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The Overuse of Antibiotics in Food Animals Threatens Public Health

Antibiotics have been used since the 1940s and have led to a dramatic reduction in illness and death from infectious diseases. But according to the federal Interagency Task Force on Antimicrobial Resistance, "[t]he extensive use of antimicrobial drugs has resulted in drug resistance that threatens to reverse the medical advances of the last seventy years."[1] Since antibiotics have been used so widely and for so long, antibiotic resistance has become a major public health threat.

In response, there has been a concerted effort by the Centers for Disease Control and Prevention (CDC) and others to encourage doctors and patients to use antibiotics more wisely. Unfortunately, little progress has been made to reduce the use of antibiotics on farms, where most of these drugs are administered.

Approximately 80 percent of the antibiotics sold in the United States are used in meat and poultry production.[2] The vast majority is used on healthy animals to promote growth, or prevent disease in crowded or unsanitary conditions. The meat and poultry production industry argues, however, that that there is no harm in this. They say for example that "animal use contributes little, if anything, to the burden of human antibiotic resistance..."[3].

A key question is, can antibiotic use in animals promote the development of hard-to-treat antibiotic-resistant superbugs that make people sick? And if it can, are the illnesses rare occurrences, and the risks theoretical, or could current usage in animals pose a serious threat to human health.

But Consumers Union has concluded that the threat to public health from the overuse of antibiotics in food animals is real and growing. Humans are at risk both due to potential presence of superbugs in meat and poultry, and to the general migration of superbugs into the environment, where they can transmit their genetic immunity to antibiotics to other bacteria, including bacteria that make people sick.

Numerous health organizations, including the American Medical Association, American Public Health Association, Infectious Disease Society of America, and the World Health Organization, agree and have called for significant reductions in the use of antibiotics for animal food production.

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[1] Pg 5 in Interagency Task Force on Antimicrobial Resistance, 2012. A Public Health Action Plan to Combat Antimicrobial Resistance. Washington, D.C. at: http://www.cdc.gov/drugresistance/pdf/actionplan-2012.pdf

[2] Confirmed: 80 Percent of all antibacterial drugs used on animals, endangering human health. At: http://www.louise.house.gov/index.php?option=com_content&task=view&id=2697&Itemid=100065

[3] Pg 5 in American Farm Bureau Federation et al June 12, 2012 letter to Congressperson Slaughter

History of Expert Opinion

Scientific expert bodies for more than two decades have concluded that there is a connection between antibiotic use in animals and the loss of effectiveness of these drugs in human medicine. In 1988, the Institute of Medicine (part of the National Academy of Sciences) concluded that "the committee believes that important, although as yet sparse, data show the flow of distinct salmonella clones from farm animals medicated with antibiotics in subtherapeutic concentrations, through food products, to humans, who thus acquire clinical salmonellosis."[4]

Ten years later, the National Research Council (part of the National Academy of Sciences) concluded that "a link can be demonstrated between the use of antibiotics in food animals, the development of resistant microorganisms in those animals, and the zoonotic spread of pathogens to humans."[5]

In 2003, an Expert Workshop co-sponsored by the World Health Organization, Food and Agricultural Organization (FDA), and World Animal Health Organization (OIE) concluded "that there is clear evidence of adverse human health consequences due to resistant organisms resulting from non-human usage of antimicrobials. These consequences include infections that would not have otherwise occurred, increased frequency of treatment failures (in some cases death) and increased severity of infections"[6].

In 2010, the U.S. Food and Drug Administration, U.S. Department of Agriculture, and the CDC all testified before Congress that there is a connection between the routine use of antibiotics for meat production and the declining effectiveness of antibiotics for people.[7] Dr. Thomas R. Frieden, Director of the CDC, noted that "there is strong scientific evidence of a link between antibiotic use in food animals and antibiotic resistance in humans."[8]

Most recently in 2012, the FDA stated "Misuse and overuse of antimicrobial drugs creates selective evolutionary pressure that enables antimicrobial resistant bacteria to increase in numbers more rapidly than antimicrobial susceptible bacteria and thus

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[4] Pg. 2 in Institute of Medicine (IOM). 1988. *Human Health Risks with the Subtherapeutic Use of Penicillin or Tetracyclines in Animal Feed*. National Academies Press. Washington, D.C.
[5] Pg. 6 in IOM. 1998. *The Use of Drugs in Food Animals: Benefits and Risks*. National Academies Press. Washington, D.C.
[6] Pg. 1 in WHO/FAO/OIE. 2003. *Joint FAO/OIE/WHO Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial Resistance: Scientific assessment, Geneva, December 1-5, 2003.* At: http://www.who.int/foodsafety/publications/micro/en/amr.pdf
[7] Hearing: Antiobiotic Resistance and the Use of Antibiotics in Animal Agriculture, Subcommittee on Health, Energy and Commerce Committee, U.S. House of Representatives, July 12, 2010
[8] Letter from Thomas R. Frieden, Director, Centers for Disease Control and Prevention, to Keeve Nachman, Program Director, Farming For the Future, at http://www.livablefutureblog.com/wp-content/uploads/2010/11/ar-m455n_20101129_182057.pdf

increases the opportunity for individuals to become infected by resistant bacteria."[9] Also in 2012, the FDA, in its final rule banning certain extralabel uses of cephalosporin antimicrobial drugs in certain food producing animals, stated "In regard to antimicrobial drug use in animals, the Agency considers the most significant risk to the public health associated with antimicrobial resistance to be human exposure to food containing antimicrobial-resistant bacteria resulting from the exposure of food-producing animals to antimicrobials."[10]

Nevertheless, the livestock industry continues to argue that while antibiotic use may have something to do with antibiotic resistance in bacteria on the farm, it is not an important human health issue, and little change in current practices are needed.

What Happens on the Farm

Numerous studies have demonstrated that routine use of antibiotics on the farm promotes drug-resistant superbugs in those facilities. Some of the most dramatic evidence came as a result of FDA approval of flouroquinolones--a class of antibiotics that includes Cipro (ciprofloxacin), which has been used in poultry production since 1995. By 1999 nearly 20 percent chicken breasts sampled contained ciprofloxacin-resistant *Camplobacter*, a disease-causing bacteria.[11] After a long fight in the courts, FDA finally banned use of the drug in 2005, at which point nearly 30 percent of *C. coli* found in chicken breasts were ciprofloxacin resistant; by 2010, resistance to ciprofloxacin had declined to 13.5 percent.[12]

The reason for this is that when you feed antibiotics to animals, the bacteria in and around the animals are exposed to the drug, and many of them die. But there are always some that the drug can't kill, and those survive and proliferate. Voila, superbugs.

While not disputing these facts, the industry argues essentially that what happens on the farm stays on the farm. There may be some superbugs there, but they don't affect people. There are two main routes, however, by which superbugs can leave the farm and infect humans. One is a direct route, in meat and poultry products, and the other is an indirect route through the environment.

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[9] Pg. 3 in Food and Drug Administration (FDA). 2012. Guidance #209: the Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals. At: http://www.fda.gov/downloads/animalveterinary/guidancecomplianceenforcement/guidanceforindustry/ucm216936.pdf

[10] Pg. 738 in FDA. 2012. New Animal Drugs; Cephalosporin Drugs; Extralabel Animal Drug Use; Order of Prohibition. Federal Register, Vol. 77(4). http://www.gpo.gov/fdsys/pkg/FR-2012-01-06/pdf/2012-35.pdf

[11] Smith KE, Besser JM, Hedberg CW, Leano FT, Bender JB, Wicklund JH, Johnson BP, Moore KA, Osterholm MT et al. 1999. Quinolone-resistant *Camplybacter jejuni* infections. *New England Journal of Medicine*, 340(20): 1525-1532. At: http://loyce2008.free.fr/Microbiologie/diarrh%E9es%20infectieuses/Campylobacter/bla.pdf

[12] Food and Water Watch. 2012. *Antibiotic Resistance 101: How Antibiotic Misuse on Factory Farms Can Make You Sick*. 21pp. At: http://documents.foodandwaterwatch.org/doc/AntibioticResistance.pdf

Superbugs Move From Farm to Kitchen

Once they appear on the farm, superbugs most definitely move from the farm to the kitchen, via uncooked meat and poultry. *Consumer Reports* tests of chicken in both 2006[13] and 2010[14] revealed widespread presence of antibiotic-resistant pathogens in retail poultry products. In both years, more than two thirds of chicken samples were contaminated with *Salmonella* and/or *Campylobacter*, and more than 60 percent of those bacteria were resistant to one or more antibiotics.

The industry argues that even this is not a concern because people know to cook poultry thoroughly. Indeed they do, but packages can drip in the refrigerator, or cutting boards can become contaminated, as well as other problems. There aren't good data on how frequently this causes illness, especially difficult-to-treat illness, because most people just ride out an infection and it fades into the background of the estimated 48 million cases of food borne illness we have annually in the US.

But occasionally a superbug outbreak is serious enough to command the attention of the Center for Disease Control. One such case occurred in 2011, in which ground turkey was linked to 136 illnesses and one death, all caused by a strain of *Salmonella* resistant to four different antibiotics, ampicillin, streptomycin, tetracycline and gentamicin.[15] Some 36 million pounds of ground turkey were recalled.

Another case was ground beef from the Hannaford grocery store chain in New England linked in 2011 to 19 infections and at least seven hospitalizations, all caused by a strain of *Salmonella* resistant to multiple antibiotics, including amoxicillin/clavulanic acid, ampicillin, ceftriaxone, cefoxitin, kanamycin, streptomycin, and sulfisoxazole.[16]

Superbugs Move From Farm to the Environment

Superbugs can also spread beyond the farm and threaten public health through environmental transmission. This can happen in various ways, particularly via workers, or farm runoff. Once farm-raised superbugs make it off the farm, they can exchange genetic material and give their resistance to other bacteria, even of other genera and species, that have never been anywhere antibiotics. This can happen in lakes, in wild animals, and even in the human digestive tract.

Workers are particularly likely to pick up resistant bacteria from animals and take them elsewhere. A study of poultry workers in the Delmarva peninsula found they were 32 times more likely to carry gentamicin-resistant *Escherichia coli*, and more than five times more likely to carry multi-drug resistant *E. coli*, compared to other community

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[13] Consumer Reports, 2007. Dirty Birds. January 2007, pp. 20-23. Consumers Union.
[14] Consumer Reports, 2010. How safe is That Chicken. January 2010, pp. 19-23. Consumers Union.
[15] Centers for Disease Control (CDC). 2011. Investigation Update: Multistate Outbreak of Human *Salmonella* Heidelberg Infections Linked to Ground Turkey. At: http://www.cdc.gov/salmonella/heidelberg/111011/index.html
[16] CDC. 2012. Investigation Update: Multistate Outbreak of Human *Salmonella* Typhimurium infections Linked to Ground Beef. At: www.cdc.gov/salmonella/typhimurium-groundbeef/010512/index.html

members.[17] A study performed in the Midwest found methicillin-resistant *Staphylococcus aureus* (MRSA) in 70 percent of the pigs and 64 percent of the workers at one facility, while no MRSA was found in pigs or workers at a facility in another state, strongly suggesting that the MRSA strain moves between pigs and humans.[18] Indeed, a careful genetic analysis has found that a particular MRSA strain found in pigs (e.g. ST398) originated as a methicillin-susceptible *S. aureus* (MSSA) in humans, jumped into pigs, where it acquired resistance to methicillin and tetracycline, and then jumped back to humans, where it's known as livestock-associated MRSA (LA-MRSA).[19] This LA-MRSA (e.g. ST398) is quite prevalent in the Netherlands, where it is responsible for over 20% of all MRSA.[20]

However, resistant bacteria can also escape from a large livestock operation (often known as a confined animal feeding operation, or CAFO) by a number of routes, including via manure applied to fields as fertilizer,[21] from trucks transporting animals,[22] the wind leaving hog facilities[23] or even via flies attracted to the manure which can pick up and transmit resistant bacteria.[24] A recently released study of the South Platte River found that antibiotic resistance genes (coding for resistance to sulfonamides) were 10,000 times higher in river sediments downstream from larger feedlots (ones with 10,000 cattle)

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[17] Price LB, Graham JP, Lackey LG, Roess A, Vailers R and E Silbergeld. 2007. Elevated risk of carrying gentamicin-resistant *Escherichia coli* among U.S. poultry workers. *Environmental Health Perspectives*, 115(12): 1738-1742. At: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2137113/pdf/ehp0115-001738.pdf

[18] Smith TC, Male MJ, Harper AL, Kroeger JS, Tinkler GP, Moritz ED, Capuano AW, Herwalt LA and DJ Diekema. 2009. Methicillin-resistant *Staphylococcus aureus* (MRSA) strain ST398 is present in midwestern U.S. swine and swine workers. *PLoS One*, 4(1): e4258. At: http://www.plosone.org/article/info:doi/10.1371/journal.pone.0004258

[19] Price LB, Stegger M, Hasman H, Aziz M, Larsen J, Andersen PS, Pearson T, Waters AE, Foster JT et al. 2012. *Staphylococcus aureus* CC398: Host adaptation and emergence of methicillin resistance in livestock. *mBio*, 3(1): e00305-11 At: http://mbio.asm.org/content/3/1/e00305-11.full.pdf

[20] van Loo I, Huijsdens X, Tiemersma E, de Neeling A, van de Sande-Bruinsma N, Beaujean D, Voss A and J Kluytmans. 2007. Emergence of methicillin-resistant *Staphylococcus aureus* of animal origin in humans. *Emerging Infectious Diseases*, 13(12): 1834-1839. At:

[21] Chee-Sanford JC, Mackie RI, Koike S, Krapac IG, Lin Y-F, Yannarell AC, Maxwell S and RI Aminov. 2009. Fate and transport of antibiotic residues and antibiotic resistance genes following land application of manure waste. *Journal of Environmental Quality*, 38(3): 1086-1108. At: https://www.crops.org/publications/jeq/articles/38/3/1086

[22] Rule AM, Evans SL and EK Silbergeld. 2008. Food and animal transport a potential source of community exposure to health hazards from industrial farming (CAFOs). *Journal of Infection and Public Health*, 1(1): 33-39. At: http://www.academia.edu/591772/Food_animal_transport_a_potential_source_of_community_exposures_to_health_hazards_from_industrial_farming_CAFOs_

[23] Gibbs SG, Green CF, Tarwater PM, Mota LC, Mena KD and PV Scarpino. 2006. Isolation of antibiotic-resistant bacteria from the air plume downwind of a swine confined or concentrated animal feeding operation. *Environmental Health Perspectives*, 114(7): 10323-1037. At: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1513331/pdf/ehp0114-001032.pdf

[24] Graham JP, Price LB, Evans SE, Graczyk TK and EK Silbergeld. 2009. Antibiotic-resistant Enterococci and Staphylococci isolated from flies collected near confined poultry feeding operations. *Science of the Total Environment*, 407(8): At: http://www.jhsph.edu/sebin/q/h/AntibioticResistantEntero.pdf

compared to river sediment upstream from such feedlots.[25] The same study found these same antibiotic resistance genes were only 1,000 times higher from sewage treatment plants that discharge ten million gallons of effluent per day, compared to pristine sediments.

Bacteria in many environments can readily exchange genes coding for antibiotic resistance with neighboring bacteria. Antibiotic resistance genes are often located on mobile genetic elements, especially plasmids, transposons and integrons which can easily move between bacteria of the same or different species, which facilitates the spread of resistance to multiple drugs by multiple types of bacteria.[26]

The industry says that 40 percent of all the antibiotics used on the farm are drugs (called ionophores) not used in human medicine, so it doesn't matter if bacteria become resistant to them. However, a study by scientists from the United States Department of Agriculture (USDA) and Cornell University involving monensin, one of the most commonly used ionophores in cattle production in the U.S., demonstrated that use of monensin in cattle feed and the selection of monensin-resistant ruminal bacteria lead to a 32-fold increase in resistance to bacitracin, which is used in human medicine.[27] This study demonstrates that one cannot claim that ionophores cannot select for cross resistance to any antibiotic used in human medicine. The study called for more research.[28] So, it is appropriate to consider ionophore use as part of the antibiotics used in animal agriculture.

Conclusion

Use of antibiotics on the farm most definitely poses a risk to human health. Antibiotic use can promote creation of superbugs which can contaminate meat and poultry and cause hard-to-cure disease in people.

Superbugs can also exit the farm via farm workers, wind, runoff, and wildlife. Even if they don't immediately cause illness, bacteria are uniquely equipped to exchange genetic immunity via their plasmids, with other bacteria wherever they encounter them.

It is for these reasons that the public health community and FDA have been proposing to limit use of antibiotics on livestock for more than three decades (see list below). Consumers Union believes that as a prudent measure, we should drastically reduce use of antibiotics on food animals, and eliminate use altogether for growth promotion or disease prevention in healthy animals.

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[25] Pruden A, Arabi M and HN Storteboom. 2012. Correlation between upstream human activities and riverine antibiotic resistance genes. *Environmental Science & Technology*, dx.doi.org/10.1021/es302657r At: http://pubs.acs.org/doi/abs/10.1021/es302657r

[26] Marshall BM and SB Levy. 2011. Food animals and antimicrobials: impacts on human health. *Clinical Microbiology Reviews*, 24(4): 718-733. At: http://cmr.asm.org/content/24/4/718.full.pdf

[27] Houlihan AJ and JB Russell. 2003. The susceptibility of ionophores-resistant *Clostridium aminophilum* F to other antibiotics. *Journal of Antimicrobial Chemotherapy*, 52: 623-628. At: http://jac.oxfordjournals.org/content/52/4/623.full.pdf

[28] Pg. 627 in Ibid.

Some of the Organizations Supporting Restrictions on the Use of Antimicrobials in Animal Production

American Medical Association, 2001

Adopted Resolution 508, Antimicrobial Use and Resistance, which states, in part, "AMA is opposed to the use of antimicrobials at non-therapeutic levels in agriculture, or as pesticides or growth promoters, and urges that non-therapeutic use in animals of antimicrobials (that are used in humans) should be terminated or phased out".[29]

American Public Health Association, 1999, 2004

Policy Number 9908: Addressing the Problem of Bacterial Resistance to Antimicrobial Agents and the Need for Surveillance, which urged "FDA to work for regulations eliminating the non-medical use of antibiotics and limiting the use of antibiotics in animal feeds"[30] In 2004, passed a resolution urging "bulk purchasers of foodstuffs to adopt procurement policies that encourage and, where feasible, require procurement of meat, fish, and dairy products produced without nontherapeutic use of medically important antibiotics."[31]

Infectious Diseases Society of America, 2009

"IDSA supports efforts to phase out the use of antimicrobial drugs for growth promotion, feed efficiency, and routine disease prevention in food animals."[32]

World Health Organization, 2001

The WHO Global Strategy for Containment of Antimicrobial Resistance, recommends that governments "terminate or rapidly phase out the use of antimicrobials for growth promotion if they are also used for treatment of humans."[33]

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[29] http://www.keepantibioticsworking.com/new/KAWfiles/64_2_36325.pdf

[30] http://www.keepantibioticsworking.com/new/Library/UploadedFiles/American_Public_Health_Association_Policy_Numb.htm

[31] http://www.keepantibioticsworking.com/new/KAWfiles/64_2_37751.pdf

[32] http://www.keepantibioticsworking.com/new/KAWfiles/64_2_107287.pdf

[33] Pg. 10 in http://www.who.int/drugresistance/WHO%20Global%20Strategy%20-%20Executive%20Summary%20-%20English%20version.pdf