Long-Term Low Rate of Macrolide-Resistant *Mycoplasma pneumoniae* Strains in Germany

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Mycoplasma pneumoniae is a frequent cause of infections of the lower and upper respiratory tracts of humans. During incidence peaks, which are reported at 3- to 7-year intervals, up to 40% of community-acquired pneumonia cases can be attributed to these bacteria (1). As species of the *Mollicutes* class lack the classical bacterial cell wall, *M. pneumoniae* is intrinsically resistant to all beta-lactam antibiotics. Furthermore, tetracyclines and quinolones are not recommended for children, who are the main patients affected by these infections. Therefore, macrolides are the first-line therapeutic agents for treatment of severe infections. Unfortunately, an increase in macrolide-resistant strains has been reported in many regions worldwide, critically narrowing the treatment options for pediatric patients. Resistance is based on mutations in domain V of the peptidyl transferase loop of the single copy of 23S rRNA of *M. pneumoniae*. More than 95% of resistant strains investigated worldwide show A-to-C/G/T transitions at position 2058 or 2059 (*Escherichia coli* numbering [2]). Previous studies confirmed a low rate of macrolide resistance in *M. pneumoniae* strains circulating in Germany (Table 1). However, different reports described not only regional differences in resistance rates but also relatively rapid change in these (3), requiring regular surveillance of clinical strains for adequate public health measurements.

We retrospectively collected *M. pneumoniae*-positive DNA of respiratory tract samples from patients with symptoms of lower respiratory tract infections in different laboratories. Samples were taken between January 2016 and December 2018 in the eastern part (Dresden, Leipzig, and Berlin regions) of Germany. The 23S rRNA of *M. pneumoniae* was partially amplified and sequenced as described previously (4).

Among 166 samples tested, macrolide resistance was found in 5 specimens (Table 1) sampled in the years 2016 (2 samples), 2017 (2 samples), and 2018 (1 sample), respectively. All strains showed an A-to-G mutation at position 2059.

The low rate of *M. pneumoniae* resistance in Germany corresponds to the situation in other countries in central and northern Europe (5–7). Interestingly, a recent report from neighboring Switzerland demonstrated a rate of macrolide resistance of 9% (8) in samples in a tertiary-care hospital, suggesting differences between out- and inpatients. Four of the five macrolide-resistant strains found in the present study are from inpatients, supporting the hypothesis that not only more-severe cases but also cases with a history of unsuccessful antibiotic treatment may accumulate in hospitals. The constant rate of resistant strains over a period of more than 20 years suggests that resistant strains lack a competitive advantage in a human population moderately exposed to macrolides (9). Nevertheless, clinicians should be aware of treatment failures in a limited number of patients that can result from an infection with a resistant strain as well from the development of resistance in an initially susceptible strain during adequate antibiotic therapy (10). This seems a rare event among the samples of this report, or it is underestimated in clinical practice, as follow-up samples are not taken in

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TABLE 1 Rates of macrolide-resistant strains of *Mycoplasma pneumoniae* in respiratory tract samples from patients in Germany

Time period (yr)	No. of strains	Rate of resistance (%)	Reference
1991–2009	266	1.9	11
2009–2012	84	3.6	12
2011–2012	96	3.1	4
2016–2018	166	3.0	This study

most cases. Despite the limitations of the study, such as the missing demographic data of patients and lack of information about antibiotics prescribed during the course of infection, the results indicate continued low macrolide resistance among *M. pneumoniae* strains in Germany.

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