

PACCARB

Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria

Meeting Summary

Fifth Public Meeting of the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria

January 25, 2017

**Department of Health and Human Services
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Meeting Proceedings

Welcome and Overview

Martin Blaser, M.D., Chair

Dr. Blaser called the meeting to order at 9:33 a.m. and welcomed the participants.

Roll Call and Rules of Engagement

Bruce G. Gellin, M.D., M.P.H., Designated Federal Official

Dr. Gellin said this PACCARB meeting will center on infection prevention in human health. He explained the rules governing the PACCARB under the Federal Advisory Committee Act and conflict-of-interest guidelines. He then called the roll.

U.S. Food and Drug Administration (FDA) and the 21st Century Cures Act

Peter Lurie, M.D., Associate Commissioner for Public Health Strategy and Analysis, FDA

Dr. Lurie focused on provisions related to antimicrobials in the 21st Century Cures Act. The act establishes a new process for approval of limited-population antibacterial drugs (LPADs). It enables approval based on a streamlined development program mutually agreed on by FDA and the sponsor in which the sources of evidence may vary from the traditional. Notably, LPADs must still meet the existing standard for approval, which requires “substantial evidence.” Labels must specify that the drug is indicated for limited populations, and promotional materials must be submitted to FDA in advance for review.

The act also requires FDA to identify interpretive criteria for susceptibility testing at the time of drug approval or licensure or as soon as possible. Within a year, FDA must create a website describing new or updated interpretive criteria standards and maintain the website, posting updates rapidly. Under the act, FDA evaluation of standards can include information provided by interested third parties. In lieu of requiring that labels provide the interpretive criteria, labels must include a link to the website. Information on the website may relate to off-label use.

Patient Story

Alicia Cole, PACCARB Member

Speaking by phone, Ms. Cole explained that she was calling from her hospital bed, where she was recovering from severe sepsis and necrotizing fasciitis for the second time in 10 years. Her experiences give her a unique perspective on the topic of infection prevention and its role in antibiotic resistance. Ms. Cole summarized her medical history, which began in 2006 with a routine surgery to remove uterine fibroids. Sepsis developed, triggering a cascade of conditions all made worse by antibiotic resistance. Ms. Cole became an advocate for addressing antibiotic resistance. Late in 2016, Ms. Cole went to the hospital with a sinus infection, which again triggered a series of infections.

From her recent experience, Ms. Cole concluded that while awareness of the need for infection prevention has been raised, glaring gaps remain in hospital and clinician adherence to protocols. She called for efforts to ensure that policies, procedures, and incentives sufficiently address the danger from pathogens that health care providers and patients face daily. The public must understand the urgency of the situation, because antibiotic resistance is harming and killing people now.

Ms. Cole called for policies and incentives that promote timely, practical education. Incentives should be devised to encourage health care providers to specialize in wound care and infection prevention. The urgency of antibiotic-resistant pathogens should be communicated. There must be accountability to enforce policies aimed at strengthening adherence to best practices.

Infection Prevention Best Practices—Lessons Learned and Gaps

Moderator: Sara Cosgrove, M.D., M.S., PACCARB Member

Dr. Cosgrove thanked Ms. Cole for her strong role in pushing the topic of infection prevention to the forefront. The Infection Prevention and Antibiotic Stewardship Working Group has categorized its areas of focus as 1) best practices; 2) implementation; 3) workforce, education, and leadership; and 4) surveillance. Today's presentations address workforce, education, and leadership issues in human health. Dr. Cosgrove said animal health and antibiotic stewardship would be addressed in future discussions.

The CDC Prevention Epicenters Program: Addressing Gaps in Healthcare-associated Infections (HAIs)/Antibiotic Resistance Prevention Practices

John Jernigan, M.D., M.S., Centers for Disease Control and Prevention (CDC)

Dr. Jernigan explained that while substantial progress has been made in reducing infections, for example, central-line-associated bloodstream infections (CLABSIs), that progress has slowed, and there has been little decline in others. Even perfect implementation of current best practices will not achieve the goal of eliminating HAIs, so prevention is key. Continued investment is needed to discover new prevention strategies.

The Prevention Epicenters Program uses collaborative agreements to align public health priorities with academic investigation. For example, CDC investigators identified the link between postoperative infections and contaminated heater-cooler devices used during open heart surgery, then used the program network to evaluate new management strategies rapidly. The network also links investigators across institutions so they can share promising prevention strategies and test them in multiple centers at once. The program also facilitated the rapid uptake of chlorhexidine bathing for infection control.

The Prevention Epicenters Program was instrumental in a study that determined the extensive impact of one long-term care facility on the spread of antibiotic-resistant bacteria throughout a region, spurring a large-scale prevention effort. Dr. Jernigan outlined other infection prevention and antibiotic stewardship initiatives facilitated by the program. He concluded that more tools are needed to improve prevention, and the Prevention Epicenters Program is expanding the toolbox.

Lessons Learned and Gaps in Community Hospitals

Deverick Anderson, M.D., M.P.H., Duke Infection Control Outlook Network

Dr. Anderson pointed out that the majority of hospitals in the United States are small, non-teaching, community hospitals with fewer than 200 beds. Best practices for infection prevention often emerge from research conducted at large hospitals. Small hospitals often lack the support and expertise to implement these practices.

Duke University established infection prevention and antibiotic stewardship networks of community hospitals throughout the southeastern United States. To address the notion that community hospitals do not see the same resistant bacterial infections as large hospitals, the Duke networks collect and provide hospital-specific data. Evidence shows that community hospitals saw an increase in carbapenem-resistant Enterobacteriaceae (CRE) and extended-spectrum β -lactamase-producing *Escherichia coli* parallel to rates at large hospitals. In fact, the more hospitals assessed their own rates of HAIs, the more incidents of CRE they found.

Barriers to implementing best practices include the lack of access to infectious disease (ID) specialists or individuals trained in infection prevention or antibiotic stewardship. In addition, hospitals experience frequent turnover in leadership, which derails initiatives. Small hospitals lack the personnel and resources to fully institute best practices. Infections that occur infrequently may not be recognized in time. Small facilities lack needed data or do not use data effectively.

These gaps affect outcomes. For example, small facilities with low volumes of surgery have higher rates of surgical site infection and postoperative ventilator use than medium-size facilities with higher volume. Smaller hospitals are also more likely than others to prescribe antibiotics inappropriately for bloodstream infections, said Dr. Anderson.

Infection Prevention and Antibiotic-Resistant Bacteria

Hilary Babcock, M.D., M.P.H., Washington University, St. Louis

Dr. Babcock said knowledge gaps persist as to how, when, and in what settings to implement basic measures such as hand hygiene and standard precautions. Effective infection prevention requires a lot of education combined with audits and feedback, all of which require more resources. Traditionally, infection control practices have targeted highest-risk settings, such as intensive care units (ICUs), but HAIs have high impact wherever they occur.

Prevention involves a combination of practices. Once various elements are introduced, it is difficult to assess the impact of a given element, especially in different contexts, and even harder to remove elements that may not be useful. The situation is complicated by the allure of promising new products, which may divert resources from the investments needed to sustain existing practices.

Dr. Babcock gave examples of challenges to infection prevention posed by new medical devices (e.g., heater-coolers and endoscopes). Medical devices are usually designed by

engineers without consideration for how the device will be cleaned to ensure sterility. Dr. Babcock concluded that infection prevention is critical to combat antibiotic resistance but is challenging to implement across facilities.

Contact Precautions

Anthony Harris, M.D., M.P.H., University of Maryland

Dr. Harris described the results of the Benefits of Universal Glove and Gown (BUGG) study to assess whether universal contact precautions more effectively prevented the spread of methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE) than contact precautions used only with patients known to be colonized with these bacteria. The study showed a 40-percent decrease in MRSA acquisition but no effect on VRE. Dr. Harris pointed out that participation in infection prevention studies tends to raise awareness and improve results in the control group.

The BUGG study concluded that those using universal precautions increased their hand hygiene practices. They also visited one less patient per hour than those not routinely donning gloves and gowns. While previous observational studies suggested that seeing patients less often leads to poorer care, the BUGG study found that fewer visits translated to fewer adverse events.

The size of the BUGG study led to more definitive answers about contact precautions than previous studies. Such precautions remain an important part of preventing antibiotic resistance, especially in high-risk settings. Dr. Harris acknowledged that gowns and gloves are inconvenient, so more research is needed to determine when they are not beneficial and also how to implement best practices once identified.

Council Discussion

Dr. Blaser posited that gloves and gowns may be more effective in preventing the spread of MRSA, which persists on the skin, than VRE, which is enteric. Studies underway on the effect of universal precautions in preventing CRE will tip the balance of thinking about implementing such practices, he added.

Dr. Harris noted that some microbes spread from patient to patient via the health care worker as a vector; in other cases, patients may be admitted with undetected colonization that manifests when antibiotics destroy healthy microbes or foreign bodies are not managed optimally. Dr. Jernigan added that contact precautions do not reduce the burden at their source. More attention to maintaining or restoring a healthy microbiome could lead to less reliance on precautions.

Jay C. Butler, M.D., said one way to address the problem of leadership turnover is to work with state hospital associations to convene hospital leaders. He asked whether efforts have been made to collaborate with national groups like the American Hospital Association or the American College of Healthcare Executives to highlight infection control and antibiotic stewardship. Dr. Anderson said some such contacts have occurred, but more outreach would be a good strategy. He noted that it is easier to reach leaders

when regulations assign a monetary value to patient outcomes, although he would prefer to make the case for quality of care rather than financial advantages.

Helen W. Boucher, M.D., FIDSA, FACP, asked how to increase funding for research on basic prevention. Dr. Harris said CDC's Prevention Epicenter Program network is one mechanism for study. He pointed out that compliance with hand hygiene is still a challenge, despite 40 years of evidence. Multifaceted interventions are needed at every step along the path. The ability to capture real-time, individualized data on hand hygiene could improve compliance. More and better interventions are needed, Dr. Harris said. Dr. Jernigan agreed that hand hygiene is the most important intervention to decrease antibiotic resistance in health care settings; he echoed the sentiment that more innovations are needed.

Asked about the impact of visitors, Dr. Jernigan and Dr. Babcock stated that the risk of infections posed by visitors to health care institutions is likely to be much lower than the risk of transmission via health care workers. Both said more facilities are discouraging or restricting people with respiratory viruses from visiting.

Discussion turned to the importance of improving antibiotic stewardship. There was agreement that it is integral to infection prevention.

John H. Rex, M.D., asked how to improve evaluation of new tools and technology. Dr. Harris said collaboration across agencies is critical to ensure that approved products have meaningful outcomes for patients. Dr. Anderson said many products lack effectiveness data on real-world use. Dr. Jernigan said it is difficult to demonstrate how effective a product is in preventing a distal outcome like bacterial infection. As with vaccine studies, surrogate markers of protection are needed. Also like vaccines, it would be helpful to evaluate the benefits to a population of preventing transmission. Dr. Jernigan noted that CDC is sponsoring some environmental studies.

Infection Prevention Implementation—How to Translate Evidence into Practice

Moderator: Angela Caliendo, M.D., Ph.D., FIDSA, PACCARB Member

AHRQ's Perspective on Translating Evidence into Practice

James I. Cleeman, M.D., Agency for Healthcare Research and Quality (AHRQ)

Dr. Cleeman emphasized that implementing HAI prevention strategies must be based on research that provides insight into what to do and how. Facilities need tools to help them translate that research effectively. The AHRQ website offers, for example, the Enhanced Protocol for Universal Decolonization, a research-based protocol combined with clinician-friendly tools that address protocol adoption, timing of implementation, and the need for clinician champions, among other things. The CRE Prevention Toolkit helps users gain support from leadership and plan for implementation of CDC guidelines.

The Comprehensive Unit Safety Program (CUSP) promotes implementation of HAI prevention by focusing on a culture of safety and enhanced teamwork and

communication. Dr. Cleeman said the CUSP addresses the need for behavioral changes to improve adherence to best practices. Nationally, AHRQ-funded projects to implement CUSP have yielded toolkits for reducing CLABSIs and catheter-associated urinary tract infections in various settings. The CUSP approach is being applied to numerous topics, including antibiotic stewardship.

Dr. Cleeman concluded that HAI prevention requires support for research on what works to prevent infection as well as research on how facilities can take those steps (i.e., implementation science). Research must then be translated into tools to facilitate implementation. Implementation must be promoted via methods such as CUSP that address human behavior, which is crucial.

Implementation Pearls for Decolonization in Health Care: The Process of Adoption

Susan Huang, M.D., M.P.H., University of California, Irvine

Dr. Huang emphasized the importance of decolonization to prevent the spread of multidrug-resistant organisms. The Randomized Evaluation of Decolonization vs. Universal Clearance to Eliminate MRSA (REDUCE MRSA) trial found that universal decolonization successfully decreased MRSA and other bloodstream infections. Dr. Huang offered seven pearls of wisdom on implementing decolonization:

1. Fund more pragmatic trials (i.e., studies in real-world conditions) on infection prevention with the goal of rolling out prevention practices in various settings.
2. Provide easy-to-use, language-appropriate, education-appropriate tools to disseminate information quickly and make practices easy to implement.
3. Require and provide regular training on infection prevention practices. (Dr. Huang said some clinicians not experienced with bathing patients or providing wound care and may avoid cleaning the most important areas of a patient's body.)
4. Assess adherence to practices. Such information will help determine whether practices are being implemented adequately and how to maximize the impact of effective practices.
5. Foster comparison and collaboration. Public reporting is helpful and encourages public health entities and facilities to work together within hospitals, across counties, and across regions.
6. Ensure that findings are disseminated (e.g., fund dissemination grants). Translation requires explaining how to apply the findings in various settings. (Dr. Huang said REDUCE MRSA had funding to roll out its protocol to 100 hospitals, and they saw significant reductions in infection. Within three years of the study, 85 percent of hospitals are using decolonization techniques.)
7. Assess the value of practices in other settings. Decolonization can prevent transmission across facilities and may stem the spread of antibiotic-resistant bacteria across regions.

Effectively Translating Evidence into Practice

Sean Berenholtz, M.D., Johns Hopkins University

Dr. Berenholtz said successful infection prevention programs combine technical and adaptive approaches. Technical approaches define effective practices and the mechanics

of putting them in place, such as requiring hand hygiene in hospital standards and protocols. Adaptive approaches focus on creating the conditions that help people implement practices, such as fostering a culture of safety in which individuals can hold each other accountable. Organizations with strong safety cultures tend to demonstrate good clinical and patient outcomes and less burnout and turnover among staff.

One model of the technical approach is Translating Evidence Into Practice, which summarizes the key evidence and identifies barriers to local implementation (e.g., lack of education, disagreement about the evidence, or competing priorities). Performance is measured, and results are provided to frontline staff and patients. The CUSP is the best validated adaptive approach to improving teamwork and safety culture, said Dr. Berenholtz. It engages frontline staff, incorporates a multistep iterative process, and relies on up-to-date education. Staff are encouraged to identify barriers and offer suggestions to improve practice. Senior leadership work with staff to help them better navigate complex systems and better understand how to align new practices with organizational priorities.

Dr. Berenholtz summarized a successful project to reduce CLABSIs that combined technical and adaptive work, including a significant investment by AHRQ in implementation science. The effort also relied on clinicians to lead the work and created a clinician community to improve communication across facilities.

Dr. Berenholtz called for more research funding, especially for implementation science, and more focus on creating infrastructures that enable health care workers to put best practices in place (e.g., data collection tools and time for documentation). Efforts need to engage staff and give them the means to improve patient safety. Staff need opportunities to share with and learn from their peers within and outside of their own systems. Finally, Dr. Berenholtz called for improving transparency of reporting and accountability through public reporting at the hospital level.

CRE: Implementing a Regional Response

Michael Lin, M.D., M.P.H., Rush University

Dr. Lin explained that CRE outbreaks are regional events that require regional control. Infections spread as patients move across facilities, but key patient health information is poorly shared. Post-acute-care facilities bear the highest burden of CRE, so focusing on these high-risk facilities offers an opportunity to improve public health. Key strategies for regional control are implementing infection prevention strategies to reduce CRE at high-risk facilities and improving communication across facilities.

To kick off a regional response, the Chicago PROTECT Project combined two approaches. First, it incorporated a bundle of common CDC interventions proven to reduce CRE infection. Second, it leveraged the Illinois Extensively Drug-Resistant Organism Registry, which facilitates reporting about CRE infections. Any health care facility can query the registry to determine whether a patient has a record of CRE infection. Dr. Lin said efforts are underway to automate the system so that hospitals are alerted when a patient with a history of CRE is admitted.

Chicago PROTECT used mathematical modeling to identify the highest impact facilities, conducted cost-benefit analysis of the feasibility of interventions, and implemented targeted interventions for CRE and use of the registry. Dr. Lin hoped that Chicago's successful work to control the spread of CRE infection regionally could serve as a model for other communities.

Prevention: Public Expectations

Lisa McGiffert, Consumer Reports

Ms. McGiffert said that consumers expect the health care system to protect them from harm, and when a provider demonstrates a pattern of failure, consumers expect action to address it. She reminded the group of the devastating toll that HAIs and antibiotic-resistant infections take on the population. While PACCARB has delved into new science around antibiotic-resistant bacteria, effective prevention comes down to basics—such as having enough nurses and cleaning staff with the right equipment. Ending the misuse of antibiotics should be simple, yet efforts to that end have not been successful.

Ms. McGiffert recommended three strategies: 1) public reporting; 2) significant funding for training, education, and implementation of best practices; and 3) financial incentives and penalties. Outbreaks should be reported publicly. A national system for reporting HAIs should be developed, similar to CDC's database for foodborne infections. A 2016 *Consumer Reports* survey found strong support for reporting outbreak information.

Concerns abound about secrecy. Investigation into infections related to heater-cooler devices revealed flaws in the system, such as the failure to warn patients who may be disease carriers of their risk. There are no systems currently available to support patients in reporting HAIs. The cultural firewall between facilities and public health authorities prevents data sharing. Current patterns of care pose a threat to public health, said Ms. McGiffert, so relying on voluntary compliance with infection control standards is ineffective. Inspectors and regulators should have complete information about facilities and the ability to impose monetary fines and require meaningful corrective action plans.

Mandates work, as exemplified by the Department of Veterans Affairs (VA's) systematic, comprehensive protocols to drive down MRSA. Medicare should leverage its payment policies to stop the misuse of antibiotics. Agencies like the Centers for Medicare and Medicaid Services (CMS) and CDC should have full access to prescribing information from U.S. pharmacies to help them identify prescription patterns that support misuse and overuse, Ms. McGiffert concluded.

Council Discussion

Kent E. Kester, M.D., FACP, FIDSA, FASTMH, asked for input on how the federal government can adopt a holistic approach to implement best practices, rather than the current approach, which supports "islands of excellence" yet leaves out many facilities. Dr. Cleeman said with CUSP implementation, AHRQ has helped about 25 percent of U.S. hospitals. He said the CMS Partnership for Patients is a model program for broad efforts to reduce HAIs and saves lives and dollars. Denise Cardo, M.D., said CDC has set goals and supported programs but now needs new strategies and polices at the federal and state

levels to move forward. She agreed with Ms. McGiffert that facilities face barriers to implementing interventions known to be effective.

Marjory Cannon, M.D., pointed to CMS' strategies to initiate quality control initiatives and best practices at the hospital level, and then expand them regionally and nationally. Collaboration with AHRQ, CDC, and the Office of the Assistant Secretary for Health has established national targets and programs to reach them at the local level. Dollars spent have had an impact, as seen in the results of quality improvement initiatives in hospitals and the Partnership for Patients. Ms. McGiffert noted that the new administration is focused on job creation, so the federal government could invest in workforce development for infection control.

Asked how to encourage cooperation across facilities, Dr. Lin said regional, state, and local health departments were already thinking about regional control before Chicago PROTECT started. He said the environment is ripe for collaboration. Dr. Huang said Department of Health and Human Services (HHS) requirements can catalyze cooperation toward the same goals. Dr. Cleeman agreed that established goals are critical in making the case for working together, but facilities also need technical advice on how to achieve those goals. Dr. Cannon said that thanks to collaboration, facilities now hear consistent messages about best practices from various agencies. Dr. Berenholtz reiterated the need for adaptive work to make changes stick.

To combat concerns about declining federal financial support for health care, Michael Craig suggested continuing to make the case that failure to invest in work to prevent antibiotic resistance now will be very costly later. Dr. Cleeman said the international community has made combating antibiotic resistance a top priority.

To address the barriers posed by lack of strong leadership, Ms. McGiffert said that demonstrating the costs of infections to a facility gets the attention of senior leaders. Dr. Lin said that in long-term care facilities, leaders are less concerned with infection control and more about the costs of antibiotics and readmissions. It is important to align incentives with greater social interests, he observed.

Infection Prevention Workforce and Education

Moderator: Helen Boucher, M.D., FIDSA, FACP, PACCARB Member

Society for Healthcare Epidemiology of America (SHEA)

Louise Dembry, M.D., M.S., M.B.A.

Dr. Dembry described the membership, mission, and activities of SHEA. She said health care epidemiologists are usually physicians with diverse responsibilities, including acting as program advocates, working with external stakeholders (including public health authorities, federal agencies, and The Joint Commission), and providing training and professional development. Health care epidemiologists serve as subject matter experts, quality and performance improvement leaders, administrators, researchers, liaisons, teachers, and antibiotic stewards.

Even those in the field of infection prevention and epidemiology sometimes lack knowledge needed for effective stewardship. For example, they may not have good leadership training, may be unfamiliar with implementation science, or may lack experience in behavioral science and modification. They may need to learn how to engage senior leadership and change culture. Dr. Dembry said SHEA provides workforce training and development for health care epidemiologists through courses, publications, conferences, and mentoring programs. It places special focus on those working in community settings and recognizes the need for diversity among faculty and members.

Dr. Dembry stressed the need to incorporate effective education during medical training, because changing ingrained behavior is hard. Health care workers need appropriate, relevant training that acknowledges gaps and reinforces effective behavior. The current health care epidemiology workforce is insufficient to meet current needs, so SHEA is seeking funding sources and partnerships to encourage training those in ID fellowships.

Association for Professionals in Infection Control and Epidemiology (APIC)

Linda Greene, R.N., M.P.S., CIC, FAPIC

Ms. Greene explained that APIC's members function across multiple settings and play critical roles in infection prevention. As Dr. Dembry observed, the competencies required to translate evidence into practice cover broad ground. Because of the potential consequences that even one case of infection can have on the system, a workforce is needed that can bring infection prevention interventions to the bedside.

A survey of APIC members identified inadequate staffing as the most urgent and common concern. A significant percentage of experienced infection preventionists are on the cusp of retirement. To address the problem, APIC is promoting a competency model for the infection prevention workforce at all career stages. It is partnering with SHEA on training and certification. Also, APIC is working with the American Nurses Association, establishing standard criteria for a robust infection prevention program and launching a recognition program.

Ms. Greene identified the key gaps in practice and education, which are particularly important in patient transitions (e.g., to long-term care facilities). They include lack of basic infection prevention training, especially for frontline staff, and lack of education on antibiotic stewardship. She called for aggressive initiatives to train a specialized infection prevention workforce and improve performance to protect patients from harm.

Infectious Diseases Society of America (IDSA)

Bill Powderly, M.D., FIDSA

As others noted, ID physicians play many roles and often need additional training and education to serve as hospital epidemiologists and infection preventionists, said Dr. Powderly. He stressed the importance of infection control in supporting advances in medical science. It is necessary to lay the foundation for appropriate use of antibiotics during medical education and throughout continuing education. At the same time, infection prevention must be recognized as key to reducing the need for antibiotics. Regarding mandates for antibiotic stewardship, Dr. Powderly said The Joint Commission

is developing requirements under the misguided notion that an adequate infection prevention workforce is in place, with sufficient resources, which is not the case.

Dr. Powderly described the broad training required to become an ID physician. He said IDSA must recognize how to position ID physicians for a lifelong career. Unfortunately, the field is attracting fewer candidates, primarily because the average salary is among the lowest of all internal medicine specialties. Salaries are driven by a reimbursement structure that does not appropriately compensate for the care of patients with complex problems. At the same time, ID physicians are expected to lead the way in quality improvement and antibiotic stewardship, yet are not paid for those efforts. Because of the sizable average debt incurred for advanced medical training, salary is a major concern.

To address some of the barriers, IDSA aims to document the value that ID physicians provide and to estimate the number of ID physicians needed in the field. Ample data show that involvement of ID physicians in patient care is associated with significant benefit to patients, including reduced mortality. Also, ID physicians play a role in combating antimicrobial resistance at every stage, from basic research to public policy. Dr. Powderly said the federal government can assist in the following ways:

- Maintain emphasis on antimicrobial resistance and alternative treatments
- Finalize the CMS stewardship rule
- Provide resources for stewardship and prevention
- Invest in the workforce

Pediatric Infectious Diseases Society (PIDS)

Paul Spearman, M.D., FPIDS

Dr. Spearman described some unique considerations faced by ID physicians who specialize in treating children. For example, they operate in a broad range of settings, from the neonatal ICU to school-based clinics, with patients ranging from neonates to teenagers. They are deeply involved in promoting vaccines (a fantastic infection prevention tool). They also engage in research, recognizing that evidence gleaned from adults does not always translate to children.

Salaries for pediatric ID physicians are very low, said Dr. Spearman, and PIDS hopes to shine a light on the value of such specialists. These physicians have little opportunity for private practice; most are hospital based. As with adult ID physicians, the field is not attracting enough candidates to fill available training slots. However, those entering the field are becoming more involved in antibiotic stewardship.

To address these challenges, Dr. Spearman called for increased recognition of specialists as leaders in pediatric hospitals and ambulatory settings. Medical training should develop career tracks to encourage the pursuit of infection prevention as part of pediatric ID fellowships. Pediatric ID specialists should be invited to take part in infection prevention efforts like this PACCARB forum. Advocates should press for more pediatric research, with results widely disseminated. Finally, PIDS and related societies should coordinate with each other and with federal agencies to address infection prevention.

Accreditation Council for Graduate Medical Education (ACGME)

Mary W. Lieh-Lai, M.D.

Dr. Lieh-Lai described the role of the ACGME in accreditation, noting that program requirements are revised every 10 years. The ACGME does not dictate the content of curricula but requires programs to train students to achieve competency. In addition to accrediting nearly 10,000 programs in the United States, ACGME International accredits some programs in the Middle East and Singapore, with more in the pipeline.

The ACGME communicates regularly with a large audience through emails and its website; leadership also engages with specialty societies and program directors. The ACGME recently launched on-site reviews to assess patient safety and health care quality, with an emphasis on infection control.

At a 2015 White House forum, ACGME's chief executive officer (CEO) expressed a commitment to partner with PACCARB and CDC to promote antibiotic stewardship among accredited programs. Dr. Lieh-Lai said that although the ACGME does not dictate specific content, infection control and antibiotic stewardship are special issues of worldwide significance, so the organization will commit to ensure students receive education on these topics.

Council Discussion

Dr. Blaser was enthusiastic about the opportunity to reach medical students through the ACGME. Dr. Lieh-Lai said the organization is in the middle of its 10-year review, so the time is right to incorporate changes. She suggested that a representative of PACCARB or CDC join the ACGME's strategic planning group for internal medicine.

Asked about the role of compensation in attracting more people to the field, Ms. Greene said that money is part of the problem but so is the lack of recognition for people in infection prevention. When their efforts are successful, they appear unnecessary, but they are vital in times of crisis. Once the crisis is over, funding for education and training are often cut, said Ms. Greene. Dr. Dembry said salary is a bigger concern for physicians, who typically have much higher education debt than nurses. She echoed that many in the field do not feel supported or lack training to pursue infection control. Dr. Spearman added that uncertainty about the future is another deterrent to specialists, as research grants are increasingly harder to win, leaving few sources of additional support.

Thomas R. Shryock, Ph.D., called for suggestions on incentives to increase the workforce. Dr. Powderly said that National Institutes of Health support for students who commit to research careers have benefited many ID faculty. He suggested the concept be expanded; for example, dangerous pathogens and the possibility of more resistant organisms may pose a national security threat and thus merit investment from other sectors of government. Dr. Powderly stressed the need to recognize the role that specialists play in patient care and overall quality of care and to pay them accordingly. Dr. Cannon said CMS is studying the issue of reimbursement. She noted that raising awareness and advocating for infection prevention workforce development are helpful.

Lonnie J. King, D.V.M., M.S., M.P.A., ACVPM, asked panelists for ideas on addressing infection prevention and antibiotic stewardship through interprofessional education. Dr. Powderly acknowledged the pressing need for such education and said the ACGME can help by making stewardship a core value of medical education. Dr. Lieh-Lai said the ACGME is pursuing interdisciplinary relationships.

Dr. Blaser pointed out that fear of lawsuits drives some unnecessary prescribing practices. Also, salaries are low because the reimbursement system is based on revenue, while infection control is a cost center that is undervalued (and systems are not accountable for outcomes like infections). Currently, the system pays for individual treatment without concern for the public good. Dr. Blaser said the real cost of antibiotics is underestimated.

Dr. Spearman observed that many hospitals did not have antibiotic stewardship programs until *U.S. News and World Report* surveys asked about them, creating a very public awareness about hospital and CEO performance. Dr. Powderly said such surveys would do better by asking whether hospital programs have metrics to measure their performance. He said incentives or penalties are needed to ensure action. For CEOs, it is important to demonstrate the value of stewardship or how the lack of it can lead to catastrophic losses.

Dr. Cosgrove reminded the group of insights from earlier presenters about the need for adaptive approaches, such as training in teamwork, communication, and behavioral science, in addition to education. She said basic education in all fields is a necessary start, and teaching the basics takes much more than lectures.

Council Reflections

Dr. Cosgrove encouraged PACCARB members to consider how to operationalize the observations made by the invited speakers. Dr. King said he appreciated the importance of adaptive approaches. He also felt PACCARB should focus on making the business case to demonstrate the cost-savings associated with infection control and antibiotic stewardship.

Dr. Caliendo said she was struck by the chaos and instability of the health system (as demonstrated by high turnover among leadership and uncertainty about payment mechanisms). Current resources are insufficient, so more attention should be paid to discontinuing practices that have little or no value, she stated. Dr. Boucher said the role of time—for example, the time it takes for experts to do their work—must be factored into the value proposition.

Aileen M. Marty, M.D., FACP, said prevention is always better than treatment but its value is hard to prove. Research is needed to show how extraordinarily cost-effective infection prevention is. Dr. Rex countered that plenty of information demonstrates the value of infection prevention and ID consultants. He suggested focusing on mechanisms similar to CMS' Conditions of Participation to compel facilities to provide more resources for infection prevention.

Dr. Cosgrove said more discussion is needed about alternative approaches to pay for infection control, such as reimbursement for baseline prevention and exceptional prevention practices. Dr. Blaser said he believes sufficient money is available but not enough is allocated for prevention. Payers must figure out ways to better address antibiotic resistance, he said.

Dr. Kester agreed with Dr. Rex that plenty of data demonstrate the value of infection prevention; the challenge is finding better ways to generalize those data. Once the data are widely accepted, infection prevention will become part of basic clinical education.

Public Comment

Kevin Kavanagh, M.D., M.S., of Health Watch USA, said the VA published the results for the last 10 years of their MRSA prevention approach, which included active detection and isolation. The VA saw an 87-percent reduction in infections in the ICU and an 80-percent reduction in non-ICU settings. However, a National Academy of Sciences (NAS) report on CRE found evidence of multiple chains of transmission and resistance mechanisms, indicating a high rate of CRE carriage. The NAS suggested an aggressive approach of carrier surveillance and isolation. The urgency of these reports is underscored by the recent patient death in Nevada from totally resistant CRE.

In addition to inadequately tracking carriers, said Dr. Kavanagh, the United States does not even have a comprehensive system to track multi-resistant infections. At least five different initiatives have published data about MRSA epidemiology, all with conflicting results. The CDC's National Healthcare Safety Network is the most comprehensive resource but only captures a small portion of MRSA infections. Dr. Kavanagh said the United States has missed most of its national infection control goals. He strongly encouraged PACCARB to recommend a mandatory, publicly reported, comprehensive surveillance system designed to detect carriers and infections resulting from these dangerous pathogens.

Carol Moss, representing Nile's Project, said that on behalf of the American public, her organization recommends that PACCARB take two bold actions. First, PACCARB should establish a working group to build the CDC guidelines for infection prevention into a toolkit that every health care facility must adopt if they want to do business in the United States. Second, PACCARB should establish a working group to focus on accountability among health departments. State-level infection prevention oversight has been lacking for preventing HAIs. Ms. Moss referred to the firewall that exists between those gathering data and those who protect the public. Information is not getting to those who protect the public because of a culture of harm and secrecy in which hospitals are not held accountable and patients feel the pain.

The basics of infection prevention are well known, said Ms. Moss, yet in California, for example, HAI rates have risen. Even with the generous investments of over \$7 million from the CDC and HHS and other substantial support, preventable infections continue to rise. Ms. Moss called on PACCARB to consider the amount of antibiotics used for the estimated 70,000 people in California alone who are infected with preventable infections

every year. A state accountability working group would finally shine a light on inactions in states that are not protecting the public. Such action would save lives and dramatically reduce antibiotic use, Ms. Moss concluded.

Helen Haskell of Mothers Against Medical Error said prevention is foundational to solving the problem of antibiotic resistance and appreciated PACCARB dedicating so much time to it. She said today's presentations talked about leadership and training and, in that context, the problem of small hospitals where personnel may not have the training or experience or sense of urgency to handle infectious diseases properly. She confirmed these observations on the basis of her own experience, but said large hospitals face the same problems. Many frontline caregivers are learners who may not yet know how to deal properly with infection. While discussion focused on best practices, only tangential attention was given to the problem of recognition and diagnosis, which not only allows for timely treatment but also helps prevent spread of infection.

As a patient, Ms. Haskell said she was shocked about the lack of data on the extent of the problem and the fact that doctors, facilities, and hospitals are not required to report infections or to collaborate on the treatment of infected patients. The protocols of the Chicago PROTECT Project should be standard national practice, said Ms. Haskell. She pointed to the risks arising from some standard practices, such as exposing healthy elderly people to pathogens in long-term care settings; invasive screening such as endoscopic retrograde cholangiopancreatography and prostate biopsy; and other scheduled surgical procedures in which infection prevention procedures are rushed.

Finally, Ms. Haskell observed that efforts to promote hand washing should have demonstrated that training has its limitations and more focus is needed on human factors as well as forcing functions like public reporting and trying to thoughtfully restrict use of procedures that put patients at risk.

Stephanie Fox-Rawlings of the National Center for Health Research said the development of new antibiotics will only help if they actually improve the health of patients with resistant infections. Drugs that are not as safe and effective as antibiotics already on the market or those that are not studied on patients with resistant bacteria will not be effective in this respect. The FDA often relies on non-inferiority trials for antibiotics, which can result in drugs that are somewhat less effective than an approved version. After several rounds of comparing new drugs to older drugs that are slightly less effective than previously approved drugs, the system ends up with new antibiotics that are much less effective than the best available. Furthermore, if they are chemically similar, new drugs add to rather than reduce the problem of antibiotic resistance.

Ms. Fox-Rawlings said the 21st Century Cures Act could easily increase the number of antibiotics that do not benefit patients. Already, FDA's efforts to speed up drug approvals have led to relatively high rates of antibiotics later removed from the market because they were not effective. Relying on smaller clinical trials for limited populations could compound the problem by increasing the risk that results are due to chance. These small studies may include patients who do not have resistant bacteria. Once approved, drugs

often are promoted and prescribed for a wider patient population than included in trials, which can expose patients to unnecessary risks, lower effectiveness, and generate resistant bacteria. Prevention and control requires methods to make sure antibiotics work on resistant bacteria and are limited to those cases. Bolstering prevention and control includes developing rapid testing options for researchers to determine which antibiotics are most effective. Further, health care and veterinary practitioners must ensure antibiotics are targeted for approved uses, said Ms. Fox-Rawlings.

Casey Farrington representing Waxman Strategies read a letter to PACCARB from former congressional representative Henry Waxman on antibiotic manufacturing pollution, an often overlooked aspect of antimicrobial resistance that can contribute to the development of superbugs. Pollution from drug manufacturing facilities producing antibiotics, predominantly in India and China, is under-examined. Recent research showed that the release of antibiotics into soil and waterways creates a perfect storm for antimicrobial resistance to develop and spread. A study in the *Journal of Hazardous Materials* showed antibiotic concentrations downstream of several drug manufacturing plants in India and China exceeding those expected in a patient being treated for infection. Other researchers concluded that for every bacterium that entered a waste treatment plant in Northern China, four or five resistant bacteria were released into the water system.

To safeguard against worsening the crisis, factories identified as serial polluters should be pressured to change or be blacklisted by the industry, including by major buyers such as hospital systems and retail pharmacies. Good manufacturing practices should be redefined to include environmental impact, and regulators should be encouraged to make antibiotic pollution a priority. Addressing antibiotic manufacturing pollution fits into the One Health approach. It will take a concerted global effort on multiple fronts within multiple industries and multiple countries to successfully address antimicrobial resistance, and wider recognition of pollution as a contributor will go a long way toward fostering worldwide changes in active pharmaceutical ingredient manufacturing.

PACCARB received and reviewed additional written comments from WaterAid and Ken Kagawa.

Closing Remarks

Sara Cosgrove, M.D., M.S., PACCARB Member

Dr. Cosgrove observed that although best practices are recognized, many questions remain unanswered, and continued research is needed to determine which practices truly have the most value. How to implement best practices remains an underlying theme of efforts. The need to improve communication persists (among facilities and health care workers and across professions). Dr. Cosgrove believes adaptive approaches may help break down the silos that still exist.

Final Comments and Adjournment

Martin Blaser, M.D., Chair

Lonnie King, D.V.M., M.S., M.P.A., ACVPM, Vice Chair

Dr. King thanked the panelists. He said Ms. Cole's presentation put a very real face on the need for prevention and the important work that PACCARB is undertaking. Mr. Blaser announced that the next PACCARB meeting will be May 3–4, 2017, and will focus on infection prevention in animal health. He thanked the speakers, PACCARB staff, public commenters, and the audience for their participation. Dr. Blaser adjourned the meeting at 4:04 p.m.

Appendix A: Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) Members

January 25, 2017

PACCARB Voting Members Present

Martin J. Blaser, M.D., Chair
Lonnie J. King, D.V.M., M.S., M.P.A., ACVPM, Vice Chair
Michael D. Apley, D.V.M., Ph.D., DACVCP
Helen W. Boucher, M.D., FIDSA, FACP
Angela Caliendo, M.D., Ph.D., FIDSA
Alicia R. Cole (by phone)
Sara E. Cosgrove, M.D., M.S.
Peter Robert Davies, B.V.Sc., Ph.D.
Kent E. Kester, M.D., FACP, FIDSA, FASTMH
Aileen M. Marty, M.D., FACP
John H. Rex, M.D.
Thomas R. Shryock, Ph.D.
Randall Singer, D.V.M., M.P.V.M., Ph.D.

Organizational Liaisons Present

Animal Health Institute
Richard Carnevale, V.M.D.
Association of State and Territorial Health Officials
Jay C. Butler, M.D. (by phone)
National Pork Producers Council
Elizabeth Allen Wagstrom, D.V.M., M.S.
The Pew Charitable Trusts
Elizabeth Jungman, J.D., M.P.H.

Ex Officios Present

U.S. Department of Health and Human Services
Luciana Borio, M.D. (Alt. for Peter Lurie, M.D.), Acting Chief Scientist, Office of the Chief Scientist, Food and Drug Administration (FDA)
Marjory Cannon, M.D. (Alt. for Shari Ling, M.D.), Medical Officer, Office of Clinical Standards and Quality, Centers for Medicare and Medicaid Services (CMS) (afternoon)
Denise Cardo, M.D. (Alt. for Michael Craig, M.P.P.), Director, Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention (CDC)
Michael Craig, M.P.P., Senior Advisor for Antibiotic Resistance Coordination and Strategy, National Center for Emerging and Zoonotic Infectious Diseases, CDC
Dennis M. Dixon, Ph.D., Chief, Bacteriology and Mycology Branch, Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health (NIH) (morning)

Jane Knisely (Alt. for Dennis M. Dixon, Ph.D.), Program Officer, Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases, NIH

Shari Ling, M.D., Deputy Chief Medical Officer, Center for Clinical Standards and Quality, CMS (by phone)

Peter Lurie, M.D., Associate Commissioner for Public Health Strategy and Analysis, Office of the Commissioner, FDA

U. S. Department of Defense

Paige Waterman, M.D., FACP, FIDSA, Director, Translational Medicine, Walter Reed Army Institute of Research

U. S. Department of Agriculture

Neena Anandaraman, D.V.M., M.P.H., (Alt. for Jeffrey Silverstein, Ph.D.), Senior Advisor for Animal Health, Production, and Products, Office of the Chief Scientist, Food Safety and Inspection Service

Brian McCluskey, D.V.M., Ph.D., Chief Veterinary Officer and Deputy Administrator for Veterinary Services, Animal and Plant Health Inspection Service

Jeffrey Silverstein, Ph.D., Deputy Administrator, Office of National Programs Animal Production and Protection, Agricultural Research Service

Designated Federal Official

Bruce G. Gellin, M.D., M.P.H., Deputy Assistant Secretary for Health, Office of the Assistant Secretary for Health, Department of Health and Human Services

Advisory Council Staff

Tiffany Allen Archuleta, M.P.H., M.Ed., Senior Research Coordinator, PACCARB, New York University Langone Medical Center

Laura Gottschalk, Ph.D., Antibiotic-Resistance ORISE Fellow

Jomana F. Musmar, M.S., Ph.D.c, Advisory Council Manager, Office of the Assistant Secretary for Health, Department of Health and Human Services

MacKenzie Roberston, Committee Management Officer, Office of the Assistant Secretary for Health, Department of Health and Human Services

Ayah O. Wali, M.P.H., Committee Management Officer, Office of the Assistant Secretary for Health, Department of Health and Human Services

Glossary of Abbreviations

ACGME	Accreditation Council for Graduate Medical Education
AHRQ	Agency for Healthcare Research and Quality
APIC	Association for Professionals in Infection Control and Epidemiology
BUGG	Benefits of Universal Glove and Gown (Study)
CDC	Centers for Disease Control and Prevention
CEO	chief executive officer
CLABSI	central-line-associated bloodstream infection
CMS	Centers for Medicare and Medicaid Services
CRE	carbapenem-resistant Enterobacteriaceae
CUSP	Comprehensive Unit Safety Program
FDA	Food and Drug Administration
HAI	Healthcare-associated infection
HHS	Department of Health and Human Services
ICU	intensive care unit
ID	infectious disease
IDSA	Infectious Diseases Society of America
LPAD	limited-population antibacterial drug
MRSA	methicillin-resistant <i>Staphylococcus aureus</i>
NAS	National Academy of Sciences
PACCARB	Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria
PIDS	Pediatric Infectious Diseases Society
REDUCE MRSA	Randomized Evaluation of Decolonization vs. Universal Clearance to Eliminate MRSA
SHEA	Society for Healthcare Epidemiology of America
VA	U.S. Department of Veterans Affairs
VRE	vancomycin-resistant enterococci