Zika Virus: The Olympics and Beyond

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Disclosures

• I have no disclosures to report
Objectives

- Review history of Zika virus
- Describe epidemiology of recent outbreaks of Zika virus infection in South America
- Discuss clinical aspects of Zika virus infection including congenital infection

Structure

<table>
<thead>
<tr>
<th>Genome or genomic region</th>
<th>Length</th>
<th>African MR764 prototype strain</th>
<th>French Polynesia H120217</th>
</tr>
</thead>
<tbody>
<tr>
<td>5' NCR</td>
<td>106 nt</td>
<td>107 nt</td>
<td>105 nt</td>
</tr>
<tr>
<td>Capsid</td>
<td>122 aa</td>
<td>125 aa</td>
<td>123 aa</td>
</tr>
<tr>
<td>PRM</td>
<td>178 aa</td>
<td>187 aa</td>
<td>179 aa</td>
</tr>
<tr>
<td>Envelope</td>
<td>569 aa</td>
<td>573 aa</td>
<td>573 aa</td>
</tr>
<tr>
<td>NS1</td>
<td>342 aa</td>
<td>352 aa</td>
<td>352 aa</td>
</tr>
<tr>
<td>NS2A</td>
<td>226 aa</td>
<td>217 aa</td>
<td>217 aa</td>
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<tr>
<td>NS2B</td>
<td>150 aa</td>
<td>159 aa</td>
<td>159 aa</td>
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<tr>
<td>NS3</td>
<td>617 aa</td>
<td>619 aa</td>
<td>619 aa</td>
</tr>
<tr>
<td>NS4A</td>
<td>127 aa</td>
<td>127 aa</td>
<td>127 aa</td>
</tr>
<tr>
<td>NS4B</td>
<td>252 aa</td>
<td>253 aa</td>
<td>253 aa</td>
</tr>
<tr>
<td>NSS</td>
<td>992 aa</td>
<td>994 aa</td>
<td>994 aa</td>
</tr>
<tr>
<td>3' NCR</td>
<td>628 nt</td>
<td>628 nt</td>
<td>628 nt</td>
</tr>
</tbody>
</table>

[Genetic info: Musso et al, CMR 2016]
Zika Virus

- Arbovirus
- Genus *Flavivirus*
  - Includes Dengue, Yellow Fever virus, Japanese encephalitis virus, West Nile virus
- First identified in Uganda in a sentinel monkey in 1947

Zika Virus

- 1947 – virus identified in a monkey from Zika Forest, Uganda
- 1954-2007 – Zika fever reported sporadically in Africa and Asia
  - 1954 – first human case in Africa
  - 1977 – first human case in Indonesia
- Major outbreaks
  - 2007 – Yap State (Micronesia) outbreak (49 confirmed, 59 suspected)
  - 2013 – Zika outbreak in French Polynesia (8746 suspected cases)
  - 2015 – Zika outbreak Brazil (similar to strain from French Polynesia), 440,000-1,300,000 estimated infections
- February 2016 WHO declares “Public Health Emergency of International Concern”

Laboratory confirmed Zika virus disease cases reported to ArboNET (United States 2015-16 as of July 13, 2016)

- Culex West Nile Virus
- Aedes albopictus
- Aedes aegypti
- Dengue
- Chikungunya
- Yellow Fever
- Zika Virus
Transmission

- Mosquito bites
- Sexual transmission
  - Cases reported of Zika confirmed disease in patients without travel but sexual contact with persons with Zika
  - Zika virus detection in semen. Virus persists in semen longer than blood.
- Transfusion?
- Lab contamination
- Maternofetal transmission
  - Transplacental
  - Perinatal
  - Breastmilk?

Zika Virus Disease

- Incubation (3 days-2 weeks)
- Viremia 3-4 days from symptom onset (0-11 days)(urine detection longer)
- Symptoms include fever, maculopapular rash (pruritic), non purulent conjunctivitis, arthralgia, myalgia, headache
- Estimated 80% of infections are asymptomatic
- Severe disease rare
- Associated Guillain Barré syndrome
GBS and Zika virus infection

*Fig 9: Temporal association between cases of Zika fever (blue columns) and GBS (red line) during the French Polynesian outbreak.*

Musso et al, CMR 2016
### Phenotypic findings of first 35 patients enrolled in the Brazilian Society of Medical Genetics-Zika embryopathy Task Force Registry – Brazil 2015

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash (trimester 1/2/3)</td>
<td>21 (57%)/ 5 (14%)/ 9 (26%)</td>
</tr>
<tr>
<td>Term</td>
<td>31 (91%)</td>
</tr>
<tr>
<td>Weight &lt; 2500 g</td>
<td>9 (26%)</td>
</tr>
<tr>
<td>Weight ≥ 2500 g</td>
<td>26 (74%)</td>
</tr>
<tr>
<td>HC &gt;3 SD</td>
<td>25 (71%)</td>
</tr>
<tr>
<td>HC &gt;2 SD to 3 SD</td>
<td>10 (29%)</td>
</tr>
<tr>
<td>Excessive and redundant scalp skin</td>
<td>11 (31%)</td>
</tr>
<tr>
<td>Clubfoot</td>
<td>5 (14%)</td>
</tr>
<tr>
<td>Arthrogryposis</td>
<td>4 (11%)</td>
</tr>
<tr>
<td>Abnormal funduscopic exam</td>
<td>2 (18%)</td>
</tr>
<tr>
<td>Abnormal neurologic exam</td>
<td>17 (49%)</td>
</tr>
<tr>
<td>Abnormal imaging (27)</td>
<td>27 (100%)</td>
</tr>
<tr>
<td>Calcifications</td>
<td>20 (74%)</td>
</tr>
<tr>
<td>Ventricular enlargement</td>
<td>12 (44%)</td>
</tr>
<tr>
<td>Neuronal migration disorders</td>
<td>9 (33%)</td>
</tr>
</tbody>
</table>

Schuler-Faccini et al. MMWR 2016
Clinical features in infants

- Fetal brain disruption sequence
  - Severe microcephaly
  - Overlapping sutures
  - Occipital bone prominence
  - Scalp rugae
- Cerebral calcifications

Russell et al, AJMG 1984

Fig 5: Mild microcephaly. Axial non-contrast CT images (A and B) shows multiple cerebral calcifications in the junction between cortical and subcortical white matter (white arrow). Axial susceptibility weighted image (C) shows multiple flecks of T2 hypointensity in subcortical frontal white matter (black arrow), and axial T2 weighted images (D) show linear or punctiform hypointensity of T2 shortening (white arrow), which correspond to the calcifications on CT. Axial T1 weighted image (E) shows bilateral frontal and thalamic calcifications, and hyperintense black arrow. Note the thickened and irregular cortical white matter junction. Sagittal T1 weighted image (F) shows enlarged corona radiata (black arrow) and hypointense corona callosa (white arrow).

Vasca Aragao BMJ 2016
Clinical features in infants

- Eye abnormalities (microphthalmia, lens subluxation, cataracts, intraocular calcifications, optic n. atrophy, optic nerve hypoplasia, macular pallor, macular chorioretinitis, chorioretinal atrophy)
- Arthrogryposis, clubfoot

Diagnostic challenges

- Symptoms can be seen in many other clinical conditions
- PCR – most definitive however viremia is limited in duration (~ 1 week) Urine detection is better (up to 3 weeks.)
- Serology – cross reaction with other flaviviruses (eg. Dengue, yellow fever) which also have similar symptoms
- PCR tests for Zika virus are available from some commercial laboratories. Serology and PCR testing is currently done through the health department at no charge (SDDHHS Epidemiology - 619-515-6620)
Diagnosis

• Who to test? Travel history combined with clinical symptoms
• What tests to order?
  – Acute infection: pcr most definitive, check blood and urine
  – Past infection: serologic tests (IgM, IgG)
  – Patients should also be tested for dengue, Chikungunya

Treatment

• No current vaccine or treatment available
• Supportive care (avoid NSAIDS if dengue possible)
• Report to the health department
• Precautions on mosquito bites and sexual transmission
Prevention

- Prevention of transmission and infection
  - Decrease mosquito bites
    - Decrease standing water sources
    - Insect repellent
    - Long sleeves, long pants
  - Avoid pregnancy when going to high risk areas
  - Avoid unprotected sexual contact when traveling to endemic areas or with persons recently in endemic areas.
Recommendations for Travel

- If pregnant and considering travel to an area with active Zika virus transmission
  - Postpone travel if possible
  - Avoid mosquito bites
    - Long sleeves, long pants
    - EPA registered insect repellents
    - Stay/sleep in screened or air conditioned rooms

CDC, Interim guidelines for pregnant women during a Zika virus outbreak, United States 2016

Recommendations for prevention of sexual transmission of Zika Virus
(for men who have travelled or reside in an area with active Zika transmission)

- Woman pregnant
  - YES
    - Condoms or abstinence for duration of pregnancy*
  - NO
    - Man has traveled to area with active Zika virus transmission
      - Confirmed or suspected Zika virus infection
        - Condoms or abstinence x 6 months
      - No symptoms
        - Condoms or abstinence x 8 weeks
  - Women should wait 8 weeks from last exposure or onset of suspected Zika disease before attempting conception

- Man resides in area with active Zika virus transmission
  - Condoms/abstinence until active transmission declines

*minimizes exposure

CDC, Interim Guidelines for Prevention of Sexual Transmission of Zika Virus and Guidelines for women of reproductive age, United States 2016
Recommendations for screening infants

- Infants with mothers potentially exposed to Zika virus with microcephaly/intracranial calcifications
  - Test mother (Zika IgM/neut Ab, dengue IgM/neut Ab)
  - Test infant (Zika RNA pcr, IgM/neut Ab, dengue IgM/neut Ab)
  - CSF – Zika RNA pcr, IgM/neut Ab, dengue IgM/neut Ab
  - Placenta evaluation
  - Eye exam
  - Hearing evaluation (birth, 6 months)
  - Head imaging
  - Work up for other congenital infection
  - Genetics/neurology evaluation
  - CBC/D, liver enzymes, other
Question:
Zika Virus is most commonly transmitted:
A. By mosquitoes
B. Sexual contact
C. Blood transfusion

Question:
The most common congenital abnormality seen in infants with maternal Zika virus infection is:
A. Poor birth weight
B. Thrombocytopenia
C. Microcephaly
Question:
The best way to protect yourself today from Zika virus infection is:

A. Vaccination
B. Preventing mosquito bites
C. Prophylactic antibiotics

Conclusions:

• Zika virus is now established in Central and South America
• There are no documented cases of Zika virus transmission via mosquitoes in the United States but the potential exists
• Zika virus infection is not usually severe in older children and adults but can lead to devastating neurologic outcomes in the developing fetus
• Recent research suggests Zika virus infection is neurotropic and leads to cell death in developing brains.
• Testing with pcr and serology are available through the health department
Thank You!

Rio Olympics Signs Official Bug Repellant Sponsor

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San Diego County Department of Health and Human Services
619-515-6620

CDC: [www.CDC.gov](http://www.CDC.gov) (Zika)