

COMMENT

SCIENCE-FICTION A look at H. G. Wells's contributions to science — and *Nature* p.162

TELEVISION *Star Trek*'s science legacy, 50 years after the first episode p.165



TERMINOLOGY Spiders don't sting; they bite. What's the difference? p.167

OBITUARY Ahmed Zewail, Nobel-winning chemist, remembered p.168

STRAPP/GETTY



Antibiotic use in livestock has contributed to drug resistance around the world.

Use antimicrobials wisely

The United Nations must reframe action on antimicrobial resistance as the defence of a common resource, argue **Peter S. Jørgensen, Didier Wernli** and colleagues.

The effectiveness of antibiotics has been waning since they were introduced into modern medicine more than 70 years ago. Today, our inability to treat infections ranks alongside climate change as a global threat^{1,2}. New classes of antimicrobial drugs are unlikely to become widely available any time soon¹; if and when they do, bacteria, viruses and other microbes will again evolve resistance³. In

any case, waging war on microbes is not tenable³ — our bodies and planet depend on them⁴ (see Supplementary Information; go.nature.com/2c03p6n).

Addressing resistance requires global collective action. Like the ozone layer, a stable climate or biodiversity, the global population of susceptible microbes is a common pool resource — one shared by all. But no individual or country has a strong enough

incentive to conserve this 'commons'. It has been depleted by the massive use of antimicrobial compounds and the growing competitive advantage of resistant microbes. It is a classic 'tragedy of the commons'.

This intimate relationship with microorganisms predates modern humans. It is the result of many millions of years of co-evolution. Our bodies need particular kinds of microbes for digestion, immune ►

► function and general health. Equally, microbes support planetary health, for example, through nutrient cycles, including those that maintain soil and water quality⁴. In other words, microbes sustain human civilization. Yet our understanding of the complex interactions and uncertainties that govern the relationships between humans and microbes is limited.

The 2015 *Global Action Plan on Antimicrobial Resistance*, drafted by the World Health Organization (WHO) with support from the United Nations Food and Agricultural Organization (FAO) and the World Organisation for Animal Health (OIE), recognizes the need for multisectoral cooperation to address resistance (see go.nature.com/2bbijap). But, in our view, it does not go far enough in recognizing the life support we receive from the global microbiome. Tackling resistance urgently requires the scaling back of the massive overuse of antibiotics to secure the liveability of Earth in the long term.

On 21 September, heads of state will meet to take further action at the United Nations high-level meeting on antimicrobial resistance in New York City. A UN declaration currently under discussion must set global targets, accelerate implementation of the global action plan, plug its gaps and ensure stronger accountability and interagency coordination. It must emphasize the many benefits of microbes.

Parties should aim to build the resilience of society and the microbiome. In our opinion, this is the way to maintain low levels of resistance amid the many surprises of a rapidly changing planet. Advances from studying resilience in other common pool resources such as fisheries and forests⁵ suggest key steps for antimicrobial resistance, which we set out below. Achieving these will require changes to institutions, regulations, education, community norms and expectations, notably in medicine and agriculture.

EDUCATE TO LEARN

Until now, political and financial investments have focused largely on creating incentives to fuel drug innovation and new or faster diagnostics. Currently, such technological fixes appeal to and benefit mainly rich nations in the 'global north'. Incentives must be targeted to benefit not only large pharmaceutical companies in the north, but also to enlist research and development efforts globally. One of the most important outcomes of the UN meeting should be national commitments to the broadest and most creative participatory education campaigns about resistance² and the importance of the microbial world.

Why? Because the level of ignorance about the calamity that is antimicrobial resistance is staggering. A 2015 WHO survey across 12 countries found that 64% of the



Limited access to quality antimicrobials in the developing world drives unregulated sales.

public think that antibiotics also work for, for instance, viral infections such as influenza and colds (see go.nature.com/2c7zvf). Such basic knowledge gaps lead patients and physicians to reach for antibiotics without appreciating the costs.

Instead, institutions and citizens must understand the central facts, context and risks in a way that allows them to learn more independently. This goal requires awareness campaigns to be revised and scaled up by orders of magnitude², as well as investment in new communication tools. Initiated in 2007, Thailand's Antibiotics Smart Use project sets a direction for upscaling. It enables patients in pharmacies to self-diagnose on the basis of the appearance of their sore throat to verify whether they need antibiotic treatment⁶. For further learning, citizen-science programmes in which participants monitor their own microbiomes should be extended to cover, for example, self-testing for resistance in various parts of the body⁷.

Such campaigns could engage communities and change norms about how and when to use antibiotics. Campaigns will need to be coordinated internationally for quality and impact, and adapted to suit

regional perspectives. Engagement can be spread through schools, mass media and social media.

JOIN UP

Resistance affects animal and environmental health as well as human health, and so requires coordinated action across economic sectors. No single concern exemplifies this better than the high rate of antibiotic use in agriculture (largely as growth promoters or disease prevention). In the United States, 70–80% of all antimicrobials consumed are given to livestock; agricultural use in the BRICS emerging economies (Brazil, Russia, India, China and South Africa) is expected to double by 2030, as compared to 2010 levels⁸ (see 'Farm forecast'). As a result, antibiotics and resistance genes enter the food chain, soil and the water table, threatening human health.

The European Union has phased out the use of medically important antibiotics for growth promotion in agriculture. Other countries, including Mexico and Taiwan⁹, have sought to reduce it. In the United States, a directive discourages the use of antibiotics for growth promotion through voluntary measures and stronger veterinary oversight

of therapeutic use. However, the powerful industrial farming lobby and a lack of perceived urgency have so far stalled stronger mandates.

Stronger political action to change how we use antibiotics, whether by humans or animals, requires citizens to be better informed. For instance, the public should have online access to surveillance that tracks how human resistance increases in settlements near farms. In the meantime, consumer groups play a crucial part by calling on retail chains to switch where their meat is sourced. For example, US food chains Chipotle, McDonald's and Chick-fil-A have responded (to varying degrees) to public demands with stricter limits on antibiotic use in the meat they sell.

A particularly worrying issue that is not confined to the use of antimicrobials in food production is the international spread of resistance genes, especially those conferring resistance to many drugs of 'last resort'. Most recently, a mobile plasmid gene carrying resistance to the last-resort antibiotic colistin has been found in Asia, Europe and North America. Clearly, countries cannot act alone to deal with the problem without jeopardizing the benefits of globalization.

Much better surveillance and containment is needed of the most dangerous multiresistant strains in people and food². A global routine-surveillance initiative could help to prevent the spread of resistance. It could screen medical tourists or patients returning from hospitals abroad to identify carriers of multiple resistant strains. Hospitals that are centres of international travel for medical treatment must lead the way; funding and learning mechanisms must be increased for other hospitals to follow suit.

The International Health Regulations, revised by WHO member states in 2005, are a legally binding instrument that aims to provide global surveillance and response. Properly financed, they could be effective¹⁰. Yet the resources needed to respond to emerging diseases do not flow commensurately to low- and middle-income countries as they do in the global north — a key lesson of the recent Ebola outbreak. All governments have a collective responsibility to improve capacities for rapid response to resistance. Greater support by donor countries to new and existing funding mechanisms such as the Global Fund to Fight AIDS, Tuberculosis and Malaria is needed in low- and middle-income countries.

EXTEND COALITIONS

International and national coalitions must be broadened. The global action plan strengthens the established collaboration between the WHO, FAO and OIE. This should be extended to cover other relevant sectors, including trade, development and environment. The model set up by UNAIDS (the Joint

United Nations Programme on HIV/AIDS) in 1996 serves as an example of how to intensify collaboration, leverage resources, involve more parties and reduce barriers.

The UN meeting must commit to driving learning between institutions. Global platforms are needed for sharing best practices and the latest data about resistance levels and antibiotic consumption, for instance, among national agencies. Such exchange happens in Europe for resistant human bloodstream infections, and human and veterinary antimicrobial consumption. This must be scaled up to monitor resistance in communities, food industry and the environment. A relevant model for exchange at the global level is the WHO's Pandemic Influenza Preparedness Framework. To engage the public effectively, more-frequent updating, vivid visualizations and engaging communications are needed.

As in the Paris climate agreement, countries should submit to the UN voluntary but monitored targets on limiting resistance. Parties may go further by making shortfalls subject to potential sanctions. A key priority is to establish measurable indicators at the country level, such as the median yearly consumption of antibiotics per person.

As for the climate issue, non-state actors from business to civil society can be central to societal transformations. Such stakeholders were consulted during the development of the WHO global action plan. But their participation in the long run must become more integral to the global coalition responsible for tackling resistance.

Available governance instruments range from binding treaties to guidelines, with each approach having pros and cons. A first step to holding companies accountable would be an international code on

the promotion of antibiotics (promotional spending in the United States in 1998 amounted to US\$1.6 billion), akin to that adopted by the WHO in 1981 on the marketing of breast-milk substitutes.

ACT NOW

The complexity and gravity of resistance call for the immediate mass mobilization of society. Maintaining the susceptibility of microbes to drugs for global health is a matter of sustainable development. Improving understanding about humankind's dependence on the global microbiome should lead to action on many other important issues

“Building global resilience to resistance is a long game.”

involving micro-organisms. These issues include infectious diseases, food security, natural resources and

environmental conservation. Action here could, in turn, lead to more-equitable forms of national progress across the sustainable-development goals³.

Building global resilience to resistance is a long game. But changes can be surprisingly fast when the time is ripe and a plan is ready. This month's UN high-level meeting is a rare opportunity for global collective action on human interactions with microbes. It must protect both the lifesaving power of antibiotics and the ability to use them when necessary. ■

Peter S. Jørgensen is a researcher at the *Global Economic Dynamics and the Biosphere, Royal Swedish Academy of Sciences, Stockholm, Sweden*. **Didier Wernli** is a senior research associate at the *Global Studies Institute, University of Geneva, Geneva, Switzerland*. **Scott P. Carroll, Robert R. Dunn, Stephan Harbarth, Simon A. Levin, Anthony D. So, Maja Schlüter and Ramanan Laxminarayan**. e-mail: psjorgensen@kva.se

1. Laxminarayan, R. *et al. Lancet* **387**, 168–175, (2016).
2. *Review on Antimicrobial Resistance: Tackling Drug-Resistant Infections Globally — Final Report and Recommendations* (Wellcome Trust, UK Government, 2016).
3. Carroll, S. P. *et al. Science* **346**, 1245993 (2014).
4. Whitmee, S. *et al. Lancet* **386**, 1973–2028 (2015).
5. Biggs, R. *et al. Ann. Rev. Environ. Res.* **37**, 421–448 (2012).
6. Bigdeli, M., Peters, D. H., Wagner, A. K. (eds) *Medicines in Health Systems: Advancing Access, Affordability and Appropriate Use* (World Health Organization, 2014).
7. Hulcr, J. *et al. PLoS ONE* **7**, e47712 (2012).
8. Van Boeckel, T. P. *et al. Proc. Natl Acad. Sci. USA* **112**, 5649–5654 (2015).
9. Maron, D. F., Smith, T. J. & Nachman, K. E. *Glob. Health* **9**, 48 (2013).
10. Wernli, D. *et al. PLoS Med.* **8**, e1001022 (2011).

Full author affiliations and supplementary information accompany this article online: see go.nature.com/2c03p6n.

FARM FORECAST

By 2030, the use of antimicrobials in agriculture in Asia alone could equal 82% of global agricultural consumption in 2010. The drugs are largely given to promote growth or prevent infections, rather than to treat disease.

