CD Summary

October 14, 1997
Vol. 46, No. 21

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VISA: NOT WELCOME HERE

THE PRE-ANTIBIOTIC era is something most practicing physicians know only from history books.* As discussed recently in these pages,[1] vancomycin-resistant enterococci (VRE) have been a reminder of those days, although the intrinsic low virulence of VRE renders them non-threatening to all but the most severely immunocompromised.

Staphylococcus aureus, on the other hand, is a virulent organism equipped with nasty enzymes and toxins. Anyone with a minor abrasion in the skin is susceptible to *S. aureus* infection, which can range in severity from an annoying case of folliculitis to a rapidly fatal case of acute bacterial endocarditis. For the past half century, physicians and their patients have gone to sleep secure in the knowledge that antibiotics effective against *S. aureus* were on pharmacy shelves. Sure, along the way we lost penicillin, and more recently have been losing even extended-spectrum analogues, such as methicillin, and then cephalosporins. But, although it's expensive, we've still had vancomycin.

A further shot across the bow came in July with the case report of a 4-year-old Japanese boy, who during the summer of 1996 had developed a nosocomial surgical-site MRSA infection. After treatment for several weeks with vancomycin and other antimicrobial agents, *S. aureus* with a vancomycin minimum inhibitory combination (MIC) of 8 µg/mL was recovered from purulent surgical-site discharge.[2] This level of susceptibility was deemed "intermediate,"[3†] and the organism dubbed Vancomycin-Intermediate (susceptibility) *Staphylococcus aureus* (VISA). Following a script written many years ago, it wasn't long before VISA was identified elsewhere—in Michigan.

In July 1997, a Michigan patient undergoing continuous ambulatory peritoneal dialysis contracted peritonitis, apparently caused by VISA (MIC, 8 µg/mL). During the previous 6 months, the patient had been treated with multiple courses of vancomycin for peritonitis caused by MRSA.[4] This August, VISA (MIC, 8 µg/mL) was isolated from the blood of a New Jersey patient following multiple courses of vancomycin treatment during the preceding five months for bloodstream infection with MRSA.[5]

WHENCE THE RESISTANCE?

Despite predictions that staphylococcal resistance to vancomycin would originate in transfer of genetic elements from VRE, the reduced susceptibility to vancomycin seen in the Japanese case was apparently unrelated to mechanisms of resistance seen in VRE.[2] In the two U.S. cases, different susceptibility profiles to other antimicrobial agents tested led investigators to conclude that the strains were unrelated to each other in any direct sense. In other words, the reduced susceptibility to vancomycin was developing de novo as a result of exposure to vancomycin.[5] Call it convergent evolution. For this reason, the most important step in preventing vancomycin resistance is reducing the use of vancomycin, reserving it for those situations in which it is clearly needed.[1,6]

WHAT IS TO BE DONE?

To decrease the likelihood that staphylococci with reduced vancomycin susceptibility will emerge, and to recognize and control them if they do, CDC and the Hospital Infection Control Practices Advisory Committee (HICPAC) have developed interim guidelines.[7] What follows is a summary of these guidelines. The complete text is available on the internet (URL= http://www.cdc.gov/ncidod/hip/Aresist/vre.htm). The guidelines recommend that every health-care facility should develop a plan (before the fact) in which responsibilities for critical personnel are clearly delineated. Key elements of any plan should include:

- **Restricting vancomycin use.** Medical and other staff members responsible for formulary decisions should review their hospital's use of vancomycin, restrict its use to accord with published guidelines,[1,6] and ensure that use of other antimicrobial agents is appropriate.
- **Testing staphylococcal isolates for vancomycin susceptibility using a MIC method** (broth dilution, agar dilution, or agar-gradient diffusion) with a full 24-hour incubation. (N.b.: strains of staphylococci with a MIC = 8 µg/mL were not detected using the current disk diffusion procedure.) Although staphylococci are not considered to be "intermediate" unless the MIC is at least 8 µg/mL, all strains with a vancomycin MIC 4 µg/mL are suspect. They should be retested for susceptibility after the laboratory has ensured that the isolate is in pure culture and confirmed its genus and species. If, after repeat testing, species identification and vancomycin test results are consistent, laboratory staff should contact the Health Division immediately (503/731-4024; nights and weekends 503/731-4030) to report presumptive identification of VISA. We will help arrange confirmatory testing at CDC.
- **A plan to prevent the spread of VISA when it is identified.** The identifying laboratory should immediately notify infection control personnel, the clinical unit, and the attending physician. In turn, infection control personnel should immediately notify the Health Division.**

* sensu lato

† susceptible, ≤4 µg/mL; intermediate, 8-16 µg/mL; resistant, ≥32 µg/mL.

** yes, we realize that means two calls in one night, but we have a belt-and-suspenders attitude about reporting.

CD Summary (ISSN 1058-7888) published biweekly, free of charge, by the Oregon Health Division, a part of the Dept. of Human Resources.
800 NE Oregon St., Portland, Oregon 97232
Second Class Postage paid at Portland, Oregon.
Postmaster—send address changes to:
CD Summary, 800 NE Oregon St., Suite 730, Portland, OR 97232.

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SECOND CLASS POSTAGE **PAID** Portland, Oregon

When VISA is identified, infection control personnel should initiate an epidemiological and laboratory investigation in collaboration with Health Division epidemiologists, to determine the extent and pattern of spread of the organism. This will involve obtaining baseline cultures (even before initiation of contact precautions) for staphylococci with reduced susceptibility to vancomycin from the anterior nares and hands of all health-care workers, roommates, and others with direct patient contact. All personnel who provide direct care for such patients must be informed of the epidemiologic implications of such strains and of the infection-control precautions necessary for their containment.

Compliance with contact precautions and other recommended infection-control practices must be monitored and strictly enforced. The efficacy of these precautions should be assessed by culturing health-care personnel for staphylococci with reduced susceptibility to vancomycin. The Health Division should be consulted before discharging colonized or infected patients. Long term patient follow-up may be indicated.

Hospitalized patients with VISA infections should be isolated in a private room; appropriate contact precautions (gown, mask, glove, and antibacterial soap for hand washing) as recommended for multidrug-resistant organisms are necessary.[8] The number of persons with access to colonized or infected patients must be minimized. Perhaps most onerously, specific health-care workers should be dedicated to the care of these patients. (Yes, doc, that means you, too.)

APOCALYPSE SOON?

The arrival of vancomycin-resistant *S. aureus* has been predicted for many years. Whether this will be as bad as many have feared or will turn out to be the Comet Kohoutek of emerging pathogens remains to be seen. Few seem to be betting on the second scenario, however. Treatment of patients with VISA or VRSA will obviously be a challenge. For information about investigational antimicrobial agents, contact the FDA's Division of Anti-infective Drug Products (301/827-2120). Investigational drug-seeking physicians will be required to send isolates to CDC for microbiologic and epidemiologic evaluation.

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Increase in aseptic meningitis

SEVERAL ALERT PORTLAND-AREA clinicians called OHD during August and September of this year to report an increase in pediatric cases of aseptic meningitis. This malady is known to be most prevalent during the late summer months. Aseptic meningitis is not reportable in Oregon, however, so we have no surveillance baseline against which to judge an increase. Medical records personnel at two large Portland-area hospitals provided us with aseptic meningitis case counts among patients <18 years of age, using discharge ICD-9 codes 047.0 through 047.9. August totals for the two hospitals were 4 cases in 1995, 10 cases in 1996, and 29 cases in 1997.

The number of cases of pediatric aseptic meningitis seen in these hospitals does not ~~seem to be explained~~ merely by ~~seasonal~~ variation; the impressions of our concerned clinicians are borne out by the data. Reasons for the increase are unclear. One hospital sent to the Oregon State Public Health Laboratory viral isolates obtained from CSF or stool of pediatric patients with aseptic meningitis; of 6 isolates typed, two were ECHO 30, two were enterovirus 71, one was ECHO 29, and one was Coxsackie B1. Therefore, our community-wide increase does not represent a point-source infection or even invasion of the area by a single virulent virus.

Aseptic meningitis is usually caused by enteroviruses, which are acquired by the fecal-oral route. This increase in cases may be a good occasion to remind your patients of the importance of hand washing following defecation.