Zika Virus: Transmission, Clinical Manifestations & Diagnosis

Kauser Akhter, MD
Assoc. Program Director, Infectious Disease Fellowship, Orlando Regional
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My Sources of Information

- CDC.gov website
- MMWR
- Florida Department of Health website
- *New England Journal of Medicine*
- *Lancet*, the *Lancet Infectious Diseases* journals
Zika Virus: Overview

• Flavivirus spread mainly through mosquitoes
• Same family as Dengue, West Nile, Yellow fever & Japanese encephalitis
• Originally identified in 1947 from Zika forest of Uganda
• In 2014, the virus spread across the Pacific Ocean to French Polynesia, Easter Island, and in 2015 to Central America, the Caribbean, and South America
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
Zika Virus: Transmission

• Mainly via bite of an infected *Aedes* species mosquito
• The mosquitoes breed in water-holding containers; they are daytime biters and feed indoors and outdoors
• Perinatal, *in utero* & sexual transmission (males to their sex partners) have also been reported (11/618 sexually transmitted cases as of 6/1/16)
• Blood transfusion-associated transmission reported abroad, but NO cases in the U.S to date
Zika: Clinical Signs & Symptoms
Zika: Clinical Signs & Symptoms

- 1 in 5 infected people (20%) become symptomatic
- ? incubation period, but likely a few days to a week
- Findings: acute onset of fever with maculopapular rash, joint pain, or non-purulent conjunctivitis
- Other common symptoms: myalgia, headache
- Illness usually mild, with symptoms lasting for several days to a week after infection
- Illness likely confers immunity to future Zika infection
Zika: Fever

- Not as high as the fever caused by Dengue or Chikungunya (both mosquito-transmitted)
- Zika-induced fever comes on acutely
- Fever usually up to 38.5 C/101.3 F; with the above infections, fever can be up to 104-105 F
Zika Virus Rash

- Maculopapular (flat & bumpy spots)
- Morbilliform (spots, 2-10 mm) or scarlatiniform (smaller ones)
- Rash begins on the face on the first day of illness and spreads all over the body
- Rash fades within 2-3 days. Gone within a week
Zika: Joint pain

- The Zika virus can cause pain and swelling of the joints
- Some patients may also experience muscle pain
- These symptoms usually subside within a week
- The joint pain is not as severe as in e.g. Chikungunya
Zika Virus Conjunctivitis

- Conjunctivitis is an inflammation of the surface of the eye which can cause redness
- The eye waters, feels sticky and painful
- The fluid is infectious so patients have to be wary of spreading the infection
- Vision not affected
- Some patients experience eye pain as well
Zika & Guillain-Barre Syndrome

• Data from the Zika outbreak in French Polynesia in 2013-2014 documented 42 cases of Guillain–Barré syndrome (GBS) in a population of approximately 270,000 (Petersen et al, 2016: Int J Infect. Dis 2016: 44: 11-15; Cao-Lormeau, April 2016: 1531-9)

• All of these 42 people tested positive for Zika

• As of June 1, 2016, 1/618 U.S states cases had GBS
What is Guillain-Barre Syndrome?

• Uncommon disorder of the nervous system in which a person’s own immune system damages the nerve cells → muscle weakness, and sometimes, paralysis

• Guillain-Barre (GBS) may be triggered by Zika, as well as other infectious causes, e.g (a bacterial pathogen which causes food poisoning)

• Symmetric muscle weakness of the arms and legs. The muscles which control eye movement or swallowing, or in severe cases, breathing, may be affected

• Symptoms can last a few weeks or several months

• Most people fully recover, but 1 out of 20 people die
# Zika vs Dengue vs Chikungunya

<table>
<thead>
<tr>
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<th>ZIKA</th>
<th>DENGUE</th>
<th>CHIKUNGUNYA</th>
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<tbody>
<tr>
<td>Fever</td>
<td>Low-grade</td>
<td>High</td>
<td>High</td>
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<tr>
<td>Rash</td>
<td>Most patients</td>
<td>&gt;50% patients</td>
<td>40-75% patients</td>
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<td>Myalgias</td>
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<td>Conjunctivitis</td>
<td>Yes</td>
<td>If hemorrhage</td>
<td>No</td>
</tr>
<tr>
<td>Cytopenias</td>
<td>No</td>
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Zika Fetal or Neonatal Complications
Microcephaly Cases in Brazil: 2015

Microcephaly cases in Brazil spike
Cases per year

Typical 176
2015 3,530

Source: Centers for Disease Control and Prevention

Daniel Wheaton • U-T
Microcephaly

• Microcephaly: head circumference $\geq 2$ SD’s below the mean for sex & gestational age at birth

• Microcephaly is rare: ~6 cases per 10,000 live born infants in the U.S
Normal Head Circumference vs Microcephaly
Microcephaly
Zika Fetal or Neonatal Complications

• Microcephaly & other brain abnormalities in babies have now been described in case reports & case studies to be due to Zika infection occurring in the late first or early second trimester of pregnancy (NEJM, May 2016)

• WHO experts also warn about Zika-induced spasticity, seizures, irritability, feeding difficulties, vision problems and severe brain abnormalities
Zika Fetal or Neonatal Complications

- Zika virus infections occurring later in pregnancy have been associated with poor intrauterine growth, fetal death, or in some pregnancies, defects on prenatal ultrasounds that have not yet been confirmed post-natally because the pregnancies are ongoing.

- Extra scalp skin, joint contractures & club foot have all been described as a result of Zika infection (NEJM, May 2016)
How Does Zika Cause Microcephaly?

- Zika has been detected in the amniotic fluid of at least 7 pregnant women in Brazil, whose fetuses had microcephaly (Lancet Infect Dis 2016; WHO)
- Zika virus has been detected in the brains of fetuses & infants with microcephaly
- In mice models of infection (Cell Stem Cell, May 2016), Zika virus was shown to target immature neurons after crossing the placenta → killing off of these cells by apoptosis (programmed cell death) & self-ingestion (autophagy)
How Does Zika Cause Microcephaly?

- ?? Does Zika affect a glucose transporter $\rightarrow$ decreased glucose transport across the placenta $\rightarrow$ microcephaly (Lancet Infect Dis, June 2016)
Zika Diagnosis: Overview

- Preliminary diagnosis is based on the patient’s clinical features, travel, and activities
- See your physician, who will then need to contact the FLA Department of Health &/or CDC
- Lab diagnosis: i) serum, urine or CSF rRT-PCR (real time reverse transcriptase polymerase chain reaction), ii) virus-specific immunoglobulin M (blood or CSF) (Zika MAC-ELISA) and iii) plaque reduction neutralizing antibodies (PRNT)
Zika Virus: Diagnostic Testing

- A positive rRT-PCR = Zika infection, & no antibody testing is needed
- Zika RNA in blood lasts up to 7 days, so the rRT-PCR in blood after 7 days of symptoms may be negative
- Virus-specific IgM develops near day 4 of illness, lasts up to 12 weeks, & can be checked if Zika suspected (cross-reaction with other flaviviruses is common) & the rRT-PCR is negative
- Neutralizing antibodies (IgG) develop shortly after IgM antibodies. Thought to confer lifelong immunity
- A plaque reduction neutralization test (PRNT) can be done after the IgM, to exclude other flaviruses
Zika Virus: Diagnostic Testing

• CDC, as of May 10, 2016, new recommendations:
• <= 14 days after symptom onset, send Zika virus rRT-PCR on urine (reverse real-time transcription-polymerase chain reaction)
• <= 7 days after symptoms: serum + urine rRT-PCR
• A positive Zika rRT-PCR = current Zika infection
• A negative rRT-PCR does not necessarily rule out Zika, as viremia decreases over time
Zika Testing: FLA Dept of Health/CDC

• If you think you have Zika, see your physician
• Your doctor will contact the health department to request Zika virus testing for patients meeting the following criteria:
• 1) Currently pregnant women who (while pregnant) experienced two or more of the following signs/symptoms: fever, maculopapular rash, arthralgia, or conjunctivitis within two weeks of travel to an area reporting Zika virus activity regardless of the time since the travel/illness occurred
Zika Testing: FLA Dept of Health/CDC

2) Mothers of an infant or fetus with microcephaly or intracranial calcifications and with history of travel to an area with Zika virus activity during pregnancy

3) If not pregnant, persons with two or more of the following signs/symptoms: fever, maculopapular rash, arthralgia or conjunctivitis and a history of travel to an area reporting Zika activity in the two weeks prior to illness onset or is a suspect local case
CDC: Congenital Zika Evaluation

• Zika rRT-PCR, antibody testing as above
• If microcephaly or intracranial calcifications, CDC also recommends geneticist evaluation, pediatric neuro evaluation, testing for syphilis, TORCH
• Ophthalmology exam at birth/within 1 month of birth, hearing screen, occipitofrontal circumference measurements & monitoring of milestones
Thank You!

Sorry, mosquito...

Everybody hates you.