NVAC NATIONAL VACCINE ADVISORY COMMITTEE

September 17–18, 2019, Meeting Minutes

Committee Members in Attendance

Robert H. Hopkins Jr., M.D., MACP, FAAP; Chair
Melody Anne Butler, B.Sc.N., RN
Timothy Cooke, Ph.D.
John Dunn, M.D., M.P.H.
David Fleming, M.D.
Leonard Friedland, M.D.
Ann Ginsberg, M.D., Ph.D.
Mary Anne Jackson, M.D., FAAP, FPIDS, FIDSA
Melissa Martinez, M.D., FAAFP
Cody Meissner, M.D., FAAP
Larry Pickering, M.D., FAAP, FIDSA

NVAC Ex Officio Members

Limone Collins, M.D. (for Tonya Rans, M.D.), Department of Defense (DoD)
Mary Beth Hance (for Jeffrey Kelman, M.D., M.M.Sc.), Centers for Medicare and Medicaid Services (CMS)
Troy Knighton, M.Ed., Ed.S., LPC, Department of Veterans Affairs (VA)
Linda Lambert, Ph.D. (for Rick Bright, Ph.D.), Biomedical Advanced Research and Development Authority (BARDA)
Valerie Marshall, M.P.H. (for Marion Gruber, Ph.D.), Food and Drug Administration (FDA), *day two only*
Justin A. Mills, M.D., M.P.H., Agency for Healthcare Research and Quality (AHRQ)
Barbara Mulach, Ph.D., National Institutes of Health (NIH)
Sam Posner, Ph.D., (for Nancy Messonnier, M.D.) Centers for Disease Control and Prevention (CDC)
Mary Rubin, M.D., (Division of Injury Compensation Programs (DICP), Health Resources and Services Administration (HRSA)
Judith Steinberg, M.D., M.P.H., Bureau of Primary Health Care (BPHC), HRSA

NVAC Liaison Representatives

James S. Blumenstock, Association of State and Territorial Health Officials (ASTHO)
Gina Charos, Public Health Agency of Canada (PHAC)
Rebecca Coyle, M.S.Ed., American Immunization Registry Association (AIRA)
John Douglas, M.D., National Association of County and City Health Officials (NACCHO)
Kristen R. Ehresmann, RN, M.P.H., Association of Immunization Managers (AIM)
Nathalie El Omeiri, Ph.D., Pan American Health Organization (PAHO)
Hana El Sahly, M.D., Vaccine and Related Biological Products Advisory Committee
Brian Wall, Pharm.D. (for Jean-Venable "Kelly" Goode, Pharm.D., BCPS, FAPhA, FCCP), American Pharmacists Association (APhA)
Christopher Regal, M.S., America's Health Insurance Plans (AHIP), *day one only*

Acting Designated Federal Officer

Ann Aikin, M.A., Office of Infectious Disease and HIV/AIDS Policy (OIDP), Department of Health and Human Services (HHS)

Proceedings
Day One—September 17, 2019

Call to Order and Rules of Engagement—Ann Aikin, M.A., Acting Designated Federal Officer, OIDP, HHS

Ms. Aikin called the meeting to order at 9:07 a.m. and welcomed the participants. She briefly outlined the agenda and described key parts of the Federal Advisory Committee Act, its conflict-of-interest rules, and standards of ethical conduct for NVAC members. Ms. Aikin thanked the NVPO staff for their support in organizing the meeting and called the roll.

Office of Infectious Disease and HIV/AIDS Policy (OIDP) Update—Tammy R. Beckham, D.V.M., Ph.D., Director, OIDP

Dr. Beckham welcomed David Kim, M.D., the new director of the Division of Vaccines and Immunization at OIDP, and Tommy Acciani, Ph.D., a research consultant who is supporting NVAC. OIDP is implementing and expanding HHS's strategy for improving human papillomavirus (HPV) vaccination. The HPV Roundtable recognized HHS' communications efforts, led by Ms. Aikin and Jordan Broderick, which stemmed from NVAC's recommendations to improve HPV vaccination rates.

Through regional stakeholder meetings on the National Adult Immunization Plan, OIDP gathered input from nearly 500 stakeholders in almost every state. The meetings sparked activity at the regional and national levels to establish or revive coalitions and offer training on using immunization registries, among other efforts. Several states strengthened the partnerships between their corrections and health departments as a result of the stakeholder engagement. The final National Adult Immunization Plan will be presented to NVAC next year.

Dr. Beckham looked forward to NVAC's recommendations for the next *National Vaccine Plan*. She thanked the Working Group (WG) for taking on a difficult task with a very short timeline.

Chair's Welcome—Robert H. Hopkins Jr., M.D., MACP, FAAP, NVAC Chair

Dr. Hopkins welcomed the participants to the public meeting, which was accessible by webcast and telephone. He described the meeting proceedings and the agenda for this meeting. The minutes of the June 5–6, 2019, meeting were approved by a majority of NVAC members.

Written comments can be sent to NVAC for consideration by e-mail (mnvac@hhs.gov). The agenda, minutes, and presentations of past meetings are available online. In 2020, NVAC is scheduled to meet on February 13–14, June 9–10, and September 23–24. (See the appendix for a list of abbreviations used in this report.)

Opening Remarks—ADM Brett P. Giroir, M.D., Assistant Secretary for Health (ASH), HHS

Dr. Giroir observed that it has been a challenging year for promoting immunization, with several outbreaks of vaccine-preventable diseases around the world, which the World Health Organization (WHO) deemed a top global health threat. He expressed dismay about the resurgence of measles, which had been eliminated in the United States. More than 75 percent of measles cases in the United States were linked to the outbreak in New York City. Public health workers, clinicians, and other stakeholders there worked hard to address and contain the outbreak.

The city estimates it spent more than $6 million and deployed over 500 staff for the response. The highly contagious virus spread rapidly in insular communities with pockets of unvaccinated and undervaccinated people. Clearly, there are opportunities to improve public awareness of the value of immunization to avoid future outbreaks, Dr. Giroir said.

The United States has also been experiencing a widespread hepatitis A outbreak, with 30 states reporting more than 25,000 cases, 15,000 hospitalizations, and 259 deaths since 2016. Vaccinating as recommended for hepatitis A is important, said Dr. Giroir.

In addition, the country experienced one of the longest influenza seasons in a decade, with activity continuing into May. Influenza has public health and economic implications, ranging from school attendance and employee absenteeism to the extreme strain on the health system. During the 2018–2019 influenza season, about 37 million people were ill, 500,000 were hospitalized, and 36,000 died from influenza. Annual vaccination remains the single best way to prevent influenza and related complications. Improving the approach to influenza, vaccines, and the infrastructure for pandemic response are of great importance to HHS, Dr. Giroir emphasized.

An August 2019 HHS report found an increase in HPV-associated cancers. Vaccination can prevent 92 percent of HPV-associated cancers, but only 51 percent of teens are fully vaccinated. On the positive side, the National Cancer Institute found that vaccinating women and girls provides some herd protection that extends to unvaccinated adult men (although not to unvaccinated women). Dr. Giroir said these findings reinforce the urgency of preventing HPV cancers, the societal benefits of vaccination, and the need to advance the national strategy launched by HHS, based on NVAC recommendations, to improve U.S. HPV vaccination rates.

Promoting vaccination and raising vaccine confidence are among HHS' top priorities, Dr. Giroir continued. Recently, HHS Secretary Alex M. Azar II released a video for National Immunization Awareness month highlighting the importance of staying up to date with childhood vaccines. Dr. Giroir's blog offers advice on improving vaccine uptake. Through social media, HHS and its partners are raising awareness about the benefits of vaccines.

Due to feedback from partners, including NVAC members, Dr. Giroir decided to include in Healthy People 2030 objectives that support immunizations across the lifespan and a measure to ensure increased documentation of age-appropriate vaccinations through immunization information systems (IIS). The upcoming revision of Healthy People will serve as a benchmark for immunization and infectious disease prevention, Dr. Giroir observed.

The next National Vaccine Plan will play a critical role in articulating the vision for uniting immunization systems and improving vaccination uptake across the lifespan. Dr. Giroir appreciated NVAC members' providing their time and expertise to help HHS deliver a thoughtful plan with strategic recommendations that will help guide immunization research policy and practice over the next 3–5 years. He believed that the field has laid the foundation for progress toward a new decade of immunization. As examples of progress already made, Dr. Giroir cited early success with an experimental vaccine against Ebola virus in the Democratic Republic of Congo, which is facing an outbreak of the deadly virus. In addition, WHO announced that Africa is expected to be free of wild-type polio in early 2020. Finally, Dr. Giroir praised Dr. Beckham for her leadership of OIDP, which has stepped up to address domestic and global public health threats.

National Vaccine Plan WG Update and Vote—Robert H. Hopkins Jr., M.D., MACP, FAAP, NVAC Chair

Dr. Hopkins reiterated the charge to NVAC. At the June meeting, NVAC members approved the following:

> NVAC recommends that HHS keep five, broad goals in the 2020 National Vaccine Plan to reflect the entire immunization system. After thorough review and discussion, NVAC recommends updating these goals, the rationale for goal inclusion, and the three top priorities for each goal that are poised to make the greatest impact on the U.S. immunization system in the next 5 years.

Also in June, the WG proposed five new goals and accompanying priorities for the National Vaccine Plan. Following input from NVAC members and further deliberations, the WG revised the goals and priorities as follows (revisions are identified with italics):

- Goal 1: Foster innovation in vaccine development and related technologies.
  1. Prioritize the development of innovative vaccines to prevent infectious diseases of *patient and* population health significance.
  2. Enhance systems for vaccine production, storage, and delivery.
  3. *Identify current vaccines in need of improved effectiveness.*
- Goal 2: Continue to leverage the vaccine safety system.
  1. Sustain and enhance current tools, standards, and approaches used to assess vaccine safety.
  2. Develop new methods to rapidly and accurately assess the safety of all recommended vaccines.
  3. Disseminate lessons learned from the vaccine safety system.
- Goal 3: Enhance knowledge of and confidence in routine vaccines and the immunization system.
  1. Research effective communication strategies to reach underimmunized populations, including messaging, outreach strategies, and cultural and linguistic approaches.
  2. Unify and promote vaccination standards across the lifespan.
  3. Enhance the delivery of vaccine safety and effectiveness messages to providers and the public.
- Goal 4: Optimize access to and utilization of all routinely recommended vaccines across the lifespan.
  1. Eliminate geographic, racial/ethnic, and socioeconomic barriers to vaccine access across the lifespan and improve care through quality improvement initiatives.
  2. Increase the use of, and data exchange within, electronic health records (EHRs) and IIS to collect and track immunization data, support clinical decision-making, assist with vaccine forecasting, and identify areas of need.
  3. Strengthen public, private, and community-based partnerships and the public health infrastructure to *improve manufacturing capabilities and* delivery of immunizations for routine use and for protection during outbreaks.
- Goal 5: Promote global immunization.
  1. Improve global surveillance for vaccine-preventable diseases and track progress against goals.
  2. Support international vaccine research and development and delivery programs to ensure vaccines are available to address global disease prevention.
  3. Sustain partnerships to prepare for emerging diseases and ongoing vaccine-preventable challenges.

Discussion

Ann Ginsberg, M.D., Ph.D., said the original intent of the revised priority in Goal 1 went beyond identifying which vaccines need improvement. She proposed changing the language to "identify and optimize."

In recognition of WHO calling out vaccine hesitancy as a public health threat, John Douglas, M.D., suggested that Goal 3, Priority 1, include the phrase "reduce vaccine hesitancy."

Troy Knighton, M.Ed., Ed.S., LPC, asked that Goal 4, Priority 2, acknowledge the need for secure data exchange. Rebecca Coyle, M.S.Ed., noted that security is usually part of the package for data exchange.

Ms. Coyle said Goal 4, Priority 3, seems to focus narrowly on manufacturing despite the need to improve overall delivery.

Public Comment

Joe Martinez said that vaccines are the biggest scam in modern history, but the people in this room run from the debate. He said he had 157 peer-reviewed from PubMed showing that vaccines cause autism and another 1,200 studies to support the finding. Nobody is dying from these diseases, said Mr. Martinez. People stopped dying from them long before these vaccines even came out. In 1960, people had more chance of dying from getting stuck by lightning than measles. In 1963, the vaccine came out, and one in 500,000 people were dying. In 1921, there was 0.19-percent chance of getting diphtheria. The diphtheria-tetanus-pertussis vaccine came out in 1940. Seven percent of the population was dying at that point. Now nobody is dying. From 1980 to 2003, there has not been one death from diphtheria, tetanus, or pertussis, Mr. Martinez said. The tetanus vaccine is a complete failure, he added.

Only 1 percent of the adverse reactions that occur are reported to the Vaccine Adverse Event Reporting System (VAERS), Mr. Martinez continued. Vaccines are killing more people than they are helping, he said. Only in places like Africa, where people are drinking out of mud puddles and are vitamin-A deficient, are people dying from these communicable diseases, said Mr. Martinez. He said millions of people are not anti-vaccine but rather ex-vaccinees, because they learned their lesson the hard way. They were forced into this fight, and now they are not backing down; millions of people would not be forced to vaccinate.

Mr. Martinez said he had 13,000 studies, including studies on aluminum and all the adjuvants, all peer-reviewed and published. There are studies of vaccinated versus unvaccinated people that show that vaccinated children are unhealthy, he said. Unvaccinated children in America are far healthier than vaccinated children, and there is no science to show anything other than that, Mr. Martinez said. The influenza vaccine is 85-percent ineffective, said Mr. Martinez, and he believes that people are dying from the vaccine but their deaths are being covered up. He called for an open, scientific debate with people like Suzanne Humphries, Andrew Wakefield, and Neil Miller.

Proposed Changes

Ms. Aikin presented the proposed changes to the WG's goals and priorities (new language in italics):

- Goal 1, Priority 3: Identify *and optimize* current vaccines in need of improved effectiveness.

- Goal 3, Priority 1: Research effective communication strategies to reach underimmunized populations *and address vaccine hesitancy*, including messaging, outreach strategies, and cultural and linguistic approaches.
- Goal 4, Priority 2: Increase the use of, and *secure* data exchange within, electronic health records (EHRs) and IIS to collect and track immunization data, support clinical decision-making, assist with vaccine forecasting, and identify areas of need.
- Goal 4, Priority 3: Strengthen public, private, and community-based partnerships and the public health infrastructure to increase delivery of immunizations for routine use and for protection during outbreaks. (*Revert to previous language*.)

Vote: NVAC members unanimously approved the WG's recommendation with the changes proposed.

The WG was also tasked with identifying new stakeholders to engage in development of the National Vaccine Plan. The WG offered the following recommendations:

- To represent the entire system, NVAC recommends the engagement of stakeholders representing each goal of the National Vaccine Plan and the priorities developed.
- NVAC recognizes the impact of disparities and therefore recommends that stakeholders representing populations at risk for disease be consulted in the development of the next National Vaccine Plan with a focus on underrepresented groups to address disparities that may prohibit vaccine coverage equally across the U.S. population.
- NVAC stresses the need for focused attention on adult and maternal vaccination and recommends engaging stakeholders focused on improving immunization across the lifespan.
- NVAC supports the National Biodefense Strategy and recommends that the ASH and OIDP engage partners working to protect Americans from biological threats and those engaged in responding to current vaccine-preventable disease outbreaks to learn how the system can better support disease threats.

Discussion

Dr. Hopkins noted that, rather than suggest individual stakeholder organizations, the WG created a list of categories of stakeholders (providers, purchasers, patients, academics, policy-makers, manufacturers, and so on) to broaden outreach. Ms. Aikin said the subgroup reviewed a list of proposed stakeholders and provided them to the OIDP for use in developing the stakeholder engagement strategy for the development of the report. Hana El Sahly, M.D., asked whether school districts were recognized as stakeholders. Dr. Hopkins said there was a broader discussion about public health outreach but not schools in particular. He said there was general agreement that educators and administrators play an important part in the childhood vaccination process.

Vote: NVAC members unanimously approved the WG's recommendations.

Experiences in the Field: Pediatric Tetanus Hospitalization Case in Oregon—Judith A. Guzman-Cottrill, D.O., Professor of Pediatrics, Division of Infectious Diseases, Oregon Health and Science University

Dr. Guzman-Cottrill described the first case she and her colleagues had ever seen of tetanus infection in an unvaccinated child. The child, who had received no childhood immunizations, was playing outside on a farm when he fell and cut his head. Six days later, he came to the emergency department with obvious symptoms of tetanus.

Dr. Guzman-Cottrill described the occurrence and spread of tetanus infection. The United States had 197 cases of tetanus infection from 2009 to 2015, with 16 deaths, all in people over age 55 years. Worldwide, WHO estimated more than 34,000 neonatal deaths from tetanus in 2015 alone.

The infected child had impending respiratory failure on arrival, requiring emergency intubation, and was admitted to the pediatric intensive care unit. The child received one dose of tetanus vaccine and antibiotic treatment, but the parents refused any other vaccinations, including the second dose of tetanus vaccine. The child required surgical care, including tracheostomy, followed by mechanical ventilator support for 44 days. Dr. Guzman-Cottrill outlined the cardiac and neurological care provided to minimize the child's severe pain. By day 57 of hospitalization, the child was finally well enough to transfer to an inpatient rehabilitation facility. Follow up one month after the child's discharge from the rehabilitation facility determined that the child was doing well, and the child returned to normal activity soon after.

Dr. Guzman-Cottrill calculated the costs of the 57-day inpatient hospital stay (48 days of which were in the critical care unit) as $811,929. That figure does not include the transportation to facilities, inpatient rehabilitation (17 days), or follow-up outpatient visits. Since Dr. Guzman-Cottrill published this case study, she has been contacted about other cases of tetanus infection.

Discussion

Melody Anne Butler, B.Sc.N., RN, asked why the parents of the affected child continued to refuse vaccination. Dr. Guzman-Cottrill said that some vaccine-hesitant parents get advice from physicians who do not believe in the safety and efficacy of vaccines. However, she has used this case to educate health care providers and the general public about the importance of vaccination. Dr. Guzman-Cottrill and her staff were deeply moved by the severe, prolonged suffering that tetanus infection caused the hospitalized child. Leonard Friedland, M.D., agreed that health care providers, especially younger ones, need to see examples of the real-world effects of vaccine-preventable diseases. Dr. Guzman-Cottrill said she and her colleagues will be publishing a follow-up article describing their care for the child in more detail.

Mary Anne Jackson, M.D., FAAP, FPIDS, FIDSA, described a similar event in her hospital. In that case, the parents allowed the affected child to be vaccinated in the hospital but refused vaccination for the child's siblings.

John Dunn, M.D., M.P.H., called attention to the number of health care providers, including physicians, who do not support vaccination, often because they feel there are conflicting data. It is true that not many people in the United States die from tetanus—as this case illustrates—so people who are against vaccines might see this case as a win. The child was saved by the hospital's care but suffered nearly 2 months of excruciating pain, followed by rehabilitation. Dr. Dunn emphasized the importance of highlighting cases like this to explain that failure to vaccinate can cause severe morbidity, not just mortality.

Dr. Guzman-Cottrill said the child in this case was lost to follow-up. When she cares for children who suffer or die from vaccine-preventable disease, she noted, she spends a lot of time with the parents, which often helps her understand and address their concerns about vaccination. This case was an extraordinary deviation, she noted. Dr. Guzman-Cottrill also observed that this family had minimal interaction with the health care system.

Better Immunity for Better Protection from Infectious Diseases

Overview of Human Immunosenescence)—Al Shaw, M.D., Ph.D., Professor of Medicine, Section of Infectious Diseases, Yale School of Medicine

By 2050, about 88 million people in the United States will be over age 65, making up a large proportion of the population. The same phenomena (the aging population) will have an even larger impact in other parts of the world. Older people have more morbidity and mortality from infectious diseases, and vaccine efficacy is different in older people than younger people. The demographic shift will have a profound impact on health care and on society in general.

Dr. Shaw described the pathophysiology of innate immune response to explain why it becomes less vigorous with aging and why vaccines are less effective in older adults. To improve vaccine response in older adults, the following approaches are being evaluated:

- Higher dose vaccines (e.g., for influenza)
- Alternative vaccine delivery systems (e.g., intradermal)
- Adjuvants that target older adults (e.g., adjuvanted influenza vaccine [Fluad] and adjuvanted zoster vaccine [Shingrix])
- Immunity-bolstering agents (e.g., sirolimus [Rapamycin] analogs, metformin, nicotinamide adenine dinucleotides, and senolytics)

Sex and Gender as Drivers for Better Design and Efficacy of Vaccines—Sabra L. Klein, Ph.D., Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health

Factors influenced by sex, a biological construct, and gender, a social construct, affect males and females differently across the lifespan. Women tend to have more robust immunity to infections than men. Vaccines tend to convey more immunity to women than men. Women have a stronger immune response than men do to a number of common vaccines; they also have more adverse reactions to certain vaccines than men do. Adverse reactions may be a function of reporting bias, and gender may influence reporting. However, biological factors should be considered.

Uptake and completion of the HPV vaccine regimen is higher in females, which might reflect gender bias and stigma associated with HPV vaccination in boys. Sex-specific messaging might be needed, Dr. Klein said. Adverse events are mild but more frequently reported by females; again, biological factors should be considered. Immunogenicity is similar in male and female adolescents but differs in adults.

Women who have injection-site inflammation following influenza vaccine have more inflammation than men do. Women have higher antibody titers in response to influenza vaccine than men. Furthermore, women ages 18–45 years have greater immunity than males of similar age; after age 65, the sex differences disappear, primarily driven by decreased immunity in women but not men. Hormone levels also correlate with influenza immunity; women experience a dramatic reduction in estrogen at menopause, while men have a less drastic decline of testosterone over time. These findings underscore the need to consider how sex differences affect vaccine efficacy, particularly the interaction of sex and age. Dr. Klein asked participants to consider whether all people should get equal doses of vaccine to achieve the same protection.

Acellular Pertussis Vaccine Waning: Impact on Evolving Pertussis Epidemiology—Nicola Klein, M.D., Ph.D., Director, Kaiser Permanente Vaccine Study Center

Dr. Klein summarized findings from an evaluation of electronic medical records from Kaiser Permanente Northern California to assess pertussis rates in California, which had outbreaks in

2010 and 2014. In both, pertussis infection spiked in children 7–10 years of age, but in 2014, adolescents and teens also experienced a spike in cases. Researchers concluded that protection from the fifth dose of acellular diphtheria-tetanus-pertussis (DTaP) vaccine waned, and risk increased each year afterward. Protection from the tetanus-diphtheria-pertussis vaccine (Tdap) booster, recommended at ages 11–12, also waned, with risk increasing afterward by 35 percent per year, on average. Notably, teenagers who received whole-cell pertussis vaccine as children were more protected than teens who received acellular vaccine as children.

Since the 2010 recommendation that all pregnant women receive Tdap vaccination, Kaiser Permanente Northern California has achieved a vaccine uptake rate of 89 percent. Data indicate the Tdap vaccine is 91-percent effective in preventing pertussis in neonates of women who were vaccinated during pregnancy. However, effectiveness drops to 69 percent by the time the infants reach 12 months of age. Evidence is accumulating that the maternally received Tdap interferes with antibody production following infant DTaP doses. However, cases of pertussis among infants in the first year of life are down 76 percent since before routine maternal immunization, supporting the hypothesis that the interference is not clinically significant.

A study of school-age children estimated the risk of pertussis in relation to DTaP vaccine coverage and the number of years since the last DTaP dose. From 2006 to 2017, about 82 percent of cases occurred in children who were age-appropriately vaccinated. Starting at age 19 months, as time passed since the last DTaP dose, the risk of pertussis increased. These data show that immunity played a major role in the recent pertussis outbreaks, Dr. Klein observed.

Although there have been no epidemics since 2014, some small outbreaks have occurred, mostly in teens, so the burden of disease remains. As DTaP cohorts age, pertussis incidence may increase among young adults, especially during periodic outbreaks. There will be an increasing need for improved detection in young adults (especially as they have children) and longer-lasting vaccines.

Improving Vaccine Efficacy with Adjuvants—Wolfgang W. Leitner, M.Sc., Ph.D., Chief, Innate Immunity Section, Basic Immunology Branch, Division of Allergy, Immunology, and Transplantation, National Institute of Allergy and Infectious Diseases (NIAID), NIH

Adjuvants can help overcome some of the limitations of vaccines. For example, adjuvants can not only strengthen immune response but also improve the quality of response to vaccine. They can drive adaptive immune response by promoting T-cell helper cell subsets and inducing cytotoxic T-cell activation. They can overcome waning immunity by extending the immune response duration.

Infants and newborns respond poorly to most vaccines and adjuvants. However, research is promising for two new products—a combination adjuvant that induces toll-like receptor 9 expression and another that targets toll-like receptor 7/8 to overcome the newborn's immunosuppressed state. Dr. Leitner described an intranasally delivered nanoemulsion adjuvant used in an animal study to promote production of more effective antibodies, resulting in a stronger response. The research indicates that pertussis vaccine can be improved by a booster vaccine with a different adjuvant. Mouse studies using existing adjuvants found that one combination was particularly good at inducing long-term immunity against influenza.

Dr. Leitner summarized the overall goals of studying vaccine adjuvants:

- Overcome reduced immunogenicity in vulnerable populations

- Improve vaccine efficacy
    - Increase magnitude and quality of immune response
    - Induce the desired type of immune response
    - Faster onset and longer duration of protection
- Allow vaccine delivery by alternative routes
    - Intranasal, sublingual, oral, transdermal
- Promote dose-sparing

Discussion

Larry Pickering, M.D., FAAP, FIDSA, asked about adverse events involving adjuvants. Dr. Leitner responded that one goal of adjuvant use is to reduce adverse events by uncoupling inflammation from immunogenicity, for example. The more that is known about adjuvants, the more researchers can use them to target defined receptors and minimize adverse events.

Melissa Martinez, M.D., FAAFP, asked how pregnancy affects vaccine immunogenicity. Dr. Sabra Klein said few studies compare vaccination in pregnant and nonpregnant women. Dr. El Sahly said some studies have shown the responses were largely comparable.

Dr. El Sahly asked whether influenza vaccine effectiveness is affected by age or sex. Dr. Sabra Klein said data show distinct differences by age but are not sufficient to show differences by sex. The biggest differences between male and female responses to influenza vaccine occur when the vaccine composition changes dramatically. Immunity that builds up over time may dampen the differences seen with age, said Dr. Sabra Klein.

Dr. Jackson asked whether increased Tdap vaccination in pregnant women might have translated to lower overall rates of pertussis in recent years, as mothers can be vectors for transmission. Dr. Nicola Klein agreed that rates are surprisingly low this year, but she was not sure why.

Cody Meissner, M.D., FAAP, asked whether any research addresses vaccine effectiveness in relation to the stage of a woman's menstrual cycle at the time of administration. Dr. Sabra Klein said she is among those studying the question. Dr. Meissner asked whether giving pregnant women Tdap vaccine earlier in gestation would elicit a better antibody response in their neonates. Dr. Nicola Klein said studies have reached conflicting findings on the matter.

Vaccines for Uncommon Diseases and Small Patient Populations

Vaccines and Antimicrobial Resistance—Leonard Friedland, M.D., FAAP, Vice President and Director, Scientific Affairs and Public Health, GSK Vaccines

Infectious diseases remain the leading cause of death worldwide. Discovering innovative technologies and developing new vaccines requires a lot of time, capital, and expertise, but it is worth the investment, said Dr. Friedland. Decisions about where to invest time and money should look beyond direct health and economic benefits to encompass the moral, social, and ethical impact of vaccines. The use of vaccines can reduce antibiotic use and resistance. Vaccines can also promote health equity, improve community health, improve the function of the health care system, and benefit the economic health of a society. Without recognizing the full benefits and contribution to society of vaccines, stakeholders may undervalue the next generation of vaccines, and policy recommendations may result in underutilization.

Vaccines in development must take into account the growing problem of antimicrobial resistance. Overuse of antimicrobials in humans and animals has led to resistance, including multidrug resistance, which leaves some infectious diseases untreatable. Antimicrobial resistance is widely

recognized as a major threat to global health and security. Some economic incentives have been implemented to motivate development of new antibiotics, but progress has been minimal. The role of vaccines has been acknowledged, but no concrete changes in policies or resource allocation have supported development of vaccines to counter antimicrobial resistance.

Vaccines can prevent bacterial diseases (e.g., diphtheria, meningitis, pertussis, and pneumonia) that would require antibiotic treatment and nonbacterial diseases (e.g., influenza, rotavirus) that often trigger inappropriate antibiotic use. NVAC and the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria have called for increased funding and incentives to develop vaccines that can decrease antibiotic use. Many global initiatives to address antimicrobial resistance are underway.

Technological advances have paved the way for substantial progress in vaccine development. All 12 of WHO's priority pathogens for antimicrobial resistance are addressed by vaccine candidates currently in development. The challenge is sustaining development through to commercialization and then to ensure that policies support use of the vaccines. More work is needed to expand and strengthen the evidence base on vaccines and antimicrobial resistance. Economic models are needed that illustrate the value of reduced use of antimicrobials as a result of mass vaccination and targeted vaccinations. Policy-makers and public health authorities should take into account the value of vaccines that counter antimicrobial resistance.

Dr. Friedland called for the following:

- Prioritize vaccination by allocating funding, increasing access, encouraging vaccination, and raising awareness about the role of vaccines in preventing antimicrobial resistance.
- Incentivize development of vaccines to address antimicrobial resistance through new funding models and include antimicrobial resistance as part of regulatory review.
- Enhance the body of data through research and surveillance to support decision-making.
- Continued annual reporting to NVAC on the progress in supporting the role of vaccines in strategies to combat antimicrobial resistance (as called for in NVAC's 2015 recommendations).
- Support for a comprehensive approach to antimicrobial resistance that includes vaccine development.

Perspectives on Progress in Developing a Globally Effective HIV Vaccine—Larry Corey, M.D., Principal Investigator, NIAID-Supported HIV Vaccine Trials Network; Past President and Director, Fred Hutchinson Cancer Research Center; Professor of Laboratory Medicine and Medicine, University of Washington

Throughout the world, HIV infection remains a serious threat, despite the availability of effective treatment and prevention methods. In the past, vaccines have been the only way to control infections that are acquired and transmitted asymptomatically. Developing an HIV vaccine has been particularly difficult because HIV is more genetically diverse than other pathogens. Its envelope is less immunogenic than other virus envelope proteins, and its envelope structure is unique and difficult to simulate. Animal models are expensive and not predictive of human efficacy. The human immune system does not have the capacity to self-cure HIV.

Nonetheless, four clinical trials are underway to define whether neutralizing or non-neutralizing antibodies can be tweaked to provide reasonable vaccine efficacy in high-risk areas. Scientific advances are fueling vaccine-related discovery. Although the 2003–2006 Thai trial that combined two HIV vaccine candidates found low efficacy, it revealed a new target for later vaccine efforts.

In 2010, the Pox Protein Public–Private Partnership formed to build on the findings and advance research efforts. Current clinical trials are exploring techniques for making neutralizing antibodies through active immunization by injection, which is how most vaccines work. Others are assessing passive immunization methods that administer broadly neutralizing antibodies intravenously. Dr. Corey noted that an HIV vaccine would complicate diagnosis, as vaccinees will develop antibodies to HIV and have seropositive test results.

The ongoing trials involve two strategies that incorporate non-neutralizing antibodies, and it may be that successful immunization requires both neutralizing and non-neutralizing antibodies, said Dr. Corey. Other efforts are focusing on products with an extended half-life that could be self-administered by subcutaneous injection.

If any of the vaccines or antibodies are effective in clinical trials, the results will unleash new scientific approaches toward the goal of HIV prevention. The resulting HIV vaccine is likely to be the most complex vaccine ever designed, with a regimen that complicates implementation and disrupts diagnosis but overcomes the barriers to controlling HIV. The science will also catalyze other research. Significant investment is needed to bring the work to fruition, said Dr. Corey.

Need for and Challenges with Hepatitis C Vaccine Development—Andrea L. Cox, M.D., Ph.D., Professor and Medicine and Oncology, Viral Hepatitis Center, Johns Hopkins Medicine

Hepatitis C virus (HCV) infects millions worldwide and kills about 20,000 Americans every year. Given the availability of vaccines for hepatitis A, B, and E and antiviral medications that can suppress hepatitis B and cure HCV, WHO established targets for eliminating viral hepatitis by 2030, but even high-income countries are not on track to meet those goals.

In the United States, HCV transmission occurs primarily among men who have sex with men and people who inject drugs (PWID); the opioid crisis has contributed to rising HCV rates (while hepatitis B rates have decreased because a vaccine is available). The public health focus has been on diagnosing and curing HCV, not prevention. However, treatment is expensive, and most of the easy-to-treat patients have already been treated. Uptake of treatment is declining.

People who are infected have nonspecific symptoms until the late stages of disease, so they are difficult to identify. Those at highest risk tend to be marginalized. There is limited knowledge about infection status. Notably, drugs do not prevent reinfection, and late-stage treatment does not fully reverse disease. More focus on HCV prevention is needed, said Dr. Cox.

One study found that about a quarter of PWID with HCV spontaneously cleared the infection, and 83 percent spontaneously cleared reinfection. These findings indicate that people can develop protective immunity to HCV, which offers some promise for a vaccine. However, limited culture systems make production of a live attenuated or inactivated whole HCV vaccine challenging. The virus has significant genetic diversity. There is no animal model for HCV. It is difficult to conduct research in PWID, who have the highest incidence of disease.

Research is underway on a vector that delivers HCV antigen and spurs innate and adaptive immune responses. The Vaccine Is Prevention study enrolled more than 500 PWID who are at high risk but are not infected with HCV. Preliminary findings demonstrated that the experimental vaccine induced T-cell responses and was safe but did not reduce progression to chronic infection. The full results of the trial will be presented later this year.

Dr. Cox concluded that there is a desperate need for an HCV vaccine to reverse global increases in HCV infections and deaths. Vaccination should be part of a comprehensive strategy that includes prevention, harm reduction, diagnosis, and treatment.

Vaccines for Uncommon Diseases: The Issue of Cost—Cody Meissner, M.D., Professor of Pediatrics, Tufts University School of Medicine

Successful vaccine development requires the interest of a robust pharmaceutical industry plus financial incentives to pursue research and development. Stable funding for effective vaccines and adequate supplies are needed to ensure that all those at risk receive the vaccine according to public health recommendations. The notion of withholding a safe, effective vaccine because the disease affects a small population is troubling and raises questions about whether a vaccine can be "too expensive" to make. If so, what are the contributing factors, and what constitutes a vaccine that is too expensive?, Dr. Meissner asked.

The cost of development for a vaccine of limited use will be similar to that for a vaccine with broad application. Some have used quality-adjusted life-years (QALY) saved as a standard, but Dr. Meissner questioned whether that measure is equitable and whether it is fair for children and adolescents. Moreover, he questioned whether the measure is sustainable: some vaccines are cost-saving, while others can be very expensive by any measure. Finally, Dr. Meissner asked whether the pharmaceutical industry answers only to its stockholders or whether it also has a responsibility to the community.

In the United States, health care spending accounts for nearly a fifth of the gross domestic product, with costs rising annually. The value to society of a vaccine can be calculated according to the reduced burden of disease, mortality, and direct and indirect costs. With estimates that developing a new vaccine costs $1 billion, it is difficult to ensure investors that they will see a reasonable rate of return. There is no widely accepted standard for determining rate of return and no mechanism for incorporating economic analysis into the decision-making about developing or recommending vaccines. There is no agreement on what society is willing to pay for a vaccine.

Lyme disease vaccine offers a good case study for the issues of cost and value. Of two safe, effective vaccine candidates, one became commercially available in the late 1990s and was withdrawn within a few years because of limited demand. Lyme disease primarily occurs in only a few states. The recommendation for Lyme vaccination was weak, targeting only a small fraction of the U.S. population. The vaccine was fairly expensive and required frequent boosters. Health care providers were not well educated about the vaccine. Most importantly, the maker was sued by people who believed the vaccine caused arthritis. Although the allegation proved to be incorrect, the vaccine was removed from the market. Currently, there is renewed interest in a Lyme vaccine, but it will likely face the same challenges around consumer demand. Dr. Meissner concluded by emphasizing the success of vaccines in preventing and, in some cases, eliminating life-threatening diseases.

Discussion

Given the number of potential targets, Dr. Friedland said that in determining which to pursue, the pharmaceutical industry considers the unmet medical need, the depth of understanding about the pathogen, and the available technology. The field has already addressed the low-hanging fruit, so it is now faced with the most challenging pathogens and target populations. Partnerships are needed to ensure sustainability throughout the long process of developing, manufacturing, and administering vaccines. Dr. Friedland added that decisions about what to pursue should be made

jointly by the field, with input from economists, social scientists, and others in addition to those traditionally involved.

David Fleming, M.D., asked what regulatory and policy changes could advance the field. Dr. Corey said sustainability requires public–private partnerships that address the regulatory components. Society must ask how much it is willing to invest in subsidizing development. Dr. Corey did not believe the pharmaceutical industry has a moral obligation to society to develop effective vaccines; rather, society must recognize the broader benefits of new vaccines and adjust its investments accordingly. It must take into account the need for prevention and rising antibiotic resistance, for example. Dr. Corey said the mindset must change so that vaccines are not looked at solely as commodities.

Dr. Meissner said a lot of taxpayer dollars are already invested in vaccine-related research. Dr. Corey responded that the highest costs come from clinical research, which is borne by the pharmaceutical industry. He reiterated the need to consider the larger societal benefit of investment. Dr. Corey said progress on HIV stalled when the decision of whether to pursue an HIV vaccine was left to the industry. Academia had to build the infrastructure to advance the vaccines, which Dr. Corey said was an example of the structural changes needed.

Dr. Hopkins said that because of the nature of transmission, HIV and HCV elicit strong biases, which affects progress. He emphasized that biases should not be part of the mission of improving health. Dr. Cox said broad recommendations help mitigate bias. However, insurance providers pay more for treatment than prevention. Moreover, the most problematic effects of HIV and HCV arise 10 or 20 years after infection, which also complicated QALY cost analyses. There is general recognition that treatment alone is not effective for controlling severe infectious disease. Ideally, evidence could show the cost benefit of preventing the spread of pathogens over decades.

Dr. Friedland reminded the group that NVAC established the Immunization Equity Subgroup to address some of the issues raised. NVAC can work to influence stakeholders about the importance of vaccines for all, including racial/ethnic minorities, those who are economically disadvantaged, those without access, and PWID. The impact of preventing disease on marginalized and high-risk populations (e.g., the benefits of obtaining education on overall health) should be factored into economic analyses.

Dr. Martinez said vaccines make the world a better place and save a lot of money, but there is no framework for thinking about the cost savings that vaccines could yield. She called for new economic models that evaluate costs fully.

Timothy Cooke, Ph.D., added that CDC has published findings clearly describing the value of vaccines, demonstrating that they save the government money. Other drugs and devices are assessed in terms of cost-effectiveness relative to other interventions, but vaccines clearly save money. However, that means the vaccine developer makes less money. Dr. Cooke raised the concern about the small number of vaccine manufacturers. He also noted that investors are not as interested in funding vaccine and infectious disease research as they are in funding gene therapy for cancer, for example. Dr. Cooke said public–private partnerships will have to step in to support vaccine development.

What Works: Equity in Adult Immunization

Cultural Beliefs and Influenza Vaccination in Today's Social Media World—Sandra Crouse Quinn, Ph.D., University of Maryland School of Public Health

Dr. Quinn's research found that African Americans perceive the risks of side effects of influenza vaccine as higher and more serious than whites do, which results in lower uptake. Trust in vaccines and the vaccine process increases uptake, but many people do not understand the process. More knowledge translates to higher uptake, but knowledge alone is not sufficient.

Further analysis revealed that African Americans are more likely than whites to perceive racial discrimination in health care settings, which leads to less trust, more use of alternatives to vaccination, a propensity for conspiracy theories around vaccination, vaccine refusal, and perceived higher risks of side effects. Exploration of misgivings uncovered a belief that different communities get different vaccines. Some hold lingering mistrust of the health care system because of the Tuskegee syphilis experiments and similar events (although some expressed that it is time to move beyond those concerns). While there is high trust in CDC, some believe FDA is influenced by pharmaceutical companies that see consumers as test subjects.

Another study found that Russian bots and trolls fed social media with vaccine messages (pro-vaccine, anti-vaccine, and neutral) that sowed misinformation about risks and promoted conspiracy theories. Given the pervasiveness of social media, Dr. Quinn said providers play a critical role in talking with patients honestly about the risks and side effects associated with the vaccine, not just the disease. They can convey the message that even when the vaccine fails to prevent influenza, it can still prevent hospitalization. Providers should be prepared to make a recommendation and provide vaccine at the same visit. Dr. Quinn said she was shocked by how many healthcare workers do not believe in influenza vaccination.

Dr. Quinn advised public health agencies to help people understand the rationale for vaccines, the vaccine process, and the recommendations. Public health entities should maintain a social media presence that educates the public and strengthens norms around vaccination. With social media, responding to anti-vaccination arguments only exacerbates the problem, so, "Don't feed the trolls," Dr. Quinn recommended. Messaging should be positive, focusing on vaccines as a way to protect one's self, one's family, and one's community and prevent serious illness. Messages should be developed through collaboration with providers, families, communities, and other stakeholders. Traditional communication methods remain critical, Dr. Quinn concluded.

Lessons Learned from Immunization Providers: Strategies for Successful Immunization Efforts Among Medicare Patients—Melissa G. French, M.S., Director, Roundtable on Health Literacy, National Academies of Sciences, Engineering, and Medicine

While the definition of "health literacy" tends to focus on the capacities of the individual, "organizational health literacy" is the ability of an organization to respond to the needs of the people it serves. Low health literacy as well as structural and cultural components—such as the ease of getting a vaccination—affect vaccine uptake. Interviews with medical providers, public health providers, and pharmacy professionals in diverse settings demonstrated that the most successful vaccination efforts occurred in organizations that saw immunization as part of the mission and worked to make it available throughout the community. Knowing the current guidelines and expressing confidence during interactions with patients were key to uptake.

Interviewees all said that resistance to vaccination could usually be overcome with clear, respectful explanations in a context in which providers can give patients their undivided attention. Providers earn trust when they are part of the community. Trust is vital, especially among populations thought to be consistently resistant to vaccination. While it was clear that successful

organizations adapt their methods to suit the population served, several key themes emerged from the interviews around what improves vaccine uptake:

- Strong leadership, regardless of the size of the organization
- A team approach, enacted by knowledgable, trained staff at every point of patient contact
- A designated champion who maintains immunization as an organizational priority
- Workflows that facilitate immunization, such as standing orders
- Minimization of steps and visits (e.g., combining vaccinations when possible)
- Patient-centered approach that enables the provider to listen to the patient
- Recognition that the core mission is a dedication to serving patients, customers, and community
- Persistence in recommending vaccines, even to those who have refused in the past
- Prioritization of immunization through reminders and consistent recommendations
- Continuous improvement that enables tracking and gives incentives for improvement
- Accountability; using immunization as an indicator of high-quality care

Tracking immunizations is difficult when vaccines are given outside of the provider's office, which translates to difficulty ordering and maintaining vaccine supplies, especially in smaller clinics. Even when the cost of vaccine is covered, low-income people face barriers to getting vaccine, such as transportation or time constraints.

Discussion

Dr. Fleming asked what strategies work to improve immunization rates in target populations. Dr. Quinn said making it easy for people to get vaccines by setting up services in the community could help them overcome barriers. Going where the people are is key—particularly providing vaccinations in settings that people trust where they feel they will be treated fairly. Ms. French added that corporate chain pharmacies do a lot of outreach, and the pharmacists often look like or come from the same communities as the people they serve, which makes them more relatable.

Dr. Friedland asked what access points might be good hosts for vaccine clinics. Dr. Quinn said her organization established the black barbershop network to get health care providers into those settings, which serve clients across the socioeconomic spectrum. Churches have a long history of providing health services, she added. Ms. French added that pharmacies have pioneered outreach through churches, libraries, and community centers, and they might have billing data to support a research effort.

Ms. Aikin asked how the field could learn from those within the African American community who believe it is time to move past the historic events that have led to mistrust in the medical system. Dr. Quinn said that when people raise the history of abuse or mistreatment, providers should be honest and acknowledge that history, then explain what has changed. She added that all providers, regardless of race/ethnicity, must begin to work to overcome the distrust; the field cannot wait until it has enough providers who look like the patients they serve. Listening carefully and being respectful are key.

Dr. El Sahly observed that for adults, vaccine delivery is centered around provider offices and pharmacies, which poses a structural barrier. Dr. Hopkins said providers should assess vaccine status, administer vaccines, and document immunization status at every visit. Providers who serve adolescents and adults should foster a team approach to address gaps and opportunities for vaccination throughout the practice. Everyone involved should make vaccination a priority, he noted. The team should include pharmacists or others who can reach healthy adults.

Dr. Quinn pointed out that broad communication in venues throughout the community strengthens the message. Providers and pharmacies should create vaccination opportunities outside the health care system. Specialty providers should adopt the team approach and reinforce the message. Ms. French added that nonclinical settings can be more comfortable and less intimidating places to discuss concerns or fears about vaccines.

Dr. Quinn added that systemic barriers in the clinical setting must be addressed; even if a specialist recommends vaccination, the process requires a separate financial transaction and a visit to a pharmacist or clinic. Dr. Jackson noted that many people do not have a primary care provider, and only 25 percent of primary care providers stock all recommended vaccines in their offices.

Immunization Equity Subgroup Update—Melissa Martinez, M.D., FAAFP, Subgroup Co-Chair

NVAC established the Subgroup with the following charge:

1. Review and summarize the complex and interrelated factors that contribute to vaccination disparities, such as access, affordability, awareness, acceptance, and activation.
2. Deliver a set of system-wide recommendations for overcoming drivers of immunization disparities and reducing gaps in coverage that will provide the foundation for development of a collaborative immunization equity strategy.
3. Report findings for a vote during the September 2020 NVAC meeting.

So far, the group has reviewed previous NVAC recommendations on disparities, examined CDC data on disparities among adults, and heard presentations from experts in vaccine confidence. The Subgroup is planning a literature review on health literacy and other barriers to vaccine uptake, such as needle phobia, access, and cost, and factors contributing to disparities (e.g., race/ethnicity, geography, religious and cultural beliefs, gender, and age). The subgroup will also evaluate policies that address disparities and identify gaps in research.

Ms. Martinez requested input on other factors the subcommittee should address, such as provider knowledge of vaccine recommendations and schedule, provider dismissal, and provider stocking of vaccines. The group plans to submit a draft report to NVAC at the June 2020 meeting for review and public comment, followed by a final report at the September 2020 meeting.

Discussion

Dr. Jackson suggested the subgroup address provider hesitancy, especially among young physicians. More education is needed, ideally through the medical training curricula, she noted. Knowledge gaps may prevent providers from communicating with patients who are vaccine-hesitant. Providers also might not stock vaccine because of the cost or because they believe primary care providers and internists are solely responsible for vaccinating adults. Ms. Coyle recommended evaluating the impact of the Affordable Care Act on rural populations; for some rural citizens, an in-network provider is hundreds of miles away.

Public Comment

Brad Rollins expressed concerns about the increasing anti-vaccine movement. Anti-science positions are gaining a bit of steam, he said, as seen with climate change denial, the anti-vaccine movement, and people who believe the earth is flat. As a public health professional, Mr. Rollins said he is alarmed by the propensity for some people to take what should be normal levels of

skepticism and dive straight into conspiracy theories and to trust entities that are opposed to the medical consensus. He proposed finding ways to better educate, particularly those who might be vulnerable to propaganda by the anti-vaccine moment. Mr. Rollins encouraged NVAC to focus on reaching out to medical universities where the next generation of doctors are being trained, opening up more workshops, providing more training on these issues, and talking with future doctors about how to build trust with their patients.

Mr. Rollins suggested that education focus not just on the mortality aspects of vaccine prevention but also the morbidity aspects. As was seen in the case described of the young boy with tetanus, there is a lot to be learned in that area.

Theresa Wrangham of the National Vaccine Information Center (NVIC) said the National Vaccine Plan appears to reflect a continued lack of integration of goals relating to vaccine safety and awareness, VAERS, and the Vaccine Injury Compensation Program (VICP). This lack of balance within the plan can contribute to the ongoing erosion of trust in government agencies and vaccine-hesitancy, as it appears that vaccine development is a higher priority than safety and the compensation of those harmed, said Ms. Wrangham.

Additionally, the approach to identifying stakeholders—excluding groups that may have historically represented concerns about the plan goals—appears exclusionary and does not support meaningful public engagement. The risk of this approach is continued erosion of trust and vaccine-hesitancy.

The thoughtful presentation on sex and gender would also appear to require some adjustment within the plan in terms of safety, given that women may be at a higher risk for vaccine injury. As mentioned in previous public comments, many of NVIC's concerns stem from the federal law that governs NVAC, which states that there is a responsibility to achieve optimal prevention of human infectious diseases through immunization and to achieve optimal prevention against adverse reactions to vaccines.

The National Vaccine Plan as it currently stands places a disproportionate emphasis on vaccine innovation and development and not enough on closing existing vaccine safety deficits, described by the Institute of Medicine, and preventing vaccine-related adverse events and deaths. The plan's policies, goals, and strategies undermine the individual's right to decide what risk is acceptable to them through informed consent. Mandating vaccination for the greater good is based on inadequate science and represents a violation of basic human rights. In essence, it treats those harmed by vaccines as acceptable collateral damage, with no respect for individuals making different choices under informed consent.

In relation to the tetanus case, publishing the protocol that aided in this child's recovery is necessary to help in the rare cases that do occur in the United States and abroad. The efforts of this child's medical team are both valuable as a teaching tool and representative of the great advances in medicine that we all benefit from. However, Ms. Wrangham believed that another tetanus case in Colorado occurred in a vaccinated person. In general, vaccination status appears to be acknowledged when disease occurs in the unvaccinated but not when disease occurs as the result of vaccine failure. It seems likely that there are medical costs associated for those who contract many diseases regardless of vaccination status. Transparency is needed in that respect and should be a part of the conversation relating to economic impacts associated with treatment of these diseases when they occur. Referring to this case as "a win" for the anti-vaccine community is counterproductive to transparency and to individuals' right to make an accurate risk-benefit decision as they consider vaccination.

Ms. Wrangham reiterated that distrust and hesitancy are the result of the lack of transparency by federal agencies in communicating the frequency and severity of disease complications, conflicts of interest, and the lack of independent vaccine safety monitoring and information on vaccine failures and the associated cost. Access to vaccines is important, as is the respect for the exercise of informed consent to vaccinate, inclusive of refusal, she concluded.

Adjournment

Dr. Hopkins adjourned the meeting for the day at 4:50 p.m.

Day Two—September 18, 2019

Chair's Welcome—Robert H. Hopkins Jr., M.D., MACP, FAAP, NVAC Chair

Dr. Hopkins recapped the first day of the meeting. Among the takeaways from day one were 1) the need to think about different targets for different vaccines and populations in the context of vaccine and adjuvant development, 2) the numerous opportunities to advance vaccines given a sufficient return on investment, 3) the potential need to refine definitions of what constitutes a successful vaccination product, and 4) the importance of spreading positive messages through social media while not engaging with trolls. Dr. Hopkins outlined the agenda for the day.

NVAC Liaison Updates

AIM—Kristen R. Ehresmann, RN, M.P.H.

AIM is partnering with ASTHO on the HPV Extension for Community Healthcare Outcomes (ECHO) Project and with CDC to train new managers about state immunization programs. AIM members also attended the AIRA conference and had a joint meeting with AIRA and CDC around what is next for IIS. AIM held a brainstorming session on vaccine confidence with 12 program managers in August to discuss challenges and successes in addressing vaccine confidence. The session was facilitated by the University of Michigan Child Health Evaluation and Research section, and a report will be forthcoming. Ms. Ehresmann encouraged people to check out the link to the AIM IIS infographic.

AIRA—Rebecca Coyle, M.S.Ed.

AIRA held its national meeting in August in Indianapolis; a number of keynote speakers focused on big data and how to utilize it, particularly in the context of public health. One speaker said that organizations can greatly improve the quality of their data by cleaning up the addresses, which are often used as a matching tool to identify patients. AIRA offers an address cleansing and geocoding service. The service has been extended through 2024. AIRA recently completed some measurement and improvement initiatives. To improve clinical decision support, it is assessing jurisdictions' ability to look at an individual record and compare it with Advisory Committee on Immunization Practices (ACIP) recommendations. AIRA was awarded funding through a multiyear cooperative agreement to look at strengths, opportunities, and strategies for better incorporating adults into an IIS.

APhA—Brian Wall, Pharm.D.

APhA provides webinars after each ACIP meeting to inform members and pharmacists broadly on ACIP activities. During the July 2019 webinar, concern was expressed about new pneumococcal recommendations and the use of shared decision-making, so APhA requested the opportunity to participate in the development of implementation guidelines and procedures.

APhA uses pulse surveys to gather information; in response to a recent survey, APhA held a webinar on vaccine storage. APhA held a roundtable discussion with physicians and pharmacists in June about vaccine referral and data exchange. Discussions centered on collaboration among health care providers, referral methods, and billing processes. Some discussion was also devoted to pandemic planning and how barriers to access and collaboration can be overcome during pandemic responses. This offers a potential model for future collaboration.

APhA published its *Practice Insights, Global Edition*, on September 6 on pharmacy-based immunization. APhA's Jean-Venable "Kelly" Goode is presenting at the International Federation of Pharmacists meeting in Abu Dhabi later this month. Dr. Goode and others will speak about how community pharmacists across the globe can provide immunizations and vaccines. APhA also conducted a webinar related to pharmacy technicians and immunization provision. The organization has released some educational modules for pharmacy technicians and pharmacists about how to activate the full team around immunization. Other related publications appear in *Pharmacy Today* and on the APhA website.

ASTHO—James S. Blumenstock

ASTHO produced a video on the importance of HPV vaccination in preventing oral cancer as an executive learning tool. Adults react better to listening and viewing information than reading, so ASTHO is aiming to convey information in new formats. Its videos feature a subject matter expert sharing some thoughts and strategies with colleagues in the impacted community on a key public health issue of concern. The HPV vaccination video features Nathaniel Smith, M.D., Secretary of Health for the State of Arkansas, the president-elect for ASTHO, and a former NVAC member. Mr. Blumenstock hoped NVAC members and liaisons would share the video, which is available online, with their constituents.

NACCHO—John Douglas, M.D.

NACCHO's annual conference featured extensive discussion about immunizations and a preconference workshop on vaccine hesitancy that was quite well attended. Every year, NACCHO honors model practices in local public health departments. As always, several this year were related to immunization and attempts to address vaccine hesitancy. The NACCHO Immunization Work Group remains active, and some new members have joined recently. That group's work includes a July 2019 policy statement on comprehensive immunization programs across the lifespan, which aligns with NVAC's recommendations for the National Vaccine Plan. It also updated a policy statement on school and childcare immunization requirements, looking across states at best practices, even at the local level, where documentation and sharing lessons learned are very useful.

NACCHO continues to be involved in promoting immunization awareness and education. It held a webinar on principles to address vaccine resistance and hesitancy. The webinar was highlighted as a kickoff to National Immunization Awareness Month in August and talked about vaccines and lessons learned from CDC's research with providers. A webinar at the end of August addressed the emerging issue of vaccine-preventable diseases in detention facilities, such as the mumps outbreaks across the country. One state health department is working with Immigration and Customs Enforcement to provide measles-mumps-rubella (MMR) vaccination for staff and detainees who have not been previously vaccinated.

PAHO—Nathalie El Omeiri, Ph.D.

In July, PAHO's Technical Advisory Group (TAG) on Vaccine-Preventable Diseases convened its 25th meeting in Cartagena, Colombia, with 220 participants from 33 countries and territories

in the Americas. CDC, PHAC, Emory University, and other immunization partners and experts. The TAG reviewed the goals of the immunization program in the Americas: sustaining the immunization achievements, completing the unfinished agenda, tackling new challenges, introducing new vaccines and assessing their impact, and strengthening health services for effective vaccine administration. While 22 out of 50 countries and territories in the region have increased coverage for diphtheria, tetanus, and pertussis vaccine (DTP3), overall regional coverage was 88 percent, implying that approximately 1.8 million children have not been vaccinated in a timely manner.

The increase in recent years in the number of unvaccinated children was influenced by the decline in coverage in countries with large cohorts of children under the age of one year in Brazil, Mexico, Argentina, Paraguay, and Venezuela, among others. During 2016, the Americas were declared free of endemic measles transmission, and 33 of 35 member states have sustained elimination for the past 17 years. However, in Venezuela and Brazil, low coverage has led to the reestablishment of endemic measles transmission in June 2018 and February 2019, respectively, after 12 months of continuous measles circulation. As of August 31, 2019 there were 4,597 cases of measles confirmed this year in 14 countries and territories of the Americas, with 56 percent of confirmed cases being reported by Brazil and 27 percent by the United States. In Venezuela, the number of measles cases drastically decreased following vaccination of approximately 9 million children (from ages 6 months to 19 years) last year. To support Venezuela, PAHO and its partners have mobilized over $7.4 million for vaccination campaigns.

PAHO recently convened a regional commission to support countries in monitoring and reverification of measles and rubella elimination. Outbreaks of diphtheria in Haiti and Venezuela and yellow fever in Brazil, for which PAHO provided technical cooperation, were also analyzed.

The TAG also discussed Tdap immunization, HPV vaccination, and progress towards elimination of vertical transmission of hepatitis B. To address vaccine hesitancy in a more comprehensive way, the TAG recommended that countries identify barriers to and drivers of vaccination and generate evidence on vaccine access, acceptance, and demand to develop tailored interventions at the local level. The full meeting report is available on PAHO's website. PAHO's Directing Council will meet in October with the participation of the ministries of health from the entire region; it will also review the progress and challenges of the immunization program, with a focus on the measles outbreaks.

PHAC—Gina Charos

Canada updates its figures on measles weekly, typically on Fridays. In 2019, it has seen 111 cases, of which 41 were imported. Ten of those imported cases resulted in domestic transmission. One measles outbreak is underway now, in the province of Quebec, of 34 cases. Ms. Charos said there is hope that this outbreak might be declared over by the end of this week, given the date of onset of the last case's symptoms.

Advisory Commission on Childhood Vaccines (ACCV)—Cody Meissner, M.D., FAAP

ACCV conducted its 111th quarterly meeting on September 6, 2019. The meeting began with program updates from DICP, the Department of Justice, and an ACCV workgroup. ACCV also received program updates from the CDC's Immunization Safety Office, NIAID, the Center for Biologics Evaluation and Research at FDA, and the OIDP. ACCV is required to review all new and modified vaccine information statements, based on the National Childhood Vaccine Injury Act of 1986. The group reviewed the vaccine information statements for live attenuated and inactivated influenza vaccines, MMR vaccine, varicella vaccine, hepatitis B vaccine, meningococcal ACWY vaccine, and meningococcal B vaccine to ensure the language in certain

sections is consistent. During the discussion, several minor suggestions were made, which will be relayed to CDC for its consideration. The next scheduled ACCV meeting is in December of this year.

DISCUSSION

Ms. Ehresmann agreed to circulate AIM's document on vaccine challenges to NVAC members when it becomes available.

AHRQ and the U.S. Preventive Services Task Force (USPSTF)—Justin A. Mills, M.D., M.P.H.

USPSTF finalized its recommendation for hepatitis B screening in pregnant adults and released it in July. It is an A-level recommendation, meaning there is a high certainty that the screening provides a substantial net benefit, so clinicians should screen all pregnant women. USPSTF found convincing evidence that universal prenatal screening for hepatitis B infections substantially reduces prenatal transmission of hepatitis B virus and subsequent development of chronic hepatitis B infection. The Task Force does not make recommendations on treatment, but it does review that evidence. In this case, USPSTF found adequate evidence that vaccination of all infants against hepatitis B infection and providing post-exposure prophylaxis with hepatitis B immunoglobulin at birth to infants of mothers infected with hepatitis B substantially reduces the risk of acquisition of hepatitis B infection in infants. There is a systematic review in process to update the 2014 recommendation on hepatitis B screening in nonpregnant adolescents and adults.

BARDA—Linda Lambert, Ph.D.

BARDA is supporting late-stage manufacturing activities of two Ebola virus vaccines—the Merck single-dose vaccine and the Janssen prime-boost vaccine. Using the Merck vaccine, a WHO-sponsored ring vaccination study in the Democratic Republic of Congo has vaccinated more than 221,000 individuals so far. FDA has accepted Merck's biological license application for the vaccine and granted Merck a priority review. The Prescription Drug User Fee Act (PDUFA) target action date is in March 2020. It is hoped that Janssen's prime-boost vaccine will be procured under Project BioShield; several studies are ongoing in Rwanda.

BARDA is supporting development of Bavarian Nordic's smallpox vaccine in a lyophilized formulation to provide a longer shelf life as well as a liquid formulation. The liquid frozen formulation of that vaccine is under review by the FDA with a PDUFA date later this month.

BARDA has preliminary results from a two-dose safety and dose range immunogenicity study of a recombinant H7N9 influenza vaccine, administered with adjuvants ASO3 or MS59. The antibody responses were as expected. There is an effective immune response against tested antigens, and the safety analysis showed that the vaccine and the adjuvants were within accepted local systemic reactive immunogenicity. The take-home message from that study is similar to what has been seen for subunit influenza vaccines—that there is broader protection and broader cross-reactive antibodies when administered with adjuvants than without.

In September, BARDA issued a request for proposals for the recompetition of BARDA's clinical studies network. The network involves three components: an entity that conducts clinical trials, a statistical data-coordinating center, and a biological specimen and investigational product storage facility. More information is available on BARDA's website. Because of the recompetition and general need, BARDA is actively looking for physicians who are interested in working for the Federal government.

CDC—Sam Posner, Ph.D.

WHO defines elimination as the absence of endemic measles virus transmission in a defined geographic area for at least 12 months in the presence of a working surveillance system. Countries lose their elimination status if a given outbreak is ongoing for more than 12 months. The measles outbreaks in New York City and New York State began in September 2018 and have been unusual in their determination and size, relative to other recent outbreaks. Thanks to extraordinary efforts by the public health officials on the ground in New York City and counties around New York State, these outbreaks appear to be winding down. Incidence peaked in 2019 in New York City, which recently declared its outbreak over after passing more than 42 days (or two incubation periods) without a case. However, the United States could still lose measles elimination status if new measles cases arise that are potentially associated with these outbreaks.

New York State's outbreak appears to be winding down. There have been no new cases in the past week. The last case of measles onset (i.e., rash) was August 19. CDC continues to work with New York State to end the outbreak and prevent loss of elimination. However, CDC is implementing a communications plan and partner outreach plan to manage the possible loss of measles elimination status. If in fact the United States loses measles elimination, HHS will make a formal announcement.

From January 1 to September 12, 2019, 1,241 cases of measles were reported in in 31 states, with no new cases reported in the past week. Even if the United States loses elimination status, vaccine coverage remains high, so the majority of the population remains at low risk of infection. CDC will continue to work with state and local health departments to keep measles from becoming endemic across the country. CDC will also be working with states and other partners to find innovative ways to identify communities with low vaccine coverage and strengthen vaccine confidence in these communities to prevent future outbreaks.

CDC has a new strategic framework, Vaccinate Confidently, which aims to promote vaccine confidence in responding to outbreaks of measles and other vaccine-preventable diseases. Recent outbreaks have been characterized by pockets of low vaccine coverage in insular and close-knit communities along with the spread of vaccine misinformation targeting these specific communities. Vaccinate Confidently has three major priorities, the first of which is to protect communities. Undervaccinated communities are at risk for disease outbreaks, and CDC is leading the way to help states, cities, and counties find these communities and take steps to protect them. For example, CDC is working with AIRA to provide states and localities with the resources and technical expertise to maximize and leverage IIS data to identify communities at risk for low vaccination using small-area analysis. This effort will provide local officials with critical capacity to respond to hotspots before outbreaks occur.

The second priority is empowering families. Every parent should feel confident in the decision to vaccinate, and every health care provider should be comfortable answering parents' questions about vaccines. CDC is working with the American Academy of Pediatrics to implement a diverse set of communication strategies to increase vaccine confidence in parents, with a special focus on parents with very young infants. The American Academy of Pediatrics will also be reaching out to pediatricians, obstetricians, pregnant women and their families, and families of young children.

The third priority area is to stop myths. Public health does not have the capacity to go after every vaccine myth online. Therefore, public health must work with local partners and messengers to improve trust and confidence in vaccines in key risk groups. Efforts to contain the spread of misinformation are demonstrated through the recent public health collaborations on social media

with Pinterest and Facebook. CDC also aims to reach new stakeholders to provide clear, accurate information about vaccination and the critical role it plays in American public health. CDC will hold a webinar at the end of this month with more information about this strategy.

DoD—Limone Collins, M.D.

A number of changes have been occurring in the military health system, so DoD is also changing its instructional textbooks (but that should not affect implementation of the immunization program.) DoD started its immunization program for the 2019–2020 season. As always, DoD's goal is to achieve 90-percent vaccination for a myriad of areas, particularly all active-duty service members, selected reserve components, and health care practitioners, by January 15, 2020. In regards to the yellow fever vaccine, particularly in the past year with supply difficulties, DoD has continued with unrestrictive ordering and focused on operational requirements.

DoD has focused on two force-protection areas related to two particular vaccines. First, there is interest in using the southern hemisphere influenza vaccine for operational forces. Second, DoD is preparing to use the Bavarian Nordic smallpox vaccine. The Pragmatic Assessment of Influenza Vaccine Effectiveness in DoD is starting its second year. It is looking at the three candidates for influenza vaccinations. The target enrollment is about 15,000 people. DoD seeks to add three sites to the original five.

FDA—Valerie Marshall, M.P.H.

FDA approved supplements for the biologics license applications for seasonal influenza vaccines to include the 2019–2020 U.S. formulation and associated labeling provisions. On September 16 and 17, 2019, FDA, NIAID, and the Coalition for Epidemic Preparedness Innovation had a public workshop on identification and use of biomarkers to advance development of preventive vaccines. This workshop brought together representatives of government agencies, academia, industry, and other stakeholders to discuss scientific, clinical, and regulatory challenges and identification, characterization, and qualification of biomarkers for preventive vaccines for infectious disease indications. Ms. Marshall anticipated that the transcripts would be publicly available within a few weeks.

HRSA BPHC—Judith Steinberg, M.D., M.P.H.

The BPHC funds and administers the Health Center program, which provides comprehensive, affordable, and quality primary care services to medically underserved people around the country. In 2018, there were approximately 1,400 health center organizations (grantees) that operated about 12,000 sites across the country in every State and territory. They served more than 28 million individuals, which represents one in 12 people in the country, one in three living in poverty, and one in five living in rural communities.

Grantees are required to report their data on an annual basis through the Uniform Data System, which includes two measures of immunizations. The first is a clinical quality measure, aligned with the electronic clinical quality measure from CMS (to reduce reporting burden), that assesses the percentage of children 2 years of age who received age-appropriate vaccines by their second birthday. In 2016, the definition of this measure changed from the third birthday to the second birthday, and since then, several vaccines have been added to the list of recommended childhood vaccines. As a result, it has been challenging for health centers to reach their prior performance levels on this measure. In 2018, nearly 40 percent of children aged 2 years had received the appropriate vaccinations by their second birthday, consistent with 2017 results.

The second measure evaluates service provision, so it is not a clinical quality measure. In 2018, almost 3.8 million children received the selected pediatric vaccinations—an 11-percent increase over 2017. Also in 2018, more than 4.4 million patients received the influenza vaccine, which is a 10-percent increase over 2017. BPHC is exploring the addition of a measure on adolescent vaccinations, which would include HPV vaccination.

HRSA DICP—Mary Rubin, M.D.

The VICP has continued to process an increased number of claims. In fiscal year (FY) 2018, 1,248 claims were filed, $199.6 million was awarded to petitioners, and $26.9 million was awarded in attorneys' fees and costs (including fees for compensated, dismissed, and interim cases). In FY 2019, as of September 1, a total of 1131 claims had been filed with the program, and $206.2 million had been awarded for petitioners and attorneys' fees and costs. HRSA has a backlog of 818 claims alleging vaccine injury awaiting review. As of August 1, 2019, the Countermeasures Injury Compensation Program has compensated 39 claims totaling $5.5 million.

In response to Dr. Pickering, Dr. Rubin said the most common claims involve shoulder injury related to vaccine administration (about 50 percent of claims) and Guillain-Barré syndrome (GBS). Dr. Friedland pointed to a position statement from the American Academy of Orthopedic Surgeons titled, "Rotator Cuff Tendinopathy, Adhesive Capsulitis, and Arthritis Cannot Be Caused by Vaccine Administration." Dr. Rubin said DICP can only make changes to the Vaccine Injury Table based on published, peer-reviewed scientific literature.

NIH—Barbara Mulach, Ph.D.

Over the summer, NIH made an award to the University of Alabama at Birmingham to begin an acute flaccid myelitis (AFM) natural history study, in collaboration with CDC and other partners. The idea is to put together an international multisite study to learn more about the incidence and distribution of AFM and to better understand how it develops and progresses in children. The written submission to NVAC from NIH provides more detail.

NIH, in partnership with OIDP, organized two consultation meetings. The first was on July 2 on the development of a group A streptococcal vaccine. The second will take place on September 24 and address overcoming waning immunity on pertussis vaccines. NIAID recently published an article in the *Journal of Infectious Diseases* about the need for research on sexually transmitted infections to refocus efforts on vaccines, therapeutics, and diagnostics. In response to that need, NIAID launched an initiative involving six new sexually transmitted infection cooperative research centers that will work to develop vaccines for syphilis, gonorrhea, and chlamydia. Later today, NVAC will hear about a universal influenza vaccine in clinical trials, which is part of NIAID's overall strategic plan for universal influenza vaccines.

VA—Troy Knighton, M.Ed., Ed.S., LPC

VA annually reviews and updates its websites, policies, recommendations, and guidance, including its clinical guidance statement for influenza vaccines. Influenza vaccine has arrived across the country in VA facilities, and vaccinations have started. Through its contract, which also includes the Indian Health Service and the Bureau of Prisons, VA gets vaccine in two shipments, half by September 15 and the rest by October 15. Once the second shipment arrives, there will be a major vaccination drive through clinics and other big vaccination events within VA. Vaccinations start mid-September, peak in October, and then start to go down in November. Mr. Knighton estimated that VA delivers about 90 percent of its vaccine within those 3 months, although vaccination continues as long as influenza is spreading and there is vaccine on hand that has not expired.

VA is continuing its partnership with Walgreens, which is entering its fifth year. The program is considered very successful, because it has helped increase access to influenza vaccine for enrolled veterans, who receive the vaccine at no cost. Last year, about 104,000 veterans went to a local Walgreens to get their influenza vaccination. Access to influenza and other vaccines will increase under the VA Community Care Network, which is part of the VA Maintaining Internal Systems and Strengthening Integrated Outside Networks (MISSION) Act.

DISCUSSION

Dr. Meissner asked why USPSTF recommended screening rather than vaccination for hepatitis B in pregnant women. Dr. Mills said USPSTF does not make recommendations for treatment.

Dr. Meissner asked what the consequences would be of losing measles elimination status. Dr. Posner did not know all the implications, but any such declaration would immediately prompt CDC to form a reverification committee and to work to reestablish elimination status.

In relation to the AFM study mentioned, Dr. Jackson observed that in 2014, enterovirus D68 (EV-D68) emerged in the United States with a large outbreak. It appears to be implicated in AFM cases, although it may not be the only virus implicated. The virus circulates every other year. This year is likely to see low rates of EV-D68. The virus has not been mentioned in NVAC's discussions of targets for vaccine development. Dr. Jackson suggested adding EV-D68 to the list of viruses to be addressed, particularly as AFM is evaluated more carefully.

Ms. Charos asked whether organizations are expecting any delay in starting influenza vaccination programs because WHO was late in issuing its recommendations this year. Dr. Posner did not know of any shortages, and the vaccine has been shipped, so vaccinations should begin on time.

Influenza Vaccine Safety Monitoring—Frank DeStefano, M.D., M.P.H., Director, Immunization Safety Office, CDC

Dr. DeStefano outlined the key mechanisms for monitoring U.S. vaccine safety and some recent findings from the data. VAERS, which is co-managed by CDC and FDA, can rapidly identify potential problems and rare events, but it is subject to underreporting, incomplete reporting, reporting bias, and other problems. Its data are not sufficient to make associations about causality. A more thorough investigation of VAERS reports for the 2018–2019 influenza season found that only 4–6 percent of reports were for serious conditions, which is consistent with other vaccines. During that period, a few episodes of GBS, anaphylaxis, and febrile convulsion were reported to VAERS, but FDA data mining did not identify any signals of those events, and there were no safety concerns for any of the 2018–2019 influenza vaccines (including those given during pregnancy).

The Vaccine Safety Datalink (VSD) gathers data from eight large health systems, which have computerized immunization records, allowing researchers to link vaccinations with other health care diagnoses and visits. It also enables researchers to evaluate adverse event reports by looking at individual medical records. CDC uses rapid-cycle analysis for near-real-time monitoring to detect signals or potential problems. More signals arose in 2018–2019 than previous seasons, which might reflect the increasing number of vaccines being monitored. In-depth analysis found that none of the reports of anaphylaxis could be confirmed, and a single report of Bell's palsy appears to be a programming error. Researchers did find an increased risk of febrile seizures in children ages 6–59 months, resulting in 2–4 additional cases per 100,000 doses of vaccine,

depending on age. Similar findings of febrile seizures in previous seasons were more pronounced in children who received other vaccines at the same time as influenza vaccine.

Using VSD data, CDC investigators were able to confirm only one GBS case related to the high-dose influenza vaccine. FDA evaluated Medicare beneficiary data and found a slight increased risk, equating to about one case per million vaccinations, which is consistent with findings from previous seasons.

The Clinical Immunization Safety Assessment (CISA) project conducts prospective studies on complex vaccine safety questions, in response to questions raised by U.S. health care providers; it also undertakes clinical research studies. The Post-Licensure Rapid Immunization Safety Monitoring program is a large distributed database for active surveillance and research, maintained by FDA with partner organizations.

Discussion

Dr. Meissner asked whether GBS is correctly associated with modern influenza vaccines, whether it is more common in unvaccinated people, and why there is a precaution to monitor for recurrent GBS for 6 weeks. Dr. DeStefano said occurrences of GBS vary from season to season, and in most seasons, no increased risk is found. In a few seasons, the risk is increased but very small—about 1–2 cases per million vaccines. Influenza infection carries a greater risk of GBS than influenza vaccine. The 6-week interval was derived from the 1976 experience with swine influenza. Recurrence might be hypothetical, said Dr. DeStefano; one study of 10 years' worth of vaccinations found no instances of recurrent GBS.

Dr. Dunn appreciated the concise summary of all the U.S. monitoring approaches. Many members of the public do not understand what VAERS does or how safety monitoring works, nor do many health care providers. Dr. Dunn asked whether any agencies provide a succinct overview of VAERS for the public and providers. Dr. DeStefano said his office would look into creating such materials. Dr. Douglas hoped to better communicate the success of the vaccine safety monitoring system.

Given the long history of vaccine safety monitoring, Mr. Knighton said it is not clear to him why some individuals have concerns about vaccine safety. Dr. DeStefano said there is a communication challenge that deserves attention. Ms. Aikin noted that CDC has a good infographic and corresponding video, The Journey of Your Child's Vaccine, which includes a description of vaccine safety monitoring, and tested well in parent focus groups.

Dr. DeStefano said the Immunization Safety Office can respond to most questions, but the CISA sites delve into the most complex issues. Each case goes through rigorous evaluation and discussion by multiple specialists. The CISA program addresses about 12 cases each year. Dr. Collins said DoD collaborates with CISA and also offers a similar program specifically for DoD members.

Props to Prevent Influenza Properly

Tools for Influenza Vaccine Safety from the National Adult and Influenza Immunization Summit (NAIIS)—Kelly McKenna, M.A., Manager, Quality and Research Initiatives, American Academy of Hospice and Palliative Medicine

NAIIS has developed tools to ensure safe vaccine administration in nontraditional settings, such as satellite, temporary, or offsite locations. The effort was spurred in response to incidents that raised concerns. Its checklist of best practices offers a comprehensive, step-by-step guide for

those overseeing vaccination clinics. The checklist addresses vaccine shipment, transport, storage, and handling; clinic preparation and supplies; administration; and documentation. It also includes helpful resources.

In addition, NAIIS created a pledge for organizations that hold vaccine clinics to sign, indicating they will use the checklist and follow CDC's best practices. Organization executives are asked to sign the pledge every year and publicize it on their organization websites. The NAIIS website offers other resources, and Ms. McKenna encouraged NVAC members to spread the word about NAIIS' materials.

Tools and Materials to Help in Improving Influenza Vaccination Efforts—Diane Peterson, Immunization Action Committee (IAC)

IAC offers hundreds of handouts online to help health care providers implement ACIP recommendations. These include a short, self-administered screening checklist that patients can complete; standing orders for influenza vaccination; a vaccine-dosing guide for children; guidance on managing reactions; and many others. IAC also provides an annually updated table of vaccines available each season, with information on each and the corresponding medical codes. Through its Ask the Experts page, users can find in-depth discussions of uncommon issues around vaccination. The site also provides vaccine information statements in multiple languages.

IAC maintains an honor role for organizations that mandate influenza vaccination and require employees who refuse vaccination to take strict preventive measures throughout the influenza season. The website also has case studies of unvaccinated people that demonstrate the consequences of vaccine refusal.

Ms. Peterson also manages NAIIS' influenza vaccine availability tracking system, available online. Manufacturers and distributors register that they have vaccine available, so clinics that run out of vaccine know where to look.

Immunizing Health Care Providers for Influenza in 2019: Why Does It Matter and What Works?—Amy Behrman, M.D., Medical Director, Occupational Medicine, University of Pennsylvania

Dr. Behrman said the NAIIS Influenza Working Group targeted influenza vaccination coverage among health care providers in long-term care facilities (LTCFs). Most hospitalizations and deaths from influenza occur among elderly patients, who are more vulnerable than younger people and have a weaker response to influenza vaccination. Influenza outbreaks are common in LTCFs. Studies show that increasing influenza vaccination among health care providers in LTCFs decreases morbidity and all-cause mortality, but such facilities lag behind all other settings in coverage rates. Education improves uptake to a limited extent. In acute care settings, mandates improve coverage dramatically.

In 2004, the University of Pennsylvania's medical center required its health care providers to be vaccinated against measles, mumps, rubella, and varicella and recommended annual influenza vaccination. The center implemented many programs to raise awareness, address myths, and make vaccination easily accessible. Compliance with the required vaccines was near 100 percent with few objections, but influenza vaccination rates remained below 50 percent. On evaluation, Dr. Behrman identified some lessons learned about mandatory versus voluntary workplace vaccination programs:

Voluntary Programs	Required Programs
• Nobody likes being compelled, especially annually	• May reduce efforts to educate and improve voluntary measures
• May produce resentment	• There may be real limits to voluntary programs
• Expensive to monitor and enforce	• Even 80–90% coverage rates do not maximize risk reduction
• Rare voluntary programs have achieved 80–90% coverage	• Compliance with mandated measles, mumps, rubella, and varicella immunization approached 100% with negligible objections
	• Early mandatory influenza vaccine programs for health care providers reported more than 95% vaccination rates, doubling prior rates
	• Health care providers are generally healthy, younger adults with optimal vaccine responses (in contrast to medically fragile patients)

The medical center began requiring annual influenza vaccination in 2009, achieving coverage rates above 98 percent. Dr. Behrman said it remains difficult to demonstrate that vaccinating health care providers reduces overall risk for patients in hospital settings, but the benefits are clear in LTCFs. Voluntary measures have not increased coverage among health care providers.

NAIIS' Influenza Working Group developed a guidance document on mandatory vaccination in LTCFs that is available free online. It has forged partnerships with the Gerontological Society of America, CMS, and AMDA–The Society for Post-Acute and Long-Term Care Medicine. Since October 2018, the number of LTCFs on IAC's honor roll for mandatory vaccination increased from six to 130, and IAC created a dedicated honor roll for LCTFs to highlight who has committed to this effective intervention. Dr. Behrman urged participants to review the guidance, offer feedback, and share it with their colleagues.

Discussion

In response to Dr. El Sahly, Dr. Behrman said some studies show absenteeism declines in acute care settings with employee vaccination requirements. She believes the findings are applicable to LTCFs.

Dr. Dunn said early efforts in Seattle to establish mandatory requirements met with a lot of resistance. However, once the first system implemented requirements, other organizations had an easier time. A critical mass developed, and vaccination requirements began to be seen as a community standard. Dr. Dunn asked whether independent LTCFs are reluctant to require vaccinations without a community-wide move in that direction. Dr. Behrman agreed with Dr. Dunn's assessment and added that LTCFs face many other challenges, including staff retention and tight profit margins. She believed that with more publicity about organizations achieving success with vaccine mandates, a community norm might develop.

Dr. Behrman said that of the 130 LTCFs on IAC's honor roll, almost all belonged to a large group with a centralized policy. Another large group is planning to require staff and patients to be vaccinated, she added.

Ms. Butler asked what challenges IAC and NAIIS face getting information out to medical and nursing providers coming into the field. Ms. Peterson said young health care professionals are the most challenging group to reach. IAC used to push information to residency programs but now relies on individuals to subscribe to its materials. Ms. Peterson and Ms. McKenna said they rely on individuals and partners to spread the word.

Dr. Douglas asked if there were data from places like Colorado, where vaccine mandates were put in place several years ago. Dr. Behrman said Colorado's mandate informed the NAIIS guidance document for LTCFs. She pointed out that "mandatory" has very different meanings in different states; the consequences range from negligible to loss of employment. However, all mandates help increase vaccine coverage rates. Courts have mostly upheld the right of health care organizations to mandate vaccination. Dr. Douglas pointed out that CMS can play a role, given that most residents of LTCFs are Medicare beneficiaries. Dr. Behrman said the NAIIS Influenza Working Group would be happy to see CMS include mandatory influenza vaccination as part of the grading and approval of LCTFs. Hospitals are already required to submit staff influenza vaccination coverage data to CMS, but Dr. Behrman said she was not sure whether LCTFs must do so. Dr. Hopkins said CDC's Public Health Professionals Gateway has State-by-State data on legislation regarding employee vaccination requirements in LCTFs.

Dr. Douglas wondered what proportion of hospitalizations related to influenza in a given season could be attributed to infection acquired in an LTCF. Dr. Behrman did not have data but guessed the rates must be high, because infections spread so easily in an LCTF setting.

Dr. El Sahly said that previous presentations to NVAC demonstrate that when broad policies such as school entry requirements are in place, many of the issues around vaccine hesitancy and opting out become less important. Policies lead to increased vaccine coverage much faster than leaving the issue up to individuals or institutions.

Dr. Friedland said HHS, CDC, and others' infographics are helpful for showing the impact of infectious disease. Given the high rates of morbidity and mortality among elderly people, public health agencies should consider creating infographics that highlight this population.

Dr. Collins said mandates are built into the foundation of DoD health care. He suggested that immunization experts evaluate exemptions to ensure they are consistent across facilities within a system that mandates vaccination. Dr. Collins also noted that DoD has a lot of experience and educational resources with vaccine shipping, storage, handling, and temperature maintenance that may be of interest to NAIIS.

Vaccine Research Center (VRC)/NIAID Update on a Phase I Trial of a Universal Influenza Vaccine Candidate—Grace Chen, M.D., M.P.H., Clinical Trials Program, Vaccine Research Center, NIAID, NIH

Dr. Chen outlined the need for a universal influenza vaccine. In the past 10 years, new technologies and approaches have laid the foundation for overcoming the challenges. The goals of a universal influenza vaccine are consistent efficacy of more than 75 percent against medically attended illness caused by seasonal and pandemic strains of influenza, a single product that does not require annual revision and durable immunity for greater than one year.

To overcome some of the biological challenges, VRC is leveraging recent technological advances in structure-guided approaches to design antigens, including natural and designer nanoparticles,

as well as different delivery techniques to develop vaccine platforms. In addition, VRC is also focused on advancements in assessing the immune response to vaccination.

In the past 2 years, VRC has conducted two trials around development of a universal vaccine. The first assessed the platform, which consists of an H1 influenza virus stem fused to a *Helicobacter pylori* ferritin platform and the hemagglutinin (HA) head removed. Preliminary data indicate the platform is safe and well tolerated.

The second trial is evaluating the influenza vaccine candidate using the new platform. The stem portion of HA has more conserved epitopes than the immunodominant HA head. In the currently licensed seasonal influenza vaccines, the HA head predominantly drives the immune response. By taking the HA head out of the vaccine, researchers hope to improve the breadth of response. In preclinical studies and animal models, the vaccine was safe and immunogenic and showed some protection against H5N1 influenza. Enrollment is underway for the Phase I clinical trial.

Discussion

In response to Dr. El Sahly, Dr. Chen said the study would look at the effect of the vaccine not only on the strain contained in the vaccine but also other strains. Investigators will use different types of neutralization assays and possibly different binding assays to evaluate the results. In response to Dr. Douglas, Dr. Chen clarified that *H. pylori* was selected for the platform because it allows presentation of the antigen in a fairly realistic way that investigators hope will generate a pronounced immune response.

Public Comment

No public comments were offered.

Wrap Up and Adjournment—Robert H. Hopkins Jr., M.D., MACP, FAAP, NVAC Chair

Dr. Hopkins thanked the participants and the NVPO staff and adjourned the meeting at 12:39 p.m.

APPENDIX: Abbreviations

ACIP	Advisory Committee on Immunization Practices
ACCV	Advisory Commission on Childhood Vaccines
AFM	acute flaccid myelitis
AHIP	America's Health Insurance Plans
AHRQ	Agency for Healthcare Research and Quality
AIM	Association of Immunization Managers
AIRA	American Immunization Registry Association
APhA	American Pharmacists Association
ASH	Assistant Secretary for Health
ASTHO	Association of State and Territorial Health Officials
BARDA	Biomedical Advanced Research and Development
BPHC	Bureau of Primary Health Care
CDC	Centers for Disease Control and Prevention
CISA	Clinical Immunization Safety Assessment
CMS	Centers for Medicare and Medicaid Services
DICP	Division of Injury Compensation Programs
DoD	Department of Defense
DTaP	acellular diphtheria-tetanus-pertussis
EHR	electronic health record
EV-D68	enterovirus D68
FDA	Food and Drug Administration
FY	fiscal year
GBS	Guillain-Barré syndrome
HA	hemagglutinin
HCV	hepatitis C virus
HHS	Department of Health and Human Services
HPV	human papillomavirus
HRSA	Health Resources and Services Administration
IAC	Immunization Action Committee
IIS	immunization information systems
LTCF	long-term care facility
MMR	measles-mumps-rubella [vaccine]
NACCHO	National Association of County and City Health Officials
NAIIS	National Adult and Influenza Immunization Summit
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NVAC	National Vaccine Advisory Committee
NVIC	National Vaccine Information Center
OIDP	Office of Infectious Disease and HIV/AIDS Policy
PAHO	Pan American Health Organization
PDUFA	Prescription Drug User Fee Act
PHAC	Public Health Agency of Canada
PWID	people who inject drugs
QALY	quality-adjusted life-years
TAG	Technical Advisory Group (PAHO)
Tdap	tetanus-diphtheria-pertussis vaccine
USPSTF	U.S. Preventive Services Task Force
VA	Department of Veterans Affairs
VAERS	Vaccine Adverse Event Reporting System

VICP	Vaccine Injury Compensation Program
VRC	Vaccine Research Center
VSD	Vaccine Safety Datalink
WG	working group
WHO	World Health Organization