Commentary

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One Health Approach to Combat Antibiotic Resistance in Developing Countries

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INTRODUCTION

The global use of antibiotics is increasing, and the global annual consumption of antibiotics for the treatment of infectious diseases is estimated at 70 billion doses per year [1]. Since the discovery of the first antibiotic, penicillin, in 1926 by Alexander Fleming and other antibiotics discovered later, antimicrobial resistance (AMR) was discovered as an anticipated consequence [2]. Even before antibiotics were discovered, some scientists argued that AMR was an inevitable natural pathway [3]. On the other hand, according to records, since the discovery of the first antibiotic used to treat human infectious diseases, doctors' and veterinarians' abuse and misuse of antibiotics has also affected the rise of AMR [4]. Today, approximately 7 million people die worldwide due to AMR, and it is estimated that by 2050 nearly 10 million people with infectious diseases worldwide will die each year from infections caused by antimicrobial-resistant organisms [5,6]. As AMR rises globally, treating human, plant, and animal infections is difficult. AMR poses a threat to the progress of the healthcare system for the treatment of diseases in the entire ecosystem [7]. In the case of Uganda, infectious diseases account for a 50% morbidity and 50% mortality rate [8]. Infectious disease resistance to antimicrobials has also led to longer hospital stays, increased drug costs, and increased morbidity and mortality [9]. To address this burden of disease, the Ugandan National Academy of Sciences made an analysis, in 2015, on antimicrobial resistance and reported increased threats of AMR [8]. The reasons behind AMR have been debatable. Some scientists agree that AMR is due to the misuse and overuse of antimicrobials among physicians, veterinarians, and farmers, while others argue it's an inevitable natural consequence of antimicrobial use for the treatment and prevention of infectious diseases. This paper aims to show how AMR can be minimized through a multisector approach to improve health in developing countries.

Background

Antimicrobial resistance occurs when bacteria, fungi, and parasites adapt to antimicrobial drugs and stop responding [10]. AMR has been developing since the 20th century and is now a global health issue [4]. If no action is taken to curb AMR, it is estimated that global drug-resistant infections will increase, mostly in developing countries like Uganda, leading to extreme poverty [11].

In the case of Uganda, due to the lack of AMR monitoring data, researchers have observed AMR in the increase of infections. As time goes by, the effectiveness of antibacterial drugs is getting worse, and infections are becoming more difficult to treat [12]. A study conducted by the Uganda National Academy of Sciences reported that the country's antibiotic resistance in humans and animals was increasing [12]. Therefore, if no action is taken and it is not correctly done, preventable deaths will occur from previously treatable infections by antimicrobial drugs, and simple infections won't be treatable. This will increase morbidity, thus hindering the viability of the current health system, which will also affect global health, agricultural well-being, and our common environment [2]. However, it is important to properly identify the root cause of the rapid AMR rise and curb it to take adequate action.

The root cause of rapid AMR (Human - Animal - Environment)

Since the first use of antibiotics to treat humans, animals and plants, and the environment, AMR has been occurring. It is commonly attributed to the misuse and abuse of antimicrobial drugs [4]. It is empirical to ask ourselves how antibiotics, "the wonder drug" of all times, reached this point of causing a global threat. As seen in Figure 1, using antibiotics to treat humans, animals, and plants continue to play a role in the persistence of AMR by releasing antibiotics in the environment.

Regarding human health, antibiotics are considered the best treatment for communicable diseases, which gives a leeway to misuse antimicrobial medicine for all infectious diseases [12]. In Uganda, for example, most antibiotics are available over the counter (OTC) and are affordable [13]. So many people in the community can easily purchase them without bearing the cost of formal consultation with a doctor [14]. As the health system allows people to decide how and when to administer antibiotics to themselves, people tend to misuse them either by under-dosing, overdosing, or not finishing the course of the medication (poor adherence). Subsequently, all these excess antibiotics leave residues in the environment, contributing to AMR. Moreover, doctors over-prescribing antibiotics to heal patients promotes AMR. A study done in Ethiopia to evaluate the knowledge and perception among physicians and nurses concluded that there's a vast knowledge gap among healthcare providers about AMR, which explains the complacent behaviors in their use of antibiotics [15].

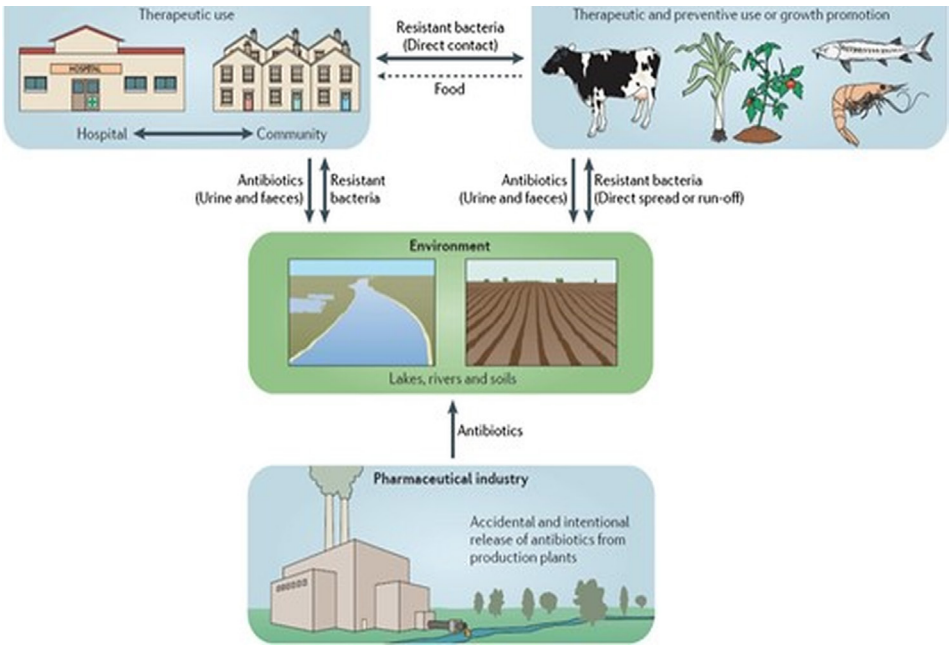

Figure 1: *An integrated ecosystem of the dissemination of AMR shows the critical need for a One Health approach to the issue (Adapted from D. I. Andersson and D. Hughes, 'Microbiological effects of sublethal levels of antibiotics', Nature Reviews Microbiology, vol. 12, no. 7, pp. 465–478, 2014, doi: 10.1038/nrmicro3270*

On the other hand, animal husbandry, plant production, and aquaculture are prominent areas that use antibiotics for therapeutic purposes. In these sectors, the misuse of antibiotics has also been identified. A study conducted in Rwanda showed that approximately 97% of farmers inappropriately use antibiotics in their livestock to prevent disease and promote growth while knowing almost nothing about antibiotics or AMR [16]. This practice of farmers in food production also leads to antibiotic residues in human food and the environment.

Lastly, pharmaceutical factories accidentally release antibiotics waste into the environment (Figure 1). As they release them into water bodies and through the vapors, antibiotics residues further accumulate in the environment.

As antibiotics accumulate in the environment, the environment becomes a reservoir for antibiotic-resistant genes [17]. In both soil and water, bacteria adapt to the antibiotic residue, and over time, these antibiotics are rendered ineffective to the now-adapted bacteria. Eventually, these bacteria are reintroduced into the food chain as animals, plants, and humans rely on the affected water and soil. Then, as a response, more and stronger antibiotics are needed to combat these new infections. Still, these new antibiotics also end up being misused and, in return, further contribute to AMR.

The cycle of AMR clearly shows the interrelationship between humans, animals, and the environment when it comes to antimicrobial drugs. Therefore, when dealing with AMR challenges, each of these three sectors must be considered: human health, animal health, and the environment.

One Health Strategy to Combat AMR

To address AMR globally, the WHO understood that the antimicrobials used in humans are the same as those used in animals and plants; therefore, AMR affects the whole ecosystem globally as migration from one country to the other has become easier with modernization. Thus, a One Health approach was incorporated into the fight against antimicrobial resistance. The One Health approach comes in handy because the multi-sectoral and interdisciplinary approach will allow all sectors involved and other relevant stakeholders to conduct a deeper analysis of the problem under one umbrella and then develop a common solution.

Hence, the World Health Organization (WHO), the World Organization for Animal Health (OIE), and the Food and Agriculture Organization (FAO) have joined forces to combat antimicrobial resistance globally. One of the commitments of WHO/OIE/FAO is to support countries in formulating policies on the appropriate use of antibiotics, establishing institutional and regulatory frameworks and networks, and promoting infection and prevention and control to reduce the use of antibiotics [19].

In addition, WHO/OIE/FAO created the AMR Multi-Partner Trust Fund to curb AMR, expand investment and reduce any financial bottlenecks that hinder the progress of health-oriented AMR national action plans in developing countries [20]. This further proves that the One Health approach was the missing key in the fight against AMR in developing countries.

Counterargument

Some scholars have challenged the use of a One Health approach to minimize antimicrobial resistance. They also questioned the misuse and overuse of antimicrobials by humans and animals as the only absolute cause of AMR. The argument stems from certain authors' emphasis on antimicrobial resistance as an inevitable natural pathway, and new antibiotic drugs are needed to combat AMR [21]. To support this statement, they explain AMR using two different mechanisms: The intrinsic bacterial mechanism, by which bacteria are naturally resistant to an antimicrobial drug, and acquired resistance, where bacteria adapt themselves and resist antimicrobials [21]. With this understanding, some scientists and leaders advocate for novel technologies and stronger arsenals of antibiotics to curb AMR.

Conclusion

AMR in developing countries and globally is on the rise as consumption of antimicrobials increases in human health, animal, plants, and the environment. AMR affects all sectors of the ecosystem. Therefore, it is in our best interest globally to put aside the silos of health and gather under the same umbrella of health to tackle the health threat at hand. As pharmaceutical companies are committed to launching new and stronger antibiotics, all relevant stakeholders should work

to alleviate the problem of antibiotic resistance to improve people's health in developing countries. AMR is a multisector problem that needs a multisector solution.

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