Editorial

Prevention and Control of Vancomycin Resistance in Gram-Positive Coccal Microorganisms: Fire Prevention and Fire Fighting

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Vancomycin was introduced 40 years ago for use against penicillin-resistant staphylococci, but, because of its toxicity and the introduction of methicillin, vancomycin soon became an alternate agent and assumed the role of second-line therapy.[1] With the appearance of methicillin resistance in *Staphylococcus aureus* and coagulase-negative staphylococci in the past two decades and penicillin resistance in enterococci in the last decade, vancomycin has been reintroduced as an important therapeutic agent. The vancomycin preparations now available are purer, and their use is fraught with fewer reactions than the preparation introduced 40 years ago. Thus, vancomycin now is used extensively for treatment of infections caused by gram-positive coccal microorganisms resistant to b-lactam antibiotics. The use of vancomycin has been increased further by the discovery of *Clostridium difficile* as the cause of antibiotic-associated colitis and by the finding that vancomycin given orally is effective therapy.[2]

The widespread use of vancomycin has led to the appearance of vancomycin resistance in enterococci and in *Staphylococcus haemolyticus.*[3-8] The exact role for other antibiotics in the selection of vancomycin resistance is unclear, but the use of other antibiotics also has been shown to be related to the acquisition of vancomycin-resistant enterococci (VRE).[6,8] Given the intrinsic resistance of enterococci to third-generation cephalosporins, it would be interesting to speculate that selection for vancomycin resistance occurred against the background of increased numbers of enterococci in the gastrointestinal tracts of seriously ill patients, selected out by treatment with these agents. Gentamicin resistance in enterococci appeared more than a decade ago, and many strains of VRE also are resistant to gentamicin.[9] This high level of multiple-drug resistance has made it difficult, if not impossible, to treat many infections due to VRE and has given VRE a selective advantage for colonization and infection of seriously ill patients with suppressed host defenses who receive multiple antibiotics.

With the emergence of VRE has come multiple reports of VRE outbreaks in hospitals.[5-7,10-15] Thus, once again, fire prevention has failed, and it is necessary to find the resources needed for fire fighting. In an editorial in this journal 4 years ago, Goldmann summed it up well.[16] "Rapid detection must be accompanied by speedy deployment of effective containment and control measures. Prompt initiation of an effective strategic plan requires an alert, well-trained, interdisciplinary 'strike force,' including individuals with expertise in infection control, epidemiology, and microbiology." He also aptly noted that hospital epidemiologists would need to prepare themselves for a struggle with hospital administrators as they tried to muster these resources. As managed care moves across the country, fire departments will

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shrink in size, further highlighting the necessity for effective fire prevention.

While many outbreaks have been controlled, some have not been controlled.[5-7,11,15] Even when control is successful, permitting outbreaks to occur and then controlling them will always cost more than prevention, aside from the cost of the morbidity and mortality in patients who become infected.

In September 1995, a fire-fighting manual entitled *Recommendations for Preventing the Spread of Vancomycin Resistance* was published by the Centers for Disease Control and Prevention (CDC).[3] The document was prepared by the Hospital Infection Control Practices Advisory Committee (HICPAC). A unique feature of this document was that recommendations for prevention were placed first. This section, entitled "Prudent Vancomycin Use," provided a list of appropriate uses for vancomycin and a list of situations for which vancomycin use should be discouraged. At the end of this section, two important points were made for enhancing compliance with recommendations:

- "Although several techniques may be useful, further study is required to determine the most effective methods for influencing the prescribing practices of physicians.
- Key parameters of vancomycin use can be monitored through the hospital's quality assurance/improvement process or as part of the drug-utilization review of the pharmacy and therapeutics committee and the medical staff."[3]

In this issue of *Infection Control and Hospital Epidemiology,* Evans and Kortas lead the way in publishing the first comparison of vancomycin use in a hospital with the HICPAC recommendations.[17] They made use of readily obtainable data and commonly used survey techniques to define the degree of compliance of vancomycin-prescribing patterns in their hospital with HICPAC recommendations. The survey apparently was done prior to any attempt at the authors' institution to implement the HICPAC recommendations, and the results represent vancomycin use at baseline. The finding that about two thirds of the vancomycin prescribed was used inappropriately confirms our suspicions that vancomycin has been misused extensively and that major efforts need to be directed toward control and prevention of this misuse. While this study was performed at a single institution, it is hard to imagine that, in the absence of formal control programs, this is not the situation at most institutions across the country.

Armed with these data, Evans and Kortas plan to design and implement a program to improve the prescribing patterns of vancomycin in their institution. We all will have to perform similar studies if we want to be more fire marshals than fire fighters and, to the extent possible, replace control with prevention.

In addition to being the first to publish this type of study, Evans and Kortas made two other important contributions. First, the authors defined an approach in assessing compliance with the first HICPAC recommendation for appropriate use of vancomycin. While this recommendation indicates that vancomycin should be used for treatment of serious infections caused by b-lactam–resistant gram-positive microorganisms, it fails to distinguish between patients with culture-proven infections and patients with presumptive infections (cultures yielding gram-positive cocci in clusters) and between patients with culture-proven infections with b-lactam–resistant gram-positive microorganisms and patients with culture-proven infections with presumptive b-lactam–resistant gram-positive microorganisms (antibiotic susceptibility test results pending). They considered all of these situations appropriate for administration of vancomycin pending culture results, but considered empiric use of vancomycin inappropriate if cultures had not been obtained prior to initiation of therapy. This approach to assessing compliance with the first HICPAC recommendation for vancomycin use seems rational and might be considered for use by those who perform such studies in the future.

The second contribution made by these authors was their delineation of three other appropriate indications for the use of vancomycin not contained in the HICPAC recommendations. These included combination of vancomycin with cefotaxime for treatment of presumed *Streptococcus pneumoniae* meningitis, in areas with a high prevalence of penicillin-resistant pneumococci; treatment of *Clostridium difficile* colitis in children who cannot swallow metronidazole tablets or tolerate the metronidazole suspension; and treatment (pending culture results) of patients known to be colonized with methicillin-resistant *Staphylococcus aureus* and, therefore, at increased risk of infection with this microorganism.

Other investigators also may define additional appropriate uses of vancomycin in the future. HICPAC was created by the Hospital Infections Program at the CDC to provide advice on infection control matters, and to prepare and revise guidelines for the prevention of nosocomial infections. Unlike the working groups assembled for the preparation of each guideline in the past, HICPAC is the only group responsible for preparation and revision of infection control guidelines. Without having to wait for many years,

HICPAC can revise any guideline at any time as new scientific information becomes available. HICPAC will need to consider modification of its recommendations for the use of vancomycin as new data like those of Evans and Kortas become available.

HICPAC should be at the forefront of the national effort to prevent the emergence of resistant microorganisms in all healthcare delivery settings. HICPAC published recommendations for the appropriate use of vancomycin, and Evans and Kortas have shown us how these recommendations can be used for development of a program for prevention. A similar approach will be needed to prevent the emergence of nosocomial pathogens resistant to other antibiotics.

If S aureus becomes resistant to vancomycin, it will be conflagration fighting rather than fire fighting. This may be the most urgent reason for making use of Evans and Kortas' approach for developing a preventive program.

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