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ZIKA VIRUS PREPAREDNESS AND RESPONSE: OPERATIONAL ISSUES, CHALLENGES, AND OPPORTUNITIES

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ABSTRACT:
On February 1, 2016, the World Health Organization (WHO) declared that the Zika virus disease (ZVD) outbreak constituted a public health emergency of international concern. ZVD is usually mild with symptoms lasting for several days to a week after being bitten by an infected mosquito. However, there have been reports of increased microcephaly cases and Guillain-Barré syndrome associated with the infection. Due to the large number of international travelers visiting the Washington, District of Columbia (DC) metropolitan area, health care workers within the city were asked to screen all patients about their recent travel history outside the United States (US). In addition, Washington, DC has a large population of frequent travelers, since many residents work in governmental or international non-governmental organizations. Our challenge was to not only develop and optimize a DC Zika surveillance protocol, but also to develop a regional protocol in collaboration with the neighboring jurisdictions of Maryland and Virginia. This report discusses planning for ZVD surveillance and response, including some ongoing challenges and opportunities to build and strengthen public health capacity to respond to emerging infectious diseases.

Keywords: Zika virus, surveillance, *Aedes aegypti, Aedes albopictus*, Washington, DC
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INTRODUCTION:

Zika virus is a flavivirus generally transmitted by mosquitos that have recently spread throughout Central and South America, the Caribbean, and Mexico. The lack of immunity to the virus and the presence of suitable and efficient vectors effectively spread the disease to vulnerable countries and regions. On February 1, 2016, the alarming threat from this disease caused the World Health Organization (WHO) to declare that "the recent cluster of neurological disorders and neonatal malformations reported in the Americas constituted a public health emergency of international concern" [1]. Although the disease was reported in Uganda in 1947, over the last few decades only occasional outbreaks have been reported in a few countries [2]. In contrast, the recent outbreak that started in Brazil in May 2015 has spread to several

surrounding countries. Since 2007, 55 countries in the Americas, Asia, Africa and Oceania have identified local transmission of the virus but not at the scale of the current epidemic that has affected almost 1.5 million people in Brazil [3].

Zika virus disease (ZVD) is usually mild with symptoms lasting for several days to a week after being bitten by an infected mosquito. Eighty percent (80%) of cases are asymptomatic [3]. Symptoms include acute onset of fever, rash, arthralgias, and conjunctivitis [4]. Although the symptoms of ZVD are mild, there have been reports of increased microcephaly cases and Guillain-Barré syndrome associated with this infection. In 2015, an increase in the number of cases of microcephaly was reported to the Ministry of Health of Brazil. By January 2016, a total of 3,530 suspected microcephaly cases had been reported, many of which occurred in infants born to women who lived in or had visited areas where ongoing Zika virus transmission was occurring [5]. By the end of 2015, 4,180 suspected cases of microcephaly had been reported [6]. More recently, instances of sexual transmission of the virus have been reported. The United States (US) Centers for Disease Control and Prevention (CDC) received reports of 14 cases of suspected sexual transmission of ZVD between February 6 and 22, 2016. This included two laboratory-confirmed cases and four probable cases of ZVD that were identified among women whose only known risk factor was unprotected sexual contact with a symptomatic male partner that recently travelled to an area with ongoing Zika virus transmission [7].

Health authorities in affected countries have to face the challenges of dealing with a new pathogen that they may know very little about [8]. Mounting an appropriate response is even more exigent in most tropical and subtropical countries where the mosquito vectors *Aedes aegypti* and *Aedes albopictus* are widely distributed and the introduction of the virus to these areas could readily result in endemic transmission of the disease [9]. The US Department of Health and Human Services decided that there was an urgent need for additional research to better characterize ZVD, focusing in particular on the mode of transmission and infection during pregnancy [10]. Even though, the US has been faced with several emerging and re-emerging infectious disease threats in the past, important gaps remain in core areas of public health system readiness. It is recognized that stable, sustained investments are required to establish a solid foundation for achieving necessary national public health emergency preparedness and response capacity [11]. This report describes planning for ZVD surveillance and control, some challenges typically faced by local and state health departments in the US, and opportunities to build and strengthen public health capacity to respond to emerging infectious diseases.

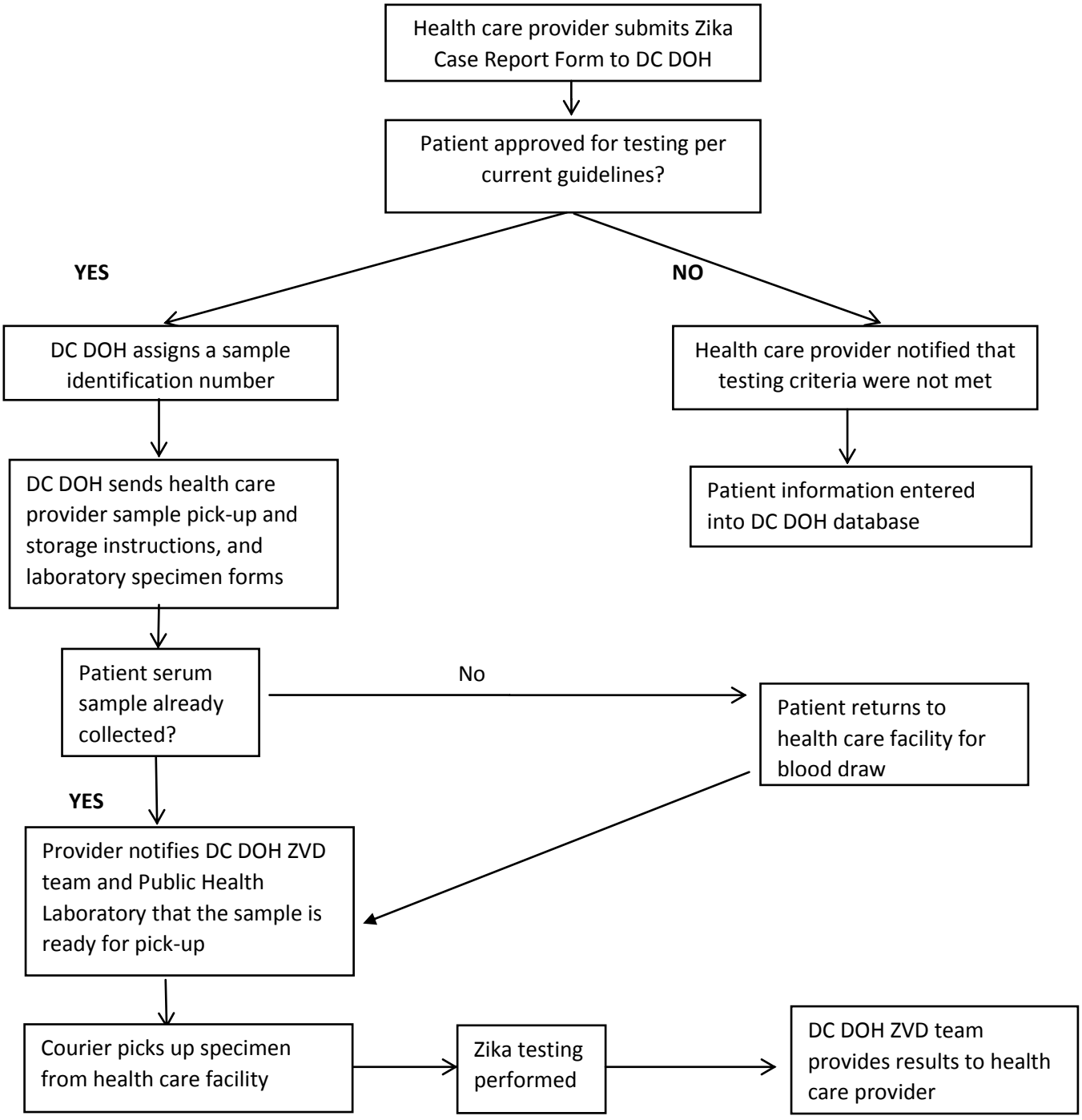
Zika Virus Preparedness and Response:

The DC Department of Health (DC DOH) Zika Virus Surveillance Program was initiated in January 2016. DC DOH Epidemiologists conducted active surveillance for travelers returning from areas with ongoing ZVD transmission in collaboration with health care workers when patients present to DC health care facilities (Figure 1). Due to the large number of international travelers in the Washington, DC metropolitan area, health care workers within the city were asked to screen all patients about their recent travel history outside the US. Patients who had traveled to areas with ongoing ZVD transmission within the previous two weeks are screened for the following symptoms: fever (both subjective and objective), non-purulent conjunctivitis, rash, and arthralgia. Non-pregnant patients displaying at least one symptom are recommended for Zika virus testing. Pregnant patients (and those who become pregnant within 8 weeks of returning from an area with ongoing ZVD transmission) are recommended for Zika virus testing 2 to 12 weeks from the last day of travel, regardless of symptom status. The DC Public Health Laboratory (PHL) performs Polymerase Chain Reaction (PCR) testing for Zika virus RNA on all samples collected within 7 days of symptom onset. Immunoglobulin M (IgM) antibody testing is performed at CDC facilities in Fort Collins, Colorado, on samples collected more than 7 days after symptom onset and for all samples from asymptomatic pregnant patients (or patients that became pregnant within 8 weeks of travel) (Figure1).

Mosquito Control:

Starting in April 2016, DC DOH is enhancing its vector-borne disease surveillance program by beginning surveillance activities two months earlier than in previous years, and therefore expanding the surveillance period to 6 months. Surveillance involves trapping adult mosquitoes in each of the eight DC wards, using gravid traps and carbon dioxide (CO2) traps. Trapped mosquitos are sorted by both sex and species weekly and submitted to the DC PHL for PCR Testing. The DC PHL performs testing on all female mosquitos for the following diseases of public health importance: Chikungunya virus, Dengue virus, West Nile virus, and Zika virus. Test results are posted on the DC DOH website daily, and weekly totals are reported to the CDC. DC DOH mosquito-control personnel also place insecticides that target the juvenile larval-stage of mosquitoes (larvicides) in areas with standing water and catch basins. DC DOH will hold two community education campaigns during the mosquito season to present information on how to reduce mosquito breeding sites in the community and around homes, as well as preventative measures individuals can take to reduce personal exposure to mosquito.

Figure 1: District of Columbia Department of Health (DC DOH) Zika Patient Processing Protocol



Challenges:

Communication with stakeholders:

Communication with stakeholders is always a critical part of response activities. As previously mentioned, Washington, DC has a large population of frequent travelers, which means that there is a large population of residents who potentially needed testing. This creates a challenge responding to e-mails and telephone calls from stakeholders who request guidance or have questions. Responding to inquiries can become time consuming to the extent that it hinders our ability to perform other response activities, such as reviewing and processing case report forms and interviewing patients referred for testing. Responding to stakeholders on an individual basis becomes even less feasible when intense media attention increases public fear, as was the case with ZVD.

DC DOH is responsible for providing official data on cases of Zika virus among DC residents to the media (such as through press releases) and responding to media inquiries. One of the challenges this creates is balancing the responsibility to share information with the need to ensure the individual privacy of patients. This has been particularly important given that the number of confirmed cases in DC (all travel-associated) is very small (n=4 as of May 9, 2016).

Another challenge in communicating with stakeholders is that instead of a single message, multiple, targeted messages must be developed and distributed to various audiences. For example, health care workers need detailed technical information so that they can appropriately manage patients and refer patients for Zika virus testing. Patients suspected to have Zika virus need specific information regarding testing and risk of infection. In addition, the messages communicated to each group evolve over time. When the CDC updates its guidance or releases new recommendations on testing criteria, mosquito control practices, as potential for Zika virus exposure changes over time (e.g., during mosquito season or summer vacation), or as we implement changes in our local surveillance protocol (e.g., updated Zika case report form), new messages need to be released. The public also needs general information presented in lay terms on prevention of mosquito bites. Development of a communications plan that includes public education about preventing the breeding of mosquitoes, personal protection guidance, and the participation of the necessary agencies and other stakeholders is critical to the success of the program.

Regional Coordination:

As the response heightened, DC DOH increasingly received ZVD case report forms for residents of the neighboring states of Maryland and Virginia who visited DC health

care facilities. Each jurisdiction had developed their own process for specimen collection and routing, submission of appropriate documentation by providers (e.g., case report and laboratory forms), and testing approval criteria. However, it soon became evident that each jurisdiction could not operate in isolation. This created a challenge to not only develop and optimize a DC ZVD surveillance protocol, but also to develop a regional protocol in collaboration with Maryland and Virginia.

Testing Limitations:

There have been several challenges associated with testing persons for ZVD. A major challenge has been that testing for Zika virus cannot be performed by commercial laboratories. Initially testing was only possible at the CDC Arbovirus Diagnostic Laboratory. Even with the expansion of PCR testing at the DC PHL, confirmatory testing must still be performed by the CDC for all samples. In addition, PCR testing is only appropriate for persons whose serum sample was collected within 7 days of symptom onset and very few patients met these criteria. Testing requires coordination of multiple partners both internal and external to DOH. When a sample is approved for testing, information must be communicated to all partners in a timely manner to facilitate timely testing and minimize sample storage times.

Recommendations about who should be tested and test result interpretation has been challenging because the epidemiology of ZVD is not well understood at this point in time. Testing criteria have changed over the course of the response as more data have become available, particularly with regard to sexual transmission. Many persons with a positive travel history but without symptoms want to be tested, especially since the general public is aware that 80% of people do not develop symptoms. However, the predictive value of the test in asymptomatic individuals is unknown and, therefore, test in this population is not currently recommended. As testing criteria expanded to include all pregnant women with a positive travel history, the wait-times for results increased past 4 weeks as the number of samples received daily by the CDC increased. This makes it difficult for patients and health care providers to make any clinical decisions based on test results alone, and have led to prolonged anxiety, especially among pregnant women.

Lessons Learned:

As part of the Zika virus response, DC DOH was tasked with balancing the need to respond to inquiries for guidance and information, while also performing other response activities, maintaining awareness of media messages, developing multiple communications tailored to specific stakeholders, and providing accurate and updated information in a timely manner. As the outbreak expanded, this communication

needed to transition from one-on-one interaction to more efficient strategies.

The most efficient means of addressing these communication challenges, particularly for the public, was to develop a specific webpage on Zika on the DC DOH website. The website directs members of the public to contact or visit their health care provider to determine whether they should be tested for ZVD. DC health care providers are e-mailed updated health notices, which can be accessed through a link on the DC DOH ZVD webpage. The health notices provided information about testing criteria, protocols for reporting suspected cases, and coordinating sample pick-up for testing. Members of the public are advised to send an e-mail to the DC DOH ZVD team using an e-mail address displayed on the DC DOH ZVD webpage if they needed additional information. A general telephone line was reserved as another means for health care providers to contact DC DOH, in addition to the DC DOH ZVD team e-mail address. As new information is posted on the DC DOH ZVD website or shared with the media, the levels of details included are closely monitored due to privacy concerns. Protecting the privacy of the patient is of paramount importance, and must be balanced when communicating public health information. We also discovered the importance of establishing key contacts at each health care facility and at the CDC to ensure that protocols were followed and to facilitate accurate and timely testing. Once we communicate information to the key contact(s) at health care facilities, they can then convey our messages to all the health care providers working at their facility.

In a situation where fear can play a large role, addressing misconceptions in the community early is important. This supports health care workers in providing appropriate care for their patients, and allows DC DOH to plan and execute an appropriate response to address current healthcare needs. Because ZVD is a mosquito-borne disease, there were continual questions from the community and the media regarding vector control. To mitigate fears, the DC DOH ZVD team presented information at community meetings as well as during a community-based educational campaign to take place throughout the mosquito season. There has also been focused communications prepared to inform residents that there has been no local transmission of ZVD by mosquitoes in the continental US and to address other misconceptions around ZVD.

Given the uniqueness of the Washington, DC metropolitan area, DC DOH could not work in isolation to develop its Zika Virus response activities. Therefore, DC DOH held weekly conference calls with Maryland and Virginia to share state and local protocols and establish a process for handling cases from neighboring jurisdictions. These conference calls were also an opportunity to share strategies and challenges. Close collaboration with neighboring jurisdictions also ensured that DC

DOH could appropriately inform health care providers about the processes that needed to be followed based on their patient's state of residence, and that health care providers received consistent messages about how to report suspected ZVD cases regardless of the health department they contacted for guidance.

DC DOH worked closely with key contacts at health care facilities to explain testing criteria and the reasons people were not cleared for testing to ensure testing was only performed when appropriate. To account for changing testing criteria, records were retained for all patients who were not approved for testing so that if they were to become eligible in the future as guidelines changed, their health care providers could be contacted.

CONCLUSIONS:

Although we faced several challenges, this experience continues to add to our effectiveness in addressing the demands of controlling future emerging infectious diseases. Meeting these challenges when they occur will ensure the accomplishment of better outcomes in the future. Priorities for control of ZVD must include provision of adequate information and education to stakeholders, who visit endemic areas, prevention of transmission by local vectors, and developing an integrated vector management program. In our rapidly changing and unpredictable environment, developing detailed protocols and increased collaborative efforts are essential keys to success.

Author Contributions:

John Davies-Cole supervised the surveillance and response activities and led the writing; Preetha Iyengar, Sasha McGee and Andrew Hennenfent conducted surveillance and response activities and wrote separate sections. Vito DelVento supervised the mosquito control activities and reviewed the manuscript. Anicet Dahorou coordinated samples referral and laboratory testing. Fern Johnson-Clarke reviewed and edited the manuscript.

REFERENCES:

1. World Health Organization (WHO). Zika Outbreak: WHO's Global Emergency Response Plan. WHO website. March 3, 2016. http://www.who.int/emergencies/zika-virus/response/en/. Accessed March 21, 2016.
2. The World Health Organization (WHO). The History of Zika Virus. WHO website. 2016.http://www.who.int/emergencies/zika-virus/timeline/en/. Accessed March 21, 2016.
3. Centers for Disease Control & Prevention (CDC). Zika: Symptoms, Diagnosis and Treatment. CDC Website. March 11, 2016. http://www.cdc.gov/zika/symptoms/index.html. Accessed March 20, 2016.
4. Carod-Artal FJ. Epidemiology and neurological complications of infection by the Zika virus: a new emerging

neurotropic virus. Rev Neurol. 2016; 62:317-328.

5. Kleber de Oliveira W, Cortez-Escalante J, De Oliveira WT, do Carmo GM, Henriques CM, Coelho GE, Araújo de França GV.Increase in reported prevalence of microcephaly in infants born to women living in areas with confirmed Zika virus transmission during the first trimester of pregnancy - Brazil, 2015. MMWR Morb Mortal Wkly Rep. 2016; 65: 242-7. doi: 10.15585/mmwr.mm6509e2.
6. Teixeira MG, da Conceição N Costa M, de Oliveira WK, Nunes ML, Rodrigues LC. The epidemic of Zika virus-related microcephaly in Brazil: detection, control, etiology, and future scenarios. Am J Public Health. 2016; 106:601-5. doi: 10.2105/AJPH.2016.303113.
7. Hills SL, Russell K, Hennessey M, Williams C, Oster AM, Fischer M, Mead P. Transmission of Zika virus through sexual contact with travelers to areas of ongoing transmission - continental United States, 2016. MMWR Morb Mortal Wkly Rep2016; 65:215–216
8. Villa, R. Zika, or the burden of uncertainty. Clin Ter.2016; 167:7-9. doi: 10.7417/CT.2016.1907.
9. Wong SS, Poon RW, Wong SC. Zika virus infection-the next wave after dengue?J Formos Med Assoc. 2016; Mar 7. pii: S0929-6646(16)00077-2. doi: 10.1016/j.jfma.2016.02.002.
10. Snair J, Hermann J, Brown L, Wollek S, Balogh E, Maxfield K. Potential Research Priorities to Inform Public Health and Medical Practice for Domestic Zika Virus: Workshop in Brief (2016). Institute of Medicine; Division on Earth and Life Studies; National Academies of Sciences, Engineering, and Medicine, Washington (DC). February 2016. http://www.nap.edu/read/23404/chapter/1#8. Accessed March 19, 2016.
11. Duchin JS. US public health preparedness for Zika and other threats remains vulnerable. Disaster Med Public Health Prep. 2016; 8:1-2.