

# Antimicrobial resistance in the age of COVID-19

Action is needed to prevent COVID-19 from casting a long shadow over antimicrobial resistance.

A peek under the hood of studies reporting on patients hospitalized with coronavirus disease 2019 (COVID-19) reveals widespread use of antimicrobial therapies as part of the package of clinical care in some countries. For example, in a retrospective cohort analysis of 191 patients from two hospitals in Wuhan, Zhou et al. write that 95% of patients were treated with antibiotics and 21% were treated with antivirals<sup>1</sup>. But practices differ around the world. A retrospective case series of 393 patients in New York revealed that only 5.6% of patients had bacteraemia and none of them received antibiotics<sup>2</sup>. In a recent letter, Cox et al. highlighted a need to prospectively monitor coinfections in patients with COVID-19 to understand whether coinfection affects disease progression, and to enable antimicrobial stewardship<sup>3</sup>. It is of the utmost importance that the potential of the global pandemic to increase antimicrobial resistance (AMR) is taken seriously.

AMR is a growing problem that has implications for global health and the world economy<sup>4</sup>. Our sister title, *Nature Reviews Microbiology*, published a comprehensive collection of articles addressing the AMR crisis in April 2020. In a Viewpoint published as part of this collection, Årdal et al. noted that “the best infection is the one that never happened, due to clean food and water” (among other factors)<sup>5</sup>. One troubling aspect of the AMR crisis is that lower- and middle-income countries (LMICs) — where clean water is in short supply due to poor water and waste infrastructure — are affected more by the burden of AMR than wealthier countries. Further, LMICs are potential hotspots for AMR transmission, as discussed in a *Perspective* by Amy J. Pickering and colleagues in this issue of *Nature Microbiology*.

The authors highlight environmental transmission of AMR in LMICs in urban informal settlements, also known as ‘shanty towns’ or ‘slums’. They explore the impacts

of behavioural, environmental and societal factors on the growth of AMR in these crowded communities. Importantly, they identify opportunities for research and potential strategies that are tailored to urban informal settlements to mitigate the spread of resistance, such as improvements in water and waste infrastructure. Understanding transmission in urban informal settlements and finding solutions that work in the field are needed to enable policy makers to take actions that reduce the burden of AMR.

The World Bank has called for improvements in water and sanitation infrastructure to tackle AMR, but Pickering et al. highlight the lack of evidence for the positive effects of water treatment and sanitation on AMR incidence in crowded urban settings. This is because diarrhoea, and not AMR, has been used as the main outcome measured for intervention studies looking at the effects of water treatment, sanitation or hand washing on health. Monitoring of human gut colonization with antimicrobial-resistant bacteria and resistance genes, and of the effectiveness of water treatment or sanitation measures, is also lacking. Ultimately, policy makers need evidence to convince governments to spend the money necessary to tackle AMR at the root causes. The publication of the *Perspective* by Pickering et al. champions efforts to identify low-cost and scalable interventions to interrupt the transmission of pathogens and AMR.

Population densities in urban informal settlements are estimated to be 125,000 persons per square kilometre and the five largest such settlements are in Africa and Asia. To set this in context, around 30,000 people live in a square kilometre in New York City. At the time of writing, the incidence of COVID-19 in LMICs was low but starting to increase, raising serious concerns given the poor quality of healthcare and limited preparedness for outbreaks (among other factors) in many LMICs. An increase in AMR in LMICs

could be augmented by a large COVID-19 outbreak. Coupled with substantial antibiotic use in China and other countries, the potential for a pandemic followed by a surge in AMR is clear.

Although antibiotic treatment of secondary bacterial pneumonia associated with influenza is accepted clinical practice, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is not influenza. In patients with COVID-19 who have coinfections, antibiotic or antiviral treatment is appropriate. But those patients may be in a minority. Writing in *Clinical Microbiology and Infection*, a group of European clinicians admit that it can be difficult to differentiate COVID-19 from bacterial pneumonia, which means that some patients without bacterial infections are receiving unnecessary antibiotics<sup>6</sup>. Nonetheless, they advocate for continued stewardship and outline a series of measures to try and limit antibiotic treatment during the pandemic. These include measures such as reserving antibiotic treatment for those patients with the most severe presentations and limiting duration of antibiotic treatment to five days.

Before the SARS-CoV-2 pandemic, overcoming AMR already demanded urgent global action. Now that we are in the midst of a pandemic, understanding the pathogenesis of SARS-CoV-2 infection, and the potential for bacterial coinfections, is imperative. Until then, efforts to prioritize antibiotic stewardship around the world must be redoubled. □

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