CD Summary

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VANCOMYCIN-RESISTANT ENTEROCOCCAL INFECTIONS

SINCE THE DAWN of antimicrobial therapy, bacteria have found ways to resist killing by successive generations of antimicrobial agents. Perhaps most illustrative of such bacterial cunning is the enterococcus.

Enterococcus (né *Streptococcus*) *faecalis* and its less well-known cousin *E. faecium* are part of the normal flora of the human GI tract, but they are a significant cause of nosocomial urinary tract, surgical site, and blood-stream infections.[1] They have always been more difficult to kill than the average Gram-positive coccus; bactericide has generally required synergistic combinations of cell-wall antibiotics and aminoglycosides.[2] In 1979, high-level resistance to gentamicin (MIC's >16,000 µg/ml!) was reported, and in 1983, β-lactamase-producing enterococci were seen. For bacteria resistant to penicillins and aminoglycosides, bacteriostatic activity could be achieved only with vancomycin, and bactericidal activity was wishful thinking.

The final blow was struck in 1986, when resistance to vancomycin was discovered among enterococci in England and in France; in 1987, vancomycin-resistant enterococci (VRE) were isolated from the blood of a U.S. patient. By 1995, 10% of nosocomial enterococcal infections were caused by VRE.[3]

Clinically significant infections with VRE obviously represent a therapeutic nightmare, since they are often resistant to all currently available antimicrobial agents.[4] But more frightening still is the specter of transmission of vancomycin resistance to the more virulent *Staphylococcus aureus*. Vancomycin is the drug of choice for the treatment of infection caused by methicillin-resistant *S. aureus* (MRSA),[5] and we trust that our readers appreciate the gravity of the scenario wherein the gene for vancomycin resistance is transferred from VRE to MRSA. Daring investigators in Scotland accomplished just this *in vitro* and on mouse skin,[6] —subsequently assuring a horrified medical community that all "VRSA" isolates were thereafter destroyed.

OREGON'S DEFENSES BREACHED

Over the last few years, VRE strains, which heretofore predominated in the northeastern United States, have become firmly entrenched in Oregon. A patient colonized with multidrug-resistant *E. faecium* was identified in a Portland-area hospital in October 1994. This patient had been transferred from a facility in the Midwest, where colonization with VRE presumably occurred. Think your patients are safe? Since this first Oregon case was recognized, hundreds more patients have had VRE in this and in several other hospitals in Oregon, and nursing homes have also reported sightings (and no, not all in the Portland area). Most of the patients have merely been colonized, but a few highly compromised individuals have developed bacteremia, recurrent abscesses, or other serious infections.

VRE are survivors, and with each of us providing over 7 meters of colonization opportunities, they are difficult to eradicate. Moreover, once found in patients, investigation often finds them on nearby bed rails, pulse oximeters, glucose monitors, blood pressure cuffs, toilet surfaces, electrocardiographic monitors, doorknobs, nurses' gowns, and in family members. (In one hospital outbreak, VRE was passed from patient to patient on the rectal probe handles of electronic thermometers.[7])

Once colonization with VRE occurs, it has been found to persist for median of 7 weeks, and at least as long as 19 months.[8] Controlling spread of this organism within hospitals has proved difficult. While some facilities have checked VRE outbreaks with stringent contact isolation protocols,[9] others have not found such strenuous efforts worthwhile.[10]

Because VRE infections are very difficult to treat and nearly impossible to eradicate, it is imperative that transmission be stopped. In the hospital, strains of VRE spread predominantly from one person to another on the hands and possibly the clothes of health-care workers. For this reason, CDC and the Hospital Infection Control Practices Advisory Committee (HICPAC) have recommended that contact precautions be used in the management of patients who are colonized or infected with VRE.[11] Contact precautions begin with placement of VRE cases in either private rooms or rooms occupied by other VRE cases. Then, through the use of gloves, gowns, dedicated equipment (e.g., stethoscopes), and hand washing after glove removal, health-care workers can avoid transmitting VRE among patients.

THE ROLE OF VANCOMYCIN

Not unexpectedly, receipt of vancomycin has been identified consistently as a risk factor for colonization or infection by VRE.[11] The best strategy for reducing the number of VRE in the world is ultimately to reduce the selective pressure in their favor—i.e., to reduce vancomycin use and force the VRE to compete on a level playing field with other denizens of the gut. To that end, HICPAC has developed guidelines on prudent vancomycin use. The table (*verso*) lists indications for vancomycin use that are considered appropriate, as well as providing examples of usage patterns to be discouraged. For more detailed recommendations, consult the guidelines[11] (available at *http://www.cdc.gov/ncidod/hip/Aresist/vre.htm*).

Physicians who prescribe vancomycin are encouraged to compare their use with these guidelines. Consult your local infectious disease physician about your favorite indications for vancomycin; try to reduce the selective pressure on your local enterococci.

VRSA NIGHTMARES COMING TRUE?

After years of prognostications, infections caused by "naturally" occurring *S. aureus* with at least intermediate levels of vancomycin resistance have now been reported in Japan and—in the August 22 issue of the MMWR—in the United States as well. We'll have more on this in the *CD Summary* presently.

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Physicians and microbiologists who encounter VRE should report the finding immediately to their infection control practitioners. Isolation of VRE does not *ipso facto* necessitate antimicrobial treatment, but for serious VRE infections (e.g., endocarditis) treatment with quinupristin/dalfopristin (RP 59500=*Synercid*®; Rhône-Poulenc Rorer) can be considered; the compassionate use administrator for this investigational new drug combination is Sharon Cerwinka, 610/454-3071; FAX 610/454-5904.

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VANCOMYCIN: GOOD DOGG E (Uses Endorsed by Experts)

- Treatment of serious infections caused by β-lactam-resistant Gram-positive microorganisms (e.g., MRSA).
- Treatment of infections caused by Gram-positive microorganisms in patients who have serious allergies to β-lactam antimicrobials.
- Treatment of antibiotic-associated colitis that fails to respond to metronidazole therapy or is severe and potentially life-threatening.
- Prophylaxis, as recommended by the American Heart Association, for endocarditis following certain procedures in patients at high risk for endocarditis.[12]
- Prophylaxis for major surgical procedures involving implantation of prosthetic materials or devices (e.g., cardiac and vascular procedures and total hip replacement) at institutions that have a high rate of infections caused by MRSA or methicillin-resistant *S. epidermidis*. A single dose of vancomycin administered before surgery is sufficient unless the procedure lasts >6 hours, in which case the dose should be repeated. Prophylaxis should be discontinued after a maximum of two doses.

VANCOMYCIN: BAD DOGGIE (Inappropriate Use)

- Routine surgical prophylaxis (unless the patient has a life-threatening allergy to β-lactams).
- Empiric therapy for a febrile neutropenic patient, unless initial evidence indicates that the patient has an infection caused by Gram-positive microorganisms (e.g., at an inflamed exit site of Hickman catheter) *and* the prevalence of infections caused by MRSA in the hospital is substantial.
- Treatment in response to a single blood culture positive for coagulase-negative staphylococcus, if other blood cultures taken during the same time frame are negative (i.e., if contamination of the blood culture is likely).
- Continued empiric use for presumed infections in patients whose cultures are negative for β-lactam-resistant Gram-positive microorganisms.
- Systemic or local (e.g., antibiotic lock) prophylaxis for infection or colonization of indwelling central or peripheral intravascular catheters.
- Selective decontamination of the digestive tract.
- Eradication of MRSA colonization.
- Primary treatment of antibiotic-associated colitis (does the word "metronidazole" mean anything to you?).
- Routine prophylaxis for patients on continuous ambulatory peritoneal dialysis or hemodialysis.
- Treatment (chosen for dosing convenience) of infections caused by β-lactam-sensitive Gram-positive microorganisms in patients who have renal failure.