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Review article

# THE USE OF ANTIBIOTICS IN FOOD ANIMALS – A THREAT TO HUMAN HEALTH

Rozalina Yordanova[1], Magdalena Platikanova[2], Petya Hristova[2]
*1) Medical College, Trakia University, Stara Zagora, Bulgaria*
*2) Department of Hygiene, Epidemiology, Microbiology, Parasitology, and Infectious Diseases, Faculty of Medicine, Trakia University, Stara Zagora, Bulgaria.*

**ABSTRACT:**

**Background:** Antibiotics are widely used in food animals to prevent disease, promote growth and maintain productivity. Modern animal production practices involve regular use of antimicrobials, but abusive use can lead to harmful consequences. The aim of this review was to provide comprehensive information regarding the risk of regular application of antibiotics in food animals, the potential consequences and impact on human health, and options for the prevention of antibiotic resistance in the food chain.

**Review Results:** Although organizations such as WHO, UN, and EU have taken steps to reduce and limit the use of antibiotics in animals, these are proving insufficient in developing countries. In many countries, the antibiotics used in animals appear to exceed that in humans. The abuse in food animals promotes the development of antibiotic-resistant bacteria and resistance genes that can be transmitted to humans through food consumption and direct contact with animal food or environment mechanisms. This can lead to human infections with antibiotic-resistant bacteria, causing treatment failure and, therefore, more severe and longer-lasting illnesses, increased hospitalization rates, more deaths and higher costs to society. Furthermore, as food animals and animal-derived foods are traded globally, they contribute to antibiotic resistance in countries far from where the problem originates.

**Conclusion:** Overcoming the problem of antibiotic resistance requires a multidisciplinary approach with effective action coordination and information exchange between the agricultural, food, veterinary and health sectors. Through international cooperation, efforts should focus on reducing unnecessary antibiotics use and reducing the spread of antibiotic-resistant bacteria, but national-level action on antibiotic resistance and food safety is also essential.

**Keywords:** antibiotics, antibiotic-resistant bacteria, food animals, food safety, public health treat,

## BACKGROUND

Humanity has benefited from the availability of antibiotics to treat bacterial infections for decades. However, the excessive use of antibiotics puts pressure on bacteria to develop resistance against these drugs, leading to the emergence of untreatable “superbugs” [1, 2]. The significant worldwide increase in the number of multidrug resistant bacteria, i.e. resistant to at least three different groups of antibiotics, is also a serious cause for concern [3]. In 2021, the World Health Organization (WHO) reported that antimicrobial resistance is among the top ten global public health threats facing humanity [4].

Antibiotics are widely used in food animals to prevent disease, promote growth, and maintain productivity. Modern animal production practices involve the regular use of antimicrobials. However, in many countries, antibiotics use in animals appears to exceed that in humans, and the abusive use can lead to important public health implications and harmful consequences - serious side effects, severe pathologies and contribution to the spread of antimicrobial-resistant pathogens in livestock and humans. Furthermore, as food animals and animal-derived foods are traded globally, they contribute to antibiotic resistance in countries far from where the problem originates. Although organizations such as the WHO, the United Nations (UN), and the European Union (EU) have taken steps to reduce and limit the use of antibiotics in animals, these are proving insufficient in developing countries where the consumption of animal products continues to grow every year.

The aim of this review was to provide comprehensive information regarding the risk of the regular application of antibiotics in food animals, the potential consequences and impact on human health, and options for the prevention of antibiotic resistance in the food chain.

## REVIEW RESULTS

### 1. Use of antibiotics in food animals

#### 1.1. Worldwide antibiotic consumption trends

In the 1950s, alongside the onset of intensive farming practices, the use of antibiotics in food animals was permitted in order to improve feed transformation, accelerate growth rates and minimize disease [5]. In 2006, the

EU banned the feeding of livestock with antibiotics and related growth-promoting drugs, and the rules governing the use of antimicrobial drugs in animals in the United States (US) were recently introduced. The new rules eliminate the use of medically important antibiotics to promote growth and allow the use of these drugs only for therapeutic or preventive purposes under the supervision of a veterinarian [6]. However, many developing countries, have no legislation on using antimicrobials use in livestock. For example, in African countries, the use and control of antimicrobials remain unregulated mainly [7]. An exception is South Africa, which has developed and implemented a National Strategic Framework for Antimicrobial Resistance 2014–2024, with one of the strategic objectives being to promote the appropriate use of antimicrobials in human and animal health [8].

The antibiotics choice and the pattern of antimicrobials consumption show geographical differences across the continents, influenced by the food animal species, regional production patterns and types of production system, intensive or extensive farming, purpose of farming (commercial, industrial or domestic), unclear legislative framework or policies regarding the use of antibiotics, and the size and socioeconomic status of the population and particularly of farmers [9]. Antimicrobial growth promoters (AGP) have been used in livestock production in the US and other developed countries for more than 60 years. Favourable outcomes on productivity in poultry and pigs were first recorded in 1946 and 1950 [10].

The annual global consumption of antimicrobials in livestock between 2010 and 2030 will increase by 67%, from 63,1 ± 1,5 tons to 105,596 ± 3,605 tons [11]. Among the 50 countries with the largest amount of antimicrobials used in livestock in 2010, the five countries with the greatest projected percentage increases in antimicrobial consumption by 2030 are likely to be Myanmar (205%), Indonesia (202%), Nigeria (163%), Peru (160%), and Vietnam (157%) [11]. In addition, it is estimated that over 80% of food producing animals are currently treated with antibiotics [12]. Antimicrobials are currently used in 8,927 tonnes of animals in the EU [13]. The world's largest producer and consumer of antimicrobials, China, consumed almost 30,000 tonnes of antimicrobials for its livestock production in 2018, with more than half of this consumption (53%) used to promote animal growth [14].

### 1.2. Livestock antibiotic consumption

Livestock farming is an integral part of the global economy and a major source of food and materials in developing countries. In order to promote growth and weight gain, entire herds of farm animals are routinely fed low doses of antibiotics in their food or water. Antibiotics are also used to prevent disease in animals living in often crowded and unsanitary spaces [15]. They are used especially during the early part of an animal's life – for example, in broiler chickens and in weaning pigs and calves [16]. All this leads to a massive accumulation of antibiotics in the environment and the acquisition of antibiotic resistance in microorganisms that come into contact with the antibiotic [17]. Antibiotic consumption in the livestock sector is the highest in China (23%), the US (13%), Brazil (9%), and India (3%), accounting for the majority of worldwide sale of antibiotics [11].

### 1.3. Antibiotic residues in food

Due to the improper use of antibiotics, they can end up as residues in food products, thus exerting a harmful effect on the consumers' health [18, 19]. These foods are mainly obtained from poultry (chicken meat and eggs), cattle (beef carcasses, milk and meat) and pigs (pork meat). If the use of antibiotics is necessary for the treatment or prevention of various animal diseases, a withholding period must be respected until antibiotic residues are no longer detected [20]. The presence of antibiotic residues in meat from various species of economic interest is considered a significant danger to public health [21].

### 1.4. Antibiotics use in aquaculture

In aquaculture, increased stocking density, poor sanitation and the inability to separate healthy fish from infected ones result in high susceptibility to fish diseases and the rapid spread of infections among them [22]. Bacterial infections account for a relatively high percentage of losses in the total annual production and, in the last few years, have resulted in billions of dollars lost to the countries of Asia, the largest aquaculture producer in the world [23]. Precisely, in order to reduce economic loss, various antibiotics are widely used due to the wrong belief that the use of large amount of antimicrobials in fish cultivation (e.g. carp and chub and various other types of marine fish species) guarantees abundant production [24].

### 1.5. Impact on human health

#### 1.5.1. Spread of antibiotic resistance

It has been established that the exposure of bacteria to low doses of antibiotics is likely to lead to bacterial adaptation, making them more resistant and more virulent [25]. Overuse or misuse of antibiotics leads to drug resistance, which threatens both animal and human health. Antimicrobial resistance in food animals has a significant impact on animal health and may be associated with resistant infections in humans as well [26]. Long-term antibiotics use in food animals creates ideal conditions for the development and spread of resistant bacterial strains. Antimicrobial resistant bacteria originating in an animal can be transmitted to humans through the environment, food products, and/or by direct contact [27]. Similar strains of resistant bacteria are found in food animals and humans, suggesting bacterial transmission from animals to humans [28]. The studies conducted worldwide report an increasing and alarming number of genes for resistance to antibiotics in livestock each year [29].

There are a number of studies reporting that the use of antibiotics in the diet of food animals leads to an increasing prevalence of resistant strains such as *Escherichia coli, Klebsiella pneumoniae, Salmonella*, Methicillin-resistant *Staphylococcus aureus* in animals, animal products, environment and patients and to the observation of increasing resistance to antibiotics, such as tetracyclines, sulfonamides, â-lactams and penicillin [30, 31, 32]. Plasmid-mediated resistance in *E. coli, Salmonella* and *Klebsiella* to colistin, a last line group of antimicrobial drug, is reported in both food animals and humans in countries from North America, Europe, Africa and Asia [33]. According to a study, a substantial proportion of human extra-intestinal extended spectrum cephalosporin-resistant *E. coli* infections originate from food animals [34]. Resistant bacteria in animals can directly or indirectly reach humans through food, water, mud and manure, which are used as fertilizers. Farm and slaughterhouse workers, veterinarians, and those in close contact with agricultural workers are easily infected with resistant bacteria through daily exposure to infected animals. Several studies have reported a high prevalence of resistant gut bacteria among farm workers compared to the general population or farm workers where antibiotics are not used [26].

Consumers may also be exposed to resistant bacteria through contact with or consumption of animal products. Evidence exist that foods from various animal sources and at all stages of processing contain large numbers of resistant bacteria and genes encoding antibiotic resistance [35]. The genes encoding antibiotic resistance identified in foodborne pathogens are also demonstrated in foodborne pathogens isolated from humans, which confirms the risk of consuming the various food products colonized by resistant bacteria [26].

**1.5.2. Allergic reactions**

Several studies have reported that antibiotic residues can cause allergic reactions, mainly associated with the use of beta-lactam antibiotics [29]. Allergic reactions have been reported in humans who consumed milk and meat, all containing penicillin residues [36, 37]. Other studies have mentioned that aminoglycosides, sulfonamides and tetracyclines residues can also cause allergic reactions [38].

**1.5.3. Mutations, reproductive disorders and teratogenic effects**

Several authors reported that antibiotic residues adversely affect human fertility can cause reproductive disorders and teratogenic effects, which is an extreme threat to the human population [36, 37, 39]. In a recent research, summarizing data from more than 70 scientific studies reporting antimicrobial residues in animal products readily available for sale, mutation rates were reported to increase with antibiotic residues [40].

**2. Strategies and recommendations for antibiotic resistance prevention in relation to food safety**

At present, most countries have no system for surveillance of antibiotic use, and different methodologies are used to collate and present the available data. For this reason, reliable data are lacking in most countries, and the available data are usually not comparable between countries. Improved surveillance of antibiotic use is urgently needed [16]. Therefore, more and better national data antibiotic resistance in relevant bacteria from food animals, food products and people, as well as data on the usage of various types of antibiotics in different kinds of food animals, are needed. Tackling antibiotic resistance requires international and cross-sectoral cooperation, collaboration and communication, as this problem crosses borders and sectors. In addition, international activities are required to guide and support the work needed at the national level [16]. An intersectoral national strategy and action plan on antibiotic resistance, including the food safety perspective and regulatory framework for authorizing and controlling veterinary medicines, including antibiotics should be established. Antibiotics should not be used as growth promoters and should be reduced in animal husbandry by improving animal health through biosecurity measures, disease prevention, and good hygiene and management practices and by finding their alternatives. Such an alternative is, for example, the unique bee product propolis. Due to its rich chemical composition and valuable properties, it offers great potential for application in the food industry as a natural and safe preservative with high antimicrobial and antioxidant activity and as a means of increasing the nutritional value of foods [41]. Because of its ability to inhibit food spoilage microorganisms and foodborne pathogens, propolis can prevent undesirable physical, chemical, microbiological and organoleptic changes in food, thereby protecting the quality and improving the expiration date of food products of animal origin [41].

## CONCLUSION

Modern food-animal production uses large amount of antibiotics not only for therapeutic purposes but also to prevent disease and promote animal growth. As a result, healthy animals are routinely or often exposed to antibiotics, which provides favourable conditions for the emergence, development, spread and persistence of antibiotic-resistant bacteria capable of causing infections not only in animals but also in people. Because food animals and foods of animal origin are traded worldwide, antibiotic resistance affecting the food supply of one country becomes a potential problem for others. Overcoming the problem of antibiotic resistance requires a multidisciplinary approach with effective action coordination and information exchange between the agricultural, food, veterinary, and health sectors. Through international cooperation, efforts should focus on reducing unnecessary antibiotics use and reducing the spread of antibiotic-resistant bacteria, but national-level action on antibiotic resistance and food safety is also essential.

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**Address for correspondence:**
Dr Rozalina Yordanova,
Medical College, Trakia University, Stara Zagora,
9, Armeiska Str., 6000 Stara Zagora, Bulgaria
Email: rozalina.yordanova@trakia-uni.bg