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Letters to the Editor

Clarithromycin Resistance in *Mycobacterium abscessus*

We read with interest the article by Sanguinetti et al. titled "Fatal Pulmonary Infection Due to Multidrug-Resistant *Mycobacterium abscessus* in a Patient with Cystic Fibrosis," which appeared in the February 2001 issue (5). We would like to point out some additional information relating to the authors' comment, "to our knowledge, this is the first evidence of true resistance to clarithromycin, which is considered the most active drug against *M. chelonae*." First, the case report involves *Mycobacterium abscessus*, not *M. chelonae*. The two names are not synonymous and should not be used interchangeably (10). The organisms have different biologies, are readily differentiated in the laboratory, and have different drug susceptibilities (2, 3, 6, 8). (Essentially all cases of chronic lung disease caused by rapidly growing mycobacteria in the setting of cystic fibrosis are due to *M. abscessus* [3].)

Second, there have been several previous reports of acquired clarithromycin resistance in isolates of *M. abscessus* and the closely related *M. chelonae*, and the genetics of this resistance have been well characterized (7, 9, 11). We would especially call the authors' attention to an article describing the study of clarithromycin resistance in a series of 800 isolates of *M. chelonae* and *M. abscessus*. Eighteen of 800 clinical isolates (2.3%) submitted for susceptibility testing between 1990 and 1995 were found to be resistant to clarithromycin; 10 of these isolates were *M. abscessus* (9). The underlying conditions most commonly associated with the development of macrolide resistance in *M. abscessus* following clarithromycin therapy were cystic fibrosis (as in the case reported by the authors) and disseminated cutaneous disease. Sequencing studies of the 23S rRNA gene revealed that 94% of the clarithromycin-resistant isolates had a mutation involving the adenine at position 2058 or 2059 (*Escherichia coli* numbering system). Selected laboratory mutants resistant to clarithromycin had the same mutations, as have other species of mycobacteria and bacteria with acquired clarithromycin resistance (1, 4). The study also revealed that *M. chelonae* and *M. abscessus* have only a single copy of the ribosomal operon in their genome and hence demonstrate susceptibility to a single point mutation resulting in high-level (clinical) resistance.

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Authors' Reply

We thank Dr. Wallace and Dr. Brown-Elliott for their interest in our article, and we appreciate their comments, which were occasioned by the following sentence: "To our knowledge, this is the first evidence of true resistance to clarithromycin, which is considered the most active drug against *M. chelonae*." Regarding the first comment, *M. chelonae* is different from *M. abscessus*; therefore, the use of the term *M. chelonae* was a mistake, due to the fact that *M. abscessus* was formerly designated *M. chelonae* subsp. *abscessus*. It is known that *M. abscessus* is the rapidly growing mycobacterial species most frequently involved in infections of patients with cystic fibrosis (3, 4), but *M. chelonae* (1) and *M. fortuitum* (2) also cause severe lung disease in these patients. With regard to the second comment, our intention was to stress the concept that the described case was the first fatal case of *M. abscessus* infection in a cystic fibrosis patient being associated with a multidrug resistance pattern (including resistance to clarithromycin). In fact, even though there are some reports of infections caused by *M. chelonae* and *M. abscessus* resistant to clarithromycin, as underlined by Dr. Wallace and Dr. Brown-Elliott, only infections caused by *M. chelonae* (5, 7) have been clinically well defined. On the other hand, while Wallace et al. (6) interestingly reported the insurgence of clinical resistance to clarithromycin in rapidly growing mycobacteria, such as *M. abscessus* and *M. chelonae*, isolated from patients with disseminated or chronic lung disease, no mention of the outcome of disease for any patient was made. However, in our report we highlighted the fatal outcome of the *M. abscessus* infection associated with the multidrug resistance pattern of the isolate. In conclusion, we apologize for our inappropriate sentence, recognizing that it should have read as follows: "To our knowl-

edge, this is the first evidence of a fatal infection due to a *M. abscessus* isolate resistant to several drugs, including clarithromycin, which is considered the most active drug against rapidly growing mycobacteria."

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