Catheter-Associated Urinary Tract Infection Is Rarely Symptomatic

A Prospective Study of 1497 Catheterized Patients

Paul A. Tambyah, MBBS; Dennis G. Maki, MD

Background: Catheter-associated urinary tract infection (CAUTI) is the most common nosocomial infection, accounting for more than 1 million cases each year in US hospitals and nursing homes.

Objective: To define the clinical features of CAUTI.

Setting and Patients: A university hospital; 1497 newly catheterized patients.

Design: Every day that the catheter was in place, a quantitative urine culture and urine leukocyte count were obtained, and the patient was queried by a research worker regarding symptoms. To more precisely define the role of CAUTI in patients' symptoms, a subset of 1034 patients, 89 of whom developed CAUTI with more than 10^3 colony-forming units per milliliter, who did not have another potentially confounding site of infection besides the urinary tract, was analyzed.

Outcome Measures: Presence of fever, symptoms commonly associated with community-acquired urinary tract infection, and peripheral leukocytosis.

Results: There were 235 new cases of nosocomial CAUTI during the study period. More than 90% of the infected patients were asymptomatic; only 123 infections (52%) were detected by patients' physicians using the hospital laboratory. In the subset analysis, there were no significant differences between patients with and without CAUTI in signs or symptoms commonly associated with urinary tract infection—fever, dysuria, urgency, or flank pain—or in leukocytosis. Only 1 of the 235 episodes of CAUTI that were prospectively studied was unequivocally associated with secondary bloodstream infection.

Conclusions: Whereas CAUTIs are a major reservoir of antibiotic-resistant organisms in the hospital, they are rarely symptomatic and infrequently cause bloodstream infection. Symptoms referable to the urinary tract, fever, or peripheral leukocytosis have little predictive value for the diagnosis of CAUTI.

Arch Intern Med. 2000;160:678-682

C ATHETER-associated urinary tract infection (CAUTI) is the most common nosocomial infection, accounting for up to 40% of all nosocomial infections and more than 1 million cases in US hospitals and nursing homes each year.[1-3] Up to half of the patients requiring an indwelling urethral catheter for 5 days or longer will develop bacteriuria or candiduria.[1-3] Silent catheter-associated bacteriuria comprises a huge reservoir of antibiotic-resistant organisms in the hospital, particularly on critical care units.[4-13]

Although there have been recommendations to treat CAUTIs only when they are symptomatic,[3,14,15] the symptoms associated with CAUTI have not been clearly defined. We report the findings of a prospective study of 1497 newly catheterized hospitalized patients that was undertaken to determine the prevalence of signs and symptoms attributable to CAUTI and the relative contribution of CAUTI to nosocomial bloodstream infection.

See also page 673

RESULTS

A total of 1497 evaluable newly catheterized patients were studied prospectively. There were 235 CAUTIs in 224 patients (14.9%); 85% of the patients had more than 10^5 CFU/mL in 1 or more cultures, and most showed active infection in serial cultures for more than 3 days (mean ± SD duration of bacteriuria or candiduria, 4.0 ± 3.9 days). The incidence of CAUTI was much higher in women (147/633 [23.2%]) than in men (77/864 [8.9%]; relative risk, 1.7; 95% confidence interval, 1.6-2.0; *P*<.001) (**Table 1**). Of the

From the Section of Infectious Diseases, Department of Medicine, University of Wisconsin Medical School, Madison.

PATIENTS AND METHODS

PATIENTS

Patients participating in 2 randomized trials of 2 novel urinary catheters—one a nitrofurazone-impregnated silicone catheter,[16] and the other, a silver-polyurethane hydrogel catheter[17]—formed the study population. Neither medicated catheter was associated with any irritative urinary tract symptoms or with increased sterile pyuria, as compared with the control catheters used in each trial.[16,17] Participants in both trials were hospitalized patients scheduled to receive an indwelling urethral (Foley) catheter who were expected to be catheterized for more than 24 hours; patients were excluded if they were younger than 18 years, pregnant, or had a known allergy to silicone, nitrofurazone, or silver. Both studies were approved by the institutional Human Subjects Committee, and written informed consent was obtained from all patients.

DATA COLLECTED

Baseline demographic and clinical data bearing on potential risk factors for CAUTI[18-20] were collected, including age, sex, structural urologic disease, underlying systemic diseases such as diabetes mellitus and cancer, immunosuppressive therapy, hospital service, confinement in an intensive care unit, severity of illness according to the Acute Physiology and Chronic Health Evaluation (APACHE) II score,[21] recent surgery, and the purpose for catheterization. On entry into the study and daily thereafter, approximately 3 mL of urine was aspirated from the sampling port of the catheter with a sterile syringe, after the port was disinfected with 10% povidone iodine. Each specimen was immediately brought to the laboratory and cultured using a technique capable of detecting 1 colony-forming unit (CFU) per milliliter,[22] evenly spreading 1 mL of undiluted urine and serial dilutions on predried sheep's blood agar plates. After aerobic incubation at 37°C for 24 to 48 hours, each colony type was enumerated and fully identified using standard techniques and criteria.[23] In accordance with the study protocol, the results of research urine cultures in this study were not communicated to patients' physicians.

Every day, in addition to providing a urine sample for culture, the patients were questioned by a research nurse regarding any discomfort or other symptoms potentially associated with the catheter, eg, urethral or pelvic pain, sense of urgency, or dysuria. Patients' records were also reviewed for fever and other clinical and laboratory data suggesting infection. Peripheral white blood cell counts were recorded, as they were ordered by the primary team taking care of the patients. Urine leukocyte counts were measured daily, using a hemocytometer (Hausser Scientific Partnership, Horsham, Pa).[24]

DEFINITION OF CAUTI

The new appearance of bacteriuria or funguria with a count of more than 10^3 CFUs/mL was considered to represent nosocomial CAUTI. We have previously shown that isolation of more than 10^3 CFUs/mL is highly predictive of CAUTI.[22] If intercurrent antimicrobial therapy is not given to the patient, the level of bacteriuria or candiduria uniformly rises to more than 10^5 CFUs/mL within 24 to 48 hours.

DEFINITIONS OF NOSOCOMIAL BLOODSTREAM AND OTHER INFECTIONS

Nosocomial bloodstream infection was defined as the isolation of a recognized pathogen from a blood culture, with no evidence that the infection was present or incubating at the time of hospital admission. With coagulase-negative staphylococci and other skin commensals, at least 2 positive cultures were required unless an intravascular device had also been shown by culture to be infected by the same species.[25] Other infections were defined according to the criteria of the National Nosocomial Infection Study of the US Center for Disease Control and Prevention.[25]

STATISTICAL ANALYSIS

An unpaired *t* test was used to determine the significance of differences with continuous variables, and the Fisher exact test was used to assess dichotomous data. All *P* values refer to 2-sided tests of significance.

---

235 CAUTIs, 220 (94%) were unimicrobial and 15 (6%) were polymicrobial, most commonly with enterococci and gram-negative bacilli. Ninety-seven infections (39%) were caused by gram-negative bacilli, 85 (34%) by enterococci and staphylococci, and 68 (27%) by *Candida* species. Only 123 (52%) of 235 CAUTIs were diagnosed by the patients' physicians using the hospital laboratory; thus, fewer than 50% of the CAUTIs were treated. The microbial profile of the infections that were not diagnosed clinically was similar to that of the infections that were detected during hospitalization and, usually, treated.

The majority of subjects (86.7% of patients with CAUTI; 89.5% of patients without CAUTI) were able to consistently respond to daily questions regarding symptoms. Overall, only 15 (7.7%) of 194 patients with CAUTI who could respond reported subjective symptoms referable to the urinary tract, pain, urgency, or dysuria.

Most surgical patients were receiving analgesics postoperatively. However, symptom scores in surgical patients (9.2% with 1 or more symptoms) were similar to those in nonsurgical patients (6.5%; *P* = .15), a far smaller proportion of whom were receiving analgesics or anti-inflammatory drugs.

Four hundred sixty-three patients had another active infection unrelated to the urinary tract: lower respiratory tract infection (n = 212), intra-abdominal infection (n = 57), primary bloodstream infection (n = 46), skin or soft tissue infection (n = 53), or other infections (n = 95). The patients in this subset were far more likely than the patients without other active unrelated infections to have fever (43% vs 19%; *P*<.001). However, symptoms referable to the urinary tract in

Table 1. Epidemiological Characteristics of 1273 Patients Without CAUTI and 224 Patients With 235 Nosocomial CAUTIs Identified in a Prospective Study of Catheterized Patients*

Characteristic	Without CAUTI	With CAUTI	P
Age, mean ± SD, y	55.0 ± 17.3	56.0 ± 18.3	.47
Sex, No. (%)			
Male	787 (62)	77 (34)	<.001
Female	486 (38)	147 (66)	
Service, No. (%)			
Surgical	1024 (80)	138 (62)	<.001
Medical	249 (20)	86 (38)	
Antibiotics per catheter-day, mean ± SD	2.4 ± 1.9†	1.6 ± 1.7‡	<.001
APACHE II score, mean ± SD	16.2 ± 6.3	16.4 ± 6.5	.58
Days catheterized before onset of infection, mean ± SD	4.4 ± 3.8†	6.4 ± 6.1	<.001

*CAUTI indicates catheter-associated urinary tract infection; APACHE II, Acute Physiology and Chronic Health Evaluation II.[21]
†Total days catheterized.
‡Days preceding CAUTI.

Table 2. Symptoms Referable to the Urinary Tract, Fever, Leukocytosis, and Quantitative Pyuria in a Subset of 1034 Hospitalized Patients With Urinary Catheters*

	Without CAUTI (n = 945)	With CAUTI (n = 89)	P
Proportion with symptoms, %			
Pain	5.9	4.8	.81
Urgency	7.6	6.0	.68
Dysuria	8.0	6.0	.66
Temperate >38.5°C	19.8	17.7	.77
Highest temperature, mean ± SD, °C	38.1 ± 0.7	37.8 ± 0.5	<.01
Peripheral white blood cell count, mean ± SD, ×10⁹/L	11.3 ± 4.1	10.7 ± 3.6	.14
Highest urine white blood cell count, mean ± SD, /µL†	11 ± 100	309 ± 1065	.009

*Other than catheter-associated urinary tract infection (CAUTI), which was detected in 89 patients, no infections were identified. The proportion of patients with and without CAUTI who could respond to daily questions regarding symptoms was identical in the 2 groups: 94%.
†Excludes kidney transplant patients, whom we have found show a burst of sterile pyuria following transplantation.

patients with CAUTI in the 2 groups were again virtually identical. Thus, to more precisely analyze the effect of CAUTI on patients' symptoms—especially fever—and peripheral leukocyte counts, a subset of 1034 patients, who did not have another, potentially confounding site of infection besides the urinary tract, was analyzed; 89 had developed CAUTI with more than 10^3 CFUs/mL. In this large subset (**Table 2**), there were no significant differences between patients with and without CAUTI in subjective symptoms commonly associated with urinary tract infections; most were afebrile. There were also no significant differences between the 2 groups in mean peripheral leukocyte counts, although there were significant elevations in urine white blood cell counts in patients with CAUTI compared with uninfected catheterized patients; the largest differences were seen in patients infected with gram-negative bacilli.[26]

During the study, 79 nosocomial bloodstream infections (5.3%), 67 primary bloodstream infections (38 originating from an intravascular device) and 12 secondary bloodstream infections, were identified in the study population. There were only 4 concordant bloodstream infections with the same organism isolated from a catheterized urine specimen and subsequent blood cultures: 2 with gram-negative bacilli (*Klebsiella pneumoniae* and *Enterobacter cloacae*), 1 with coagulase-negative staphylococci, and 1 with *Candida lusitaniae*. In the latter 2 cases, an infected central venous catheter could not be excluded as the source of the patient's bloodstream infection, because the infecting organism was also recovered in large numbers from a semiquantitative culture of a central venous catheter. In 1 case with *K pneumoniae*, the patient had a concordant ventilator-associated pneumonia. In only a single case, with *E cloacae*, did a nosocomial bloodstream infection appear unequivocally to have derived from a CAUTI; interestingly, this patient had no symptoms, whatsoever, referable to the urinary tract.

COMMENT

Although most authorities[14,15] and case definitions[25] make a distinction between symptomatic CAUTI and asymptomatic catheter-associated bacteriuria, we are unaware of prospective studies which have rigorously sought to determine the utility of signs and symptoms in the detection of CAUTI. We prospectively studied a large number of hospitalized patients with indwelling urinary catheters and found that fewer than 10% of patients with microbiologically documented CAUTI, most with active infection and pyuria for many days, reported symptoms commonly encountered with community-acquired urinary tract infection unrelated to a urinary catheter. By further analyzing a subset of catheterized patients without other potentially confounding infections (Table 2), we were able to show that symptoms referable to the urinary tract not only are infrequent in patients with CAUTI, but also have little predictive value for the diagnosis of infection.

The presence of an indwelling urinary catheter alone, unrelated to CAUTI, can clearly cause dysuria or urgency; our data indicate that these symptoms in a catheterized patient usually do not denote CAUTI. Moreover, peripheral leukocytosis is not predictive of CAUTI (Table 2).

The association between fever and CAUTI has also not been convincingly demonstrated in other studies. In a prospective study of elderly patients in a nursing home, Kunin et al[27] found that although 74% of catheterized patients developed CAUTI, fewer than 2% had temperatures higher than 38°C. More recently, in a study of the contribution of CAUTI to febrile morbidity in a long-term care facility, urinary tract infection was found to be the cause of fewer than 10% of episodes of fever, despite of a high prevalence of bacteriuria.[28] Warren et al[29] evaluated 47 women in a nursing home with long-term urinary catheters, all of whom had chronic bacteriuria, and reported a very low incidence of febrile episodes of urinary tract origin.

Symptomatic comunity-acquired pyelonephritis has been shown to be associated with more virulent "pyelonephritogenic" strains of *Escherichia coli*,[30-32] and Guyer et al[33] recently reported that *E coli* strains from patients with CAUTI were less likely to carry virulence genes (59%) than patients with community-acquired urinary tract infections unrelated to catheters (82%). Relatively few (13%) of the CAUTIs identified in our study, however, were caused by *E coli*. Nosocomial bacteremias stemming from CAUTI are most often caused by Enterobactericae other than *E coli*, such as Enterococci, *Pseudomonas aeruginosa*, or *Candida* species,[1-3,34,35] and we are doubtful that the lack of virulence of nosocomial catheter-associated uropathogens is the reason that most patients with CAUTI are asymptomatic

We hypothesize that the asymptomatic nature of most patients' CAUTIs derives from 2 physiologic factors. First, the presence of a catheter in the urethra prevents continuous exposure of the urethral mucosa to large numbers of organisms in infected urine, implicitly preventing infectious urethritis, which produces dysuria and urgency in infected noncatheterized patients. Second, a patent urinary catheter ensures that the urinary tract is continuously decompressed, preventing urgency and frequency associated with distension of an inflamed bladder, as well as vesicoureteral reflux. In support of this hypothesis, it is universally recognized that urinary tract obstruction rapidly converts silent bacteriuria to symptomatic urosepsis, which, if unrelieved, culminates in bacteremia and septic shock.[36,37] Harding et al[38] reported that of 27 catheterized patients with asymptomatic CAUTI, 7 (26%) subsequently developed symptoms referable to the urinary tract only after catheter removal.

The paucity of secondary bloodstream infections found in this study—only 4 possible cases among 235 documented new-onset CAUTIs, most occurring in patients with major underlying diseases and comorbidities (mean APACHE II score, 16; Table 2)—lends further credence to our hypothesis that the continuous decompression of the urinary tract associated with catheter drainage accounts for the asymptomatic nature of most CAUTIs and may also be the major reason that bacteremia is an infrequent complication of CAUTI. Whereas the urinary tract has been reported to be the source of as many as 15% to 40% of nosocomial bloodstream infections,[39-43] other prospective studies of CAUTI which, like ours, obtained daily urine cultures to reliably detect all infections also found low rates (1%-4%) of secondary bacteremia in patients with CAUTI.[36,43-45]

Recently, a prospective study of catheter replacement in patients with long-term indwelling catheters detected transient bacteremia after catheter exchange in only 5 of 120 instances, none of which was clinically symptomatic.[46]

We conclude that CAUTI is rarely symptomatic and infrequently causes bloodstream infection. However, nosocomial CAUTIs comprise a huge silent reservoir of antibiotic-resistant bacteria and yeasts.[4-13] Thus, efforts to prevent CAUTIs by improved catheter care and deployment of technologic advances designed for prevention[1-3,16,17] must continue to receive high priority in institutional infection control programs.

REFERENCES

1. Kunin CM. Care of the urinary catheter. In: *Urinary Tract Infections: Detection, Prevention and Management.* 5th ed. Baltimore, Md: Williams & Wilkins; 1997: 227-279.
2. Stamm WE. Catheter-assosciated urinary tract infections: epidemiology, pathogenesis and prevention. *Am J Med.* 1991;91(suppl 3B):65S-71S.
3. Warren JW. The catheter and urinary tract infection. *Med Clin North Am.* 1991; 75:481-493.
4. Siebert JD, Thomson RB, Tan JS, Gerson LW. Emergence of antimicrobial resistance in gram-negative bacilli causing bacteremia during therapy. *Am J Clin Pathol.* 1993;100:47-51.
5. Jarlier V, Fosse T, Philippon A. Antibiotic susceptibility in aerobic gram-negative bacilli isolated in intensive care units in 39 French teaching hospitals. *Intensive Care Med.* 1996;22:1057-1065.
6. Bjork DT, Pelletier LL, Tight RR. Urinary tract infections with antibiotic resistant organisms in catheterized nursing home patients. *Infect Control.* 1984;5:173-176.
7. Gaynes RP, Weinstein RA, Chamberlin W, Kabins S. Antibiotic-resistant flora in nursing home patients admitted to hospital. *Arch Intern Med.* 1985;145:1804-1807.
8. Kirby WMM, Corpron DO, Tanner DC. Urinary tract infections caused by antibiotic-resistant coliform bacilli. *JAMA.* 1956;162:1-4.
9. Schaberg DR, Haley RW, Highsmith AK, Anderson RL, McGowan JE. Nosocomial bacteriuria: a prospective study of case clustering and antimicrobial resistance. *Ann Intern Med.* 1980;93:420-424.
10. Lam S, Singer C, Tucci V, Morthland VH, Pfaller MA, Isenberg HD. The challenge of vancomycin-resistant enterococci: a clinical and epidemiologic study. *Am J Infect Control.* 1995;23:170-180.
11. Shlaes DM, Lehman MH, Currie-McCumber CA, Kim CH, Floyd R. Prevalence of colonization with antibiotic resistant gram-negative bacilli in a nursing home care unit: the importance of cross-colonization as documented by plasmid analysis. *Infect Control.* 1986;7:538-545.
12. Rice L, Willey SH, Papanicolau GA, et al. Outbreak of ceftazidime resistance caused by extended-spectrum β-lactamases at a Massachusetts chronic-care facillity. *Antimicrob Agents Chemother.* 1990;34:2193-2199.
13. Naber KG, Witte W, Bauernfeind A, et al. Clinical significance and spread of fluoroquinolone resistant uropathogens in hospitalized urological patients. *Infection.* 1994;22(suppl 2):S122-S127.
14. O'Grady NP, Barie PS, Bartlett J, et al. Practice parameters for evaluating new fever in critically ill adult patients. *Crit Care Med.* 1998;26:392-408.
15. National Institute on Disability and Rehabilitation Research. The prevention and management of urinary tract infections among people with spinal cord injuries:

National Institute on Disability and Rehabilitation Research Consensus Statement. *J Am Paraplegia Soc.* 1992;15:194-204.

16. Maki DG, Knasinski V, Tambyah PA. A prospective investigator-blinded trial of a novel nitrofurazone-impregnated indwelling urinary catheter [abstract]. *Infect Control Hosp Epidemiol.* 1997;18(suppl):50.

17. Maki DG, Knasinski V, Halvorson K, Tambyah PA. A novel silver-hydrogel–impregnated indwelling catheter reduces CAUTIs: a prospective double-blind trial. In: Program and abstracts of the Eighth Annual Meeting of the Society for Healthcare Epidemiology of America; April 5, 1998; Orlando, Fla.

18. Garibaldi RA, Burke JP, Dickman ML, Smith CB. Factors predisposing to bacteriuria during indwelling urethral cathteterization. *N Engl J Med.* 1974;291:215-219.

19. Platt R, Polk BF, Murdock B, Rosner B. Risk factors for nosocomial urinary tract infection. *Am J Epidemiol.* 1986;124:977-985.

20. Burke JP, Riley DK. Nosocomial urinary tract infections. In: Mayhall CG, ed. *Hospital Epidemiology and Infection Control.* Baltimore, Md: Williams & Wilkins; 1996: 139-153.

21. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med.* 1985;13:818-829.

22. Stark RP, Maki DG. Bacteriuria in the catheterized patient: what quantitative level of bacteriuria is relevant? *N Engl J Med.* 1984;311:560-564.

23. Balows LE, Hausler W, Shadomy H, eds. *Manual of Clinical Microbiology.* 5th ed. Washington DC: American Society for Microbiology; 1991.

24. Stamm WE. Measurement of pyuria and its relation to bacteriuria. *Am J Med.* 1983;75(suppl 1B):53-58.

25. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. *Am J Infect Control.* 1988;16:128-140.

26. Tambyah PA, Maki DG. The relationship between pyuria and infection in patients with indwelling urinary catheters: a prospective study of 761 patients. *Arch Intern Med.* 2000;160:673-677.

27. Kunin CM, Chin QF, Chambers S. Morbidity and mortality associated with indwelling urinary catheters in elderly patients in a nursing home: confounding due to the presence of associated diseases. *J Am Geriatr Soc.* 1987;35: 1001-1006.

28. Orr PH, Nicolle LE, Duckworth H, et al. Febrile urinary tract infection in the institutionalized elderly. *Am J Med.* 1996;100:71-77.

29. Warren JW, Damron D, Tenney JH, Hoopes JM, Deforge B, Muncie HL. A prospective microbiologic study of bacteriuria in patients with chronic indwelling urinary catheters. *J Infect Dis.* 1987;6:1151-1158.

30. Johnson JR. Virulence factors in *Escherichia coli* urinary tract infection. *Clin Microbiol Rev.* 1991;4:80-128.

31. Ulleryd P, Lincoln K, Scheutz F, Sandberg T. Virulence characteristics of *E. coli* in relation to host response in men with symptomatic urinary tract infection. *Clin Infect Dis.* 1994;18:579-584.

32. Stamm WE, Hooton TM, Johnson JR, et al. Urinary tract infections: from pathogenesis to treatment. *J Infect Dis.* 1989;159:400-406.

33. Guyer DM, Kao JS, Mobley HL. Genomic analysis of a pathogenecity island in uropathogenic *Escherichia coli* CFT073: distribution of homologous sequences among isolates from patients with pyelonephritis, cystitis and catheter-associated bacteriuria and from fecal samples. *Infect Immun.* 1998;66:4411-4417.

34. Bronsema DA, Adams JR, Pallares R, Wenzel RP. Secular trends in rates and etiology of nosocomial urinary tract infections at a university hospital. *J Urol.* 1993;150:414-416.

35. Horan TC, Culver DH, Gaynes RP, Jarvis WR, Edwards JR, Reid CR. Nosocomial infections in surgical patients in the United States, January 1986-June 1992. *Infect Control Hosp Epidemiol.* 1993;14:73-80

36. Bryan CS, Reynolds KL. Hospital acquired bacteremic urinary tract infection: epidemiology and outcome. *J Urol.* 1984;132:494-498.

37. Quintiliani R, Klimek J, Cunha BA, Maderazo EG. Bacteraemia after manipulation of the urinary tract: the importance of preexisting urinary tract disease and compromised host defences. *Postgrad Med J.* 1978;54:668-671.

38. Harding GK, Nicolle LE, Ronald AR, et al. How long should catheter-acquired urinary tract infection in women be treated? *Ann Intern Med.* 1991;114:713-719.

39. Kreger BE, Craven DE, Carling PC, McCabe WR. Gram-negative bacteremia: reassessment of etiology, epidemiology and ecology in 612 patients. *Am J Med.* 1980;68:332-343.

40. Rudman D, Hontanosas A, Cohen Z, Mattson DE. Clinical correlates of bacteremia in a Veterans Administration extended care facillity. *J Am Geriatr Soc.* 1988; 36:726-732.

41. Krieger JN, Kaiser DL, Wenzel RP. Urinary tract etiology of bloodstream infections in hospitalized patients. *J Infect Dis.* 1983;148:57-62.

42. Stamm WE, Martin SM, Bennett JV. Epidemiology of nosocomial infections due to gram-negative bacilli: aspects relevant to development and use of vaccines. *J Infect Dis.* 1977;136(suppl):S151-S160.

43. Siegman-Igra Y, Kulka T, Schwartz D, Konforti N. Polymicrobial and monomicrobial bacteremic urinary tract infection. *J Hosp Infect.* 1994;28:49-56.

44. Hartstein AI, Garber SB, Ward TT, Jones SR, Morthland VH. Nosocomial urinary tract infection: a prospective evaluation of 108 catheterized patients. *Infect Control.* 1981;2:380-386.

45. Platt R, Polk BF, Murdock B, Rosner B. Mortality associated with nosocomial urinary tract infection. *N Engl J Med.* 1982;307:637-641.

46. Bregenzer T, Frei R, Widmer AF, et al. Low risk of bacteremia during catheter replacement in patients with long-term urinary catheters. *Arch Intern Med.* 1997; 157:521-525.