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Viewpoint | March 1, 2016

The Emerging Zika Pandemic Enhancing Preparedness

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The Zika virus (ZIKV), a flavivirus related to yellow fever, dengue, West Nile, and Japanese encephalitis, originated in the Zika forest in Uganda and was discovered in a rhesus monkey in 1947. The disease now has “explosive” pandemic potential, with outbreaks in Africa, Southeast Asia, the Pacific Islands, and the Americas.¹ Since Brazil reported Zika virus in May 2015, infections have occurred in at least 20 countries in the Americas.² Puerto Rico reported the first locally transmitted infection in December 2015, but Zika is likely to spread to the United States. The *Aedes* species mosquito (an aggressive daytime biter) that transmits Zika virus (as well as dengue, chikungunya, and yellow fever) occurs worldwide, posing a high risk for global transmission. Modeling anticipates significant international spread by travelers from Brazil to the rest of the Americas, Europe, and Asia.³ What steps are required now to shore up preparedness in the Americas and worldwide?

MILD DISEASE BUT GROWING CONCERNS ABOUT MICROCEPHALY

Zika virus infection usually is asymptomatic or causes mild illness, such as fever, rash, muscle/joint pain, and conjunctivitis; severe disease and fatalities are uncommon. Health authorities, however, are investigating severe clinical manifestations, including neurological and autoimmune-like illness, particularly Guillain-Barré syndrome (GBS) and congenital neurological malformations. Most concerning is a possible association between Zika virus and microcephaly in Brazil and, retrospectively, in French Polynesia.

Brazil has reported nearly 4000 cases of suspected microcephaly in 2015, representing a 20-fold increase from 2010 through 2014.¹ Evidence of the virus has been found in the placenta and amniotic fluid of mothers and in the brains of fetuses or newborns. Yet causation between Zika virus and microcephaly is not yet established. On January 15, 2016, Hawaii reported the first domestic case of microcephaly in a newborn whose mother had lived in Brazil. Days later, Florida, Illinois, and Texas reported several infected individuals (some pregnant) after international travel.

NATIONAL HEALTH SYSTEM CAPACITIES

The International Health Regulations (IHR) requires every country to develop core health system capacities, but most fail to meet international standards. To ensure national preparedness for Zika, countries—including the United States—should fund and adopt these strategies, particularly countries already affected and those with significant *Aedes* mosquito populations.

Vector Control. Mosquito-borne diseases require reducing source populations, including physical (eg, removing water-containing sources) and biological (eg, fish that feed on larvae) controls. Insecticide spraying of mosquito habitats or adult populations can be effective. Although it remains controversial due to ecological concerns, releasing genetically modified sterile male mosquitoes could reduce disease-transmitting mosquito larvae. All these strategies require effective mosquito surveillance to ensure focused interventions.

Risk Communication. Health information campaigns should advise the public to avoid mosquito exposure, such as by wearing appropriate clothing, using insect repellents, and spraying insecticide in indoor spaces. Staying inside protected dwellings during peak mosquito biting hours can also reduce risk. Using physical barriers such as screens, closed windows, and bed nets can reduce mosquito populations around residential areas.

Enhanced Zika Surveillance. The Pan American Health Organization (PAHO) issued a series of epidemiological updates and alerts in 2015 urging enhanced surveillance for Zika virus, as well as neurological, autoimmune, and congenital malformation associations.⁴ The IHR requires countries to report unusual Zika-related cases. PAHO's guidance prompted El Salvador to find and report an increase in GBS between December 2014 and January 2015. Training health workers to observe and report Zika-related disease and robust systems for collecting and analyzing surveillance data will complement public health strategies.

Travel Advisories. To minimize harm to high-risk travelers, agencies should consider issuing travel advisories. Given rapidly evolving epidemiological and virological data, the Centers for Disease Control and Prevention (CDC) issued a "level 2" Alert on January 15 advising pregnant women to consider postponing travel to countries with ongoing Zika virus transmission—the agency's first-ever alert for pregnant women.⁵ (The Public Health Agency of Canada and the Taiwan CDC issued similar advice.) The CDC stopped short of a more restrictive "level 3 warning" against nonessential travel. Travel advisories for the wider public could include guidance on reducing mosquito exposure and greater awareness of symptoms. On returning home, symptomatic individuals should report their travel histories to their physician.

Clinical Management. An estimated 80% of Zika infections are asymptomatic, and most of the remainder are self-limited. No specific antiviral treatment is available and care is supportive, with symptoms usually resolving within 7 days.¹ Severe GBS cases can require intensive care, including mechanical ventilation. On January 19, the CDC issued new guidelines for pregnant women with suspected or proven Zika virus infection, including an algorithm for offering laboratory testing. (Diagnostic testing is not optimal because antibody tests could cross-react, giving false-positive results due to other flavivirus infections.) Commercial tests are unavailable, but the CDC and several state laboratories have testing capability. Pregnant women with laboratory evidence of Zika virus in serum or amniotic fluid should consider serial fetal ultrasounds every 3 to 4 weeks.⁵

Accelerated Research and Development. When Zika infection was seen as usually asymptomatic and self-limited, researchers had little incentive to develop reliable countermeasures. The emerging data on fetal complications,⁴ however, have altered this equation, with research on new vaccines becoming urgent. Similarly, understanding which individuals are at increased risk of GBS could allow specific antiviral treatment.

A safe and effective Zika virus vaccine is probably 3 to 10 years away even with accelerated research. The National Institutes of Health launched a Zika vaccine initiative in late 2015, and Brazil has expedited vaccine development. Vaccines against yellow fever and Japanese B encephalitis have been licensed for decades, and Brazil, Mexico, and the Philippines approved the first dengue vaccine in 2015.

Public Health Emergency Declarations. A national declaration of a public health emergency can focus political attention, while financing a surge in resources. Public health agencies also have increased authority during public health emergencies. Brazil, for example, proactively declared a public health emergency in November 2015.⁴ Countries experiencing major Zika virus outbreaks with possible neurological, autoimmune, and congenital malformation associations could invoke heightened emergency powers.

WORLD HEALTH ORGANIZATION LEADERSHIP

The World Health Organization (WHO) Ebola Panel in July 2015 said that urgent warnings "either did not reach senior leaders or senior leaders did not recognise their significance."⁶ By many accounts the agency's failure to act decisively cost thousands of lives.⁷ Despite internal reforms, however, WHO is still not taking a leadership role in the Zika pandemic. On January 18, WHO said it is "supporting countries to control Zika," citing the need for surveillance, laboratories, vector control, and clinical care. Yet, the global dimensions of Zika are quite clear, with fresh urgency as the 2016 Olympics in Rio de Janeiro loom.

Despite the global threat, the WHO director-general has not convened an IHR Emergency Committee to advise countries on critical issues such as vector control, health system preparedness, travel advisories, and avoiding punitive measures. An emergency committee should be convened immediately to advise the director-general about the conditions necessary to declare a Public Health Emergency of International

Concern (PHEIC). The very process of convening the committee would catalyze international attention, funding, and research. While Brazil, PAHO, and the CDC have acted rapidly, WHO headquarters has thus far not been proactive, given potentially serious ramifications.

Convening an emergency committee does not mean that the director-general should declare a PHEIC. WHO, for example, convened an emergency committee on 10 occasions to review global data on the Middle East respiratory syndrome (MERS). Yet the emergency committee has not advised to declare a PHEIC for MERS but has offered detailed recommendations to guide member states. The director-general has the sole authority under the IHR to convene an emergency committee, and she is uniquely empowered to declare a PHEIC subject to the committee's advice.

The director-general was widely criticized for waiting 4 months after the first cross-border transmission of Ebola before declaring a PHEIC.^{8,9} A key lesson learned from that searing experience was the need for an intermediate-level response to emerging crises, thus avoiding overreaction while still galvanizing global action. Functionally, the director-general could achieve a similar result by convening an emergency committee on Zika virus. The international community cannot afford to wait for WHO to act.

ARTICLE INFORMATION

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