Updates in Infectious Diseases

Kelley Struble, DO, MS
St. John Physicians – Infectious Disease
September 30, 2016
Disclosures

- No financial relationships or affiliations to disclose
Overview

Activity

- Pre-Test
- Lecture
- Post-Test

Topics

- Ebola
  - Where are we now?
- Zika Virus (Adults)
  - History
  - Transmission
  - Domestic Impact
  - Diagnosis
  - Treatment / Prevention
Pre-Test

Which of the following infections should be ruled out before initiating treatment for Zika virus infection?

A. Herpes Simplex  
B. HIV  
C. Dengue  
D. Brucellosis
Ebola
Where are we now?

• October 23, 2014 - Last known diagnosis of Ebola infection in United States

• March 31, 2016 - CDC deactivates the EOC for the 2014-2016 Ebola response

2016 Flare Ups

- Sierra Leone
  - January 2016
  - 2 cases

- Guinea & Liberia
  - March 2016
  - 13 cases
  - >1200 contacts
  - Sexual transmission suspected

Zika Virus
Zika Virus

- Flavivirus
- Dengue, Chikungunya, Yellow Fever, West Nile Virus
History
• 1947

• Zika forest in Uganda
  • Rhesus monkey

http://www.who.int/emergencies/zika-virus/history/en/
• 1952
• Uganda
• United Republic of Tanzania

http://www.who.int/emergencies/zika-virus/history/en/
http://www.who.int/emergencies/zika-virus/history/en/
Zika Virus Outbreak on Yap Island, Federated States of Micronesia


- New illness
- Rash
- Conjunctivitis
- Fever
- Arthralgia / Arthritis

- Cases peaked May – July
- Viral genome sequenced 2006
• Attack rates variable
• 74% of residents infected
  • Zika virus IgM
• No deaths or hospitalizations
• No virus detected in mosquito populations sampled
Transmission
Transmission

Adults

- **Mosquito bite from vector**
  - Aedes species
  - A.aegypti
    - Comanche, Jackson, Oklahoma counties
  
- “Daytime biters”
- Early morning / late afternoon

www.ok.gov/health
Transmission

Estimated range of *Aedes aegypti* and *Aedes albopictus* in the United States, 2016*

*Aedes aegypti* mosquitoes are more likely to spread viruses like Zika, dengue, chikungunya than other types of mosquitoes such as *Aedes albopictus* mosquitoes.

- These maps show CDC’s best estimate of the potential range of *Aedes aegypti* and *Aedes albopictus* in the United States.
- These maps include areas where mosquitoes are or have been previously found.
- Shaded areas on the maps do not necessarily mean that there are infected mosquitoes in that area.

*Maps have been updated from a variety of sources. These maps represent CDC’s best estimate of the potential range of *Aedes aegypti* and *Aedes albopictus* in the United States. Maps are not meant to represent risk for spread of disease.*

Transmission

Adults

- **Sexual transmission**
  - 2008 – first report in continental U.S.
  - Males and females at equal risk
  - “Activities that might expose a sex partner to genital secretions”

- **Men: up to 6 months after onset of illness**
- **Women: up to 8 weeks after onset of illness**
Transmission

Adults

• **Blood Transfusion**
  • No cases in the United States.
  • Multiple cases in Brazil currently under investigation
  • 2013 French Polynesian outbreak:
    • 2.8% donors tested positive for Zika
  • Zika virus has been found in blood donors from previous outbreaks

• **August 26, 2016**: FDA guidance calls for all blood collection centers in the U.S. to screen all donated blood for Zika virus.

http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm518218.htm
Transmission

Infants

- Perinatal

- Intrauterine
  - Microcephaly
  - Eye defects
  - Hearing loss
  - Impaired growth
  - Fetal loss

US Zika Pregnancy Registry

- Local / State health departments
- Individual providers
- CDC website updated weekly
Prevalence
Pregnant Women with Any Laboratory Evidence of Possible Zika Virus Infection in the United States and Territories, 2016

<table>
<thead>
<tr>
<th>US States and the District of Columbia*</th>
<th>US Territories**</th>
</tr>
</thead>
<tbody>
<tr>
<td>749</td>
<td>1,348</td>
</tr>
</tbody>
</table>

*Includes aggregated data reported to the US Zika Pregnancy Registry as of September 15, 2016

**Includes aggregated data from the US territories reported to the US Zika Pregnancy Registry and data from Puerto Rico reported to the Zika Active Pregnancy Surveillance System as of September 15, 2016
# Prevalence in Adults

- **Nationally notifiable condition**
- **ArboNET for January 01, 2015 – September 21, 2016**

## United States
Locally acquired mosquito-borne cases reported: 43  
Travel-associated cases reported: 3,314  
Laboratory acquired cases reported: 1  

**Total: 3,358**  
- Sexually transmitted: 28  
- Guillain-Barré syndrome: 8

Areas of Active Transmission:  
- Miami-Dade County, Florida - As of July 29, 2016

## U.S. Territories
Locally acquired cases reported: 19,706  
Travel-associated cases reported: 71  

**Total: 19,777**  
- Guillain-Barré syndrome: 37

*U.S. Territories include Puerto Rico, American Samoa, and U.S. Virgin Islands*
Laboratory-confirmed Zika virus disease cases reported to ArboNET by state or territory (as of September 21, 2016)

Active Zika Virus Transmission in Florida

What about Oklahoma?

Clinical Signs and Symptoms
Signs/Symptoms

- Fever
- Maculopapular rash
- Arthralgia
- Conjunctivitis
- Myalgia
- Headache
Clinical features: Zika virus compared to Dengue and 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>
<tr>
<td>Shock</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Rabe, Ingrid MBChB, MMed “Zika Virus- What Clinicians Need to Know?” (presentation, Clinician Outreach and Communication Activity (COCA) Call, Atlanta, GA, January 26 2016)
Zika Virus and the Guillain–Barré Syndrome — Case Series from Seven Countries

August 31, 2016 | DOI: 10.1056/NEJMc1609015

B. Case Series of ZIKV Disease and GBS Aligned to the Week of Peak Incidence of ZIKV Disease

[Diagram showing the alignment of ZIKV and GBS cases to the week of peak incidence of ZIKV epidemic.]
Testing
Tests

Zika virus RT-PCR

- Urine with matched serum
  - Also available for CSF
- <2 weeks after symptom onset or last exposure
- Positive test confirms infectivity

Zika virus immunoglobulin (IgM) ELISA

- Serum only
- 2-12 weeks after symptom onset or last exposure
- Positive test requires PRNT confirmation for Zika to exclude cross-reactivity with other flaviviruses

- There are no IgG assays available for Zika virus
- Testing is not indicated >12 weeks after exposure

Testing

Confirmation of recent/active infection:

• 1) Zika virus RNA in any body fluid or tissue specimen

  • OR

• 2) Positive or equivocal Zika virus IgM antibody test results on serum or CSF

  • PLUS

• Positive (≥10) PRNT titer for Zika virus AND negative (<10) PRNT titer for dengue virus
Tests available at OKDHS

- Testing available by Emergency Use Authorization only
  - Requires phone consultation and approval by ADS Epidemiologist on call

- Zika virus RT-PCR (CDC)
  - CDC Trioplex rRT-PCR
  - Zika, Dengue, and Chikungunya virus

- Zika IgM antibody (CDC)
  - Zika MAC-ELISA
  - Zika virus only
  - If Dengue or Chikungunya IgM testing necessary, then specimen will be forwarded to CDC
Evaluation
When and whom to test?

Areas of Active Zika virus transmission

• When and whom to test?

  • Infants/Children – not addressed in this presentation

  • Non-pregnant individuals
    • With Symptoms
      • Lived in / travel to area of active Zika transmission within 2 weeks of symptom onset
      • Unprotected sexual contact with infected individual or person who has lived in or traveled to active area within 12 weeks of departure from the area
    • No Symptoms
      • Exposure through unprotected sex

  *4 out of 5 patients with active Zika virus infection are asymptomatic*
Symptomatic < 14 days from symptom onset (or exposure)

2016 Zika Response: Algorithm for U.S. Testing of Symptomatic Individuals*
Specimens Collected <14 days Following Symptom Onset

Serum and Urine Specimens Received (possibly with CSF or amniotic fluid)

Test all specimens by rRT-PCR

Note: Urine and amniotic fluid are not acceptable specimen types for dengue and chikungunya rRT-PCR.

Dengue**
Serum or CSF positive, patient positive for dengue virus infection.

Serum or CSF positive, patient positive for dengue virus RNA.

Chikungunya**
Serum or CSF, if tested, negative for chikungunya virus infection.

Zika
Any specimen positive, patient positive for Zika virus infection.

All specimens negative, patient positive for Zika virus RNA.

Serological testing
Serum specimens should be tested by:
- Zika MAC-EUISA* OSDH*
- a dengue IgM assay**

If any IgM assay yields positive or equivocal results for a specimen, results must be confirmed by PRNT.

One or both tests positive or equivocal.
Forward for confirmation by PRNT

All tests negative.
No further testing of specimen required.

PRNT
Serum tested by CDC or CDC-designated Confirmatory Testing Lab.
Combine PRNT results with results of other diagnostic tests to determine overall interpretation. See table on p. 8.

NOTE: Report all test results. Results should be considered in the context of symptoms, exposure risk and time point.

Symptomatic >14 days from symptom onset (or exposure)

- Testing not indicated >12 weeks after exposure
- No IgG test available for Zika
Asymptomatic, possible sexual transmission

- No published algorithms
- Guidelines for testing same as for symptomatic individuals
- No testing performed after 12 weeks from partner’s departure from Zika-affected area
• No testing indicated for asymptomatic individuals with no exposure history.
Pregnant individuals

- Assess for exposure at each prenatal visit

- CDC strongly advises NO travel to areas of active transmission for duration of pregnancy
- Protect from mosquito bites / barrier precautions with sexual activity if patient travels

Indications for testing:
- Unprotected sexual contact with infected individual
- Travel to area of active transmission

- Up to 12 weeks from date of last possible exposure
Pregnant / Asymptomatic

Serum and Urine from Asymptomatic Pregnant Women Meeting Epidemiologic Criteria

Serum and urine received

Specimens collected <14 days after return from travel or exposure

Test serum and urine by rRT-PCR for ZIKV only

Either specimen positive, patient positive for Zika virus infection.
Zika MAC-ELISA negative. No further testing of specimen required.

Both negative, patient negative for Zika virus RNA.
Health care provider should request collection of a follow-up serum specimen 2-12 weeks following exposure or return from travel.
Test follow-up serum by Zika MAC-ELISA

Zika MAC-ELISA positive or equivocal.
Forward for confirmation by PRINT

Specimens collected 2-12 weeks after return from travel or exposure or from women living in areas with ongoing Zika transmission

Test serum by Zika MAC-ELISA

Zika MAC-ELISA positive or equivocal.
Test serum and urine by rRT-PCR

Either specimen positive, patient positive for Zika virus infection.

Both negative, patient negative for Zika virus RNA.
Forward serum for confirmation of Zika MAC-ELISA by PRINT

Zika MAC-ELISA negative.
No further testing of specimen required.

PRINT
Serum tested by CDC or CDC-designated confirmatory testing lab.

Have a patient that needs to be tested?

- Download Screening Form from OSDH website
- Fill out and fax to Acute Disease Service (Fax: 405-271-6680)
- Call Epidemiologist on call (Phone: 405-271-4060)
  - Not approved for testing: No further action
  - Approved for testing:
    - Download Lab Requisition form from OSDH website
    - Fill out a lab requisition form for each specimen to be submitted
    - Send patient to lab with requisition form (or fax form to lab)
      - Do not send patient directly to public health department
Treatment and Prevention
Treatment

- No antiviral treatments available
- Vaccine in testing

- Supportive treatment only
  - Fluids
  - Rest
  - NSAIDS

- NOTE: must rule out Dengue before recommending NSAID therapy. Risk of hemorrhage with Dengue infection or co-infection with use of NSAIDS

- Dengue virus is NOT sexually transmitted

NIH image gallery (flickr)
Prevent mosquito bites

Everyone living in or traveling to areas with Zika should take steps to prevent mosquito bites:

- Cover exposed skin by wearing long-sleeved shirts and long pants.
- Use EPA-registered insect repellents that contain one of the following active ingredients: DEET, picaridin, IR3535, or oil of lemon eucalyptus or para-methane-diol. Always use as directed.
  - Pregnant and breastfeeding women can use all EPA-registered insect repellents according to the product label.
  - Most repellents can be used on children older than 2 months old. To apply, adults should spray insect repellent onto hands and then apply to a child’s face.
    - Do not use products containing oil of lemon eucalyptus (OLE) or para-methane-diol (PMD) on children under 3 years old.
- Use permethrin-treated clothing and gear (boots, pants, socks, tents). You can buy pre-treated items or treat them yourself.*
- Stay and sleep in screened-in or air-conditioned rooms.
- Sleep under a mosquito bed net if air conditioned or screened rooms are not available or if sleeping outdoors.
- Mosquito netting can be used to cover babies younger than 2 months old in carriers, strollers, or cribs to protect them from mosquito bites.

Prevention

- Sexual Transmission
- Abstinence
- Condom use

- Men: up to 6 months after onset of illness
- Women: up to 8 weeks after onset of illness

Prevent spread through sex

Condoms can reduce the chance of getting Zika from sex. To be effective, condoms should be used from start to finish, every time during vaginal, anal, and oral sex and the sharing of sex toys. Zika can be passed from a person with Zika before their symptoms start, while they have symptoms, and after their symptoms end.

- All pregnant women with sex partners who live in or have traveled to an area with Zika should use condoms or not have sex during their pregnancy, even if their partners do not have Zika symptoms, or if their symptoms have gone away.
- Couples who traveled to the area can consider using condoms or not having sex for at least 8 weeks after travel.
- Anyone concerned about sexual transmission of Zika can consider using condoms or not having sex while there is Zika in the area.

Training for Healthcare Providers

Post-Test
Which of the following infections should be ruled out before initiating treatment for Zika virus infection?

A. Herpes Simplex 
B. HIV 
C. Dengue 
D. Brucellosis 

Answer: C 

Treatment for Zika virus infection consists of supportive care measures only, including rest, fluids, and use of analgesics and antipyretics. Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided until dengue can be ruled out to reduce the risk of hemorrhage.

Thank you!

kelley.struble@sjmc.org