Chikungunya and dengue fever are both caused by viruses transmitted by mosquitoes\(^1\)\(^-\)\(^6\). The two most important vector species involved in transmission are *Aedes aegypti* and *Aedes albopictus*\(^1\)\(^-\)\(^6\). The two viruses have similar epidemiological, environmental, entomological, and clinical patterns and will be discussed in the same section. As of this writing, neither virus is locally-acquired in Arizona, and cases are associated with travel to endemic areas\(^7\)\(^-\)\(^9\). However, imported cases are also a public health concern because *Aedes aegypti* mosquitoes are present in Arizona and infected humans can spread the disease to mosquitoes\(^7\)\(^-\)\(^9\). There have been recorded outbreaks caused by both of these viruses throughout tropical regions of the world, including but not limited to, sub-Saharan Africa, India, South America, and Southeast Asia\(^1\)\(^-\)\(^6\).

For additional background information on chikungunya virus and dengue fever please see the ADHS Arboviral Handbook.

A. Agent:

Chikungunya virus is an alphavirus, which is a genus in the *Togaviridae* family of viruses\(^3\)\(^-\)\(^6\). The family is comprised of enveloped, single-stranded RNA viruses\(^10\). Dengue virus is in the genus flavivirus in the family *Flaviviridae*\(^1\)\(^-\)\(^3\). Viruses of the flavivirus genus are linear, single-stranded, positive-sense RNA\(^11\). Dengue virus has four distinct serotypes: DENV-1, DENV-2, DENV-III, DENV-IV\(^1\)\(^-\)\(^3\)\(^,9\).

B. Clinical Description:

Dengue fever and chikungunya fever present with very similar clinical symptoms\(^1\)\(^-\)\(^9\). Both are acute febrile illnesses sometimes accompanied by headache, rash, myalgia, arthralgia, general weakness, and extreme fatigue\(^1\)\(^-\)\(^9\). It is believed that nearly 75% of dengue cases are asymptomatic\(^1\)\(^-\)\(^3\)\(^,7\)\(^,9\). For chikungunya virus, between 10-20% of infections are thought to remain asymptomatic\(^4\)\(^-\)\(^6\)\(^,8\)\(^-\)\(^9\).

*Chikungunya fever* is more likely to present with a severe rash and extreme arthritis\(^4\)\(^-\)\(^6\)\(^,8\)\(^-\)\(^9\). The arthritis is the most distinguishing symptom, and can be severe and long lasting\(^4\)\(^-\)\(^6\)\(^,8\)\(^-\)\(^9\).

*Dengue fever* is more likely to present with general muscle/bone pain, and lead to more severe disease with hemorrhagic manifestations\(^5\)\(^-\)\(^3\)\(^,7\)\(^,9\).

C. Reservoirs:

Infected humans are the primary reservoir that keeps chikungunya virus and dengue virus circulating in the environment\(^1\)\(^-\)\(^9\). In some parts of the world, non-human primates may act as a reservoir for these viruses, but they are not a necessary component of the transmission cycle\(^1\)\(^-\)\(^9\). The *Aedes* mosquito vector is also an important and required component of viral survival\(^1\)\(^-\)\(^9\).

D. Mode of Transmission:

Transmission occurs in a human-mosquito-human cycle\(^1\)\(^-\)\(^9\). Humans and mosquitoes are the only *required* factors in transmission\(^1\)\(^-\)\(^9\). The virus spreads when an infected mosquito feeds
on a human and the human contracts the infection\textsuperscript{1-9}. Next, another uninfected mosquito feeds on that same human and picks up the virus during the blood meal\textsuperscript{1-9}. During another blood meal the mosquito may spread the virus to a new human host\textsuperscript{1-9}.

E. Incubation Period:
Both have an average incubation period of 3-7 days (range is 3-10 days for dengue fever and 1-12 days for chikungunya) following the bite of an infected mosquito\textsuperscript{1-6,9}.

F. Period of Communicability:
Person-to-person transmission of dengue or chikungunya virus is not possible\textsuperscript{1-6,9}. When infected, people can be viremic and infectious to mosquitoes during the first few days of illness—usually for less than 5 days after symptom onset\textsuperscript{1-6,9}.

G. Susceptibility and Resistance:
Generally, all individuals are susceptible to disease\textsuperscript{3,6,9}. Following the clearance of an infection with either of these pathogens, the host has acquired immunity\textsuperscript{3,6,9}. With chikungunya, this is believed to mean lifelong protection against disease\textsuperscript{3,9}. With dengue, people only acquire immunity to the strain to which they were exposed\textsuperscript{1-3,9}. Therefore, repeat infections with a separate serotype are possible\textsuperscript{1-3,9}. In fact, second infections with a novel serotype typically lead to more serious outcomes, due to an overreaction of the host’s immune system to the dengue virus antigens\textsuperscript{1-3,9}. Vaccines are in production for both viruses, but none are currently available\textsuperscript{1-6,9}.

H. Treatment:
There is no specific treatment, cure, or vaccine for either chikungunya or dengue virus\textsuperscript{1-6,9}. The best course of action is bed rest, fluids to prevent dehydration, and analgesics for pain control\textsuperscript{1-6,9}. For dengue, fever-reducing analgesics with acetaminophen can be used; aspirin, non-steroidal anti-inflammatory drugs (NSAIDS), and corticosteroids should be avoided due to an increased risk of bleeding and hemorrhagic symptoms\textsuperscript{1-3,9}. Supportive therapy can also be helpful\textsuperscript{1-6,9}.

I. Clinical Case Definition\textsuperscript{11}:
An illness characterized by one or more of the following clinical features:

Chikungunya - a case presenting with fever or chills 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.

Dengue – Clinical Syndromes

Dengue-Like Illness\textsuperscript{12-13} - Defined as a fever reported by the patient or healthcare provider.

Dengue\textsuperscript{12-13} - Defined by 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
- Aches and pains (e.g., headache, retro-orbital pain, joint pain, myalgia, arthralgia)
- Tourniquet test positive
- Leukopenia (a total white blood cell count of <5,000/mm\textsuperscript{3})
- Any warning sign for severe dengue\textsuperscript{1-3,9}
  - Abdominal pain or tenderness
- Persistent vomiting
- Extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites)
- Mucosal bleeding at any site
- Liver enlargement >2 centimeters
- Increasing hematocrit concurrent with rapid decrease in platelet count

**Severe Dengue**\(^\text{12-13}\) - Defined as dengue with any 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 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) ≥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

### J. Laboratory Criteria for Diagnosis:

<table>
<thead>
<tr>
<th>Chikungunya (Arboviral) Case Classification(^\text{12,14})</th>
<th>(See also the chikungunya case classification flowchart on page 11 of the ADHS Arboviral Handbook)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Confirmed</strong></td>
<td>A clinically compatible case presenting with fever or chills 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—with one or more of the following laboratory criteria:</td>
</tr>
<tr>
<td></td>
<td>● Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, OR</td>
</tr>
<tr>
<td></td>
<td>● Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, OR</td>
</tr>
<tr>
<td></td>
<td>● Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen</td>
</tr>
<tr>
<td><strong>Probable</strong></td>
<td>A clinically compatible case presenting with fever or chills 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—with the following laboratory criteria:</td>
</tr>
<tr>
<td></td>
<td>● Virus-specific IgM antibodies in CSF or serum but with no other testing</td>
</tr>
<tr>
<td><strong>Not a Case</strong></td>
<td>A case that does not match the above clinical picture or have any of the above lab or epidemiological results.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dengue Case Classification(^\text{12-13})</th>
<th>(See also the dengue case classification flowchart on page 23 of the ADHS Arboviral Handbook)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Confirmed</strong></td>
<td>A confirmed case is defined as a clinically compatible case of dengue-like illness, dengue or severe dengue AND having any one or more of the following test results:</td>
</tr>
<tr>
<td></td>
<td>● Detection of DENV nucleic acid in serum, plasma, blood, cerebrospinal fluid (CSF), other body fluid or tissue by validated reverse transcriptase-PCR</td>
</tr>
</tbody>
</table>

Chikungunya and Dengue Virus Protocol
Last Revised: 3/14/2022
| Detection of DENV antigens in tissue by a validated immunofluorescence or immunohistochemistry assay |
| Detection in serum or plasma of DENV NS1 antigen by a validated immunoassay |
| Cell culture isolation of DENV from a serum, plasma, or CSF specimen |
| Detection of IgM anti-DENV by validated immunoassay in a serum specimen or CSF in a person living in a dengue endemic or non-endemic area of the U.S. without evidence of other flavivirus transmission (e.g., WNV, SLEV, or recent vaccination against a flavivirus (e.g., YFV, JEV)) |
| Detection of IgM anti-DENV in a serum specimen or CSF by validated immunoassay in a traveler returning from a dengue endemic area without ongoing transmission of another flavivirus (e.g., WNV, JEV), clinical evidence of co-infection with one of these flaviviruses, or recent vaccination against a flavivirus (e.g., YFV, JEV) |
| IgM anti-DENV seroconversion by validated immunoassay in acute (i.e., collected <5 days of illness onset) and convalescent (i.e., collected >5 days after illness onset) serum specimens |
| IgG anti-DENV seroconversion or ≥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) with a >4-fold higher end point titer as compared to other flaviviruses tested |

**Probable**

A probable case has as a clinically compatible case of dengue-like illness, dengue or severe dengue AND one or more of the following:

- Detection of IgM anti-DENV by validated immunoassay in a serum specimen or CSF in a person living in a dengue endemic or non-endemic area of the U.S. with evidence of other flavivirus transmission (e.g., WNV, SLEV), or recent vaccination against a flavivirus (e.g., YFV, JEV).
- Detection of IgM anti-DENV in a serum specimen or CSF by validated immunoassay in a traveler returning from a dengue endemic area with ongoing transmission of another flavivirus (e.g., WNV, JEV), clinical evidence of co-infection with one of these flaviviruses, or recent vaccination against a flavivirus (e.g., YFV, JEV).

**Suspect**

A suspect is defined as a clinically compatible case of dengue-like illness, dengue or severe dengue AND a negative IgM anti-DENV 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*.

*The person under investigation is not a case if there is no laboratory or epidemiological evidence supporting the diagnosis.

**Not a Case**

A case that does not match the above clinical picture or have any of the above lab or epidemiological results.

**K. Classification of Import Status:**

A case is considered imported if the person became infected outside of the U.S. This should be considered when there is opportunity for exposure and epidemiological evidence more suggestive of infection elsewhere. A case may also be imported from one state into another, or one local jurisdiction into another. All opportunities for exposure and epidemiological evidence should be documented for assessment of import status. The majority of dengue and chikungunya in the U.S. are imported cases; however, it is crucial to always confirm travel history1-6,9. To assess import status, focus on the travel history two weeks prior to
symptom onset. If the case traveled to an endemic area in that time period they may have imported it, if not, it may be a local case. Because both chikungunya and dengue are emerging diseases, an accurate assessment of importation status is very important.

L. Laboratory Testing:
For both dengue fever and chikungunya, submit serum for PCR, IgM EIA and, if needed, PRNT testing to the Arizona State Public Health Lab, together with patient travel history and date of symptom onset.

<table>
<thead>
<tr>
<th>TEST</th>
<th>SPECIMEN</th>
<th>METHOD</th>
<th>NOTES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serological Assay</td>
<td>Serum or blood sample, both acute and convalescent phase serum preferred</td>
<td>Detection of virus-specific IgM or rising titers of IgG</td>
<td>Flaviviruses can cross react on serologic assays. Consider plaque reduction neutralization assay to confirm serological assay results.</td>
</tr>
<tr>
<td>Immunohistochemistry</td>
<td>Tissue, blood or CSF</td>
<td>Detection of antigen</td>
<td></td>
</tr>
<tr>
<td>PCR</td>
<td>Tissue, blood or CSF</td>
<td>Detection of virus-specific RNA sequence</td>
<td></td>
</tr>
</tbody>
</table>

M. Assessing 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 circulate, serologic testing for more than one virus may be needed and results compared to determine the specific causative virus. Flaviviruses with potential cross-reaction include West Nile, St. Louis encephalitis, Powassan, Dengue, Japanese encephalitis virus, and Zika viruses. If the case was imported from outside of the jurisdiction consider testing for other arboviral diseases endemic to the area where the patient traveled.

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

N. Outbreak Definition:
A chikungunya or dengue outbreak is defined as any amount of confirmed or probable cases which outnumber the expected amount in a specific time and geographic location. Because dengue and chikungunya have never been locally acquired before, any locally acquired cases would be considered an outbreak. In addition, an increase in travel-associated cases could be considered an outbreak. However, importation status should be assessed prior to the outbreak assessment.

O. Time Frame:
Providers must submit a report to the Local Health Department within 5 working days after a case or suspect case is diagnosed, treated, or detected. Laboratories must submit a report to ADHS within 5 working days after obtaining a positive test result.
P. Forms:
- ADHS Dengue Investigation Form:
- ADHS Chikungunya Investigation Form:

Q. Investigation Steps:

- Confirm Diagnosis
  i. Before contacting the patient or family, determine what information is available from medical records, lab reports, and healthcare providers.
  ii. Obtain information that supports clinical findings in the case definition:
      ● Onset date, order of the symptoms, symptom severity and duration, hospitalization, and outcome/status.
  iii. Obtain information on any laboratory tests that were performed, along with results or date results are expected.
      ● If laboratory tests have not been run coordinate testing to confirm the case.
      ● Testing should be coordinated with ADHS.
        - Local Health Departments should request approval for testing by sending the following information to vbzd@azdhs.gov:
          o Age:
          o Gender:
          o Travel History (country AND state or city, if possible):
          o Mosquito Exposure (Y/N):
          o Dates of Travel:
          o Symptomatic/Asymptomatic:
          o Onset Date:
          o Symptoms:
          o Dengue Testing Requested (Y/N):
          o Chikungunya Testing Requested (Y/N):
          o Zika Testing Requested (Y/N):
          o Pregnant/#weeks:
          o MEDSIS ID:
        - ADHS will approve testing requests based on estimate of risk and current lab capacity.
        - ADHS staff will send epi info (along with name & date of birth) to the Virology/Serology department of ASPHL.
        - Local public health should ensure a lab submission form accompanies all specimens that go to the State Lab. The lab submission form should be included with the specimen (one form for each specimen submitted).

Conduct Case Investigation
Epidemiological investigation report should be submitted in MEDSIS by filling out the full DSO and Travel Table.
  i. Collect information as specified on the Communicable Disease Report:
     ● Demographic data (birth date, county, sex, race/ethnicity), dates of exposure, reason for infection (e.g. known mosquito contact, outdoor activities, etc.), and occupation.
     ● Resident of your county? If not, determine if the case is an international import or an out-of-state import.
● Travel history:
  - Dates of exit from and reentry to Arizona.
  - Locations (include dates of locations traveled).

ii. Focus on the 2-week incubation period. Did the patient travel outside the area in the past 2 weeks? If yes, should other arboviruses from that area be considered?

**Conduct Contact Investigation**

i. Susceptible contacts are anyone who came into contact with the same exposure source as the first patient. If the case was imported this may include anyone who was traveling with the case. If the case was acquired locally it would include anyone living in the household. The mosquito vectors involved in transmission have a preference for living in and around human homes.

**Initiate Control and Prevention Measures**

i. Any suspicious cases should be reported to the appropriate health authority. Chikungunya and dengue are not transmitted person-to-person, but can be spread by infected mosquitoes\(^1\)\(^{-9}\). Efforts should focus on identifying suspect cases and cooperating with vector control to apply insecticide at the exposure source and location, when possible\(^9\). If the case was locally acquired, vector control is considered *high priority* and should be conducted as soon as possible\(^9\). If the case was imported, vector control should still be notified of the case location and encouraged to focus surveillance and control efforts on that area\(^9\). The case’s household should also be educated about how to protect themselves from mosquito bites to prevent additional virus transmission into the local mosquito population. Messages can include\(^1\)\(^{-9}\):

  ● Proper use of DEET and other insect repellents. Always apply after sunscreen and reapply as needed.
  ● When experiencing symptoms it’s best to remain indoors.
  ● Use air conditioning instead of leaving doors and windows open to the outside, or make sure screens are intact and effective.
  ● Don’t let sitting water accumulate on your property (i.e. don’t leave out buckets, soda cans, or other containers). If water does accumulate, empty and scrub the container.
  ● If you experience more mosquitoes on your property call your local pest management agencies.

**Isolation and Restrictions**

i. Isolation is not required, but patients should be encouraged to avoid mosquitoes for 2 weeks following disease onset either by staying indoors or practicing increased vigilance with DEET-based insect repellents\(^1\)\(^{-9}\).

**Contact Management**

i. Focus should be on vector control and environmental interventions in and around cases’ homes. In imported cases, it’s important to evaluate travel companions for risk and illness. In locally acquired cases, members of the household should be evaluated for symptoms and instructed to take extra precautions.
• **Notifications**
  i. Report all cases by telephone to ADHS within 5 working days\(^{16}\).
  ii. Encourage the consideration of a chikungunya or dengue diagnosis in those fitting the clinical case definition and travel history.
  iii. As appropriate, notify the case, contacts, and other individuals or groups.

R. **Outbreak Guidelines:**
Refer to Outbreak Section of the Disease Investigation Manual.
References


