Chikungunya, Dengue, and Zika

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Infectious Diseases
Reading Health System
Deaths resulting from mosquito bites outnumber all other animal-related deaths combined. A staggering more than 1 million people die each year from diseases transmitted by mosquitoes. In addition to mortality, mosquito-borne vectors are responsible for the suffering of hundreds of millions of people. Each year, an estimated 700 million people are infected by mosquito bites, with almost all serious cases of mosquito-borne illnesses occurring in developing countries.
Although there are hundreds of mosquito species that feed on human blood, two species, *A. aegypti* (shown) and *Aedes albopictus*, are responsible for the transmission of numerous arboviruses.[21] *A. aegypti*, the yellow fever mosquito, originated in Africa, and *A. albopictus*, the Asian tiger mosquito, originated in Asia, but both species have expanded to new geographic locations and become cosmopolitan.

In addition to yellow fever, *A. aegypti* is the primary vector for transmitting dengue fever, Zika virus, and chikungunya virus,[22] as well as several other viral pathogens. *A. albopictus* also transmits dengue fever, Zika virus, and chikungunya.

### Zika virus

- Single stranded RNA Virus
- Genus Flavivirus, Family Flaviviridae
- Closely related to dengue, yellow fever, Japanese encephalitis and West Nile viruses
- Transmitted to humans primarily by *Aedes* (Stegomyia) species mosquitoes
**Vectors: *Aedes* Mosquitoes**

- *Aedes* species mosquitoes
  - *Ae aegyptimore* efficient vectors for humans
  - *Ae albopictus*
- Also transmit dengue and chikungunya viruses
- Lay eggs in domestic water-holding containers
- Live in and around households
- Aggressive daytime biters

**Geographic distribution in the US**

- *Aedes aegypti*
- *Aedes Albopictus*
Zika Virus Transmission Cycles

- Sylvatic (jungle) cycle
- Epidemic (urban) cycle
Other modes of transmission

- Maternal-fetal
  - Intrauterine
  - Perinatal
- Other
  - Sexual
  - Blood transfusion
  - Laboratory exposure
- Theoretical
  - Organ or tissue transplantation
  - Breast milk

Recommendations for prevention of sexual transmission of Zika virus for couples in which a man has traveled to or resides in an area with active Zika virus transmission

Couples in which a woman is pregnant

- Couples in which a woman is pregnant should use condoms consistently and correctly or abstain from sex for the duration of the pregnancy.

Other couples concerned about sexual transmission

- Couples in which a man had confirmed Zika virus infection or clinical illness consistent with Zika virus disease should consider using condoms or abstaining from sex for at least 6 months after onset of illness.

- Couples in which a man traveled to an area with active Zika virus transmission but did not develop symptoms of Zika virus disease should consider using condoms or abstaining from sex for at least 8 weeks after departure from the area.

- Couples in which a man resides in an area with active Zika virus transmission but has not developed symptoms of Zika virus disease might consider using condoms or abstaining from sex while active transmission persists.
**Zika Virus Epidemiology**

- First isolated from a monkey in Uganda in 1947
- Prior to 2007, only sporadic human disease cases reported from Africa and southeast Asia
- In 2007, first outbreak reported on Yap Island, Federated States of Micronesia
- In 2013–2014, >28,000 suspected cases reported from French Polynesia*

Zika Virus in the Americas

- May 2015, the first locally-acquired cases in the Americas were reported in Brazil
- As of March 23, 2016, there are outbreaks in 39 countries or territories in the Americas, including the Commonwealth of Puerto Rico, the US Virgin Islands, and American Samoa
- Spread to other countries is likely
Zika Virus in the Continental United States

- Local transmission of Zika virus has not been reported in the continental United States.
- Since 2011, there have been laboratory-confirmed Zika virus cases identified in travelers returning from areas with local transmission.
- With current outbreaks in the Americas, cases among U.S. travelers will most likely increase.
- Imported cases may result in virus introduction and local spread in some areas of U.S.

Zika Virus in the United States, 30 March 2016

- US States
  - 312 travel-associated cases
  - 27 pregnant women
  - 6 sexually transmitted
  - 0 locally-acquired vector-borne cases
- US Territories
  - 3 travel-associated cases
  - 349 locally acquired cases
  - 37 pregnant women
Zika Virus Clinical Disease Course and Outcomes

- Incubation period: 3-14 days
- Clinical illness usually mild
- Symptoms last several days to a week
- Severe disease requiring hospitalization uncommon
- Fatalities are rare
- Guillain-Barre syndrome reported in patients following suspected Zika virus infection
  - Relationship to Zika virus infection under investigation

Zika Virus Disease

Most Common Symptoms
- Rash
- Fever
- Joint pain
- Conjunctivitis

- Other symptoms
  - Muscle pain
  - Headache
Clinical signs and symptoms reported by 115 residents of U.S. states and the District of Columbia with laboratory evidence of Zika virus disease — January 1, 2015–February 26, 2016

<table>
<thead>
<tr>
<th>Sign/symptom</th>
<th>Yes† No. (%)</th>
<th>No. (%)</th>
<th>Unknown No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>113 (98)</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Fever</td>
<td>94 (82)</td>
<td>20 (17)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>76 (66)</td>
<td>33 (29)</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Headache</td>
<td>65 (57)</td>
<td>37 (32)</td>
<td>13 (11)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>63 (55)</td>
<td>38 (33)</td>
<td>14 (12)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>43 (37)</td>
<td>53 (46)</td>
<td>19 (17)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>22 (19)</td>
<td>63 (55)</td>
<td>30 (26)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6 (5)</td>
<td>79 (69)</td>
<td>30 (26)</td>
</tr>
</tbody>
</table>

Zika Virus and Guillain-Barré syndrome (GBS)

- Unclear how many people have GBS after ZV infection
  - Brazil, 2015: 6 patients aged 2–57 years with neurologic syndromes (GBS and acute disseminated encephalomyelitis) after ZV infection
  - French Polynesia, 2014: 38 cases of GBS, non among children
  - US: 1 case in the States and 1 in the territories

- Overall, GBS incidence appears to increase with age

Zika Virus and Microcephaly in Brazil

- Reports of a substantial increase in number of babies born with microcephaly in 2015 in Brazil; true baseline unknown
  - Zika virus infection identified in several infants born with microcephaly (including deaths) and in early fetal losses
  - Some of the infants with microcephaly have tested negative for Zika virus
- Incidence of microcephaly among fetuses with congenital Zika infection is unknown
Diagnostic Testing for Zika Virus

- Reverse transcriptase-polymerase chain reaction (RT-PCR) for viral RNA in serum collected ≤7 days after illness onset
- Serology for IgM and neutralizing antibodies in serum collected ≥4 days after illness onset (duration 12 weeks)
- Immunohistochemical (IHC) staining for viral antigens or RT-PCR on fixed tissues

Serology Cross-Reactions with Other Flaviviruses

- Zika virus serology (IgM) can be positive due to antibodies against related flaviviruses (e.g., dengue and yellow fever viruses)
- Neutralizing antibody testing may discriminate between cross-reacting antibodies in primary flavivirus infections
- Difficult to distinguish infecting virus in people previously infected with or vaccinated against a related flavivirus
- Healthcare providers should work with state, territorial, and local health departments to ensure test results are interpreted correctly
Laboratories for Diagnostic Testing for Zika Infection

- No commercially available diagnostic tests
- Testing performed at CDC and a few state health departments
- CDC is working to expand laboratory diagnostic testing in states through the Laboratory Response Network
- Healthcare providers should contact their state or territorial health department to facilitate diagnostic testing
**Initial Assessment and Treatment of Patients**

- No specific antiviral therapy
- Treatment is supportive (i.e., rest, fluids, analgesics, antipyretics)
- Patients with suspected ZV infections should be evaluated and managed for possible dengue or chikungunya virus infections
- Aspirin and other NSAIDs should be avoided until dengue can be ruled out to reduce the risk of hemorrhage

**Zika Virus Preventive Measure**

- No vaccine or medication to prevent infection or disease
- Primary prevention measure is to reduce mosquito exposure
- Pregnant women should consider postponing travel to areas with ongoing ZV outbreaks
- Protect infected people from mosquito exposure during first week of illness to prevent further transmission
Mosquito Control in the United States

- Coordinated and funded locally in most areas
  - Divided into mosquito control or abatement districts

- Many mosquito control programs are stand-alone divisions of local governments
  - Need to link mosquito control districts with both state and local health departments

- State and local jurisdictions may have different laws and ordinances concerning mosquito control
  - Stand alone program or connected to health departments
  - Especially relevant concerning property access

Description
The official World Health Organization (WHO) Zika App. Get the latest information from WHO on the Zika virus disease by downloading this app.

Screenshots
Dengue Virus

- 4 closely related serotypes
- Positive strand ssRNA virus, Flavivirus
- Infection with one does not confer protection to other serotypes
- Transmitted by mosquitoes (A. aegypti and A. albopictus), vectors
- Found in tropical and subtropical areas
- Can cause a mild or severe disease
- More than 400 million people are infected yearly
- Emerged as a worldwide problem since the 1950’s

Dengue Transmission

- Transmission occurs when a mosquito feeds on a person during a 5 day period when large amounts of virus are in the blood
- The virus then requires 8-12 days of incubation before it can be transmitted to another human
- The mosquito remains infected for life, which might be days or weeks
- In rare cases it can be transmitted in organ transplants or blood transfusions from infected donors
Dengue Symptoms

• Symptoms begin 4-7 days after the mosquito bite and typically last 3-10 days
• Fever, as high as 106 F (41 C)
• Headaches
• Muscle, bone and joint pain (aka breakbone fever)
• Pain behind the eyes
• Rash (face, thorax, extensor surfaces, skip areas)
• Nausea vomiting
Dengue Hemorrhagic Fever

- Bleeding from nose and mouth
- Severe abdominal pain
- Persistent vomiting
- Bleeding under the skin (might look like bruising)
- Problems with lungs, liver and heart leading to shock and in some cases death
- More likely if infected previously with different strain

Dengue Risk Factors

- Living or traveling in tropical areas
  - Southeast Asia
  - Western Pacific Islands
  - Latin America
  - Caribbean
- Prior infection with dengue fever virus
- Nearly all cases in the US (48 continental) were acquired by travelers or immigrants
- Reportable disease
Dengue Treatment/Management

• No treatment, supportive
  • Fluids
  • Antipyretics
  • Avoid ASA
  • Rest
• Vaccine not available in US, several in development
• Skin repellent
• Long sleeves and pants
• Mosquito netting

Dengue Case Definitions
Dengue without warning signs

• Fever and two of the following
  • Nausea, vomiting
  • Rash
  • Aches and pains
  • Leukopenia
  • Positive tourniquet test

• How to do a Tourniquet Test
  • 1. Take the patient's blood pressure and record it, for example, 100/70.
  • 2. Inflate the cuff to a point midway between SBP and DBP and maintain for 5 minutes.
    \[ \frac{100 + 70}{2} = 85 \text{ mm Hg} \]
  • 3. Reduce and wait 2 minutes.
  • 4. Count petechiae below antecubital fossa. See image at right.
  • A positive test is 10 or more petechiae per 1 square inch.
Dengue with Warning Signs**

- Dengue as defined above with any of the following:
  - Abdominal pain or tenderness
  - Persistent vomiting
  - Clinical fluid accumulation (ascites, pleural effusion)
  - Mucosal bleeding
  - Lethargy, restlessness
  - Liver enlargement >2 cm
  - Laboratory: increase in HCT concurrent with rapid decrease in platelet count
- **requires strict observation and medical intervention

Severe Dengue

- Dengue with at least one of the following criteria:
  - Severe Plasma Leakage leading to:
    - Shock
    - Fluid accumulation with respiratory distress
  - Severe Bleeding as evaluated by clinician
  - Severe organ involvement
    - Liver: AST or ALT ≥ 1000
    - CNS: impaired consciousness
    - Failure of heart and other organs
Laboratory testing

• PCR (serum, plasma, blood, CSF, other body fluid or tissue)
• Immunofluorescence or immunochemistry
• IgM or IgG antibodies
  • Seroconversion or ≥4 fold rise in titer

Laboratory-Confirmed DHF in the Americas
Prior to 1981 vs. 1981 - 2003


Source: WHO/PAHO/CDC
Arbovirus Infections: Zika, Chikungunya and Dengue
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Chikungunya

- First described in outbreak in Tanzania in 1952
- RNA virus, Togaviridae family
- Derived from a word in Kimakonde language meaning “to become contorted” (due to joint pain)

Chikungunya in the US
States reporting chikungunya virus disease cases - US, 2014 (as of Feb 2015)

Arbovirus Infections: Zika, Chikungunya and Dengue
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Transmission

- Through mosquito bites
  - Mosquitoes become infected when they feed on a person already infected with the virus, infected mosquitoes then transmit to other people
  - *A aegypti* and *A. albopictus* mosquitoes, bite mostly during the daytime.

- Rarely, from mother to child
  - Around the time of birth
  - No documentation of transmission via breastfeeding

- Rarely, through infected blood
  - In theory, no known reports

Symptoms

- Begin 3-7 days after bitten
- Abrupt onset of fever (typically >39 C) and joint pain (symmetric)
- Headache
- Muscle pain
- Joint swelling
- Rash (maculopapular)
- Most people feel better in a week
- In some people joint pain may persist for weeks to months
- Unlikely to become infected again
Timeline of Infection, Symptoms, and Biomarkers.


Table 1. Frequency of acute symptoms of CHIKV infection.*

<table>
<thead>
<tr>
<th>Symptom or sign</th>
<th>Frequency range (% of symptomatic patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>76–100</td>
</tr>
<tr>
<td>Polyarthralgias</td>
<td>71–100</td>
</tr>
<tr>
<td>Headache</td>
<td>17–74</td>
</tr>
<tr>
<td>Myalgia</td>
<td>46–72</td>
</tr>
<tr>
<td>Back pain</td>
<td>34–50</td>
</tr>
<tr>
<td>Nausea</td>
<td>50–69</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4–59</td>
</tr>
<tr>
<td>Rash</td>
<td>28–77</td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>12–32</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>3–56</td>
</tr>
</tbody>
</table>

Majority (72-97%) of infected persons are symptomatic.
Diagnosis

• Consider in patients with acute onset fever and polyarthalgia, especially in travelers from endemic areas

• Laboratory testing
  • PCR
  • Serologies (IgG, IgM)
  • Viral culture

Differential Diagnosis

• Leptospirosis
• Malaria
• Rickettsia
• Group A strep
• Rubella
• Measles
• Parvovirus
• Enteroviruses
• Adenovirus
• Other alphavirus infections
• Dengue
• Zika
• etc
Treatment

- No medicine to treat
- No vaccine at this time
- Symptomatic
  - Plenty of rest
  - Plenty of fluids
  - Antipyretics, analgesics

Clinical Features: Zika, Dengue, Chikungunya

<table>
<thead>
<tr>
<th>Features</th>
<th>Zika</th>
<th>Dengue</th>
<th>Chikungunya</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Rash</td>
<td>+++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Myalgia</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Headache</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
</tbody>
</table>
Distinguishing Zika from Dengue and Chikungunya

• Dengue and chikungunya viruses transmitted by same mosquitoes with similar ecology

• Dengue and chikungunya can circulate in same area and rarely cause co-infections

• Diseases have similar clinical features

• Important to rule out dengue, as proper clinical management can improve outcome*


Prevention (for all discussed)

• Use air conditioning or window/door screens to keep mosquitoes outside. If you are not able to protect yourself from mosquitoes inside your home or hotel, sleep under a mosquito bed net.

• Help reduce the number of mosquitoes outside your home or hotel room by emptying standing water from containers such as flowerpots or buckets.

• When weather permits, wear long-sleeved shirts and long pants.

• Use insect repellents
  • Repellents containing DEET, picaridin, IR3535, and oil of lemon eucalyptus or para-menthane-diol provide long-lasting protection.
  • If you use both sunscreen and insect repellent, apply the sunscreen first and then the repellent.
  • Do not spray repellent on the skin under your clothing.
  • Treat clothing with permethrin or purchase permethrin-treated clothing.
  • Always follow the label instructions when using insect repellent or sunscreen.
Arbovirus Infections: Zika, Chikungunya and Dengue

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**Prevention Tips:**

- Wear long-sleeved shirts, trousers, hats
- Use EPA-registered insect repellents
- Sleep under mosquito nets on beds if overseas or outside
- Empty/clean containers that hold water
- Stay in places with air conditioning or screens on windows
- Treat clothing and gear with permethrin (insecticide)

**Cartoon:**

Infectious Microbe Research Lab

The most important thing in this job is not letting the little things get to you.