Zika Update

Kristina M. Angelo DO, MPH-TM

Travelers’ Health Branch
Division of Global Migration and Quarantine
National Center of Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention

ACOI Conference
October 28, 2016
I have no financial relationships to disclose.

Kristina Angelo
kangelo@cdc.gov
Outline

- Overview
- Epidemiology
- Clinical Course and Disease Outcomes
- Clinical Guidance
- Diagnostics
- Prevention
- Vaccine Development
- Clinical Resources
Zika Virus (ZIKV) Overview
ZIKV

- Single stranded RNA virus
- Genus *Flavivirus*, family *flaviviridae*
- Closely related to dengue, yellow fever, Japanese encephalitis (JEV), and West Nile virus (WNV)

Transmission electron microscope image of negative-stained, Fortaleza-strain ZIKV (red), isolated from a microcephaly case in Brazil.

Photo Credit: www.niaid.nih.gov
Modes of Transmission

- **Bite from an infected *Aedes* species mosquito**
  - *Ae. aegypti* and *Ae. albopictus*
- **Maternal-fetal**
  - Intrauterine
  - Perinatal
- **Sexual transmission from ANY infected partner**
- **Laboratory exposure**
- **Probable: blood transfusion**


# Vector Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Ae. aegypti</th>
<th>Ae. albopictus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of Blood Meal</td>
<td>Bite during the day and night</td>
<td></td>
</tr>
<tr>
<td>Number of Blood Meals</td>
<td>Multiple (Ae. aegypti), single (Ae. albopictus)</td>
<td></td>
</tr>
<tr>
<td>Preferred Host(s)</td>
<td>Humans (Ae. aegypti), humans and other mammals (Ae. albopictus)</td>
<td></td>
</tr>
<tr>
<td>Preferred Site to Lay Eggs</td>
<td>Containers of standing water (i.e., tires, flower pots)</td>
<td></td>
</tr>
<tr>
<td>Vector-borne Diseases</td>
<td>Dengue, yellow fever, chikungunya, ZIKV</td>
<td></td>
</tr>
<tr>
<td>Environment</td>
<td>Urban (Ae. aegypti), urban and rural (Ae. albopictus)</td>
<td></td>
</tr>
</tbody>
</table>

- Anthropophillic and anthropophagic

Estimated Potential Range of ZIKV Vectors, United States

Incubation Period, Viremia, and Transmissibility

- Incubation period: 3–14 days
- Viremia: few days–1 week
- Virus can be shed in semen and urine after viremia has resolved
  - Viral RNA has been detected in semen as long as 188 days after illness onset
  - Duration of transmissibility not established
  - To date, cases of sexual transmission have involved exposure within a few weeks of illness onset

ZIKV Epidemiology
Where was ZIKV Discovered?

Uganda, 1947


Where were the Previous Reported ZIKV Outbreaks?


ZIKV Lineages

- **2 distinct lineages**
  - African
  - Asian

- **Despite being genetically distinct, all strains are the same serotype**
  - Identical surface antigens
  - Antibodies elicited after infection with the Asian lineage potently inhibit both Asian and African lineage strains in vitro

ZIKV Detected in the Americas (2015–2016)

Brazil, 2015

Countries and Territories with Active ZIKV Transmission: AMERICAS
(current as of October 19, 2016)

- Anguilla
- Antigua and Barbuda
- Argentina
- Aruba
- The Bahamas
- Barbados
- Belize
- Bolivia
- Bonaire
- Brazil
- British Virgin Islands
- Cayman Islands
- Colombia
- Costa Rica
- Cuba
- Curaçao
- Dominica
- Dominican Republic
- Ecuador
- El Salvador
- French Guiana
- Grenada
- Guadeloupe
- Guatemala
- Guyana
- Haiti
- Honduras
- Jamaica
- Martinique
- Mexico
- Nicaragua
- Panama
- Paraguay
- Peru
- Puerto Rico
- Saba
- Saint Barthélemy
- Saint Lucia
- Saint Martin
- Saint Vincent and the Grenadines
- Saint Eustatius
- Saint Maarten
- Saint Kitts and Nevis
- Suriname
- Trinidad and Tobago
- Turks and Caicos
- United States
- U.S. Virgin Islands
- Venezuela

Countries and Territories with Active ZIKV Transmission: OUTSIDE THE AMERICAS
(current as of October 19, 2016)

- **Oceania/Pacific Islands**
  - American Samoa
  - Fiji
  - Kosrae, Federated States of Micronesia
  - Marshall Islands
  - New Caledonia
  - Papua New Guinea
  - Samoa
  - Tonga

- **Africa**
  - Cape Verde

- **Asia**
  - Singapore

Novel Genetic Findings

- Molecular clock phylogeny suggests ZIKV arrived to the Americas between May–December 2013
- Current epidemic strains are more closely related to the Asian lineage
- Significant change in amino acid and nucleotide sequences in the past 50 years
  - All strains from the Americas have 99% nucleotide homology
- Virus pre-membrane precursor protein has high variability
  - Variability contributes to significant structural change
  - May partially explain the capacity to spread through the Americas

Zika by the Numbers (as of October 20, 2016): WORLDWIDE

- 67 countries (since 2015)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Countries (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reported evidence of person-to-person transmission (sexual)</td>
<td>12</td>
</tr>
<tr>
<td>Reported evidence of microcephaly or other CNS malformation potentially associated with ZIKV or suggestive of congenital infection</td>
<td>23</td>
</tr>
<tr>
<td>Reported increased incidence of Guillain-Barré (GBS) or confirmed ZIKV in the setting of GBS</td>
<td>19</td>
</tr>
</tbody>
</table>
Zika by the Numbers (as of October 19, 2016):

### US STATES

<table>
<thead>
<tr>
<th>Case Classification</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Locally acquired mosquito-borne cases</td>
<td>137</td>
</tr>
<tr>
<td>Travel-associated cases</td>
<td>3,878</td>
</tr>
<tr>
<td>Laboratory acquired cases</td>
<td>1</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>4,016</strong></td>
</tr>
</tbody>
</table>

Zika by the Numbers (as of October 19, 2016):

**US STATES**

<table>
<thead>
<tr>
<th>Special Classification (n=4,016)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexually-transmitted</td>
<td>32</td>
</tr>
<tr>
<td>Guillain-Barré syndrome</td>
<td>13</td>
</tr>
<tr>
<td>Pregnant women*</td>
<td>899</td>
</tr>
<tr>
<td>Liveborn infants with birth defects*</td>
<td>23</td>
</tr>
<tr>
<td>Pregnancy losses with birth defects*</td>
<td>5</td>
</tr>
</tbody>
</table>

*Reported to the Zika Pregnancy Registry, as of October 13, 2016

Zika by the Numbers (as of October 19, 2016):

<table>
<thead>
<tr>
<th>State</th>
<th>Travel-associated cases n (%)</th>
<th>Locally acquired cases n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=4,016)</td>
<td>(N=137)</td>
</tr>
<tr>
<td>Florida</td>
<td>708 (18)</td>
<td>137 (100)</td>
</tr>
<tr>
<td>New York</td>
<td>884 (23)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>California</td>
<td>296 (8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Texas</td>
<td>231 (6)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Zika by the Numbers (as of October 19, 2016): US TERRITORIES

<table>
<thead>
<tr>
<th>Case Classification</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Locally acquired mosquito-borne cases</td>
<td>27,314*</td>
</tr>
<tr>
<td>Travel-associated cases</td>
<td>88</td>
</tr>
<tr>
<td>Laboratory acquired cases</td>
<td>0</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>27,402</strong></td>
</tr>
</tbody>
</table>

*26,798 (98%) are in Puerto Rico
# Zika by the Numbers (as of October 19, 2016): US TERRITORIES

<table>
<thead>
<tr>
<th>Special Classification</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexually-transmitted</td>
<td>N/A</td>
</tr>
<tr>
<td>Guillain-Barré syndrome</td>
<td>40</td>
</tr>
<tr>
<td>Pregnant women*</td>
<td>1,927</td>
</tr>
<tr>
<td>Liveborn infants with birth defects*</td>
<td>1</td>
</tr>
<tr>
<td>Pregnancy losses with birth defects*</td>
<td>1</td>
</tr>
</tbody>
</table>

*Reported to the Zika Pregnancy Registry, as of October 13, 2016

Zika Disease Clinical Course and Outcomes
Zika Virus Infection Clinical Course

- Clinical illness is usually mild
- Many infections are asymptomatic
- Symptoms last several days to a week
- Severe disease requiring hospitalization is uncommon
- Fatalities are rare
Symptoms

- **Most common symptoms**
  - Acute onset of fever
  - Maculopapular rash
  - Joint pain
  - Conjunctivitis

- **Other symptoms**
  - Muscle pain
  - Headache

Differential Diagnosis

- Based on typical clinical features, the differential diagnosis for Zika infection is broad

- Dengue
- Chikungunya
- Leptospirosis
- Malaria
- Rubella
- Measles
- Parvovirus
- Enterovirus
- Adenovirus
- Other alphaviruses (e.g., Mayaro, Ross River, Barmah Forest, o’nyong-nyong, Sindbis viruses)
Clinical Features: ZIKV Compared to Dengue and Chikungunya

<table>
<thead>
<tr>
<th>Clinical Feature</th>
<th>ZIKV</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>
<tr>
<td>Shock</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Adapted from Rabe, Ingrid MBChC, Mmed “Zika Virus-What Clinicians Need to Know?” (presentation, Clinical Outreach and Communication Activity (COCA) call, Atlanta, GA, January 26 2016)

ZIKV and Guillain-Barré Syndrome (GBS)

- CDC research suggests a temporal and geographic relationship between GBS and ZIKV

- French Polynesia (2013):
  - 38 cases of GBS occurred among an estimated 28,000 persons
  - Case-control study revealed a strong association (OR >34) between GBS and previous Zika infection

- Case series from 7 countries (2015–2016)
  - Increase in incidence of GBS between 100–877%

- Brain ischemia, meningoencephalitis, and acute myelitis complicating Zika virus infection also have been reported

ZIKV in Pregnancy

- Incidence of Zika virus infection in pregnant women is not known
- Infection can occur in any trimester
- No evidence of more severe disease compared with non-pregnant women
- No evidence of increased susceptibility

CDC, *CDC Health Advisory: Recognizing, Managing, and Reporting Zika Virus Infections in Travelers Returning from Central America, South America, the Caribbean and Mexico*, 2016.


Case Definition of Microcephaly

- **Definite congenital microcephaly for live births**
  - Head circumference (HC) at birth < 3rd percentile for gestational age and sex
  - If HC at birth is not available, HC < 3rd percentile for age and sex within the first 2 weeks of life

- **Definite congenital microcephaly for still births and other pregnancy losses**
  - Postnatal HC < 3rd percentile for gestational age and sex
  - Prenatal HC >3 SD below the mean on prenatal ultrasound
Congenital Zika Syndrome

- Microcephaly
- Intracranial calcifications
- Other brain anomalies (ventriculomegaly, hydrocephalus, atrophy, etc)
- Eye anomalies
- Other anomalies (club foot, contractures)
Congenital Zika Syndrome Brain Anomalies
ZIKV and Ocular Findings

- Case series of 29 infants with microcephaly born to mothers with Zika virus infection during pregnancy
  - Ocular abnormalities were found in 10/29 (34.5%)
    - 7/10 (70%) infants had bilateral disease
    - 11/17 (65%) affected eyes had focal pigment mottling of the retina and chorioretinal atrophy
    - 8/17 (47%) affected eyes had optic nerve abnormalities

- Infants with possible congenital Zika virus infection should be screened for eye disease

---


Adverse Outcomes and ZIKV

- Linked to miscarriage and stillbirth
  - Evidence insufficient to confirm ZIKV as cause
- Problems related to brain injury
  - Eye abnormalities
  - Hearing impairment
  - Seizures
  - Swallowing impairment
  - Limb abnormalities
  - Severe irritability
  - Developmental delay
  - Growth abnormalities

Confirmation of ZIKV in Fetal Tissues

- **ZIKV identified in**
  - Amniotic fluid
  - Placenta
  - Brain
  - Products of conception

(CDC lab, Brazil clinical specimens)
Digitally-colorized transmission electron micrograph (TEM) of Zika virus. Virus particles, here colored red, are 40 nm in diameter, with an outer envelope, and an inner dense core.
Zika Virus Infection Clinical Guidance
Guidance for Health Care Providers Caring for Pregnant Women with Possible ZIKV Exposure

Clinical Management of Positive or Inconclusive ZIKV Testing Results During Pregnancy

- **Antepartum**
  - Consider serial ultrasounds every 3–4 weeks
  - Referral to maternal-fetal medicine specialist

- **Postpartum**
  - Histopathology of the placenta and cord
  - Frozen placental tissue and cord tissue for ZIKV RNA
ZIKV and Immunocompromised Persons

- Information is lacking on whether the risk for Zika virus infection or the severity of illness is different for people with HIV infection or other causes of immune suppression
- 3 cases of ZIKV in HIV-infected adults (Brazil) to date
  - Mild illnesses
- Close clinical monitoring of HIV-infected patients with ZIKV should be considered


ZIKV Diagnostics
Diagnostic Testing for Symptomatic Individuals for ZIKV

- Real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) for viral RNA in serum and urine specimens (possibly CSF or amniotic fluid) collected < 14 days after illness onset
- Serology for ZIKV IgM in serum (possibly CSF) collected ≥ 14 after illness onset
- Plaque reduction neutralization test (PRNT) for confirmation of virus-specific neutralizing antibodies in paired serum samples
- Immunohistochemical (IHC) staining for viral antigens or RT-PCR on fixed tissues
Serology Cross-reactions with Other Flaviviruses

- ZIKV 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 and local health departments to ensure test results are interpreted correctly
Laboratories for Diagnostic Testing

- Testing is performed at CDC, select commercial labs, and a few state health departments
  - CDC is working with commercial labs to expand testing
- Healthcare providers should contact their state, local, or territorial health department to facilitate diagnostic testing
Zika Reporting

- Zika virus disease and Zika virus infection without disease, including congenital Zika virus infection, are nationally notifiable conditions.
- Report all cases to your state, local, tribal, or territorial health department.
Zika Pregnancy Registries

- CDC established the **US Zika Pregnancy Registry** to collect information and learn more about pregnant women/infants with Zika virus infection
  - Zika Active Pregnancy Surveillance System in Puerto Rico

- Data collected will be used to update recommendations for:
  - Clinical care
  - Services for pregnant women and families
  - Prevention of Zika virus infection during pregnancy

- If you are a healthcare provider & have registry questions, please email or call 770-488-7100 (ask for the Zika Pregnancy Hotline). For other questions, call 800-CDC-INFO
Zika Virus Infection Prevention
Recommendations for Prevention of Sexual Transmission

- Couples in which a woman is pregnant
  - Use condoms or abstain from sex throughout pregnancy

- Couples who are not pregnant and one or both partners have traveled to or live in an area with ZIKV
  - Use condoms (male or female) or abstain from sex (vaginal, anal, oral, and sharing of sex toys) as follows:
    - Men: At least 6 months after symptom onset or last possible exposure (if asymptomatic)
    - Women: At least 8 weeks after symptom onset or last possible exposure (if asymptomatic)

Mosquito Bite Protection

- Wear long-sleeved shirts and long pants
- Stay and sleep in places with air conditioning, when possible, and use window and door screens to keep mosquitoes outside
- Take steps to control mosquitoes indoors and outdoors
- Personal protection:
  - Use EPA-registered insect repellents with either DEET, picaridin, IR3535, or oil of lemon eucalyptus (OLE), 2-undecanone, or para-menthane-diol (PMD) and follow label directions
    - OLE and PMD should not be used in children <3 years
  - Apply sunscreen before insect repellent

http://www.nc.cdc.gov/travel/page/avoidbug-bites
What People Infected with ZIKV or Possibly Exposed to ZIKV can do to Protect Others

- Protect from mosquito bites for 3 weeks after leaving a Zika-affected area when ZIKV can be found in the blood
  - 3 weeks = Incubation week + viremic week
  - When viremic, ZIKV can be passed to a mosquito and to others
ZIKV Vaccine Development
Stages in the Development of a New Vaccine

- Exploratory Stage
- Pre-clinical Stage
- Clinical Development
- Regulatory Review and Approval
- Manufacturing
- Quality Control

http://www.cdc.gov/vaccines/basics/test-approve.html
Stages in the Development of a New Vaccine

- **Phase 1**: Small numbers of people
- **Phase 2**: Intended population
- **Phase 3**: Large numbers of people and tested for efficacy and safety

[http://www.cdc.gov/vaccines/basics/test-approve.html](http://www.cdc.gov/vaccines/basics/test-approve.html)
NIH/NIAID ZIKV Vaccine Candidates

- **DNA-based vaccine**
  - Similar to an investigational vaccine for WNV
  - Phase 1 clinical trial underway

- **Live-attenuated vaccine**
  - Building on a similar vaccine approach for dengue virus
  - Dengue vaccine: safe and immunogenic in early-phase trials; being evaluated in a large Phase III study in Brazil

https://www.niaid.nih.gov/topics/Zika/ResearchApproach/Pages/vaccineResearch.aspx
NIH/NIAID Vaccine Candidates

- Genetically engineered version of vesicular stomatitis virus (VSV)
  - VSV: successfully used in an investigational Ebola vaccine
  - Plans to evaluate the ZIKV vaccine in tissue culture/animal models

- Whole-particle inactivated vaccine
  - Based on a similar approach used by the Walter Reed Army Institute of Research for JEV and dengue viruses

https://www.niaid.nih.gov/topics/Zika/ResearchApproach/Pages/vaccineResearch.aspx
Zika Virus Infection Clinical Resources
CDC Consultation Service

• CDC maintains a 24/7 consultation service for health officials and healthcare providers caring for pregnant women with Zika virus infection (suspect or confirmed)
  • To contact the service:
    o Call: 770-488-7100
    o Email: ZIKAMCH@cdc.gov

• For other questions call:
  • 800-CDC-INFO
Additional Resources

Questions?
Thank you!

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
Visit: www.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info

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.