TELECONFERENCE OF THE BOARD OF SCIENTIFIC COUNSELORS, OFFICE OF INFECTIOUS DISEASES

Centers for Disease Control and Prevention
Atlanta, Georgia

December 6, 2018
10:00 AM – 1:30 PM (EST)

A half-day, open public meeting of the Board of Scientific Counselors (BSC), Office of Infectious Diseases (OID),[1] took place as a teleconference on Thursday, December 6. In addition to Board members and staff of the Centers for Disease Control and Prevention (CDC), representatives of several public health partner organizations and members of the public attended the meeting (appendix). Due to the declaration of December 5 as a National Day of Mourning in memory of President George H.W. Bush, the agenda (originally planned for a one-and-a-half day, in-person meeting) was shortened to address four time-critical topics:

- The recent outbreaks of acute flaccid myelitis (AFM) and the formation of an AFM Task Force as a workgroup of the BSC
- Reports from
  - The Food Safety Modernization Act Surveillance Working Group (FSMA-SWG)
  - The new Vector-borne Diseases Workgroup (VBD WG) of the BSC/OID and the BSC, National Center for Environmental Health/Agency for Toxic Substances and Disease Registry (NCEH/ATSDR)
  - The Infectious Disease Laboratory Working Group (IDLWG)

Following the report from the FSMA-SWG, the BSC/OID unanimously passed a motion to approve the fiscal year (FY) 2018 FSMA-SWG annual report to the Secretary, U.S. Department of Health and Human Services (HHS).

Opening Remarks

BSC/OID Chair Ruth Lynfield—State Epidemiologist and Medical Director, Minnesota Department of Health—called the meeting to order and was joined in welcoming participants and facilitating introductions by Michael Iademarco, Acting CDC Deputy Director for Infectious Diseases, and Sarah Wiley, the BSC/OID Designated Federal Official. Following the roll call, Dr. Lynfield welcomed three new BSC members: Jay Butler, Acting Chief Medical Officer, Alaska Department of Health and Social Services; Kathy Talkington, Project Director, Antibiotic Resistance Project, The Pew Charitable Trusts; and Jon Temte, Professor, Department of Family Medicine and Community Health, University of Wisconsin School of Medicine and Public Health. Dr. Lynfield also welcomed alternate ex officio member Edward Cox, representing the U.S. Food and Drug Administration (FDA); a new ex officio member, Tammy Beckham, representing the National Vaccine Program Office; and two new liaison representatives—

[1] Name of BSC/OID reflects previous organizational unit. The Office of Infectious Diseases is now known as Deputy Director for Infectious Diseases.

Howard Njoo, serving as an alternate representative from the Public Health Agency of Canada (PHAC), and José Romero, representing the Advisory Committee on Immunization Practices (ACIP). No significant conflicts of interest were identified during the roll call.

Focused Discussion: Recent Outbreaks of AFM and Formation of the AFM Task Force

AFM Epidemiology in the United States, 2014–2018

Manisha Patel—Measles, Mumps, Rubella, Herpesvirus and Domestic Polio Epidemiology Team Lead, Division of Viral Diseases, National Center for Immunization and Respiratory Diseases (NCIRD), CDC—reviewed the epidemiology of AFM, which is characterized by

- Sudden onset of limb weakness within hours to a few days
- MRI findings that demonstrate spinal cord lesions largely restricted to gray matter
- Occurrence among children with a preceding respiratory or febrile illness
- No proven treatment. CDC's interim considerations for clinical management, developed in consultation with neurologists and infectious disease experts, are available on the CDC website.

Initial investigations of AFM cases began 6 years ago, in 2012, when three patients with acute limb weakness and gray matter lesions on MRIs presented within 1 month of each other in California (*Morbidity and Mortality Weekly Report* [*MMWR*], October 2014); 23 cases with this presentation were retrospectively identified as having occurred between 2012 and 2014. In 2014, 9 patients with limb weakness and spinal cord gray matter lesions were reported in Colorado. One hundred and twenty cases were identified in 34 states, after CDC issued a national alert. More than 5 cases of AFM per state were reported in California, Colorado, Massachusetts, Pennsylvania, and Utah.

AFM case definitions have evolved since national investigation began in 2014; a standardized case definition was implemented in 2015. The current case definition is as follows:

- **Confirmed**—*Acute onset of flaccid limb weakness, AND an MRI showing a spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments*
- **Probable**—*Acute onset of flaccid limb weakness, AND cerebrospinal fluid (CSF) with pleocytosis (white blood cell count >5 cells/mm^3)*

Analysis of AFM cases identified between August 2014 and October 2018 through national surveillance (n=460) indicated that

- AFM cases peaked every 2 years, with the greatest number of cases having onset of limb weakness during September in peak years (2014, 2016, and 2018).
- The median age of pediatric AFM patients was 6 years old, with relatively few infants affected. A higher proportion of cases were in boys (60%) than in girls, and 60% of case-patients were white.
- Among confirmed pediatric AFM cases identified since 2014, 37% experienced upper limb weakness only, compared with the 18% that experienced lower limb weakness only. MRI studies indicated that 80% had cervical spinal lesions. AFM cases reported in non-peak years (2015, 2017) were more likely to experience lower limb weakness and less likely to report a preceding respiratory or febrile illness than AFM cases reported in peak years (44–72% vs. 85–90%).

From August 2014 through December 1, 2018, over 1,500 specimens have been tested, including over 250 CSF specimens.

- Testing of CSF specimens:
  - PCR testing identified enterovirus-D68 (2 cases), enterovirus-A71 (1 case), and coxsackievirus A16 (1 case) in CSF samples from 4 cases of AFM reported between 2014 and 2018.
  - Metagenomic testing was also conducted on a subset of the 2014 CSF specimens; several clinically insignificant viruses were found, including GB virus C and transfusion-transmitted virus.
- Testing of upper respiratory specimens:
  - 20–30% of specimens from AFM cases that occurred in peak years were PCR positive for enterovirus-D68. However, enterovirus-D68 was also detected in some patients later classified as non-cases.
  - Other viruses (and some co-infections) were found in about one-third of upper respiratory specimens from AFM cases.
  - In the remaining one-third of upper respiratory specimens, no pathogen was detected.
  - All stool samples tested negative for poliovirus by standard World Health Organization (WHO) methods.

Clinical characteristics of confirmed pediatric AFM cases identified in 2018 (n=129) include the following:

- 96% of patients were hospitalized, with 58% admitted to an intensive care unit.
- For cases with a CSF specimen obtained, 81% had a mild or moderate pleocytosis with a lymphocyte predominance. Of note, the median time from limb weakness to CSF collection was 2 days.
- There have been no deaths reported among cases that were confirmed in 2018; however, there are deaths that have occurred in 2018 from cases with onset in prior years.
- 97% of 2018 cases had a preceding febrile or respiratory illness, and the median time between the preceding illness and limb weakness onset was approximately 2 days for fever, 2.5 days for gastrointestinal illness, and 5 days for respiratory illness.

CDC laboratory results for confirmed AFM cases from 2018 include the following:

- Two of 32 CSF specimens from AFM patients were positive for the following: enterovirus-A71 (1 adult case) and enterovirus-D68 (1 case).
- Respiratory specimens from 40 of 81 AFM patients were positive for the following viruses: enterovirus-D68 (21 cases), enterovirus-A71 (10 cases), rhinoviruses (7 cases), and parechovirus (2 cases).
- Stool specimens from 9 of 62 AFM patients were positive for the following viruses: enterovirus-A71 (1 case), enterovirus-D68 (1 case), echovirus 11 (1 case), coxsackieviruses (3 cases), parechovirus (1 case), and non-typed enterovirus/rhinovirus (2 cases).

Summary

- An increase in AFM cases occurred in 2018 compared with 2017; however, AFM is still a rare disease.
  - AFM is predominantly a pediatric illness.
  - An every-other-year increase in cases has been observed since 2014.

  - AFM cases have been reported in 44 states since 2014.
- More than 85% of AFM cases are associated with a preceding febrile or respiratory illness.
  - A virus has been detected in 50% of respiratory specimens.
  - Three different viruses have been identified in CSF specimens from 4 confirmed cases of AFM.
  - It is unclear whether AFM is the result of a direct viral invasion of spinal cord tissue or a post-infectious process. Limited biopsy or tissue specimens are available for pathologic studies.

AFM Task Force Report

Ruth Lynfield—BSC/OID Chair and Chair of the AFM Task Force—reported on the first AFM Task Force meeting, which took place on December 4, 2018. The Task Force is a workgroup of the BSC/OID and includes three BSC/OID members; one BSC/OID ex officio member, representing the Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health (NIH); and 12 additional members with clinical and research expertise in neurology, pediatric infectious diseases, myelitis, immunology, epidemiology, and infectious disease modeling. Three parents of children with AFM spoke at the Task Force meeting, describing their experiences in obtaining diagnoses and treatment for their children.

Neurologic/Clinical Session

Evidence supporting AFM as an emerging condition includes the following: multiple patients presenting with rapid onset of paralysis, the epidemiologic pattern of cases, and the degree of cervical involvement. It was noted that background cases of AFM were likely misdiagnosed as Guillain-Barré syndrome in previous years.

The Task Force agreed that the current clinical case criteria (i.e., acute flaccid weakness) was appropriate for surveillance purposes. Analysis of sub-populations will allow further characterization of the spectrum of illness, leading to a more specific definition that could inform research questions around etiology and pathogenesis.

The Task Force also concluded that

- A better understanding of lesions detected by MRI will help inform knowledge of the pathogenesis of AFM. Researchers should keep in mind that
  - The timing of the MRI is critical to the interpretation of findings.
  - AFM patients with upper limb weakness typically exhibit cervical spinal cord lesions in gray matter. In cases where MRIs indicate cervical spinal cord lesions only, lower extremity weakness is likely due to white matter involvement.
  - It is important to consider treatment modalities for both gray and white matter disease within the spinal cord.
- Rigorous and standardized long-term follow-up of AFM cases, including strength and functional assessments, is essential.
- Analysis of treatment outcomes is exceedingly difficult, due to the small patient pool and lack of standardized measurements across institutions.

Virology and Pathogen Discovery

The Task Force concluded that

- There is support for a link between preceding virus-like illness and AFM.
- Enterovirus-D68 remains a leading candidate for an AFM viral trigger, despite detections of other enteroviruses and rhinoviruses, and although the majority of respiratory specimens test negative for these viruses.
- The failure to consistently detect a pathogen in CSF specimens is likely to remain true even with planned enhanced discovery methods.
- Additional investigation is needed to confirm a link between preceding viral illness and AFM and to improve our understanding of
  - The duration of viral shedding. Data on the duration of viral shedding will facilitate interpretation of respiratory-specimen test results and determine how the timing of specimen collection affects those results.
  - Enterovirus epidemiology (temporal and geographic), with a focus on respiratory disease

Host Immune Response and Immune-Mediated Pathogenesis

To investigate the role of the human immune response in AFM, the Task Force recommends that researchers

- Measure antibody responses to infection in serum and CSF, including the presence of diagnostic antibodies (intrathecal antibodies) and pathogenic antibodies (autoantibodies) and the possibility of antibody-dependent enhancement[2]
- Use broad approaches for measuring pathogen-specific responses, such as multi-pathogen peptide microarrays and immune cell receptor repertoire profiling
- Measure and characterize enterovirus-D68 population immunity

Because the kinetics of AFM suggest that antibody-mediated pathology is unlikely, studies to measure autoantibody response are of lower priority.

Host Risk Factors

The Task Force expressed general support for assessing genetic factors associated with AFM, but recognized that host genetics studies can be complex and expensive. Priorities include studies that

- Target specific gene subsets in the central nervous system and immune system
- Target genetic factors that influence tissue susceptibility (e.g., receptor polymorphisms)
- Use detailed, structured interviews with families to uncover other potential risk factors, including environmental or behavioral risk factors

[2]Antibody-dependent enhancement is a phenomenon observed with dengue infections in which pre-existing antibodies present in the body from a primary dengue virus infection bind to an infecting dengue virus particle during a subsequent infection with a different dengue serotype. The antibodies from the primary infection cannot neutralize the virus and may allow it to infect monocytes more efficiently, leading to more severe disease.

Moving Forward

Priorities for action include

- Establish strong collaborations among CDC, NIH, academic researchers, and state and local health departments
- Understand the cause of central nervous system damage (e.g., direct pathogen effects and/or immune responses). Non-human primate models and other model systems may be useful in these studies.
- Continue work on pathogen detection
- Review and summarize clinical phenotypes of cases
- Strengthen case identification and surveillance, working with medical and public health partners to optimize recognition of AFM and use surveillance data for risk factor and other studies
- Strengthen and expand education and communication outreach
- Implement a natural history study to better understand pathogen(s), pathogenesis, and long-term outcomes
- Continue close dialogue with parents and families. One parent who spoke at the Task Force meeting emphasized the importance of improving medical record interoperability to enhance early detection and treatment.

Questions for the BSC

- Do you agree with the themes summarized from the AFM Task Force meeting?
- Any other areas to consider?
- Suggestions for ways to increase engagement of clinicians and public health?

BSC Discussion

Questions/comments from BSC members included the following:

- **How does the clinical presentation of AFM differ from that of acute poliomyelitis?** Mark Pallansch—Director, Division of Viral Diseases, NCIRD—said that AFM cases appear to have much more cervical involvement than thoracic compared with polio cases. Additionally, approximately 30% of the AFM cases had respiratory compromise, which is somewhat higher than polio.
  - AFM is similar to polio in the rapid onset of limb weakness but is more likely to affect the upper limbs versus the lower limbs.
  - Dr. Pallansch also noted that the shift from culture-based methods to molecular-based methods has facilitated detection of poliovirus in CSF specimens. Poliovirus can be detected in CSF up to 25% of the time. However, poliovirus has not been detected in either CSF or stool samples from any of the AFM patients reported to date.
- It was suggested that work should be done to highlight what is ***not*** a risk factor for AFM. A particular issue that keeps coming up is immunizations, but there are other factors.
- **What does CDC currently recommend for treatment of AFM*?*** Earlier this year, CDC updated interim considerations on clinical management of AFM, based on consultation with physicians with expertise in pediatric infectious disease and neurology, including immunology and inflammation.

Nancy Messonnier, NCIRD Director, said that pediatric neurologists and the parents of children with AFM agree that early access to rehabilitative therapy is important in regaining muscle function.

- **Should public health resources be devoted to rare diseases like AFM?** CDC made the decision to establish a Task Force to address this rare but tragic disease following the detection of three cycles of AFM (which suggested the emergence of a new condition requiring public health attention). Guidance from the Task Force will help achieve a better understanding of the epidemiology and etiology of AFM, accelerating development of strategies for effective treatments and prevention.
- **How accurate are serologic methods for detection of specific enteroviruses that may be associated with AFM?** Dr. Pallansch responded that the serologic method being used is antibody neutralization, which has been the defining way to separate enteroviruses from one another. While the test tells whether there is the presence of antibody that is capable of neutralizing a specific virus, it does not explain how it got there.
- **How strong is the virologic evidence suggesting a link between AFM and enterovirus infection?**
  - Dr. Pallansch responded that there is no question of a correlation between enterovirus-D68 (EV-D68) in the same years as the AFM increases. However, it could be somewhat of an artifact since EV-D68 came to our attention because of large outbreaks of severe respiratory disease requiring children to be admitted to intensive care units. This is how the large outbreak of EV-D68 was recognized in 2014. Additionally, EV-D68 is the only enterovirus for which there is a specific assay available, making testing and typing of EV-D68 much easier and more straightforward, which could also be an artifact.
  - Dr. Messonnier added that this is a key question that has confounded the issue. There is disagreement about whether EV-D68 has been proven to be the cause. In 2014 when there was the first discovery of a peak of AFM, it was during a very bad EV-D68 year. EV-D68 emerged and caused widespread disease in pediatric populations. While it is true that in 2016 there was an increase, it was not anywhere near what was observed in 2014. Therefore, CDC looked more broadly at other respiratory viral pathogens and still could not find a single underlying cause. This is why an even broader look is being taken in 2018. One key question is how this potentially could be EV-D68 when there are serologic data that suggest that populations in the United States have pre-existing antibodies to EV-D68.
- **By looking at the existing cases, can we tell what treatments are given at home or in the hospital for the preceding febrile or respiratory illness? Could AFM, like Reye's syndrome, be triggered by drug treatment for a preceding viral illness?** Studies are underway to gather data (e.g., from chart reviews) about treatment for preceding illnesses that AFM-affected children received at home or in the hospital.
- **What kinds of activities have been implemented thus far to educate and engage public health personnel and clinicians?** Dr. Messonnier responded that CDC has been working on this since 2014 and has engaged in numerous efforts to get messages out to clinicians, including using all of the normal channels through health departments, Health Alert Notices (HANs), et cetera. CDC has been funding health departments since 2015 to increase awareness and provide education to clinicians on AFM. CDC is also working with the American Academy of Pediatrics and all its other partners to increase awareness of AFM.
- **Does peak occurrence of AFM during the month of September suggest a back-to-school phenomenon? And what surveillance systems are in place to monitor respiratory infections?** A rise in AFM cases has not been observed every September, but only in alternate years. Dr. Pallansch noted that school-based surveillance for specific viruses would require labor-intensive viral typing to

distinguish among many common viral infections whose incidence tends to increase during the first weeks of the school year.

- **What do we understand about the natural history of AFM and what proportion of the children with AFM have persistent deficits, do the deficits improve, and is there family clustering?** Dr. Lynfield (AFM Task Force and BSC/OID) replied that the AFM Task Force absolutely agrees that a natural history study is very important, and that is being discussed. Examining the global epidemiology is also important, and is being addressed. In terms of the deficits, rehabilitation seems to be extremely important. In the coming weeks, the AFM Team will be diving deeper into the data to look at clinical phenotypes and will discuss how best to do longer term follow-up.
- **What might be the significance of the gender differential in cases of AFM?** The observation that a greater number of males than females are affected by AFM is consistent with the enterovirus hypothesis that boys tend to exhibit more severe illness than girls when infected with enteroviruses. However, this is not exclusive to enterovirus infection.
- **What proportion of children with AFM recover from the neurologic deficits?** Long-term follow-up is essential to answer this question. The clinical course of AFM varies, and rapid initiation of rehabilitation therapy is very important.
- **Is the period of transmissibility the period before onset of respiratory symptoms or paralysis?** Although AFM, the disease, is not transmissible from person to person, viruses that could cause AFM, such as enteroviruses, are. This is important because it impacts the type of isolation precautions that are used for patients with AFM in the hospital.
  - Part of the challenge is knowing the specific etiology. The suggested viruses and upper respiratory infections are transmissible but also extremely common.
  - Tom Clark, Incident Commander for the CDC AFM Response, said that contact and respiratory droplet precautions are appropriate when taking care of patients with EV-D68 respiratory disease.
- **How can CDC increase engagement of pediatricians and other clinicians in detection of AFM?**
  - CDC uses HANs to inform healthcare workers about AFM and funds state health departments to increase awareness and disseminate information about AFM to clinicians. Despite these efforts, parents of children with AFM report that clinicians may not think of AFM when they see evidence of limb weakness in a child. Lack of awareness can delay treatment as well as collection of specimens that could help identify a cause.
  - BSC members suggested that CDC
    - Work with professional societies, critical care physicians, and hospital physicians to raise awareness of AFM
    - Use data about how and where parents seek care for their children with AFM (e.g., in urgent care centers and/or emergency rooms) to inform decisions about where to focus communication efforts

In response to questions about current areas of research, Dr. Pallansch and Steve Oberste—Chief, Polio and Picornavirus Laboratory Branch, Division of Viral Diseases, NCIRD—mentioned ongoing studies on pathogen discovery (with colleagues at Columbia University and the University of California, San Francisco), on antibody-dependent enhancement, and on genetic and environmental factors that might make children more susceptible to AFM.

Other Comments from BSC Members

- The creation of an AFM Task Force is a good approach to inform collective action to address AFM. It will provide useful input to the BSC/OID, and it recalls CDC's prior use of "Team Bs" to advance the responses to the global outbreak of SARS and the Ebola outbreak in West Africa.
- A natural history study of AFM will further understanding of AFM pathogenesis.
- CDC should work with WHO and other nations to compare and advance global surveillance for AFM.
- Dr. Njoo (PHAC) observed that it might be mutually beneficial to include a Canadian representative on the AFM Task Force, because there is a similar situation in Canada. Dr. Clark agreed; CDC will consider this idea.

Public Comments

Phone lines were opened at 11:30 AM for public comments. One caller asked about the possible cause of the 6-fold increase in AFM cases in 2016 indicated in Dr. Patel's data. Dr. Lynfield said that this portion of the agenda was for the BSC/OID to receive comments from members of the public, and CDC would note the question.

Food Safety Modernization Act Surveillance Working Group Report

Tim Jones—State Epidemiologist, Tennessee Department of Health, and FSMA-SWG chair—reported on the draft annual report to the HHS Secretary and on the FSMA-SWG meeting held on December 3–4, 2018.

FY 2018 Annual Report

- The FSMA-SWG is charged with issuing an annual report to the HHS Secretary.
- The proposed timeline for the FY 2018 annual report includes completion in November 2018; BSC review and comment in December; BSC endorsement at the December BSC meeting; and submission to the HHS Secretary in January 2019.
- The FY 2018 annual report includes an introduction, a discussion of key topics, a discussion of resources, and a section on next steps. Key topics include potential use of foodborne illness surveillance data to evaluate the implementation of FSMA, CDC updates, and culture-independent diagnostic tests (CIDTs).
- Appendices to the FY 2018 annual report include (1) a list of FSMA-SWG members and (2) a list of FY 2012–17 FSMA-SWG annual reports and meeting topics.

Dale Morse—Associate Director for Food Safety, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), CDC—noted that the FY 2018 annual report includes advice and guidance developed by the FSMA-SWG during

- A FSMA-SWG meeting in December 2017 that considered how FDA might use surveillance data from industry partners and CDC to measure the impact of FSMA on foodborne illness

- A Forum on Culture-Independent Diagnostics in May 2018, at The Pew Charitable Trusts in Washington, DC, organized by CDC, Pew, the Association of Public Health Laboratories, the Council of State and Territorial Epidemiologists (CSTE), and The Ohio State University

Dr. Morse also noted that IDLWG is also reviewing CIDT issues, which are relevant to many infectious diseases areas, in addition to foodborne diseases.

BSC Discussion

Questions from BSC members included the following:

- **What is the basic task for public health in regard to use of culture-independent diagnostic tests?** Specific activities identified by Dr. Jones included
  - Preserving isolates during the transition to CIDTs (e.g., via new submission requirements and/or public health sentinel sites such as the Gonococcal Isolate Surveillance Project [GISP])
  - Resolving resource issues related to increased use of CIDTs,[3] which are more sensitive than culture-based tests. Detection of a higher volume and complexity of cases, as CIDTs come into widespread use, will require more investigative resources at the state and local level. Dr. Jones noted that the transition to tests based on whole genome sequencing (WGS) will increase data management costs and likely require cooperation and resource-sharing with medical and industry partners.
  - Revising CSTE case definitions that currently refer only to culture-based test results to include both types of test results. Changes in case definitions will affect the interpretation of disease trends based on comparisons of new data sets with those from prior years.
  - Revising return-to-work laboratory-test criteria for people in high-risk occupations (e.g., food handlers), because CIDT results do not distinguish between persons who are actively infectious and persons in the post-infection phase.
- **Will CDC address CIDT-related issues related to diagnostic stewardship[4] by clinical laboratories?** Diagnostic stewardship issues and partnerships with clinical laboratories may be considered by IDLWG as part of its consideration of CIDT issues.
- **Have CIDTs had a positive or negative impact on diagnosis of acute gastroenteritis?** Dr. Jones said that the impact of CIDTs has been largely positive, with fewer cases missed. He noted that it will take time and experience to determine which cases detected by CIDTs are of clinical and public health importance. A similar determination was necessary during the transition to PFGE (pulsed-field gel electrophoresis) testing when PulseNet first began.

BSC Endorsement

Following the discussion, the FY 2018 annual report received unanimous approval by the BSC members.

[3] FoodNet (Foodborne Diseases Active Surveillance Network) data indicate that the annual percentage of bacterial infections diagnosed by CIDTs increased from 9% in 2012–15 to 25% in 2016–17.
[4] Diagnostic stewardship refers to the appropriate use of laboratory testing to guide patient management, including treatment, in order to optimize clinical outcomes and limit the spread of antimicrobial resistance.

FSMA-SWG Meeting on December 3–4, 2018

The three meeting topics included the following:

1. **Updates on the Interagency Food Safety Analytics Collaboration (IFSAC)**
   - IFSAC—a collaboration among CDC, FDA, and the U.S. Department of Agriculture/Food Safety and Inspection Service (FSIS)—has issued updated source attribution estimates for 2014–2016 for four priority pathogens: *Salmonella*, *Escherichia coli* O157, *Listeria monocytogenes*, and *Campylobacter*.
   - IFSAC is evaluating data sources and approaches for assessing points of contamination (POC) during outbreaks of foodborne diseases. Potential data sources and approaches include
     - Accessing data sets from CDC, FDA, and FSIS that include POC information
     - Utilizing variables from the Foodborne Disease Outbreak Surveillance System (FDOSS) to classify outbreaks based on POC regulatory jurisdiction
     - Automating classification of outbreaks based on POC regulatory jurisdiction. IFSCAC has determined that 80% of outbreaks might be auto-classified in this way.

2. **CDC foodborne illness surveillance data systems and strategies**
   - The FSMA-SWG considered the complexity of CDC's surveillance systems and the need for improved integration of surveillance data. CDC's enteric illness surveillance systems include
     - *Case-based systems*, such as the National Notifiable Diseases Surveillance System (NNDSS)
     - *Isolate-based systems*, such as the Foodborne Diseases Active Surveillance Network (FoodNet), PulseNet, and the National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS)
     - *Event-based systems*, such as the National Outbreak Reporting System (NORS)
   - A state health department may report a case of *Salmonella* to NNDSS, PulseNet, NARMS, NORS, FoodNet, the National Enteric Reference Laboratory, or the Laboratory-based Enteric Disease Surveillance (LEDS) system. Moreover, state health departments currently use different reporting formats.
   - CDC is transitioning to a more efficient workflow, in which
     - The states electronically transmit surveillance data to CDC in a standardized format.
     - The surveillance data in CDC's case database are linked automatically to data in CDC's laboratory database.
   - CDC's objectives for improving data management include
     - Optimizing data collection and transmission, by increasing informatics capacity; developing message mapping guides (MMGs) to support standardized electronic data transmission by state partners; and changing data formats, processes, and systems, as needed to advance data integration
     - Linking data sources in a timely manner. Linkage requires compatible systems and defined standards for data and transmission.
     - Using surveillance data to drive action-oriented endpoints
     - Disseminating surveillance data to catalyze practical action

- MMGs enable jurisdictions to submit surveillance data in the HL7 format. MMGs are available for all foodborne pathogens and conditions and include data elements specific to certain pathogens, public health programs, and studies. Before releasing the foodborne disease MMGs, CDC incorporated feedback from the states and piloted the use of MMGs in Emerging Infections Program (EIP) and non-EIP jurisdictions.
- CDC is also assisting state partners in improving informatics capacity, via the Epidemiology and Laboratory Capacity for Infectious Diseases (ELC) Cooperative Agreement.
- ***FSMA-SWG guidance on data integration*.** FSMA-SWG members observed that
  - Although CDC's surveillance data on enteric diseases is "very rich," its data collection and management systems are antiquated, inefficient, duplicative, uncoordinated, and siloed. Public health data should be transmitted through a single entry port and be readily available for distribution to programs and partners.
  - CDC is making progress in improving data integration, with MMGs already adopted by some states. Continued infrastructure improvements are needed to advance
    - States' ability to send electronic reports to CDC
    - CDC's ability to receive electronic data; to connect systems to reduce redundancy; to adapt current systems to new technology (e.g., WGS), and to make data available to users. The NORS Dashboard and NARMS Now might be used as data-sharing models.
  - Progress updates on data integration will be requested at future BSC meetings.

3. **CDC and FDA updates on recent produce outbreaks**

   Topics included the following:

- The 2018 cyclosporiasis outbreak season, which
  - Involved 2,299 laboratory-confirmed cases reported from 33 states, with 160 hospitalizations.[5] Significant outbreaks included
    - 250 cases linked to Del Monte pre-packaged vegetable trays
    - 511 cases linked to McDonald's salads
    - Basil-associated clusters in 2 states, with a total of 16 cases
    - 3 cilantro-associated clusters at Mexican-style restaurants, with a total of 53 cases

  Work is underway to develop advanced molecular methods for detection of *Cyclospora* strains. During the 2018 outbreak season, investigators observed that
    - Many cases could not be linked to an outbreak and/or to the outbreak vehicle
    - For the first time, *Cyclospora* was associated with domestically grown products
- A 2018 outbreak of *E. coli* O157 infections linked to romaine lettuce, which was the largest outbreak of Shiga toxin-producing *E. coli* (STEC) since the 2006 outbreak associated with spinach. The 2018 outbreak involved 210 cases in 36 states, with 96 hospitalizations, 27 cases of hemolytic uremic syndrome, and 5 deaths.

[5] Casillas SM, Bennett C, Straily A. *Notes from the Field:* Multiple Cyclosporiasis Outbreaks — United States, 2018. MMWR Morb Mortal Wkly Rep 2018;67:1101–1102.

- WGS analysis indicated that
  - Clinical isolates (which fell into two sub-clades) were closely related to water isolates obtained from an irrigation canal in the region of California identified as the potential source of the lettuce.
  - The same STEC O157 strain had been detected in sporadic cases in 2017 and 2018; in disease clusters in Colorado in 2017 and Maine in 2018, possibly associated with leafy greens; and in a 2017 outbreak in California associated with contaminated stream water (and possibly with wildlife).
- Investigative challenges included difficulties in collecting data from patients (because people who eat lettuce eat it often and may not remember what type of lettuce they ate) and in testing food products (because the short shelf-life of lettuce limits opportunities to test leftover food). Another issue concerned lack of information about the growing locations of the contaminated lettuce.
- Accomplishments that helped control the outbreak included
  - Issuing a public warning about romaine lettuce within 8 days of identifying the multistate outbreak
  - Rapid investigations of sub-clusters to help confirm the outbreak vehicle
  - Demonstration of the value of WGS during outbreak investigations

Potential Future Topics for the FSMA-SWG

Future areas for discussion include

- Industry updates on data-sharing, legal issues, and product labeling to facilitate trace-back efforts
- Recurring outbreak strains and sources/vehicles of contamination
- Orphan illnesses, such as cryptosporidiosis, toxoplasmosis, and hepatitis A
- "Stealth[6]" sources of contamination
- Outbreaks due to imported foods
- Use of social media for disease surveillance
- Periodic reviews of enteric surveillance systems
- Updates on interagency collaborations (e.g., IFSAC, the Interagency Foodborne Outbreak Response Collaboration [IFORC], and the Interagency Collaboration on Genomics and Food Safety [Gen-FS])
- Identification and analyses of the root causes of contamination
- Building state capacity (e.g., via the Integrated Food Safety Centers of Excellence), including workforce development issues

[6] A "stealth food" is a food that people may eat but are unlikely to remember (e.g., spices, garnishes, and ingredients in a food product such as the filling in a snack cracker).

BSC Discussion

- Dr. Njoo (PHAC) commended collaboration among U.S. and Canadian investigators during the response to the STEC O157 outbreak associated with romaine lettuce.
- In response to a question about efforts to reduce contamination before food products reach consumers, Dr. Jones noted that interventions vary, depending on the type of food. Examples include changes in meat processing that reduce *E. coli* O157 contamination of ground beef, decontamination of irrigation water and water used in food processing, and agriculture practices that separate food animals from crops.
- Dr. Morse added that the FY 2018 annual report discusses new FDA rules and regulations on food processing that aim to reduce contamination of food. Sherri McGarry, the CDC Food Safety Liaison to FDA, reported that the outbreak associated with romaine lettuce has prompted FDA to hold discussions with industry partners about whether to revise FDA produce safety rules related to prevention of disease spread via contaminated water.

Vector-borne Diseases Workgroup Report

The Vector-borne Diseases Workgroup was established jointly by the BSC/OID and the BSC/NCEH/ATSDR to advance public health efforts to detect, prevent, and respond to VBDs. The VBD WG is co-chaired by Jim Le Duc, BSC/OID, and Melissa Perry, BSC/NCEH/ATSDR, and its membership includes scientists with expertise in public health, entomology, pesticides, and ecology. Jay Butler is a second BSC/OID member on the VBD WG.

Dr. Le Duc noted that there is wider acknowledgment that vector-borne diseases are increasing and that the United States is not fully prepared to address these risks. The VBD WG is tasked with providing guidance to CDC/ATSDR on goals and strategies to

- Develop and evaluate VBD prevention and control tools, by
  - Conducting a public health assessment of the safety, efficacy, and feasibility of existing and novel vector control methods
  - Using modeling to identify effective tactics for VBD prevention and response
  - Assessing the relative effectiveness of non-pesticidal tools (e.g., traps and genetically modified vector populations)
  - Developing strategies for collection and use of data on vectors and pathogens
- Clarify CDC/ATSDR's role in monitoring human exposures and adverse health effects related to use of pesticides for VBD control
- Establish a strong public health workforce in vector control, by developing a cadre of public health entomologists and providing targeted training in vector control for state and local health departments
- Develop, maintain, and improve mosquito control programs to improve outbreak responses and decrease the need for emergency measures
- Improve risk communications for VBD, emphasizing the need for clear and transparent language and proactive community engagement
- Enhance collaborations among partners in public health, academia, and industry to develop and improve existing VBD prevention and vector control strategies

Ben Beard—Deputy Director, Division of Vector-Borne Diseases (DVBD), NCEZID—and co-Designated Federal Official, VBD WG—reported that DBVD has developed an internal VBD strategic plan and is working with other agencies to develop a national, cross-government VBD plan. Dr. Beard mentioned the recent release of

- Illnesses on the rise from mosquito, tick, and flea bites, *Vital Signs*, May 2018
- Multistate Infestation with the Exotic Disease–Vector Tick *Haemaphysalis longicornis* — United States, August 2017–September 2018, *MMWR*, November 30, 2018

VBD WG Activities

Dr. Le Duc reported that the VBD WG has held three teleconferences:

- On July 6, the VBD WG confirmed its membership, discussed its timeline, and reviewed tasks and key issues identified by OID and NCEH.
- On October 1, the VBD WG reviewed strategic plans on VBD from DVBD and NCEH.
- On November 7, the VBD WG reviewed progress made to date; received input on its tasks and on areas of VBD expertise within DVBD and NCEH; and discussed the pending release of a report from the HHS Tick-Borne Disease Working Group established by Congress in 2016 as part of the 21st Century Cures Act. Dr. Beard is the CDC representative to the HHS workgroup.

The VBD WG has begun an in-depth discussion of risk communications and will focus next on workforce development in vector control. Progress to date includes the following:

- Identification of opportunities for collaboration between DVBD and NCEH. Common themes include
  - Training and workforce development. Current training efforts include the DVBD Regional Centers of Excellence (COEs) in Vector-Borne Diseases and the NCEH training modules on vector control for environmental health professionals.
  - Communication issues, such as the need for clear, coordinated messaging, especially during emergencies
  - Collaboration with state and local health departments as principal partners and "customers"
  - Common interests in rodents as reservoirs/vectors of disease, and common concerns about importation of exotic mosquito and tick disease vectors
- Identification of unique VBD expertise in NCEH and DVBD

BSC Discussion

Questions from BSC members included the following:

- **Does CDC use geospatial modeling as a public health tool to identify areas that are vulnerable to the emergence or re-emergence of VBDs?** Dr. Beard noted that DVBD has collaborated with the National Center for Atmospheric Research in Boulder, Colorado, to model the impact of rising temperatures and cyclical phenomena such as El Niño on the incidence, distribution, range, and seasonality of ticks and mosquitos.
- **What are CDC's plans for training entomologists?** DVBD supports five COEs through a 5-year, $50M program. These centers are located in California, Florida, Minnesota, New York, and Texas. Training activities include graduate and post-doctoral training programs in public health entomology and a range of other shorter term training opportunities. DVBD also provides funds to the Entomological

Society of America and to the American Mosquito Control Association to support certification programs in vector control. In addition to training the next generation of entomologists and VBD experts, the COEs' priorities include creating a community of practice that includes academic and health department partners and conducting operational research to produce new tools and guidelines for vector control.

- **How might CDC increase the engagement of rural primary care providers in surveillance for vector-borne diseases?** Physicians in rural areas are well positioned to observe cases of tick-borne diseases and improve detection and reporting of VBDs. BSC members suggested that CDC work with professional societies and local health departments to intensify outreach to healthcare providers in rural areas and disseminate information about VBDs.

Other Comments

- BSC members noted that the impact of climate change on vector-borne diseases is a relevant and timely topic for future consideration by the VBD WG.
- Dr. Beard noted that
  - New guidance from the ELC Cooperative Agreement combines tick-borne and mosquito-borne diseases into one VBD category, so that health departments can use ELC resources to address either problem, depending on local needs.
  - The DVBD strategic plan emphasizes VBD education for healthcare providers, including nurse practitioners and physician assistants.
- Rima Khabbaz, NCEZID Director, said that it is unusual to have a workgroup that straddles two CDC centers and two BSCs. Marilyn Radke—co-Designated Federal Official, VBD WG, from NCEH—participated in the BSC/OID meeting, and the VBD WG will report to the BSC/NCEH/ATSDR next week.

Infectious Disease Laboratory Working Group Report

Jill Taylor—Director of the Wadsworth Center, New York State Department of Health, and IDLWG co-chair—posed the following question to the BSC, on behalf of IDLWG: ***Can IDLWG play a useful role in addressing issues that arise during the transition from culture-based tests to CIDTs?***

Background

- IDLWG's initial role was to assist CDC in establishing the Advanced Molecular Detection (AMD) initiative. As described by Gregory Armstrong—Director, Office of Advanced Molecular Detection (OAMD)—at the May 2018 BSC meeting, OAMD has extended sequencing and bioinformatics capacities to state and local public health laboratories and continues to increase engagement by epidemiologists.
- Last year, IDLWG turned its attention to public health issues related to increased use of CIDTs by hospital and clinical laboratories. As discussed by the FSMA-SWG, CIDTs are a transformative and disruptive technology, causing a loss of isolates and necessitating changes in traditional epidemiologic approaches to disease surveillance and investigation of outbreaks.
- While the use of CIDTs to detect foodborne illnesses is already widespread, CIDT use will eventually affect all types of infectious diseases, including respiratory diseases and antimicrobial drug-resistant diseases.

Future Activities

- During 2019, IDLWG might
  - Continue to provide assistance to OAMD to address challenges that may arise as OAMD incorporates new techniques and expands to include all pathogens of public health importance
  - Help guide and support CDC during the transition to CIDTs and then to metagenomics
- IDLWG can coordinate input on CIDT issues from infectious disease experts, industry partners, health departments, and non-governmental organizations. Those issues may include the following: preserving isolates for public health purposes; interpreting disease trends when new data sets are based on CIDT results; addressing the need for greater investigative resources as CIDTs detect a higher volume of cases; and advancing research studies on metagenomic techniques and on methods for merging epidemiologic and laboratory data sets.
- IDLWG might hold an in-person meeting in 2019 and additional meetings via teleconference and submit an annual report on CIDT issues in December 2019.
- Susan Sharp, IDLWG co-chair, noted that IDLWG is well positioned to address CIDT issues and can bring in additional expertise, as needed.

BSC Discussion

- John Besser—Deputy Chief, Enteric Diseases Laboratory Branch, Division of Foodborne, Waterborne, and Environmental Diseases, NCEZID—agreed that the world of diagnostics is changing quickly and that guidance from the BSC and IDLWG would be welcome.
- The BSC members agreed that CIDTs are an appropriate focus and good direction for IDLWG and that IDLWG's input to the BSC on this topic would be useful.

Public Comments

Phone lines were opened at 1:20 PM for public comments. No comments were made.

Closing Comments

Dr. Lynfield thanked the BSC participants and commended two BSC members who are retiring from the BSC after completing two terms: Andy Pavia—Chief, Division of Pediatric Infectious Disease, University of Utah—and Judy Wasserheit—Chair, Department of Global Health, University of Washington. Dr. Lynfield also acknowledged two members who are rotating off the BSC: Melinda Wharton, ex officio member representing the National Vaccine Program Office, and Nancy Bennett, liaison representative from ACIP.

Dr. Lynfield, Dr. Iademarco, and Ms. Wiley thanked Robin Moseley—who is retiring from CDC later this month—for her many years of excellent and expert service to CDC and to the BSC.

The meeting was adjourned at 1:30 PM.

APPENDIX: Meeting Participants*

BSC Members

Tammy Beckham
Kristy Bradley
Jay Butler
Sheldon Campbell
Barbara Cole
Edward Cox
(representing FDA)
Jeff Duchin
Emily Erbelding
Mary Hayden
Tim Jones
Salmaan Keshavjee
Beth Lautner
Jim Le Duc
Mike Loeffelholz
Ruth Lynfield
Bonnie Maldonado
Howard Njoo
(representing PHAC)
Susan Philip
Mark Riddle
Lee Riley
José Romero
Susan Sharp
Kathy Talkington
Jill Taylor
Jon Temte
Judy Wasserheit
Debbie Yokoe

CDC Staff

Noah Aleshire
Greg Armstrong
Ben Beard
John Besser
Chris Braden
Tom Clark
Kim Distel
Marta Gwinn
Michael Iademarco
Rima Khabbaz
Alexandra Levitt
Sherri McGarry
Jono Mermin
Nancy Messonnier
Dale Morse
Robin Moseley
Steve Oberste
Mark Pallansch
Manisha Patel
Marilyn Radke
Mike Shaw
Sarah Wiley

*Participants on site and by phone also included other CDC staff, individuals from Deputy Director for Infectious Diseases partner organizations, and members of the public.

I hereby certify that to the best of my knowledge, the foregoing minutes of the proceedings of the meeting of the Board of Scientific Counselors, Office of Infectious Diseases, on December 6, 2018, are accurate and complete.

/S/
Ruth Lynfield, M.D.
Chair, BSC, OID

03/01/19
Date