The Buzz on Zika: Should We Still Be Concerned?

CA Perinatal Service Coordinators’ Annual Meeting
November 15, 2017

Neil S. Silverman, M.D.
Center for Fetal Medicine and Women’s Ultrasound
Clinical Professor, Obstetrics and Gynecology
Division of Maternal-Fetal Medicine
David Geffen School of Medicine at UCLA
Aedes aegypti
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

More members in the community become 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

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
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**

<table>
<thead>
<tr>
<th>Year</th>
<th>Microcephaly Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>153</td>
</tr>
<tr>
<td>2011</td>
<td>139</td>
</tr>
<tr>
<td>2012</td>
<td>175</td>
</tr>
<tr>
<td>2013</td>
<td>167</td>
</tr>
<tr>
<td>2014</td>
<td>147</td>
</tr>
<tr>
<td>2015-2016</td>
<td>4,568</td>
</tr>
</tbody>
</table>

- 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 (*SMFM, 2016)*
  - \( \text{HC} < 2 \text{ SD} \) for GA should trigger more detailed eval and f/u

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

* ref: Chervenak FA, et al, AJOG 1984
Zika virus intrauterine infection causes fetal brain abnormality and microcephaly: tip of the iceberg?
Fig 3 Severe microcephaly.

Maria de Fatima Vasco Aragao et al. BMJ 2016;353:bmj.i1901
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
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\(^1\)
  - 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\(^2\)
  - Birth defects related to Zika in 6%, 21 in live births
  - No risk difference regarding sx; 11% risk if exposure in 1\(^{st}\) 

Zika – Where is it and where is it not?
Aedes aegypti and Aedes albopictus Mosquitoes in California
Detection Sites by County/City

Updated October 27, 2017

Counties with **Aedes aegypti** only:
Fresno, Imperial, Kings, Madera, Riverside, San Mateo, 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.
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).

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.
Confirmed Zika Cases in Mexico by State
January 1, 2016 – August 8, 2016

N = 1,490

Data provided by the Mexican Ministry of Health
Confirmed Zika Cases in Mexico by State
January 1, 2017 – October 23, 2017

Data provided by the Mexican Ministry of Health

Ag. = Aguascalientes
Quer. = Querétaro
DF = Distrito Federal
Tl. = Tlaxcala
### 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 23 de octubre de 2017.

Nota: Estos casos están considerados dentro del acumulado general de casos confirmados autóctonos.
Zika in the US: as of Nov 1, 2017

**US States/DC (5559 cases): 331 in 2017**

- Travel-associated Zika virus disease cases reported: 5284 (50 other routes)
- Locally acquired vector-borne cases reported: 225
  - In 2017: all travel cases so far, exc 1 local and 3 sexual

**US Territories**

- Travel-associated cases reported: 147 (0 in 2017)
- Locally acquired cases reported: 37075 (including 583 so far in 2017)
  - 51 cases of Guillain-Barre syndrome
Current Zika Statistics (as of 10/17/17)

• **2246 pregnant travelers** with laboratory evidence of Zika virus in US States and DC – vast majority imported/travel-related
  o 1993 completed pregnancies
  o 98 reported liveborn infants and 8 fetal losses with Zika related birth defects

• **4503 pregnant** cases in US territories (mostly Puerto Rico) --- 3375 completed, 137 affected liveborns
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 November 3, 2017, there have been 608 travel-associated Zika virus infections in California.

- Total infections: 609
- New infections reported this week: 1
- Locally acquired infections: 0
- Cumulative number of infections due to sexual transmission: 8
- Cumulative number of infections in pregnant women: 157
- Cumulative number of completed pregnancies: 130
  - Liveborn infants with birth defects: 8
  - 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>35</td>
<td>7</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>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>17</td>
</tr>
<tr>
<td>Marin</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Mendocino</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Merced</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Monterey</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Napa</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Nevada</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Orange</td>
<td>31</td>
<td>9</td>
</tr>
<tr>
<td>Placer</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Riverside</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>Sacramento</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>San Benito</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>San Bernardino</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td>San Diego</td>
<td>36h</td>
<td>13</td>
</tr>
<tr>
<td>San Francisco</td>
<td>29</td>
<td>11</td>
</tr>
<tr>
<td>San Joaquin</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>San Luis Obispo</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>San Mateo</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>Santa Barbara</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Santa Clara</td>
<td>36</td>
<td>13</td>
</tr>
<tr>
<td>Santa Cruz</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Solano</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Sonoma</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Stanislaus</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Tulare</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Ventura</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Yolo</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Yuba</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>568</strong></td>
<td><strong>101</strong></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, picardin 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

Titilope Oduyebo, MD1; Kara D. Polen, MPH1; Henry T. Walke, MD1; Sarah Reagan-Steiner, MD1; Eva Lathrop, MD1; Ingrid B. Rabe, MBChB1; Wendi L. Kuhnert-Tallman, PhD1; Stacey W. Martin, MSc1; Allison T. Walker, PhD1; Christopher J. Gregory, MD1; Edwin W. Ades, PhD1; Darin S. Carroll, PhD1; Maria Rivera, MPH1; Janice Perez-Padilla, MPH1; Carolyn Gould, MD1; Jeffrey B. Nemhauser, MD1; C. Ben Beard, PhD1; Jennifer L. Harcourt, PhD1; Laura Viens, MD1; Michael Johansson, PhD1; Sascha R. Ellington, MSPH1; Emily Petersen, MD1; Laura A. Smith, MA1; Jessica Reichard, MPA1; Jorge Munoz-Jordan, PhD1; Michael J. Beach, PhD1; Dale A. Rose, PhD1; Ezra Barzilay, MD1; Michelle Noonan-Smith1; Denise J. Jamieson, MD1; Sherif R. Zaki, MD1; Lyle R. Petersen, MD1; Margaret A. Honein, PhD1; Dana Meaney-Delman, MD1
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 \textit{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**

- **Currently: CA, FL, TX, NY keeping prior guidelines**
August 2, 2017

Updated Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure

This time and remains as follows:

a) CDPH has decided to maintain the previous recommendations to test all asymptomatic pregnant women with recent possible Zika virus exposure, whether or not the exposure is ongoing, and

b) For asymptomatic pregnant women with ongoing possible Zika virus exposure, CDPH continues to recommend both PCR and IgM testing in accordance with the prior recommended periodicity. Those recommendations are included below in this update.

The following information was considered in arriving at the decision to retain the current
Pregnancy Management

- Microcephaly and intracranial calcifications typically detected during ultrasounds in the late 2\textsuperscript{nd}/early 3\textsuperscript{rd} trimester:
  - 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. \textit{(Paara-Saavedra et al, ObGyn 7/17)}

- If early testing negative and 2\textsuperscript{nd} trimester or early 3\textsuperscript{rd} 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
  - Outpatient management and follow-up
- Infant negative for congenital Zika virus infection
  - Routine care

*Laboratory evidence of maternal Zika virus infection includes: (1) Zika virus RNA detected by real-time reverse transcription-polymerase chain reaction (RT-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 \(^1\)
  - 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) \(^2\)
  - 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 \(^3\)

Which newborns need Zika surveillance?

- Zika testing for in 1\textsuperscript{st} 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)
Measuring head circumference for microcephaly

- Use a measuring tape that cannot be stretched
- Securely wrap the tape around the widest possible circumference of the head
  - Broadest part of the forehead above eyebrow
  - Above the ears
  - Most prominent part of the back of the head

Take the measurement three times and select the largest measurement to the nearest 0.1 cm
Optimal measurement within 24 hours after birth.

Commonly-used birth head circumference reference charts by age and sex based on measurements taken before 24 hours of age

Recommended consultation for initial evaluation and management of infants affected by Zika

- **Neurologist** - determination of appropriate neuroimaging and evaluation
- **Infectious disease specialist** - diagnostic evaluation of other congenital infections
- **Ophthalmologist** - comprehensive eye exam and evaluation for possible cortical visual impairment prior to discharge from hospital or within 1 month of birth
- **Endocrinologist** - evaluation for hypothalamic or pituitary dysfunction
- **Clinical geneticist** - evaluate for other causes of microcephaly or other anomalies if present
## Outpatient management checklist

<table>
<thead>
<tr>
<th>Infant with abnormalities consistent with congenital Zika syndrome and laboratory evidence of Zika virus infection</th>
<th>2 weeks</th>
<th>1 mo.</th>
<th>2 mo.</th>
<th>3 mo.</th>
<th>4-6 mo.</th>
<th>9 mo.</th>
<th>12 mo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid screen (TSH &amp; free T4)</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Neuro exam</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Neuro exam</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Thyroid screen (TSH &amp; free T4)</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Ophthalmology exam</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Repeat audiology evaluation (ABR)</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Developmental screening</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
</tr>
</tbody>
</table>

- Routine preventive health care including monitoring of feeding, growth, and development
- Routine and congenital infection-specific anticipatory guidance
- Referral to specialists as needed
- Referral to early intervention services

<table>
<thead>
<tr>
<th>Infant with abnormalities consistent with congenital Zika syndrome and negative for Zika virus infection</th>
<th>2 weeks</th>
<th>1 mo.</th>
<th>2 mo.</th>
<th>3 mo.</th>
<th>4-6 mo.</th>
<th>9 mo.</th>
<th>12 mo.</th>
</tr>
</thead>
</table>
| ☑ Evaluate for other causes of congenital anomalies
- Further management as clinically indicated |

<table>
<thead>
<tr>
<th>Infant with no abnormalities consistent with congenital Zika syndrome and laboratory evidence of Zika virus infection</th>
<th>2 weeks</th>
<th>1 mo.</th>
<th>2 mo.</th>
<th>3 mo.</th>
<th>4-6 mo.</th>
<th>9 mo.</th>
<th>12 mo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ophthalmology exam</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>ABR</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Consider repeat ABR</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Developmental screening Behavioral audiology evaluation if ABR was not done at 4-6 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Monitoring of growth parameters (Head circumference, weight, and height), developmental monitoring by caregivers and health care providers, and age-appropriate developmental screening at well-child visits

<table>
<thead>
<tr>
<th>Infant with no abnormalities consistent with congenital Zika syndrome and negative for Zika virus infection</th>
<th>2 weeks</th>
<th>1 mo.</th>
<th>2 mo.</th>
<th>3 mo.</th>
<th>4-6 mo.</th>
<th>9 mo.</th>
<th>12 mo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>☑ Monitoring of growth parameters (Head circumference, weight, and height), developmental monitoring by caregivers and health care providers, and age-appropriate developmental screening at well-child visits</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
</tr>
</tbody>
</table>
Pediatric evaluation and follow-up tools
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 healthcare professionals