



# 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

- The virion is approximately 40 nm in diameter with surface projections that measure roughly 5-10 nm.
- Nucleocapsid is 25-30 nm in diameter surrounded by a host-membrane derived lipid bilayer.
- Enveloped
- Icosahedral
- Contains envelope proteins E and M

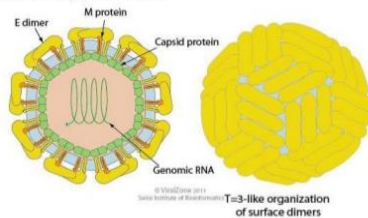


TABLE 2 Genome structures of ZIKV strains

Gene or genomic region	Length	
	African MR 766 prototype strain <sup>a</sup>	French Polynesia H/PP/2013 <sup>b</sup>
5' NCR	106 nt <sup>c</sup>	107 nt
Capsid	122 aa <sup>d</sup>	105 aa
PrM	178 aa	187 aa
Envelope	500 aa	505 aa
NS1	342 aa	352 aa
NS2A	226 aa	217 aa
NS2B	130 aa	139 aa
NS3	617 aa	619 aa
NS4A	127 aa	127 aa
NS4B	252 aa	255 aa
NS5	902 aa	904 aa
3' NCR	428 nt	428 nt
Complete genome	10,794 nt	10,617 nt

<sup>a</sup> Data are from reference 268.

<sup>b</sup> Data are from reference 216.

<sup>c</sup> nt, nucleotides.

<sup>d</sup> aa, amino acids.

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



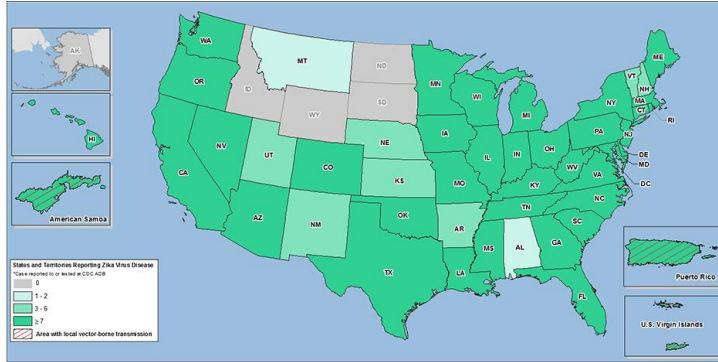
# Zika Virus

- 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”



Wikon N, Smith DR. Lancet 2016

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



Laboratory-confirmed Zika virus disease cases reported to ArboNET by state or territory — United States, 2015-2016 (as of July 13, 2016)

CDC



## Transmission



Culex  
 ↓  
 West Nile Virus



Aedes albopictus



Aedes aegypti

Dengue  
 Chikungunya  
 Yellow Fever  
 Zika Virus







Photo credit: Foy BD, et al. Probable non-vector-borne transmission of Zika virus, Colorado, USA. Emerg Infect Dis 2011;17(5):880–882.



## GBS and Zika virus infection

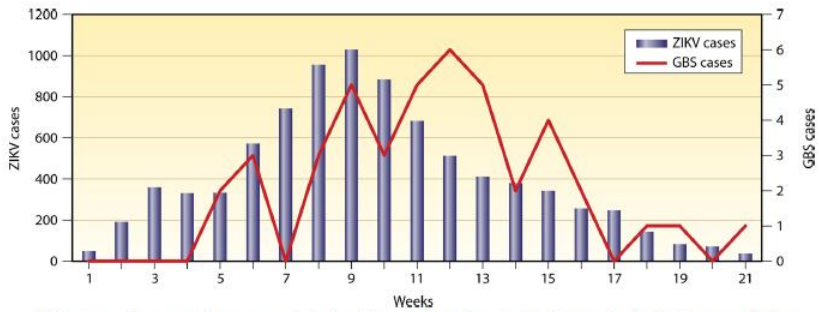


FIG 9 Temporal association between cases of Zika fever (blue columns) and GBS (red line) during the French Polynesian outbreak.

Musso et al, CMR 2016



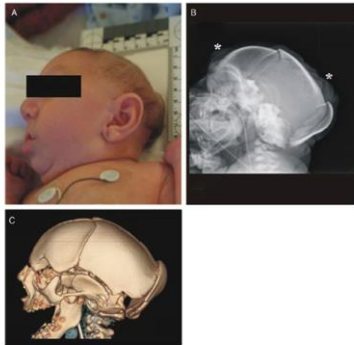


Figure 2. Photograph of the side head (A) shows severe microcephaly with occipital keel-like prominences, and normally developed face. Coronal (B) and 3D coronal tomography reconstruction (C) also show collapse of the calvarium with extensive separation of the calvarial sutures. Note the skin ridge (\*) on the occiput.



Culijat et al CID 2016



### Phenotypic findings of first 35 patients enrolled in the Brazilian Society of Medical Genetics-Zika embryopathy Task Force Registry – Brazil 2015

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

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

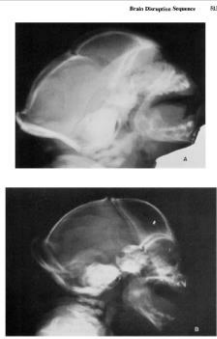


Fig. 13.18 Lateral radiograph of skull. (A) Case 1. (B) Case 2. See notes introduction to chapter.

Russell et al, AJMG 1984

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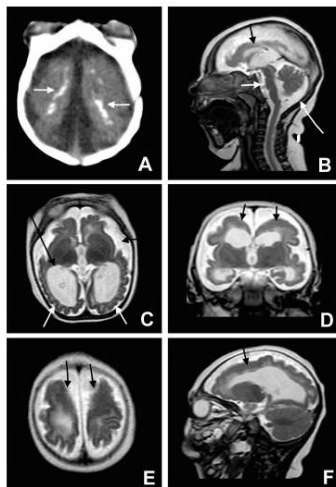
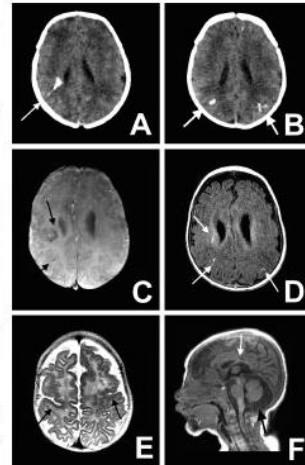


Fig 2 | Microcephaly, cortical malformation, and brain calcification. Axial CT image (A) shows many small dystrophic calcifications in the junction between cortical and subcortical white matter (white arrow) and noticeable reduction of the brain parenchyma thickness. Sagittal T2 weighted image (B) shows hypogenesis of the corpus callosum (black arrow), enlarged cisterna magna (long white arrow), and pons hypoplasia (white arrow). Axial T2-weighted image (C) shows simplified gyral pattern (white arrow), ventriculomegaly (long black arrow) widely open Sylvius fissure as well as enlargement of subarachnoid space (black arrow). Coronal T2 weighted image (D) shows pachygyria in the frontal lobes (black arrows). Note the bilateral cortical thickness in the pachygyric frontal lobe (black arrows), shown on axial and sagittal T2 weighted images (E and F).

Fig 5 | Mild microcephaly. Axial non-contrast CT image (A and B) shows multiple bilateral calcifications in the junction between cortical and subcortical white matter (white arrows). Axial susceptibility magnetic weighted image (C) shows multiple foci of T2-hypointensity in subcortical frontal white matter (black arrows), and axial T1 weighted image (D) shows linear or punctiform foci of T1-shortening (white arrows), which correspond to the calcifications on CT. Axial T2 weighted image (E) shows bilateral frontal and central sulcus polymicrogyria (black arrows). Note the thickened and irregular cortical-white matter junction. Sagittal T1 weighted image (F) shows enlarged cisterna magna (black arrow) and hypoplastic corpus callosum (white arrow).



Vasca Aragao BMJ 2016

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## 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



Figure: Chorioretinal scar on the macular region of the left eye with no associated optic disc findings in an infant without microphthalmia

## 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.

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## Mosquito Bite Prevention (United States)

Not all mosquitoes are the same. Different mosquitoes spread different viruses and bite at different times of the day.

Type of Mosquito	Viruses spread	Biting habits
<ul style="list-style-type: none"> <li>▲ <b>Aedes aegypti</b></li> <li>▲ <b>Aedes albopictus</b></li> </ul>	<ul style="list-style-type: none"> <li>▲ Chikungunya</li> <li>▲ Dengue</li> <li>▲ Zika</li> </ul>	<ul style="list-style-type: none"> <li>▲ Primarily daytime, but can also bite at night</li> </ul>
<ul style="list-style-type: none"> <li>▲ <b>Culex species</b></li> </ul>	<ul style="list-style-type: none"> <li>▲ West Nile</li> </ul>	<ul style="list-style-type: none"> <li>▲ Evening to morning</li> </ul>

**Protect yourself and your family from mosquito bites**

**Use insect repellent**

Use an Environmental Protection Agency (EPA) registered insect repellent with one of the following active ingredients. When used as directed, EPA-registered insect repellents are proven safe and effective, even for pregnant and breastfeeding women.

Active ingredient	Some brand name examples*
<ul style="list-style-type: none"> <li>Higher percentages of active ingredient provide longer protection</li> </ul>	
<ul style="list-style-type: none"> <li><b>DEET</b></li> </ul>	<ul style="list-style-type: none"> <li>Off!, Cutter, Sawyer, Ultrathon</li> </ul>
<ul style="list-style-type: none"> <li><b>Picaridin</b>, also known as <b>KBR 3023</b>, <b>Bayrepel</b>, and <b>icaridin</b></li> </ul>	<ul style="list-style-type: none"> <li>Cutter Advanced, Skin So Soft Bug Guard Plus, Aftan (outside the United States)</li> </ul>
<ul style="list-style-type: none"> <li><b>Oil of lemon eucalyptus (OLE)</b> or <b>para-menthane-diol (PMD)</b></li> </ul>	<ul style="list-style-type: none"> <li>Repel</li> </ul>
<ul style="list-style-type: none"> <li><b>IR3535</b></li> </ul>	<ul style="list-style-type: none"> <li>Skin So Soft Bug Guard Plus Expedition, SkinSmart</li> </ul>

\*Insect repellent brand names are provided for your information only. The Centers for Disease Control and Prevention and the U.S. Department of Health and Human Services cannot recommend or endorse any name brand products.

### Protect yourself and your family from mosquito bites (continued)



- Always follow the product label instructions.
- Reapply insect repellent every few hours, depending on which product and strength you choose.
  - Do not spray repellent on the skin under clothing.
  - If you are also using sunscreen, apply sunscreen first and insect repellent second.
- Natural insect repellents (repellents not registered with EPA)
  - The effectiveness of non-EPA registered insect repellents, including some natural repellents, is not known.
  - To protect yourself against diseases like chikungunya, dengue, and Zika, CDC and EPA recommend using an EPA-registered insect repellent.
  - When used as directed, EPA-registered insect repellents are proven safe and effective.
  - For more information: [www2.epa.gov/insect-repellents](http://www2.epa.gov/insect-repellents)

### If you have a baby or child



- Always follow instructions when applying insect repellent to children.
- Do not use insect repellent on babies younger than 2 months of age.
- Dress your child in clothing that covers arms and legs, or
  - Cover crib, stroller, and baby carrier with mosquito netting
- Do not apply insect repellent onto a child's hands, eyes, mouth, and cut or irritated skin.
  - Adults: Spray insect repellent onto your hands and then apply to a child's face
  - Do not use products containing oil of lemon eucalyptus (OLE) or para-menthane-diol (PMD) on children under 3 years of age.

### Treat clothing and gear



- Treat items such as boots, pants, socks, and tents with permethrin or purchase permethrin-treated clothing and gear.
  - Permethrin-treated clothing will protect you after multiple washings. See product information to find out how long the protection will last.
  - If treating items yourself, follow the product instructions.
  - Do not use permethrin products directly on skin.

### Mosquito-proof your home



- Use screens on windows and doors. Repair holes in screens to keep mosquitoes outside.
- Use air conditioning when available.
- Keep mosquitoes from laying eggs in and near standing water.
  - Once a week, empty and scrub, turn over, cover, or throw out items that hold water, such as tires, buckets, planters, toys, pools, birdbaths, flowerpots, or trash containers. Check inside and outside your home.

[www.cdc.gov/features/StopMosquitoes](http://www.cdc.gov/features/StopMosquitoes)

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## Recommendations for Travel

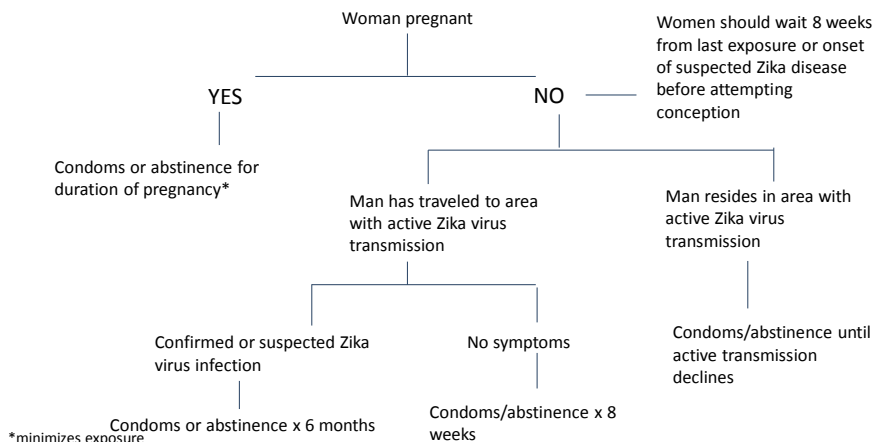
- If pregnant and considering travel to an area with active Zika virus transmission
  - Postpone travel if possible
  - Avoid mosquito bites
    - Long sleeves, long pants
    - EPA registered insect repellents
    - Stay/sleep in screened or air conditioned rooms

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)

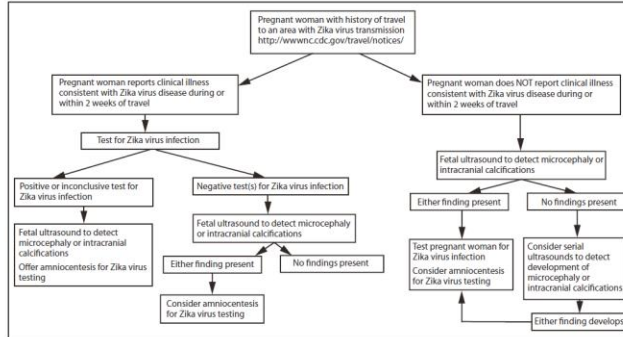


CDC, Interim Guidelines for Prevention of Sexual Transmission of Zika Virus and Guidelines for women of reproductive age, United States 2016



## Recommendations for pregnant women

FIGURE. Interim guidance: testing algorithm<sup>a,1,2</sup> for a pregnant woman with history of travel to an area<sup>3</sup> with Zika virus transmission, with or without clinical illness<sup>4</sup> consistent with Zika virus disease



<sup>a</sup> Availability of Zika virus testing is limited; consult your state or local health department to facilitate testing. Tests include Zika virus reverse transcription-polymerase chain reaction (RT-PCR) and Zika virus immunoglobulin M (IgM) and neutralizing antibodies on serum specimens. Given the overlap of symptoms and endemic areas with other viral illnesses, evaluate for possible dengue or chikungunya virus infection.

<sup>1</sup> Laboratory evidence of maternal Zika virus infection: 1) Zika virus RNA detected by RT-PCR in any clinical specimen; or 2) positive Zika virus IgM with confirmatory neutralizing antibody titers that are  $\geq 4$ -fold higher than dengue virus neutralizing antibody titers in serum. Testing would be considered inconclusive if Zika virus neutralizing antibody titers are  $< 4$ -fold higher than dengue virus neutralizing antibody titers.

<sup>2</sup> Amniocentesis is not recommended until after 15 weeks of gestation. Amniotic fluid should be tested for Zika virus RNA by RT-PCR.

<sup>3</sup> Updates on areas with ongoing Zika virus transmission are available online (<http://wwwnc.cdc.gov/travel/notices/>).

<sup>4</sup> Clinical illness is consistent with Zika virus disease if two or more symptoms (acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis) are present.

CDC, Interim guidelines for pregnant women during a Zika virus outbreak, 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
  - CBCD, liver enzymes, other

CDC, Interim guidelines for the evaluation and testing of infants with possible congenital Zika virus infection, United States 2016



## 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

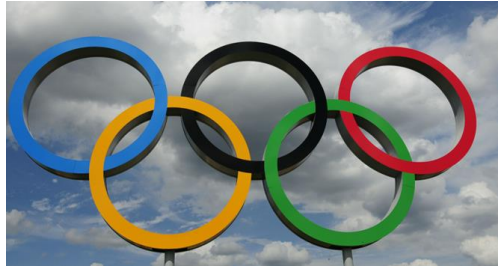


# Thank You!

HEALTH RIO OLYMPICS

## Rio Olympics Signs Official Bug Repellant Sponsor

by Madeline Fisher JULY 5, 2016, 12:28 PM EDT



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

