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Antibiotic Resistance is an Evolving Threat

The efficacy of antibiotics has come under increased attention in recent months, as health officials in the U.S. and U.K. have made statements declaring the global spread of antibiotic resistance a high priority risk.

Warnings on Antibiotic Resistance Spread

The emergence or re-emergence of several high-profile pathogens, along with a dried-up pipeline of novel drugs to treat them, has caused officials to sound alarms about the growing threat of antibiotic resistance and call for action from the global community. Dame Sally Davies, Britain's most senior medical adviser, said that antibiotic resistance should be added to the government's National Risk Register of Civil Emergencies, giving it the same prominence as pandemic influenza and terrorism. Thomas Frieden, the director of the U.S. Centers for Disease Control and Prevention has also warned of the growing number of bacteria that are resistant to carbapenem antibiotics and the difficulty of treating resistant infections acquired from hospital or healthcare settings. Carbapenems are one of the antibiotics of last resort for many bacterial infections.

Mortality

Antibiotic resistance could make common infections and routine surgeries life threatening if left unchecked. An estimated 5-10 percent of all hospital patients develop an infection, and about 90,000 of these patients die each year as a result of their infection. According to the World Health Organization, there are about 440,000 new cases of multidrug-resistant tuberculosis each year, causing at least 150,000 deaths.

The Resistance to Antibiotics has Developed Over Time

Antibiotic resistance is not a new risk; shortly after penicillin was first available in the 1940s, resistant strains began to emerge. The spread of resistance is an unavoidable consequence of the bacterial imperative to survive. Furthermore, overuse or incorrect use of antibiotics promotes the evolution of bacteria into hardier, more resilient strains that are resistant to first-line antibiotics. Over time, superbugs like MRSA have emerged, acquiring resistance to a number of widely used antibiotics.

Therefore, discovery of antimicrobials must keep pace in this biological arms race. Between 1935 and 1967, over a dozen novel antibiotics were brought to market, and for a span of 60 years the spectrum of antibiotics won out against emerging antibiotic resistance. Since the 1960s, the pace of discovery has nearly ground to a halt, and in the last couple decades, we have found ourselves once again on the losing side. A recent report by the Infectious Disease Society of America (IDSA) found that it is likely that the number of approved antibacterial drugs is reaching a plateau, with only one new drug per year.

The limits of conventional drug discovery methods are partly to blame for these shortcomings. Drug discovery does not favor extensive investment in drugs like antibiotics, used sparingly and for short periods, over investment in treatments for chronic diseases. National governments are being urged to step in, by providing incentives or easing burdensome regulations to stimulate the market proposition for new antibiotics.

Novel Approaches in Antibiotic Development

In the future, RMS sees the drought of antibiotic development being combatted by novel approaches. One such method involves expanding the library of natural compounds from which antibiotics are developed. Nearly all antibiotics have their origin in natural products isolated from microbial communities; the most commonly known example is penicillin derived from the fungus *Penicillium.* The second method involves technologies that directly attack antibiotic resistance genes. A third approach exploits the properties of bacteriophage, viruses that have evolved to infect bacteria.

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RMS® Infectious Disease Model

The RMS® Infectious Disease Model (IDM) considers the impact of using pharmaceuticals, like antibiotics and antivirals, to treat various infectious diseases in pandemic situations. The RMS IDM event set, consisting of ~4500 probability-weighted events, is designed to provide a probabilistic view of the losses that could result from the entire range of potential infectious disease pandemics, including those that are caused by antibiotic-resistant pathogens. If specific drugs or treatments are effective and available, then the RMS IDM takes into account the corresponding reduction in mortality due to the pharmaceutical intervention. RMS models a ~20% probability that a pandemic caused by an emerging or re-emerging infectious agent will be unresponsive to pharmaceuticals.

Better Use of Antibiotics and New Drugs Give Hope

Today's medical procedures, including chemotherapy and organ transplantation, rely on the effective treatment of infections. If left unchecked, the further spread of antibiotic resistance could significantly compromise the progress of modern medicine and have a significant impact on long term mortality trends. At the moment, antibiotic resistance presents a slower-moving threat than other catastrophic risks, like influenza pandemics or terrorists attacks. Much progress can be made if existing antibiotics are used stringently and novel new drugs are developed to combat resistance.