



Zika Virus

Disease Plan

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Last updated: December 5, 2019 by Dallin Peterson

Questions about this disease plan?

Contact the Utah Department of Health Bureau of Epidemiology: 801-538-6191.

✓ **CRITICAL CLINICIAN INFORMATION**

Clinical Evidence
<p>Signs/Symptoms</p> <ul style="list-style-type: none"> • Fever • Conjunctivitis • Maculopapular Rash • Arthralgia
<p>Period of Communicability</p> <ul style="list-style-type: none"> • Can be spread to unborn fetus transplacentally throughout the pregnancy. • Can be spread from man to sexual partner for up to 3 months in semen. • Can be spread from women to sexual partner for up to 2 months in vaginal fluids.
<p>Incubation Period</p> <ul style="list-style-type: none"> • The incubation period for Zika is usually 2–7 days.
<p>Mode of Transmission</p> <ul style="list-style-type: none"> • Primarily spread by mosquito, <i>Aedes aegypti</i> and <i>albopictus</i>. • Mother to infant, transplacentally. • Sexually including vaginal, anal, oral and through use of sexual toys.
Laboratory Testing
<p>Type of Lab Test/Timing of Specimen Collection</p> <ul style="list-style-type: none"> • Symptomatic pregnant women possibly exposed to Zika virus either sexually or by foreign travel should be tested by nucleic acid amplification test (NAAT) or also known as reverse transcription-polymerase chain reaction (RT-PCR) as soon as possible after symptom onset. • Symptomatic persons (pregnant and non-pregnant) should be tested for dengue. https://www.cdc.gov/dengue/healthcare-providers/testing/testing-guidance.html • Pregnant women who have a fetus with ultrasound findings consistent with congenital Zika, who currently live, have lived, or traveled to a Zika-affected area, should be tested by Zika virus NAAT or RT-PCR and IgM testing on maternal serum and NAAT or RT-PCR on maternal urine.
<p>Type of Specimens</p> <ul style="list-style-type: none"> • Serology – serum (red top tube or serum separator) at least 3 mL at 4°C if shipped within 24 hours, or frozen (-70°C) over 24 hours • RT-PCR – serum (red top tube or serum separator) and urine (sterile screw top vile) at least 1 mL 4°C if shipped within 24 hours, or frozen (-70°C) over 24 hours • Immunohistochemistry – formalin fixed or paraffin-embedded tissues at room temperature
Treatment Recommendations
<p>Type of Treatment</p> <ul style="list-style-type: none"> • No specific treatment only supportive care
<p>Prophylaxis</p> <ul style="list-style-type: none"> • None
Contact Management
<p>Isolation of Case</p> <ul style="list-style-type: none"> • None
<p>Quarantine of Contacts</p> <ul style="list-style-type: none"> • None
Infection Control Procedures
<ul style="list-style-type: none"> • Standard infection control procedures

✓ WHY IS ZIKA VIRUS IMPORTANT TO PUBLIC HEALTH?

Zika virus is primarily transmitted to humans through the bite of an infected *Aedes* species mosquito. Perinatal, *in utero*, sexual and transfusion transmission events have also been reported. Since 2016, reported cases of Zika virus in the Americas have declined, and are now outnumbered by dengue cases. However, due to areas of the world known to have endemic Zika virus transmission, travelers, especially pregnant women, should take necessary precautions to reduce the risk of infection. An association between maternal infection of Zika virus during pregnancy and microcephaly along with additional birth defects in infants has been confirmed. Other long-term health effects for infants born to Zika virus confirmed mothers have also been documented.

✓ DISEASE AND EPIDEMIOLOGY

Clinical Description

Zika is an acute, viral illness characterized by a sudden onset of fever with maculopapular rash, arthralgia (joint pain), or conjunctivitis (red eyes). Other commonly reported symptoms have included myalgia (muscle pain) and headache. Approximately 20% of people infected with Zika virus become symptomatic, and illness is usually mild, with symptoms lasting from 2–7 days. Hospitalization due to severe disease is uncommon. However, there have been reported cases of Guillain-Barré syndrome in patients following suspected Zika virus infection. Guillain-Barré is a rare disorder in which the immune system attacks part of the nervous system.

Causative Agent

The Zika virus is a mosquito-borne flavivirus that was first identified in Uganda in 1947.

Differential Diagnosis

Flavivirus infections such as dengue and yellow fever share similar vectors, geographic distribution, and symptomology as the Zika virus. Chikungunya virus is an alphavirus with similar transmission characteristics and geographic distribution. Laboratory evidence of viral infection is accomplished by testing serum to detect viral nucleic acid or virus-specific immunoglobulin M (IgM) and neutralizing antibodies. Serological cross-reactivity can occur so a positive result on an IgM ELISA test should be followed by confirmatory testing to detect viral nucleic acid or neutralizing antibodies. Because Zika IgM antibodies and neutralizing antibodies may persist for months to years following infection, detecting Zika IgM antibodies might not indicate a recent infection. Patients who have been immunized (e.g., received yellow fever or Japanese encephalitis vaccination) or infected with, another flavivirus (e.g., dengue, West Nile or St. Louis encephalitis virus) may have cross-reactive antibodies on IgM or neutralizing antibody assays.

Other differential diagnosis considerations based on symptoms include malaria, rubella, measles, parvovirus, adenovirus, enterovirus, leptospirosis, rickettsia and group A streptococcal infections.

Laboratory Identification

Testing Guidelines

Currently, diagnostic testing for Zika virus is recommended for symptomatic pregnant women, with a history of travel to an area with Zika virus transmission. At present, the Utah Public Health Laboratory (UPHL) performs the InBios Assay for Zika IgM serology test and Trioplex RT-PCR. Equivocal, inconclusive or positive test results must be sent to the CDC Laboratory in Fort Collins, CO, for confirmation.

Symptomatic pregnant patients

- Serum and urine from symptomatic pregnant woman should be collected as soon as possible after symptom onset. The maternal serum should be tested for dengue and Zika virus by NAAT or reverse transcription-polymerase chain reaction (RT-PCR) along with dengue IgM testing only.
 - If Zika NAAT or RT-PCR is positive on a single specimen, the Zika NAAT or RT-PCR should be repeated on a newly extracted RNA from the same specimen to rule out false-positive Zika NAAT or RT-PCR results. If the dengue NAAT or RT-PCR is positive, this provides evidence of a dengue infection, and no further testing is indicated.
 - If dengue IgM is positive, this is adequate evidence of dengue infection, and no further testing is indicated.
- Zika virus IgM testing is not recommended for symptomatic pregnant women due to the persistence of Zika IgM antibodies for months to years following infection along with the cross reactivity between dengue IgM and Zika IgM antibodies during serologic testing.

Asymptomatic pregnant patients

- Zika virus IgM antibody and RT-PCR or NAAT testing is not recommended for asymptomatic pregnant women with recent travel to an area with Zika virus transmission.

Symptomatic non-pregnant patients

- Symptomatic non-pregnant patients should be tested for dengue. (<https://www.cdc.gov/denque/testing>) Zika virus is not currently recommended for this group based on the current epidemiology of the viruses.

Asymptomatic non-pregnant patients

As per previous guidance, asymptomatic non-pregnant patients should NOT be tested for dengue or Zika viruses.

Congenital Zika virus infection in an infant

- Pregnant women who have a fetus with ultrasound findings consistent with congenital Zika, who currently live, have lived, or traveled to a Zika-affected area, should be tested by Zika virus NAAT or RT-PCR and IgM testing on maternal serum and NAAT or RT-PCR on maternal urine.
 - If Zika NAAT or RT-PCR is negative and the IgM is positive, confirmatory PRNT should be performed against Zika and dengue.

Bureau of Epidemiology approval is still required for the Triplex RT-PCR testing. The Bureau of Epidemiology, Utah Department of Health (UDOH) or local health department, must approve all testing requests prior to samples going to the CDC.

Specimen Collection and Shipping When Zika IgM Testing is Requested or RT-PCR is Approved by the UDOH

- Collect serum ($\geq 3\text{mL}$) in a large, red top tube.
- Refrigerate serum at 4°C, or maintain on ice for no longer than 24 hours.
- Samples collected and shipped with expected arrival the same day can be shipped on cold packs (4°C).
- If storage/transport will exceed 24 hours, serum should be frozen at -20°C or lower. These samples should be shipped on dry ice.
- Follow packaging and shipping instructions for Category B, Biological Substances.
- The UPHL requisition form will be sent to the provider or laboratory team and will accompany specimens on the respective courier. Samples submitted with incomplete information will experience delayed testing and reporting of results.
- For questions about filling out the forms or couriers, call Bureau of Epidemiology at 801-538-6191 or your local health department. Access the UPHL requisition form at http://health.utah.gov/epi/reporting/UPHL_ID_Test_Request_Form.pdf.
- UPHL will ship specimens to CDC on Monday, Tuesday, and Wednesday. Specimens received later in the week will not be shipped until the following week, and should be kept frozen over weekends.

Laboratory Tests

Assays for acute specimens

RT-PCR or NAAT should be performed on serum specimens collected as soon as possible after from last known exposure or symptom onset in symptomatic pregnant females with serum and urine specimens. Urine specimens should always be accompanied with a serum specimen.

Assays for convalescent specimens

Zika virus IgM serologic testing is not recommended for pregnant women (regardless of symptoms) and persons (regardless of symptoms) with recent travel to an area with Zika virus. This is due to the cross reactivity with dengue virus in serologic studies causing false positive results. Additionally, due to the persistence of Zika IgM antibodies for months to even years, positive Zika IgM antibody results are not indicative of acute infection of Zika virus. Pregnant patients with prenatal ultrasound findings with congenital Zika virus infection who live, have lived, or traveled to areas with a risk of Zika during her pregnancy should have Zika virus NAAT

and IgM testing performed on serum and NAAT on urine. Patients with positive Zika virus IgM results should have sample confirmed by testing for neutralizing antibodies. Plaque-reduction neutralization tests (PRNT) can be performed to measure virus-specific neutralizing antibodies, and may be able to discriminate between cross-reacting antibodies in primary flavivirus infections. However, elevation of neutralizing antibodies does not indicate acute infection.

Immunohistochemistry

Staining for viral antigens or RT-PCR on fixed tissues are not routinely recommended, but may be conducted upon consultation with UDOH staff.

Treatment

There are currently no specific treatments for Zika virus infections. Persons who think they have Zika should:

- Get plenty of rest.
- Drink fluids to prevent dehydration.
- Take medicine such as acetaminophen to relieve fever and pain. **DO NOT** take aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and naproxen. Aspirin and NSAIDs should be avoided until dengue can be ruled out to reduce the risk of hemorrhage (bleeding).
- If a person is taking medicine for another medical condition, he/she should talk to a healthcare provider before taking additional medicine.

Case Fatality

Death due to Zika virus is very rare at all ages.

Reservoir

Zika virus is spread to people primarily through the bite of an infected *Aedes* species mosquito. The virus replicates in the midgut of the mosquito, disseminates to other tissues, and infects the salivary glands. *Aedes* mosquitoes are found in warmer, tropical and subtropical climates and at altitudes below 6,500 feet (2000 meters).

Transmission

Zika virus is spread to humans primarily through the bite of an infected *Aedes aegypti* or *Aedes albopictus* mosquito. During the first week of infection, the Zika virus can be found in the blood and passed from an infected person to another mosquito through mosquito bites. An infected mosquito can then spread the virus to other people. These mosquitoes have not been identified in Utah, although they appear to be expanding their range due to climate change.

Other documented modes of transmission include intrauterine, resulting in congenital infection; intrapartum, from a viremic mother to her newborn; through blood transfusions or accidental laboratory exposure; and through sexual transmission from both a man and a woman to their partner(s).

Zika virus can be spread before, during, and after the individual have symptoms. The virus can be present in sexual fluids longer than in blood and on average remains in semen for three months. Although rare, the virus has been detected in semen as long as 370 days. On average, virus has been shown in vaginal fluids up to two months. Current recommendation for persons wanting to get pregnant is for men to wait for at least three months and women to wait for at least two months after symptom onset of last possible Zika exposure before engaging in unprotected sex.

Among 1,450 children of mothers with laboratory evidence of Zika virus infection during pregnancy reported to the U.S. Zika Pregnancy Registry, 1 in 7 infants had one or more recognized health problems possibly caused by Zika. Continued studies are underway to investigate the association of Zika virus infection and microcephaly, including the role of other contributing factors (e.g., prior or concurrent infection with other organisms, nutrition and environment). To date, there are no reports of infants getting Zika virus through breastfeeding. Because of the benefits of breastfeeding, mothers are encouraged to breastfeed, even in areas where Zika virus is present.

Susceptibility

Anyone living in, or traveling to, an area where Zika virus is found can be infected with Zika virus. Currently, the CDC has cautioned pregnant women in any trimester to postpone travel to areas where Zika virus transmission is ongoing. Pregnant women who do travel to any of these areas should consult with their healthcare provider and strictly follow steps to avoid mosquito bites during their trip. Women who are trying or thinking about becoming pregnant should consult their healthcare provider before traveling to any of these locations, and strictly follow steps to prevent mosquito bites during their trip. For up-to-date information on travel notices, see <http://wwwnc.cdc.gov/travel/page/zika-information>.

Incubation Period

The incubation period for Zika is usually 2–7 days.

Period of Communicability

After the onset of symptoms, Zika virus can be found in the blood of an ill person for about a week. The virus can be present in semen longer than in blood due to the fact the semen is shielded from the immune system. Viremia is expected to last approximately one week in the blood of patients with clinical illness. There is no evidence that a fetus conceived after Zika virus has cleared from the blood would be at risk for fetal infection. On average, Zika virus has been detected in semen for at least three months and in rare cases up to 370 days after symptom onset, and in vaginal and cervical fluids up to two months after symptoms. Current recommendations are as follows:

- Couples in which a man had confirmed Zika virus infection or clinical illness consistent with Zika virus disease should consider using condoms or abstaining from sex for at least three months after onset of illness.
- Couples in which a man traveled to an area with active Zika virus transmission but did not develop symptoms of Zika virus disease should consider using condoms or abstaining from sex for at least eight weeks or two months after departure from the area.

- Couples in which a woman had confirmed Zika virus infection or clinical illness consistent with Zika virus disease should consider using condoms or abstaining from sex for at least eight weeks or two months after onset of illness or last exposure.
- Couples in which a man resides in an area with active Zika virus transmission but has not developed symptoms of Zika virus disease might consider using condoms or abstaining from sex while active transmission persists.
- If the partner of a man suspected of having Zika virus is pregnant, the couple should either use prevention techniques during sex, such as condom use, or abstain from sex for the duration of the pregnancy.

Epidemiology

Zika virus is a mosquito-borne flavivirus that was first identified in Uganda in 1947. It is transmitted by the bite of an infected *Aedes aegypti* or *Aedes albopictus* mosquito (the same mosquitoes that transmit other arboviruses, such as dengue and chikungunya), which are found throughout much of the Americas and some regions of the United States. The virus caused sporadic human infections in Africa and Asia until 2007, when the first documented Zika virus outbreak was reported in Yap State, Federated States of Micronesia. This outbreak is estimated to have impacted 73% of the population ≥ 3 years of age. In October 2013, a subsequent outbreak occurred in French Polynesia, where approximately 28,000 cases sought medical care (nearly 11% of the population). In May 2015, the first local transmission of Zika virus in the Americas was reported by the World Health Organization (WHO), with autochthonous cases identified in Brazil. The Ministry of Health estimated that 440,000-1,300,000 suspected cases of Zika virus disease occurred in Brazil by the end of 2015. As of January 20, 2016, according to the Pan American Health Organization, Puerto Rico and 20 other countries or territories in the Americas had reported locally transmitted cases.

During the outbreak in Brazil, Zika virus RNA was identified in specimens (i.e., brain tissue, placenta, and amniotic fluid) from several infants with microcephaly, and from fetal losses in women infected with Zika virus during pregnancy. The Brazil Ministry of Health reported a marked increase from previous years in the number of infants born with microcephaly and intracranial calcifications in 2015, although it is not known how many cases are due to Zika virus infection. The incidence of Zika virus infection in pregnant women is not currently known, and no evidence suggests that pregnant women are more susceptible to Zika virus infection, or experience more severe disease during pregnancy.

PUBLIC HEALTH CONTROL MEASURES

Public Health Responsibility

- Investigate all suspect cases of disease and fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- Identify clusters or outbreaks of disease.
- Identify sources of exposure and stop further transmission.

Prevention

There is no vaccine against Zika virus. The mosquitoes that spread the Zika virus are aggressive daytime biters, but they can also bite at night. They typically lay their eggs in or near standing water in things such as buckets, bowls, animal dishes, flower pots, old tires, and vases. When traveling to, or residing in, an area of ongoing transmission, the CDC recommends taking the following steps to avoid being bitten:

- Wear long-sleeved shirts and long pants.
- Choose a hotel or lodging with air conditioning, or that uses screens on windows and doors to keep mosquitoes outside.
- Sleep under a mosquito bed net.
- Treat clothing and gear with permethrin as described by product instructions, or purchase items treated with permethrin.
 - Do not use permethrin products directly on skin. These products are intended to treat clothing.
- Use Environmental Protection Agency (EPA) registered insect repellents with active ingredients which include:
 - DEET (N, N-diethyl-m-tolua-mide). Choose a product that will provide sufficient protection for the amount of time spent outdoors. Product labels often indicate the length of time that someone can expect protection from a product. DEET is considered safe when used according to the product label.
 - Picaridin (KBR 3023), or icaridin outside of the United States. Picaridin-containing products should be used according to the product label.
 - Oil of lemon eucalyptus (OLE) or PMD (para-menthane-3,8-diol). This recommendation only applies to EPA-registered products containing the active ingredient OLE or PMD. “Pure” oil of lemon eucalyptus (essential oil not formulated as a repellent) is NOT recommended, as validation testing for efficacy and safety has not gone through similar testing.
 - IR3535 (3-[N-butyl-N-acetyl]-aminopropionic acid).
- Always follow the product label instructions.
- Reapply insect repellent as directed.
- Do not spray repellent on the skin under clothing.
- If you are also using sunscreen, apply the sunscreen before applying insect repellent. Avoid using DEET products that combine the repellent with a sunscreen. Sunscreens may need to be reapplied often, resulting in an over-application of DEET.
- For babies and children:
 - Do not use insect repellent on children younger than two months of age.
 - Dress your children in clothing that covers arms and legs.
 - Cover crib, stroller, and baby carrier with mosquito netting.
 - Do not apply insect repellent onto a child’s hands, eyes, mouth, and cut or irritated skin.
 - Adults should spray repellent onto hands, and then apply to a child’s face.
- Wash hands after application to avoid accidental exposure to eyes, or ingestion.

The CDC has identified that Zika virus can also be spread by a man to his sex partner(s). Because of the potential link between Zika virus and birth defects, pregnant women should take steps to prevent infection:

- If you practice vaginal, anal, or oral sex with a male partner who lives in, or has traveled to, an area with Zika virus, use a condom the right way, every time, during your pregnancy.
- Don't have sex with your male partner during your pregnancy. Not having sex is the best way to be sure that someone does not get sexually transmitted Zika virus.
- Your male partner should also take steps to prevent mosquito bites to prevent further spread of the virus.

Men and their non-pregnant sex partners who want to reduce the risk for sexual transmission of Zika virus should use condoms consistently and correctly during sex or abstain from sex.

Recommended duration of consistent condom use or abstinence from sex depends on clinical illness consistent with Zika virus disease. These include:

- Couples in which a man had confirmed Zika virus infection or clinical illness consistent with Zika virus disease should consider using condoms or abstaining from sex for at least three months after onset of illness.
- Couples in which a man traveled to an area with active Zika virus transmission but did not develop symptoms of Zika virus disease should consider using condoms or abstaining from sex for at least eight weeks after departure from the area.
- Couples in which a woman had confirmed Zika virus infection or clinical illness consistent with Zika virus disease should consider using condoms or abstaining from sex for at least eight weeks after onset of illness or last exposure.
- Couples in which a man resides in an area with active Zika virus transmission but has not developed symptoms of Zika virus disease might consider using condoms or abstaining from sex while active transmission persists.
- If the partner of a man suspected of having Zika virus is pregnant, the couple should either use prevention techniques during sex, such as condom use, or abstain from sex for the duration of the pregnancy.

Chemoprophylaxis

None.

Vaccine

None.

Isolation and Quarantine Requirements

Isolation: None.

Hospital: None.

Quarantine: None.

✓ **CASE INVESTIGATION**

Reporting

Table 1: Table of criteria to determine whether a case should be reported to public health authorities

Criterion	Zika Virus Disease, Non-congenital	Congenital Zika Virus Disease
<i>Clinical Evidence</i>		
Rash	O	
Acute Fever (reported or measured)	O	
Arthralgia	O	
Conjunctivitis	O	
Guillain-Barré syndrome not known or associated with another diagnosed etiology	O	
Neurologic manifestations not known to be associated with another diagnosed etiology	O	
Congenital microcephaly		O
Congenital intracranial calcifications		O
Congenital structural brain or eye abnormalities		O
Congenital central nervous system abnormalities		O
Healthcare record contains a diagnosis of Zika virus disease	S	S
Death certificate lists ZIKV as a cause of death or a significant condition contributing to death	S	S
<i>Laboratory Evidence</i>		
Culture of ZIKV from blood, body fluid, or tissue	S	S
Detection of ZIKV-specific RNA in specimens of serum, CSF, tissue or other clinical specimen (e.g., amniotic fluid, umbilical cord blood, urine, semen, saliva)	S	S
Detection of ZIKV antigen by immunohistochemical staining of tissue specimen	S	S
ZIKV-specific IgM antibodies in serum or CSF	S	S
<i>Epidemiological Evidence</i>		
Residence or travel to an area with known ZIKV transmission within two weeks of symptom onset	O	
Mother lived in or traveled to an area with ongoing ZIKV transmission during pregnancy		O
Epidemiologic link to a person with laboratory evidence of recent ZIKV infection (e.g., sexual contact)	O	O (mother)
Laboratory evidence of flavivirus infection in mother during pregnancy		O

Blood transfusion within 30 days of symptom onset	O	
Organ or tissue transplant recipient within 30 days of symptom onset	O	

Notes:

S = This criterion alone is Sufficient to report a case

N = All "N" criteria in the same column are Necessary to report a case.

O = At least one of these "O" (One or more) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to report a case.

* A requisition or order for any of the "S" laboratory tests is sufficient to meet the reporting criteria.

Case Definition

Clinical Criteria

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), **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

Zika virus disease, congenital

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 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.)

Laboratory Criteria

Recent ZIKV infection:

- Culture of ZIKV from blood, body fluid, or tissue; **OR**

- Detection of ZIKV antigen or viral RNA in serum, CSF, placenta, umbilical cord, fetal tissue, or other specimen (e.g., amniotic fluid, urine, semen, saliva), **OR**
- Positive ZIKV 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

Case Classification

Zika virus disease, non-congenital

Confirmed disease case

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.

Probable disease case

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.

Infection That Does Not Meet Clinical Criteria, Non-congenital

Confirmed ZIKV infection

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.

Probable ZIKV infection

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 virus IgM antibody test and no neutralizing antibody testing performed.

Zika virus disease, congenital

Confirmed congenital disease case

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 two days of birth; **OR**
- Positive ZIKV IgM antibody test of umbilical cord blood, neonatal serum or CSF collected within two 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.

Probable congenital disease case

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 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.

Infection That Does Not Meet Clinical Criteria, Congenital

Confirmed congenital infection without disease

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 two days of birth; **OR**
 - Positive ZIKV IgM antibody test of umbilical cord blood, neonatal serum or CSF collected within two 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.

Probable congenital infection without disease

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 two 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.

Table 2. Criteria for defining a case of Zika virus disease or infection

Criterion	Zika virus, non-congenital				Congenital Zika virus			
	Symptomatic		Asymptomatic		Symptomatic		Asymptomatic	
	Prob	Conf	Prob	Conf	Prob	Conf	Prob	Conf
<i>Clinical Evidence</i>								
Fever of acute onset	○	○	○	○				
Maculopapular Rash	○	○	○	○				
Arthralgia	○	○	○	○				
Conjunctivitis	○	○	○	○				
Guillain-Barré syndrome	○	○	○	○				
Neurologic manifestation	○	○	○	○				
Complications of pregnancy including fetal loss, or fetus or neonate with congenital microcephaly or intracranial calcifications	○	○	○	○				
Congenital microcephaly					○	○	○	○
Intracranial calcifications					○	○	○	○
Congenital structural brain or eye abnormalities					○	○	○	○

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Other congenital central nervous system abnormalities										O	O	O	O				
Absence of clinical criteria listed above					N	N	N	N						N	N	N	N
Live born infant										N	N	N	N	N	N	N	N
Illness not explained by another etiology	N	N	N	N						N	N	N	N				
<i>Laboratory Evidence</i>																	
Detection of ZIKV by culture, viral antigen or viral RNA in serum, CSF, tissue, or other specimen (e.g., amniotic fluid, urine, semen, saliva)			N					N									
Detection of ZIKV by culture, viral antigen, or viral RNA in fetal tissue, umbilical cord blood, or amniotic fluid												O				O	
Detection of ZIKV by culture or viral RNA in neonatal serum, CSF, or urine collected within two days of birth												O				O	
Positive ZIKV IgM antibody test of serum or CSF	N	N		N	N	N		N									
Positive ZIKV IgM antibody test of umbilical cord blood, neonatal serum, or CSF collected within two days of birth									N	N		N					N
Positive ZIKV neutralizing antibody titers				N				N					N				N
Negative neutralizing antibody titers against dengue or other endemic flaviviruses in region where exposure occurred				N				N					N				N
Negative dengue-specific IgM antibody test	N				N				N					N			
Positive neutralizing antibody titers against ZIKV and dengue or other flaviviruses endemic to the region where exposure occurred		N				N				N					N		
No neutralizing antibody testing performed	N				N					N				N			
<i>Epidemiological Evidence</i>																	
Resides in or has recently traveled to an area with ongoing ZIKV transmission	O	O			O	O											
Direct epidemiologic linkage to a person with laboratory evidence of recent ZIKV infection (e.g., sexual contact, in utero or perinatal transmission, blood transfusion, organ transplantation)	O	O			O	O											

Case Contact Management

In this event, the investigating health jurisdiction will follow-up with the patient's physician to receive updated clinical information, including pregnancy outcomes.

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✓ **VERSION CONTROL**

Updated June 2016 – Update assays for acute specimens.

Updated April 2016 – Created disease plan using template and updated testing guidelines.

Updated October 2016 – Updated case definitions and reporting criteria.

Updated August 2018 – Updated Critical Clinician Information, “Why is Zika Virus Important to Public Health,” Testing Guidance, Transmission, Period of Communicability, and Prevention sections.

Updated June 2019 – Updated testing recommendation from 14 days for RT-PCR to 7 days per new MMWR findings.

Updated September 2019 – Updated testing guidance due to UPHL charging \$45 for IgM testing.

Updated November 2019 – Updated testing guidance due to CDC updates

(<https://www.cdc.gov/zika/hc-providers/testing-guidance.html>)

Updated December 2019 – Updated “Why is Zika Important to Public Health,” “Differential Diagnosis,” “Laboratory Identification,” and “Laboratory Testing” sections to include pregnancy information.

✓ UT-NEDSS/EpiTrax Minimum/Required Fields by Tab

Demographic

- County
- State
- Date of Birth
- Birth Gender
- Ethnicity
- Race
- First Name
- Last Name
- Middle Name
- Area Code
- Email Address
- Extension
- Phone Number

Clinical

- Date Diagnosed
- Date of Death
- Disease
- Onset Date
- Pregnant
- Expected delivery date
- Microcephaly
- Fetal loss
- Guillain-Barre syndrome/acute flaccid paralysis

- Clinicians
- Diagnostic Facilities
- Asymptomatic
- Symptomatic

Laboratory

- Lab Test Date
- Organism
- Specimen Source
- Test Result

Epidemiological

- Transmission mode of interest

Investigation

- Did the patient travel outside the USA during the exposure period?

Contacts

NA

Reporting

- Date first reported to public health

Administrative

- State case status

✓ ZIKA VIRUS RULES FOR ENTERING LABORATORY TEST RESULTS

The following rules describe how laboratory results reported to public health should be added to new or existing events in UT-NEDSS/EpiTrax. These rules have been developed for the automated processing of electronic laboratory reports, although they apply to manual data entry, as well.

Test-Specific Rules

Test specific rules describe what test type and test result combinations are allowed to create new morbidity events in UT-NEDSS/EpiTrax, and what test type and test result combinations are allowed to update existing events (morbidity or contact) in UT-NEDSS/EpiTrax.

Test Type	Test Result	Create a New Event	Update an Existing Event
IgM Antibody	Positive	Yes	Yes
	Negative	Yes*	Yes
	Equivocal	Yes*	Yes
PCR/amplification	Positive	Yes	Yes
	Negative	Yes*	Yes
	Equivocal	Yes*	Yes
Total Antibody by EIA	Positive	Yes	Yes
	Negative	Yes*	Yes
	Equivocal	Yes*	Yes

*An initial negative/equivocal zika result will create a surveillance event in EpiTrax. If there is an existing zika case, a negative/equivocal zika result will update within the whitelist rules.

Whitelist Rules

Whitelist rules describe how long an existing event can have new laboratory data appended to it. If a laboratory result falls outside the whitelist rules for an existing event, it should not be added to that event, and should be evaluated to determine if a new event (CMR) should be created.

Zika Virus Morbidity Whitelist Rule: If the specimen collection date of the laboratory result one year or less after the event date, the laboratory result should be added to the morbidity event.

Zika Virus Contact Whitelist Rule: If the specimen collection date of the laboratory result is 30 days or less after the date of the contact event, the laboratory result should be added to the contact event.

Graylist Rule

We often receive laboratory results through ELR that cannot create cases, but can be useful if a case is created in the future. These laboratory results go to the graylist. The

graylist rule describes how long an existing event can have an old laboratory result appended to it.

Zika Virus Graylist Rule: If the specimen collection date of the laboratory result is 30 days before to seven days after the event date of the morbidity event, the laboratory result should be added to the morbidity event.

Other Electronic Laboratory Processing Rules

If an existing event has a state case status of “not a case,” ELR will never add additional test results to that case. New labs will be evaluated to determine if a new CMR should be created.