Catheter-Associated Urinary Tract Infection Is Rarely Symptomatic
A Prospective Study of 1497 Catheterized Patients
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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.

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PATIENTS AND METHODS

PATIENTS

Patients participating in 2 randomized trials of 2 novel urinary catheters—one a nitrofurazone-impregnated silicone catheter, and the other, a silver-polyurethane hydrogel catheter—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. 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 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, 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 standard techniques and criteria. After aerobic incubation at 37°C for 24 to 48 hours, each colony type was enumerated and fully identified using standard techniques and criteria.

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 measured daily, using a hemocytometer (Hauser Scientific Partnership, Horsham, Pa).

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. 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. Other infections were defined according to the criteria of the National Nosocomial Infection Study of the US Center for Disease Control and Prevention.

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 symp-
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 10^5 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.

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.

Although most authorities14,15 and case definitions25 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 al27 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 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.

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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Without CAUTI (n = 1049)</th>
<th>With CAUTI (n = 89)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>55.0 ± 17.3</td>
<td>56.0 ± 18.3</td>
<td>.47</td>
</tr>
<tr>
<td>Sex, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>787 (62)</td>
<td>77 (42)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female</td>
<td>486 (38)</td>
<td>147 (66)</td>
<td></td>
</tr>
<tr>
<td>Service, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical</td>
<td>1024 (80)</td>
<td>138 (62)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Medical</td>
<td>249 (20)</td>
<td>86 (38)</td>
<td></td>
</tr>
<tr>
<td>Antibiotics per catheter-day,</td>
<td>2.4 ± 1.9†</td>
<td>1.6 ± 1.7‡</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APACHE II score, mean ± SD</td>
<td>16.2 ± 6.3</td>
<td>16.4 ± 6.5</td>
<td>.58</td>
</tr>
<tr>
<td>Days catheterized before onset of infection, mean ± SD</td>
<td>4.4 ± 3.8†</td>
<td>6.4 ± 6.1</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*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*

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

*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.

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**COMMENT**
Symptomatic community-acquired pyelonephritis has been shown to be associated with more virulent “pyelonephritogenic” strains of Escherichia coli,30-32 and Gayer 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 Enterobacteriaceae 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 infectious urethritis, which produces dysuria and urgency in infected noncatheterized patients.28

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,1,3,39,40 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.4,11 Thus, efforts to prevent CAUTIs by improved catheter care and deployment of technologic advances designed for prevention1,3,16,17 must continue to receive high priority in institutional infection control programs.

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