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Preventing Antimicrobial Resistance Together: One Health Approach

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Introduction

Antimicrobial Resistance (AMR) is a condition in which bacteria, viruses, fungi, and parasites evolve and cease to respond to antibiotic. These resistant pathogens make infections more difficult to cure and raise the risk of disease transmission, life-threatening sickness, and death. Drug resistance makes it harder or impossible to treat diseases and renders antibiotics and other antimicrobial medications useless. *AMR causes around 25,000 deaths annually in the EU and 700,000 worldwide and is predicted to kill more people than cancer by 2050.*

Antibiotics are substances that bacteria naturally generate to prevent the growth of competing microorganisms. Due to their frequent genetic exchanges, they create genetic and biochemical mechanisms of antibiotic resistance to survive. These mechanisms have spread widely among species. Most of the antibiotic compounds produced by the pharmaceutical industry no longer work on some bacteria that are pathogenic to people and animals. This widespread problem is currently a significant public health issue.

In addition, the environment has been heavily contaminated by resistant microorganisms excreted by humans and animals who received antibiotic treatment. Bacterial flora in environmental, animal and human reservoirs are constantly exchanging. It is well recognized that the misuse and or overuse of antibiotics in livestock played a role in the development of AMR.

Amr- Global Concern

The ability to cure common diseases is still under concern due to the creation and spread of resistant bacteria to drugs, and have developed new resistance mechanisms. The increasing global development of multi- and pan-resistant bacteria, commonly referred to as "superbugs," which cause diseases that cannot be treated with current antibiotics, is highly alarming. WHO, in 2019, identified only six antibiotics in clinical development as innovative to address priority pathogens. Antibiotics are becoming increasingly less effective as antibiotic resistance increases worldwide, making diseases harder to cure and ultimately leading to mortality. According to the WHO priority pathogen list, new antibiotics are urgently needed, for example, to treat carbapenem-resistant gram-negative bacterial infections.

The main drivers of antibiotic resistance include antibiotic abuse and overuse; lack of access to clean water, sanitation and hygiene (WASH) for humans and animals; inadequate infection and disease prevention and control in healthcare facilities and farms; poor access to quality, affordable medicines, vaccines and diagnostics; lack of awareness and knowledge; and lack of law enforcement. The costs of antimicrobial resistance to national economies and healthcare systems are high. Without practical tools to prevent and adequately treat drug-resistant infections, and improved access to effective antimicrobials, the number of patients who fail treatment or die from the disease will increase.

Use Of Antimicrobial Agents in Food Animals

In the production of food animals, antibiotics are used for the following purposes:

(i) Treatment of animals exhibiting overt clinical symptoms
(ii) Prophylaxis of healthy animals at risk of infection
(iii) Infection control (metaphylaxis) of a herd or flock showing elevated morbidity or mortality, and
(iv) Better feed efficiency (growth promotion) of healthy animals.

Antimicrobials were first used as growth promoters in the 1950s because they accelerated animal growth rates and enhanced feed utilisation. The European Union has banned growth promoter antibiotics in feed because of their ability to select for resistance to antimicrobials used for treating human infections.

The widespread use of antibiotics in livestock, poultry, and farmed seafood has significantly improved the health and productivity of food animals. Most antibiotic classes used on animals raised for food include human analogues, which increases the chance that resistance to human antimicrobials will develop. These include penicillins, cephalosporins, macrolides, lincosamides, streptogramins, aminoglycosides, fluoroquinolones, tetracyclines, folate pathway inhibitors (sulfonamides and potentiated sulfonamides, e.g., trimethoprim-sulfamethoxazole), phenicols, and polypeptides. Other antimicrobial agents, which are mostly administered in feeds for growth promotion and prophylaxis, belong to classes used only in veterinary medicine, such as the arsenical compounds, pleuromutilins, quinoxalines (e.g., olaquindox), phosphoglycolipids (e.g., flavomycin) and ionophores (e.g., monensin, salinomycin, and lasalocid).

Antimicrobial usage in companion animals may provide a risk to human health. Companion animals, especially cats and dogs, may act as sources of AMR zoonotic bacteria to people. Antimicrobials are also frequently used in small animal practice to treat various illnesses, including infections of the urinary tract, respiratory tract, wounds, skin, and ears.

Use Of Antimicrobial Agents in Humans

In humans, antibiotics are used to cure or for antibiotic prophylaxis. Several tens of billions of unit doses of antibiotics are consumed annually by humans worldwide. Beta-lactam antibiotics (penicillins, cephalosporins, and carbapenems) account for around 60% of antibiotic used in human settings. Tetracyclines, macrolides, and fluoroquinolone usage is also widespread. About 80% of antibiotics are used in the community and 20% in hospitals.

Due to the wide range of antibiotics used and the high likelihood of transferring specific resistant germs from person to person, health care institutions play a significant role in spreading bacterial resistance. Some antibiotics provided to diseased patients are not used and are thus dumped into the environment along with our regular garbage. More importantly, the majority of antibiotics ingested by people are excreted in urine and faeces in their active form. Many of these antibiotics are found in wastewater treatment plants in nations with wastewater treatment infrastructure. Antibiotics (beta-lactam antibiotics, macrolides, tetracyclines, fluoroquinolones, etc.) have been found in wastewater from some treatment plants. These antibiotics are eliminated in the plant effluent, biodegraded, or absorbed in sewage sludge. While sewage effluent is released into the aquatic environment, sewage sludge can be used as fertilizer in agricultural fields (rivers).

Antibiotics are detected in some aquatic and terrestrial environments at concentrations ranging from ng to µg per litre of water or per gram of soil. Similar concentrations have also been measured in some groundwater. These antibiotics persist in the environment after contamination for periods ranging from a few days (e.g., beta-lactam antibiotics) to several months (e.g., fluoroquinolones and tetracyclines).

Strategies To Overcome Antibiotic Resistance

To slow the spread of antibiotic resistance, efforts are being made worldwide to increase the effectiveness of already existing antibiotics and to investigate novel medicines. The primary requirements for a new antibiotic are good efficacy, superior action to existing antibiotics, and an ideal safety profile. Chemical and biological methods coupled with advanced technological improvements are advantageous in advancing antimicrobial chemotherapy. Even though the development and production of effective antimicrobials are generally sluggish, several of these strategies have been studied for more than a decade.

One possible approach to the issue of antibiotic resistance is to **modify the structures** of already existing antibiotics. An antimicrobial agent that works well against Gram-positive bacteria is vancomycin. After nearly 60 years after discovering this antibiotic, vancomycin-resistant microorganisms have emerged.

Antibiotic combination therapy was also discovered to be an effective treatment. To increase the efficacy of the treatment, two or more drugs may be combined based on the susceptibility pattern of the infecting bacteria.

Adjuvants are additional compounds that could aid in boosting the activity of an antibiotic. Typically, these compounds do not kill microorganisms on their own. This **drug-adjuvant combination** approach helps delay the onset of resistance. Current medications are evaluated for their potential as adjuvants in order to find new antibiotic adjuvants. Numerous substances, including antihistamines, and inflammatory and hypotensive medications, were discovered to act against various bacteria.

Alternative to antibiotics, a newer way of combating antimicrobial resistance antibodies, lysins, vaccines, engineered phages, wildtype phages, probiotics and immune stimulation is already in clinical trials. In contrast, the antimicrobial peptides, host defense peptides, and antibiofilm peptides are in the preclinical phase. Bacteriophage, as an antibacterial agent to combat antibiotic-resistant microorganisms, is considered a possible step in overcoming antibiotic resistance.

Conclusion

Antibiotics are powerful drugs that are usually safe in treating microbial diseases in food-producing animals (FPA) for improving the health and welfare of animals. However, the indiscriminate use of antibiotics can lead to developing antibiotic resistance in animal microbiota. Due to the linkage between antibiotic use in FPA and the occurrence of antibiotic-resistant diseases in humans via the food chain, a reasonable strategy regarding the use of antibiotics under only veterinary supervision must be suggested and reinforced. By carefully regulating the food process parameters, the food chain could function as a "resistances' modulator" rather than an "AMR amplifier" to lower the occurrence of resistant microorganisms.

Good Agricultural Practices (GAP), Good Manufacturing Practices (GMP) and Good Hygiene Practices (GHP) must be implemented in livestock production and product manufacturing facilities to limit the spread of AMR pathogens.

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