IJID Regions 9 (2023) 102–103

Contents lists available at ScienceDirect

IJID Regions

journal homepage: www.elsevier.com/locate/ijregi

Editorial

Antimicrobial resistance – A global problem in need of global solutions☆

Antimicrobial resistance (AMR) has been declared one of the 10 global public health threats facing humanity by the World Health Organization. A review commissioned by the government of the United Kingdom found that by 2050 more people would die from infections with multidrug-resistant bacteria or pan-resistant bacteria than from cancer and the annual cost would at that time reach 1 trillion USD [1,2].

The AMR problem is manifold and needs political action on many levels. It is a One Health issue that has been driven by the selective pressure exerted by excessive use of antimicrobials in human and veterinary medicine and in agriculture that involves plants, livestock, poultry, fish, shellfish and other aquatic animals, alongside the concomitant contamination of the environment with antimicrobial drugs, antimicrobial resistant bacteria, and antimicrobial resistance genes [3].

Antimicrobial resistance has been accompanied by insufficient education at all levels on antimicrobial use and its consequences. Promotion of prudent and appropriate use of antimicrobial drugs needs to be accompanied by surveillance systems of antimicrobial use and resistance in humans, animals, and plants, regulatory controls and enforcement [4]. Guidelines on antimicrobial use in humans, animals, and plants must be readily available and periodically updated in line with changes in antimicrobial susceptibility.

Antimicrobials should only be available for human and veterinary medicine by prescription to prevent their misuse for non-therapeutic purposes. "Over the counter" access to antimicrobials, that is, their sale without prescription, in human and veterinary medicine, as well as in plant/animal agriculture, must be regulated and enforced. However, patients and farmers, especially in remote locations or in resource-poor settings, often do not have ready access to individuals with expertize on appropriate antimicrobial use. Innovative solutions to expand access to expert advice in those situations are required.

The unrestricted use of "prophylactic" antimicrobials in healthy poultry, livestock, fish, and other aquatic animals, often also used for "growth enhancement," must be addressed [5]. Intensive animal husbandry (called factory farming) is increasing worldwide. Overcrowding and other unhealthy conditions characteristic of intensive animal husbandry create conditions that promote transmission of infectious agents. To prevent infectious disease outbreaks on these factory farms, antimicrobials are routinely administered in feed or water to an entire group of animals, including the healthy animals. Proper biosecurity measures and improved farm management practices should be established, especially for intensive animal husbandry, to reduce the need for antimicrobials [6].

Feces from animals that are fed antimicrobials is frequently applied to agricultural lands as fertilizer, leading to ‘’enrichment" of soil with antimicrobials, multidrug-resistant bacteria, and antimicrobial resistance genes. The consequent antimicrobial-induced alterations in the plant microbiome can have a significant impact on plant health. Waterways become contaminated from run-off from fertilized farms. Humans may then be exposed to antimicrobials, multidrug-resistant bacteria and resistance genes through exposure to contaminated plants, animal products, or waterways.

Similar to environmental contamination as a result of run-off from livestock, poultry and aquatic animal farms, the inadequate management of pharmaceutical wastes at the sites of production have been identified as important sources of environmental contamination in both low/ middle-income countries (LMICs) and high-income countries [7]. In addition, wastewater from healthcare facilities contains a complex mixture of contaminants, including pharmaceutically active compounds, microorganisms including antimicrobial-resistant bacteria, and antimicrobial-resistance genes, which may survive wastewater treatment. Contamination of waterways has been documented worldwide [8,9]. Release of these contaminants into the aquatic ecosystem from hospitals, pharmaceutical facilities and farms into soil and waterways imposes a significant threat to the environment, which needs to be monitored from all these sources to assess effectiveness of the corrective measures [10].

Because antimicrobial resistance endangers human, veterinary, and plant health worldwide, many people have an interest in mitigating the loss of efficacy of antimicrobial drugs. These stakeholders include physicians, nurses, and veterinarians who prescribe antimicrobial drugs for their patients, pharmacists, pharmaceutical companies, pharmaceutical distributors, plant/animal farmers and others in the agricultural industry, policymakers and drug regulators. All these groups contribute in various ways to the overuse and misuse of antimicrobial drugs and all need to become antimicrobial stewards [11]. Patients themselves must become antimicrobial stewards, because they may pressure healthcare providers for antimicrobial prescriptions or readily self-medicate with antimicrobial drugs obtained without prescription in many localities worldwide.

Antimicrobial stewardship programs are one of the major strategies for promotion of responsible use of antimicrobials. Antimicrobial stew-

☆ This paper is being jointly published by International Journal of Infectious Diseases, IJID Regions and IJID One Health by Elsevier Inc. The articles are identical except for minor stylistic and spelling differences in keeping with each journal's style. Either citation can be used when citing this article.

https://doi.org/10.1016/j.ijregi.2023.10.005

ardship should have a high priority in pre- and post-graduate teaching of physicians and veterinarians [12,13]. Their development for farmers in plant/animal agriculture, is also critical. Antimicrobial stewardship programs should include electronic surveillance of antimicrobial use patterns to identify those with excessive and inappropriate use and analysis of the cause [14].

Antimicrobial resistance is also spreading through international mobility of people and animals [15]. This is in particular the case for travelers who took an antimicrobial drug while abroad or for patients repatriated after a hospital stay abroad [16–18]. Even healthy travelers from low AMR countries to high AMR endemic countries harbor intestinal AMR after returning home, demonstrating that AMR is spreading by travels, and the spread probably is proportional to the number of travelers [19]. This was what happened when the NDM-1, the New Delhi metallo-β-lactamase 1, was discovered in the United Kingdom and linked to travelers from India [20]. Appropriate infection control procedures should be considered when hospitalizing patients with a history of recent travel (within the past 12 months) to high AMR endemic regions. Consideration should also be given to the selection of antimicrobial therapy in such patients at high risk for a drug-resistant pathogen who require empiric antimicrobial therapy for a severe infection.

Research and development around new antimicrobials to counteract multidrug-resistant infections is expensive and these new agents are beyond the reach of patients and health programs in most LMICS. They should not take the place of strengthening antimicrobial stewardship programs and infection control and prevention policies and practices. The use of diagnostic laboratory testing needs to be encouraged to guide best antimicrobial practices and surveillance. Vaccines are an important tool in the AMR battle by reducing the overall burden of infections caused by both susceptible and resistant organisms and antimicrobial usage [21].

AMR is a global problem in need of local/regional strategies, coordinated approaches for global solutions and interventions with One-health perspective. This is a call for more action and to take collective responsibility for responding to the global AMR threat, before it is too late.

Declaration of Competing Interest

All authors declare no conflicts of interest.

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