Emerging Quinolone-Resistant *Salmonella* in the United States

We conducted a national survey of antimicrobial resistance in human clinical isolates of *Salmonella* between July 1, 1994, and June 30, 1995. Every tenth nontyphoidal *Salmonella* isolate received at state public health laboratories in the United States during this period was tested for resistance to 12 antimicrobial agents, including two quinolones, nalidixic acid, and ciprofloxacin. Emerging quinolone resistance was detected; of 4,008 isolates tested, 21 (0.5%) were resistant to nalidixic acid, and one (0.02%) was resistant to ciprofloxacin. Continued surveillance for quinolone-resistant *Salmonella* is necessary, particularly after the recent approval of a fluoroquinolone for use in animals intended for food in the United States.

Each year, an estimated 2 to 4 million human *Salmonella* infections occur in the United States (1,2). Although most of these infections cause a mild, self-limiting illness, serious sequelae, including invasive infections and death can occur (1,2). Antimicrobial therapy is not recommended for routine treatment of salmonellosis; however, appropriate antimicrobial therapy can be life-saving for patients with invasive disease. Since antimicrobial agents are essential for treating some *Salmonella* infections, isolates from such infections should be monitored for antimicrobial resistance, particularly resistance to fluoroquinolones (e.g., ciprofloxacin). Fluoroquinolones have been in human clinical use in the United States since the mid-1980s and are recommended for treating invasive *Salmonella* infections in adults (3,4). Resistance to nalidixic acid—the prototypic quinolone—has been found in some instances to precede resistance to fluoroquinolones (5).

To determine the prevalence of antimicrobial resistance among *Salmonella* isolates in the United States, we conducted a study between July 1, 1994, and June 30, 1995. All state public health laboratories sent every tenth nontyphoidal *Salmonella* isolate they received to the Centers for Disease Control and Prevention for antimicrobial testing. Isolates were tested by the disk diffusion method for resistance to 12 antimicrobial agents, including two quinolones, nalidixic acid, and ciprofloxacin. For ciprofloxacin-resistant isolates, the minimum inhibitory concentration for ciprofloxacin was also determined.

Antimicrobial resistance patterns were determined for 4,008 *Salmonella* isolates received from 51 states and territories. Emerging quinolone resistance was detected; 21 isolates (0.5%) were resistant to nalidixic acid, and one (0.02%) was resistant to ciprofloxacin. The 21 nalidixic acid-resistant strains included 13 different serotypes from 15 states. The most common serotypes were Typhimurium (5 isolates), Enteriditis (3), and Virchow (2).

The ciprofloxacin-resistant strain, *Salmonella* serotype Schwarzengrund, was isolated in January 1995 from the stool of a woman referred to a hospital in the United States for treatment of complications caused by factor VIII deficiency. She had been hospitalized in the Philippines in September 1994 for "amoebic colitis," which was treated with antimicrobial agents; the patient could not recall the names of the agents. At that time, she also received a blood transfusion for severe anemia. Examination in the U.S. hospital showed a factor VIII level of 5% with a factor VIII inhibitor titer of 20 Bethesda units. The patient was afebrile and did not have diarrhea or other gastrointestinal symptoms, however, blood was observed in her stool on the second day of hospitalization. Colonoscopy showed angiodysplasia of the right colon. She was not treated with antimicrobial agents and was discharged from the hospital after 15 days.

To our knowledge, this is only the second reported isolation of fluoroquinolone-resistant *Salmonella* in the United States; the first reported isolate was from a patient who had been treated with three courses of ciprofloxacin for 8 weeks (6). The resistant pathogen found in our study was probably acquired in the Philippines, where quinolones have been available without prescription at least since 1987 (7) and where, according to a 1992 survey, 2.5% of nontyphoidal *Salmonella* isolates were resistant to

fluoroquinolones (5). Fluoroquinolone-resistant *Salmonella* have also been reported in Asia and Europe (5,8,9). Prior hospitalization, prior antimicrobial treatment (6), and travel outside the United States have been shown to increase the risk of being infected with *Salmonella* resistant to antimicrobial agents (10).

Compared with the previous national study, conducted in 1989-1990, which found one in 758 (0.1%) *Salmonella* isolates resistant to nalidixic acid, we found a fivefold increase in the prevalence of nalidixic acid resistance. Although increasing, the low prevalence of quinolone resistance in *Salmonella* in the United States and the lack of domestically acquired fluoroquinolone-resistant strains, is in sharp contrast to the situation in England and Wales, where increasing prevalence has been reported (8), particularly among isolates of *S*. Typhimurium, *S*. Virchow, and *S*. Hadar (E.J. Threlfall, L.R. Ward, J.A. Skinner, B. Rowe, unpub. obs.). Among one particular *Salmonella* strain, *Salmonella* Typhimurium Definitive Type 104 (DT 104), which was the second most frequently isolated *Salmonella* strain from humans in the United Kingdom in 1995, the incidence of fluoroquinolone resistance has increased from 0% in 1993 to 6% in 1995 (11), and has more than doubled in 1996 (Public Health Laboratory System, unpub. data). An important factor contributing to this increase may be the licensing in 1993 of the fluoroquinolone antimicrobial enrofloxacin for general veterinary use in that country (11). Although the only fluoroquinolone-resistant *Salmonella* isolate identified in our study was apparently acquired outside, DT 104 has emerged widely in the United States (12). The recent approval of a fluoroquinolone for use in animals intended for food in the United States (sarafloxacine in poultry) (13) may contribute to the emergence and circulation of fluoroquinolone-resistant strains in a way analogous to that already observed in the United Kingdom. Since fluoroquinolones are important in treating invasive *Salmonella* infections and most DT 104 isolates are already resistant to ampicillin, chlorampenicol, streptomycin, sulphonamides, and tetracyclines, continued monitoring of salmonellas for resistance to fluoroquinolone antimicrobial drugs is warranted.

Acknowledgments

We thank the numerous microbiologists at the state public health laboratories who provided the isolates included in the study.

Hallgeir Herikstad,* Peggy Hayes,* Mohamed Mokhtar,* Margaret L. Fracaro, E. John Threlfall,‡ and Frederick J. Angulo*

*Centers for Disease Control and Prevention, Atlanta, Georgia, USA; The Presbyterian Hospital in the City of New York, New York, USA; ‡Public Health Laboratory Service, Central Public Health Laboratory, London, United Kingdom

References

1. Cohen ML, Tauxe RV. Drug-resistant *Salmonella* in the United States: an epidemiologic perspective. Science 1986;234:964-9.
2. Tauxe RV. *Salmonella*: a postmodern pathogen. Journal of Food Production 1991;54:563-8.
3. Wilcox MH, Spencer RC. Quinolones and salmonella gastroenteritis. J Antimicrob Chemother 1992;30:221-8.
4. Conte JE. Manual of antibiotics and infectious diseases. Baltimore: Williams & Wilkins; 1995.
5. Turnidge J. Epidemiology of quinolone resistance. Eastern hemisphere. Drugs 1995;49:43-7.
6. Cherubin CE, Eng RHK. Quinolones for the treatment of infections due to *Salmonella*. Rev Infect Dis 1991;13:343-4.
7. Lansang MA, Lucas-Aquino R, Tupasi TE, Mina VS, Salazar LS, Juban N, et al. Purchase of antibiotics without prescription in Manila, the Philippines. Inappropiate choices and doses. J Clin Epidemiol 1990;43:61-7.
8. Frost JA, Kelleher A, Rowe B. Increasing ciprofloxacin resistance in salmonellas in England and Wales 1991-1994. J Antimicrob Chemother 1996;37:85-91.
9. Hof H, Ehrhard I, Tschape H. Presence of quinolone resistance in a strain of *Salmonella typhimurium*. Eur J Clin Microbiol Infect Dis 1991;10:747-9.
10. Lee LA, Puhr ND, Maloney EK, Bean NH, Tauxe RV. Increase in antimicrobial-resistant *Salmonella* infections in the United States, 1989-1990. J Infect Dis 1994;170:128-34.
11. Threlfall EJ, Frost JA, Ward LR, Rowe B. Increasing spectrum of resistance in multiresistant *Salmonella typhimurium*. Lancet 1996;347:1053-4.
12. Centers for Disease Control and Prevention. Multidrug-resistant *Salmonella* serotype Typhimurium—United States, 1996. MMWR Morb Mortal Wkly Rep 1997; 46:308-10.
13. Centers for Disease Control and Prevention. Establishment of a national surveillance program for antimicrobial resistance in *Salmonella*. MMWR Morb Mortal Wkly Rep 1996;45:110-1.