Policy Brief and Recommendations #4 Misuse of Antibiotics in Food Animal Production

Antibiotic Misuse in Food Animals – Time for Change

APUA

POLICY BRIEF AND RECOMMENDATIONS #4
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AUTHOR: APUA

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EXECUTIVE SUMMARY

Antibiotics are widely used in food animal production for therapy and prevention of bacterial infections and for growth promotion. Food animals are raised in confined conditions that promote the spread of infectious diseases. Antibiotics are often used over alternatives, because of low cost and ready availability, often without prescription. Most of the antibiotics used in food animals are the same s those used in humans. Some antibiotic growth promoters (AGPs) used in food animals in the United States are drugs classified by the World Health Organization (WHO) as critically important antibiotics for use in human medicine.

Resistance has developed to virtually all antibiotics used in food animals. The most important driver of resistance selection and spread is antibiotic use [1], [2]. To slow the pace of resistance, the use of antibiotics for growth promotion should be terminated. In addition, it is recommended that antibiotic use data for animals be made available to aid in assessing the public health impacts of antibiotic use in animals and policy changes on antibiotic consumption.

Antibiotic use in food animals

INTRODUCTION

Since the 1950s antibiotics have been widely used in food animal production in the United States. They are used for many purposes, including the therapeutic treatment of clinically sick animals, for disease prophylaxis during periods of high risk of infection, and for promotion of growth and feed efficiency [3]. Food animals are raised in groups or herds, often in confined conditions that promote the spread of infectious diseases [4]. Antibiotics are frequently used to compensate for poor production practices. Most of the antibiotics used in food animals are the same as or belong to the same classes as those used in humans.

Nearly all of the classes of antibiotics used in humans have also been approved for use in animals, including most of the antibiotics classified as critically important for use in humans [5], [6]. Antibiotics are used in all of the major (cattle, pigs, poultry) and minor (e.g. sheep, goats) land-based species and in aquaculture (e.g. salmon, trout) and are administered for therapy, prophylaxis (prevention) and growth promotion / increased feed efficiency [3],[4].

In the U.S., antibiotics must be approved for use in food animals by the Food and Drug Administration (FDA), before they can legally be administered to food animals [6]. However, the vast majority of antibiotics were approved without consideration of the human health impacts due to antibiotic resistance. Therefore, the approved conditions for use are not necessarily safe for humans from the antibiotic resistance standpoint. It is only in the last decade that procedures to evaluate these impacts have been developed and adopted by FDA and similar agencies in other countries [7].

For therapy of clinical bacterial infections, animals are treated with therapeutic doses of antibiotic for a period of time that is specified on the product label. Therapeutic treatment of individual animals is common practice in dairy cattle production (e.g. treatment of pneumonia or mastitis) but occurs in other species only when it is economically or logistically feasible to handle and treat individual animals (e.g. beef claves in a feedlot, sows, breeding animals) [3]. In many cases (e.g. flocks or broiler chickens or pens of salmon), it is impractical to capture, handle and treat individual animals. In these instances, the entire group is treated, including clinically sick animals, those that may be incubating the disease, and those not infected [3].

Group-level use of antibiotics

Group-level prophylactic use of antibiotics is also very common. In some cases, for example, beef calves on arrival at the feedlot, may be administered by injection, but in most cases, prophylactic antimicrobials are administered in feed or water [8], [9]. Prophylactic treatments may be given at therapeutic or subtherapeutic doses and the duration of treatment is frequently longer than for therapy. Most commonly, prophylactic treatments are administered to all animals in a group considered to be at risk of infection due to their age or stage of production [3], [6], [8]. Examples of prophylactic treatments include: administration of ceftiofur by injection of hatching eggs or day-old turkey poults to prevent *E.coli* infection; administration of chlortetracycline to feed to beef calves to prevent liver abscess; and, administration of tylosin in feed to weaned piglets to prevent diarrhea [10], [11], [12].

Antibiotics used for growth promotion

Antibiotics are also used for growth promotion, which is also sometimes called increased feed efficiency [3], [4], [10], [6]. Most AGP is used in production of pigs, broiler chickens, turkeys, and feedlot beef cattle. The specific physiological basis of the growth promoting effects of antibiotics is unknown, but is hypothesized to involve a nutrient sparing effect in the gut and selective suppression of species of bacteria and clinical expression of infection, i.e., disease prophylaxis [3], [6]. AGPs are typically administered in sub-therapeutic doses for long periods of time (usually greater than 2 weeks), and sometimes for the entire duration of the production cycle. At one time, it was thought that AGPs improved production by 2-10%.

Recent national-level data from Denmark, however, showed that AGPs were of negligible benefit in broiler production, and only of benefit in pork production for prevention of diarrhea in weaned pigs [6]; an effect that in light of more recent data is now in some doubt [13]. Some researchers have claimed that certain AGPs may improve food safety by reducing the incidence of carriage of foodborne infections in animals, but this claim is based on limited evidence [14].

The quantity of antibiotics used in food animal production is thought to be very large, by some estimates comparable to quantities used in human medicine [4]. Unfortunately, few publicly available data on quantities of specific antibiotics used in specific species of food animals are available in the United States. This is a serious information gap that is largely attributable to the lack of a national antibiotic use monitoring system. Such data that are available are derived from targeted surveys and very limited aggregate data provided by the pharmaceutical industry [6], [15].

Selection and spread of resistance in agriculture

Use of a given antibiotic in food animals (or any other sector) selects for resistance to that particular antibiotic (direct selection), but also to related drugs in the same antibiotic class (cross-selection) and even to unrelated drugs (co-selection), when resistance genes to both drugs are present within bacteria [2]. Bacteria may be exposed to these drugs within the intestines, lungs or other locations within food animals, or in the farm environment after drugs are excreted in urine and feces.

Resistance has developed to virtually all antibiotics used in food animals

Resistance has developed to virtually all antibiotics used in food animals. For some antibiotics, resistance is somewhat slow to emerge, but in other cases, for example, among *Camphylobacter* to the fluoroquinolones, it occurs very quickly [16]. Resistance is acquired both by disease-causing (pathogenic) and harmless (commensal) bacteria found within animals and the environment. Resistant bacteria spread among groups of animals or fish, to the local environment (inside of pens, barns) and to the wider environment (adjacent soil, air and water) through spreading of manure and dissemination by in-contact wildlife, insects, and rodents [3], [17], [18], [19].

These bacteria also spread to humans, primarily through contaminated meat, but also through direct contact between food animals and humans (e.g. farmers, farm visitors) [4], [6], [20]. Moreover, resistance genes readily spread among bacteria of the same or different species [4]. Nationally, food animals are a very large reservoir of resistant bacteria. Millions of livestock are produced annually in the United States [15], and these produce millions of tons of manure, each of which contains billions of bacteria that are readily available to contaminate the environment and food chain. Once selected in food animal populations, these resistant bacteria cannot be contained on the farm. Some "biosecurity" measures are used on certain types of farms (e.g. poultry or swine) to restrict the entry and further transmission of selected infectious diseases of animal health significance, but these are not designed for preventing the introduction of further dissemination of *Camphylobacter*, *E. coli* or many other bacteria of human health significance, nor the spread of these resistant bacteria off the farm and into food and the environment.

Antibiotic use – the most important driver of resistance

The most important driver of resistance selection and spread is antibiotic use [1], [2]. AGPs are particularly potent in this regard, because they are administered in low doses (that provide sublethal injury and selective advantage to resistant mutants) for long periods of time (resistance spread is time-dependent) and in large numbers of animals (increasing the odds that resistant strains will emerge and spread) [4]. Other drivers of spread include animal density, housing and hygiene [4].

In the United States, most food animals are reared intensively in large groups that are housed in conditions of close confinement and high stocking density [6]. Examples include the rearing of tens of thousands of broiler chickens within single barns, hundreds or thousands of cattle in feedlots, and hundreds or thousands of pigs in confined swine operations. High stocking density and close confinement encourage the rapid spread of bacteria between animals, including important human pathogens such as *Salmonella*, *Camphylobacter* and *E. coli*. Huge quantities of manure are produced on these facilities, which if not composted properly, is an important source of these and other bacteria and resistance determinants for environmental contamination of soil and water.

Intensive rearing is also conducive to spread and expression of clinical diseases in animals that require antibiotic therapy. These diseases provide a rationale for widespread and often unnecessary use of prophylactic antibiotics, some of which are of critical importance to human health. Beef and veal calves are usually sourced from different locations and transported long distances prior to confinement in barns and feedlots. These conditions are stressful and lead to a host of infectious diseases for which AGPs and prophylactic antibiotics are used [6], [21]. Similarly, piglets are weaned at an early age and litters are mixed, causing stresses that precipitate diarrhea and other diseases for which AGPs are widely used [10], [9].

Animals of various species are routinely fed AGPs throughout the fattening period in order to enhance feed efficiency, promote growth and prevent clinical disease. Many of these AGPs are also used in human medicine (e.g., penicillin, tetracycline) or are members of important classes of human drugs (e.g. tylosin, a macrolide related to erythromycin, and virginiamycin, a streptogrammin) [4], [6].

Time for Some Changes

Terminate use of antibiotic growth promoters in food animal production

AGP use in the United States should be terminated to protect public health [22]. European data suggest that AGPs have little actual benefit in terms of growth promotion or increased feed efficiency [22]. AGP termination should be accompanied by appropriate steps to ensure that animal health and welfare is maintained in ways that do not result in significant increases in the use of therapeutic or prophylactic antibiotics that offset the benefits to public health from reduction in AGP use [22]. This is possible through greater implementation of non-antibiotic strategies for animal health maintenance, and where necessary, more targeted use of therapeutic antimicrobials that are less likely than AGPs to select for resistance of public health importance.

Monitor antimicrobial use and antimicrobial resistance

A major barrier to better understanding of the public health impacts of antibiotic use in animals is a lack of publicly available data on antibiotic consumption in the agricultural sector. The limited information currently available on antibiotic use in food animals in the United States is pieced together from special research studies, regional surveys and indirect estimates [23]. *Good quality national-level data are essential to risk assessment, interpretation of resistance trends, and assessment of the impact of policy changes on consumption* [22][*] In countries (e.g. northern Europe) where antibiotic use monitoring data are publicly available, it is much more feasible to evaluate the relative contributions of veterinary and human antibiotic use on resistance in bacterial populations [10].

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[*] For more information and detailed policy recommendations, see the FAAIR Report, edited by Michael Barza, MD and Sherwood L. Gorbach, MD.

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