Zika Virus Disease and Zika Virus Infection 2016 Case Definition, Approved June 2016

CSTE Position Statement(s)

- 16-ID-01

Subtype(s)

- Zika virus disease, congenital
- Zika virus disease, non-congenital
- Zika virus infection, congenital
- Zika virus infection, non-congenital

Background

Zika virus (ZIKV), a flavivirus transmitted by *Aedes* species mosquitoes, was first identified in the Zika Forest by the Virus Research Institute in Uganda in a non-human primate in 1947 and from *Aedes africanus* mosquitoes in 1948. Before 2007, there had been only 14 human ZIKV disease cases documented. In 2007, an outbreak of ZIKV disease occurred on Yap Island, Federated States of Micronesia and the ensuing investigation included the first population-based epidemiological study of ZIKV infection and disease. It was estimated that 75% (attack rate) of the island's inhabitants were infected with ZIKV resulting in 18% symptomatic and 82% asymptomatic infections. The most common symptoms documented in this outbreak were maculopapular rash, fever, arthralgia, and conjunctivitis. From 2013 to 2014 there was a large outbreak in French Polynesia where *Aedes aegypti* was considered the most important vector. There continues to be ongoing transmission in the Pacific Islands.

Due to the rapidly evolving epidemic of Zika virus infection, the Council of State and Territorial Epidemiologists (CSTE) Executive Board developed an interim position statement to establish standardized case definitions for Zika virus disease and ZIKV congenital infection dated February 26, 2016, and to add these conditions to the Nationally Notifiable Diseases List. As laboratory testing for ZIKV has been more widely performed, limitations of the interpretation of serologic test results,

including plaque reduction neutralization testing have been recognized, necessitating revisions to the laboratory criteria of the case definitions. Additionally, numerous asymptomatic persons, particularly pregnant women are tested for ZIKV infection and will meet laboratory criteria for infection. Because asymptomatic infection might be epidemiologically significant, revisions to the interim surveillance case definitions are proposed to include ZIKV infections without disease. Public health jurisdictions are encouraged to evaluate, report, and monitor identified ZIKV infections, particularly in pregnant women, that don't meet the clinical criteria of the confirmed and probable congenital and non-congenital disease case classifications.

Laboratory Criteria for Diagnosis

Recent ZIKV infection

- Culture of ZIKV from blood, body fluid, or tissue; **OR**
- Detection of ZIKV antigen or viral ribonucleic acid (RNA) in serum, cerebrospinal fluid (CSF),

  placenta, umbilical cord, fetal tissue, or other specimen (e.g., amniotic fluid, urine, semen, saliva), **OR**

- Positive ZIKV immunoglobulin M (IgM) antibody test in 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

Recent flavivirus infection, possible ZIKV

- Positive ZIKV IgM antibody test of serum or CSF with positive neutralizing antibody titers against ZIKV and dengue virus or other flaviviruses endemic to the region where exposure occurred
- Positive ZIKV 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 ZIKV transmission; **OR**
- Sexual contact with a confirmed or probable case within the infection transmission risk window of ZIKV infection or person with recent travel to an area with known ZIKV 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 vectorborne transmission

Subtype(s) Case Definition Collapse all

Zika virus disease, congenital

Clinical Criteria

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

(As part of the complete evaluation of congenital microcephaly or other central nervous system [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 anomalies should also be performed.)

Case Classification

Probable

A neonate meets clinical criteria for congenital disease; **AND**
The neonate's mother has an epidemiologic linkage or meets laboratory criteria for recent ZIKV or flavivirus infection; **AND**
The neonate has laboratory evidence of ZIKV or flavivirus infection by:

- Positive ZIKV IgM antibody test of serum or CSF collected within 2 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.

Confirmed

A neonate meets the clinical criteria for congenital disease **AND** meets one of the following laboratory criteria:

- ZIKV 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 ZIKV IgM antibody test of umbilical cord blood, neonatal serum or CSF collected within 2 days of birth **with** positive ZIKV 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), **OR**
  - maculopapular rash, **OR**
  - 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 central nervous system-related abnormalities including defects such as clubfoot or multiple joint contractures
- Guillain-Barré syndrome or other neurologic manifestations

Case Classification

Probable

Meets clinical criteria for non-congenital disease; **AND**
Has an epidemiologic linkage; **AND**
Has laboratory evidence of recent ZIKV or flavivirus infection by:

- Positive ZIKV IgM antibody test of serum or CSF with:
  - 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.

Confirmed

Meets clinical criteria for non-congenital disease; **AND**
Has laboratory evidence of recent ZIKV infection by:

- Detection of ZIKV by culture, viral antigen or viral RNA in serum, CSF, tissue, or other specimen (e.g. amniotic fluid, urine, semen, saliva); **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.

Zika virus infection, congenital

Case Classification

Probable

A neonate who does not meet clinical criteria for a congenital disease case; **BUT**
The neonate's mother has an epidemiologic linkage or meets laboratory criteria for recent ZIKV or flavivirus infection; **AND**
The neonate has laboratory evidence of ZIKV or flavivirus infection by:

- Positive ZIKV 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 ZIKV and dengue or other flaviviruses endemic to the region where exposure occurred.

Confirmed

A neonate who does not meet clinical criteria for a congenital disease case; **BUT**
The neonate has laboratory evidence of recent ZIKV or flavivirus infection by:

- ZIKV 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 ZIKV IgM antibody test of umbilical cord blood, neonatal serum or CSF collected within 2 days of birth **with** positive ZIKV 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 clinical criteria for non-congenital disease; **BUT**
Has an epidemiologic linkage; **AND**
Has laboratory evidence of recent ZIKV infection by:

- Positive ZIKV IgM antibody test of serum or CSF with:
    - positive neutralizing antibody titers against ZIKV 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 clinical criteria for non-congenital disease; **AND**
Has laboratory evidence of recent ZIKV infection by:

- Detection of ZIKV by culture, viral antigen or viral RNA in serum, CSF, tissue, or other specimen (e.g. amniotic fluid, urine, semen, saliva); **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.

Comments

CSTE approved position statement 16-ID-01 in June 2016, which modified the previous February 2016 interim case definition 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".