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CONTROLLING ANTIBIOTIC RESISTANCE THROUGH THE ONE HEALTH APPROACH

Antimicrobial Resistance: Fundamental Basis and Issues with Control

Li Yang HSU (for ReACT)

Antimicrobial resistance is the most evident manifestation of bacterial evolution. The mechanisms of resistance are ancient and many were probably selected out millions of years ago – bacteria from the Lechuguilla cave being the case in point, with resistance to multiple different modern antibiotics despite the bacteria being isolated for almost 4 million years [1]. Soon after the development of penicillin, Alexander Fleming noted that formerly susceptible bacteria could develop resistance to the compound in the petri dish, and gave one of the earliest warnings of its implications during his Nobel lecture [2]. However, the development and proliferation of multiple classes of antibiotics in the subsequent 3 decades, coupled with the excellent safety profiles of most antibiotics, resulted in lax human antibiotic prescribing standards and significant inappropriate antibiotic prescription in many parts of the world [3]. In the 1950s, the use of sub-therapeutic quantities of antibiotics was found to enhance the feed-to-weight ratio of food animals, and the practice of using antibiotics as growth promoters quickly escalated globally [4]. In the past two decades, there is accumulating evidence linking levels of human antibiotic prescription to resistance [5,6], and also nontherapeutic use in animals to antimicrobial resistance in pathogenic human bacteria [4]. Coupled with a dramatic decline in the development of novel antibiotics [7], a paradigm shift framing antibiotics as precious and potentially finite rather than limitless resources was inevitable.

The negative impact of antimicrobial resistance in humans is enormous, resulting in increased healthcare costs, higher mortality and morbidity, and productivity losses [3,4,8]. Multiple professional and civic organizations, including the World Health Organization, have put forward position papers and recommendations on how to preserve the beneficial impact of antibiotics [8]. Superficially, the way forward is clear – the recommendations are largely similar and can be broadly classified as follows:

1. More transparent, better and global surveillance of antimicrobial usage and resistance.
2. Improving the “antibiotic pipeline” – facilitating and increasing the development of novel classes of antibiotics.
3. Improving the appropriate prescription of antibiotics in both humans and animals – including reducing the use of antibiotics as growth promoters in animal husbandry and aquaculture.

4. Better infection control practices and regulation to limit the spread of antimicrobial-resistant pathogens within institutions and cross-borders, and also in animal husbandry.
5. Better education at all levels on the issues of antimicrobial resistance.

Nonetheless, progress on the control of antimicrobial resistance has been slow, and it is perhaps apt that the issue of antimicrobial resistance in recent times is increasingly being re-framed as a wicked problem. The term 'wicked problem' was originally used to describe social issues that are complex, ill defined and subject to multiple interpretations, and are virtually impossible to completely solve – "solutions" often result in making things better (or worse), the implementation of which frequently results in trade-offs and unanticipated complications [9]. Antimicrobial resistance – embedded within the complexity and scale of human and animal medicine and interactions – can no longer be viewed as a purely scientific puzzle to be overcome, but involves sociopolitical and cultural initiatives in order for progress to be made. And given the evolutionary capability of bacteria, the issue can perhaps never be completely resolved.

In the hospital setting, particularly public hospitals in less developed countries and Asia, the high patient-to-healthcare staff ratio and high hospital occupancy results in difficulties in improving compliance to infection control practices, including basic hand hygiene and isolation/cohorting of patients infected or colonized by antimicrobial-resistant bacteria. The drive for medical tourism dollars has as an indirect consequence enhanced the spread of multidrug-resistant bacteria such as the carbapenem-resistant Enterobacteriaceae [10]. Advances in medical care especially in the areas of transplantation and cancer chemotherapy have resulted in a steadily growing cohort of severely immunocompromised patients where broad-spectrum antibiotics are routinely prescribed at the first sign of infection – practices that are endorsed by professional guidelines [11]. Attempts at antimicrobial stewardship in the hospital setting not infrequently result in conflict with physicians whose perspective is in providing 'best' care for their patients, and who view antimicrobial stewardship as an encroachment on their right to prescribe [2]. In each of the abovementioned examples, competing priorities render it difficult to implement practices that can effectively bring down antimicrobial resistance rates in many institutions worldwide.

Similarly, in the case of animal husbandry and aquaculture, competing priorities and razor-thin profit margins in some cases are deterrents against stopping the practice of antibiotics as growth promoters or even withholding mass antibiotic treatment at the appearance of the first ill animal or fish [4,8]. The significance of antimicrobial resistance in animal bacteria with respect to human health is also repeatedly challenged despite the accumulated evidence [4]. The World Health Organization had comprehensively highlighted major gaps and challenges in the control of antimicrobial resistance globally, including the lack of comprehensive multidisciplinary strategies, lack of adequate regulatory frameworks, insufficient awareness and education at all levels, and the presence of incentives that encourage abuse of antibiotics [8].

Seen in the perspective of a wicked problem, how and whether antimicrobial resistance can eventually be brought under control appears unclear. Nonetheless, it is important to note the major advancements and improvements made (and that continue to be made) with other issues listed as wicked problems, including gender inequality, poverty, ethnic inequality, etc. From this perspective, any improvement is good, and continued progress better. Taking a 'One Health' approach to antimicrobial resistance in order to try to align all concerns and interests, gaining political will and commitment for the right regulatory and cross-border cooperative frameworks, education at all levels – including framing the issue in ways that people will care about, are all logical and necessary steps. Encouragement of action at all levels along with greater collection and transparency of data – while messy – is an approach that has also worked well with other issues of similar or greater complexity.

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