Vancomycin resistance among epidemic strains of methicillin-resistant Staphylococcus aureus in England and Wales

Sir,

We read with interest the recent report by Geisel et al.\(^1\) of seven strains of heterogeneous intermediate vancomycin-resistant Staphylococcus aureus (hetero-VISA) isolated in the Düsseldorf area of Germany. These isolates belonged to a single clone, an observation that supports the suggestion that some methicillin-resistant S. aureus (MRSA) lineages have greater propensities than others to develop resistance to vancomycin.\(^2\) Homogeneous VISA (homo-VISA) strains, as opposed to hetero-VISA strains, have been isolated in Japan, the USA, France and Hong Kong. All such VISA strains are regarded as ‘intermediate’ because the level of vancomycin resistance (MIC 8 mg/L) is intermediate as defined by criteria recommended by the National Committee for Clinical Laboratory Standards (NCCLS), i.e. MICs \(>4\) and \(<32\) mg/L,\(^3\) although they are ‘resistant’ when susceptibility categories are assigned according to criteria issued by a Working Party of the British Society for Antimicrobial Chemotherapy (BSAC).\(^4\)

Two homo-VISA isolates were recently recovered from two patients in a hospital in Scotland.\(^5\) The strains were unrelated on the basis of molecular typing and did not resemble the epidemic MRSA strains, EMRSA-15 or EMRSA-16 (D. Morrison, Scottish MRSA Reference Laboratory, personal communication). Isolation of a hetero-VISA strain belonging to EMRSA-15 has also been reported from Bristol.\(^6\)

EMRSA-15 and EMRSA-16 are the most prevalent MRSA strains in the UK\(^7\) and account for c. 80\% of S. aureus isolates referred to the Laboratory of Hospital Infection (LHI) for epidemiological typing. To assess the incidence of resistance and hetero-resistance to vancomycin among MRSA isolates in England and Wales, we investigated 303 epidemiologically unrelated EMRSA-15 and EMRSA-16 isolates. One hundred and fifty-four EMRSA-15 isolates and 149 EMRSA-16 isolates were selected from isolates submitted to LHI during 1998-9 by 55 and 61 hospitals, respectively. The hospitals represented all NHS regions of England and Wales and the isolates represented all of the known phage variants of EMRSA-15 and EMRSA-16 strains. The isolates were screened by a modification of the disc diffusion method described previously,\(^8\) which exploits the antagonism between \(\beta\)-lactams and vancomycin exhibited by hetero-VISA strains, but not other S. aureus strains. The isolates were grown overnight in nutrient broth (Difco, Basingstoke, UK) and the suspensions were diluted to achieve a density equivalent to that of a No. 2 McFarland standard and swabbed evenly over the surfaces of plates of brain–heart infusion agar (Difco) containing vancomycin at a concentration of 4 mg/L. Oxacillin discs (1 \(\mu\)g) were placed in the centres of the plates, which were incubated at 37°C for 24 h. Growth of the homo-VISA control, Mu50 (MIC 8 mg/L),\(^8\) was confluent, with the exception of a small zone of inhibition around the oxacillin disc (Figure). The hetero-VISA control, Mu3,\(^8\) was

**Figure.** Detection of a homo-VISA strain (left) and a hetero-VISA strain (right) by the \(\beta\)-lactam/glycopeptide antagonism test.
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inhibited by vancomycin, but there was a 5–10 mm zone of confluent growth around the oxacillin disc and individual colonies were scattered elsewhere on the plate. Three hundred and two isolates of EMRSA-15 and EMRSA-16 did not grow at all on the plates and one EMRSA-15 strain was hetero-resistant (E test MIC 3 mg/L). In pilot studies with strain Mu3, we found that discs containing amoxycillin (2 μg), ceftazidime (30 μg) or cephradine (30 μg) could be used as alternatives to oxacillin in the test; cefmetazole is used in Japan, but discs containing this antibiotic are not widely available in the UK.

Our data suggest that vancomycin resistance and heteroresistance among EMRSA-15 and EMRSA-16 isolates are rare. However, resistance can arise, in EMRSA-15 at least, and microbiologists in the UK must remain vigilant, particularly when strains of S. aureus are isolated from patients who have received prolonged courses of vancomycin or after the apparent failure of vancomycin therapy.

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References