Chikungunya in the United States

Arboviral Diseases Branch
Division of Vector-Borne Diseases
Centers for Disease Control and Prevention

April 8, 2015
Chikungunya virus disease

- Mosquito-borne viral disease characterized by acute onset of fever and severe polyarthralgia
- Often occurs in large outbreaks with high attack rates
- Outbreaks have occurred in countries in Africa, Asia, Europe, and the Indian and Pacific Oceans
- In 2013, first locally-acquired cases in the Americas reported on islands in the Caribbean
Countries with reported local transmission of chikungunya virus disease
Reported chikungunya cases and number of countries/territories with local transmission in the Americas, Dec 2013–Mar 2015

>1.3 million suspected or confirmed cases
44 countries/territories
### Chikungunya virus disease cases reported to PAHO from selected countries in the Americas, Dec 2013–Apr 2015

<table>
<thead>
<tr>
<th>Country</th>
<th>Suspected (N=1,322,693)</th>
<th>Confirmed* (N=30,309)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dominican Republic</td>
<td>539,138 (41%)</td>
<td>84 (&lt;1%)</td>
</tr>
<tr>
<td>Colombia</td>
<td>243,060 (18%)</td>
<td>1,531 (5%)</td>
</tr>
<tr>
<td>El Salvador</td>
<td>144,335 (11%)</td>
<td>157 (&lt;1%)</td>
</tr>
<tr>
<td>Guadeloupe</td>
<td>81,350 (6%)</td>
<td>430 (1%)</td>
</tr>
<tr>
<td>Martinique</td>
<td>72,520 (5%)</td>
<td>1,515 (5%)</td>
</tr>
<tr>
<td>Haiti</td>
<td>64,695 (5%)</td>
<td>14 (&lt;1%)</td>
</tr>
</tbody>
</table>

*<1% of all reported cases are laboratory-confirmed
Chikungunya virus in the United States

- Prior to 2006, chikungunya rarely identified in U.S. travelers.

- From 2006‒2013, average of 28 cases per year in the United States
  - All were travelers to affected areas in Asia, Africa, or Indian Ocean
  - None resulted in known local transmission in the United States

- In 2014, after chikungunya virus local transmission was first identified in Caribbean countries and territories
  - Number of chikungunya cases in U.S. travelers increased significantly
  - Local transmission was identified in Florida, Puerto Rico, and USVI
States reporting chikungunya virus disease cases — United States, 2014 (as of February 10, 2015)

Cases (N=2,492)

Local 11 (<1%)

Imported 2,481 (99%)
Chikungunya virus disease cases reported by state — United States, 2014 (as of February 10, 2015)

<table>
<thead>
<tr>
<th>State</th>
<th>Travel-associated (N=2,481)</th>
<th>Locally-transmitted (N=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New York</td>
<td>740 (30%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Florida</td>
<td>447 (18%)</td>
<td>11 (100%)</td>
</tr>
<tr>
<td>New Jersey</td>
<td>171 (7%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>158 (6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>96 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>43 other states</td>
<td>869 (35%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
Chikungunya virus disease cases reported by territory — United States, 2014 (as of February 10, 2015)

<table>
<thead>
<tr>
<th>Territory</th>
<th>Travel-associated (N=46)</th>
<th>Locally-transmitted (N=4,467)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Puerto Rico*</td>
<td>32 (70%)</td>
<td>4,216 (94%)</td>
</tr>
<tr>
<td>US Virgin Islands†</td>
<td>14 (30%)</td>
<td>251 (6%)</td>
</tr>
</tbody>
</table>

*30,983 suspected cases also reported to Puerto Rico Dept of Health
†1,321 suspected cases also reported to USVI Dept of Health
States reporting chikungunya virus disease cases — United States, 2015 (as of April 7, 2015)

Cases (N=77)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Local</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Imported</td>
<td>77 (100%)</td>
</tr>
</tbody>
</table>
Chikungunya virus disease cases reported by state — United States, 2015 (as of April 7, 2015)

<table>
<thead>
<tr>
<th>State</th>
<th>Travel-associated (N=77)</th>
<th>Locally-transmitted (N=0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Florida</td>
<td>16 (22%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>New York</td>
<td>12 (18%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Maryland</td>
<td>7 (10%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>California</td>
<td>6 (9%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Texas</td>
<td>4 (6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>14 other states</td>
<td>32 (42%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
Chikungunya virus disease cases reported by territory — United States, 2015 (as of April 7, 2015)

<table>
<thead>
<tr>
<th></th>
<th>Travel-associated (N=0)</th>
<th>Locally-transmitted (N=56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Puerto Rico*</td>
<td>0 (0%)</td>
<td>51 (91%)</td>
</tr>
<tr>
<td>US Virgin Islands†</td>
<td>0 (0%)</td>
<td>5 (9%)</td>
</tr>
</tbody>
</table>

*341 suspected cases also reported to Puerto Rico Dept of Health
†18 suspected cases reported to USVI Dept of Health
Chikungunya virus

- Single stranded RNA virus
- Genus *Alphavirus*
- Family *Togaviridae*
- Closely related to Mayaro, O’nyong-nyong and Ross River viruses
Chikungunya virus vectors

- Transmitted by *Aedes aegypti* and *Aedes albopictus*
- Also transmit dengue virus
- Larvae develop in discarded tires and household containers
- Aggressive daytime-biting mosquitoes

*Aedes aegypti*  
*Aedes albopictus*
Approximate geographic distribution of *Aedes aegypti* and *Aedes albopictus* mosquitoes in the United States
Primary transmission cycle

Anthroponotic transmission
(person to mosquito to person)
Other modes of transmission

- Documented rarely
  - Intrapartum from viremic mother to child
  - \textit{In utero} transmission resulting in miscarriage
  - Percutaneous needle stick
  - Laboratory exposure

- Theoretical concern
  - Blood transfusion
  - Organ or tissue transplantation

- No evidence of virus in breast milk
Primary clinical symptoms

- Majority (72%–97%) of infected people symptomatic
- Incubation period usually 3–7 days (range 1–12 days)
- Primary clinical symptoms are fever and polyarthralgia
- Arthralgia usually bilateral and symmetric
- Pain can be severe and debilitating
Other common clinical signs and symptoms

- Headache
- Myalgia
- Arthritis
- Conjunctivitis
- Nausea/vomiting
- Maculopapular rash
Clinical laboratory findings

- Lymphopenia
- Thrombocytopenia
- Elevated creatinine
- Elevated hepatic transaminases
Atypical disease manifestations

- Uveitis
- Retinitis
- Hepatitis
- Nephritis
- Myocarditis
- Hemorrhage
- Myelitis
- Cranial nerve palsies
- Guillain-Barre syndrome
- Meningoencephalitis
- Bullous skin lesions*

*Primarily described in infants
Risk factors for hospitalization or atypical disease

- Neonates exposed intrapartum
- Older age (e.g., >65 years)
- Underlying medical conditions (e.g., diabetes, hypertension, or cardiovascular disease)
Clinical outcomes

- Acute symptoms typically resolve in 7‒10 days
- Mortality is rare; occurs mostly in older adults
- Some patients have relapse of rheumatologic symptoms* in months following acute illness
- Studies report variable proportions of patients with persistent joint pains for months or years

*Polyarthralgia, polyarthritis, tenosynovitis, Raynaud’s syndrome
Diagnostic testing

- Culture for virus*
- Reverse transcriptase-polymerase chain reaction (RT-PCR) for viral RNA
- Serology for IgM and neutralizing antibodies
- Serology for ≥4-fold rise in virus-specific quantitative antibody titers on paired sera†
- Immunohistochemical staining (IHC) for viral antigens

*Virus should be handled under biosafety level (BSL) 3 conditions
†Determined by plaque reduction neutralization test (PRNT) or immunofluorescence assay (IFA)
## Timing for diagnostic testing

<table>
<thead>
<tr>
<th>Diagnostic assay</th>
<th>Days post-illness onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral culture</td>
<td>≤3 days</td>
</tr>
<tr>
<td>RT-PCR</td>
<td>≤8 days</td>
</tr>
<tr>
<td>IgM antibody tests</td>
<td>≥4 days</td>
</tr>
</tbody>
</table>
Healthcare providers should contact their local health department to facilitate diagnostic testing.

Testing performed at CDC, state health departments, and commercial laboratories.

Commercial laboratories will only perform tests that are ordered by healthcare provider.

Several IgM antibody assays are commercially-available but not yet FDA-cleared.
## CDC evaluation of commercially-available chikungunya virus IgM antibody assays

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Assay</th>
<th>Type</th>
<th>Performance†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euroimmun*</td>
<td>Anti-CHIKV IgM</td>
<td>IFA</td>
<td>High</td>
</tr>
<tr>
<td>Euroimmun*</td>
<td>Anti-CHIKV IgM</td>
<td>ELISA</td>
<td>High</td>
</tr>
<tr>
<td>Inbios*</td>
<td>CHIKjj Detect MAC</td>
<td>ELISA</td>
<td>High</td>
</tr>
<tr>
<td>Abcam (NovaTec)*</td>
<td>Anti-CHIKV IgM human</td>
<td>ELISA</td>
<td>Inconsistent</td>
</tr>
<tr>
<td>Genway (NovaTec)*</td>
<td>CHIKV IgM χ-capture</td>
<td>ELISA</td>
<td>Low</td>
</tr>
<tr>
<td>CTK Biotech</td>
<td>RecombiLISA CHIK IgM</td>
<td>ELISA</td>
<td>Low</td>
</tr>
<tr>
<td>SD Diagnostics</td>
<td>CHIKa IgM</td>
<td>ELISA</td>
<td>Low</td>
</tr>
<tr>
<td>CTK Biotech</td>
<td>On-site CHIK IgM Combo</td>
<td>Rapid</td>
<td>Low</td>
</tr>
<tr>
<td>SD Diagnostics</td>
<td>SD BIOLINE CHIK IgM</td>
<td>Rapid</td>
<td>Low</td>
</tr>
</tbody>
</table>

*Available for purchase in the United States but not FDA-cleared
†Compared to CDC IgM capture ELISA
CDC steps to increase public health testing capacity

- Publish results of the commercially-available IgM antibody assay evaluations
- Provide reagents for CDC MAC-ELISA until commercial kit evaluation is published
- Provide protocol, primers/probe sequences, and RNA lysate for CDC RT-PCR
- Distribute RT-PCR and antibody test proficiency panels
Distinguishing chikungunya from dengue

- Viruses transmitted by same mosquitoes
- Diseases have similar clinical features
- Viruses can circulate in same area and cause co-infections
- Important to rule out dengue, as proper clinical management can improve outcome

*WHO dengue clinical management guidelines:
Clinical features of chikungunya virus infections compared to dengue virus infections

<table>
<thead>
<tr>
<th></th>
<th>Chikungunya</th>
<th>Dengue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (&gt;39°C)</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>+++</td>
<td>+/-</td>
</tr>
<tr>
<td>Arthritis</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Headache</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Rash</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Myalgia</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Shock</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>
Clinical laboratory features of chikungunya virus infections compared to dengue virus infections

<table>
<thead>
<tr>
<th></th>
<th>Chikungunya</th>
<th>Dengue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphopenia</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Hemoconcentration</td>
<td>-</td>
<td>++</td>
</tr>
</tbody>
</table>
Differential diagnosis for chikungunya

- Dengue
- Leptospirosis
- Malaria
- Rickettsia
- Parvovirus
- Enterovirus
- Group A streptococcus
- Rubella
- Measles
- Adenovirus
- Post-infectious arthritis
- Rheumatologic conditions
- Other alphavirus infections (e.g., Mayaro, Ross River, Barmah Forest, O’nyong-nyong, and Sindbis viruses)
Initial assessment and treatment

- No specific antiviral therapy; treatment is supportive
- Assess hydration and hemodynamic status
- Evaluate for other serious conditions and treat or manage appropriately
- Collect specimens for diagnostic testing for chikungunya and dengue
- Manage as dengue until it is ruled out
Use of aspirin and other NSAIDs

- Aspirin and other NSAIDs can increase risk of hemorrhage in patients with dengue

- If dengue in the differential diagnosis, do not use aspirin or other NSAIDs until afebrile ≥48 hours and no dengue warning signs*

- Use acetaminophen for initial fever and pain control

- Persistent joint pain may benefit from the use of NSAIDs, corticosteroids, or physiotherapy but no clinical trials

*Warning signs for severe dengue include bleeding, pleural effusion or ascites, lethargy, enlarged liver, and hemoconcentration with thrombocytopenia
Inform travelers going to areas with known virus transmission about risk of disease

Consider chikungunya in patients with acute onset of fever and polyarthralgia

Be aware of possible local transmission in areas where *Aedes* species mosquitoes are active
Reporting chikungunya cases

- Chikungunya and dengue are nationally notifiable conditions
- Healthcare providers and reference laboratories report laboratory-confirmed cases to state health departments
- State health departments report cases to CDC through ArboNET
- Timely reporting allows health departments to assess and reduce the risk of local transmission or mitigate further spread
Preventive measures

- No vaccine or medication available to prevent infection or disease
- Primary prevention measure is to reduce mosquito exposure
- Consider advising people at risk for severe disease to avoid travel to areas with ongoing outbreaks
- Protect infected people from further mosquito exposure during first week of illness
Mosquito prevention and control

- Use air conditioning or window/door screens
- Use mosquito repellents on exposed skin
- Wear long-sleeved shirts and long pants
- Mosquito habitat control
- Appropriate applications of larvicide and adulticide
Future course of chikungunya in the Americas

- Virus will continue to spread in areas with competent vectors
  - Local transmission recently identified in Mexico
  - Anticipate some spread into U.S. border states

- Travel-associated cases will introduce virus into the U.S.
  - Imported cases will result in local transmission and outbreaks
  - Air conditioning may limit the size and scope of outbreaks
  - Colder temperatures will interrupt and possibly stop further spread

- Dengue might provide predictive model
  - In 2013, 2.4 million cases of dengue reported in the Americas
  - 773 travel-related and 49 locally transmitted cases in U.S. states
Remaining questions

- Role of *Aedes albopictus* in temperate areas
- Will enzootic cycle be established to maintain virus
- Impact of chikungunya and dengue virus co-circulation
- Burden of longer term morbidity
Chikungunya virus in the Americas summary

- Chikungunya virus continues to spread in the Americas
- Primary prevention measure to reduce mosquito exposure
- Consider in patients with acute fever and polyarthralgia, especially travelers who recently returned from areas with known local virus transmission
- Laboratory-confirmed cases should be reported to state health departments and CDC
Selected references (1)


Selected references (2)


Additional resources

- General information about chikungunya virus and disease:
  http://www.cdc.gov/chikungunya/

- Protection against mosquitoes:

- Travel notices: http://wwwnc.cdc.gov/travel/notices

- Information for travelers and travel health providers:

- Chikungunya preparedness and response guidelines:
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.