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Antibiotics: interplay between humans, animals and the environment is key

By Sabiha Essack

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Antibiotics have revolutionised health care since their introduction into clinical practice in the 1930s and 1940s by dramatically decreasing the morbidity and mortality associated with bacterial infections in humans and animals.

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Antibiotics have saved innumerable lives. They have also made possible major surgery, organ transplantation, treatment of pre-term babies, and cancer chemotherapy. They have advanced food security and food safety.

But infectious diseases remain the leading cause of death in the world. This is particularly in lower and middle income countries. Increasingly this is due to a rise in antibiotic resistance.

Antibiotic resistance has been recognised as a threat to the world economy. It affects developed and developing countries, which makes it a public health challenge with extensive health, economic and societal implications.

Antibiotic resistance is a direct consequence of the selection pressure from warranted and indiscriminate antibiotic use in human, animal and environmental health. Understanding how this happens is key to containing the problem.

How it happens

Resistance develops when bacteria no longer respond to antibiotics that were previously effective and cured infection.

This means that treatments no longer work for infections that are caused by microorganisms that have developed resistance. This is the case for both humans and animals. The increase in infections like this raises the risk of diseases spreading in communities as well as through flocks or herds.

Other outcomes are that illnesses last longer, mortality rates are higher and the cost of treatment goes up because alternatives need to be found.

The complexity and diversity of antibiotic resistance poses a further challenge. The complexity includes the fact that bacteria are becoming increasingly resistant to multiple antibiotics classes. And single isolates – or strains – exhibit multiple resistance mechanisms.

An added complexity is that resistance genes are carried on a myriad of mobile genetic elements. These are capable of exchange among – and between – bacteria in humans, animals and the environment.

What's in place

Efforts have been stepped up in recent years to manage the growth of resistance.

Three years ago the United Nations General Assembly signed a declaration on antimicrobial resistance. It also endorsed the World Health Assembly Resolution. This urged member states to have national action plans in place based on a global action plan agreed in 2017.

The plan was developed by a collaboration between the World Health Organisation, the United Nations Food and Agriculture Organisation and the World Organisation for Animal Health.

At the centre of the plan is what has been termed the One Health approach. This encourages interdisciplinary collaboration and communication on health at the human-animal-environmental interface. It's defined as

> *the collaborative effort of multiple disciplines – working locally, nationally and globally – to attain optimal health for people, animals and our environment.*

The Global Action Plan sets out five strategic objectives:

- to improve awareness and understanding of antimicrobial resistance;
- to strengthen knowledge through surveillance and research;
- to reduce the incidence of infection through infection prevention and control;
- to optimise the use of antimicrobial agents; and
- to ensure sustainable investment in countering antimicrobial resistance.

A range of countries have taken steps to implement the plan. For example, South Africa has published a framework in response to the plan.

People, food and animals

Antibiotic resistance exists in three interlocking sectors: human health, animal health and environmental health. It's therefore important to understand the relative importance of each sector in the evolution of resistant bacteria. It's also important to understand the genetic determinants of resistance, their interactions and transmission routes.

But the relative roles of the three sectors in the development, transmission and persistence of antibiotic resistant genes is poorly understood. Nevertheless, the knowledge gaps are beginning to be filled.

For example, there is a growing body of evidence that links antibiotic consumption in livestock to antibiotic resistance in the clinic. This can happen when antibiotics are used in low doses on animals over long periods. This creates optimal conditions for bacteria to entrench genes that confer resistance. These genes are subsequently transferred to human pathogens – or commensals – via people, contaminated food or the environment.

The area in which the burden of antibiotic resistance is least understood is environmental health. This is a problem for two reasons. The first is that environmental bacteria are the most prevalent. The second is that they serve as sources of resistance genes that can become incorporated into human and animal pathogens over time. This natural phenomenon is exacerbated by the influx of resistance genes from livestock and human waste into the environment. It's also made worse by other factors such as:

- the entry of antibiotic residues from pharmaceutical industries, and
- intensive livestock farming.

The world is waking up to the fact that antibiotic resistance is escalating in humans, animals and the environment. And that each sector presents antibiotic resistance reservoirs with the risk of spread within and between them.

To inform evidence-based strategies for its prevention and containment it's imperative that there's research into the nature, extent, mobility and consequences of antibiotic resistance.

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