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CAFOs and Public Health: *The Fate of Unabsorbed Antibiotics*

PUBLIC HEALTH

EXPERT REVIEWED

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Note: Traditionally, the term "antibiotic" refers to compounds that are made by microorganisms, usually yeast or bacteria, and kill other microorganisms (e.g., penicillin). Similar compounds that are synthetic or semi-synthetic are more commonly referred to "antibacterials" or "antimicrobials" (e.g., carbadox). Both are used in food animal production, and, for the purpose of this paper, will be grouped simply as "antibiotics."

Introduction

Antibiotics are used in food animal production in two basic manners: therapeutically (typically higher doses) to treat specific diseases; and subtherapeutically (typically lower doses) for increased feed efficiency or disease prevention. Some antibiotics, however, are not absorbed very well by the animal and are passed in the urine or in manure. As manure is spread on fields as fertilizer, so are the antibiotics. Some see this as a public health concern, believing the drugs could then enter ground or surface water or be taken up by edible plants where the drugs could contribute to antibiotic resistance development and/or adverse reactions in those with antibiotic allergies. What follows is an attempt to address this concern by tracing the life (and activity) of an antibiotic from administration to an animal, to excretion in feces or urine, to application to soil as fertilizer, and finally to possible entry into and contamination of human drinking water or food.

In the Animal

Regardless of the route or purpose of antibiotic use, a portion of the dose will not be absorbed by the animal and will get passed in the urine or feces. The actual amount varies from compound to compound, but in some cases the amount unabsorbed is much greater than the amount absorbed. For example, an estimated 80% of a dose of ampicillin is excreted in urine or feces; in contrast, only 20% of bacitracin is unabsorbed[1]. Most studies looking at excretion rates report that, in general, the excreted form is the active form of the drug[2].

In Manure

In most livestock operations, manure is collected in pits. In some operations, manure is then transferred to lagoons for further remediation. Several studies have detected antibiotics in these environments[3,4,5]. Whether the drugs remain active in manure pits and lagoons (and for how long) varies from antibiotic to antibiotic. For example, the half-life of tylosin in manure (i.e., the time in which tylosin loses half of its activity) is very short, approximately one week. As such, tylosin is not usually found in high quantities in aged manure. Other drugs, such as tetracyclines, are more stable in

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manure environments and can be detected, albeit at low concentrations, for more than five months[5].

In Soil

Manure is usually taken from pits or lagoons and spread on fields both to provide nutrients for crops and to further remediate the manure. It is here that unabsorbed antibiotics are truly introduced to the terrestrial environment. Several groups have shown that varying (usually low) concentrations of active antibiotics can be found in soils treated with livestock manure[5,6,7]. Once in the soil, the fate of the antibiotic is largely dictated by how well it binds to soil and how quickly it degrades[2]. Depending primarily on those two factors, the antibiotic can degrade in soil, not degrade and enter surface water as run-off, not degrade and leach into ground water, and/or be taken up by plants.

Regarding degradation, most antibiotics become much less stable once applied to soil, but this too varies from antibiotic to antibiotic. A recent study examining degradation of common veterinary antibiotics in soil reported half-lives of 20, 27, 8, 16, and 5 days for erythromycin, oleandomycin, tylosin, tiamulin, and salinomycin, respectively[8]. Antibiotics that bind strongly to soil (i.e., are immobilized in soil) and also have shorter half-lives can be completely degraded in soil. Tylosin, for example, binds strongly to soil and has a relatively short half-life. As such, it quickly degrades once applied to soil and is not usually detected in ground water, surface water, or plants.

In Surface Water

Some antibiotics may bind strongly to soil but degrade more slowly. These drugs could enter into surface waterways through run-off. One group reported that 0.091% of sulphachloropyridazine and 0.054% of oxytetracycline applied to a field in manure was lost due to run-off (both aqueous and particulate)[9]. While these are low amounts, several groups have detected different antibiotics in rivers and streams throughout the United States. In some cases, contamination was attributed to nearby livestock operations[10].

In Ground Water

Antibiotics that do not bind strongly to soil are more mobile and have a greater chance of contaminating ground water through leaching. Indeed, several groups have shown that some commonly used antibiotics, namely sulfonamides, can be detected in leachate, albeit at very low levels. It follows that a few studies have reported detecting sulfonamides in well water and one study attributed the contamination to a nearby animal housing facility[11]. The majority of other antibiotics are not regularly found in leachate.

In Plants

For those antibiotics that bind strongly to soil yet have long half-lives, there is also a concern that these drugs could be taken up by plants. This is only now being researched fully. There are a handful of reports, however, indicating that some plants can take up some antibiotics from soil. This ability apparently varies greatly with both the type of plant and the antibiotic tested. One group showed that corn, green onion, and cabbage absorbed oxytetracycline but not tylosin from spiked soil (i.e., antibiotics added to the soil)[12]. Another study that more closely resembled real-life conditions (e.g., using actual manure from antibiotic treated animals) showed that of nine antibiotics tested, only three were taken up by lettuce in detectable amounts while four were taken up by carrots. While antibiotics could be detected in the edible portions of the plants, the concentrations at which they were found were much lower than FDA acceptable daily intake levels. The authors concluded that uptake of antibiotics by plants as a result of spreading livestock manure does not pose an appreciable human health risk[13].

Significance of These Levels

While there are several studies that assess antibiotic concentrations at single sites such as manure pits, or lagoons, or different soil types, there is a notable lack of integrated studies that trace antibiotic concentrations in several different sites within a single livestock operation. Without such studies, it is difficult to assess the capacity of soil to remove antibiotics from manure.

One such study, however, is available. De Liguoro and co-workers examined antibiotic levels in feces, bedding and manure, soil of fertilized fields, and surrounding drainage courses from a cattle operation following use of both oxytetracycline and tylosin. As was seen in other studies, tylosin degraded very rapidly, was not detected in soil after 45 days, and was never detected in surrounding water. Oxytetracycline was more stable in soil (detectable after five months), but at levels ten times lower than government mandated thresholds. Oxytetracycline was never detected in surrounding water. The authors concluded that spreading manure on soil is effective at eliminating and or destroying unabsorbed antibiotics in manure[5].

In place of other integrated investigations, Table 1 is a compilation of several unrelated studies and summarizes the levels at which some antibiotics have been detected in manure, soil, plants, and surface water (compiled from ref. 14). Also included are the FDA acceptable daily intake (ADI) or tolerance levels for each drug. The table suggests that while antibiotic concentrations are initially high in manure samples, there are significant reductions in antibiotic activity with each remediation step. For example, the concentrations detected in soil samples are roughly 1000 fold less than those found in manure. It follows that the levels found in plants or surface water are almost 100,000 fold lower than those found initially in manure and between 20 to 1000 times lower than FDA ADI or tolerance levels.

Finally, it is worth noting that by most accounts the use of antibiotics in food animal production leads to increases in the concentration of antibiotic resistant bacteria in the feces. While the impact this may have on human health is beyond the scope of this current paper, it is important to note that the levels of antibiotics commonly found in waterways or even soil following application of livestock manure are not considered high enough to drive resistance in typical test bacteria (minimum inhibitory concentrations).

Conclusions

Determining the fate of unabsorbed antibiotics in livestock manure is a relatively new field of study. With only a small number of studies, it is difficult to determine whether antibiotics found in livestock manure have an effect on human health once they are released to the terrestrial environment. It is clear that antibiotics can be detected in manure and in soil fertilized with manure. In some cases, antibiotics have been detected in ground or surface water systems near livestock operations. A much smaller number of studies report that some unabsorbed antibiotics can be taken up in small quantities by some plants. A compilation of data from several studies, however, suggests that with each remediation step (*e.g.*, digestion in lagoons, degradation in soil, etc.) the amount of detectable antibiotic drops significantly. As such, the concentrations of antibiotics found in sources that could impact human health such as ground or surface water, or plants, are at least an order of magnitude less than those deemed by the FDA to be an appreciable health risk.

Table 1. *Concentrations of antibiotics detected in manure, soil, plants, and surface or ground water.*

Antibiotic	Manure conc. (mg/kg)	Soil conc. (µg/kg)	half-life (days/ environment)	Degradation Rate at 20°C % days		Plant Conc. (species/conc.) ng/g	Surface (S) or ground (G) water conc. (µg/L)	FDA ADI$^{\beta}$ or tolerance
Oxytetracycline	0.82-19.0	<7	47 (sediment)	unknown		not detected	0.07-1.34(S)	25.0µg/kg BW
Tylosin	0.1-7.9	<10	3.3-8.1 (slurry)	100	30	not detected	unknown	0.2ppm
Tetracycline	0.04-24.0	86-172	unknown	unknown		not tested	0.11(S)	25.0µmg/kg BW
Chlortetracycline	0.1-14.0	4.6-7.3	7-20 (manure)	12	30	2.0-17.0	0.15(S)	25.0µmg/kg BW
amprolium	0.0-77.0	unknown	unknown	30	90	not tested	unknown	0.5ppm±
sulfamethazine	0.13-8.7	unknown	50-100*(sediment)	unknown		not detected*	0.076-0.22$^{\alpha}$(G)	0.1ppm
sulfathiazole	traces-12.4	unknown	50-100*(sediment)	unknown		not detected*	0.08$^{\beta}$(G)	0.1ppm

$^{\beta}$ADI = acceptable daily intake; *value for sulfadiazine; BW = body weight; $^{\alpha}$ = 0.076 -0.22ppb; $^{\beta}$ = 0.08ppb); †value for monensin; ± = lowest FDA tolerance level for amprolium

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(See Lee et al., 2007 and Kumar et al., 2005a for comprehensive reviews)

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