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REVIEW
Antibiotic Use in Livestock Production

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ABSTRACT

Antibiotic usage is a useful and commonly implemented practice in livestock and production agriculture that has progressively gained attention in recent years from consumers of animal products due to concerns about human and environmental health. Sub-therapeutic usage of antibiotics has led to a concern that prophylactic supplementation leads to antimicrobial resistance, and this particular practice has come under public scrutiny. The consumer and media misconceptions about antibiotic usage and production strategies utilized in livestock production have caused a shift in consumer demands. Antibiotics directly and indirectly affect the livestock industry by treating illness and promoting the overall health of the animal, which may enhance production parameters such as growth and profitability. However, pending legislation threatens to eliminate the current antibiotic usage strategies implemented by producers. This review will address the historical and current use of antibiotics as it pertains to production animal agriculture to summarize how antibiotics promote animal health and growth performance.

Keywords: Antibiotic, livestock, animal health, review

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INTRODUCTION

Antibiotic usage in meat animal production is a hotly debated issue in the livestock industry that has acquired more attention as consumers seek to place more "natural" and "safer" products on their table (Gilbert and McBain, 2003). Consumer perception can greatly influence food animal production as has been recently observed for some common food production practices; such as lean finely textured beef ("pink slime") which was removed from meat formulations of producers due to negative media attention and consumer perception (Flock, 2012). The use of gestation crates in swine production has also drawn increasing attention, leading to the refusal of

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some retailers and restaurants to purchase pork from producers that utilize gestation crates (Food Safety News, 2013). Furthermore, antibiotic usage in animals for health benefits and growth promotion has continued to be a concern of the American consumer in recent years. In response to similar concerns, the European Union (EU) banned sub-therapeutic supplementation of animal feeds with antibiotics (Pradella, 2006). Recently, the U.S. Food and Drug Administration issued a guidance directive on the judicious use of antibiotics in food animals, and this measure has led some to believe that this is phase one of an agenda to remove sub-therapeutic antibiotic use from livestock production.

The gastrointestinal tract of animals is populated with a complex microbial ecosystem that is essential for the function, growth, and overall health of the animal (Chaucheyras-Durand and Durand, 2010). Many livestock producers currently utilize feeding and production strategies, including the use of antibiotics, that alter the microbial ecology of the gastrointestinal tract of the animal to benefit the overall health and production efficiency of their animals. As a bonus to the consumer, some of these strategies may also help eliminate or reduce foodborne pathogens that may contaminate the food supply (Perlman, 1973). If and when sub-therapeutic antibiotic use in food animals is banned in the U.S., alternative strategies must be implemented to replicate these positive effects in order for the livestock industry to remain viable.

CURRENT USE OF ANTIBIOTICS IN LIVESTOCK

Antibiotics are used in the livestock industry for a variety of reasons including treatment of disease, prophylaxis, as well as improving feed efficiency and overall growth performance (Berge *et al*., 2005; Brown *et al*., 1975). While antibiotics do not make label claims that suggest alteration of growth parameters in livestock, the association between their use and growth promotion has been reported in many species such as cattle, swine, and poultry for over 50 years (Moore *et al*., 1946; Jukes *et al*., 1950; Rogers *et al*., 1995; Salinas-Chavira *et al*., 2009). Performance parameters can be quantitatively measured in a variety of ways including, but not limited to: mortality, weight gain, meat/milk quality, and feed efficiency. While the mode of action by which antibiotics improve feed efficiency has not been fully elucidated, growth performance may be enhanced due to decreased inflammation in the small intestine (Feighner and Dashkevicz, 1987; Eyssen and DeSomer, 1963).

To further explain how antibiotics may work in conjunction to promote animal health and food safety, McCracken and Gaskins (1999) indicated that the development of the intestinal immune system occurs in conjunction with the development of the normal microflora of the animal; however chronic stimulation of the immune system may decrease the amount of protein available for growth (Gordon *et al.,* 1963). Studies comparing germ-free and conventionally raised animals have demonstrated this phenomenon and have reported alterations in immune function of these animals in conjunction with the development of the intestinal microflora (McCraken and Lorenz, 2001). Thinning of the intestinal epithelium in conjunction with the use of antibiotics may be the result of decreased microbial production of polyamines and volatile fatty acids (VFAs) that enhance intestinal cell growth and activity (Ferket *et al*., 2002). Ferket *et al*. (2002) states that intestinal mucosal thinning that may occur with the use of antibiotics may increase energy availability for growth because the animal does not have to maintain a larger intestinal mucosal layer.

Cattle

Antibiotics have been used for decades in cattle, and some of the most commonly used antibiotics in the feedlot setting are a class of compounds known as ionophores (Russell and Strobel, 1989). Ionophores were approved for use in ruminants in the 1970s (Russell and Strobel, 1989). The ionophore monensin was fed to chickens as a coccidiostat, and the manure from these poultry houses was spread on cattle pastures as a fertilizer. Cattle grazing these pastures grew more rapidly than cattle grazing pastures fertilized with manure from poultry houses where the chickens were not fed monensin (Callaway, 2013). As a result, the ionophore monensin was directly incorporated into cattle rations beginning in the 1970's, and this compound has been reported to enhance growth performance through a variety of modifications of the ruminal microbiome (Raun *et al*., 1976; Callaway *et al*., 2003). Ionophores primarily inhibit bacteria with Gram positive physiology, including lactic acid bacteria, and this improves growth efficiency, average daily gain (ADG), reduces wasteful protein degradation (by hyperammonia producing bacteria), reduces methanogenesis, and reduces ruminal acidosis via lower lactate production (Russell and Strobel, 1988). Ionophores have been reported to reduce liver abscesses by inhibiting epithelial keratinization caused by lactic acidosis and subsequent *Fusobacterium necrophorum* infections (Nagaraja and Chengappa, 1998; Lechtenberg *et al*., 1998).

While compounds such as ionophores alter the microbial ecology of the gastrointestinal tract to promote overall health and performance, other antibiotics are used to treat specific bacterial disease and illness. Some of these antibiotics may also elicit a dual effect, promoting both health and performance in the animals. Bovine respiratory disease (BRD) is the most common and expensive disease present in American cattle, and the use of antibiotics to treat/prevent this disease is a great example of this dual effect of antibiotics (Smith, 1998; Snowder *et al*., 2006). Bovine respiratory disease is a complex disease caused by exposure to various viral (e.g., Infectious Bovine Rhino-tracheitis, Bovine Viral Diarrhea, Bovine Respiratory Syncytial Virus, and Parainfluenza Virus) and/or bacterial (e.g.., *Pasteurella hemolytica*, *Pasteurella multocida, Haemophilussomnus, Mycoplasmasp.* and *Actinomycespyogenes*) pathogens. Bovine respiratory disease may be mitigated in a number of ways including vaccination, management practices, and antibiotic treatments to prevent and/or treat the disease. Addition of chloratetracycline and sulfamethazine to treat enteritis, coccidiosis, and bovine respiratory disease (BRD) in the ration of cattle arriving at the feed lot was also reported to increase ADG while decreasing the risk of bovine respiratory disease for the first 28 days at the feedlot (Guillermo and Berg, 1995; Smith *et al*., 1993). Another commonly used antibiotic in beef production is Tilmicosin which is a broad spectrum antibiotic used to treat and prevent BRD. Tilmicosin works to inhibit protein synthesis of bacteria such as *Pasteurella hemolytica* that may lead to the onset of BRD. Treatment of cattle upon arrival into feedlots with Micotil®, a solution of Tilmicosin, was shown to decrease BRD symptoms and increase dry matter intake (Galyean *et al*., 1995).

Antibiotics are also used in livestock to prevent specific physiologic disorders such as ruminal lactic acidosis, a common problem in grain fed cattle that can be chronic or acute and range from moderate to severe (Nagaraja and Titgemeyer, 2007; Slyter, 1976; Muir *et al*., 1981; Nagaraja *et al*., 1982). Ruminal acidosis is the accumulation of lactate in the rumen resulting in a lowered pH that decreases animal growth performance parameters, and leads to the development of other health problems such as laminitis, bloat, and liver abscesses (Nagaraja and Chengappa, 1998; Nocek, 1997; Enemark, 2008). In acute clinical lactic acidosis, D-lactate is the acid primarily responsible for this condition (Dunlop, 1965); however, the role of lactate in sub-acute acidosis is not fully understood (Enemark, 2009). The onset of acidosis is linked with feeding readily fermentable carbohydrates that are commonly associated with a high concentrate ration as would normally be fed in the cattle feedlot or swine finishing production systems (Owens *et al*., 1998; Russell and Hino, 1985).

Antibiotics/antimicrobials and other feedstuffs have been reported to be effective strategies to prevent the onset of ruminal acidosis (Owens *et al*.,1998; Callaway *et al*., 2003). Antibiotics may decrease the incidence of liver abscesses in cattle which may be the result of ruminal acidosis and may predict carcass performance (Rogers *et al*., 1995; Brown and Lawrence, 2010). Virginamycin is an antibiotic used to prevent necrotic enteritis in cattle and has also been reported to increase the gain to feed ratio in cattle (Salinas-Chavira *et al*., 2009). Rogers *et al*. (1995) reported an increase in ADG and feed conversion, and a decrease in liver abscesses in cattle fed virginamycin.

Swine

As in ruminants, such as cattle, antibiotics are used in swine production for many of the same reasons. These pharmaceuticals are used in swine for both prophylactic and treatment therapies, and in some cases, these antibiotics can also effect performance parameters. Jensen *et al*. (1955) reported increased gains and feed conversion in swine fed the antibiotic aureomycin. While aeuromycin was also initially reported to enhance reproductive performance in swine (Yestal *et al*., 1952), subsequent work by Davey *et al*. (1955) reported no difference in reproductive performance when swine were fed various concentrations of the antibiotic. Viability and performance of newborn and suckling piglets was also unaffected when swine were supplemented with aureomycin (Davey *et al*., 1955). Aureomycin was further reported to increase profitability by increasing belly weight and decreasing backfat thickness (Perry *et al*., 1953). Zimmerman (1986) reported that antibiotics such as chloratetracyline, furazolidone, lincomycin, salinomycin, tylosin, and virginamycin may improve average weight gain by approximately 15%. Additionally, Zimmerman (1986) reported that combined use of chloratetracycline, penicillin, and sulfamethazine (2:1:2) increased ADG in starter pigs by 25%. Multiple studies in swine also indicate that treatment by any of the aforementioned antibiotics can increase farrowing rate (Zimmerman, 1986; Ruiz *et al*., 1968; Anderson, 1969; Hays 1978). Litter size may also be increased with the addition of a combination of antibiotics (Zimmerman, 1986; Ruiz *et al*., 1968; Hays 1978). The antibiotics penicillin and streptomycin increased the growth rate of swine fed to market weight (Bridges *et al*., 1952). Penicillin and streptomycin used in conjunction are still approved for use in the swine industry, as well as bovine, equine, and ovine species, to treat bacteria such as *Arcanobacterium, Klebsiella pneumonia, Listeria* spp*., Mannheimia haemolytica, Pasteurella, Staphylococcus,* and *Salmonella* (Norbrook Laboratories, 2013). Tylosin is another antibiotic approved for use in swine that can be provided via intramuscular injection, feed, or water, and is effective in preventing and controlling porcine proliferative enteropathy (ileitis; Paradis, 2004; Marseller *et al*., 2001; McOrist *et al*., 1997). Tylosin supplemented in the drinking water of swine for 17 days decreased clinical signs of gastrointestinal infection and promoted growth performance (Paradis *et al*., 2004). Tylosin-supplemented swine showed no clinical or pathological signs of proliferative enteropathy (ileitis) after experimental infection with L*awsonia intracellularis* (McOrist *et al*., 1997). The mitigation of disease in concert with enhanced growth and reproductive performance as a result of antibiotic usage in swine help make the use of antibiotics a profitable production strategy (Zimmerman, 1986).

Poultry

Antibiotic usage is an extremely important aspect of poultry production and has been used in production and researched extensively since the 1950s (Feighner and Dashkevicz, 1987). Antibiotics used in poultry production are believed to be effective growth promotants due to the alterations they induce in the microflora of the gastrointestinal tract (Feighner and Dashkevicz, 1987). This theory is supported by experiments that report germ-free chickens grow more efficiently than commercially raised poultry, and germ-free animals do not grow faster when given antibiotics with growth promoting capabilities (Coates *et al*., 1963; Forbes and Pank, 1959). In poultry, antibiotic feeding has been reported to increase weight gain and feed conversion efficiency (feed/gain; Feighner and Dashkevicz, 1987; Bunyan *et al*., 1977). Feed efficiency has been reported to be improved in poultry supplemented with antibiotics by reducing microbial populations in competition for nutrients and reduction of pathogenic bacteria (Feighner and Dashkevicz, 1987; Eyssen and de-Somer, 1963; Barnes *et al*., 1978). Studies have reported that ammonia production by bacteria in the GI tract of monogastrics may suppress growth (Dang and Visek, 1960; Harbers *et al*., 1963; Visek, 1978). Deconjugation of bile salts may also play a role in growth suppression due to *Streptococcus faecium* in the small intestine; however, the use of antibiotics has been reported to reduce attachment of this bacterium to intestinal epithelia (Cole and Fuller, 1984; Fuller *et al*., 1984; Fuller *et al*., 1983).

Table 1. Some antibiotics used in animal agriculture that may be used to promote overall animal health and impact pathogen colonization and shedding

Some Antibiotics used in Animal Agriculture By Species			
Cattle[a]	Swine[b]	Poultry[c]	Aquaculture[d]
Amoxicillin	Apramycin	Ardacin	Amoxicillin
Ampicillin	Bacitracin	Avilamycin	Ampicillin
Enroflaxin	Bambermycin	Avoparcin	Chloramphenicol
Erythromycin	Carbadox	Bacitracin manganese	Cortimoxazole
Florfenicol	Chloratetracycline	Erythromycin	Enroflaxin
Oxytetracycline	Furazolidone	Lincomycine	Erythromycin
Penicillin	Lincomycin	Mocimycin	Florfenicol
Sulfadimethoxine	Nosiheptide	Neomycin	Furazolidine
Tilmicosin	Salinomycin	Nosiheptide	Nitrofurans
Tylosin	Tiamulin	Penicillin	Oxolinic acid
	Tylosin	Soframycin	Oxytetracycline
	Virginamycin	Tetracycline	Sarafloxacin
		Tylosin	Streptomycin
		Virginamycin	Sulphadizine
			Trimethoprim-Sulfamethoxazole

[a]Currin and Whittier, 2009

[b]Zimmerman, 1986

[c]Castanon, 2007

[d]Defoirdt *et al.*, 2011

The intestinal epithelia in poultry and other species play a large role in the growth capabilities of animals, and antibiotics can alter the intestinal microflora as well as the intestinal epithelia of animals to promote growth. As mentioned previously, thinner intestinal epithelia may result in more efficient nutrient uptake and absorption (Eyessen and deSomer, 1963; Ford and Coates, 1971; Siddons and Coates, 1972; Sieburth *et al*., 1951). Also, antibiotics reduce populations of bacteria in the intestines, thereby making more nutrients available for animal growth (Eyssen, 1962; Monson *et al*., 1954). When antibiotics reduce the microbial population in the GI tract, they may inherently reduce pathogens responsible for disease or subclinical infections (Eyssen and deSomer, 1963a; Eyssen and deSomer, 1963b; Eyssen and deSomer, 1967; Sieburth *et al*., 1951). The combination of all these effects elicited by antibiotics provides a possible explanation as to why antibiotics enhance growth performance and feed efficiency.

Aquaculture

As in mammalian production, antibiotics also play a critical role in the aquaculture industry. Diseases in production aquaculture are estimated to cause losses of approximately 3 billion dollars per year globally (Subasinghe, *et al*., 2001). There are more than 100 known pathogens to fish; however, some of these are opportunistic pathogens (Alderman and Hastings, 1998). One of the main bacterial culprits are *Vibrio* bacteria (*harveyi, cambellii,* and *parahaemolyticus*; Defoirdt *et al*., 2007). While these pathogens are detrimental to the health of the aquaculture, some bacteria such as *Vibrio cholera* and *vulnificus*, may cause human disease as well (Thompson *et al*., 2004). Some of the antibiotics used in aquaculture are chloramphenicol, gentamycin, trimethorprim, tiamulin, tetracyclines, quinolones, and sulfonamides (Table 1; Defoirdt *et al*., 2007). Most of these antibiotics are incorporated into the feed of the aquaculture at specified dosages with required withdrawal times (Alderman and Hastings, 1998). However, countries around the world have vastly different regulations regarding the administration, dosage, withdrawal, and control of antibiotics in aquaculture (Alderman and Hastings, 1998). As in many food-producing species, antibiotic-resistant bacteria such as *Aeromonas salmonicida, A. hydrophila, Vibrio anguillarum, Pseudomonas fluorescens, Pasteurella piscida,* and *Edwardsiella tarda* have been documented in aquaculture species (Aoki, 1988).

SUMMARY

Antibiotics are an important part of agriculture and food production originating from the cattle, swine, poultry, and aquaculture industries, and much research has been conducted to determine the efficacy and safety of these pharmaceuticals. These compounds are used not only to treat disease, but can also be used effectively as a prophylactic treatment. Such strategies to control pathogens in food-producing animals may, in some cases, improve growth performance parameters while simultaneously promoting the overall health of the animal. Thus, antibiotics are a critical player in the profitability of agriculture in the U.S. and throughout the world and play a vital role in feeding the ever growing world population. However, an ever changing population and shifts in consumer demand have placed pressure on the agricultural industry and governments to reduce and/or eliminate the use of antibiotics in food production. While this potential change could possibly be detrimental to current management strategies, there are potential alternatives to antibiotics that have been extensively researched in livestock to promote health, performance, profitability, and food safety.

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