

Health Care–Associated Bloodstream Infections in Adults: A Reason To Change the Accepted Definition of Community-Acquired Infections

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Background: Bloodstream infections occurring in persons residing in the community, regardless of whether those persons have been receiving health care in an outpatient facility, have traditionally been categorized as community-acquired infections.

Objective: To develop a new classification scheme for bloodstream infections that distinguishes among community-acquired, health care–associated, and nosocomial infections.

Design: Prospective observational study.

Setting: One academic medical center and two community hospitals.

Patients: All adult patients admitted to the hospital with bloodstream infection.

Measurements: Demographic characteristics, living arrangements before hospitalization, comorbid medical conditions, factors predisposing to bloodstream infection, date of hospitalization, dates and number of positive blood cultures, results of microbiological susceptibility testing, dates of hospital discharge or death, and mortality rates at 3 to 6 months of follow-up.

Results: 504 patients with bloodstream infections were enrolled; 143 (28%) had community-acquired bloodstream infections, 186 (37%) had health care–associated bloodstream infections, and 175 (35%) had nosocomial bloodstream infections. Of the 186 patients with health care–associated bloodstream infection, 29 resided in a nursing home, 64 were receiving home health care, 78

were receiving intravenous or intravascular therapy at home or in a clinic, and 117 had been hospitalized in the 90 days before their bloodstream infection. Cancer was more common in patients with health care–associated or nosocomial bloodstream infection than in patients with community-acquired bloodstream infection. Intravascular devices were the most common source of health care–associated and nosocomial infections, and *Staphylococcus aureus* was the most frequent pathogen in these types of infections. Methicillin-resistant *S. aureus* occurred with similar frequency in the groups with health care–associated infection (52%) and nosocomial infection (61%) but was uncommon in the group with community-acquired bloodstream infection (14%) ($P = 0.001$). Mortality rate at follow-up was greater in patients with health care–associated infection (29% versus 16%; $P = 0.019$) or nosocomial infection (37% versus 16%; $P < 0.001$) than in patients with community-acquired infection.

Conclusions: Health care–associated bloodstream infections are similar to nosocomial infections in terms of frequency of various comorbid conditions, source of infection, pathogens and their susceptibility patterns, and mortality rate at follow-up. A separate category for health care–associated bloodstream infections is justified, and this new category will have obvious implications for choices about empirical therapy and infection-control surveillance.

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A recent review (1) found that nearly equal proportions of bacteremias were community acquired (48%) and nosocomial (52%). In the 1970s, by contrast, nearly two thirds of 500 bacteremic episodes were nosocomial (2). At present, patients with complicated conditions, such as cancer or renal failure, are routinely cared for in outpatient settings, yet such patients are still categorized as having “community-acquired infections” when they are admitted to the hospital with bloodstream infection. The Centers for Disease Control and Prevention (CDC) surveillance definitions include only nosocomial infection (3); infections that are not nosocomial are considered to be community acquired by default.

The term *nosohusial* has been proposed to describe infections occurring in patients who are receiving care at home (4). However, this term applies only to illnesses in patients who receive care at home; it excludes patients in nursing homes and rehabilitation centers, patients receiving dialysis, and patients receiving chemotherapy in physicians’ offices. Although the authors of a recent study (5) proposed creating a more inclusive category, health care–

associated infection, no consensus definition exists for this group of infections.

We sought to devise a new classification scheme for bloodstream infections that distinguishes among and compares patients with community-acquired, health care–associated, and nosocomial infections.

METHODS

This prospective cohort study was done at Duke University Medical Center (Durham, North Carolina), Durham Regional Hospital (Durham, North Carolina), and Nash General Hospital (Rocky Mount, North Carolina). Approval of the study protocol was obtained from the institutional review boards at each hospital, which waived the requirement for obtaining informed consent.

Patient Selection

Daily microbiology laboratory reports were reviewed and case-report forms were completed by either a physician or an infection-control practitioner on consecutive adult patients who were admitted to the hospital with blood-

Context

Bloodstream infections are traditionally classified as community-acquired or hospital-acquired (nosocomial). Ideally, these classifications guide initial diagnostic and management decisions. As out-of-hospital care grows more complex, do we need finer classifications?

Contribution

This prospective study from three hospitals in North Carolina shows that about one third of patients with bloodstream infections have had recent contact with the health care system (health care–associated infections) through nursing homes, home health care programs, outpatient intravenous therapy, or recent hospitalizations. *Staphylococcus aureus* and intravascular devices were the most common pathogen and source, respectively, for both health care–associated and nosocomial infections.

Implications

Health care–associated infections often resemble nosocomial infections, a fact to be considered in selecting empirical antibiotic therapy for these infections.

–The Editors

stream infections or developed bloodstream infections during hospitalization. Patients younger than 17 years of age and patients who visited the emergency department but were not hospitalized were excluded.

Data Collection

We collected data on demographic characteristics, medication use, blood cultures, comorbid medical conditions, results of antimicrobial susceptibility testing, and dates of admission and discharge or death. Mortality data were retrieved from medical records and a Social Security death registry Web site (6). The medical record was the gold standard for assessing mortality, and we searched for deaths by Social Security number only if the medical record was not definitive. Follow-up continued for a maximum of 6 months after enrollment.

A *bloodstream-infection episode* was defined by the first set of positive blood cultures in a series or by any new positive blood culture set occurring more than 48 hours after a previous positive result, unless it was clear to the investigator that the new positive culture was part of the previous episode (2). To distinguish between true bloodstream infections and episodes of contamination, each positive blood culture was assessed critically by one investigator. All isolates were categorized as 1) true-positive, 2) contaminated, or 3) of unknown clinical significance. The determination was made after review of the patient's clinical history, physical findings, temperature at the time of blood culture, leukocyte count, number of positive blood cultures, results of cultures of specimens from other sites, imaging results, histopathologic findings, clinical course, and response to therapy (1).

Nosocomial bloodstream infection was defined by a positive blood culture obtained from patients who had been hospitalized for 48 hours or longer (3). If a patient was transferred from another hospital, the duration of inpatient stay was calculated from the date of the first hospital admission.

Health care–associated bloodstream infection was defined by a positive blood culture obtained from a patient at the time of hospital admission or within 48 hours of admission if the patient fulfilled any of the following criteria:

1. Received intravenous therapy at home; received wound care or specialized nursing care through a health care agency, family, or friends; or had self-administered intravenous medical therapy in the 30 days before the bloodstream infection. Patients whose only home therapy was oxygen use were excluded.
2. Attended a hospital or hemodialysis clinic or received intravenous chemotherapy in the 30 days before the bloodstream infection.
3. Was hospitalized in an acute care hospital for 2 or more days in the 90 days before the bloodstream infection.
4. Resided in a nursing home or long-term care facility.

Community-acquired bloodstream infection was defined by a positive blood culture obtained at the time of hospital admission or within the 48 hours after hospital admission for patients who did not fit the criteria for a health care–associated infection.

Information about comorbid medical conditions, such as diabetes, chronic obstructive pulmonary disease, liver disease, active cancer, transplantation, or HIV infection, was obtained through medical record review. Active cancer was defined as a solid tumor or hematologic malignancy (except squamous-cell or basal-cell skin cancer) diagnosed or treated in the past 5 years. Vascular disease was defined by the clinical documentation of at least one of the following: coronary artery disease, cerebrovascular disease, peripheral vascular disease, or aortic aneurysm. Renal failure was defined as a serum creatinine concentration greater than 177 $\mu\text{mol/L}$ (>2.00 mg/dL).

Factors predisposing to infection, such as chemotherapy, immunosuppressive therapy, and radiation therapy, were considered to be present if they had been administered within 30 days of the bloodstream infection. Neutropenia was defined as an absolute neutrophil count of less than 500 cells/mm³ within 30 days before the bloodstream infection. Immunosuppressive therapy included treatment with steroids, cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil, and calcineurin inhibitors.

Sources of bloodstream infection were designated as culture confirmed (if the same organism was isolated from another site) or suspected (if clinical findings of infection were seen without microbiological proof). *Primary bloodstream infections including intravascular device–associated infections* were defined according to the National Nosocomial Infections Surveillance System (3, 7). *Secondary bloodstream infection* was declared to be present when an organism iso-

lated from a blood culture was related to an infection at another site, as defined by both CDC and other published criteria (3, 8).

Microbiology

All isolates from patients were identified and speciated by using standard microbiologic techniques (2). Antimicrobial susceptibility testing was done according to National Committee for Clinical Laboratory standards (9).

Statistical Analysis

Statistical analysis was done by using SAS software, version 8.2 (SAS Institute, Inc., Cary, North Carolina). Distributions of baseline characteristics were analyzed by using the Wilcoxon rank-sum test for continuous variables. The chi-square test was used to assess associations among categorical variables, with 3×2 tables broken down into three 2×2 tables for pairwise comparisons. If any expected value for a cell in one of the 2×2 tables was less than 5, the Fisher exact test was used and two-sided *P* values were reported. Associations between epidemiologic categories of infection and other variables were analyzed by using conditional fixed-effects logistic regression. Dummy variables (0/1) were used to represent two of the three hospitals (the third hospital being the baseline) as well as two of the three epidemiologic categories of infection, thereby adjusting for clustering of epidemiologic factors and outcomes by hospital site. This technique was validated by comparison with Mantel–Haenszel chi-square. A

P value less than 0.05 was considered statistically significant.

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The funding source had no role in the collection, analysis, or interpretation of the data or in the decision to submit the manuscript for publication.

RESULTS

Between 16 October 2000 and 28 February 2001, a total of 1175 positive blood cultures were detected at the three study hospitals. Of these 1175 cultures, 476 were the result of contamination, 655 represented true bloodstream infections, and 44 were of unknown clinical significance. Seven of the 1175 were excluded from analysis because the patients were not admitted to the hospital.

Coagulase-negative staphylococci (66%), gram-positive rods (16%), and mixed skin flora (9%) constituted most of the contaminants. Either coagulase-negative staphylococci (64%) or yeast (11%) was present in three fourths of cases classified as bloodstream infection of unknown clinical significance.

Five hundred four patients had a total of 648 bloodstream-infection episodes (mean episodes per patient, 1 [range, 1 to 4]). Only the first episode of bloodstream infection was analyzed; subsequent episodes were excluded.

Of the 504 patients, 143 (28%) had community-

Table 1. Characteristics of 504 Patients with Bloodstream Infections from Three Hospitals*

Characteristic	Patients from DUMC (n = 330)	Patients from DRH (n = 110)	Patients from NGH (n = 64)	Total Patients (n = 504)	P Values		
					DUMC vs. DRH	DUMC vs. NGH	DRH vs. NGH
Mean age ± SD (median), y	58 ± 17 (59)	65 ± 19 (71)	63 ± 20 (67)	60 ± 18 (61)	<0.001	0.069	>0.2
Men, n (%)	182 (55)	57 (52)	30 (47)	269 (53)	>0.2	>0.2	>0.2
Race, n (%)							
White	194 (59)	67 (61)	18 (28)	279 (55)	>0.2	<0.001	<0.001
Nonwhite	136 (41)	43 (39)	46 (72)	225 (45)			
Living arrangements before hospitalization, n (%)							
Private residence	307 (93)	92 (84)	54 (84)	453 (90)	0.16	0.025	>0.2
Other	23 (7)	18 (16)	10 (16)	51 (10)			
Comorbid conditions, n (%)							
Vascular disease	130 (39)	49 (45)	26 (41)	205 (41)	>0.2	>0.2	>0.2
Renal failure	113 (34)	20 (18)	21 (33)	154 (31)	0.002	>0.2	0.028
Hemodialysis	46 (14)	5 (5)	10 (16)	61 (12)	0.008	>0.2	0.012
Diabetes mellitus	91 (28)	28 (25)	24 (38)	143 (28)	>0.2	0.11	0.094
Cancer	104 (32)	22 (20)	8 (13)	134 (27)	0.021	0.002	>0.2
Chronic obstructive pulmonary disease	47 (14)	23 (21)	13 (20)	83 (16)	0.098	>0.2	>0.2
Liver disease	32 (10)	1 (1)	6 (9)	39 (8)	0.002	>0.2	0.011
Transplantation	41 (12)	0	0	41 (8)	<0.001	0.003	1.0
HIV infection	15 (5)	5 (5)	5 (8)	25 (5)	1.0	>0.2	>0.2
Factors predisposing to bloodstream infection, n (%)							
Immunosuppressive therapy	73 (22)	10 (9)	8 (13)	91 (18)	0.003	0.081	>0.2
Chemotherapy	51 (15)	7 (6)	2 (3)	60 (12)	0.015	0.008	>0.2
Neutropenia	26 (8)	4 (4)	1 (2)	31 (6)	0.13	0.067	>0.2
Radiation therapy	11 (3)	1 (1)	2 (3)	14 (3)	0.18	>0.2	>0.2

* DRH = Durham Regional Hospital; DUMC = Duke University Medical Center; and NGH = Nash General Hospital.

Table 2. Comorbid Medical Conditions in 504 Patients with Bloodstream Infections, by Epidemiologic Type of Infection*

Condition	Patients with Community- Acquired BSI (n = 143)	Patients with Health Care- Associated BSI (n = 186)	Patients with Nosocomial BSI (n = 175)	P Values		
				Community- Acquired BSI vs. Health Care- Associated BSI	Community- Acquired BSI vs. Nosocomial BSI	Health Care- Associated BSI vs. Nosocomial BSI
	← n (%) →					
Renal failure	32 (22)	73 (39)	49 (28)	0.019	>0.2	0.041
Diabetes	39 (27)	57 (31)	47 (27)	>0.2	>0.2	>0.2
Vascular disease	50 (35)	80 (43)	75 (43)	>0.2	0.19	>0.2
Cancer	18 (13)	55 (30)	61 (35)	0.003	0.001	>0.2
Chemotherapy	0 (0)	32 (17)	28 (16)	>0.2	>0.2	>0.2
Neutropenia	0 (0)	13 (7)	18 (10)	>0.2	>0.2	>0.2
Chronic obstructive pulmonary disease	25 (17)	27 (15)	31 (18)	>0.2	>0.2	>0.2
Transplantation	7 (5)	17 (9)	17 (10)	>0.2	>0.2	>0.2
Immunosuppressive therapy	17 (12)	36 (19)	38 (22)	0.17	0.16	>0.2
HIV infection	13 (9)	6 (3)	6 (3)	0.032	0.060	>0.2
Liver disease	8 (6)	20 (11)	11 (6)	>0.2	>0.2	0.096

* BSI = bloodstream infection.

acquired bloodstream infections, 186 (37%) had health care–associated bloodstream infections, and 175 (35%) had nosocomial bloodstream infections. Community-acquired infections occurred more frequently at the two community hospitals (71 of 174 patients [41%]) than at the university teaching hospital (72 of 330 patients [22%]) ($P < 0.001$). Conversely, nosocomial infections occurred more frequently at the university teaching hospital (142 of 330 patients [43%]) than at the two community hospitals (33 of 174 patients [19%]) ($P < 0.001$).

First episodes of bloodstream infection comprised 577 isolates from 504 patients; that is, 114 of 504 patients (23%) had polymicrobial infections. Patients had a median of 2 positive blood culture sets (interquartile range [IQR], 1 to 2; range, 1 to 15).

The mean age of the study patients was 60 years. Approximately two thirds of the study cohort was admitted to Duke University Medical Center (Table 1). Twenty-nine percent of patients (146 of 504) either were admitted to an intensive care unit after onset of their bloodstream infection or developed a bloodstream infection while in, or within 7 days of being in, an intensive care unit.

Health Care–Associated Bloodstream Infection

Twenty-nine of 186 patients with health care–associated bloodstream infections (16%) resided in a nursing home, 64 (34%) received home health care, 78 (42%) received home- or clinic-based intravenous therapy or dialysis, and 117 (63%) had been hospitalized in the 90 days before their bloodstream infection.

Comorbid Medical Conditions and Factors Predisposing to Bloodstream Infection

The most frequent comorbid medical conditions were vascular disease (41% of the 504 total patients), renal failure (31%), and diabetes mellitus (28%). Diabetes mellitus,

vascular disease, and chronic obstructive pulmonary disease were equally common in the three groups of patients (Table 2). Renal failure was more common in patients with health care–associated infection; HIV infection was more common in those with community-acquired infection. Cancer was more common in the groups with health care–associated and nosocomial infections than in the group with community-acquired infection (Table 2).

Source of Bloodstream Infection

A proven ($n = 234$) or suspected ($n = 210$) source of bloodstream infection was identified in 444 of 504 study patients (88%). Bloodstream infections were considered to be primary in 208 patients (40%) and secondary in 296 patients (60%). An intravascular device was the most common source of bloodstream infection (148 of 444 patients [33%]), and urinary tract infection was the second most common source (114 of 444 patients [26%]).

Patients with health care–associated and nosocomial bloodstream infections had similar frequencies of intravascular-device–related and gastrointestinal tract–related bacteremias, and patients with community-acquired bloodstream infection had more bloodstream infections that were secondary to urinary tract infection (Table 3).

Pathogens

The two pathogens most often responsible for community-acquired bloodstream infections were *Escherichia coli* and *Streptococcus pneumoniae*. *Staphylococcus aureus* was the most common pathogen in patients with health care–associated and nosocomial bacteremia. The second and third most common pathogens in patients with nosocomial bloodstream infection were *Staphylococcus epidermidis* and *Enterococcus* species. *Candida* species caused only 2 of 143

community-acquired bloodstream infections, but it caused 10 of 175 nosocomial bloodstream infections ($P = 0.04$).

Microbiological Susceptibility Data

Seventy-three of the 145 patients with bloodstream infection due to *S. aureus* were infected with methicillin-resistant *S. aureus* (MRSA). Only 3 patients with community-acquired bloodstream infection were infected with MRSA (2%); in contrast, 35 of 186 patients (19%) with health care–associated bloodstream infection and 35 of 175 patients (20%) with nosocomial bloodstream infection had MRSA bacteremia. Of the 35 patients with health care–associated cases of MRSA bacteremia, 23 had been hospitalized in the previous 90 days, 15 had received home intravenous therapy or nursing care, 16 were receiving dialysis or chemotherapy, and 8 resided in a nursing home. All 3 patients with community-acquired MRSA infection had been hospitalized in the previous 12 months (one had been hospitalized 6 months before the bacteremia; one, 9 months before the bacteremia; and one, 12 months before the bacteremia).

Enterococci manifesting resistance to ampicillin and vancomycin were more common in patients with nosocomial bloodstream infection than in patients with health care–associated bloodstream infection. They were absent in patients with community-acquired bloodstream infection. Ampicillin–sulbactam and ciprofloxacin resistance occurred with similar frequency in Enterobacteriaceae isolated from patients with health care–associated and those with nosocomial bloodstream infection and was infrequent in the group with community-acquired infection.

Length of Stay and Mortality

The median duration of hospital stay for all study patients was 8.5 days (IQR, 5 to 20 days; range, 0 to 225 days). Patients with nosocomial bloodstream infection had longer median durations of hospital stay (23 days [IQR, 13.5 to 45 days]) than did patients with health care–associated bloodstream infection (7 days [IQR, 4 to 15 days]) or community-acquired bloodstream infection (6 days [IQR, 4 to 8.5 days]).

The crude inpatient mortality rate for all patients with bloodstream infection was 21% (108 of 504 patients). No

statistically significant difference was seen in inpatient mortality rates among the three hospitals. However, significantly more in-hospital deaths were seen in the group with nosocomial bloodstream infection (52 of 175 patients [30%]) than in the groups with health care–associated bloodstream infection (37 of 186 patients [20%]; $P = 0.038$) and community-acquired bloodstream infection (19 of 143 patients [13%]; $P = 0.002$). Patients with health care–associated and community-acquired infection did not differ with respect to inpatient mortality rates ($P = 0.15$). A total of 33 patients died 3 to 6 months after hospitalization (of the 504 study patients, a total of 141 died [28%]). The death rate was higher in the group with health care–associated infection than in the group with community-acquired infection (29% versus 16%; $P = 0.019$) and in the nosocomial group than in the community-acquired group (37% versus 16%; $P < 0.001$). The mortality rate at follow-up did not differ in the groups with nosocomial and health care–associated infections ($P = 0.19$).

DISCUSSION

Our definition of health care–associated bloodstream infection was empirically derived after a critical review of several studies published in the past decade. For example, we extended the definition to include patients receiving hemodialysis because they have high rates of bloodstream infection and are often infected or colonized with resistant bacteria as outpatients (10–12). Similarly, residence in a nursing home or other long-term care facility places persons at risk for colonization or infection with MRSA (13–15).

Bloodstream infections that occur in persons who reside in the community have been categorized as community-acquired bacteremias even if the persons are receiving out-of-hospital medical therapy (16, 17). For example, a recent study (18) reported that 91% of 57 episodes of *S. aureus* bacteremia in patients with HIV infection were community acquired, even though 78% of these patients had had an indwelling intravascular catheter when they developed infection. In another study (17), more than one fifth of community-acquired *S. aureus* bacteremias from

Table 3. Source of Bloodstream Infection, by Epidemiologic Type of Infection*

Source of BSI	Patients with Community-Acquired BSI (n = 125)	Patients with Health Care–Associated BSI (n = 168)	Patients with Nosocomial BSI (n = 151)	P Values		
				Community-Acquired BSI vs. Health Care–Associated BSI	Community-Acquired BSI vs. Nosocomial BSI	Health Care–Associated BSI vs. Nosocomial BSI
	← n (%) →					
Intravascular device	0	70 (42)	78 (52)	NA	NA	>0.2
Urinary tract infection	58 (46)	29 (17)	27 (18)	<0.001	<0.001	>0.2
Pneumonia	34 (27)	27 (16)	24 (16)	0.10	0.18	>0.2
Gastrointestinal tract infection	5 (4)	28 (17)	20 (13)	0.004	0.056	0.15

* BSI = bloodstream infection; NA = not available.

1990 to 1993 were related to intravascular devices; no cases from 1980 to 1983 were related to these devices. Home-based intravenous therapy has an overall incidence of bacteremia of 2% to 4.2% with an estimated risk for bloodstream infection of 2 per 1000 catheter-days (4, 16, 19, 20).

Morin and Hadler (5) recently proposed a definition for a new category, health care–associated bloodstream infections due to *S. aureus*. They categorized community-acquired *S. aureus* bloodstream infections into three groups: “health care–associated,” “with underlying medical condition,” and “with no underlying medical condition.” The category of “health care–associated bloodstream infection” included outpatients with indwelling vascular devices, patients receiving dialysis, and patients who had been hospitalized within the past 12 months. In contrast to us, Morin and Hadler categorized bloodstream infections as nosocomial if patients resided in a nursing home or long-term care facility. Sixty-two percent of patients with community-acquired bacteremia had health care–associated bacteremia, 71% had been hospitalized in the previous 12 months, 32% were receiving hemodialysis, and 49% had an indwelling device.

In results similar to those of Morin and Hadler, we found that 68 of 88 patients who had non-nosocomial bloodstream infections caused by *S. aureus* had health care–associated infections. Sixty-two percent of these 68 patients had been hospitalized in the previous 3 months, 32% were receiving hemodialysis, and 44% had received outpatient intravenous therapy before their bloodstream infection. However, unlike Morin and Hadler, who reported that only 16% of patients with health care–associated *S. aureus* bloodstream infection were infected with MRSA, we found that 51% of our patients with health care–associated bloodstream infections due to *S. aureus* had MRSA infection. This difference in rates of MRSA may reflect differences in the prevalence of MRSA and case-mix between the hospitals in the two studies.

We chose previous hospitalization within 3 months as the criterion by which to categorize patients as having health care–associated bloodstream infection, whereas Morin and Hadler used hospitalization in the preceding 12 months. Had we used Morin and Hadler’s criterion, 30 additional patients would have been classified as having had health care–associated bloodstream infections. The 3 patients who were defined as having community-acquired MRSA infection and the 4 patients with resistant gram-negative pathogens would also have been classified as having had health care–associated bloodstream infection. However, all of the remaining 23 patients with community-acquired infection who had been hospitalized within the past year had had bloodstream infections caused by antibiotic-susceptible organisms; 6 were infected with *E. coli*, and 4 were infected with *S. pneumoniae*.

Of 186 patients in our study with health care–associated bloodstream infection, 117 (63%) had been hospitalized in the preceding 3 months. Previous hospitalization is

a known risk factor for colonization with MRSA, vancomycin-resistant enterococci, and fluoroquinolone-resistant gram-negative organisms in patients residing both in the community and in long-term care facilities (14, 21, 22), and asymptomatic colonization with both MRSA and vancomycin-resistant enterococci may persist for months to years (23–25).

Patients with health care–associated bloodstream infections in our cohort closely resemble those with nosocomial infections in the following ways: 1) frequency of cancer and HIV infection, 2) source of infection, 3) frequency of *S. aureus* and MRSA as pathogens, and 4) mortality rates at follow-up. Notable differences between the two groups were seen in frequency of renal failure, duration of hospital stay, and inpatient mortality rate.

Nosocomial bloodstream infections are often caused by *S. epidermidis*, are associated with the use of intravascular catheters, and result in both increased length of stay and increased crude mortality rates (26, 27). In our study, *S. epidermidis* caused 44 of 175 nosocomial bloodstream infections (25%); intravascular catheters were the source of infection in 78 of 175 patients (45%). Length of stay and in-hospital mortality rate were greater in the group with nosocomial bloodstream infection than in other groups.

This study has limitations. Our results may have been biased by local patterns of health care and antimicrobial resistance that are different from those in other areas of the world. Given the large populations served by the three study hospitals, their overlap with areas served by other hospitals, and the many agencies providing community-based health care in the region, we could estimate neither a suitable denominator nor the actual incidence of bloodstream infection by each individual category.

Finally, our definition of health care–associated bloodstream infection may have been excessively broad in some aspects, yet imprecise in other ways. For example, the 3-month cut-off for recent hospitalization could have been expanded to 12 months in light of the long-lived persistence of colonization with resistant bacteria (23–25). In addition, our category of health care–associated infections includes a heterogeneous group of persons, and not all subsets of this group are identical in their risks for and predictors of infection.

Our results suggest that empirical antibiotic therapy for patients with known or suspected health care–associated and nosocomial bloodstream infections should be similar. In contrast, patients with community-acquired bloodstream infection are often infected with antibiotic-sensitive organisms, and their prescribed therapy should reflect this pattern.

For the reasons cited above, a category for health care–associated bloodstream infection is needed. Future studies should validate this category for infections other than bloodstream infections and examine subsets of patients with health care–associated infections. The CDC and individual hospital infection-control surveillance programs

should redefine infections to accommodate a new category of health care–associated infections. Collecting surveillance data on health care–associated and nosocomial infections would help clinicians choose empirical antibiotic therapy and would have obvious implications for professionals involved in the care of sick patients in community settings.

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References

- Weinstein MP, Towns ML, Quartey SM, Mirrett S, Reimer LG, Parmigiani G, et al. The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults. *Clin Infect Dis*. 1997;24:584-602. [PMID: 9145732]
- Weinstein MP, Reller LB, Murphy JR, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I. Laboratory and epidemiologic observations. *Rev Infect Dis*. 1983;5:35-53. [PMID: 6828811]
- Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. *Am J Infect Control*. 1988;16:128-40. [PMID: 2841893]
- Graham DR, Keldermans MM, Klemm LW, Semenza NJ, Shafer ML. Infectious complications among patients receiving home intravenous therapy with peripheral, central, or peripherally placed central venous catheters. *Am J Med*. 1991;91:95S-100S. [PMID: 1928199]
- Morin CA, Hadler JL. Population-based incidence and characteristics of community-onset *Staphylococcus aureus* infections with bacteremia in 4 metropolitan Connecticut areas, 1998. *J Infect Dis*. 2001;184:1029-34. [PMID: 11574918]
- Social Security Death Index. Accessed at www.ancestry.com/search/rectype/vital/ssdi/main.htm on 13 December 2001.
- Horan TC, Emori TG. Definitions of key terms used in the NNIS System. *Am J Infect Control*. 1997;25:112-6. [PMID: 9113287]
- Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis*. 2000;30:633-8. [PMID: 10770721]
- Performance Standards for Antimicrobial Susceptibility Testing; Eleventh Informational Supplement. NCCLS document M100-S11. Wayne, PA: National Committee for Clinical Laboratory Standards; 2001.
- Stevenson KB, Adcox MJ, Mallea MC, Narasimhan N, Wagnild JP. Standardized surveillance of hemodialysis vascular access infections: 18-month experience at an outpatient, multifacility hemodialysis center. *Infect Control Hosp Epidemiol*. 2000;21:200-3. [PMID: 10738990]
- Weinstein RA. Lessons from an epidemic, again [Editorial]. *N Engl J Med*. 2001;344:1544-5. [PMID: 11357159]
- Beltrami EM, Singer DA, Fish L, Manning K, Young S, Banerjee SN, et al. Risk factors for acquisition of vancomycin-resistant enterococci among patients on a renal ward during a community hospital outbreak. *Am J Infect Control*. 2000;28:282-5. [PMID: 10926704]
- McGowan JE Jr, Hall EC, Parrott PL. Antimicrobial susceptibility in gram-negative bacteremia: are nosocomial isolates really more resistant? *Antimicrob Agents Chemother*. 1989;33:1855-9. [PMID: 2610495]
- Warsawsky B, Hussain Z, Gregson DB, Alder R, Austin M, Bruck-schwaiger D, et al. Hospital- and community-based surveillance of methicillin-resistant *Staphylococcus aureus*: previous hospitalization is the major risk factor. *Infect Control Hosp Epidemiol*. 2000;21:724-7. [PMID: 11089657]
- Smith PW, Seip CW, Schaefer SC, Bell-Dixon C. Microbiologic survey of long-term care facilities. *Am J Infect Control*. 2000;28:8-13. [PMID: 10679131]
- Brown RB, Cipriani D, Schulte M, Corl A, Pieczarka R. Community-acquired bacteremias from tunneled central intravenous lines: results from studies of a single vendor. *Am J Infect Control*. 1994;22:149-51. [PMID: 7943925]
- Steinberg JP, Clark CC, Hackman BO. Nosocomial and community-acquired *Staphylococcus aureus* bacteremias from 1980 to 1993: impact of intravascular devices and methicillin resistance. *Clin Infect Dis*. 1996;23:255-9. [PMID: 8842259]
- Senthilkumar A, Kumar S, Sheagren JN. Increased incidence of *Staphylococcus aureus* bacteremia in hospitalized patients with acquired immunodeficiency syndrome. *Clin Infect Dis*. 2001;33:1412-6. [PMID: 11565083]
- Graham DR, Molnar VL. Nosohospital infection: a decade of surveillance for complications of home intravenous therapy [Abstract]. Fourth Decennial International Conference on Nosocomial and Healthcare-Associated Infections, Atlanta, Georgia, 5–9 March 2000.
- Darouiche RO, Musher DM. Increasing rates of *Staphylococcus aureus* bacteremia—a medical device is a merit in disguise and methicillin resistance is merely a vice [Editorial]. *Clin Infect Dis*. 1996;23:260-1. [PMID: 8842260]
- Richard P, Delangle MH, Raffi F, Espaze E, Richet H. Impact of fluoroquinolone administration on the emergence of fluoroquinolone-resistant gram-negative bacilli from gastrointestinal flora. *Clin Infect Dis*. 2001;32:162-6. [PMID: 11112677]
- Padiglione AA, Grabsch E, Wolfe R, Gibson K, Grayson ML. The prevalence of fecal colonization with VRE among residents of long-term-care facilities in Melbourne, Australia. *Infect Control Hosp Epidemiol*. 2001;22:576-8. [PMID: 11732788]
- Scanvic A, Denic L, Gaillon S, Giry P, Andreumont A, Lucet JC. Duration of colonization by methicillin-resistant *Staphylococcus aureus* after hospital discharge and risk factors for prolonged carriage. *Clin Infect Dis*. 2001;32:1393-8. [PMID: 11317238]
- Baden LR, Thiemke W, Skolnik A, Chambers R, Strymish J, Gold HS, et al. Prolonged colonization with vancomycin-resistant *Enterococcus faecium* in long-term care patients and the significance of “clearance.” *Clin Infect Dis*. 2001;33:1654-60. [PMID: 11595985]
- Henning KJ, Delencastre H, Eagan J, Boone N, Brown A, Chung M, et al. Vancomycin-resistant *Enterococcus faecium* on a pediatric oncology ward: duration of stool shedding and incidence of clinical infection. *Pediatr Infect Dis J*. 1996;15:848-54. [PMID: 8895914]
- Jarvis WR. Selected aspects of the socioeconomic impact of nosocomial infections: morbidity, mortality, cost, and prevention. *Infect Control Hosp Epidemiol*. 1996;17:552-7. [PMID: 8875302]
- Warren DK, Zack JE, Elward AM, Cox MJ, Fraser VJ. Nosocomial primary bloodstream infections in intensive care unit patients in a nonteaching community medical center: a 21-month prospective study. *Clin Infect Dis*. 2001;33:1329-35. [PMID: 11550117]

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