

**ZIKA VIRUS DISEASE
ZIKA VIRUS INFECTION
(ZIKV)**

REPORTING INFORMATION

- **Class B:** Report by the end of the next business day after the case or suspected case presents and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report to the local public health department in which the reporting health care provider or laboratory is located.
- Reporting Form(s) and/or Mechanism:
 - The Ohio Disease Reporting System (ODRS) should be used to report lab findings to the Ohio Department of Health (ODH). For healthcare providers without access to ODRS, you may use the [Ohio Confidential Reportable Disease form](#) (HEA 3334).
 - The ODH [Mosquito-borne Illness Case Investigation Form](#) is available for use to assist in local disease investigation. Information collected from the form should be entered into ODRS and not sent to ODH, unless otherwise requested. If requested, the form can be faxed to ODH at (614) 564-2456 or uploaded to the ODRS record.
- Key fields for ODRS reporting include: pregnancy status (for females), import status (whether the infection was travel-associated or Ohio-acquired), date of illness onset, symptoms, all fields in the Epidemiology module (including sexual contact questions) and travel details in the Travel History module (with accurate departure and return dates along with city, province/county, state and country).

AGENT

Zika virus is an RNA virus that belongs to the *Flavivirus* genus in the family Flaviviridae. There is substantial serologic cross reaction with other flaviviruses (e.g., dengue, Japanese encephalitis, Powassan, St. Louis encephalitis, West Nile, yellow fever viruses).

Infectious dose: A single bite of an infectious mosquito.

CASE DEFINITION

Laboratory Criteria for Diagnosis

Recent Zika virus infection:

- Culture of Zika virus from blood, body fluid or tissue or
- Detection of Zika virus antigen or viral ribonucleic acid (RNA) in serum, cerebrospinal fluid, placenta, umbilical cord, fetal tissue or other specimen (e.g., amniotic fluid, urine, semen, saliva) or
- Positive Zika virus immunoglobulin M (IgM) antibody test in serum or CSF with positive Zika virus neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred.

Recent flavivirus, possible Zika virus:

- Positive Zika virus IgM antibody test of serum or CSF with positive neutralizing antibody titers against Zika virus and dengue virus or other flaviviruses endemic to the region where exposure occurred or
- Positive Zika virus IgM antibody test and negative dengue virus IgM antibody test with no neutralizing antibody testing performed.

Epidemiologic Linkage

- Resides in or recent travel to an area with known Zika virus transmission or
- Sexual contact with a confirmed or probable case within the infection transmission risk window of Zika virus infection or person with recent travel to an area with known Zika virus transmission or
- Receipt of blood or blood products within 30 days of symptom onset or
- Organ or tissue transplant recipient within 30 days of symptom onset or
- Association in time and place with a confirmed or probable case or
- Likely vector exposure in an area with suitable seasonal and ecological conditions for potential local vector-borne transmission.

ZIKA VIRUS DISEASE, CONGENITAL

Clinical Criteria

Live-born infant with congenital microcephaly, intracranial calcifications, structural brain or eye abnormalities or other congenital central nervous system (CNS)-related abnormalities not explained by another etiology.

(As part of the complete evaluation of congenital microcephaly or other CNS] birth defects, testing for other congenital infections such as syphilis, toxoplasmosis, rubella, cytomegalovirus infection, lymphocytic choriomeningitis virus infection and herpes simplex virus infections should be considered. An assessment of potential genetic and other teratogenic causes of the congenital abnormalities should also be performed.)

Case Classification

Probable: A neonate who meets the clinical criteria for congenital disease and the neonate's mother has an epidemiologic linkage or meets laboratory criteria for recent Zika virus or flavivirus infection and the neonate has laboratory evidence of Zika virus or flavivirus infection by:

- Positive Zika virus IgM antibody test of serum or CSF collected within 2 days of birth and
 - Positive neutralizing antibody titers against Zika virus and dengue or other flaviviruses endemic to the region where exposure occurred or
 - Negative dengue virus IgM antibody test and no neutralizing antibody testing performed.

Confirmed: A neonate who meets the clinical criteria for congenital disease and meets one of the following laboratory criteria:

- Zika virus detection by culture, viral antigen or viral RNA in fetal tissue, umbilical cord blood or amniotic fluid or neonatal serum, CSF or urine collected within 2 days of birth or
- Positive Zika virus IgM antibody test of umbilical cord blood, neonatal serum or CSF collected within 2 days of birth with positive Zika virus neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred.

ZIKA VIRUS DISEASE, NON-CONGENITAL

Clinical Criteria

A person with one or more of the following not explained by another etiology:

- Clinically compatible illness that includes
 - Acute onset of fever (measured or reported),
 - Maculopapular rash,
 - Arthralgia or
 - Conjunctivitis.
- Complication of pregnancy
 - Fetal loss or
 - Fetus or neonate with congenital microcephaly, congenital intracranial calcifications, other structural brain or eye abnormalities or other congenital CNS-related abnormalities including defects such as clubfoot or multiple joint contractures.
- Guillain-Barré syndrome or other neurologic manifestations.

Case Classification

Probable: A person who meets the clinical criteria for non-congenital disease and has an epidemiologic linkage and has laboratory evidence of recent Zika virus or flavivirus infection by:

- Positive Zika virus IgM antibody test of serum or CSF with
 - Positive neutralizing antibody titers against Zika virus and dengue or other flaviviruses endemic to the region where exposure occurred or
 - Negative dengue virus IgM antibody test and no neutralizing antibody testing performed.

Confirmed: A person who meets the clinical criteria for non-congenital disease and has laboratory evidence of recent Zika virus infection by:

- Detection of Zika virus by culture, viral antigen or viral RNA in serum, CSF, tissue or other specimen (e.g., amniotic fluid, urine, semen, saliva) or
- Positive Zika virus IgM antibody test of serum or CSF with positive Zika virus neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred.

ZIKA VIRUS INFECTION, CONGENITAL

Case Classification

Probable: A neonate who does not meet the clinical criteria for a congenital disease case but the neonate's mother has an epidemiologic linkage or meets laboratory criteria for a recent Zika virus or flavivirus infection and the neonate has laboratory evidence of Zika virus or flavivirus infection by:

- Positive Zika virus IgM antibody test of serum or CSF collected within 2 days of birth and
 - Negative dengue IgM antibody test and no neutralizing antibody testing performed or
 - Positive neutralizing antibody titers against Zika virus and dengue or other flaviviruses endemic to the region where exposure occurred.

Confirmed: A neonate who does not meet the clinical criteria for a congenital case but the neonate has laboratory evidence of recent Zika virus or flavivirus infection by:

- Zika virus detection by culture, viral antigen or viral RNA in fetal tissue, umbilical cord blood or amniotic fluid or neonatal serum, CSF or urine collected within 2 days of birth or

- Positive Zika virus IgM antibody test of umbilical cord blood, neonatal serum or CSF collected within 2 days of birth with positive Zika virus neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred.

ZIKA VIRUS INFECTION, NON-CONGENITAL

Case Classification

Probable: A person who does not meet the clinical criteria for non-congenital disease but has an epidemiologic linkage and has laboratory evidence of recent Zika virus infection by:

- Positive Zika virus IgM antibody test of serum or CSF with
 - Positive neutralizing antibody titers against Zika virus and dengue or other flaviviruses endemic to the region where exposure occurred or
 - Negative dengue IgM antibody test and no neutralizing antibody testing performed.

Confirmed: A person who does not meet the clinical criteria for non-congenital disease and has laboratory evidence of recent Zika virus infection by:

- Detection of Zika virus by culture, viral antigen or viral RNA in serum, CSF, tissue or other specimen (e.g., amniotic fluid, urine, semen, saliva) or
- Positive Zika virus IgM antibody test of serum or CSF with positive Zika virus neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred.

Comments

The Council of State and Territorial Epidemiologists (CSTE) approved position statement 16-ID-01 in June 2016 which modified the previous February 2016 interim case definitions and naming convention from "Zika virus, congenital infection" to "Zika virus disease, congenital" and from "Zika virus disease, non-congenital infection" to "Zika virus disease, non-congenital."

SIGNS AND SYMPTOMS

About 1 in 5 people infected with Zika virus will develop symptoms. Symptoms are usually mild and last for several days to a week and commonly include fever, a maculopapular rash, arthralgia or conjunctivitis. Other symptoms may include headache and myalgia.

Severe disease requiring hospitalization is uncommon and case fatality is low.

Complications are rare, but there have been cases of Guillain-Barré syndrome and other neurologic complications reported in patients following suspected Zika virus infection. Zika virus infection in pregnant women has been linked with adverse pregnancy outcomes and birth defects in infants.

DIAGNOSIS

Preliminary diagnosis is often based on a patient's clinical features, places and dates of travel (if patient is from a non-endemic country or area), activities and epidemiologic history of the location where infection likely occurred. In addition to the other more common causes of encephalitis and aseptic meningitis (e.g., herpes simplex virus and enteroviruses) and febrile illnesses, arboviruses such as chikungunya, dengue, Eastern equine encephalitis, Jamestown Canyon, LaCrosse, Powassan, St. Louis encephalitis, West Nile and Western equine encephalitis viruses should also be considered in the differential etiology.

Laboratory tests used for diagnosing Zika virus include viral culture, real-time reverse transcriptase-polymerase chain reaction (rRT-PCR), detection of IgM or IgG antibodies by enzyme-linked immunosorbent assay (ELISA) or immunofluorescence assay (IFA), plaque reduction neutralization test (PRNT) and immunohistochemical staining (IHC). The optimal timing for Zika virus assays are:

- Viral culture: ≤ 3 days after illness onset or last exposure date (for asymptomatic patients)
- rRT-PCR: ≤ 7 days after illness onset or last exposure date (for asymptomatic patients)
- IgM antibody tests: ≥ 4 days after illness onset or last exposure date (for asymptomatic patients)

IgM antibodies may be detectable ≥ 4 days after illness onset and can persist for months. Serum collected within 8 days of illness onset may not have detectable IgM antibodies, and testing should be repeated on a convalescent-phase sample collected 2-3 weeks after the acute-phase sample. Urine and whole blood specimens can be tested by rRT-PCR when collected within 14 days of symptom onset, although a matching serum specimen for the patient should also be collected and tested. Testing for asymptomatic males and non-pregnant females is currently not recommended by the CDC.

Currently, there are a few commercial laboratories in the United States that perform diagnostic Zika virus testing; the CDC's Arbovirus Diagnostic Laboratory and some state public health laboratories have capacity to test for this virus. Specimens are usually blood or serum, but for cases with neuroinvasive disease, cerebrospinal fluid (CSF) may also be obtained. Birth products and fetal tissues such as placental tissue, cord blood or other autopsy tissues can be tested for infants and fetuses with suspected Zika virus infection. Other body fluids such as saliva, urine, semen and amniotic fluid may also be requested for testing.

For clinical samples being sent to ODH Laboratory, the [ODH Microbiology Specimen Submission Form](#) and the [ODH Mosquito-borne Illness Case Investigation Form](#) must accompany the specimens. Be sure the date of illness onset, list of symptoms compatible with Zika virus disease, pregnancy status and gestational age (for females), other relevant epidemiologic information and travel history for the case is completed.

For clinical samples being sent to CDC's Arbovirus Diagnostic Laboratory for testing, the [CDC Specimen Submission Form](#) must also accompany the samples. Be sure the date of illness onset, symptoms compatible with Zika virus disease, pregnancy status and gestational age (for females), other relevant epidemiologic information and travel history for the case are completed. Use test order code CDC-10282 for arbovirus serology. Please contact ODH at (614) 995-9955 to arrange for testing at CDC.

EPIDEMIOLOGY

Source

Humans serve as the primary Zika virus reservoir during epidemic periods. *Aedes aegypti* mosquitoes serve as the principal vector for Zika virus, and are widely distributed throughout the tropics. Given the vectors' distribution throughout the Americas, the entire region is susceptible to the invasion and spread of Zika virus. The *Ae. aegypti* mosquito is not known to be established in Ohio. However, *Aedes albopictus*, the Asian tiger mosquito, is established in Ohio and could potentially transmit Zika virus, although it has not yet been implicated in the transmission of human cases.

Susceptibility

All individuals not previously infected with Zika virus (naïve individuals) are at risk for infection and developing disease. Zika virus infection is thought to confer long-lasting immunity. Persons at risk for severe disease may include neonates and fetuses exposed in utero. There is also concern for Guillain-Barré syndrome following Zika virus infection; the risk for Guillain-Barré syndrome increases with increasing age.

Occurrence

Zika virus was first isolated from a monkey in 1947 in the Zika Forest of Uganda and had mostly remained in Africa, causing some small and sporadic outbreaks in Asia. In 2007, a large outbreak occurred in the Micronesian state of Yap, where 75% of the population was infected. Another large outbreak occurred in French Polynesia during 2013-2014 where there were an estimated 32,000 cases. In May 2015, local transmission of Zika virus in northeastern Brazil was reported. Since then, the virus has spread to most of the countries and territories in the Caribbean, Central America and South America. Zika virus is considered endemic in some countries in Africa, the Pacific Islands and Asia; however, the risk to travelers in these endemic areas is likely lower than it is in countries experiencing active Zika virus transmission.

Mode of Transmission

Zika virus is spread by the bite of an infected mosquito. The yellow fever mosquito, *Aedes aegypti*, is the principal vector and is not known to be established in Ohio. However, the Asian tiger mosquito, *Aedes albopictus*, is established in many Ohio counties and may serve as a potential vector. These mosquitoes become infected when they feed on a person infected with Zika virus. Infected mosquitoes can then spread the virus to other humans when they bite. While most cases are due to vector-borne transmission from an infected mosquito, vertical transmission from mother to child, blood-borne, sexual and laboratory exposure transmission have also been documented. These exposures indicate that direct contact transmission can occur. Although Zika virus has been detected in breast milk, there is no evidence that the virus has been transmitted through breastfeeding. Transmission from organ or tissue donation may be theoretically possible.

Period of Communicability

Zika virus is communicable in blood during the acute illness for a week after illness onset, as long as viremia is present. It is believed that the virus can persist longer in the semen and genital fluids of infected persons than the blood, although the exact length of time an infected person could transmit Zika virus to his/her partner is currently unknown.

Incubation Period

The incubation period is currently unknown, but is likely to range from 3 days to 2 weeks.

PUBLIC HEALTH MANAGEMENT

Case

Investigation

With serologic identification of Zika virus infection, a complete travel history for the two weeks prior to onset should be obtained. The patient should also be questioned about donating or receiving blood, blood products and organs in the 4 weeks prior to onset of symptoms. Sexual contact with partners who traveled or resided in areas with Zika virus transmission should also be asked as well as the partners' symptom status. Female patients should be asked whether they were pregnant at the time of infection, and infants should be checked whether they were breastfed before illness onset. Sites of

outdoor exposure and activities can be evaluated for the presence of *Aedes* mosquitoes by standard collection techniques (BG sentinel traps, light traps, larval samples) during mosquito season.

Organ, Tissue or Blood Donors or Recipients

If the patient is a recent organ, tissue or blood donor or recipient, notify the blood or tissue banks and ensure remaining co-component blood or tissue products are quarantined. Working with the blood or tissue bank, identify other possibly exposed patients, and notify ODH. ODH will notify CDC about the potential for transfusion or transplant transmission.

Treatment

There is no specific antiviral drug treatment for Zika virus. Symptomatic treatment is recommended after excluding more serious conditions like malaria, dengue and bacterial infections. Joint pain may benefit from the use of non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids or physiotherapy, but this should be used only after dengue has been ruled out.

Isolation and Follow-up Specimens

Although no specific isolation procedures are in place, acutely infected persons should avoid being bitten by *Aedes* mosquitoes 3 weeks after illness onset, in order to prevent further transmission of the virus. All travelers returning from areas with active Zika virus transmission should avoid mosquito exposures for 3 weeks after return. A convalescent sample 2-4 weeks after the acute may be required to confirm a case.

Public Health Significance

High in endemic areas. Identification of a locally acquired case of Zika virus in Ohio warrants a vector investigation and vector control strategies to prevent an outbreak.

Contacts

No treatment or prophylaxis of contacts is indicated.

Sexual Contacts

Testing of asymptomatic sexual contacts of women who are pregnant or trying to become pregnant who traveled to an area with active Zika virus transmission is not recommended. However, sexual contacts of pregnant women who traveled to or resided in an area with active Zika virus transmission should be advised to either abstain or use condoms consistently and correctly during sex for the duration of the pregnancy. Sexual contacts of confirmed or probable Zika virus cases should be assessed for symptoms compatible with Zika virus infection and offered testing if symptoms occurred within 2 weeks from the last sexual encounter with the confirmed or probable case. Confirmed and probable cases of Zika virus infection should be advised to either abstain or consistently and correctly use condoms during sex; for men the length of time is 6 months, for women it is 8 weeks. Couples who potentially were exposed to Zika virus but did not have symptoms and who wish to become pregnant are advised to wait 8 weeks after her last possible exposure date before trying to conceive if only a female partner traveled or 6 months after his last possible exposure date before trying to conceive if a male partner traveled.

For women who are undergoing fertility treatment, the CDC recommends following testing and timing recommendations as described above. Zika virus transmission through assisted reproductive technology has not been reported; however, transmission through gametes or embryos is theoretically possible.

Prevention and Control

Vaccination

There is no vaccine or preventive drug currently available.

Travelers

Travelers entering endemic areas should be warned to avoid mosquitoes, use mosquito repellents, occupy screened quarters and use mosquito netting over beds.

Vector Investigation

All travelers returning from areas with active Zika virus transmission are advised to avoid being bitten by mosquitoes for three weeks after return from travel in order to prevent further transmission of the virus if they were infected. Depending on local resources, environmental assessments around the homes of suspected viremic cases for *Aedes* mosquitoes may be useful to determine the risk for local transmission of Zika virus. Those jurisdictions with capacity should consider:

- Adult mosquito control:
 - *Ae. albopictus* (and *Ae. aegypti*) are most active during the day and are not effectively controlled by standard ultra-low volume (ULV) applications. Early morning or late evening applications are recommended.
 - Focus ULV or barrier applications to the areas where human cases are present to reduce local transmission.
- Larval mosquito control:
 - Remove larval habitats.
 - Encourage the public to participate in efforts by discarding materials or closing containers (e.g., flower pots, buckets, tires, garbage cans).

Mosquito Bite Avoidance

The best way to prevent Zika virus infection is to avoid mosquito bites. Prevention tips are similar to those for other viral diseases transmitted by mosquitoes, such as dengue or West Nile virus:

- Use insect repellent [registered with the U.S. Environmental Protection Agency \(EPA\)](#) on exposed skin. Always follow the directions on the package. When using both sunscreen and insect repellent, apply the sunscreen first then the repellent. EPA-registered repellents are safe to use during pregnancy.
- Wear long sleeves, pants and socks if feasible.
- Wear permethrin-treated clothing to repel and kill mosquitoes.
- Use screens on windows and doors to exclude mosquitoes. And, when available, air conditioning can make households less hospitable to mosquitoes.
- Participation in community and homeowner based vector control strategies:
 - Ensure that water does not collect in containers around the home and community by emptying water from containers such as flowerpots, buckets, barrels and tires. Change the water in pet dishes, and replace the water in bird baths weekly. Drill holes in tire swings so water drains out. Empty children's wading pools and store on their sides after use.
 - Use chemical or biological control of larvae and adult mosquitoes when necessary.

Preventing Sexual Transmission

Pregnant couples in which one or both partners live in or traveled to an area with Zika virus transmission should:

- Use condoms from start to finish every time they have sex or do not have sex during the pregnancy. This is important, even if the pregnant woman's partner does not have symptoms of Zika virus disease or feel sick.
- Not share sex toys during the pregnancy.

People with a partner who traveled to an area with Zika virus transmission can use condoms or not have sex. The period of time for taking these precautions depends on whether the traveler is male or female:

- If the traveler is female: Use condoms or do not have sex for at least 8 weeks after her return from an area with active Zika virus transmission (if she doesn't have symptoms) or for at least 8 weeks from the start of her symptoms (or Zika virus diagnosis) if she develops Zika virus disease.
- If the traveler is male: Use condoms or do not have sex for at least 6 months after his return from an area with active Zika virus transmission (if he doesn't have symptoms) or for at least 6 months from the start of his symptoms (or Zika virus diagnosis) if he develops Zika virus disease. This extended period is because Zika virus stays in semen longer than in other body fluids.

Prevention Resources

- [ODH Zika Fact Sheet \(Spanish\)](#)
- [ODH Mosquito Bite Protection Fact Sheet](#)
- [ODH Zika Information](#)
- [CDC Zika Information](#)
- [Pan-American Health Organization Zika Information](#)
- [World Health Organization Zika Information](#)