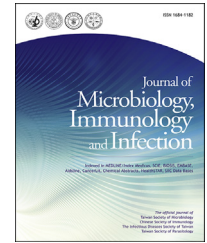


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## CORRESPONDENCE

# Increasing resistance to fluoroquinolones among *Haemophilus* species in Southern Taiwan



Dear Editor,

Fluoroquinolones have been widely used to treat respiratory tract infections. Except for several cases or strains, surveillance studies in Europe and the USA have indicated that most *Haemophilus influenzae* isolates (> 99%) are susceptible to fluoroquinolones.<sup>1,2</sup> We describe the increasing prevalence of fluoroquinolone resistance among clinical isolates of *Haemophilus* species from the respiratory tract of patients in Southern Taiwan, and such finding should be highlighted because we are losing one of the antimicrobial weapons against bacterial pathogens that cause respiratory tract infections.

According to the Clinical and Laboratory Standards Institute, the *in vitro* susceptibility of moxifloxacin among *H. influenzae* and *Haemophilus parainfluenzae* isolates has been routinely tested using disk diffusion methods at two medical centers in Southern Taiwan. The susceptibility of ciprofloxacin in *Haemophilus* species has also been tested since 2000 at Chi-Mei Hospital, Tainan, Taiwan. Between 2000 and 2015, the secular trend of ciprofloxacin susceptibility among all non-repetitive *H. influenzae* isolates decreased from 100% to 77% at CMH, and moxifloxacin susceptibility decreased from 82% to 76% from 2007 to 2015 at National Cheng Kung University Hospital, Tainan, Taiwan (Figure 1). Around the same period (2004–2015), the susceptibility of *H. parainfluenzae* to ciprofloxacin also decreased rapidly at CMH from 93% to 36%, while the susceptibility of *Streptococcus pneumoniae* to moxifloxacin saw no major change, remaining at 99% (data not shown).

Before 2004, surveillance studies from the North America, Latin America, and Europe reported that fluoroquinolone resistance accounted for only 0–0.3% of *H. influenzae* isolates.<sup>1,2</sup> A search for minimum inhibitory concentration distributions in the database of the European Committee on Antimicrobial Susceptibility Testing of 22,880 observations of *H. influenzae* from 12 data sources revealed

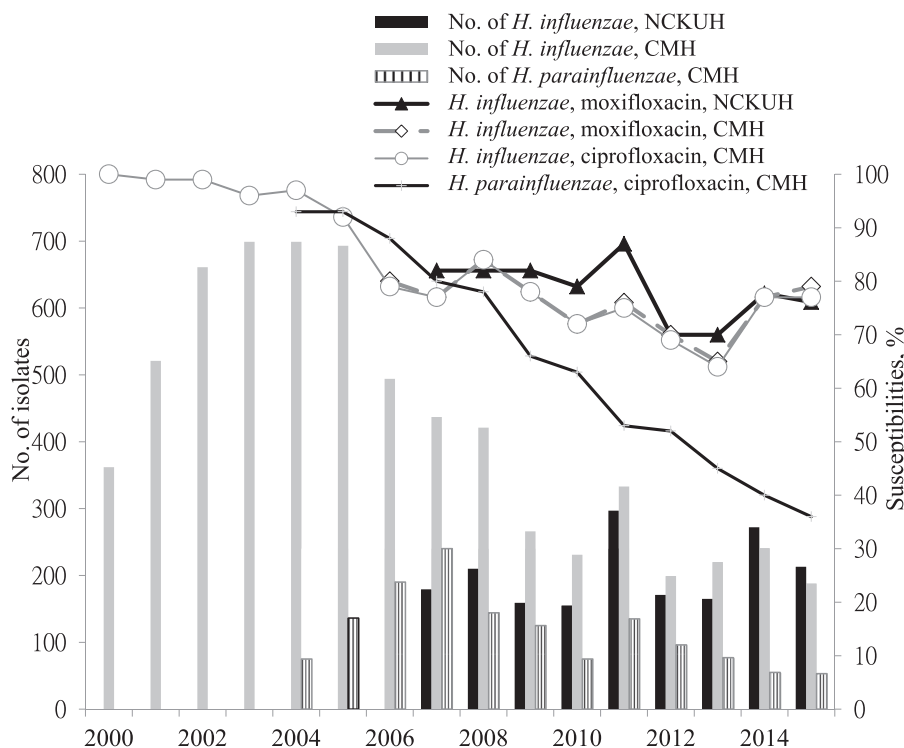
that only 0.13% of isolates exhibited a levofloxacin MIC of  $\geq 2$   $\mu\text{g}/\text{mL}$ , primarily 2–8  $\mu\text{g}/\text{mL}$ .<sup>2</sup> However, the percentage of resistance among *H. influenzae* isolates was 2.6% between 2002 and 2004 in Japan.<sup>3</sup> In 2007, 20 (42%) of 48 *H. influenzae* isolates derived from surveillance cultures of throat swabs and sputum at four nursing homes in Southern Taiwan in 2007 were resistant to levofloxacin and 10 had a levofloxacin MIC of  $> 32$   $\mu\text{g}/\text{mL}$ .<sup>4</sup>

A previous study reported that *H. influenzae* isolates with reduced susceptibility to fluoroquinolones carried amino acid changes at positions 84 and/or 88 in *gyrA* and/or at the analogous positions (84, 88) in *parC*.<sup>3</sup> Fluoroquinolone resistance in Gram-negative bacteria arose in a multistep fashion with mutations in *gyrA* occurring as the first step. However, in some Gram-positive bacteria such as *S. pneumoniae*, *parC* subunit of topoisomerase IV is the primary target of fluoroquinolones.<sup>5</sup> The reason for discrepancy of fluoroquinolone resistance among *H. influenzae*, *H. parainfluenzae*, and *S. pneumoniae* isolates during the past decade requires further study.

In 2004, a clonal outbreak of fluoroquinolone-resistant *H. influenzae* spread in a long-term care facility in New York, USA, and previous use of levofloxacin was associated with the outbreak.<sup>5</sup> Because of substantial incidence and nonspecific presentation of bacterial infections, oral fluoroquinolones might be prescribed frequently for empirical therapy of suspected infection events in older and multi-comorbid residents. With increasing clinical prescriptions of fluoroquinolones,<sup>6</sup> the emergence and regional spread of fluoroquinolone resistance in *H. influenzae* isolates might eventually occur among institutionalized adults, particularly debilitated elderly people. If this resistance trend continues, it might threaten the therapeutic efficacy of fluoroquinolones as empirical therapy for hospitalized adults with respiratory tract infections. Our data show that fluoroquinolones might no longer be safely assumed to be

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**Figure 1.** Secular trends of fluoroquinolone susceptibilities among *Haemophilus* isolates. CMH = Chi-Mei Hospital; NCKUH = National Cheng Kung University Hospital.

an effective treatment for *Haemophilus* infections. Routine susceptibility testing is essential, and continued surveillance programs for antimicrobial resistance are warranted.

### Conflicts of interests

None declared.

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### References

- Biedenbach DJ, Jones RN. Five-year analysis of *Haemophilus influenzae* isolates with reduced susceptibility to fluoroquinolones: prevalence results from the SENTRY antimicrobial surveillance program. *Diagn Microbiol Infect Dis* 2003;46:55–61.
- The European Committee on Antimicrobial Susceptibility Testing – EUCAST Antimicrobial wild type distributions of microorganisms Available at: <http://217.70.33.99/Eucast2/SearchController/search.jsp?action=performSearch&BeginIndex=0&Micdif=dif&NumberIndex=50&Antib=-1&Specium=10> [accessed 03.04.15].
- Yokota S, Ohkoshi Y, Sato K, Fujii N. Emergence of fluoroquinolone-resistant *Haemophilus influenzae* strains among elderly patients but not among children. *J Clin Microbiol* 2008;46:361–5.
- Chang CM, Lauderdale TL, Lee HC, Lee NY, Wu CJ, Chen PL, et al. Colonisation of fluoroquinolone-resistant *Haemophilus influenzae* among nursing home residents in southern Taiwan. *J Hosp Infect* 2010;75:304–8.
- Nazir J, Urban C, Mariano N, Burns J, Tommasulo B, Rosenberg C, et al. Quinolone-resistant *Haemophilus influenzae* in a long-term care facility: clinical and molecular epidemiology. *Clin Infect Dis* 2004;38:1564–9.
- Kuo SC, Shih SM, Yang Lauderdale TL, Chen YC, Hsiung CA. Fluoroquinolone prescribing in Taiwan, 2000 to 2010. *J Microbiol Immunol Infect* 2015;48:S88.

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