CHIKUNGUNYA VIRUS INFECTION
(CHIKV)

REPORTING INFORMATION

- **Class B:** Report by the end of the next business day after the case or suspected case presents and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report to the local public health department in which the reporting health care provider or laboratory is located.
- Reporting Form(s) and/or Mechanism:
    - The Ohio Disease Reporting System (ODRS) should be used to report lab findings to the Ohio Department of Health (ODH). For healthcare providers without access to ODRS, you may use the Ohio Confidential Reportable Disease Form (HEA 3334, rev. 1/09).
    - The ODH Mosquito-borne Illness Case Investigation Form is available for use to assist in local disease investigation. Information collected from the form should be entered into ODRS and not sent to ODH, unless otherwise requested. If requested, the form can be faxed to ODH at (614) 564-2456.
- Key fields for ODRS reporting include: import status (whether the infection was travel-associated or Ohio-acquired), date of illness onset and all fields in the Epidemiology module.

AGENT

Chikungunya virus is an RNA virus that belongs to the *Alphavirus* genus in the family Togaviridae. The name chikungunya comes from an African word meaning "that which bends," describing the stooped appearance of persons suffering with the characteristic painful arthralgia.

Infectious dose: A single bite of an infectious mosquito.

CASE DEFINITION

Clinical Description

Most arboviral infections are asymptomatic. Clinical disease ranges from mild febrile illness to severe encephalitis. For the purpose of surveillance and reporting, based on their clinical presentation, arboviral disease cases are often categorized into two primary groups: 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 headache, myalgia, stiff neck, altered mental status, seizures, limb weakness or cerebrospinal fluid (CSF) pleocytosis. AFP may result from anterior myelitis, peripheral neuritis or post-infectious peripheral demyelinating neuropathy (i.e., Guillain-Barre 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 (e.g., West Nile fever) that may include headache, myalgia, arthralgia, rash or gastrointestinal symptoms. Some viruses can also cause more characteristic clinical manifestations, such as severe polyarthralgia or arthritis due to chikungunya virus or other alphaviruses (e.g., Mayaro, Ross River, O'nyong-nyong).

Clinical Criteria for Diagnosis
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 (chills) as reported by the patient or a healthcare 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.

Laboratory Criteria for Diagnosis
- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, cerebrospinal fluid (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 or serum.

Case Classification
Probable:
- Neuroinvasive disease: A case that meets the above clinical criteria for neuroinvasive disease and with virus-specific IgM antibodies in CSF or serum but with no other testing.
- Non-neuroinvasive disease: A case that meets the above clinical criteria for non-neuroinvasive disease and with virus-specific IgM antibodies in serum but with no other testing.

Confirmed:
- Neuroinvasive disease: A case that meets the above clinical criteria for neuroinvasive disease and one or more the following laboratory criteria:
  - 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 IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen or
  - Virus-specific IgM antibodies in CSF, with or without a reported pleocytosis, and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred.
- Non-neuroinvasive disease: A case that meets the above clinical criteria for non-neuroinvasive disease and one or more of the following laboratory criteria:
  - 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 IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen.

** It is important to distinguish chikungunya virus from dengue due to the potential for worse outcomes (including death) from dengue. The two diseases can occur together in the same patient.

Comments

Imported Arboviral Diseases

Human disease cases due to dengue or yellow fever viruses are nationally notifiable to CDC using specific case definitions. However, many other exotic arboviruses (e.g., Japanese encephalitis, tick-borne encephalitis, Venezuelan equine encephalitis and Rift Valley fever viruses) are important public health risks for the United States as competent vectors exist that could allow for sustained transmission upon establishment of imported viral pathogens. Healthcare providers and public health officials should maintain a high index of 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 appropriate local/state health agencies and CDC.

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 may be needed and results compared to determine the specific causative virus. For example, such testing might be needed to distinguish antibodies resulting from infections within genera (e.g., flaviviruses such as West Nile, St. Louis encephalitis, Powassan, dengue 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.
- Persistence of IgM antibodies: Arboviral IgM antibodies may 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.
- 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).

- Other information to consider: Vaccination history, detailed travel history, date of onset of symptoms and knowledge of potentially cross-reactive arboviruses known to circulate in the geographic area should be considered when interpreting results.

SIGNS AND SYMPTOMS

Unlike other arboviral infections, most people infected with chikungunya virus will develop symptoms. Symptoms usually begin 3-7 days after being bitten by an infected mosquito and most commonly include fever (typically >39°C [102°F]) and polyarthralgia. Joint symptoms are usually bilateral and symmetric and can be severe and debilitating. Other symptoms may include headache, myalgia, arthritis, conjunctivitis, nausea/vomiting or maculopapular rash.

Infection with chikungunya virus does not often result in death, but the symptoms can be severe and disabling. Most patients' symptoms resolve within 7-10 days, but in some people, joint pain may persist or relapse for months to years. Complications are rare, but can include uveitis, retinitis, myocarditis, hepatitis, nephritis, bullous skin lesions, hemorrhage, meningo-encephalitis, myelitis, Guillain-Barre syndrome and cranial nerve palsies.

DIAGNOSIS

Preliminary diagnosis is often based on a patient's clinical features, places and dates of travel (if patient is from a non-endemic country or area), activities and epidemiologic history of the location where infection likely occurred. In addition to the other more common causes of encephalitis and aseptic meningitis (e.g., herpes simplex virus and enteroviruses), arboviruses such as LaCrosse, St. Louis encephalitis, Eastern equine encephalitis, Western equine encephalitis, Powassan and West Nile viruses should also be considered in the differential etiology.

Laboratory tests used for diagnosing chikungunya include viral culture, reverse transcriptase-polymerase chain reaction (RT-PCR), detection of IgM or IgG antibodies by enzyme-linked immunosorbent assay (ELISA) or immunofluorescence assay (IFA), plaque reduction neutralization test (PRNT) and immunohistochemical staining (IHC). The optimal timing for chikungunya virus assays are:

- Viral culture: $\leq$ 3 days after illness onset
- RT-PCR: $\leq$ 5 days after illness onset
- IgM antibody tests: $\geq$ 5 days after illness onset

IgM antibodies are generally first detectable 4-8 days after illness onset and can persist for months. Serum collected within 8 days of illness onset may not have detectable IgM antibodies, and testing should be repeated on a convalescent-phase sample collected 2-3 weeks after the acute-phase sample.

Currently, there are five laboratories in the United States that perform diagnostic chikungunya testing: CDC Arbovirus Diagnostic Laboratory; California, Florida and New York state public health laboratories; and FOCUS Diagnostics. Specimens are usually blood or serum, but for cases with neuroinvasive disease, cerebrospinal fluid (CSF) may also be obtained.

For clinical samples being sent to CDC's Arbovirus Diagnostic Laboratory for testing, the CDC Specimen Submission Form must accompany the samples. Be sure the date of illness onset and travel history fields are completed. Use test order code CDC-10282 for arbovirus serology. Please contact ODH at (614) 995-9955 to arrange for testing at CDC.

EPIDEMIOLOGY

Source

Humans serve as the primary chikungunya reservoir during epidemic periods. During inter-epidemic periods, several vertebrates have been implicated as potential reservoirs, including non-human primates, rodents, birds and some small mammals. There are two main vectors of chikungunya: *Aedes aegypti* and *Aedes albopictus*. Both mosquito species are widely distributed throughout the tropics with *Ae. albopictus* also present at more temperate latitudes. Given the vectors' distribution throughout the Americas, the entire region is susceptible to the invasion and spread of chikungunya virus.

Susceptibility

All individuals not previously infected with chikungunya (naïve individuals) are at risk for infection and developing disease. Chikungunya virus infection is thought to confer life-long immunity. Persons at risk for severe disease include neonates exposed intrapartum, older adults (e.g., > 65 years) and persons with underlying medical conditions (e.g., hypertension, diabetes, or cardiovascular disease).

Occurrence

Chikungunya virus was first isolated from the blood of a febrile patient in Tanzania in 1953 and has since been cited as the cause of numerous human epidemics in many areas of Africa and Asia and most recently in limited areas of Europe. A 2007 outbreak in northern Italy highlighted the risk of local transmission of the virus via imported cases. Like Italy, the United States harbors competent mosquito vectors and naïve hosts, which creates a potential for emergence of chikungunya virus. In late 2013, local transmission of chikungunya virus on the Caribbean island of St. Martin was reported. Since then, the virus has spread to other countries and territories in the Caribbean and South America.

Mode of Transmission

Chikungunya virus is spread by the bite of infected *Ae. aegypti* and *Ae. albopictus* mosquitoes. Mosquitoes become infected when they feed on a person infected with chikungunya virus. Infected mosquitoes can then spread the virus to other humans when they bite. While most cases are due to vector-borne transmission from an infected mosquito, vertical transmission from mother to child, blood-borne and laboratory transmission have also been documented. These exposures indicate that direct contact transmission can occur. There is no evidence that the virus is transmitted through breast milk. Transmission from organ donation is theoretically possible.

Period of Communicability

Chikungunya is communicable during the acute illness for a week after illness onset, as long as viremia is present.

Incubation Period

The incubation period is 1-12 days, but is usually 3-7 days.

PUBLIC HEALTH MANAGEMENT

Case

<u>Investigation</u>

With serologic identification of chikungunya virus infection, a complete travel history for the three weeks prior to onset should be obtained. The patient should also be questioned about donating or receiving blood, blood products and organs in the 4 weeks prior to onset of symptoms. Female patients should be asked whether they were pregnant at the time of infection, and infants should be checked whether they were breastfed before illness onset. Sites of outdoor exposure and activities can be evaluated

for the presence of *Aedes* mosquitoes by standard collection techniques (light traps, larval samples).

Organ, Tissue or Blood Donors or Recipients
If the patient is a recent organ, tissue or blood donor or recipient, notify the blood or tissue banks and ensure remaining co-component blood or tissue products are quarantined. Working with the blood or tissue bank, identify other possibly exposed patients, and notify ODH and CDC.

Treatment
There is no specific antiviral drug treatment for chikungunya. Symptomatic treatment is recommended after excluding more serious conditions like malaria, dengue and bacterial infections. Persistent joint pain may benefit from use of non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids or physiotherapy.

Isolation and Follow-up Specimens
Although no specific isolation procedures are in place, acutely infected persons should avoid being bitten by *Aedes* mosquitoes during the week after illness onset, in order to prevent further transmission of the virus. A convalescent sample 2-4 weeks after the acute may be required to confirm a case.

Public Health Significance
High in endemic areas. Identification of a locally acquired case of chikungunya in Ohio warrants a vector investigation and vector control strategies to prevent an outbreak.

Contacts
No treatment or prophylaxis of contacts is indicated.

Prevention and Control
Vaccination
There is no vaccine or preventive drug currently available.

Vector Investigation
Acutely infected persons must avoid being bitten by *Aedes* mosquitoes during the week after illness onset, in order to prevent further transmission of the virus. Depending on local resources, environmental assessments around the homes of suspected viremic cases for *Aedes albopictus* mosquitoes may be useful to determine the risk for local transmission of chikungunya. Those jurisdictions with capacity should consider:

- Adult mosquito control:
    - *Ae. albopictus* (and *Ae. aegypti*) are most active during the day and are not effectively controlled by standard ultra-low volume (ULV) applications. Early morning or late evening applications are recommended.
    - Focus ULV or barrier applications to the areas where human cases are present to reduce local transmission.
- Larval mosquito control:
    - Remove larval habitats.
    - Encourage the public to participate in efforts by discarding containers (e.g., flower pots, buckets, garbage cans, tires, etc.).

Mosquito Bite Avoidance

The best way to prevent chikungunya virus infection is to avoid mosquito bites. Prevention tips are similar to those for other viral diseases transmitted by mosquitoes, such as dengue or West Nile virus:

- Use insect repellent containing DEET, picaridin, oil of lemon eucalyptus, IR3535 or para-menthane-diol products on exposed skin. Always follow the directions on the package. When using both sunscreen and insect repellent, apply the sunscreen first then the repellent.
- Wear long sleeves, pants and socks if feasible.
- Wear permethrin-treated clothing to repel and kill mosquitoes.
- Use screens on windows and doors to exclude mosquitoes. And, when available, A/C can make households less hospitable to mosquitoes.
- Participation in community and homeowner based vector-control strategies:
    - Ensure that water does not collect in containers around the home and community by emptying water from containers such as flowerpots, buckets, barrels and tires. Change the water in pet dishes, and replace the water in bird baths weekly. Drill holes in tire swings so water drains out. Empty children's wading pools and store on their sides after use.
    - Use chemical or biological control of larvae and adult mosquitoes when necessary.

What is chikungunya?
Chikungunya is a viral disease transmitted by mosquitoes. The name chikungunya is derived from an African word that roughly means "that which bends," describing the stooped appearance of persons suffering with the characteristic painful arthritis. The disease has occurred in Africa, Southeast Asia, Southern Europe and islands in the Indian and Pacific Oceans. In late 2013, chikungunya was found for the first time in islands in the Caribbean.

What are the symptoms of chikungunya?
Symptoms of chikungunya include a sudden onset of high fever (typically greater than 102°F [39°C]) and severe joint pain, often in the hands and feet. Other symptoms may include headache, muscle aches, joint swelling or rash.

How long after being infected do symptoms appear?
The incubation period (time from infection to illness) can be 1-12 days, but is usually 3-7 days. Most people infected with the virus will develop some symptoms. Chikungunya virus infection is thought to confer life-long immunity. Fatalities related to chikungunya virus are rare.

How long do symptoms last?
Most people feel better within a week, but some patients have prolonged joint pain which may last for weeks or months.

How can I get chikungunya?
A person can get chikungunya by being bitten by an infected mosquito. Rarely, chikungunya has been transmitted from an infected mother to her unborn child and through infected blood. Transmission from blood transfusion or organ transplantation is theoretically possible, but has not been documented. There is no evidence that the virus is transmitted through breast milk.

Who is at risk?
Anyone who has not previously had chikungunya (naïve individuals) is at risk of acquiring infection and developing disease. It is believed that once exposed to chikungunya, individuals will develop long-lasting immunity that will protect them against re-infection. Persons at risk for severe disease include babies exposed at birth, older adults (> 65 years) and persons with underlying medical conditions (e.g., hypertension, diabetes or cardiovascular disease).

What should I do if I think I have chikungunya?
See your healthcare provider, who will ask you to submit blood specimens to see if you have been exposed to the virus.

What is the treatment for chikungunya?
There is no vaccine or specific antiviral treatment currently available for chikungunya. Treatment includes rest, fluids and medicines to relieve symptoms of fever and aching such as ibuprofen, naproxen, acetaminophen or paracetamol. Aspirin should be avoided. Infected persons should avoid further mosquito exposure (staying indoors in areas with screens and/or under a mosquito net) during the first week of the illness so they do not contribute to the transmission cycle.

How can I prevent chikungunya?
There are no known cases of chikungunya cases that have been acquired in the continental United States or Ohio. Cases have been reported in travelers who have traveled to areas where chikungunya is in the mosquito population. Travelers to chikungunya infected areas can reduce their risk of being infected by using insect repellent, wearing protective clothing, and staying indoors while mosquitoes are most active.

Reducing exposure to mosquitoes is the best defense against infection with chikungunya and other mosquito-borne viruses. There are several approaches you and your family can use to prevent and control mosquito-borne diseases.

- Use repellent: When outdoors, use insect repellent containing DEET, picaridin, IR3535, or oil of lemon eucalyptus on exposed skin as well as on clothing (mosquitoes will bite through thin cloth).
    - Permethrin is a repellent/insecticide that can be applied to clothing and will provide excellent protection through multiple washes. You can treat clothing yourself (always follow the directions on the package!) or purchase pre-treated clothing. For best protection it is still necessary to apply other repellent to exposed skin.
- Wear protective clothing: Wear long sleeves, pants and socks when weather permits.
- Avoid peak biting hours: Avoid outdoor activity or use protective measures when mosquitoes are active (*Aedes aegypti* are most active during the day, and *Aedes albopictus* typically feeds in the daytime in addition to at dusk and dawn).
- Install and repair screens: Have secure, intact screens on windows and doors to keep mosquitoes out.
- Keep mosquitoes from laying eggs near you: Mosquitoes can lay eggs even in small amounts of standing water. Get rid of mosquito breeding sites by emptying standing water from flower pots, buckets, barrels and tires. Change the water in pet dishes and replace the water in bird baths weekly. Drill holes in tire swings so water drains out. Empty children's wading pools and store on their side after use.

For more information, please visit these websites:

- ODH Chikungunya Information: http://www.odh.ohio.gov/chikv
- CDC Chikungunya Information: http://www.cdc.gov/chikungunya
- CDC Insect Repellent Use & Safety: http://www.cdc.gov/westnile/faq/repellent.html
- World Health Organization: http://www.who.int/mediacentre/factsheets/fs327/en/
- Pan-American Health Organization: http://www.paho.org/hq/index.php?option=com_topics&view=article&id=343&Itemid=40931