Nosocomial Infections in the ICU*

The Growing Importance of Antibiotic-Resistant Pathogens

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Patients hospitalized in ICUs are 5 to 10 times more likely to acquire nosocomial infections than other hospital patients. The frequency of infections at different anatomic sites and the risk of infection vary by the type of ICU, and the frequency of specific pathogens varies by infection site. Contributing to the seriousness of nosocomial infections, especially in ICUs, is the increasing incidence of infections caused by antibiotic-resistant pathogens. Prevention and control strategies have focused on methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant Enterococcus, and extended-spectrum β-lactamase-producing Gram-negative bacilli, among others. An effective infection control program includes a surveillance system, proper handwashing, appropriate patient isolation, prompt evaluation and intervention when an outbreak occurs, adherence to standard guidelines on disinfection and sterilization, and an occupational health program for health-care providers. Studies have shown that patients infected with resistant strains of bacteria are more likely than control patients to have received prior antimicrobials, and hospital areas that have the highest prevalence of resistance also have the highest rates of antibiotic use. For these reasons, programs to prevent or control the development of resistant organisms often focus on the overuse or inappropriate use of antibiotics, for example, by restriction of widely used broad-spectrum antibiotics (*eg*, third-generation cephalosporins) and vancomycin. Other approaches are to rotate antibiotics used for empiric therapy and use combinations of drugs from different classes. ***(CHEST 1999; 115:34S–41S)***

Key words: antimicrobial resistance; broad-spectrum antibiotics; drug-resistant pathogens; nosocomial infections

Abbreviations: CDC = Centers for Disease Control and Prevention; MRSA = methicillin-resistant *Staphylococcus aureus;* NNIS = National Nosocomial Infections Surveillance; SHEA/IDSA = Society for Healthcare Epidemiology of America/Infectious Diseases Society of America; VRE = vancomycin-resistant Enterococcus sp

Since the 1980s, infectious disease specialists have recognized that ICU patients acquire nosocomial infections at a much higher rate than patients elsewhere in the hospital. For ICU patients, the risk is as much as 5 to 10 times greater than for those on general medical wards.[1–4] This increased risk of nosocomial infection results from three major factors: (1) intrinsic risk factors related to the need for intensive care, such as severe underlying disease, multiple illnesses, malnutrition, extremes of age, and immunosuppression; (2) invasive medical devices, such as endotracheal tubes for mechanical ventilation, intravascular catheters, and urinary tract catheters; (3) crowding (*eg*, neonatal ICU) and animate reservoirs (*eg*, colonized or infected patients), which increase the risk of cross-infection in the ICU.

The most representative data on nosocomial infection rates have been provided by the National Nosocomial Infections Surveillance (NNIS) system.[5] NNIS data indicate that today's typical hospitalized patient may be sicker than in former years. Data from surveys of NNIS hospitals between 1988 and 1995 demonstrate a significant increase in the number of ICU beds and a slight decrease, not reaching statistical significance, in total beds.[6]

Surveillance data from ICUs are available for the years 1986 through 1997 (Table 1).[7] Risk adjustment is provided by stratifying the data by type of ICU and type of invasive medical device (*ie*, ventilator, central venous catheter, urinary tract catheter) and by presenting the infection rate as infections per 1,000

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Table 1—*Device-Associated Infection Rates by Type of ICU*[7]

Type of ICU	Ventilator-Associated Pneumonia,* Mean (10%–90%)†	Central Line-Associated Bloodstream Infections,‡ Mean (10%–90%)†	Urinary Catheter-Associated Urinary Tract Infections,§ Mean (10%–90%)†
Coronary	10.2 (0.0–19.1)	5.0 (0.0–10.3)	7.1 (1.1–14.0)
Medical	8.9 (1.6–17.6)	6.1 (1.7–12.1)	8.0 (2.2–12.7)
Medical/surgical	11.8 (3.6–18.3)	4.5 (0.0–8.2)	5.4 (1.3–10.1)
Neurosurgical	18.3 (2.6–30.2)	5.7 (0.0–9.9)	8.5 (1.7–14.9)
Pediatric	5.8 (0.0–10.7)	8.1 (1.3–13.6)	5.3 (1.0–12.1)
Surgical	14.5 (4.2–23.8)	4.9 (0.8–9.2)	5.3 (0.7–9.2)
Burn	24.1	14.6	10.5
Respiratory	6.7	4.6	7.1
Trauma	17.2	7.2	8.3

*Cases of ventilator-associated pneumonia per 1,000 ventilator-days.
†Values represent the pooled mean, 10th percentile value, and 90th percentile value of hospitals reporting data to the CDC.
‡Number of infections per 1,000 central-line days.
§Number of infections per 1,000 urinary-catheter days.

device days. Further risk adjustment has been performed for infections in neonatal ICUs by stratifying patients by birth weight.[7,8]

From the NNIS data, one may conclude the following: the relative frequency of different sites of nosocomial infections (*ie*, ventilator-associated pneumonia, bloodstream infections, urinary tract infections) and the absolute risk of infection (per 1,000 device days) vary by type of ICU; the relative frequency of different nosocomial pathogens varies by site of infection (Table 2); and the site-specific rates of nosocomial infections in similar types of ICUs vary 10- to 20-fold among hospitals.[7]

Drug-Resistant Pathogens in the ICU

In the hospital, concern about drug-resistant pathogens has focused on methicillin-resistant *Staphylococcus aureus* (MRSA),[9,10] vancomycin-resistant Enterococcus sp (VRE),[11–13] extended-spectrum β-lactamase-producing Gram-negative bacilli,[14] multidrug-resistant *Mycobacterium tuberculosis*,[15] fluconazole-resistant Candida sp,[16] and most recently, strains of *S aureus* with reduced susceptibility to vancomycin—because such strains have now been isolated in Japan and the United States.[17] This concern has been fueled by multiple reports of outbreaks of infection caused by these pathogens and increasing rates of endemic infection in ICU patients. However, only limited data are available regarding the prevalence of these pathogens in ICUs throughout the United States. Data obtained from the NNIS system documents the increasing frequency of VRE in US hospitals (Fig 1).[17,18] Archibald and colleagues[6] reported the prevalence of drug-resistant pathogens isolated from different patient populations of eight hospitals between 1994 and 1995 (Table 3). For five of these antimicrobial/pathogen combinations, the percentage of resistant isolates was significantly higher in the ICU than in the two other settings.[6]

Control of Nosocomial Infections in the ICU

Weinstein[19] has summarized the traditional infection-control measures used in ICUs (Table 4). Unfortunately, as noted by Weinstein, these control measures often fail because frequently patients are already colonized with "nosocomial" bacteria when hospitalized and because endogenous flora in ICU patients is often amplified by antibiotics and gastric alkalization. Other factors include selection by antibiotic pressure on antibiotic-resistant bacterial subpopulations and spontaneous bacterial resistance mutation, lapses in aseptic care during a crisis, spread on hands of personnel caring for ventilator-dependent patients who have heavy respiratory tract

Table 2—*Distribution of the Five Most Common Nosocomial Pathogens Isolated From the Four Major Infection Sites in the ICU, January 1986–April 1997*[7]

Bloodstream		Pneumonia		Surgical Site		Urinary Tract	
Pathogen	%	Pathogen	%	Pathogen	%	Pathogen	%
CoNS*	33.5	*Pseudomonas aeruginosa*	17.4	Enterococcus sp	15.3	*Escherichia coli*	19.2
S aureus	13.4	*S aureus*	17.4	CoNS*	12.6	*C albicans*	14.4
Enterococcus sp	12.8	Enterobacter sp	11.4	*S aureus*	11.2	Enterococcus sp	14.1
Candida albicans	5.8	*Klebsiella pneumoniae*	6.7	*P aeruginosa*	10.3	*P aeruginosa*	11.2
Enterobacter sp	5.2	*Haemophilus influenzae*	4.9	Enterobacter sp	9.5	*K pneumoniae*	5.8
Other	29.3	Other	42.2	Other	41.1	Other	35.3
Total	100.0	Total	100.0	Total	100.0	Total	100.0

*CoNS = coagulase-negative staphylococcus.

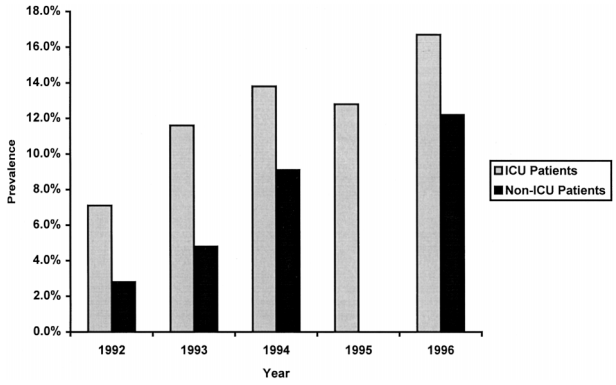

FIGURE 1. Nosocomial Enterococcus in the United States, 1992 through 1996. From Summary of Notifiable Diseases, United States, 1996 *MMWR.*[49]

colonization or infection, unrecognized environmental reservoirs, and new devices that break through anatomic barriers.[19]

Key elements of an effective infection control program include a surveillance system,[20] proper hand washing before and after contact with each patient or patient equipment,[21] appropriate isolation of patients with transmissible pathogens, prompt evaluation and intervention in cases of outbreaks,[22] adherence to standard guidelines on disinfection and sterilization of medical equipment,[23] and an effective program of occupational health focusing on preexposure and postexposure management of health-care providers.[24] Proper hand washing, isolation, and disinfection are critical to prevent transmission of resistant pathogens between patients via contaminated equipment or contaminated hands of health-care providers. GI tract colonization of health-care providers with resistant pathogens does not appear to be a reservoir of these infectious agents.[25]

Table 4—*Traditional Infection Control Measures in ICUs

Infection Control Measures
1. Identify reservoir
• Colonized and infected patients
• Environmental contamination; common sources
2. Halt transmission among patients
• Improve hand washing and asepsis
• Barrier precautions (gloves, gown) for colonized and infected patients
• Eliminate any common source; disinfect environment
• Separate susceptible patients
• Close unit to new admissions if necessary
3. Halt progression from colonization to infection
• Discontinue compromising factors when possible (*eg,* extubate, remove nasogastric tube, discontinue bladder catheters, as clinically indicated; rotate IV catheter sites; proper ventilator and pulmonary care)
4. Modify host factors
• Treat underlying disease and complications
• Control antibiotic use (rotate, restrict, or cease)

*From Weinstein,[19] with permission.

PREVENTION AND CONTROL OF ANTIMICROBIAL RESISTANCE

Consensus statements have been published recently that delineate strategies to prevent and control the emergence and spread of antimicrobial-resistant microorganisms in hospitals.[26,27] Prevention strategies are based on minimizing the transmission of antibiotic-resistant pathogens between patients (Tables 5 and 6) and developing a program to prevent or reduce antimicrobial resistance (Table 7). The Centers for Disease Control and Prevention (CDC) has published general isolation guidelines to minimize the risk of transmission of infectious agents from colonized/infected patients to other patients or health-care providers.[21] Detailed infection-control

Table 3—*Resistance to Specific Antimicrobials in Isolates From Inpatients vs Outpatients for Sentinel Antimicrobial/Pathogen Combinations

Antimicrobial/Pathogen Combination	No. of Resistant Isolates/Total No. of Isolates Tested (%)		p Value
	Inpatients	Outpatients	
Methicillin/coagulase-negative Staphylococcus†	922/1,881 (49.0)	250/796 (35.9)	< 0.01
Methicillin/*S aureus*†	861/2,633 (32.7)	233/1,594 (14.6)	< 0.01
Ceftazidime/*Enterobacter cloacae*†	145/559 (26.0)	15/126 (11.9)	< 0.01
Imipenem/*P aeruginosa*	164/1,368 (12.0)	31/477 (6.5)	< 0.01
Ceftazidime/*P aeruginosa*†	147/1,889 (7.8)	25/631 (4.0)	< 0.01
Vancomycin/Enterococcus sp†	92/1,459 (6.3)	8/575 (1.4)	< 0.01
Ciprofloxacin/*E coli*	16/3,189 (0.5)	28/3,997 (0.7)	NS‡
Ceftazidime/*E coli*	5/2,348 (0.2)	9/1,887 (0.5)	NS‡

*Adapted from Archibald et al,[6] with permission.
†Antimicrobial-resistant isolates significantly higher in ICU than in other two settings.
‡NS = not significant.

Table 5—*Four-Phase Approach to the Management of an MRSA Outbreak

Management Approach
Phase I
A. Basic epidemiology
1. Compile line lists
B. Management steps
1. Notify personnel on affected wards to
a. Isolate new cases following the CDC guidelines for isolation precautions
b. Intensify basic infection control measures, such as hand washing
Phase II
A. Generate initial epidemiologic hypothesis
1. Use line listing to confirm clustering and identify a common source of transmission
2. Instruct microbiology laboratory to save organisms
3. Review antibiograms to determine whether isolates are possibly related
B. Management steps
1. Notify management that there may be a problem
2. Continue infection control measures
Phase III
A. Confirmation of hypothesis through standard epidemiologic workup
1. Recruit employee health records to identify personnel from whom cultures should be made
2. Perform and save nasal cultures in personnel and other patients who were in contact with the case patient
3. Evaluate MRSA rates in other patient care units
4. Compare current rates with past rates
B. Management steps
1. Consider mupirocin calcium use for high-risk patients
2. Notify public relations department of the problem as appropriate
3. Continue infection control measures
Phase IV
A. Confirmation of hypothesis through microbiology
1. Determine strain types to establish spread of a single strain
B. Management steps
1. Continue infection control measures
2. Continue involvement of hospital administration
3. Arrange meeting of the risk-management team to review the data
4. Consider mupirocin calcium use for appropriate prophylaxis/nasal decolonization, even before typing is completed

*From Wenzel et al,[28] with permission.

Table 6—*Recommended Use of Vancomycin

Recommended Use
The use of vancomycin is appropriate or acceptable
1. For treatment of serious infections caused by β-lactam-resistant Gram-positive microorganisms
2. For treatment of infections caused by Gram-positive bacteria in patients with serious allergies to β-lactam antibiotics
3. When antibiotic-associated colitis does not respond to metronidazole or is severe and possibly life threatening
4. For prophylaxis, as recommended by the American Heart Association, following certain procedures in patients at high risk for endocarditis
5. For prophylaxis for major surgical procedures involving implantation of prosthetic materials or devices at institutions that have a high rate of infections caused by MRSA or methicillin-resistant *Staphylococcus epidermidis;* vancomycin should be administered once immediately before surgery and repeated if the procedure lasts > 6 h. Prophylaxis should be discontinued after 2 days
The use of vancomycin should be discouraged for
1. Routine surgical prophylaxis
2. Empiric therapy for a febrile neutropenic patient, unless evidence indicates that the patient's infection is caused by Gram-positive bacteria and the prevalence of MRSA infections in the hospital is high
3. Treatment in response to a single blood culture positive for a coagulase-negative Staphylococcus, if other blood cultures taken during the same time frame are negative
4. Continued empiric use in patients whose cultures are negative for β-lactam-resistant Gram-positive microorganisms
5. Prophylaxis for infection or colonization of indwelling central or peripheral intravascular catheters
6. Selective decontamination of the digestive tract
7. Eradication of MRSA colonization
8. Primary treatment of antibiotic-associated colitis

*Adapted from CDC.[18]

recommendations have been published to minimize the transmission of MRSA,[28] VRE,[18] and *S aureus* with reduced susceptibility to vancomycin.[17]

Consensus guidelines define an MRSA outbreak as "an increase in the rate of MRSA cases or a clustering of new cases due to the transmission of a single microbial strain in a health-care institution, including long-term care facilities."[28] The following threshold rates (number of new nosocomial cases per 100 hospital admissions/number of new nosocomial cases per 100 patient days) for identifying high rates of MRSA transmissions are provided: < 200 hospital beds, 0.13/0.25; 200 to 499 hospital beds, 0.25/0.3; and, ≥ 500 hospital beds, 0.5/0.6. A four-phase approach to control is recommended (Table 5).

The proper use of vancomycin (Table 6)[18] is especially important because vancomycin use has risen dramatically in recent years, and vancomycin use is one of the strongest risk factors for VRE colonization/infection. The CDC guidelines for preventing the spread of VRE include recommendations on the prudent use of vancomycin, an educational program on VRE for hospital personnel, routine testing of all enterococci isolated from blood and sterile body sites (except urine) for vancomycin resistance, screening of all enterococcal isolates for vancomycin resistance if VRE are detected, and appropriate use of isolation precautions for all VRE-infected or colonized patients.[18]

The focus on control of antimicrobial use stems from compelling evidence of a causal association between antimicrobial use in hospitals and resistance of pathogens to these antimicrobials.[29] The Society

Table 7—*Elements of an Optimal Antimicrobial Control Program to Study the Prevention or Reduction of Antimicrobial Resistance

Elements
Precise definitions of antimicrobial resistance for antimicrobials and organisms
A system for monitoring the frequency of resistance (clinical and environmental)
A determination of which antimicrobial(s) to control
A method to achieve usage control
A determination of who will be responsible for maintaining control
A method to educate and enroll prescribers in the control process
A stable system of hospital infection control
A system to measure use of controlled and uncontrolled antimicrobials
A method to determine antimicrobial use per geographic area per unit of time
Ability to distinguish community from nosocomial isolates
Ability to identify isolates by body site and hospital location
A method to ensure that clinical care will not be harmed by control measures
Ability to identify known mechanisms of antimicrobial resistance
Ability to type organisms phenotypically or genetically

*Adapted from Shlaes et al,[27] with permission.

for Healthcare Epidemiology of America/Infectious Diseases Society of America (SHEA/IDSA) guidelines point out the following: changes in the use of antibiotics parallel changes in the prevalence of resistance to them. Resistance is more prevalent in nosocomial bacterial strains than in those from the community. Hospital patients infected with resistant strains are more likely than control patients to have received prior antimicrobials. Hospital areas that have the highest prevalence of resistance also have the highest rates of use of antibiotics. The longer a patient is exposed to antimicrobials, the greater the likelihood of colonization with resistant organisms.[27]

Risk Factors

Multiple case-control studies have analyzed the risk factors associated with infection or colonization with MRSA or VRE. Both univariate analysis in individual case studies and multivariate analysis have demonstrated that antibiotic exposure[30–33] and cephalosporin use are risk factors for infection with MRSA.[33,34]

To prevent or control antimicrobial resistance, the SHEA/IDSA guidelines propose the following: the selective removal, control, or restriction of antimicrobial agents or classes; the rotation of antimicrobial agents; and use of combination antimicrobial therapy. The SHEA/IDSA guidelines also review specific methods to implement antibiotic control policies (Table 8). The goal is to have all patients receive the most effective, least toxic, and least costly antibiotic for the precise period needed to cure or prevent an infection.[27]

Table 8—*Methods to Implement Antibiotic Control or Restriction Policies*

Methods
Written hospital guidelines
Educational efforts aimed at changing prescribing practices of physicians
Restriction of hospital formulary through pharmacy and therapeutics committee
Cyclic rotation of antimicrobials within a class
Antibiotic order forms
Antibiotic stop orders (therapeutic use, prophylactic use)
Restriction of use
Removal of specific agents
Review of medical records by pharmacists
Usage feedback to physicians
Computerized review
Group purchasing practices
Generic substitution
Utilization review with guidelines for rational and appropriate use
Requirement of consultation with infectious disease subspecialists for certain antimicrobial choices
Antimicrobial susceptibility reporting
Reduction of pharmaceutical promotion

*Adapted from Shlaes et al,[27] with permission.

Restriction of Antibiotic Use

By the early 1980s, most teaching hospitals had adopted restriction policies for the use of selected expensive agents.[35] Himmelberg and colleagues[36] demonstrated that institution of restriction policies was associated with reduced antibiotic expenditures, but elimination of a restriction policy resulted in an increase of 103% in the cost of the previously restricted antibiotics.

In another study, implementation of a rigid protocol for the use of preoperative prophylactic antibiotics resulted in cost savings of 57%.[37] While antibiotic restriction policies clearly result in lower cost, the influence of these programs on the prevalence of resistance and on clinical outcomes has been less well defined. Decreased use of broad-spectrum cephalosporins has been associated temporally with decreased antibiotic resistance among Gram-negative bacilli,[38–41] and decreased use of third-generation cephalosporins and vancomycin has been associated with a decreased incidence of VRE.[42] Investigators have also found that antibiotic control policies resulted in a stable median-length stay and a reduction in the number of nosocomial infections treated with antimicrobial drugs.[37] White and colleagues[43] evaluated the institution of a policy that required prior authorization for selected parenteral antibiotics. Total parenteral antimicrobial expenditures decreased by 32% and susceptibilities to all β-lactam and quinolone antibiotics increased. Im-

portantly, for patients with bacteremia caused by Gram-negative bacilli, the restrictions did not change overall survival. Further, there were no differences in the median time from positive blood culture to the prescription of an appropriate antibiotic or in the median time to discharge from the hospital. Evans and coworkers[44] developed a computerized decision-support program to assist physicians in the use of anti-infective agents. Patients who received antibiotics recommended by the computer program had significant reductions in the cost of anti-infective agents, total hospital costs, and length of hospital stay.

Substitution or rotation of antibiotics has been proposed as a method for decreasing the prevalence of antibiotic-resistant pathogens. Gerding et al[45] reported that substitution of amikacin for gentamicin led to a significant reduction in resistance to gentamicin and tobramycin among Gram-negative bacilli. However, the first attempt to reintroduce gentamicin led to a resurgence of gentamicin resistance. Kollef and coworkers[46] replaced ceftazidime with ciprofloxacin for empiric therapy for ventilator-associated pneumonia and demonstrated a reduction in the incidence of ventilator-associated pneumonia attributed to antibiotic-resistant Gram-negative bacteria. However, limitations with this study preclude accepting its conclusion that a scheduled change of antibiotic classes can reduce the incidence of ventilator-associated pneumonia. First, the incidence of pneumonia declined for unclear reasons. Second, only a single change was evaluated rather than multiple changes. Finally, the follow-up period was only 6 months.

Conclusions

Nosocomial infections, especially those caused by antibiotic-resistant pathogens, represent an important source of morbidity and mortality for the patient hospitalized in an ICU. Important antibiotic-resistant nosocomial pathogens include MRSA, VRE, Gram-negative bacilli (especially, Klebsiella and Enterobacter) producing extended-spectrum β-lactamases, multiple drug-resistant *M tuberculosis,* and fluconazole-resistant Candida sp.

The key to control of antibiotic-resistant pathogens in the ICU is rigorous adherence to infection control guidelines and prevention of antibiotic misuse. Antibiotic restriction policies clearly result in reduced drug costs. Evidence suggests that reducing use of certain antibiotics may lead to a decreased prevalence of antibiotic-resistant pathogens: vancomycin, VRE; gentamicin, gentamicin-resistant Gram-negative bacilli; and, ceftazidime, Gram-negative bacilli producing extended-spectrum β-lactamases. Limited data suggest that measures to control antibiotic use do not adversely affect—and may actually improve—patient outcomes (*eg*, decreased length of stay, risk of subsequent infection).

Unfortunately, relatively few appropriately designed studies have evaluated the impact of antibiotic- and infection-control interventions on the prevalence of antibiotic resistance among nosocomial pathogens and on patient outcomes. The efficacy of intensive antibiotic control should be assessed in multicenter studies designed to avoid methodologic flaws.[47] Preventing the emergence of multidrug-resistant microorganisms requires the adoption of a multifaceted approach.[48]

Appendix/Discussion

Dr. Weber: I just want to go over briefly the nosocomial guidelines from the American Thoracic Society. These have a complicated scheme based on risk factors, onset of disease, etc. One of the weaknesses of the guidelines is that they just tell you to use a quinolone or a β-lactam/β-lactamase inhibitor combination. I do not think many of us would use ampicillin/sulbactam in the ICU for nosocomial pneumonia, but that would meet the American Thoracic Society guidelines. I have updated this and added specific drugs. I believe that appropriate drugs would include piperacillin/tazobactam, cefotaxime, ceftriaxone, and cefepime. If you have anaerobes, they suggest adding clindamycin. If you are worried about that, you can use piperacillin/tazobactam alone.

If the patient has severe pneumonia, then it is an aminoglycoside, ciprofloxacin, or trovafloxacin plus one of the other drugs we just mentioned. In the ICUs in general, people are going to pick one of the combinations of piperacillin/tazobactam, ceftazidime, cefepime, imipenem, or meropenem with ciprofloxacin, trovafloxacin, or an aminoglycoside. I think that is going to be the standard therapy in ICUs, plus or minus vancomycin, depending on MRSA.

So antibiotic resistance is a growing problem and control of antibiotic use is crucial, but few guidelines can aid the clinician in what interventions to use. There are very limited data demonstrating effective control measures for outcomes other than cost. Most guidelines and multiple studies suggest that vancomycin should be limited, and that an increase in cephalosporin use increases the likelihood of VRE and extended-spectrum β-lactamase. Obviously piperacillin/tazobactam is an excellent therapy for several common ICU infections, such as pneumonia, and may have a reduced risk of precipitating resistance.

Dr. Campbell: For prior authorization of an antibiotic, does the prescribing physician call the infectious disease specialist to ask, "May I use this drug?"

Dr. Weber: That is what we were doing up to about 8 years ago. The prescribing physicians would have to call the infectious diseases specialist, and then the infectious diseases specialist would ask, "Why do you want to use that?"

Dr. Campbell: This may work in a university or Veterans Affairs hospital, but once you try to move it into private hospitals—you cannot do it.

Dr. Weber: I agree that it is particularly hard in the private hospitals. Now we have moved away from prior authorization, and pharmacy has a set of guidelines as to which antibiotics should be used, depending on the clinical issues.

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