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How Can You Prevent Antimicrobial Resistance?

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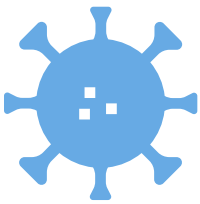
How can you prevent antimicrobial resistance?

As deadly as it has already proven to be, COVID-19 could result in even more health-related disruptions in the future. Several studies estimate that 70% to 97% of hospitalized patients with COVID-19 received antibiotic therapy. Here's the problem: Increased antibiotic usage accelerates antibiotic resistance.

The irony is, SARS-CoV-2 is a virus with respiratory symptoms, and no antibiotic is yet available against it. Inappropriate prescribing could have been avoided with diagnostic testing for influenza, Respiratory Syncytial Virus, group A strep, etc., prior to prescription and treatment. COVID-19 pandemic reminds us of the value of infectious diseases diagnostics. Even though economic value of infectious diseases diagnostics is not always easily quantifiable, diagnostics play a valuable and critical role in effective patient care. Diagnostics helps to determine the disease etiology, influence treatment modalities, and enable public health surveillance. Moreover, advances in Point-Of-Care (POC) testing have further improved patient care.

Antimicrobial resistance

Microbes are survivors. To paraphrase German philosopher Friedrich Nietzsche, what doesn't kill them makes them stronger. When exposed to conditions that inhibit growth, such as antibiotics, microbes make changes that help them survive. Those that acquire resistance can multiply rapidly and spread the resistance to other microbes.



Per Rodney Rohde, PhD, professor, and chair for the Clinical Laboratory Science (CLS) Program in the College of Health Professions at Texas State University, COVID-19 pandemic can worsen the threat posed by antimicrobial resistance.

In 2019, the World Health Organization declared antibacterial resistance one of the top 10 threats to global health. Left unchecked, drug-resistant diseases could cause 10 million deaths each year by 2050, warns the UN Ad hoc Interagency Coordinating Group on Antimicrobial Resistance.

In the United States, antibiotic-resistant bacteria and fungi cause more than 2.8 million infections and 35,000 deaths each year— nearly twice as many annual deaths from antibiotic resistance as reported in 2013. The Centers for Disease Control and Prevention's 2019 AR Threats Report includes two new urgent threats: drug-resistant *Candida auris* and Carbapenem-resistant *Acinetobacter*. These were added to three identified in 2013: Carbapenem-resistant Enterobacteriaceae (CRE), *Neisseria gonorrhoeae*, and *Clostridioides difficile*.

Friedrich Nietzsche

Enter COVID-19

COVID has exacerbated the threat. In 2020, the World Health Organization reported on a study that showed that while 72% of COVID-19 patients received antibiotics, only 8% demonstrated bacterial or fungal co-infections. WHO also reported that early in the pandemic, azithromycin was widely used with hydroxychloroquine in the mistaken belief it could quell the virus. Azithromycin has since been shown to have no effect on SARS-CoV-2.

Another factor exacerbating antibiotic resistance has been the upswing in telehealth during the pandemic. Studies have shown that antibiotics are prescribed for a broader set of symptoms in the absence of physical examinations or laboratory tests -- e.g., telehealth.

Hospital admissions increase the risk of healthcare-associated infections and the transmission of multi-drug-resistant organisms. Disruptions to health services during the pandemic also led to interruptions to treatments, such as for tuberculosis and human immunodeficiency virus, which can lead to selection for drug resistance. Similarly, disruptions to vaccination services increase the risk of infection, potentially leading to an overuse of antimicrobials.

The widespread use of biocidal agents for environmental and personal disinfection represents another threat. Low-level exposure to biocidal agents can select for drug-resistant strains and enhance the risk of cross-resistance to antibiotics, particularly those that treat Gram-negative bacteria.

What now?

Outsmarting microbes will never be easy. After all, they've been at it for a long time. Researchers believe that *Enterococci* bacteria – which cause thousands of multidrug-resistant infections in patients each year – were carried onto land in the guts of the world's first terrestrial animals *425 million years ago*. Still, efforts are being made to slow down the growth of antibiotic resistance. For the duration of the current pandemic, the World Health Organization recommends:

1. Training health workers to identify signs and symptoms of severe COVID-19 and those of bacterial or fungal disease; evaluate the need for medical devices that increase the chances of healthcare-associated infections; and implement strict infection prevention and control measures.
2. Ensuring the regular supply of quality-assured antimicrobials, including antiretroviral and tuberculosis drugs, and vaccines.
3. Reducing the turnaround time of COVID-19 testing by improving testing methods and expanding testing facilities, especially for presumed patients, to reduce the urge to initiate antibiotics.
4. Exercising caution in the use of biocides for environmental and personal disinfection, and prioritizing biocidal agents with a low selection pressure for antibiotic resistance.

In the long run

Government agencies, academic institutions, and nonprofit and industry groups around the world are sharing their expertise and aligning clinical trials and resources to tackle the growing problem. For example, the Antibacterial Resistance Leadership Group, funded by the U.S. National Institute of Allergy and Infectious Diseases (NIAID) is collaborating with groups in 19 countries and has initiated more than 40 clinical studies at 130 sites.

In 2019, the UN Interagency Coordination Group on Antimicrobial Resistance recommended countries support awareness programs for prudent use of antimicrobials by professionals in human, animal and plant health; invest in research and development for new technologies to combat antimicrobial resistance; and urgently phase out the use of critically important antimicrobials as growth promoters in agriculture.

In 2020, NIAID proposed a four-pronged approach to the challenge:

- Support research into promising therapeutics. For example, the Institute is funding research projects to develop models to predict the potency of therapeutics based on an understanding of how molecules enter and leave Gram-negative pathogens.
- Optimize existing antibiotics, that is, developing regimens of older antibiotics to more effectively treat infections and suppress the emergence of resistance.
- Develop microbiome-based approaches. For example, NIAID scientists collaborated with researchers in Thailand on a project that showed that Bacillus -- a "good" bacterium commonly found in probiotic digestive supplements -- helps eliminate *Staphylococcus aureus*.
- Explore phage therapy. Bacteriophages (phages) are viruses that selectively infect and kill bacteria. Phage therapy has been used to treat patients with severe, multi-drug-resistant infections under compassionate use conditions with promising results. However, knowledge gaps have hindered its development in the U.S.

Diagnostics an essential component

The need for antibiotic stewardship programs has never been more urgent. The UK's National Institute for Health and Care Excellence (NICE) defines such programs as "an organizational or healthcare-system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness." They emphasize education and training about antimicrobial resistance, providing regular feedback to prescribers, and integrating audits into existing quality improvement programs.

In the U.S., the National Action Plan for Combating Antibiotic-Resistant Bacteria, 2020-2025 recognizes the importance of rapid and innovative diagnostics as a tool to ensure appropriate antimicrobial use. Specifically, the authors call for researchers to:

- Develop new or enhance existing diagnostics that use isolates and primary samples to determine the presence, severity, or antimicrobial susceptibility or resistance of bacterial or fungal infections and to identify appropriate treatment.
- Stimulate research to better understand the appropriate use of diagnostics to determine the presence, severity, or antimicrobial susceptibility or resistance of bacterial or fungal infections in human and veterinary care.
- Develop evidence-based guidance to promote the appropriate use of new diagnostics and to improve the use of existing diagnostics that determine the presence, severity, or antimicrobial susceptibility or resistance of bacterial or fungal infections in human clinical care.

To summarize,

- Detect, respond to, and contain emerging resistance
- Prevent and stop spread of resistant infections in healthcare and community settings.
- Improve antibiotic use.

In addition to the above, Point-of-Care (POC) testing can play a crucial role in antibiotic stewardship. A study in a UK hospital demonstrated that a point-of-care test (POCT) for viral respiratory infections reduced the number of inappropriate hospital admissions and antibiotic prescriptions. With advancement in POC testing and conscious efforts towards antibiotic stewardship we can prevent antimicrobial resistance.

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