Understanding Vancomycin-intermediate (VISA) and Vancomycin-resistant (VRSA) *Staphylococcus aureus.*

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Vancomycin has been the "last resort" antibiotic for methicillin-resistant *Staphylococcus aureus* (MRSA) infections for many years. Enterococci acquired vancomycin-resistance (typically mediated by the resistance gene *vanA*) in the 1980's. Since then, scientists and physicians have predicted that staphylococci would also acquire the same resistance mechanism, since it is known that these two organisms exchange genes through conjugative plasmids. Fortunately, staphylococci did not acquire that resistance mechanism until recently.

The overwhelming majority of *S. aureus* isolates are vancomycin-susceptible, having an MIC in the range of 0.5-2 μg/ml. Vancomycin-intermediate *S. aureus* (VISA) isolates were first described in Japan in 1997 (Hiramatsu *et al.*, 1997) and subsequently isolated in the United States later that same year. These isolates have a vancomycin MIC between 8-16 μg/ml. The mechanism of resistance in VISA isolates is not completely understood but involves the thickening of the peptidoglycan layer. "True" vancomycin-resistance within *S. aureus* (vancomycin-resistant *S. aureus*-VRSA) was not described until 2002 (Chang *et al.*, 2003). Since that time, two unrelated *S. aureus* strains have been isolated in the United States. These isolates have vancomycin MICs $\geq$32 μg/ml and the resistance is mediated by *vanA* (encoded on a conjugative plasmid). It is important to note that the vancomycin-intermediate result in VISA isolates is not mediated by the same resistance mechanism as found in the enterococci (*vanA*).

Detection methods

Most, but not all, routine automated susceptibility testing methods will detect VISA. These methods include both conventional Microscan® panels (Dade MicroScan, West Sacramento, CA), Vitek® (bioMerieux, Hazelwood, MO.), Vitek® 2, and E-test (using a 0.5 MacFarland suspension; AB Biodisk, Piscatway, NJ) (Marlowe *et al.*, 2001; Tenover *et al.*, 1998; Walsh *et al.*, 2001). Notably, standard 24 hour disk-diffusion methodology will not detect VISA and is therefore not a recommended (Tenover *et al.*, 1998). Laboratories that rely on disk diffusion are recommended to use the vancomycin agar screen plate (composed of brain-heart infusion agar containing 6 μg/ml of vancomycin) which reliably detects VISA. VISA may appear atypical (small-pinpoint colonies) on standard laboratory media and may take 48 hours to grow. Both VRSA isolates were detected using automated susceptibility testing methods, however, more research is needed to fully determine the best methodology to detect these highly resistant pathogens.

Figure 1 denotes a flow chart for the identification of VISA and VRSA. VISA and VRSA are extremely rare in the United States. There have been fewer than 15 confirmed cases of VISA in the United States and only 2 confirmed cases of VRSA. Consequently, all *S. aureus* isolates that are either intermediate or resistant to vancomycin must be confirmed before reporting. If you have any questions regarding VISA or VRSA, or susceptibility testing in general, please call Dr. Paul Fey at 402-559-2122.

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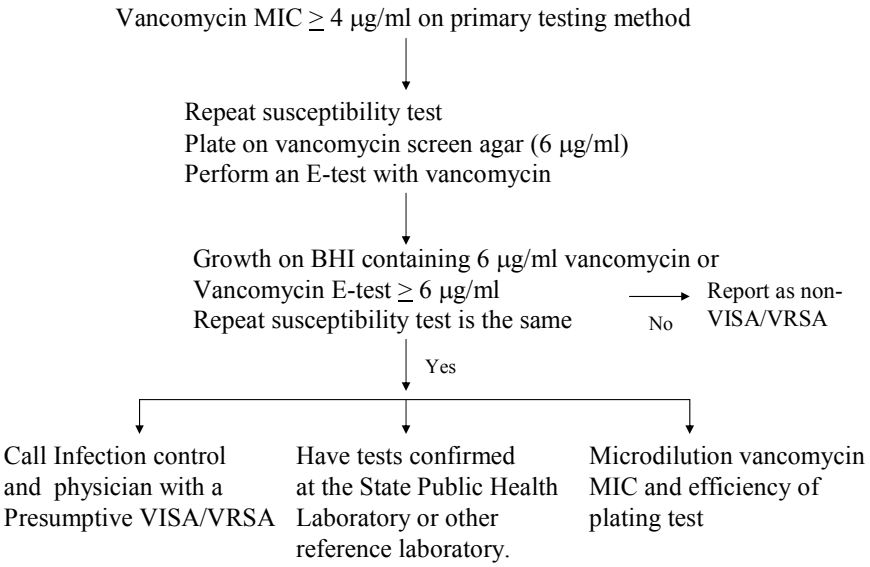
Walsh, T. R., Bolmstrom, A., Qwarnstrom, A., Ho, P., Wootton, M., Howe, R. A., MacGowan, A. P. & Diekema, D. (2001). Evaluation of current methods for detection of staphylococci with reduced susceptibility to glycopeptides. *J Clin Microbiol* **39**, 2439-2444.



If all tests confirm the presence of VISA or VRSA, the isolate will be sent by the NPHL to CDC for confirmation testing.