

Global antimicrobial resistance



ANTIMICROBIALS AND MODERN MEDICINE — The development of medicines that control bacteria, viruses, parasites and fungi ushered in the era of modern medicine over the last century. The new antimicrobial drugs not only curbed the toll of infectious diseases, but by improving the safety of surgery, hospital procedures and treatment for cancers, enabled medical care to which millions of people worldwide have owed their lives and longevity. Starting with the 1928 discovery of penicillin, advances in antibiotics led to an array of medicines that a 1975 New York Academy of Medicine summary described as “an embarrassment” of choicesⁱ.

GROWING THREATS, A DIMINISHING ARSENAL — But those choices already were dwindling as microbes evolved into strains resistant to the effects of the medicines that had been created to combat them, while research toward new antimicrobial drugs slowed. The discovery of new types of antibiotics had peaked in the 1950s with the development of nine new medicines, and plateaued during the 1960s and 70s with the development of five in each of those decades. The early 1980s saw two new antibiotic types, and the beginning of a hiatus for antibiotic development that continues to this day. Every antibiotic available now came from one developed between 1900 and 1984. And while the effectiveness of the existing arsenal to fight microbial infections diminished, the years following the 1970s saw the discovery of more than three dozen previously unidentified infectious diseasesⁱⁱ including HIV, SARS, Lyme disease, hepatitis C, a new form of cholera, and a variety of waterborne and foodborne diseases.

PRACTICES PROMOTE RESISTANCE — While microbes develop resistance to medicines naturally over time, excessive and incorrect use of the drugs have accelerated the process. Over the years since the last new classes of antibiotics were developed, rising incomes and access to the drugs led to increased use, with global consumption of antibiotics for medical use climbing by nearly 40 percent between 2000 and 2010ⁱⁱⁱ. In many countries worldwide, the number of courses of treatment prescribed per year exceeds one course per person. In other countries, access to antibiotics and other antimicrobial medicines without prescription also promotes excessive and inconsistent use. Lack of regulatory capacities in low-income countries also enables marketing of substandard and counterfeit antimicrobial drugs, further exacerbating resistance.

At the same time, rising incomes have driven growing global demand for animal protein, leading to increasing use of antibiotics to prevent disease and promote the growth of food-producing animals. Antibiotic use in farming now exceeds human use, and results in the spread of resistant bacteria in livestock, poultry and farmed fish, to which humans are exposed through consumption and environmental pollution. And while only four classes of medicines to treat fungal infections exist (compared to 20 types of antibiotics to treat bacterial infections) fungicides used to protect crops are fueling resistance to treatments for fungi that cause illness in humans.

THE CHALLENGE — These practices have fueled the development of deadly and increasingly treatment-resistant infections transmitted in hospital and community settings that include MRSA – or Methicillin Resistant Staphylococcus aureus – as well as multi- and extensively drug-resistant tuberculosis. Globalization and urbanization have accelerated both the spread of infections and of resistance to the medicines used to treat them. While in the United States an estimated 70 percent of roughly 2 million infections acquired in hospitals each year are resistant to at least one treatment, low- and middle-income countries bear the brunt of antimicrobial resistance. More than 200,000 newborns are lost each year to infections that don’t respond to available treatments, and an estimated 480,000 people become sick with tuberculosis that is resistant to multiple drugs – requiring longer, more toxic and less effective treatments. The harms of antimicrobial resistance include hospital-acquired infections that challenge care in wealthy countries, and emerging resistance to parasitic disease treatments in low-income countries. Global impacts of antimicrobial resistance include harms to individual and public health, and to national economies, security and stability. The world faces a growing need to work together across health, environmental, and agricultural endeavors to protect existing medicines and to promote the development of new ones.

RECOGNITION AND RESPONSES — While health system weaknesses that have fueled antimicrobial resistance globally have also challenged efforts to track its impacts, in 1998 the World Health Organization recognized antimicrobial resistance as a problem affecting countries across the economic spectrum, spread by international trade and travel.

In 2004, the Infectious Diseases Society of America published [Bad Bugs, No Drugs](#), examining needs for antimicrobial research and development incentives, and included among its recommendations a commission to prioritize antimicrobial

discovery for public health threats, and partnerships between the National Institutes of Health and pharmaceutical companies to develop new antibiotic drugs.

The dangers of antimicrobial resistance received new international attention in 2005 when the WHO named it a threat to global health security. When the WHO proclaimed antimicrobial resistance the central focus of World Health Day in 2011, IDSA released [Combating Antimicrobial Resistance: Policy Recommendations to Save Lives](#), urging Congress to enact incentives and provide leadership and funding to promote development of new medicines, improve surveillance of resistance, and support efforts to control treatment resistant infections.

The WHO, in turn, highlighted inconsistent standards and capacities to detect resistance, monitor and regulate use of antimicrobials, and to assess the impacts of those efforts. In 2014^{iv} the agency made its first attempt to assess global preparedness to address resistance, and found significant gaps in surveillance, standards and coordination. The effort found multidrug-resistant tuberculosis to be growing, widely under-reported, and uncontrolled. It found spreading resistance to malaria treatments, and, among people starting treatment for HIV, increasing levels of transmitted resistance to antiretroviral medicines. The agency found high rates of resistance to treatments for bacterial infections limiting options to expensive, toxic, and, in resource-limited settings, inaccessible, treatments of last resort. And it found that MRSA was limiting not only treatment for skin and wound infections, but also the effectiveness of antibiotics used before surgery to prevent infections.

That year also saw the first report from the United Kingdom's Review on Antimicrobial Resistance panel, which asserted that without policies to reverse the spread of antimicrobial resistance, the toll from infections no longer responsive to treatment would grow from the current estimated 700,000 deaths each year to a yearly toll of 10 million by 2050, with a quarter of those lives lost to tuberculosis. It projected the cost of lost productivity alone would be around \$100 trillion.

In 2014 the White House launched the Global Health Security Agenda in partnership with 28 other countries and recognized combating antimicrobial resistance worldwide as one of its priorities. Among its activities, the initiative works with individual countries to develop their own plans of action to monitor and control antimicrobial use and effectiveness.

NEXT STEPS — In 2015, the White House released a [National Action Plan for Combating Antibiotic Resistant Bacteria](#). Goals for the next three years outlined in the plan include partnerships between the National Institutes of Health and pharmaceutical companies toward development of at least two new antibiotic drugs entering late stage clinical trials, collaboration with countries to build infection control measures, and at least four documents on antibiotic containment to guide low- and middle-income countries. The White House followed the plan that year with its [National Action Plan for Combating Multidrug Resistant Tuberculosis](#), setting deadlines to reach 25 percent of MDR-TB patients with appropriate treatment in 10 countries with the highest disease burdens by 2016, to 35 percent of patients with MDR-TB by 2018, and to 50 percent of patients by 2020. The plan called for accelerated research and development of new treatment, diagnostic and preventive tools to fight tuberculosis, but did not set specific targets or deadlines for those products.

In 2015, also, the World Health Organization released a [Global Action Plan on Antimicrobial Resistance](#) outlining strategies to improve awareness and surveillance of antimicrobial resistance, reduce incidence of infections, optimize use of existing medicines and ensure support for research and development of new ones.

The UK [Review on Antimicrobial Resistance](#) panel released [the final of its series of reports](#) this year, recommending improved access to clean water and sanitation, development of rapid point-of-care diagnostics, increased funding and incentives for antimicrobial research and development, efforts to build the ranks of infectious diseases physicians, and a global campaign to educate patients, policy makers, health providers and animal farmers to reduce use of antibiotics. Those efforts would require a global investment of \$40 billion over 10 years, authors projected, calling for the nations representing the world's 20 largest economies to collaborate on creating a means to gather the necessary financial investments.

A START — At the September 2016 United Nations High Level Meeting on antimicrobial resistance, member nations issued a Political Declaration affirming a commitment to undertake the strategies outlined in the 2015 WHO [Global Action Plan on Antimicrobial Resistance](#), and recognizing that sustained funding would be necessary to achieving the plan's aims. Singling out resistance to antibiotics, including those used to treat tuberculosis as the most significant threat, the plan also called for international cooperation to build surveillance and service capacities in low-income countries. Providing a potential starting point for an era of global cooperation toward new antibiotics, diagnostics, and vaccines and toward building the needed health and science workforce, the declaration recognized that antimicrobial resistance is a worldwide challenge, demanding international collaboration, coordination, and accountability.

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ⁱ Spring, Maxwell: A Brief Survey of the History of the Antimicrobial Agents, Bulletin of the New York Academy of Medicine, October 1975

ⁱⁱ IDSA, *Bad Bugs, No Drugs*, 2004

ⁱⁱⁱ The Review on Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations, December 2014

^{iv} World Health Organization: Antimicrobial Resistance Global report on surveillance 2014

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