Antibiotics in the Environment and Antibiotic Resistance

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Background

We share the world with a wide range of living organisms, from microscopic bacteria to gigantic whales. Although we cannot see them, bacteria are all around us and are a normal part of our ecosystem and our lives. Various kinds of bacteria are in competition with one another for nutrients and living space. Bacteria are specialized and fill various niches in the environment. For example, the soil is full of bacteria that live off of soil nutrients, moisture and decaying material. Other bacteria live best in the bodies of people and animals, benefiting them; others cause disease.

Some soil bacteria naturally produce substances (antibiotics or antimicrobials) that inhibit the growth of other bacteria. Scientists cultivate these soil bacteria and collect the antibiotics produced. The antibiotic may be given to people to help fight infections or disease caused by other bacteria. Not all bacteria are affected the same way by the specific type of antibiotic. While the growth of non-resistant bacteria is suppressed, resistant bacteria can continue to live in the presence of antibiotics. Resistance is the inherent ability of some bacteria to resist being killed by an antibiotic. Resistance was present prior to the use of antibiotics and occurs as a result of genetic mutation or when extra chromosomal DNA (plasmid) is acquired from other bacteria. In theory, antibiotic use selects for resistant bacteria, allowing them to multiply without the competition of antibiotic-susceptible bacteria.

The literal meaning of the word “antibiotic,” used commonly for decades, is “against life.” It is less precise than the term “antimicrobial,” which means “against microbes.” Here the two names are used interchangeably, despite the scientifically more accurate meaning of the term “antimicrobial.”

Antimicrobials are used in human medicine and animal agriculture to reduce incidences of disease and death. They are given by injection, orally, and in food and water to prevent or treat diseases and as growth promoters. Exact amounts currently manufactured and used are not available.

Antibiotics used for growth promotion lessen the effects of subclinical disease; thus food consumption, weight gain and the efficiency of food use for growth are improved. They are not effective when disease is absent.

What about antibiotics from livestock production entering the environment? Will antibiotics used in livestock production have a negative impact on groundwater or surface water?

Chemicals used in homes, manufacturing and agriculture can enter the environment in wastewater. A 1999 study by the Toxic Substances Hydrology Program of the U.S. Geological Survey found a range of chemicals in residential, industrial and agricultural wastewaters and at low concentrations in surface waters. The chemicals included human and veterinary pharmaceuticals (including antibiotics), natural and synthetic hormones, detergent metabolites, plasticizers, insecticides and fire retardants. Measured concentrations of pharmaceuticals in wastewaters were much lower than would be found if a person or animal were

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consuming the chemical. Most are detected in water at concentrations less than 1 microgram per liter. These amounts are relatively small compared with the dosages provided to humans and animals to treat disease. For example, the antibiotic tetracycline may be given to humans at a rate of 2 grams per day, usually in two to four pills taken orally. If given to pigs as a growth promoter, the dosage is 0.05 gram per day. Higher concentrations occurred in sediments because of sorption. In Huron County, Michigan, a USGS study found both human-use and veterinary-use antibiotics in stream (surface) water but not in groundwater (Duris and Haack, 2004). Whether these findings are of biological, environmental or health consequence are currently unknown. Research is being proposed and conducted.

Up to 40 percent or more of the antibiotic dose may be excreted, especially for antibiotics given at therapeutic doses (Boxall et al., 2004). This is true for both humans and animals. However, various classes of antibiotics are more or less metabolized. Antibiotics are excreted in urine and feces either unchanged or metabolized in the form of the conjugated, oxidized or hydrolyzed products of parent compounds.

Antibiotics may enter the environment in wastewater or when human waste solids and animal manures are applied to cropland as plant fertilizer. Some antibiotics degrade quite slowly, possibly surviving the processes of storage and handling, and may be present in land-applied biosolids. The continual land application of biosolids could cause the rates of antibiotic accumulation in soils to exceed the rates of degradation. However, accumulation in soils is less probable as environmental regulations and voluntary generally accepted management practices limit manure application so that applied nutrients meet the requirement of the crop being grown.

Understanding the fate and transport of antibiotics in the environment is essential to assess their impact and subsequent risks to ecosystems. Sorption (absorption, taking up; and adsorption, holding) by soil plays a determinant role in controlling transport, bioavailability and, hence, fate of antibiotics in the environment. The complicated chemical structures of antibiotics lead to multiple interactions with soils (Tolls, 2001). In general, soil organic matter and minerals are the two soil components responsible for holding antibiotics. A few studies have attempted to address the sorption mechanisms, but so far they are far from being fully understood.

Do antibiotics used in animal agriculture enter the human food chain through plant uptake? If so, at what level?

In 2005, Kumar and others reported that green onion, cabbage and corn plants can take up small amounts (2 to 17 nanograms per gram of fresh tissue) of chlortetracycline from soil that had been amended with swine manure known to contain that antimicrobial. Uptake of the antibiotic tylosin was not observed. Other researchers have not been able to produce similar results. The assay to detect the antibiotics was an enzyme-linked immunosorbent assay (ELISA). This assay reportedly suffers from significant detection interferences from natural organic matter that can be derived from plant tissues (Huang and Sedlak, 2001). A carefully designed and laborious clean-up procedure may enhance the accuracy of ELISA measurements; however, the results should be confirmed with more conclusive analysis techniques such as gas chromatography and mass spectrometry or liquid chromatography and mass spectrometry.

Will antibiotics used in animal agriculture lead to antibiotic resistance in human strains of bacteria?

It is possible, but a link between agricultural use of antimicrobials and antibiotic-resistant human infections has not been proven, only speculated. The incidence of human disease caused by antibiotic-resistant organisms is not greater in people working on livestock farms than in those who do not. In the past, cases of what was believed initially to be resistant bacteria from animals spreading to humans were headlined in the press. But when these potential examples were examined closely, other more usual risk factors, such as antibiotics already in people before infection or a hospital stay, were present and much more of a health risk.

Antibiotics have been used in animals for more than 60 years. Antibiotic resistance only recently has become a major medical concern in hospitals. Whenever a population of bacteria of importance to animals or humans is exposed to an antibiotic, it encourages the predominance of the most resistant strains of the bacteria. The most well-known example of this is how rapidly gonorrhea became resistant to penicillin. It is possible for resistant bacteria from animals to make their way into humans, but many barriers stand in their way. Most bacteria that cause animal diseases are specialized for that species (species-specific) and poorly invade humans. Zoonotic bacteria, such as certain species of Escherichia coli and Salmonella are of greater concern because they are transmissible from animals to humans. Usual precautions of washing hands and thoroughly cooking foods eliminate the spread of these to humans, but these procedures do not help prevent environmental transmission (e.g., to drinking water).

Antibiotic resistance can occur in bacteria even when the antibiotics have not been used. Researchers found tetracycline- and tylosin-resistant bacteria in manure samples taken from storage facilities of swine farms where antimicrobials were not being used (Chander et al., 2006). Likewise, Smith and others (2007) reported that resistance of *E. coli* to tetracycline, sulfonamides and streptomycin was similarly prevalent in feces of broiler chickens both receiving and not receiving antibiotics. Chander and others (2006) also reported that tetracycline- and tylosin-resistant bacteria were isolated in soil of fields where manure was applied "regularly" and in the feces of dogs kept as pets on the farm. But, the prevalence of resistant bacteria did not differ among farms using or not using antimicrobials as a feed additive for growth promotion.

Bacteria have complex genetic means for transferring resistance. Some scientists hypothesize that cause (antibiotic use) and effect (antibiotic resistance) may be linked. Doubtless, detailed exploration of microbial genetics will evaluate this suggestion in the future.

If we discontinue the use of antibiotics for growth promotion and disease prevention, will that decrease the risks associated with using antibiotics in animal agriculture?

This was the thinking in Denmark and some European countries, where use of low levels of many antibiotics in livestock was banned. Monitoring the prevalence of antibiotic-resistant bacteria in animal manure found lower numbers after the ban. The designers of the antibiotic ban used this finding to claim success. However, when examining a more immediate outcome, such as the level of resistant infections in people, the results were not clear. The animals raised for food in these countries now have a lower health status and their mortality rate has increased. Because of the lower health status, it is more expensive to raise food, and the incidence of resistant infections affecting people has not decreased. Total antimicrobial use has decreased slightly, but therapeutic usage has surpassed growth promoter usage prior to the ban (DANMAP, 2005). Banning use of antimicrobials for growth promotion did not affect the incidence of antimicrobial residues in foods or the incidence of Salmonella, Campylobacter or Yersinia infections in humans (WHO, 2003).

Are animals raised in large facilities healthier or less healthy than animals raised on small and medium-sized farms?

It is very difficult to conclude that animal health is related to the size of the farm. There have been no controlled studies evaluating this. Retrospective data suggest that this is true, if one assumes that the amount of antibiotic use is correlated positively with the amount of disease. A survey conducted by the National Animal Health Monitoring System (NAHMS, 2002) found that 78 percent of farms with 2,000 or fewer pigs used feed-grade antibiotics, compared with 94 percent of farms with 10,000 or more. However, in 2005, NAHMS released a report on dairy farming documenting that a greater percentage of large (500 or more cows) and medium-sized (100 to 499 cows) operations fed antimicrobials in heifer (pre-lactation) rations than did small (fewer than 100 cows) operations (36 percent, 30 percent and 15 percent, respectively). Note that antibiotics that might appear in milk are not approved for feeding to lactating dairy cows. Antibiotics are not allowed to be present in milk for public sale according to the Federal Drug Administration's Grade A Pasteurized Milk Ordinance under the Federal Food, Drug and Cosmetics Act. Similar percentages of small (1,000 to 7,999 head) and large (8,000 head or more) beef feedlots practice antimicrobial feeding and/or watering (NAHMS, 1999). However, the assumption that the amount of antibiotic use and the amount of disease may be related may not be valid because large farms have better record-keeping systems and make greater use of veterinary services and disease diagnostics. Simply, there are more accurate data and greater veterinary use on large farms for reasons other than disease occurrence alone.

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