Antibiotics and Their Use in Food Animals

Use of antibiotics may transfer antibiotic resistance to humans

by Don Michalski, MS, RPh

Antibiotics are used for the treatment and prevention of disease in companion and food production animals. Approximately 35-40 % of all antibiotics produced in the United States are used in food animal agriculture and production. These antibiotics, human and veterinary approved, are used in a variety of situations including companion animals (pets), food production and aquaculture.

There are concerns about the further development of resistant bacteria due to repeated and sub-therapeutic exposure of food producing animals to commonly used antibiotics.

Veterinarians prescribe antibiotics for companion animals, approximately 130 million dogs and cats in the United States, for a variety of indications including respiratory, orthopedic, and soft tissue infections, abscesses, and urinary tract infections. However, more critically, food production veterinarians utilize numerous antibiotics including cephalosporins (ceftiofur, cephapirin), penicillin G, sulfadimethoxine, florphenicol, oxytetracyline, ampicillin, and amoxicillin for the management and prevention of a variety of clinical indications including pulmonary and soft tissue infections and mastitis (mammary) in dairy cattle.

Many different chemical classifications of antibiotics and anti-infectives are used in food animals for numerous clinical situations. Many of these drugs are used at seemingly sub-therapeutic levels for increasing growth and feed efficacy. A major drug category that is used is the ionophores such as monensin and lasolocid, which are indicated for improved feed efficacy in confined cattle and for the prevention and control of coccidiosis, *Emeria bovis* and *E. zuerni* in poultry.

Ionophores are drugs that, in addition to their anti-coccidiosis effect, produce a more efficient utilization of cellulose into fatty acids (propionic acid), which serve as energy sources for ruminants (cattle and related species). Tylosin is a macrolide that is used in swine for controlling swine dysentery and is also used to reduce the incidence of liver abscesses due to *Fusabacterium*. In poultry, tylosin increases feed efficacy and increases weight gain, up to 34% increase in feed utilization. Licensed feed mills most frequently compound these substances as a Type A medicated article in a concentration of 10-100 grams per ton of feed.

Many food-borne pathogens such as enterococci and *Salmonella* originate on the skin or in the gastrointestinal tract of food animals. During the slaughtering or milking process, these bacteria can enter the human food chain. There are suggestions that the most significant antibiotic selection process occurs in the calf, swine and poultry processing industry.

Although many drugs are metabolized or hydrolyzed, a significant number of these drugs are excreted unchanged and may be carried into surface and ground water. Effluent from sewage treatment has contained product concentration in the mg/liter range. Hagedorn, et al conducted an analysis of fecal contamination of surface water for resistance profiles with human and animal origin. The investigators concluded that differences in resistance patterns reflected the differences in antibiotic selection process.

In addition to the use of antibiotics in animal feed, as previously mentioned, significant amounts of antibiotics continue to be used for the management of disease in food animals. A major issue about the use of antibiotics in food animals is the concern regarding antibiotic residues in edible tissue including milk and eggs and in meat from beef, veal, swine, poultry and fish (aquaculture).

Veterinarians use antibiotics prudently because of very strict regulations about antibiotic residues mandated from the FDA, USDA and the Federal Milk Ordinance. Of equal concern is the significant evidence of the relationship of the clinical use of antibiotics in food animals to the transfer of antibiotic resistance to humans. Reports have shown this relationship to *Campylobacter* resistance in humans in Spain, staphylococcal resistance to erythromycin in poultry and human isolates, and enterococcal resistance patterns identified among humans and animals. The use of avopacin, a glycopeptide (vancomycin) used in Europe as a feed additive, has created significant concern about vancomycin-resistant enterococci (VRE). This situation led to the banning of this drug in Europe and subsequent banning of this drug category for food animals in the United States.

Of equal concern is the availability of many antibiotics (procaine penicillin G, oxytetracycline, and gentamicin) as oral and injectable products for over-the-counter (OTC) use by farmers and ranchers. Availability of intra-mammary antibiotics (amoxicillin, cephapirin, etc.) for mastitis management contributes extensively to the exposure of food production animals to antibiotics. These products can be acquired from feed stores (e.g. Farm & Fleet) for treatment of diseases that are diagnosed by the farmer. There are strict limitations such as following the exact OTC labeling that usually recommends less than therapeutic doses that may be prescribed by veterinarians. This potential indiscriminate use raises concerns about the further development of resistant bacteria due to repeated and sub-therapeutic exposure of food producing animals to commonly used antibiotics.

One mandate is that all users of veterinary antibiotics must abide by rigid withdrawal time policies for all drugs including antibiotics in food animals. These withdrawal times usually reflect 10 half-lives of antibiotics, which ensure that no significant amounts of antibiotics remain in edible tissue (1ppb =1 part of antibiotic per billion part of edible tissue). The withdrawal times are typically one day to 180 days from the time of the last dose administered to time of the meat or milk going into the human food market. The withdrawal time depends upon the drug, its pharmacokinetics in a particular species, and the product formulation.

Because of antibiotic resistance patterns (identified and supported by the CDC, AMA and AVMA) and direct toxicity, certain drugs are illegal to use in food animals. These include metronidazole, aminoglycosides, fluoroquinolones (two exceptions), chloramphenicol, vancomycin, and some sulfonamides. Fluoroquinolones (enrofloxacin which is metabolized to ciprofloxacin) and glycopeptides are specifically banned because of the concern of transferring antibiotic resistance to humans. Failure to abide by these regulations can result in civil and criminal prosecution.

Bacterial resistance in animals has related to human clinical cases such as the deaths of two patients in Denmark due to resistant *Salmonella*, a poultry worker who developed a life-threatening infection which had similar resistance patterns seen in the poultry farms, and a 12-year-old boy from Nebraska who developed a life threatening multi-drug resistant (including ceftriaxone) *Salmonella* infection. The 12-year-old individual, whose father was a veterinarian treating four adjacent beef herds, acquired severe GI symptoms. Although ceftriaxone was not used in the herds, ceftiofur, a closely related antibiotic, had been used extensively on the family farm. Fortunately, this boy quickly recovered with alternative therapies.

Epidemiologists continue to review the probable links of extensive and perhaps misuse of antibiotics in the agricultural community and its effect on human antibiotic sensitivity patterns and utilization. Surveillance by regulatory and professional groups will continue to identify future episodes of the human –animal antibiotic resistance link. This entire issue can best be stated by a quote by W. Witte, who stated, "The medical consequences of antibiotics in agriculture have been proposed to be the end of the road of the ecological network of resistance: agriculture and veterinary use contribute to selective pressure, resistance reservoirs and routes of transmission." ●

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