

A Coordinated and Sustained Response to the Threat of Antibiotic Resistance Is Critical: Lessons Learned From Israel

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The global spread of antibiotic resistance (AR) has reached alarming levels, leading the United Nations to declare AR “the greatest threat to human health, development and security” [1]. In this issue of *Clinical Infectious Diseases*, Schwaber and Carmeli report on how Israel was compelled to develop a national infection prevention program in the setting of a *Klebsiella pneumoniae* carbapenemase (KPC) outbreak. By March 2007, 1275 patients in 27 hospitals across Israel had acquired KPC sequence type 258. At the time of the outbreak, most acute care hospitals and long-term care facilities lacked formal infection prevention programs, and surveillance for hospital-acquired infections (HAIs) and multidrug-resistant organisms (MDROs) was not performed consistently or reported nationally. In addition, there was no emergency preparedness plan to deal with high-consequence pathogens. Once the outbreak was evident, the government supported the formation of the National Center for Infection Control,

which implemented timely interventions that led to outbreak containment.

The KPC outbreak triggered a profound change in the Israeli health system’s approach to infection prevention and antibiotic stewardship (AS). The approach included augmented information technology and microbiology laboratory capacity, increased infection prevention resources, and creation of a central regulatory body to oversee all infection prevention and AS activities in the country. Five years later, dramatic progress was observed, with a 50% reduction in central line–associated bloodstream infection rates in intensive care units and marked improvement in antibiotic use in hospitals. Israel’s experience reminds us that coordinated and funded federal efforts to reduce the spread of infectious diseases and, in particular, AR are critical to preserving human health. Over the past few years, significant progress has been made in addressing the AR threat in the United States. However, looming budget cuts to AR prevention programs and medical research put this progress at risk.

Multidrug-resistant gram-negative bacteria pose the greatest and most immediate public health threat. These bacteria have the potential to rapidly disseminate due to plasmid-mediated resistance and the very limited therapeutic options available to treat the infections they cause. KPC production is the most common mechanism of carbapenem

resistance among *Enterobacteriaceae* spp. in the United States. Carbapenem-resistant *Enterobacteriaceae* (CRE) acquisition was initially observed in hospitals; however, the long-term care setting is now recognized as an important reservoir for these organisms, with 25% of *K. pneumoniae* clinical isolates in long-term acute care hospitals in the United States being KPC producers [2].

Until recently, minimal attention has been given to understanding and developing approaches to coordinate activities to reduce CRE transmission and AR infections across healthcare facilities and public health departments in the United States. Such coordination was clearly critical in controlling the KPC outbreak in Israel. Using mathematical modeling, one study estimated that if US healthcare sites both improved local infection prevention and AS work and shared information about CRE test results using public health departments as a coordinating entity, an estimated 74% fewer patients would be infected with CRE over a 5-year period [3].

Recognizing the urgent need to tackle AR, executive order 13676, Combating Antibiotic Resistant Bacteria [4], was issued in 2014. In 2015, the National Action Plan for Combating Antibiotic Resistant Bacteria [5] was released, and federal budget funding directed at AR prevention, diagnosis, and treatment increased significantly, facilitating

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national coordination of AR work. With this increased funding, the Centers for Disease Control and Prevention (CDC) implemented the Antibiotic Resistance Solutions Initiative (ARSI) [6], which aims to improve national infrastructure in order to detect, respond to, and contain AR infections across healthcare settings and communities; expand AS efforts; and support innovative research. As part of the ARSI initiative, the State HAI/AR Prevention Program was created to codify and implement the coordinated approach among acute care and long-term care settings and state health departments. The Antibiotic Resistance Laboratory Network was developed to provide the infrastructure and laboratory capacity for 7 regional laboratories. The CDC has spearheaded the national movement to define optimal AS activities and promote stewardship across acute care, long-term care, and ambulatory care settings, including development of the Core Elements of AS documents [7]. The CDC also increased funding for its Prevention Epicenters Program, which supports research in HAI and AR, including development of a multifacility CRE patient alert system and a bundle of interventions to halt CRE spread in the long-term care setting [8, 9].

This combined work has formed the initial building blocks needed to develop a coordinated national infrastructure to combat CRE and other MDROs, but sustained funding and continued expansion are needed given the size and complexity of the US healthcare system. Thus, it is particularly disheartening that the proposed fiscal year (FY) 2018 US federal budget has alarming recommendations that would reduce AR funding across the Department of Health and Human Services [4]. The CDC's AR funding could be reduced by \$37 million, and these cuts include the funds that support the State HAI/AR Prevention Program and Antibiotic Resistance Laboratory Network. In addition, the administration is recommending that all CDC AR funding be supported by transfers from the Prevention and Public Health Fund (PPHF), which is authorized

by the Affordable Care Act, rather than through budget authority (ie, funding allocated by Congress). However, if the ACA is repealed, the PPHF will dissolve, and additional funds would need to be appropriated by Congress to fund CDC's AR work. Funding for the National Healthcare Safety Network (NHSN) remains in the budget but without an increase to expand capacity for AR and antibiotic use surveillance. The FY2018 budget also proposes a \$1.2 billion cut to the CDC's overall funding, which could impact NHSN and AR funding.

Beyond the proposed CDC cuts, the Budget Blueprint to Make America Great Again [10] recommends additional significant reductions that affect AR research, including a \$1 billion cut to the National Institute of Allergy and Infectious Diseases (NIAID) and folding the Agency for Healthcare Research and Quality (AHRQ) into the National Institutes of Health. These recommendations would potentially impact NIAID's Antibacterial Resistance Leadership Group, which has made significant research contributions to developing and evaluating diagnostic testing to improve antibiotic use, producing novel treatment approaches for MDROs, and establishing a repository of CRE isolates. This repository serves as a resource for testing new antibiotic agents and for expanding knowledge of the molecular epidemiology of these organisms [11]. For research that defines the best approaches to preventing and treating MDROs in order to improve the care of patients, ways to disseminate it into practice are essential. Thus, reductions in funding to or elimination of AHRQ would greatly impact its work in implementing evidence-based best practice in HAI and AR prevention and AS at the point of care.

The consequences of budgetary restrictions to infectious disease programs in the United States have proven to be devastating in the past. New York City saw a remarkable rise in the incidence of MDR tuberculosis when its tuberculosis control programs were reduced in the late 1980s [12]. In the context of budget cuts to more than half of the state's sexually transmitted

infection (STI) programs, STIs reached the highest number ever in 2015 [13]. The United States' coordinated response to containing AR is in its infancy but has seen rapid progress over the past few years. Reversing this progress will endanger the health of US residents and contribute to the global burden of AR.

Notes

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