MAYO CLINIC

Zika Virus in the Americas: A Review for Clinicians

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CME Activity

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Abstract

Zika virus has recently emerged as a new public health threat. An arthropod-borne virus named after the Zika forest in Uganda, it was first discovered in 1947. The virus caused only sporadic cases of Zika infection in Africa and Southeast Asia until 2007, when the first large outbreak occurred in the Yap State in the Federated States of Micronesia. Another outbreak in French Polynesia in 2013 was notable for being associated temporally with an increase in cases of Guillain-Barré syndrome. In 2015, the virus was first reported in Brazil and since then has spread explosively through several additional countries in South and Central America and the Caribbean. Simultaneously, several of these countries have seen a dramatic increase in the incidence of infants born with microcephaly. The rapid spread of Zika virus through the Americas, together with the association of infection with microcephaly and Guillain-Barré syndrome, has resulted in the World Health Organization declaring a public health emergency. Zika virus has the potential to spread to new areas where the *Aedes* mosquito vector is present and therefore presents a risk to the United States. This concise review describes the clinical features of Zika virus infection and provides advice for clinicians on counseling travelers and others about the disease.

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HISTORY AND EPIDEMIOLOGY

The Zika virus was first identified in 1947 in the Zika forest near Kampala, Uganda, in a rhesus monkey that was part of a yellow fever research study.[1] Serologic studies identified human Zika infections in several African countries including Uganda, Nigeria, Tanzania, Egypt, Central African Republic, Ivory Coast, Sierra Leone, and Gabon over the next several decades. In addition, sporadic cases were reported in Southeast Asia including Malaysia, Indonesia, India, Cambodia, Pakistan, Philippines, Singapore, Thailand, and Vietnam. In April 2007, an epidemic of rash, conjunctivitis, and arthralgia was reported from Yap State, Federated States of Micronesia.[2] This epidemic represented the first documented outbreak of Zika virus infection; it was estimated that 70% of the island's population was infected with Zika virus over a 13-week period. In 2013, another large outbreak was reported in French Polynesia. This outbreak was notable because although most clinical cases presented with mild disease, an association with Guillain-Barré syndrome (GBS) was first noted.[3,4] The incidence of GBS cases during the outbreak was 20-fold higher than expected. There were subsequent small outbreaks in Oceania but relatively few cases until May 2015, when another outbreak was identified in Brazil.[5] Since then, the virus has been detected at an increasing rate in several countries in South and Central America and the Caribbean (Figure 1).[6] In September 2015, reports of an increase in the number of infants born with microcephaly in Zika virus–affected areas began to emerge.[7] On February 1, 2016, the World Health Organization (WHO) declared that the Zika virus outbreak constituted an international public health emergency because of the possible link to microcephaly and other neurologic syndromes. The WHO declaration represents its highest level of alert and has only been invoked 3 other times so far—in 2009 during the H1N1 influenza epidemic, in May 2014 when poliomyelitis reemerged in Pakistan and Syria, and in August 2014 with Ebola virus.

TRANSMISSION

Zika virus is primarily transmitted to humans through bites from *Aedes* mosquitoes. Both *Aedes aegypti* (confined to tropical and subtropical regions) and *Aedes albopictus* (found in temperate regions in addition to tropical and subtropical areas) are capable of transmitting Zika virus and have been implicated in outbreaks of Zika virus. Both *Aedes* species are present in the United States. *Aedes albopictus* is of particular concern because it has a much wider range than *A aegypti*. It was originally imported from Southeast Asia and has been remarkably adaptable to cooler climates. *Aedes albopictus* is now firmly established in several states in the United States.[8] It is an aggressive daytime biter and thrives in densely populated urban environments. As the number of returning travelers with Zika virus disease increases, the presence of the *Aedes* vector in the United States makes local spread a serious possibility (Figure 2).

Other modes of transmission are possible, but it is unclear how much of a role they play in propagating outbreaks. Sexual transmission of Zika virus was first reported in 2011.[10] An American researcher acquired Zika virus in Senegal, became ill after returning home to Colorado, and transmitted the infection to his wife who had not traveled outside the United States. There have been 2 lab-confirmed cases of sexual transmission of Zika virus in the US during the current Zika outbreak; several additional cases are under investigation.[11] The virus was first isolated from sperm during the Polynesian outbreak.[12] It is not known how long the virus persists in sperm or whether asymptomatic persons infected with Zika virus can transmit infection to sexual partners. The disease is associated with viremia, so not surprisingly, transfusion-related transmission has been reported.[13] The virus is detectable in breast milk,[14] but breastfeeding-associated transmission has not been reported so far.

PATHOGENESIS

Zika virus is an RNA virus that is closely related to other flaviviruses including yellow fever, dengue virus, Japanese encephalitis, and West Nile virus. Little is known about its pathogenesis; however, it is thought that viral replication occurs in local dendritic cells after inoculation from a mosquito with subsequent spread to lymph nodes and the bloodstream. Viremia is generally seen within 3 to