

# Arboviral Disease

<b>Signs and Symptoms</b>	<ul style="list-style-type: none"> <li>• Eastern/western equine encephalitis, chikungunya, dengue, Japanese encephalitis, St. Louis encephalitis, La Crosse encephalitis, Powassan, California serogroup, Zika</li> <li>• Most infections asymptomatic</li> <li>• Neuroinvasive: aseptic meningitis, encephalitis, or acute flaccid paralysis</li> <li>• Non-neuroinvasive: acute febrile illness; may be headache, muscle or joint aches, rash, or gastrointestinal symptoms</li> </ul>
<b>Incubation</b>	Varies with agent
<b>Case classification (not used for clinical diagnosis)</b>	<p>Classifications differ for each of the categories below. See Section 3.</p> <ul style="list-style-type: none"> <li>• Neuroinvasive arboviral disease (excludes West Nile virus)</li> <li>• Non-neuroinvasive arboviral disease (excludes West Nile virus)</li> <li>• Dengue (dengue-like, dengue, severe dengue)</li> <li>• Zika virus disease case, non-congenital; Zika virus disease, congenital</li> <li>• Zika virus infection, non-congenital; Zika virus infection, congenital</li> </ul>
<b>Differential diagnosis</b>	<p>Different agents difficult to distinguish due to cross-reactivity and persisting IgM (years). Other illnesses: hepatitis, influenza, leptospirosis, malaria, viral rash illness, viral hemorrhagic fever, viral meningitis, cholecystitis</p>
<b>Treatment</b>	Supportive
<b>Duration</b>	Varies with agent
<b>Exposure</b>	<p>Vector: varies with agent, may be mosquitoes, ticks, flies, or midges</p> <p>Reservoirs: varies with agent, may be birds or small mammals; transmission among people via mosquitoes occurs for dengue, chikungunya, yellow fever, and Zika</p>
<b>Laboratory testing</b>	<p>Local Health Jurisdiction (LHJ) and Communicable Disease Epidemiology (CDE) can arrange testing</p> <ul style="list-style-type: none"> <li>• <b>Best specimens:</b> generally <b>serum or CSF</b>; also urine for Zika</li> <li>• Keep specimens <b>cold or if already frozen keep frozen (dry ice), ship</b> with Virology/Serology form or the Zika virus test form  <a href="https://www.medialab.com/dv/dl.aspx?d=1615463&amp;dh=e4b87&amp;u=69790&amp;uh=0e2a1">https://www.medialab.com/dv/dl.aspx?d=1615463&amp;dh=e4b87&amp;u=69790&amp;uh=0e2a1</a>  <a href="http://www.doh.wa.gov/Portals/1/Documents/5230/ZikaRequisitionForm.pdf">http://www.doh.wa.gov/Portals/1/Documents/5230/ZikaRequisitionForm.pdf</a></li> <li>• Specimen Collection and Submission Instructions  <a href="https://www.doh.wa.gov/Portals/1/Documents/5240/SCSI-WNV-MIA-V2.pdf">https://www.doh.wa.gov/Portals/1/Documents/5240/SCSI-WNV-MIA-V2.pdf</a>  <a href="http://www.doh.wa.gov/Portals/1/Documents/Pubs/420-167-ZikaSpecimenCollectionShipping.pdf">http://www.doh.wa.gov/Portals/1/Documents/Pubs/420-167-ZikaSpecimenCollectionShipping.pdf</a></li> </ul>
<b>Public health actions</b>	<p>LHJ can consult with CDE 877-539-4344 for testing</p> <ul style="list-style-type: none"> <li>• Confirm diagnosis – confirmatory testing may be needed</li> <li>• Identify potential exposures, particularly local or in the United States</li> <li>• Notify CDE promptly for locally acquired cases (e.g., no out-of-state travel)</li> <li>• Advise no blood donation for 6 months; for Zika advise about potential sexual transmission or about follow-up during pregnancy</li> </ul> <p><i>Infection Control:</i> standard precautions</p>

# Arboviral Disease

(except West Nile virus and Yellow Fever)

## 1. DISEASE REPORTING

### A. Purpose of Reporting and Surveillance

1. To distinguish arboviral infections acquired locally or in the United State from those related to international travel.
2. To better understand the epidemiology of these infections in Washington State in order to target education and control measures.
3. To identify emerging arboviral infections in Washington.

### B. Legal Reporting Requirements

1. Health care providers and health care facilities: notifiable to **local health jurisdiction** within 3 business days.
2. Laboratories: Arboviral (eastern and western equine encephalitis, dengue, St. Louis encephalitis, La Crosse encephalitis, Japanese encephalitis, Powassan, California serogroup, chikungunya, Zika) any positive result excluding IgG notifiable to local health jurisdiction within 2 business days; submission on request – specimen associated with positive result excluding IgG, within 2 business days.
3. Veterinarians: animal cases notifiable to Washington State Department of Agriculture. See: <https://app.leg.wa.gov/WAC/default.aspx?cite=16-70>
4. Local health jurisdictions: notifiable to Washington State Department of Health (DOH) Communicable Disease Epidemiology (CDE) within 7 days of case investigation completion or summary information required within 21 days.

### C. Local Health Jurisdiction Investigation Responsibilities

1. Consult CDE about endemically acquired cases or for assistance with testing. CDE maintains [criteria for Zika virus testing through public health](#).
2. Facilitate transport of specimens (e.g., serum, urine, whole blood or CSF) to the Washington State Public Health Laboratories (PHL) if initial testing or confirmatory testing is needed. Please call CDE prior to submitting specimens (206-418-5500), or submit a [Zika virus intake form](#) to CDE if submitting specimens for Zika virus testing. For assistance in determining appropriate specimen type, call CDE, or for Zika, refer to [Zika virus detailed laboratory ordering guidance](#).
3. Report all *confirmed*, *probable*, and *suspect* cases to CDE (see definitions below). Complete the Arboviral Disease case report form <https://www.doh.wa.gov/Portals/1/Documents/5100/210-066-ReportForm-Arbovirus.pdf> and enter the data into the Washington Disease Reporting System (WDRS) as “Arboviral Disease.” Cases of West Nile virus disease and yellow fever are

discussed in separate guidelines and should be reported separately in WDRS as “West Nile Virus” and “Yellow Fever.”

## 2. THE DISEASE AND ITS EPIDEMIOLOGY

For information about West Nile virus and yellow fever, see disease specific guidelines at <https://www.doh.wa.gov/Portals/1/Documents/5100/420-085-Guideline-WNV.pdf> and <https://www.doh.wa.gov/Portals/1/Documents/5100/420-086-Guideline-YellowFever.pdf>.

### Background

Arboviral (arthropod-borne viral) diseases are transmitted by arthropods (e.g., mosquitoes, sandflies, ticks, or midges). More than 130 arboviruses are known to cause human disease. Most arboviruses of public health importance belong to one of three virus genres: *Flavivirus*, *Alphavirus*, and *Bunyavirus*.

Arboviral diseases include West Nile virus disease (discussed separately), eastern and western equine encephalitis (WEE), dengue, chikungunya, St. Louis encephalitis (SLE), La Crosse encephalitis, Japanese encephalitis, Powassan virus encephalitis, yellow fever (discussed separately), Zika, and other less common infections. In addition, there are other arthropod-borne viruses that cause hemorrhagic fevers and other illnesses that are diseases with international importance (e.g., Rift Valley fever and Crimean-Congo hemorrhagic fever viruses); for reporting purposes in Washington they have been included under the condition “Viral Hemorrhagic Fever.”

### A. Etiological Agent

See Table 1 for selected arboviral agents (excludes West Nile virus and yellow fever, which are discussed separately).

### B. Description of Illness

Arboviral infections cause four main clinical syndromes: 1) acute central nervous system (CNS) illnesses, 2) acute benign fevers of short duration with or without rash, 3) hemorrhagic fevers, and 4) polyarthritides and rash with or without fevers (see Table 1). Zika infection during pregnancy has been linked to certain birth defects, including microcephaly.

### C. Arboviral Diseases in Washington State

One to 23 cases of travel-associated dengue are reported each year. Prior to 2013, 0-3 travel-associated chikungunya cases were reported annually. In late 2013, the first local transmission of chikungunya virus was identified in the Caribbean; widespread local transmission was then identified in many countries in Central and South America. In 2014, 11 cases of chikungunya virus infection were identified in travelers returning from the Caribbean and in 2015, 40 travel-associated cases were reported in Washington. Since 2016, chikungunya cases have decreased to pre-outbreak levels. In 2015, a Zika outbreak began in Brazil and quickly spread to many countries in South and Central America, the Caribbean, and the South Pacific. Increased testing for Zika virus due to concerns about birth defects likely led to increased detections of chikungunya and dengue. The circulation of multiple flaviviruses and their cross-reactivity on serologic testing led to inability to distinguish virus types in some cases. During 2016, more than 60 cases of

travel-associated Zika virus disease were reported in Washington residents, decreasing to 16 cases of Zika virus disease in 2017, and no Zika virus disease cases in 2018.

Rare reports of other travel-associated arboviral diseases include Colorado tick fever and Japanese encephalitis in 2008, and St. Louis encephalitis and Toscana virus in 2009.

Other than West Nile virus, the last reported human illness due to an arboviral infection acquired in Washington State was WEE in 1988. SLE has also occurred in Washington, primarily in the central valley east of the Cascade Mountains. SLE infections were detected in sentinel chickens in Benton county in 2005 (Source: DOH Environmental Health-Zoonotic Disease Program).

#### **D. Vectors and Reservoirs**

Most arboviruses are maintained in enzootic cycles involving arthropods and birds or small mammals. Humans are usually “dead end hosts,” in that they do not contribute to the spread of the virus. However, some arboviral infections (e.g., dengue, yellow fever, chikungunya, Zika) can be indirectly spread from one person to another by a mosquito. Vector mosquitoes and ticks are present in Washington for some (SLE, WEE), but not all (dengue, chikungunya, Zika) arboviruses. See Table 1 below.

#### **E. Modes of Transmission**

Arboviruses are most commonly transmitted by the bites of arthropods (e.g., mosquitoes, ticks, flies, or midges). Some arboviruses have been shown to be transmitted on rare occasions through blood transfusions, organ transplantation, unprotected sexual intercourse, transplacentally during pregnancy or perinatally during birth, consumption of unpasteurized dairy products, breast feeding, and laboratory exposures.

#### **F. Incubation Period**

Varies with agent. See Table 1.

#### **G. Period of Communicability**

Except for rare cases of transplacental transmission, organ transplantation, sexual transmission, or blood transfusion, most arboviruses are transmitted by an arthropod vector from animal to human. Dengue, chikungunya, Zika, and yellow fever are exceptions because mosquitoes can transmit the virus from one viremic human to an uninfected human. During their periods of high viremia, usually 3-5 days before fever onset until the fever subsides, humans can infect mosquitoes with dengue and Zika. Infection with Zika virus during pregnancy can cause fetal infection which may result in birth defects or stillbirth, although many women with infections have normal infants. Sexual transmission of Zika virus has been documented up to several weeks after illness onset or last exposure.

#### **H. Treatment**

Treatment is supportive.

**Table 1: Geographic Distribution and Clinical Characteristics of Selected Arboviral Infections\***

Note that separate guidelines are available for both West Nile virus and Yellow fever.

Genus	Disease (Etiologic agent)	Arthropod	Geographic distribution	Incubation period	Clinical syndrome
<i>Bunya-virus</i>	California serogroup viral encephalitis (Jamestown Canyon, Keystone, La Crosse, Snowshoe hare, Trivittatus, and California encephalitis viruses)	Mosquito	Widespread in the United States and Canada; most prevalent in Midwest and Southeast; also South America, Europe, Asia	5–15 days	Encephalitis
<i>Alpha-virus</i>	Chikungunya fever (Chikungunya virus)	Mosquito	Africa; Asia; Caribbean; Central and South America, potentially Florida (2014)	3-7 days (range 1-12 days)	Fever, arthralgia, rash (hemorrhage rare)
<i>Colti-virus</i>	Colorado tick fever (Colorado tick fever virus)	Tick	Western United States and Canada	1–14 days	Febrile illness, rarely with encephalitis or myocarditis
<i>Flavi-virus</i>	Dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS) (dengue viruses)	Mosquito	Tropical areas worldwide: Central and South America, Caribbean, Asia, Australia, Oceania, Africa; recently Florida and Hawaii	Commonly 4–7 days (range: 3–14 days)	Febrile illness; hemorrhagic fever and shock (particularly with second infection)
<i>Alpha-virus</i>	Eastern equine encephalitis (EEE virus)	Mosquito	Eastern seaboard and Gulf states of the United States; Canada; South and Central America	4–10 days	Febrile illness, encephalitis
<i>Flavi-virus</i>	Japanese encephalitis (Japanese encephalitis virus)	Mosquito	Asia; Pacific Islands; Northern Australia	5–15 days	Encephalitis, fever
<i>Flavi-virus</i>	Powassan encephalitis (Powassan encephalitis virus)	Tick	Canada; northeastern and upper Midwestern United States; Russia	4–30 days	Encephalitis, meningitis
<i>Flavi-virus</i>	St. Louis encephalitis (SLE virus)	Mosquito	Much of the United States; Manitoba and southern Ontario; Caribbean area; South America	4–14 days	Febrile illness, Encephalitis,
<i>Alpha-virus</i>	Venezuelan equine encephalitis (VEE virus)	Mosquito	Central and South America; southern United States	1–4 days	Fever, encephalitis
<i>Alpha-virus</i>	Western equine encephalitis (WEE virus)	Mosquito	Central and western United States; Canada; Argentina, Uruguay, Brazil	2–10 days	Fever, encephalitis
<i>Flavi-virus</i>	Zika	Mosquito	Central and South America, parts of Caribbean, Pacific Islands and Africa	2-14 days	Fever, arthralgia, rash, conjunctivitis. Congenital Zika virus syndrome.

\*Sources: American Academy of Pediatrics. Arboviruses. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on the Infectious Diseases*. 27<sup>th</sup> ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006:212–14.

Arthropod-borne Viral Diseases. In: Heymann DL, ed. *Control of Communicable Diseases Manual*. 18<sup>th</sup> ed. Washington D.C.: American Public Health Association; 2004: 31–34.

### 3. CASE DEFINITION

**NOTE:** - West Nile and yellow fever are discussed in separate guidelines;

- Dengue is discussed in Section 3B of this guideline.
- Zika is discussed in Section 3C of this guideline.

#### A. Neuroinvasive and Non-Neuroinvasive Arboviral Diseases (2014)

##### 1. Clinical Description *(for dengue, see Section 3B; for Zika, see Section 3C)*

Most arboviral infections are asymptomatic. Clinical disease ranges from mild febrile illness to severe encephalitis. For the purposes of surveillance and reporting, arboviral disease cases are often categorized into two primary groups based on their clinical presentation: neuroinvasive disease and non-neuroinvasive disease.

**Neuroinvasive disease:** Many arboviruses cause neuroinvasive disease such as aseptic meningitis, encephalitis, or acute flaccid paralysis (AFP). These illnesses are usually characterized by the acute onset of fever with stiff neck, altered mental status, seizures, limb weakness, cerebrospinal fluid (CSF) pleocytosis, or abnormal neuroimaging. AFP may result from anterior ("polio") myelitis, peripheral neuritis, or post-infectious peripheral demyelinating neuropathy (i.e., Guillain-Barré syndrome). Less common neurological manifestations, such as cranial nerve palsies, also occur.

**Non-neuroinvasive disease:** Most arboviruses are capable of causing an acute systemic febrile illness that may include headache, myalgias, arthralgias, rash, or gastrointestinal symptoms. Other physical complaints may include vertigo, stiff neck, or muscle weakness without progression to more clinically apparent neurological involvement.

##### 2. Clinical Criteria for Diagnosis *(for dengue, see Section 3B; for Zika, see Section 3C)*

A clinically compatible case of arboviral disease is defined as follows:

###### Neuroinvasive disease

- Meningitis, encephalitis, acute flaccid paralysis, or other acute signs of central or peripheral neurologic dysfunction, as documented by a physician, **AND**
- Absence of a more likely clinical explanation. Other clinically compatible symptoms of arbovirus disease include: headache, myalgia, rash, arthralgia, vertigo, vomiting, paresis and/or nuchal rigidity.

###### Non-neuroinvasive disease

- Fever or chills as reported by the patient or a health-care provider, **AND**
- Absence of neuroinvasive disease, **AND**
- Absence of a more likely clinical explanation. Other clinically compatible symptoms of arbovirus disease include: headache, myalgia, rash, arthralgia, vertigo, vomiting, paresis and/or nuchal rigidity.

### 3. Laboratory Criteria for Diagnosis (for dengue, see Section 3B; for Zika, see Section 3C)

#### Neuroinvasive disease:

##### *Confirmatory:*

- Isolation of virus from or demonstration of specific viral antigen or nucleic acid in tissue, blood, CSF, or other body fluid, **OR**
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, **OR**
- Virus-specific immunoglobulin M (IgM) antibodies in serum with confirmatory\* virus-specific neutralizing antibodies in the same or a later specimen, **OR**
- Virus-specific IgM antibodies in CSF and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred.

##### *Presumptive:*

- Virus-specific IgM antibodies in CSF or serum but with no other testing.

#### **Non-neuroinvasive disease:**

##### *Confirmatory:*

- Isolation of virus from or demonstration of specific viral antigen or nucleic acid in tissue, blood, or other body fluid, excluding CSF, **OR**
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, **OR**
- Virus-specific immunoglobulin M (IgM) antibodies in serum with confirmatory\* virus-specific neutralizing antibodies in the same or a later specimen.

##### *Presumptive:*

- Virus-specific IgM antibodies in serum but with no other testing.

\***Arboviral serologic assays:** Assays for the detection of IgM and IgG antibodies commonly include enzyme-linked immunosorbent assay (ELISA), microsphere immunoassay (MIA), or immunofluorescence assay (IFA). These assays provide a presumptive diagnosis and should have confirmatory testing performed. Confirmatory testing involves the detection of arboviral-specific neutralizing antibodies utilizing assays such as plaque reduction neutralization test (PRNT).

### 4. Case Definition (2014) (for dengue, see Section 3B; for Zika, see Section 3C)

#### *Confirmed:*

- **Neuroinvasive:** a case that meets the clinical criteria and one or more of the confirmatory laboratory criteria for neuroinvasive disease.
- **Non-neuroinvasive:** a case that meets the clinical criteria for and one or more of the confirmatory laboratory criteria for non-neuroinvasive disease.

#### *Probable:*

- **Neuroinvasive:** a case that meets the clinical criteria and the presumptive laboratory criterion for neuroinvasive disease.

- **Non-neuroinvasive:** a case that meets the clinical criteria and the presumptive laboratory criterion for non-neuroinvasive disease.

## 5. Comments on Interpreting Arboviral Laboratory Results

- **Serologic cross-reactivity.** In some instances, arboviruses from the same genus produce cross-reactive antibodies. In geographic areas where two or more closely-related arboviruses occur, serologic testing for more than one virus using PRNT may be needed to determine the specific causative virus. For example, such testing might be needed to distinguish antibodies resulting from infections from viruses within a genus, e.g., flaviviruses such as West Nile, St. Louis encephalitis, Powassan, dengue, Zika, or Japanese encephalitis viruses.
- **Rise and fall of IgM antibodies.** For most arboviral infections, IgM antibodies are generally first detectable at 3 to 8 days after onset of illness and persist for 30 to 90 days, but longer persistence has been documented (e.g., up to 500 days for West Nile virus). Serum collected within 8 days of illness onset may not have detectable IgM and testing should be repeated on a convalescent-phase sample to rule out arboviral infection in those with a compatible clinical syndrome. A negative IgM antibody test on a specimen collected >12 weeks after illness onset does not rule out infection.
- **Persistence of IgM antibodies.** Arboviral IgM antibodies may still be detected in some patients months or years after their acute infection. Therefore, the presence of these virus-specific IgM antibodies may signify a past infection and be unrelated to the current acute illness. Finding virus-specific IgM antibodies in CSF or a fourfold or greater change in virus-specific antibody titers between acute- and convalescent-phase serum specimens provides additional laboratory evidence that the arbovirus was the likely cause of the patient's recent illness. Clinical and epidemiologic history also should be carefully considered.
- **Persistence of IgG and neutralizing antibodies.** Arboviral IgG and neutralizing antibodies can persist for many years following a symptomatic or asymptomatic infection. Therefore, the presence of these antibodies alone is only evidence of previous infection and clinically compatible cases with the presence of IgG, but not IgM, should be evaluated for other etiologic agents.
- **Other information to consider.** Vaccination history, detailed travel history, possible sexual or congenital exposures, date of onset of symptoms, and potentially cross-reactive arboviruses known to circulate in the geographic area of exposure should be considered when interpreting results.
- **Imported arboviral diseases.** Many exotic arboviruses (e.g., dengue, Zika, chikungunya, Japanese encephalitis, Tick-borne encephalitis, Venezuelan equine encephalitis, and Rift Valley fever viruses) are potential public health risks for the United States as competent vectors exist in some states that could allow for sustained transmission upon establishment of imported arboviral pathogens. Healthcare providers and public health officials should maintain a high index of clinical suspicion for cases of potentially exotic or unusual arboviral etiology, particularly in international travelers. If a suspected case occurs, it should be reported to the local



health jurisdiction, then to DOH Communicable Disease Epidemiology for reporting to the Centers for Disease Control and Prevention (CDC).

## **B. Dengue: Dengue-like Illness, Dengue, Severe Dengue (Includes Dengue Hemorrhagic Fever, Dengue Shock Syndrome)**

### **1. Clinical Criteria for Diagnosis**

- **Dengue-like Illness** is defined by fever as reported by the patient or healthcare provider.
- **Dengue** is defined by the presence of fever as reported by the patient or healthcare provider and the presence of one or more of the following signs and symptoms: nausea/vomiting, rash, headache, retro-orbital or ocular pain, myalgia, arthralgia, tourniquet test positive, leukopenia (a total leukocyte count  $<5,000/\text{mm}^3$ ), abdominal pain or tenderness, extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites), mucosal bleeding at any site, liver enlargement  $>2$  cm, or increasing hematocrit concurrent with rapid decrease in platelet count.
- **Severe Dengue** is defined as dengue (above) with one or more of the following:
  - Severe plasma leakage evidenced by hypovolemic shock and/or extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites) with respiratory distress. A high hematocrit value (an increase in hematocrit  $\geq 20\%$  above average for age or a decrease in hematocrit  $\leq 20\%$  of baseline following fluid replacement therapy) for patient age and sex offers further evidence of plasma leakage.
  - Severe bleeding from the gastrointestinal tract (e.g., hematemesis, melena) or vagina (menorrhagia) as defined by requirement for medical intervention including intravenous fluid resuscitation or blood transfusion.
  - Severe organ involvement, including any of the following:
    - Elevated liver transaminases: aspartate aminotransferase (AST) or alanine aminotransferase (ALT)  $\geq 1,000$  units per liter (U/L)
    - Impaired level of consciousness and/or diagnosis of encephalitis, encephalopathy, or meningitis
    - Heart or other organ involvement including myocarditis, cholecystitis, and pancreatitis

### **2. Laboratory Criteria for Diagnosis (*Dengue-like, Dengue, Severe Dengue only*)**

Confirmatory:

- Detection of DENV nucleic acid in tissue, blood, serum, cerebrospinal fluid (CSF), or other body fluid by validated reverse transcriptase-polymerase chain reaction (PCR) test **OR**
- Detection of dengue virus antigens in tissue by a validated immunofluorescence or immunohistochemistry assay, **OR**
- Detection in serum or plasma of dengue virus NS1 antigen by a validated immunoassay, **OR**

- Cell culture isolation of dengue virus from a serum, plasma, or CSF specimen, **OR**
- Detection of dengue-specific IgM antibodies by validated immunoassay in a serum specimen or CSF in a person living in a dengue endemic or non-endemic area of the United States without evidence of other flavivirus transmission (e.g., WNV, SLEV, or recent vaccination against a flavivirus (e.g., YFV, JEV)); **OR**
- Detection of dengue-specific IgM antibodies by validated immunoassay in a serum specimen or CSF in a traveler returning from a dengue endemic area without ongoing transmission of another flavivirus (e.g., WNV, JEV, YFV), clinical evidence of co-infection with one of these flaviviruses, or recent vaccination against a flavivirus (e.g., YFV, JEV), **OR**
- Seroconversion from negative dengue virus-specific serum immunoglobulin M (IgM) antibody in an *acute* phase specimen (collected  $\leq 5$  days after symptom onset) to positive dengue-specific serum IgM antibodies in a convalescent-phase specimen (collected  $\geq 5$  days after symptom onset), **OR**
- Dengue-specific IgG antibody seroconversion or  $\geq 4$ -fold rise in titer by a validated immunoassay in serum specimens collected  $> 2$  weeks apart, **AND** confirmed by a neutralization test (e.g. plaque reduction neutralization test).
- Virus-specific immunoglobulin M (IgM) antibodies in serum with confirmatory\* virus-specific neutralizing antibodies in the same or a later specimen.

Presumptive:

- Detection of dengue-specific IgM antibodies by validated immunoassay in a serum specimen or CSF in a person living in an area of the United States with evidence of other flavivirus transmission, **OR** a traveler returning from a dengue endemic area with ongoing transmission of another flavivirus, **OR** clinical evidence of co-infection with another flavivirus, **OR** recent vaccination against a flavivirus (e.g., YFV, JEV).

Suspected:

- The absence of dengue-specific IgM by validated immunoassay in a serum or CSF specimen collected  $< 5$  days after illness onset and in which molecular diagnostic testing was not performed in a patient with an epidemiologic linkage.

**\*Dengue serologic assays:** Assays for the detection of IgM and IgG antibodies commonly include enzyme-linked immunosorbent assay (ELISA), microsphere immunoassay (MIA), or immunofluorescence assay (IFA). These assays provide a presumptive diagnosis and should have confirmatory testing performed if infection with other flaviviruses is a possibility. Confirmatory testing involves the detection of dengue-specific neutralizing antibodies utilizing assays such as plaque reduction neutralization test (PRNT).

### 3. Exposure (*Dengue-like, Dengue, Severe Dengue only*)

Criteria for epidemiologic linkage are dependent upon exposure, which is defined as:

- Travel to a dengue endemic country or presence at location with ongoing outbreak of dengue-like illness within two weeks of illness onset, **OR**

- Association in time and place with a confirmed or probable dengue case.

#### 4. Case Definition (2015) (*Dengue-like, Dengue, Severe Dengue only*)

*Suspect*: a clinically compatible case of dengue-like illness, dengue, or severe dengue that is epidemiologically linked to a confirmed case or by travel, as defined above.

*Probable*: a clinically compatible case of dengue-like illness, dengue, or severe dengue with laboratory results indicative of presumptive infection.

*Confirmed*: a clinically compatible case of dengue-like illness, dengue, or severe dengue with confirmatory laboratory results.

#### 5. Comment

An asymptomatic blood or tissue donor is defined as having dengue virus-specific viral antigen or genomic sequences demonstrated in donated blood or organs during screening and confirmatory testing in the absence of symptoms in the donor. In 2009, CDC requested reporting of dengue virus positive asymptomatic donors, however, no cases have been identified. Reporting is now limited to persons with symptomatic dengue virus infection.

Dengue viruses are flaviviruses and have sufficient antigenic similarity to yellow fever virus, Japanese encephalitis virus, Zika virus, and West Nile virus that previous infection or vaccination may raise cross-reactive serum antibodies. In such situations, the result of ELISA testing may be unreliable and PRNT may be needed to correctly identify the infecting virus. However, high-titers of cross-reactive antibody produced from multiple previous flavivirus infections cannot be resolved by PRNT.

### C. Zika

#### 1. Clinical Description (*Zika disease and infection only*)

**Zika virus disease case, 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 nervous system-related abnormalities including defects such as clubfoot or multiple joint contractures
- Guillain-Barré syndrome or other neurologic manifestations

**Zika virus disease case, 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.

## 2. Laboratory Criteria for Diagnosis (*Zika disease and infection only*)

### *Confirmed, non-congenital*

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

### *Probable, non-congenital*

- 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
- Positive Zika virus IgM antibody test AND negative dengue virus IgM antibody test with no neutralizing antibody testing performed

### *Confirmed, congenital*

- 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.

### *Probable, congenital*

- 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

## 3. Exposure (*Zika disease and infection only*)

Criteria for epidemiologic linkage are dependent upon exposure, which is defined as:

- 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 vectorborne transmission

#### 4. Case Definition (2016) (*Zika disease and infection only*)

##### **Zika Virus Disease, Non-congenital:**

###### *Confirmed case*

Meets clinical criteria for non-congenital case AND has confirmatory laboratory evidence of recent Zika virus infection.

###### *Probable case*

Meets clinical criteria for non-congenital disease, AND has an epidemiologic linkage, AND has probable laboratory evidence of recent Zika virus or flavivirus infection.

##### **Zika Virus Disease, Congenital:**

###### *Confirmed case*

A neonate meets the clinical criteria for congenital disease AND meets one of the confirmed congenital laboratory criteria

###### *Probable case*

A neonate 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 probable Zika virus or flavivirus infection

##### **Zika Virus Infection, Non-congenital:**

###### *Confirmed case*

Does not meet clinical criteria for non-congenital disease, AND has confirmatory laboratory evidence of recent Zika virus infection.

###### *Probable case*

Does not meet clinical criteria for non-congenital disease, BUT has an epidemiologic linkage, AND has probable laboratory evidence of recent Zika virus infection.

**Zika Virus Infection, Congenital:**

*Confirmed:* Neonate who does not meet clinical criteria for a congenital disease case, BUT meets one of the confirmed congenital laboratory criteria

*Probable:* 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 Zika virus or flavivirus infection; AND

The neonate has laboratory evidence of probable Zika virus or flavivirus infection.

**Comment**

An asymptomatic blood or tissue donor is defined as having Zika virus-specific viral antigen or genomic sequences demonstrated in donated blood or organs during screening and confirmatory testing in the absence of symptoms in the donor. In 2016, CDC requested reporting of Zika virus positive asymptomatic donors. Zika virus is a flavivirus and has sufficient antigenic similarity to dengue, yellow fever virus, Japanese encephalitis virus, and West Nile virus that previous infection or vaccination may raise cross-reactive serum antibodies. In such situations, the result of ELISA testing may be unreliable and PRNT may be needed to correctly identify the infecting virus. However, high-titers of cross-reactive antibody produced from multiple previous flavivirus infections cannot be resolved by PRNT.

**4. DIAGNOSIS AND LABORATORY SERVICES****A. Diagnosis**

Laboratory diagnosis is primarily made by detection of viral specific antibodies in serum or CSF, or by detection of nucleic acid in serum or tissue. See Section 3A (5) for additional information about serologic testing.

**B. Tests Available at the Washington State Health Public Health Laboratories (PHL)**

PHL can test for West Nile virus (WNV)-specific and St. Louis encephalitis (SLE) virus-specific IgM antibody in serum or CSF by microsphere immunoassay (MIA). PHL can also test for Zika-specific IgM antibody in serum by enzyme-linked immunosorbent assay (ELISA), for Zika, chikungunya, and dengue nucleic acid by RT-PCR on serum, and for Zika RNA by RT-PCR on urine. PHL also has emergency capacity for dengue and chikungunya IgM serology testing; consult with CDE to request this testing. In certain situations (e.g. inconclusive results, concern for cross-reactivity), PHL will send samples to the CDC for additional testing by plaque reduction neutralization test (PRNT). See WNV guideline for additional information.

PHL sends specimens to the CDC for all other arboviral tests. For details of specimen requirements see:

<https://www.doh.wa.gov/ForPublicHealthandHealthcareProviders/PublicHealthLaboratories/MicrobiologyLabTestMenu>

Details on criteria for Zika virus testing through public health, detailed laboratory ordering guidance, and specimen collection instructions can be found here:

<https://www.doh.wa.gov/YouandYourFamily/IllnessandDisease/ZikaVirus/healthcareprovidersClinicallabs#Zika>

Note that PHL require all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

### C. Specimen Collection

Serum and/or CSF should be refrigerated and transported cold or frozen. Other specimens should be held at initial storage temperature (e.g., maintain frozen specimens with dry ice.) Specimens should be submitted with a completed PHL Serology/Virology form (<https://www.medialab.com/dv/dl.aspx?d=1615463&dh=e4b87&u=69790&uh=0e2a1>) or the Zika virus test request form (<https://www.doh.wa.gov/Portals/1/Documents/5230/ZikaRequisitionForm.pdf>).

Please call DOH Communicable Disease Epidemiology (206-418-5500) to request testing and obtain shipping instructions for specimens other than serum or CSF.

## 5. ROUTINE CASE INVESTIGATIONS

Interview the case and others who may be able to provide pertinent information.

### A. Evaluate the Diagnosis

If the case tests positive for an arboviral infection at a laboratory other than a Public Health Laboratories, discuss the need to perform confirmatory testing with DOH Communicable Disease Epidemiology (206-418-5500). As needed, facilitate transport of the specimen to PHL for further testing.

Evaluate whether the patient had a previous infection with West Nile virus or another arboviral disease or was vaccinated for an arboviral disease (e.g., Japanese encephalitis, tick-borne encephalitis, or yellow fever).

### B. Manage the Case

1. Hospitalized patients should be treated with standard precautions. Infected persons should be advised not to donate blood, tissues or organs for 6 months after infection has cleared
2. Pregnant women with a positive or inconclusive test for Zika virus should be followed by serial ultrasound examination every 3-4 weeks to monitor fetal growth and anatomy, particularly neuroanatomy.
  - Referral to a maternal-fetal medicine or infectious disease specialist is recommended
  - Amniocentesis can be considered for further Zika virus testing
3. Infants born to mothers with laboratory evidence of Zika virus infection during pregnancy should have a standard evaluation at birth that includes a comprehensive physical examination and Zika virus NAT (serum and urine) and IgM (serum) testing as soon as possible after birth. In addition, by 1 month of age, these infants should have a postnatal head ultrasound, comprehensive ophthalmologic exam, and hearing assessment by auditory brainstem response (ABR) testing. For infants with findings of Congenital Zika Syndrome (CZS), Zika virus NAT and IgM testing should be considered on cerebrospinal fluid (CSF); these infants should also be evaluated for other causes of

congenital abnormalities and referred to developmental and other specialists based on their clinical findings. See detailed CDC guidance:

<https://www.cdc.gov/pregnancy/zika/testing-follow-up/documents/pediatric-evaluation-follow-up-tool.pdf>

4. Women with laboratory evidence of Zika virus infection should wait at least 2 months after their symptoms first appeared or their last date of possible travel or sexual exposure before trying to get pregnant
5. Men with laboratory evidence of Zika virus infection should wait at least 3 months after their symptoms first appeared or their last date of possible travel or sexual exposure to have unprotected sex
6. Zika virus-infected persons with a pregnant partner should use barrier methods consistently and correctly or abstain from sex for the duration of pregnancy.
7. There is no current recommendation for mothers infected with arboviral disease to discontinue breastfeeding. In the case of Zika infection, current evidence suggests that the benefits of breastfeeding outweigh the risk of Zika virus spread through breast milk.
8. Assess evidence or risk of local transmission. Neither *Aedes aegypti* nor *Ae. albopictus*, the primary mosquito vectors for dengue, Zika, and chikungunya, are endemic to Washington State, so the risk of a case infecting mosquitoes which could subsequently infect other humans is very low. However, autochthonous dengue infections have been identified in Florida, Texas, and Hawaii; likewise autochthonous chikungunya cases were identified in the Caribbean in late 2013 and in Florida in July 2014. Patients with dengue and chikungunya in areas where the vectors are likely present should be sequestered from mosquitoes while viremic to avoid local transmission.

### C. Identify Potential Sources of Infection

Obtain a detailed travel history, including specific locations and travel dates, and ask about arthropod exposures during the likely exposure period. For suspected Zika virus infection, also ask about unprotected sexual exposures to a person who traveled to an area where Zika virus is circulating. If exposure within the United States is suspected for dengue, Zika, or chikungunya, notify DOH Communicable Disease Epidemiology immediately (206-418-5500).

Ask about receiving blood products or about organ or tissue transplants.

### D. Identify Close Contacts or Other Potentially Exposed Persons

Identify others who traveled with the patient. Determine if the patient donated blood or organs, breastfed, or gave birth in the month preceding illness onset.

### E. Management of Contacts/Others Exposed

Arboviral infections are not generally transmitted from person-to-person, except for rare cases of sexual transmission, transplacental transmission, organ transplantation, or blood transfusion. If the patient donated blood or organs, inform the blood or tissue bank of the potential exposure. In cases of potential mother-to-infant transmission, monitor the infant



for compatible signs and symptoms.

Instruct others persons potentially exposed to the same source to seek medical attention if symptoms of arboviral disease develop. Even if no symptoms developed from travel to an area affected by Zika, after travel, men should use condoms consistently and correctly when having sex with pregnant women (for the duration of pregnancy) or women who could become pregnant (for 3 months after last exposure date), and women who travel should avoid unprotected sex with pregnant women (for the duration of pregnancy), or for 2 months after last exposure date.

## F. Environmental Evaluation/Management

Consider outreach to educate the public about avoiding arthropod exposure.

Environmental measures to reduce local arboviral transmission may include the elimination of mosquito breeding habitats and the use of chemical (i.e., pesticides) and biological controls. Notify local environmental health program and/or vector control of locally acquired cases, so that they may determine and institute appropriate intervention measures. In outbreak settings, an investigation may assist in identifying and controlling factors favoring transmission.

## 6. MANAGING SPECIAL SITUATIONS

Not applicable

## 7. ROUTINE PREVENTION

### A. Immunization Recommendations

#### Japanese Encephalitis Vaccine:

Persons planning to travel or reside in areas where Japanese encephalitis is endemic or epidemic should consult with a travel medicine health provider regarding the need for Japanese encephalitis vaccine.

To learn more about vaccine indications, contraindications and side effects, see the CDC website <https://www.cdc.gov/japaneseencephalitis/qa/index.html> and the recommendations from the ACIP (Centers for Disease Control and Prevention. Inactivated Japanese Encephalitis Virus Vaccine Recommendations of the Advisory Committee on Immunization Practices [ACIP], MMWR. Jan. 8, 1993;42:11. Available at <https://www.cdc.gov/mmwr/preview/mmwrhtml/00020599.htm>).

### B. Prevention Recommendations

To prevent arboviral diseases, persons should avoid arthropod bites by:

- Considering postponing travel to areas with active Zika transmission if pregnant or trying to become pregnant.
- Wearing a long sleeve shirt, long pants, and a hat when going into mosquito- or tick-infested areas, such as wetlands or woods. Tuck pant legs into socks or boots and shirts into pants to keep ticks on the outside of clothing where they can be more easily spotted and removed.

- Using mosquito repellent when necessary. The most effective mosquito repellents contain the EPA-approved active ingredients DEET (N, N-diethyl-m-toluamide), Picaridin, oil of lemon eucalyptus, or IR3535. Read and follow instructions on the label. Permethrin is another long-lasting repellent that is intended for application to clothing and gear, but not directly to skin. In general, the more active ingredient (higher concentration) a repellent contains, the longer time it protects against mosquito bites. Do not over use repellents. Take special care when using repellent on children.
- When traveling, using mosquito bed nets when exposure to mosquitoes may occur at night.
- Additional information regarding the use of repellents can be found on the CDC website at: <https://www.cdc.gov/westnile/faq/repellent.html>.

Persons traveling to arboviral endemic areas should consult with a travel clinic health care provider regarding additional measures which should be taken in specific areas.

## ACKNOWLEDGEMENTS

This document is a revision of the Washington State Guidelines for Notifiable Condition Reporting and Surveillance published in 2002 which were originally based on the Control of Communicable Diseases Manual (CCDM), 17<sup>th</sup> Edition; James Chin, Ed. APHA 2000. We would like to acknowledge the Oregon Department of Human Services for developing the format and select content of this document.

## UPDATES

July 2008: In Section 2C, the number of dengue fever cases reported each year was changed from 0–8 to 0–10. In Section 8B, IR3535 was added as a safe and effective mosquito repellent.

March 2010: In Section 1B, requirements for the veterinarian were clarified to distinguish animal and human case reporting. In Section 1C, reporting of suspect cases was included (to reflect new 2010 CSTE dengue case definition). Section 3A was revised to include a clinical illness description and to differentiate the laboratory criteria for diagnosis from the case definitions. In Section 3B, the dengue case definition was updated. Sections 4B and 4C, the laboratory testing available at PHL was updated. In Section 5, case investigation guidelines were amended.

January 2011: The Legal Reporting Requirements section has been revised to reflect the 2011 Notifiable Conditions Rule revision. In section 2, modes of transmission were updated (E) and the CAL serogroup was updated in Table 1. Section 3A was completely replaced to reflect the 2011 CSTE case definition for Arboviral disease (non-dengue). In Section 3B, the laboratory criteria were updated to clarify the requirements for P/N ratio. Section 4B was modified to reflect current test availability at PHL as of November 2010.

July 2014: Section 3A was revised to reflect the 2014 CSTE case definition for Arboviral disease (non-dengue), in which the requirement about documented temperature of fever was changed. For arboviral diseases (other than dengue), fever has been removed entirely from the criteria for neuroinvasive disease; it no longer needs to be measured for non-neuroinvasive disease. The laboratory criteria were differentiated for neuroinvasive disease and non-neuroinvasive disease. The “Routine Case Investigation” and “Controlling Further Spread” sections were merged into a single section.

January 2015: Section 2C was updated to reflect the recent travel-associated cases of chikungunya virus infection in Washington State. Section 3B was revised to reflect the 2015 CSTE case definition for dengue. This revision changed the categories for clinical description from dengue fever, dengue hemorrhagic fever, and dengue shock syndrome to dengue-like illness, dengue, and severe dengue. Clinical and lab criteria for classification were updated to reflect the national definition. Section 5B was revised to include information on length of time a person diagnosed with a dengue infection is prohibited from blood or organ donation.

April 2015: Section 3B(2) was revised to include classification for a person living in a dengue endemic or non-endemic area of the United States without evidence of other flavivirus transmission.

January 2017: The following sections were revised to include Zika virus information: Sections 1C, 2B, C, E, G, and H, 4B, 5B, C and E, and 7B. Section 3C was added to include the 2016 CSTE case definitions for Zika virus disease congenital, Zika virus disease non-congenital, Zika virus infection congenital, and Zika virus infection non-congenital.

Mar 2019: Routine updates, edited Table 1 to include genus. Edited the dengue case definition laboratory evidence to include IgM positive result combined with a PRNT result as criteria for lab confirmation. Updated guidelines for breastfeeding women infected with Zika. Updated Section 5B to reflect updated Zika guidance.

December 2022: For 2023 WAC revision combined provider and facility reporting requirement (Section 1B1-2), updated laboratory submission (Section 1B3)

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