



# Zika Virus

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

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GEISEL  
— SCHOOL OF —  
MEDICINE  
AT DARTMOUTH

# 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



# The Vector

- “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 29<sup>th</sup> 2015 USVI
  - Feb 5<sup>th</sup> 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



[http://www.cdc.gov/zika/images/zik-world-map\\_active\\_02-03-2016\\_web.jpg](http://www.cdc.gov/zika/images/zik-world-map_active_02-03-2016_web.jpg)



# 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

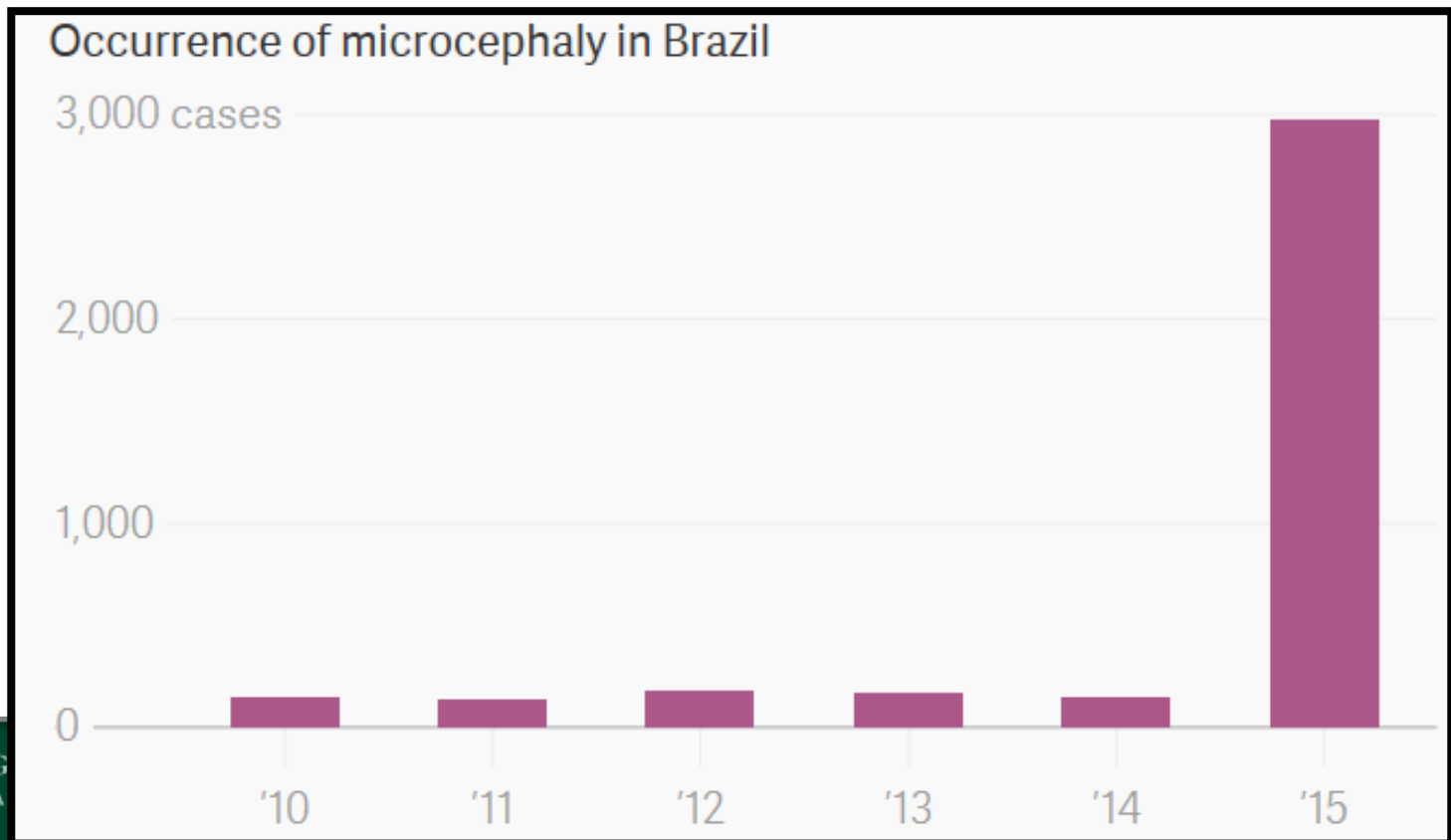
- Seven states involved, esp northeast
  - MOH estimates 1.3 million infected
  - Concurrent unprecedented dengue epidemic
- First ever deaths from Zika confirmed
  - Adult and 16yo
- Rainy season between January and May  
anticipating spike in arboviruses

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: Espirito Santo (78.6%), Rio de Janeiro (60.9%)
- Most states experiencing circulation of Zika, chikungunya, and dengue virus

<http://www.who.int/csr/don/8-february-2016-gbs-brazil/en/>



# 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

**Dengue**

 **Febre alta**

**Tontura** **Manchas vermelhas**

**Dor nas articulações** **Naúseas e vômitos**

**Fraqueza** **Perda de peso**

**Sangramento no nariz e na gengiva** **Dor de cabeça**

**Dor atrás dos olhos**

**Chikungunya**

**Dores intensas nas articulações de pés e mãos** **Dor de cabeça**

**Dor muscular** **Manchas vermelhas**

**Febre alta**

**ZikaV**

 **Dor muscular**

**Dor de cabeça** **Febre baixa**

**Lesões com pontos brancos e vermelhos na pele** **Dor nas articulações**

**Olhos vermelhos** **Dor nas costas**

Fonte: Ministério da Saúde



# 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/cdcs/alerts/index.htm>

To sign up for HAN notifications, e-mail:

[Health.Alert@nh.gov](mailto:Health.Alert@nh.gov)



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## Health Alert Network (HAN) Messages

### [Archived 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](#)

10/06/2015 [Shiga Toxin-producing E. coli \(STEC\) O157:H7 Outbreak in Vermont](#)

09/21/2015 [Ebola Virus Disease \(EVD\) Preparation in New Hampshire: Update #5](#)

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](#)

05/06/2015 [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](#)

### Program Information

- ✦ Bureau of Infectious Disease Control
- ✦ Avian Flu
- ✦ Disease Handbook for Child Care Providers
- ✦ Disease Reporting Forms
- ✦ EEE & West Nile Virus
- ✦ Healthcare-Associated Infections
- ✦ Hepatitis A
- ✦ Hepatitis C
- ✦ Influenza
- ✦ Lyme Disease
- ✦ Meningitis
- ✦ NH Health Alert Network
- ✦ Rabies
- ✦ Salmonella
- ✦ SARS
- ✦ Staph
- ✦ Surveillance
- ✦ Tuberculosis
- ✦ Publications
- ✦ Contact Bureau of Infectious Disease Control

### Related Resources

- ✦ CDC Health Alert Network
- ✦ Healthy Insights



# Main Concern for Zika Virus Infection

Fetuses/Infants born to pregnant  
women infected with Zika virus

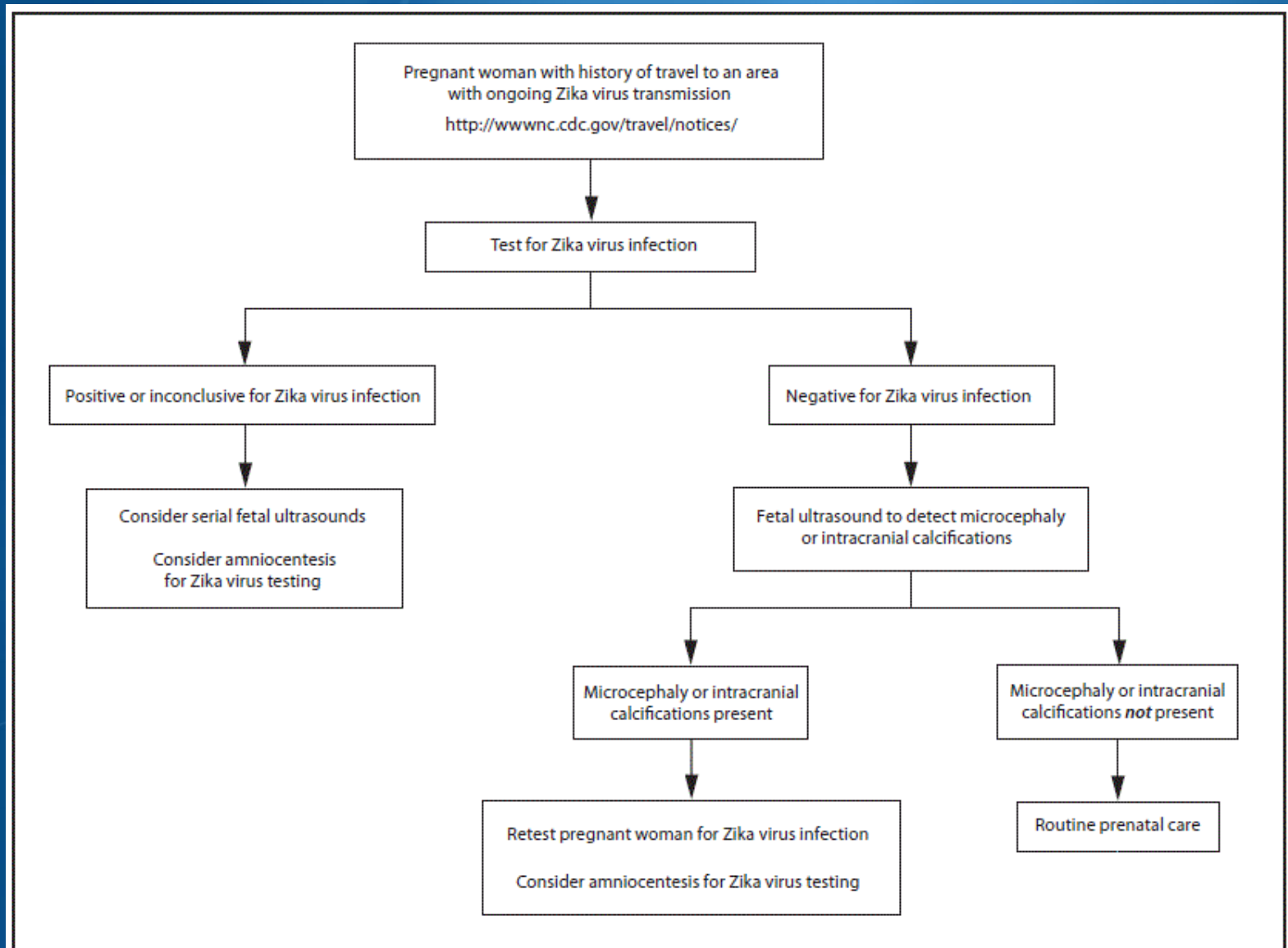
# Question

- 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

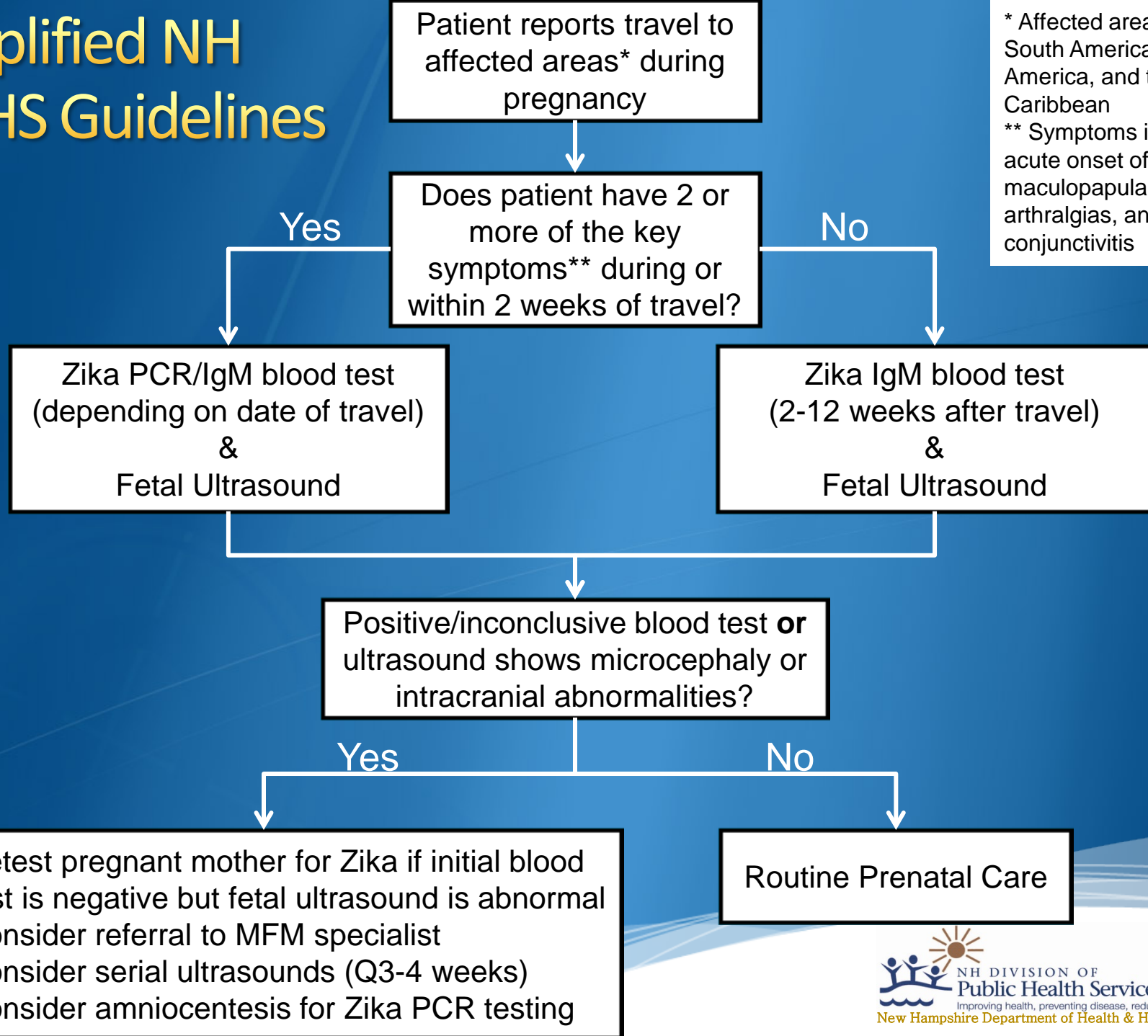
- Pregnant Women should postpone travel to Zika affected areas
- Anybody that does travel, especially pregnant women or women trying to become pregnant, should follow strict guidance to avoid mosquito bites:  
<http://www.cdc.gov/zika/prevention/index.html>
- If a pregnant woman did travel... there is 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



# Simplified NH DHHS Guidelines

\* 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



## Interim Guidelines for the Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection — United States, 2016

Weekly / January 29, 2016 / 65(3);63–67

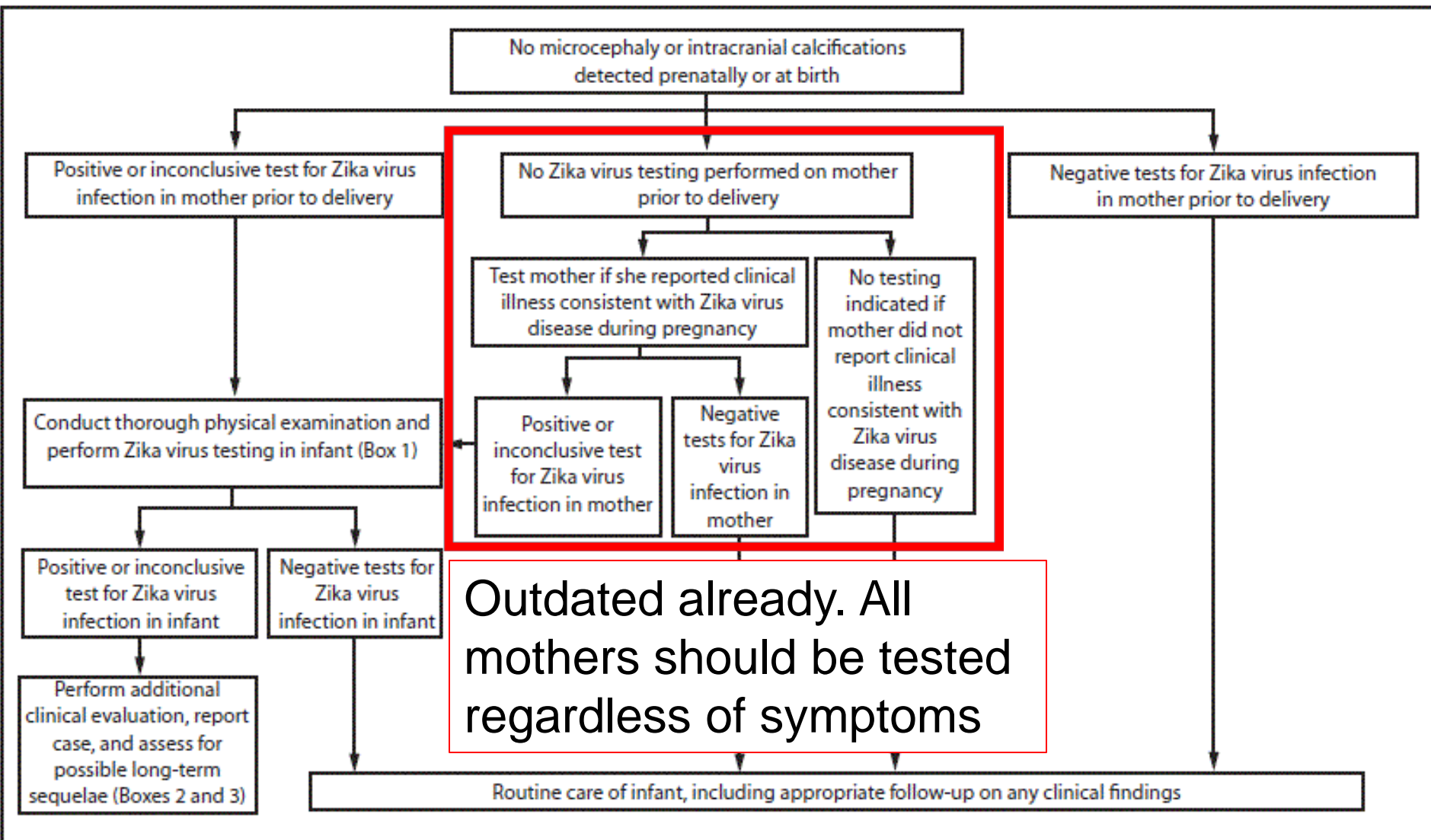
- Guidance for healthcare providers caring for infants born to mothers who traveled to, or resided, in Zika affected areas during pregnancy
  - Infants with microcephaly
  - Infants without microcephaly

- Guidelines can be found at:

<http://www.cdc.gov/mmwr/volumes/65/wr/mm6503e3.htm>



# Testing Infants Without Microcephaly



# 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**  
*Safe families, healthy lives.*

Dallas County Health and Human Services

### CONTACTS

Erikka 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**

DISPATCHES

Emerg Infect Dis 2011

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

Brian D. Foy, Kevin C. Kobylinski,  
Joy L. Chilson Foy, Bradley J. Blitvich,  
Amelia Travassos da Rosa, Andrew D. Haddow,  
Robert S. Lanciotti, and Robert B. Tesh

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.

# CDC Guideline Key Points (1)

- 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



# CDC Guideline Key Points (2)

- 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

# Questions?