Medical Summary

ZIKA

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INTRODUCTION

Zika virus infection, transmitted by *Aedes* mosquitoes, is caused by a flavivirus closely related to dengue, West Nile virus, and Japanese encephalitis. Infection is symptomatic in approximately 1 of 5 cases; when symptomatic, infection usually presents as an influenza-like syndrome and is often mistaken for dengue or chikungunya. Because of cross-reaction in commonly used dengue antibody tests, until recently Zika was likely often misdiagnosed as mild dengue infection. With more frequent utilization of modern pan-flavivirus molecular screening in reference laboratory settings, characterization of Zika virus infection previously mistaken for dengue has enhanced understanding of the expanding geographic range and manifestations of this infection.

MODE OF TRANSMISSION

Humans and non-human primates are likely the main reservoirs of the virus, and anthroponotic (human-to-vector-to-human) transmission occurs during outbreaks. *Aedes aegypti* is the most important vector to humans; *Aedes albopictus* and *Aedes hensilii* have been identified as potential vectors.

Transfusion-derived and sexual transmission occur uncommonly.

EPIDEMIOLOGY

Zika virus was initially identified in 1947 in the Zika Forest in Uganda in the Rhesus macaque population; the first human cases were reported in 1952. Historically, Zika epizootics have inexplicably tended to follow chikungunya epizootics and epidemics.

Until 2007, limited case reports and sero-surveys indicated infrequent, sporadic human infection in at least a dozen countries of Africa and Southeast Asia. However, in 2007, Zika caused a large outbreak in Yap, Micronesia, marking the first detection of the virus beyond Africa and Asia. Since then, the virus has spread to French Polynesia (occurring in 2013-14) and a few other Pacific Islands, and subsequently in early 2015, to Brazil (largest outbreak to date), countries in Central and South America, the Caribbean, and then to Cape Verde.

RISK FACTORS

All persons residing in or visiting an endemic area when there is ongoing transmission are at risk of acquiring Zika.

CLINICAL PRESENTATION

The incubation period is 3-12 days. The majority of cases present with fever, headache, malaise, maculopapular rash, arthralgia, myalgia, and conjunctivitis. Other non-specific features are less common. The self-limited illness with symptoms lasting 2-7 days is almost always mild without serious forms (such as with dengue) and without long-term arthritic sequelae (such as with chikungunya). Hemorrhagic fever

has not been reported in Zika infection. Nevertheless, in the early stages of the disease, Zika is indistinguishable from dengue and chikungunya, which often coexist in the same locations.

Although severe disease requiring hospitalization is uncommon, there are reports of increased rates of Guillain-Barré syndrome (GBS), an autoimmune complication that occurs after many different viral infections, from the previous outbreak in French Polynesia and in the current outbreak in Brazil and other Latin American countries. The case fatality is low.

An association between infection during pregnancy and congenital microcephaly is under investigation, but conclusive evidence is lacking at present. In Brazil, more than 3,500 microcephaly cases, a large increase over normal incidence, were reported between October 2015 and January 2016. A role for increased reporting is possible. How many of the microcephaly cases are associated with Zika virus infection has not been systematically investigated to date, although Zika antibodies indicating infection at some point during pregnancy have been found in a small number of cases. Appropriate case-control and cohort studies which are needed to prove a causal association are ongoing in Brazil; no data have been released to date. In 1 Brazilian cohort of 35 cases from Zika affected areas, 26 (74%) of mothers of infants with microcephaly and neuroimaging abnormalities self-reported recalling a rash during the first (n=15) or second (5) trimester; Zika virus testing is pending. Testing for other pathogens associated with microcephaly was negative. In addition, Zika virus RNA has been isolated from brain tissue in 4 severely affected fetuses/perinatal deaths in Brazil, from amniotic fluid in 2 others, and from placenta in 1 case. No other flavivirus, including Zika virus over the past 60 years, is known to be teratogenic. No increase in microcephaly rates in other currently affected countries or in pregnant travelers to other Zika-affected countries have been reported. The full spectrum of outcomes that might be associated with infection during pregnancy and the factors that might increase risk to the fetus in certain, and perhaps unusual, circumstances are not yet fully understood. Until more is known, many authorities are recommending that pregnant women (in any trimester) or those trying to become pregnant should consider postponing travel to Zika-affected areas. (See Travax Destinations for specific geography).

PREVENTION STRATEGIES

Insect precautions and personal protection measures against day-biting mosquitoes are the main prevention strategy. Of importance in terms of prevention, *Aedes* mosquitoes, unlike malaria-transmitting *Anopheles*, are daytime feeders, with 2 peaks of biting activity during the day: the first 2-3 hours after dawn and the mid-to-late afternoon hours. This pattern, however, turns to one of all-day activity indoors or during overcast days. In risk areas, travelers (especially pregnant travelers) should be especially vigilant in applying repellent during daytime hours, particularly during peak biting times (early morning hours and late afternoon). Insect repellents containing DEET and picaridin are considered safe during all trimesters of pregnancy. See *Insect Precautions*.

In addition, containers with stagnant water can serve as breeding sites for *Aedes* mosquitoes, and travelers should be instructed to empty them or remove them from the proximity of human habitations whenever possible.

NEED FOR MEDICAL ASSISTANCE

Medical assistance is not normally necessary, as serious complications are extremely rare, in contrast with dengue fever, in which patients may develop shock and hemorrhage. Most Zika infections resolve spontaneously over a few days. There is no specific antiviral treatment for Zika virus infection. Self-medication with paracetamol (acetaminophen) may help relieve some symptoms.

Testing is not indicated for travelers returned from non-Zika transmission areas. Testing is not recommended for pregnant women who visited Zika transmission areas who did not have compatible symptoms during or within 2 weeks of return.

Pregnant women who report 2 or more symptoms consistent with Zika virus infection during or within 2 weeks of travel to risk areas or who have ultrasound findings of fetal microcephaly or intracranial calcifications should be tested for Zika virus in consultation with public health authorities. Pregnant women with laboratory evidence of Zika virus infection should be referred for expert management.

Infants with microcephaly or intracranial calcifications born to women who traveled or resided in risk areas during pregnancy or any infant born to women with positive or inconclusive test results should be tested for Zika virus in consultation with public health authorities.

Specific commercial antibody testing for Zika is unavailable. In the U.S., specimens should be routed via State Health Departments to the CDC. During the first week of illness, reverse transcriptase-polymerase chain reaction (RT-PCR) on serum is usually positive. Virus-specific IgM develop toward the end of the first week of illness. Cross-reaction with related flaviviruses (e.g., dengue and yellow fever viruses) is common and positive tests must be confirmed at a reference laboratory. Both RT-PCR and serologic testing of infants who are being evaluated for evidence of a congenital Zika virus infection are necessary.
