

FDA/CDC/USDA Antibiotic Resistance Monitoring Program

Linda Tollefson, DVM, MPH, Marissa Miller, DVM, MPH, Paula J. Fedorka-Cray, PhD,
Frederick J. Angulo, DVM, PhD, and Stephen F. Sundlof, DVM, PhD

Development of antimicrobial resistance has emerged as a global problem. Expert scientific groups such as the Institute of Medicine, the American Society for Microbiology and the World Health Organization have expressed apprehension about the national and global increase in antibiotic resistance and the complex issues surrounding this increase in both the community and institutional settings (1,4). Antibiotic use selects for populations of resistant bacteria in target pathogens and normal bacterial flora, including food borne pathogens such as *Salmonella*, *Campylobacter*, and *E. coli*. If resistant food borne pathogens are present in food animal species, these bacteria may contaminate food products at the time of slaughter and be transmitted to humans through the food chain (3). Extensive antibiotic use increases the spread of antibiotic-resistant bacteria by creating selective pressure favoring resistant bacteria (6). The public health impact of resistance on the population includes increased morbidity and mortality from treatment failures and increased health care costs as newer, more expensive antibiotics are needed to treat infections (1).

Because of the public health concerns associated with the approval of fluoroquinolones for use in food-producing animals in the United States, in 1996 the Food and Drug Administration, the Centers for Disease Control and Prevention (CDC) and the Department of Agriculture (USDA) established the National Antimicrobial Resistance Monitoring Program to prospectively monitor changes in antimicrobial susceptibilities of zoonotic enteric pathogens from human and animal clinical specimens, from healthy farm animals, and from carcasses of food-producing animals at slaughter plants (2,5). The Program is continuous and monitors changes in susceptibilities of zoonotic enteric pathogens to a number of antimicrobials.

The goals and objectives of the National Antimicrobial Resistance Monitoring Program are to provide descriptive data on the extent and temporal trends of antimicrobial susceptibility in *Salmonella* and other enteric organisms from the human and animal populations; facilitate the identification of resistance in humans and animals as it arises; provide timely information to veterinarians and physicians; prolong the life span of approved drugs by promoting the prudent

use of antibiotics; identify areas for more detailed investigation; and guide research in the area of antibiotic resistance.

The Program consists of two parallel arms. Veterinary testing of non-typhoid *Salmonella* isolates is conducted at USDA; *Campylobacter* isolates are also tested as of January 1, 1998. CDC's Foodborne Disease Laboratory in the National Center for Infectious Diseases is testing human isolates, non-typhoid *Salmonella*, *E. coli* O157, and *Campylobacter jejuni* and *coli* submitted by 16 State Public Health Laboratories (CA, CO, CT, FL, GA, KS, Los Angeles County, MA, MD, MN, NJ, NY, New York City, OR, WA, and WV). Both the CDC and USDA laboratories are using a semi-automated system (Sensititre™, Accumed, Westlake, Ohio) for the testing of isolates; comparable methods for isolate handling are used in both laboratories.

As of January 1, 1997, both laboratories are using the same preconfigured panel designed for the Sensititre™ system to determine minimum inhibitory concentrations (MICs) for the same 17 antimicrobial agents: amikacin, amoxicillin/clavulanic acid, ampicillin, apramycin, ceftiofur, ceftriaxone, cephalothin, chloramphenicol, ciprofloxacin, gentamicin, kanamycin, nalidixic acid, streptomycin, sulfamethoxazole, tetracycline, ticarcillin, and trimethoprim/sulfamethoxazole.

DISCUSSION

The National Antimicrobial Resistance Monitoring Program is only a sentinel: it can not tell us how or why, from what source, or by what mechanism resistance has emerged. More focused analytical studies will be needed to fully determine the association between antimicrobial resistance in the human and animal populations. To begin to address these limitations, several enhancements of the Program are planned under the National Food Safety Initiative (FSI).

The goal of the FSI is to reduce, to the greatest extent possible, the incidence of food borne illness. Six specific areas are targeted under the FSI: Surveillance, Inspections, Risk Assessment, Research, Education, Outbreak Coordination, and Strategic Planning. The designers of the FSI worked from the premise that an effective and comprehensive food safety program must have several interrelated components which together have far greater impact on reducing the incidence of food borne illness than is possible to attain with any single component. FDA Center

for Veterinary Medicine components in the FSI fall into two main elements for 1998: Surveillance and Research.

The goal of the Surveillance Initiative is the rapid detection of food borne illness outbreaks, dissemination of information to facilitate immediate control mechanisms, and reduction of the transfer of resistant animal pathogens to humans. The National Antimicrobial Resistance Monitoring Program is FDA's focal point under the Surveillance Initiative. Ongoing national surveillance of antimicrobial resistance will be expanded to new sites and new sources of isolates. Outbreak investigations and field studies will be initiated as a result of major shifts or changes in resistance patterns in either animal or human isolates. These efforts will include a trace back system to determine the source of the infection and the circumstances that led to the resistance. If similar strains of *Salmonella* appear in both the veterinary and the human populations studied in the monitoring system (same serotype and same antimicrobial resistance pattern), we will attempt molecular comparison of strain characteristics in the same laboratory to define their degree of similarity. Other data collection efforts are planned including prescribing surveys of physicians and veterinarians to assess the impact of antimicrobial drug use on resistance patterns and prevalence to guide regulatory policy as well as education campaigns on the prudent use of antibiotics.

Beginning in 1998, we plan to increase collection of *Salmonella* isolates from healthy animals at slaughter plants. These isolates will be obtained from the USDA which has mandated slaughter plants to sample for *Salmonella* to ensure compliance with pathogen reduction performance standards as part of a plant's Hazard Analysis and Critical Control Point program (7). This program must be in effect on January 25, 1998 for slaughter plants with 500 or more employees. These large slaughter plants in total account for 75% of the annual meat and poultry production in the U.S. Also in 1998, FDA plans to establish veterinary sentinel sites at veterinary diagnostic laboratories in the states of Washington, New York, and California in order to facilitate comparisons between the animal and human isolates at the local level.

FDA Center for Veterinary Medicine projects under the research component of the FSI include development of improved detection methods for food borne pathogens in animal feed, identification and characterization of factors that lead to the development of antimicrobial drug resistance in food borne pathogens in farm animals and aquaculture, and expanded investigation

of techniques to limit or avoid resistance. FDA is encouraging the development of alternative strategies to antibiotic usage such as improved management techniques and novel drug treatments to reduce both the overall prevalence of pathogens carried by animals and specifically target resistant pathogens.

The identification of emerging resistance and the capability to investigate resistance patterns and trends identified through the National Antimicrobial Resistance Monitoring Program are essential elements to facilitate timely and appropriate public health response activities. Further development of a multi-agency coordinated response will promote punctual communication, informed decision making, and proactivity in assisting veterinarians and physicians in the prudent use of antimicrobial agents. The ultimate outcome will be to prolong the efficacy of existing and new antimicrobial agents which are needed to control both human and animal disease and to minimize the spread of resistant zoonotic pathogens to humans.

References

1. American Society for Microbiology Public and Scientific Affairs Board. Report of the ASM Task Force on Antibiotic Resistance, Washington, D.C., March 16, 1995.
2. Centers for Disease Control and Prevention. Notice to Readers: Establishment of a national surveillance program for antimicrobial resistance in *Salmonella*. Morbidity and Mortality Weekly Report 1996, 45:110-111.
3. Holmberg, S.D., Osterholm, M.T., Senger, K.A., Cohen, M.L. Drug-resistant *Salmonella* from animals fed antimicrobial agents. N. Engl. J. Med. 1984, 311:617-622.
4. Institute of Medicine Committee on Emerging Microbial Threats to Health, Lederberg, J., Shope, R. E., and Oaks, S. C. (Eds.). Emerging Infections: Microbial Threats to Health in the United States, National Academy Press, Washington, D.C., 159-160, 1992.
5. Tollefson, L. FDA reveals plans for antimicrobial susceptibility monitoring. J. Amer. Vet. Med. Assoc. 1996, 208:459-460.
6. U.S. Congress, Office of Technology Assessment. Impacts of Antibiotic-Resistant Bacteria, OTA-H-629, Washington, D.C., U.S. Government Printing Office, September, 1995.
7. U.S. Department of Agriculture. Pathogen Reduction; Hazard Analysis and Critical Control Point (HACCP) Systems; Final Rule. Federal Register 61(144):38806-38989, July 25, 1996.