The Commonality of Risk Factors for Nosocomial Colonization and Infection with antimicrobial-resistant **Staphylococcus aureus**, Enterococcus, Gram-Negative Bacilli, **Clostridium difficile**, and Candida

Nasia Safdar, MD, and Dennis G. Maki, MD

Recent years have witnessed a rapidly growing crisis in antimicrobial resistance, especially among microorganisms that cause nosocomial infection. To better understand common risk factors among multiresistant organisms, this review explores risk factors for nosocomial infection with methicillin-resistant **Staphylococcus aureus**, vancomycin-resistant enterococcus, **Clostridium difficile**, extended-spectrum β-lactamase–producing gram-negative bacilli, and Candida. This review comprises data from 74 published studies; 53 (71%) were retrospective studies and addressed few risk factors or did not quantify risk. The analysis shows impressive commonality of risk factors across these diverse multiresistant organisms: advanced age; underlying diseases and severity of illness; inter-institutional transfer of the patient, especially from a nursing home; prolonged hospitalization; gastrointestinal surgery or transplantation; exposure to invasive devices of all types, especially central venous catheters; and exposure to antimicrobial drugs, especially cephalosporins.

Beginning in the late 20th century, we have witnessed a rapidly growing crisis in antibiotic resistance, especially among microorganisms that cause nosocomial infection (1–4). Most notable among these are methicillin-resistant **Staphylococcus aureus** (5), vancomycin-resistant enterococcus (6), **Clostridium difficile** (7), extended-spectrum β-lactamase–producing gram-negative bacilli (8), and Candida (9). Infections caused by these microorganisms increase hospital stays and attributable mortality (1–9).

The success of programs to curtail antimicrobial resistance—especially in controlling endemic infections—has been limited. Strategies for preventing nosocomial infection are more likely to succeed if they are guided by a full understanding of the factors that put hospitalized patients at increased risk (10).

Numerous studies have identified risk factors for nosocomial colonization or infection by individual multiresistant pathogens. After reviewing the published studies on this subject, we conclude that the most important risk factors for colonization or infection with the various multiresistant microorganisms are common and universal.

In this review, we do not differentiate between colonization or infection because nosocomial colonization is the precursor to clinical infection. The risk for nosocomial infection is 11% to 38% with colonization by methicillin-resistant **S. aureus** (11, 12), 25% with colonization by vancomycin-resistant enterococcus (13), 25% with colonization by extended-spectrum β-lactamase–producing gram-negative bacilli (14), and as high as 38% with colonization by **Candida** (15). We included in our review published papers or abstracts that used multivariable techniques of statistical analysis to identify risk factors in adults.

We found 74 studies with data on nosocomial colonization (n = 24) or infection (n = 50) by methicillin-resistant **S. aureus** (11, 12, 16–26), vancomycin-resistant enterococcus (n = 22) (27–48), extended-spectrum β-lactamase–producing gram-negative bacilli (n = 9) (49–57), **C. difficile** (n = 20) (58–77), or Candida (n = 10) (78–87). Only 21 studies (29%) were conducted prospectively; the remainder retrospectively analyzed colonization or infection as determined by clinical cultures obtained by patients’ caregivers. Most studies examined few risk factors; only 59 (80%) quantified risk by calculating odds ratios or relative risk.

More restricted use of antibiotics, especially cephalosporins, and strategies to prevent medical device–related infection and cross-infection in the hospital would yield benefit with all types of resistant organisms. Preemptive isolation of all patients with risk factors for infection by resistant organisms would very likely reduce secondary spread within the hospital. Conversely, programs that focus on only one organism or one antimicrobial drug are unlikely to succeed. Prospective studies of sufficient size that address all potential risk factors, especially individual anti-infective agents, and that use matched controls who are shown by surveillance cultures to be free of colonization by resistant organisms would enhance understanding of the epidemiology of antimicrobial resistance in institutions and guide efforts to develop more effective strategies for prevention.
Thirty-five studies (49%) examined a broad, general hospital population; the remainder focused on selected subgroups, such as patients in an intensive care unit (ICU) (16 studies), patients with HIV infection or malignant solid organ or hematologic conditions (7 studies), patients in nursing homes (6 studies), patients receiving hepatic transplants (4 studies), patients undergoing general surgery (3 studies), or patients requiring hemodialysis (2 studies).

Table 1 shows risk factors that predicted nosocomial colonization or infection with individual multiresistant organisms. Seven types of risk factors were most likely to

Table 1. Risk Factors for Nosocomial Colonization or Infection with Methicillin-Resistant *Staphylococcus aureus*, Vancomycin-Resistant Enterococcus, *Clostridium difficile*, Extended-Spectrum β-Lactamase–Producing Gram-Negative Bacilli, and *Candida*

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<tr>
<td>Advanced age</td>
<td>1.2 to 1.3 (17, 23)</td>
<td>2.6 (45)</td>
<td>NS (49, 51, 54, 56)</td>
<td>1.0 to 14.1 (60, 69, 74, 77)</td>
<td>1.5 (78)</td>
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<tr>
<td>Underlying disease</td>
<td></td>
<td></td>
<td>t (51), NS (49, 56, 57)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<tr>
<td>Renal failure</td>
<td>t (12, 17, 18, 22, 23, 26)</td>
<td>4.4 to 6.98 (35, 42)</td>
<td>t (51), NS (49, 56, 57)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<tr>
<td>Hematologic cancer</td>
<td>t (12, 17, 23, 26), NS (22)</td>
<td>8.4 (33)</td>
<td>t (51), NS (49, 56, 57)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<tr>
<td>Hepatic failure</td>
<td>t (12, 17, 23, 26)</td>
<td>2.3 to 6.1 (29, 30, 32, 47)</td>
<td>t (51), NS (49, 56, 57)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<tr>
<td>Severity of illness</td>
<td>1.9 (24)</td>
<td>3.6 (52)</td>
<td>t (51), NS (49, 56, 57)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<tr>
<td>Intercatheter transfer of a patient; patient from a nursing home</td>
<td>6.9 (24)</td>
<td>3.6 (52)</td>
<td>t (51), NS (49, 56, 57)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<tr>
<td>Extended length of stay</td>
<td>1.7 to 17.5 (16–19, 21–23, 25, 26)</td>
<td>1.1 to 2.9 (32, 45)</td>
<td>t (51), NS (49, 56, 57)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<tr>
<td>Invasive procedures or devices</td>
<td></td>
<td></td>
<td>t (51), NS (49, 56, 57)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<td>Gastrointestinal surgery</td>
<td>t (17)§</td>
<td>3.3 to 6.93 (31, 48)</td>
<td>t (51), NS (49, 56, 57)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<tr>
<td>Transplantation</td>
<td>t (12, 18, 23, 25)</td>
<td>2.5 to 13 (49, 56)</td>
<td>t (51), NS (49, 56, 57)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<tr>
<td>Central venous or arterial catheter</td>
<td>2.7 (38)</td>
<td>1.8 (51, 52)</td>
<td>t (58–77), NS (63)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<tr>
<td>Urinary catheter</td>
<td>NS (11, 17, 18, 22, 26)</td>
<td>2.5 to 12.8 (51, 54, 55)</td>
<td>t (58–77), NS (63)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
</tr>
<tr>
<td>Intubation and mechanical ventilation</td>
<td>t (18)§</td>
<td>1.2 to 2.8 (51, 54, 55)</td>
<td>t (58–77), NS (63)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<tr>
<td>Tube feeding</td>
<td>5.5 (19)</td>
<td>1.3 to 6.1 (33, 36)</td>
<td>t (58–77), NS (63)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<tr>
<td>Anti-infective therapy</td>
<td></td>
<td></td>
<td>t (81, 85–87)</td>
<td>1.71 to 6.7 (66, 76)</td>
<td>1.4 to 22.1 (79, 84)</td>
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<td>Cephalosporins</td>
<td>3.1 (24)</td>
<td>1.6 to 13.8 (39, 41, 44)</td>
<td>NS (49, 52, 54–56), NS (52, 56)</td>
<td>1.4 to 28.6 (64, 65, 69)</td>
<td>NS (81, 86, 87)</td>
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<td>Penicillins</td>
<td>NS (22, 23), t (11, 12, 17, 18)</td>
<td>t (34, 36, 48), NS (37, 38, 40, 44)</td>
<td>NS (49, 55), t (51, 52, 54, 56)</td>
<td>3.4 to 4.9 (59, 68)</td>
<td>NS (81, 86, 87)</td>
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<tr>
<td>Clindamycin</td>
<td>t (12, 17, 18, 22, 26)</td>
<td>2.3 to 11.0 (27, 29, 32, 33, 40, 42, 44–46, 48)</td>
<td>NS (49, 55), t (51, 52, 54, 56)</td>
<td>15.6 to 42 (61, 62)</td>
<td>NS (81, 86, 87)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>t (11, 17, 18, 23), NS (22)</td>
<td>2.3 to 11.0 (27, 29, 32, 33, 40, 42, 44–46, 48)</td>
<td>t (49, 51, 52, 54, 55)</td>
<td>3.1 (59)</td>
<td>275 (81)</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>1.7 to 11.3 (16, 19, 21, 24, 26)</td>
<td>1.6 to 14.5 (42, 43, 45, 47)</td>
<td>t (49, 50, 53, 56)</td>
<td>1.4 to 8.77 (49, 56, 57)</td>
<td>1.6 to 22.6 (63, 65, 70, 72, 74)</td>
</tr>
<tr>
<td>Multiple antibiotics</td>
<td>1.7 to 11.3 (16, 19, 21, 24, 26)</td>
<td>1.6 to 14.5 (42, 43, 45, 47)</td>
<td>t (49, 50, 53, 56)</td>
<td>1.4 to 8.77 (49, 56, 57)</td>
<td>1.6 to 22.6 (63, 65, 70, 72, 74)</td>
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*NS = not significant.
† Not evaluated.
‡ According to Acute Physiology and Chronic Health Evaluation II (APACHE II) score or Simplified Acute Physiology Score (SAPS).
§ Found significant in a multivariable model but magnitude of increased risk not quantified.
result in colonization or infection with multiresistant species: advanced age (odds ratio [OR], 1.2 to 14.1); severity of illness (OR, 1.9 to 11.6); inter-institutional transfer of the patient (OR, 2.9 to 21.3); prolonged hospital stay (OR, 1.3 to 17.5); gastrointestinal surgery (OR, 2.5 to 6.9); transplantation (OR, 3.2 to 6.7); exposure to medical devices, especially central venous catheters (OR, 1.8 to 26.4); and, universally, heavy exposure to broad-spectrum antimicrobial drugs (OR, 1.6 to 25.1), especially cephalosporins (OR, 1.6 to 28.6).

**DISCUSSION**

Numerous reports have documented a striking increase in the incidence of nosocomial infection caused by the multiresistant species examined in this study (1–9). Data on ICU patients from the nearly 300 U.S. hospitals participating in the National Nosocomial Infection Surveillance Study of the Centers for Disease Control and Prevention (88) showed that by 1998, nosocomial infections caused by methicillin-resistant *S. aureus* accounted for 55% of all *S. aureus* infections; those caused by vancomycin-resistant enterococcus, 26% of all enterococcal infections; and those caused by gram-negative bacilli resistant to third-generation cephalosporins (and presumably, extended-spectrum *β*-lactamase producers), 36% of all *Enterobacter* infections, 20% of all *Pseudomonas aeruginosa* infections, and 9% of all *Klebsiella* infections. A similar prospective study of antimicrobial resistance in 40 U.S. medical centers, the Intensive Care Antimicrobial Resistance Epidemiology Project (89), documented similar trends. The five pathogens we reviewed now account for approximately 50% of all nosocomial infections in U.S. hospitals (88, 89). These trends in endemic nosocomial infection, as well as the increasing number of reports of outbreaks of *Candida* infection (90), indicate that current infection-control efforts to target multiresistant pathogens are failing dismally.

Although many studies have identified risk factors that are specific to individual pathogens, few studies have attempted to establish commonality of risk factors among these organisms or even to explore their relationships with each other. It has been shown that infection by *C. difficile* can facilitate transmission of vancomycin-resistant enterococcus (43, 91) and that successful control of vancomycin-resistant enterococci results in a commensurate reduction in *C. difficile* infections (92). In a review of the relationship between vancomycin-resistant enterococcus and *C. difficile*, Gerding (93) showed that persons infected with these organisms share many common risk factors, including type of antimicrobials received; advanced patient age; extended length of stay; severity of underlying disease; and exposure to electronic thermometers, enteral feeding, and environmental contamination.

Our analysis is limited by the modest size of the included studies and, especially, by their mostly retrospective nature, which limits confidence that all of the control patients were indeed free of colonization by the resistant pathogen in question. Nonetheless, our analysis shows an impressive commonality of risk factors across the five groups of diverse multiresistant pathogens. We believe these data indicate that infection-control programs that focus on one organism or only one antimicrobial agent are unlikely to succeed. For maximum benefit, we believe that infection-control programs must apply global strategies aimed at all resistant organisms (Table 2) (94–153).

**Severity of Illness and Underlying Disease and Extended Length of Stay**

It is clear that patients with serious underlying disease and a high severity-of-illness score, particularly those who have undergone complicated surgery or organ transplantation or who have renal or other organ failure, are at greatly increased risk for infection by multiresistant organisms. This increase in risk results from the patients’ exposure to invasive devices and other procedures (each of which increases risk), as well as from depressed host defenses and extensive exposure to antibiotics. Almost invariably, the duration of hospitalization is considerably longer in these patients than in patients with less severe illness.

Obviously, little can be done to modify illness severity. Thus, we believe that strategies to protect intrinsically vulnerable patients (Table 2) must focus on limiting and improving the use of antimicrobial therapy; more consistent application of basic infection-control measures, such as hand-related hygiene; and the adoption of novel prevention-related technology, such as anti-infective–coated vascular (95–97) or urinary (98–101) catheters.

However, we should also consider the reality that our current paradigm for preventing spread of resistant organisms in the hospital—waiting until colonization or
infection by a resistant organism is reported by the laboratory before isolating the patient, usually in a single room, and requiring gloves with or without a gown for all contacts with that patient—has failed. Prolonged wearing of gloves in the hospital, a very common practice, may paradoxically increase the risk for nosocomial cross-infection (154, 155).

Considerable data indicate that cohort nursing for patients with known colonization or infection by multiresistant organisms can reduce cross infection (102–105). However, for every patient with known colonization of infection by multiresistant organisms, many more patients with unrecognized colonization are already in the medical center—probably in the same unit (20, 33, 43, 44, 156). A more logical strategy is the preemptive use of barrier precautions for all high-risk patients to prevent contamination of the hands of health care workers by multiresistant organisms during contact with patients who have silent colonization and to prevent cross-infection to other uncolonized patients. Studies have shown that the preemptive use of barrier precautions—also called “protective isolation”—is highly effective at preventing the spread of multiresistant organisms, such as methicillin-resistant Staphylococcus aureus or vancomycin-resistant enterococcus in an epidemic setting (107–109). Some studies have also shown a strong correlation between preemptive use of barrier precautions in high-risk populations, such as patients in the intensive care unit (ICU), and prevention of endemic nosocomial infection, including by multiresistant organisms (110–114).

Objects in the hospital environment also appear to play a significant role in the transmission of resistant pathogens. The use of stethoscopes (157), sphygmomanometers (158), and electronic thermometers (159, 160) on multiple patients provides further opportunity for

**Table 2. Risk Factors and Potential Control Measures for Colonization or Infection with Antimicrobial-Resistant Nosocomial Pathogens Amenable to Control**

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Control Measures (References)</th>
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<tr>
<td>Underlying disease; severity of illness; interinstitutional transfer; patients undergoing transplantation or gastrointestinal surgery; extended institutional length of stay</td>
<td>Focused and improved hand-related hygiene (94)</td>
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<td>Focused use of novel technology designed for prevention, such as anti-infective–coated vascular (95–97) or urinary catheters (98–101)</td>
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<td>Cohort nursing for patients with known colonization or infection by resistant organisms (102–105)</td>
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<td></td>
<td>Screening for cultures on admission, with targeted isolation of identified carriers (106)</td>
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<td></td>
<td>Preemptive use of barrier precautions (protective isolation) for all high-risk patients (107–114)</td>
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<td>Closely monitored antimicrobial therapy (115–117)</td>
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<td>Invasive medical devices</td>
<td>Formal institutional training in vascular access and care; close monitoring and supervision of trainees (118–120)</td>
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<tr>
<td>Intravascular devices</td>
<td>Intravenous therapy teams to insert and care for catheters (121, 122)</td>
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<td>Maximal sterile barrier precautions at the time of insertion of device (123, 124)</td>
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<td></td>
<td>Use of chlorhexidine for cutaneous antisepsis (125–127)</td>
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<td></td>
<td>Use of novel technology for prevention, such as antiseptic dressings, anti-infective–coated catheters, contamination-resistant catheter hubs, and anti-infective–containing lock solutions (95–97, 127, 128)</td>
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<td>Institutional training of staff who perform insertions (129)</td>
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<td></td>
<td>Use of novel technology, such as antiseptic-coated catheters (98–101)</td>
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<td>Routine use of gloves for all contact involving patients with catheters (130)</td>
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<td></td>
<td>Use of novel technology—endotracheal tubes that remove pooled supraglottic secretions (131, 132)</td>
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<td></td>
<td>Preemptive use of barrier precautions in all patients (107–114)</td>
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<td></td>
<td>Focused use of perioperative prophylaxis to greatly limit prolonged postoperative administration (133)</td>
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<td>Active perioperative rewarming of hypothermic patients (134)</td>
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<td>Hyperoxygenation in the perioperative period (135)</td>
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<td>Institutional guidelines (136–138)</td>
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<td></td>
<td>Focused educational programs (139)</td>
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<td></td>
<td>Restrictions on the use of key agents (140–150)</td>
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<td>Policies of the microbiology laboratory (140–150)</td>
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<td></td>
<td>Close monitoring of anti-infective use and frequent audits (115–117)</td>
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<td>“Cycling” or rotation of antibiotic classes (151)</td>
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<td></td>
<td>Computer-assisted prescribing of antibiotics (152, 153)</td>
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<td>Urinary catheters</td>
<td>Closely monitored antimicrobial therapy (115–117)</td>
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<td>Intubation and mechanical ventilation</td>
<td>Closely monitored antimicrobial therapy (115–117)</td>
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<tr>
<td>Surgery</td>
<td>Closely monitored antimicrobial therapy (115–117)</td>
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<td>Antimicrobial therapy</td>
<td>Closely monitored antimicrobial therapy (115–117)</td>
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the spread of multiresistant organisms. Surfaces contiguous to a patient in the ICU should be wiped down with the general hospital disinfectant at least daily, and all high-risk patients should have a designated stethoscope and sphygmomanometer that are decontaminated when the patient is discharged.

**Invasive Medical Devices**

Modern-day medicine is synonymous with cutting-edge “high-tech” medicine, such as mechanical ventilatory support; hemodynamic monitoring; total parenteral nutrition; hemodialysis; intracranial-pressure monitoring; innovative forms of surgery; and a huge arsenal of drugs, including anti-infectives of every genre (1). Such technology, more than anything else, has forced medicine to accept the necessity of nosocomial infection control. Invasive devices of all types generally play a far more important role in increasing susceptibility to nosocomial infection than underlying diseases (10) (Table 1). However, this fact should be viewed as welcome news, because there is far greater promise in being able to reduce nosocomial infections by innovative improvements in aseptic techniques and especially technologic advances in medical devices than by breakthroughs that will reverse chronic organ failure or degenerative diseases (1).

In general, risk factor analysis for nosocomial infection has shown very clearly that most nosocomial infections, whether they are caused by susceptible or multiresistant organisms, derive from surgery (161) or exposure to invasive procedures or medical devices. Such devices include intravascular catheters in the case of nosocomial bloodstream infection (162), urinary catheters with nosocomial urinary tract infections (163), intubation and mechanical ventilatory support with nosocomial pneumonia (164), and ventriculostomy (165) with nosocomial meningitis.

Intravascular devices, particularly central venous catheters of all types, cause nearly two thirds of all nosocomial bloodstream infections in U.S. hospitals (162, 166). Several key preventive measures can greatly reduce this risk (167)—namely, ongoing training and monitoring of house officers in techniques of vascular access and care (120), use of nurse intravenous therapy teams to insert and care for many types of vascular catheters (121, 122), use of maximal sterile barriers during insertion of central venous catheters (123, 124), and use of chlorhexidine instead of iodine-based antisepsics for disinfection of catheter access sites (125–127). Perhaps the most promising factor is the growth of application of novel technologies designed for prevention. Placing cuffs on surgically implanted tunneled catheters has greatly reduced the risk for infection in patients requiring prolonged central access, such as for hemodialysis (168, 169). The most important advance during the past four decades may be the recent development of short-term, noncuffed central venous catheters with anti-infective surfaces to reduce colonization on the skin and biofilm formation—the precursor to device-related bloodstream infection. An anti-infective coating can reduce by 50% to 90% the risk for intravenous device–related bloodstream infection (95–97).

The use of antiseptic coatings on urinary catheters has recently also been shown to reduce the risk for nosocomial urinary tract infections, including those caused by multiresistant organisms (98–101). Novel endotracheal tubes that incorporate an additional lumen to continuously aspirate pooled secretions above the glottis have been shown in randomized trials to reduce the incidence of ventilator-associated pneumonia by nearly 50% (131, 132). The patients who are most likely to benefit from novel technologies are those at highest risk for nosocomial infection with multiresistant organisms.

**Antimicrobial Therapy**

The crisis in antimicrobial resistance is due in greatest measure to the indiscriminate use of systemic antibiotics worldwide in the past 30 years, especially in hospitals (1–9). Antimicrobial therapy has its greatest ecologic impact in the close confines of a hospital, particularly in ICUs (170). In fact, most nosocomial outbreaks caused by antibiotic-resistant organisms (171) have occurred in ICUs. Antibiotic pressure, which promotes the exchange of resistance genes by various transfer mechanisms (172), has been proven to be the single most important factor predisposing patients to infection by resistant organisms. Broad-spectrum antimicrobial therapy is the root cause of antibiotic-associated diarrhea and colitis caused by *C. difficile* (58–77).

It is clear that antimicrobial agents are widely overused and misused. More than 75% of patients in U.S. hospitals receive antimicrobial agents, and studies indicate that more than one half of hospitalized patients receiving antimicrobial therapy have no evidence of infection or clear indication for antibiotics (140–150,
173). Vancomycin use in one university hospital increased 20-fold from 1981 to 1991, and indications for its use were often not in keeping with published guidelines (174). Moreover, most antibiotics used within hospitals are very-broad-spectrum or extended-spectrum penicillins, second- and third-generation cephalosporins, carbapenems, aminoglycosides, or fluoroquinolones. A recent meta-analysis that controlled for variability in selection of control groups and length of stay (175) found only a modest association between vancomycin use and colonization by vancomycin-resistant enterococcus. Exposure to other broad-spectrum antimicrobials, such as third-generation cephalosporins and other drugs with anaerobic activity, is more important in promoting colonization and spread of vancomycin-resistant enterococci than is use of vancomycin (29, 39, 41–45, 47, 176). It is imperative that greater efforts be directed to improving the use of all systemic antibiotics, especially within hospitals.

The Joint Commission on Accreditation of Healthcare Organizations now mandates that hospitals periodically audit their use of antimicrobial agents (177). Such audits should scrutinize the need for antimicrobial therapy by checking for clear evidence of infection, justification for prophylactic use, the appropriateness of the regimen selected, and monitoring for efficacy and side effects during therapy. Educational programs and institutional guidelines for antimicrobial use that permit a hospital staff to set standards on the basis of local needs and judgments should be established and guided by published criteria (136–138). Other important strategies for controlling antimicrobial use include a restricted formulary (140–150), policies of the clinical microbiology laboratory for reporting susceptibility testing (140), automatic stop orders for surgical prophylaxis (133), and the “cycling” or “rotating” of classes of broad-spectrum antibiotics in ICUs (151). Many institutions now restrict selected costly and essential drugs (such as third-generation cephalosporins, carbapenems, amikacin, new fluoroquinolones, fluconazole, or lipid-associated amphotericin), requiring physicians who wish to use these drugs to justify their use to a member of an institutional antibiotic review committee. However, the most innovative and promising approach to improving the use of antiinfective therapy may be the use of computer-assisted prescribing—user-friendly, expert systems available at the point of use (152, 153).

**Summary**

The greatest challenge for nosocomial infection control has long been consistent implementation of control measures that have proven to be effective (1). Prospective studies of sufficient size that address all potential risk factors, especially individual anti-infective agents, and that use matched control patients shown by sequential surveillance cultures to be free of colonization by resistant organisms would greatly improve our understanding of the epidemiology of antimicrobial resistance in institutions. Such studies would also guide efforts to develop more effective strategies for prevention.

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**References**


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