Zika in Pregnancy

September 17, 2017

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Maternal Fetal Medicine
Medical University of South Carolina
Disclosure

• I have no financial disclosures
Remember when.....

• A couple of years ago, an encounter with a mosquito did not pose a major health concern to most of the developed world.

• Unfortunately, with the dire effects of Zika virus
Goals

• History
• Infection
• Transmission
• Fetal sequelae
• Testing algorithm
• Updates
Zika Virus

• Single stranded RNA Virus
• Belongs to the Flavivirus family
• Mosquito born illnesses due to Flaviruses include:
  • Yellow Fever
  • Dengue Fever
  • Japanese Encephalitis
  • West Nile Virus
  • Zika Virus
• Primarily transmitted to humans by *Aedes (Steomyia)* species mosquito
History

• Initially identified – 1947 Rhesus monkey
History
History

• First human cases in 1950’s
• 2007 Yap Island – Micronesia
  • 73% population infected
• 2013-2014 French Polynesia
  • 10% population infected (25K persons)
  • 2 cases vertical transmission – neurologic complications
• 2015 Brazil
Laboratory-confirmed symptomatic Zika virus disease cases* reported to ArboNET by states and territories—United States, 2017 (Provisional data as of August 16, 2017)

States and Territories Reporting Zika Virus Disease, 2017

- 0 cases
- 1 - 11 cases
- 12 - 22 cases
- 23 - 49 cases
- 50 - 100 cases
- > or = 101 cases

*Case counts include all symptomatic Zika virus disease cases, including cases in travelers returning from affected areas, cases acquired through presumed local mosquito-borne transmission and cases acquired through other routes. Cross hatching signifies areas with reported local mosquito-borne transmission in 2017.
Air Travel Between U.S. and Zika-Affected Areas

Courtesy Dr. Thomas Quinn
Director, Center for Global Health
JHU
US Zika virus cases (all)

Laboratory-confirmed symptomatic Zika virus disease cases* reported to ArboNET by states – United States, 2016–2017 (provisional data from January 1, 2016 – August 16, 2017)
**Zika pregnancy registry**

- Outcomes for US States and District of Columbia

<table>
<thead>
<tr>
<th>Completed with or without birth defects</th>
<th>Liveborn infants with birth defects</th>
<th>Pregnancy losses with birth defects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,180</td>
<td>93</td>
<td>4</td>
</tr>
</tbody>
</table>

- Outcomes for US Territories

<table>
<thead>
<tr>
<th>Completed with or without birth defects</th>
<th>Liveborn infants with birth defects</th>
<th>Pregnancy losses with birth defects</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,130</td>
<td>128</td>
<td>7</td>
</tr>
</tbody>
</table>

CDC.Gov – Data as of 08/08/2017
MUSC Information – since June 2016

• **As of August 21, 2017:** Total 85 samples for Zika testing to SC DHEC.

• Since March 2017, we have submitted 24, all of which have been negative.

• We continue to provide Zika testing free of charge using S.C. DHEC.

• Prices of private tests:
  • Zika RNA PCR testing on serum and urine are about $1000.00
  • Zika IgM serology testing is around $300.00.
Zika Virus Infection

- Incubation 3-12 days
- Viremia ~7 days, but up to 60 days
- 80% of infected patients have no symptoms
- Symptomatic disease (sx’s start 2-7 days after bite)
  - Mild most common
    - Some have severe disease
  - Fever
  - Maculopapular rash
  - Arthralgia (joint pain)
  - Non-purulent conjunctivitis
## 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>
</tbody>
</table>
Zika Virus Infection

- Adult disease sequelae
  - Rare to have severe disease or death
  - Guillain-Barre syndrome
  - Fetal complications

Meaney-Delman et al Obstet Gynec 2016;0:1-7
ZIKV Transmission

- *Aedes* genus of mosquito is the common vector (*Aedes aegypti* and *Aedes albopictus*)
- Vertical transmission
  - Antepartum
  - Intrapartum
  - Breastfeeding – no cases but ZIKV RNA is found in breast milk. Official recommendation is to allow breastfeeding
- Sexual transmission
- Blood bank
- Laboratory exposure
ZIKV Sexual Transmission

• Case reports
  • Musso et al 2/2015  Potential Sexual Transmission of Zika Virus
    • 12/2013 French Polynesia Male developed hematospermia – ZIKV isolated.
  • Colorado and then Texas confirmed transmission Male to Female
  • Several new cases now being investigated
    • 2/23/2016 CDC Health Advisory
    • All male to female and all from symptomatic males

Men and women traveling in an area with risk of Zika should consider using condoms every time they have sex or not have sex while traveling.

<table>
<thead>
<tr>
<th>Affected Partner</th>
<th>Timeframe to Prevent Sexual Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>If a couple has a male partner and <strong>only he travels</strong> to an area with risk of Zika</td>
<td>The couple should consider using condoms or not having sex for at least <strong>6 months</strong></td>
</tr>
<tr>
<td></td>
<td>• After the male partner returns, even if he doesn't have symptoms, or</td>
</tr>
<tr>
<td></td>
<td>• From the start of the male partner’s symptoms or the date he was diagnosed with Zika.</td>
</tr>
<tr>
<td>If a couple has a female partner and <strong>only she travels</strong> to an area with risk of Zika</td>
<td>The couple should consider using condoms or not having sex for at least <strong>8 weeks</strong></td>
</tr>
<tr>
<td></td>
<td>• After the female partner returns from to an area with risk of Zika, even if she doesn't have symptoms, or</td>
</tr>
<tr>
<td></td>
<td>• From the start of the female partner’s symptoms or the date she was diagnosed with Zika.</td>
</tr>
<tr>
<td>If the couple contains both a male and female partner and <strong>both travel</strong> to an area with risk of Zika</td>
<td>The couple should consider using condoms or not having sex for at least <strong>6 months</strong></td>
</tr>
<tr>
<td></td>
<td>• After returning from an area with risk of Zika, even if they don't have symptoms, or</td>
</tr>
<tr>
<td></td>
<td>• From the start of either partner’s symptoms or from the date either were diagnosed with Zika.</td>
</tr>
</tbody>
</table>
Zika and human effects

**Zika Neural tropism**

**Fetal**
- NPC
  - Microcephaly
  - Cognitive defects
- Neuro retina
  - Retinal blindness

**Adult**
- NPC
  - Stem cell niche loss
- Immune activation
  - Post-infectious polyradiculopathy
- Neuro retina
  - Uveitis
  - Conjunctivitis

CAUSE AND EFFECT?

• Increased number of cases of microcephaly in Brazil
• Zika virus detected in amniotic fluid of pregnant women whose fetus had sonographic evidence of microcephaly
• Zika virus additionally isolated in culture from amniotic fluid, placenta and fetal brain in other affected pregnancies.

De Carvalho et al 2017.
Skepticism

1.) The last time an infectious pathogen was discovered to cause an epidemic of fetal defects was more than 50 years ago (i.e., rubella virus)

2.) No flavivirus has ever been shown definitively to cause birth defects in humans

3.) No reports of adverse pregnancy or birth outcomes were noted during previous outbreaks of ZIKV virus disease
Zika fetal neuropathogenesis

• ZIKV can infect human induced pleuripotent stem cell-derived neural progenitor cells, human neurospheres and brain organoids in vitro → dysregulation of cell cycle-related pathways and increased apoptosis

Hypotheses for Zika induced fetal neuropathogenesis

- Transcytosis across placenta
- Placental infection by Zika
- Transmission of Zika-infected maternal cells across placenta at any stage of pregnancy

Zika infection induces immune response and deregulation of microcephaly associated genes

Li et al, 2016.

Expression of microcephaly-associated genes between viral injection side of brains and controls as determined by real-time PCR
Fetal effects

• Microcephaly

• Abnormal neurologic image findings
  • Calcifications (periventricular, intraparenchymal)
  • Ventriculomenagly
  • Cerebellar hypoplasia
  • Lissencephaly

• Eye

• Joints – limited range of motion (clubfeet)

• Increased muscle tone
What is Microcephaly....

• Head significantly smaller than would be expected at a specific gestational age and sex

• Associated with
  • Genetic disorders (Chromosomal and single gene disorders)
  • Environmental
    • Perinatal infections
    • Prenatal exposure to drugs or chemicals
    • Perinatal hypoxia or trauma
• February, 2016
  
  • Isolated fetal microcephaly ≥ 3 SD below mean for GA
  • Pathologic microcephaly if ≥ 5 SD below mean for GA
  • If > 2 SD, careful intracranial anatomy evaluation and repeat in 3-4 weeks
<table>
<thead>
<tr>
<th>Gestational age, wk</th>
<th>Mean, mm</th>
<th>Head circumference, mm: SD below mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>-1</td>
</tr>
<tr>
<td>20</td>
<td>175</td>
<td>160</td>
</tr>
<tr>
<td>21</td>
<td>187</td>
<td>172</td>
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<tr>
<td>22</td>
<td>198</td>
<td>184</td>
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<tr>
<td>23</td>
<td>210</td>
<td>195</td>
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<tr>
<td>24</td>
<td>221</td>
<td>206</td>
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<tr>
<td>25</td>
<td>232</td>
<td>217</td>
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<td>26</td>
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<td>27</td>
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<td>28</td>
<td>262</td>
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<td>29</td>
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<td>30</td>
<td>281</td>
<td>266</td>
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<td>31</td>
<td>289</td>
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<td>32</td>
<td>297</td>
<td>283</td>
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<td>33</td>
<td>305</td>
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<td>34</td>
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<td>297</td>
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<td>35</td>
<td>319</td>
<td>304</td>
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<td>36</td>
<td>325</td>
<td>310</td>
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<td>37</td>
<td>330</td>
<td>316</td>
</tr>
<tr>
<td>38</td>
<td>335</td>
<td>320</td>
</tr>
<tr>
<td>39</td>
<td>339</td>
<td>325</td>
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<td>40</td>
<td>343</td>
<td>328</td>
</tr>
<tr>
<td>41</td>
<td>346</td>
<td>331</td>
</tr>
<tr>
<td>42</td>
<td>348</td>
<td>333</td>
</tr>
</tbody>
</table>


### Table 2: Ultrasound findings at different gestational ages

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>16–20 weeks of gestation (n=12)</th>
<th>20–24 weeks of gestation (n=10)</th>
<th>24–28 weeks of gestation (n=5)</th>
<th>28–32 weeks of gestation (n=4)</th>
<th>Total fetuses scanned (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal ultrasound</td>
<td>4 (33%)</td>
<td>9 (90%)</td>
<td>5 (100%)</td>
<td>4 (100%)</td>
<td>14 (100%)</td>
</tr>
<tr>
<td>Ventriculomegaly greater than 10 mm</td>
<td>3 (25%)</td>
<td>5 (50%)</td>
<td>4 (80%)</td>
<td>4 (100%)</td>
<td>12 (86%)</td>
</tr>
<tr>
<td>Cortical atrophy with enlarged pericerebral spaces</td>
<td>3 (25%)</td>
<td>6 (60%)</td>
<td>4 (80%)</td>
<td>4 (100%)</td>
<td>11 (79%)</td>
</tr>
<tr>
<td>Cortical calcifications</td>
<td>2 (17%)</td>
<td>7 (70%)</td>
<td>5 (100%)</td>
<td>4 (100%)</td>
<td>10 (71%)</td>
</tr>
<tr>
<td>Abnormal corpus callosum</td>
<td>2 (17%)</td>
<td>7 (70%)</td>
<td>5 (100%)</td>
<td>4 (100%)</td>
<td>10 (71%)</td>
</tr>
<tr>
<td>Calcifications in basal ganglia nuclei</td>
<td>3 (25%)</td>
<td>2 (20%)</td>
<td>4 (80%)</td>
<td>4 (100%)</td>
<td>10 (71%)</td>
</tr>
<tr>
<td>Microcephaly less than third percentile</td>
<td>2 (17%)</td>
<td>4 (40%)</td>
<td>3 (60%)</td>
<td>4 (100%)</td>
<td>9 (64%)</td>
</tr>
<tr>
<td>Abnormal gyration</td>
<td>0</td>
<td>1 (10%)</td>
<td>2 (40%)</td>
<td>4 (100%)</td>
<td>6 (43%)</td>
</tr>
<tr>
<td>Abnormal posterior cranial fossa</td>
<td>3 (25%)</td>
<td>3 (30%)</td>
<td>1 (20%)</td>
<td>1 (25%)</td>
<td>5 (36%)</td>
</tr>
<tr>
<td>Abnormal pons</td>
<td>1 (8%)</td>
<td>0</td>
<td>0</td>
<td>2 (50%)</td>
<td>3 (21%)</td>
</tr>
<tr>
<td>Polymalformative syndrome*</td>
<td>1 (8%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Intrauterine growth restriction</td>
<td>2 (17%)</td>
<td>2 (20%)</td>
<td>0</td>
<td>1 (25%)</td>
<td>4 (29%)</td>
</tr>
</tbody>
</table>

Data are n (%). At 12–16 weeks of gestation, 0 of 14 scans showed any ultrasound abnormalities. Data in first four columns are number of scans with abnormality out of total number of scans done during the specified time period; final column shows total number of fetuses in which each abnormality was seen. *Encephalocele, anophthalmia, arthrogryposis, and hydrops fetalis.
Intracranial calcifications
Absent normal vermis
Dysgenesis of the corpus callosum
Brain atrophy
Severe asymmetric Ventriculomegaly
Absent thalamus, Eye calcifications
Fetal/Neonatal effects

• Eye abnormalities
  • 29 infants with microcephaly in Brazil
    • 35% had ocular abnormalities (chorioretinal atrophy and focal pigment mottling)

Freitas and Colleagues, JAMA Ophthal February 9, 2016 Online
If infected what % babies have anomalies

### Pregnancy Outcomes After Maternal Zika Virus Infection During Pregnancy - U.S. Territories, January 1, 2016-April 25, 2017

<table>
<thead>
<tr>
<th>Characteristic</th>
<th># Brain abnormalities/ Microcephaly</th>
<th># of completed pregnancies</th>
<th>% ZIKAV associated BD (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any laboratory evidence of recent possible ZIKA V infection</td>
<td>108</td>
<td>2,549</td>
<td>5 (4-6)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal symptom status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sx ZIKAV</td>
<td>68</td>
<td>1,561</td>
<td>5 (4-6)</td>
</tr>
<tr>
<td>Asx</td>
<td>38</td>
<td>966</td>
<td>4 (3-6)</td>
</tr>
<tr>
<td>Timing of symptoms or specimen collection date</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First trimester</td>
<td>27</td>
<td>536</td>
<td>6 (4-8)</td>
</tr>
<tr>
<td>Second trimester</td>
<td>46</td>
<td>1,096</td>
<td>5 (4-6)</td>
</tr>
<tr>
<td>Third trimester</td>
<td>31</td>
<td>876</td>
<td>4 (3-6)</td>
</tr>
</tbody>
</table>

Shapiro-Mendoza CK, MMWR Morb Weekly Rep 2017; 66-621
ZIKV Testing

- RT-PCR validated
  - Serum, amniotic fluid, placenta, fetal tissues, semen
  - Good about 7 days of symptom onset
- Serologic testing
  - IgM (ELISA) turns positive ~ 4-7 days
    - Cross-reaction with other flaviviruses, including vaccination and infections
    - Plaque reducing neutralization test
- Immunohistochemical staining
- Nationally notifiable disease

Meaney-Delman et al Obstet Gynecol 2016;0:1-7
CDC’s Response to Zika

UPDATED INTERIM PREGNANCY GUIDANCE: SYMPTOMATIC PREGNANT WOMEN WITH POSSIBLE ZIKA VIRUS EXPOSURE

Testing Recommendations and Interpretation of Results for Healthcare Providers

ASK PREGNANT WOMEN ABOUT

WHOM to test?

Pregnant women reporting possible exposure during current pregnancy and symptoms of Zika virus disease* 

WHEN to test?

Test as soon as possible, through 12 weeks after symptom onset

WHICH tests?

Zika virus NAT (serum and urine) AND Zika virus IgM serology (serum)*

RESULTS and ADDITIONAL tests

ACUTE ZIKA VIRUS INFECTION

ZIKA VIRUS INFECTION, TIMING OF INFECTION CANNOT BE DETERMINED

"For pregnant women without Zika virus exposure before the current pregnancy, a positive IgM result represents recent Zika virus infection."

FLAVIVIRUS INFECTION, SPECIFIC VIRUS AND TIMING OF INFECTION CANNOT BE DETERMINED

"For pregnant women without Zika virus exposure before the current pregnancy, a positive IgM result represents recent unspecified flavivirus infection."

NO EVIDENCE OF ZIKA VIRUS INFECTION

INTERPRETATION

https://www.cdc.gov/mmwr/volumes/66/wr/mm6629e1.htm?s_cid=mm6629e1_w

*Not all results are positive, despite exposure or possiblepositive. Testing should be performed in accordance with local public health guidelines. 

Note: For the purpose of this guidance, recent exposure to Zika virus includes exposure to individuals who tested positive for Zika virus within 6 weeks of the current pregnancy.

U.S. Department of Health and Human Services
Center for Disease Control and Prevention

OS06738-4 - July 24, 2017
## When to test

<table>
<thead>
<tr>
<th>If your patient…</th>
<th>Testing recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Was exposed to Zika AND has symptoms of Zika virus infection or a history or symptoms at any time during her pregnancy</td>
<td>• She should be tested for Zika as soon as possible. Concurrent RNA nucleic acid test (NAT) testing and Zika virus IgM testing is recommended as soon as possible or through 12 weeks after symptom onset.</td>
</tr>
<tr>
<td>Lives in or frequently travels to an area with risk of Zika but does not have symptoms of Zika virus infection.</td>
<td>She should be offer testing three times during pregnancy using RNA NAT testing.</td>
</tr>
<tr>
<td>Traveled to or had sex without a condom with a partner who lived in or traveled to an area with risk of Zika but does not have symptoms of Zika virus infection</td>
<td>Testing is not routinely recommended. Testing should be considered using a shared decision-making model that includes pretest counseling, individualized risk assessment, clinical judgment, patient preferences, and the jurisdiction’s recommendations.</td>
</tr>
<tr>
<td>Was exposed to Zika AND had birth defects potentially associated with Zika detected on a prenatal ultrasound</td>
<td>Concurrent RNA NAT testing and Zika virus IgM testing is recommended. If amniocentesis is being done for clinical care, healthcare providers should also test the amniotic fluid for Zika genetic material. Testing of placental and fetal tissues may also be considered if results of maternal Zika virus testing are not definitive.</td>
</tr>
</tbody>
</table>
Pregnant woman with history of travel to an area with ongoing Zika virus transmission

Test for Zika virus infection

Positive or inconclusive for Zika virus infection
- Consider serial fetal ultrasounds
  - Consider amniocentesis for Zika virus testing

Negative for Zika virus infection
- Fetal ultrasound to detect microcephaly or intracranial calcifications
  - Microcephaly or intracranial calcifications present
    - Retest pregnant woman for Zika virus infection
    - Consider amniocentesis for Zika virus testing
  - Microcephaly or intracranial calcifications not present
    - Routine prenatal care
Pregnant woman with history of travel to an area with ongoing Zika virus transmission

Test for Zika virus infection  

Positive or inconclusive for Zika virus infection
- Consider serial fetal ultrasounds
  - Consider amniocentesis for Zika virus testing  

Negative for Zika virus infection
- Fetal ultrasound to detect microcephaly or intracranial calcifications  
  - Microcephaly or intracranial calcifications present
    - Retest pregnant woman for Zika virus infection
      - Consider amniocentesis for Zika virus testing  
  - Microcephaly or intracranial calcifications not present
    - Routine prenatal care
Pregnancy Effects

• Unknown if pregnant women are more susceptible
• Disease does not appear to be any worse in pregnancy
• Transmission to the fetus has been documented in all trimesters
  • Zika RNA in abortus tissues, AF, placenta and term neonates
The unknowns for counseling

• Incidence among pregnant women
• Rate of vertical transmission
• Rate of clinical manifestations of the fetus is infected

• If a woman was infected prior to pregnancy and up to 4 weeks, not expected to have any fetal effects
Recommendations for Pregnant Women

• CDC Recommends all pregnant women consider postponing travel to areas of ongoing Zika virus transmission if possible
  • http://wwwn.cdc.gov/travel/notices

• If pregnant women have to travel, avoid mosquito bites
  • Protective clothing
  • U.S. EPA-registered insect repellent
  • Screened-in or air-conditioned areas
If an infant is Zika infected...

The prognosis for infants with congenital Zika virus infection is not known. In infants with severe microcephaly from other causes, a range of neurologic sequelae have been reported (e.g., intellectual disability, hearing loss, vision loss, and seizures). These problems can range from mild to severe, are often life-long, and in some cases can be life-threatening.
Current Commentary

Zika Virus and Pregnancy
What Obstetric Health Care Providers Need to Know
Dana Meaney-Delman, MD, MPH, Sonja A. Rasmussen, MD, MS, J. Erin Staples, MD, PhD, Titilope Oduyebo, MD, Sascha R. Ellington, MSPH, Emily E. Petersen, MD, Marc Fischer, MD, and Denise J. Jamieson, MD, MPH

• Great summary for anyone working in the field of Women’s Health
### PRECONCEPTION COUNSELING

<table>
<thead>
<tr>
<th>Preconception Counseling</th>
<th>Red</th>
<th>Yellow</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>With Zika symptoms and/or diagnosis</strong></td>
<td>Women and men who are planning to conceive in the near future should be advised to wait <strong>at least 8 weeks</strong> if a woman had Zika symptoms and/or diagnosis, and <strong>at least 6 months</strong> if a man had Zika symptoms and/or diagnosis, before attempting conception.</td>
<td>Women and men who are planning to conceive in the near future should consider waiting <strong>at least 8 weeks</strong> if only the woman was exposed and <strong>at least 6 months</strong> if the man was exposed after the end date of the last possible exposure before attempting conception.</td>
</tr>
<tr>
<td><strong>No Zika symptoms, and without ongoing exposure</strong></td>
<td>Women and men who are planning to conceive in the near future should be advised to wait <strong>at least 8 weeks</strong> if only the woman was exposed and <strong>at least 6 months</strong> if the man was exposed after the end date of the last possible exposure before attempting conception.</td>
<td>Women and men who are planning to conceive in the near future should consider waiting <strong>at least 8 weeks</strong> if only the woman was exposed and <strong>at least 6 months</strong> if the man was exposed after the end date of the last possible exposure before attempting conception.</td>
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</tbody>
</table>
| **No Zika symptoms and with ongoing exposure** | • Women and men who are planning to conceive in the near future should be counseled on the possible risk for Zika virus infection during the periconceptional period and about the potential consequences of Zika virus infection to the fetus during pregnancy. Healthcare providers should discuss reproductive life plans with patients and review factors that might influence pregnancy timing (e.g., duration of Zika virus outbreak, fertility, age, reproductive history, medical history, personal values and preferences).  
• Women and men who live in or travel to red or yellow areas should be advised to remain aware of Zika virus transmission and strictly follow [steps to prevent mosquito bites](#). | |
CDC recommendations

- Consider postponing travel to affected areas (see prior slides)
- If traveling there:
  - Strictly follow steps to avoid mosquito bites
  - These mosquitoes bite
    - Mostly during the daytime
    - Indoors and outdoors
What can travelers do to prevent Zika?

There is no vaccine to prevent or medicine to treat Zika. Travelers can protect themselves by preventing mosquito bites:

- Cover exposed skin by wearing long-sleeved shirts and long pants.
- Use EPA-registered insect repellents containing DEET, picaridin, oil of lemon eucalyptus (OLE), or IR3535. Always use as directed.
  - Pregnant and breastfeeding women can use all EPA-registered insect repellents, including DEET, according to the product label.
  - Most repellents, including DEET, can be used on children aged >2 months.
- Use permethrin-treated clothing and gear (such as boots, pants, socks, and tents). You can buy pre-treated clothing and gear or treat them yourself.

- Stay and sleep in screened-in or air-conditioned rooms.

https://www.cdc.gov/westnile/faq/repellent.html

https://www.epa.gov/insect-repellents/find-repellent-right-you
Latest CDC update (7/24/2017)

1.) Declining prevalence of ZIKAV in Americas
2.) Evidence prolonged detection of Zika IgM Ab
Latest CDC update (7/24/2017)

1.) All pregnant women US/Territories asked about Zika exposure EVERY visit
2.) Pregnant/recent exposure AND symptoms = TEST through 12 weeks after symptoms
3.) Asymptomatic – ONGOING exposure – offer NAT 3x during pregnancy
4.) NO LONGER recommends routine Zika virus testing for asymptomatic pregnant women without ongoing exposure
5.) Possible exposure and ultrasound findings = Testing NAT/IgM
6.) Preconception ZIKAV IgM NOT recommended
Zika Vaccine

- Many flavivirus diseases are vaccine preventable
- Vaccines are available for YFV, JEV, and TBEV,
- Problems preventing development of safe and effective vaccines for WNV and DENV
  - Multiple viral strains
  - No robust animal models
  - Antibody-dependent enhancement
- Zika
Antiviral Therapy

- ZIKAV replication machinery in genome similar to Hepatitis C
  - NS2B-NS3 protease

- Shiryaev, et al 2017
  - NSC157058 decreases ZIKV in mice

Shiryaev SA, Antiviral Research 143 (2017) 218e229
Table 1. Selected viral TORCH pathogens and associated morbidity. After [75].

<table>
<thead>
<tr>
<th>Viral TORCH Pathogen</th>
<th>Symptoms</th>
<th>First or Second Trimester Teratogen</th>
<th>Third Trimester Teratogen</th>
<th>Primary microcephaly</th>
<th>Spontaneous abortion or fetal death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubella virus (German measles)</td>
<td>Defects in multiple organ systems, including the ophthalmic (cataracts and microphthalmia), cardiac, and neurological (deafness, mental retardation), and increased risk of type 1 diabetes in childhood</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Mental retardation, sensorineural hearing loss, jaundice, hepatosplenomegaly, petechiae, preterm birth, preeclampsia, and fetal growth restriction</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Herpes simplex virus</td>
<td>Encephalitis, sepsis, cataracts, pneumonia, myocarditis, hepatosplenomegaly, chorioretinitis, and mental retardation</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Varicella zoster virus (chickenpox)</td>
<td>Skin lesions, neurological and eye defects, limb hypoplasia, fetal growth restriction, and defects of multiple organ systems</td>
<td>+</td>
<td>-</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Zika virus</td>
<td>Microcephaly, facial disproportionality, cutis gyrata, hypertonia and/or spasticity, hyperreflexia, and irritability; abnormal neuroimages include calcifications, ventriculomegaly, and lissencephaly</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

doi:10.1371/journal.pntd.0004877.t001

• Thank you