PACCARB

Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria

Meeting Summary

20th Public Virtual Meeting of the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria March 2, 2022

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Meeting Proceedings

Welcome and Overview

Martin Blaser, M.D., Council Chair, and Michael D. Apley, D.V.M., Ph.D., DACVCP, Vice Chair

Dr. Blaser opened the meeting at 10 a.m. ET and welcomed the participants. He gave an overview of the agenda and acknowledged retiring Council members: voting members Lonnie J. King, D.V.M., M.S., M.P.A., ACVPM, who served as vice chair; Sara E. Cosgrove, M.D., M.S.; and Kent E. Kester, M.D., FACP, FIDSA, FASTMH; and liaison members Rima Khabbaz, M.D., of the Centers for Disease Control and Prevention's (CDC's) National Center for Emerging and Zoonotic Infectious Diseases and Lawrence Kerr, Ph.D., of the Office of Pandemics and Emerging Threats, Office of Global Affairs, at the U.S. Department of Health and Human Services (HHS). Dr. Blaser said that Dr. King had been a great partner in leading the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB).

Dr. King expressed gratitude to the PACCARB staff and the Council members for their efforts during his tenure, adding that federal agency representatives do not always receive the recognition they deserve for their work. He noted that since the inception of PACCARB, Council members have solidified the Council's purpose, focused its capacity, and advanced efforts to address antimicrobial resistance (AMR). Dr. Apley also thanked the retiring members, especially Dr. King for his leadership.

Roll Call

Jomana F. Musmar, M.S., Ph.D., Designated Federal Official, Advisory Council Committee Manager, Office of the Assistant Secretary for Health (OASH), HHS, and Taylor Simmons, M.P.H., OASH, HHS

Dr. Musmar called the meeting to order. She described the Council's establishment and charter and summarized the rules governing the Council under the Federal Advisory Committee Act and conflict-of-interest guidelines. Ms. Simmons called the roll. (See the appendix for the list of Council members and staff.)

Opening Remarks from the Assistant Secretary for Health, Swearing-In of New Council Members, and Honoring Retiring Members

ADM Rachel L. Levine, M.D., Assistant Secretary for Health, HHS

ADM Levine thanked the Council members for their advice, recommendations, and continued commitment to stopping the spread of AMR. She offered sincere condolences to all those who have suffered and lost loved ones as a result of COVID-19 and expressed gratitude and respect to the public health workers and health care workers on the front lines of the pandemic, as well as the federal, state, and local partners striving to address the pandemic.

COVID-19 highlights the importance of robust pandemic preparedness that considers the effects of secondary infections. The Council's mission was formally expanded in 2020 to include pandemic preparedness with the recognition that combating AMR plays an integral part. ADM Levine voiced the administration's continued support for a One Health perspective, particularly

for pandemic preparedness. She thanked today's meeting presenters for bringing diverse viewpoints and sharing critical information.

ADM Levine emphasized the importance of transparency in efforts to act aggressively and make progress. She urged stakeholders to keep pushing the envelope around the use of the One Health approach to novel outbreaks so that the country will be more prepared in the future—because the nation's health depends on it.

On behalf of HHS Secretary Xavier Becerra and herself, ADM Levine thanked the outgoing Council members for their valuable contributions of time and expertise and their leadership. She welcomed and administered the oath of office to four new PACCARB members:

- Voting Member Virginia R. Fajt, D.V.M., Ph.D., DACVCP, Clinical Professor, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University
- Voting Member Payal K. Patel, M.D., M.P.H., Assistant Professor, The University of Michigan Health System
- Voting Member Julia E. Szymczak, Ph.D., Assistant Professor of Epidemiology, University of Pennsylvania Perelman School of Medicine
- Liaison Member James Adaskaveg, Ph.D., Minor Crop Farmer Alliance

Community Story

Rep. John Burkel, Minnesota House of Representatives, Turkey Grower

Rep. Burkel shared photos and stories of the heart-wrenching experience of losing most of his turkey flock in a matter of days to the highly pathogenic avian influenza (HPAI) pandemic of 2015. On April 13, 2015, Rep. Burkel observed that something about his flock seemed "off." He immediately contacted the Minnesota Board of Animal Health and conducted tracheal swabs using materials he had onsite, then sent the results to the University of Minnesota for evaluation. By April 15, tests confirmed the swabs were positive for HPAI, and the turkeys were immediately quarantined. By April 18, Rep. Burkel had lost 99 percent of his flock of 7,000.

The next step in the process was depopulating the remaining flock, including a group of 10-day-old poults, using a lethal foam. The Minnesota Department of Health and the Minnesota Board of Animal Health were involved in the process. A local case manager, rather than a representative from the U.S. Department of Agriculture (USDA), helped Rep. Burkel with swift decision making and response, which likely prevented the infection from spreading throughout the area. No other flocks in the area experienced infection, even though other parts of the state and region had outbreaks.

Rep. Burkel said the stress of the event was significant. Following depopulation, he took charge of composting the remains, working closely with state authorities and industry representatives to comply with guidelines. The composting process was followed by thorough cleaning and disinfection of the premises. Rep. Burkel's entire family helped with the cleaning processes, recognizing that the sooner it was accomplished, the sooner the business could restart. After cleaning and testing to ensure that no infectious material remained, the business began repopulating in mid-July 2015. Rep. Burkel salvaged about one-third of his normal production

year in 2015 and rebuilt the enterprise, in part with support from the state's disaster assistance program, which provided low-interest, 10-year loans and other assistance.

Discussion

Rep. Burkel noted that although his farm followed good biosecurity practices, he believes that the virus came from wild birds, possibly aided by the unusually warm and windy weather, and that he might have tracked the virus into the barn on his shoes. He added that his farm is located many hours away from the other outbreaks in the region. Rep. Burkel said that the flock's bedding material contained sunflower and other seeds that might have attracted wild birds. He has since switched to organic wood shavings exclusively.

The farm eventually returned to full production in 2016. Rep. Burkel noted that everyone in the industry is on high alert in light of new avian influenza strains and the upcoming spring wild bird migration. His farm has increased biosecurity practices and taken steps to ensure that all employees know the protocols and remain mindful of potential breaches.

Rep. Burkel described the process of receiving financial assistance, which involved getting an appraisal of the value of the flock to facilitate compensation. Having materials on site enabled him to quickly test the flock for infection, which helped to swiftly move the process forward. Although HPAI draws a lot of attention, less-pathogenic influenza viruses circulate frequently among poultry. Growers are aware of the threat and test when signs of infection appear, said Rep. Burkel. Surveillance is generally effective, and Minnesota has had plans in place for managing avian and swine influenza outbreaks for decades, he added.

Avian Influenza: 2014–2015 HPAI Outbreak

H5N1 Avian Influenza in Humans, 1997–2021: Anticipate, Recognize, Act

Daniel Lucey, M.D., M.P.H., Georgetown University

According to the World Health Organization (WHO), since 2003, there have been 863 confirmed cases of H5N1 influenza in humans and 455 deaths. No sustained, person-to-person transmission has been reported. Stemming the spread of the virus requires anticipation, recognition that infected birds can infect humans, and action. The virus is typically susceptible to oseltamivir. Secondary bacterial pneumonia is not commonly reported.

Dr. Lucey said the first cases of H5N1 HPAI were reported in China in 1996, and the first cases in humans were identified in 1997. It is now endemic in poultry there with occasional cases in humans. Vietnam experienced an outbreak in 2003 and 2004, and H5N1 has since become endemic in poultry in that country. The Vietnam 2004 H5N1 isolate was used to make the vaccine that currently resides in the U.S. Strategic National Stockpile, and Dr. Lucey said he is skeptical that vaccine would be effective against current mutations of the virus. Thailand rapidly addressed a 2004 outbreak with comprehensive action and has reported no additional cases in humans. In 2005, the United States initiated pandemic preparedness and global actions against H5N1 in more than 100 countries. The highest case fatality rates have been reported in Indonesia (80 percent) and the lowest in Egypt (33 percent), where the population has rapid access to diagnostics for birds and humans and to oseltamivir for treatment and prophylaxis.

Dr. Lucey outlined gain-of-function research conducted in 2010 and 2011 that provided insight on the capacity of H5N1 virus to mutate and transmit among mammals. He emphasized the importance of anticipation because the next significant virus likely exists already.

Federal Response to the 2015 Outbreak

Fidelis N. Hegngi, D.V.M., Animal and Plant Health Inspection Service (APHIS), USDA

Dr. Hegngi emphasized that the United States has one of the strongest systems in the world for detecting animal disease outbreaks and preventing their spread, which is key to preventing human infection. For avian influenza, USDA surveillance mechanisms cover agricultural poultry production, live bird marketing systems (also called wet markets), backyard flocks, and wild birds, among others. Ensuring the safety of responders is a primary consideration. As he described the steps for addressing outbreaks, Dr. Hegngi noted that emergency vaccination might be considered in severe outbreaks. However, it would prohibit other countries from importing U.S. poultry and has never been used in U.S. flocks.

The 2014–2015 H5N1 HPAI U.S. outbreak affected birds in 21 states and resulted in depopulation of more than 50 million birds in commercial poultry systems, representing the most significant animal health event ever in the United States. The U.S. HPAI National Response Plan requires USDA to activate an incident command system. The outbreak response illustrated the benefit of establishing an incident management team that would be available for future outbreaks; creating a rotation schedule for responders that involves some overlap to enhance communication; maintaining consistency through protocols and standard procedures; and establishing local site managers to help growers understand the remediation processes. Notably, responders must recognize the economic and emotional strain such events place on growers.

By working with affected producers, states, and academic institutions throughout the outbreak, APHIS gathered information to develop a biosecurity self-assessment tool, education and reference materials, and a list of 14 biosecurity principles for preventing disease. Producers can use the principles to design site-specific biosecurity plans.

Dr. Hegngi concluded that USDA continues to work on increasing biosecurity; enhancing surveillance and rapid detection; expanding response capacity at all levels; supporting research into new, more efficient methods of humane euthanization and disposal; and improving public communication. He emphasized that there is no single source of transmission, but more stringent biosecurity measures benefit everyone and help contain the spread of infection.

State Public Health Response to HPAI Outbreak

Joni Scheftel, D.V.M., M.P.H., Dipl. ACVPM, Minnesota Department of Public Health

Minnesota, the largest turkey producer in the country, was hardest hit by the 2015 HPAI outbreak. The Minnesota Department of Public Health has a seat on the state's Board of Animal Health and was fully involved in the planning and response to the HPAI outbreak. Existing collaborations offered an understanding of industry perspectives and an opportunity to build relationships with animal health experts that proved valuable in the 2015 response effort.

Dr. Scheftel noted that the outbreak posed no threat to food safety or the general public; rather, the focus was on maintaining occupational safety among poultry workers. The department

recommended that workers receive the seasonal influenza vaccine and use personal protective equipment (PPE) to minimize exposure. Department personnel interviewed poultry workers about their contacts and use of PPE, assessed their exposures, and recommended antivirals according to CDC recommendations. Interviews were critical to understanding and monitoring the situation, clarifying recommendations, and providing emotional support. Dr. Scheftel said that ongoing monitoring via phone, email, and text messaging was time-consuming but strongly appreciated. Fact sheets were translated into languages common among Minnesota poultry workers (Spanish and Karen). Ongoing surveillance revealed two small outbreaks of infectious disease (Campylobacteriosis and influenza B) but no avian influenza.

Cooperation between poultry companies and occupational health experts contributed to the success of the effort. Minnesota shared its materials and protocols with other states affected by the outbreak. The use of text messaging was innovative at the time and spread widely, leading to automated systems for monitoring health. The incident revealed the challenges of identifying and contacting state and USDA responders rather than relying on them to self-monitor.

Minnesota is planning its response to an anticipated 2022 H5N1 HPAI outbreak by convening industry, local, state, and federal stakeholders; emphasizing PPE use; encouraging producers to prepare contact lists in advance; standing up databases and mechanisms for automated daily monitoring; and planning phone interviews. Dr. Scheftel underlined the clear need for public health agencies to be full partners in HPAI response.

Industry Response to Avian Influenza Outbreaks

Michelle Kromm, D.V.M., M.P.H., M.A.M., Food Forward, LLC

Dr. Kromm explained that the poultry industry is organized around a just-in-time delivery system, with schedules set weeks to years in advance to ensure supply. No operations are designed to hold birds or products beyond the time needed for normal supply situations. In case of a disease outbreak, responders come from around the country and industry representatives play a key role in explaining how local operations and supply chains work. Good, transparent communication is important to contain the outbreak and minimize the economic impact.

A number of adjustments to policies and practices emerged in response to the 2015 HPAI outbreak. For example, Minnesota had diagnostic tools for HPAI but doubled daily testing and focused on new infections in at-risk populations to resolve laboratory capacity barriers. Electronic mechanisms for indemnity were implemented and streamlined, so that producers faced fewer hurdles in the process. Capacity for depopulation during the outbreak was insufficient; there is now a joint expectation for collaboration to depopulate quickly. Stakeholders are working together to address repopulation in the face of a prolonged outbreak.

During the outbreak, frequent, regular meetings between industry representatives and the unified command leaders helped determine how to disseminate limited resources to minimize disease spread. Collaboration around communication ensured that all the stakeholders delivered a united message that poultry was safe to eat, which in turn allowed all stakeholders to focus on the response.

In the aftermath, stakeholders determined that more active surveillance was needed during bird migration seasons, paid for by the industry. Through broad active and passive surveillance, index cases of various avian influenza viruses can be identified and addressed early. Dr. Kromm commented that birds can develop secondary bacterial pneumonia and are more susceptible to it as a result of COVID-19 infection. Treatment for bacterial disease in poultry could contribute to AMR. In conclusion, Dr. Kromm said that collaboration, communication, and planning are key, but stakeholders must have flexibility to respond to the unique demands of an outbreak.

Discussion

Although the science exists to develop avian vaccines, export restrictions prevent use of vaccines in U.S. flocks. Moreover, the United States supplies the genetic material for poultry around the world, which further prevents the use of vaccines. However, Dr. Hegngi noted, European poultry producers have been devastated by HPAI and thus might be more amenable to vaccines in the future.

Dr. Lucey reiterated that secondary bacterial pneumonia does not seem to have contributed very much to deaths or illness from H5N1 influenza, but if the virus achieved sustained transmission, then that could change and affect AMR. Partial or complete resistance to oseltamivir has been reported, so that possibility should be anticipated. None of the presenters were aware of specific work underway to assess birds that were exposed but did not succumb to H5N1 HPAI to understand the genetics of resistance.

Dr. Hegngi emphasized that U.S. surveillance for HPAI is strong, as is surveillance for less-pathogenic avian influenza viruses, capturing most cases. Among backyard flocks, the greater concern is salmonellosis and other bacterial diseases. Dr. Scheftel added that in Minnesota, backyard flocks had very few disease outbreaks until recently. The Minnesota Department of Public Health and its partners are working diligently to educate people with backyard flocks about biosecurity, infection control, and biocontainment.

The presentations all highlighted the need for speedy collaboration and collective action to stop outbreaks. Dr. Scheftel noted that building relationships among stakeholders takes time and an understanding of the varied interests involved. Public health entities are often excluded from animal health response efforts because they do not account for the risks that producers face of losing their commodity. Public health responses that only protect humans at risk for infection are not feasible. Dr. Hegngi described extensive collaboration and preparation to prevent disease spread in wet markets in New York City and elsewhere. National conferences facilitate ongoing communication and information sharing. Dr. Kromm said that building relationships is key so that stakeholders are not meeting each other for the first time in the midst of an emergency.

Dr. Hegngi said that USDA provides information for backyard flock owners on monitoring, testing, and reporting requirements and underwrites the cost of diagnosis. Eradication of the 2015 H5N1 HPAI outbreak cost nearly $1 billion, including $300 million for indemnity and compensation to producers. The event cost the United States $6 billion in trade.

The USDA National Poultry Improvement Plan includes recommendations for limiting interactions between wild and domestic birds. Dr. Hegngi noted that when incidents occur, USDA works with the agency that certifies free range and organic producers to address issues.

2009–2010 H1N1 Pandemic

2009–2010 H1N1 Pandemic Overview and One Health and AMR Implications

Andrew Bowman, D.V.M., Ph.D., The Ohio State University

Dr. Bowman described the emergence of the pandemic H1N1 influenza, which surfaced in swine about a decade before it was detected and transmitted to humans. Once in humans, the virus spread rapidly around the world. In contrast to seasonal influenza, most deaths from H1N1 influenza occurred in people younger than 65 years, possibly because older people had been exposed to a similar strain. Dr. Bowman stated that most pandemic viruses ultimately become endemic, seasonal influenza viruses, replacing the previous seasonal strain, and the 1918 influenza virus was endemic for decades. The 2019–2020 influenza season was marked primarily by the 2009 H1N1 virus and caused significant morbidity and mortality.

From 11 to 35 percent of influenza patients experience secondary bacterial infections or bacterial coinfections. About 75 percent of influenza-related pneumonia includes bacterial coinfection. From 29 to 55 percent of the 2009 H1N1 pandemic mortalities had secondary bacterial pneumonia. Data from 10 years of influenza cases indicated that about two-thirds of patients received antivirals, antibiotics, or both, and they had lower hospitalization rates than untreated patients. Dr. Bowman said that the reasons for practitioner use of antibiotics in these cases remain unclear.

Once H1N1 influenza spread to humans, humans around the world transmitted it back to swine. In swine, influenza viruses from previous pandemics coexist, and swine populations carry a broad diversity of influenza types, mostly resulting from human-to-swine transmission. Influenza A plays a role in about 20 percent of cases of porcine respiratory disease, which also involves several coinfections. Swine experience high morbidity but low mortality unless a secondary infection occurs, so producers focus heavily on controlling disease spread. Dr. Bowman concluded that bidirectional transmission of influenza between humans and swine has a significant effect on population health and is expected to continue, so tackling disease spread at the interface is key.

Federal Response to the H1N1 Pandemic

James Lawler, M.D., M.P.H., University of Nebraska Medical Center

Recognition of pandemic influenza is always delayed, Dr. Lawler stated. By the time the 2009 H1N1 virus was detected in the United States, a huge outbreak had been underway for weeks—despite the fact that some cases had been identified early as part of an ongoing study. Successfully addressing such a public health emergency involves developing a plan rapidly. In 2009, responders quickly created a national strategy aimed at mitigating the effects of the disease, slowing the spread, and protecting social and economic functioning. Planners projected possible trajectories, using historic data, various models, lessons learned from the 2018 and 1976 influenza pandemics, and strategic pandemic response planning that began in 2005. During the

2009 outbreak, the CDC incident management system included a team of experts, some of whom had been involved in the CDC response to the 1976 influenza outbreak.

Dr. Lawler maintained that historical perspective is important because nothing is new. The concepts of flattening the curve of infection and the fundamentals for managing COVID-19 were also applied in 2009. Once the 2009–2010 H1N1 pandemic subsided, retrospective analysis confirmed that the projections made as part of national strategic planning were very accurate. The total U.S. morbidity and mortality—61 million cases and 12,000 deaths—were similar to that of a mild seasonal influenza virus, but because many of the victims were young or middle-aged (rather than elderly, as with seasonal influenza), the toll in adjusted life years lost was much worse than usual. During the pandemic, focusing on the potential impact on younger people led responders to push for active distribution of antivirals to mitigate the effects.

Finally, Dr. Lawler highlighted the importance of high-level leadership in responding to pandemics. Leaving emergency planning to state and local entities in the midst of the COVID-19 outbreak led to disjointed and inefficient execution, he said. The national-level pandemic planning that took place from 2005 to 2006 drove the 2009 planning and response, so federal responders were well positioned to oversee state and local activities and coordinate a coherent response. Even at the federal level, leaving decisions to individual agencies results in turf battles and blocks attention to larger strategic elements. The response to pandemic and emerging infectious diseases ultimately falls on elected leaders, not public health officials, said Dr. Lawler, and those leaders need sufficient technical insight from knowledgeable experts to guide a coordinated response.

Swine Industry Response to and Impacts of the H1N1 Pandemic

Heather Fowler, Ph.D., V.M.D., National Pork Board

Dr. Fowler illustrated the industry's One Health approach to disease response, which focuses on pig health, worker health and safety, and public health. The principles translate into validated practices that are implemented through the Pork Quality Assurance Plus program and the Transport Quality Assurance program.

When the 2009 H1N1 influenza outbreak began, the National Pork Board had an influenza working group in place with representation from various agencies and state and federal partners. It created a crisis response team and developed a response plan. The main goal of response was ending the pandemic, and a key objective was communicating to the public that pork remained safe to eat. The Board developed materials for producers on how to protect their pigs, improve biosecurity, participate in surveillance, and prevent disease transmission. The Board sought to be open and transparent about modern practices for recognizing, controlling, and preventing the spread of disease. Another vital step was addressing misinformation by educating producers and consumers domestically and internationally.

Although response was swift and the pandemic ended relatively quickly, producers lost equity and revenue and suffered from disruptions in exports. From April 2009 to April 2010, the industry lost about $2 billion in revenue. The experience underscored the need to maintain relationships that support a One Health approach. The USDA national swine influenza virus surveillance program gathers information from regulatory agencies and industry to create reports

that can be shared with producers and inform disease prevention efforts. The industry engages with state partners on influenza research to understand the transmission and evolution of viruses. Broad partnerships provide opportunities to share information, strengthen relationships, and engage new communities.

Discussion

Dr. Bowman observed that the industry needs more rapid diagnostics. Currently, some practitioners might provide antibiotics because they feel pressured to do something to prevent secondary infection, even if they do not know whether the primary infection is viral or bacterial. Dr. Fowler agreed that early disease detection is key. She said that the National Swine Veterinary Conference provides a forum for disseminating research, education, and best practices.

Dr. Bowman pointed out that endemic influenza is common in swine production, and producers are willing to vaccinate swine herds to control it. Much discussion is underway about the possibility of eradicating endemic influenza in sow herds, which could have a dramatic effect downstream. Dr. Bowman noted that producers are frustrated by current limited vaccine options. Dr. Lawler added that a cost-benefit analysis drives the willingness to vaccinate swine: one chicken is worth only a few dollars, yet one pig can draw hundreds of dollars. Dr. Fowler said that the return on investment is part of decision making, but producers also consider their options and downstream effects.

Dr. Fowler offered some steps for bolstering the One Health approach, such as sharing stories about effective One Health efforts, inviting stakeholders to engage in research or participate in online or in-person tours with producers, and encouraging experts to ask questions of their knowledgeable colleagues. She encouraged more conversation and openness to learning.

1918 Influenza Pandemic

Understanding the Scale of the 1918 Pandemic and the Role of Bacterial Coinfections on Mortality

Jeffery Taubenberger, M.D., Ph.D., National Institute of Allergy and Infectious Diseases, National Institutes of Health

From 1918 to 1919, influenza killed 50 million to 100 million people worldwide, including 675,000 people in the United States. Of the approximately 100,000 U.S. troop casualties during World War I, about 43,000 were deaths from influenza. Researchers who recreated the 1918 virus found that unlike most human influenza viruses, the 1918 virus was pathogenic for almost every animal model. In addition, it is estimated that at least 94 percent of cases in humans involved secondary bacterial infection.

Dr. Taubenberger explained that the 1918 virus damaged the lungs, causing viral pneumonia, which was widely reported in the medical literature at the time. Such infection was severe but rarely fatal, according to autopsy reports. Instead, secondary bacterial pneumonia caused most of the influenza-related deaths. Similarly, in 2009, H1N1 virus caused primary lung damage, and bacterial pneumonia led to death. In 2009, many patients faced methicillin-resistant *Staphylococcus aureus*, most of which was community-acquired. Some experimental animal

research on copathogenesis of the 1918 influenza virus found that it caused severe morbidity in animals, and the addition of streptococcal pneumonia proved fatal. Dr. Taubenberger added that bacteria have a more complicated genomic makeup than influenza viruses, and bacterial virulence can change in response to the environment.

Analysis of the COVID-19 pandemic revealed similarities with the 1918 influenza virus, although secondary pneumonia is not as closely related to fatalities from COVID-19. Understanding the interplay between virulent influenza infection and secondary infections is important to planning future pandemic response, said Dr. Taubenberger.

Public Health Policy and the Public's Behavior During Pandemics

Nancy Bristow, Ph.D., University of Puget Sound

Dr. Bristow observed that the current pandemic was comparable to the 1918 influenza pandemic in terms of the lack of preparedness, inadequate response, politicization, and inequity. She stated that in 1918, Americans had confidence in the ability of medicine and public health measures to protect the populace based on recent successes in bacterial disease treatment and new community hygiene measures that improved public health. World War I heightened awareness of and respect for the burgeoning profession of public health.

The first wave of the 1918 pandemic influenza went largely unnoticed outside of the military. The second wave struck rapidly and caused severe and visible symptoms, and even individuals who seemed to recover could die from secondary pneumonia. Most of the victims were ages 20–40 years. Public health officials attempted to control the chaos, and federal agencies offered guidelines, but state and local responses varied. First steps included education and recommendation of basic preventive measures, followed by increasingly restrictive steps, such as closing public gathering places. Many localities followed closure recommendations; fewer were willing to impose mask-wearing or quarantines.

As preventive steps moved from voluntary to mandatory, compliance was high, partly because they were framed as patriotic duties and partly because of the confidence in public health and medicine. But some resistance emerged from the beginning; for example, a small number of people decried the preventive measures as tyrannical overreach by the federal government.

Dr. Bristow noted the tendency of public health leaders at the time to mislead and misinform the public out of a desire to maintain calm. People resisted some protective measures because the problem was not clearly described and because officials overpromised what public health could do to ensure community safety. High expectations soon led to disappointment. In addition, effective nonpharmacologic interventions were often overlooked in the midst of the pandemic. Eventually, public compliance worsened. For example, Seattle and San Francisco saw anti-mask protests, and courts heard challenges to the closures of theaters, churches, and schools.

Racial injustice and prejudice also played a significant role in the 1918 pandemic. African Americans were often excluded from hospitals or confined to separate wards. Indigenous people were prohibited from leaving their reservations, and their tribal health practices were disregarded. Dr. Bristow highlighted that some aspects of the public response to the COVID-19 pandemic were predictable, but public health in general failed to reckon with the lessons of the

1918 pandemic. She emphasized the need for honesty and transparency, broad preparedness at all levels and across geographic boundaries, depoliticization of the pandemic and the response, and rectification of longstanding health inequities.

Discussion

Dr. Taubenberger said that the reasons why younger people were more likely than others to die from the 1918 influenza virus remain unclear. He noted that mortality among older people was less than expected, suggesting that exposure to prior years' virus strains had some protective effect. Dr. Taubenberger added that children ages 5–10 years had the highest infection rates and the lowest mortality rates.

Dr. Bristow acknowledged that public health messaging is very difficult. She noted that some communities, such as Milwaukee and Seattle, did very well during the 1918 pandemic, achieving good community cooperation and relatively low mortality rates. One effective approach was to signal to the community from the outset that more restrictive measures would be needed if the situation did not improve, ramping up response as needed. Dr. Bristow noted that people want to be reassured, and doing so gains public favor, but public health messaging must be clear and truthful.

Dr. Bristow said that the lack of good data on death rates hampered the ability to address the inequities of care that occurred during the 1918 pandemic. As the COVID-19 pandemic emerged, widely available data quickly highlighted inequities already known to exist. The strong desire to return to normal could result in a lost opportunity to make needed changes. Dr. Bristow urged participants to fight against the urge to move on.

Dr. Taubenberger said that the 1918 pandemic spread quickly throughout military camps. However, in the United States and globally, mortality rates were similar among young and middle-aged adults, regardless of gender. After the pandemic ended, public health and military experts in the United States, Europe, Australia, and elsewhere conducted extensive investigations and extremely comprehensive studies. The results of those efforts are available today, and Dr. Taubenberger hoped that similar efforts would be undertaken to assess the current pandemic.

Remarks from Panel Moderators

Dr. Apley, who moderated the panel on the 2014–2015 HPAI outbreak, noted the recurring themes of the importance of communication and its effect on behavior. He acknowledged that many lessons must be learned about communication and how to address social issues related to health.

Paul Plummer, D.V.M., Ph.D., DACVIM, DECSRHM, who moderated the panel on the 2009–2010 H1N1 pandemic, also noted the emphasis on communication. He highlighted the important One Health perspectives raised by presentations that discussed the human–animal interface and species-specific disease management approaches. He appreciated the attention to bidirectional transmission, which is often overlooked. The panelists raised the need for better, faster diagnostics on which to base immediate decisions and for management interventions and alternatives to antibiotics, all of which have been raised in discussions about improving antibiotic stewardship. Dr. Plummer noted that mechanisms exist to accelerate the development of

antibiotics and diagnostics for humans, although more are needed. In animal and plant health, such efforts are hindered by the lack of resources and opportunities. Both fields would benefit from the development of new diagnostics that are cost-effective, available at the point of care, and integrated with biosecurity measures.

Dr. Blaser, who moderated the panel on the 1918 influenza pandemic, said that the COVID pandemic underscored that public health matters and that how public health messages are communicated matters. The best available tools are not helpful if they are not used. With COVID-19, an effective vaccine is available, but a substantial proportion of the population does not believe in it. As a result, people are not benefiting from the great science that has been conducted.

Dr. Blaser added that the panels underscored the importance of rapid, accurate diagnosis so that people can make informed decisions. Pandemics are dynamic and do not follow an expected course, so public health entities must be prepared to communicate about an emerging and changing situation. The panels also demonstrated the importance of secondary bacterial infections during viral outbreaks.

Dr. Blaser noted that in the 20th century, most epidemic diseases were viral, compared with previous bacterial epidemics, such as cholera and typhoid. It is possible that vaccines could be the solution to future viral epidemics, and COVID-19 demonstrated the capacity of researchers to isolate a virus and produce a vaccine in a matter of days.

Public Comment: Innovation Spotlight

Dr. Musmar explained that the Innovation Spotlight is an opportunity for public comment open to all those with relevant new and emerging technologies they wish to present to the Council. The Council does not endorse or sponsor any of the companies or products described.

Kyle Bozentko of the Center for New Democratic Processes described his organization's work to involve the public in policy decision making in a meaningful way through an innovative approach to patient-centered research that engages the public. For example, the organization convened a citizen's jury in Liverpool, England, that was charged with exploring attitudes about public–private collaborations to monitor and address AMR, and the results are informing the development of a multiparty data surveillance project led by Health Innovation Liverpool to investigate and tackle AMR. A citizen's jury provides useful data for policymaking. It promotes diversity and equity by involving a broadly representative group of citizens. Individuals assess the tradeoffs, guide research and development, and establish acceptable parameters for policies and practices (in this case, data access and use). Such an approach is critical to AMR data initiatives, including those using artificial intelligence, because it provides insights on how to monitor AMR without causing harm. In the United States, such data initiatives are a challenge because there is no central health database from which to draw. Mr. Bozentko said that the challenge can be overcome by engaging people impacted by and historically excluded from decision making. He anticipated future opportunities for collaborative, patient-centered research partnerships that involve government and public health agencies, academic and research institutions, pharmaceutical and biomedical companies, and AMR-focused collaborative bodies.

Bradley Burnam of Turn Therapeutics explained that he worked in medical device sales for 10 years, during which he acquired an antibiotic-resistant infection in a hospital setting. He endured multiple surgeries and saw firsthand the lack of innovation in addressing skin infections. Mr. Burnam identified a liquid biocide used primarily as a preservative in cosmetics and a liquid wound cleanser that was used in Europe. He patented a process for combining them with a petroleum carrier to create Hexagen, a topical treatment approved by the U.S. Food and Drug Administration (FDA) for chronic wound care in 2016. Mr. Burnam said that the triple-antibiotic ointment Neosporin was never approved by FDA for treating skin infection; rather, FDA allowed such use through a grandfathering clause. The overuse of Neosporin has resulted in high allergy and resistance rates. Hexagen has the same consistency as Neosporin but includes no antibiotic. It offers broad-spectrum efficacy against WHO-designated priority pathogens and has not been shown to lead to resistance. Clinical trials are scheduled for this year to determine the therapeutic effectiveness of Hexagen for skin infections, which would make it the first product of its kind in that respect.

Public Comment

Lisa Morris of Consana Health described the role of senior care pharmacists, who provide expert advice on medication use, specifically for older adults, in various settings. During the pandemic, senior care pharmacists and long-term care pharmacies have played a critical role in the successful deployment, administration, and reporting of COVID vaccines. More than 229.2 million doses of COVID vaccine have been administered and reported by pharmacies across programs in the United States, and of those, 8 million doses were administered onsite to long-term care facilities in the early days of the vaccination program. The numbers make it clear that there is an ongoing role for pharmacists in deploying, administering, and reporting any vaccine, not just COVID. Ms. Morris said it is important to ensure that pharmacists can support others in administering care. Pharmacists should be recognized as providers of vaccine services under Medicare Part B and state Medicaid programs so that operations can be scaled up in times of need to improve domestic and global health outcomes. Senior care pharmacists have a critical role in combating AMR wherever older adults reside or receive care. Senior care pharmacists facilitate evidence-based communication among providers, prescribers, and nurses. They develop, disseminate, and implement clinical practice guidelines for common infectious diseases and encourage prescribers to review antimicrobial regimens and stewardship routinely.

Ms. Morris said that senior care pharmacists also conduct pharmacokinetic monitoring and focus on increasing conversion and use of oral instead of intravenous antibiotics, seeking the shortest effective duration of antibiotic use to reduce resistance. She emphasized that antimicrobial stewardship is not about withholding treatment but rather using knowledge to provide the most effective antibiotic for the optimal duration for the best outcomes and to preserve the efficacy of antibiotics for others. Recognizing the skill set of senior care pharmacists could pave the way for better future outcomes and quicker response to future pandemics, Ms. Morris concluded.

Final Comments and Adjournment

Martin Blaser, M.D., Chair, and Michael D. Apley, D.V.M., Ph.D., DACVCP, Vice Chair

Dr. Blaser thanked the participants and presenters for providing a lot of useful material to increase understanding of future pandemics and their relationship to AMR. He reiterated his

gratitude to those members leaving the Council and looked forward to the contributions of new members. Dr. Apley thanked the Council staff for their excellent efforts. Dr. Blaser adjourned the meeting at 3:07 p.m.

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

March 2, 2022

PACCARB Voting Members Present
Martin J. Blaser, M.D., Chair
Michael D. Apley, D.V.M., Ph.D., DACVCP
Stephanie Black, M.D., M.Sc.
Helen W. Boucher, M.D., FIDSA, FACP
Virginia R. Fajt, D.V.M., Ph.D., DACVCP
Paula J. Fedorka Cray, Ph.D.
Christine Ginocchio, Ph.D., MT
Locke Karriker, D.V.M., M.S., DACVPM
Elaine Larson, Ph.D., RN
Ramanan Laxminarayan, Ph.D., M.P.H.
Payal K. Patel, M.D., M.P.H.
Paul Plummer, D.V.M., Ph.D., DACVIM, DECSRHM
Julia E. Szymczak, Ph.D.
David White, M.S., Ph.D.

Organizational Liaisons Present
American Association of Extension Veterinarians
Carla L. Huston, D.V.M., Ph.D., Dipl. ACVPM

American Veterinary Medical Association
Joni Scheftel, D.V.M., M.P.H., Dipl. ACVPM

Biotechnology Innovation Organization
Emily Wheeler

Healthcare Infection Control Practices Advisory Committee
Lisa Maragakis, M.D., M.P.H.

Minor Crop Farmer Alliance
James Adaskaveg, Ph.D.

Pediatric Infectious Diseases Society
Jason Newland, M.D., M.Ed.

Society of Infectious Disease Pharmacists
Elizabeth Dodds Ashley, Pharm.D., M.H.S., FCCP, BCPS

Wellcome Trust
Timothy Jinks, Ph.D.

Regular Government Employees Present
U.S. Department of Health and Human Services

Marjory Cannon, M.D. (for Shari Ling, M.D.), Centers for Medicare & Medicaid Services
Dennis M. Dixon, Ph.D., National Institute of Allergy and Infectious Diseases, National Institutes of Health
Lynn Filpi, Ph.D., Office of Pandemics and Emerging Threats, Office of Global Affairs
William Flynn, D.V.M., Center for Veterinary Medicine, Food and Drug Administration
Christopher Houchens, Ph.D., Biomedical Advanced Research and Development Authority, Office of the Assistant Secretary for Preparedness and Response
Rima Khabbaz, M.D., National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention
Melissa Miller, M.D., M.S., FCCM, Agency for Healthcare Research and Quality

U.S. Department of Agriculture
Neena Anandaram (for Emilio Esteban, D.V.M., M.BA., M.P.V.M., Ph.D.), Food Safety and Inspection Service
Chelsey Shivley, D.V.M., Ph.D., DACAW (for Sarah Tomlinson, D.V.M.), Animal and Plant Health Inspection Service
Jeffrey Silverstein, Ph.D., Agricultural Research Service

U.S. Department of Defense
Paige Waterman, M.D., FACP, FIDSA, Walter Reed Army Institute of Research

U.S. Environmental Protection Agency
Jay Garland, Ph.D., Center for Environmental Solutions and Emergency Response

Designated Federal Official
Jomana F. Musmar, M.S., Ph.D., Advisory Council Committee Manager, Office of the Assistant Secretary for Health (OASH), Department of Health and Human Services (HHS)

Advisory Council Staff
Mark Kazmierczak, Ph.D., Gryphon Scientific
Haley Krem, Committee Management Officer, OASH, HHS
Chloe Loving, M.P.H., CHES, CPH, ORISE Fellow, HHS
Sarah McClelland, M.P.H., Public Health Advisor, OASH, HHS
Taylor Simmons, M.P.H., ORISE Fellow, HHS

Glossary of Abbreviations

APHIS	Animal and Plant Health Inspection Service
AMR	antimicrobial resistance
CDC	Centers for Disease Control and Prevention
COVID-19	coronavirus disease 2019
FDA	U.S. Food and Drug Administration
HHS	U.S. Department of Health and Human Services
HPAI	highly pathogenic avian influenza
OASH	Office of the Assistant Secretary for Health
PACCARB	Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria
PPE	personal protective equipment
USDA	U.S. Department of Agriculture
WHO	World Health Organization