


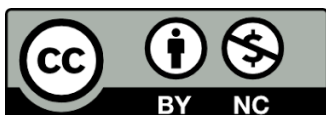


## Antimicrobial resistance: global concern and the critical need for new antibiotics

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Antimicrobial resistance (AMR) is a manifestation of evolution in real-time in response to chemical warfare against bacteria through the medicinal and non-therapeutic use of antimicrobial agents. Antibiotic resistance, which is a result of fast genetic evolution in bacteria, not only contributes to worldwide disease outbreaks but also reduces people's ability to effectively control significant human illnesses. Since sulfonamide and penicillin were first used in clinical settings in the 1930s and 1940s, respectively, many have believed that antibiotics are completely effective against infectious infections. However, due to the extensive use of antibiotics, a significant public health issue known as antibiotic resistance is currently evident. The evolution of bacteria has been ongoing for a very long time. Many of the resistance mechanisms have, in fact, been chosen over millions of years, according to a recent study. Lechuguilla cave in New Mexico, which has been a deserted cave for the past 4 million years, provided samples of microbes that tested positive for resistance to 14 different antibiotics [1]. While multidrug-resistant "superbugs," raises concerns, it also provides cause for optimism because the promotion of resistance in nature suggests the existence of mechanisms that prevent bacterial growth and thus promote resistance (in fact, previously unidentified mechanisms of resistance like daptomycin hydrolysis were discovered in the cave's microbial flora). The use, abuse and overuse of once-highly efficient anti-infective medications, have become a global challenge after decades in which it looked like human

ingenuity had outwitted microorganisms, thus, hastens this process and causes damage. There is currently no antibiotic that does not cause resistance to grow. In fact, even the most modern drugs, like the ceftaroline-avibactam combo, can produce persistent mutants in the lab [2]. Additionally, fungi and viruses are starting to develop resistance. It is generally known that the H1N1 influenza virus exhibit oseltamivir resistance [3] and echinocandin resistance by *Candida albicans* [4]. In light of this, it is a positive development that earlier substances like pleuromutilins, which prevent protein synthesis, are being used again [5]. The first pleuromutilin for systemic use, BC 3781, was found in 1951 [6] and put to the test in a phase II trial in 2011 [7]. In order to effectively combat antibiotic resistance, a strategy that encourages the development of novel as well as well-known but underutilized compounds, permits efficient development, minimizes unnecessary overuse, and restricts the spread of bacteria that are already resistant calls for collaboration, vision, and leadership [8].

Infectious diseases continue to be among the world's leading causes of morbidity and mortality [9]. Resistance to microbial therapies, whether bacterial, viral, or parasitic, is neither surprising nor new. However, as drug resistance develops and accelerates over space and time, the scope and magnitude of this phenomenon are becoming an ever-increasing global public health issue. Some bacteria and viruses are now resistant to all but one antibiotic, and some may soon be without effective remedies in the "medicine chest". Multidrug-resistant strains of organisms that cause AIDS, tuberculosis, gonorrhea, malaria, influenza, pneumonia, and diarrhea cause disease burdens in both industrialized and developing countries.

AMR is a serious threat and has far-reaching effects on world health, which includes higher rates of death and morbidity. Approximately 700,000 fatalities per year are attributed to AMR; if no effective measures are taken, this number is expected to rise to 10 million by the year 2050 [10]. AMR also causes treatment failures, protracted illnesses, and disabilities, which lowers patient quality of life and raises healthcare expenses. AMR has a significant financial impact since it entails longer hospital stays, greater use of healthcare resources, and higher treatment costs. AMR increases morbidity, mortality, and healthcare expenditures while decreasing the efficacy of antimicrobial-agent-dependent therapies. AMR also compromises the efficacy of other therapies, including



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cancer chemotherapy, organ transplantation, and critical care. Children, the elderly, and people with compromised immune systems are among the vulnerable populations who bear a disproportionate share of the socioeconomic costs associated with AMR. AMR also hinders the growth of healthcare infrastructure in low- and middle-income nations. A thorough and coordinated strategy that includes better infection prevention and control methods, a decrease in the overuse of antibiotics, and funding for the creation of novel antimicrobial medicines is important to address these issues. We can only lessen the effects of AMR and protect global health by making such efforts.

The development and application of novel antibiotics is a difficult scientific and economic challenge. There haven't been many new antibiotic classes created in the last 50 years [11], and resistance isolates can appear quite quickly, endangering their ability to be used effectively and sustainably [12]. Antibiotic stewardship promotes more prudent antibiotic usage and reduces the selection forces that fuel resistance development. Antibiotic use is decreased with infection control. The requirement for antibiotic therapy and the selection pressure that fuels the emergence of resistance can both be significantly diminished by vaccinations. When it comes to bacterial vaccines, vaccines that lower the frequency of antibiotic use can help to lower selection for AMR in the target pathogen as well as in bystander bacterial species like *Escherichia coli*, *Klebsiella pneumoniae*, or *Staphylococcus aureus* that can spread and cause disease [13]. Some vaccinations may be able to decrease antibiotic use to a greater extent than the percentage of illness syndromes caused by the vaccine target pathogen. A vaccination that is effective against group A *Streptococcus* would lessen the requirement for pharyngitis patients to have presumptive antibiotic treatment. Vaccines that are effective against the main microorganisms responsible for a specific clinical state may eventually have a synergistic effect on the consumption of antibiotics, leading to lower levels of resistance. The Wellcome Trust evaluated the viability of creating vaccines for these infections [14], and the World Health Organization (WHO) compiled a list of antibiotic-resistant microorganisms for which new medications are urgently needed [15, 16]. The following activities are needed to address diverse pathogen clusters: improve acceptance, bring to market, advance early research and development, gather data, and consider alternatives.

Improved antibiotic stewardship, improved infection control procedures, increased accessibility to appropriate diagnostics, public awareness campaigns, and more stringent laws governing the use of antibiotics in agriculture and environmental protection are all necessary components of a multifaceted strategy to address these contributing factors. Collectively addressing these issues will help us slow the spread of AMR and ensure that antimicrobial drugs

continue to be effective for both the present and the future. By 2050, it is extremely likely that there will be major economic losses due to lost productivity and societal disturbance if there is not a swift and comprehensive response to prevent and manage AMR [17]. To combat AMR, it will be necessary to make advancements in infection control, antimicrobial stewardship, and antimicrobial discovery, according to the Global Action Plan on Antimicrobial Resistance [18] and other reports [19].

Despite the fact that the discovery of antibiotics is one of the biggest medical advances in history, infectious diseases continue to be a top medical and scientific priority [20]. Since the early introduction of sulfonamides and penicillins into clinical usage, it has been demonstrated that bacterial pathogens are capable of developing resistance to new antibiotics [21, 22]. We must keep developing new antibiotics to keep up with the emergence of antibiotic resistance in bacterial pathogens. Rethinking methods for maintaining and prolonging the effective life of antibiotics, like rotating antibiotic use and combination antibiotic therapy, is also crucial. Only by comprehending the basic biology of interactions between bacterial pathogens and their hosts and by appreciating antibiotics as valuable, finite resources will the problems be overcome.

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