Zika Virus Update

WELL

THAT ESCALATED QUICKLY
• What is it? (Microbiology/History)
• What does it do? (Clinical Implications/Microcephaly)
• What should we do? (Testing/Diagnosis)
• Prevention
• What’s next?
Microbiology & History
What is it and where did it come from?

I ♥ Microbiology
Microbiology

• “Arbovirus” (ARthropod-BOrne virus) is a descriptive term applied to hundreds of predominantly RNA viruses that are transmitted by arthropods, notably mosquitoes and ticks.
  – Four families of viruses: Bunyaviridae, Flaviviridae, Reoviridae, Togaviridae

• Until recently, only a few had caused clinically significant human diseases, the most historically important of these is yellow fever virus.

• Two lineages of Zika: African and Asian with current outbreak (& French Polynesian outbreak) most similar to Asian strain
History-Viral Family

- These viruses started to emerge millennia ago, when North African villagers began to store water in their dwellings.
- Connection between arthropods and disease first postulated in 1881 by Cuban doctor Carlos Finlay who hypothesized that Yellow fever may be transmitted by mosquitoes.
- Confirmed by Major Walter Reed in 1901.
- Primary vector, Aedes aegypti, spread globally from 15th-19th centuries.
- Four unexpected arrivals of important arthropod-borne viral diseases in the Western Hemisphere over the past 20 years:
  - dengue, which entered this hemisphere stealthily over decades and then more aggressively in the 1990s;
  - West Nile virus, which emerged in 1999; and
  - chikungunya, which emerged in 2013.
What does it do?
What is Zika?

Zika is a virus transmitted by the Aedes mosquito, which also transmits dengue and chikungunya.

Zika can cause:

- Mild fever
- Conjunctivitis
- Headache and joint pain
- Skin rash

Onset is usually 2-7 days after the mosquito bite.

1 in 4 people with Zika infection develops symptoms.
Zika virus infection during pregnancy can cause microcephaly and other severe fetal brain defects. Infection during pregnancy has also been linked to adverse outcomes including pregnancy loss, and eye defects, hearing loss, and impaired growth in infants.

— CDC
At A Glance - Zika in the U.S. (as of June 30, 2016)

- Pregnant Women with Any Lab Evidence of Zika Virus Infection*
  - US States and DC: 320
    - LB with birth defects: 7
    - SB with birth defects: 5 (actually includes SAB, SB, TAB)
  - US Territories: 279
    - LB with birth defects: 0
    - SB with birth defects: 1

*Updated weekly on CDC website from Zika registry through HDs/CDC
* Includes microcephaly, calcium deposits in the brain, ventriculomegaly, absent or poorly formed brain structures, abnormal eye development, or other problems resulting from damage to the brain that affects nerves, muscles and bones, such as clubfoot or inflexible joints
What we don’t know

• If a pregnant woman is exposed
  – We don’t know how likely she is to get Zika.

• If a pregnant women is infected
  – how likely it is that Zika will pass to her fetus.
  – if the fetus is infected, how likely are birth defects or pregnancy loss
  – when in pregnancy the infection might cause harm to the fetus (studies are suggesting that earlier exposure may be more severe than later exposure)
  – whether her baby will have birth defects or long term sequelae
  – if sexual transmission of Zika virus poses a different risk of birth defects than mosquito-borne transmission.
one study utilizing modeling based on the ZIKV outbreak in French Polynesia suggested microcephaly would occur in 1% of babies born to mothers infected in the first trimester, and a recent cohort study from Brazil found abnormal outcomes including stillbirth, growth restriction, and microcephaly and other sonographic abnormalities in 29% of fetuses of Zika-infected mothers in all trimesters (Cauchemez, 2016, Brasil, 2016)
Microcephaly-SMFM

- **Isolated Fetal Microcephaly**
  - $\geq3SD$ below the mean for GA
  - Case series suggest mostly normal outcome

- **Pathologic Microcephaly**
  - $\geq5SD$ below the mean or other findings

- If 2SD below the mean, detailed intracranial assessment is indicated
  - Echogenic foci, ventriculomegaly, cerebellar hypoplasia

- **Profile assessment**

- **Reference charts available on CDC website, SMFM website**
TESTING/DIAGNOSIS

What do we do?
Updated Interim Guidance:

Testing Algorithm for a Pregnant Woman with Possible Exposure to Zika Virus\(^1\), Not Residing in an Area with Active Zika Virus Transmission\(^2\)

1. Pregnant woman with possible exposure to Zika virus
   - Test for Zika virus infection
     - Positive or inconclusive for Zika virus infection
       - Consider serial fetal ultrasounds
     - Negative for Zika virus infection
       - Fetal ultrasound to detect abnormalities consistent with Zika virus disease\(^4\)
         - Fetal abnormalities consistent with Zika virus disease present
           - Retest pregnant woman for Zika virus infection
         - Fetal abnormalities consistent with Zika virus disease not present
           - Routine prenatal care

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\(^1\) Possible exposure to Zika virus includes travel to an area with active transmission of Zika virus [http://www.cdc.gov/travel/notices/], or sex without a condom with a man who traveled to, or resided in, an area with ongoing transmission of Zika virus.

\(^2\) Testing is not currently recommended for pregnant women with possible sexual exposure to Zika virus if both partners are asymptomatic.


\(^4\) Fetal abnormalities consistent with Zika virus disease include microcephaly, intracranial calcifications, and brain and eye abnormalities. Fetal ultrasounds might not detect abnormalities until late second or early third trimester of pregnancy.
CDC’s Response to Zika

Updated Interim Guidance:

Testing Algorithm for a Pregnant Woman Residing in an Area with Active Zika Virus Transmission\(^1\), with or without Clinical Illness\(^2\) Consistent with Zika Virus Disease\(^3\)

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1. Pregnant woman residing in an area with local Zika virus transmission
   - Pregnant woman reports clinical illness consistent with Zika virus disease
     - Test for Zika virus infection
       - Positive or inconclusive for Zika virus infection
         - Consider serial fetal ultrasounds
          - Fetal abnormalities consistent with Zika virus disease\(^4\) present
            - Retest pregnant woman for Zika virus infection
              - Routine prenatal care
              - Test for Zika virus infection mid-2\(^{nd}\) trimester
              - Consider an additional fetal ultrasound

   - Pregnant woman does not report clinical illness consistent with Zika virus disease
     - Test for Zika virus infection upon initiation of prenatal care
       - Fetal ultrasound
         - Fetal abnormalities consistent with Zika virus disease\(^4\), or
           - Positive or inconclusive test result for Zika virus infection
             - Consider serial fetal ultrasounds
               - Routine prenatal care
               - Test for Zika virus infection mid-2\(^{nd}\) trimester
               - Consider an additional fetal ultrasound

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2. Positive or inconclusive for Zika virus infection
   - Consider serial fetal ultrasounds

3. Negative for Zika virus infection
   - Fetal ultrasound
     - Fetal abnormalities consistent with Zika virus disease\(^4\) not present
     - No fetal abnormalities consistent with Zika virus disease\(^4\), and
       - Negative test result for Zika virus infection
         - Fetal abnormalities consistent with Zika virus disease\(^4\), consider retest for Zika virus infection

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1. Local health officials determine when to implement testing of asymptomatic pregnant women based on information about levels of Zika virus transmission and laboratory capacity.

2. Clinical illness is consistent with Zika virus disease if one or more signs/symptoms (acute onset of fever, rash, arthralgia, or conjunctivitis) are present: [http://www.cdc.gov/zika/symptoms/index.html](http://www.cdc.gov/zika/symptoms/index.html)


4. Fetal abnormalities consistent with Zika virus disease include microcephaly, intracranial calcifications, and brain and eye abnormalities. Fetal ultrasounds might not detect abnormalities until late second or early third trimester of pregnancy.

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www.cdc.gov/zika
Clinical Management-Positive or Inconclusive Zika virus testing

**Antepartum**
- Consider serial ultrasounds every 3-4 weeks.
- Referral to maternal-fetal medicine specialist

**Postpartum**
- Histopathologic examination of the placenta and umbilical cord.
  - Testing of frozen placental tissue and cord tissue for Zika virus RNA.
  - Testing of cord serum for Zika and dengue virus IgM and neutralizing antibodies.
• PCR
  – Serum: present during 1st week of illness
  – Urine: present during first 14 days of illness

• Serology
  • IgM: typically develops at end of 1st week of illness, cross-reactivity with other flaviviruses

• Plaque-reduction neutralization (PRNT)

• Currently, the Utah Public Health Laboratory (UPHL) performs the Zika IgM MAC-ELISA and RT-PCR tests. Equivocal, inconclusive or positive test results must be sent to the CDC laboratory in Fort Collins, CO, for confirmation, including PRNT testing.
Testing will be performed according to the following:

a) If a pregnant woman is within seven days of onset of symptoms, the maternal serum will be tested for reverse transcription-polymerase chain reaction (RT-PCR).

b) If a pregnant woman is asymptomatic and has specimen drawn after travel, her serum will be tested for anti-Zika IgM antibody.

c) If Zika IgM antibody testing is positive, her serum will be additionally tested for dengue to rule out cross-reactive antibodies with this disease. Note: these tests will not be performed on Zika IgM-negative women.

d) If the test results are either positive or inconclusive, fetal ultrasound(s) should be performed to detect microcephaly or intracranial calcifications.

e) Zika virus testing is recommended for pregnant women with possible sexual transmission exposure to Zika virus if either she or her male partner developed symptoms consistent with Zika virus disease.

f) Due to the limited understanding of the duration and pattern of shedding of Zika virus in the male genitourinary tract, neither serum nor semen testing for men for the purpose of assessing risk for sexual transmission is currently recommended. The preferred recommendation is that such men abstain from sexual activity or consistently use condoms during sex for the duration of pregnancy. This is because the persistence of Zika virus in semen is not known, but in one instance was shown to be >60 days.
Steps

• Dallin Perterson at UDOH Bureau of Epidemiology
  – 801-538-6191 (ph)
• Fill out clinical and state lab form (pre-checked boxes on requisition)
• Send Lab requisition with patient to lab
• Fax copies of both to Dallin
  – 801-538-9923 (f)
# INFECTIOUS DISEASE TEST REQUEST FORM

**UTAH PUBLIC HEALTH LABORATORY**
4831 SOUTH 2700 WEST
TAYLORSVILLE, UTAH 84129
TELEPHONE: (801) 965-2400
FAX: (801) 965-2651
http://health.utah.gov/lab/infected-disease

**PLEASE PRINT CLEARLY FOR ACCURACY**

## PATIENT INFORMATION:

<table>
<thead>
<tr>
<th>Patient State of Residence:</th>
<th>Patient County of Residence:</th>
</tr>
</thead>
<tbody>
<tr>
<td>UT</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Zip Code</th>
<th>Date of Birth (mm/dd/yyyy)</th>
<th>Age</th>
<th>Sex</th>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Patient Name (Last, First):</th>
<th></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Patient ID #: (Public Health)</th>
<th>ethnicity:</th>
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</thead>
<tbody>
<tr>
<td>(Public Health)</td>
<td>Hispanic</td>
</tr>
<tr>
<td></td>
<td>Non-Hispanic</td>
</tr>
</tbody>
</table>

## PROVIDER INFORMATION:

<table>
<thead>
<tr>
<th>Provider Code:</th>
<th>Provider Phone:</th>
<th>Provider Email:</th>
<th>Secure Fax #:</th>
</tr>
</thead>
</table>

## SPECIMEN SOURCE/SITE (CHOOSE 1):

<table>
<thead>
<tr>
<th>Specimen Source/Site</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## BACTERIOLOGY/TUBERCULOSIS TESTS:

**Bacterial Specimen**

<table>
<thead>
<tr>
<th>Required Shipping Temperature:</th>
<th>Bacterial Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>(e.g. Cold)</td>
<td>(e.g. Heat)</td>
</tr>
</tbody>
</table>

## VIROLOGY/IMMUNOLOGY TESTS:

**Viral Specimen**

<table>
<thead>
<tr>
<th>Required Information:</th>
<th>Blood draw date/time</th>
<th>Incubation at 37°C completed:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Signature:</td>
<td>Incubation start date/time:</td>
</tr>
<tr>
<td></td>
<td>Incubation end date/time:</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specimen Type:</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</table>

## BIOTERRORISM TESTS:

<table>
<thead>
<tr>
<th>Notify Lab before submitting:</th>
<th></th>
<th></th>
</tr>
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<tbody>
<tr>
<td></td>
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<tr>
<th>Specimen Type:</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

## ADDITIONAL INFORMATION:

<table>
<thead>
<tr>
<th>Other Disease Suspected:</th>
<th>Referral Test to CDC (form REQUIRED) specify:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Contact UPHL for CDC form</td>
</tr>
</tbody>
</table>

## COMMENTS:

|                        | |
|------------------------||


# Zika Virus Disease Case Investigation Form

**Arboviral Diseases Branch**

**FOR ARBOVIRAL DISEASE BRANCH USE ONLY**

<table>
<thead>
<tr>
<th>CDC R-number</th>
<th>ZIKVID</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Reporting Jurisdiction**

<table>
<thead>
<tr>
<th>Jurisdiction (state/territory):</th>
<th>UT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agency:</td>
<td></td>
</tr>
<tr>
<td>Contact Name:</td>
<td></td>
</tr>
<tr>
<td>Contact Phone:</td>
<td></td>
</tr>
<tr>
<td>Contact Position:</td>
<td></td>
</tr>
<tr>
<td>Contact Email:</td>
<td></td>
</tr>
</tbody>
</table>

**Demographic Information**

<table>
<thead>
<tr>
<th>State ID number(for public health):</th>
<th>Age:</th>
<th>Years</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Initials:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>State of residence:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex:</td>
<td>Male</td>
<td>Female</td>
<td></td>
</tr>
<tr>
<td>Pregnant:</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>If yes, gestational week at illness onset:</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Travel History**

<table>
<thead>
<tr>
<th>Dates of travel:</th>
<th>Country(s) visited:</th>
</tr>
</thead>
</table>

**Vaccination History**

<table>
<thead>
<tr>
<th>Previously vaccinated for any of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yellow Fever</td>
</tr>
<tr>
<td>Japanese Encephalitis</td>
</tr>
<tr>
<td>Tickborne Encephalitis</td>
</tr>
</tbody>
</table>

**Illness Information**

<table>
<thead>
<tr>
<th>Illness onset date:</th>
<th>□ Hospitalized</th>
<th>□ Died</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical syndrome:</td>
<td>□ Guillain-Barre syndrome / Acute flaccid paralysis</td>
<td>□ Microcephaly</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fever</th>
<th>□ Yes</th>
<th>□ No</th>
</tr>
</thead>
<tbody>
<tr>
<td>if yes:</td>
<td>Subjective fever</td>
<td>Measured fever (Maximum measured temperature: _____)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rash</th>
<th>□ Yes</th>
<th>□ No</th>
</tr>
</thead>
<tbody>
<tr>
<td>if yes:</td>
<td>Type: □ Maculopapular □ Petechial □ Purpuric □ Other</td>
<td>Pruritic: □ Yes □ No</td>
</tr>
<tr>
<td></td>
<td>Distribution:</td>
<td></td>
</tr>
</tbody>
</table>

**Additional clinical symptoms**

<table>
<thead>
<tr>
<th>□ Arthralgia</th>
<th>□ Headache</th>
<th>□ Vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Conjunctivitis</td>
<td>□ Myalgia</td>
<td>□ Diarrhea</td>
</tr>
</tbody>
</table>

**Specimen Information**

<table>
<thead>
<tr>
<th>Specimen 1 collected:</th>
<th>Type: □ Serum □ CSF □ Amniotic fluid □ Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specimen 2 collected:</td>
<td>Type: □ Serum □ CSF □ Amniotic fluid □ Tissue</td>
</tr>
</tbody>
</table>
Testing

• Refer to CDC website for details on collection of fetal /placental tissue
• Blood/urine usually takes about 3w (per CDC)
Prevention

• Travel Advisories
• Sexual Transmission
• Mosquito control and Avoidance
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

More members in the community become infected

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
Aedes Mosquitoes

- Zika virus is transmitted to people primarily through the bite of an infected Aedes species mosquito (Ae. aegypti and Ae. albopictus). These are the same mosquitoes that spread dengue and chikungunya.

- These mosquitoes typically lay eggs in and near standing water in things like buckets, bowls, animal dishes, flower pots and vases. They prefer to bite people, and live indoors and outdoors near people.

- Mosquitoes that spread chikungunya, dengue, and Zika are aggressive daytime biters, but they can also bite at night.
Pregnant?
Warning: Zika might be linked to birth defects
There is no vaccine to prevent Zika virus infection

Protect yourself from mosquito bites

Daytime is most dangerous
Mosquitoes that spread chikungunya, dengue, and Zika are aggressive daytime biters. They can also bite at night.

Use insect repellent
It works!
Look for the following active ingredients:
- DEET
- PICARIDIN
- IR3535

Wear protective clothes
Wear long-sleeved shirts and long pants and use insect repellent. For extra protection, treat clothing with permethrin.

Mosquito-proof your home
Use screens on windows and doors. Use air conditioning when available. Keep mosquitoes from laying eggs in and near standing water.
Mosquito Bite prevention

- Use Environmental Protection Agency (EPA)-registered insect repellents with one of the following active ingredients: DEET, picaridin, IR3535, oil of lemon eucalyptus, or para-menthane-diol.
- Do not spray repellent on the skin under clothing.
- If you are also using sunscreen, apply sunscreen before applying insect repellent.
Sexual Transmission

• ZIKV can also be transmitted through sex with a male partner.

• Patients should be advised to take the following steps to protect themselves from sexual transmission of ZIKV:
  – If a man develops symptoms of ZIKV disease, he should use a condom the right way, **every time** he has vaginal, anal, or oral or should not have sex **for 6 months** after illness starts.
  – If a man does not develop symptoms of ZIKV disease, he should still use condoms for **at least 8 weeks** after the last date of exposure (the last day he is in an area with active ZIKV transmission) to avoid sexual transmission to his partner. This is especially important if he has any plans to try to conceive with his partner after returning from travel.
  – Use condom for entire pregnancy
Preconception Exposure

• One or more symptoms of ZIKV disease (fever, rash, arthralgia or conjunctivitis)
  – Female traveler: 8w
  – Male traveler: 6m

• NO symptoms or + testing: 8w (m/f)
Geography

• US Territories
  – Local mosquito-borne transmission of Zika virus has been reported in the Commonwealth of Puerto Rico, the US Virgin Islands, and American Samoa

• US States
  – No local mosquito-borne Zika virus disease cases have been reported in US states, but lab tests have confirmed Zika virus in travelers returning to the United States. These travelers have gotten the virus from mosquito bites and some non-travelers got Zika through sex with a traveler
What Now?

WE ARE DOOMED
Future Directions

- Vaccine—in investigation
- Mosquito control with usual measures
- Oxitec mosquito
  - May reduce mosquito population by 95%
  - Oxford University 1999
  - Inability to develop past the larval stage
- Study clinical implications
  - Obtain data for clinical counseling
  - CDC currently in Brazil conducting case-control study
Final Points

• Follow national/international guidelines
  – Check back frequently!
  – ACOG, SMFM, CDC, WHO, PAHO
  – State Health Departments can help with testing

• Remember that in our patient population (US), other public-health risks likely pose a much greater maternal-fetal threat and should continue to be emphasized
  – Vaccines (flu, tdap)
  – Seatbelt use
  – Substance use
  – Many others (CMV)
If families would like to speak to someone about a possible Zika virus infection or diagnosis during pregnancy and risk to the baby, please contact MotherToBaby. MotherToBaby experts are available to answer questions in English or Spanish by phone, text, or chat. The free and confidential service is available Monday - Friday from 8am - 5pm (local time). To reach MotherToBaby:

- Call 1-866-626-6847
- Text questions to 855-999-3525 (standard text messaging rates may apply)
- Chat live or send an email through the MotherToBaby website
- CDC maintains a 24/7 clinical consultation service for health care providers evaluating and caring for pregnant women and infants with possible ZIKV infection. Call CDC's Zika Pregnancy Hotline for Healthcare Providers at 770-488-7100 or e-mail zikamch@cdc.gov for any concerns related to clinical management.