

Will the Overuse of Antibiotics During the Coronavirus Pandemic Accelerate Antimicrobial Resistance of Bacteria?

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The coronavirus pandemic is one of mankind's biggest challenges of modern day. Viruses can cause deadly pandemics, yet another enemy should not be forgotten: Bacterial pathogens. From a biomedical perspective, bacterial infections should be easier to control, as prokaryotes exhibit structures and biochemical processes that differ from humans, and thus are easier to target. Viruses, however, employ human cells to propagate and are, therefore, more complicated to target by drugs.

Until the true dimensions of the current coronavirus pandemic became clear, it felt as though we lived in a world where we could trust that the shelves of pharmaceutical companies would be full with medication to treat almost any human infection. The real challenges for drug development were surely the noncommunicable diseases such as cancer, heart disease, and stroke. These still are the leading causes of death globally, in particular in developed nations, however, while emerging viruses are evermore on our minds, we have to think about another potential apocalypse: Antibiotic-resistant bacteria. Over the decades, and with every successive deployment of a new antibiotic, resistant bacterial strains have emerged; some pathogens are now extensively drug resistant, where an infection might be lethal or at least have a severe impact on morbidity.

With the pandemic on our minds, why should we care about antimicrobial resistance (AMR)? Treating severe SARS-CoV-2 infections, physicians often prescribe prophylactic antibiotics.^{1–3} In many countries antibiotic courses are even prescribed to non-hospitalized patients. The rationale behind the decision to deploy prophylaxis is simple: Without antibiotics, the risk of a bacterial

infection is drastically increased. Secondary bacterial infections establish easily in patients who suffer from a viral induced infection of the lungs, due to a plethora of reasons, including an altered immune response, reduced clearance of mucus and increased attachment of bacteria to epithelial cells.^{1,2,4} Such infections further reduce the rate of survival.¹

Before SARS-CoV-2, many countries had started programs for antibiotic stewardship under the umbrella of the “one health” concept, with people, animals, and the environment all interconnected; if we use antibiotics in farming for example, resistance genes can be transferred to human pathogens. Antibiotic stewardship was aimed to reduce the misuse and overuse of antibiotics, and only to treat infections appropriately and where necessary to reduce the rate of development of AMR, thereby preventing the spread of AMR genes. However, these well thought of programs are now at risk of being discontinued under the pressure doctors face during this unprecedented time. Studies summarising published clinical reports show that 60% to 70% of COVID-19 patients had received antibiotics.^{1,5} Depending on the country and the healthcare setting, a maximum of 20% of patients exhibit secondary bacterial or fungal infections.^{1,2} While this indicates that some patients will require antibiotic treatments, the prophylactic use of such drugs is questionable.

With tens of millions of people being tested positive for SARS-CoV-2 and possibly millions of fatal cases if current trends continue, antibiotic use in the clinical management of COVID-19 globally will be enormous. The long-term rehabilitation and management of health consequences of COVID-19 are unknown; some individuals may suffer of long term effects such as an impaired lung function, leading to susceptibility to bacterial and fungal infections. Only time will tell, but it is likely that this pandemic and its clinical management will exacerbate the rise of antibiotic resistant superbugs. Now that the coronavirus is here to stay, countries must embrace the concept of antibiotic stewardship even more and do all they can to avoid the emergence and spread of resistant bacteria post-pandemic. Government programs and big pharma will need to commit to supporting these efforts.

Up until the 1990s, almost every major pharmaceutical company was developing antibiotics. Most of them, including Bayer, Eli Lilly, and Bristol-Myers Squibb discontinued their antimicrobial R&D efforts over a decade ago. In 2016, a joint declaration issued by over 100 pharmaceutical companies announced the “AMR Industry Alliance.” Sadly, within a few years of this declaration the major payers had announced their disengagement in discovery programs in the search for novel antibiotics.^{6,7}

New hope has arrived with yet another 360° strategy turn: On the 9th of July, 2020, a consortium that includes Roche, Novartis, GlaxoSmithKline, Bayer Pfizer, Johnson & Johnson, Eli Lilly, Boehringer Ingelheim, and Merck, together with the Wellcome

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Trust, the WHO, and the European Investment Bank, announced to support the development of two to four novel antibiotics until 2030.⁸ “With the AMR Action Fund, the pharmaceutical industry is investing nearly US\$1 billion to sustain an antibiotic pipeline that is on the verge of collapse, a potentially devastating situation that could affect millions of people around the world,” announced Dave Ricks, Chairman and CEO of Eli Lilly who is also the President of the *International Federation of Pharmaceutical Manufacturers & Associations*. The pledged 1 billion dollars may not go far; the development of a single drug compound costs approximately the same sum.^{9,10}

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