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## Combating Antimicrobial Resistance and Protecting the Miracle of Modern Medicine

The COVID-19 pandemic has forced society to confront human vulnerability to microbial pathogens (e.g., viruses, bacteria, parasites, and fungi) in a way that has not been necessary in much of the world for a century. Before the mass production of penicillin in the 1940s, deaths from bacterial infections were common, elevating the risk of common illnesses such as pneumonia, but also risks associated with surgery and other lifesaving procedures. Antimicrobial medicines have changed these risks drastically. They have helped reduce mortality not just from infectious disease, but also from cancer, surgery, and various chronic conditions, as well as routine life events such as childbirth.

As antimicrobials have been used (sometimes overused), microbes' resistance to them has grown, threatening to undermine a century of health gains. Efforts to mitigate the emergence and spread of resistant pathogens are complicated by various factors. Antimicrobial resistance is notoriously difficult to measure. Although most obvious in human health, resistance emerges in animal health and in the environment, as microbes can live in humans and other animals as well as in the environment. Moreover, microbes can spread quickly and do not recognize borders, making cooperation among countries and across sectors necessary for an effective response.

### THE COMMITTEE'S CHARGE

A concern with the problem of antimicrobial resistance prompted Congress to direct the National Institute of Allergy and Infectious Diseases to support a consensus committee study under the auspices of the National Academies of Sciences, Engineering, and Medicine to examine progress against the national strategy on combating antibiotic resistant bacteria. The committee's charge included questions on managing effective surveillance for infections related to antimicrobial resistance, measuring the health and economic consequences of



antimicrobial resistance, interventions in animal health, and the incentives for developing new medical products to prevent and treat resistant infections.

## **THE SCOPE OF THE PROBLEM**

Antimicrobial resistance is a global health problem or, more accurately, a web of related problems, where actions in one setting affect outcomes in others, often in ways that are hard to predict. It is difficult to predict where and in what bug-drug combinations resistance will emerge, persist, and spread.

The use of antimicrobial medicines in both human and animal health drives antimicrobial resistance. Biosecurity measures, good husbandry, and other practices used in modern animal production systems can greatly reduce and sometimes eliminate the need for antimicrobials in animal agriculture. Vaccines and other preventive tools are important alternatives to antimicrobials, but there is a shortage of affordable vaccines for animals.

The One Health approach emphasizes the mutual dependence of human and animal health and the health of the environment, and is therefore well suited to the complex problem of antimicrobial resistance. A One Health analysis requires an interdisciplinary, multisectoral collaboration, and includes attention to the often neglected environmental dimension of resistance—especially important in light of climate change, which will likely aggravate the problem.

## **INFECTION PREVENTION AND STEWARDSHIP**

Almost 90 percent of hospitals in the United States have programs that incorporate all seven of the Centers for Disease Control and Prevention's core elements of antimicrobial stewardship—up from only about 40 percent in 2014. Yet, many practice settings (e.g., nursing homes, dialysis centers, long-term acute care hospitals) still see considerable use of antimicrobials. These settings also treat a population of patients who are often immunocompromised or infirm. The report recommends increased attention to these settings, describing how telemedicine and steps to modernize records may be necessary. The report also encourages including antimicrobial stewardship in the quality measures on the Care Compare website, a public clearinghouse for quality indicators.

The same principles of antimicrobial stewardship apply to human and animal medicine, although key barriers are different. Veterinarians often work in relatively small practices and dispense medicines directly from their clinics, making the roles of both administrators and pharmacists far less relevant than in human stewardship programs. Partly for these reasons, there is a greater emphasis on veterinarians' individual responsibility to serve as stewards of antimicrobial medicines.

Tracking antimicrobial use is a key part of any stewardship program, but the United States does not have a strong system to track antimicrobial use in animals. The report encourages the Food and Drug Administration to promote better antimicrobial stewardship by investing in strategies to advance the use of electronic prescriptions in veterinary medicine and to encourage the sharing of prescription information currently held in proprietary hands.

## **BRINGING NEW PRODUCTS TO MARKET**

The challenge of bringing new antimicrobials to market is at the center of much of the public discussion about antimicrobial resistance. The medicines needed to treat resistant infections are complicated to develop and have a relatively small market in terms of both duration of use (usually only a few days) and need. Although there are over 2.8 million resistant infections every year in the United States, infections with any one resistant pathogen are relatively uncommon. When new antimicrobials are brought to market, good stewardship requires that older drugs be used first, even if there were no difference in price. There is, therefore, a mismatch in society's need for new antimicrobials and industry's willingness to invest in them.

The government invests in drug development to help fill this gap, offering different programs working at different places on the development pipeline. Such incentives have overall improved the number of products in the antimicrobial drug pipeline by about 10 percent between 2014 and 2019, but most of these products and the others in the pipeline do not appear to be meaningfully different from existing medicines. Market entry reward payments could draw more attention to bringing useful, novel antimicrobials to market. These payments depend on identifying those medicines that offer additional clinical value, something that is often not readily apparent when a drug is approved. The committee recommends that a government interagency committee establish well-targeted, objective criteria to identify novel antimicrobials with high potential for filling a critical, unmet need.

The Department of Health and Human Services should then support trials to establish the additional clinical benefit and optimal use of these drugs.

## **ROLE OF THE UNITED STATES IN COORDINATED GLOBAL ACTION**

The effectiveness of a national strategy to combat antimicrobial resistance will depend on global investment and sustained international engagement integrated across human, animal, and environmental health. Part of the challenge of responding to antimicrobial resistance is that, while the U.S. strategy and action plans, like that of most countries, evoke a One Health grounding, putting it into practice is difficult. Ultimately, every implementing agency involved in the response to antimicrobial resistance has its own mandate and mission.

The integration of surveillance data from human, animal, and environmental sources will be a critical component of a global strategy against antimicrobial resistance. The largest increases in antibiotic consumption over the past two decades, for both humans and livestock, have occurred in low- and middle-income countries. These countries also have a high burden of infectious disease and a growing demand for animal-source foods that could contribute to increased antimicrobial use. Serious international investment in combating antimicrobial resistance is both morally compelling and in the best interest of the United States. A national response proportionate to the size and scope of the threat would work across government agencies and in collaborative, bilateral, and multilateral relationships internationally. A program modeled on the President's Emergency Plan for AIDS Relief may be best suited to this problem.

This ambitious, global program will require coordination with an increasingly large group of stakeholders both in the United States and abroad. A designated national leader modeled on the Global AIDS Coordinator would be crucial to managing this coordination and efficient response. By supporting a truly systemic, One Health response, the recommended program may be able to drive progress on a range of health indicators, including, but not limited to, the burden of resistant infections.

For a full list of the committee's recommendations, view the recommendations insert or the full report at [nationalacademies.org/combatingAMR](http://nationalacademies.org/combatingAMR).

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