that might require antibiotic treatment and the prescribing physician.

Stephanie Natsch, Marjo E. E. van Kasteren, Bart-Jan Kullberg, and Jos W. M. van der Meer
Division of General Internal Medicine, Department of Medicine, University Hospital Nijmegen, Nijmegen, the Netherlands

References

Reprints or correspondence to: Dr. Jos W.M. van der Meer, Division of General Internal Medicine (541), P.O. Box 9101, 6500 HB Nijmegen, the Netherlands.

Clinical Infectious Diseases 1998;26:1482–3
© 1998 by the Infectious Diseases Society of America. All rights reserved. 1058–4838/98/2606–0054$03.00

Reply
Sir—I am grateful for the comments of Drs. Natsch, van Kasteren, Kullberg, and van der Meer in response to the guidelines published in Clinical Infectious Diseases [1]. The authors raise three key issues: (1) specific recommendations on actions to be taken to reduce the emergence of resistance are lacking, (2) no attention was paid to the streamlining of antimicrobial therapy, and (3) no attention was paid to the role of the clinical microbiology laboratory. We will address their concerns in reverse order. The section on surveillance for resistant organisms including table 2, wherein specific antibiotic testing guidelines are proposed, and the first recommendation in table 7 address the importance of the microbiology laboratory. Although we note that stewardship of antibiotic use will be required to control resistance, it is our belief that a single superior method for attaining this goal has not yet been scientifically established. Hence, several possible approaches are indicated in tables 8 and 9. Finally, the recommendations provided in table 7 are specific but focus on the gathering of data. The problem we encountered is that individual hospitals face quite different problems of resistance and patterns of antimicrobial use. Therefore, we devised the more general guideline illustrated in figure 1, wherein each hospital establishes its own policies based upon local data. In our scheme, the outcomes resulting from implementation of these policies are then monitored to provide a system of continuous improvement within each individual institution.

We hope our response helps clarify the proposed guidelines and the limits of our ability to make specific recommendations based on scientifically sound principles.


From Wyeth-Ayerst Research (Dr. Shlaes), Pearl River, New York; Veterans’ Affairs Lakeside Medical Center (Dr. Gerding), Chicago, Illinois; UMDNJ-Robert Wood Johnson Medical School (Dr. John), New Brunswick, New Jersey; William S. Middleton Memorial Veterans’ Hospital (Dr. Craig), Madison, Wisconsin; SUNY Health Science Center (Dr. Bornstein), Syracuse, New York; Lahey Clinic (Dr. Duncan), Burlington, Massachusetts; Duluth Clinic Limited (Dr. Eckman), Duluth, Minnesota; St. Elizabeth Hospital (Dr. Farrer), Elizabeth, New Jersey; University Hospital (Dr. Greene), State University of New York, Stony Brook, New York; Bronx-Lebanon Hospital Center (Dr. Lorian), Bronx, New York; Tufts University School of Medicine (Dr. Levy), Boston, Massachusetts; Grady Memorial Hospital (Dr. McGowan), Atlanta, Georgia; New Jersey Department of Health (Dr. Paul), Trenton, New Jersey; Kaiser Permanente Medical Center (Dr. Ruskin), Los Angeles, California; Centers for Disease Control and Prevention (Dr. Tenover), Atlanta, Georgia; and St. Elizabeth Hospital Medical Center (Dr. Watanakunakorn), Youngstown, Ohio

References

Reprints or correspondence: Dr. David M. Shlaes, Wyeth-Ayerst Research, 401 North Middletown Road, Pearl River, New York 10965.

Clinical Infectious Diseases 1998;26:1483
© 1998 by the Infectious Diseases Society of America. All rights reserved. 1058–4838/98/2606–0055$03.00

Lactobacillus Bacteremia and Endocarditis

Sir—The article on lactobacillemia by Husni et al. [1] further emphasizes the importance of lactobacillemia as a cause of morbidity and mortality among both immunocompromised and immunocompetent hosts. However, we would like to point out that Lactobacillus should not be considered a contaminant in any case, as was suggested by Husni et al. First, Lactobacillus was not noted to be a contaminant in a large study of blood cultures by Weinstein et al. [2]. Second, there have been no reports that this organism is a skin pathogen. Third, there have been no reports to date of central line infections caused by Lactobacillus. These facts were borne out in our study [3] and by a report of 12 additional cases [4]. Finally, some bacteremias can clear without specific treatment,
and it would be hard to define contamination in such cases in the absence of a known skin or line source. Therefore, when lactobacill-
emia is detected, we would encourage clinicians to consider it a true infection and treat it accordingly.

Suresh Antony, Stephen Dummer, and Charles Stratton
Texas Tech University Medical Center, and Texas Oncology PA, El Paso, Texas; and Vanderbilt University School of Medicine, Nashville, Tennessee

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 antibiotic 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 resist-

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 inocu-

lum 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 ex-
posed 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.

Jacques Acar
Laboratoire de Microbiologie Médicale, Universite Pierre et Marie
Curie, Paris, France

References
1. Limaye AP, Gautum RK, Black D, Fritsch TR. Rapid emergence of resis-


3. Milatovic D, Braveny I. Development of resistance during antibiotic ther-


4. Peterson LR. Clinical infections associated with resistance development.
In: Hooper DC, Wolfson JS, eds. Quinolone antimicrobial agents. 2nd

5. Sanders WE Jr, Sanders CC. Inducible β-lactamases: clinical and epidemi-
ologic implications for use of newer cephalosporins. Rev Infect Dis 1988;
10:830–8.


7. Péchere JC, Vladotiana IR. Development of resistance during ceftazidime

Activity of cefepime against ceftazidime-resistant gram-negative bacilli

Reprints or correspondence: Prof. Jacques Acar, Laboratoire de Microbiolo-
gie Médicale, 185 rue Raymond Losserand, 75674 Paris Cédex 14, France.

Clinical Infectious Diseases 1998;26:1484 © 1998 by the Infectious Diseases Society of America. All rights reserved. 1058–4838/98/2606–0057$03.00

Reply

Sir—Our report on the rapid development of resistance to cefe-
pime 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).