of all of the organisms, 90% were identified by the research laboratory, compared with 69% identified by the commercial laboratory ($P < 0.05$). Within the nine species categories of organisms in Table 2, the research laboratory identified more in six, and the commercial laboratory identified more in three.

All comparisons. In total, the research laboratory identified 92% of all isolates, and the commercial laboratories identified 62% ($P < 0.001$). There was no significant difference in isolation frequency between the research laboratory and the commercial laboratories for each of *E. coli*, *K. pneumoniae*, and *P. mirabilis*. These organisms are the most common urinary isolates in noncatherized patients with bacteriuria (7). Combining them into a group designated common uropathogens still revealed no significant difference between the laboratories (49 of 54 organisms identified by the research laboratory versus 47 of 54 identified by the commercial laboratories). However, the research laboratory identified significantly more of the less common pathogens—*P. stuartii*, *P. aeruginosa*, *M. morganii*, and enterococci.

Several species of both gram-negative and gram-positive organisms were each isolated infrequently enough that they were not listed separately. Each of these, by definition, is an uncommon uropathogen, and the comparison of isolation frequencies between the research laboratory and commercial laboratories for these uropathogens was similar to that of the uncommon individual species noted above. The research laboratory identified 41 of 47 organisms (87%), and the commercial laboratories identified 22 of 47 organisms (47%) ($P < 0.001$).

DISCUSSION

The uncatheterized urinary tract is commonly sterile, and when bacteriuria develops, it is usually caused by a single species (7). Once a urethral catheter is put in place, bacteriuria occurs with an incidence of 3 to 10% per day (21). In acute-care hospitals, the catheter stays in place for 2 to 4 days in most patients, and only 10 to 20% of patients develop bacteriuria (15). However, in nursing homes, some patients may remain catheterized for longer periods of time, and most become bacteriuric after 30 days of catheterization. With continued catheterization for months and years, as is often the case in nursing homes, bacteriuria becomes polymicrobial and dynamic, with a variety of common (*E. coli*, *P. mirabilis*, and *K. pneumonia*) and uncommon (*P. stuartii* and *M. morganii*) uropathogens (22).

Therefore, the bacteriology of long-term urethral catheters is qualitatively and quantitatively different from that of other types of urine specimens. Our studies have demonstrated that nursing home patients with catheters in place for months and, in some cases, years invariably have a polymicrobial bacteriuria. As many as 95% of urine specimens from such patients contain at least two bacterial species present at concentrations of 10^5 CFU/ml or more. Indeed, some urine specimens contain six or more bacterial species at these concentrations (22). Therefore, polymicrobial bacteriuria in long-term-catheterized patients is a real and common clinical situation. This fact should be recognized, and its implications for the clinical microbiology laboratory should be considered.

In this study, the findings in both the retrospective and prospective comparisons were consistent and indicated that the commercial laboratories isolated fewer organisms than did our research laboratory. Furthermore, it seems clear that this was not a random discrepancy. The common uropathogens, such as *E. coli*, *P. mirabilis*, and *K. pneumoniae*, were isolated in equivalent frequencies by both the research laboratory and the commercial laboratories. The discriminating feature was that the research laboratory consistently isolated more uncommon uropathogens, such as *P. stuartii* and *M. morganii*.

The study did not address reasons for this discrepancy. However, the likely causes include differences in the techniques used by the laboratories. One technique of possible importance is the research laboratory's dilution of urine before inoculation. Our observations suggest that the median

concentration of organisms of all species is $\geq 10^8$ CFU/ml of undiluted urine in these long-term-catheterized patients. A 0.001-ml loop would inoculate 10^5 colonies upon an agar plate. The commercial laboratories used undiluted urine, and their technologists were seeking separate species, each at 100 colonies or more on the plate. Among the profusion of organisms on the plate, the technologists may have had difficulties in finding separate species and in estimating appropriate colony counts.

Other than a desire for accuracy, are there other reasons for obtaining the complete bacteriology of urine specimens from long-term-catheterized patients? We believe that there are at least four reasons. (i) Patients experience morbidity and mortality from polymicrobial bacteriuria. (ii) Many of the uncommon organisms causing bacteriuria are resistant to antibiotics. (iii) Infection epidemiology and control may be improved by accurate identification and reporting of isolates. (iv) More-inclusive reportings may lead to a better understanding of the complications of bacteriuria associated with long-term urinary catheterization.

Clearly, morbidity and mortality are consequences of bacteriuria associated with long-term catheterization. Fevers from urinary tract infections appear to be the most common type of febrile episodes in long-term-catheterized patients (Warren et al., IVth Int. Symp. Pyelonephritis, 1986). Because these patients are always bacteriuric, fevers are sometimes difficult to attribute to the catheterized urinary tract. However, the identification of bacteremia clarifies for the clinician the source of infection, as well as the pathogenic importance of the bacteriuric species. Bacteremias caused by these uncommon uropathogens occur (16, 18, 19; Warren et al., IVth Int. Symp. Pyelonephritis, 1986) and may be associated with deaths (9, 10).

Treatment of these infections depends upon knowledge of antibiotic susceptibility patterns. Ironically, some of the bacteriuric organisms least likely to be isolated and reported by commercial laboratories are those with the greatest prevalences of resistance to commonly used antibiotics (3, 6, 14, 17, 19). Knowledge of the prevalent organisms of an institution and their antibiotic susceptibilities is important in the empiric selection of appropriate antibiotic therapy for the symptomatic patient. Clearly, deaths can occur from bacteremia with these uncommon uropathogens for which empiric therapy has been limited to antibiotics to which the bacterial strain is resistant (9, 10).

A related issue is the epidemiology of nosocomial infections. These organisms can be passed from patient to patient (2, 8, 13, 17). Furthermore, plasmids encoding numerous phenotypic characteristics, including antibiotic resistance, may be passed from organism to organism, even between species (14). Accurate assessment of polymicrobial bacteriuria of patients in a medical care unit is necessary to understand the epidemiology of organism and plasmid transfer.

Although a number of bacterial species may colonize or infect the urinary tracts of long-term-catheterized patients, it seems likely that some are more pathogenic than others. For instance, urease-producing organisms may more commonly be associated with urinary tract stones (11) and perhaps with catheter obstruction (5). Some organisms may more likely lead to bacteremia than other organisms (15). Better reporting of bacterial species may lead to epidemiologic associations with fevers, catheter obstructions, urinary stones, epididymitis, prostatic abscesses, chronic tubulointerstitial nephritis, etc.

What recommendations can be made? First, it seems reasonable that each microbiology laboratory specimen slip should have a section whereupon it can be noted whether the specimen is from a patient with a long-term catheter. This would allow the laboratory to discriminate between contaminated specimens from noncatheterized patients and true polymicrobial specimens from long-term-catheterized patients.

Second, studies comparing techniques for isolating the variety of organisms found in long-term-catheterized urinary tracts would be appropriate. These might include transportation and storage procedures and the use of diluted urine specimens, as well as inoculation of a variety of differential and selective media.

Third, because of the increased effort, time, and materials required for proper identification of multiple organisms, inclusive reporting of urine cultures from patients with long-term catheters will be more costly than routine cultures. Consequently, educational efforts and institutional policies should be directed towards the development of prudence in the ordering of studies of urine bacteriology of such patients. Urine cultures from catheterized patients with fever or urinary symptoms or both seem to be appropriate. For the study of urine specimens from asymptomatic patients, proper guidelines are less clear. As more data regarding the complications of bacteriuria associated with long-term catheterization are obtained, appropriate guidelines may become evident. Until such a time, it seems reasonable that each institution develop its own policies regarding surveillance urine cultures for individual patient care, as well as for infection control.

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