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Urease-Positive Bacteriuria and Obstruction of Long-Term Urinary Catheters

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Long-term urethral catheterization (≥30 days), a management technique for urinary incontinence, results in polymicrobial bacteriuria. We frequently found urease-producing bacteria: of 1,135 weekly urine specimens from 32 long-term-catheterized patients, 86% had urease-positive bacterial species at $\geq 10^5$ CFU/ml. The most common species were *Proteus mirabilis* and *Morganella morganii*, each found in over half the specimens. *P. mirabilis*, but not other urease-positive species, was significantly associated with the 67 obstructions observed in 23 patients. *M. morganii* had a more complex association and in some way may protect the catheter from obstruction.

Long-term urethral catheterization, a common management technique for intractable urinary incontinence or urinary retention, is universally complicated by polymicrobial and dynamic bacteriuria (3, 7, 10, 12, 14). The sequelae of this bacteriuria may include fevers, bacteremia, acute pyelonephritis, peri-urinary tract infections, urinary stones, chronic renal inflammation, renal failure, and death (7, 11, 13). A large proportion of the bacteriuric species are *Proteeae*, including *Proteus mirabilis*, *Morganella morganii*, and *Providencia stuartii* (10, 14). This tribe commonly produces urease, an enzyme which catalyzes the hydrolysis of urea in the urine (0.4 to 0.5 M), resulting in a rapid rise of pH (6). The alkaline environment prompts the precipitation of polyvalent cations and anions, including struvite ($MgNH_4PO_4 \cdot 6H_2O$) and carbonate-apatite [$Ca_{10}(PO_4\ CO_3OH)_6(OH)_2$] crystals (1, 2, 5, 6, 11), structural components of renal calculi called "infection stones." Catheter encrustations are also composed of struvite and carbonate-apatite (2).

Over a period of 1 year, we studied 32 women ≥65 years of age who had silicone-coated latex urethral catheters in place for ≥100 consecutive days. Antimicrobial agents were not routinely administered during the study. Weekly urine specimens were collected and processed as described previously (14). Urease production was determined by reaction of the Minitek Enterobacteriaceae II system (BBL Microbiology Systems, Cockeysville, Md.). Additionally, urease production of 50 representative isolates of the more common species and all isolates of those less common was confirmed on urease segregation agar (4). Catheter obstruction, defined as complete blockage requiring irrigation or replacement, was sought each day by research assistants. No change in urine volume in the collection bag was used as an index of obstruction of the catheter lumen. Informed consent was obtained from all patients.

Of 1,135 weekly urine specimens, 972 (86%) yielded urease-positive bacterial species at $\geq 10^5$ CFU/ml. A total of 5,088 facultative or aerobic bacterial species, of which 1,816 (36%) produced urease, were isolated. The most common urease-producing organisms were *P. mirabilis* and *M. morganii*, each found in over half the specimens (Table 1).

During the study, 23 patients experienced at least one catheter obstruction (a total of 67 obstructions). Of the 831 specimens obtained from these patients, 758 (91%) contained at least one urease-positive bacterial species. On the other hand, of nine patients with no obstructions, 76% (231 of 304 specimens) contained urease-positive species ($P < 0.001$ by chi square).

P. mirabilis was significantly associated with obstructed catheters. Specimens from patients with obstructions more frequently contained *P. mirabilis* (539 of 831 specimens [65%]) than did those from unobstructed patients (121 of 304 specimens [40%]) ($P < 0.001$ by chi square). The bacteriology of the patients with obstructions was further studied (Table 2). From these patients, those specimens immediately preceding an obstruction (obstructed specimens) were compared with all other specimens from these patients (unobstructed specimens). *P. mirabilis* appeared in 73% of obstructed specimens, compared with 64% of unobstructed specimens. Thus, a progressive association of *P. mirabilis* and catheter obstruction was seen: from patients with obstructions, 73% of obstructed specimens and 64% of unobstructed specimens and from patients without obstructions, 40% of specimens. Furthermore, when obstructing material was quantitatively cultured, *P. mirabilis* was isolated from 9 of 10 catheters at $\geq 10^5$ CFU/g.

The association of *M. morganii* and catheter obstruction was more complex. Like *P. mirabilis*, *M. morganii* was found more frequently in patients with obstructions (470 of 831 specimens [57%]) than in patients with no obstructions (142 of 304 specimens [47%]) ($P < 0.005$ by chi square). However, directly counter to the findings for *P. mirabilis*, *M. morganii* was identified significantly more often in unobstructed than obstructed specimens from patients who had experienced catheter obstructions (59 versus 33% [$P < 0.001$]) (Table 2).

The data indicate no association or even trend between the presence of the other urease-positive species (*P. stuartii*, *Klebsiella pneumoniae*, *Providencia rettgeri*, and *Proteus vulgaris*) and catheter obstruction.

P. mirabilis is strongly correlated with obstruction of long-term urethral catheters, but other urease-producing bacterial species are not. In other studies, we found that ureases of *P. mirabilis* hydrolyzed urea 6 to 10 times faster than did ureases from other species (*M. morganii*, *P.*

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TABLE 1. Frequency of urease-positive isolates in 1,135 weekly urine specimens from 32 long-term-catheterized patients

Species	No. (%)	
	Specimens[a]	Patients
P. mirabilis	660 (58)	28 (88)
M. morganii	612 (54)	29 (91)
P. stuartii	257 (23)[b]	14 (44)
K. pneumoniae	198 (17)[c]	19 (59)
P. rettgeri	47 (4)	7 (22)
P. vulgaris	16 (1)	2 (6)
Other gram-negative organisms	26 (2)	14 (44)
Urease-positive organisms	972 (86)	32 (100)

[a] Includes only urease-positive isolates at $\geq 10^5$ CFU/ml.
[b] Urease-positive *P. stuartii* isolates represented 37% of a total of 700 *P. stuartii* isolates. Isolates were differentiated from closely related *Providencia* and *Proteus* species by fermentation of adonitol, inositol, galactose, and trehalose (8). Fifty-five of sixty-six representative urease-positive isolates reacted with *P. stuartii* O antisera as tested by John Penner, University of Toronto. Eight isolates were nontypeable rough, and three were nontypeable smooth.
[c] Urease-positive *K. pneumoniae* isolates represented 82% of a total of 241 *K. pneumoniae* isolates.

stuartii, *K. pneumoniae*, *P. rettgeri*, and *P. vulgaris*) (8a). This was so even though *P. mirabilis* urease had lower affinity for urea than did that of the other species. In urine, because of the high concentration of urea, low affinity of the enzyme is not a disadvantage, because the enzyme is saturated with substrate and thus works at maximum rate. Although we believe that urease plays the critical role in crystallization leading to obstruction, we cannot rule out the possible involvement of the elongated swarm cell, slime production, or attachment to the catheter surface by fimbriae in this process.

We found that the effect of *M. morganii* upon catheter obstruction was more complex. *M. morganii* may in some way tend to prevent catheter obstruction. Other urease-producing species were not directly or inversely associated with catheter obstruction.

TABLE 2. Catheter obstruction and presence of urease-positive bacterial species in urine

Species	No. of isolates (%) in patients:		
	With obstructions		With no obstructions (304 specimens)[a]
	Obstructed specimens (n = 67)[b]	Unobstructed specimens (n = 764)[a]	
P. mirabilis	49 (73)	490 (64)	121 (40)
M. morganii	22 (33)	448 (59)	142 (47)
P. stuartii	18 (27)	169 (22)	70 (23)
K. pneumoniae	11 (16)	148 (19)	39 (13)
P. rettgeri	2 (3)	44 (6)	1 (0)
P. vulgaris	3 (4)	10 (1)	3 (1)

[a] Weekly urine specimens not followed by onset of catheter obstruction.
[b] Weekly urine specimens preceding onset of catheter obstruction.

Others have demonstrated that the immersion of glass rods (6) or other foreign bodies (9) in urine containing *P. mirabilis* is a useful model for crystal morphogenesis and calculus formation. The long-term-catheterized urinary tract containing *P. mirabilis* may represent an in vivo model of calculus formation.

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