Zika Virus

Rethinking “just another Aedes-transmitted arbovirus” and the “mild cousin of Dengue”

Elizabeth A. Talbot MD
Assoc Professor, ID and Int’l Health
Deputy State Epidemiologist, NH
The Pathogen

- Zika virus (ZIKV) in *Flavivirus* genus, *Flaviviridae* family, Spondweni group
  - SS RNA
- First isolated in
  - 1947 from monkey in Zika forest, Uganda
  - 1948 in mosquitoes (*Aedes africanus*) same forest
  - 1952 in a human in Nigeria
- ZIKV lineages: African and Asian
  - Asian emerged in Pacific and Americas
"Another noxious virus to a list of several other viruses that are widely transmitted by Aedes: dengue, Chikungunya, Zika, Mayaro, JE, yellow fever virus”

Major vector is A. aegypti
- Also Ae. africanus, Ae. albopictus, Ae. polynesiensis, Ae. unilineatus, Ae. vittatus and Ae. hensilli

Bite during the day
Aedes Aegypti
Additional Modes of Transmission

• Perinatal by transplacental transmission or during delivery
  – Confirmed in French Polynesia

• Transfusion-derived transmission
  – One confirmed in Brazil
  – 3% of banked blood in French Polynesia seropositive
    • Not necessarily infectious
Sexual Transmission

• Sexual transmission reported in three cases
  – Scientist who visited Senegal in 2011 contracted
    • Few weeks after return to US, wife diagnosed
  – 2016: male traveler returns to TX; wife confirmed
• Known present in semen for 2w after symptom onset
• Many questions remain
Identified in Other Body Fluids

- Breastmilk
  - No confirmed transmission
  - Risk benefit favors breastfeeding
- Urine and saliva
  - Uncertain if can transmit
Clinical Features

• Incubation ~3-12 days after bite
• 60-80% of infections asymptomatic
• Symptoms usually mild: self-limiting febrile illness of 4–7 days duration without severe complications
• Main symptom: acute fever, maculopapular rash, arthralgia, non-purulent conjunctivitis/conjunctival hyperemia, myalgia and headache
  – Retro-orbital pain and GI signs rare
Rash

Rash often starts on face and then spreads throughout body
Clinical Sequelae

- French Polynesia
  - Guillain-Barré syndrome
  - Other autoimmune: thrombocytopenic purpura, leukopenia
- Brazil
  - GBS
  - Neurological and neurodevelopmental conditions such as microcephaly in fetuses and newborns from mothers exposed to ZIKV
- Especially first 2 trimesters of pregnancy
Previous Epidemiology

• Before 2007, ZIKV circulation included only tropical Africa and Southeast Asia
  – Based on serosurveys and viral isolation in mosquitoes and humans, and with reports of travel-associated cases
  – Detection of specific antibodies in animal species
    • Orangutans, zebra, elephants, water buffaloes and rodents

• No large human outbreaks reported
Recent Epidemiology

- April to July 2007, outbreak on **Yap Island**
  - First outbreak identified outside of Africa and Asia
  - Affected nearly 75% of population of ~12,000
- 2013 - 2015 several outbreaks in Pacific region including large outbreak in **French Polynesia**
  - ~28,000 of 270,000 population
And Beyond

- August 2014 Rapid spread in South and Central America
  - Arrived via FIFA World Cup, based on phylogenetic analysis
- 28 countries and territories affected
  - Jan 29th 2015 USVI
  - Feb 5th 2016 Puerto Rico
- WHO estimates 3–4 million cases of Zika in next 12m
  - Mathematical modelling based on regional dengue dynamics and Zika in Brazil

Global Response

• Jan 28, WHO Director General Margaret Chan said Zika virus, now “spreading explosively” in the Americas, was “deeply concerning”

• Although causal relation between infection and birth malformations and neurological syndromes has not been established, it is strongly suspected

• Chan noted. “The possible links...have rapidly changed the risk profile of Zika, from a mild threat to one of alarming proportions. The increased incidence of microcephaly is particularly alarming, as it places a heart-breaking burden on families and communities.”

• Feb 1 declared Public Health Emergency of International Concern
The Brazil Outbreak

• Seven states involved, esp northeast
  – MOH estimates 1.3 million infected
  – Concurrent unprecedented dengue epidemic

• First ever deaths from Zika confirmed
  – Adult and 16yo

• Rainy season between January and May
  anticipating spike in arboviruses

Marcondes CB and de Melo Ximenes MDFF. Zika virus in Brazil and the danger of infestation by Aedes (Stegomyia) mosquitoes. Revista da Sociedade Brasileira de Medicina Tropical http://dx.doi.org/10.1590/0037-8682-0220-2015
The Microcephaly Association

• Through Dec 2015, >1,248 cases of microcephaly reported among newborns in Brazil
  – 20-fold increase in rate noted coincident with Zika
  – >40 deaths, tremendous disabilities
Microcephaly Research

• Plausible: in mice, ZIKV is highly neurotropic

• Research in Brazil
  – In 35 cases, 26 (74%) of mothers of infants with microcephaly/neuroimaging abnormalities self-reported rash during first (n=15) or second (5) trimester
    • Zika virus testing is pending
    • Testing for other pathogens negative
  – Viral RNA detected in
    • Amniotic fluid of 2 pregnant women with fetal microcephaly
    • Brain tissue in 4 severely affected fetuses/perinatal deaths
    • Placenta of one affected infant
  – Some affected infants have not had Zika RNA detected

Marcondes CB and de Melo Ximenes MDFF. Zika virus in Brazil and the danger of infestation by Aedes (Stegomyia) mosquitoes. Revista da Sociedade Brasileira de Medicina Tropical http://dx.doi.org/10.1590/0037-8682-0220-2015
Reporting, Classification Biases

• Several national reporting systems
• Likely reporting biases
• Definition of microcephaly has tightened
• Some cases initially classified as microcephalic have since been re-classified; others shown due to other causes
Why Microcephaly Now?

• No evidence of new Zika strain
• Another cause?
• Unnoticed in smaller Zika outbreaks
  – French Polynesia has retrospectively confirmed increase in congenital malformations
GBS in Brazil

• 22 January 2016, National IHR Focal Point of Brazil notified PAHO/WHO of national increase of Guillain-Barre Syndrome (GBS)

• Data from hospital-based surveillance system reveal that, between January and November 2015, 1,708 cases of GBS were registered nationwide. Compared with 2014
  – Some states increasing: Alagoas (516.7%), Bahia (196.1%), Rio Grande do Norte (108.7%), Piauí (108.3%)
  – Some decreasing: Espírito Santo (78.6%), Rio de Janeiro (60.9%)

• Most states experiencing circulation of Zika, chikungunya, and dengue virus

Diagnosis

• In acutely ill patients, flaviviral RNA detected then sequenced for specific viruses
  – Viremic period 3–5 days after symptom onset
  – Detected in urine up to 10 days after symptom onset
• IgM can be detected 2-12 weeks following infection
  – Serological results interpreted acc to vaccination and previous exposure to other flaviviral infections
  – Confirmed by
    • Neutralization (PRNT)
    • Seroconversion
    • Four-fold antibody titer increase in paired serum samples
Treatment

- Differential or co-clinical diagnostics should be considered
  - Dengue, chikungunya and malaria

- Symptomatic treatment
  - Pain relief, fever reduction, anti-histamines for pruritic rash

- Discourage treatment with aspirin or NSAIDs
  - Hemorrhagic syndrome reported
  - Reye's syndrome
Recommendations for Testing Travelers for Zika Virus

Benjamin P. Chan, MD, MPH
February 10, 2016
NH Division of Public Health Services
Health Alert Network (HAN) Notifications

For more information:
http://www.dhhs.state.nh.us/dphs/cdcas/alerts/index.htm

To sign up for HAN notifications, e-mail:
Health.Alert@nh.gov
Health Alert Network (HAN) Messages

2016
02/05/2016  Zika Virus Transmission in the Americas: Update #1
02/05/2016  Increase in Norovirus Activity in New Hampshire
01/20/2016  Zika Virus Transmission in the Americas

2015
12/23/2015  Perfluorochemical (PFC) Blood Testing Program: Update #3
10/07/2015  Opioid Abuse/Misuse Response in New Hampshire
10/05/2015  Shiga Toxin-producing E. coli (STEC) 0157:H7 Outbreak in Vermont
09/21/2015  Ebola Virus Disease (EVD) Preparation in New Hampshire: Update #3
09/17/2015  First Confirmed Cases of Influenza in New Hampshire, 2015-2016
09/16/2015  Arboviral Illness Update: West Nile Virus Identified in Mosquito Batch--Manchester, NH
08/17/2015  Release of Individual Perfluorochemical (PFC) Blood Test Results
08/13/2015  Updated Centers for Disease Control (CDC) 2015 Sexually Transmitted Disease (STD) Treatment Guidelines
07/01/2015  Arboviral Disease in New Hampshire: Preparation for the 2015 Season
06/15/2015  Individual Perfluorochemical (PFC) Blood Test Results Release
06/12/2015  Middle East Respiratory Syndrome Coronavirus- (MERS-CoV) Situational Update and Guidelines for Patient Evaluation
06/10/2015  Highly Pathogenic Avian Influenza
05/05/2015  Lyme Disease and Other Tickborne Diseases in New Hampshire
04/29/2015  Confirmed Measles Case with Travel to New Hampshire
04/03/2015  Perfluorochemical (PFC) Contamination of the Drinking Water at the Pease Tradeport
03/12/2015  Multi-State Measles Outbreak & Influenza Update, March 2015
02/04/2015  Influenza Season Update #2
01/30/2015  Multi-State Measles Outbreak, January 2015
Main Concern for Zika Virus Infection

Fetuses/Infants born to pregnant women infected with Zika virus
Question

How can pregnant women get Zika virus disease (and then transmit to the fetus)?

1. Travel (via infected *Aedes* mosquito bite)
2. Travel
3. Travel
4. Possible sexual transmission from men
5. Unlikely from blood transfusion

No evidence of transmission through other body fluids (breast milk, saliva, urine, etc.)
Prevention

Pregnant Women should postpone travel to Zika affected areas

Anybody that does travel, especially pregnant women or women trying to become pregnant, should follow strict guidance to avoid mosquito bites:

If a pregnant woman did travel... there is guidance for testing women and monitoring fetuses

If a male traveled who has a pregnant female partner... there is guidance for preventing sexual transmission to the woman
Updated CDC Guidelines for Pregnant Women

Pregnant woman with history of travel to an area with ongoing Zika virus transmission

Test for Zika virus infection

Positive or inconclusive for Zika virus infection
Consider serial fetal ultrasounds
Consider amniocentesis for Zika virus testing

Negative for Zika virus infection
Fetal ultrasound to detect microcephaly or intracranial calcifications

Microcephaly or intracranial calcifications present
Retest pregnant woman for Zika virus infection
Consider amniocentesis for Zika virus testing

Microcephaly or intracranial calcifications not present
Routine prenatal care

Patient reports travel to affected areas* during pregnancy

Does patient have 2 or more of the key symptoms** during or within 2 weeks of travel?

Yes

Zika PCR/IgM blood test (depending on date of travel) & Fetal Ultrasound

No

Zika IgM blood test (2-12 weeks after travel) & Fetal Ultrasound

Positive/inconclusive blood test or ultrasound shows microcephaly or intracranial abnormalities?

Yes

Retest pregnant mother for Zika if initial blood test is negative but fetal ultrasound is abnormal
• Consider referral to MFM specialist
• Consider serial ultrasounds (Q3-4 weeks)
• Consider amniocentesis for Zika PCR testing

No

Routine Prenatal Care

* Affected areas include: South America, Central America, and the Caribbean
** Symptoms include: acute onset of fever, maculopapular rash, arthralgias, and conjunctivitis
Testing Asymptomatic Pregnant Women

“Serologic testing for Zika virus can be offered to asymptomatic women who traveled to an area with ongoing Zika virus transmission” (CDC guidelines)

IgM antibodies are expected to be present at least 2 weeks after virus exposure and persist for up to 12 weeks.

A negative IgM result would suggest recent infection did not occur and could preclude the need for serial ultrasounds.

A negative serologic test result cannot definitively rule out Zika virus infection.

Summary for Testing/Monitoring Pregnant Women

- Ask about travel
- If travel, ask about symptoms:
  - Acute onset fever
  - Maculopapular rash
  - Arthralgias
  - Conjunctivitis
- If travel (regardless of symptoms):
  - Zika blood test
  - Fetal ultrasound
- Symptoms will affect the timing of the blood test
Guidance for healthcare providers caring for infants born to mothers who traveled to, or resided, in Zika affected areas during pregnancy

- Infants with microcephaly
- Infants without microcephaly

Guidelines can be found at:
http://www.cdc.gov/mmwr/volumes/65/wr/mm6503e3.htm

Outdated already. All mothers should be tested regardless of symptoms.
Sexual Transmission of Zika

Emerg Infect Dis 2015

Potential Sexual Transmission of Zika Virus

Didier Musso, Claudine Roche, Emilie Robin, Tuxuan Nhan, Anita Teissier, Van-Mai Cao-Lormeau

In December 2013, during a Zika virus (ZIKV) outbreak in French Polynesia, a patient in Tahiti sought treatment for hematospermia, and ZIKV was isolated from his semen. ZIKV transmission by sexual intercourse has been previously suspected. This observation supports the possibility that ZIKV could be transmitted sexually.

DCHHS

Dallas County Health and Human Services

CONTACTS
Eriikka D. Neroes, Public Information Officer
214.819.6329 (office) 214.394.8109 (cell)

Zachary Thompson, Director
214.755.9299 (cell)

FOR IMMEDIATE RELEASE

DCHHS Reports First Zika Virus Case in Dallas County Acquired Through Sexual Transmission

Emerg Infect Dis 2011

Probable Non-Vector-borne Transmission of Zika Virus, Colorado, USA


Clinical and serologic evidence indicate that 2 American scientists contracted Zika virus infections while working in Senegal in 2008. One of the scientists transmitted this arbovirus to his wife after his return home. Direct contact is implicated as the transmission route, most likely as a sexually transmitted infection.
Men who have traveled to an area of active Zika virus transmission and who have a pregnant partner should abstain from sexual activity or consistently and correctly use condoms during sex (vaginal, anal, or oral intercourse) for the duration of the pregnancy.

Zika virus testing for the assessment of risk for sexual transmission is of uncertain value -- incidence and duration of shedding in the male genitourinary tract is limited to one case report in which Zika virus persisted longer than in blood.

Testing of men for the purpose of assessing risk for sexual transmission is not recommended

NH DHHS will consider testing non-pregnant individuals on a case-by-base basis if it impacts clinical management or decision making.
Limitations of Testing

- Within 7 days of symptoms: serum RT-PCR
- 4 days or later after symptoms: serum IgM
- IgM antibodies are expected to be present at least 2 weeks after virus exposure and persist for up to 12 weeks
- Cross reactivity of Zika IgM with other related flavivirus infection or vaccination (e.g. dengue, chikungunya, yellow fever)
- IgM needs confirmation with PRNT assays (antibody neutralization)
Nuances of Testing

What if a pregnant woman has traveled and is symptomatic, then gets tested with PCR and/or IgM before 2 weeks (from date of travel) and their serum testing is negative... do they need to be retested after 14 days?

CDC doesn’t offer guidance about repeat testing

You could test for Zika IgM again after 2 weeks have elapsed since travel