

**Meeting of the Board of Scientific Counselors, Office of Infectious Diseases
Centers for Disease Control and Prevention
Tom Harkin Global Communications Center
Atlanta, Georgia**

December 5, 2012

A one-day, open public meeting of the Board of Scientific Counselors (BSC), Office of Infectious Diseases (OID), was held on December 5, 2012, at the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. In addition to Board members and CDC staff, the meeting was attended by representatives of several public health partner organizations (Appendix).

A key theme of the meeting was strengthening the clinical and public health interface, with a focus on two areas: (1) addressing pertussis and (2) implementing new recommendations for reducing morbidity and mortality due to infection with hepatitis C virus (HCV). The meeting began with reports from the BSC Food Safety Modernization Act Surveillance Working Group (FSMA SWG) and the Antimicrobial Resistance Working Group (ARWG). The meeting also included updates on CDC's infectious disease activities, including a presentation on the multistate outbreak of fungal meningitis, and a discussion with CDC Director Dr. Thomas Frieden.

OPENING REMARKS

BSC Chair Dr. Ruth Berkelman, Rollins Professor, Emory University, called the meeting to order and was joined in welcoming participants and facilitating introductions by Dr. Rima Khabbaz, CDC Deputy Director for Infectious Diseases, and Robin Moseley, the BSC/OID Designated Federal Officer. Dr. Berkelman welcomed three new board members: Dr. Kristy Bradley, Oklahoma State Epidemiologist and State Public Health Veterinarian; Dr. Scott Ratzan, Vice President, Global Health, Johnson & Johnson; and Dr. Jill Taylor, Interim Director, Wadsworth Center, New York State Department of Health.

Dr. Berkelman said that Dr. Frieden has expressed strong support for the BSC. She also mentioned a letter published in *Politico* by former CDC directors that highlights CDC's work in infectious diseases as an example of how CDC safeguards the health of the American people (*Americans Depend on a Strong CDC*; <http://www.politico.com/news/stories/1112/84286.html>).

I. BSC WORK GROUP REPORTS

FSMA Surveillance Working Group

BSC member and working group chair Dr. Jim Hadler, Public Health Consultant, reported on the activities of the FSMA SWG, which met December 3-4, immediately prior to the BSC meeting. The working group is charged with providing advice and recommendations to CDC (and through CDC to the Secretary, Department of Health and Human Services [HHS]) on criteria for the designation of Integrated Food Safety Centers of Excellence (CoEs) and on enhancements to improve foodborne illness surveillance. Working group members include two representatives from the BSC (Dr. Hadler and Dr. Harry Chen, Commissioner, Vermont Department of Health); one each from CDC, the U.S. Department of Agriculture (USDA) Food Safety and Inspection Service (FSIS), and the U.S. Food and Drug Administration (FDA); three from academia; three from consumer groups; three from the food industry; and seven from state and local health and agricultural organizations.

Since the May BSC meeting, the working group has focused on the following topics:

Integrated Food Safety Centers of Excellence. Based on criteria developed by the working group (see [May 2012 BSC meeting minutes](#)), CDC has designated five CoEs in Colorado, Florida, Minnesota, Oregon, and Tennessee (<http://www.cdc.gov/foodsafety/fsma.html#section399>). CoE representatives met on Nov 28-29, 2012, to consider their scope of work in light of limited funding. Discussion topics included terms of reference, performance metrics, and specialization to avoid duplication of effort. Five working groups were established, each led by a CoE: Academic Coordination (Florida), Workforce Development (Colorado), Communications/Website (Tennessee), Performance Metrics (Minnesota), and Research Issues (Oregon).

To help facilitate their success, the FSMA SWG suggested that the CoEs serve as regional resources that

- Complement ongoing capacity-building assets such as FoodCORE and the Council to Improve Foodborne Outbreak Response (CIFOR)
- Conduct economic analyses of public health efforts to detect, investigate, control, and prevent foodborne diseases.

Preservation of PulseNet. Dr. Hadler stressed the importance of PulseNet, a network of laboratories that work to identify similar cases of foodborne illness that might signal an outbreak by comparing DNA patterns of bacteria from patient specimens submitted to CDC from different geographic locations. Clinical laboratories are increasingly using molecular tests that do not require pathogens to be grown in culture. As a result, fewer isolates are available for subtyping by PulseNet, and for other infectious disease surveillance systems, including many that monitor foodborne disease such as FoodCORE, OutbreakNet, FoodNet, the National Antimicrobial Resistance Monitoring System (NARMS), the FDA Coordinated Outbreak Response and Evaluation (CORE) Network, and the Predictive Analytics component of the USDA/FSIS Public Health Information System. Efforts are needed to ensure modernization of these surveillance systems.

The FSMA SWG emphasized that the public health community must preserve culture-based testing and maintain PulseNet until longer term solutions are identified and implemented. For the short term, public health laboratories will need additional capacity and legal authority to work with clinical laboratories that use non-culture-based tests to obtain duplicate specimens for culture. For the long-term, CDC and partners will need to develop, validate, and implement standardized non-culture-based tests that provide information that is at least equivalent to the information currently available to PulseNet. The working group suggested that CDC identify costs for these short- and long-term solutions and identify resources to fulfill them (e.g., from government, the food industry, and the healthcare sector).

Economic Analyses to Document the Impact of Foodborne Diseases Surveillance and Prevention.

The FSMA SWG discussed the methods and preliminary findings of two ongoing studies that illustrate the impact and cost-effectiveness of public health surveillance and prevention efforts. The first study assessed the number of cases of *Escherichia coli*, *Campylobacter*, and *Listeria* infections averted in 2010 by prompt public health action. A preliminary analysis found that the averted cases represented \$96 million savings in direct medical costs. The second study, still under analysis, documented cost-savings due to rapid detection of foodborne outbreaks by PulseNet.

The FSMA SWG emphasized that the findings of these analyses should be communicated to policy makers once the analyses are complete and when publicly available. CDC should coordinate additional economic analyses to document the impact of public health surveillance and prevention and identify differences in disease incidence and public health capacity among states.

Enhancements to CDC Data-Sharing and Surveillance Activities. Recent examples of CDC's activities in this area include

- Establishment of user-friendly, consumer-oriented sites that provide data more rapidly and in searchable format
- Development of improved surveillance tools, including a new PulseNet Portal, which allows direct querying of the PulseNet database, and a new Palantir-based platform for secure data-sharing, which integrates real-time outbreak data from multiple states into a central dashboard display that is available to all responders.

Priorities for 2013. Over the coming year, the FSMA SWG will focus on state and local surveillance capacity, performance indicators and metrics, and surveillance of antibiotic resistance in foodborne microbes. Other areas of interest may include risk-based prioritization of surveillance activities (e.g., detection of infections such as norovirus, toxoplasma, cryptosporidium, and *Vibrio vulnificus*); updates on CoEs; and issues related to culture-independent diagnostic testing and attribution of foodborne disease to particular pathogens and food products.

FSMA SWG Annual Report. The working group has drafted an annual report that will be sent to the BSC for review and submission to the HHS Secretary, as required under FSMA. The 2012 Annual Report will emphasize the recent loss of capacity at state and local levels and the need for additional resources to build on existing surveillance systems to fill existing and emerging data gaps. It will also summarize the advice provided to CDC on selection criteria for the CoEs; feedback on the draft Interagency Food Safety Analytics Collaboration (IFSAC) strategic and operational plan; and guidance on areas where improvement of foodborne illness surveillance is needed, including

- Interagency linkages and coordination at local, state, federal, and tribal levels
- Development and use of meaningful foodborne illness surveillance performance measures
- More complete collection, standardization, and analysis of information on factors contributing to foodborne illness
- Loss of ability to track and link organisms to detect outbreaks and trace contaminated foods due to increased use of culture-independent diagnostic tests
- Building of state and local surveillance capacity on which national surveillance is based
- Communication with partners and external stakeholders, especially when investigating and responding to outbreaks affecting many states.

The FSMA SWG annual report will be submitted to the HHS Secretary, most likely in February.

BSC Discussion

BSC and the FSMA SWG. In response to a question about the relationship between the working group and the BSC, Dr. Berkelman explained that the FSMA SWG was constituted under the BSC to fulfill specific provisions of FSMA. As the federal advisory committee overseeing the working group, the BSC must discuss working group reports and approve any formal recommendations. For example, all BSC members will have an opportunity to review and comment on the working group's annual report.

Global Trends. In response to a question about addressing the impact on food safety of two major global factors—climate change and the globalization of the food supply—Dr. Hadler noted that FSMA addresses the globalization of the food supply as an FDA regulatory issue, and global warming issues are usually regarded as part of disease prevention rather than disease surveillance. Nevertheless, the working group can raise these issues in the context of improving disease surveillance (e.g., enhancing global capacity to monitor emerging global foodborne threats).

Loss of Microbial Isolates. BSC member Dr. Andy Pavia, Chief, Division of Pediatric Infectious Diseases, University of Utah, suggested that the working group make the issue of obtaining microbial isolates a major priority because of their importance to disease surveillance and outbreak investigation. For example, the working group could suggest ideas for short- and long-term solutions to address the loss of culture tests for foodborne disease surveillance and present these to the full board. Dr. Hadler said that that these might be included in the 2013 Annual Report. Although the working group meets only a few times a year and the agenda is already full, it might be possible to find time between meetings to address this important issue.

This issue is already under consideration by other CDC groups, and not restricted to the context of foodborne diseases. Dr. Beth Bell, Director, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), noted that the increasing use of non-culture-based tests is a major focus of CDC's bioinformatics activities. A request was made that CDC report back to the BSC on activities in this area. Dr. Hadler also noted that issues related to increasing use of non-culture diagnostics will be mentioned as a future priority in the cover letter to the HHS Secretary that will accompany the 2012 Annual Report.

Emergency Health Communications. Another focus area for the working group might be identifying and integrating communication strategies that link public health partners and external stakeholders when foodborne disease outbreaks occur. Dr. Hadler noted that three members of the FSMA SWG have expressed interest in public health communications as a future priority.

Antimicrobial Resistance Working Group

BSC member and working group chair Dr. Bob Weinstein, System Chair and Department Chair, Department of Medicine, Cook County Health and Hospitals System, reported on the first two of four tasks undertaken by the ARWG to assist CDC in fulfilling provisions of the 2011 Generating Antibiotic Incentives Now (GAIN) Act (H.R. 2182). The four tasks are as follows:

- Development of methodology for antimicrobial resistance (AR) threat assessment and categorization
- Evaluation of efforts to measure antimicrobial use and implement antimicrobial stewardship programs
- Identification of the most successful strategies for preventing and controlling antimicrobial resistance
- Identification of laboratory diagnostic needs and issues.

AR Threat Assessment and Categorization. The goal of the first task is to create a methodology for assessing which types of currently identified AR problems pose the greatest threat to public health. During conference calls on September 7 and October 30, 2012, the ARWG completed a third revision of AR threat assessment criteria related to disease severity, economic impact, transmissibility, preventability, and effectiveness of treatment. This draft was included in the December 2012 BSC briefing book. The working group met on December 4 and made additional revisions after testing the criteria against five AR problems. CDC plans to use the final version of the criteria (expected by mid-January) to assess a broad range of drug-resistant bacteria and fungi under consideration for inclusion in a GAIN Act list of AR problems that require urgent attention.

The GAIN Act requires an all-or-none assessment of AR threats. However, the ARWG has decided to develop (in addition) a systematic categorization of AR threats to facilitate more effective use of public health resources. Three categories are under consideration: Urgent, Serious, or Emerging. A fourth category might include AR problems not requiring proactive public health action at this time.

12/4/12 ARWG meeting outcome: The ARWG supports CDC's efforts to develop a methodology for AR threat assessment. CDC may follow up by proposing additional changes to the threat assessment criteria and will keep the ARWG apprised of progress.

Antimicrobial Stewardship and Antibiotic Safety. ARWG member Dr. Sara Cosgrove, Assistant Professor of Medicine, Division of Infectious Disease, Johns Hopkins University School of Medicine, led a discussion at the December 4 ARWG meeting about whether to re-brand "antimicrobial stewardship" as "antibiotic safety." The group decided to maintain the "stewardship" brand but add complementary messages and "tag-lines" on using drugs wisely, smartly, and/or safely, as appropriate for different audiences.

The ARWG also reviewed CDC's efforts to measure antimicrobial use, following a presentation at the December 4 working group meeting by CDC staff members Drs. Lauri Hicks (Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases [NCIRD]) and Scott Fridkin and Arjun Srinivasan (both from the Division of Healthcare Quality Promotion, NCEZID). Data on antimicrobial use in outpatient settings will be obtained from private sources, while data on antimicrobial use in inpatient settings will be collected through a National Healthcare Safety Network (NHSN) surveillance module that is currently under development. As part of the discussion, the ARWG considered ways to engage all levels of the health system in improving antimicrobial use.

Dr. Weinstein noted that CDC and FDA (through HHS) are required to submit a report to Congress within 5 years of the start of the GAIN Act, evaluating U.S. programs that measure the use of antibiotics and the implementation and effectiveness of antimicrobial stewardship programs.

12/4/12 ARWG meeting outcome: The ARWG discussed ideas regarding antimicrobial use measurement and possible metrics for assessing implementation and success of stewardship programs in outpatient and inpatient settings.

Next Steps. The ARWG plans to hold two conference calls before its next meeting (in May) to discuss CDC updates on implementation of the ARWG's recommendations. The topic proposed for the May 2013 meeting is the third task in fulfilling provisions of the GAIN Act: *Identifying the most successful strategies for preventing and controlling antimicrobial resistance*. The working group will also begin considering the fourth task: *Identifying laboratory diagnostic needs and issues*. As part of that task, the ARWG is likely to address the issue raised by the FSMA SWG about the decreasing availability of cultures for testing (see page 2), as it relates to AR surveillance.

BSC Discussion

ARWG co-chair Dr. Andy Pavia suggested that the working group begin identifying effective stewardship interventions during its upcoming conference calls.

In response to a question about addressing (1) animal sources of resistance genes and (2) introduction of resistance problems from other countries, Dr. Weinstein noted that the ARWG charge concerns human health issues only. However, issues related to AR emergence in animals will be discussed at a joint meeting of the ARWG and the FSMA SWG, tentatively scheduled for December 2013. International issues are part of the third GAIN Act task on identifying effective prevention and control strategies.

Comments from BSC members included the following:

- The ARWG should focus on identifying ways to mitigate the problems that the working group has categorized as priority AR threats. Dr. Weinstein noted that the decision to address categorization (in addition to the all-or-nothing assessment required by the GAIN Act) was

intended to help guide public health action. However, the ARWG's agenda was intentionally limited to the four GAIN Act tasks, in an effort to remain focused while addressing a huge problem with many aspects.

- AR categorization might help the ARWG in identifying prevention and control strategies (the third task). It would be helpful if the ARWG identified healthcare venues where interventions could make the most impact (e.g., with respiratory outpatients).
- AR data are essential to understand where and how antibiotics are being over-used.

During the December 4 working group meeting, Dr. Hicks presented data on antibiotic use by zipcode (e.g., for respiratory sinusitis) to help target resources and education efforts. Dr. Hicks noted that more than 58% of antibiotics are used to treat upper respiratory infections for which they are not needed. Rates of misuse differ by state and by neighborhood, occurring most often in the Southeast. Dr. Weinstein stressed that rapid point-of-care diagnostics are needed to indicate when an infection is viral rather than bacterial. This intervention will be discussed as part of the fourth task. Antibiotics also tend to be over-used in treating hospitalized patients who are very ill. Once the drugs are started, they often are not stopped or decreased even when it becomes clear that they are not needed.

In response to a comment on using checklists to catalyze behavior change, Dr. Weinstein noted that the CDC-supported Southeastern Pennsylvania Adult and Pediatric Prevention Epicenter Network met last week at the University of Pennsylvania to develop a checklist for antimicrobial stewardship related to care of adults. The Network also plans to develop checklists related to pediatric care and intensive care.

Dr. Pavia noted that CDC has documented progress in improving antibiotic use in outpatient settings. However, it is difficult to gain an accurate picture of antibiotic use in hospitals. Dr. Weinstein said that the new AR surveillance module under development by NHSN is based on an electronic medication administration record (eMAR) interface that is in use by 65% of hospitals. Some state laws that mandate reporting of antibiotic use to NHSN also mandate use of eMAR.

It was suggested that the National Association of County and City Health Officials (NACCHO), Association of State and Territorial Health Officials (ASTHO), and the Council of State Epidemiologists (CSTE) work with public health departments to advance AR interventions and stewardship strategies that address antibiotic use at the provider level. Dr. Berkelman said that if the ARWG would like to bring formal recommendations to the BSC for discussion and vote, that option is open.

II. OID UPDATES

Dr. Khabbaz provided updates from OID and from the three infectious disease national centers.

Dr. Khabbaz began by reviewing recent outbreak investigations of public health importance, and noted that Dr. Beth Bell will be giving an update on the ongoing investigation of fungal meningitis later in the day (see page 17). Examples of recent outbreaks include hantavirus infection among visitors to Yosemite National Park; cases of influenza A (H3N2) variant reported from multiple states; and cases of *Clostridium difficile* among pediatric oncology patients in Colorado. Recent multistate foodborne disease outbreaks included *Salmonella* infections linked to cantaloupes and mangoes; *Listeria* infections associated with soft cheese; and Shiga toxin-producing *Escherichia coli* O157:H7 infections linked to contaminated leafy greens. Among international outbreak responses, CDC has helped investigate Ebola hemorrhagic fever outbreaks in Uganda and the Democratic Republic of the Congo; Nodding syndrome in Tanzania, Uganda, and South Sudan; cholera in Sierra Leone; and anthrax in humans and animals in the Republic of Georgia.

Other updates included the following:

CDC Personnel. Leadership changes at CDC include new positions or departures for Dr. Kevin DeCock, former Director of the Center for Global Health (CGH); Dr. Steve Thacker, former Director of the Office of Surveillance, Epidemiology and Laboratory Services (OSELs); and Dr. Kevin Fenton, former Director of the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP). Until permanent new directors are identified, those positions will be covered by Dr. Anne Schuchat (CGH), Dr. Denise Cardo (OSELs), and Dr. Rima Khabbaz (NCHHSTP). Dr. Schuchat's current position as Director of NCIRD will be filled by Dr. Melinda Wharton, and Dr. Khabbaz will continue as CDC Deputy Director for Infectious Diseases and Director of OID. Dr. Thomas Hearn, Deputy Director, NCEZID, is also retiring, after 35 years of distinguished service.

Recognitions and Awards. Examples of awards received by CDC infectious disease experts include the following:

- Dr. Kevin Fenton: Second-year recipient of *The Root Award* honoring the top 100 black influencers and achievers
- Dr. Anne Schuchat: Infectious Diseases Society of America (IDSA) / American Medical Association award for excellence in public health emergency communication
- Dr. Hazel Dean, Deputy Director, NCHHSTP: Trailblazer Award (a *Chief Learning Officer Learning in Practice Award*)
- Dr. Toby Merlin, Director, Division of Preparedness and Emerging Infections, NCEZID: Association of Public Health Laboratories (APHL) 2012 Presidential Award.

CDC Budget. The FY13 budget remains uncertain, with a Continuing Resolution (CR) in place through March 27.

- Under the CR, existing programs can be continued or modified but no new programs can be created or existing programs expanded.
- The CR does not address the automatic "sequester" mandated by the 2011 Budget Control Act. But even if sequestration is avoided, budget cuts are likely.
- CDC is exercising caution in making grant awards above last year's levels, in making new awards, and in adding significant funding to existing contracts.

Dr. Khabbaz also referred to the supportive letter published in *Politico* by former CDC Directors (see page 1) and other letters of support from public health partners. She mentioned the positive Congressional response to Dr. Bell's testimony before the U.S. Senate Committee on Health, Education, Labor and Pensions about the multistate outbreak of fungal meningitis (http://www.cdc.gov/washington/testimony/pdf/testimony_20121115.pdf; see also page 17), noting that Senator Lamar Alexander called CDC's public health response "A-plus."

Cross-Cutting Issues. Examples of recent cross-cutting infectious disease activities include the following:

- A human papillomavirus (HPV) program review was held in July involving NCHHSTP, NCIRD, NCEZID, CGH, and the National Center for Chronic Disease Prevention and Health Promotion. CDC may use a *Winnable Battle*-type format to help support and prioritize activities and use of shared resources for HPV prevention efforts.
- An external inspection of CDC's Building 18 Animal Biosafety Level 3 (ABSL-3) vivarium was conducted by experts from the Public Health Agency of Canada and two U.S. biosafety experts. The inspection concluded that the facility is "is compliant with all U.S. regulatory requirements and guidelines and poses no risk to the health and safety of the public."

- Onsite review of CDC's animal resource programs was completed by the Association for Assessment and Accreditation of Laboratory Animal Care International in early November. The reviewers found no deficiencies and recommended continued full accreditation for CDC.

Advanced Molecular Technologies. OID is facilitating efforts to enhance public health bioinformatics capacity by ensuring that CDC laboratories have cutting-edge molecular tools. Priorities include

- Creating web-accessible, searchable databases on infectious pathogens for use by CDC and public health partners
- Establishing training fellowships with academic partners to address bioinformatics workforce needs
- Developing and standardizing molecular epidemiology tools to modernize national infectious disease surveillance systems
- Creating and enhancing screening, modeling, and tracking systems to improve prediction and early recognition of infectious threats.

Dr. Khabbaz and Dr. Berkelman suggested that consideration should be given to formation of a laboratory work group to advise CDC on advanced molecular diagnostics and other laboratory issues. This issue will be discussed in more detail at a future BSC meeting.

Programmatic Updates. Selected program accomplishments include the following:

- **NCHHSTP**
 - Vital Signs report on *HIV Among Youth in the U.S.* (<http://www.cdc.gov/vitalsigns/HIVAmongYouth/index.html>)
 - The *Let's Stop HIV Together* campaign (<http://www.cdc.gov/features/LetsStopHIV/>)
 - New treatment guidelines for gonorrhea (<http://www.cdc.gov/std/gonorrhea/treatment.htm>)
- **NCEZID**
 - A new 5-year strategic *NCEZID Strategic Plan*, aligned with the *CDC ID Framework* and CDC's five agency-wide priorities (http://www.cdc.gov/ncezid/pdf/strategicplan_NCEZID.pdf)
 - Documentation of national declines in healthcare-associated infections, including central line-associated bloodstream infections (CLABSI), catheter-associated urinary tract infections (CAUTI), surgical site infections, and methicillin-resistant *Staphylococcus aureus* (MRSA)
 - New public health intervention programs designed to improve refugee and public health
- **NCIRD**
 - CDC Pandemic Influenza Functional Exercise, held on September 11-23
 - Publication of prevention information on influenza A (H3N2) variant virus: *Key Facts for People Exhibiting Pigs at Fairs* (<http://www.cdc.gov/flu/swineflu/h3n2v-pigs-at-fairs.htm>)
 - Significant progress toward polio eradication, with the number of outbreaks dropping from 11 in 2011 to 0 in 2012 and cases reported in 2012 from only 4 countries (Chad, Afghanistan, Nigeria, and Pakistan).

BSC Discussion

Contingency Planning. In response to questions about contingency planning for a possible sequester, Dr. Khabbaz said that CDC has held challenging discussions about which activities to cut/cancel if the sequester should occur. She noted that BSC advice and input might be requested sometime in the future, depending on outcome. The emergence of rare or previously unknown diseases makes it especially difficult to prioritize public health needs related to infectious diseases. For example, no one would have prioritized fungal diseases in the United States, prior to the fungal meningitis outbreak.

Dr. Khabbaz mentioned that Senator Tom Harkin talked about the importance of sustaining public health programs at the Senate committee hearing on the fungal meningitis outbreak. It was suggested that CDC estimate the costs of the SARS response in 2003 and what would be needed to address a similar emergency in 2013.

III. STRENGTHENING THE CLINICAL AND PUBLIC HEALTH INTERFACE

1) Addressing pertussis

Dr. Tom Clark, Epidemiology Team Lead, Meningitis and Vaccine Preventable Diseases Branch, Division of Bacterial Diseases, NCIRD, discussed the resurgence of pertussis (whooping cough) that has occurred in spite of high rates of vaccine coverage.

Dr. Clark began by reviewing the use of pertussis vaccines in the United States. The incidence of pertussis dropped dramatically in the 1950s after the introduction of the DTP vaccine (diphtheria and tetanus toxoids, plus pertussis whole-cell vaccine). In the mid-1990s, a new vaccine, called DTaP (diphtheria and tetanus toxoids, plus pertussis acellular vaccine) was recommended for administration in five doses for infants at 2, 4, and 6 months of age, for toddlers at 15-18 months, and for pre-school children at 4-6 years. With the introduction of DTaP, the incidence of pertussis in infants over 6 months dropped significantly, with pertussis deaths mostly occurring in infants less than 2 months of age.

However, illness among children and teens began to rise in the mid-2000s, despite high vaccination rates. In 2005, the Advisory Committee on Immunization Practices (ACIP) recommended that teenagers receive a booster shot of Tdap vaccine (a reformulation of DTaP that is also recommended for unvaccinated adults). By 2011, Tdap coverage of teens had risen to 78% and Tdap coverage of children was 95%. Nevertheless, pertussis rates continued to rise, with significant outbreaks occurring in California in 2010 and Washington State in 2012.

To determine the cause of the resurgence, CDC compared pertussis rates in population cohorts who received the acellular vaccine only (the youngest children) and those whose pertussis immunizations included a combination of whole-cell and acellular vaccines. In 2004, the highest disease incidence was among teens (11-18 years of age), peaking at age 13. By 2006, however, more school-aged children (7-10 years of age) than teens contracted pertussis. By 2010, rates had risen among pre-school children (1-4 years of age) and the peak among older children had fallen to 10 years of age, with few cases occurring among older teens who had received both whole-cell and acellular vaccines.

In examining reasons for these increases, a case-control study conducted in California in 2010 determined that the effectiveness of the DTaP vaccine—though initially 98%—begins to fall off after vaccination, moderately but immediately, and continues to decrease each year (<http://www.ncbi.nlm.nih.gov/pubmed/22970945>). Five years after the last (fifth) childhood dose, immunity to pertussis is about 71%. These data—along with the information on vaccine coverage and disease incidence among birth cohorts—suggest that waning immunity is driving disease resurgence. Thus, children are susceptible to pertussis not because of poor rates of vaccination but despite vaccination. Data collected in Washington State support this conclusion (<http://www.ncbi.nlm.nih.gov/pubmed/22810264>).

CDC and partners have considered a number of other hypotheses. For example, the apparent increase in pertussis could be due to improved disease diagnosis and reporting (i.e., surveillance bias). However, the data on the changing incidence among birth cohorts suggest that the increase is real. Another possibility

is that the minor variability in the antigen content of DTaP vaccines might cause some DTaP vaccines to be more effective than others. However, a child's series of five doses most often includes more than one type of DTaP vaccine. A third hypothesis is that the selective pressure of vaccination on circulating strains has led to the emergence of strains with antigens that vary from those included in the DTaP vaccine. However, several studies indicate that short-term vaccine effectiveness is excellent.

BSC Discussion

Health Communications. Many jurisdictions have documented significant increases in cases of pertussis. Dr. Clark emphasized that vaccination against pertussis is still the best way to protect your child. Waning immunity as the child gets older does not imply a lack of protection. When vaccinated children get pertussis, they have shorter and less severe illnesses and are less likely to transmit infection to others. The bottom line is that the pertussis vaccine protects against severe disease and it is especially important for babies.

Population Factors. In response to a question about whether population factors such as obesity or diabetes affect the antigenicity of pertussis vaccines, Dr. Clark said that immunogenicity studies have thus far been conducted in healthy populations only. In those studies, no evidence of reduced immunogenicity has been detected by measuring vaccine-induced antibody levels, which suggests that antibody levels do not correlate precisely with the degree of protection.

Unvaccinated Children. In response to a question about the 7%-8% of children in the California study who had not been vaccinated against pertussis, Dr. Clark noted that the parents of those children had requested waivers, although the reasons for the waivers were not recorded. The proportion of unvaccinated control (0.9%) was too small to affect the study's conclusions.

Vaccination of Pregnant Women and Caregivers of Infants. Suggestions for ways to overcome barriers to pertussis vaccination of adults included

- Incorporating pertussis vaccination into prenatal care programs that aim to reduce premature births
- Making postpartum vaccination part of routine medical practice, for mothers who are not immunized during pregnancy
- Providing vaccination or a prescription for vaccination to new fathers and making vaccination of other infant caregivers (e.g., grandparents and babysitters) part of routine hospital practice
- Enlisting partners such as
 - Pediatricians in encouraging new parents to get vaccinated against pertussis.
 - Pharmacies in encouraging people who request flu shots to get pertussis shots as well
 - Pharmacies, daycare centers, and members of the American Congress of Obstetricians and Gynecologists (ACOG) in explaining to infant caregivers why being immunized against pertussis is an important way to protect babies, including very young infants who have not yet received their first dose of vaccine
- Exploring the use of Section 317 funds to overcome state and local financial barriers to immunization of fathers, grandparents, babysitters.

Dr. Clark noted that in 2011 ACIP recommended immunization of pregnant women for those not previously vaccinated. Last October, ACIP also voted to recommend vaccination with Tdap during each pregnancy, regardless of patient's prior vaccination history. Thus far, feedback suggests good adherence to this recommendation.

In response to a question about identifying obstacles to having obstetricians and gynecologists administer vaccines to pregnant women, Dr. Clark said that CDC expects to complete a survey of postpartum vaccination of women this spring. Additional data on logistical and financial barriers are also being collected by the CDC Behavioral Risk Factor Surveillance System. Also noted, ACOG is planning to conduct a provider survey addressing barriers to vaccination of pregnant women, including logistics, physicians' attitudes, and financing. The Pan American Health Organization and WHO are also interested in this topic, which may be addressed by the WHO Strategic Advisory Group of Experts (SAGE) on Immunization.

Vaccine Development and Use. Data from Australia suggest that one option might be to recommend a mixed schedule, using the whole-cell vaccine as the first dose. However, it would be better to develop a new acellular vaccine that is more like a whole-cell vaccine in composition and antigenicity. Dr. Clark noted that no vaccine of that kind is currently in the pipeline. A new live, attenuated intranasal vaccine is available in France that manufacturers might decide to market here. A new acellular vaccine might involve different antigens or adjuvants, or be made in a new way.

In response to a suggestion about moving up the timing of the first dose of DTaP, so that (like the hepatitis B vaccine) it is delivered before a newborn leaves the hospital, Dr. Clark said that ACIP considered recommending moving the timing of pertussis vaccine down to 6 weeks of age, but concluded that the benefit would be small. In addition, data suggest that giving the first dose later provides better protection.

In response to a question about the benefits of using school entry requirements to increase vaccine coverage in children or teens, Dr. Clark noted that the data suggest that the incidence of pertussis is not rising because of changes in the schedule but because immunity is already waning in 3- and 4-year olds, before they enter school. Forthcoming data from the Washington State outbreak, like the data from California, will help us decide which actions to take.

Pertussis Detection. In response to a question about whether increased recognition of pertussis cases could be due to increased use of DNA tests—which miss fewer strains than culture-based methods—Dr. Clark noted that PCR has been used to confirm pertussis cases since 1997. The absolute number of cases has probably increased because of better testing, but better testing does not explain the resurgence of pertussis in school-aged kids. Dr. Clark added that the CDC pertussis laboratory has worked with APHL, state laboratories, and private clinical laboratories to standardize diagnostic tests for *Bordetella pertussis*.

Vaccination of Healthcare Workers. It was suggested that healthcare workers who receive flu shots be provided information about the DTaP vaccine for adults. This is the practice at the Mayo Clinic, where it is mandatory for employees to have a flu shot, although they can request waivers. In this way, hospitals, in their role as employers, can help prevent the spread of pertussis, if the reservoir of pertussis among older people with waning immunity is a significant part of the problem.

Recommendations for Outbreak Control. In response to questions about recommended public health measures and health communications on this issue, Dr. Clark noted that CDC plans to update its recommendations on pertussis prophylaxis, with newer recommendations having more flexibility and a greater focus on household and infant risks of transmission. Dr. Clark also noted that CDC is working with ACOG to help pediatricians and other providers engage parents.

Final Comments. Additional comments included the following:

- CDC and the National Institute for Allergy and Infectious Diseases (NIAID) at the National Institutes of Health (NIH) should consider the need for new pertussis vaccines that provide longer-lasting immunity.

- IDSA will hold a meeting on March 6, with NIH, FDA, CDC, and other partners to address vaccine issues, including development of new vaccines and pathways to licensure.
- FDA has also convened a workgroup to address scientific gaps in vaccine development.

Dr. Berkelman requested that the BSC receive an update on pertussis activities at the next BSC meeting.

2) Implementing new recommendations for reducing HCV morbidity and mortality

Dr. John Ward, Director, Division of Viral Hepatitis, NCHHSTP, discussed CDC's new, birth-year-based HCV testing recommendations (<http://www.cdc.gov/hepatitis/hcv/GuidelinesC.htm>) and the proposed HCV testing recommendations of the U.S. Preventive Services Task Force (USPSTF).

The U.S. burden of chronic HCV infection is substantial, with HCV mortality rates surpassing those of HIV in 2007. However, new HCV therapies are in the pipeline that can clear HCV from the system (i.e., virologic cure) and prevent the development of cirrhosis and liver cancer. During the early 1990s, injected interferon, which had limited success and many adverse effects, was the only treatment for HCV infection. Today, 12-week oral regimens that are 90% effective and have few side effects may soon be available, with FDA approval expected by 2014. Nevertheless, many persons living with viral hepatitis remain undiagnosed and do not take advantage of these new treatments.

Rationale for Age-Based Recommendations. The previous HCV testing recommendations were based on risk and on medical indications. Testing was recommended for injection drug users, HIV-positive persons, infants of HCV-infected mothers, people with signs of liver disease or on chronic hemodialysis, and people who received blood transfusions or organ transplants prior to 1992 or blood products made prior to 1987. Despite these recommendations, 45%-85% of HCV-infected persons remain unidentified.

HCV surveillance data suggest that detection efforts should be targeted to the baby boomer generation, which accounts for 74% of the 2.7-3.9 million HCV infections in the United States as well as 73% of all HCV-associated mortality. Prevalence among baby boomers is 5.3 times higher than that for other age groups.

Development of Age-Based Recommendations. CDC conducted an evidence-based review of HCV surveillance and treatment data, based on the procedures of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group (<http://www.gradeworkinggroup.org/>). The review concluded that a recommendation of one-time testing and linkage to care of individuals born between 1945 and 1965 could reduce the risk of liver cancer by 70% and reduce all-cause mortality by 50%. The age-based recommendation was identified as a "strong recommendation" based on a "moderate quality of evidence."

That evidence included a study which estimated that age-based testing could identify about 800,000 additional cases of HCV infection, averting 200,000 cases of cirrhosis, 47,000 cases of hepatocellular cancer, 15,000 liver transplants, and 120,000 deaths (<http://annals.org/article.aspx?articleid=1132687>). Savings in medical costs could approach \$2.5 billion per year; the monetary benefit in terms of quality-adjusted life years was calculated to be \$35,700 per patient. The study was conducted by scientists from the University of Chicago, CDC, RTI International, Kaiser Permanente, and the University of North Carolina at Chapel Hill.

The new CDC recommendations underwent peer-review, HHS clearance, a public comment period, and further clearance before publication in the *MMWR* (<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6104a1.htm>).

Implementation of Age-Based Recommendations. Implementation of the new recommendations includes the following activities:

- ***Educating the public to increase demand for testing.*** HHS has launched a public health campaign that includes a U.S. Hepatitis Testing Day (May 19) and White House observance of World Hepatitis Day (July 28). The campaign, which has generated significant media interest, includes participation by the U.S. Department of Veterans Affairs and the Indian Health Service. The CDC Director held a media conference on August 16, 2012, to announce the new recommendations, and billboard notices have been posted on donated space at airports and transit stops. In addition, CDC has developed a web-based tool that individuals can use to assess their HCV risk (<http://www.cdc.gov/hepatitis/riskassessment/start.html>).
- ***Training providers to improve HCV testing and management.*** CDC is preparing an inventory of educational materials (<http://cdcnpin.org>); developing curricula for medical students and health trainees (<http://knowhepatitis.org>); expanding web-based education for clinicians (<http://depts.washington.edu/hepstudy/>); and participating in training programs developed by Medscape and the International Antiviral Society-USA (IAS-USA). CDC is also working with public health and medical partners to organize meetings of healthcare providers (with IDSA and the American Association for the Study of Liver Diseases [AASLD]) and medical education groups (e.g., AMA's Continuing Medical Education program). CDC is also organizing meetings of other important stakeholders, including insurers (with IDSA, AASLD, and America's Health Insurance Plans), public health officials (with ASTHO and APHL), and federal partners (with the Office of the Assistant Secretary for Health, HHS).
- ***Augmenting capacity for HCV testing and linkage to care.*** In FY12, CDC received \$5 million in PPHF funds and \$500,000 from the CDC Foundation for HCV testing. These funds supported testing at 16 primary care settings, 10 settings that serve persons who inject drugs, and 2 settings that use telemedicine techniques developed by Project ECHO (<http://www.rwjf.org/en/grants/grantees/project-echo.html>).
- ***Monitoring the implementation and impact of recommendations.*** As co-chair of the Physician Consortium for Performance Improvement, CDC is spearheading efforts to develop performance measures for HCV testing of high-risk patients and of persons born between 1945 and 1965. When complete, these measures will be submitted for review by the National Quality Forum.
- ***Improving implementation of the new recommendations.*** CDC is reviewing the testing and management of about 10,000 HCV patients, with respect to hospitalization or ambulatory care, mortality prevention, treatment, costs, and outcomes. CDC is also supporting seven new HCV surveillance sites and revising the HCV case definition and testing algorithm. CDC also plans to include questions on HCV testing in the National Health Interview Survey (NHIS) and The National Health and Nutrition Examination Survey (NHANES).

CDC is also continuing to develop best practices and improve HCV testing technologies and procedures.

Dr. Ward noted that CDC's budget for viral hepatitis prevention is limited and that many components of the implementation effort, including HCV prevention research studies and the "Know More Hepatitis" campaign, depend on the work of the Viral Hepatitis Action Coalition (VHAC), which is funded by the CDC Foundation. VHAC includes 17 partners, from industry, community groups, and public health organizations.

USPSTF Recommendations. Dr. Ward concluded his presentation by reviewing the draft USPSTF recommendations for HCV testing. The draft document recommends

1. Screening for HCV infection in adults at high risk including those with any history of intravenous drug use or blood transfusions prior to 1992 - Grade B (*moderate certainty that the net benefit is moderate to substantial*)
2. That clinicians consider offering screening for HCV infection in adults born between 1945 and 1965 - Grade C (*likely a small net benefit*).

These recommendations are available for public comment through December 24, 2012

(<http://www.uspreventiveservicestaskforce.org>). According to Dr. Ward, although the second recommendation is in good accord with CDC's new age-based recommendation, the assignment of Grade C affects insurance coverage since only procedures recommended as Grade A or B are covered by insurers as no-copay priority preventive services. As such, assignment of a Grade C will affect implementation of HCV testing recommendations for persons born during 1945-1965.

BSC Discussion

Linkage to Care. In response to a question about ensuring referral to treatment when a person tests positive for HCV, Dr. Ward said that the CDC cooperative agreements on HCV testing require a plan for linkage to care. In response to a comment about the need for careful auditing, Dr. Ward said that CDC has procedures in place to track referral to care. As with HIV, ensuring referral to care after testing can be challenging, especially among persons who are poorly insured, non-compliant, and/or addicted to drugs.

It was suggested that it might be too early to recommend expanded HCV testing, because new therapies with fewer side effects may not be available until 2014. Dr. Ward noted that policy implementation takes time, so having 1-2 years of lead time could be beneficial. Also, some individuals may derive significant benefit from care (e.g., assessments of liver health and liver disease) even if they do not receive immediate treatment for HCV. In fact, only about one in four HCV-positive persons develops cirrhosis and therefore requires drug treatment. In those cases, healthcare providers can help HCV-positive patients decide whether to defer treatment in anticipation of the more tolerable agents that will be available in the near future.

Safeguarding the Health of Younger Persons with HCV Infection. In response to a question about a second wave of younger people who test positive for HCV, Dr. Ward said that state-level data indicate that older adolescents and young adults, both male and female, are becoming infected. To some extent, these infections are occurring among users of oxycodone who move on to injectable heroin when they become tolerant to oxycodone. Dr. Ward referred to a National Institute on Drug Abuse (NIDA) article about HCV incidence in eastern Kentucky and noted that we need to develop new ways to identify and intervene in this emerging population. This topic will be discussed by CDC and NIDA in upcoming meetings.

USPSTF Recommendations. In regard to a question about the data on which the Grade C designation was based, Dr. Ward said that USPSTF may have made a distinction based on HCV prevalence. Although a small difference, HCV prevalence is 6% among at-risk persons and 3% among baby boomers. In its comments to USPSTF (due December 24), the Division of Viral Hepatitis would like to emphasize that the benefit is the same, regardless of the pathway by which patients are identified and referred to care

and to suggest that USPSTF delay finalization of their HCV testing recommendations since additional data are forthcoming.

Dr. Berkelman observed that testing recommendations from different federal agencies and other national entities should be in good alignment if at all possible. She returned to this issue at the end of the meeting (see page 19).

IV. DISCUSSION WITH CDC DIRECTOR TOM FRIEDEN

Dr. Tom Frieden, CDC Director, requested BSC advice and feedback on CDC's infectious disease activities. In his introductory remarks, he reminded the BSC that his own background is in infectious diseases. He reviewed ongoing threats, including new diseases, antimicrobial resistance, rapid disease spread due to the globalization of travel and trade, and genetic modification to increase transmission or virulence. He said that CDC is committed to doing more to address these and other infectious disease issues, including healthcare-associated infections and foodborne diseases. He mentioned ongoing efforts to improve CDC capacity for advanced molecular diagnostics and public health bioinformatics. He also mentioned the need to help other countries strengthen their laboratory networks, epidemiology capacity, and institutional capacities. In conclusion, he noted that CDC's innovations, including rapid tests for dengue and plague, are providing significant health benefits throughout the world.

Dr. Frieden asked for input from BSC members. Dr. Hadler stressed the need to modernize and sustain PulseNet in light of changing laboratory practices and asked that CDC take the lead in ensuring that public health does not lose its ability to detect and control foodborne diseases. Dr. Frieden agreed that PulseNet is important to the nation's health. One short-term approach under consideration is to have FDA approvals of rapid diagnostic tests include a requirement that when test results are positive, a sample must be forwarded to the state health laboratory or retained for future work. However, Dr. Frieden noted that it will be difficult to identify funding to support public health laboratories in isolating pathogens from these samples. He referred to the Laboratory Efficiencies Initiative (LEI), a partnership between CDC and APHL that aims to find cost-effective ways to maintain diagnostic capacities at state laboratories (<http://www.cdc.gov/OSELS/lspppo/lei/>).

BSC member Dr. Frank Cockerill, President and CEO, Mayo Medical Laboratories, asked whether private laboratories like the Mayo Clinic (the largest private reference laboratory in the world) can help CDC with laboratory issues. He also mentioned that Mayo is exploring the use of home genetic testing as a disease surveillance tool. Dr. Frieden stated that the best way to help CDC is to provide advice on strategic direction, and information. Over the next few years, CDC plans to focus on two broadly overlapping areas: protecting Americans from threats to health and addressing the leading causes of illness, injury, and death (most of which are not infectious). For both categories, CDC works in four spheres:

- Understanding what needs to be done and whether current efforts are working
- Changing default behaviors so that the healthy choice is the default choice
- Interacting with the healthcare system
- Enhancing health communication with the public, providers, specialists, and insurers.

BSC advice is welcome in all of these areas, and especially in regard to interacting with the healthcare system to improve disease prevention. CDC has good community linkages and is developing new partnerships with healthcare providers and insurers. The agency can also build on long-standing partnerships to prevent disease through vaccination.

BSC member Dr. Jill Taylor spoke about the impact of point-of-care tests and other advanced molecular diagnostic tests on the public health laboratory system. She observed that the detection of the fungal meningitis outbreak depended on having the right person in place at the right time. Dr. Frieden agreed that our laboratory-based surveillance systems must be preserved and strengthened. Public health laboratories must continue to implement efficiencies such as joint procurement of laboratory supplies and equipment and move toward more consolidation of services and less fragmentation.

BSC member Dr. Kristy Bradley observed that resources for basic public health services are a major concern at the state level. The Oklahoma Public Health Laboratory, for example, has had significant reductions in Epidemiology and Laboratory Capacity for Infectious Diseases Cooperative Agreement (ELC) funding for foodborne disease and influenza diagnostics. She asked whether CDC has a timeline or strategic plan to help the states with laboratory efficiencies. Dr. Frieden said that CDC's ability to provide additional ELC resources depends on the FY13 budget, and it is possible that CDC will be funded under a CR for the rest of the year. In view of continued uncertainty and financial constraints, more must be done with existing resources. He noted that Dr. May Chu, Director, Laboratory Science, Policy and Practice Program Office, OSELS, and Dr. Judy Monroe, Director, Office for State, Tribal, Local and Territorial Support, are working with APHL and state health laboratories to implement LEI.

BSC member Dr. Judy Wasserheit, Professor of Medicine and Global Health, and Vice Chair, Department of Global Health, University of Washington, said that global climate change—as underscored by our experience with Superstorm Sandy—is another trend that will have a profound long-term impact on health. She emphasized that climate change will affect infectious diseases (e.g., foodborne diseases), as well as disaster relief, and asked what role CDC might take in addressing environmental health and infectious diseases.

Dr. Frieden stated that CDC is considering ways to increase resilience in the face of environmental changes. Despite much uncertainty, the public health community can use traditional surveillance tools to better understand how these changes impact the nation's health. Thus far, CDC has limited environmental health activities related to infectious diseases. We know that parts of the United States will be more prone to vectorborne diseases as temperatures rise, necessitating a greater emphasis on mosquito control, especially in the aftermath of floods.

BSC member Dr. John Bennett, Chief, Clinical Mycology Section, Laboratory of Clinical Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, commented that advanced informatics can help address infectious disease issues related to global warming by facilitating the development of strategic and predictive models of climate change.

Dr. Pavia asked whether CDC is thinking about a longer-term vision. Dr. Frieden responded that while he was not specifically working on a long-term plan, he would welcome advice on long-term issues and trends. Dr. Pavia suggested public health IT and social changes, such as decreased health literacy, as areas for long-term planning.

BSC member Dr. Scott Ratzan stressed the importance of advancing health literacy. He mentioned that a Johnson & Johnson tool developed to help individuals assess their chronic disease risk might be adapted to assess infectious disease risk as well. He asked Dr. Frieden how health literacy might be used by CDC and HHS to improve compliance with preventive care practices, as well as to advance global health diplomacy and security. Dr. Frieden expressed interest in the Johnson & Johnson assessment tool, noting that it is more common to transfer infectious disease tools to the chronic disease world, rather than the reverse. He said that CDC's health communication and health literacy efforts aim to provide two types of information that reinforce each other: general health information and information on specific preventive

measures. For example, to reduce diabetes, CDC provides information on healthy aging as well as diabetes-specific control measures.

Dr. Wassherheit asked about implementation of the global aspects of the CDC HPV program review. Dr. Frieden stated that commitment in this area is strong but scale-up of global programs is difficult. CDC and international partners might develop pilot programs to advance HPV prevention overseas (e.g., incorporating HPV vaccination into HIV prevention programs).

Dr. Chen noted that state health departments—which rely on partnerships and resources from the federal government—are struggling to find their proper role in the new healthcare system. A major component may be demonstrating the value of preventive measures to providers and insurers, to build a business case for disease prevention and public health action.

Dr. Frieden closed by stating that defining the new public health role and demonstrating value, as Dr. Chen suggested, is an important challenge. That role may include

- Using data to identify health trends and emerging threats
- Providing increased assistance with quality assurance
- Identifying essential services (e.g., preventive services) that should be provided in medical clinics
- Building new and improving existing connections between clinical and public health efforts (e.g., promoting tobacco quit lines).

V. CDC RESPONSE TO THE MULTISTATE FUNGAL MENINGITIS OUTBREAK

Dr. Beth Bell provided an update on the healthcare-associated outbreak of fungal meningitis and other infections among patients who received contaminated steroid injections. The outbreak response involved 23 state health departments, CDC, and FDA, as well as healthcare providers and experts in fungal infection. Larry Altman of *The New York Times* called the outbreak “one of the most shocking outbreaks in the annals of American medicine.”

CDC’s Emergency Operations Center was activated in October 2012 to serve as a hub for notification of nearly 14,000 exposed patients, development of diagnostic and treatment guidance, provision of advanced testing at CDC laboratories, public health surveillance to identify risk exposures, and coordination with FDA to identify contaminated medication. CDC has used websites, conference calls, and social media to reach out to patients, clinicians, and response partners. CDC guidance called for symptomatic patients to be referred for clinical evaluation, while exposed but asymptomatic persons should be provided with clinical information to help them recognize any future symptoms that might develop.

The investigation was initiated in mid-September when an infectious disease physician informed the Tennessee Department of Health (TDH) about a meningitis patient with culture-confirmed *Aspergillus fumigatus* who had received an epidural steroid injection at a pain clinic on July 30. TDH, in consultation with CDC, subsequently identified several culture-negative meningitis cases among persons who had received injections at the same clinic. Each of the patients had received at least one of three lots of methylpredisolone acetate (MPA) compounded by the New England Compounding Center (NECC).

On September 26, NECC voluntarily recalled the three lots of MPA, which included 17,000 vials distributed to 75 facilities in 23 states. On October 4, FDA and CDC held a joint telebriefing announcing the finding of visible fungal contamination of sealed vials and FDA recommended that healthcare professionals cease use and remove all NECC products from their pharmaceutical inventories.

As of December 3, 541 cases and 36 deaths had been reported in 19 states. *Exserohilum rostratum* (a common mold found in soil and plants, but rarely infecting humans) was identified in patient samples by

the Virginia Department of Health and by CDC. Laboratory testing of unopened MPA vials identified *Exserohilum rostratum* and two fungal species not known to cause human illness (*Rhodotorula laryngis* and *Rhizopus stolonifer*).

The spectrum of illness is still evolving. In addition to the large number of meningitis cases, other conditions have included stroke, spinal or paraspinal infections, and peripheral joint infections. By November, it became evident that a significant number of meningitis patients, as well as some exposed persons without previous symptoms, had developed spinal or paraspinal infections at or near the site of injection. CDC developed guidance to help clinicians appropriately diagnose these injection site infections.

Dr. Bell noted that responding to the outbreak meant “navigating uncharted waters.” Diagnostic tools and experience in treating infections with this rare organism were limited. CDC developed a PCR assay, optimized to detect *Exserohilum rostratum* in CSF specimens. Because clinical experience with this organism was very limited, CDC convened a group of clinical mycology specialists who provided ongoing consultation about diagnosis and treatment to inform CDC guidance.

Dr. Bell concluded by observing that the public health response to the fungal meningitis outbreak “showed the value of public health to the American people.” The role of the state health departments—from sounding the alarm to contacting the 14,000 patients to conducting ongoing surveillance—was pivotal. The outbreak response also highlighted CDC’s critical roles with the states. A considerable proportion of the outbreak responders in the states were directly supported by CDC’s financial and in-kind support through, for example, the Emerging Infections Program (EIP), the ELC, and the state Healthcare-Associated Infection Coordinators. CDC’s long-term investments in laboratory training to state health departments also proved critical, and the agency’s leadership “kept everyone moving in the same direction.”

BSC Discussion

Dr. Bell emphasized CDC’s difficulty in making public health’s value evident in the absence of a major outbreak. As mentioned in earlier discussion during the meeting, the public pays attention during high-profile outbreaks, but when CDC is successful at preventing outbreaks, the agency’s work often goes unnoticed. She added that CDC’s ability to step up successfully makes it difficult to explain that CDC and state health departments are “skating close to the edge,” in terms of resources.

Comments and Suggestions from Individual BSC Members.

- CDC should help determine why many of the patient samples obtained during the outbreak investigation were culture-negative. A better understanding of whether symptoms are due to current infection or to inflammation following infection would help guide treatment decisions about the use of antifungals and anti-inflammatory drugs.
- CDC could also assist FDA in revising laws or regulations involving compounding pharmacies.
- The investigation went well from a state perspective, with good collaboration on all levels. CDC was responsive to medical and public health questions and brought in FDA and clinical experts to provide advice and consultation.
- CDC should tell this story to policy makers and the public, emphasizing the following points:
 - The size and scope of the outbreak, and the ability of the rapid public health response to minimize harm
 - The underlying public health infrastructure that makes such a response possible
 - The fact that the response was conducted “on a shoe string.” If public health resources are further reduced, such investigations will likely not go as well

- The fact that the fungal meningitis outbreak does not represent an isolated, atypical situation, and states must often respond to more than one high-profile outbreak at the same time.

Follow-up of Outbreak Patients. In response to a question about medical follow-up of fungal meningitis patients, Dr. Bell called the fungal meningitis outbreak “an acute outbreak with long-term implications.” She said that CDC plans to set up a patient registry in partnership with universities and other clinical partners to determine whether patients experience any long-term medical complications and to investigate disease course in culture-positive and culture-negative persons.

Outbreak Detection. In response to a question about whether the outbreak could have been detected even earlier, Dr. Bell emphasized the strong linkages between TDH and its clinical community, and noted that not all states have these capacities. In addition to being an EIP site, TDH also had a highly competent staff member leading the investigation—Dr. Marion Kainer, Director of the TDH Healthcare Associated Infections and Antimicrobial Resistance Program—who immediately followed up on the suggestion of a possible problem at the pain clinic that served the index patient. Events might not have played out this way in a state with even more limited public health resources. It was further noted that the infectious disease physician who informed Dr. Kainer about the index case held an MPH degree from Vanderbilt University, where she was taught by Dr. Tim Jones, the Tennessee State Epidemiologist, who is also an alumnus of the Epidemic Intelligence Service.

Quality Control of the Compounding Pharmacy. In response to a question about quality control procedures at NECC before the outbreak, Dr. Bell responded that FDA has posted its most recent inspection reports on the web:

<http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/ORA/ORAElectronicReadingRoom/UCM325980.pdf>.

Laboratory Issues. In response to a question about laboratory surge capacity, Dr. Bell noted that very few laboratories are able to test for this form of fungal infection, although CDC provides training courses to interested state public health laboratories. During the outbreak, many state laboratories sent their samples to the CDC Mycotic Diseases Laboratory, which recruited laboratorians from other CDC programs to assist with the large volume of testing.

Dr. Berkelman requested that BSC receive an update on the meningitis outbreak in 6 months (i.e., at the next BSC meeting).

VI. CLOSING

In closing, Dr. Berkleman posed two questions to the board:

- 1) Should the BSC establish a laboratory working group?

Dr. Khabbaz thought it would be useful for CDC to have BSC input on how to provide leadership in meeting the opportunities and challenges posed by rapid diagnostics, in light of limited resources. She suggested that a BSC laboratory working group might also advise OID in prioritizing the recommendations of the CDC Blue Ribbon Panel on Bioinformatics (see [November 2011 BSC meeting minutes](#)).

Other issues that might be considered by a laboratory working group include:

- Laboratory quality assurance issues, including the evaluation of laboratory tests by CDC
- The intersection of clinical practice and public health (e.g., the need for specimens)

- Regionalization of laboratory tests for selected pathogens
- The impact of evolving molecular diagnostics on public health surveillance.

Dr. Berkelman concluded that more discussion is needed. She suggested that CDC work with interested board members to draft a laboratory working group charge that can be presented to BSC during a teleconference.

- 2) How might the BSC address the lack of alignment between the CDC and USPSTF guidelines on HCV testing?

Dr. Chen suggested that the BSC draft a letter to the USPSTF, which has requested comments by December 24. Dr. Berkelman agreed that a BSC letter, if it is in accordance with policies of the Federal Advisory Committee Act,¹ might carry more weight than individual letters by BSC members. Such a letter might

- Highlight the difficulties in having two sets of national recommendations on HCV testing
- Ask the USPSTF to clarify the basis for assigning Grade C rather than Grade B to its age-based HCV testing recommendation
- Stress that the evidence base for HCV testing in the age group is rapidly changing
- Ask the USPSTF to consider postponing the final version and revisiting the draft when additional data become available.

Dr. Berkelman and Dr. Khabbaz thanked the Board members for their service and their support for the CDC mission.

The next BSC meeting will be held on May 8, 2013. One or more phone meetings may be held over the course of the year to follow up on today's discussion.

¹ The BSC is charged with providing advice to the HHS Secretary; therefore, board members drafted a letter to the Secretary (rather than the USPSTF) outlining their concerns with the lack of alignment between the two sets of guidelines.

**APPENDIX
MEETING PARTICIPANTS**

BSC Members

Ruth Berkelman
Jack Bennett
Nancy Bennett (*representing CDC Advisory Committee on Immunization Practices on behalf of Jon Temte*)
Kristy Bradley
Harry Chen
Frank Cockerill
Matt Erdman (*representing U.S. Department of Agriculture on behalf of Beth Lautner*)
John Gittleman
Jesse Goodman (*participated by phone*)
Jim Hadler
Linda Lambert (*representing National Institute of Allergy and Infectious Diseases on behalf of Carole Heilman*)
Jeanne Marrazzo
Steve Ostroff
Andy Pavia
Scott Ratzan
Bob Sautter
Ken Scott (*representing Public Health Agency of Canada on behalf of Rainer Engelhardt*)
Kim Smith
Julio Sotelo
Jill Taylor
Bob Tesh
Judy Wasserheit
Bob Weinstein
Mary Wilson

Partners and Public Visitors

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Jane Getchell (*Association of Public Health Laboratories*)
Joe Hilinski (*Pediatric Infectious Diseases Society*)
Lilly Kan (*National Association of County and City Health Officials*)
Harry Keyserling (*American Academy of Pediatrics*)
Ruth Lynfield (*Infectious Diseases Society of America*)
Christy Phillips (*Pediatric Infectious Diseases Society*)
Bill Schaffner (*National Foundation for Infectious Diseases*)
Kathy Talkington (*Association of State and Territorial Health Officials*)
Joe Toerner (*Food and Drug Administration; BSC/OID Antimicrobial Resistance Working Group*)
Kimberly Walker (*American Society for Microbiology*)

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Cyndy Whitney
Sarah Wiley

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 5, 2012, are accurate and complete.

Ruth Berkelman, M.D.
Chair, BSC, OID

Date