encouraging cooperation a dozen years ago. Those reasons are still valid today and opportunities for mutually beneficial research are even better.

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Tracking Antibiotics Up the Food Chain

AMONG THE COSTS OF USING ANTIBIOTICS IS the gradual loss of their effectiveness as bacteria evolve resistance to them. S. Falkow and D. Kennedy suggest in their Editorial "Antibiotics, animals, and people—again!" that the best policy to minimize these costs for a class of antibiotics called fluoroquinolines is to ban their use in farm animals (*Science*'s Compass, 19 Jan., p. 397). But evidence does not support their analysis. The suggested policy would deny the public benefits of antibiotic use in animals without materially extending effective use of these drugs in humans.

From our perspective as professional risk analysts, the Editorial presents a flawed diagnosis of the problem. Falkow and Kennedy blame increasing antibiotic resistance on veterinary use because resistance has increased in humans while fluoroquinolines are being used to treat poultry. Our analysis of the Center for Disease Control and Prevention (CDC) study and other published results suggests that the evolution of resistance to fluoroquinolines in human commensal bacteria arises independently of use in animals. Strains of *Campylobacter jejuni* resistant to fluoroquinolines existed before this use. The prevalence of resistant strains in people increases at roughly the same rate in countries that do not use fluoroquinolines in farm animals as in countries that do (*1*), whereas resistance in farm animals has no obvious association with use in farm animals (*2*). Indeed, as inoculation theory predicts, the presence of *C. jejuni* strains in chickens protects those who handle (*3*) and eat (*4*) the infected birds against severe diarrhea and campylobacteriosis.

The use of antibiotics in animal husbandry benefits the public in several ways. It can reduce the cost of meat and the numbers of infective microbes in food (*5*). People are healthier as a result. The U.S. Food and Drug Administration (FDA) should develop an approach to managing antibiotic use that allows us to reap the benefits of these drugs while maximizing their effectiveness. Recent CDC data now being analyzed might allow the FDA to do so. Effective policy-making cannot be based on logic that attributes blame for rising resistance to relatively minor use of antibiotics in animals while neglecting the far more likely cause represented by increasing use in humans.

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"[P]olicy-making cannot be based on logic that attributes...rising resistance to relatively minor use of antibiotics in animals"

"800 tons of fluoroquinolines are used annually in humans, 120 tons in animals; the latter use, hardly minor, threatens the former."

Response

WE POINTED OUT IN OUR EDITORIAL THAT 25 years ago the issue of antibiotics in animal feeds had become an argument in which scientific evidence defaults to risk assessment. The response by Daniel Byrd and coauthors suggests that times haven't changed. They argue that the benefits of continued use of fluoroquinolines in animals outweigh the costs to human and animal health. To support that case, they assert that the use of fluoroquinolines in animals is "minor," while ignoring its human uses.

In fact, 800 tons of fluoroquinolines are used annually in humans, 120 tons in animals; the latter use, hardly minor, threatens the former. Byrd *et al.* point out that resistance to fluoroquinolines in human commensal bacteria arises independently of fluoroquinolone use in animals. That is correct, but irrelevant to our case; the question is whether the animal uses *add* to the resistance load. The weight of epidemiological evidence shows that food of animal origin is the source of most food-borne bacterial infections caused by Campylobacter (as well as non-typhoid Salmonella, Yersinia, *Escherichia coli* 0157, and other pathogens). So the question is whether the use of these drugs in animal feeds contributes to the increase of resistant *C. jejuni* and *E. coli*. Such increases were seen in Europe after the introduction of enrofloxacin in veterinary medicine, and again in the United Kingdom after the approval of quinolines for the same purpose. The increase in the United States reported in our Editorial was the third case, and one can only hope it will be the last [see (*1*) for an authoritative review of these human costs].

To buttress their case for benefits, Byrd *et al.* say that the presence of *C. jejuni* strains in chickens protects handlers and consumers against severe diarrhea and campylobacteriosis. Actually, between 60 and 80% of chickens sold for consumption in U.S. supermarkets have some Campylobacter contamination. Antibiotic use has little effect on that proportion, but what it does do is to make more of the bacteria antibiotic-resistant. The data we cited show that the eventual result is an increase in the proportion of resistant pathogens in people who are buying and eating the chickens. There are about 2.4 million cases of Campylobacter disease in the United States each year (*2*). Clearly, exposure to these bacteria is not a protective event. Why Byrd *et al.* count it as a benefit is not clear.

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Taiwan Seeks to Solve Its Resistance Problems

THE IMPORTANT ROLE OF FOOD ANIMALS IN antibiotic resistance was emphasized in the Editorial by Stanley Falkow and Donald Kennedy. Taiwan has had a serious antibiotic resistance problem for many years. In 1997, the National Health Research Institutes (NHRI), an institute modeled after the U.S. National Institutes of Health, established a program to address it. The program includes social advocacy and a national surveillance program to ascertain the extent of the resistance problem in human medicine. The results of the study revealed that the major resistance problems were associated with the cheaper "first-line" antibiotics such as penicillins, first-generation cephalosporins, gentamicin, and erythromycin, rather than the more expensive second- and third-generation cephalosporins, carbapenems, fluoroquinolines, and vancomycin (*1*). These latter were being regulated in hospital practice by requiring proof of indication or by consultation.

Our work attracted the attention of the Control Yuan, a governmental oversight body on the same level as the executive, legislative, and judiciary branches of government. The Control Yuan pointed out that regulations of the Department of Health and the Commission on Agriculture (COA) concerning the production, import, and use of antibiotics were inadequate, mutually contradictory, or not enforced. Both departments responded with major efforts that continue today to address the criticisms.

Although such corrective measures are laudable, they alone are not sufficient to reduce the problem of antibiotic resistance. Physicians and their patients must also be involved. On the basis of the experiences of other countries, it is clear that to reduce antibiotic resistance, the consumption of antibiotics must be substantially reduced (*2*). We identified two areas of substantial abuse: antibiotic prophylaxis for clean surgeries (*3*) and antibiotic use for upper respiratory infections in outpatient practice (unpublished data). If these abuses were corrected, the total consumption of first-line antibiotics could be lowered by as much as 25%. Taiwan's Department of Health and the National Health Insurance Bureau have now targeted these two areas of antibiotic abuse for correction: in February 2001, the latter announced that it will no longer pay for antibiotics prescribed for acute upper respiratory infections or the common cold.

The importance of transmission of antibiotic-resistant bacteria from food animals is also being addressed. In 2000, after action by the Control Yuan, the COA prohibited the use of seven antibiotics (including avoparcin) for growth purposes. We found in chickens a substantial number of vancomycin-resistant Enterococci, as well as *Escherichia coli* and Salmonella with reduced susceptibility or resistance to ciprofloxacin (*2*). In July 2000, the COA instituted, with the participation of NHRI, a national surveillance program to determine the extent of antibiotic use in chickens and pigs and the extent of antibiotic-resistant bacteria in their fecal flora, data which can then be used to assess the types of antibiotic resistance in animals that might be a threat to human health.

Thus, in the last 2 years, Taiwan has begun a significant national effort to address the issue of antibiotic resistance, which, if carried out conscientiously, should have a substantial impact on the problem.

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Antibiotic Resistance Affects Plant Pathogens

FALKOW AND KENNEDY'S EDITORIAL OUTLINES the current problems with selection for clinically relevant antimicrobial resistance in bacterial pathogens of animals, and presents a challenge for the development of novel antimicrobials specific for animal pathogens. The situation with antibiotics and plant bacterial disease management is similar. Resistance to streptomycin and tetracycline, antibiotics used mostly on fruit crops such as apple and peach in the United States, is widespread among plant-pathogenic and plant-associated bacteria in some nursery and orchard environments (*1*). The common resistance determinants encoded by these bacteria are very similar to those found in clinical pathogens (*2*), indicating that plants can also serve as a reservoir for antibiotic resistance in the environment.

The co-mingling of agricultural issues (for example, transgenic crops and animals, food safety, water use and quality) and human health issues will become increasingly apparent in the 21st century. Our ability to effectively manage crop diseases hinges on the availability of choices of antimicrobials or other alternatives that will have limited effects on clinical pathogens. Thus, genomics efforts must also be directed toward studying plant pathogens with the goal of improving the efficiency of agricultural production with minimal adverse effects on human and environmental health.

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CORRECTIONS AND CLARIFICATIONS

NEWS FOCUS: "Patience yields secrets of seed longevity" by K. Brown (9 Mar., p. 1884). In column 3, paragraph 2, Flanders Field was incorrectly identified as being in The Netherlands instead of Belgium.

LETTERS: "Discovery of earliest hominid remains" by M. Pickford (9 Feb., p. 986). In both the text of the letter and in the caption of the accompanying figure, Brigitte Senut's first name was misspelled.

REPORTS: "Central role for the lens in cave fish eye degeneration" by Y. Yamamoto and W. R. Jeffery (28 Jul. 2000, p. 631). In the Abstract, the sentence beginning on line 5 should have read "Conversely, eye growth and development are retarded after transplantation of a cave fish lens into a surface fish optic cup or lens extirpation."

CREDIT: (LEFT) JOHN HAMILTON SMITH/CORBIS; (CENTER) JOE VALBUENA/USDA; (RIGHT) SCOTT BAUER