An HSUS Report: Human Health Implications of Non-Therapeutic Antibiotic Use in Animal Agriculture

Abstract

For decades, the U.S. meat industry has fed medically important antibiotics to chickens, pigs, and cattle to accelerate their weight gain and prevent disease in the stressful and unhygienic conditions that typify industrialized animal agriculture production facilities. A strong scientific consensus exists, asserting that this practice fosters antibiotic resistance in bacteria to the detriment of human health. In response to this public health threat, the European Union has banned the non-therapeutic feeding of a number of antibiotics of human importance to farm animals. Given these serious concerns as well as recent data that suggest an overall lack of financial benefit, the U.S. meat industry should discontinue this risky practice.

Introduction

In 1951, the U.S. Food and Drug Administration (FDA) approved the addition of penicillin and tetracycline to chicken feed as growth promoters, encouraging pharmaceutical companies to mass-produce antibiotics for animal agriculture.[1] By the 1970s, nearly 100% of all birds commercially raised for meat in the United States were being fed antibiotics.[2] By the late-1990s, poultry producers were using 5 million kg (11 million lb) of antibiotics annually, more than a 300% increase from the 1980s.[3] The thousands of tons of antibiotics used in animal agriculture are typically not for treatment of sick and diseased animals. Rather, the drugs are used for non-therapeutic purposes. More than 90% of U.S. pig farms, for example, feed the animals antibiotics for such non-treatment reasons as promotion of weight gain.[4]

Although the European Union has banned the use of a number of antibiotics of human importance in farm animals for non-treatment purposes since 1998, producers in the United States continue to mix more than one dozen different antibiotics into farm animal feed. The Union of Concerned Scientists (UCS) estimates that 70% of antimicrobials used in the United States are fed to chickens, pigs, and cattle for non-therapeutic purposes,[5] primarily to birds raised for meat due to the scale and intensification of the poultry industry. Additionally, three antibiotics have been approved by the FDA for therapeutic use in the U.S. aquaculture industry, which consumes tons of antibiotics annually.[6] Globally, it is estimated that half of the antibiotics produced in the world go not to human medicine but to usage on the farm.[7]

Antibiotics and Growth Promotion

The scientific community is still uncertain as to why the low-level feeding of antibiotics promotes faster weight gain in animals raised for meat.[8] One possible explanation is the “resource allocation theory”: Since only a certain amount of energy, protein, and other nutrients enter an animal’s system at any one time, resources directed towards mounting an effective immune response are diverted from building muscle (meat), thereby introducing a potential trade-off between production traits desirable for industry and immunocompetence.[9,10] According to this explanation, feeding antibiotics at a low level reduces immune system activity, freeing more resources for growth and weight gain.

For example, germ-free chicks raised in germ-free environments grow faster than chickens living in unsanitary conditions.[11] Exposure to the normal microbial flora of the gut are enough of an immune stimulus to reduce growth rates significantly.[12] Indeed, even without tissue damage or evidence of disease, immune function can divert energy from maximal growth.[13] Animals raised in more sanitary environments and given antibiotics experience no change in growth rates, whereas animals in commercial production who are fed antibiotics demonstrate a remarkable spurt in growth.[14]

The maintenance of an effective immune system is metabolically very costly.[15] Macrophage immune cells burn about half as much energy as maximally functioning heart muscle cells.[16] Because antibodies are made of protein, when the body is producing thousands of antibodies per second, there may be less protein available for growth. One study showed that chickens capable of mounting a decent antibody response have lower weight and lower feed efficiency than chickens with suboptimal antibody production.[17]

Immune challenges can result in a greater than 20% decline in daily weight gain for farm animals, while increasing protein demands as much as 30%,[18] demonstrating the inverse relationship between growth and immunity. In the unhygienic conditions of intensive confinement animal production operations, normal physiological processes like growth may be impaired in light of the infectious load to which animals are exposed. A constant influx of antibiotics may reduce that load.[19]

Unnaturally rapid growth[*] due to genetic manipulation can result in pathological conditions that can further stress the animals, such as painful crippling leg and joint deformities.[20] Animal agriculture industry journal *Feedstuffs* reports that "broilers [chickens raised for meat] now grow so rapidly that the heart and lungs are not developed well enough to support the remainder of the body, resulting in congestive heart failure and tremendous death losses."[21] Pharmacological growth acceleration adds additional stress.

Concern regarding the relationship between inappropriate production conditions and antibiotic usage spans decades. "Present production is concentrated in high-volume, crowded, stressful environments, made possible in part by the routine use of antibacterial in feed," the congressional Office of Technology Assessment wrote in 1979. "Thus the current dependency on low-level use of antibacterial to increase or maintain production, while of immediate benefit, also could be the Achilles' heel of present production methods."[22]

Potential Risks to Human Health

Indiscriminate use of antibiotics may lead to the evolution of resistance by selecting directly for drug-resistant pathogens as well as for mobile genetic elements carrying resistance determinants to both human and non-human animal pathogens. Antibiotics and antibiotic-resistant bacteria can be found in the air, groundwater, and soil around farms and on retail meat,[23] and people can be exposed to these pathogens through infected meat, vegetables fertilized with raw manure, and water supplies contaminated by farm animal waste.[24]

According to the Centers for Disease Control and Prevention (CDC), at least 17 classes of antimicrobials are approved for farm animal growth promotion in the United States,[25] including many families of antibiotics that are critical for treating human disease, such as penicillin, tetracycline, and erythromycin.[26] As the bacteria become more resistant to the antibiotics fed to chickens and other animals raised for meat, they may become more resistant to the antibiotics needed to treat sick people. Resistance genes that emerge can then be swapped between bacteria. Italian researchers published a DNA fingerprinting study in 2007 showing that these antibiotic-resistance genes could be detected directly in meat products from chickens and pigs.[27]

The world's leading medical, agricultural, and veterinary authorities have reached consensus that antibiotic overuse in animal agriculture is contributing to human public health problems. A joint scientific analysis co-sponsored by the World Health Organization, the Food and Agriculture Organization of the United Nations, and the World Organisation for Animal Health concluded: "[T]here is clear evidence of adverse human health

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[*] For more information, see: "An HSUS Report: Welfare Issues with Selective Breeding for Rapid Growth in Broiler Chickens and Turkeys" at www.hsus.org/farm/resources/research/practices/fast_growth_chickens_turkeys.html.

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."

This conclusion was derived from multiple lines of evidence including epidemiological studies tracing drug-resistant human infections to specific farm animal production facilities; temporal associations demonstrating antibiotic use in farm animal populations preceding the emergence of the same resistance in humans; and microbial studies showing that antibiotic-resistant bacteria from farm animals not only infect humans, but may transfer that resistance to other bacteria that colonize the human gut.[28] The strongest evidence may be data from Europe's experience, which showed that after antibiotics were banned for growth promotion in animal agriculture, there was a subsequent decrease in the levels of antibiotic-resistant bacteria in farm animals, on meat, and within the general human population.[29]

According to the head of the CDC's food poisoning surveillance program, "[t]he reason we're seeing an increase in antibiotic resistance in foodborne diseases [in the United States] is because of antibiotic use on the farm."[30] However, antibiotic resistance is escalating not only in the United States, but globally. The Director-General of the World Health Organization fears that this worldwide rise in antibiotic-resistant "superbugs" is threatening to "send the world back to a pre-antibiotic age."[31] As resistant bacteria become resistant to second- and third-line drugs, CDC medical epidemiologist David M. Bell was quoted as saying that "we're skating just along the edge."[32] The bacteria seem to be evolving resistance faster than our ability to create new antibiotics. "It takes us seventeen years to develop an antibiotic," explains National Institutes of Health medical historian David Morens. "But a bacterium can develop resistance virtually in minutes. It's as if we're putting our best players on the field, but the bench is getting empty, while their side has an endless supply of new players."[33] Remarked University of Illinois microbiologist Abagail Salvers, "Never underestimate an adversary that has a three-point-five-billion-year head start."[34]

Case Studies: Drug-Resistant *Campylobacter*, *Salmonella*, *E. coli*, MRSA, and Influenzavirus A

The poultry industry blames the dramatic rise in antibiotic-resistant bacteria on overuse of all antibiotics, including the over-prescription of antibiotics by physicians for their patients.[35] While doctors undoubtedly play a role, according to the CDC, evidence is accumulating that overuse by animal agriculture industries is a public health threat.[36] The September 2005 FDA decision against the Bayer Corporation is illustrative of this point.

Campylobacter is a spiral-shaped poultry bacterium that corkscrews its way into the lining of the intestine "with a speed that cannot be matched by other bacteria."[37] Typically, *Campylobacter* causes only a self-limited diarrheal illness ("stomach flu") that does not require antibiotics. However, if the gastroenteritis is particularly severe or if doctors suspect that the bacteria may be crossing the gut into the bloodstream, the initial preferred drug is typically a quinolone antibiotic like Cipro. Quinolone antibiotics have been used in human medicine since the 1960s, but widespread antibiotic-resistant *Campylobacter* did not arise until after quinolones were licensed for use in chicken production in the mid-1990s.[38] In countries like Australia, which reserved quinolones exclusively for human use, resistant bacteria are practically unknown.[39]

The FDA concluded that the use of Cipro-like antibiotics in chicken production compromised the treatment of nearly 10,000 Americans annually, meaning that thousands of people infected with *Campylobacter* who sought medical treatment were initially treated with an antibiotic to which the bacteria was resistant,[40] forcing the doctors to switch to more powerful drugs. A study involving thousands of patients with *Campylobacter* infections showed that resistant strains led to up to nearly ten times more complications—including infections of the brain, the blood, and, the most frequent serious complication they noted, death.[41]

When the FDA announced that it intended to join other countries and ban quinolone antibiotic use on U.S. poultry farms, the drug manufacturer Bayer initiated legal action that successfully delayed the ban for five years.[42] During that time, Bayer continued to dominate the market, estimated at $15 million annually,[43] and resistance continued to climb.[44]

Antibiotic-resistant *Salmonella* has also led to serious human medical complications.[45] Foodborne *Salmonella* emerged in the U.S. Northeast in the late-1970s and has since spread throughout North America. One theory holds that multidrug-resistant *Salmonella* was disseminated worldwide in the 1980s via contaminated feed made out of farmed fish[†] who had been fed routine antibiotics.[46] The practice of using antimicrobial agents in fish farming has been criticized by the CDC.[47] The CDC is especially concerned about the recent rapid dissemination of a strain resistant to nine separate antibiotics, including the primary treatment used in children.[48] *Salmonella* kills hundreds of Americans every year, hospitalizes thousands, and sickens more than 1 million.[49] Under industry pressure, the FDA recently delayed and then revoked its ban on the off-label use of third-generation cephalosporins in animal agriculture,[50] the drugs of choice for invasive *Salmonella* infections in children.[51]

Evidence is mounting that antibiotic-resistant bladder infections may be tied to farm animal drug use as well.[52] Urinary tract infections (UTIs) are the most common bacterial infections in women of all ages,[53] affecting millions every year in the United States. From a physician's perspective, UTIs are increasingly difficult to treat, as antibiotic resistance among the chief pathogen, *E. coli*, becomes more common.[54]

Perhaps the most familiar *E. coli* strain is *E. coli* O157:H7, perhaps best known for a Jack-in-the-Box restaurant outbreak that sickened hundreds and killed four children in 1993. Clinically, human infection starts as hemorrhagic colitis (profuse bloody diarrhea) and can progress to kidney failure, seizures, coma, and death. This class of toxin-producing foodborne bacteria remains the leading cause of acute kidney failure in North American children.[55] Though fewer than 100,000 Americans get infected every year and fewer than 100 die,[56] millions get "extraintestinal" *E. coli* infections—UTIs that can invade the bloodstream and are responsible for an estimated 36,000 deaths annually in the United States.[57] While the source of human *E. coli* O157:H7 infection is known to be fecal contamination from the meat, dairy, and egg industries,[58] only recently have scientists traced the path of UTI-type *E. coli*.

Medical researchers at the University of Minnesota took more than 1,000 food samples from multiple retail markets and found evidence of fecal contamination in 69% of the pork and beef tested, and 92% of the poultry samples as evidenced by the presence of *E. coli*. More than 80% of the *E. coli* they recovered from beef, pork, and poultry products were resistant to one or more antibiotics, and greater than half of the samples of poultry bacteria were resistant to more than five drugs. Nearly half of the poultry samples were contaminated with the extraintestinal pathogenic *E. coli* bacteria, abbreviated ExPEC, further supporting the notion that UTI-type *E. coli* may be foodborne pathogens as well.[59] Scientists suspect that by eating chickens and other animal products, women infect their lower intestinal tract with these antibiotic-resistant bacteria, which can then migrate into their bladder.[60]

Alarmingly high rates of methicillin-resistant *Staphylococcus aureus* (MRSA) detection in farm animals and retail meat in Europe has led to increased scrutiny of the agricultural use of antibiotics. The Dutch Agriculture, Nature, and Food Standards Minister, Cees Veerman, was recently reported as saying that "the high usage of antibiotics in livestock farming is the most important factor in the development of antibiotic resistance, a consequence of which is the spread of resistant microorganisms (MRSA included) in animal populations."[61] The 2008 discovery of MRSA in North American pigs suggests the potential public health risk attributed to farm animal-associated MRSA may be a global phenomenon.[62] Recently, the majority (70%) of pigs tested in Iowa and Illinois were found to be carrying MRSA.[63] According to 2009 published findings from Louisiana State University, 5.6% of retail pork samples were contaminated with human-type MRSA.[64]

Drug resistance is not limited to bacteria. In the 2005 *Washington Post* exposé, "Bird Flu Drug Rendered Useless," it was revealed that for years Chinese chicken farmers had been lacing the animals' water supply with the antiviral drug amantadine to prevent economic losses from bird flu.[65] The use of amantadine in the water

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[†] For more information, see: "An HSUS Report: The Welfare of Animals in the Aquaculture Industry" at www.hsus.org/farm/resources/research/welfare/welfare_aquaculture.html.

supply of commercial poultry as prophylaxis against avian influenza[‡] was pioneered in the United States after the 1983 outbreak in Pennsylvania. Even then it was shown that drug-resistant mutants arose within nine days of application.[66] The practice in China has been blamed for the emergence of widespread viral resistance to a life-saving drug that could be used in a human pandemic.[67] "In essence," wrote Frederick Hayden, the Stuart S. Richardson Professor of Clinical Virology in Internal Medicine at the University of Virginia School of Medicine, "this finding means that a whole class of antiviral drugs has been lost as treatment for this virus."[68]

Calls to Ban the Use of Non-Therapeutic Antibiotics in Animal Agriculture

The European science magazine *New Scientist* editorialized in 1968 that the use of antibiotics to make animals grow faster "should be abolished altogether."[69] Pleas for caution in the overuse of antibiotics can be traced back farther to the discoverer of penicillin himself, Sir Alexander Fleming, who told *The New York Times* in 1945 that inappropriate use of antibiotics could lead to the selection of "mutant forms" resistant to the drugs.[70] While the European Union banned the use of certain medically important antibiotics as farm animal growth promoters years ago,[71] no such comprehensive step has yet taken place in the United States.

The American Medical Association, the American Public Health Association, the Infectious Diseases Society of America, and the American Academy of Pediatrics are among the 350 organizations nationwide that have endorsed efforts to phase out the use of antibiotics important to human medicine as animal feed additives.[72]

In 2001, Donald Kennedy, editor-in-chief of *Science*, and Stanley Falkow, professor of Microbiology and Immunology at Stanford University, wrote that the continued feeding of medically important antibiotics to farm animals to promote growth goes against a "strong scientific consensus that it is a bad idea."[73] An editorial the same year in the *New England Journal of Medicine* entitled "Antimicrobial Use in Animal Feed—Time to Stop" came to a similar conclusion.[74]

Despite the consensus among the world's scientific authorities, debate on this issue continues. The editorial board of *Nature Reviews Microbiology* journal offered an explanation: "A major barrier is the fact that many scientists involved in agriculture and food animal producers refuse to accept that the use of antibiotics in livestock has a negative effect on human health….It is understandable that the food-producing industry wishes to protect its interests. However, microbiologists are aware of, and understand, the weight of evidence linking the sub-therapeutic use of antibiotics with the emergence of resistant bacteria. Microbiologists also understand the threat that antibiotic resistance poses to public health. As a profession, we must be vocal in supporting any policy that diminishes this threat."[75]

An editorial in the *Western Journal of Medicine* identified erroneous claims made by the pharmaceutical and meat industries and concluded: "The intentional obfuscation of the issue by those with profit in mind is an uncomfortable reminder of the long and ongoing battle to regulate the tobacco industry, with similar dismaying exercises in political and public relations lobbying and even scandal."[76]

This is not the first time the animal agriculture industry has used growth-promoting drugs at the potential expense of human health. Decades ago, the poultry industry pioneered the use of the synthetic growth hormone diethylstilbestrol (DES) in agriculture, despite the fact that it was a known carcinogen. Although some women were prescribed DES during pregnancy—a drug advertised by manufacturers to produce "bigger and stronger babies"[77]—the chief exposure for Americans to DES was through residues in meat. Even after it was proven that women who were exposed to DES gave birth to daughters with high rates of vaginal cancer, the meat industry was able to stonewall a ban on DES in chicken feed for years.[78] According to a Stanford University health policy analyst, only after a study found DES residues in marketed poultry meat at 342,000 times the levels found to be carcinogenic did the FDA finally ban it as a growth promoter in poultry production in 1979.[79]

[‡] For more information, see: "An HSUS Report: Human Health Implications of Intensive Poultry Production and Avian Influenza" at www.hsus.org/farm/resources/research/pubhealth/public_health_avian_influenza.html.

Kennedy, who served as commissioner of the U.S. Food and Drug Administration from 1977 to 1979, describes the antibiotic debate as a "struggle between good science and strong politics." When meat production interests pressured Congress to shelve an FDA proposal to limit the practice, Kennedy concluded: "Science lost."[80]

Financial Ramifications

The U.S. Government Accountability Office released a 2004 report on the use of antibiotics as growth promoters in farm animals. Though the GAO acknowledged that the bulk of studies "found that the use of antibiotics in animals poses significant risks for human health," a ban could, in part, result in a "reduction in profits" for the industry. The report published fears that even a partial ban might "increase costs to producers, decrease production, and increase retail prices to consumers."[81]

An unsubstantiated industry estimate[82] of the costs associated with a total ban on the widespread feeding of antibiotics to farm animals in the United States is an increase in the price of poultry products from 1-2 cents per pound and an increase in the price of pork or beef between 3-6 cents per pound. This could cost the average U.S. meat-eating consumer as much as $9.72 a year.[83]

Antibiotic-resistant infections in the United States from all sources may cost billions of dollars every year[84] and may kill 63,000 people annually.[85]

A major analysis of the elimination of growth-promoting antibiotics in Denmark, one of the world's largest pork producers,[86] showed that the move led to a marked reduction in bacterial antibiotic resistance without significant adverse effects on productivity.[87] U.S. industry, however, has argued that the Danish experience cannot be extrapolated to the United States.[88] This led Johns Hopkins University researchers to carry out an economic analysis based on data from Perdue, one of the largest poultry producers in the United States.

The Johns Hopkins University Bloomberg School of Public Health study, published in 2007, examined data from 7 million chickens and concluded that the use of antibiotics in chicken feed *increases* costs of poultry production. "Contrary to the long-held belief that a ban against GPAs [growth-promoting antibiotics] would raise costs to producers and consumers," the researchers concluded, "these results using a large-scale industry study demonstrate the opposite."[89] They found that the conditions in Perdue's facilities were such that antibiotics did accelerate the birds' growth rates, but the money saved was insufficient to offset the cost of the antibiotics themselves. Growth-promoting antibiotics may end up costing producers more in the end than if they hadn't used antibiotics at all. A similar study at Kansas State University also showed suggested no economic benefits from feeding antibiotics to "finishing" pigs.[90]

Conclusion

The practice of feeding antibiotics to farm animals to promote faster growth is being phased out in countries around the world to protect the public's health. Given the lack of demonstrable benefits, the U.S. meat industry should heed the call of the U.S. public health community and global authorities to follow this lead. With few, if any, new classes of antibiotics in clinical development,[91] an expert on antibiotics at the Institute for Agriculture and Trade Policy warned that "we're sacrificing a future where antibiotics will work for treating sick people by squandering them today for animals that are not sick at all."[92]

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The Humane Society of the United States is the nation's largest animal protection organization—backed by 10 million Americans, or one of every 30. For more than a half-century, The HSUS has been fighting for the protection of all animals through advocacy, education, and hands-on programs. Celebrating animals and confronting cruelty. On the Web at humanesociety.org.