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Antibiotics Use in Animal Husbandry and Their Public Health Impact

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Demand for animal and bird's meat is increasing due to increase in population. In order to meet the need of consumers, selection of superior breed has become essential. However, it has also resulted in compromising the welfare issues in animal and birds rearing. Vaccination, antibiotics and probiotic treatment have comparatively improved the health status of animal and birds. Drugs necessary to treat infected animal and birds are a direct cause of economic damage, owing to their costs. The cost of drugs varies between countries, depending on the legislation and the infrastructure of the country. Till date broad spectrum antibiotics are injected to reduce financial loss. It leads to serious side effects. Therefore, alternative therapies are required for the effective treatment.

Keywords: Antibiotics, drug, animal, birds, therapies.

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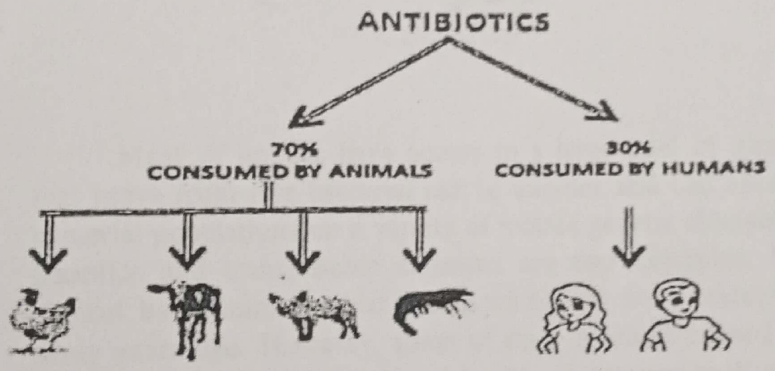
The precise quantity of antimicrobials used in food production globally is difficult to estimate, but the evidence suggests that it is at least as great as the amount used by humans. Indeed, in some parts of the world antimicrobial use is far greater in animals than in humans; in the US, for instance, more than 70 percent of medically important antibiotics are used in animals. The relative use in agriculture, without better policies, is likely to grow even more due to the rise of economic growth, wealth, and with these, food consumption of the emerging world. Consumption of antimicrobials by animals to produce meat products, in the BRICS countries (the major emerging economies of Brazil, Russia, India, China and South Africa) alone, for example, is set to double between 2010 and 2030.

Effects of antibiotics

Higher use of antibiotics drives increased drug resistance, as



bacteria are exposed more often to the antibiotics used to treat them. This is also true for other medicines, such as antifungals. The risks associated with the high use of antimicrobials are threefold.

Firstly, it presents the risk that drug-resistant strains are passed on through direct contact between humans and animals (notably farmers). Secondly, these drug-resistant strains have the potential to be passed onto humans more generally through the food chain, i.e. when consumers prepare or eat the meat itself. Finally, there is a further indirect threat to human health as result of animal excretion. Both resistant bacteria, as well as significant volumes of antibiotics consumed, are then excreted by animals (with most of the active ingredient unmetabolised). This both releases resistant bacteria into the environment as well as causing the environment to be tainted with antibiotics, providing further opportunities for exposure to bacteria and creating additional selective pressure that leads to the development of drug resistance.

Antimicrobial resistance

Many bacterial species multiply rapidly enough to double their numbers every 20-30 minutes, and their ability to adapt to changes in the environment and survive unfavourable conditions often results in the development of mutations that protect them. In addition, a factor contributing to their adaptability is that individual cells do not rely on their own genetic resources alone.

Many, if not all, have access to a large pool of itinerant genes that move from one bacterial cell to another and can spread through bacterial populations on a variety of mobile genetic elements, of which plasmids and transposable elements are two examples. In order to control bacterium, chemicals and antibiotics were widely applied in many years ago. However, some of their residues caused the serious impact in both environment and health of consumers (Kumaran *et al.*, 2018).Bacterial capacity to adapt to external changes using these mechanisms is called resistance development in the face of selection pressures, and the development of resistance allows the resistant organisms to proliferate in the prevailing conditions.

Resistance Takes Two Forms.

- Inherent or intrinsic resistance, i.e. the species is not normally susceptible to a particular drug. This may be due to the inability of the antibacterial agent to enter the bacteria cell and reach its target site, or lack of affinity between the antibacterial and its target (site of action), or absence of the target in the cell.
- Acquired resistance, where the species is normally susceptible to a particular drug but certain strains express drug resistance,

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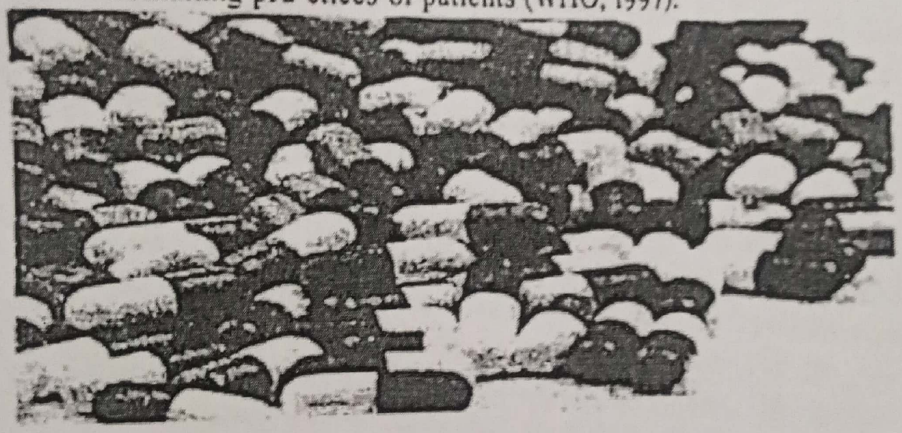
which may be mediated through a number of mechanisms that will be discussed later in this document.

When resistance develops, the antibiotic is no longer capable of curing or treating the disease caused by the infective agent. A low level of resistance may be detected by a slight increase in the minimal inhibitory concentration (MIC) for the antibiotic from the usual value, which is not necessarily of clinical significance. A higher degree of resistance is characterized by an MIC that exceeds, sometimes by several orders of magnitude, the concentrations of drug safely attainable in the patient's tissues.

Overuse of antibiotics

There is no doubt that the overuse and/or misuse of antibiotics in humans are contributing factors to the development of antibiotic resistance (EMEA, 1999; WHO, 2000; Levin, 2001; UCS, 2002), which are related to the prescribing practices of health workers and to medicationtaking pra ctices of patients (WHO, 1997).



Antimicrobials have been increasingly used in efforts to control disease and promote growth of livestock. Nevertheless, in recent years there has been a move away from the use of antibiotics as growth promotants in countries such as the UK, Sweden and Denmark. The European Union has also made moves to ban antibiotics for growth promotion in food animals and the WHO also recommend that use of antimicrobial growth promoters should be terminated or rapidly phased out (WHO, 2001). Antibiotics can be used in livestock production in sub-therapeutic doses to favour growth or in low-level doses for prophylactic purposes, as well as in therapeutic doses to treat infections. Unfortunately, the non-therapeutic use of antimicrobial agents is also considered to have led to an increase in resistant bacteria. Antibiotics are also used to treat fruit trees and fruit for prevention of bacterial diseases.

In some areas there is misuse of antibiotics in aquaculture to control diseases, which is directly related to increasing or maintaining production. For instance, the illegal use of chloramphenicol or nitrofurans in some Asian countries for controlling shrimp diseases has been highlighted recently by the EU through the bans placed on imported shrimps containing unacceptable residues from China (EC, 2002a), as well as Thailand, Vietnam and Myanmar (EC, 2002b). Chemicals such as tributyl tin used to control pond organisms (e.g. snails) may also be a problem that could lead to residues. The invention of novel drugs or the use of alternatives to antibiotics should also be encouraged Kumaran and Citarasu (2018).

Application methods

Medicated feed

More often than not medicated feeds are commercially prepared, either as sinking or floating pellets, although such feeds have a limited shelf life. As already mentioned, one problem with the use of medicated feeds is that diseased fish stop eating and this may be compounded by unpalatable feed caused by the presence of the drug itself, which makes the problem worse. Consequently, good diagnosis that includes an antibiotic sensitivity test plays an important role in the use of the correct early treatment.

The incorporation of an antibiotic in the feed is usually via a powdered premix in conjunction with a binder, such as gelatin (up to 5%), fish or vegetable oil. One of the important considerations is that the feed and the drug have to be mixed thoroughly to give an even distribution of the drug and coating of the pellets. The dosage required for treatment with a medicated feed depends on the original level of active ingredient/kg fish body weight. The feed is then administered for a recommended treatment period, according to the specific disease to be treated and the instructions of a veterinary practitioner. It is also important that treated fish must not be harvested for food use until a specified withdrawal period has elapsed. Medicated feed needs to be kept under adequate storage conditions, such as in a cool dry place kept separate from other feeds, to avoid any deterioration of the feed quality and drug efficacy.

Injection

Injection of antibiotics can be a more effective treatment for bacterial infections than using a medicated feed, particularly for advanced infections. However, it is usually only practical for valuable individual fish, such as broodstock or ornamental fish (e.g. koi carp).

rather than fish in large scale production facilities. Injection quickly leads to high blood and tissue levels of antibiotic. Normally, an individual fish will also need to be anaesthetized before treatment. Typical injection sites include the intraperitoneal cavity and the intramuscular route.

The volume required for injection of antibiotics is based on the weight of fish to be treated, the recommended dosage for the antibiotic being used and its supplied concentration. This is usually expressed as:

$$\text{Volume of antibiotic required (kg)} = \frac{\text{recommended dosage (mg/kg)} \times \text{weight of fish}}{\text{supplied solution concentration (mg/ml)}}$$

Topical

Topical treatments are usually only necessary for more valuable individual fish, such as ornamental varieties or brood stock. Open sores or ulcers can be treated with a topical antiseptic microbicide, such as an iodine-based solution, followed if necessary, by a topical antibiotic. Nevertheless, it is possible that ulcers can heal themselves with improved water quality and the elimination of parasites.

Baths and Dips

Baths and dips are not as effective as some of the other treatment methods, particularly for systemic infections, because of generally poor internal absorption of the antibiotic being used.

The method of application can therefore be used for surface infections such as fin rot, bacterial gill disease, superficial fungal infections and ectoparasitic infestations. Another disadvantage with bath type treatments is that a lot more antibiotic is required when compared with oral (feed) treatments or injections. Bath treatments are also not recommended for recirculation systems or aquarium systems using biological filters. Consequently, fish treatment by bath usually uses a separate container, tank or simply with the flow stopped. Additional aeration may also be required for bath treatments. Accurate calculation of the volume of water in the tank, pond or cage is also required (Bruno and Munro, 1991).

Avoiding Antimicrobial Agents

There is a hypothesis of disease propagation that demonstrates that the cause of all disease is stressor overload (Wilken, 2002). Consequently, the reduction of unnecessary stress is the main aim of any satisfactory programme of improved health, whether it be human,

animal or fish. However, elimination of all stressors is virtually impossible and, therefore, reduction of only the unnecessary stressors, the so-called destructive stressors, should be attempted. In general, the FAO have defined the development of affordable vaccines, the use of immunostimulants and non-specific immune-enhancers, and the use of probiotics and bioaugmentation for the improvement of aquatic environmental quality as major areas for further research in disease control in aquaculture (Subasinghe, 1997), which would help to reduce the use of antimicrobial agents.

Approaches to minimizing antibiotics use in food-animal production

As growth promoters (feed supplementation)

There are some options that might be considered as alternatives to the use of antibiotics as growth promoter factors. The potential of some of these options represents a new area that requires further research.

Enzymes and probiotics

This approach aims to obtain a situation where a greater share of the nutrients supplied in the feed is made available for absorption by the animal. Improvement in feed efficiency has been associated with antibacterial feed additive (AFA) use (probiotics).

Organic acids

These products are widely distributed in plants and animals and are also fermentation products, and their salts are often used as food preservatives and to acidify feeds. At low pH (around 3.5), digestion of proteins and the population of beneficial bacteria (*Lactobacilli*) are maximized, and harmful bacteria are inhibited. This is another approach that has been used to replace antibiotics as growth promoters. A greater weight gain was observed when fumaric acid was used to supplement piglet feed. The possible mechanism of growth promotion includes inhibition of undesirable microflora, increased digestibility of proteins and changes in the intestinal morphology.

Minerals

The use of zinc oxide in Denmark has led to decreased use of antibiotics in swine feed. Zinc improves pig performance and reduces incidence and severity of diarrhoea in piglets. Rare earth elements have been used in China as feed additives. Recently, a rare earth mixture containing lanthanum, cerium and praseodymium was tested in swine, significantly improving weight gain and feed conversion (He and Rambeck, 2000).

Conjugated linoleic acid

Conjugated linoleic acid (CLA) comprises a mixture of positional and geometric isomers of linoleic acid, with conjugated double bonds in the region of carbon atoms8-13. With pigs fed up to 1 percent CLA in the diet, small improvements were seen in average daily weight gain and feed efficiency (Jahreis *et al.*, 2000).

Phospholipids

It has recently been reported that lysoforte, a phospholipid, can aid in nutrient uptake from the digestive tract, significantly improving growth and feed conversion in piglets (Doyle, 2001).

Seaweed extracts

Seaweed shows that cattle feed containing forage treated with, or directly fed, seaweed meal and extract showed marked positive

effects on the animal's immune system, weight gain, carcass quality and even shelf life of finished meats.

Immunologically-active compounds

Some of the growth-promoting effects of the sub therapeutic use of antibiotics in feeds may result from their action against subclinical infections or competitive intestinal bacteria. Several immunologically-active compounds, such as egg yolk antibodies (IgY), cytokines, spray-dried plasma and freeze-dried eggs, have been shown to affect the immune response and may enhance resistance to disease. For this reason, it has been suggested that the addition of these immunoactive compounds to feed may accomplish the same purpose.

Conclusion

Good availability of vaccines for bacterial diseases and they have resulted in reduced use of antimicrobial agents, although there is still a need for improvements in delivery methods and efficacy, as well as the development of viral vaccines. Additional control measures such as good husbandry, adequate feed composition, movement restrictions, immunostimulants and biological control could contribute to reduced antimicrobial usage throughout the aquaculture industry. Many disincentives also exist to curtail antibiotic usage in aquaculture, including the increasing marginal cost-effectiveness of their use in disease treatment, the increasing need to be HACCP compliant, as well as the growing concern over the negative impact that some seafood products have had recently in connection with antibiotic residues. If these factors are taken into account and the potential problems related

to the use of antimicrobial agents can be overcome, then a positive outlook could be generated for reduced reliance on antibiotic-based management strategies in the future.

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