Mupirocin resistance in methicillin-resistant *Staphylococcus aureus* and mupirocin consumption over 10 years in a tertiary hospital

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Introduction and Aims

- Topical mupirocin is widely used to eradicate carriage and prevent infection with methicillin-resistant *Staphylococcus aureus* (MRSA).
- Mupirocin inhibits bacterial protein synthesis by reversibly binding to the enzyme isoleucyl-tRNA-synthetase.
- Two levels of mupirocin resistance have been described: low-level resistance (L-MuR) and high-level resistance (H-MuR) (Table 1).2
- Resistance is reported in up to 65% of MRSA isolates in some institutions.3
- There have been conflicting reports regarding the association between mupirocin use and the emergence of resistance.1,4
- At the University of Geneva Hospitals, mupirocin resistance in MRSA was noted to increase from 9% in 1999 to 80% in 2007 (Figure 1). In 2008, more than 99% of resistant isolates had L-MuR and a sample of 12 non-clonal L-MuR isolates all possessed the V588F point mutation in the isoleucyl-tRNA-synthetase gene5 which was responsible for this resistance phenotype.
- This study aimed to:
  - Determine the prevalence and molecular mechanisms of mupirocin resistance in MRSA blood culture isolates in our institution.
  - Correlate mupirocin use and prevalence of resistance over time.

### Methods

- The study was conducted at the University of Geneva Hospitals (HUG), Switzerland, a tertiary care centre with 2032 beds and 48 314 admissions in 2008. Topical intranasal mupirocin has been used at HUG to decolonise known MRSA carriers since 1994.
- The first 20 non-duplicate MRSA blood culture isolates per year (1999-2008) were selected (1 isolate per patient). Non-viable/contaminated isolates were excluded.
- Isolates were screened for mupirocin resistance using a 0.5 McFarland suspension on Mueller-Hinton agar with a 5μg disk (Becton Dickinson) at 35°C for 18-24 hours.6 Resistance was defined as a zone of inhibition of < 14mm.
- Resistant isolates had MICs with Etests (AB Biodisk, Solna, Sweden)7,8: MIC 8-256 μg/mL = L-MuR; MIC > 256 μg/mL = H-MuR.
- All MRSA isolates had an allelic discrimination assay for the V588F point mutation9 and resistant isolates had a mupA PCR.6
- Mupirocin consumption data (2000-2008) were obtained from pharmacy records.
- Results were analysed using Stata software, version 11.0.

### Results

- The prevalence of mupirocin resistance in our institution is increasing and predominantly consists of L-MuR characterised by the V588F point mutation.
- The V588F point mutation was found in all L-MuR MRSA but was also present in 12 of 14 (86%) H-MuR MRSA and 2 of 85 (2%) sensitive MRSA (Table 2).
- mupA gene was found in all H-MuR MRSA but also in 3 of 89 (3%) L-MuR MRSA.

### Conclusions

- The prevalence of mupirocin resistance in our institution is increasing and predominantly consists of L-MuR characterised by the V588F point mutation.
- This correlates with an increase in mupirocin use over this period.
- Emergence of mupirocin resistance and its impact should be monitored in institutions considering widespread use of this antibiotic for decolonisation.

### References

1. Laupland KB, Conly JM. Clin Infect Dis 2003; 37: 933-938

### Table 1. Phenotypic and genotypic resistance to mupirocin

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>MIC (μg/mL)</th>
<th>Molecular Mechanism</th>
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<tbody>
<tr>
<td>Sensitive (Mu-S)</td>
<td>≤ 4</td>
<td>Wild type</td>
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<td>Low-level Resistance (L-MuR)</td>
<td>8 - 64</td>
<td>Mutations in native tRNA synthetase</td>
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<tr>
<td>High-level Resistance (H-MuR)</td>
<td>≥ 512</td>
<td>Plasmid-mediated mupA</td>
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<td>(novel tRNA synthetase)</td>
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### Figure 1. Mupirocin resistance in MRSA 1999 to 2008

![Figure 1](image1.png)

### Figure 2. Mupirocin resistance in MRSA blood cultures and mupirocin consumption 1999 to 2008

![Figure 2](image2.png)

### Figure 3. Relationship between mupirocin consumption per year and mupirocin resistance

![Figure 3](image3.png)