7. Sahm DF, Thornsberry C, Jones ME, Blasser R, Critchley IA, Evangelista AT, Karlowsky YA. Antimicrobial susceptibility of Enterobacteriaceae and Pseudomonas aeruginosa from inpatient infections in the U.S.: 1999–2002 TRUST surveillance. Critical Care Congress, 2003, Abstract 2015.

8. Gillespie T, Masterton RG. Investigation into the selection frequency of resistant mutants and the bacterial kill rate by levofloxacin and ciprofloxacin in non-mucoid Pseudomonas aeruginosa isolates from cystic fibrosis patients. Int J Antimicrob Agents 2002;19:377–82.

9. Zhanel GG, Walters M, Laing N, Hoban DJ. In vitro pharmacodynamic modeling simulating free serum concentrations of fluoroquinolones against multidrug-resistant Streptococcus pneumoniae. J Antimicrob Chemother 2001;47:435–40.

10. Biedenbach DJ, Barrett MS, Croco MA, Jones RN. Bay 12-8039, a novel fluoroquinolone, activity against important respiratory tract pathogens. Diagn Microbiol Infect Dis 1998;31:45–50.

11. Thornsberry C, Ogilvie PT, Holley HP Jr, Sahm DF. Survey of susceptibilities of Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis isolates to 26 antimicrobial agents: a prospective U.S. study. Antimicrob Agents Chemother 1999;43:2612–23.

12. Thornsberry C, Ogilvie PT, Holley HP Jr, Sahm DF. Survey of susceptibilities of Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis isolates to 26 antimicrobial agents: a prospective U.S. study. Antimicrob Agents Chemother 1999;43:2612–23.

13. Biedenbach DJ, Barrett MS, Croco MA, Jones RN. Bay 12-8039, a novel fluoroquinolone, activity against important respiratory tract pathogens. Diagn Microbiol Infect Dis 1998;31:45–50.

14. Thornsberry C, Ogilvie PT, Holley HP Jr, Sahm DF. Survey of susceptibilities of Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis isolates to 26 antimicrobial agents: a prospective U.S. study. Antimicrob Agents Chemother 1999;43:2612–23.

15. Thornsberry C, Ogilvie PT, Holley HP Jr, Sahm DF. Survey of susceptibilities of Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis isolates to 26 antimicrobial agents: a prospective U.S. study. Antimicrob Agents Chemother 1999;43:2612–23.

16. Zhanel GG, Ennis K, Vercaigne L, Walkty A, Gin AS, Embil J, et al. A critical review of the fluoroquinolones: focus on respiratory infections. Drugs 2002;62:13–59.

17. Lacey MK, Lu W, Xu X, Tessier PR, Nicolau DP, Quintiliani R, Nightingale CH. Pharmacodynamic comparisons of levofloxacin, ciprofloxacin, and amoxicillin against Streptococcus pneumoniae in an in vitro model of infection. Antimicrob Agents Chemother 1999;43:672–7.

18. Nightingale CH, Grant EM, Quintiliani R. Pharmacodynamics and pharmacokinetics of levofloxacin. Chemotherapy 2000;46 (Suppl 1):6–14.

19. Ambrose PG, Grasela DM, Grasela TH, Passarell J, Mayer HB, Pierce PF. Pharmacodynamics of fluoroquinolones against Streptococcus pneumoniae in patients with community-acquired respiratory tract infections. Antimicrob Agents Chemother 2001;45:2793–7.

20. Kolhepp SJ, Grunkemeier G, Leggett JE, Dworkin RJ, Slaughter SE, Gilbert DN. Phenotypic resistance of penicillin-susceptible and penicillin-resistant Streptococcus pneumoniae after single and multiple in vitro exposures to ciprofloxacin, gatifloxacin, levofloxacin, moxifloxacin, and trovafloxacin. Annual Meeting Infectious Diseases Society of America, 2000, Abstract 97.

21. Klepser M, Ernst E, Petzold CR, Rhomberg P, Doern GV. Comparative bactericidal activities of ciprofloxacin, clinafloxacin, grepafloxacin, levofloxacin, moxifloxacin, and trovafloxacin against Streptococcus pneumoniae in a dynamic in vitro model. Antimicrob Agents Chemother 2001;45:673–8.

22. Low D, de Azavedo J, Weiss K, Mazzulli T, Nicolau DP, Quintiliani R, Nightingale CH, Passarell J, Mayer HB, Pierce PF. Comparative bactericidal activity of levofloxacin and ciprofloxacin in non-mucoid Pseudomonas aeruginosa isolates from cystic fibrosis patients. Int J Antimicrob Agents 2002;19:377–82.

23. Nightingale CH, Grant EM, Quintiliani R. Pharmacodynamics and pharmacokinetics of levofloxacin. Chemotherapy 2000;46 (Suppl 1):6–14.

24. Evangelista AT, Loeloff M, Pfelger S, Davies TA, Evangelista AT. Characterization of U.S. clinical Streptococcus pneumoniae strains from 2000–2001 that are cross-resistant to ciprofloxacin, gatifloxacin, levofloxacin, and moxifloxacin. Annual Meeting Infectious Disease Society of America 2002, Abstract 78.

25. Davies TA, Evangelista A, Pfleger S, Bush K, Sahm DF, Goldschmidt R. Prevalence of single mutations in topoisomerase type II genes among levofloxacin-susceptible clinical isolates of Streptococcus pneumoniae isolated in the United States in 1992–1996 and 1999–2000. Antimicrob Agents Chemother 2002;46:119–24.

26. Davies TA, Evangelista A, Pfleger S, Bush K, Sahm DF, Goldschmidt R. Prevalence of single mutations in topoisomerase type II genes among levofloxacin-susceptible clinical isolates of Streptococcus pneumoniae isolated in the United States in 1992–1996 and 1999–2000. Antimicrob Agents Chemother 2002;46:119–24.

27. Davidson R, Covalcanti R, Brunton JL, Bast DJ, De Azavedo JC, Kibsey P, et al. Resistance to levofloxacin and failure of treatment of pneumococcal pneumonia. N Engl J Med 2002;346:747–50.

28. Horcajada JP, Via J, Moreno-Martínez A, Ruiz J, Martínez J, Sánchez M, Soriano E, et al. Molecular epidemiology and evolution of resistance to quinolones in Escherichia coli after prolonged administration of ciprofloxacin in patients with prostatitis. J Antimicrob Chemother 2002;49:55–9.

29. Hoellman DB, Kelly LM, Jacobs MR, Appelbaum PC. Comparative antianaerobic activity of BMS 284756. Antimicrob Agents Chemother 2001;45:589–92.

30. Ednie LM, Jacobs, Appelbaum PC. Activities of gatifloxacin compared to those of seven other agents against anaerobic organisms. Antimicrob Agents Chemother 1998;42:2459–62.

31. Zhanel GG, Laing NM, DeCorby M, Nichol KA, Homan DJ. Pharmacodynamic activity of fluoroquinolones in a mixed infection simulating an artificial bowel: effect of eradicating Bacteroides fragilis. American Society for Microbiology, 2002, Abstract A-145.

Address for correspondence: James A. Karlowsky, Focus Technologies, 13665 Dulles Technology Drive, Suite 200, Herndon, VA 20171-4603, USA; fax: (703) 480-2654; email: jkarlowsky@focusanswers.com

International Travel and Sexually Transmitted Disease

To the Editor: Recent articles in the professional literature (1–3) have offered advice regarding the importance of taking a careful travel history, particularly in this time of unprecedented levels of international travel.
(4). Such screening serves an important public health purpose as well, especially for sexually transmitted disease (STD) control.

Sexual behaviors associated with travel can change the level of risks for STD transmission (5–7), and the epidemiology of STDs is not uniform throughout the world (8,9). These geographic differences may increase the risk of a traveler’s becoming infected, or, conversely, increase the risk of a traveler’s introducing a sexually transmitted pathogen, possibly one that is resistant to treatment, into a low-incidence area (10). In addition, different strains of pathogens may be common in different parts of the world (11–14). For example, quinolone-resistant Neisseria gonorrhoeae (QRNG) is much more common in Asia (up to 40% of all isolates) (15). These strains of QRNG were first introduced in the United States by persons who engaged in sexual activity abroad, but now California and Hawaii have an increasing incidence of infection attributable to these strains (16). Indeed, QRNG has become endemic in those states, and incidence is no longer related to travel. During 1999–2001, only 3 QRNG isolates (0.28%) were identified among the 1,066 gonococcal isolates cultured in the STD Laboratory, State Laboratory Institute, Massachusetts Department of Public Health (Massachusetts Department of Public Health, unpub. data). However, in 2002, 9 (2.1%) of 425 isolates of Neisseria gonorrhoeae were quinolone resistant. None of the persons recently infected reported a history of travel outside of New England. Unfortunately, few had reliable information to identify their partner(s). Those partners who were identified were either not located or did not agree to speak with the disease intervention specialist.

This experience with antimicrobial resistance of Neisseria gonorrhoeae should serve as a model for STD prevention planning and programming. It highlights the importance of retaining the laboratory capacity to monitor antimicrobial susceptibilities of bacterial STD isolates. Treatment protocols should be adjusted in light of the prevalence of resistant strains of sexually transmitted pathogens. In cases in which symptoms associated with a bacterial STD persist after what is usually considered appropriate treatment, clinicians should obtain cultures and perform susceptibility tests on isolates. Nucleic acid amplification technologies do not provide critical antibiotic susceptibility information. In this situation, the public health STD program or laboratory should be contacted for guidance. Determining the sensitivity pattern of the pathogen in an expeditious fashion will ensure that appropriate and timely therapy can be initiated for the infected patient as well as enable more effective follow-up and treatment to sexual contacts. Asking patients who seek treatment for a possible STD about their own and their partner’s travel histories is important to broaden the differential diagnosis (17). The increase in population mixing facilitated by travel and Internet-generated contacts may be diminishing the importance of the focality of traditional STD epidemiology. Finally, STD prevention messages should be a part of the health advice offered to travelers (7,18,19).

Acknowledgments

We thank Alfred DeMaria and Ralph Timperi for their thoughtful reviews and comments regarding this material.

Paul Etkind,* Sylvie Ratelle,* and Harvey George*

*Massachusetts Department of Public Health, Jamaica Plain, Massachusetts, USA

References

1. Ryan ET, Wilson ME, Kain KC. Illness after international travel. N Engl J Med 2002;347:505–16.
2. Ryan ET, Kain KC. Health advice and immunizations for travelers. N Engl J Med 2000;342:1716–25.
3. Harry TC. Infectious syphilis and importance of travel history. Lancet 2002;359:447–8.
4. World Health Organization. The state of the world health. In: The world health report 1996: fighting disease, fostering development. Geneva: The Organization; 1997. p. 1–62.
5. Matteelli A, Carosi G. Sexually transmitted disease in travelers. Clin Infect Dis 2001;32:1063–7.
6. Cabada MM, Echevarria JI, Seas CR, Navarte G, Samalvides F, Freedman D, et al. Sexual behavior of international travelers visiting Peru. Sex Transm Dis 2002;29:510–3.
7. Bloor M, Thomas M, Hood K, Abdeni D, Goujon C, Hauser D, et al. Differences in sexual risk behaviour between young men and women travelling abroad from the UK. Lancet 1998;352:1664–8.
8. Gerbase AC, Rowley JT, Mertens TE. Global epidemiology of sexually transmitted diseases. Lancet 1998;351(Suppl 3):2–4.
9. Wasserheit JN, Aral SO. The dynamic topology of sexually transmitted disease epidemics: implications for prevention strategies. J Infect Dis 1996;174(Suppl 2):S201–13.
10. Thompson MM, Najera R. Travel and the introduction of human immunodeficiency virus type 1 non-B subtype genetic forms into western countries. Clin Infect Dis 2001;32:1732–7.
11. World Health Organization/Global Program on AIDS. Global prevalence and incidence estimates of selected curable sexually transmitted diseases: Overview and estimates. Geneva: The Organization; 1995. p. 1–26.
12. Van Dyck E, Crabbe E, Neila N, Bogaerts J, Munyabikali JP, Gips Y, et al. Increasing persistence of Neisseria gonorrhoeae in west and central Africa. Consequence on therapy of gonococcal infection. Sex Transm Dis 1997;24:32–7.
13. Tapsall JW, Phillips EA, Schultz TR, Thacker C. Quinolone-resistant Neisseria gonorrhoeae isolated in Sydney, Australia, 1991 to 1995. Sex Transm Dis 1996;23:425–8.
14. Lewis DA, Bond M, Butt KD, Smith CP, Shafi MS, Murphy SM. A one-year survey of gonococcal infection seen in the genitourinary medicine department of a London district general hospital. Int J STD AIDS 1999;10:588–94.
15. WHO Western Pacific Gonococcal Antimicrobial Surveillance Programme. Surveillance of antibiotic resistance in Neisseria gonorrhoeae in the WHO Western Pacific Region, 2000. Commun Dis Intell 2001;25:274–6.
LETTERS

16. Centers for Disease Control and Prevention. Increases in fluoroquinolone-resistant Neisseria gonorrhoeae—Hawaii and California. MMWR Morb Mortal Wkly Rep 2002;51:1041–4.
17. Kingston M, Warren C, Carlin E. Tropical warts. Lancet 2001;358:808.
18. Mulhall BP. Sexual behaviour in travellers. Lancet 1999;353:595–6.
19. Abdullah AS, Hedley AJ, Fielding R. Sexual behaviour in travellers. Lancet 1999;353:595–6.

Address for correspondence: Sylvie Ratelle, Bureau of Communicable Disease Control, Massachusetts Department of Public Health, 305 South Street, Jamaica Plain, MA 02130, USA; fax: 617-983-6925; email: sylvie.ratelle@state.ma.us

---

Salmonella in Denmark

To the Editor: In the large study by Evans and Wegener recently published in Emerging Infectious Diseases (1), salmonellae in broiler chickens and pigs significantly decreased after routine in-feed antimicrobial drug use for growth promotion was terminated in Denmark. Avoparcin was a frequently used growth promoter in poultry until its ban in Denmark in 1995 because of its association with the development and spread of vancomycin-resistant enterococci. On examining Evans and Wegener’s data, I noticed that a precipitous drop in salmonellae in broiler chickens appeared to have occurred in early 1996. Do the authors think this drop was due to the withdrawal of avoparcin? As the authors note, avoparcin has been associated with increased shedding of salmonellae (including a dose-response effect) in a number of studies (2,3). If the large drop (from approximately 25% positive samples in 1995 to approximately 10% in 1996) is not due to withdrawal of avoparcin, what do the authors suggest could have caused it?

Do the authors have sufficient numbers of samples to reanalyze their data in broiler chickens for three periods instead of just two (i.e., the periods January 1995–December 1995, January 1996–December 1997, and January 1998–December 2000)? This change would take into account the potential effect of avoparcin withdrawal in 1995.

Also, the most important reason for decreasing food animals’ carriage of salmonellae is to protect people from becoming ill with Salmonella. Do the authors have any figures on domestically acquired human infections with salmonellae in Denmark since early 1995? Is there any temporal association with the withdrawal of growth promoters?

Peter Collignon*
*Sydney University, Woden, Australia

References
1. Evans MC, Wegener HC. Antimicrobial growth promoters and Salmonella spp., Campylobacter spp. in poultry and swine, Denmark. Emerg Infect Dis 2003;9:489–92.
2. Barrow PA, Smith HW, Tucker JF. The effect of feeding diets containing avoparcin on the excretion of Salmonella by chickens experimentally infected with natural sources of Salmonella organism. J Hyg (Lond) 1984;93:439–44.
3. Barrow PA. Further observations on the effect of feeding diets containing avoparcin on the excretion of Salmonella by experimentally infected chickens. Epidemiol Infect 1989;102:239–52.

Address for correspondence: Peter Collignon, Professor, Canberra Clinical School, Sydney University, P. O. Box 11, Woden, ACT. 2607, Australia; fax: 61 2 6281 0349; email: peter.collignon@act.gov.au

---

In Reply: The drop in Salmonella organisms in broiler chickens becomes evident in September 1995. The ban on avoparcin occurred in May 1995. These two facts suggest that the first flocks of broiler chickens produced without avoparcin were slaughtered in August 1995. Thus, the temporal relationship is evident. We have reanalyzed the data for the three strata January 1994–December 1995, January 1996–December 1997, and January 1998–December 2000. Each stratum is significantly different from the two others (p < 0.0001).

Arguing in favor of a causal relationship, apart from the temporal relationship, one would say that no changes in the Salmonella control program in this period could explain this reduction. Arguing against a causal relationship, one would say that the levels momentarily bounced back to nearly the pre-ban level in 1997, despite the avoparcin ban. The subsequent drop and consistent low level could be explained by changes in the control program (introduction of serologic Salmonella monitoring in 1997 to 1998). On the basis of our data, drawing a conclusion one or the other is not possible.

There is a clear temporal association between reduction in Salmonella in broiler chickens and reduced incidence of domestically acquired Salmonella infections that can be attributed to domestically produced broilers. This finding was recently reported in this journal (1).

Mary E. Patrick* and Henrik C. Wegener†
*DeKalb County Board of Health, Decatur, Georgia, USA; and †Danish Veterinary Institute, Copenhagen, Denmark

Reference
1. Wegener HC, Hald T, Wong DLF, Madsen M, Korsgaard H, Bager F, et al. Salmonella control programs in Denmark. Emerg Infect Dis 2003;9:774–80.

Address for correspondence: Mary Evans Patrick, DeKalb County Board of Health, 445 Winn Way, Decatur, GA 30030, USA; fax: 404-294-3842; email: mcevans@gdh.state.ga.us