Quinolones 1992

FLUOROQUINOLONES ARE SYNTHETIC DERIVATIVES OF nalidixic acid, which was introduced and widely used for treatment of urinary tract infections in the 1960s. Because of their activity against a very wide range of bacteria, these agents have been promoted as the new wonder drugs. Fluoroquinolones are active against *Staphylococcus aureus*, *Staph epidermidis*, *Haemophilus influenzae*, *Neisseria meningitidis*, *N gonorrhoeae*, *Escherichia coli* and other coliforms, *Pseudomonas aeruginosa*, *Salmonella typhi*, *S enteridis*, shigella, campylobacter, legionella, chlamydia, rickettsia, brucella and some mycobacteria. Unfortunately their activity against *Streptococcus pneumoniae*, and group A and group B streptococci are disappointing. They are not active against anaerobic bacteria.

Fluoroquinolones are bactericidal; their major antibacterial action is mediated by inhibition of bacterial DNA replication. There is no cross-resistance with other classes of antibiotics. Resistance may develop when fluoroquinolones are used, especially with pseudomonas.

Fluoroquinolones are well-absorbed and well-tolerated after oral administration. They have a long half-life and can be administered once or twice daily. Gastrointestinal distress has been reported in a small proportion of patients. Fluoroquinolones can interfere with theophylline metabolism; blood levels of the latter must be followed carefully if the drugs are used concurrently.

Three fluoroquinolones have been licensed in Canada: norfloxacin (Norfoxin; Merck Frosst Canada Inc), ciprofloxacin (Cipro; Miles Canada Inc) and ofloxacin (Floxin; Ortho-McNeil Inc). More than 20 other fluoroquinolones are under clinical investigation. None of the fluoroquinolones is recommended for use in prepubertal children because a unique toxicity has been observed in animals, including rats, rabbits,

guinea pigs, dogs, horses and monkeys. Damage to articular cartilage of weight-bearing joints occurs at dose regimens equivalent to those used in humans. Susceptibility is greatest in young animals. The damage is dose-related. Human embryonic chondrocytes in cell culture have been shown to be very susceptible to fluoroquinolone-induced injury.

Joint damage has not been proven to occur in adults treated with fluoroquinolones. Moreover, joint damage was not found in long term follow-up of children who had received nalidixic acid many years before. Joint toxicity has not yet been reported in children studied with a number of fluoroquinolones during clinical trials.

Conditions in which fluoroquinolones may prove to be very useful include: urinary tract infections, especially those caused by pathogens resistant to amoxicillin or trimethoprim-sulphamethoxazole; invasive bacterial diarrhea due to enteropathogenic *E coli*, shigella, salmonella or campylobacter; chronic salmonella carrier state; legionellosis; cystic fibrosis lung infections; and infections caused by bacteria resistant to commonly used antibiotics.

Because of the relatively poor activity against streptococci, including pneumococci, fluoroquinolones should **not** be used to treat community-acquired respiratory tract infections. Severe and sometimes fatal pneumococcal infections – including bacteremia and meningitis – have developed in adults treated with fluoroquinolones.

If the safety of the fluoroquinolones in children can be established, they will become valuable additions in pediatrics. Because less expensive, equally effective and less toxic antibiotics are available for most ordinary infections in children, fluoroquinolones should be reserved for situations in which alternatives are not available.

All material presented in Pediatric Infectious Disease Notes has been reviewed and approved by the chairperson, Canadian Pediatric Society Board and representative members of the Canadian Pediatric Society Committee on Infectious Diseases and Immunization

*R Gold, MD, FRCPC
Toronto, Ontario*