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Short Communication

Antibiotics in agriculture and problems of contamination of meat and meat products

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Abstract

The widespread and uncontrolled use of antibiotics (AB) in animal husbandry has led to an "explosive" increase in the scale of their use, which gives rise to a spectrum of global consequences. On the one hand, AB in foods at a level higher than residual amounts (RA) affects the intestinal microflora in the human body, leading to sensitization, allergies, and other consequences. On the other hand, the constant background of veterinary ABs in the intestines of animals and in the waste they produce, acting collectively as a huge bioreactor, contributes to the formation of resistant forms of bacteria, including pathogens for humans. The research results obtained at the Federal State Budgetary Institution for Nutrition and Biotechnology showed a high level of antibiotic-resistant strains isolated from poultry products: 88 - 96% *C. jejuni* are resistant to ciprofloxacin, nalidixic acid and tetracycline, 34% to erythromycin; *Enterobacter* spp. up to 73% resistant to tetracycline AB. The presence of resistance of these groups of bacteria leads to the ineffectiveness of AB in the treatment of people. The widespread use of AB for preventive purposes and for fattening young animals: broiler chickens, piglets and calves, requires special attention when controlling the AB content in meat and meat products obtained from these species. The presence in the Russian Federation of an effective control and monitoring system has contributed to a decrease in the proportion of cases of AB detection in food products over the past decade from 1.5 to 0.5%. Given the possible risk of preserving veterinary AB in the animal's body, it is important to consider their highest concentration in the excretory organs: skin, kidneys, and also in the liver. It is advisable to purchase products of animal origin in retail chains with a high level of control of the products sold, if there is clear information about the origin of the products, expiration dates, and storage conditions.

Keywords: *Veterinary Antibiotics; Antibiotic Resistance; Meat Products; Poultry Products; C. jejuni; Enterobacter spp*

The use of antibiotics in animal husbandry to stimulate the growth and prevention of infections in healthy livestock, which began in the 50s of the 20th century, led to an "explosive" increase in the scale of their use. The volume of antibiotics used in veterinary medicine for productive animals, poultry and aquaculture, according to WHO, today is more than 2 times the volume of drugs used in medicine, using the same types or classes of antimicrobials as for humans [1]. According to the European Union and the WHO FAO, tetracyclines are the most prevalent in the entire spectrum of antibiotics for agriculture due to their availability and low prices [2]. The number of tetracyclines (per 1 kg of biomass of farm animals) in the EU countries is more than half of all sold antibiotics for veterinary medicine [1].

The same situation is typical for other countries. The widespread and sometimes uncontrolled use of antibiotics in agriculture gives rise to a range of global consequences.

Antibiotics in farm animals are used to treat infections, as well as to prevent diseases and stimulate growth, it is especially important that in the last two options, antimicrobials in large quantities are given simultaneously to a large number of animals. This practice makes up the main difference between the use of antibiotics for humans and for animals [3]. In accordance with safety requirements, before the slaughter of productive animals, the so-called withdrawal period must be maintained in order to remove antibiotics from organism, non-compliance leads to the fact that the remnants of the drugs used through animal feed fall into food.

According to the State register of veterinary drug (SRVD) and feed additives at the beginning of 2016, 2318 drugs were registered in the Russian Federation, of which more than 20% are veterinary drug (VD) with antimicrobial effects. In addition, antibiotics account for more than half of the substances approved for import and production from which the most popular dosage forms are produced in the territory of the Russian Federation. There is also the practice of introducing antibiotics into the feed of productive animals [2].

To prevent contamination of meat products with antibiotics, control should be carried out at all technological stages from the receipt of raw meat (input control of each batch) to the finished product. Checking meat raw materials and processed products for compliance with the requirements of the Technical Regulations of the Customs Union TR CU 021/2011 "On Food Safety" and TR CU 034/2013 "On the Safety of Meat and Meat Products" is mandatory for levomycetin (chloramphenicol), tetracycline groups and bacitracin at the level of residual quantities, and control of unearned raw materials in relation to a wide range of antibiotics and antimicrobial agents (more than 50), given in Appendix 4 of the Unified Sanitary and Epidemiological sanitary and hygienic requirements for products (goods) subject to sanitary and epidemiological surveillance (control)", if they were used by manufacturers of raw meat, which should be reflected in the accompanying documentation for each batch of raw materials. It should be noted that the responsibility for observing the relevant rules on the use of antibiotics in agriculture lies entirely with the manufacturer.

The presence of antibiotics in food products in quantities exceeding maximum residual levels (MRLs) may expose the consumer to the risk of receiving them with food, having a direct effect directly on the body itself. The indirect effect of antibiotics occurs through the formation of antibiotic-resistant pathogenic microflora in the environment and an increased risk of infectious diseases in humans with aggravated consequences.

The scale of antibiotic use in animal husbandry is reflected in the scale of environmental impact, which in turn forms a response human exposure. Antibiotics, when ingested in animals, in therapeutic, prophylactic doses or with food as growth stimulants, interact with the intestinal microflora. Farm animals and the waste they produce together act as huge bioreactors in which conditions are created for the formation of bacteria resistant to antimicrobials, including pathogens for humans. The appearance of, in particular, zoonotic bacteria such as nontifoid serovars *Salmonella enterica* [4] and various *Campylobacter* species has been documented [5,6]. Among bacteria that are resistant to clinically significant medicinal antimicrobials that are used in farm animals, we can name *Escherichia coli* and various *Salmonella* species that are resistant to β-lactam antibiotics and 3rd and 4th generation cephalosporins and to fluoroquinolones; various *Campylobacter* species resistant to macrolides and fluoroquinolones; *Staphylococcus aureus* resistant to all beta-lactam antibiotics (i.e., methicillin-resistant *Staphylococcus aureus*); enterococci resistant to vancomycin (vancomycin-resistant enterococcus) [3].

Research is being conducted at the FRC of Nutrition and Biotechnology to study the antibiotic resistance of microbial contaminants isolated from various types of meat raw materials and food products. Thus, when analyzing the phenotypic antibiotic resistance profiles of 55 *Campylobacter jejuni* strains isolated from raw poultry products and flushing from equipment surfaces of poultry processing enterprises, the presence of resistance to 15 antimicrobial preparations of 8 pharmacological groups was revealed: the majority of 40% of the strains of the studied cultures were 96.3% to ciprofloxacin, almost 90% of cultures to nalidixic acid, 88.6% to tetracycline, 34% to erythromycin, and 40% of the strains were multi-resistant 4 antibiotics and more. The data obtained indicate a high prevalence of antibiotic-resistant strains among *Campylobacteria* that contaminate poultry products in the process of production and processing of raw materials [7].

In another study, also conducted by the Federal State Budgetary Institution of Nutrition and Biotechnology, on the study of the antibiotic resistance of enterobacteria and enterococci isolated from food products, including poultry and livestock, it was found that in "meat" enterobacterial isolates the highest level of resistance was detected to tetracycline antibiotics: doxycycline (73%), tetracycline (38%), ampicillin (53%); strains insensitive to chloramphenicol, nitrofurantoin, ciprofloxacin, levofloxacin, nalidixic acid were less common. Among the studied strains, two were highly resistant - *E. coli* from cattle liver and *E. coli* from turkey mince (multi-resistant to 8 antibiotics) [8].

The presence of *Campylobacteria, Enterobacteria, Enterococci* and *Escherichia* antibiotic resistance of the quinolone group (ciprofloxacin, ciprofloxacin, nalidixic acid) causes concern, since this group of antimicrobials along with cephalosporins (third and subsequent generations) of macrolides and ketolides, glycopeptides and polymyxins in the last list of antibiotics "critical" for medicine, published in April 2017 [9].

With the widespread use of antibiotics in animal husbandry, along with resistance of pathogens and the ineffectiveness of antibiotics (including drugs of the latest generations) in treating people today, a whole range of negative consequences for humans (the growth and spread of non-infectious human diseases associated with the modification of normal intestinal microflora, such as sensitization of the body and allergies, dysbiosis, atopy, obesity, irritable bowel syndrome), as well as for the environment - increased frequency contamination by resistant bacteria, the spread of microdoses of antibiotics and the continuation of the resistance chain reaction; induction of horizontal resistance gene transfer from extraneous microorganisms to biotechnological microflora in the products fermented by it [2].

Resistant bacteria carried by farm animals can be transmitted to humans, mainly through the consumption of meat and poultry products that have not undergone sufficient heat treatment, through contact with raw foods or through cross-contamination of other foods, as well as through the environment (e.g. contaminated water) and direct contact with animals. Moreover, transmission factors can also be vegetables and fruits grown using organic fertilizers obtained from animals.

Particularly sensitive to the effects of antibiotics are people with weakened immune systems and children. The most dangerous in terms of adverse effects for humans is the entry of antibiotic-resistant pathogenic bacteria into the human body, and especially the child, since if an infectious process occurs, the effectiveness of the use of clinical antibiotics may be insufficient, resulting in an increase in the duration of treatment, the number of hospitalizations, and an increased risk of deaths.

In farm animals, antibiotics are used mainly for the treatment and prevention of respiratory and intestinal infections in groups of intensively fed animals. They are especially widely used in young animals, for example, broiler chickens, as well as piglets and calves. The high density of animals and poultry on farms contributes to the rapid spread of infections, and as a result to a high mortality of animals (or "death of animals"), to prevent which antibiotics are given to all animals without exception. And given the intensive breeding rates and the use of antibiotics as growth stimulants, most farm animals and birds (broiler chickens, piglets) receive them throughout their lives. Moreover, the bird is more susceptible to infectious diseases than other animals whose meat is eaten. Therefore, meat and meat products from poultry, as well as piglets and calves, require special attention when controlling the content of antibiotics. According to specialists, antibiotics are used in 99% of poultry farms in Russia, and the high density in poultry farms increases the risk of the formation of antibiotic-resistant strains of bacteria [10].

The growth in domestic meat production according to the Federal State Statistics Service of the Russian Federation (FSSS RF) shifts the pattern of consumption in favor of poultry and pork. So, if in 2006 poultry accounted for 31% of all meat produced in slaughter weight, which was approximately on the same level as pork 32.6% and cattle - 33%, then in 2015, poultry already 45% of all meat produced in Russia, then came pork - 30%, cattle - 21%, sheep and goats - 3%, and other animal species - 1%. At the same time, chicken products are invariably leading the market due to the greatest affordability. A high level of consumption of poultry meat by children and adults increases the risk of getting into the body of a residual amount of antibiotics (RAA).

In the Russian Federation, a system for assessing the safety, control and monitoring of livestock products obtained using VDs with antimicrobial activity has been created and is functioning. About 100 standards (MRL) have been developed and put into practice on MRLs of VDs in milk and dairy products, meat and poultry products, cage fish, honey, which are included in technical regulations.

According to the Federal Service for Supervision of Consumer Rights Protection and Human Well-Being (Rospotrebnadzor) over the past decade, the proportion of cases of detection of antibiotics in food products has decreased from 1.5 to 0.5%. Most likely to meet antibiotic residues in poultry products - up to 1.2%, least likely - in baby food (less than 0.1%) [2].

Given the possible risk of preserving veterinary antibiotics in the animal's body, it is important to know that they are most concentrated in the excretory organs: skin, kidneys, and also in the liver. Studies on the effect of heat treatment on the content of antibiotics in meat showed the following results. After cooking cattle, pork and poultry meat for 1 hour, the distribution of antibiotics (chloramphenicol, tetracycline, bacitracin) was as follows: 7 - 12% were found in meat, 19 - 20% were destroyed, and 67-78% turned into broth (broth after cooking must be drained). In the manufacture of cooked sausages using hot steam, 89-93% of antibiotics (chloramphenicol, tetracycline, streptomycin and benzipenicillin) were found in the final product - there was no significant decrease [11].

Despite the existence of effective control measures for the content of antibiotics, the consumer should remember that it is advisable to purchase products of animal origin (meat, eggs, dairy products) in retail chains that have proven themselves to have a high level of control of the products sold, from trusted sellers and authorized markets where veterinary and sanitary control is established. When purchasing food products, you should pay attention to the clarity of the labeling, which should contain information about the name of the food product; its composition, name and location of the food manufacturer, date of manufacture, shelf life and storage conditions of the product, as well as recommendations and (or) restrictions on use, a single sign of product circulation on the market of the Member States of the Customs Union.

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