voricazoline. Primary treatment with amphotericin B or quickly switching from azoles to amphotericin B seems to be mandatory for good clinical outcome. There is no evidence of a clear correlation between the MICs of amphotericin B and outcome of treatment, but high MICs should be taken into consideration for antifungal alternatives. The combination of amphotericin B with caspofungin could have been beneficial in this case.

The patient described here was exposed to azoles previously, in contrast to the majority of azole-naive patients described in the Netherlands. Resistance in antifungal-exposed patients may be expected as any antimicrobial treatment is associated with selective pressure and therefore with a risk of resistance emergence. A. fumigatus resistant to medical azoles has also been recovered from the environment. Molecular typing confirmed that environmental and clinical isolates harbouring cyp51A mutations were clustered, suggesting environmental transmission to azole-naive patients. This suggests that selection through a fungicide-based route may have taken place. TR6/Y121F/T289A-bearing strains have been found throughout the environment in the Netherlands and Belgium, but also recently in India. TR46/Y121F/T289A environmental strains in India were similar to the Dutch clinical strains. All these cases may indicate the rapid and worrisome geographical spread of these new resistance mechanisms, possibly following the same path as TR34/L98H, which now causes therapy-refractory infections worldwide.

Funding
This study was conducted as part of our routine work.

Transparency declarations
None to declare.

References
strain of Acinetobacter baumannii, Hornsey et al. demonstrated that telavancin and colistin in combination was significantly more active than either drug used alone.

As daptomycin does not appear to pose a risk for nephrotoxicity, it is unfortunate that we observed no synergy and a high rate of antagonism (41.2%) in the colistin+daptomycin combinations. To our knowledge, this has not been reported by other workers. Körber-Irrgang et al. reported no antagonism when testing the combination against 10 P. aeruginosa strains using Mueller–Hinton broth supplemented with 50 mg/L calcium. In time–kill studies that involved testing colistin+daptomycin against 15 clinical A. baumannii isolates, Malmberg et al. reported an increase in the initial kill rate (1–4 h) in 13 of the 15 strains compared with colistin alone. They used Mueller–Hinton II broth and agar, which is cation adjusted to a standard calcium ion concentration of 25 mg/L. (C. Malmberg, Antibiotic Research Unit, Uppsala University and Uppsala Academic Hospital, Uppsala, Sweden, personal communication).

We wonder if the antagonism we found with colistin+daptomycin is genuine or is perhaps an artefact of the method used to assess this combination. Daptomycin Etests incorporate daptomycin is genuine or is perhaps an artefact of the method used to assess this combination. Daptomycin Etests incorporate daptomycin combinations.

It is possible, therefore, that direct contact with the calcium from the daptomycin Etest is inhibiting the colistin. This would decrease the availability of colistin for antimicrobial action, resulting in elevation of the MIC, which is borne out by the MIC50/90 of colistin when combined with daptomycin. Whether this explains the antagonism we observed or whether it is indeed genuine remains to be seen. Until this can be resolved, we would urge caution in the selection of methodology for testing colistin+daptomycin combinations.

Funding
This was conducted as part of our routine work.

Transparency declarations
In his capacity as President of the International Society of Chemotherapy I. M. G. frequently requests meeting support for a wide range of diagnostic and pharmaceutical companies, including many of those involved in the manufacture of diagnostics and antibiotics for MRSA. He is also a consultant and/or speaker board member to AstraZeneca, GlaxoSmithKline, Merck, Sharp and Dohme, Novartis and Pfizer, and consultant for Astellas, Becton Dickinson, bioMérieux, Cepheid, Clinigen, Cubist and The Medicines Company. K. E. M.: none to declare.

References

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Pharmacokinetics of oral isavuconazole in a patient after Roux-en-Y gastric bypass surgery

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Keywords: mucormycosis, zygomycosis, antifungal therapy, salvage therapy

Sir,

This is a report describing pharmacokinetic aspects of an orally administered azole antifungal agent, in particular of the investigational agent isavuconazole, in a patient after Roux-en-Y gastric bypass surgery. The patient gave written consent for publication of their medical details.

Table 1. Results of testing colistin in combination with telavancin and daptomycin using Etest against 17 strains of P. aeruginosa

<table>
<thead>
<tr>
<th>Combination</th>
<th>Synergy, FICI ≤0.5</th>
<th>No interaction, FICI &gt;0.5–4.0</th>
<th>Antagonism, FICI ≥4.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colistin + telavancin</td>
<td>1 (5.9%)</td>
<td>16 (94.1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Colistin + daptomycin</td>
<td>0 (0%)</td>
<td>10 (58.8%)</td>
<td>7 (41.2%)</td>
</tr>
</tbody>
</table>