Wisconsin Department of Health Services
Division of Public Health
P-02066 (01/2018)

Communicable Disease Case Reporting and Investigation Protocol

ZIKA VIRUS INFECTION

I. IDENTIFICATION AND DEFINITION OF CASES

A. **Clinical Description:** Zika virus (ZIKV) is an arbovirus closely related to dengue, yellow fever, Japanese encephalitis, and West Nile viruses. ZIKV infection may be asymptomatic or result in acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis. Other common symptoms include headache, myalgia, and photophobia. In adults, ZIKV infection has been associated with Guillan-Barré Syndrome. ZIKV is primarily transmitted by the bite of an infected *Aedes* species mosquito, but also through sexual contact, blood transfusion, organ transplantation, laboratory exposure, and from a mother to her fetus through transplacental transmission. Congenital ZIKV infection can lead to congenital Zika virus syndrome, a pattern of birth defects described by severe microcephaly, other neurological abnormalities such as intracranial calcifications, brain atrophy and asymmetry, ocular abnormalities, joint contractures, and hypertonia.

Clinical criteria for diagnosis: Since there is no difference in the risk of ZIKV-associated birth defects among asymptomatic and symptomatic ZIKV infections during pregnancy, asymptomatic infection is epidemiologically significant. ZIKV infections are divided up into the following four clinical subgroups:

- **Zika virus disease, congenital**: Liveborn infant with congenital microcephaly, or intracranial calcifications, or 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, lymphocytic choriomeningitis virus, and herpes simplex virus should be considered. An assessment of potential genetic and other teratogenic causes of the congenital anomalies should also be performed.)
- **Zika virus disease, non-congenital**: 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 such as fetal loss or fetus or neonate with birth defect consistent with congenital Zika virus syndrome.
  - Guillain-Barré syndrome or other neurological manifestations.
- **Zika virus infection, congenital**: An infant who is asymptomatic (i.e., does not meet the clinical criteria for a congenital disease case).
- **Zika virus infection, non-congenital**: A person who is asymptomatic (i.e., does not meet the clinical criteria for a non-congenital disease case).

B. **Laboratory Criteria:**

- Confirmatory **congenital** laboratory evidence:
  - ZIKV detection by culture, viral antigen, or viral RNA in fetal tissue or amniotic fluid; or neonatal serum, CSF, or urine collected within two days of birth; OR
  - Positive ZIKV immunoglobulin M (IgM) antibody test of neonatal serum or CSF collected within two days of birth WITH positive ZIKV neutralizing antibody titers and negative neutralizing titers against dengue or other flaviviruses endemic to the region where exposure occurred.
- Supportive **congenital** laboratory evidence: Positive ZIKV IgM antibody test of neonatal serum or CSF collected within two days of birth, AND
  - Positive neutralizing antibody titers against ZIKV 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.
- Confirmatory **non-congenital** laboratory evidence:
  - ZIKV detection by culture, viral antigen, or viral RNA in serum, CSF, urine, tissue, or amniotic fluid; OR

- Positive ZIKV IgM antibody test of serum or CSF WITH positive ZIKV neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred.
- Supportive **non-congenital** laboratory evidence: Positive ZIKV IgM antibody test of serum or CSF, AND
  - Positive neutralizing antibody titers against ZIKV 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.

Note: Fee-exempt ZIKV testing is available at the Wisconsin State Laboratory of Hygiene (WSLH) for qualifying patients. All requests for fee-exempt ZIKV testing must be approved by a Wisconsin Division of Public Health epidemiologist prior to specimen submission to WSLH. Updated information on who meets fee-exempt ZIKV testing criteria can be found here (www.dhs.wisconsin.gov/zika/lab-testing.htm).

Positive results from a single ZIKV serologic test can be misleading because serologic cross-reactivity often occurs between closely related arboviruses (e.g., Zika, dengue, Japanese encephalitis, yellow fever viruses). It is, therefore, critical that plaque reduction neutralization testing (PRNT) be performed on any ZIKV IgM positive specimen to confirm a ZIKV infection. ZIKV IgM positive specimens at WSLH are automatically sent to CDC for PRNT confirmation.

ZIKV transmission can vary according to geographic location, local climatic conditions, and sexual behaviors, and in some patients, ZIKV-specific IgM antibody can be detectable more than 12 weeks following infection. Therefore, the importance of a recent travel history, possible sexual exposures, and thorough serologic testing cannot be overemphasized. Immunoglobulin G (IgG) antibody can likely be detected throughout a person's lifetime after an infection. Thus, a positive IgG and a negative IgM may indicate previous ZIKV infection at some point in time.

C. **Wisconsin Surveillance Case Definition:**
- **Confirmed/Probable congenital disease**: A neonate who meets the above clinical criteria for congenital disease **AND** meets at least one of the above confirmed/supportive laboratory criteria, **AND** whose mother has an epidemiological link (i.e., reported travel to a ZIKV-affected area and/or sexual contact with a traveler to a ZIKV-affected area) or meets laboratory criteria for a recent ZIKV or flavivirus infection.
- **Confirmed/Probable non-congenital disease**: A case that meets one of the above clinical criteria for non-congenital disease **AND** meets at least one of the above confirmed/supportive laboratory criteria, **AND** has an epidemiological link (i.e., reported travel to a ZIKV-affected area and/or sexual contact with a traveler to a ZIKV-affected area).
- **Confirmed/Probable congenital infection**: An infant who is asymptomatic **AND** meets at least one of the above confirmed/supportive laboratory criteria, **AND** whose mother has an epidemiological link (i.e., reported travel to a ZIKV-affected area and/or sexual contact with a traveler to a ZIKV-affected area) or meets laboratory criteria for a recent ZIKV or flavivirus infection.
- **Confirmed/Probable non-congenital infection**: A case that is asymptomatic **AND** meets at least one of the above confirmed/supportive laboratory criteria, **AND** has an epidemiological link (i.e., reported travel to a ZIKV-affected area and/or sexual contact with a traveler to a ZIKV-affected area).
- **Suspect**: A case that meets one of the above clinical criteria for diagnosis, OR has an epidemiological link or whose mother has an epidemiological link. (i.e., reported travel to a ZIKV-affected area and/or sexual contact with a traveler to a ZIKV-affected area).

II. REPORTING

A. **Wisconsin Disease Surveillance Category II – Methods for Reporting:** This disease shall be reported to the patient's local health officer or to the local health officer's designee within 72 hours of recognition of a case or suspected case, per Wis. Admin. Code § DHS 145.04 (3) (b). Report electronically through the Wisconsin Electronic Disease Surveillance System (WEDSS), or mail or fax a completed Acute and Communicable Disease Case Report (F-44151) to the address on the form.

B. **Responsibility for Reporting**: According to Wis. Admin. Code § DHS 145.04(1), persons licensed under Wis. Stat. ch. 441 or 448, laboratories, health care facilities, teachers, principals, or nurses serving a school or day care center, and any person who knows or suspects that a person has a communicable disease identified in Appendix A.

C. **Clinical Criteria for Reporting:** Clinically compatible illness for either congenital or non-congenital disease.

D. **Laboratory Criteria for Reporting:** Laboratory evidence of infection by detection of ZIKV-specific IgM, ZIKV-specific IgG, ZIKV-specific ribonucleic acid sequence by polymerase chain reaction (PCR) in clinical specimens, isolation of ZIKV in cell culture, or detection of specific Zika viral antigen by immunohistochemistry.

III. CASE INVESTIGATION

A. **Responsibility for case investigation**: It is the responsibility of the local health department (LHD) to investigate or arrange for investigation of suspected or confirmed cases as soon as is reasonably possible. A case investigation may include information collected by phone, in person, in writing, or through review of medical records or communicable disease report forms, as necessary and appropriate.

B. **Required Documentation:**
1. Complete the WEDSS disease incident investigation report, including appropriate, disease-specific tabs. This may be facilitated by completing an Arbovirus Infection Follow-up form.
2. Upon completion of investigation, set WEDSS disease incident process status to "Sent to State."

C. **Additional Investigation Responsibilities**
1. Obtain detailed travel history and vaccination history against related viruses (i.e., yellow fever or Japanese encephalitis vaccines).
2. Determine if the patient has had a previous arboviral illness diagnosis and, if so, the month and year when this illness occurred.
3. If investigating a possible congenital case, collect contact information for the infant's primary care provider and enter this information into the notes section in WEDSS for the purpose of infant follow-up.

IV. PUBLIC HEALTH INTERVENTIONS AND PREVENTION MEASURES

A. In accordance with Wis. Admin. Code § DHS 145.05, local public health agencies should follow the methods of control recommended in the current editions of *Control of Communicable Diseases Manual*, edited by David L. Heymann, published by the American Public Health Association, and the American Academy of Pediatrics' *Red Book: Report of the Committee on Infectious Diseases*, unless otherwise specified by the state epidemiologist.

B. To prevent ZIKV infection during pregnancy, women and couples trying to conceive should be advised to avoid travel to areas with a risk of ZIKV transmission. For updated information on countries with a risk of ZIKV transmission, visit the CDC's Zika website https://wwwnc.cdc.gov/travel/page/zika-information or the World Health Organization's Zika website http://www.who.int/emergencies/zika-virus/classification-tables/en/.

C. After a possible ZIKV exposure, educate the patient on preventing further ZIKV transmission. Persons with a possible ZIKV exposure should:
1. Avoid mosquito bites for three weeks after illness onset or after last possible exposure (if asymptomatic). In persons who were recently infected with ZIKV, mosquito avoidance is critical to prevent the introduction of ZIKV to local mosquito populations in Wisconsin. Mosquito bite prevention can be achieved through the use of an Environmental Protection Agency-registered repellent on exposed skin, the use of permethrin on clothing, staying indoors, excluding mosquitoes from dwellings by installing window and door screens in good repair, and the use of air conditioning.
2. Abstain from sexual contact (vaginal, oral, or anal) or use condoms during sex (vaginal, oral, or anal) to avoid sexual transmission to any partners. Women should avoid unprotected sex for at least eight weeks after illness onset or after last possible exposure (if asymptomatic). Men should avoid unprotected sex for at least six months after illness onset or after last possible exposure (if asymptomatic). Men who have a partner who is pregnant should abstain or use condoms for the entire duration of the pregnancy.
3. Delay conception for at least eight weeks if only the woman has a possible exposure, or for at least six months if a male partner has a possible exposure to avoid ZIKV transmission to a fetus.

V. CONTACTS FOR CONSULTATION

A. Local health departments and tribal health agencies: https://www.dhs.wisconsin.gov/lh-depts/index.htm

B. Bureau of Communicable Diseases, Communicable Diseases Epidemiology Section: 608-267-9003

C. Wisconsin State Laboratory of Hygiene: 1-800-862-1013

VI. RELATED REFERENCES

A. Heymann DL, ed. Arthropod-Borne Viral Diseases In: *Control of Communicable Diseases Manual*. 20th ed. Washington, DC: American Public Health Association, 2015: 26-42.

B. Pickering LK, ed. Arbovirus Infections In: *Red Book*: *2015 Report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2015: 240-246.

C. Centers for Disease Control and Prevention, Zika virus website: https://www.cdc.gov/zika/.

D. Centers for Disease Control and Prevention, Morbidity and Mortality Weekly Zika Reports: https://www.cdc.gov/mmwr/zika_reports.html.