One hundred years of success in antimicrobials: but what will the next 100 years bring?

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Summary

In the past 100 years, thanks to the discovery and development of antimicrobial therapies, human and veterinary medicine have made a leap forward in treating infectious diseases.

However, resistance mechanisms quickly appeared and spread in all sectors – human, animal and environment – throughout the world, thus jeopardising the progress made. Awareness has been raised only gradually but is now prominent at the global level, due in large part to the action of international organisations such as the World Organisation for Animal Health (WOAH), the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO), and antimicrobials are considered a global public health good to be preserved.

Under the leadership of WOAH in particular, the actions undertaken in research, surveillance, information, training, awareness and communication are moving in the right direction towards responsible and prudent use of antimicrobials.

In the next 100 years, the fight against antimicrobial resistance will undeniably remain a crucial challenge for public health, veterinary public health and agriculture. Concerted efforts and scientific innovations, such as in functional genomics and artificial intelligence, could offer solutions to mitigate the impact of this growing threat.

A multidisciplinary and comprehensive One Health approach is necessary to successfully address antimicrobial resistance. International collaboration remains crucial, and international organisations such as WOAH, WHO, FAO and the United Nations Environment Programme must continue their essential role in coordinating these efforts.

Keywords

Antimicrobial resistance – Antimicrobials – Artificial intelligence – Functional genomics – International collaboration – One Health – Quadripartite.

Introduction

Since their discovery nearly 100 years ago, antibiotics have revolutionised the field of medicine by enabling the effective treatment of bacterial infections. They have become essential drugs in both human and veterinary medicine, where they are used for curative or preventive purposes. However, this major advance has been accompanied by the growing challenge of antimicrobial resistance. Over time, bacteria have developed mechanisms to escape the effects of antimicrobial agents, and these bacteria are then transmitted through food or the environment to humans and animals, thus threatening the effectiveness of treatments. The therapeutic effectiveness of existing antimicrobial agents must be preserved as a common good for human and animal health, animal welfare and food safety.

This phenomenon constitutes a crucial issue for public health, animal health and ecosystem health. The fight against antimicrobial resistance has thus become a major challenge on a global scale, failure of which could lead to major health crises. A general holistic and global mobilisation must be put in place before it is too late. International organisations including the World Organisation for Animal Health (WOAH) have been committed to this for many years.

From the discovery of antimicrobial agents to the appearance of their resistance

In the 1920s, Alexander Fleming discovered penicillin, the first antibiotic, which effectively combated previously fatal infections. This paved the way for further research and the development of other antimicrobial agents over the following decades. Penicillin was used successfully during World War II to treat wounded soldiers, ushering in the era of antimicrobial agents and their significant use in both human and veterinary medicine.

Since the 1940s, research has led to the emergence of many other antibiotics, such as aminoglycosides, polymyxins, macrolides, streptomycin and tetracycline. Scientists have begun to understand the mechanisms of action of these drugs and to develop them further. Antimicrobial agents have become omnipresent in medicine and human and animal health.

As antimicrobial agents became more commonly used, the first signs of antimicrobial resistance appeared, as early as the 1930s. Bacteria began to develop mutations and other mechanisms that allowed them to survive antimicrobial treatments. Physicians and veterinarians were confronted with infections that were increasingly difficult to treat and had to resort to more powerful antimicrobials.

The 2000s were marked by growing awareness of the phenomenon of antimicrobial resistance and the importance of prudent use. Antimicrobial resistance has become a major global concern in this decade. Drug-resistant infections have become more common and more difficult to treat. The globalisation of exchanges of goods and people has accelerated this phenomenon, such that resistance genes for antimicrobials mainly used in China or India have been found in Europe. Experts have warned that, if concrete measures are not taken, there is a risk of returning to a pre-antimicrobial era in which common infections could once again be deadly. The health projections for 2050 are alarming, in terms of both the number of deaths and the economic impact.

Major efforts have been made to curb this ‘silent pandemic’. Faced with this threat, governments, health organisations, the pharmaceutical industry, physicians and veterinarians have worked together to encourage responsible and prudent use of antimicrobials, develop new drugs (vaccines, new active substances, etc.) and promote research into new methods of alternative treatment.

Educational campaigns have been launched to raise awareness of antimicrobial resistance among health professionals and the general public, and surveillance systems have been developed to monitor the evolution of the phenomenon.

Role of the World Organisation for Animal Health in combating antimicrobial resistance

WOAH has long played a crucial role in combating antimicrobial resistance as it relates to animal health. Since its creation in 1924, WOAH has implemented several types of actions to prevent and control animal diseases worldwide. When the problem of antimicrobial resistance became apparent, WOAH quickly rolled out health policies to combat antimicrobial resistance as it did for other animal diseases.

Standards and recommendations

In the late 1990s, WOAH worked on the development of standards to establish recommendations for the responsible and prudent use of antimicrobial agents in animals,

for risk analysis for antimicrobial resistance, for harmonised programmes for monitoring and surveillance of bacterial resistance, and for monitoring the quantities of antimicrobials used in animals. This included guidance on regulating the manufacture and use of veterinary medicinal products. These standards are subject to regular review in order to rapidly adapt to developments in science and knowledge.

Scientific expertise

In 2001, WOAH set up an *ad hoc* committee of international scientific experts to carry out targeted risk assessments for human and animal health on the development of antimicrobial resistance. The mission of this working group was to develop a list of antimicrobial agents of veterinary importance; that list, first published in 2007, is updated regularly and broken down to species level.

Monitoring and reporting

Based on established international recommendations and standards, WOAH has developed the necessary tools for collecting data relating to the use of antimicrobials in all of its Members. Since 2016, WOAH has published an annual report on the use of antimicrobial agents in animal health and has developed an interactive database, ANIMUSE, to facilitate access to data for everyone.

Collaborating Centres

WOAH has designated Collaborating Centres for veterinary medicine and antimicrobial resistance that provide scientific support and technical advice and participate in Focal Point training. They are also a source of support for Members wishing to improve their surveillance system or their means of combating antimicrobial resistance.

Training and awareness

Through its network of Focal Points for Veterinary Products, WOAH offers training programmes to promote its standards and recommendations. The subject of good practices in the use of antimicrobial agents and in resistance monitoring was on the programme of the first training cycle in 2010 and has been included in each subsequent cycle. Two global conferences were organised with the aim of raising awareness on issues related to antimicrobial resistance, providing scientific information and promoting international standards relating to stewardship of antimicrobial agents.

Communication

WOAH organises awareness campaigns to inform animal owners and animal health professionals about the risks of antimicrobial resistance and the best practices to follow. It provides its Members with communication tools and organises an annual week of events dedicated to the fight against antimicrobial resistance.

Support to Members of the World Organisation for Animal Health

WOAH provides support to its Members to help them implement standards and recommendations. Various programmes make it possible to provide support, such as through evaluations of Veterinary Services (the Performance of Veterinary Services tool), or to analyse the problems encountered in the application of standards (the Observatory). Donors play an essential role by funding countries' development of improvement programmes based on assessments carried out by international organisations. To this end, in 2004 WOAH developed the World Animal Health and Welfare Fund, a multi-donor trust fund.

Thus, from the start, WOAH has been aware of the extent of the problem of antimicrobial resistance and has mobilised its resources and tools to offer its Members and the global community an approach to control, as it does for major epizootics.

International collaboration

But above all, WOAH is committed to international collaboration. Since 2000, WOAH has worked with the World Health Organization (WHO) on antimicrobial resistance, and since 2007 it has collaborated closely with WHO and the Food and Agriculture Organization of the United Nations (FAO) within the framework of the Tripartite (FAO, WHO and WOAH) initiative to fight in particular against antimicrobial resistance. The United Nations Environment Programme joined this collaboration to form a Quadripartite with a One Health approach towards tackling the problem, which the United Nations recognised as a major global public health problem in 2016. For more than seven years, a global action programme has enabled better mobilisation of all countries on this major global public health issue. The fight against antimicrobial resistance is also one of six action points in the Joint Plan of Action of the Quadripartite.

What is the future of antimicrobials?

The prospect of the fight against antimicrobial resistance in the coming years is complex and full of challenges, but also full of opportunities. It must be versatile, multisectoral and global. Objectives and focuses include:

- **Ever more responsible and prudent use of antimicrobial agents**: Awareness of the importance of responsible and prudent use should continue to grow. Standards and guidelines to reduce unnecessary use of antimicrobial agents (such as use as growth promoters in animals) should be strengthened, with increased monitoring of international trade.
- **Development of new alternatives**: Research in the human and animal health sectors must focus on the development of alternatives to antimicrobial agents to fight infectious diseases. Research into and development of probiotics, prebiotics, bacteriophages, vaccines, autogenous vaccines and natural substances should be intensified. These alternatives could play a key role in preventing and treating infections while minimising the risk of resistance.
- **The evolution of veterinary medicine with better adapted treatments** thanks to advances in animal genomics, thus allowing more targeted antimicrobial treatments.
- **Rapid and accurate diagnostics** to help identify specific pathogens and choose the most effective treatments.
- **Improvement of antimicrobial resistance surveillance** with a focus on the environment, including wastewater monitoring.
- **New technologies**, such as artificial intelligence, biotechnology and nanotechnology, that could revolutionise the fight against antimicrobial resistance. New methods of detection, treatment and prevention could emerge from these areas. Innovation in research, technology and agricultural practices is expected to continue. New ideas and solutions could emerge, such as for wastewater treatment.
- **Strengthening the capacities** of developing countries to improve stewardship of antimicrobial agents. This will benefit everyone by supporting monitoring of antimicrobial resistance, implementation of prevention programmes, adoption of better regulation and increased training. International aid and partnerships between countries play a crucial role in a One Health approach.

- **Education and awareness** of the general public, animal health professionals and policy-makers. Such efforts remain crucial to maintain vigilance against antimicrobial resistance. Awareness campaigns should continue to highlight risks and best practices.

The fight against antimicrobial resistance will require a multidisciplinary approach, international collaboration and a combination of different actions. The One Health approach, which recognises the interconnection between human, animal and environmental health, must remain at the core of efforts to combat antimicrobial resistance. Although the challenges are significant, technological and scientific advances offer great potential to preserve the effectiveness of antimicrobial agents and promote long-term health of humans, animals and the environment.

Conclusions

The fight against antimicrobial resistance will continue to represent a major challenge in human, animal and environmental health. Further efforts to advocate for stewardship and prudent use are essential, as are increases in research, surveillance, information, training, awareness and communication. However, there are reasons for optimism, as concerted efforts and scientific innovations (such as functional genomics and artificial intelligence) could offer solutions to mitigate the impact of this growing threat.

A multidisciplinary and comprehensive global approach is necessary to address antimicrobial resistance. Countries need to exchange information, coordinate strategies and share surveillance data to monitor resistance and identify emerging trends. International bodies such as the Quadripartite must continue their essential role in coordinating these efforts.

Further resources

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