

QUALITY CONTROL OF ANIMAL DEVELOPMENT, ANIMAL PROTECTION, AND QUARANTINE

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Summary

Veterinary drugs are widely used in modern animal husbandry not only for therapeutic and prophylactic purposes but also for better breeding efficiency. Although their use contributes to higher food production, better food supply, and cheaper food, there are also negative consequences, primarily antimicrobial resistance. The harmful effect of drugs having hormonal activity and the toxicity of some chemical residues should be mentioned. To assure safety of the food supply, a reduction of risks is necessary. Good veterinary practices search for natural alternatives such as antimicrobials, while efficient regulations at national and international levels may be the main tools.

1. Introduction

Plant growing and animal farming have been major human activities for many thousands of years. These two activities have been closely interrelated because animal farming makes possible the conversion of low-energy, often indigestible, plant material into high-value, proteinaceous products such as meat, milk, and eggs. The growing human population and parallel growing needs for animal products have, over the years, stimulated efforts toward improving feed conversion and realizing faster growth of animals to achieve lower cost and higher profit. As a result of these efforts, new practices in animal husbandry have been designed by controlling various factors such as genetics, nutrition, health, management, and the environment.

To achieve optimal productivity and profitability, modern animal husbandry is trying to achieve the fastest growth of animals and the best feed conversion efficiency to produce milk, meat, and eggs at the lowest cost. In addition, an important factor of effectiveness in animal husbandry is the reduction of losses caused by disease and unplanned death of animals.

Major components in the structure of any modern farming system are several antibacterial agents, including pharmacologically active compounds of both natural and synthetic origin, primarily antibiotics. Apart from treatments such as injections, most of these agents are administered to animals as feed additives, or in drinking water, to cure outbreaks of disease whenever they occur. Their use has become essential in intensive livestock farming because the rearing conditions of a large number of animals in close confinement could hardly be more favorable for frequent incidence and rapid spread of disease.

Veterinary drugs in general are used for both therapeutic and prophylactic purposes. A third application is the use of growth promoters that are generally specified compounds or mixtures of compounds. To these belong, among others, steroids and other substances that have similar pharmacological activity and are used to improve the efficiency of protein conversion. The better this conversion, the faster the animal grows and the earlier it can be slaughtered. These are obvious economic reasons that do not take into account the possible harmful effects for the consumer of the products derived from the slaughtered animal.

The thyrostats, which are sometimes called antihormones, are used for inhibition of the activity of the thyroid gland. Lower thyroid activity means lower basic energy requirement, which may thus result in higher body weight gain.

A new class of compounds has found its way into animal breeding. The beta-agonists, sometimes referred to as repartitioners, are licensed only for respiratory diseases in cattle and horses. They are being used, however, because they increase the ratio of lean tissue to fat. The improvement of lean meat ratio may also be achieved by supplementation of feed with substances containing chromium in the form of the compound chromium picolinate.

Corticosteroids (e.g., dexamethason) are also being used in animal husbandry. Their exact role in animal metabolism is not yet fully clarified.

An important feature of thyrostats, beta-agonists, and corticosteroids is that they are, in general, orally active. This means that they can be given via fodder or drinking water, leaving no trace of percutaneous administration, which is one of the annoying indications with injections of orally inactive steroids.

A trend of the late 1990s in animal husbandry was the use of *nutraceuticals* as an alternative to antibiotics to reduce negative effects of the residue of antimicrobial agents in animal products, and consequently of potential health hazards for the consumer. The streams of research papers on such topics as probiotics, prebiotics, organic acids,

enzymes, herbs, and spices became a veritable torrent of data, covering everything from bacteria to Chinese herbal medicine.

Many new products, developed as alternatives to such growth promoters as antibiotics, became readily available at the market, and still more are under development. Two major approaches, which appear time and again when assessing new feed additives, claim to be growth promoting. First, natural substances that achieve similar effects to the classic antibiotic approach could be used. Second, the digestive processes of animals could be enhanced. In the future, it may be possible to genetically manipulate animals so that the digestive system catches up with the genetic potential for growth.

2. Negative Effects of the Use of Veterinary Drugs

2.1 Residual Growth Promoters, Factors Influencing Residue Level

The significance of residual antibacterials, growth promoters, and other compounds used for therapeutic purposes in food, is the object of intensive studies, and has been one of the most vexing problems in food science. Since the safety of the food supply is of utmost importance to public health, the concept of zero tolerance, which refers to the absence of residues, seemed to be the best solution to avoid risks posed by the presence of residues in food. However, it became evident that this concept guaranteeing the highest degree of food safety is not realizable. Whether antibacterial or other residues could or could not be found in meat, milk, and eggs depends on the detection limits of analytical methods. However, as the sensitivity of analytical methodology increased, it was found that animal-derived food formerly believed to be free of residues was contaminated after all. It was realized that the goal of producing food free of residues in absolute terms is, to all practical purposes, impossible to achieve. Such a target could theoretically be attained by entirely abandoning the use of veterinary drugs, but this is an unacceptable option in modern animal farming because veterinary pharmaceuticals have been and are a key element in increasing the productivity of animal husbandry. Therefore, possible hazards for human health must be cautiously weighed against benefits, and judgment must be made that reflects the appropriate “safe” balance.

When evaluating potential risks connected with residues, it is necessary to make a difference between risks associated with residues from illegal and accidental contamination and uncontrolled treatment of food animals and with veterinary drugs and residues that are permitted by regulation and associated with the well-controlled, ordinary use of veterinary drugs. For detection of illegal, uncontrolled use, continuous monitoring is necessary to ensure that only approved veterinary drugs are used, in addition to the normal food inspections.

Major factors governing the occurrence of violative antibacterial and growth promoter residues in animal products are considered to be the lack of adherence to withdrawal times and extralabel use. In most violative cases, the withdrawal time has been deliberately disobeyed, whereas in the case of emergency slaughtering, compliance can never be attained. Sometimes, the withdrawal time is unknown to the farmer because of an incorrectly labeled formulation, whereas in a few cases the antibacterial has been administered to an animal species different from that for which it was originally

intended. In the latter cases, high levels of violative residues often appear, and adverse toxicological effects on the treated animals may be observed. Residues can appear in animal products from contamination of feed and drinking water by carryover from former medicated batches. Since this carryover is usually low, violative residues are normally not expected. Sometimes direct contamination occurs in the animal product itself, such as when milk is collected from different farms that include a farm where a cow was treated with an antibiotic for mastitis, and the total quantity of collected milk may be contaminated with the antibiotic.

The procedure of establishing legal limits for residues and guaranteeing safe food of animal origin for consumers is a complex one and requires profound knowledge of the metabolism of residues and their physiological effect on humans.

Based on numerous published studies, many factors influencing the fate of antibacterials and growth promoters in the animal organism have been detected. In the following sections, some of them will be briefly treated. Variations in the oral intake of antibacterials because of disease or normal differences between animals will influence the absorption and elimination profile. For example, renal failure may result in the diminished elimination of antibacterials that are normally readily secreted, such as the β -lactams and the amyloglicosides, and therefore in longer withdrawal times. On the other hand, the elimination of sulfadimethoxine or amoxicillin from pigeons may be distinctly accelerated in cases of coccidia or salmonella infection. An abnormal elimination profile may also be observed when other pharmaceuticals are given concurrently; induction or inhibition of hepatic enzymes with an androgen hormone has been found to result in decreased or increased persistence of sulfamethazine residues. Improper injections may also result in slow absorption, giving rise to high levels of residues at the injection site and low levels in the other tissues.

Residual antibacterials and growth promoters appear in meat and eggs at generally low concentrations, therefore the risks of acute human toxicity are practically excluded. Exceptions are some severe non-dose-related side effects, such as irreversible aplastic anemia, which arises from chloro-amphenicol in susceptible individuals, and allergic reactions that may arise from β -lactam residues in sensitized consumers.

Next to acute toxicity, possible hazards with respect to the presence of antibacterial residues in food may be mutagenic or carcinogenic, or in the nature of antibiotic resistance. Long-term, low-level mutagenic or carcinogenic effects, if any, are by far the most relevant from a public health point of view. A number of mutagenic or carcinogenic antibacterials, such as the nitrofurans and quinoxaline 1,4-dioxides, have been used in food-producing animals for a long time and still play an important role in livestock farming. All of them are under legal control, and their use is being reevaluated from the viewpoint of human food safety.

Apart from public health impact, residual antibacterials may bring about technoeconomic losses, especially in the dairy industry, by inhibiting the growth of starter cultures and thus preventing or delaying the formation of good quality fermented dairy products.

2.2 Microbiological Aspects

From a microbiological point of view, the antibacterial agents are primarily important for evaluation of potential risks. Although it is generally accepted that antibacterial residues in foods cannot cause harm, the widespread incorporation of some antibacterials in animal feeds gives rise to concern related to the appearance of antibacterial-resistant microorganisms. Pathogenic bacteria, such as the *Salmonella* species colonizing the gastrointestinal tract of the animal, may favor the production of populations resistant to the administered antibacterial agent. Additionally, resistance initially developed in nonpathogenic bacteria, such as strains of *Escherichia coli*, may be transferred over time to pathogenic bacteria. These aspects of resistance, transfer, and colonization have been discussed at length but are still controversial.

The relatively widespread use of antimicrobials in agriculture has led many medical practitioners and researchers to question whether this may also have contributed to the presence of antimicrobial-resistant organisms in the human population. This question has not yet been definitely answered. Although there is no question that antimicrobial resistant organisms exist among the livestock population, it is questionable whether these microorganisms contribute to the existence of the variety of antimicrobial microorganisms among human populations. Nevertheless it is true that both human medicine and animal husbandry cannot ignore this risk. It is an important need in agriculture to review its practices in this area.

2.3 Other Residues

In the European Union, the use of substances having hormonal action is prohibited in livestock farming. The so-called natural hormones (testosterone, progesterone, 17, beta-estradiol) may be permitted for therapeutic purposes under strict controls, which prevent misuse of them. Although under good agricultural and veterinary conditions, the level of hormone residues is lower than the concentration generally evaluated as safe, continued monitoring is necessary to ensure that permitted limits are not exceeded.

Among feed supplements, some contain selenium or chromium. Chromium salts or chromium-enriched yeast are added as a supplement to pork feed to improve the carcass quality by increasing lean meat ratio. Because both selenium and chromium may be toxic, the concentration of residues of the two microelements should be controlled.

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Biographical Sketch

Árpád Bata received his M.Sc. Degree in chemical engineering in 1977 and his Ph.D. Degree in 1987 in mycotoxins from Budapest University of Technology and Economics. In 2000 he obtained the D.Sc. title in the science of animal feeding and animal feed supplements. He is the general Director of the Hungarian-Canadian R and D Company Ltd. in Ocsa, Hungary, and a lecturer at the University of Veterinary Sciences in Budapest, Hungary. Dr. Bata's main research activities are the biochemistry of animal feeding, and analysis of residues in food and feed.