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Commentary: Missing opportunities on the Presidential Advisory Council on Combating Antibiotic Resistance (PACCARB)

Timothy Landers, PhD, RN, CNP, CIC¹

Kevin T. Kavanagh, MD, MS²

¹ The Ohio State University College of Nursing, Columbus, OH

² Health Watch USA, Somerset, KY

Antimicrobial resistance is a critically important impending public health crisis that not only threatens the treatment of infectious disease but also the very foundations of modern health care from transplantation to cancer chemotherapy. Many types of surgeries and the health of immunocompromised patients, including diabetics, will be placed at risk as antibiotics are no longer to prevent or treat infections. Even minor illnesses or injuries such as a scrape or paper cut become life threatening in the absence of effective antibiotics.

In response to this impending public health catastrophe, President Obama issued Executive Order 13676 that mandated the United States Government to issue the “National Strategy for Combating Antibiotic Resistance” (2014) and directed the development of a federal “National Action Plan for Combating Antibiotic Resistance” (NAP) (2015) to direct interagency coordination and cooperation to address antibiotic resistance.^{1,2} In addition, Executive Order 13676 announced a planned doubling of federal funding for antibiotic resistance research to \$1.2 billion in the federal budget proposal (2016).³

In addition to the NAP and increased federal research support, Executive Order 13676 also authorized the establishment of a 30-member Presidential Advisory Council on Combating Antibiotic Resistance (PACCARB). The goal of this paper is to review the current membership of PACCARB, identify gaps that impair the ability of PACCARB to address antibiotic resistance in a coordinated and integrated fashion, and propose additional areas of expertise that are required to adequately address the impending epidemic of antibiotic resistant organisms.

BACKGROUND

National and international organizations have identified antibiotic resistance as a major public health problem. The World Health Organization issued a comprehensive report on antibiotic resistance surveillance (2013), outlined options for action (2014), and has developed a global strategy (2015) to address this emerging public health crisis.⁴⁻⁶ In the US, the Centers for Disease Control and Prevention issued a threat report on antibiotic resistance and the “catastrophic consequences of inaction” (2013).⁷

The President's Council of Advisors on Science and Technology issued recommendations on addressing the problem of antibiotic resistance (2014).⁸

The defining characteristic of the National Strategy and Action Plan (NAP) is the need for a sustained, coordinated and integrated approach to antibiotic resistance prevention and control. A One Health approach addressing humans, animals and the environment is recognized in the National Strategy and NAP as the foundational model for antibiotic resistance prevention activities. The vision of these efforts is that “the United States will work domestically and internationally to prevent, detect, and control illness and death related to infections caused by antibiotic-resistance bacteria by implementing measures to mitigate the emergence and spread of antibiotic resistance and ensuring the continued availability of therapeutics for the treatment of bacterial infections.”¹

The scope of the NAP addresses pathogens identified as urgent or serious public health threat by the Centers for Disease Control and Prevention. The five overarching goals of the National Strategy and NAP are shown in Table 1. The first goal recognizes that “it is also critical to prevent transmission of bacteria-causing infections that are resistant to treatment across community and healthcare settings. Outbreaks can be prevented through regional efforts to rapidly detect and control infections that are hard to treat, and also through prompt communications regarding the management and transfer of infected patients within and between healthcare facilities.”¹

1. Slow the emergence of resistance bacteria and prevent the spread of resistant infections.
2. Strengthen national One-Health surveillance efforts to combat resistance
3. Advance development and use of rapid and innovative diagnostic tests for identification and characterization of resistance bacteria.
4. Accelerate basic and applied research and development for new antibiotics, other therapeutics, and vaccines.
5. Improve international collaboration and capacities for antibiotic resistance prevention, surveillance, control and antibiotic research development.

Table 1. Five goals of the National Action Plan to Combat Antibiotic Resistance

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RESPONSIBILITIES OF PACCARB

Executive Order 13767 specifies that the PACCARB is to provide advice, information and recommendations to the Secretary of Health and Human Services regarding: 1) the optimization of antibiotic use, 2) acceleration of research on combating resistance including stewardship, 3) advancing human and animals diagnostics, 4) furthering research on new treatments, 5) the development of antibiotic alternatives for livestock, 6) maximizing dissemination of information to the public, human clinical and veterinary audiences, and 7) improving international collaboration. In addition to this charge, Health and Human Services (HHS) Secretary Sylvia M. Burwell issued a task letter to PACCARB requesting that the committee to consider and address the best ways to incentivize new drug and non-drug therapeutics, novel diagnostic tests in humans and animals, and to prioritize elements to promote maximum influence.

Although addressed in the National Strategy and NAP, the spread of antibiotic resistant pathogens, either by preventing infections or by preventing patient-to-patient transmission was not specified in the directive. As a result, it receives little attention in the PACCARB initial assessment¹⁰ of the NAP.

In contrast, other countries emphasize infection prevention and control as a key component of addressing antibiotic resistance. For example, an action plan produced by United Kingdom specifies as their second intervention to “improve sanitation and prevent the spread of infections.”¹¹ The United Kingdom has had significant success in reduction of methicillin-resistant staphylococcus aureus (59% reduction between 2007 and 2009) through the implementation of standardized national protocols to prevent spread.^{12,13} In currently available international action plans, infection prevention and control is highlighted as a key strategic initiative. A library of these national strategies is available at:

<http://www.who.int/drugresistance/action-plans/library/en/>.

PACCARB EXPERTISE

Following an internal selection process, HHS announced the 30 members of PACCARB in March, 2015. A total of 30 members were appointed including 15 (50%) voting public members, 5 (17%) non-voting liaison members, and 10 (33%) non-voting ex-officio members. Among all voting and non-voting members, 19 (63%) are male. Physicians account for 53% of voting members (8/15) and 53% of the total membership (16/30) with all physicians having infectious disease backgrounds as identified by designation as a Fellow of the Infectious Disease Society of America or serving as an IDSA organizational representative. Of the members appointed, 33% of voting (5/15) and 30% of the total membership (9/30) are trained in agriculture or veterinary sciences (DVM/VMD/PhD in food science/veterinary epidemiology). One Registered Nurse serves as a non-voting liaison representative from long-term care administration and one consumer representative was appointed as a voting public member.

GAPS IN PACCARB MEMBERSHIP

Given the importance of a coordinated, integrated approach to addressing antibiotic resistance, it is critical that PACCARB members represent the professional expertise and engagement of relevant stakeholders. Despite the expertise of members of PACCARB, serious deficiencies exist in the expertise and background which will hamper the ability of the committee to address antibiotic resistance using a coordinated, integrated One Health perspective.

Gaps in expertise on PACCARB must be addressed so that the National Strategy and NAP can be fully implemented and the federal government can prioritize issues and investments in antibiotic resistance. With intense pressure on industry to control this emerging epidemic, conflicts of interest of the PACCARB members need to be publicly declared. To date, there has been limited disclosure of conflicts of interest. Conflicts – whether actual or perceived – could undermine public confidence in PACCARB and its findings. This is particularly true because the expert members of PACCARB are well-regarded and respected researchers, academicians, policy makers and clinicians.

Additional areas of expertise that would help advance the mission of PACCARB are given in Table 1.

| Expertise | Personnel Sample Source Organizations | Rationale |
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| Drug regulation | United States Food & Drug Administration | In alignment with PACCARB’s mission to accelerate new drug discovery and diagnostic tests, the FDA can play a role in the approval and licensing of new tests. The FDA also set regulations regarding drug indications and which is important for implementation of antibiotic stewardship. |

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| Worker Safety | National Institute of Occupational Safety and Health Collective bargaining organizations (unions) | The safety and working environment of the healthcare worker needs to be addressed. Recommendations for pathogen screening and exposure to pathogens should be established. |
| Hospitals | American Hospital Association | Preventing infections from antibiotic resistant bacteria (ARB) in hospital settings through prevention of infections, ABR transmission and stewardship requires organizational and management support of these efforts. Leadership engagement is recognized as a core component of stewardship programs. ARB not only place patients at risk but also healthcare workers and the operational integrity of a facility. Hospitals need to commit ample resources for the accomplishments of these goals. |
| Nursing | American Nurses Association | The 3.4 million Registered Nurses in the United States administer every dose of antibiotics in hospitals and are at the front line of patient care in non-acute care programs. Nurses play critical roles in patient education and patient safety. |

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| <p>Infection Prevention</p> | <p>Association of Professionals in Infection Prevention and Epidemiology</p> | <p>Infection Preventionists are responsible for surveillance, detection, control and prevention of healthcare associated infections. Infection prevention programs must work synergistically with antibiotic stewardship programs to reduce the risk of infection and transmission of ABR pathogens. In addition, there are concerns for worker safety and staffing limitations which hinder adoption of prevention protocols.</p> |
| <p>Pharmacists</p> | <p>American Pharmacists Association National Community Pharmacists Association</p> | <p>Pharmacists play critical roles in stewardship programs, in patient education and detection of inappropriate antibiotic utilization. As experts in drug utilization, they must be included in effective stewardship programs.</p> |
| <p>Private Insurers</p> | <p>Anthem, Humana, ETNA</p> | <p>Insurers can exert a tremendous impact by incentivizing antibiotic stewardship through payment policies. Currently, evaluation and management visits are tiered, and have differing payments depending upon the complexity of the visit. Prescription of an antibiotic is one way a higher tier and payment can be justified. This financial incentive needs to be reversed.</p> |

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| <p>Primary care clinicians</p> | <p>American Academy of Family Physicians American Academy of Nurse Practitioners American Academy of Nurse Practitioners</p> | <p>Appropriate antibiotic utilization in primary care settings is impacted by patient demand, delays in obtaining culture or lab-based pathogen identification. Antibiotics may be inappropriately prescribed in 60% of outpatient diagnoses. In these settings, care is often provided by teams of physicians and other advanced practice providers who must engage with setting-specific stewardship practices.</p> |
| <p>Public policy expertise</p> | <p>American Public Health Association</p> | <p>Incentives for inappropriate antibiotic use or over-utilization of diagnostic test can be driven by public policy regarding reimbursement and expertise in public policy should be included to comprehensively address ABR.</p> |
| <p>Health professions education</p> | <p>American Association of College of Nursing National League for Nursing American Association of Medical Colleges Association of Public & Land Grant Universities American Association of Veterinary Medical Colleges</p> | <p>Education and training are important elements of stewardship. By educating and training health professions students, future practice can be impacted. Interdisciplinary curricula that are evidence-based and outcomes-oriented programs should be developed for practicing clinicians and students.</p> |

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| Social and behavioral expertise | | Social determinants of health and health disparities are widely recognized as an important issue and can help address the socio-cultural determinants of antibiotic use and resistance. |
| Retailers | Grocery stores Retail clinic administrators | Driven largely by consumer demand, antibiotic-free meat products are increasingly popular. This represents an opportunity to address the demand-side of inappropriate antibiotic utilization. The rise of loss-leader “free antibiotic” programs by some retail pharmacies is a worrisome trend and requires the engagement of industry and trade groups. In addition, retail based clinics provide increasingly important access points for upper respiratory infections, urinary tract infections and other conditions for which an antibiotic may be prescribed. While current evidence does not show that antibiotics are not over-used in these settings, it is important to engage grocery stores and retail clinic providers. |

Antibiotic resistance is a global issue and requires comprehensive action. For example, limited US control of antibiotic production in China and India may contribute to the emergence of resistance. Antibiotic residuals and resistant organisms have been demonstrate in the water supply of China, India and other developing countries. However, US and international agencies (e.g., U.S. State Department, World Trade Organization, G7) which can influence international trade policies, foreign aid and travel incentivizing proper antibiotic utilization are not represented on the PACCARB.

The daunting task of prevention of international spread of bacterial resistance in third world countries with underdeveloped healthcare delivery systems also underscores the importance of also having an effective system for surveillance of carriers and prevention of person-to-person transmission. This is a component of the National Strategy and NAP which is mentioned but noticeably underdeveloped in CARB's action plan.

WHY IT IS CRITICAL TO GET IT RIGHT

The timeline of the history of medicine has a number of crucially important milestones. We are rapidly approaching one of the most important – the looming threat of a post-antibiotic era. Losing the ability to fight infection may reverse many important medical advances and have a tragic impact on public health and longevity.

Expanding the expertise of PACCARB would permit it to address antibiotic resistance in a coordinated, integrated fashion using a One Health perspective.

These additional areas include prioritized research needs and substantial investment in research on the standards for infection prevention research to ensure that research findings are valid, reliable, and generalizable.¹⁴

Adequate attention to infection prevention requires sustained organizational investment in infection prevention and control programs. As infection prevention is the key way to combat antibiotic resistant infections and dissemination, it should serve as a cornerstone of national efforts. Infection prevention is the ultimate antibiotic stewardship program, for if an infection does not take place, an antibiotic is not given. Since many infections are nurse-sensitive outcomes, it is important to support adequate staffing across settings. Furthermore, the impact of AMR as an occupational or employee health issue should be addressed to ensure that the health care work force is protected from occupationally acquired infections.

Strict standards for environmental cleaning in healthcare and community-based facilities including occupied and terminal room cleaning should be developed based on the best available evidence and research should be supported to determine the impact on pathogen environmental load and the development and dissemination of antibiotic resistant organisms.

Similarly, the over-the-counter antiseptics and antibiotics should be closely evaluated. Two notable examples include the use of triclosan, a suspected environmental toxicant, in consumer antibacterial products and polymixin in topical OTC products, which may induce resistance to other polymixins such as colistin.

A One Health approach should also underscore the attention to the health of an individual's microbiome. It is increasingly recognized that the microbiome confers both beneficial, and potentially harmful effects.

Attention should be paid to financial incentives and novel economic models, including linking federally funded drug development to antibiotic stewardship initiatives.

CONCLUSION

Similar to other industrialized countries with national healthcare, the United States needs to set prioritized standards which can be implemented with near uniformity across our healthcare system. This will not be an easy task, but how the leaders in public health and infectious disease address this epidemic at this juncture will be studied for millennia and their actions dissected for centuries to come. Their decisions will determine their legacy and the future of modern health care as a whole.

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