Jackson Health System’s
Innovations In Obstetrical, Neonatal, And Pediatric Care Symposium
Our Goals

Ebola:
- Symptoms
- Transmission
- Outcomes

Zika:
- Symptoms
- Transmission
- Prevention
- Maternal and fetal outcomes

Time for questions and discussion
The short and the sweet of Ebola and pregnancy
Ebola in Pregnancy, for Healthcare Workers in the US: CDC Key Points

Healthcare providers caring for pregnant women in U.S. hospitals should be prepared to screen patients for EVD and have a plan in place to triage these patients.

Obstetric management of pregnant women with EVD, particularly decisions about mode of delivery for women in labor, needs to consider risks to the woman, risks of exposure for healthcare providers, and potential benefits to the neonate.

Healthcare workers who are pregnant should not care for patients with EVD.

Pregnant workers or patients with confirmed EVD should be hospitalized, and CDC guidance should be followed.

Early Symptoms

Symptoms can appear from 2 to 21 days after exposure.

- Fever
- Headache
- Diarrhea
- Vomiting
- Stomach pain
- Unexplained bleeding or bruising
- Muscle pain

When is someone able to spread the disease to others?

A person is only contagious after Ebola symptoms begin.

After 21 days, if an exposed person does not develop symptoms, they will not become sick with Ebola.

EVD in pregnancy is associated with a high rate of obstetric complications and poor maternal and perinatal outcomes:

- spontaneous abortion
- prelabour rupture of membranes
- preterm labor/preterm birth
- antepartum and postpartum hemorrhage
- intrauterine fetal death
- Stillbirth
- maternal death
- neonatal death
Ebola in pregnancy: Mortality

Non pregnant mortality: ~75%

Pregnant mortality: 95%

Neonatal/infant mortality: approaching 100%
IPC precautions for pregnant women at risk of EVD transmission during childbirth and complication management

- Comprehensive Ebola IPC precautions as recommended for care of EVD cases should be applied in the management of pregnant women and newborns at risk of EVD transmission (4, 5, 6):
  - full personal protective equipment (PPE), including head cover, face mask, goggles or face shield, boots, coverall or gown, apron, double gloving with outer elbow length gloves;
  - rigorous hand hygiene;
  - appropriate waste, sharps and laundry management (*special attention should be given to sharps disposal*)
  - environmental cleaning and decontamination (*special attention should be given to decontamination of reusable instruments*)
**Full PPE**

For Childbirth Care with EVD Transmission Risk

- head cover
- face mask
- goggles or face shield
- coverall or gown
- apron
- double gloving with outer elbow length gloves
- rubber boots

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**Standard PPE**

For Childbirth Care

- face shield, or face mask and goggles
- gown
- elbow length gloves
- rubber boots, or closed shoes and overshoes

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- Pregnant women with EVD
- Pregnant women who survive EVD (with an ongoing pregnancy)
- Pregnant contacts of EVD cases (during 21 day monitoring period)
- EVD survivors who become pregnant after recovery
- All other pregnant women who do not belong in risk groups for Ebola virus transmission during pregnancy

*PPE = personal protective equipment  EVD = Ebola virus disease*
Breast feeding and Ebola

Lactation and EVD

EVD survivors who were pregnant or lactating when infected: Limited evidence suggests that breast milk can remain positive for Ebola for more than 2 months after symptom onset. Further IPC precautions are required to prevent exposing others to the virus.

Transition to a more pressing emerging disease...
Zika virus (Zika)

- Single stranded RNA virus
- Genus *Flavivirus*, family *Flaviviridae*
- Closely related to dengue, yellow fever, Japanese encephalitis, and West Nile viruses
- Primarily transmitted through the bite of an infected *Aedes* species mosquito (*Ae. aegypti* and *Ae. albopictus*)

Modes of transmission

• Bite from an infected mosquito

• Maternal-fetal
  – Intrauterine
  – Perinatal

• Sexual transmission from an infected person to his or her partners (with or without symptoms)

• Laboratory exposure

• Theoretical: blood transfusion, organ and tissue transplant, fertility treatment, and breast feeding

Updated Cases of Zika: United States & Territories
September 7

US States
- Locally acquired mosquito-borne cases reported: 43
- Travel-associated cases reported: 2,920
- Laboratory acquired cases reported: 1
- Total: 2,964
  - Sexually transmitted: 24
  - Guillain-Barré syndrome: 7

US Territories
- Locally acquired cases reported: 15,809
- Travel-associated cases reported: 60
- Total: 15,869*
  - Guillain-Barré syndrome: 31
Incubation and viremia

- Incubation period for Zika virus disease is 3–14 days.
- Zika viremia ranges from a few days to 1 week.
- Some infected pregnant women can have evidence of Zika virus in their blood.
- Virus remains in semen longer than in blood.

Zika Viremia in Pregnancy

CDC Zika Pregnancy Registry: Prolonged Zika virus RNA detection in serum in 4 symptomatic pregnant women up to 46 days

1 asymptomatic pregnant woman 53 days postexposure.

Unclear relationship to neonatal disease severity

Meaney-Delman et al, 2016 Obstetrics and Gynecology.
Symptom onset: 19 days after travel
Ultrasound: HC: 18.6 cm; 3rd percentile
Serum RT-PCR+: ZIKV IgM+ (20 days)
Urine RT-PCR+: ZIKV IgM+ (20 days)
Ultrasound: HC: 22.9 cm; 4th percentile
Serum RT-PCR+: ZIKV IgM+ (44 days)
Urine RT-PCR+: ZIKV IgM+ (44 days)
Ultrasound: HC: 26.9 cm; 11th percentile
Serum RT-PCR+: ZIKV IgM+ (51 days)
Urine RT-PCR+: ZIKV IgM+ (51 days)
Ultrasound: HC: 30.4 cm; 17th percentile
Serum RT-PCR+: ZIKV IgM+ (62 days)
Urine RT-PCR+: ZIKV IgM+ (62 days)
Ultrasound: HC: 31.9 cm; 6th percentile
Ongoing Pregnancy

Meaney-Delman et al, 2016 Obstetrics and Gynecology.
Zika detection in saliva and semen

Male in 30s, January 2016: history of fever and erythematous rash during a stay in Haiti.

Return to Italy: ZIKV RNA detected in urine and saliva 91 days after symptom onset, and semen up to day 188,
Reported clinical symptoms among confirmed Zika virus disease cases

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macular or popular rash</td>
<td>90%</td>
</tr>
<tr>
<td>Subjective fever</td>
<td>65%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>65%</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>55%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>15%</td>
</tr>
<tr>
<td>Headache</td>
<td>14%</td>
</tr>
<tr>
<td>Retro-orbital pain</td>
<td>39%</td>
</tr>
<tr>
<td>Edema</td>
<td>19%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10%</td>
</tr>
</tbody>
</table>

(n = 31)
Recommendations

- CDC recommends Zika virus testing for
  - Symptomatic people who live in or recently traveled to an area with active Zika transmission, and
  - People who have had unprotected sex with someone confirmed to have Zika virus infection or who lives in or traveled to an area with active Zika transmission.
- All pregnant women in the US should be assessed for possible Zika exposure at each prenatal care visit.

Diagnostic testing for Zika virus

- During first two weeks after the start of illness, Zika virus infection can often be diagnosed by performing real-time reverse transcriptase polymerase chain reaction (rRT-PCR) on serum and urine.

- Serology for IgM and neutralizing antibodies in serum collected up to 12 weeks after illness onset

- Plaque reduction neutralization test (PRNT) for presence of virus-specific neutralizing antibodies in paired serum samples

- Immunohistochemical (IHC) staining for viral antigens or RT-PCR on fixed tissues

Diagnostic testing for Zika virus

In Florida: Pregnant women have access to free IgM and PCR testing (serum, urine) via FL DOH

Non-pregnant women and men: Testing via FL DOH only if symptomatic (serum, urine)

Non-pregnant women and men: Private labs (? Covered via insurance) when not symptomatic, trying to plan pregnancy, etc

No commercially available semen testing
• Zika virus disease is a nationally notifiable condition. Report all confirmed cases to your state health department.
Zika virus can pass from a pregnant woman to her fetus during pregnancy or around the time of birth.

Zika infection in pregnancy is a cause of microcephaly and other severe brain defects. Other problems include:

- Eye defects, hearing loss, impaired growth, and fetal loss.

Case definition of microcephaly

Definite congenital microcephaly for live births

• Head circumference (HC) at birth is less than the 3rd percentile for gestational age and sex.
• If HC at birth is not available, HC less than the 3rd percentile for age and sex within the first 6 weeks of life

Definite congenital microcephaly for still births and early termination

• HC at delivery is less than the 3rd percentile for gestational age and sex.
Figure 1. Projection of birth months after Zika virus transmission and occurrence of microcephaly, Salvador, Bahia State, Brazil. Weekly pregnancy cohorts are based on 40-week pregnancies and monthly reports of infants with microcephaly in Bahia State, Brazil, in relation to periods of high risk for Zika virus transmission. The epidemic curve shows cases treated for illness with rash in Salvador, Brazil, estimated from (14). Complete monthly report data for January–March 2016 are not yet available.
Zika Virus Pregnancy related Complications: French Polynesia

Retrospective study, French Polynesia, September 2013-July 2015

66% of population was infected in ~ 1 year (total population 270,000)

8 microcephaly cases identified (average 4100 births/year)
   - five abortions (median age 30 weeks)
   - three live-births
Zika Virus Pregnancy related Complications: French Polynesia

**Modeling:** national seroprevalence, probability of infection in pregnancy, trimester of infection, incidence of microcephaly

Predicted association between first trimester exposure and increase in microcephaly cases

Predicted a 1% risk of microcephaly when mother is Zika (+)

Cauchemez et al Lancet 2016
Zika Virus
Pregnancy related Complications

Cohort Study Brazil: Oct 2016-Feb 2016

Inclusion: Pregnant with rash > Testing of serum and urine RT-PCR Zika

2 Miscarriages
70 women followed
  > 60% had prenatal US (others without access)
  All negative CMV, Rubella, Syphilis
  88% Dengue IgG positive on entry

Zika Virus
Pregnancy related Complications

Ultrasonographic findings in our cohort showed serious and frequent problems in fetal and central nervous system development, affecting 29% of the 42 women whose fetuses were evaluated by ultrasonography.

<table>
<thead>
<tr>
<th>Fetus No.</th>
<th>Week of Gestation at Infection</th>
<th>Week of Gestation at Ultrasound Examination</th>
<th>Abnormal Findings on Doppler Ultrasonography</th>
<th>Findings at Birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>8</td>
<td>35</td>
<td>Microcephaly, cerebral calcifications, abnormal middle cerebral artery, intrauterine growth restriction</td>
<td>Microcephaly, cerebral calcifications on CT, global cerebral atrophy, macular lesions</td>
</tr>
<tr>
<td>40</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>12</td>
<td></td>
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<tr>
<td>41</td>
<td>12</td>
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<td>12</td>
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<td>10</td>
<td>25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>26</td>
<td></td>
<td>Microcephaly, cerebral calcifications, growth restriction (95th percentile on the pulsatile index), intrauterine growth restriction</td>
<td>Microcephaly, cerebral calcifications, growth restriction proportional to body size</td>
</tr>
<tr>
<td>38</td>
<td>27</td>
<td>35</td>
<td>Cerebral calcifications, ventriculomegaly, brachycephaly</td>
<td>Still in utero</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>34</td>
<td>None</td>
<td>Normal at birth</td>
</tr>
<tr>
<td>3</td>
<td>31</td>
<td>33</td>
<td>None</td>
<td>Normal at birth</td>
</tr>
<tr>
<td>53</td>
<td>32</td>
<td>38</td>
<td>Fetal death</td>
<td>Stillbirth</td>
</tr>
<tr>
<td>23</td>
<td>35</td>
<td>40</td>
<td>Anhydramnios, intrauterine growth restriction</td>
<td>Normal growth measure, poor sucking reflex, EEG abnormalities</td>
</tr>
</tbody>
</table>
Columbia and Zika


65,726 clinical cases of Zika, 2485 (4%) positive on RT-PCR (confirmed)

1850 women who had delivered and had complete information on the gestational week at the time of symptom onset.

532 >> first trimester > 84% still pregnant
702 >> second trimester > 71% still pregnant
616 >> third trimester > 82% of infants born, no microcephaly

(four microcephalic/Zika + infants reported since publication)
### Pregnant Women with Any Laboratory Evidence of Possible Zika Virus Infection

<table>
<thead>
<tr>
<th>US States and the District of Columbia*</th>
<th>US Territories**</th>
</tr>
</thead>
<tbody>
<tr>
<td>671</td>
<td>1,080</td>
</tr>
</tbody>
</table>

*Includes aggregated data reported to the US Zika Pregnancy Registry as of September 1, 2016

**Includes aggregated data from the US territories reported to the US Zika Pregnancy Registry and data from Puerto Rico reported to the [Zika Active Pregnancy Surveillance System](#) as of September 1, 2016
<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liveborn infants with birth defects*</td>
<td>17</td>
<td>Includes aggregated data reported to the US Zika Pregnancy Registry as of September 1, 2016</td>
</tr>
<tr>
<td>Pregnancy losses with birth defects**</td>
<td>5</td>
<td>Includes aggregated data reported to the US Zika Pregnancy Registry as of September 1, 2016</td>
</tr>
</tbody>
</table>

**Pregnancy Outcomes in the United States Territories**

<table>
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<th>Number</th>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>Liveborn infants with birth defects*</td>
<td>1</td>
<td>Includes aggregated data from the US territories reported to the US Zika Pregnancy Registry and data from Puerto Rico reported to the Zika Active Pregnancy Surveillance System as of September 1, 2016</td>
</tr>
<tr>
<td>Pregnancy losses with birth defects**</td>
<td>1</td>
<td>Includes aggregated data from the US territories reported to the US Zika Pregnancy Registry and data from Puerto Rico reported to the Zika Active Pregnancy Surveillance System as of September 1, 2016</td>
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</table>
Zika and pregnancy

• Learning the full range of other potential health problems caused by Zika virus infection during pregnancy.
• No reports of infants getting Zika through breastfeeding
• No evidence that previous infection will affect future pregnancies

Evaluation for all infants with positive or inconclusive Zika virus test results

- Physical examination, measurement of head circumference, and assessment of gestational age
- Evaluation neurologic abnormalities, dysmorphic features, enlarged liver or spleen, and rash/other skin lesions
- Cranial ultrasound
- Ophthalmologic evaluation before hospital discharge or within 1 month after birth
- Evaluation of hearing by evoked otoacoustic emissions testing or auditory brainstem response testing before hospital discharge or within 1 month after birth
- Consultation with appropriate specialist for any abnormal findings

Additional evaluation for infants with microcephaly or findings consistent with congenital Zika virus infection

- Consultation with clinical geneticist or dysmorphologist and pediatric neurologist
- Testing for other congenital infections; consider consultation with pediatric infectious disease specialist
- Complete blood count, platelet count, and liver function and enzyme tests
- Genetic or other teratogenic causes should be considered if additional anomalies are identified.

Long term follow up for infants with positive or inconclusive Zika virus test results

- Additional hearing screen at 6 months of age and audiology follow up of abnormal newborn hearing screening
- Continued evaluation of developmental characteristics and milestones, as well as head circumference, through 1st year of life
- Consultation with appropriate medical specialists (e.g., pediatric neurology, developmental and behavioral pediatrics, physical and speech therapy) if any abnormalities are noted and as concerns arise
