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Time to tackle AMR together

As resistance against antimicrobials continues to grow, collective action must be taken to turn the tide against this global public-health concern.

November marks World AMR Awareness Week (18–24 November) and this year's theme, a continuation from 2022, is "Preventing antimicrobial resistance together". Antimicrobial resistance (AMR) has been recognized as a growing threat for many years, and while there have been numerous calls for action, research into the increasing burden of AMR and breakthroughs in the development of new antimicrobials, the overall impact on this sizeable problem has been negligible. The European Centre for Disease Prevention and Control (ECDC) reported that annual deaths attributable to bacterial AMR in the European Union and European Economic Area increased over a three-year period — from an average of 30,730 deaths in 2016 to 38,710 deaths in 2019 (ref. 1). A study published in *The Lancet* reported that bacterial AMR was associated with an estimated 4.95 million deaths worldwide in 2019, with 1.27 million deaths being a direct result of bacterial AMR[2]. These worrying statistics are likely to be underestimated considering the increasing burden of fungal, viral and parasitic AMR for which effective antimicrobials are limited. Those living in lower- and middle-income countries are disproportionately affected by AMR, and infants and older individuals are most at risk of nosocomial infections by resistant pathogens. Urgent and concrete action is clearly needed and we must work together to successfully tackle AMR.

When we think of AMR, hospital-associated infections by antibiotic-resistant bacteria typically come to mind. Indeed, the ECDC reported that methicillin-resistant *Staphylococcus aureus* (MRSA) and third-generation cephalosporin-resistant *Escherichia coli* and *Klebsiella pneumoniae* were responsible for the largest burden of disease between 2016 and 2020 (ref. 1). A previously unappreciated threat to AMR comes in the form of biocides, such as disinfectants and antiseptics that are routinely used in clinical settings. In this issue of *Nature Microbiology*, Li et al. show that clinically relevant biocides can target multiple genes in the multidrug-resistant pathogen *Acinetobacter baumannii*, resulting in altered membrane potential and promotion of antibiotic tolerance. The use of biocides is largely unregulated and this study adds further support for biocide stewardship alongside that of antimicrobials.

Beyond clinical settings, antimicrobials are increasingly used in livestock and agricultural practices, thus creating further risk to health and food security. Several surveillance studies have alerted to the growing burden of AMR across farms worldwide[3,4]. One study detected antibiotic resistance genes (ARGs) across ten large-scale poultry farms and four linked abattoirs in China. These ARGs were potentially mobile and associated with clinically relevant bacteria, indicating a risk of bacterial AMR transmission to humans[3]. Importantly, this study linked ARG presence to temperature and humidity, raising further concerns in light of the growing threat of climate change. Other studies have reported sharing of microbes and resistomes (the pool of resistance determinants encoded by a microbiome) between food animals, domestic animals, wildlife and humans[5,6]. These transmission events pose an important risk to One Health, so action must extend beyond clinical settings for there to be tangible results. This risk is likely to worsen in the face of other global crises, including climate change, conflict and displacement.

Parasitic, viral and fungal pathogens are also developing resistance against a relatively limited pool of antimicrobials. While artemisinin remains effective against most *Plasmodium falciparum* infections, the causative agent of malaria, resistance is emerging and is accompanied by mutations that render diagnostics ineffective[7]. Historically neglected by the press, the public and funding bodies[8], fungal pathogens have become a priority in the wake of COVID-19-associated fungal infections causing a number of unprecedented cases and deaths and the emergence of the multidrug-resistant pathogen *Candida auris*[9]. The World Health Organization (WHO) launched its fungal priority pathogens list[10] at the end of 2022 to give these microbes overdue recognition as threats to human, animal and ecosystem health. Widespread use of broad-spectrum fungicides in agriculture has compounded the issue of antifungal resistance, again highlighting the key link between AMR and One Health.

The future of AMR may seem bleak but there is hope. The WHO recently announced its global research agenda[11] for AMR in human health comprising 40 research priorities across prevention, diagnosis and treatment, with a special focus on drug-resistant tuberculosis. This agenda will put a spotlight on areas that require the most attention, such as the implementation and assessment of water, sanitation and hygiene (WASH) practices, vaccine development, rapid point-of-care diagnostics, antimicrobial stewardship and improved surveillance, as well as ensuring that these strategies are effective, affordable and can be integrated into national policies. Meanwhile, governments and funding bodies are also realizing the urgency of the situation. The UK government has pledged £210 million of funding to support AMR surveillance by the Fleming Fund. This project aims to invest in sequencing capacity, training and systems to enable better surveillance of AMR across 25 lower- and middle-income countries where the burden is most acute. Additionally, antimicrobial development is advancing. For years, there has been very little in the way of new antifungals, but several new drugs are undergoing clinical trials or have been approved by regulatory bodies to treat invasive fungal diseases, for example the use of intravenous rezafungin for invasive candidiasis when treatment options are limited. Research groups are turning to alternative sources, such as nematode symbionts and soil bacteria, to mine new antibiotics that are effective against important bacterial pathogens[12,13]. Whether these new antibiotics will reach the clinic is unclear, but the existence of accelerators such as CARB-X can provide funding and support to help translate preclinical research to clinical trials. These developments spark optimism but to ensure that these targets come to fruition and have impact, stakeholders must work together.

So what else can we do? Improved surveillance, new drugs and prioritizing research are certainly key to tackling AMR, but this cannot overcome the problem of AMR unless we preserve the effectiveness of current and future antimicrobials. In this issue, Jimmy Nkaiwuatei, the Head of Research, Discovery

and Innovations at Students Against Superbugs Africa, writes about how education and outreach can promote effective antimicrobial stewardship and stop AMR in its tracks. Growing up in Kenya, Nkaiwuatei noticed behaviours that were contributing to the AMR crisis — sharing of antibiotics, unfinished treatment courses and inappropriate dispensing, as well as poor WASH practices. As a result, he instigated a programme of AMR educational workshops with a group of students that now includes collaborations with healthcare professionals and AMR leaders across 11 African countries. We hope that this Turning Point article will inspire other scientists to become AMR leaders in their communities.

AMR is a complex, multifaceted issue that requires action at all levels. Collaboration between sectors such as basic research, healthcare and agriculture is essential, as is support from funders, policymakers and educators. AMR poses a threat to all of us and we must work together to stop it.

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