Zika Virus Disease
North Carolina 2024 Case Definition

NOTE: A surveillance case definition is a set of uniform criteria used to define a disease for public health surveillance. Surveillance case definitions enable public health officials to classify and count cases consistently across reporting jurisdictions. Surveillance case definitions are not intended to be used by healthcare providers for making a clinical diagnosis or determining how to meet an individual patient's health needs.

CSTE Position Statement 23-ID-10

Subtype(s)

- Congenital Zika Virus Disease
- Non-congenital Zika Virus Disease

Background

Zika virus is a flavivirus that is primarily transmitted through the bite of an infected *Aedes* species mosquito. Intrauterine, perinatal, sexual, laboratory, and transfusion-associated transmission have also been reported.

Most people infected with Zika virus have asymptomatic infections or mild clinical disease characterized by acute onset of fever, maculopapular rash, arthralgia, and nonpurulent conjunctivitis. Other common symptoms can include myalgia, headache, edema, vomiting, retroorbital pain, or lymphadenopathy. Hospitalization and death are uncommon. Guillain-Barré syndrome, encephalopathy, meningoencephalitis, myelitis, uveitis, and severe thrombocytopenia rarely occur. Transmission of the virus to the unborn child during pregnancy can lead to congenital Zika virus infection and may cause serious birth defects of the brain and eyes, including severe microcephaly, intracranial calcifications, cerebral or cortical atrophy, chorioretinal abnormalities, and optic nerve abnormalities.

Development of surveillance case definitions for Zika virus infection and disease (16-ID-01) occurred in 2016 during a rapidly evolving Zika virus disease outbreak in the Western Hemisphere. Since that time, levels of Zika virus transmission in the Americas have declined considerably. The 23-ID-10 position statement revises the standardized case definition for Zika virus disease to address the changing epidemiology and current knowledge of the laboratory and clinical findings associated with Zika virus disease. It also removes non-congenital and congenital Zika virus infection without disease from the case definition, thus removing these subtypes from the Nationally Notifiable Conditions list.

Epidemiologic Linkage

- Resided in or traveled to an area with a risk* of Zika virus transmission in the 14 days before the onset of symptoms, in the 28 days before the onset of Guillain-Barré syndrome, or during pregnancy; **OR**
- Laboratory exposure to Zika virus before onset of symptoms or during pregnancy; **OR**
- Receipt of blood, blood products, organ transplant, or tissue transplant within 30 days of symptom onset or during pregnancy from a person who has either been diagnosed with Zika virus infection or returned from traveling to an area with risk of Zika virus transmission; **OR**
- Sexual contact, within 14 days of symptom onset or during pregnancy, with a person who in the last 90 days has either been diagnosed with Zika virus infection or has returned from traveling to an area with a risk of Zika virus transmission.

*Consult with CDC as needed for assistance with geographic risk determinations.

Criteria to Distinguish a New Case from an Existing Case

A person not previously enumerated as a case that meets the confirmed or probable case classification.

Note: Infection with Zika virus is expected to provide lifelong immunity. However, in persons who are severely immunocompromised, viral persistence following infection may occur, which can lead to persistent disease. Immunocompromised individuals may also be vulnerable to reinfection with Zika virus.

Congenital Zika Virus Disease

Clinical Criteria

†To meet the clinical criteria for congenital Zika virus disease, the liveborn infant must not have an identified genetic or other cause for the findings, including a positive test for another likely etiology††, and should have one or more of the following brain or eye anomalies or neurological sequelae specific for congenital Zika virus disease and typically identifiable in the neonatal period:

- Microcephaly (occipital frontal circumference >2 standard deviations below the mean for age and sex) at birth or postnatal onset,
- cortical hypoplasia or abnormal gyral patterns (polymicrogyria, lissencephaly, heterotopia),
- increased volume of cerebrospinal fluid (CSF) (hydrocephalus ex vacuo, unspecified hydrocephalus, ventriculomegaly) due to loss of brain parenchyma,
- intracranial calcifications (most commonly between the cortex and subcortex),
- congenital contractures of major joints (arthrogryposis) associated with structural brain anomalies,
- congenital paralysis of the diaphragm associated with structural brain anomalies,
- corpus callosum agenesis/hypoplasia,
- cerebellar hypoplasia,
- scarring of the macula with coarse deposits of pigment in the retina (focal retinal pigmentary mottling) **OR**
- other structural eye anomalies (microphthalmia, cataracts, chorioretinal atrophy, optic nerve hypoplasia).

†Clinical findings can be observed during prenatal or postnatal evaluations. Consult with CDC as needed for assistance with congenital Zika virus disease clinical determinations.

††**Other clinical considerations for congenital Zika virus disease**: Among congenital infections, cytomegalovirus infection has clinical findings most consistent with Zika virus infection and should be ruled out by diagnostic testing. While other infectious etiologies (e.g., rubella virus, varicella zoster virus, herpes simplex virus, lymphocytic choriomeningitis virus, Toxoplasma gondii, or Treponema pallidum) have clinical findings less consistent with congenital Zika virus disease, testing for these infections should be considered as part of the complete evaluation for congenital disease.

Laboratory Criteria

Confirmatory laboratory evidence:

- Detection of Zika virus, viral antigen, or viral RNA in infant CSF, blood, urine, or postmortem tissue‡ **OR**
- Detection of anti-Zika virus IgM antibodies in infant CSF or blood‡, with positive anti-Zika virus-specific neutralizing antibody titers.

Presumptive laboratory evidence:

- Detection of Zika virus, viral antigen, or viral RNA in amniotic fluid, placenta, umbilical cord, or cord blood‡; **OR**
- Detection of anti-Zika virus IgM antibodies in infant CSF or blood‡ with no neutralizing antibody testing performed.

Note: The categorical labels used here to stratify laboratory evidence are intended to support the standardization of case classifications for public health surveillance. The categorical labels should not be used to interpret the utility or validity of any laboratory test methodology.

‡To prevent misclassifying postnatal Zika virus infections as congenital cases, in Zika virus endemic areas specimens should be collected within 4 weeks after birth.

Case Classification

Probable

- Meets the clinical criteria for congenital Zika virus disease, **AND**
- Meets presumptive laboratory criteria for congenital Zika virus disease, **AND**
- Whose gestational parent meets:
  - epidemiologic linkage criteria, **OR**
  - confirmatory laboratory criteria for non-congenital Zika virus disease during this pregnancy.

Confirmed

- Meets the clinical criteria for congenital Zika virus disease, **AND**
- Meets confirmatory laboratory criteria for congenital Zika virus disease, **AND**
- Whose gestational parent meets:
  - epidemiologic linkage criteria, **OR**
  - confirmatory laboratory criteria for non-congenital Zika virus disease during this pregnancy.

Non-congenital Zika Virus Disease

Clinical Criteria

To meet the clinical criteria for non-congenital Zika virus disease, the person should have one or more of the following not explained by another etiology.

- Acute onset of one or more of the following symptoms: fever (measured or reported), generalized rash, arthralgia, or non-purulent conjunctivitis,
- Guillain-Barré syndrome,
- Loss of a fetus at greater or equal to 20 weeks gestation.

Laboratory Criteria

Confirmatory laboratory evidence:

- Detection of Zika virus, viral antigen, or viral RNA in a body fluid or tissue; **OR**

- Detection of anti-Zika virus IgM antibodies in blood or CSF, with positive Zika virus-specific neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred[§]

Presumptive laboratory evidence:

- Detection of anti-Zika virus IgM antibodies in blood or CSF with a negative anti-dengue virus IgM antibody test in the same specimen with no neutralizing antibody testing performed; **OR**
- Four-fold or greater rise in anti-Zika virus-specific neutralizing antibody titers in paired blood specimens; **OR**
- In the setting of a Zika virus outbreak[§§] with minimal circulation of other endemic flaviviruses, detection of anti-Zika virus IgM antibodies in blood or CSF.

Note: The categorical labels used here to stratify laboratory evidence are intended to support the standardization of case classifications for public health surveillance. The categorical labels should not be used to interpret the utility or validity of any laboratory test methodology.
[§]If Zika and dengue virus IgM antibodies are detected and neutralizing antibodies are unable to differentiate flaviviruses, consider reporting as Flavivirus disease, not otherwise specified (See ArboNET Surveillance Guide).
[§§]Consult with CDC as needed for assistance with outbreak status determinations.

Case Classification

Probable

- Meets the epidemiologic linkage criteria, and clinical and presumptive laboratory criteria for non-congenital Zika virus disease.

Confirmed

- Meets the epidemiologic linkage criteria, and clinical and confirmatory laboratory criteria for non-congenital Zika virus disease.