



Vancomycin-Resistant *S. aureus* : Now & Future

Keiichi Hiramatsu

Department of Bacteriology
Juntendo University, Japan

Vancomycin is still a choice of treating severe MRSA infection throughout the world. However, its low cyto-killing activity against MRSA and its low achievable tissue concentration both set limitations to the clinical effectiveness of the drug. First of all, inability of vancomycin to kill MRSA cells allow them to remain in the patients' bodies even after their infections have been successfully treated after vancomycin therapy. In this way, everyday in the world, MRSA cells survive after being exposed to and "selected" by vancomycin, which evidently become more "resistant" to the antibiotic. The increase of vancomycin resistance achieved in this way may not be apparent as can be appreciated easily by MIC determination, since the vancomycin MICs for "susceptible" MRSA strains (0.5~2 mg/L*) and the available tissue concentrations (2~5 mg/L depending on the tissue) are very close. Strains with MIC of 4 mg/L are difficult to treat as reported recently; thus the NCCLS breakpoint for vancomycin (4 mg/L and less, as susceptible) is not valid clinically. It seems that MRSA is increasingly "resistant" to vancomycin within the "susceptible" MIC range defined by NCCLS. Within this groups of strains are hetero-VRSA (or hVISA), which are defined as strains that generate subpopulations of cells with increased vancomycin resistance including those of MIC 8 mg/L (Low-level VRSA:L-VRSA or VISA) at high frequency. First discovered in 1996, the type of vancomycin resistance seems to have become prevalent throughout the world. With this regard, it is curious that two strains of MRSA have been identified that carried *vanA*-gene plasmid. The strains called High-level VRSA (H-VRSA or VRSA) are known to have high MIC of 128 mg/L or above. This "unnecessarily" high level of vancomycin resistance for a human pathogen is reminiscent of the fact that the genes have been derived from the avoparcin-resistant enterococci in the animal farm. Considering the difference in the mechanism of resistance between L-VRSA (thickening of cell wall) and H-VRSA (altered cell-wall component, murein monomer), the latter should have less fitness cost of resistance and grow much faster than the former. Then do we expect rapid dissemination of H-VRSA throughout the world in the near future? Are there any other factor affecting the scenario with regard to the clinical fate of vancomycin?