

APPENDIX E: MICROBIOLOGY

MICROBIOLOGY: 3 CASE REPORTS

- In the first case [Perez-Trallero et al., 2003], a telithromycin-resistant isolate of *S. pneumoniae* was selected under clarithromycin therapy. In January 2002, a 71-year-old Spanish man, who was allergic to penicillin and had a history of chronic obstructive pulmonary disease (COPD), was hospitalized due to pneumonia. The first *S. pneumoniae* strain was isolated from sputum obtained before antibiotic treatment with intravenous levofloxacin was begun. It was susceptible to quinolones, macrolides and telithromycin. On Day 4, intravenous clarithromycin was added but withdrawn after 4 doses. On Day 14, clinical and radiological conditions had deteriorated, and treatment was changed to intravenous clarithromycin and intravenous ciprofloxacin. On the same day, a second pneumococcal isolate resistant to levofloxacin and clarithromycin and intermediate to telithromycin was obtained. Initially, this second isolate was incorrectly reported as clarithromycin-susceptible because of an erroneous record of the result of the disk diffusion method. On Day 24, the patient was discharged with oral clarithromycin. Twenty-four hours later, the patient was readmitted with exacerbation of the RTI and 2 pneumococcal isolates resistant to levofloxacin, clarithromycin, and telithromycin were found within 6 hours. The patient received trimethoprim-sulfamethoxazole for 5 days; a fifth pneumococcal isolate was obtained from a pleural effusion specimen. This isolate was still resistant to levofloxacin and clarithromycin but had reversed susceptibility to telithromycin. The pneumonia completely resolved after 10 days of treatment with vancomycin.
- The second case [Faccone et al., 2005] reports the isolation of a telithromycin resistant *S. pneumoniae* after azithromycin and telithromycin therapy. In July 2002, a 29-year-old woman was admitted to the Instituto de Cardiología y Cirugía Cardiovascular Fundación Favaloro (Argentina) with symptoms of AECB. The patient had a history of COPD and was treated with several courses of antibiotics, including levofloxacin. *Streptococcus pneumoniae* M4256 was isolated from a sputum sample taken at the time of admission, and the patient was empirically treated with azithromycin. The isolate exhibited resistance to levofloxacin and azithromycin but susceptibility to telithromycin. After 3 days of azithromycin treatment, the therapy was switched to 10 days of telithromycin with a good clinical response. A month later, the patient received the same telithromycin scheme as prophylaxis. In October 2002, the patient was readmitted with respiratory symptoms and deteriorating clinical signs. A second *S. pneumoniae*, designated M4243, was isolated from sputum but this time displayed no zone of inhibition to telithromycin by disk diffusion testing. The patient received ampicillin plus vancomycin for 21 days, showing a good clinical outcome. The initial strain was resistant to azithromycin by efflux [*mef(A)* gene] and had an alteration in ribosomal protein L4 in comparison with the typical wild strain R6. The second strain had 2 additional alterations in ribosomal ARN and L22 protein. As stated by the authors, the second strain was isolated after 2 courses of telithromycin, but there were insufficient data to evaluate the role of prior therapy with azithromycin in the selection of the telithromycin resistant strain.
- The third case, in France [Goldstein et al., 2005], describes a patient hospitalized for pneumonia after a 5-day course of telithromycin for AECB with isolation of a telithromycin-resistant *S. pneumoniae*. This case is poorly documented as no initial strain was isolated before telithromycin treatment, making differentiation between emergence of resistance and

treatment failure due to an antibiotic-resistant strain impossible. Here again, the authors describe previous macrolide treatment (roxithromycin).