



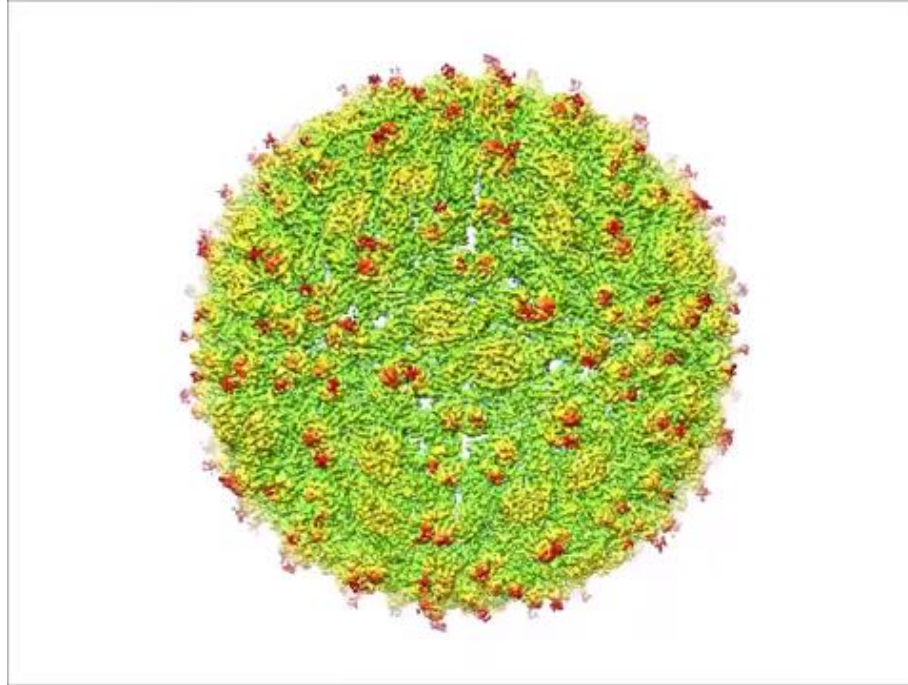
Zika: at the Crossroad of Vector Borne Emerging Infectious Diseases and Teratogenicity

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Development in Puerto Rico (CRECE)
Zika in Infants and Pregnancy (ZIP)**

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Zika Virus Structure as Demonstrated by Researchers from Purdue University



Presentation Outline

- Summarize epidemiology, diagnosis, clinical manifestations, and management of Zika virus disease
- Discuss association between Zika virus disease, microcephaly and Guillain-Barré syndrome
- Provide status on the Zika virus epidemic in Puerto Rico and continental United States
- Examine the importance of primary prevention, including role of Integrated pest management (IPM)
- Discuss the complexity of risk assessment and communication



Puerto Rico Braces for Its Own Zika Epidemic

Intensive efforts to stop the virus have begun on the island, where a quarter of the population will get it within a year, the C.D.C. predicts.

By DONALD G. McNEIL Jr. MARCH 19, 2016

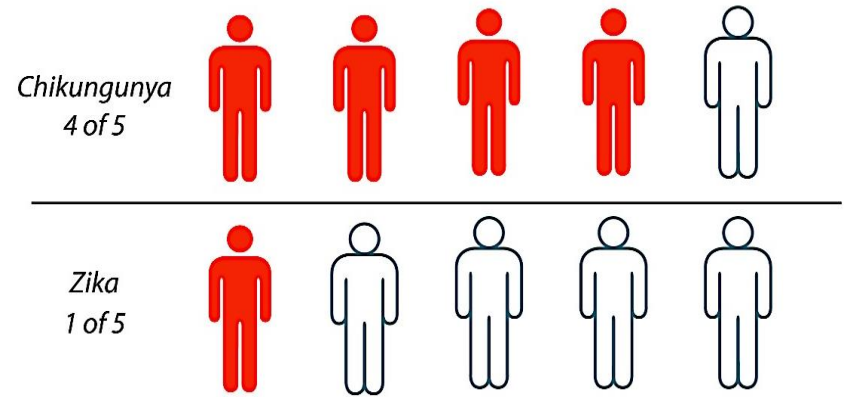
What is Zika Virus?

- Flavivirus (*Flaviviridae* family)
 - Yellow fever, dengue, West Nile viruses
- Spreads to people primarily through the bite of an infected *Aedes* species mosquito
- Closely related to dengue virus
 - Transmitted by same mosquito
 - Cross reactivity on currently available antibody testing
- Infection causes either asymptomatic or mild illness with symptoms lasting for several days to a week

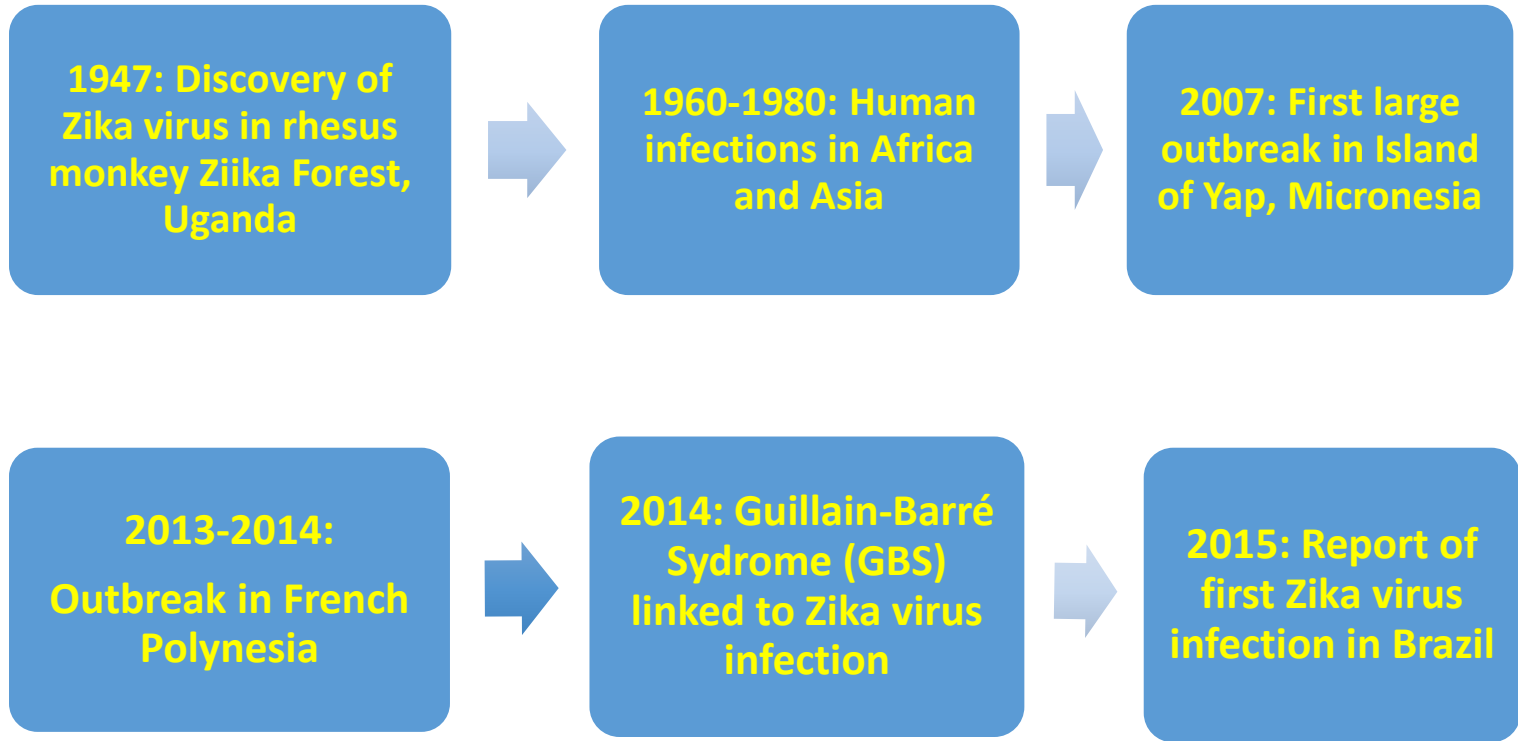
Zika is a Silent Epidemic

- Dengue & Chikungunya spread by same mosquito species
- Dengue has infected 80-90% of people in Puerto Rico
- Chikungunya infected 1 of every 4 people in Puerto Rico in less than a year
- The same pattern with Zika would lead to at least 6,900 pregnant women becoming infected in 2016

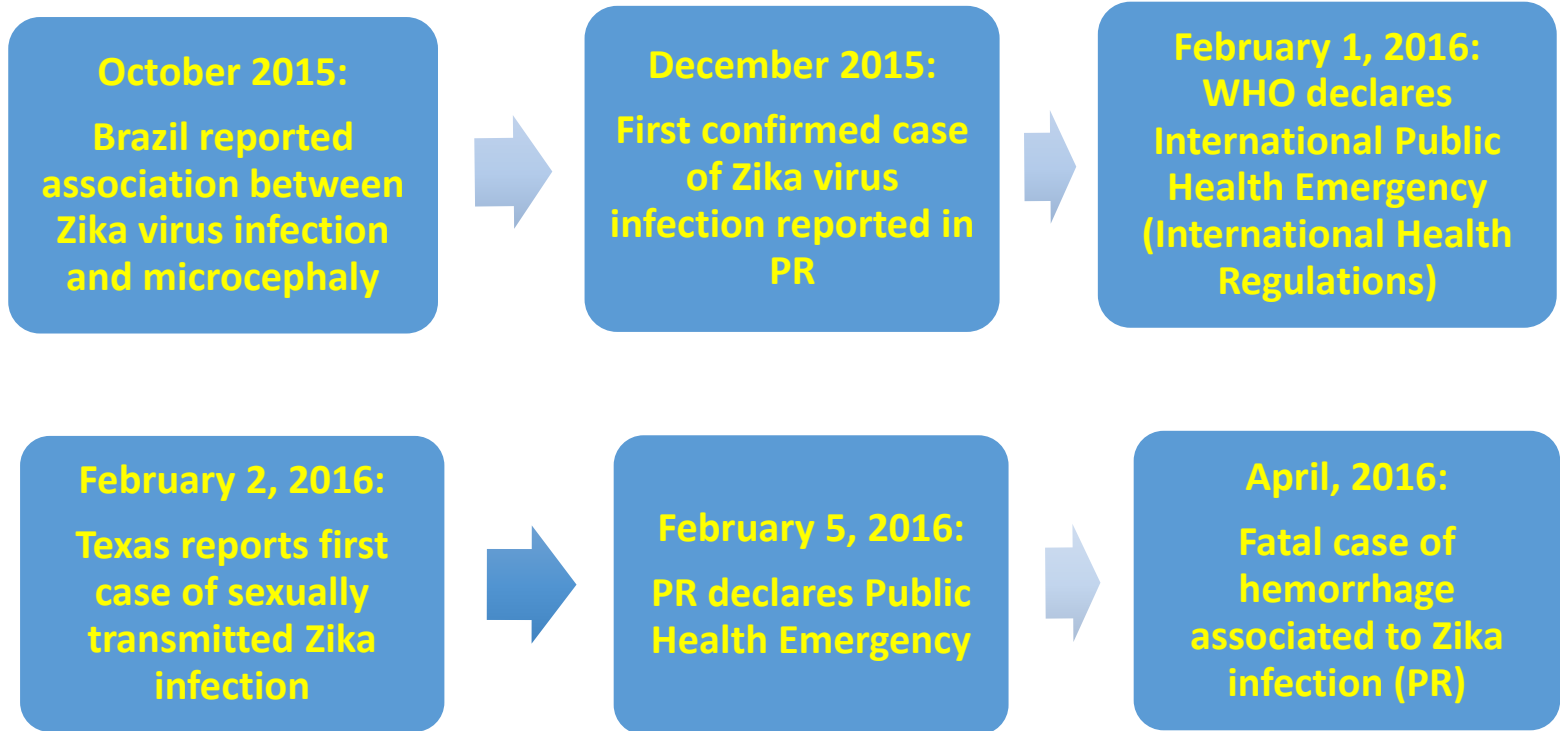
Proportion of people who manifest symptoms when they have infection with Chikungunya or Zika



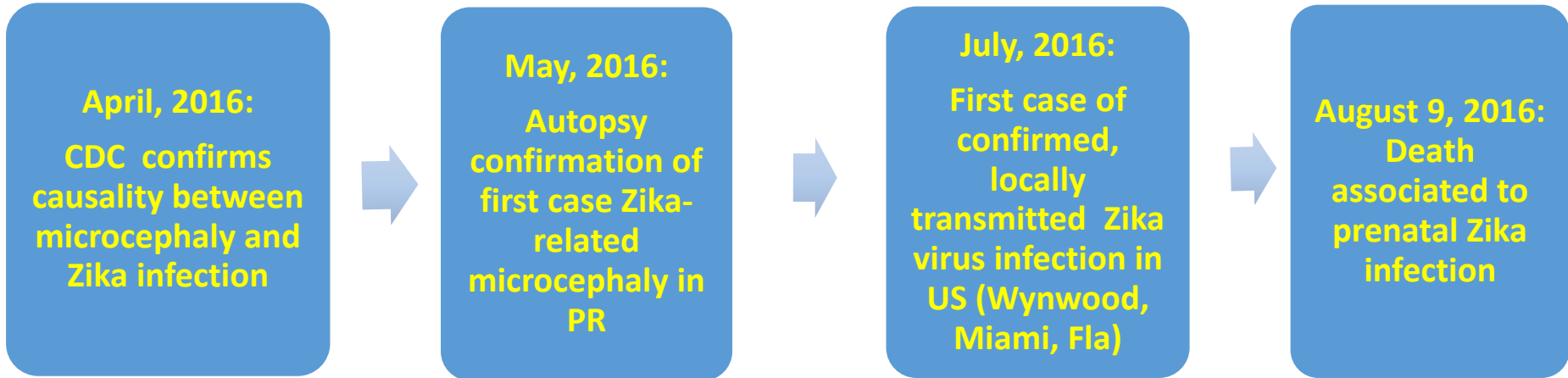
History of an Emerging Infectious Disease



History of an Emerging Infectious Disease



History of an Emerging Infectious Disease



Zika Virus Infection and Pregnancy



Taking a pre-baby trip has become a tradition for some expectant moms. But a new health risk, the Zika virus, has some of them thinking twice. (quintanilla / Getty)

(Chicago Tribune, April 3, 2016)

Interim Guidelines for Healthcare Providers

- Care of pregnant women and women of reproductive age with suspected Zika infection
- Care of infants and children with suspected Zika infection
- Prevention of sexual transmission of Zika virus

<http://www.cdc.gov/zika/hc-providers/clinical-guidance.html>

Zika Virus Disease

- Incubation period:
 - 3-14 days
 - Virus detected in blood (viremia): 7-10 days
 - Prolonged viremia reported in some pregnant women
- No vaccine (yet)
 - 8 agencies and companies worldwide
 - Clinical trials (Butantan Institute São Paulo, Brazil)

Zika Virus Disease

- Most common symptoms are mild and last 2-7 days:
 - Low grade fever
 - Rash (+/- pruritus) → common symptom
 - Arthralgia (+/- swelling of hands, feet)
 - Conjunctivitis sicca
- Tx: Rest, hydration and acetaminophen
- Full recovery without severe complications
- Hospitalization rates are low
- Life-long immunity?

Conjunctivitis



(Medscape, 2016)

Rash



(Gredia Huerta-Montanez, 2016)

Clinical Features: Zika Virus Compared to Dengue and Chikungunya

Features	Zika	Dengue	Chikungunya
Fever	++	+++	+++
Rash	+++	+	++
Conjunctivitis	++	-	-
Arthralgia	++	+	+++
Myalgia	+	++	+
Headache	+	++	++
Hemorrhage	-	++	-
Shock	-	+	-

Transmission of Zika Virus

Other Modes of Transmission

- Maternal-fetal
 - Intrauterine
 - Perinatal
- Other
 - Sexual
 - Blood transfusion
 - Laboratory exposure
- Theoretical
 - Organ or tissue transplantation
 - Breast milk



(U.S. Centers for Disease Control and Prevention, 2016)

Zika and Adverse Pregnancy Outcomes

- Zika as a teratogen
 - First mosquito-borne cause of human birth defects ever known
 - First new infectious major cause of birth defects in 50 years
 - No reports of adverse pregnancy or birth outcomes were noted during previous outbreaks of Zika virus disease in Pacific Islands
 - Sufficient evidence has accumulated to infer a causal relationship between prenatal Zika virus infection and microcephaly and other severe brain anomalies (S. Rasmussen, et al., NEJM)

Zika and Adverse Pregnancy Outcomes

- Transplacental transmission
 - Increased risk of adverse outcomes earlier in pregnancy?
 - Microcephaly
 - Hydranencephaly (absent or ↓ cerebral hemispheres)
 - Central nervous system lesions (calcifications)
 - Others: ocular involvement, hearing problems, hydrops fetalis, abnormal amniotic fluid volume
 - Fetal loss (miscarriage, stillbirth)

Microcephaly

- Head circumference measurement technique
- > 2 SDs below mean (below 3rd percentile for age and gender)
 - Primary- abnormal head growth (genetic)
 - Secondary- arrested growth/cerebral tissue destruction
- Irreversible
- Cognitive and neurological problems

Microcephaly

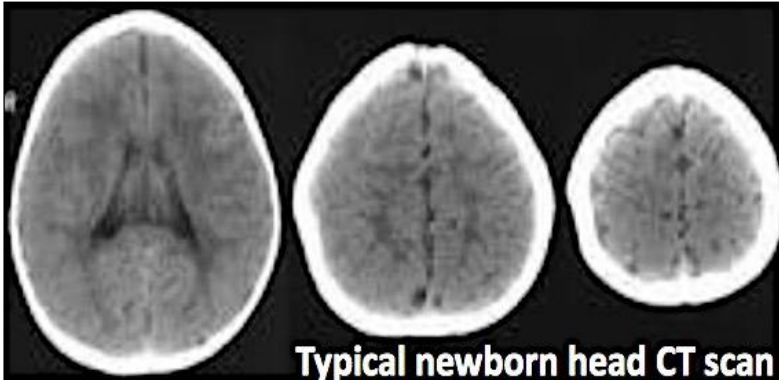


(U.S. Centers for Disease Control and Prevention,
National
Center on Birth Defects and Developmental Disabilities,
2016)

Infants with Microcephaly



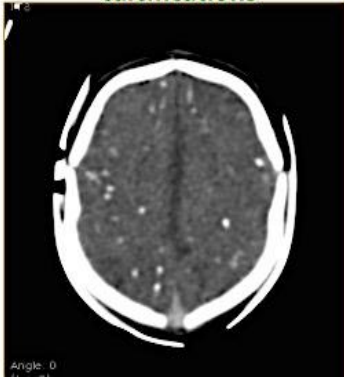
AP Photos/Felipe Dana



Typical newborn head CT scan



scattered intracranial calcifications



enlarged ventricles and volume loss



(U.S. Centers for Disease Control and Prevention, 2016)

Congenital Zika Syndrome

- Fetal brain disruption sequence
 - Severe microcephaly
 - Intracranial calcifications
 - Other brain anomalies
 - Eye findings
 - Redundant scalp skin
- Arthrogryposis
- Clubfoot

Diagnosis of Zika Infection

- **Trioplex** (RT-PCR or reverse transcription polymerase chain reaction)
 - Viral particles of chikungunya, zika and dengue viruses
 - Serum (<7 days), urine (<14 days)
- **Zika Antibody Detection (Zk-IgM ELISA)**
 - Delayed immune response
 - Cross reactivity with dengue
 - Days after illness onset for up to \approx 12 weeks

PREGNANT WOMAN

Assess for possible Zika virus exposure
Evaluate for signs and symptoms of Zika virus disease

A**B**

- Symptomatic : <2 weeks after symptom onset, **or**
- Asymptomatic and **NOT** living in an area with active Zika virus transmission: <2 weeks after possible exposure

- Symptomatic: 2–12 weeks after symptom onset, **or**
- Asymptomatic and **NOT** living in an area with active Zika virus transmission: 2–12 weeks after possible exposure, **or**
- Asymptomatic and living in an area with active Zika virus transmission: 1st and 2nd trimester

Zika virus rRT-PCR on serum and urine

Zika virus IgM and dengue virus IgM[§] on serum

Positive Zika virus rRT-PCR on serum or urine:
Recent Zika virus infection

Negative Zika virus rRT-PCR on serum and urine

Dengue virus IgM positive or equivocal and Zika virus IgM negative:
Presumptive dengue virus infection

Zika virus IgM positive or equivocal and any result on dengue virus IgM:
Presumptive recent Zika virus or flavivirus infection

Zika virus IgM and dengue virus IgM negative:
No recent Zika virus infection

Zika virus IgM and dengue virus IgM negative:
No recent Zika virus infection

Zika virus IgM or dengue virus IgM positive or equivocal
Presumptive recent Zika virus or dengue virus or flavivirus infection

Reflex Zika virus rRT-PCR on serum and urine

Plaque reduction neutralization test (PRNT)

Negative Zika virus rRT-PCR on serum

Positive Zika virus rRT-PCR on serum:
Recent Zika virus infection

Zika virus PRNT ≥10 and dengue virus PRNT <10:
Recent Zika virus Infection

Zika virus PRNT ≥10 and dengue virus PRNT ≥10:
Recent flavivirus infection, specific virus cannot be identified

Zika virus PRNT <10:
No recent evidence of Zika virus infection

Questions Needing Answers

- **How common is the infection?**
 - Symptoms nonspecific, mild or absent
 - *flavivirus* antibody cross-reactivity
- **What is the risk of adverse outcome in pregnancy? How does it change gestational age?**
- **What is the spectrum of clinical outcomes?**

Questions Needing Answers

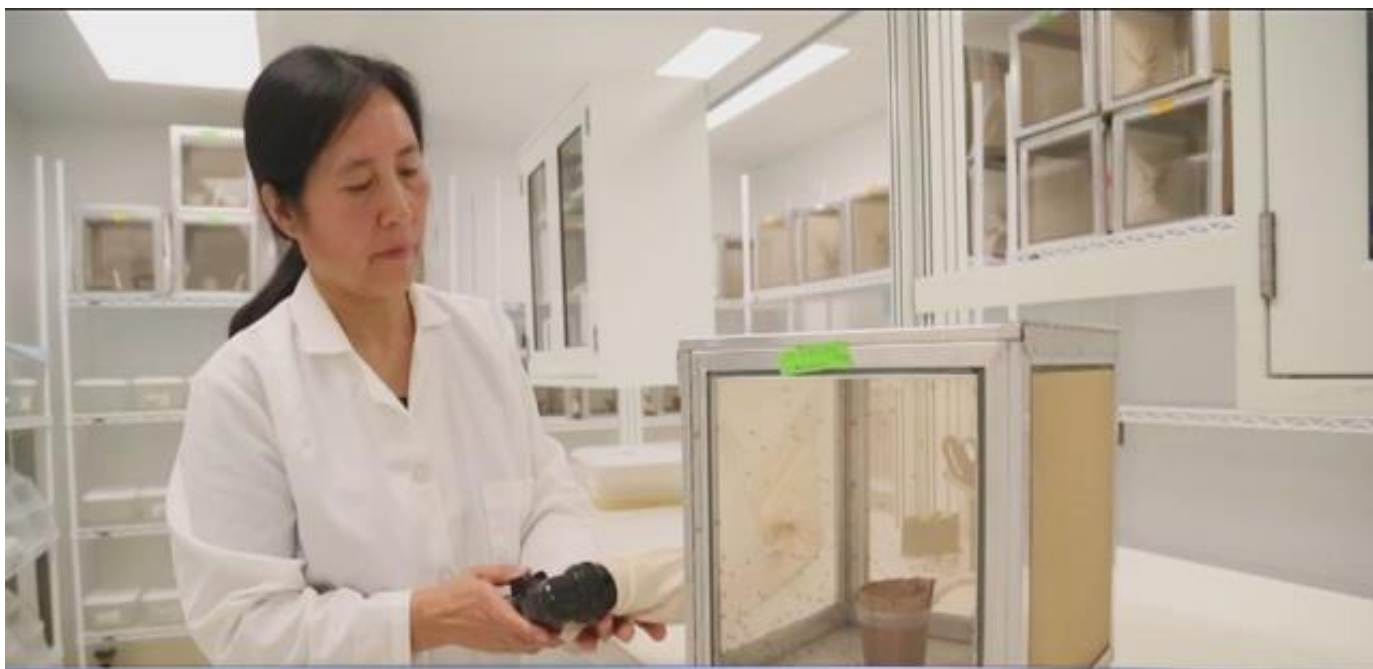
- **Can mild or asymptomatic Zika infection damage the fetus?**
- **Will normocephalic infants born to Zika-infected mothers have other long-term neurological adverse effects?**
- **Co-factors involved in fetal outcomes?**
 - Genetic susceptibility
 - Nutrition
 - Viral load
 - Maternal environmental exposures
 - Prior infection with virus in same class
 - Antibody dependent enhancement (ADE)

Guillain-Barré Syndrome (GBS) and Zika

- Autoimmune disorder
 - Progressive muscle weakness and paralysis
 - 5% mortality
 - 30% need ventilatory support
 - 10% relapse
- Early recognition and treatment is key
 - Intensive care
 - Immunomodulatory tx (plasmapheresis and immune globulin (IVIG))

Guillain-Barré Syndrome (GBS) and Zika

- In Puerto Rico
 - Guillain-Barré Syndrome Surveillance
 - 30 cases associated with Zika infection
- Incidence
 - Baseline 1-2/100,000
 - Zika-related suspected 1/10,000



FOX 26

9:13 74°

**DALLAS REPORTS CASE OF ZIKA VIRUS
TRANSMITTED SEXUALLY**

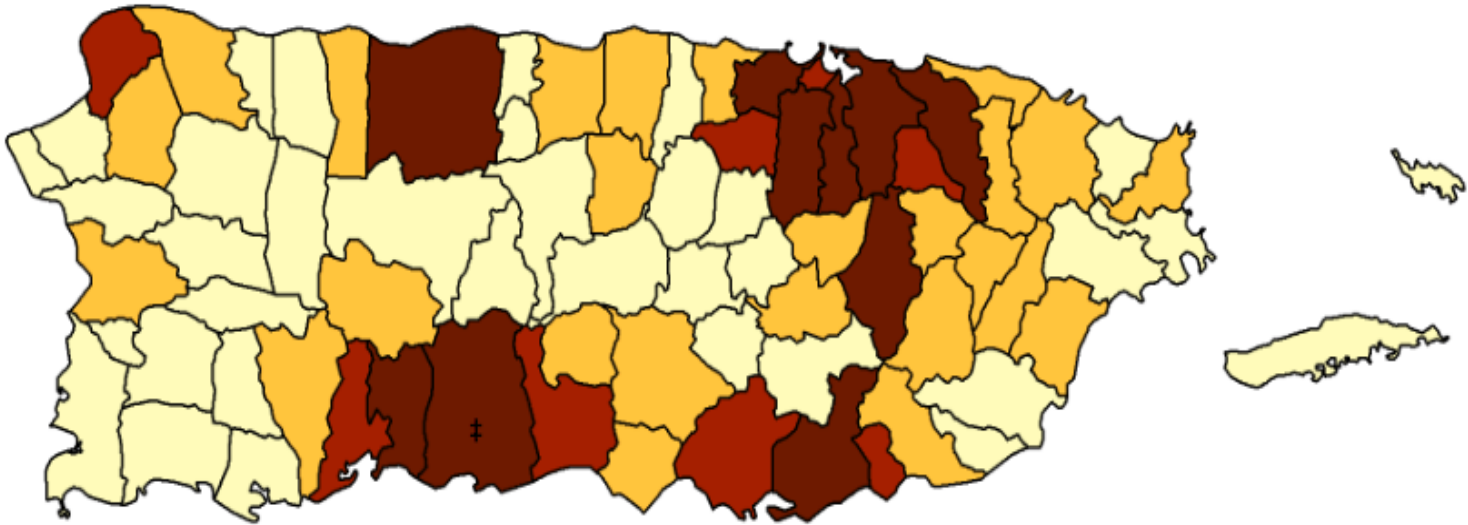
YOUR DALLAS-COAST WEATHER AUTHORITY

Zika Distribution (US CDC)



Zika Virus Disease in Puerto Rico

Casos confirmados (n = 10,415)[†] de ZIKV, 2015–hasta semana 30-2016



(Weekly report PRDOH arboviral diseases-August 11,2016)

Zika in Puerto Rico

- Testing, mosquito abatement, protection of blood supply
- Prevention messaging
 - Public service announcements, billboards, bus stops, digital media
- Community engagement efforts
- Surveillance systems: arboviral diseases, GBS and microcephaly

Prevention of Zika Virus Transmission



Zika Vector Control



Aedes aegypti



Aedes albopictus

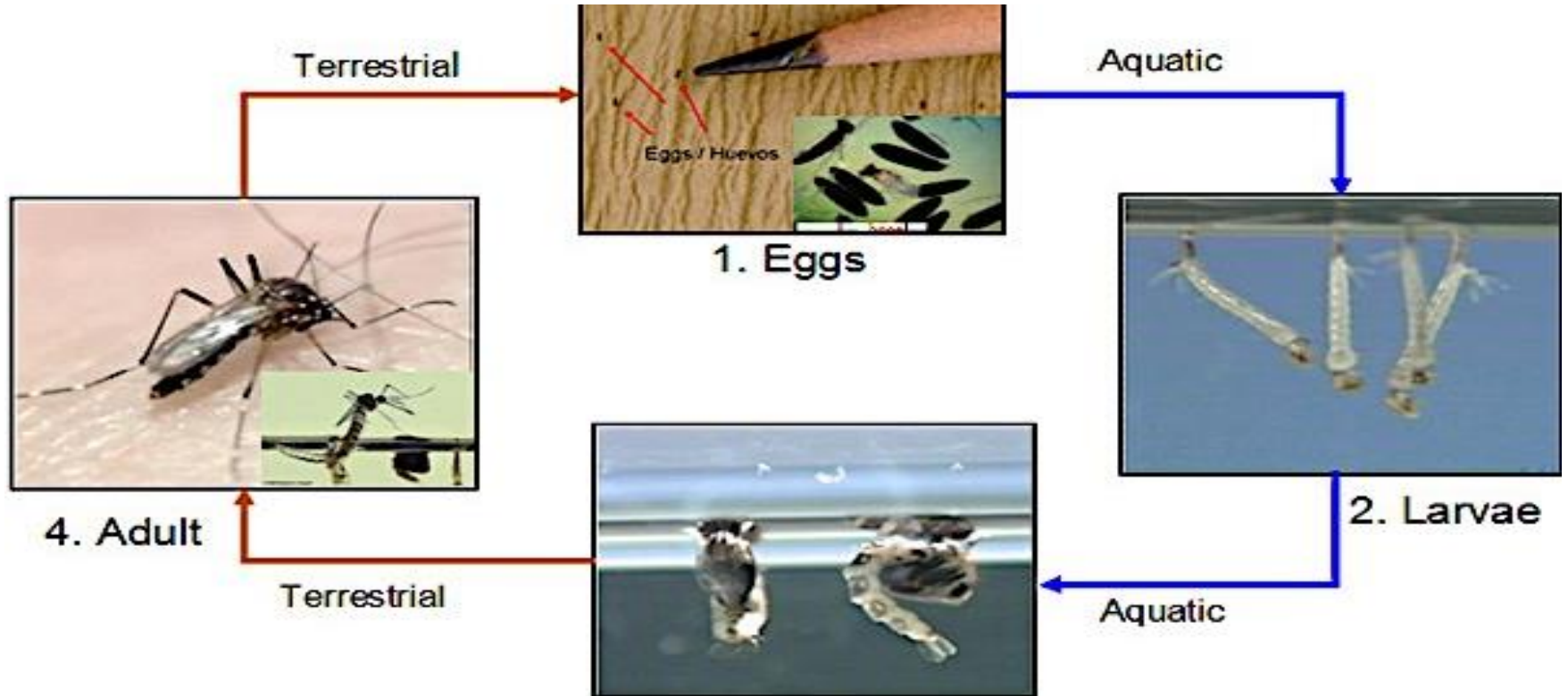
Aedes aegypti

- Household mosquito
- Bites during the day; rests in cooler, darker places
- Resilience and adaptability
 - Eggs can last > 1year
 - Adapts to environmental changes
 - Thrives in impoverished, crowded areas
 - Container breeder
 - Oviposition: 100-200 eggs, several places

Aedes aegypti

- “Sip feeder”
 - Aggressive biters
 - Dawn to dusk
- Dengue incidence in America increased 30X in 50 years (WHO, 2016)
 - Climate change
 - Alterations in geographic range (latitude and altitude) and seasonality of vector-borne diseases

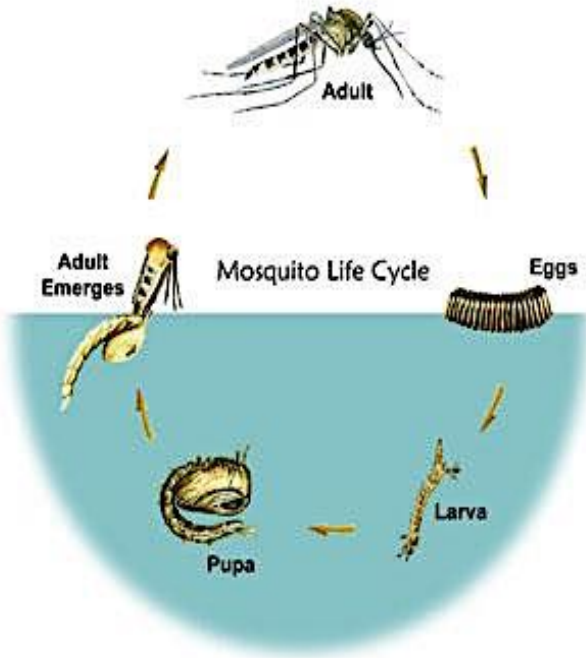
Aedes aegypti Life Cycle





(U.S. CDC, 2016; Gredia Huerta-Montanez, 2014)

Mosquito Control



- Should target ALL mosquito life stages
- Most effective:
 - **Elimination of breeding sites**
- Communities engagement challenges:
 - **Virus is new, mosquito is not**

(US EPA, March 2016)

Integrated Pest Management (IPM) during a Public Health Emergency

- IPM principles
 - Prevention as first line of pest control
 - Effective and environmentally sensitive (cultural, physical and biological measures)
 - Combination of common-sense practices and knowledge of the life cycles of pests and their interaction with the environment
 - Least possible hazard to people, property, and the environment (chemical)

Children are More Vulnerable



(CDC, 2016)

“Children are not little adults”

IPM and Mosquito Control

- Mosquito surveillance
- Source reduction methods
- Public education on preventive measures
- Evaluation of efficacy and mitigation of human health risks with special consideration to children's vulnerability and susceptibility
- Direct control procedures (i.e., adulticiding and larviciding)

IPM: Biological and Physical Controls

- Biological control
 - Life predators to kill *A. aegypti*
- Physical control
 - Mosquito-proof screens
 - Bed nets
 - Use of air-conditioner
- Repellents and skin protection
 - *N,N*-Diethyl-*m*-toluamide (DEET), ER3535, picaridin
 - Re-application necessary
 - Clothing application of DEET and permethrin
 - Review recommendations for use in children and pregnant women

IPM: Chemical Control

- Pesticide application alone is **NOT** effective in controlling mosquito populations
- Most pesticides used for adult mosquitoes do not provide long-term residual control
- **Resistance** from overuse

IPM: Chemical Control

Adult mosquitoes:

- Residual insecticides (Targeted Indoor and outdoor residual spraying (IRS/ORS)→
 - Chemically stable pesticide applied to surfaces
 - Ideally lasts for several months
 - > 80% households in an area to be effective
- Aerosol treatments
 - Widely used
 - Only effective while the particles are airborne
 - Pressurized cans, hand-held “foggers”, trunk-mounted sprayers, aircraft application



(www.bbc.com, 2016)



(U.S. Centers for Disease Control and Prevention, 2016)

ULV and Aerial Applications

- Adulcicides
 - Very concentrated pesticide in very small volumes (droplet 15-50 microns)
 - Minimum of 2,000 acres
 - naled (Dibrom)- OP applied by air to over 11 million acres in US and for adult mosquito control after natural disasters
- Larvicidals
 - Bacillus thuringiensis (Bti), (S)-Methoprene
 - Community larviciding of key containers

Innovative Methods for Vector Control

- Autodissemination traps (CDC-Autocidal Gravid Ovitrap (AGO), In2Care)
- Genetically modified mosquitoes
 - OX513A
- Sterile insect technique
- Wolbachia-infected mosquitoes



(<http://univares.com/in2care>)



Pregnant?

Warning: Zika is linked to birth defects
There is no vaccine to prevent Zika virus infection

Protect your pregnancy

From getting Zika from mosquito bites



Daytime is most dangerous

Mosquitoes that spread Zika are aggressive daytime biters. They can also bite at night.

Use insect repellent

It's safe and it works! Read the label and follow the directions.



Cover your skin

Wear long-sleeved shirts and long pants. For extra protection, treat clothing with permethrin.

Mosquito-proof your home

Use screens on windows and doors.
Use air conditioning when available.
Eliminate standing water.



From getting Zika from sex



Don't have sex

Don't have sex with your male partner during your pregnancy.

OR

Use a condom

Use a condom the right way every time you have vaginal, anal, or oral sex during your pregnancy.



Talk to your healthcare provider

If you think your male partner may have or had Zika, tell your healthcare provider if you had sex without a condom.

Zika Prevention Kit



(U.S. Centers for Disease Control and Prevention, 2016)



¿Embarazada?

Advertencia: El virus del Zika puede estar asociado a defectos congénitos

No existe una vacuna para prevenir la infección por el virus del Zika



¡Protéjase de las picaduras de mosquitos!



Durante el día es más peligroso

Los mosquitos que propagan el chikunguña, el dengue y el zika pican agresivamente durante el día y también pueden picar por la noche.



Use repelente de insectos

¡Funcional

Busque los siguientes ingredientes activos:

• DEET • Picaridina • IR3535



Utilice ropa que la proteja

Póngase camisas de manga larga y pantalones largos y use repelente de insectos. Para protección adicional, trate la ropa con permetrina.



Mantenga su hogar libre de mosquitos

Use una malla o tela metálica en las puertas y ventanas. Use el aire acondicionado si está disponible. Elimine el agua acumulada para que los

Concluding Thoughts

- **Protect the next generation**

- Mobilize when adverse outcome has not been detected yet
- Protect pregnant women from mosquitoes
 - Zika Prevention Kits and education on personal protection
- IPM for mosquito control

Concluding Thoughts

- Herd immunity will slow further transmission
 - Need for immediate and long-term prevention and control strategies
- Pesticides as a bridge to long-term, integrated vector management
- Messaging to the communities is key

Resources

- <http://www.cdc.gov/zika/>
- <https://www.epa.gov/insect-repellents>
- <https://www.epa.gov/mosquitocontrol/joint-statement-mosquito-control-united-states>
- <http://pediatrics.aappublications.org/content/early/2016/03/22/peds.2016-0621>
- <http://www.who.int/mediacentre/factsheets/zika/en/>

THANKS

“Intergenerational solidarity is not optional, but rather a basic question of justice, since the world we have received also belongs to those who will follow us”.

(Pope Francis, *Laudato Si'*, 2015)



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