

Zika virus infection

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■ INTRODUCTION

Zika virus is spread to people through mosquito bites. It is a mosquito-borne flavivirus, recently appearing in the Western hemisphere. The virus is related to other flaviviruses, including dengue virus, West Nile virus, and Japanese encephalitis virus. Clinical manifestations of Zika virus infection includes: fever, rash, headache, arthralgia, myalgia, and conjunctivitis. Zika virus infection has also been associated most recently with congenital microcephaly and fetal losses among women infected during pregnancy; further investigation is ongoing.(1)

EPIDEMIOLOGY

During large outbreaks in French Polynesia and Brazil in 2013 and 2015 respectively, national health authorities reported potential neurological and auto-immune complications of Zika virus disease. Recently in Brazil, local health authorities have observed an increase in Zika virus infections in the general public, as well as an increase in babies born with microcephaly in northeastern Brazil. Agencies investigating the Zika outbreaks are finding an increasing body of evidence about the link between Zika virus and microcephaly. However, more investigation is needed before we understand the relationship between microcephaly in babies and the Zika virus. Other potential causes are also being investigated.(8)

Outbreaks of Zika virus infection have occurred in Africa, Southeast Asia, and the Pacific Islands. Currently, there is an ongoing Zika virus outbreak in the Americas.(2,3). In January 2016, the United States Centers for Disease Control and Prevention (CDC) advised that pregnant women considered postponing travel to any area where Zika virus transmission is ongoing, given an association between congenital microcephaly in parallel with the Zika virus outbreak in Brazil(1). Named as Zika, after the Ugandan

forest where it was first isolated in a rhesus monkey in 1947, it spread to Southeast Asia, where it was associated with sporadic infections. The first major outbreak occurred in the Yap Islands of Micronesia in 2007.(4,6) Another large outbreak occurred in French Polynesia in 2013, where public health officials estimated infection rates of 70 percent in some islands.

Zika virus infection appeared in the Western hemisphere in February 2014 on Chile's Easter Island; the virus continued to be detected there until June 2014. Zika virus infection in Brazil was confirmed in May 2015.(7) As of January 2016, countries with autochthonous circulation of Zika virus in the Americas include Brazil, Colombia, Ecuador, El Salvador, French Guiana, Guatemala, Guyana, Haiti, Honduras, Martinique, Mexico, Panama, Paraguay, Saint Martin, Suriname, and Venezuela.(8)

In December 2015, Zika virus infection was detected in Puerto Rico. Local transmission of Zika virus infection has not yet been reported in the continental United States, but cases of imported Zika infection have been reported in travelers.

Transmission

1) THROUGH MOSQUITO BITES

It is transmitted to humans primarily via the bite of an infected *Aedes* mosquito. Zika virus is carried by the *Aedes aegyptii* mosquito, which lives only in tropical regions; however, the *Aedes albopictus* mosquito, which lives in temperate regions, is also capable of carrying it. *Aedes* mosquitoes usually bite during the daytime and breed in standing water.(9,10)

2) VERTICAL PERINATAL TRANSMISSION

It has been described.(11) Data on maternal-to-child transmission of Zika virus during pregnancy and childbirth are limited; further study is underway.(9) The virus has been isolated from blood and semen; these appear to be infrequent mechanisms for disease transmission.(12-15)

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3) POSSIBLY THROUGH INFECTED BLOOD OR SEXUAL CONTACT

There has been one report of possible spread of the virus through blood transfusion and one report of possible spread of the virus through sexual contact.(1)

CLINICAL MANIFESTATIONS

1 About 1 in 5 people infected with Zika virus become ill (i.e., develop the zika disease).

2 The most common symptoms of zika are fever, rash, joint pain, or conjunctivitis (red eyes). Other common symptoms include muscle pain and headache.

3 The illness is usually mild with symptoms lasting for several days to a week.

4 Severe disease requiring hospitalization is uncommon. Deaths are rare.

Symptoms typically include acute onset of low-grade fever (37.8 to 38.5°C) with maculopapular rash, arthralgia (notably the small joints of hands and feet), or conjunctivitis (nonpurulent). Other commonly reported clinical manifestations include myalgia, headache, retro-orbital pain, and asthenia.(16) Rarely observed symptoms and signs include abdominal pain, nausea, diarrhea, mucus membrane ulcerations, and pruritus.(17)

Symptoms and signs typically appear 2 to 12 days after the mosquito vector bite.

The illness is usually mild; symptoms usually resolve within two to seven days. Asymptomatic infection is common; symptoms develop in 20 to 25 percent of individuals who become infected with Zika virus.

Pan American Health Organization case definition:(18)

- A suspected case consists of a patient with rash or fever with one or more of the following symptoms or signs (not explained by other medical conditions): arthralgia or myalgia, nonpurulent conjunctivitis or conjunctival hyperemia, and headache or malaise. A confirmed case is a suspected case with positive laboratory test result for Zika virus.

- Severe disease requiring hospitalization is uncommon, and case-fatality rates are low. (16) An increase in the rate of Guillain-Barré syndrome has been observed in association with Zika virus infection; a direct causal relationship has not yet been definitively established. (18-20)

A large number of Brazilian newborns with microcephaly has been observed in parallel with the current Zika outbreak(19-26). Zika virus infection has been confirmed in several infants with congenital microcephaly and in fetal losses among women infected during pregnancy.(1) The spectrum of outcomes that may be associated with infection during pregnancy is not yet fully understood, nor are the factors that may increase fetal risk; further investigation is ongoing.

DIFFERENTIAL DIAGNOSIS

- Dengue virus and Zika virus infections present with similar clinical manifestations and are transmitted by the same mosquito vector. Clinically dengue infection usually

presents with relatively high fever and relatively severe muscle pain, which may also be associated with hemorrhage. Coinfection with Zika, chikungunya, and dengue viruses has been described.(27)

- Chikungunya virus and Zika virus infections present with similar symptoms and signs and are transmitted by the same mosquito vector. Clinically chikungunya usually presents with relatively high fever and relatively intense joint pain, affecting the hands, feet, knees, and back. The infection can be disabling, causing patients to bend over so that they cannot walk, or rendering individuals unable to perform simple manual tasks.

- Parvovirus, rubella, measles, other viruses may also cause arthritis, including enterovirus, adenovirus, and alphaviruses. Rickettsial infections must also be considered in the differential diagnosis.

- Leptospirosis is characterized by fever, rigors, myalgia, conjunctival suffusion, and headache. Less common symptoms and signs include cough, nausea, vomiting, diarrhea, abdominal pain, and arthralgia. It may be distinguished from Zika virus infection by the presence of jaundice. The diagnosis is established by serology.

- Malaria is characterized by fever, malaise, nausea, vomiting, abdominal pain, diarrhea, myalgia, and anemia. The diagnosis of malaria is established by visualization of parasites on peripheral smear.

DIAGNOSIS

A Zika virus infection should be suspected in individuals with characteristic clinical symptoms (fever, rash, headache, arthralgia, myalgia, and conjunctivitis) and relevant epidemiologic exposure (residence in or travel to an area where the Aedes mosquito is present and where imported or local cases have been reported, within two weeks prior to the onset of illness).

We can use a rapid screening test, however the diagnosis is definitively established by polymerase chain reaction (PCR) or serology performed by a specialized test:(1,28,29)

On the first week following onset of symptoms, the diagnosis of Zika virus infection may be established by serum PCR for detection of Zika virus RNA. In addition, acute serum should be obtained to compare with convalescent serum obtained two to three weeks later. PCR testing for dengue virus and chikungunya virus should also be pursued.

Four or more days following onset of symptoms, the diagnosis may be established by Zika virus serologic testing (IgM and neutralizing antibody testing) performed by the CDC or the Pan American Health Organization/World Health Organization. Acute and convalescent sera should be obtained to detect an increased antibody titer in paired samples with an interval of two to three weeks. Serologic

testing for dengue virus infection and chikungunya virus infection should also be pursued. All serologic results should be interpreted with caution since there can be cross-reactivity with other flaviviruses (including dengue virus and West Nile virus).

The optimal approach to evaluation for presence of possible intrauterine infection is uncertain; further study is needed. During the current outbreak in Brazil, Zika virus RNA has been identified in tissues from several infants with microcephaly and from fetal losses in women infected during pregnancy.(1,26)

MANAGEMENT

There is no specific treatment for Zika virus infection.

Management consists of rest and symptomatic treatment including drinking fluids to prevent dehydration and administration of acetaminophen to relieve fever and pain. (30) Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) should be avoided until dengue infection has been ruled out, to reduce the risk of hemorrhage.

Women who are pregnant or planning to become pregnant should have routine prenatal care. Fetuses and infants of women infected with Zika virus during pregnancy should be evaluated for possible congenital infection and neurologic abnormalities.(1)

PREVENTION

There is no vaccine for prevention of Zika virus infection.

Preventive measures include personal protective measures to prevent mosquito bites and implementation of measures to eliminate and control mosquito breeding sites.(12)

Personal protective measures to prevent mosquito bites include wearing long sleeves and long pants, using insect repellent, and staying indoors as feasible (with air conditioning, window/door screens, and/or mosquito nets to minimize contact between mosquitoes and people). Individuals with Zika virus infection may reduce spread of infection to others by following the same precautions to avoid mosquito bites during the first week of illness.

Potential mosquito breeding sites should be identified and eliminated. Mosquito larvae can breed in standing water; therefore, individuals should be instructed to avoid allowing standing water to collect outdoors (such as in flower pots, buckets, bottles, jars, and containers that collect water). Domestic water tanks should be covered so that mosquitoes cannot enter, and drains that could accumulate standing water should be eliminated.

Pregnant women should be particularly careful regarding adherence to mosquito protective measures and about traveling to areas where transmission of Zika virus and other mosquito-borne viruses is high. In January 2016, the United States Centers for Disease Control and Prevention advised

that pregnant women consider postponing travel to any area where Zika virus transmission is ongoing.(1)

WHO is supporting countries to control Zika virus disease by:

1. Strengthening surveillance.
2. Building the capacity of laboratories to detect the virus.
3. Working with countries to eliminate mosquito populations.
4. Preparing recommendations for the clinical care and monitoring of persons with Zika virus infection.
5. Defining and supporting priority areas of research into Zika virus disease and possible complications.

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