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## RESEARCH ARTICLE

### COMBATTING ANTIMICROBIAL RESISTANCE; ETHICAL CONSIDERATIONS AND CONSEQUENCES

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#### ABSTRACT

The ongoing pandemic of COVID-19 has emphasized the interrelatedness of health, economics, and political governance. It has also highlighted the importance of anticipating and addressing threats proactively. Our actions or inactions have ramifications for global health. Antimicrobial resistance (AMR) is a threat motivated by a rational over-dependence on pharmaceutical intervention, the economics of satisfying it, and the politics of safely regulating use. Closely considering the moral obligations in the context of AMR remains vital for the ethical significance of AMR to be included more widely into policy making, practice guidelines and training programs to ensure the threat is eliminated. Here, we examine the ethical implications for AMR in the contexts of healthcare, economics, regulation, consumption and agriculture.

#### INTRODUCTION

The issue of AMR has received critical attention globally. A Global Action Plan (GAP) against AMR was adopted by the World Health Organization (WHO) in 2015, and subsequently in 2016, a political declaration of the high-level meeting of the General Assembly of the UN on antimicrobial resistance was made. Many national governments have also developed their own National Action Plans (NAPs) for combatting AMR. However, challenges remain in terms of availability of information about the global governance of AMR as it relates to the enormity of the problem and how effective and efficient national responses are (Wernli, 2017). Bringing this global challenge under control requires robust and unfettered cooperation and coordination among countries and across various spheres to include human and animal health, the environment, economic development, agriculture and trade. Antimicrobial resistance (AMR) development can be attributed to a wide range of factors ranging from over-prescription of antibiotics, non-adherence to antibiotic dosage, overuse of antibiotics in livestock and fish farming, poor infection prevention and control in health facilities, lack of new antibiotics, and ability of bacteria to acquire and transfer resistant genes (World Health Organization, 2020).

Tackling and reducing the development of AMR can be achieved through multiple approaches. These include, improved global public health awareness on AMR, reduction of unnecessary use of antimicrobials in agriculture and their release into the environment, improving sanitation and preventing the spread of infections in healthcare settings, and enhancing global surveillance of drug resistance and microbial consumption.<sup>3</sup> Controlling the use of antibiotics as much as possible to ensure efficacy is critical towards containing AMR. However, the global community has fallen short of ensuring adequate availability of antibiotics to many parts of the world. The use of Broad-spectrum antibiotics, such as quinolones, carbapenems and third-generation cephalosporins is reported to be below 20% of total antibiotics used in some countries vis-a-vis more than 50% in others.<sup>4</sup> In many of the places, over-the-counter sales of antibiotics have resulted in unregulated and uncontrolled sale and use of antibiotics. Broadly, a conundrum that the world currently faces is the need to ensure adequate access to antibiotics where there is insufficiency, but yet minimizing misuse in other parts of the world. Highlighting the key considerations of AMR for nations and the global health community becomes imperative in the midst of these ethical implications.

#### Key Considerations for AMR

**Mechanism of Antimicrobial Resistance:** Antimicrobial resistance generally acquired through four important mechanisms.

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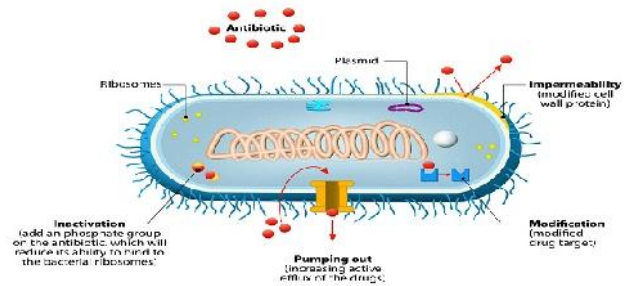
As illustrated below (Figure 1), these mechanisms are: reduced cell permeability, production of drug-inactivating enzymes, pumping out of drugs from the cell and modification of an existing target. Introduction of a new antimicrobial into clinical practice usually results in the development of resistant strains of bacteria that were initially susceptible. This has caused a significant reduction in the long-term therapeutic value of many antimicrobial drugs (Reygaert *et al.*, 2018). At the community level, *Enterobacteriaceae* such as *Salmonella spp.* and *Shigella spp.*, *Mycobacterium tuberculosis*, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria gonorrhoeae* are common organisms in which resistance is a serious problem, while Multi-resistant Gram-negative rods, methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *enterococci* are major culprits of resistance in the hospital setting. Prevalence of antibacterial resistance depends both on acquisition and spread. Hence, controlling indiscriminate use of antimicrobials should lessen the rate of acquisition and spread (Sefton, 2002).

**Healthcare and IPC Practices:** Institutions providing healthcare such as hospitals, clinics and nursing homes remain hotspots for the development of antibacterial resistance with rapid spread between patients easily occurring. It has been estimated that more than 70% of the bacteria causing hospital acquired infections caused by resistant strains of bacteria and 35–55% or more of these infections are preventable with proper IPC practices in place.

It is therefore critical to establish clear cut standards in facilities as per when and how antibiotics may be prescribed (Ministerie van Volksgezondheid, 2020), with oversight in place to offer feedback on individual implementation of IPC guidelines. Failure to take necessary actions and initiate interventions may result in dire consequences for treatment of acute bacterial infections and increased risk for medical procedures in which antibiotics are used. This raises serious moral issues in terms of failure to provide safe and secure medical care.

**Economic Burden:** Antimicrobial resistance (AMR) not only constitutes an enormous threat to global health, but it comes with immense economic burden to society. The fight to address AMR globally is being challenged by multiple economic factors ranging from market incentives that stimulate the development of novel antimicrobials and vaccines, to equipment for detecting and determining the need for antimicrobials for therapeutic use. Developing a new pharmaceutical product, including antibiotics use is very expensive with no guaranteed return on investment, and the drug development process is often stalled or left incomplete due to insufficient funding, particularly in its initial phases (International Monetary Fund, 2020). Meanwhile, in parallel to lack of investment in drug development, AMR is leading to growing cost to society. It has reported that by 2050, AMR will lead to 10 million deaths every year, costing the world up to \$100 trillion, with an accompanying reduction in Global Gross Domestic Product (GDP) of 2 to 3.5 percent (WHO, 2013). In a report commissioned by the UK government in 2015, it was suggested that failure to halt today's levels of infection and resistance rates would bring cumulative global economic losses of almost \$6 trillion over the next four decades<sup>7</sup>. Key reports such as these have indicated enhanced understanding of the consequences of non-intervention and its ethical undertone (Taylor, 2016).

## MECHANISMS OF ANTIMICROBIAL RESISTANCE



Source: 1985 - 2020 BioSpace.com.

**Unregulated sale and consumption:** Antimicrobials are reported to be the most commonly misused of all the drugs. This is particularly prevalent in developing countries, where the availability of antibiotics without prescription enables self-medication and provides a ready mechanism for the spread of antimicrobial resistance. Irrational medication use is related to systemic issues such as high frequency of expired medications and insufficient numbers of trained healthcare providers. In many cases, health facility dispensaries are also poorly maintained and personnel do not often consult the standard treatment guidelines and essential medicines list when prescribing (Ayukeybong, 2017). Controlling antibiotics use to ensure effectiveness in regulating over-the-counter sales of antibiotics remain critical and requires making difficult ethical choices that have implications on personal livelihoods and businesses.

**Agricultural use:** The use of antimicrobials in animals and food production remains important for the welfare of animals and the economic benefits for agriculture. Globally, agricultural antibiotic use likely exceeds human consumption with the absolute quantity of antibiotics used in animals being 4 times more than what is being used in humans (World Health Organization). This remains a major contributor to AMR development through its misuse especially as growth promoters in farm animals. Residues of antibiotics are passed on humans and thereby creating conditions for AMR development (Smith, 2019). Although the development of AMR through food can be curtailed by implementing good food safety management practices, fragility and fragmentation of food control systems and processes remain a challenge for many countries. Very often, the proper infrastructure, regulation framework and technical capabilities required to implement and regularly monitor the safety of food at national and sub-national levels are lacking. It therefore becomes imperative to develop robust and well-coordinated national food safety control systems which should include the proper governance and operational mechanisms tackle the global challenge of AMR. Additionally, striking a balance between antimicrobial use in agriculture and the potential for development of AMR in humans due to consumption of animal and animal products require serious ethical consideration.

## Conclusion

Antibiotic resistance gives rise to several ethical questions and management of these issues is complex. Across all spheres, ranging from healthcare to agriculture and trade, predicaments will surface and decisions made will have to be made so consciously, with due considerations to impending consequences.

Closely considering the moral obligations in the context of AMR remains vital for the ethical significance of AMR to be included more widely into policy making, practice guidelines and training programs. No time is like the present for such action. With a significant percentage of severe and hospitalized cases of Covid-19 being administered antibiotics, and an undetermined but likely vast number of people injudiciously self-administering antibiotics in attempts to protect themselves against the disease, Covid-19 may just be begetting another pandemic of a subtle but monumental proportion.

**Conflict of Interest Statement:** The authors declares that there are no conflicts of interest in this paper.

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