Detection and Relevance of Hetero-VISA

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Evidence to support the clinical significance of heterogeneous vancomycin resistance in strains of *Staphylococcus aureus* (hetero-VISA or hVISA) continues to accumulate. Although confirmed hVISA isolates are associated with high rates of vancomycin failure, many vancomycin treatment failures appear not to be due to hVISA or VISA. Hetero-VISA strains test "susceptible" in the routine clinical laboratory using the vancomycin breakpoint or interpretive criteria for *Staphylococcus* spp. of the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS). Specifically, these strains have vancomycin MICs ≤ 4 μg/mL as opposed to true VISA strains with "intermediate" vancomycin MICs of 8 to 16 μg/mL. However, h-VISA strains contain subpopulations of daughter cells with vancomycin MICs in the 8 to 16 μg/mL range. Routine susceptibility testing will not reliably detect h-VISA strains because the concentration of the subpopulation of cells expressing resistance is low (1 in 10^4 or 1 in 10^7) and generally below the usual inoculum concentration used in a broth microdilution MIC or standard disk diffusion test. Most of the h-VISA strains that have been reported were MRSA but it has occurred in MSSA. Laboratories are faced with the same problems in detecting hVISA strains as they encountered with the detection of some highly heterogeneous MRSA strains and better methods are needed. Although there are no standardized methods to identify h-VISA, several investigative methods have been described. These include: 1) population analysis profiling (PAP) on vancomycin agar; 2) a variety of spot inoculum screening tests using either BHIA or MHA media containing various concentrations of vancomycin; and 3) the Etest method using a variety of standardized inocula concentrations and agar media. In addition, unusual colony morphology after incubation for 24 to 48 hours can be a clue to h-VRSA. It is important that clinicians alert the clinical microbiology laboratory when they have patients on vancomycin therapy with persistent signs and symptoms of infection ≥ 7 days after initiation of vancomycin therapy, thus allowing a more targeted search for possible hVISA strains in their cultures.