Reduction in Rates of Methicillin-Resistant *Staphylococcus aureus* Infection after Introduction of Quarterly Linezolid–Vancomycin Cycling in a Surgical Intensive Care Unit

ROBERT L. SMITH,¹ HEATHER L. EVANS,¹ TAE W. CHONG,¹
SHANNON T. MCELEARNEY,¹ TRACI L. HEDRICK,¹ BRIAN R. SWENSON,¹
W. MICHAEL SCHELD,² TIMOTHY L. PRUETT,^{1,2} and ROBERT G. SAWYER^{1,3}

ABSTRACT

Background: The burden of infection with antibiotic-resistant gram-positive cocci, including methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE), continues to increase, leading to substantial morbidity and high mortality rates, particularly in intensive care units (ICUs). Creative interventions may be required to reverse or stabilize this trend.

Methods: The efficacy of empiric cycling of antibiotics active against gram-positive organisms was tested in a before–after intervention in a single surgical ICU. Four years of baseline data were compared with two years of data compiled after the implementation of a strategy where the empiric antibiotic of choice for the treatment of gram-positive infections (linezolid or vancomycin) was changed every three months. Whatever the initial choice of drug, if possible, the antibiotic was de-escalated after final culture results were obtained. The rates of all gram-positive infections were analyzed, with a particular focus on MRSA and VRE. Concurrently, similar outcomes were followed for patients treated on the same services but outside the ICU, where cycling was not practiced.

Results: During the four years prior to cycling, 543 infections with gram-positive organisms were acquired in the ICU (45.3/1,000 patient-days), including 105 caused by MRSA (8.8/1,000 patient days) and 21 by VRE (1.8/1,000 patient-days). In the two years after implementation of cycling, 169 gram-positive infections were documented (28.1/1,000 patient-days; $p < 0.0001$ vs. non-cycling period), including 11 caused by MRSA (1.8/1,000 patient-days; $p < 0.0001$ vs. non-cycling period). The percentage of *S. aureus* infections caused by MRSA declined from 67% to 36%. The rate of infection with VRE was unchanged. Outside the ICU, the yearly numbers of infections with both MRSA and VRE increased over time.

Conclusion: Quarterly cycling of linezolid and vancomycin in the ICU is a promising method to reduce infections with MRSA.

Departments of ¹Surgery, ²Internal Medicine, and ³Public Health Sciences, University of Virginia, Charlottesville, Virginia.

THE EFFICACY OF CYCLING OR ROTATING antibiotic classes in reversing or forestalling antimicrobial resistance remains controversial. Whereas some studies have implied improvements in antimicrobial resistance patterns or outcomes with cycling, other trials have been largely negative or have even led to worsening of resistance. The majority of these efforts have been in intensive care units (ICUs), undoubtedly because of the greater incidence of isolation of antimicrobial-resistant pathogens in such facilities compared with outpatient or non-ICU wards. In addition, all previous studies have analyzed the utility of cycling to prevent resistance among gram-negative pathogens, likely because of the availability of at least five antibiotic classes to treat the prototypical ICU pathogen, *Pseudomonas aeruginosa*.

Nonetheless, infections caused by resistant gram-positive cocci, most notably methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE), continue to cause substantial morbidity and mortality rates in ICUs, and efforts to reduce their frequency seem worthwhile. Despite the magnitude of the problem, no efforts to reduce resistance in gram-positive organisms specifically by using cycling have been undertaken to date, probably because of the previous unavailability of broad-spectrum agents active against these bacteria. The regulatory approval of linezolid has afforded the opportunity to examine this intervention. Logically, intermittent cycling of linezolid and vancomycin would be expected to decrease the rate of resistance among enterococci, with the periodic relief of VRE selection pressure during periods of linezolid use and vancomycin non-use. The current study was undertaken to test the hypothesis that quarterly cycling of linezolid and vancomycin would reduce the rate of infection with VRE in a surgical ICU and that it would not significantly alter the prevalence of MRSA.

PATIENTS AND METHODS

This study was approved by the University of Virginia Human Investigation Committee. Data were collected from 1 December 1997 to 30 November 2003. All patients admitted to the surgical/trauma ICU who were on the trauma,

general surgery, or transplant surgery services were evaluated for the presence of infection, identified by every-other-day chart review, house staff/attending interviews, and review of daily antibiotic usage and laboratory and microbiologic data. To ensure consistency, all data were reviewed and entered in a computer format by a single investigator (RGS). Data were coded and analyzed without patient identifiers according to Institutional Review Board standards.

The experimental format was a before–after design. During the first four years of the study (1 December 1997 to 30 November 2001), patients with a possible gram-positive infection were given either vancomycin or a beta-lactam antibiotic empirically according to the clinical situation. In general, vancomycin was used in patients known to be colonized or infected with MRSA, or who had gram-positive cocci on initial Gram stain of a clinical specimen if there was suspicion of a new infection. A beta-lactam antibiotic or sometimes another antibiotic class was used empirically in patients with mixed infections or in whom only gram-negative pathogens were suspected. During the final two years of study (1 December 2001 to 30 November 2003), the antibiotic of choice for the empiric treatment of gram-positive infections was cycled every three months between linezolid (first cycle, 1 December 2001 to 28 February 2002) and vancomycin (first cycle, 1 March 2002 to 31 May 2002). The empiric choice was modified occasionally by allergy or a high suspicion of infection with VRE, in which case, linezolid was preferred. De-escalation to a different class of antimicrobial (most commonly a beta-lactam agent) was practiced during all six years. Throughout the study, vancomycin was given in a dose that achieved a trough serum concentration of 15–20 mcg/mL. The duration of therapy was left to the discretion of the treating physician, as no guidelines were in place with regard to this treatment parameter. Generally, antibiotics were stopped on the basis of the clinical status, including the resolution of fever and leukocytosis, and weaning from mechanical ventilation in the case of pneumonia.

Intensive insulin therapy with a serum glucose target of 80–110 mg/dL was initiated early in 2003. Also, for more than a decade, patients in our hospital have undergone weekly screen-

TABLE 1. DEMOGRAPHICS AND INFECTION RATES OF PATIENTS ADMITTED TO THE ICU, BY PERIOD

	No cycling	Cycling	P value
Months	48	24	—
Dates	12/1/97–11/30/01	12/1/01–11/30/03	—
Admissions	2,765	1,429	—
Patient days	11,979	6,012	—
Mean age (years)	55.6 ± 0.2	56.2 ± 0.4	0.13
Condition (%)			
Trauma	1,038 (38)	504 (35)	—
Non-trauma, non-transplant	1,589 (57)	849 (60)	—
Transplant	138 (5)	76 (5)	—
APACHE II score	18.7 ± 0.3	18.3 ± 0.3	>0.2
ICU-acquired infections	1,096	419	—
Per 100 admissions	39.6	29.3	<0.0001
Per 1,000 patient-days	91.5	69.7	<0.0001
Infections with gram-positive organism	543	169	—
Per 100 admissions	19.6	11.8	<0.0001
Per 1,000 patient-days	45.3	28.1	<0.0001
Infections with resistant gram-positive cocci	126	25	—
Per 100 admissions	4.6	1.7	<0.0001
Per 1,000 patient-days	10.5	4.2	<0.0001

APACHE = Acute Physiology and Chronic Health Evaluation; ICU = intensive care unit.

ing for nasal colonization with MRSA and rectal colonization with VRE unless they are known to be colonized or infected with these pathogens already. Patients found to be infected or colonized are kept in strict contact isolation until three negative screening cultures have been obtained. During the period of the study, the percentage of new admissions to the ICU who were found to be colonized was 4% for MRSA and 1% for VRE, and this did not change between the non-cycling and cycling periods. Dispensers for alcohol hand gel hand were in use uniformly in our hospital throughout the study. The majority of our current ventilator-associated pneumonia bundle also was in place during the entire study, including elevation of the head of the bed to 30° when possible, early aggressive extubation, daily reduction in sedation, and chlorhexidine mouth rinses.

All patients admitted to the ICU had basic demographic data recorded, as well as calculation of the Acute Physiology and Chronic Health Evaluation (APACHE) II score [1] based on variables within 24 h of ICU admission. The U.S. Centers for Disease Control and Prevention definitions were used for all infections [2], including quantitative cultures from an endotracheal aspirate for the diagnosis of pneumonia, where isolation of $> 10^5$ colony-forming units (CFU)/mL of a predominant organism from an appropriately obtained culture was re-

quired. For each infection, multiple variables were recorded, including demographic, microbiologic, and pharmacologic data. The APACHE II score was recalculated at the time of diagnosis of infection. Additional categorical variables were recorded, including established comorbidities, need for transfusion of blood products, and presence of trauma or an allograft. Concurrently, similar data were collected on all patients treated for infection on the non-ICU trauma, general, and transplant surgery units. All infected patients were followed until the end of their hospitalization for any subsequent infection or in-hospital death.

The primary outcome measure was the incidence of infection, specifically with gram-positive cocci and resistant gram-positive cocci, defined as MRSA or VRE. All microbiology testing was performed in the University of Virginia Health System clinical laboratories. For each infection, each isolate was counted only once. Rates of infection were normalized to both 100 ICU admissions and 1,000 ICU patient-days.

Continuous variables were compared using the Student *t*-test, and categorical variables were compared using χ^2 analysis with Yates correction. All *p* values are two-tailed, and values ≤ 0.05 were considered statistically significant. Except as otherwise specified, the values provided are means $\pm$ standard errors or percentage of the group of origin.

TABLE 2. INFECTION AND MORTALITY RATES FROM INFECTIONS WITH *S. aureus* AND ENTEROCOCCI

	No cycling	Cycling	P value
All <i>S. aureus</i> infections	157	31	—
Per 100 admissions	5.7	2.2	<0.0001
Per 1,000 patient-days	13.1	5.2	<0.0001
In-hospital deaths (per year)	56 (14.0)	2 (1.0)	—
Methicillin-sensitive <i>S. aureus</i>	52	20	—
Per 100 admissions	1.9	1.4	>0.2
Per 1,000 patient-days	4.3	3.3	>0.2
In-hospital deaths (per year)	15 (3.8)	0	—
Methicillin-resistant <i>S. aureus</i>	105	11	—
Per 100 admissions	3.8	0.77	<0.0001
Per 1,000 patient-days	8.8	1.8	<0.0001
In-hospital deaths (per year)	41 (10.3)	2 (1.0)	—
All enterococci	115	62	—
Per 100 admissions	4.2	4.3	>0.2
Per 1,000 patient-days	9.6	10.3	>0.2
In-hospital deaths (per year)	39 (9.8)	25 (12.5)	—
Vancomycin-resistant enterococci	21	14	—
Per 100 admissions	0.76	0.98	>0.2
Per 1,000 patient-days	1.8	2.3	>0.2
In-hospital deaths (per year)	11 (2.8)	5 (2.5)	>0.2

RESULTS

Table 1 gives the basic demographics for all patients admitted during either period of study, as well as the infection rates for all pathogens, all gram-positive cocci, and all targeted resistant gram-positive cocci, defined as MRSA and VRE. The baseline admission demographics were similar in the two periods of the study. The overall rate of ICU-acquired infection decreased significantly after the institution of antibiotic cycling, as did the rates of all gram-positive infections and infections caused by MRSA or VRE.

Table 2 presents a further analysis of the rates of infection with and death caused by *S. aureus* and enterococci. Quarterly cycling of linezolid and vancomycin was associated with a significant decline in the rate of infection with MRSA, as well as a decline in the mean yearly number of deaths after MRSA infection, from 10.3 to 1.0. There was no change in the rates of infection with methicillin-sensitive *S. aureus* (MSSA), any *Enterococcus*, or VRE. All VRE were *E. faecium*.

Table 3 presents data regarding the site of all *S. aureus*, MSSA, and MRSA infections. For both organisms, the lung was the predominant site. As noted before, cycling was associated with a decrease in the rate of isolation of MRSA

from all sites. A significant decrease also was noted for pneumonia and vascular catheter infections caused by MRSA.

Figure 1 depicts the number of MRSA infections treated by the surgical services in the ICU, the non-ICU wards (where cycling was not practiced), or outside the hospital during all six years of the study. After initiation of cycling in the ICU between years 4 and 5, infections caused by MRSA became more common outside than inside the ICU, and the predominant drug-resistant gram-positive pathogen isolated in the ICU became VRE rather than MRSA. Ideally, statistical analysis would be performed on the rates of infection on the ICU and non-ICU wards, but accurate denominators for admissions to the non-ICU wards could not be derived because of the mixture of surgical and non-surgical patients on those units.

Figure 2 gives the percentage of all infections caused by *S. aureus* that were MRSA for infections acquired inside (N = 116) and outside (N = 160) the ICU. Although the percentage of all *S. aureus*-caused infections that were MRSA was stable across the two study periods for non-ICU-acquired infections, it declined from 66.9% to 35.5% (p = 0.002) for ICU-acquired infections after the initiation of cycling. As expected, the distribution of sites of infection was

TABLE 3. SITES OF INFECTION WITH *S. AUREUS*

	No cycling	Cycling	P value ^a
All <i>S. aureus</i>	157	31	—
Lung	99 (3.6 /8.3)	24 (1.7 /4.0)	0.0005
Blood	17 (0.61/1.4)	3 (0.21/0.50)	0.07
Vascular catheter	15 (0.54/1.3)	0 (0 /0)	>0.2
Surgical site	9 (0.33/0.75)	2 (0.14/0.33)	>0.2
Abdomen	6 (0.22/0.50)	2 (0.14/0.33)	>0.2
Urine	4 (0.14/0.33)	0 (0 /0)	>0.2
Pleura	3 (0.11/0.25)	0 (0 /0)	>0.2
Other	4 (0.14/0.33)	0 (0 /0)	>0.2
Methicillin-sensitive <i>S. aureus</i>	52	20	—
Lung	41 (1.5 /3.4)	17 (1.2 /2.8)	>0.2
Blood	6 (0.22/0.50)	0	0.18
Vascular catheter	1 (0.04/0.08)	0	>0.2
Surgical site	0	2 (0.14/0.33)	>0.2
Abdomen	0	1 (0.07/0.17)	>0.2
Urine	2 (0.07/0.17)	0	>0.2
Pleura	3 (0.11/0.25)	0	>0.2
Other	2 (0.07/0.17)	0	>0.2
Methicillin-resistant <i>S. aureus</i>	105	11	—
Lung	58 (2.1 /4.8)	7 (0.49/1.2)	<0.0001
Blood	11 (0.40/0.92)	3 (0.21/0.50)	>0.2
Vascular catheter	14 (0.51/1.2)	0	0.01
Surgical site	9 (0.33/0.75)	0	0.07
Abdomen	6 (0.22/0.50)	1 (0.07/0.17)	>0.2
Urine	2 (0.07/0.17)	0	>0.2
Pleura	3 (0.11/0.25)	0	>0.2
Other	2 (0.07/0.17)	0	>0.2

^aDifference in rates per 100 admissions. All significant numbers also are significant as measured by 1,000 patient-days.

different for ICU-acquired and non-ICU-acquired infections. The most common sites of ICU-acquired MRSA infections were lung (65 cases; 56%), blood (34 cases; 21%), abdomen (25 cases; 16%), and surgical site (22 cases; 14%); among non-ICU-acquired infections, they were lung (40 cases; 25%), blood (14 cases; 12%), catheter (14 cases; 12%), surgical site (9 cases; 8%), and abdomen (7 cases; 6%).

Table 4 gives outcomes for all gram-positive infections segregated by initial treatment with vancomycin, linezolid, or any other agent (including no antibiotic) during the four baseline years without linezolid–vancomycin cycling. It has been postulated that treatment with vancomycin leads to inferior outcomes than treatment with other agents. No statistically significant differences were seen in the number in-hospital deaths according to initial empiric therapy, although there was a trend toward a higher in-hospital death rate with the empiric use of vancomycin for all gram-positive infections ($p = 0.06$ for the difference) and lung in-

fections ($p = 0.08$ for the difference) during the four years without cycling.

Table 5 gives the outcomes of gram-positive infections by initial treatment during the two years of linezolid–vancomycin cycling. Outcomes were not different according to the antibiotic given initially. In Tables 4 and 5, the relatively high associated unadjusted in-hospital mortality rates probably are related to the severity of the underlying illness rather than the infections themselves. In addition, a number of the surgical site infections were organ/space infections and would be expected to have associated mortality rates closer to that observed after hospital-acquired intra-abdominal infections than to those associated with incisional infections.

Throughout all six years, all *S. aureus* isolated exhibited a minimum inhibitory concentration (MIC) for vancomycin of ≤ 1 mcg/mL. No linezolid resistance was observed among VRE isolated from ICU-acquired infections, although during the final two years of the study, two iso-

FIG. 1. Number of infections with methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE, all of which were *E. faecium*) treated on surgical services at the University of Virginia Hospital by year and location of acquisition. Linezolid–vancomycin cycling was practiced in the surgical intensive care unit (ICU) during years 5 and 6.

lates from infections on the non-ICU ward had intermediate sensitivity (MIC, 4 mcg/mL). Finally, the rate of ICU-acquired *Clostridium difficile* colitis was similar in the non-cycling period (20 infections; 0.72/100 admissions and 1.7/1,000 patient-days) and the cycling period (7 infections; 0.49/100 admissions and 1.2/1,000 patient-days).

DISCUSSION

The higher rate of antibiotic resistance among bacteria isolated from infections has become one of the key problems among hospitalized patients, particularly those treated in the ICU. A wide variety of methods to reduce these rates have been proposed, including those that are relatively non-specific, such as better hand hygiene, and others that are more specific, such as restricting the use of specific antimicrobials associated with specific pathogens, such as third-generation cephalosporins. Although it is acknowledged widely that antimicrobials exert selective pressure on bacte-

ria, leading to resistance, whether it is possible to manipulate this pressure to improve resistance rates is unclear.

One controversial technique to alter antibiotic pressure beneficially in a geographically defined area involves cycling or rotating the antimicrobials used to treat infections. To date, studies of cycling have had inconsistent results, although some have demonstrated benefits, as judged by various outcomes [3–7]. On the other hand, mathematical models suggest that a strategy of greater antibiotic heterogeneity might lead to better outcomes [8], although one clinical study specifically testing this hypothesis suggested otherwise [9]. Probably because of the wide variety of classes of agents available, all clinical studies to date have analyzed the utility of cycling to improve the rates of resistance among gram-negative pathogens. However, the introduction of linezolid enabled cycling of this drug and vancomycin for the empiric treatment of gram-positive infections in critically ill patients. We report here the first study of cycling of agents active against gram-positive organisms in an attempt to alter the re-

FIG. 2. Percentage of isolates of *Staphylococcus aureus* that were methicillin resistant (MRSA) causing infections on surgical services at the University of Virginia Hospital by location of acquisition. Linezolid–vancomycin cycling was practiced only in the surgical intensive care unit (ICU).

sistance rates for two problematic pathogens, MRSA and VRE.

Although the study was designed to reduce the incidence of VRE in the ICU, this goal was not achieved. Rather, a marked reduction in the rate of infection with MRSA was noted after the introduction of cycling with no change in the rate of recovery of MSSA, leading to a significant reduction in the percentage of *S. aureus* that were MRSA. These changes appeared to be isolated to the ICU, where cycling was practiced, because there was no change in either the

number of MRSA or MSSA infections treated or the percentage of all *S. aureus* that were MRSA outside the ICU on the same surgical services during the same six-year period.

The mechanism of the near-eradication of MRSA from the ICU under study is unclear. It is possible that the intermittent use of linezolid allowed the environmental deletion of *S. aureus* clones subclinically less susceptible to vancomycin that persisted during the four years of baseline data collection. There are no direct data to support this hypothesis, because iso-

TABLE 4. OUTCOMES ACCORDING TO INITIAL EMPIRIC GRAM-POSITIVE ANTIBACTERIAL AGENT WITHOUT CYCLING

	Vancomycin		Linezolid		Other	
	Number	Died (%)	Number	Died (%)	Number	Died (%)
All gram positive	390	119 (31)	3	1 (33)	150	3 (22)
Lung	102	31 (30)	—	—	51	8 (16)
Blood	118	32 (27)	1	1 (100)	36	9 (25)
Vascular catheter	75	29 (39)	—	—	23	5 (22)
Surgical site	22	6 (27)	—	—	14	2 (14)
Other	73	21 (29)	2	0	26	9 (35)
Methicillin-sensitive <i>S. aureus</i>	29	10 (35)	—	—	23	5 (22)
Methicillin-resistant <i>S. aureus</i>	102	40 (39)	—	—	3	1 (33)

TABLE 5. OUTCOMES ACCORDING TO INITIAL EMPIRIC GRAM-POSITIVE ANTIBACTERIAL AGENT DURING CYCLING

	<i>Vancomycin</i>		<i>Linezolid</i>		<i>Other</i>	
	<i>Number</i>	<i>Died (%)</i>	<i>Number</i>	<i>Died (%)</i>	<i>Number</i>	<i>Died (%)</i>
All gram positive	77	22 (29)	58	16 (28)	34	9 (27)
Lung	18	4 (22)	13	2 (15)	14	2 (14)
Blood	30	4 (13)	19	3 (16)	4	1 (25)
Vascular catheter	10	5 (50)	5	1 (20)	1	1 (100)
Surgical site	8	4 (50)	7	5 (71)	6	2 (33)
Other	11	5 (46)	14	5 (36)	9	3 (33)
Methicillin-sensitive <i>S. aureus</i>	6	0	8	0	6	0
Methicillin-resistant <i>S. aureus</i>	8	1 (13)	3	1 (33)	0	0

lates were not tested for heteroresistance, and, in fact, there was never any evidence of MIC “creep” that might have been expected with a relative loss of vancomycin sensitivity. On the other hand, the in-hospital mortality rate in patients infected with *S. aureus* who were treated with any agent decreased after the introduction of cycling (although the numbers were too small to confirm statistical significance), perhaps implying the environmental loss of one or more virulent clones.

It is possible that the reduction in the rate of MRSA infection was related to other changes in care unrelated to cycling. No systematic changes in infection control practice were made between the two periods studied, however. The same isolation procedures, use of alcohol-based hand hygiene, infection prevention techniques (such as full barrier precautions for the placement of central venous catheters and semirecumbency for mechanical ventilation), and methods for the diagnosis of infection were used throughout. It is possible, of course, that compliance with all of these preventive steps improved over time; this was not measured. If this was the case, however, one would have expected to see a reduction in all infections and no change in the ratio of MRSA to MSSA infections. We did note a decrease in the rate of pneumonia caused by gram-negative organisms during the same period (data not shown), but to a much lesser degree than seen for MRSA, and did not find a significant decline in gram-negative catheter-related blood stream infections. In addition, any undocumented changes in infection control or prevention

process would have been expected to affect the rates of non-ICU acquired infection similarly, as they would have been prescribed by the same protocols, but this result was not observed. Finally, another possible explanation for changes in the prevalence of MRSA is undocumented changes in the usage of other antimicrobial agents. For example, changes in the use of cephalosporins with activity against MSSA might change selection for MRSA. Although there was no documented change in the therapeutic use of cephalosporins between the periods studied, alterations in prophylactic use (which was not tracked) may have occurred.

Several weaknesses of the current study deserve mention. First, it was carried out in a single ICU, and the applicability to other ICUs or patient populations is unproved. Second, the overall approach was a before–after design, rather than randomization, a design forced by the lack of availability of an appropriate control unit. Theoretically, a follow-up period without cycling demonstrating a return to baseline rate of MRSA infections would have strengthened the results, but the authors instead have undertaken a second study examining daily cycling as a model of heterogeneity, the results of which are being analyzed. Third, these data do not address the supposition that completely heterogeneous use of linezolid and vancomycin would improve results further, as predicted by mathematical models. As noted, a two-year analysis of this question has been completed, and the data from this intervention are being analyzed. Fourth, subtle or undocumented changes in the usage of other

antibiotics (therapeutic or prophylactic) may have occurred, leading to variations in MRSA selection pressures that were not taken into account. Finally, the cost of linezolid is greater than that of vancomycin, and specific antibiotic cost data for these patients in our ICU are not available. However, the significant reduction in the empiric use of either vancomycin or linezolid attributable to a decrease in the number of all gram-positive infections, as well as the ability to de-escalate more frequently to beta-lactam antibiotics with a reduction in the number of MRSA infections, probably led to relative cost neutrality with cycling.

It is interesting that quarterly cycling of classes of antimicrobials for infections with gram-negative bacteria has been relatively unsuccessful in changing resistance rates, at least in medical ICUs [10]. There could be several reasons, including the fact that the number of gram-negative pathogens targeted is greater than for cycling of drugs against gram-positive organisms, and that the relative representation of various sites of infection is different in medical and surgical ICUs. In addition, the rapidity with which relevant gram-positive bacteria, including MRSA, become resistant to either vancomycin or linezolid probably is less than for gram-negative pathogens against the antimicrobial agents used to treat them. Thus, it is possible a three-month cycle of a gram-negative agent will lead to resistance more frequently than will a three-month cycle of either linezolid or vancomycin.

Overall, the data suggest that quarterly cycling of linezolid and vancomycin for the empiric treatment of gram-positive infections in the ICU may be effective in reducing the frequency of infections with MRSA. Further studies will be needed in other ICUs with high rates of isolation of this pathogen to confirm these findings.

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Address reprint requests to:
Dr. Robert G. Sawyer
Department of Surgery
University of Virginia HSC
Charlottesville, VA 22908-0709

E-mail: rws2k@virginia.edu