Antibiotics, Animals, and People—Again!

Nearly 25 years ago, we were both involved in a proposal to terminate the use of certain antibiotics then being added to animal feeds in the United States to promote the growth of livestock (the United Kingdom had wisely restricted the most prevalent uses years earlier). One of us (Don Kennedy) was commissioner of the U.S. Food and Drug Administration (FDA); the other (Stanley Falkow) was a member of an expert panel commissioned by the FDA to assess the associated risks. At that time, evidence linking antibiotic resistance in bacteria inhabiting livestock to resistance in human pathogens was indirect, though it was plain to us and to most microbiologists that using the same antibiotics in people and animals was a bad idea. The FDA proposed eliminating the subtherapeutic growth-promotant uses of penicillin and two other antibiotics, but livestock production interests persuaded Congress to put the regulation on the shelf.

Science lost that time, but of course science didn't stand still. Molecular epidemiology was unheard of in 1977, and studies on the transfer of resistance plasmids among different kinds of bacteria were in their infancy. Now there are unmistakable links between the subtherapeutic use of antibiotics and the prevalence of resistant bacteria. Two studies by the U.S. National Academy of Sciences, while recognizing that link, found that there was insufficient evidence for a direct influence on human health, thereby shifting the debate from molecular genetics to risk assessment. Denmark, Finland, and Sweden have all eliminated the use of antibiotics for growth promotion, and the World Health Organization has advised against the practice of dosing animals with some of the same antibiotics we rely on in human medicine. Yet the practice continues in the United States and many other nations.

An additional and potentially more serious problem has now emerged. In 1996, the FDA approved the use of fluoroquinolines in chickens and turkeys, primarily to prevent mortality associated with *Escherichia coli* infection. This inexplicable decision was reached despite strong opposition from the Centers for Disease Control (CDC), which cited the extraordinary value of these compounds in treating community- or hospital-acquired enteric infections in humans. Subsequent events showed that the CDC's concerns were prescient: Fluoroquinoline resistance quickly appeared in *Campylobacter* isolated from chickens, and by 1999 17.6% of *C. jejuni* and 30% of *C. coli* isolated from human patients showed fluoroquinoline resistance. *Campylobacter* infections are the leading cause of food-borne illness in the United States. Adding to the human and economic costs are chronic sequelae associated with *C. jejuni* infection: Guillain-Barré syndrome and reactive arthritis. Armed with such evidence, the FDA's Center for Veterinary Medicine proposed on 31 October 2000 to withdraw the approval of fluoroquinolines for animal use. Of the two manufacturers, Abbott Laboratories agreed voluntarily to cease manufacture of its product; Bayer Corporation did not, and is submitting its case for continued marketing along with its request for a hearing. We think the FDA should pursue its case aggressively to stop Bayer from marketing.

Using the same antibiotics in people and animals is a bad idea.

In the end, the FDA has taken the right stand, and we may dodge this bullet. The CDC played a strong role in developing the epidemiological context for the action and deserves to be congratulated. But we will be wise to reflect on the problems that remain. It is hardly surprising that compounds useful in human health also help animals. Both humans and animals are heir to related bacterial pathogens; indeed, most human bacterial pathogens can be traced in evolution to microbes that infect animals. Nearly half of the total volume of antibiotics used in the United States is fed to animals, and this practice continues despite a strong scientific consensus that it is a bad idea. The resulting struggle between good science and strong politics has simmered fruitlessly for a quarter of a century; it's time to end it, and some entrepreneurial energy might do the trick. In human medicine, the goal has been to develop broad-spectrum compounds effective against a range of pathogens, and it is natural for veterinary medicine to deploy these rather than develop new ones. However, we now know enough about bacterial genomics and bacterial pathogenesis, and we have enough new biochemical technologies, to begin developing novel antimicrobials that work specifically against animal pathogens yet do not create resistance in human ones. It looks to us like an economic opportunity as well as a scientific challenge. Anyone out there care to try?

Stanley Falkow and Donald Kennedy

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