Preventing and Managing Congenital Zika and Congenital Syphilis Infections

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Disclosures

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Initially identified in 1947 in a rhesus monkey in the Zika Valley in Uganda through a yellow fever surveillance program

First human case reported in Uganda in the 1950s

Spread from Northern Africa to South East Asia
  - Limited to small-scale epidemics until 2007 when it hit the Yap Islands
Initial reports of possible congenital infection associated with ZIKV infection

- 2013-2014 French Polynesia
  - ZIKV seropositivity before outbreak 0-1.7%
  - Estimated 10% of the population were infected (~28,000 persons)
  - GBS 40 cases, several cases neonatal neurologic complications and 2 cases vertical transmission (very limited data)
Northeastern Brazil May 2015 first reported at the same time Dengue was circulating.

September, 2015 an increase in microcephaly cases reported in the same areas as the Zika epidemic (20 cases per 10,000 live births – 20 fold increase).
Zika Virus Associated with Microcephaly

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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
Microcephaly and intracranial calcifications

- Vertical transmission – symptoms at 13 weeks gestation
- Ultrasound at 14 and 20 weeks normal anatomy and growth
- 29 weeks gestation “abnormal”
- 32 weeks: IUGR <3%, normal AFI, placental calcifications, HC <2%, moderate ventriculomegaly, numerous intracranial calcifications and “blurred anatomy” Dopplers all normal

NEJM Brief Report 2/12/2016
Pregnancy termination: 5%, prominent microcephaly at the 1%, whole brain weight 4SD below average. Small cerebellum and brain stem, complete agyria and internal hydrocephalus, numerous calcifications. Virus particles identified with EM, RT-PCR positive in brain only, negative for other flaviviruses.
Congenital Zika Syndrome

- Pattern of birth defects in fetuses and infants infected with Zika virus during pregnancy
At a Glance – Zika in the US
April 12th, 2017

- **US States**
  - Travel-associated cases reported: 4,935
  - Locally acquired vector-borne cases reported: 223
  - Total: 5,234
    - Sexually transmitted: 46

- **US Territories**
  - Travel-associated cases reported: 143
  - Locally acquired cases reported: 36,383
  - Total: 36,526
At a Glance – Zika in the US
April 12th, 2017

- Maryland
  - Local cases: 0
  - Travel Associated Cases: 134 (3)

- Virginia
  - Local Cases: 0
  - Travel Associated Cases: 115 (2)
5,177 Laboratory Evidence Zika infections in pregnant women
- 1,716 in the United States
- 3,461 in the U.S. territories
- ~55% had clinical symptoms
U.S. Zika Pregnancy Registry

- Laboratory evidence of possible recent Zika virus infection (mother, placenta or fetus/neonate)
- 12/1/2015 through 12/27/2016 completed pregnancies
- 1,297 pregnancies from 44 States
  - 972 completed pregnancies with reported outcomes (895 Liveborn and && pregnancy loss)
Overall 5% of the completed pregnancies were affected with CZS if lab evidence of possible infection
- 6% of symptomatic moms and 5% asymptomatic moms
- 9% First trimester exposure

If there was confirmed evidence of Zika infection, 10% of the infants had CZS
- 15% if exposure in the first trimester

30 times higher than the pre-Zika years
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
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**
Global *Aedes aegypti* Distribution Predicted the Spread of Zika Virus

Aedes aegypti mosquitoes are more likely to spread viruses like Zika, dengue, chikungunya and other viruses than other types of mosquitoes such as Aedes albopictus mosquitoes.

These maps show:
- Exact locations of numbers of mosquitoes living in an area
- Risk of likelihood that these mosquitoes will spread viruses

**These maps show**
- CDC's best estimate of the potential range of *Aedes aegypti* and *Aedes albopictus* in the United States
- Areas where mosquitoes are or have been previously found

*Maps have been updated from a variety of sources. These maps represent CDC's best estimate of the potential range of *Aedes aegypti* and *Aedes albopictus* in the United States. Maps are not meant to represent risk for spread of disease.*

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention
Evaluation - Maternal

- Test all pregnant woman with travel to an affected area (Algorithms)
  - Symptoms within 2 weeks of travel
    - RT-PCR and IgM
  - No symptoms
    - IgM 2-12 weeks after exposure
- Pregnant women living in an endemic area algorithm
- Infants and Children Guidelines
ZIKV Testing (11/25/2016 MMWR)

- RT-PCR validated
  - Serum, amniotic fluid, urine, placenta, fetal tissues, semen
  - Good about 7-14 days of symptom onset (urine up to 14 days)

- Serologic testing
  - IgM (ELISA) turns positive ~ 4-7 days
    - Cross-reaction with other flaviviruses, including vaccination and infections
  - Plaque reducing neutralization test (PRNT)

- Still no approved IgG
Recommendations for Pregnant Women

- CDC Recommends all pregnant women consider postponing travel to areas of ongoing Zika virus transmission if possible
- If pregnant women have to travel, avoid mosquito bites
  - Protective clothing
  - U.S. EPA-registered insect repellent
  - Screened-in or air-conditioned areas
CDC’s Response to Zika

PREGNANT? Read this before you travel

What we know about Zika

- Zika can be passed from a mother to her fetus during pregnancy.
- Infection with Zika during pregnancy is linked to birth defects in babies.
- Zika is spread mostly by the bite of an infected Aedes species mosquito.
  - These mosquitoes are aggressive daytime biters. They can also bite at night.
- There has been no local transmission of Zika in the continental US.
- There is no vaccine to prevent or medicine to treat Zika.
- Zika can be spread by a man to his sex partners.

What we don’t know about Zika

- If there’s a safe time during your pregnancy to travel to an area with Zika.
- If you do travel and are infected, how likely it is that the virus will infect your fetus and if your baby will have birth defects from the infection.

Travel Notice

CDC has issued a travel notice (Level 2-Practice Enhanced Precautions) for people traveling to areas where Zika virus is spreading.

- For a current list of places with Zika outbreaks, see CDC’s Travel Health Notices: http://wwwnc.cdc.gov/travel/page/zika-travel-information
- This notice follows reports in Brazil of microcephaly and other poor pregnancy outcomes in babies of mothers who were infected with Zika virus while pregnant.

Your Best Protection: Prevent Mosquito Bites

Clothing

- Wear long-sleeved shirts and long pants.
- Treat clothing and gear with permethrin or purchase permethrin-treated items.
- Treated clothing remains protective after multiple washings. See product information to learn how long the protection will last.
- If treating items yourself, follow the product instructions carefully.
- Do NOT use permethrin products directly on skin. They are intended to treat clothing.

Indoor Protection

- Stay in places with air conditioning or that use window and door screens to keep mosquitoes outside.
- Sleep under a mosquito bed net if air conditioned or screened rooms are not available or if sleeping outdoors.

Repellent

Use Environmental Protection Agency (EPA)-registered insect repellents. When used as directed, these insect repellents are safe and effective for pregnant and breastfeeding women.

- Always follow the product label instructions.
- Reapply as directed.
- Do not spray repellent on the skin under clothing.
- If you are also using sunscreen, apply sunscreen before applying insect repellent.

Symptoms of Zika

About 4 out of 5 people with Zika won’t even know they have it. The illness is usually mild with symptoms lasting for several days to a week.

The most common symptoms of Zika are:

- Fever
- Rash
- Joint Pain
- Conjunctivitis (red eyes)

www.cdc.gov/zika
STD Coffee Break

March 3, 2017
CONGENITAL SYPHILIS
NOTE: Data collection for syphilis began in 1941; however, syphilis became nationally notifiable in 1944. Refer to the National Notifiable Disease Surveillance System (NNDSS) website for more information: https://wwwn.cdc.gov/nndss/conditions/syphilis/.
Primary and Secondary Syphilis — Rates of Reported Cases Among Women Aged 15–44 Years by Age Group, United States, 2006–2015

Rate (per 100,000 population)

Year


20-24 25-29 30-34 35-39 40-44
Primary and Secondary Syphilis — Rates of Reported Cases by Age Group and Sex, United States, 2015

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Rate (per 100,000 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-14</td>
<td>0.0</td>
</tr>
<tr>
<td>15-19</td>
<td>2.8</td>
</tr>
<tr>
<td>20-24</td>
<td>5.1</td>
</tr>
<tr>
<td>25-29</td>
<td>4.5</td>
</tr>
<tr>
<td>30-34</td>
<td>2.9</td>
</tr>
<tr>
<td>35-39</td>
<td>2.3</td>
</tr>
<tr>
<td>40-44</td>
<td>1.5</td>
</tr>
<tr>
<td>45-54</td>
<td>0.9</td>
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<tr>
<td>55-64</td>
<td>0.3</td>
</tr>
<tr>
<td>65+</td>
<td>0.0</td>
</tr>
<tr>
<td>Total</td>
<td>1.4</td>
</tr>
</tbody>
</table>

For Men:
- 50: 13.7
- 40: 22.6
- 30: 35.7
- 20: 29.9
- 10: 8.0
- 0: 0.0

For Women:
- 50: 41.8
- 40: 5.7
- 30: 1.0
- 20: 0.0
- 10: 0.1
- 0: 0.0
The total rate of primary and secondary syphilis for the United States and outlying areas (Guam, Puerto Rico, and Virgin Islands) was 7.6 cases per 100,000 population.
Congenital Syphilis — Reported Cases by Year of Birth and Rates of Primary and Secondary Syphilis Among Women, United States, 2006–2015

* CS = Congenital syphilis; P&S = Primary and secondary syphilis.
Why is Congenital Syphilis on the Rise?

- There was a 36% increase when comparing 2015 to 2011
  - 56% increase in primary and secondary syphilis rates during the same time period
  - 22% of the cases in 2014 had no prenatal care
    - If they had prenatal care, 43% did not receive prenatal treatment
      - 16% not tested
      - 39% seroconverted during pregnancy
    - 17% were treated <30 days prior to delivery

CDC STD Surveillance data 2015
<table>
<thead>
<tr>
<th>Category</th>
<th>Adequate Treated</th>
<th>Inadequate Treated</th>
<th>Untreated</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Natal Care (PNC) 172</td>
<td>101</td>
<td>33</td>
<td>38</td>
<td>172</td>
</tr>
<tr>
<td>No PNC 34</td>
<td></td>
<td>19</td>
<td></td>
<td>34</td>
</tr>
<tr>
<td>Adequate Treated</td>
<td>14</td>
<td></td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>Inadequate Treated</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Untreated</td>
<td>19</td>
<td></td>
<td></td>
<td>19</td>
</tr>
<tr>
<td>Inadequate Treated</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Adequate Treated</td>
<td>14</td>
<td></td>
<td></td>
<td>14</td>
</tr>
</tbody>
</table>

**MISSED OPPORTUNITIES**

206 Congenital Syphilis (CS) Cases, Maryland 2006-2015
<table>
<thead>
<tr>
<th>Rank</th>
<th>State</th>
<th>Cases</th>
<th>Rate per 100,000 Live Births</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Louisiana</td>
<td>53</td>
<td>83.9</td>
</tr>
<tr>
<td>2</td>
<td>California</td>
<td>141</td>
<td>28.5</td>
</tr>
<tr>
<td>3</td>
<td>Maryland</td>
<td>18</td>
<td>25.0</td>
</tr>
<tr>
<td>4</td>
<td>Nevada</td>
<td>8</td>
<td>22.8</td>
</tr>
<tr>
<td>5</td>
<td>Illinois</td>
<td>30</td>
<td>19.1</td>
</tr>
<tr>
<td>6</td>
<td>Florida</td>
<td>38</td>
<td>17.6</td>
</tr>
<tr>
<td>7</td>
<td>Arizona</td>
<td>14</td>
<td>16.4</td>
</tr>
<tr>
<td>8</td>
<td>Georgia</td>
<td>21</td>
<td>16.3</td>
</tr>
<tr>
<td>9</td>
<td>Oregon</td>
<td>6</td>
<td>13.3</td>
</tr>
<tr>
<td>10</td>
<td>Arkansas</td>
<td>5</td>
<td>13.2</td>
</tr>
<tr>
<td>11</td>
<td>Oklahoma</td>
<td>7</td>
<td>13.1</td>
</tr>
<tr>
<td>12</td>
<td>Texas</td>
<td>49</td>
<td>12.7</td>
</tr>
<tr>
<td></td>
<td>U.S. TOTAL</td>
<td>487</td>
<td>12.4</td>
</tr>
<tr>
<td>13</td>
<td>Ohio</td>
<td>17</td>
<td>12.2</td>
</tr>
<tr>
<td>14</td>
<td>Hawaii</td>
<td>2</td>
<td>10.5</td>
</tr>
<tr>
<td>15</td>
<td>Michigan</td>
<td>11</td>
<td>9.7</td>
</tr>
<tr>
<td>16</td>
<td>Delaware</td>
<td>1</td>
<td>9.2</td>
</tr>
<tr>
<td></td>
<td>HP 2020 TARGET</td>
<td></td>
<td>9.1</td>
</tr>
<tr>
<td>17</td>
<td>New Mexico</td>
<td>2</td>
<td>7.6</td>
</tr>
<tr>
<td>18</td>
<td>North Carolina</td>
<td>9</td>
<td>7.6</td>
</tr>
<tr>
<td>19</td>
<td>Tennessee</td>
<td>5</td>
<td>6.3</td>
</tr>
<tr>
<td>20</td>
<td>Indiana</td>
<td>5</td>
<td>6.0</td>
</tr>
<tr>
<td>21</td>
<td>Washington</td>
<td>5</td>
<td>5.8</td>
</tr>
<tr>
<td>22</td>
<td>Massachusetts</td>
<td>4</td>
<td>5.6</td>
</tr>
<tr>
<td>23</td>
<td>South Carolina</td>
<td>3</td>
<td>5.3</td>
</tr>
<tr>
<td>24</td>
<td>Alabama</td>
<td>3</td>
<td>5.2</td>
</tr>
<tr>
<td>25</td>
<td>New York</td>
<td>12</td>
<td>5.1</td>
</tr>
<tr>
<td>26</td>
<td>Pennsylvania</td>
<td>7</td>
<td>5.0</td>
</tr>
<tr>
<td>27</td>
<td>Missouri</td>
<td>3</td>
<td>4.0</td>
</tr>
<tr>
<td>28</td>
<td>Virginia</td>
<td>3</td>
<td>2.9</td>
</tr>
<tr>
<td>29</td>
<td>Minnesota</td>
<td>2</td>
<td>2.9</td>
</tr>
<tr>
<td>30</td>
<td>Connecticut</td>
<td>1</td>
<td>2.8</td>
</tr>
<tr>
<td>31</td>
<td>Kentucky</td>
<td>1</td>
<td>1.8</td>
</tr>
</tbody>
</table>
## Maryland STI Ranking by Rates, 2015

(latest year for which national data are available)

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MD Ranking</td>
<td>MD Rate</td>
<td>U.S. Rate</td>
</tr>
<tr>
<td>Syphilis (primary &amp; secondary)</td>
<td>10&lt;sup&gt;th&lt;/sup&gt;</td>
<td>8.5</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(509 cases)</td>
<td></td>
</tr>
<tr>
<td>Congenital Syphilis*</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt;</td>
<td>25.0</td>
<td>12.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(18 cases)</td>
<td></td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>24&lt;sup&gt;th&lt;/sup&gt;</td>
<td>114.8</td>
<td>123.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(6,858 cases)</td>
<td></td>
</tr>
<tr>
<td>Chlamydia</td>
<td>23&lt;sup&gt;rd&lt;/sup&gt;</td>
<td>459.3</td>
<td>478.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(27,450 cases)</td>
<td></td>
</tr>
</tbody>
</table>

Syphilis, gonorrhea, and chlamydia rates are cases per 100,000 population

*Congenital syphilis rate is cases per 100,000 live births

Source: STD Surveillance 2015. Centers for Disease Control and Prevention
**Congenital Syphilis**

- *T. pallidum* is transmitted across the placenta from a pregnant woman to her fetus
- May occur during any stage of syphilis and in any trimester
- Manifestations may not be noted at birth
  - Early lesions inflammatory
  - Late lesions immunologic and destructive
The diagnosis is surprisingly difficult

- All infants born to mothers with reactive syphilis serology should have an RPR or VDRL performed on the serum (not umbilical cord sample)
- No adequate IgM available at this time
- Physical exam: hydrops, HSM, jaundice, rhinitis, pseudoparalysis, skin rash
- Examine the placenta and umbilical cord
- Darkfield microscopy if suspicious lesions or available body fluids
Serologic Testing for Syphilis

- Serologic detection requires the detection of two types of antibodies
  - Non-treponemal antibodies
    - Directed against lipoidal antigens
    - RPR and VDRL, TRUST
  - Treponemal antibodies
    - Antibodies directed against *T. pallidum* proteins
    - TP-PA, MHA-TP, FTA-ABS, EIAs, CIAs, MBIA
Benefits (and Problems) of Each

- **Traditional**
  - Detects active infection
  - High rate of biologic false positives so needs confirmation
  - Can miss early primary and treated infection

- **Reverse sequence algorithm**
  - Detects early and treated infection
  - Non-treponemal test needed to detect active infection
  - EIAs and CIAs are nonspecific with high false positive rate
The only way to prevent congenital syphilis is to prevent or at least treat maternal syphilis.
Identification of pregnant women infected with syphilis

- Screen ALL pregnant women
  - First prenatal visit
  - In Maryland screen again at 28 weeks and then again at delivery in high prevalence communities
- No infant should ever be discharged from the hospital without confirmation of negative maternal serology
- Screen anyone who delivers a stillborn infant after 20 weeks gestation
Congenital Syphilis at Parkland Hospital 1988 to 1998

- Primary (N=26): 23% Congenital Syphilis, 60% Stillbirth
- Secondary (N=53): 36% Congenital Syphilis, 60% Stillbirth
- Early Latent (N=145): 20% Congenital Syphilis
- Late Latent (N=27): 7% Congenital Syphilis
- Unknown (N=97): 20% Congenital Syphilis

Legend:

- Dark Purple: Stillbirth
- Light Gray: Congenital Syphilis
Syphilis Therapy Efficacy by Stage

Syphilis Treatment Efficacy by Gestational Age

Weeks’ gestation (N)

- <21 (126)
- 21 - 25 (51)
- 26 - 30 (59)
- 31 - 35 (46)
- 36 - 40 (28)
- 40 - 43 (3)

Success | Failure
---|---
99% | 1
100% | 0
93% | 4
100% | 0
93% | 2
100% | 0

1999; 93:5-8
The State and Local Health Departments are your allies in the fight against both CZS and Congenital Syphilis

- Do not hesitate to contact them with any questions. They are there to help with contact notification, researching prior treatment and helping interpret results
- If they contact you regarding a possible case, follow up with them
- These are reportable diseases
Maryland Confidential Morbidity Report Form (DHMH 1140)

http://phpa.dhmh.maryland.gov/Pages/what-to-report.aspx
Zika Virus Information

(Aedes Mosquito)

Zika Virus Basics:

Zika virus is a virus spread to people through mosquito bites of Aedes species mosquitoes. Aedes
Resources

Maryland Department of Health and Mental Hygiene
Bureau of Infectious Disease Prevention and Health Services
Center for Sexually Transmitted Infection Prevention
410-767-6690.
http://phpa.dhmh.maryland.gov/OIDPCS/CSTIP/SitePages/cstip-for-healthcare-providers.aspx

Bureau of Infectious Disease Epidemiology & Outbreak Response Bureau
Zika Virus Information for Marylanders & Guidance for Maryland Providers

Centers for Disease Control and Prevention (CDC)
Zika
- Zika Virus Information for Healthcare Providers
- Zika Virus and Pregnancy

Syphilis
- Syphilis During Pregnancy, 2015 STD Treatment Guidelines
Resources

American Congress of Obstetricians and Gynecologists
Zika Virus Resource Summary for Ob-Gyns and Health Care Providers
http://www.acog.org/About-ACOG/ACOG-Departments/Zika-Virus

Additional ACOG Resources
Zika Toolkit
http://www.acog.org/zikatoolkit
- ACOG Zika Virus Practice Advisory
- State contact list for local testing, ACOG member access only
- State Zika Registry contact list, ACOG member access only
- US Pregnancy Registry
- Zika Screening Tool (PDF)
- Visit the acog.org/zika page for all ACOG Zika Virus Updates
STD Clinical Consultation Network (STDCCCN)

- Provides STD clinical consultation services within 1-3 business days, depending on urgency, to healthcare providers nationally.
- Your consultation request is linked to your regional STD/HIV Prevention Training Center’s expert faculty.
- We are just a click away!
- www.STDCCCN.org
E-mail questions for the presenter to: maphtc@jhsph.edu

Presented by:

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