



# The Evolving Buzz on Zika and Pregnancy: An Update for Clinicians

August 19, 2016



## Webinar Instructions:

1. Everyone will be muted on entry.
2. Questions can be typed in the Q&A Box and addressed at the end.
3. The meeting is being recorded and a link will be posted on the CMQCC and CDPH websites.



# The Evolving Buzz on Zika and Pregnancy: An Update for Clinicians

August 19, 2016

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**PublicHealth** 

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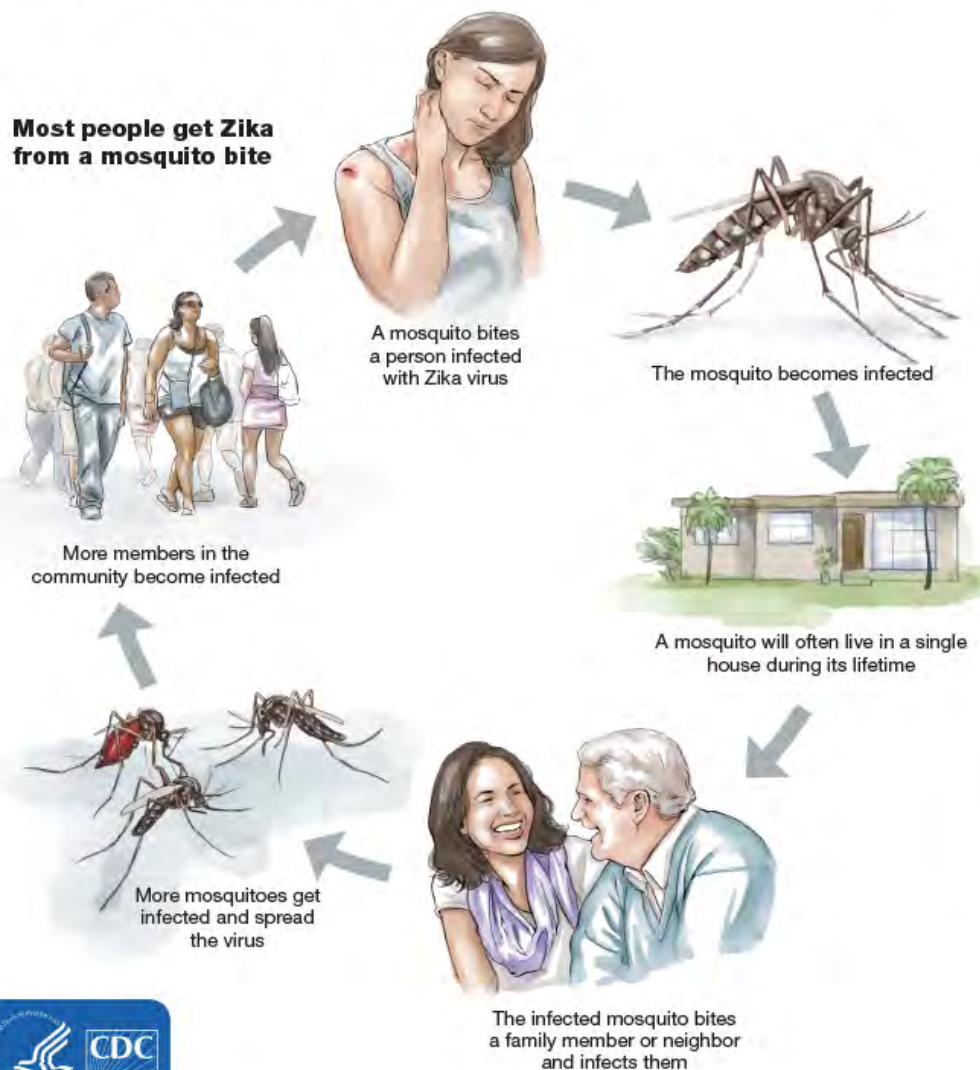
# Background

- Zika virus is transmitted to humans primarily through the bite of infected *Aedes* mosquito
  - Nearly all Zika outbreaks due to *aegypti* & *albopictus*
  - These are the same mosquitoes that transmit dengue and chikungunya
  - The mosquito vectors typically breed in domestic water-holding containers
  - *Aegypti* -- feeds primarily on humans, multiple humans in a single meal, lives close to humans , also daytime and nighttime feeders

# PROTECT YOUR FAMILY AND COMMUNITY:

## HOW ZIKA SPREADS

### Most people get Zika from a mosquito bite



### 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

## 37 STATES



## PUERTO RICO

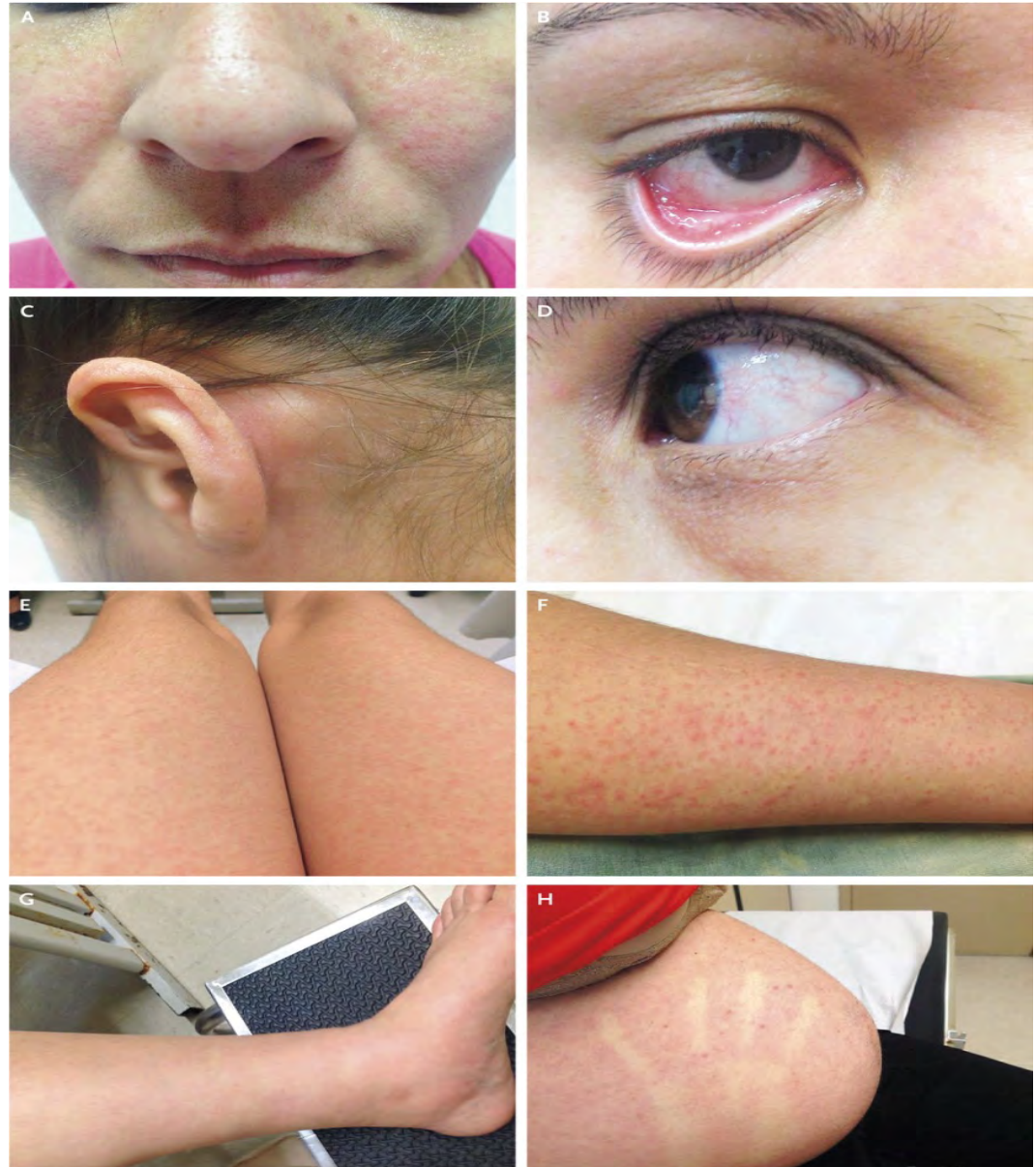
SOURCE: CENTERS FOR DISEASE CONTROL AND PREVENTION

# Zika – Disease and Risks

# Clinical Disease

- About 20% of people infected with Zika virus become symptomatic (*but % based on earlier outbreaks*)
- Among those with clinical illness
  - Symptoms mild, typically develop within 1 week from exposure, lasting several days to a week
  - Characteristic clinical findings: acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis.
  - Severe disease requiring hospitalization is uncommon and fatalities are rare.
- Guillain-Barré syndrome also has been reported at increased rates in patients following Zika infection
  - 50% increase in cases in Colombia since Oct 2015

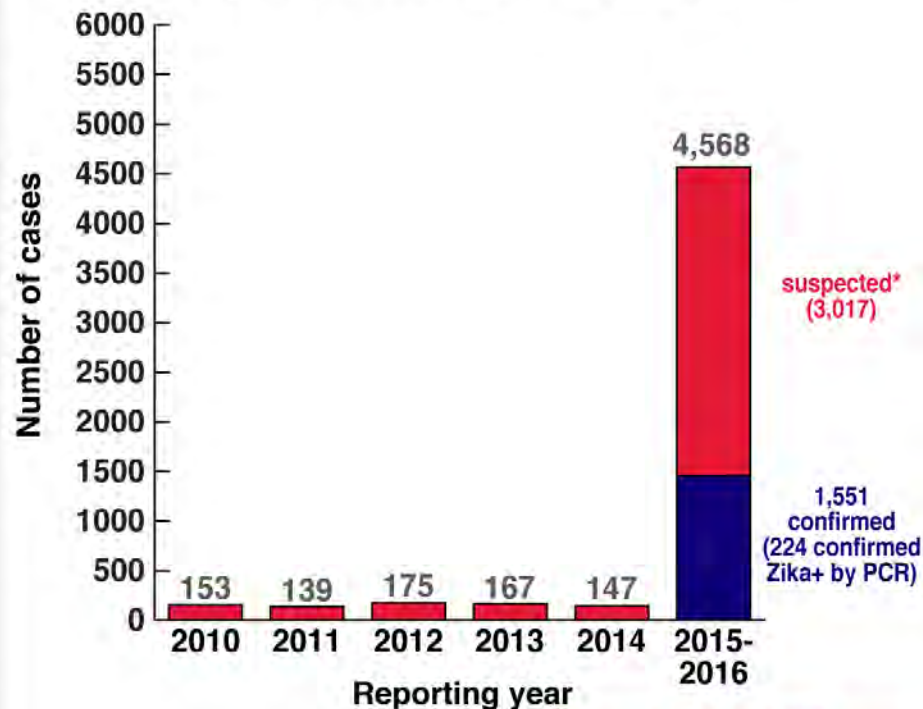
# Clinical Features of Zika Virus Infection in Pregnant Women.



# Brazil Zika Outbreak

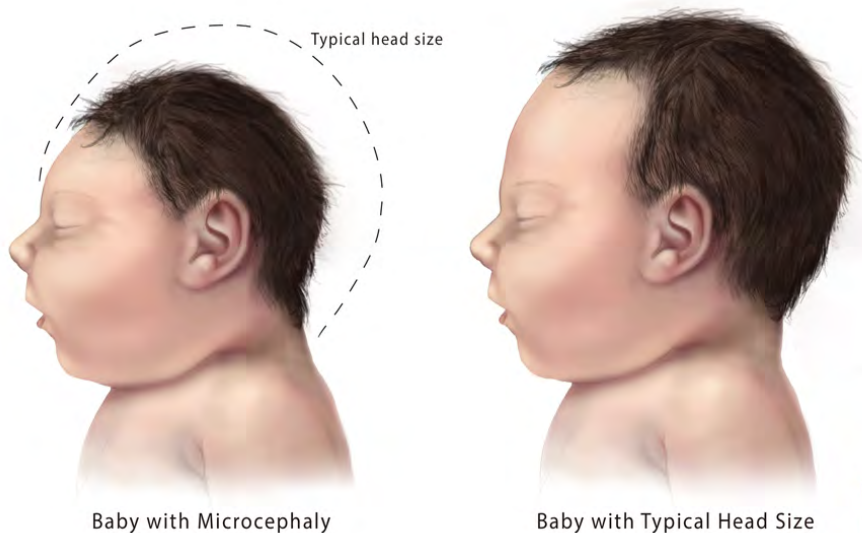
- May 2015: First infection in Brazil
- October 2015: increase in microcephaly

Microcephaly cases in Brazil 2010-14;  
suspected/confirmed cases 2015-2016



\*does not include 3,262 cases  
investigated and discarded

Source: Brazilian MOH; data as of 6/4/2016.



# Microcephaly: the *most apparent* marker?

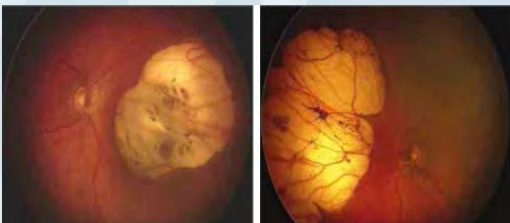
- Microcephaly is a very specific diagnosis, and typically unusual as an isolated finding: initially seen in **newborns**
  - On ultrasound, typically defined as HC < 3<sup>rd</sup> %ile for GA
- Microcephaly became an **early trigger** to search for Zika association, but spectrum of disease became apparent
  - Microcephaly can occur as a result of a **fetal brain disruption sequence**: this appears to be pathology of Zika infection
- Polynesia outbreak in 2014: higher rates of fetal CNS abnormalities in some women who tested positive for Zika, though none had had symptoms (*Euro Ctr Dis Prev Control 2015*)

# Fetal Brain Anomalies

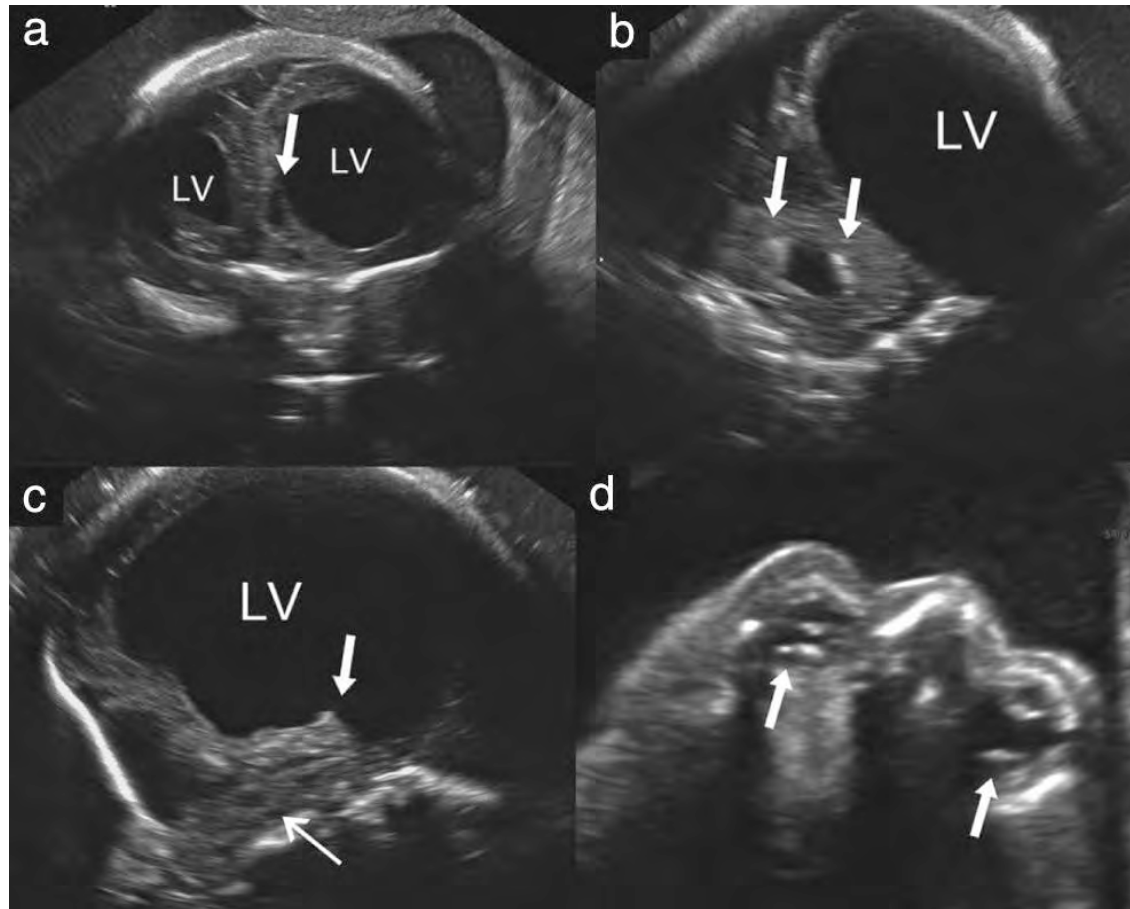
- Microcephaly
- Hydrocephalus/hydranencephaly
- Absent structures: (CC, pons, cerebellar vermis)
- Neuronal migration disorders (lissencephaly)
- Fetal brain disruption sequence
- Cerebral calcifications
- Brain asymmetry

# Zika Associated Pregnancy Outcomes

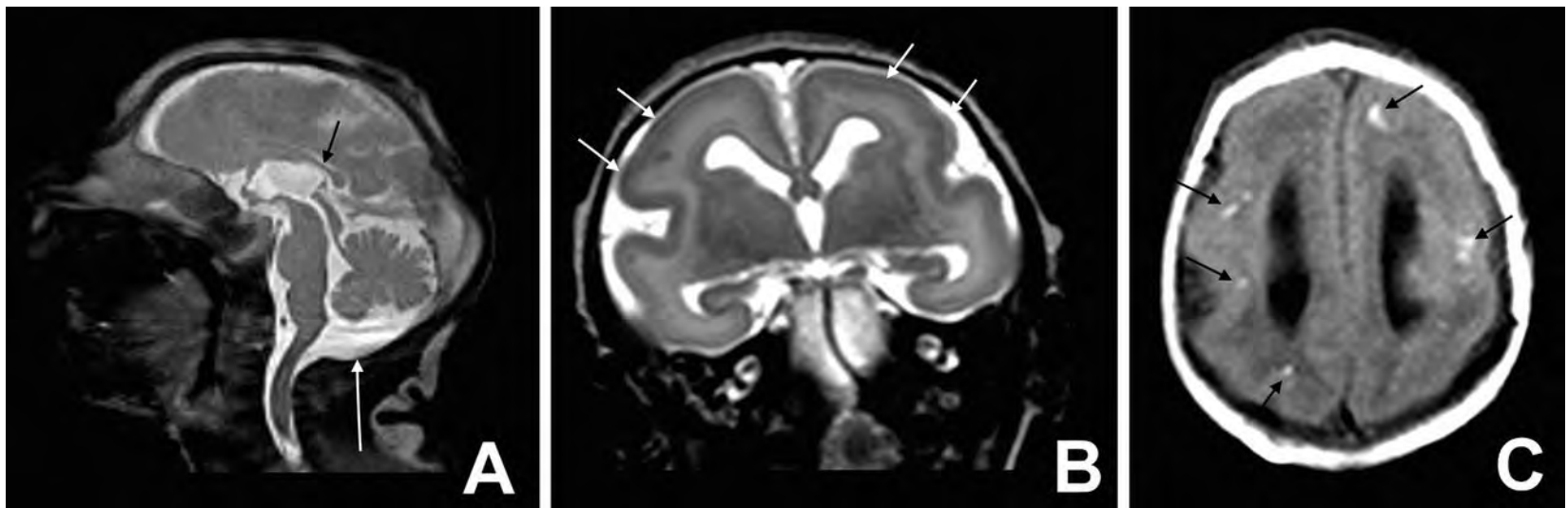
- Fetal loss/miscarriage, stillbirth
- Fetal growth abnormalities
- Fetal brain anomalies
  - Microcephaly
  - Ventriculomegaly
  - Intracranial calcifications
- Eye abnormalities
- Neurologic
  - Hypertonia
  - Arthrogryposis
  - Seizures
  - Neurobehavioral anomalies



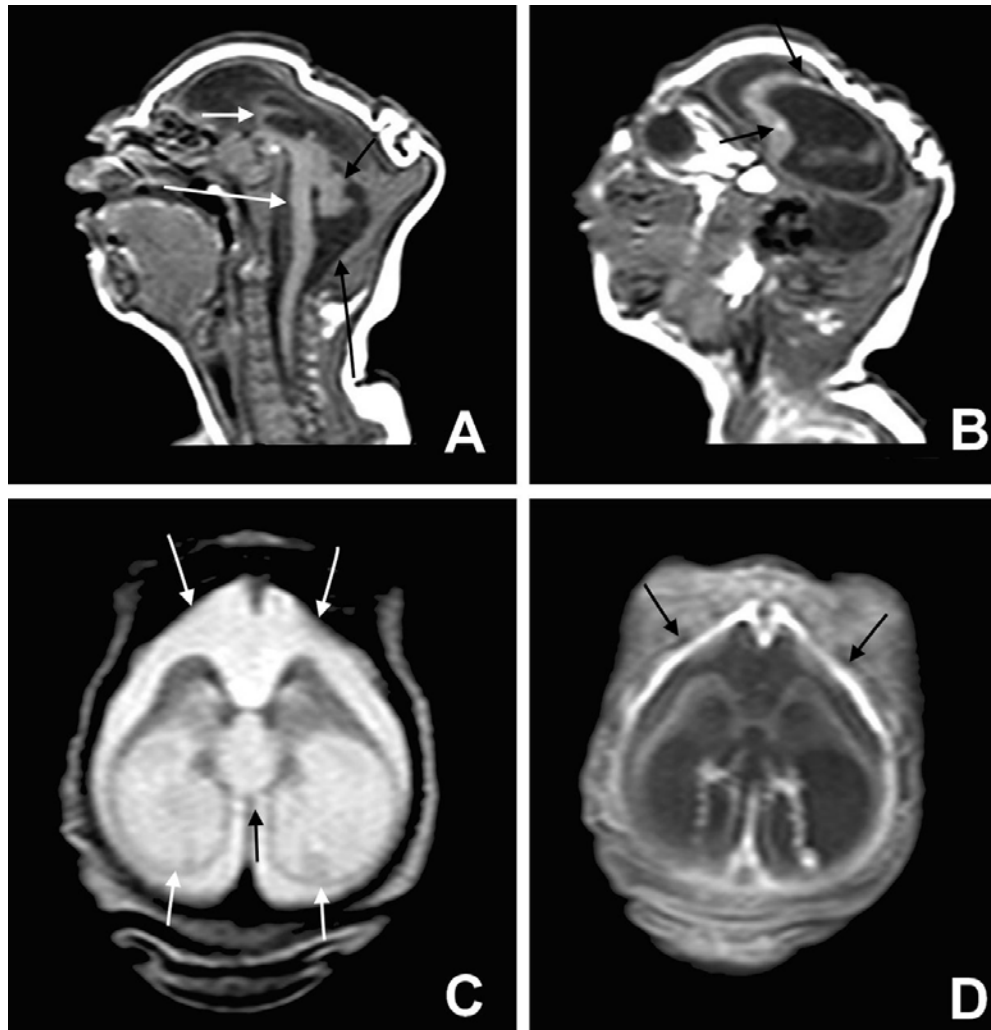
## Zika virus intrauterine infection causes fetal brain abnormality and microcephaly: tip of the iceberg?



**Fig 4 Microlissencephaly.**



**Fig 3 Severe microcephaly.**



Maria de Fatima Vasco Aragao et al. BMJ  
2016;353:bmj.i1901

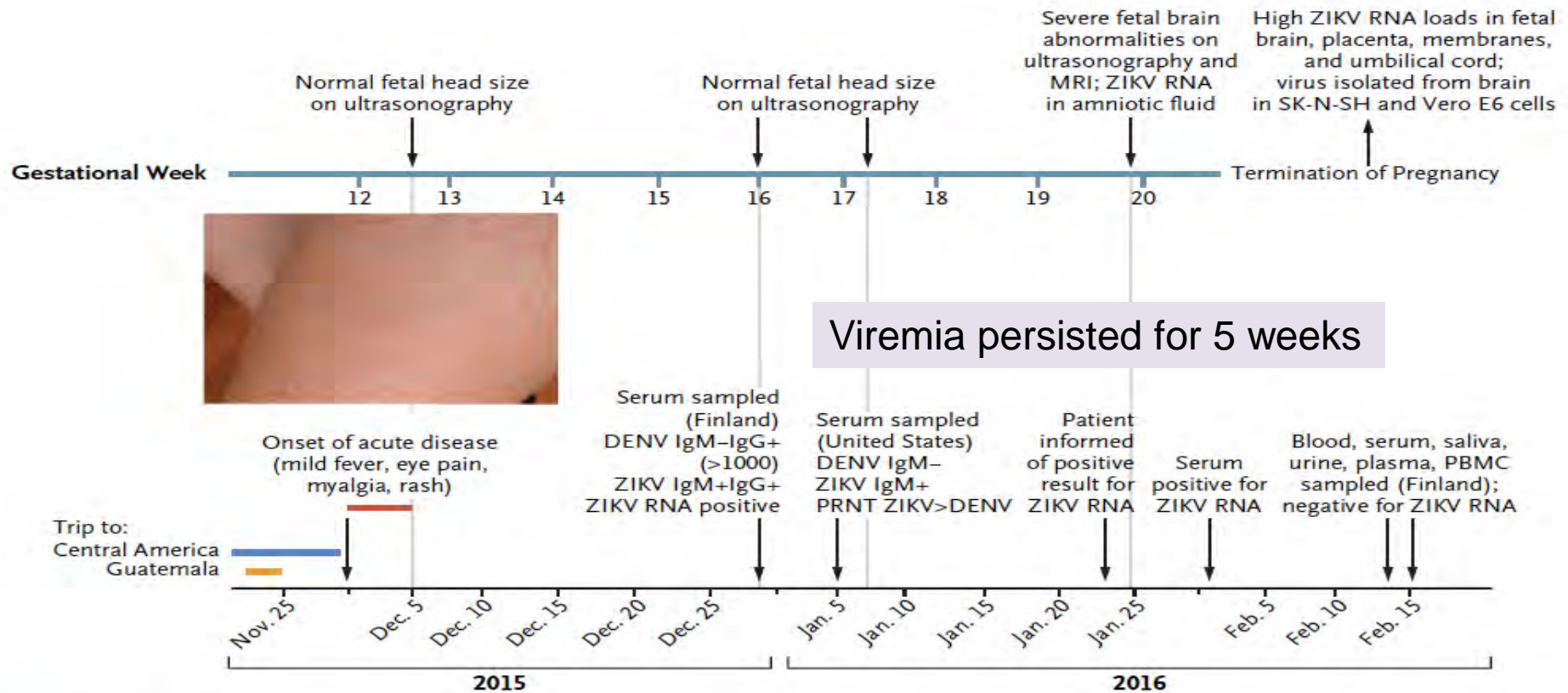
# Prospective NEJM series, Brazil: Background

- Brazil group had been conducting surveillance for dengue in population of Rio de Janeiro since 2007
  - In 2015, noted increase in dengue-like illness with rash, coinciding with surge of similar cases in NE Brazil → ID as Zika
- Study cohort: 88 symptomatic pregnant women (9/15-2/16)
  - 82% (72/88) tested positive for ZIKV (PCR) in blood, urine, or both
  - Serial U/S done: 20-30+ weeks
  - Timing of infection: 5-38 weeks of gestation

# Prospective NEJM series, Brazil: Results

- Of 72 women with PCR-positive test results
  - > 50% reported an ill family member; **21%: partner had been ill**
- 2 women miscarried in 1<sup>st</sup> Δ; 42 (60%) of others had u/s
  - 28 women declined u/s: either too far or fear of finding anomalies
- **Abnormal u/s results seen in 12/42 (29%) pts with Zika infx**
  - No abnormalities seen in any of the 16 Zika-negative women
  - IUGR in 5/12 fetuses (42%), with or without microcephaly
  - Cerebral calcifications in 4/12, other CNS anomalies in 2 fetuses
  - 2 IUFDs @ 30 and 38 wks: women infected at 25 and 32 wks

# Pregnancy: Prolonged Viremia



**Figure 1. Timeline of Symptoms and Radiographic and Laboratory Studies.**

This timeline highlights the symptoms of Zika virus (ZIKV) infection in the mother (bottom row) and the corresponding radiographic and laboratory findings in the fetus (top row). The inset photograph shows the mother's rash at the time of the onset of the acute illness. DENV denotes dengue virus, MRI magnetic resonance imaging, PBMC peripheral-blood mononuclear cells, and PRNT plaque-reduction neutralization test.

# Long Term Pregnancy Outcomes: Evolving

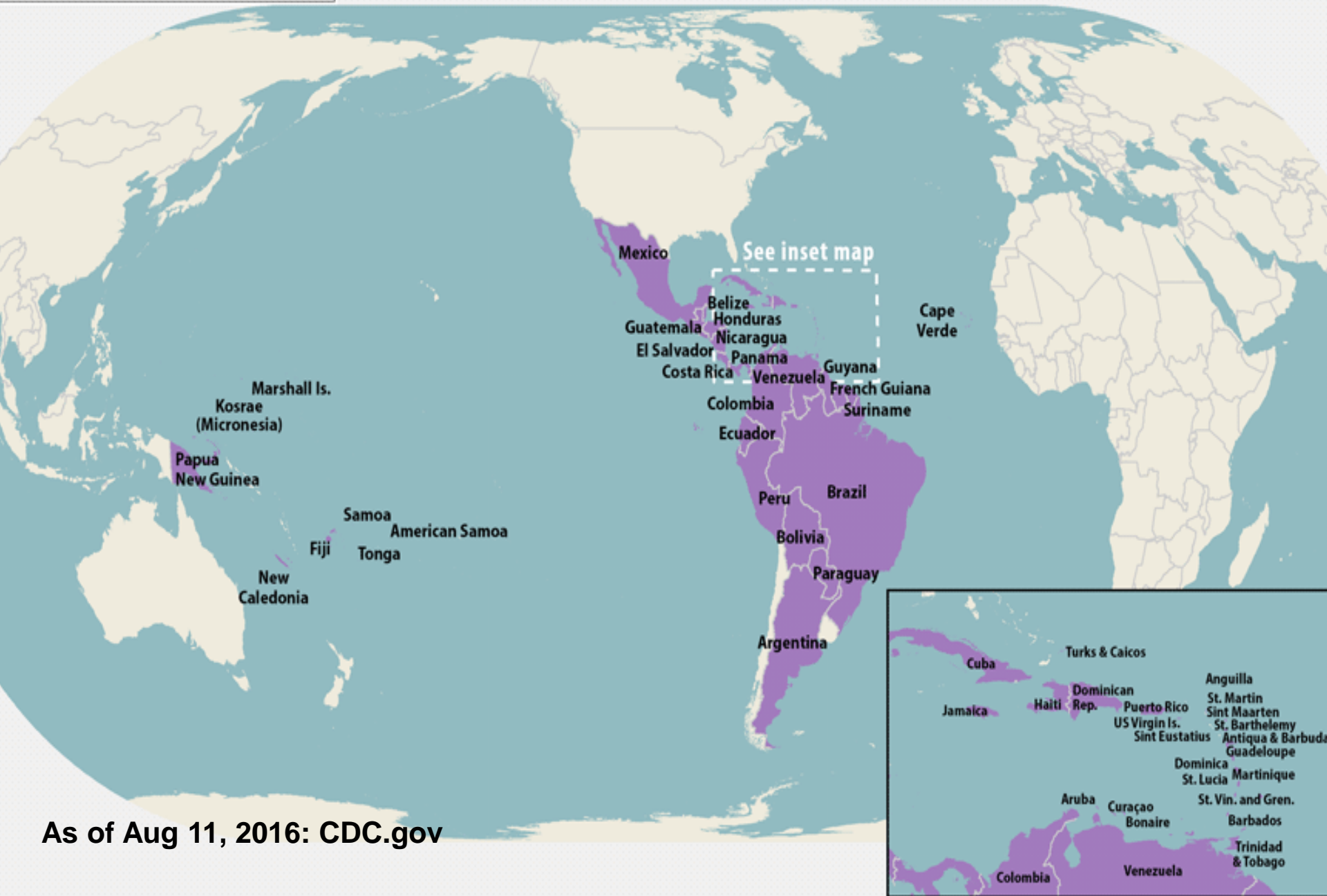
- Emerging reports and series of long-term functional motor and sensory abnormalities
  - van der Linden et al, *BMJ* 8/16: 7 infants with microcephaly and abnormal MRI: also with arthrogryposis: neurologic not muscular
  - Pestorius et al, CDC, 8/4/16: “late-onset microcephaly” in series from Brazil: normal head size at birth, abnormal by 6 months
- Anticipate a spectrum of outcomes?
  - Developmental delay
  - Intellectual impairments
  - Mental disorders – autism, schizophrenia, etc
  - Motor abnormalities

# Zika-Related Arthrogryposis



**Zika – Where is it  
and where is it not?**

Reported active transmission



As of Aug 11, 2016: CDC.gov

# Zika in the US

## (as of August 10, 2016)

### **US States and DC**

- Travel-associated Zika virus disease cases reported: 1955 (22 sexually transmitted)
  - 6 cases of Guillain-Barre syndrome
- Locally acquired vector-borne cases reported: 33\*
- No Zika-related hospitalizations or deaths among women
  - 1 recent Zika-attributable death in Utah (elderly traveler)

### **US Territories**

- Travel-associated cases reported: 31
- Locally acquired cases reported: 6587 (all but 112 in Puerto Rico)
  - 20 cases of Guillain-Barre syndrome

# Zika Pregnancy Statistics

(as of August 11, 2016)

## US States and DC

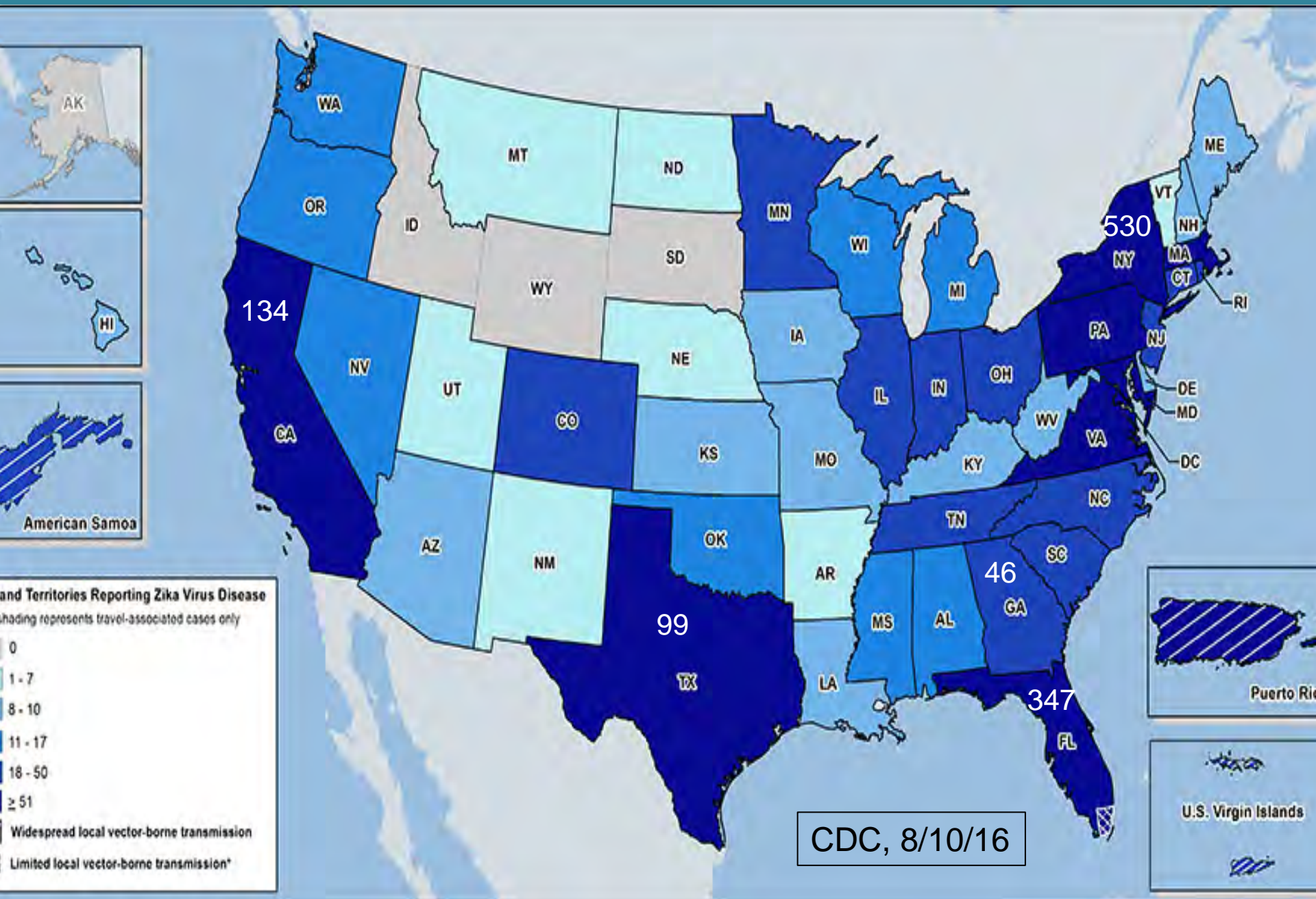
- 529 **pregnant travelers** with laboratory evidence of Zika virus—  
all imported/travel-related, **no native cases**
  - 16 reported liveborn infants and 5 fetal losses with Zika  
related birth defects

## US Territories

- 691 **pregnant** cases (mostly Puerto Rico)
  - 1 liveborn infant and 1 fetal loss with Zika related birth defects

## California (as of August 12, 2016)

- 24 **pregnant** cases
  - 2 liveborn infant and 0 fetal losses with Zika related birth  
defects



**Imported Zika Cases  
2015-2016**





Legend:

- No reported cases
- 1-10 reported cases
- 11-20 reported cases
- 20+ reported cases

N = 153 (as of 2016)

Map Data (Number of cases by state):

State	Number of Cases
Alabama	7
Arizona	1
Arkansas	0
California	12
Colorado	0
Connecticut	0
Delaware	0
Florida	28
Georgia	5
Hawaii	0
Idaho	0
Illinois	0
Indiana	0
Iowa	0
Kansas	0
Kentucky	0
Louisiana	0
Maine	0
Maryland	0
Massachusetts	0
Michigan	0
Minnesota	0
Mississippi	0
Missouri	0
Montana	0
Nebraska	0
Nevada	0
New Hampshire	0
New Jersey	0
New Mexico	0
New York	0
North Carolina	0
North Dakota	0
Ohio	0
Oklahoma	0
Oregon	0
Pennsylvania	0
Rhode Island	0
South Carolina	0
South Dakota	0
Tennessee	0
Texas	34
Utah	0
Vermont	0
Virginia	0
Washington	0
West Virginia	0
Wisconsin	0
Wyoming	0

 No reported cases  
 1-10 reported cases  
 11-20 reported cases  
 20+ reported cases



**CDPH Weekly Update on Number of Zika Virus Infections in California  
August 12, 2016**

The following table provides the number of travel-associated infections with Zika virus in California residents in 2015 and 2016. CDPH is following CDC testing guidelines. This table is updated every Friday. As of August 12, 2016, there have been 153 travel-associated Zika virus infections in California.

- Total infections: **153**
- Cumulative number of infections due to sexual transmission: **1**
- Cumulative number of infections in pregnant women: **24<sup>a</sup>**
  - Liveborn infants with birth defects: **2<sup>b</sup>**
  - Pregnancy losses with birth defects: **0<sup>c</sup>**

Zika virus infections in California, 2015-2016 <sup>d</sup> (as of August 12, 2016)		
County	Travel-associated <sup>e</sup>	Locally acquired <sup>f</sup>
Alameda	10	0
Contra Costa	7	0
Fresno	1	0
Kern	1	0
Lake	1	0
Los Angeles	34	0
Marin	1	0
Merced	3	0
Monterey	1	0
Napa	2	0
Orange	10	0
Riverside	5	0
Sacramento	2	0
San Bernardino	7	0
San Diego	28 <sup>g</sup>	0
San Francisco	12	0
San Joaquin	3	0
San Mateo	3	0
Santa Clara	11	0
Santa Cruz	1	0
Solano	1	0
Sonoma	2	0
Stanislaus	2	0
Tulare	2	0
Yolo	2	0
Yuba	1	0
<b>Total</b>	<b>153</b>	<b>0</b>

# Imported Zika Cases in California, 2015-2016

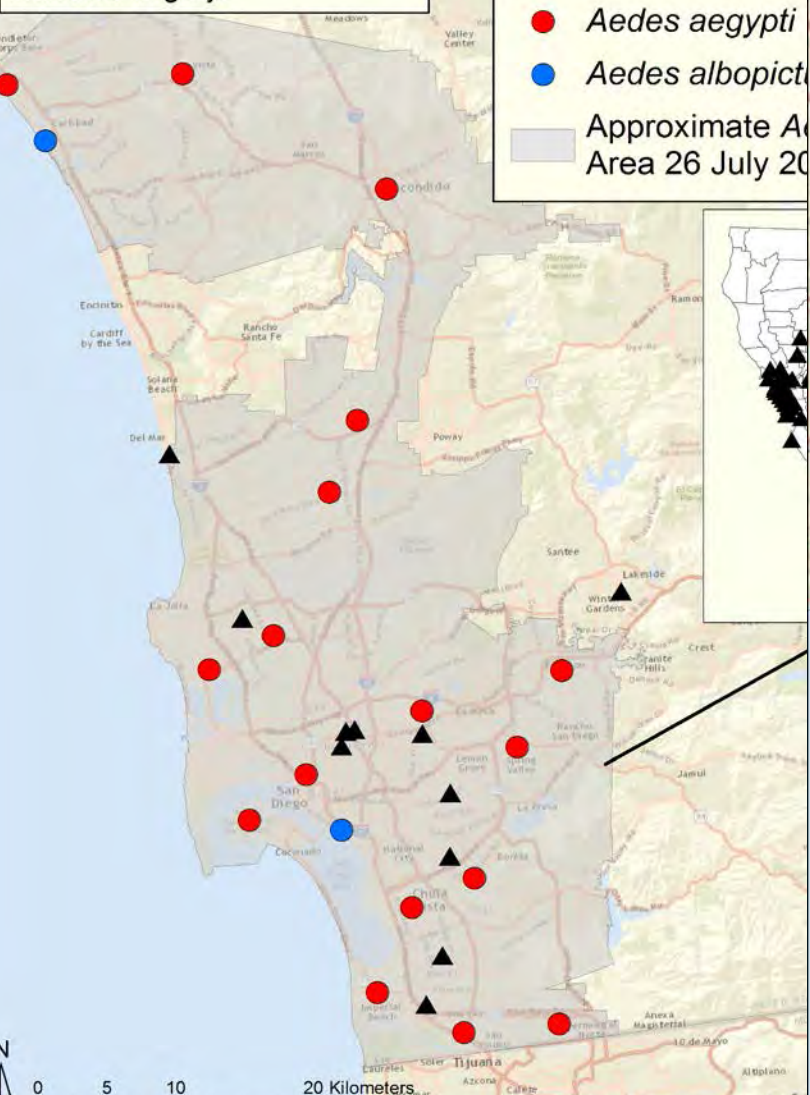
Country Traveled To	Number of Imported Cases in California
Mexico	36
El Salvador	22
Dominican Republic	15
Guatemala, Honduras	31
Puerto Rico	13
Jamaica, Nicaragua	27
Costa Rica	7
Venezuela	5
Brazil, Colombia	8
Haiti	2
American Samoa, Belize, French Polynesia, Kiribati, Saint Lucia, Trinidad	7

Note: Individuals may have traveled to more than one country.  
California Department of Public Health

## Travel-Associated Zika Cases and *Aedes* Detections in San Diego County\*

\* *Aedes* may not be found throughout the contiguous area indicated in gray.

- ▲ Zika Cases as of 26 July 2016
- *Aedes aegypti*
- *Aedes albopictus*
- Approximate *Aedes* Infestation Area as of 26 July 2016

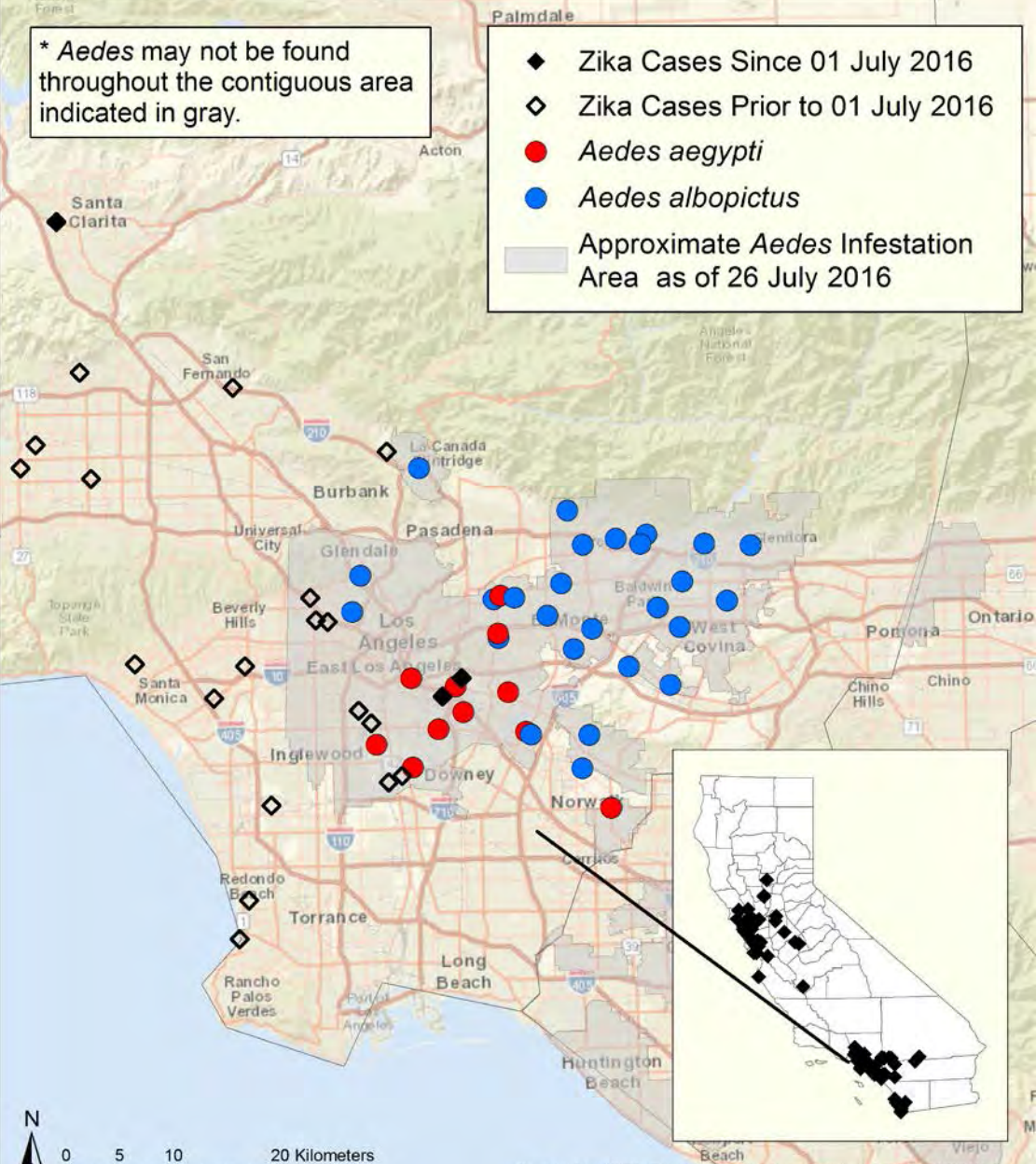


Sources: Esri, HERE, DeLorme, USGS, Intermap, increment P Corp., NRCAN, Esri Japan, METI, Esri China (Hong Kong), Esri (Thailand), Mapbox, Swg, and the GIS User Community

## Travel-Associated Zika Cases and *Aedes* Detections in Los Angeles County\*

\* *Aedes* may not be found throughout the contiguous area indicated in gray.

- ◆ Zika Cases Since 01 July 2016
- ◇ Zika Cases Prior to 01 July 2016
- *Aedes aegypti*
- *Aedes albopictus*
- Approximate *Aedes* Infestation Area as of 26 July 2016



Sources: Esri, HERE, DeLorme, USGS, Intermap, increment P Corp., NRCAN, Esri Japan, METI, Esri China (Hong Kong), Esri (Thailand), Mapbox, Swg, and the GIS User Community

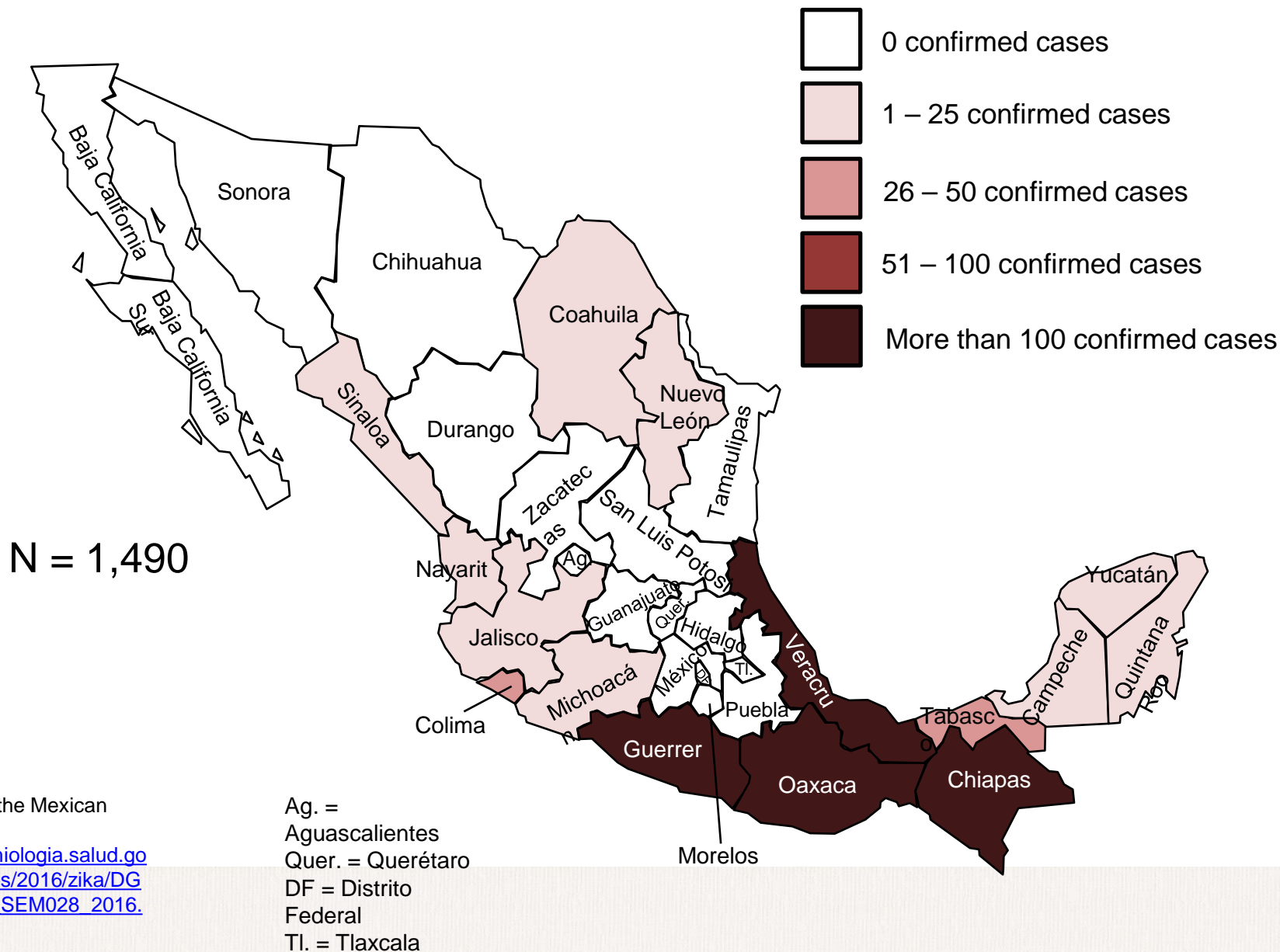
# Culex sp. mosquitoes as a Zika risk?

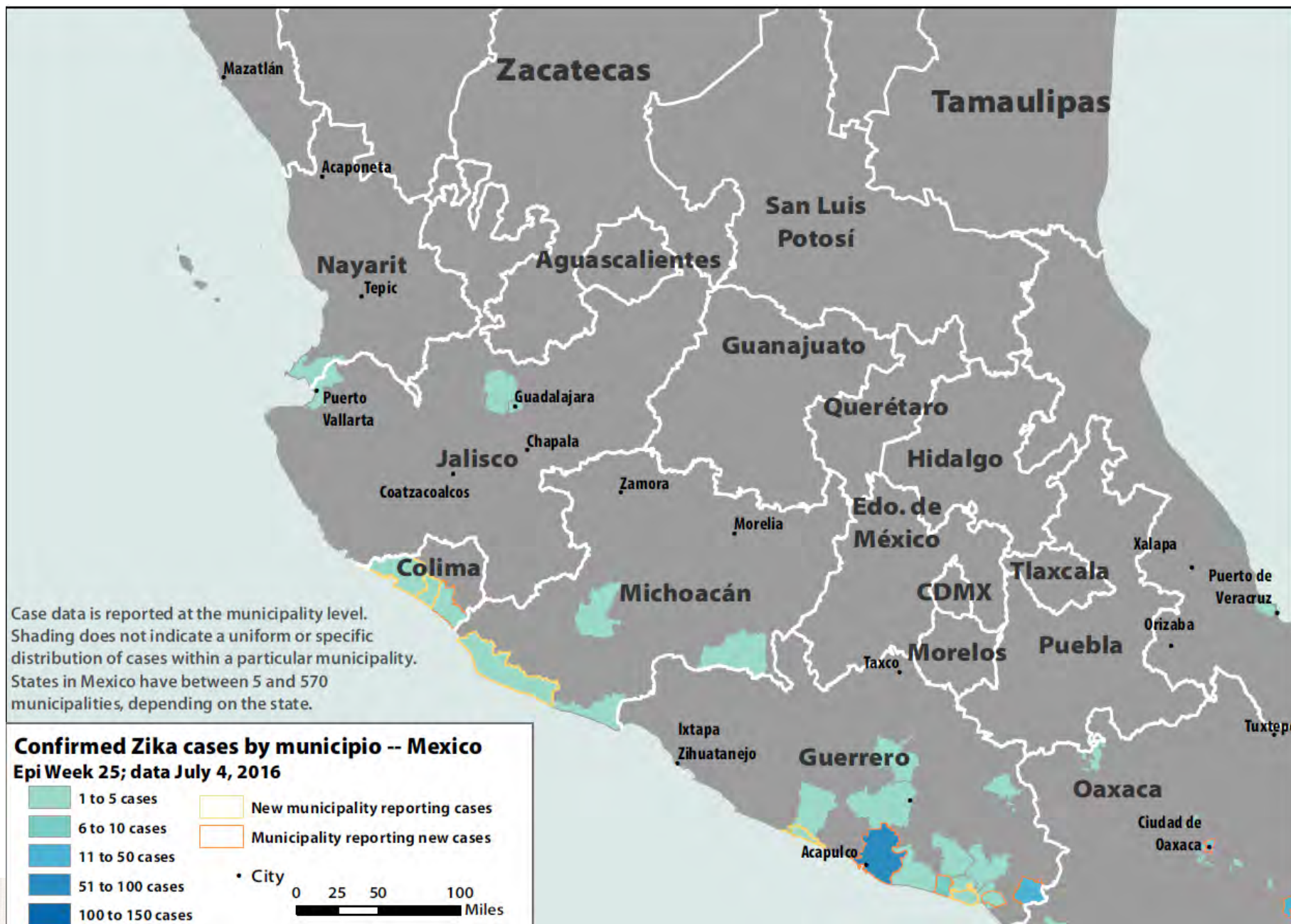
- Recent reports from Brazil suggested *Culex* (Southern house) mosquito as source of Zika transmission (also West Nile virus)
- Latest research from UT Galveston (Aug 4): *Culex* NOT an efficient vector for Zika transmission and confirmed *Aedes aegypti* to be
  - Researchers captured both species in wild and fed infected blood, measured Zika in bodies and saliva of mosquitoes
  - Released data ahead of upcoming publication as public health issue



# Confirmed Zika Cases in Mexico by State

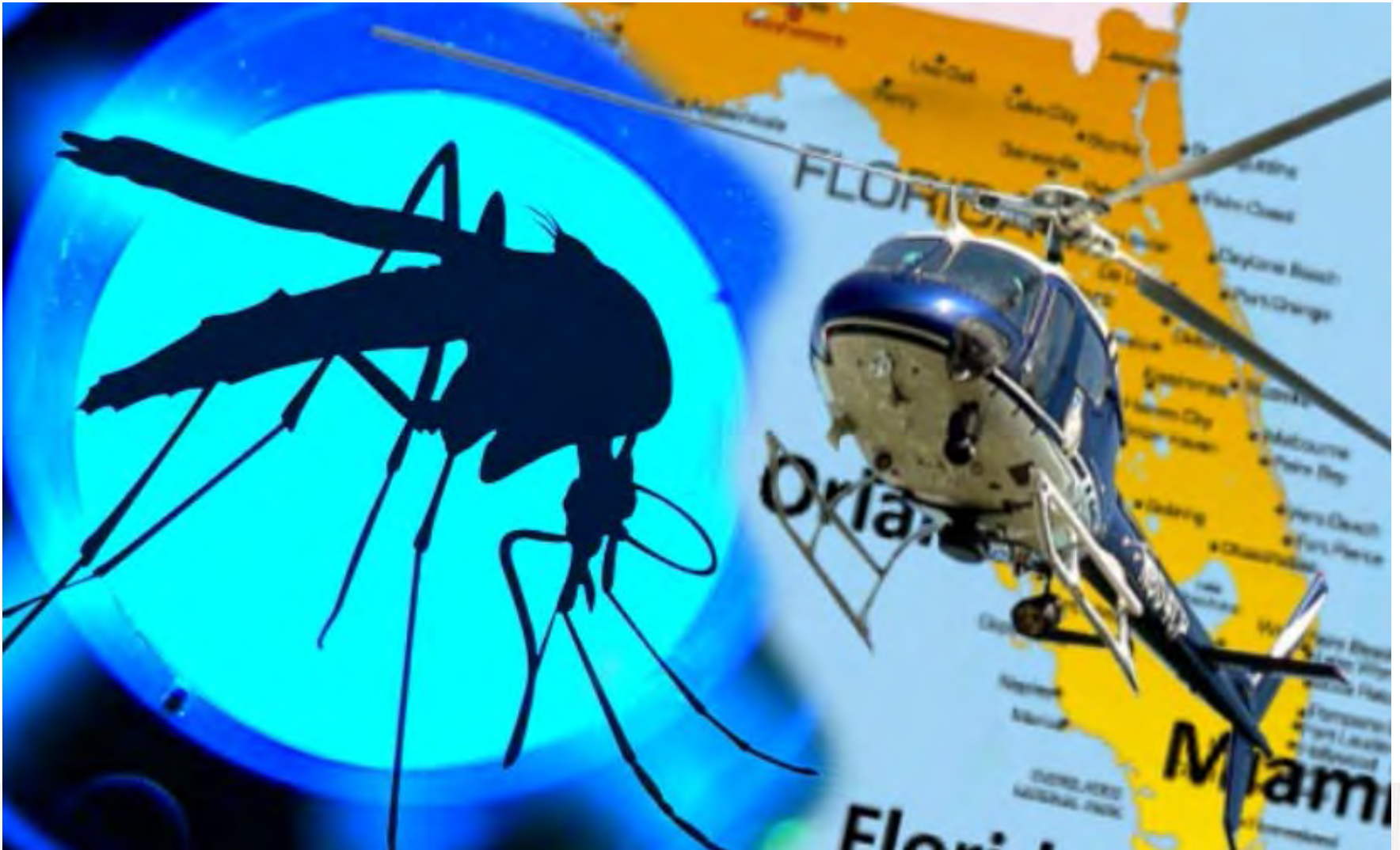
## January 1, 2016 – August 8, 2016







# Local Zika Transmission in Florida





### *It's a New Day in Public Health.*

The Florida Department of Health works to protect, promote & improve the health of all people in Florida through integrated state, county, & community efforts.

[Programs & Services](#)[Licensing & Regulation](#)[Statistics & Data](#)[Certificates](#)

## Department of Health Responds to Local Zika Cases

By Florida Department of Health, Office of Communications

July 29, 2016

## DEPARTMENT OF HEALTH RESPONDS TO LOCAL ZIKA CASES

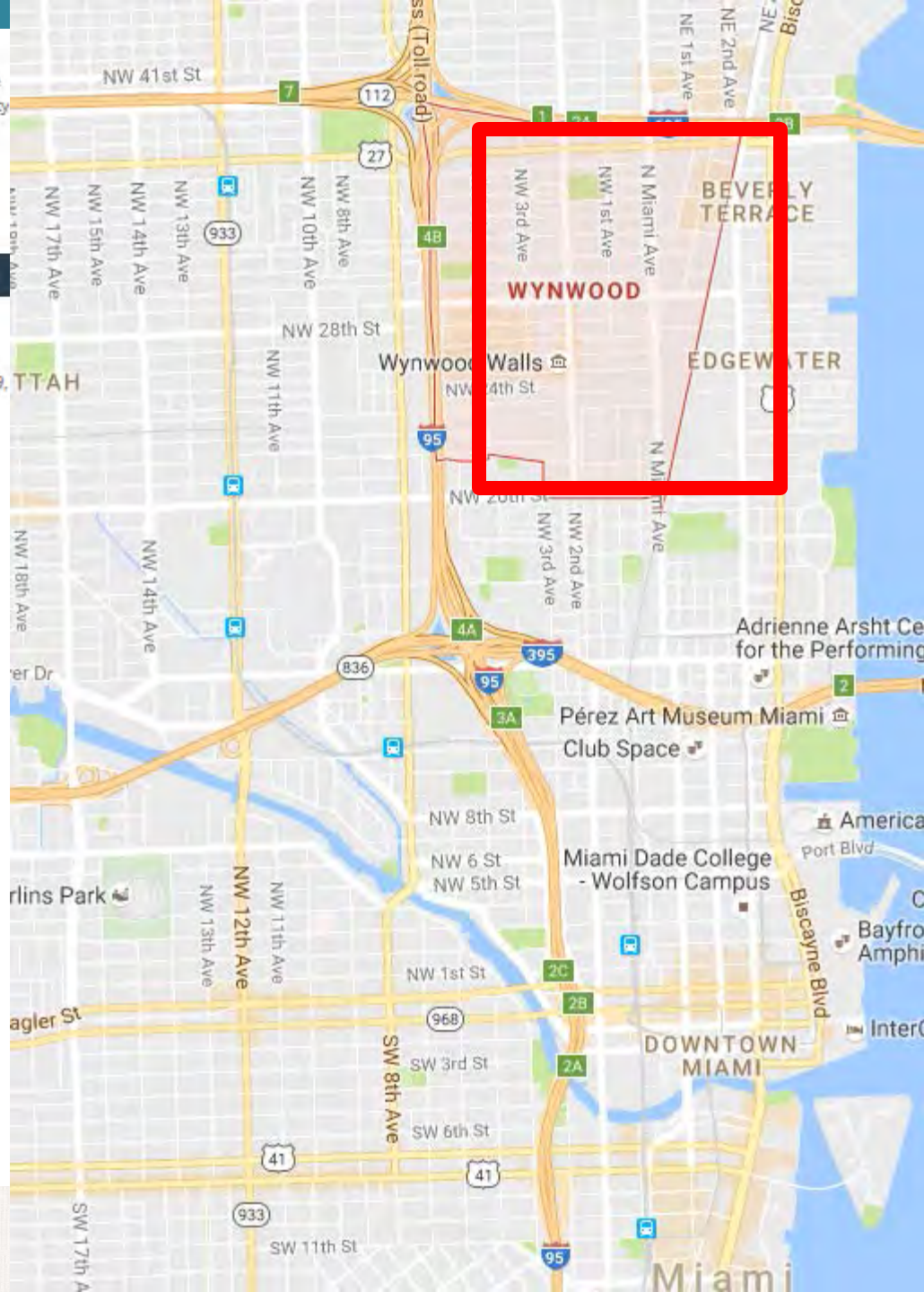
### Contact:

Communications Office

[NewsMedia@flhealth.gov](mailto:NewsMedia@flhealth.gov)

(850) 245-4111

**Tallahassee, Fla.**—The Florida Department of Health has gathered enough information as part of its ongoing investigation into non-travel related cases of Zika in Miami-Dade and Broward counties to conclude that a high likelihood exists that four cases are the result of local transmission. At this time, the department believes that active transmission of the Zika virus are occurring in one small area in Miami-Dade County, just north of downtown. The exact location is within the boundaries of the following area: NW 5th Avenue to the west, US 1 to the east, NW/NE 38th Street to the north and NW/NE 20th Street to the south. This area is about 1 square mile and a map is below to detail the area. While no mosquitoes trapped tested positive for the Zika virus, the department believes these cases were likely transmitted through infected mosquitoes in this area.



# Local Zika Transmission in Florida

## (August 17, 2016)

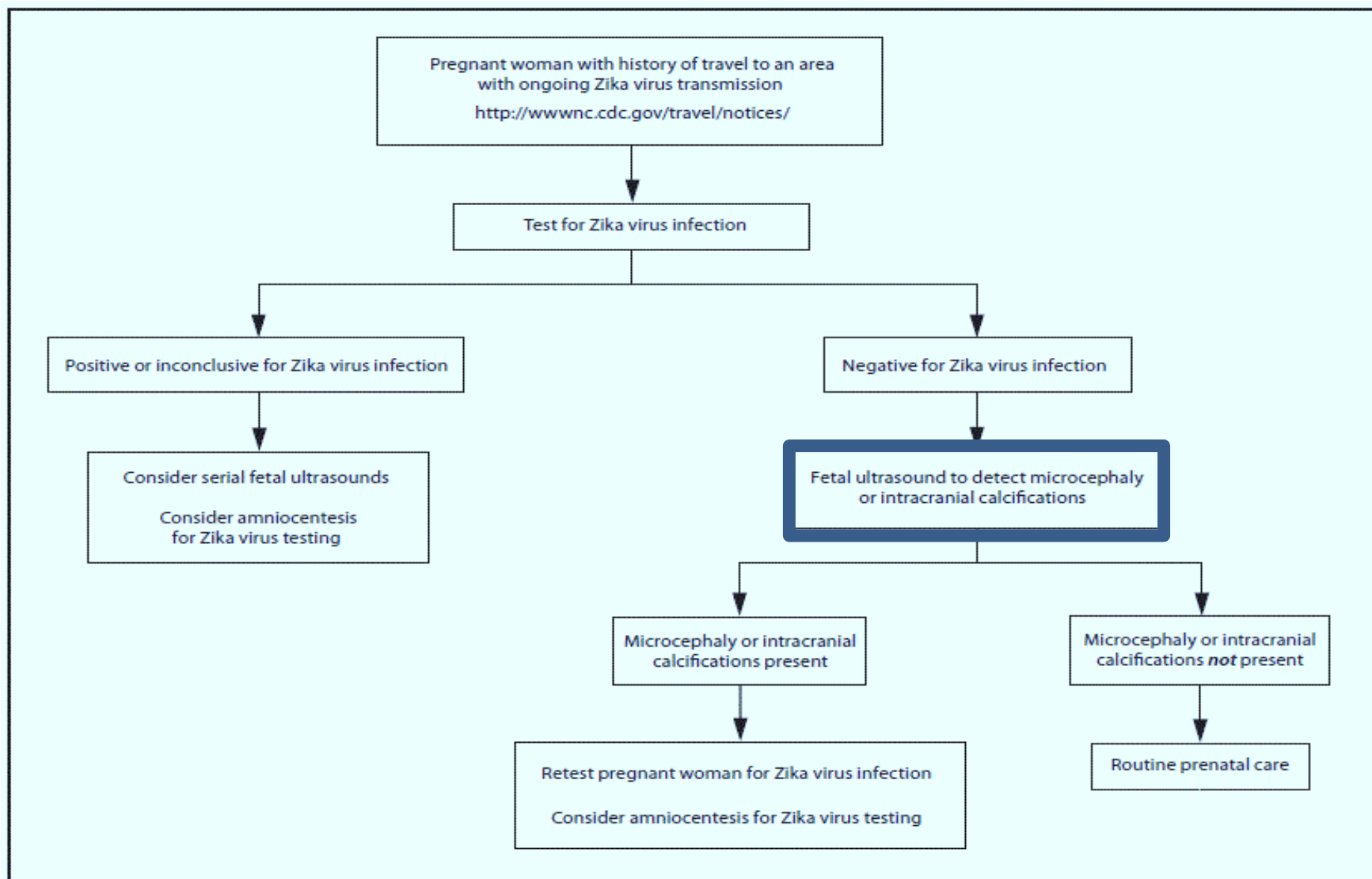
- 33 cases of locally-acquired Zika infection
  - 4 original cases (Miami-Dade and Broward)
    - 23 additional cases
  - 5 cases (Miami-Dade)
  - 1 case (Palm Beach)
- Florida DOH believes transmission still limited to 1-square mile in Wynwood
- Door to door outreach and sampling ongoing
- Mosquito abatement and reduction ongoing

# Zika – Education and Testing

# What do we tell our pregnant patients?

- How much fetal risk with confirmed maternal infection?
  - Based on current data, **range may be as high as 29%**
  - Rates are derived from methodologically diverse studies
- Despite earlier reports, recent data suggest later GA at infection does not exclude potential adverse impact
- Pregnant women **should not travel** to areas with active Zika transmission
- If in an area with transmission, protection and prevention strategies are important – **and repellent for 3 weeks after return from these areas**
  - DEET, picaridin most effective --- both fine for use during pregnancy

# Testing algorithm for a pregnant woman possible Zika exposure



## Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States, July 2016

Titilope Oduyebo, MD<sup>1</sup>; Iroquo Igbinosa, MD<sup>2</sup>; Emily E. Petersen, MD<sup>1</sup>; Kara N.D. Polen, MPH<sup>2</sup>; Satish K. Pillai, MD<sup>3</sup>; Elizabeth C. Ailes, PhD<sup>2</sup>; Julie M. Villanueva, PhD<sup>3</sup>; Kim Newsome, MPH<sup>2</sup>; Marc Fischer, MD<sup>4</sup>; Priya M. Gupta, MPH<sup>5</sup>; Ann M. Powers, PhD<sup>4</sup>; Margaret Lampe, MPH<sup>6</sup>; Susan Hills, MBBS<sup>4</sup>; Kathryn E. Arnold, MD<sup>2</sup>; Laura E. Rose, MTS<sup>3</sup>; Carrie K. Shapiro-Mendoza, PhD<sup>1</sup>; Charles B. Beard, PhD<sup>4</sup>; Jorge L. Muñoz, PhD<sup>4</sup>; Carol Y. Rao, ScD<sup>7</sup>; Dana Meaney-Delman, MD<sup>8</sup>; Denise J. Jamieson, MD<sup>1</sup>; Margaret A. Honein, PhD<sup>2</sup>

*On July 25, 2016, this report was posted as an MMWR Early Release on the MMWR website (<http://www.cdc.gov/mmwr>).*

CDC has updated its interim guidance for U.S. health care providers caring for pregnant women with possible Zika virus exposure, to include the emerging data indicating that Zika virus RNA can be detected for prolonged periods in some pregnant women. To increase the proportion of pregnant women with

exposure. For asymptomatic pregnant women who live in areas without active Zika virus transmission and who are evaluated <2 weeks after last possible exposure, rRT-PCR testing should be performed. If the rRT-PCR result is negative, a Zika virus IgM antibody test should be performed 2–12 weeks after the exposure. Asymptomatic pregnant women who do not live in an area with active Zika virus transmission, who are first evalu-



The American College of  
Obstetricians and Gynecologists  
WOMEN'S HEALTH CARE PHYSICIANS



Society for  
Maternal-Fetal  
Medicine

## Practice Advisory on Zika Virus

### In the Zika Practice Advisory

- [Background](#) (Updated: August 3, 2016)
- [Travel Restrictions](#) (Updated: August 3, 2016)
- [Prevention](#) (Updated: August 3, 2016)
- [Reproductive Counseling](#) (Updated: August 3, 2016)
- [Testing, Evaluation, and Management of Pregnant and Postpartum Women](#) (Updated: August 3, 2016)
- [Reporting and the U.S. Pregnancy Registry](#) (Updated: August 3, 2016)
- [Infection Control Considerations](#) (Updated: August 3, 2016)
- [Zika and Blood Transfusion](#) (Updated: August 3, 2016)
- [References](#) (Updated: August 3, 2016)

## Zika Testing – What's new (this time)?

- Expanded testing for pregnant women
  - Attempt to increase the proportion of pregnant women with Zika infection who receive definitive dx
  - Ask about Zika exposure (travel, sex) at **each prenatal visit**
    - Only test pregnant women with (+) exposure history
  - Recognizing risks of sexual transmission regardless of whether sexual partner who traveled to risk area had symptoms or not → also ask partner travel hx
  - Recognizing longer time for viral RNA detection in some pregnant women compared to nonpregnant adults
- Still no testing for asymptomatic partner of a pregnant woman → *still emphasize condoms thru pregnancy*

# Zika Testing – What Testing should be done?

- PCR done for all pts with symptoms within **2 weeks after onset of symptoms**: test blood AND urine
- PCR for asymptomatic: only in pregnant women with exposure in past 2 weeks (including sex w/ male **or** female partner who traveled)
  - If PCR on pregnant woman negative, still do antibody testing **2-12 weeks after exposure**
- All other pregnant patients with exposure (including sexual contact with traveler): testing for **Zika-specific IgM antibodies**
  - Typically develop toward the end of the first week of illness
  - **Testing in asymptomatic patients no earlier than 2 weeks after exposure (no later than 12 weeks) : TAT 2-3 weeks**
  - If Ab (+), then further testing done to confirm

# Should I request a test for Zika virus from my doctor?

Did you or your sexual partner travel from one of the countries or territories affected by Zika virus within the past two weeks?

**NO**

**YES**

Are you pregnant?

**NO**

**YES**

*You don't need a test.*

Did you or your partner experience any of the following symptoms during your travels or within two weeks of travel?

*Fever, rash, joint pain or conjunctivitis*

**NO**

**YES**

*Go to your doctor, who will determine, based on your travel dates, activities and symptoms, whether or not to request a Zika virus test. It could also be malaria, Chikungunya virus or other diseases, so medical attention is necessary no matter what it turns out to be.*

*Pregnant women can request a Zika diagnostic test anytime from two to 12 weeks after they return from a Zika virus-affected area. They should request a test immediately if they experience symptoms like fever, rash, joint pain or conjunctivitis.*

New (July 25)

*Pregnant women get PCR test if travel or other exposure within 2 weeks, even if no symptoms (including sex with male partner who traveled), then antibody test if PCR negative*

# Zika Testing – How?

- Emergency-approved commercially available test for PCR has a very specific role in new guidelines, especially for pregnant women
  - Cost and collection issues
  - **PCR now a test for pregnant women w/o symptoms but with exposure within 2 weeks**
- One company recently approved for CDC MAC-ELISA IgM testing: advertised TAT 5-7 days
  - Again, collection protocol needs to be followed
- Clinicians should still be aware of current guidelines for testing
  - Take a travel history of pt and partner
  - Be aware of current travel advisories ([cdc.gov](https://www.cdc.gov))

# Sexual Transmission: What We Don't Know

- For how long after the infection semen/vaginal fluids can infect a sexual partner
  - *Lancet* 6/7/16: transmission through semen 34-41 d after infection
  - *Lancet* 8/2016: Zika RNA found in semen after 90 days
  - *Eurosurveillance* 8/11/16: RNA (+) in urine up to 91 days and in semen 134 days after sx
- If Zika can be transmitted through saliva or other bodily fluids
- Transmission risk/duration after ***asymptomatic*** infection

# Sexual Partner concerns/guidelines

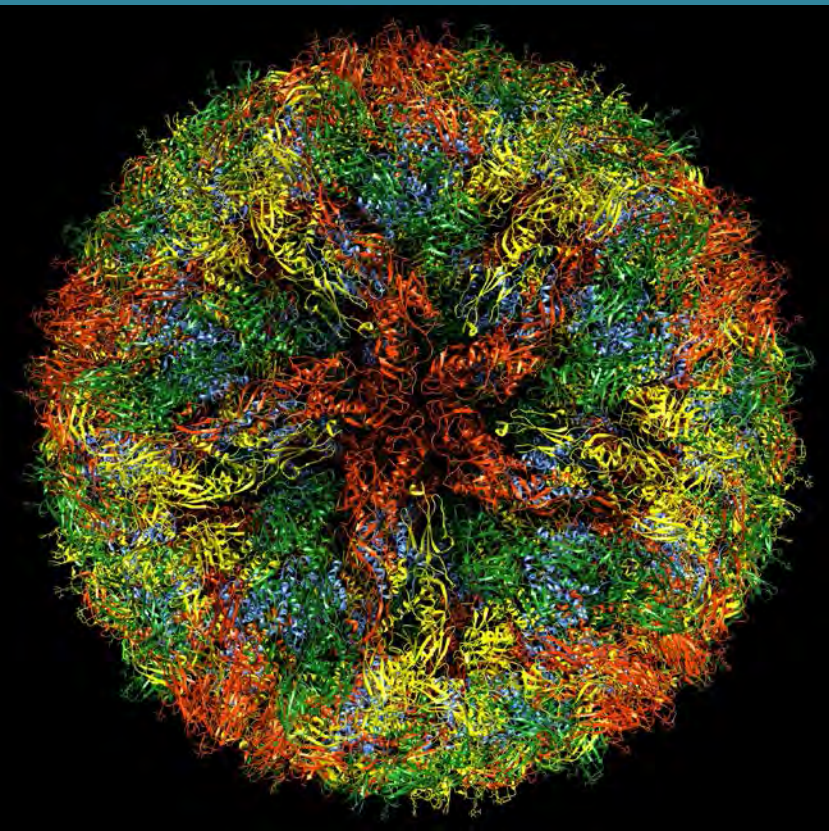
- Sexual transmission of Zika virus can occur
  - Male/female, female/male, male/male all reported
- Pregnant women whose male partners have or are at risk for Zika virus infection should consider using condoms or abstaining from sexual intercourse – ***duration of pregnancy***

## Suggested timeframe to wait before trying to get pregnant

Possible exposure via recent travel or sex without a condom with a man infected with Zika		
	Women	Men
<b>Zika symptoms</b>	Wait at least 8 weeks after symptoms start	Wait at least 6 months after symptoms start
<b>No Zika symptoms</b>	Wait at least 8 weeks after exposure	Wait at least 8 weeks after exposure. Talk with your healthcare provider
People living in areas with Zika		
	Women	Men
<b>Zika symptoms</b>	Wait at least 8 weeks after symptoms start	Wait at least 6 months after symptoms start
<b>No Zika symptoms</b>	Talk with doctor or healthcare provider	Talk with doctor or healthcare provider

# Zika's Additional Impact on OBGYN Care

- Tissue/organ donation – including egg/sperm donors
  - Donors are ineligible for 6 months if dx'd with ZKVD, in an area with active transmission, or had sex with a male partner with either of those risks
  - Also applies to umbilical cord blood and placenta
  - *FDA 3/1/16, affirmed by ASRM 3/4/16*
- Blood donation
  - Major impact on blood bank capabilities: for US, greatest impact in Puerto Rico (*also Miami*) -- no reported cases via transfusion, but local blood collections stopped 3/1 pending PCR
  - Investigational use of Zika PCR for PRBCs/WB (Apr 4)
  - FDA statement (2/16/16): 4 week waiting period for potential donors -- after illness, travel, or sexual contact



# Zika in Pregnancy: Evaluating the Impact on the Fetus and Neonate

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Mother with laboratory evidence of Zika virus infection during pregnancy

Perform a comprehensive PE, head U/S, hearing test, and Zika testing (Box 1)

Russell K, et al. Update: Interim Guidance for the Evaluation and Management of Infants with Possible Congenital Zika Virus Infection — United States, August 2016. MMWR. ePub: 19 August 2016.

# Testing at Delivery: Box 1

## **For possible congenital Zika virus infection**

- Test infant serum for Zika virus RNA, Zika virus immunoglobulin M (IgM) and neutralizing antibodies, and dengue virus IgM and neutralizing antibodies. The initial sample should be collected either from the umbilical cord or directly from the infant within 2 days of birth, if possible.
- If cerebrospinal fluid is obtained for other studies, test for Zika virus RNA, Zika virus IgM and neutralizing antibodies, and dengue virus IgM and neutralizing antibodies.
- Consider histopathologic evaluation of the placenta and umbilical cord with Zika virus immunohistochemical staining on fixed tissue and Zika virus reverse transcription-polymerase chain reaction (RT-PCR) on fixed and frozen tissue.
- If not already performed during pregnancy, test mother's serum for Zika virus IgM and neutralizing antibodies, and IgM and neutralizing antibodies for other potentially cross-reacting viruses as appropriate.

\*Indications for testing for congenital infection include 1) an infant with microcephaly or intracranial calcifications born to a woman who traveled to or resided in an area with Zika virus transmission while she was pregnant or who had unprotected sex during her pregnancy with a man who experienced symptoms of acute Zika virus infection within 2 weeks of returning to an area with Zika virus transmission, or 2) an infant born to a mother with a positive or inconclusive test result for Zika virus infection.

**Table 1: Specimen Collection and Storage of specimens for Zika virus testing in infants (updated 2/26/16)**

Specimen	When to Collect	Preferred Amount	Container	Storage and Shipment Conditions	Tested at CDC	Tested at VRDL
Serum (infant)†	<2 days post onset	≥2 ml (one tube preferred)	red or tiger top tube	cold	serology, PCR	serology, PCR
Serum (mother)	at time of collection of infant serum	≥2 ml (one tube preferred)	red or tiger top tube	cold	serology, PCR	serology, PCR
CSF	if collected for other studies	≥1 ml	sterile cryovial	cold	serology, PCR	N/A
Amniotic Fluid	when available	≥1 ml	sterile cryovial	frozen	PCR	N/A
Cord Blood	when available	0.5-1 ml	sterile cryovial	cold or frozen	PCR	serology, PCR
Placental/Fetal Tissue§	when available	0.5-1.0 cm	sterile container	both a.) cold formalin fixed and b.) frozen tissues	HP, IHC, PCR	N/A

† Infant serum or cord blood are acceptable specimens for serological and PCR testing.

§ For additional information on collecting placental and fetal or infant tissues, see <http://www.cdc.gov/zika/hc-providers/tissue-collection-submission.html>

# Evaluation for all infants with possible congenital Zika virus infection

## ○ Physical Examination

- Comprehensive physical examination, including careful measurement of occipitofrontal circumference, length, weight, and assessment of gestational age.
- Evaluation for neurologic abnormalities, dysmorphic features, splenomegaly, hepatomegaly, and rash or other skin lesions.

## ○ Additional Clinical Evaluation

- Cranial ultrasound
- Evaluation of hearing by evoked otoacoustic emissions testing or auditory brainstem response testing, either before discharge from the hospital or within 1 month after birth.
- Ophthalmologic evaluation, including examination of the retina, either before discharge from the hospital or within 1 month after birth.
- Other evaluations specific to the infant's clinical presentation.

Mother with laboratory  
evidence of Zika virus  
infection during  
pregnancy

Perform a  
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## Box 2: Further evaluation for infants with lab-confirmed Zika and abnormalities c/w congenital Zika

### Consults:

- Pediatric neurologist to determine appropriate brain imaging
- Pediatric infectious disease specialist and testing for other congenital infections
- Ophthalmologist for comprehensive eye exam and evaluation for possible cortical visual impairment prior to discharge from the hospital or within 1 month of birth.
- Endocrinologist for evaluation for hypothalamic or pituitary dysfunction.
- Clinical geneticist or dysmorphologist
- Consider: Orthopedist, PT, pulmonologist, GI, lactation, nutrition, Speech/OT, ENT

### Testing:

- Complete blood count with platelet count and liver function and enzyme tests
- Perform auditory brainstem response to assess hearing

Mother with laboratory evidence of Zika virus infection during pregnancy

Perform a comprehensive PE, head U/S, hearing test, and Zika testing (Box 1)

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Infant with findings c/w congenital Zika syndrome

Initial evaluation (Box 2)

## Box 3: Outpatient management of congenital Zika syndrome

- Establish medical home with PCP visits monthly for first 6 months
- Follow growth and development; provide routine immunizations, anticipatory guidance, and psychosocial support; and ensure infants receive necessary testing and consultations.
- Neurologic examination by the primary care provider at 1 and 2 months of age.
  - Refer to neurology for any abnormalities, or concerns.
- Refer to developmental specialist and early intervention services.
- Repeat comprehensive ophthalmologic exam at age 3 months
  - Refer to ophthalmology for any abnormal findings, or concerns.
- Repeat auditory brainstem response testing at age 4–6 months
  - Refer to audiology for any abnormal findings, or concerns.
- Repeat testing for hypothyroidism at age 2 weeks and 3 months, even if the initial results were normal.
  - Refer to endocrinology for any abnormal findings.
- Provide family and supportive services.

Mother with laboratory  
evidence of Zika virus  
infection during  
pregnancy

Perform a  
comprehensive PE,  
head U/S, hearing test,  
and Zika testing (Box 1)

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Infant with findings c/w  
congenital Zika  
syndrome

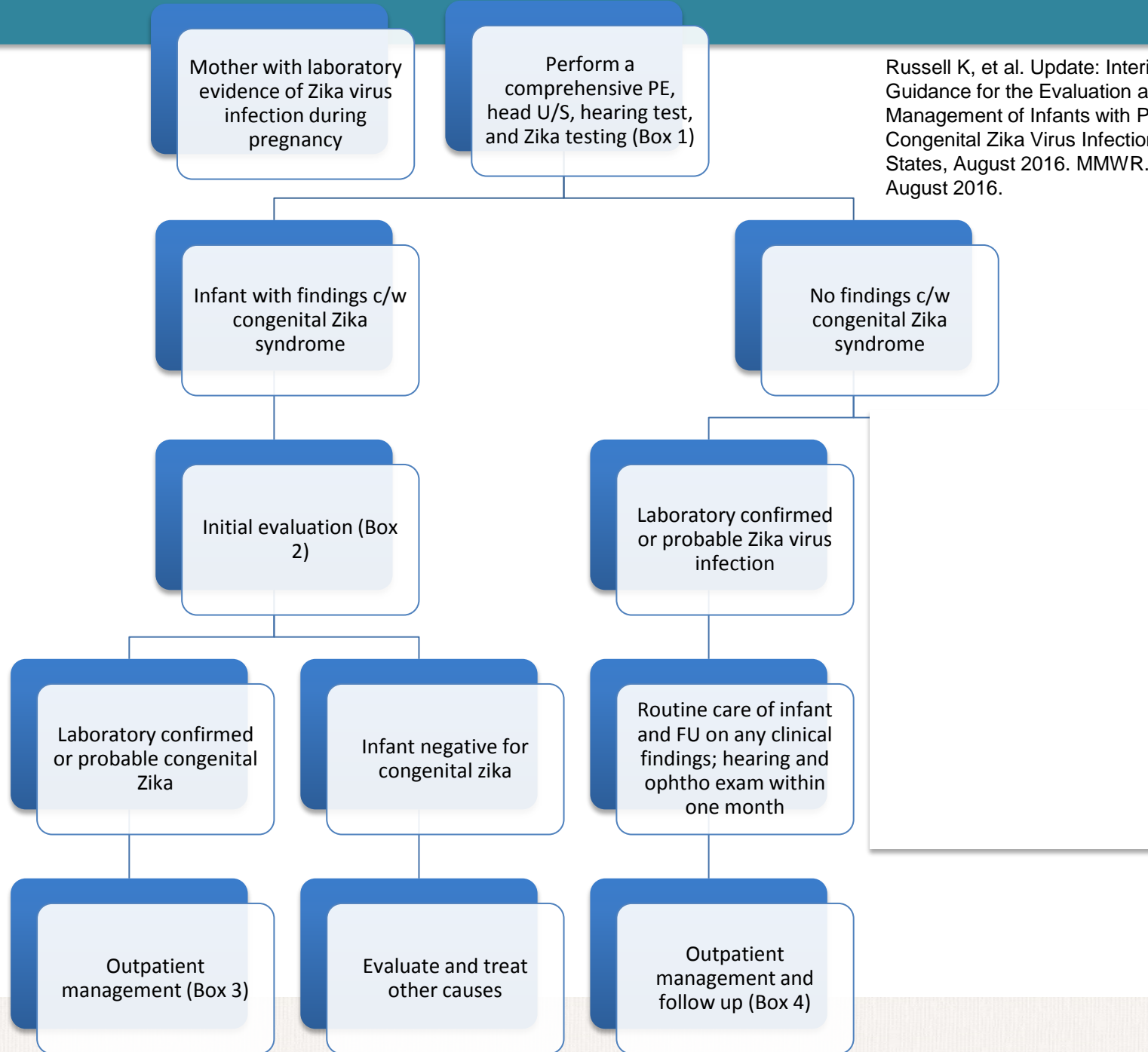
Initial evaluation (Box  
2)

Laboratory confirmed  
or probable congenital  
Zika

Outpatient  
management (Box 3)

## Box 4: Outpatient management of laboratory confirmed Zika without abnormalities c/w congenital Zika

- Establish medical home with PCP visits
  - Follow growth parameters, and perform developmental screening at each well child visit.
  - Emphasize anticipatory guidance for families regarding developmental milestones, feeding and growth, sleep and irritability, and abnormal movements
- Screen development: Use a standardized, validated developmental screening tool at 9 months as currently recommended, or earlier for any concerns.
- Referral to ophthalmology for comprehensive eye exam within one month of birth. Perform vision screening and assess visual regard at every well child visit, and refer to ophthalmology for any abnormal findings, or concerns.
- Perform auditory brainstem response within one month of birth. Consider repeat auditory brainstem response at 4–6 months or perform behavioral diagnostic testing at 9 months of age and refer to audiology for any abnormal findings, or concerns.
- Provide family and supportive services.



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Mother	Infant clinical exam	Before hospital discharge	Infant testing	2 wks.	1 mo.	2 mos.	3 mos.	4–6 mos.	9 mos.	12 mos.
Laboratory evidence of Zika virus infection*	No evidence of abnormalities	Routine newborn care: PE, HC, weight/length, and neurologic exam Hearing screen Head US Infant Zika virus testing (Table 1)	Negative for Zika virus infection	Routine care, including monitoring of OFC and development at every well child visit and age-appropriate developmental screening						
			Laboratory evidence of Zika virus infection*	Ophthalmology exam ABR					Consider repeat ABR	Behavioral audiology if ABR not done at 4–6 mos.
			Monitoring of OFC and development at every visit and age-appropriate developmental screening (Box 4)							
	Abnormalities consistent with congenital Zika syndrome	As above plus: Consider transfer to hospital with subspecialty care CBC, metabolic panel, LFTs, ophthalmology exam ABR Consider	Negative for Zika virus infection	Evaluate for other causes of congenital anomalies Further management as clinically indicated						
			Laboratory evidence of Zika virus infection*	Thyroid screen	Neurologic exam	Neurologic exam	Thyroid screen, ophthalmology exam	Repeat ABR	Routine preventive health care including monitoring of feeding and growth Routine and congenital infection-specific anticipatory guidance Referral to specialists, including evaluation of other causes of congenital	
		advanced neuroimaging (Box 2)		anomalies as needed (Box 3)						

Not tested, or tested outside of appropriate window <sup>†</sup>	No evidence of abnormalities	Maternal Zika virus testing <sup>†</sup> Consider Zika virus placental testing Routine newborn care: PE, HC, weight/length and neurologic exam Hearing screen Head US	Perform infant Zika virus testing if evidence of Zika virus infection on maternal testing <sup>*,†</sup>	Outpatient management for appropriate infant clinical exam and test results
	Abnormalities consistent with congenital Zika syndrome	As above, plus: Consider transfer to hospital with subspecialty care. CBC, metabolic panel, LFTs, ophthalmology exam ABR Consider advanced neuroimaging Infant Zika virus testing (Table 1)	Negative for Zika virus infection  Laboratory evidence of Zika virus infection <sup>*</sup>	Evaluate for other causes of congenital anomalies Further management as clinically indicated  Refer to outpatient management for infant with abnormalities consistent with congenital Zika syndrome

# Zika Resources

- CDC Zika website: [www.cdc.gov/zika](http://www.cdc.gov/zika)
- ACOG's Zika webpage: [www.acog.org/zika](http://www.acog.org/zika)
- CDC Zika Pregnancy Hotline for Healthcare Providers: [770-488-7100](tel:7704887100) or email [ZikaPregnancy@cdc.gov](mailto:ZikaPregnancy@cdc.gov) for concerns related to clinical management
- CA Department of Public Health webpage for health care professionals
  - [www.cdph.ca.gov/zika](http://www.cdph.ca.gov/zika) see Information for Health Professionals

## QUESTIONS?