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Point/Counterpoint

Does Misuse of Antibiotics in Food Animals Threaten Human Health?

NO

By Dr. Richard Carnevale
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After 50 years and a mountain of published research, it is clear that the use of antibiotics to keep food animals healthy presents an extremely small risk to humans. In fact, recent data suggest that the greater risk to food safety is making decisions to ban antibiotics without sufficient scientific basis.

Antibiotics are used in food animals to treat disease, prevent disease, and control disease, and to maintain health and promote growth. Less than 10% of the antibiotics used in animals fall into the last category. The use of other terms and estimates to describe antibiotic use are simply mechanisms of obfuscation.

The evidence documenting the very small risk to humans is strong and growing.

Overwhelmingly, the major problems with antimicrobial resistance in human medicine, as documented by physicians, have little if anything to do with animals or food. MRSA, by all accounts the biggest resistance concern, is not the result of antibiotic use in animals.

Clear and dramatic reductions in foodborne pathogens in our meat supply, and the reduced incidence of foodborne infections as reported by USDA and the Centers for Disease Control and Prevention, cut the already small risk of resistant foodborne bacteria being transferred to humans.

Quantitative, data-driven risk assess-

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YES

By David Wallinga, M.D., M.P.A
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More and more, public health experts agree that agricultural overuse of antibiotics harms human health. Last December, the World Health Organization concluded, "There is clear evidence of the human health consequences" from agricultural use of antibiotics, including "infections that would not have otherwise occurred, increased frequency of treatment failures (in some cases death) and increased severity of infections."[1] In 2003, the National Academy of Sciences likewise stated, "Clearly, a decrease in antimicrobial use in human medicine alone will have little effect on the current situation. Substantial efforts must be made to decrease inappropriate overuse in animals and agriculture as well."[2]

Although some quantitative risk assessments purport to show low human health risks from antibiotic use in food animals, those assessments ignore key aspects of the issue — notably the transferability of resistance determinants. Indeed, methods to quantify this critical attribute of bacteria do not now exist.

To date, quantitative assessments have focused solely on potential treatment failures for traditional foodborne pathogens. Moreover, those assessments have ignored nonfood pathways for transmitting resistant pathogens or resistance determinants, including

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ments show very small risks. For example, a study of the use of two macrolide products concluded their use is accompanied by a very low risk to public health. As one of the scientists said, "People would be more likely to die from a bee sting than for their antibiotic treatment to fail because of macrolide-resistant bacteria in meat or poultry."

Other studies have also demonstrated the danger of making decisions about antibiotic use without a scientific risk assessment. A risk assessment on the use of fluoroquinolones to treat sick chickens showed that withdrawal of the product would increase the incidence of foodborne illness by more than 100 cases for each incidence of antibiotic-resistant disease avoided, due to more foodborne pathogens contaminating slaughter plants.

Any serious discussion of risk and risk management options must be done on the basis of specific drug/pathogen combinations. A common mistake is to make reference to the risks associated with broad antibiotic use and to confuse potential hazards with risks. Critics like to cite numerous published studies where resistance to antimicrobials in enteric bacteria has been reported and then conclude that human health is being compromised. Yet the evidence that those bacteria actually arose due to animal use and then led to untreatable human infections is rarely if ever available.

Another common mistake is to confuse risk with the amounts of antibiotics used. Clearly, those who wish to attribute risk based on overall quantities used in animals have an agenda outside of scientific risk assessment. The amount of use of a particular drug may be an important data point in an accurate risk assessment of the compound, but it is not a substitute for quantitative risk assessment.

The European experience in banning the growth promotion uses of antibiotics without scientific basis demonstrates the unintended consequences of making policy decisions without a firm scientific basis. Danish statistics show the ban on growth-promoting antibiotics spurred an increase in animal disease. While overall antibiotic use declined, therapeutic use significantly increased. While rates of resistant bacteria in animals declined, there was no decrease in resistance in human clinical infections. So where is the public benefit of this action?

Current protections built into the use of antibiotics safeguard public health while allowing for the use of these products to preserve animal health. The veterinary community has written and follows principles of proper use for antibiotics in animals. Monitoring and surveillance systems to watch for the rise of resistant bacteria are in place, and can be strengthened. As many experts have pointed out, the best protection against the foodborne spread of resistant bacteria is improvement in food hygiene, and data show large gains have been made in that arena. Finally, science-based, data-driven risk assessments on both new and existing antibiotic products should be the basis for policy decisions about their use.

Data and experience show that non-science based decisions about antibiotic use are likely to have unintended, negative consequences for animal health and food safety.

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through occupational exposure and the environment. While a quantitative determination that merely examines part of the problem can suffice to show a risk, the converse is *not* true: no credible claim that antibiotic use is safe can be made without also examining transferability of resistance determinants, and the full range of pathways.

Articles purporting to find no impact typically have been written by authors connected to industry. In one instance, authors noted they were "initially convened as an advisory board" by the Animal Health Institute (AHI), the trade association representing producers of agricultural antibiotics. They stated, "We are grateful to AHI who kindly agreed to cover the costs of the preparation of this review: circulation of drafts, acquisition and circulation of references, and production of fair copy based on the drafts."[3] The Deputy Director of FDA's Center for Veterinary Medicine noted that the article "contains several factual errors" and that the assessment "diverges from the majority of the peer-reviewed scientific literature on the subject, casting doubt on how objectively the authors reviewed the published data."[4]

Ample evidence thus supports restrictions on agricultural use of antibiotics — particularly the long-term, relatively low-dose use of antibiotics as feed additives, a practice particularly likely to stimulate spread of resistance determinants. These additives are used not to treat sick animals, but rather for non-therapeutic purposes, i.e., to promote growth and to prevent disease more likely to result from crowded, often stressful conditions. APUA's own exhaustive report in 2002 reviewed 500 studies and concluded, "The elimination of non-therapeutic use of antimicrobials in food animals and agriculture will lower the burden of antimicrobial resistance... with consequent benefits to human and animal health."[5] The Union of Concerned Scientists estimates that this use constitutes 70%[6] of total antimicrobial use in the U.S. By contrast, the Animal Health Institute cites the deceptively low figure of "less than 10%" of antibiotics being used in animals for growth promotion, an estimate that disregards the widespread and routine use of antibiotics for disease prophylaxis.

The FDA acknowledges that its cumbersome process for withdrawing agricultural drugs takes six to 20 years to complete *per drug or drug class*.[7] Bipartisan legislation has been introduced to more expeditiously phase out use of feed additives of antibiotics that belong to classes of drugs also used in human medicine. The American Medical Association and dozens of other health organizations endorse the legislation.

It's already clear that industry can meet this challenge. Both McDonald's Corporation and the major food-service company Bon Appétit have developed meat procurement policies aimed at reducing agricultural use of antibiotics. However, we ultimately need legislation to level the playing field and to fully address this problem. WHO-selected experts have

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reviewed the phase-out of antimicrobial feed additives as growth promoters by Denmark — the world's largest pork exporter — and found a 54% reduction in antimicrobial use in food animals. The phase-out had "no serious negative effects" on efficiency of food animal production, animal health, food safety and consumer prices, but was "very beneficial in reducing antimicrobial resistance in important food animal reservoirs," thereby reducing the threat of resistance to public health.[8]

To paraphrase the title of a 2001 guest editorial from the *New England Journal of Medicine*: "Antibiotic use in animal feed — time to stop."[9]

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cern, since severe foodborne disease (FBD) cannot be effectively treated and may result in therapeutic failure and death.[1] Scientific evidence from industrialized nations points to antimicrobial agents used for livestock and poultry as the main risk factor for the development of resistance in foodborne pathogens (FBP). [1,2]

While most industrialized countries established foodborne antimicrobial resistance monitoring programs during the last decade, very few, if any, Latin American countries have established such surveillance systems. Moreover, there is very little information on how food animal production contributes to FBP resistance in countries where diarrheal diseases are endemic.

In response to the need to generate information on FBP antimicrobial resistance in Mexico, the Fundación Mexicana para la Salud, Capitulo Peninsular (Mexico) and the U.S. Food and Drug Administration (FDA) Center for Veterinary Medicine initiated the Resistvet Project, a surveillance program in four agricultural states. Prior to the establishment of the official network in 2002 with a three-year cooperative agreement awarded by the FDA, participating laboratories received a series of training courses to ensure standardization of methods and a minimum standard of performance.

Network Capacities

Each participating center conducts statewide active surveillance in slaughterhouses, retail meats, and ill and asymptomatic humans. The slaughterhouse and meat surveillance is closely integrated with the state government program and is jointly conducted with official inspectors. Each laboratory has capacity for the isolation and identification of *Salmonella, Campylobacter* and *Escherichia coli*. Susceptibility testing is performed by disk diffusion and agar dilution using NCCLS standards. Serotyping and molecular analysis of isolates are performed at the coordinating laboratories. This paper presents the most relevant findings of the network to date and discusses their implications for regulatory policy and intervention strategies.

Salmonella and *Campylobacter* Surveillance

Salmonella Enteritidis and *Salmonella* Typhimurium are the two top serotypes isolated from ill humans. In 2002, they represented 22% and 12%, respectively, of all serotypes from this source. In addition, *S.* Typhimurium is the most multidrug resistant serotype isolated. The number of resistance determinants in *S.* Typhimurium has progressively increased in the last four years. In 2002, a strain resistant to ten antibiotics, including third-generation cephalosporins, was detected in Yucatan. This has now become the predominant strain of *S.* Typhimurium in humans and retail meats in that state.

The prevalence of *Salmonella* in humans and retail meat varies considerably by geographic location and season. During the summer, up to 45% of diarrheal samples and 33% of fecal samples from healthy kindergarten children have *Salmonella*. Similarly, *Salmonella* can be isolated in up to 90-100% of retail meat. Molecular analysis of *Salmonella* strains of human and food animal origin has shown that many of these are genetically identical.[3] The high prevalence of *Salmonella* in humans and retail meats, and the genetic similarity between these strains suggests that in Mexico considerable transfer from food animals to humans occurs via the food chain.

Quinolone-resistant *Salmonella* and fluoroquinolone-resistant *Campylobacter* are emerging problems, with the prevalence of these resistant organisms higher than in industrialized countries such as the U.S. and Denmark (Table 1). In Mexico, nalidixic acid-resistant *Salmonella* is highest in samples of poultry origin, particularly in *S.* Meleagridis, *S.* Enteritidis, and *S.* Albany.[4] Ciprofloxacin resistance is highly prevalent in *Campylobacter jejuni* of human and poultry origin, and over half of the isolates are non-susceptible to erythromycin. Multidrug resistance to ciprofloxacin, erythromycin and gentamicin is highest in *C. coli* from pork.[5] These results strongly suggest heavy use of fluoroquinolones and tylosin by poultry and swine producers in Mexico.

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