NBSB National Biodefense Science Board

National Biodefense Science Board December 3, 2019 Proceedings:

Assessing Best Practices to Improve National Training and Readiness for Health Care Providers/Clinicians to Deliver Appropriate Care during Disasters

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

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Summary

The National Biodefense Science Board (NBSB or the "Board") meets periodically in person and in public as required by legislation to review, discuss, and evaluate information and perspectives relevant to selected topics. Within the Department of Health and Human Services (HHS) through the Office of the Assistant Secretary for Preparedness and Response (ASPR):

> *The Board provide[s] expert advice and guidance … regarding current and future chemical, biological, nuclear, and radiological agents, whether naturally occurring, accidental, or deliberate … [and] on other matters related to public health emergency preparedness and response.*[1]

The Board held a public meeting in Washington, DC, on December 3, 2019, to consider a number of matters, including topics assigned to the two active working groups, such as modeling requirements for emerging infectious diseases such as Eastern Equine Encephalitis Virus and an update on the recently completed, national-level public health emergency exercise organized by ASPR called Crimson Contagion.

The general public were invited to attend the Board's meeting via the Federal Register by phone and webinar. The designated federal official (DFO) instructed members of the public to email comments or questions to NBSB@hhs.gov or post them in the chat box for the webinar. A quorum of appointed board members were present during the roll call, either in person or by phone. Also present were *ex officio* representatives from ASPR, the Centers for Disease Control and Prevention (CDC), the National Aeronautics and Space Administration (NASA), the Food and Drug Administration (FDA), and the Environmental Protection Agency (EPA).

Mr. Mike Moore, Exercise Branch Chief in the ASPR Division of Exercise, Evaluation, and After Action (E2A2), provide an overview and summary of the after-action review for the 2019 Crimson Contagion exercise. Crimson Contagion was an HHS National Level Exercise, involving multiple federal agencies, state agencies, and major hospitals to test the ability of the U.S. government to respond to a devastating influenza pandemic. There were a number of lessons

[1] Section 319M of the Public Health Service (PHS) Act (42 U.S.C. 247d-7f) as added by section 402 of the Pandemic and All-Hazards Preparedness Act of 2006 and amended by section 404 of the Pandemic and All Hazards Preparedness Reauthorization Act and Section 222 of the PHS Act (42 U.S.C. § 217a).

learned, and areas for exploration and improvement identified, including promotion of timely and effective vaccine development and procurement of other medical countermeasures. Delays in this funding can result in delays in vaccine availability. In the event of a pandemic, it will also be important to ensure that global manufacturing capacity is sufficient to meet global demand regarding medical supplies and raw materials.

Following the presentation by Mr. Moore and discussion among the board members, the Board received progress updates from the All-Hazards Response (AHR) Working Group. The AHR Working Group discussed "Anticipatory Modeling of Requirements for Emerging Infectious Diseases – Review of Gaps and Challenges to Respond to Eastern Equine Encephalitis Virus" (EEEV) led by Ms. Anna Tate, ASPR Requirements Division analyst, and board member Dr. Elizabeth Leffel. The Acting Director for the ASPR Office of Strategy, Policy, Planning, and Requirements, Dr. Kristin DeBord, had previously sent a letter to the NBSB (Appendix 2) requesting that the Board examine the current EEEV epidemiologic situation, national surveillance, and federal preparedness for a more significant outbreak of EEEV; and develop recommendations to be better prepared for mosquito-borne infectious diseases in general.

The AHR Working Group also continued a discussion from prior meetings led by board member Dr. Gray Heppner on "Strategic Considerations to Accelerate Development and Deployment of Vaccine for High Consequence Emerging Infectious Diseases". Following this, the Board began a discussion led by Dr. Dele Davies on "Integrating Clinical Disaster Response Training with Community- and State-based Emergency Planning", which is an extension of the recommendations to improve clinical disaster medicine training that were approved in September 2019.

Before the end of the meeting, Dr. Robert Kadlec, the HHS Assistant Secretary for Preparedness and Response, attended the meeting to acknowledge the fine work of the four members of the board who are reaching the end of their appointment to the NBSB. Drs. Virginia Caine, Tammy Spain, Catherine Slemp, and Noreen Hynes are all at the end of their second full term on the NBSB, which is the maximum allowed by legislation. Although those four board members will continue to serve on the board until new board members are appointed, Dr. Kadlec formally presented their certificates and letters of appreciation signed by him and HHS Secretary Alex Azar.

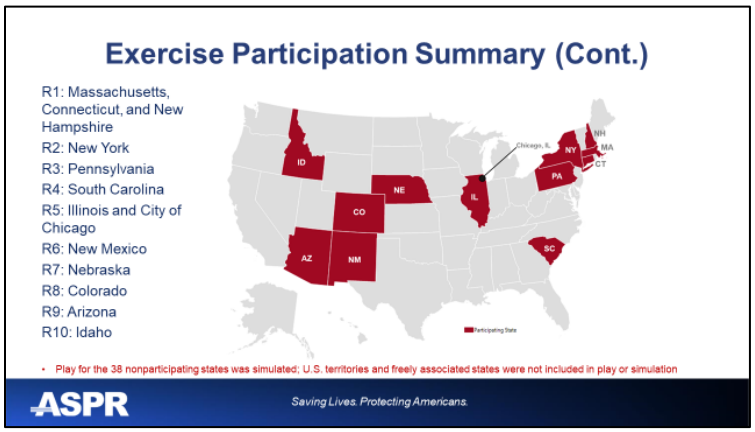
The NBSB public meeting adjourned at approximately 4:30 p.m. Eastern Time (ET) on December 3, 2019. The next public meeting is scheduled for May of 2020.

Section 1: ASPR Program Updates

Abstracts of Presentations

After Action Review of Crimson Contagion, 2019 National Level Exercise – William (Mike) Moore, MEP, Exercise Branch Chief, E2A2, ASPR.

Crimson Contagion was a national-level, multi-level exercise using a novel and highly lethal, naturally occurring strain of influenza A to evaluate pandemic preparedness across the federal government and the capacity for effective federal coordination with state and local stakeholders. The full exercise series included a number of preparatory events among HHS internal staff, among federal agencies, and with state, county, and hospital partners from January 23 to May 15; and a relocation (continuity of operations) exercise in the National Capital Region for HHS senior leaders on July 24. The exercise series culminated with a functional exercise August 13-16, 2019, which involved 35 federal, state, and local entities to examine cross-cutting strategies for operational coordination and communications, stabilization and restoration of critical lifelines, national security, public health response to a biological threat, and continuity of operations. Through collection of data and observations from participating stakeholders, the E2A2 staff developed 22 interim "key findings."



At the over-arching, strategic level, the exercise evaluation team observed that initiating vaccine development and procuring other medical countermeasures may benefit from immediate, additional appropriations to mitigate delays in vaccine deployment and to ensure competitive procurement of medical supplies from the limited stock available among national and international vendors. United States domestic manufacturing capacity and/or raw materials for pandemic influenza medical countermeasures is another area for further exploration and improvement. In the event of a pandemic, it will be important to ensure that global manufacturing capacity is sufficient to meet global demand regarding medical supplies and raw materials.

Section 2: Interim Progress Updates for Current Topics

Summaries of Presentations and Discussion

Anticipatory Modeling of Requirements for Emerging Infectious Diseases – Review of Gaps and Challenges to Respond to Eastern Equine Encephalitis Virus (EEEV) – CAPT Christopher Perdue, DFO; Elizabeth Leffel, PhD, MPH; and Anna Tate, MPH, Requirements Division, SPPR, ASPR.

EEEV is a rare cause of brain infections (encephalitis). Most cases occur in eastern or Gulf Coast states. The Board received a briefing on EEEV from ASPR staff detailing currents rates of morbidity and mortality. More information is detailed in the letter from Dr. Kristin DeBord (see Appendix 2). The Board was asked to assist in collaborating with federal and non-federal partners to define and prospectively plan for a situation in which targeted federal actions are required in response in the event of sustained and/or significantly increased EEEV infections. If appropriate, these recommendations could be to address broader emerging infectious disease (EID) contexts.

The objectives of prospective planning are (1) to understand the current risks and risk perceptions regarding EEEV and evaluate potential for future outbreaks of EEEV; (2) to review current programmatic approaches to conducting surveillance and reducing incidence of EEEV infections; (3) to evaluate potential options for public health preparedness forecasting and/or modeling, and, if appropriate, to make recommendations for anticipatory actions; and (4) to evaluate the appropriateness and feasibility of extrapolating EEEV prospective threat planning to broader EID contexts.

The discussion was taken up in Working Group sessions and deliberated in detail.

Strategic Considerations to Accelerate Development and Deployment of Vaccine for a High Consequence Emerging Infectious Diseases - Gray Heppner, MD.

Dr. Gray Heppner discussed the outline for a potential NBSB white paper, an initial draft of which has been circulated among members of the NBSB All Hazards Response Working Group (not yet available for public review), describing the aspirational requirements to develop an

effective vaccine against a previously unknown, highly lethal, and transmissible infectious disease (Disease X) within 28 days. The World Health Organization (WHO) has recently warned that the epidemic potential of a yet unknown pathogen, Disease X, poses a threat to the public's health in the absence of safe and effective MCM. In the event of a Disease X pandemic, multiple analyses have indicated that the length of time required to administer an effective vaccine is the major determinant for the numbers of lives saved. One question that remains is, "How fast is fast enough?" The working group will continue to discuss this topic and suggest best practices and refinements to a potential white paper in preparation for review during a future public meeting.

Integrating Clinical Disaster Response Training with Community- and State-based Emergency Planning - H. Dele Davies, MD and MPH.

On September 11, 2019, the NBSB approved the Disaster Medicine Working Group recommendations on best practices to improve national training and readiness for health care providers (clinicians of various types) to deliver appropriate care during disasters. These recommendations were intentionally focused on training for providers in the healthcare delivery system and others most closely associated with direct patient care (rather than training for public health and community response system practitioners). Additionally, that document did not include specific recommendations for integrating health care providers into public health and community response systems (e.g. state and local health departments, incident command systems, or community-based organizations such as Medical Reserve Corps or the Citizen Emergency Response Teams). The Board recognized that integration of the direct delivery of medical care and public health emergency response is critical, which is the new topic of discussion in the working group. Board members will meet with subject matter experts over the following months and develop additional recommendations, if needed, to be review at the next public meeting of the NBSB.

Appendix 1: Principle Attendees at the NBSB Public Meeting on December 3, 2019

Voting Members

Prabhavathi Fernandes, PhD (retired)
NBSB Chairperson
Chapel Hill, NC

Carl Baum, MD., FAAP, FACMT
Professor of Pediatrics, Yale University School of Medicine
New Haven, CT

Mark Cicero, MD
Associate Professor in Pediatrics (Emergency Medicine) & Director of Pediatric Disaster Preparedness
Yale University School of Medicine
New Haven, CT

H. Dele Davies, MD, M.Sc., M.H.C.M.
Vice Chancellor for Academic Affairs & Dean for Graduate Studies, University of Nebraska Medical Center
Omaha, NE

Donald G. Heppner, MD
Chief Medical Officer and Managing Partner, Crozet BioPharma Consulting, LLC
Crozet, VA

Noreen A. Hynes, MD, MPH
Director, Geographic Medicine Center in the Division of Infectious Diseases, Associate Professor at Johns Hopkins University School of Medicine & Associate Medical Director of Johns Hopkins Hospital Biocontainment Unit
Baltimore, MD

Elizabeth Leffel, PhD, MPH
President, Leffel Consulting Group, LLC
Berryville, VA

David Schonfeld, MD, FAAP
Professor of the Practice in the University of Southern California School of Social Work and Pediatrics & Director of the National Center for School Crisis and Bereavement
Los Angeles, CA

Joelle N. Simpson, MD, MPH
Medical Director for Emergency Preparedness, Children's National Health System &
Program Director for Emergency Medical Services for Children - DC Program
Washington, DC

Catherine Slemp, MD, MPH
Public health consultant to West Virginia Department of Health
Milton, WV

Tammy Spain, PhD
CMC Project Manager, Paragon BioTeck, Inc.
Tampa, FL

Federal agency representatives (non-voting)

Chris Hassel, PhD
Senior Science Advisory, ASPR
Washington, DC

Joanne Andreadis, PhD
Associate Director for Science (Acting), Center for Preparedness and Response, Centers for Disease Control and Prevention
Atlanta, GA

Marc Shepanek, PhD
Deputy Chief of Medicine of Extreme Environments & Research Assistant Professor at the Uniformed Services University Medical School
Washington, DC

Gregory Sayles, PhD, MS
Director of National Homeland Security Research Center, U.S. Environmental Protection Agency
Washington, DC

Brooke Courtney, JD, MPH
Senior Regulatory Counsel, Office of Counterterrorism and Emerging Threats, U.S. Food and Drug Administration
White Oak, MD

Eric Carlson
Bureau of Oceans and International Environmental and Scientific Affairs
Department of State
Washington, DC

ASPR National Advisory Committee Staff

CDR Christopher L. Perdue, MD, MPH
Senior Policy Coordinator, SPPR, ASPR & NBSB Designated Federal Officer
Washington, DC

Darrin Donato
Chief, Domestic Policy Branch, SPPR, ASPR
Washington, DC

Maxine Kellman, DVM, PhD, PMP
Biotechnology Analyst, SPPR, ASPR & NBSB Alternate Designated Federal Officer
Washington, DC

CDR Cliffon Smith, MPA
Evaluation/Public Health Analyst, SPPR, ASPR
Washington, DC

Mariam Haris, MPP
Policy Analyst, SPPR, ASPR
Washington, DC

Appendix 2: Letter from ASPR Office of Strategy, Policy, Planning, and Requirements to the NBSB

DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary

Office of the Assistant Secretary
for Preparedness & Response
Washington, D.C. 20201

National Biodefense Science
Board

November 6, 2019

Prabha Fernandes, PhD
Chairperson, National Biodefense Science Board (NBSB)
114 Milton Avenue
Chapel Hill, NC 27514

Dear NBSB Dr. Fernandes,

Domestic incidence of Eastern Equine Encephalitis (EEE) virus, a zoonotic alphavirus and rare cause of fatal encephalitis, has been markedly high in 2019. A number of federal programs are in place to conduct surveillance and reduce the incidence of EEE in human and equid populations. We would like to request assistance from a working group of the National Biodefense Science Board (NBSB) to collaborate with federal and non-federal partners to define and prospectively plan for a situation in which targeted, federal actions are required in response to sustained and/or significantly increased EEE virus infections. Additionally, it may be possible to expand any recommendations from the NBSB to broader emerging infectious disease (EID) contexts, as appropriate.

The objectives of prospective planning are (1) to understand the current risk perceptions regarding EEE virus and evaluate the potential for future outbreaks of EEE; (2) to discuss and evaluate current programmatic approaches to conducting surveillance and reducing incidence of EEE virus infections; (3) to evaluate potential options for public health preparedness forecasting and/or modeling, and, if appropriate, to make recommendations for anticipatory actions; and (4) to evaluate the appropriateness and feasibility of extrapolating EEE prospective threat planning to broader EID contexts.

Background

As of October 29, 2019, 35 EEE cases and 13 deaths have been reported across 8 US states, which represents a six-fold increase in the number of reported cases during same period in 2018 and the highest single-year case count since the 1960s. While most cases are asymptomatic or produce mild illness, 4-5 percent of human EEE virus infections result in EEE, which has a >30% mortality rate with death usually occurring 2-10 days after symptom onset. EEE virus is transmitted to humans via mosquito species that acquire the virus from infected wild birds; infected humans and horses do not appear to be able to further transmit the virus (directly or indirectly). The transmission cycle occurs primarily in freshwater hardwood swamps (such as the Eastern and Gulf Coast states). EEE is nationally notifiable and is reported by states to CDC via ArboNET, though it is widely underreported given the passive nature of the system. See the attached *Fact Sheet* for more details.

The National Biodefense Strategy calls for promoting measures to prevent or reduce the spread of naturally occurring infectious disease (Objective 2.1) and ensuring a vibrant and innovative national science and technology base to support biodefense (Objective 3.1). It also calls for enhancing preparedness to save lives through medical countermeasures (MCMs) (Goal 3.5) and includes objectives to enhance MCM development, sustainment, and availability. A decision framework and models to promote objective determinations regarding alphaviruses and their potential for escalation would inform decisions regarding medical countermeasure requirements and other public health and emergency medical resource allocations within HHS.

In deliberating issues related to preparedness for a potential, federal-level EEE emergency response, the NBSB should consider a number of activities:

1. Review current federal programs for public health surveillance and response to EEE virus infections;
2. Describe, to the extent possible, elements of a systematic approach to improving preparedness for sustained, increased incidence and/or a significant outbreak of EEE (e.g. a preparedness framework) in the United States;
3. Provide recommendations for high priority actions that HHS and its planning partners could consider immediately and in the future based on epidemiologic thresholds outlined in the preparedness framework;
4. Provide recommendations on additional coordination activities among federal and non-federal partners;
5. Identify gaps in the current science, threat assessments, and intervention systems that may require additional resources.
6. Other considerations as deemed necessary by the NBSB in consultation with the Executive Director.

Resources and Timeline

The ASPR National Advisory Committee (NAC) team will use existing resources to coordinate teleconferences and in-person meetings as needed. Board members may coordinate among themselves to discuss the issues, but meetings of a working group require the presence of a designated federal officer. Requests for other assistance should be sent to NAC team. The working group should be prepared to provide a progress report to the full board during the public meeting on December 3, 2019.

Additional questions or concerns about this proposal can be directed to the Designated Federal Officer / Executive Director, CAPT Christopher Perdue, christopher.perdue@hhs.gov.

Kristin DeBord, PhD
Director, Strategy Division
Activing Director, Office of Strategy, Policy, Planning, and Requirements

Attachment:
EEE virus Fact Sheet

Appendix 2: EEE Virus Fact Sheet
Fact Sheet: Eastern Equine Encephalitis

EEEV/EEE Domestic Epidemiology

As of October 26, 2019, 35 human EEE cases and 15 deaths have been reported across 8 US states, which represents a six-fold increase in the number of reported cases during same period in 2018 and the highest single-year case count since the 1960s. EEEV is transmitted to humans via mosquito species that acquire the virus from infected wild birds; humans and horses are considered to be dead-end hosts. The transmission cycle occurs primarily in freshwater hardwood swamps (e.g., in Eastern and Gulf Coast states).

EEE is highly virulent and has an incubation period ranging from 4-10 days. While most cases are asymptomatic or produce mild illness, 4-5 percent of human EEV infections result in EEE, of which there is a >30% mortality rate (with death usually occurring 2-10 days after symptom onset). Clinical manifestation and severity of disease is correlated with age (among other host factors), with persons ≥50 years and ≤15 years of age at greatest risk for developing EEE. EEEV infection is thought to confer life-long immunity against re-infection but does not confer significant cross-immunity against other alphaviruses, or any cross-immunity against flaviviruses.

EEE is nationally notifiable and is reported by states to CDC via ArboNET, though both human and equine cases are widely underreported given the passive nature of the system; thus, true prevalence is likely underestimated. Sentinel EEEV testing and reporting for other non-human animals varies across states. The United States Department of Agriculture (USDA) and the Department of Defense's (DoD) Armed Forces Health Surveillance Division (AFHSD) rely on ArboNET for their own EEE tracking and reporting purposes.

It is difficult to predict future seasonality and geographic distribution of EEEV, though Florida is considered to be an important source of EEEV epidemics with its year-round transmission and high EEEV genetic diversity. Analyses suggest that US geographic regions vary in their EEEV epidemiological dynamics, with enzootic EEEV viruses in Florida appearing to migrate and seed epidemics in northern states. Given the geographic range of the virus does not always correspond to human EEE cases, it is likely the ecologic conditions conducive for EEEV to transition from the enzootic to the epizootic cycle are not present in all geographic locations.

Factors related to vector expansion (e.g., climate change) and their potential impact on long-term epidemiology of EEEV must also be considered. There has been a recent geographic shift in West Nile Virus (WNV) incidence (i.e., higher than average incidence in Western states and lower than average incidence in Northeastern states), combined with a 25 percent increase in incidence in 2018 compared to 2017-2018. Similarly, 2019 has been marked by a recent and significant shift in equine cases of WNV and EEE, with about twice as many expected EEE cases

and about half as many than expected WNV cases. Together, these recent shifts in transmission dynamics serve as examples of the potential ecological and epidemiologic implications of arborviral vector expansion.

In addition to naturally-occurring outbreaks, there is also concern for the aerosol threat that EEEV poses in the bioterrorism context – i.e., a deliberate release of aerosolized EEEV. CDC classifies EEEV as a Category B bioterrorism agent. EEEV is highly infectious via the aerosol route, is relatively easily produced with high-titer, and has a relatively low infectious dose, making it a viable candidate for use as a biological weapon. Data from nonhuman aerosol studies indicate rapid pathogenesis. A number of indicators could potentially trigger a bioterrorism investigation, including abnormally high incidence (temporally or geographically), close proximity of cases unnaturally temporally clustered, or a shorter than average incubation period.

Public Health Preparedness and Response Strategies

Several existing public health preparedness and response strategies are vital to EEEV mitigation efforts. Such efforts include coordinated human, avian/animal, and mosquito surveillance; comprehensive vector control (including Integrated Mosquito Management [IMM]); and targeted risk communication (particularly regarding prevention of mosquito bites and mosquito control, as well as vaccination among equines).

Diagnostics, Vaccines, and Antiviral Treatments

Preliminary diagnosis of EEEV in humans is based on a combination of clinical features and epidemiology, but confirmatory testing at a laboratory (typically serology) is required. Since it is generally difficult to isolate EEEV from clinical samples, the majority of isolates and positive polymerase chain reaction (PCR) samples come from cerebrospinal fluid (CSF) or brain tissue. Treatment for EEE is supportive; there are no available human vaccines or specific antiviral/therapeutic treatments. As such, there is a need for licensed vaccines and antiviral therapeutics for human use, particularly those that are developed and tested for efficacy against EEEV/alphavirus inhalation exposure.

Targeted Research and Development

Several human vaccines and post-exposure prophylaxis treatments are undergoing evaluation for EEEV. VRC 313, a trivalent vaccine (WEVEE) sponsored by NIAID, is currently undergoing Phase 1 clinical trial evaluation. The United States Army Medical Research Institute of Infectious Disease (USAMRIID) is also currently evaluating a DNA vaccine for EEE (TSI-GSD 104), as well as a combination vaccine, that protects against aerosol challenge. A (poorly immunogenic, formalin-inactivated) EEEV vaccine from the 1960s administered to at-risk workers also remains under Investigational New Drug (IND) status. Trobaugh et al. (University of Pittsburg)

demonstrated productive strategy (informed mutation of virulence loci) for production of live attenuated viruses for virulent arboviruses like EEEV. Finally, Painter et al. (Emory Institute for Drug Development) recently published results from mouse model studies supporting potential preclinical development of EIDD-1931 as a potential anti-alphavirus drug, as it demonstrated broad activity against alphaviruses in vitro. A number of other vaccine and therapeutic studies exist.

Additional References (not exhaustive)

EEEV background: CDC, USDA, VDCI, NNDSS case definition

EEEV in the United States, 2003-2016 (CDC)

Complex Epidemiological Dynamics of EEEV in Florida

Large-Scale Complete-Genome Sequencing and Phylodynamic Analysis of EEEV Reveals Source-Sink Transmission Dynamics in the US (Tan et al, **2018** [Am. Society for Microbiology])

Validation of a Risk Index Model for Predicting EEEV Transmission to Horses in Florida (2018)

Improving Decision Support for Infectious Disease Prevention and Control (RAND)

Vaccine development for biothreat alphaviruses (J Bioterrorism & Biodefense, 2011)

Characterization and pathogenesis of aerosolized EEE in the common marmoset (DTRA-funded; Virol J, 2017)