percentiles calculated. Applying the BSAC formula to pharmacokinetic data ($C_{\text{min}}$ of ~3.2 µg/L following an oral dose of 250 mg with a terminal half-life of 7–8 h), an MIC susceptible breakpoint (BP) of 0.4 mg/L was calculated.

MIC data were reviewed to ascertain the ABT-492 MIC ranges for the ‘wild sensitive’ populations. For Enterobacteriaceae, *M. catarrhalis*, haemolytic streptococci, *S. milleri*, *N. meningitidis* and *E. faecalis*, ABT-492 MICs for the population lacking a mechanism of resistance were 0.015–0.12 mg/L, 0.004–0.06 mg/L, 0.008–0.06 mg/L, 0.004–0.06 mg/L, 0.001 mg/L and 0.06–2 mg/L, respectively. In the case of staphylococci, the MIC range for the susceptible population was 0.001–0.015 mg/L. In contrast, for the 25 MRSA isolates that had reduced susceptibility to ciprofloxacin (ciprofloxacin MIC range 64–128 mg/L), ABT-492 MICs ranged from 0.25 to 1 mg/L. For *S. pneumoniae*, ABT-492 MICs ranged between 0.002 and 0.015 mg/L except for the three isolates of *S. pneumoniae* with ciprofloxacin MICs of 128 mg/L. These organisms had corresponding ABT-492 MICs of 0.03 mg/L. In the case of *H. influenzae*, MICs for the susceptible population were between 0.001 and 0.004 mg/L. For the isolate with no zone of inhibition to a nalidixic acid 30 µg disc (ciprofloxacin MIC 0.06 mg/L), the ABT-492 MIC was 0.004 mg/L and therefore indistinguishable from the susceptible population. Five isolates of *N. gonorrhoeae* with reduced susceptibility to the quinolones (no zone of inhibition to a nalidixic acid 30 µg disc) had ABT-492 MICs between 0.03 and 0.25 mg/L. For the organisms lacking a mechanism of resistance, MICs ranged between 0.001 and 0.002 mg/L.

For all isolates except *E. faecalis*, zones for disc contents of 2 and 5 µg were unacceptably large, susceptible organisms having zones larger than 40 mm (data not shown). Zone diameter data for a 1 µg disc were therefore analysed for all genera except *E. faecalis*, looking at the populations lacking a mechanism of resistance. A summary of MIC and zone diameter BPs for interpreting susceptibility and expected MIC and zone diameter ranges for a 1 µg disc is the most appropriate concentration for determining susceptibility by BSAC methodology except for *E. faecalis* where a 5 µg disc is more suitable. For the detection of low-level quinolone resistance in *H. influenzae* and *Neisseria* spp., it would be prudent for a 30 µg nalidixic acid disc to be used (recommended by the BSAC).

These data indicate that an ABT-492 disc content of 1 µg is the most appropriate concentration for determining susceptibility by BSAC methodology except for *E. faecalis* where a 5 µg disc is more suitable. For the detection of low-level quinolone resistance in *H. influenzae* and *Neisseria* spp., it would be prudent for a 30 µg nalidixic acid disc to be used (recommended by the BSAC).

### References


### Correspondence

Sir,  
*Mycoplasma pneumoniae* infects persons of all age groups and is responsible for as much as 25–50% of community-acquired pneumonias. It is also a common cause of tracheobronchitis. Fatal pneumonias and disseminated infections involving the central nervous system, joints and other organs sometimes occur. Disease may be especially severe and prolonged in persons who are immunosuppressed. Cost and limited availability of diagnostic tests mandate that treatment for *M. pneumoniae* infections must be given empirically in most settings. Macrolides and tetracyclines possess bacteriostatic activity, but fluoroquinolones represent the only drugs likely to be bactericidal against this organism.

Levofoxacin has been shown to be active in vitro against *M. pneumoniae*. This study was undertaken to evaluate the *in vitro* activity of levofloxacin against a large number of recent clinical isolates of *M. pneumoniae* recovered from patients with proven respiratory tract disease and to assess its bactericidal activities against a subgroup of these organisms by determining MBCs and carrying out time–kill assays.

One-hundred and two *M. pneumoniae* isolates were tested. These organisms were isolated from the respiratory tract of individuals with proven respiratory disease from six different countries between 1992 and 2000. Several of the isolates were obtained from outbreaks in the United States within the past 5 years. Some of these organisms have been evaluated *in vitro* against various fluoroquinolones in earlier studies. A microbroth dilution method was used to determine MICs. A subgroup of 12 randomly chosen isolates was tested to determine MBCs of levofloxacin directly from microtitre plates used to determine MICs. Two of these isolates were chosen for time–kill assays. Methods for each of these assays have been described in detail elsewhere.

All 102 *M. pneumoniae* isolates were inhibited by levofloxacin within clinically achievable concentrations ranging from 0.063 to 0.2 µg/L. Levofloxacin, fluoroquinolones, bactericidal activity, respiratory tract infections

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2 mg/L with MIC$_{50}$ = 0.5 mg/L and MIC$_{90}$ = 2.0 mg/L. MBCs for 10 of 12 (83%) isolates were 2 – 4 times the MIC, indicating bactericidal effect.

Plots of time–kill assays for two isolates with levofloxacin MICs = 0.5 mg/L and MBCs = 2 mg/L (4 × MIC) are shown in Figure 1.

Bactericidal effect for time–kill assays (99.9% killing) or reduction in inoculum by ≥ 3 log$_{10}$ dilutions occurred after 24 h at 8 × MIC in one isolate and after 48 h in both isolates at concentrations ≥ 2 × MIC. No regrowth exceeding 10$^2$ cfu/mL was observed.

This is the first report describing MICs, MBCs and time–kill assays to assess bactericidal activity of levofloxacin against M. pneumoniae in the largest collection of clinical isolates reported to date. In 10 out of 12 randomly selected isolates, a bactericidal effect was demonstrated, supporting the use of levofloxacin against M. pneumoniae infections, including serious infections in which killing the organism may be of importance.

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References


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