



**Department  
of Health**

# Zika Virus

## What New York State Clinicians Need to Know

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NYS Commissioner of Health**

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# Objectives

At the conclusion of this webinar, clinicians will be able to:

- Describe the epidemiology, clinical manifestations, management, and prevention of Zika virus disease
- Discuss diagnostic testing for Zika virus infection available through NYSDOH's Wadsworth Center and interpretation of test results
- Articulate the importance of early recognition and reporting of cases
- State the recommendations for pregnant women and possible Zika virus exposure

# Zika Virus

- Single stranded RNA Virus
- Genus *Flavivirus*, Family *Flaviviridae*
- Closely related to dengue, yellow fever, Japanese encephalitis and West Nile viruses
- Transmitted to humans primarily by *Aedes* species mosquitoes

# Zika Virus Vectors

## Aedes Mosquitoes

- *Aedes* species mosquitoes
  - *Ae aegypti*: more efficient vectors for humans
  - *Ae albopictus*: found in some parts of NYS
- Also transmit dengue and chikungunya viruses
- Lay eggs in domestic water-holding containers
- Live in and around households
- Aggressive daytime biters

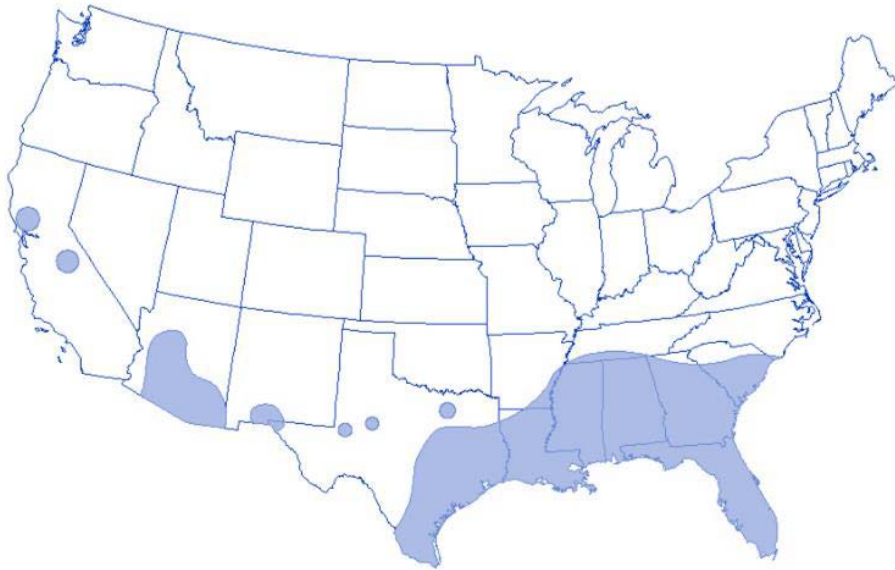


*Aedes aegypti*

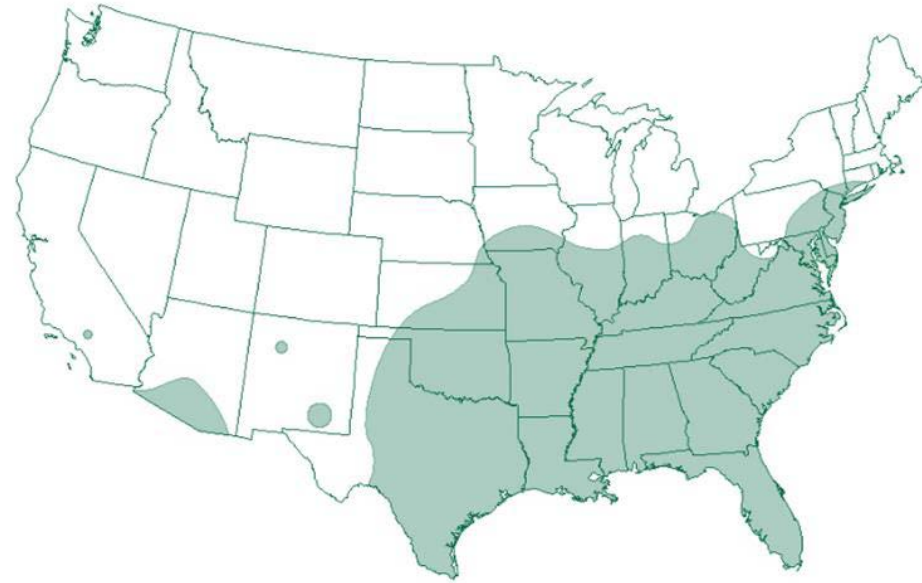


*Aedes albopictus*

# *Aedes aegypti* and *Aedes albopictus* Mosquitoes: Geographic Distribution in the United States

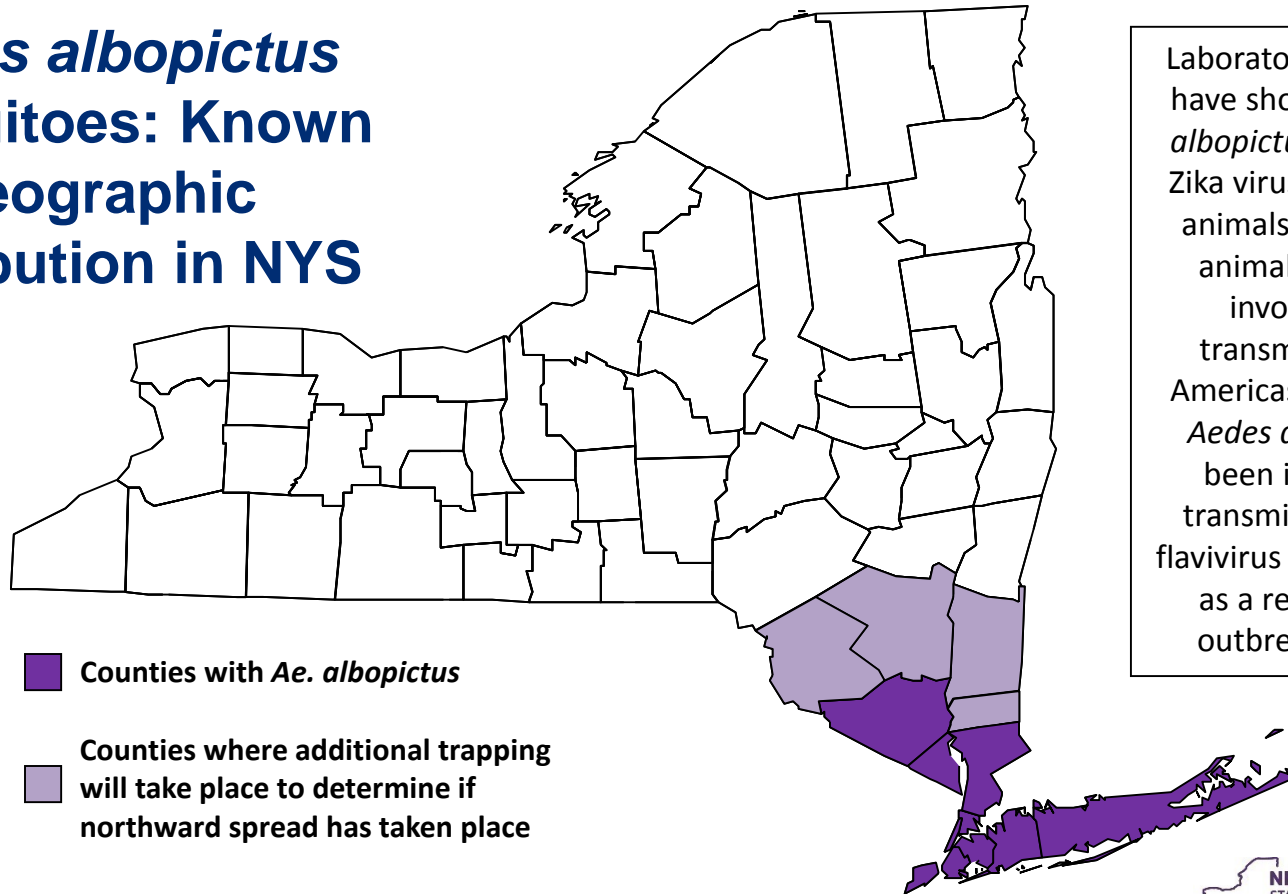


*Aedes aegypti*



*Aedes albopictus*

# *Aedes albopictus* Mosquitoes: Known Geographic Distribution in NYS



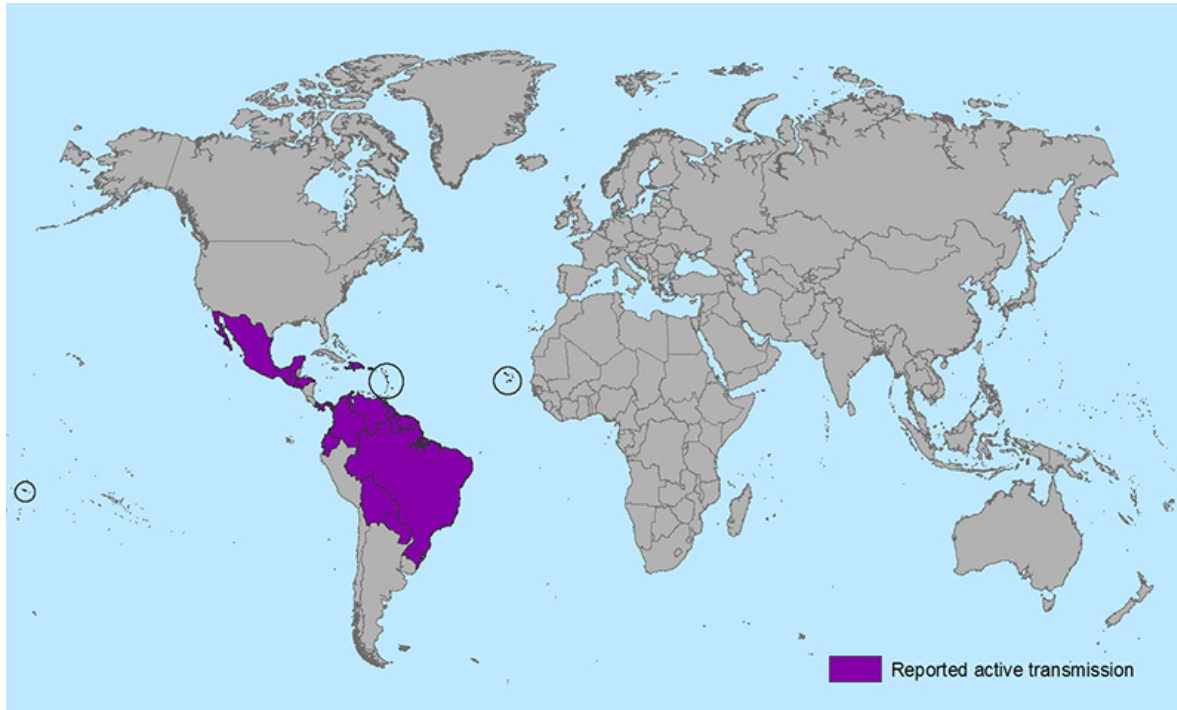
Laboratory experiments have shown that *Aedes albopictus* can transmit Zika virus from infected animals to uninfected animals. Its current involvement in transmission in the Americas is not known. *Aedes albopictus* has been implicated in transmission of other flavivirus outbreaks, such as a recent Dengue outbreak in Hawaii.

# Modes of Transmission

- Mosquito Bite
  - From infected to uninfected humans and primates by bite of a mosquito
- Maternal-fetal
  - Intrauterine
  - Perinatal
- Other possibilities
  - Sexual
  - Blood transfusion
- Theoretical
  - Organ or tissue transplantation
  - Breast milk



# Zika Virus: Countries and Territories with Active Zika Virus Transmission



As of January 30, 2016



# Zika Virus Epidemiology

- First isolated from a monkey in Uganda in 1947
- Prior to 2007, only sporadic human disease cases reported from African and southeast Asia
- In 2007, first outbreak reported on Yap Island, Federated States of Micronesia
- In 2013-2014, >28,000 suspected cases reported from French Polynesia\*

\*<http://ecdc.europa.eu/en/publications/Publications/Zika-virus-French-Polynesia-rapid-risk-assessment.pdf>



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# Zika Virus Incidence and Attack Rates

Infection rate: 73% (95%CI 68–77)

Symptomatic attack rate among infected: 18%(95%CI 10-27)

All age groups affected

Adults more likely to present for medical care

No severe disease, hospitalizations, or deaths

Note: Rates based on serosurvey on Yap Island, 2007 (population 7,391)

Duffy M. N Engl J Med 2009



# Zika Virus Clinical Disease Course and Outcomes

- Clinical illness usually mild
- Most common symptoms are a maculo or papular rash, fever, arthralgia, conjunctivitis, myalgia, and headache
- Symptoms last several days to a week.
- Severe disease requiring hospitalization uncommon
- Fatalities are rare, typically only with comorbidities
- Guillain-Barré syndrome reported in patients following suspected Zika virus infection
  - Relationship to Zika virus infection is not known



# Differential Diagnosis for Zika Virus Disease in Returning Travelers

- Dengue
- Chikungunya
- Leptospirosis
- Malaria
- Rickettsia
- Parvovirus
- Group A streptococcus
- Rubella
- Measles
- Adenovirus
- Enterovirus

# Laboratories for Diagnostic Testing

- No commercially-available diagnostic tests
- Testing performed at NYSDOH's Wadsworth Center and CDC
- CDC is working to expand laboratory diagnostic testing to other states
- Health care providers should contact their local health department to facilitate diagnostic testing at Wadsworth

# Diagnostic Testing for Zika Virus

- Real-time PCR assay to detect viral RNA in serum and urine collected  $\leq 7$  days after illness onset
- Serological assays to detect either IgM or IgG in serum collected  $\geq 4$  days after illness onset. Detects both Zika-specific and cross-reactive antibody
- Plaque reduction neutralization test (PRNT) to detect a  $\geq 4$ -fold rise in Zika virus-specific neutralizing antibodies in paired sera

# Serology Cross-Reactions with Other Flaviviruses

- Zika virus serology (IgM) can be positive due to antibodies against related flaviviruses (e.g., dengue and yellow fever viruses)
- Neutralizing antibody testing may discriminate between cross-reacting antibodies in individuals who have never had a flavivirus infection before
- Difficult to distinguish infecting virus in people previously infected with or vaccinated against a related flavivirus
- Health care providers should work with NYSDOH and local health departments to ensure test results are interpreted correctly



# Specimens

## Serum

Collect whole blood in red top tubes  
minimum 6ml



Centrifuge and remove serum  
minimum 3ml



Freeze serum and  
urine -70 to -80°C

## Urine

Minimum 3ml





### Infectious Diseases Requisition

Patient Demographics				* denotes required information
Last Name *		First Name *	MI	DOB * / /
Street Address		City	State	Zip Code
NYS County of Residence *		NYS DOH Outbreak Number	DOH Case Number	Submitter's Reference Number
Submitter (Laboratory report will be sent to)				* denotes required information
Name and Address *				Laboratory PFI _____
				Contact Person _____
				Telephone Number (____) _____
Specimen Information				* denotes required information
Specimen is: <input type="checkbox"/> Isolate <input type="checkbox"/> Primary Specimen <input type="checkbox"/> Autopsy Specimen		Collection Date * ____/____/____		
Source / Specimen Type *		Time Collected (if applicable for test) ____:____		
Laboratory Examination Requested				<a href="http://www.wadsworth.org/IDtesting">www.wadsworth.org/IDtesting</a>
<input type="checkbox"/> Bacterial <input type="checkbox"/> Fungal <input type="checkbox"/> Mycobacterial <input type="checkbox"/> Parasitic <input type="checkbox"/> Serology <input type="checkbox"/> Viral				
Suspected Organism / Agent _____				
<input type="checkbox"/> Identification / Confirmation		<input type="checkbox"/> Susceptibility (specify antimicrobial(s)) _____		
<input type="checkbox"/> TB Fast Track <a href="http://www.wadsworth.org/microbio/tbtrack.htm">www.wadsworth.org/microbio/tbtrack.htm</a>		<input type="checkbox"/> Serology (specify test and define onset date)		
<input type="checkbox"/> Viral Encephalitis Panel <a href="http://www.wadsworth.org/clinical/fields/enceph/term.htm">www.wadsworth.org/clinical/fields/enceph/term.htm</a>		<input type="checkbox"/> Other (specify) _____		
Submitting lab findings: Smear/Stain/Other results _____ Comments _____				
Specimen submitted on/in: Media _____ Preservative _____ Tissue cell line _____				
Relevant Exposure: <input type="checkbox"/> Contact known case <input type="checkbox"/> Food/water <input type="checkbox"/> Nosocomial				
<input type="checkbox"/> Travel _____ Location & Date _____ <input type="checkbox"/> Animal _____ Type _____ <input type="checkbox"/> Arthropod _____ Type _____				
Clinical History				
Name of patient's healthcare provider _____ Telephone Number _____				
Diagnosis: _____ Hospitalized? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown If hospitalized, hospital name: _____				
Pregnant (trimester): _____ Symptoms: <input type="checkbox"/> Acute <input type="checkbox"/> Chronic <input type="checkbox"/> Other _____ Onset of symptoms: ____/____/____				
Fever: max _____ duration _____ CSP: Glu _____ Prot _____ RBC _____ WBC _____				
Relevant Treatment: _____ Date ____/____/____ Relevant Immunization: _____ Date ____/____/____				
Symptoms/Clinical Epidemiology (check all that apply):				
Central Nervous System: <input type="checkbox"/> Altered Mental Status <input type="checkbox"/> Coma <input type="checkbox"/> Encephalitis <input type="checkbox"/> Headache <input type="checkbox"/> Meningitis <input type="checkbox"/> Paralysis <input type="checkbox"/> Seizures				
Gastrointestinal: <input type="checkbox"/> Diarrhea <input type="checkbox"/> Blood/Mucus <input type="checkbox"/> Nausea <input type="checkbox"/> Vomiting				
Respiratory: <input type="checkbox"/> Bronchitis <input type="checkbox"/> Bronchiolitis <input type="checkbox"/> Cough <input type="checkbox"/> Pneumonia <input type="checkbox"/> Upper Respiratory Infection				
Skin/hair/nails: <input type="checkbox"/> Hemorrhagic <input type="checkbox"/> Maculopopular Rash <input type="checkbox"/> Petechial Rash <input type="checkbox"/> Vesicular				
Cardiovascular: <input type="checkbox"/> Endocarditis <input type="checkbox"/> Myocarditis <input type="checkbox"/> Pericarditis				
Miscellaneous: <input type="checkbox"/> Arthralgia <input type="checkbox"/> Conjunctivitis <input type="checkbox"/> Cystitis <input type="checkbox"/> Hepatitis <input type="checkbox"/> Hepatomegaly <input type="checkbox"/> Immunocompromised <input type="checkbox"/> Jaundice				
<input type="checkbox"/> Keratitis <input type="checkbox"/> Lymphadenopathy <input type="checkbox"/> Malaise <input type="checkbox"/> Myalgia <input type="checkbox"/> Pleurodynia <input type="checkbox"/> Splenomegaly <input type="checkbox"/> Ulcer(s) <input type="checkbox"/> Urethritis				
Other Symptoms: _____				

- ← Patient name and address
- ← Physician name and address
- ← Specimen details
- ← Test request
- ← Travel history – location and dates
- ← ? Pregnant ? trimester
- ← Clinical symptoms



# Packaging, shipping and certification



IATA  
DOT  
Certification

# Initial Assessment and Treatment

- No specific antiviral therapy
- Treatment is supportive (i.e., rest, fluids, analgesics, antipyretics)
- Suspected Zika virus infections should be evaluated and managed for possible dengue or chikungunya virus infections
- Aspirin and other NSAIDs should be avoided until dengue can be ruled out to reduce the risk of hemorrhage

# Zika Virus in the Continental United States

- Local transmission of Zika virus has not been reported in the continental United States
- Since 2011, there have been laboratory-confirmed Zika virus cases identified in travelers returning from areas with local transmission
  - 9 cases in NYS, all in returning travelers
- With current outbreaks in the Americas, cases among U.S. travelers will most likely increase
- Imported cases may result in virus introduction and local spread in some areas of U.S.



# Zika Virus Disease Surveillance

- Consider in travelers with acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis within 2 weeks after return
- Inform and evaluate women who traveled to areas with Zika virus transmission while they were pregnant
- Evaluate fetuses/infants of women infected during pregnancy for possible congenital infection and microcephaly
- Be aware of possible local transmission in areas where *Aedes* species mosquitoes are active.

# Reporting Zika Virus Disease Cases

- As an arboviral disease, Zika virus disease is a nationally notifiable disease
  - Health care providers are required to report all suspected cases to their local health department
- Timely reporting allows NYSDOH and local health departments to assess and reduce the risk of local transmission or mitigate further spread

# Zika Virus Preventive Measures

- No vaccine or medication to prevent infection or disease
- Primary prevention measure is to reduce mosquito exposure
- Pregnant women should consider postponing travel to areas with ongoing Zika virus outbreaks
- Because bites to them may infect mosquitoes, infected people need to be protected from mosquito exposure during first week of illness to prevent further transmission



# Zika Virus and Pregnancy



- Limited information is available
- Existing data show:
  - No evidence of increased susceptibility
  - Infection can occur in any trimester
  - Incidence of Zika virus in this population is not known
  - No evidence of more severe disease

Centers for Disease Control and Prevention, *CDC Health Advisory: recognizing Managing and reporting Zika Virus Infections in Travelers Returning from Central America, South America, the Caribbean and Mexico*, 2016.

Besnard, M., et al., Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014. *Euro Surveill*, 2014. 19(14): p. 1-5.

Oliveira Melo, A., et al., Zika virus intrauterine infection causes fetal brain abnormality and microcephaly: tip of the iceberg? *Ultrasound in Obstetrics & Gynecology*, 2016. 47(1): p. 6-7.



# Maternal-Fetal Transmission of Zika Virus

- Evidence of maternal-fetal transmission
  - Zika virus infection confirmed in infants with microcephaly in Brazil and in infants whose mothers have traveled to Brazil but delivered in the US
  - Zika virus RNA identified in specimens of fetal losses
  - Zika virus detected prenatally in amniotic fluid
    - Two women at ~30 weeks gestation with a history of symptoms consistent with Zika infection
    - Fetal microcephaly and intracranial calcifications detected on ultrasound
    - Amniotic fluid testing positive for Zika virus RNA by RT-PCR

# Zika Virus and Microcephaly in Brazil

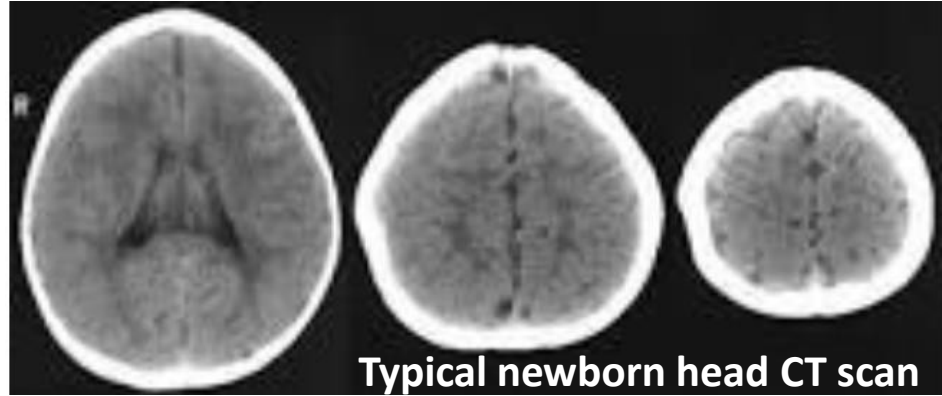
- Over 4,000 babies born with microcephaly since outbreak started in Brazil, an over 20-fold increase
  - Zika virus infection identified in several infants born with microcephaly (including deaths) and in early fetal losses
  - Some of the infants with microcephaly have tested negative for Zika virus
- Incidence of microcephaly among fetuses with congenital Zika infection is unknown
- Microcephaly can have many causes, not just Zika virus



# Infants with Microcephaly



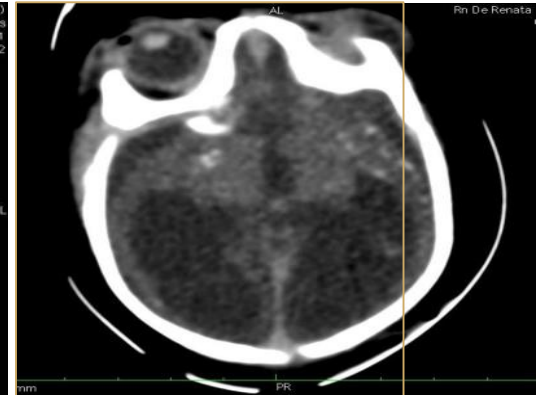
AP Photos/Felipe Dana



Typical newborn head CT scan

scattered intracranial  
calcifications

enlarged ventricles  
and volume loss



# CDC Recommendations: Pregnancy and Women Considering Travel

- Pregnant women in any trimester should consider postponing travel to areas where Zika is present
- Pregnant women who do travel to one of these areas should talk to their Health care provider and strictly follow steps to avoid mosquito bites during the trip
- Women attempting to become pregnant should also follow these recommendations

# Zika Virus Disease Prevention: Pregnant Women

Pregnant women who must travel to one of these areas should talk to their doctor or other health care provider first and strictly follow steps to avoid mosquito bites during the trip:

- Use repellent products registered with the US Environmental Protection Agency (EPA)
- Do not overuse repellent – only apply as much as you need to provide protection
- Read and follow label directions before using any kind of repellent
- Dress in long-sleeved shirts and long pants
- Stay indoors when mosquitoes are most active.
- Aedes mosquitoes are active during the day



# Evaluation of Pregnant Women

- Obtain recent travel history from pregnant women
- NYSDOH recommends and will provide testing for symptomatic, pregnant women who traveled to an area with ongoing Zika virus transmission during pregnancy
  - Provide information to pregnant women and their provider to help inform clinical management and decision making

# Zika Virus Laboratory Testing of Infants\*

- Recommended for
  1. Infants with microcephaly or intracranial calcifications born to women who traveled to or resided in an area with Zika virus transmission while pregnant
  2. Infants born to mothers with positive or inconclusive test results for Zika virus infection

\*Refer to the “Interim Guidelines for the Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection” – MMWR, 2016

# Zika Virus Remaining Questions

- Incidence of maternal-fetal transmission by trimester
  - Factors that influence (e.g., severity of infection, maternal immune response)
- Need and implications of testing of asymptomatic pregnant women
- Likelihood of sexual transmission and testing needs and implications
- Risk of microcephaly and other fetal and neonatal outcomes
- Risk of Guillain-Barré syndrome
- Potential for long-term reservoirs of Zika virus



# Summary

- Zika virus continues to circulate and cause locally-transmitted disease in the Americas
- Consider the possibility of Zika virus infection in travelers with acute fever, rash, arthralgia, or conjunctivitis within 2 weeks after return
- Pregnant women in any trimester should consider postponing travel to areas of Zika virus transmission

Slides courtesy of the Centers for Disease Control and Prevention.