and it would be hard to define contamination in such cases in the absence of a known skin or line source. Therefore, when lactobacill­

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References

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Rapid Emergence of Resistance to Cefepime During Treatment

SIR—I was extremely interested in the article by Limaye et al. [1] about the rapid emergence of resistance to cefepime during treatment, as well as the accompanying editorial by Medeiros [2]. Both raise additional questions concerning the development of resistance to antibacterial agents.

Limaye et al. [1] describe a patient who received ciprofloxacin followed by ceftazidime. Treatment with these antimicrobial agents has been associated clinically with the rapid emergence of resistance, particularly in cases of high-density infections. Reports on the quinolones suggest a 10%–15% risk of emergence of resistant organisms during treatment [3,4]. For the third-generation cephalosporins, the estimated risk of the emergence of resistant Enterobacter species following treatment is 19%–44% [5,6].

As Medeiros explained [2], when a bacterial strain is derepressed it may become resistant to fourth-generation cephalosporins, either through the overproduction of β-lactamases or through an alteration in the permeability of the bacterial outer membrane. The risks of these types of mutations have not yet been assessed clinically. In experimental studies [7], the two-step process for resistance selection has been detailed. Data from studies with use of a high inoculum suggest the prior existence of derepressed bacterial isolates with a subpopulation containing the outer membrane alteration, given that imipenem activity was also reduced [8].

Because of the risk of sequential resistance selection among Enterobacter, Citrobacter, Serratia, and Morganella species expressed initially to third-generation cephalosporins, might it be wiser to initiate therapy with a fourth-generation cephalosporin at the time that the bacterial strains are still susceptible to the third-generation cephalosporins? Patients would benefit from the potency of these compounds and their lower affinity for class 1 β-lactamases and, at the same time, the risk of emergence of resistant strains would be decreased.

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References

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Reply

SIR—Our report on the rapid development of resistance to cefepime during the treatment of a liver transplant recipient with a hepatic abscess underscores the difficulties associated with the management of serious gram-negative infections, particularly among immunocompromised hosts [1]. The accompanying editorial highlights the known in vitro mechanisms of resistance in Enterobacter species and points out the limitations inherent in in vitro resistance testing, particularly as related to the detection of infrequent subpopulations of resistant bacteria [2]. Even with the availability of more sensitive methods for the detection of these subpopulations of resistant bacteria, it is not clear that clinical failure could be accurately predicted, especially in the presence of other adjunctive measures to deal with infection (e.g., a functional immune system and drainage of infected material).