The Buzz on Zika: Should We Still Be Concerned?

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Aedes aegypti
Background

- Zika virus is transmitted to humans primarily through the bite of infected *Aedes* sp. mosquito
  - Nearly all Zika outbreaks due to *aegypti* & *albopictus*
  - These are the same mosquitoes that transmit dengue and chikungunya
    - Dengue and Zika are flaviviruses (YF); chikungunya: alphavirus
    - West Nile also arbovirus/flavivirus, but spread by Culex sp.
  - The mosquito vectors typically breed in domestic water-holding containers
  - *Aegypti* -- high “vectorial capacity”: feeds primarily on humans, multiple humans in a single meal, lives close to humans, also daytime and nighttime feeders
PROTECT YOUR FAMILY AND COMMUNITY:
HOW ZIKA SPREADS

Most people get Zika from a mosquito bite

A mosquito bites a person infected with Zika virus

The mosquito becomes infected

A mosquito will often live in a single house during its lifetime

More mosquitoes get infected and spread the virus

The infected mosquito bites a family member or neighbor and infects them

More members in the community become infected

Other, less common ways, people get Zika:

During pregnancy
A pregnant woman can pass Zika virus to her fetus during pregnancy. Zika causes microcephaly, a severe birth defect that is a sign of incomplete brain development

Through sex
Zika virus can be sexually transmitted by a man to his partners

Through blood transfusion
There is a strong possibility that Zika virus can be spread through blood transfusions

CDC
Centers for Disease Control and Prevention
Clinical Disease

- About 20% of people infected with Zika virus become symptomatic.

- Among those with clinical illness:
  - Symptoms mild, typically develop within 1 week from exposure, lasting several days to a week.
  - Characteristic clinical findings: acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis.
  - Severe disease requiring hospitalization is uncommon and fatalities are rare.

- Guillain-Barré syndrome also has been reported at increased rates in patients following Zika infection.
Clinical Features of Zika Virus Infection in Pregnant Women.
Brazil Zika Outbreak

- May 2015: First infection in Brazil
- October 2015: increase in microcephaly

Microcephaly cases in Brazil 2010-14; suspected/confirmed cases 2015-2016

- 1,551 confirmed (224 confirmed Zika+ by PCR)
- Suspected* (3,017)

*does not include 3,262 cases investigated and discarded

Source: Brazilian MOH; data as of 6/4/2016.
Microcephaly: the tip of the iceberg?

- Microcephaly is a very specific diagnosis, and typically unusual as an isolated finding: initially seen in newborns
  - On ultrasound, defined as $\text{HC} < 3 \text{ SD}$ for GA \textit{(SMFM, 2016)}*
  - $\text{HC} < 2 \text{ SD}$ for GA should trigger more detailed eval and f/u

- Microcephaly became an \textit{early trigger} to search for Zika association, but spectrum of disease became apparent
  - Microcephaly can occur as a result of a \textit{fetal brain disruption sequence}: this appears to be pathology of Zika infection

\*\textit{ref: Chervenak FA, et al, AJOG 1984}
Zika virus intrauterine infection causes fetal brain abnormality and microcephaly: tip of the iceberg?
CT Scans Reveal Extensive Abnormalities

23 infants with microcephaly in Pernambuco, Brazil

- Intracranial calcifications
- Global cortical hypogyratation
- Ventriculomegaly
- Global cerebellar hypoplasia
Fig 3 Severe microcephaly.
Zika Associated Pregnancy Outcomes

- Fetal loss/miscarriage, stillbirth
- Fetal growth abnormalities
- Fetal brain anomalies
  - Microcephaly
  - Ventriculomegaly
  - Intracranial calcifications
- Eye abnormalities
- Neurologic
  - Hypertonia
  - Arthrogryposis
  - Seizures

Miranda-Filho et al, AJPH April 2016, Vol 106 No. 4
Ophtho criteria for CZS

- First ophthalmological examination has to be performed within 30 days of birth.
  - Red Reflex Test does NOT work for diagnosis in cases of CZS
  - 72 patients with CZS -- normal RRT

- SIGNS: Focal pigment mottling of the retina and circular lesions of chorioretinal atrophy including the macula, along with optic nerve abnormalities
  - Identified in 30% of newborns with microcephaly (Frietas et al, JAMA Ophtho 2/16)

- UNIQUE CHORIORETINAL ATROPHY
Zika-Related Arthrogryposis

van der Linden at al, BMJ 8/16
Long Term Pregnancy Outcomes: Evolving

- Update on 13 infants born without microcephaly but ZKV-infected (Brazil)
  - 11 referred for small head size but > 2SD, 2 for devel. lag (5, 7 mos)
  - Neuroimaging abnormal in all: all w/ ↓ brain volume, +/- ↑ vents
  - 10 w/dysphagia, 3 w/chorioretinitis, all hypertonic (MMWR 11/16)

- Recent Brazil cohort Zin AA, et al. JAMA Pediatrics 7/17/17
  - 112 mother-infant pairs w/confirmed maternal infx
  - 10/24 with eye findings (42%) did not have microcephaly, while 8 (33%) had no CNS findings

- Anticipate a spectrum of outcomes?
  - Developmental and/or intellectual delay
  - Motor abnormalities
Pregnancy Risk Estimates

- **Brasil et al: Rio cohort**: Prospective study cohort of 134 symptomatic pregnant women with confirmed ZKV infection
  - Overall, 49/117 (42%) liveborn ZKV-exposed infants had abnormal findings by 1\(^{st}\) month of life [5% in ZKV(-): p< 0.001]

- Adverse outcomes seen regardless of trimester of infx
  - 55% risk if maternal infx in 1\(^{st}\), 52% if in 2\(^{nd}\), 29% if in 3\(^{rd}\)

- Updated report from US Zika Pregnancy Registry
  - Birth defects related to Zika in 6%, 21 in live births
  - No risk difference regarding sx; 11% risk if exposure in 1\(^{st}\)

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Health and Development at Age 19–24 Months of 19 Children Who Were Born with Microcephaly and Laboratory Evidence of Congenital Zika Virus Infection During the 2015 Zika Virus Outbreak — Brazil, 2017

Ashley Satterfield-Nash, DrPH; Kim Kotzky, MPH; Jacob Allen, MPH; Jeanne Bertolli, PhD; Cynthia A. Moore, MD, PhD; Isabela Ornelas Pereira; André Pessoa, MD; Flavio Melo, MD; Ana Carolina Faria e Silva Santelli, MD; Coleen A. Boyle, PhD; Georgina Peacock, MD

ZODIAC Study: compiled comprehensive description of children > 12 months of age born with microcephaly (< 3rd %ile at birth) and (+) Zika IgM from Oct 2015-Jan 2016

19 infants, mean age at followup 22 months (range 19-24 months)

15/19 infants had HC ranging from 3.7-8.4 SD below the mean (avg 6.3 SD)  
All of these infants were symptomatic and had developmental testing < 6 mos.

4/19 infants had HC within 1 SD of mean, all had testing results for > 6 mos.
TABLE 1. Growth measurements* of children aged 19–24 months with confirmed or probable congenital Zika virus infection†,§ and microcephaly classification at birth¶,** — Paraíba, Brazil, August–October 2017

<table>
<thead>
<tr>
<th>Growth</th>
<th>Male (n = 10)</th>
<th>Female (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head circumference††</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;3 SD below mean for age and sex§§</td>
<td>7 (70)</td>
<td>8 (89)</td>
</tr>
<tr>
<td>Length¶¶</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–3 SD below mean for age and sex***</td>
<td>6 (60)</td>
<td>7 (78)</td>
</tr>
<tr>
<td>Weight†††</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 to &gt;3 SD below mean for age and sex§§§</td>
<td>6 (60)</td>
<td>7 (78)</td>
</tr>
</tbody>
</table>
TABLE 3. Health and developmental outcomes of 19 children aged 19–24 months with confirmed or probable congenital Zika virus infection, *, † and microcephaly classification §, ¶ at birth — Paraíba, Brazil, August–October 2017

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medical findings</strong></td>
<td></td>
</tr>
<tr>
<td>Seizures**, ††</td>
<td>11 (58)</td>
</tr>
<tr>
<td>Retinal abnormalities§§</td>
<td>4 (21)</td>
</tr>
<tr>
<td><strong>Hospitalization</strong>**</td>
<td>8 (42)</td>
</tr>
<tr>
<td>Pneumonia/Bronchitis</td>
<td>6 (75)</td>
</tr>
<tr>
<td>Intestinal infection</td>
<td>1 (14)</td>
</tr>
<tr>
<td>High fever</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Failure to thrive/feed</td>
<td>1 (14)</td>
</tr>
<tr>
<td><strong>Functional outcomes</strong></td>
<td></td>
</tr>
<tr>
<td>Sleeping difficulties**</td>
<td>10 (53)</td>
</tr>
<tr>
<td>Feeding difficulties**</td>
<td>9 (47)</td>
</tr>
<tr>
<td>Impaired response to auditory stimuli (hearing asymmetric or no response)¶¶</td>
<td>13 (68)</td>
</tr>
<tr>
<td>Impaired response to visual stimuli¶¶</td>
<td>11 (58)</td>
</tr>
<tr>
<td><strong>Neurologic outcomes</strong></td>
<td></td>
</tr>
<tr>
<td>Severe motor impairment ¶¶</td>
<td>15 (79)</td>
</tr>
<tr>
<td>Cerebral palsy***</td>
<td>14 (74)</td>
</tr>
</tbody>
</table>
Summary

What is already known about this topic?

Congenital Zika virus infection has been linked to increased rates of microcephaly and a unique pattern of birth defects among infants. Although children with microcephaly and laboratory evidence of Zika virus infection have been described in early infancy, the subsequent health and development in young children have not been well characterized, constraining planning for the care of these children.

What is added by this report?

The growth and development of 19 children, aged 19–24 months, with laboratory evidence of Zika virus infection were thoroughly assessed. All children had at least one adverse outcome including feeding challenges, sleeping difficulties, severe motor impairment, vision and hearing abnormalities, and seizures, and these outcomes tended to co-occur.

What are the implications for public health practice?

Children with microcephaly and laboratory evidence of Zika virus infection face medical and functional challenges that span many areas of development, some of which become more evident as children age. They will continue to require specialized care from clinicians and caregivers. These data allow for anticipation of medical and social services needs of affected children and families, such as early intervention services, and planning for resources to support these families in healthcare and community settings.
Zika – Where is it and where is it not?
Aedes aegypti and Aedes albopictus Mosquitoes in California Detection Sites by County/City

Updated January 5, 2018

Counties with Aedes aegypti only:
Fresno, Imperial, Kings, Madera, Riverside, Merced, Tulare

Both Aedes aegypti and Aedes albopictus:
Kern, Los Angeles, Orange, San Bernardino, San Diego

See pages 2 and 3 for Aedes detections by city or census-designated place in each county.
Health & Fitness

Mosquito Capable Of Carrying Zika Found In Pasadena

Eggs from the type of mosquito that can transmit Zika, dengue and chikungunya have been detected in Pasadena: BREAKING

By Paige Austin (Patch Staff) - Updated July 3, 2017 10:36 pm ET
Figure 2. Distribution of suspected and confirmed Zika cases by epidemiological week and sub-region. Region of the Americas, 2016 – 2017 (as of EW 18).16

Source: Data provided by countries and territories and reproduced by PAHO/WHO
Figure 3. Distribution of suspected and confirmed Zika cases by EW. Argentina, Brazil, Ecuador, and Peru, EW 25 of 2015 to EW 18 of 2017.
Zika as an Endemic Infection

- Zika virus is considered **endemic** in some countries, and a large number of local residents are likely to be immune. However, US travelers to endemic areas may not be immune to Zika virus and infections have occurred among travelers to Asia and Africa.

- Zika evolving as an outbreak like other arboviruses: areas of endemicity but high potential (like West Nile and chikungunya) for ongoing sporadic cases and local outbreaks. *(Paules C, Fauci A: JAMA 1/12/17)*
Confirmed Zika Cases in Mexico by State
January 1, 2016 – August 8, 2016

Data provided by the Mexican Ministry of Health
### Casos Confirmados Autóctonos de Enfermedad por Virus del Zika en Mujeres Embarazadas, por Entidad de Infección, México 2015-2017*

<table>
<thead>
<tr>
<th>Entidad Federativa</th>
<th>Casos Confirmados 2015-2016</th>
<th>Casos Confirmados 2017</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baja California Sur</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Campeche</td>
<td>53</td>
<td>2</td>
<td>55</td>
</tr>
<tr>
<td>Coahuila</td>
<td>2</td>
<td>105</td>
<td>107</td>
</tr>
<tr>
<td>Colima</td>
<td>203</td>
<td>0</td>
<td>203</td>
</tr>
<tr>
<td>Chiapas</td>
<td>561</td>
<td>1</td>
<td>562</td>
</tr>
<tr>
<td>Guerrero</td>
<td>472</td>
<td>8</td>
<td>480</td>
</tr>
<tr>
<td>Hidalgo</td>
<td>134</td>
<td>13</td>
<td>147</td>
</tr>
<tr>
<td>Jalisco</td>
<td>36</td>
<td>31</td>
<td>67</td>
</tr>
<tr>
<td>México</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Michoacán</td>
<td>20</td>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>Morelos</td>
<td>200</td>
<td>98</td>
<td>298</td>
</tr>
<tr>
<td>Nayarit</td>
<td>7</td>
<td>168</td>
<td>175</td>
</tr>
<tr>
<td>Nuevo León</td>
<td>504</td>
<td>63</td>
<td>657</td>
</tr>
<tr>
<td>Oaxaca</td>
<td>209</td>
<td>1</td>
<td>210</td>
</tr>
<tr>
<td>Puebla</td>
<td>33</td>
<td>32</td>
<td>65</td>
</tr>
<tr>
<td>Querétaro</td>
<td>0</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Quintana Roo</td>
<td>330</td>
<td>4</td>
<td>334</td>
</tr>
<tr>
<td>San Luis Potosí</td>
<td>20</td>
<td>295</td>
<td>315</td>
</tr>
<tr>
<td>Sinaloa</td>
<td>24</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td>Sonora</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Tabasco</td>
<td>278</td>
<td>8</td>
<td>286</td>
</tr>
<tr>
<td>Tamaulipas</td>
<td>95</td>
<td>464</td>
<td>559</td>
</tr>
<tr>
<td>Veracruz</td>
<td>870</td>
<td>14</td>
<td>884</td>
</tr>
<tr>
<td>Yucatán</td>
<td>915</td>
<td>9</td>
<td>924</td>
</tr>
<tr>
<td>Zacatecas</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>5,065</strong></td>
<td><strong>1,327</strong></td>
<td><strong>6,392</strong></td>
</tr>
</tbody>
</table>

* FUENTE: SINAVE/DGE-SS: Sistema de Vigilancia Epidemiológica de Enfermedad por virus del Zika.
* Hasta el 25 de octubre de 2017.

Nota: Estos casos están considerados dentro del acumulado general de casos confirmados autóctonos.
L.A. County officials confirm first case of sexually transmitted Zika virus

By Soumya Karlamangla · Contact Reporter

Aedes aegypti mosquitoes, responsible for transmitting Zika, sit in a petri dish at the Fiocruz Institute in Recife, Brazil. (Felipe Dana / AP)

JANUARY 4, 2018, 12:10 PM
Zika in the US: as of Jan 10, 2018

**US States/DC (5635 cases): 407 in 2017**
- Travel-associated Zika virus disease cases reported: 5355 (50 other routes)
- Locally acquired vector-borne cases reported: 228
  - In 2017: all travel cases, except 4 local and 5 sexual

**US Territories**
- Travel-associated cases reported: 147 (0 in 2017)
- Locally acquired cases reported: 36,976 (631 in 2017)
  - 51 cases of Guillain-Barre syndrome
Current Zika Statistics (as of 10/17/17)

• 2364 pregnant travelers with laboratory evidence of Zika virus in US States and DC – vast majority imported/travel-related
  o 2143 completed pregnancies
  o 102 reported liveborn infants and 9 fetal losses with Zika related birth defects (5.2% affected)

• 4690 pregnant cases in US territories (mostly Puerto Rico) --- 3738 completed, 150 affected liveborns or losses (4.0%)
## Imported Zika Cases in California, 2015-17

(n = 609, through Nov 3, 2017, with 101 total in 2017 so far)

<table>
<thead>
<tr>
<th>Country Traveled To</th>
<th>Number of Imported Cases in California (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mexico</td>
<td>195 (36%)</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>61 (11%)</td>
</tr>
<tr>
<td>Guatemala</td>
<td>49 (9%)</td>
</tr>
<tr>
<td>El Salvador</td>
<td>37 (7%)</td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>26 (5%)</td>
</tr>
</tbody>
</table>

These 5 countries account for 68% of travel cases in CA

Median age 35

66% in women
The following table provides the number of travel-associated infections with Zika virus in California residents during 2015 – 2017. CDPH is following CDC testing guidelines. This table is updated the first Friday of every month. As of January 5, 2018, there have been 634 travel-associated Zika virus infections in California.

- Total infections: 634
- New infections reported this month: 15
- Locally acquired infections: 0
- Cumulative number of infections due to sexual transmission: 9
- Cumulative number of infections in pregnant women: 108
- Cumulative number of completed pregnancies: 142
  - Liveborn infants with birth defects: 10
  - Pregnancy losses with birth defects: 0

<table>
<thead>
<tr>
<th>County</th>
<th>Travel-associated 2015-2016</th>
<th>Travel-associated 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alameda</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>(City of Berkeley)</td>
<td>(3)</td>
<td>(3)</td>
</tr>
<tr>
<td>Butte</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Contra Costa</td>
<td>26</td>
<td>4</td>
</tr>
<tr>
<td>Fresno</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Humboldt</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Imperial</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Kern</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Kings</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Lake</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>114</td>
<td>22</td>
</tr>
<tr>
<td>(City of Long Beach)</td>
<td>(6)</td>
<td>(1)</td>
</tr>
<tr>
<td>(Pasadena)</td>
<td>(1)</td>
<td>(0)</td>
</tr>
<tr>
<td>Marin</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Mendocino</td>
<td>0</td>
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</tr>
<tr>
<td>Merced</td>
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<tr>
<td>Monterey</td>
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<td>Napa</td>
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<td>Nevada</td>
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<td>Orange</td>
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<td>Placer</td>
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<td>0</td>
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<tr>
<td>Riverside</td>
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<tr>
<td>Sacramento</td>
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<td>0</td>
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<tr>
<td>San Benito</td>
<td>1</td>
<td>0</td>
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<tr>
<td>San Bernardino</td>
<td>18</td>
<td>7</td>
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<tr>
<td>San Diego</td>
<td>85</td>
<td>20</td>
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<tr>
<td>San Francisco</td>
<td>29</td>
<td>11</td>
</tr>
<tr>
<td>San Joaquin</td>
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<tr>
<td>San Mateo</td>
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<td>Santa Barbara</td>
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<td>Solano</td>
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<td>Sonoma</td>
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<td>0</td>
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<td>Tulare</td>
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<tr>
<td>Yuba</td>
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<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>508</td>
<td>126</td>
</tr>
</tbody>
</table>
Zika – Education and Testing
What do we tell our pregnant patients?

- How much fetal risk with confirmed maternal infection?
  - Based on current data, range may be as high as 29%
  - Rates are derived from methodologically diverse studies

- Despite earlier reports, recent data suggest later GA at infection does not exclude potential adverse impact

- Pregnant women **should not travel** to areas with active local Zika transmission
The role of prevention

- If in an area with transmission, protection and prevention strategies are important – *and repellent for 3 weeks after return from these areas*

- DEET, picaridin fine for use in pregnancy
  - Consumer Reports (Sept 2017): Deet at 25-30% concentrations works best, picardin 20% (spray, not lotion), oil of lemon eucalyptus 30% (Repel better than Coleman)
Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States (Including U.S. Territories), July 2017

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What informed the new testing guidelines?

- While consequences of Zika infection are better understood, accurate diagnosis continues to be challenging
  - Virus present in body fluids only transiently
  - Serologic testing (IgM) can’t always reliably time infection
  - Serology prone to false-positive results and cross-reaction with other flaviviruses
- With declining prevalence of Zika infection, probability of false-positive tests increases
- Changing epidemiology further limits diagnostic capabilities of existing tests
Zika Immunity

- Presumption has been that Zika infection confers immunity after the IgM response
- Based on experience with other flaviviruses, previous Zika infection is likely to confer prolonged, likely lifelong immunity
  - If true, prior infection would prevent risks for a future pregnancy
- However, no commercially-available IgG testing exists, and IgM duration limited
- New tests on the horizon .. NS1-based
New guidelines – what do the changes reflect?

- As many areas in the Americas move into a 2\textsuperscript{nd} or 3\textsuperscript{rd} mosquito season after introduction of Zika virus, testing becomes more complex.
- Given the evolving epidemiology and the better-realized limitations of testing, updated testing algorithms for symptomatic and asymptomatic pregnant women emphasize a **shared decision-making model**.
- Need for pre- and post-test counseling, with results interpreted in context of limitations.
New guidelines: what’s the same (mostly)?

- **Screen pregnant women for Zika exposure risk and/or symptoms** at every prenatal and hospital visit
  - Knowledge of potential exposure before and during pregnancy is critical information for test interpretation

- **Symptomatic pregnant women with recent possible Zika exposure: testing still recommended**
  - Concurrent NAT (blood/urine) and IgM as soon as possible, through 12 weeks post-exposure *(can consider if > 12 wks, but..)*

- **Pregnant women with exposure and u/s findings:** still test

- **Asymptomatic women with ongoing possible Zika exposure: testing still offered once/trimester**
  - **NAT testing of blood and urine, not IgM (diagnostic limits)**
New guidelines: what’s different (mostly)

- Asymptomatic women with recent possible Zika exposure **but not ongoing exposure**
  - Testing now *not routinely recommended* for this group
  - BUT: shared-decision making and *consideration of local/regional epidemiologic risks* involved for this group
  - CDC acknowledges that data indicate that while perinatal Zika risk doesn’t differ by maternal symptoms, routine testing in a low-prevalence group increases risk of false-positives in absence of any prevention or therapies
  - If testing done, default to algorithm for symptomatic/no ongoing exposure: **PCR and IgM**

- **Until recently: CA, FL, TX, NY kept prior guidelines**
C. Asymptomatic Pregnant Women with recent but without ongoing exposure are not routinely tested but instead should be assessed carefully for factors that increase the likelihood of Zika infection. A patient’s risk tolerance and decision-making regarding the pregnancy may be sufficient justification to test for Zika virus infection.

California has substantially declined. These factors together lead to a lower pre-test probability of infection when considering testing pregnant women and their newborns. As of November 24, 2017, 162 pregnant women with travel-associated Zika infection have been reported in California since 2015. Of these, 136 women have had completed pregnancies and 9 infants have been born with microcephaly and other Zika-associated anomalies. More than half of the infants born in California with Zika-associated birth defects were born to Zika-exposed mothers who were asymptomatic for Zika infection.
ZIKA SCREENING ALGORITHM

FOR CHILDREN AND ADULTS

IS THERE A HISTORY OF POSSIBLE ZIKA EXPOSURE?
Recent travel to an area with risk of Zika virus (see list of areas with risk of Zika virus*) OR Recent unprotected sexual contact with:

- A male who has traveled in the past 6 months to an area with risk of Zika virus
- A female who has traveled in the past 6 weeks to an area with risk of Zika virus

IS THE PATIENT PREGNANT?

DOES OR DID THE PREGNANT PATIENT HAVE SYMPTOM(S) OF ZIKA VIRAL DISEASE?
One or more of the following symptoms within 2 weeks of travel or sexual exposure:

- Maculopapular rash
- Fever (over 100.4°F/38°C)
- Arthralgias
- Conjunctivitis

ASYMPTOMATIC PREGNANT WOMEN WITH AN EPISODE OF ZIKA EXPOSURE
• Do not routinely test, but instead assess carefully for factors that increase the likelihood of Zika infection. See California’s Updated Guidance (www.cdph.ca.gov/CDPHGuidance) for a list of risk factors to consider.
• A patient’s risk tolerance and decision-making regarding the pregnancy may be sufficient justification for Zika virus testing.
• If choosing to test, follow testing instructions for Symptomatic Pregnant Women.

ASYMPTOMATIC PREGNANT WOMEN WITH ONGOING POSSIBLE ZIKA EXPOSURE
• Recommend sexual abstinence (vaginal, anal, or oral) or condom use (male or female) for all exposed patients, especially pregnant occupants.
• Males: For at least 6 months after last potential Zika exposure
• Females: For at least 2 months after last potential Zika exposure
• If not pregnant, recommend delay pregnancy for the above periods of time and prescribe effective contraceptive methods
• Advise use of mosquito repellent for 3 weeks after return from an area with risk of Zika
• For counseling recommendations, see: www.cdph.ca.gov/CDPHGuidance

ALL PATIENTS WITH EXPOSURE:
Recommended self-examination of genital, oral, and anal area for any rash that may develop. If rash develops, see health care provider.

SYMPOMATIC INDIVIDUALS
• NPT testing of serum and urine within 1 week of symptom onset.
• IgM antibody testing <12 weeks since symptom onset
• If negative IgM and Zika virus NAT negative, confirm with PRNT

FOR INFANTS
INFANT ZIKA VIRUS TESTING FOR SUSPECTED CONGENITAL ZIKA VIRUS INFECTION
• Indications for testing include maternal exposure history plus any of the following:
  • Maternal laboratory evidence of Zika virus infection
  • Infant findings consistent with congenital Zika syndrome regardless of maternal test results

Newborn specimen collection:
• Zika virus NAT testing on infant serum and urine and Zika virus IgM antibody testing on infant serum. If non-negative IgM and negative Zika virus NAT, confirm with PRNT
• If CSP is collected for other purposes, NAT and IgM antibody testing should be performed on CSP

For infants with findings consistent with congenital Zika syndrome with unknown etiology, consider CSF for Zika virus NAT and IgM antibodies.

Birth hospitals may consider collecting infant specimens for congenital Zika virus testing if maternal testing is done. See www.cdph.ca.gov/CDPHGuidance for more information on Zika virus testing or results. Contact your local health department: www.cdph.ca.gov/LHDContactInfo
Pregnancy Management

- Microcephaly and intracranial calcifications typically detected during ultrasounds in the late 2nd/early 3rd Δ
  - These birth defects might be detected as early as 18-20 weeks gestation.
  - A recent study of 17 pregnancies with laboratory confirmed Zika virus infection and adverse fetal outcomes reported a median of 18 weeks from symptom onset to prenatal diagnosis of microcephaly. *(Paara-Saavedra et al, ObGyn 7/17)*

- If early testing negative and 2nd trimester or early 3rd trimester scan normal: usual care
- If confirmed/possible maternal Zika infection, consider serial u/s q 3-4 weeks
Zika “waiting periods” – not just pregnancy

- Timeframes to wait to get pregnant after travel to an area with a CDC travel notice *(CDC 7/17)*
  - Women -- 8 weeks    Men -- 6 months
  - If both partners traveled, wait 6 months + condoms

- Egg and sperm donors *(ASRM, 3/16)*
  - Wait period *6 months* after infx, travel, or contact

- Blood donors *(FDA, 2/16)*
  - 4 week waiting period
Neonatal coordination is Critical!

Evaluation and testing of infants with possible congenital Zika virus infection

Mother with laboratory evidence of Zika virus infection during pregnancy*

Perform a comprehensive physical exam on infant, head ultrasound, standard newborn hearing assessment and infant Zika virus laboratory testing

Infant with findings consistent with congenital Zika virus syndrome

Initial evaluation

Infant with laboratory confirmed or probable congenital Zika virus infection

Outpatient management and follow-up

Infant negative for congenital Zika virus infection

Continue to evaluate for other causes of congenital anomalies

Infant without findings consistent with congenital Zika virus syndrome

Infant with laboratory confirmed or probable congenital Zika virus infection

Routine newborn care; additionally, perform an ABR and ophthalmology exam within one month of life

Infant negative for congenital Zika virus infection

Routine care

Infant with laboratory evidence of Zika virus infection includes: (1) Zika virus RNA detected by real-time reverse transcription-polymerase chain reaction (rRT-PCR) in any clinical specimen; or (2) positive Zika virus immunoglobulin M (IgM) with confirmatory neutralizing antibody titers. Mother's should be tested by rRT-PCR within 2 weeks of exposure or symptom onset, or IgM within 2-12 weeks of exposure or symptom onset. Due to the decline in IgM antibody and viral RNA levels over time, negative maternal testing 12 weeks after exposure does not rule out maternal infection. Abbreviation: ABR = auditory brainstem response.

More information on the evaluation, management, and follow-up of infants with possible congenital Zika virus infection is available at www.cdc.gov/zika/hc-providers/infants-children.html.
Need for Neonatal Followup & Deficits

- Recent report on 2549 completed pregnancies (1/16-4/17)
  - 5% of fetuses/newborns of women in Puerto Rico with confirmed Zika infection had likely Zika-associated birth defects
  - Of liveborns without birth defects, only 52% had postnatal neuroimaging and 78% had hearing screens

- Recent US Pregnancy Registry Data worse (MMWR, 4/7/17)
  - Among 895 liveborns with maternal infection: postnatal neuroimaging reported for 25%, Zika testing of at least 1 infant specimen 65%

- While 98% of pregnant women in P.R. in a recent survey took at least 1 measure to avoid Zika infection, use of repellents (45%) and condoms (40%) during pregnancy overall low

Which newborns need Zika surveillance?

- Zika testing for in 1st two days after birth for infants at risk: serum and urine for PCR, serum for IgM
  - Mothers with lab-confirmed infection
  - Abnormal clinical findings suggestive of congenital Zika and potential maternal epidemiologic link, regardless of maternal test results

- All infants born to women with lab-confirmed Zika infection should get:
  - Zika testing, comprehensive exam, head ultrasound, and standard hearing assessment
  - Based on newer data, they should also get formal eye exam (not just red reflex testing)
Zika Resources

- ACOG’s Zika webpage: [www.acog.org/zika](http://www.acog.org/zika)
- CDC Zika Pregnancy Hotline for Healthcare Providers: 770-488-7100 or email ZikaPregnancy@cdc.gov for concerns related to clinical mgmt or the Zika Pregnancy Registry
- CA Dept of Public Health webpage for health care professionals