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Fluoroquinolone Resistance in Gram-negative bacilli

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Fluoroquinolone resistance is emerging in Gram-negative pathogens worldwide. Over the past 20 years, resistance to fluoroquinolones by Enterobacteriaceae has become common and widespread, and is generally not clonal. A recent surveillance of enteric bacteria in US intensive care units found that more than 10% of these organisms were resistant to ciprofloxacin. Report from the Meropenem Yearly Susceptibility Test Information Collection Surveillance Program (MYSTIC) in US revealed a continued decrease in fluoroquinolone susceptibility (ciprofloxacin and levofloxacin), especially among indole-positive *Proteae* (-22.1%), *E.coli* (-17.0%), *Enterbacter species* (-10.0%), and *Proteus mirabilis* (-7.6%). Levels of quinolone resistance in clinical *E. coli* have been reported at 40% in HongKong, 60% in Mainland China, and about 25% of healthy individuals living in Barcelona were found to be intestinally colonized with quinolone-resistant *E. coli*. A decrease in the susceptibility rates of fluoroquinolones in MYSTIC Program was also observed within the non-fermentative Gram-negative bacilli, including *Pseudomonas aeruginosa* and *Acinetobacter spp.*

Traditionally, two mechanisms of resistance have been found to determine resistance to fluoroquinolones. The most important of these mechanisms in Enterobacteriaceae is the accumulation of mutations in the bacterial enzymes targeted by fluoroquinolones: DNA gyrase and DNA topoisomerase IV. The second mechanism operates by decreasing intracellular drug accumulation by upregulation of native efflux pumps either alone or together with decreased expression of outer membrane porins. The recent discovery of plasmid-mediated quinolone resistance by Qnr protein and AAC(6')-Ib-cr provides us the new thought on the rapid increasing resistance. Both mechanisms provide low-level quinolone resistance that facilitates the emergence of higher-level resistance. The emerging of quinolone resistance has associated with resistance to other agents, such as beta-lactams and aminoglycosides. To screen for these genes at bedside for the clinical Gram-negative bacilli is needed.

Recent studies performed in US did not show a significant effect of fluoroquinolone use on percent resistance for most drug-organism combinations, except for the relationship between levofloxacin use and percent MRSA. The ecologic relationship between fluoroquinolone use and resistance is complex and requires more study. In countries, such as China and Spain, fluoroquinolones are used widely in food animals. Reducing fluoroquinolone use in food animals will improve human health. At the same time, we should advocate prudent use of fluoroquinolones in clinical practice worldwide.