Public Health Entomology Update:
NC Arboviruses/NC Zika Response/Aedes Survey Updates

Brian Byrd, PhD, MSPH

Western Carolina University | Environmental Health

Brian Byrd, PhD, MSPH

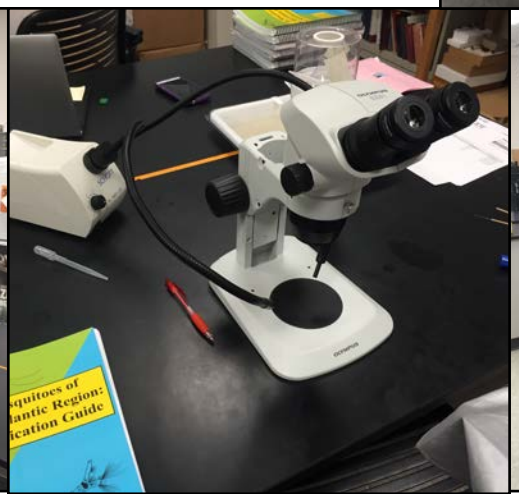
- **Training/Education**
  - BA (Biology), UNC-Asheville
  - MSPH (Public Health/Parasitology), Tulane University
  - PhD (Medical Entomology/VBID), Tulane University
  - Grad. Certificate (Field Epidemiology), UNC-CH (12/16)
- **Currently**
  - Associate Professor

    Western Carolina University
  - Supervisor

    Mosquito & Vector-borne Infectious Diseases Laboratory (mosquito.wcu.edu)

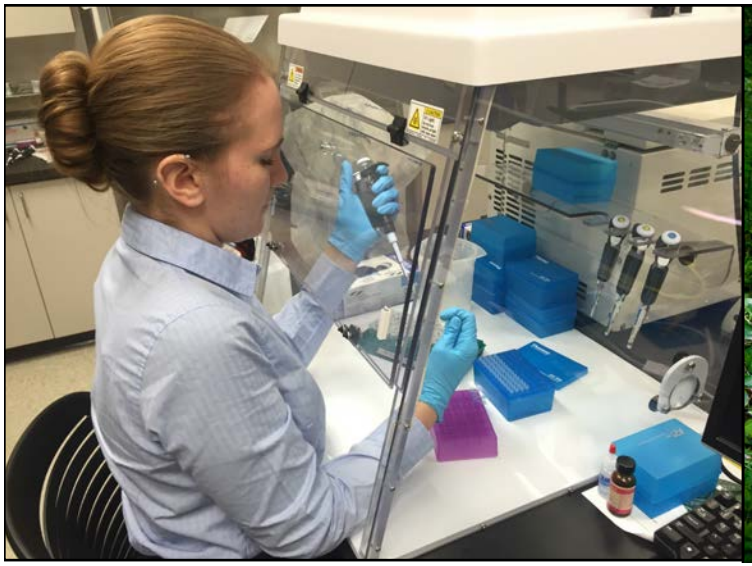
WCU "Mosquito Lab"

- **Laboratory Capacity**
  - BSL-2 Laboratory
  - Microscopy, Cell Culture, NA Testing
  - Arthropod Containment Facility
  - Training Capability
- **Field/Response Capacity**
  - Collection Devices
  - Entomologic Surveillance



Laboratory Focus

- **ENVH Training**
  - Undergraduate (BSEH) Program
  - REHS Continuing Education
- **Research**
  - La Crosse
  - Invasive Mosquito Species
  - Cryptic Species



NC Mosquito-borne Pathogens

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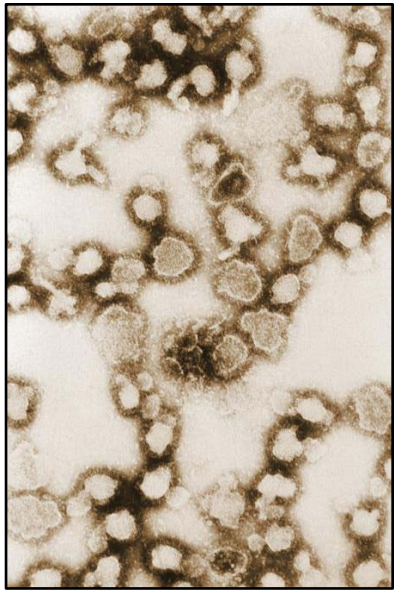
- **Zoonotic**
  - (Animal-Mosquito-Human)

    La Crosse virus
    West Nile virus
    Eastern Equine Encephalitis virus
    Saint Louis Encephalitis virus



- **"Anthroponotic"**
  - (Human-Mosquito-Human)

    Chikungunya
    Dengue
    Malaria
    Zika

    } Introduced by travel

Arboviral Disease: NC Acquired

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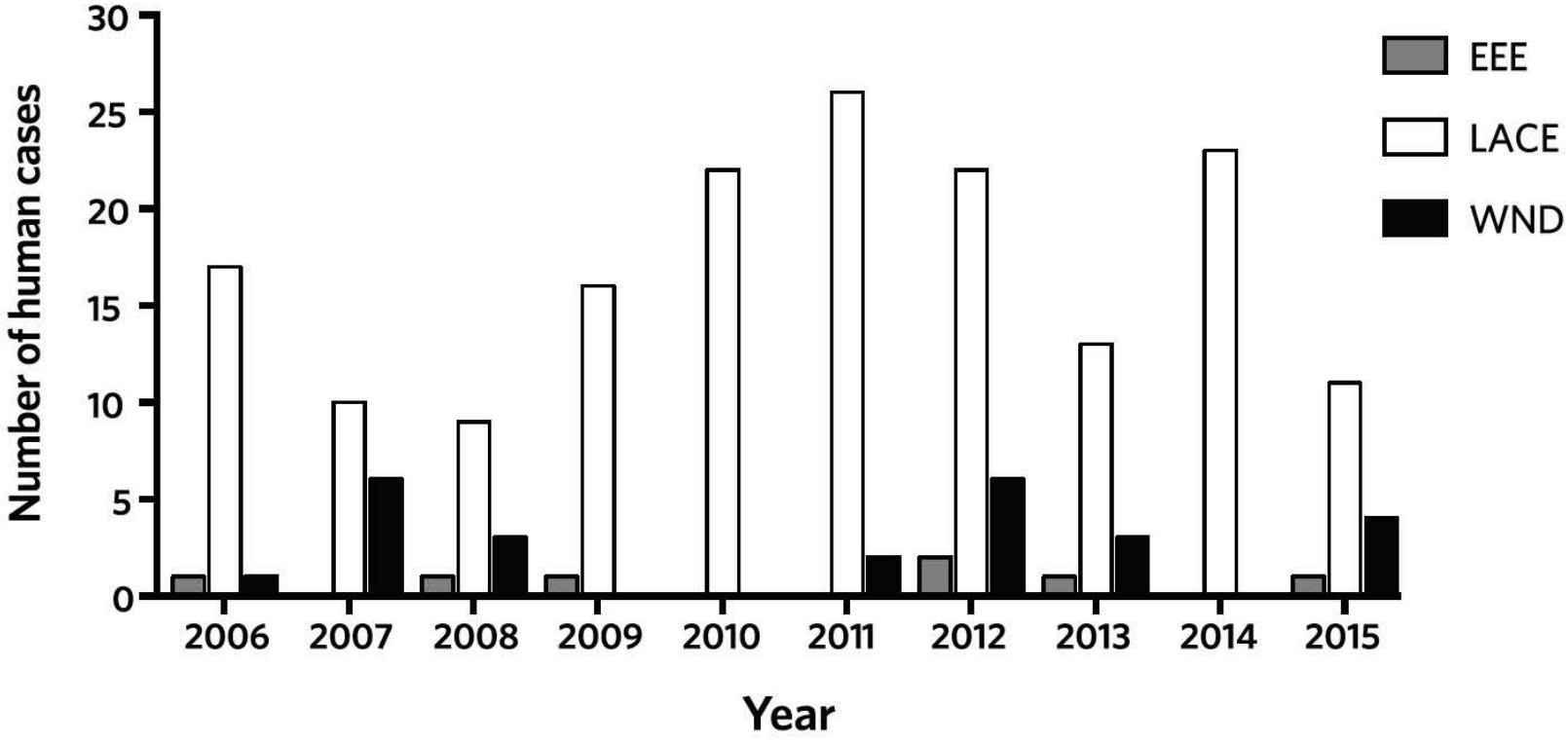
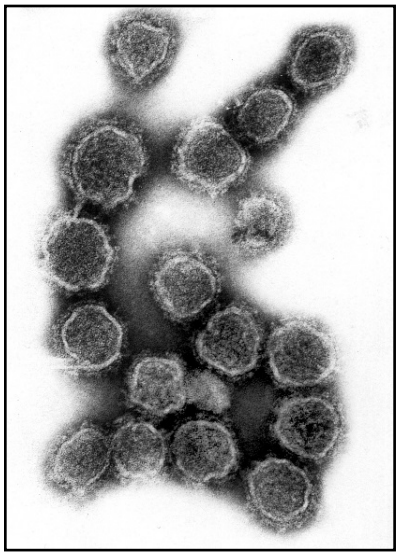
FIGURE 1.
Mosquito-Borne Arboviral Diseases in Humans, North Carolina, 2006–2015



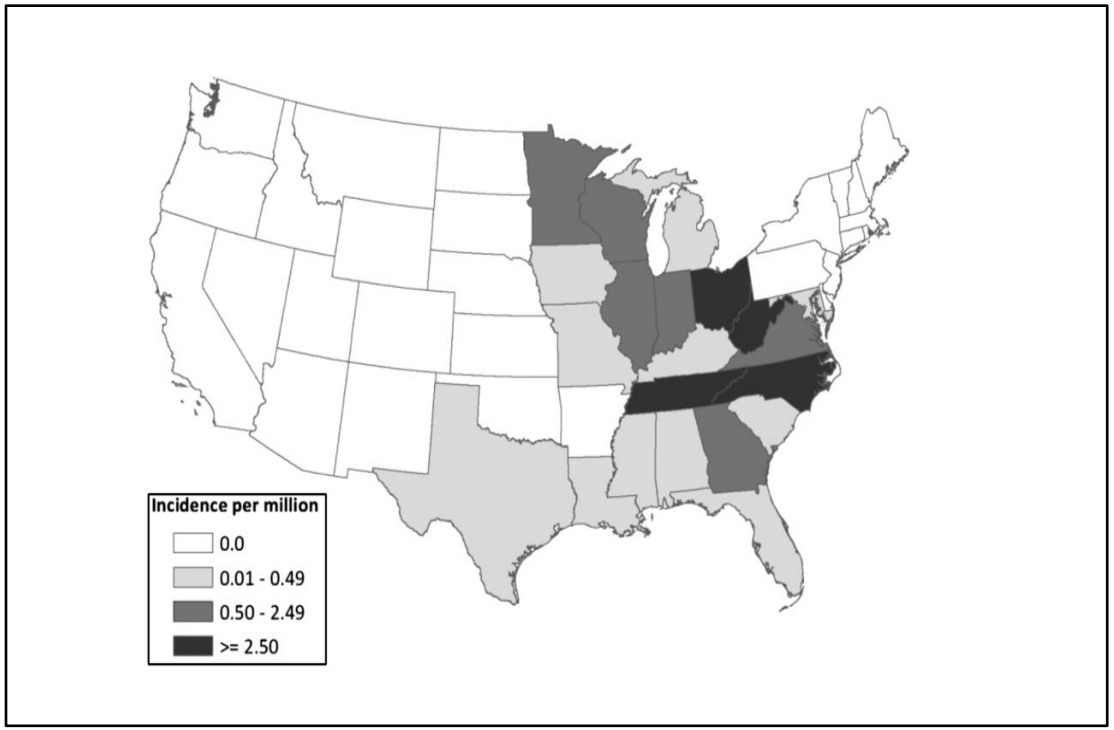
Byrd, NCMJ 2016

La Crosse Virus

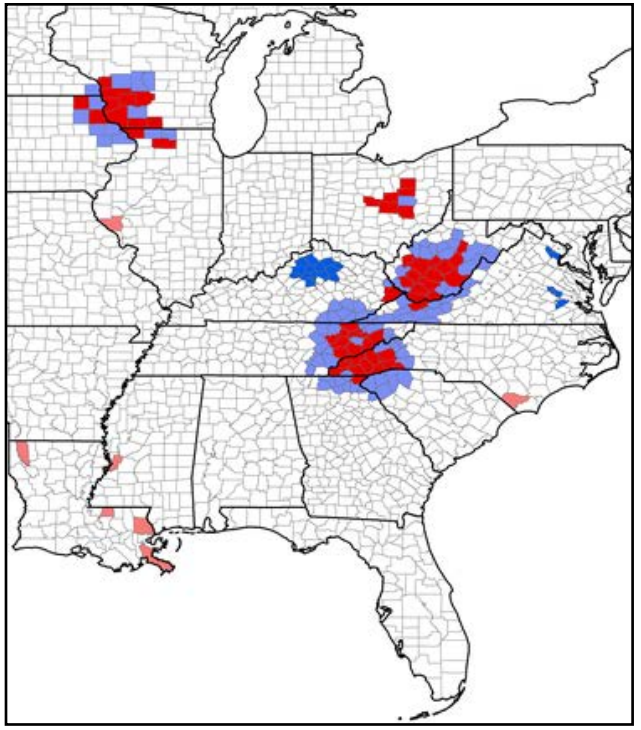
- **Isolated in 1960's in La Crosse, Wisconsin**
  - Bunyavirus (California serogroup virus)
- **Only acquired through the bite of a mosquito**
  - Eastern-tree hole mosquito (principle vector)
- **LACv is the most common arboviral cause of pediatric encephalitis in the US**



LACE Disease Geography



Gaensbauer JT, Lindsey NP, Messacar K, Staples JE, Fischer M. Neuroinvasive arboviral disease in the United States: 2003 to 2012. I. 2014 Sep;134(3):e642-50.

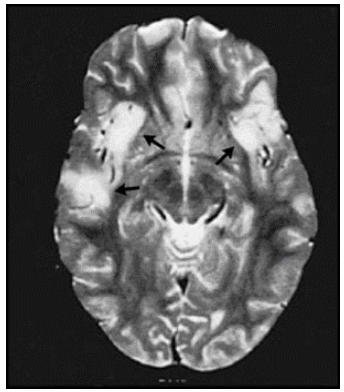


Haddow AD and Odoi A, The incidence risk, clustering, and clinical presentation of La Crosse virus infections in the eastern United States, 2003-2007. *PLoS One*. 2009 Jul 3;4(7):e6145.

Although LACE was historically found throughout the Midwest, the burden has shifted to the Appalachian region: 81% reported from Ohio, West Virginia, North Carolina, and Tennessee (2003-2012). Within NC, the western counties have the highest incidence rate of LACE. Most cases occur in Buncombe, Haywood, Henderson, Jackson, Macon, Swain, and Transylvania counties.

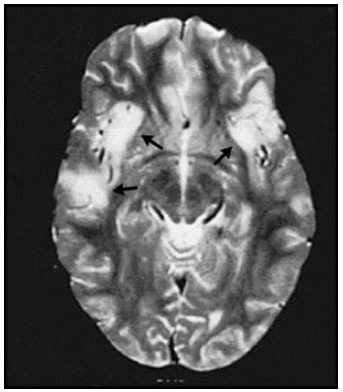
LACv Disease

- **Symptoms**
  - Incubation Period: 5-15 days
  - Fever, Headache, Vomiting, Fatigue, Lethargy
  - Severe neuroinvasive disease occurs mostly in children under 16 years
  - Seizures during acute illness are common; fatal cases are rare (<2%)
- **Neurologic Sequelae**
  - Vary in duration and severity
  - Recurrent seizures, hemiparesis, and cognitive and neurobehavioral abnormalities



LACv Disease

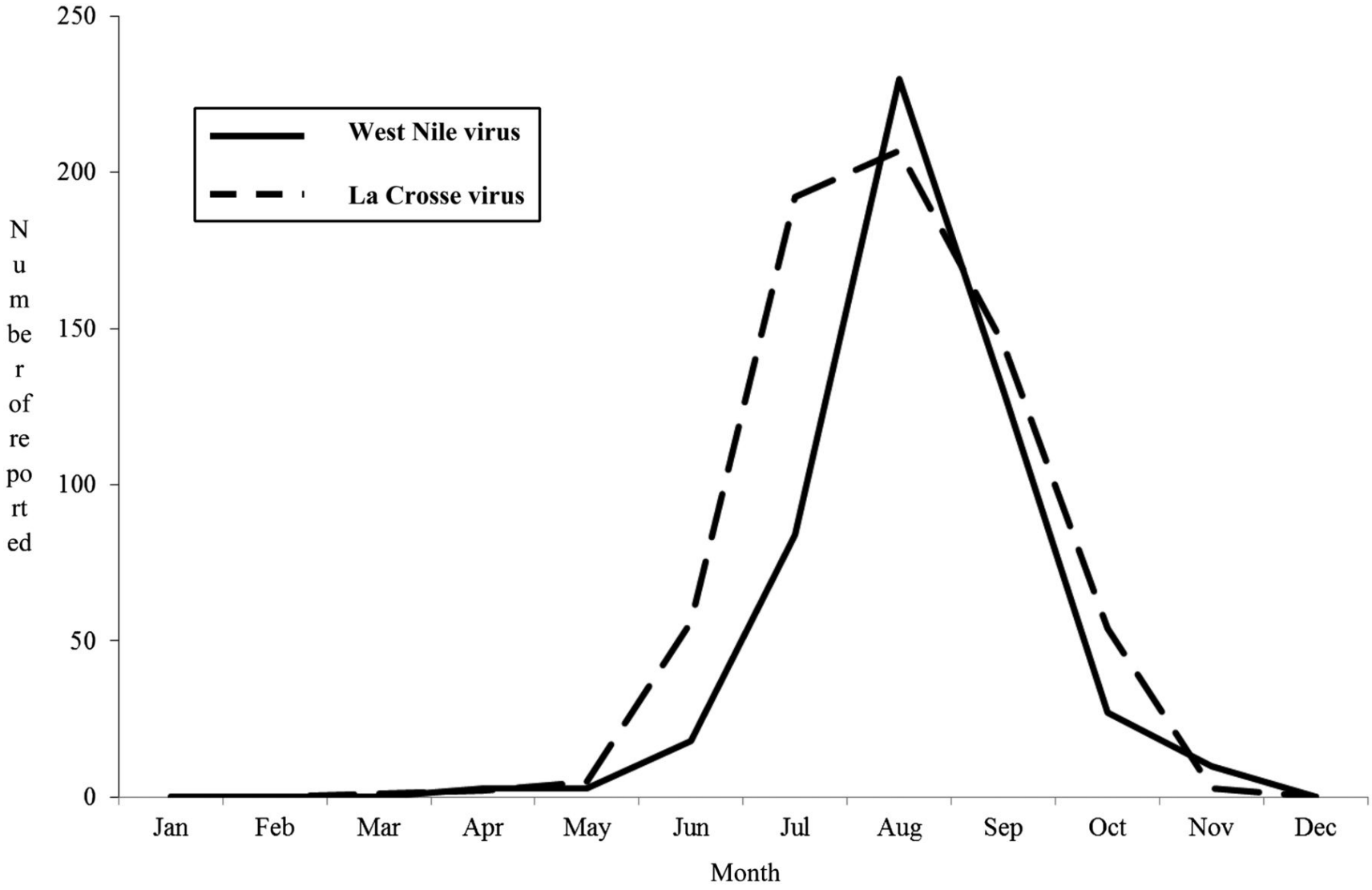
- **Treatment**
  - No vaccine
  - No specific antiviral treatment
  - Supportive treatment only
  - "Prevention is the Cure"
- **Economic and Social Impacts: High**
  - Direct and Indirect Medical Costs
    - $7,521-$175,586 (mean= $32,974)*
  - Lifelong Neurologic Sequelae
    - $48,775-$3,098,798*



*2003 USD Value

Utz et al. Economic and Social Impacts of La Crosse Encephalitis in Western North Carolina *American Journal of Tropical Medicine and Hygiene*. 69 (5) 2003.

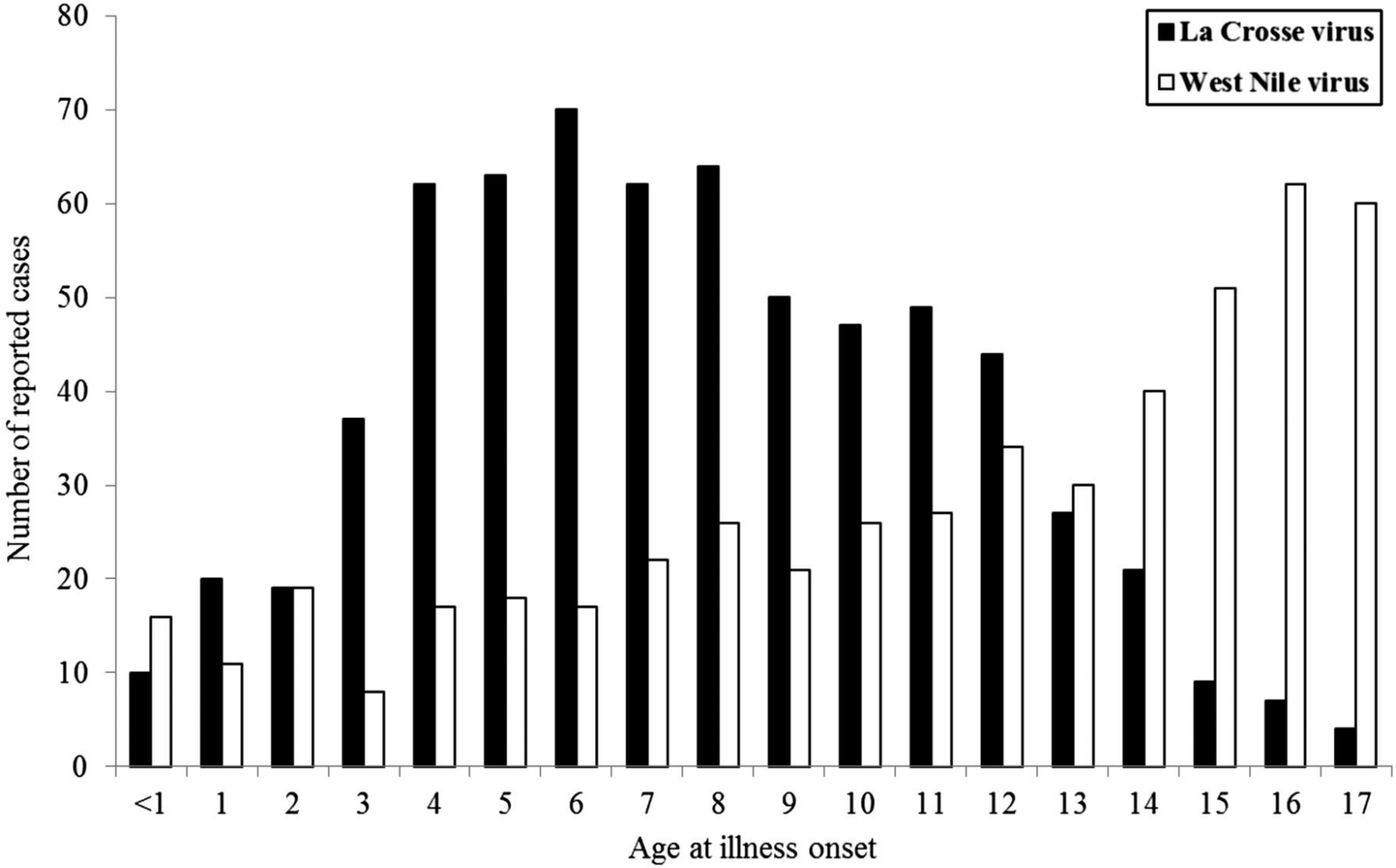
Number of reported pediatric neuroinvasive arboviral disease cases due to La Crosse and West Nile viruses, by month of illness onset: United States, 2003–2012.



PEDIATRICS®

James T. Gaensbauer et al. *Pediatrics* 2014;134:e642-e650

Number of reported pediatric neuroinvasive arboviral disease cases due to La Crosse and West Nile viruses, by age at illness onset: United States, 2003–2012.



PEDIATRICS

James T. Gaensbauer et al. *Pediatrics* 2014;134:e642-e650

LACv Infection

Largely Unrecognized

- Most infections: Asymptomatic
- Each recognized case: ~200 infections
- "Tip of the Iceberg"

Seroepidemiology of LACv infection (WNC)

Location	n	% Positive
Macon Co.	36	8.3
Swain Co.	175	8.0
Jackson Co.	225	4.9
Haywood Co.	162	2.5

Szumlas DE, Apperson CS, Hartig PC, Francy DB, Karabatsos N. Seroepidemiology of La Crosse virus infection in humans in western North Carolina. *Am J Trop Med Hyg.* 1996 Apr;54(4):332-7.

Invasive Vectors

Aedes albopictus: "Asian Tiger Mosquito"

- Can transmit La Crosse virus
- Readily feeds on Humans
- Aggressive, Daytime Feeder

Aedes japonicus: "Asian Bush Mosquito"

- Can transmit La Crosse virus
- Feeds on Humans
- Less Aggressive, Daytime/Evening Feeder

LACv IRs for *Ae. japonicus* (0.63) were lower than *Ae. triseriatus* (2.72) and *Ae. albopictus* (3.01) (Westby et al., 2015)

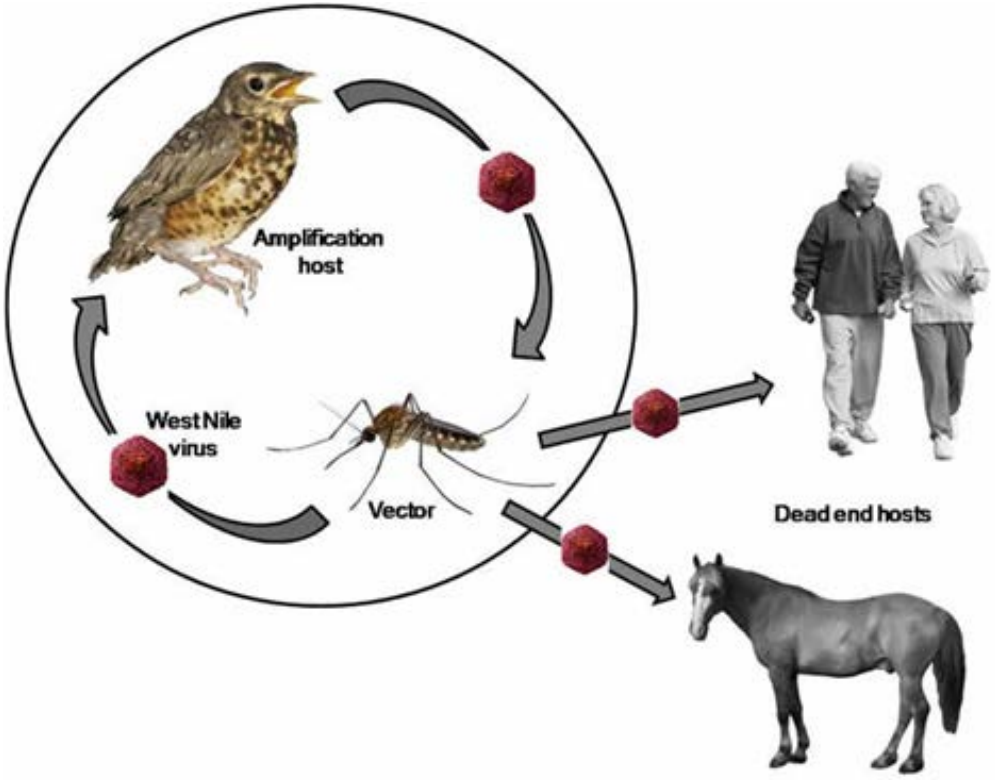
Environmental Risk Factors

- Time spent outdoors
- Residence near one or more tree holes
- Abundance of the Asian Tiger mosquito

Erwin PC, Jones TF, Gerhardt RR, Halford SK, Smith AB, Patterson LE, Gottfried KL, Burkhalter KL, Nasci RS, Schaffner W. La Crosse encephalitis in Eastern Tennessee: clinical, environmental, and entomological characteristics from a blinded cohort study. *Am J Epidemiol.* 2002 Jun 1;155(11):1060-5.

Other Zoonotic Arboviruses

- West Nile virus
- Eastern Equine Encephalitis virus
- Saint Louis Encephalitis virus



- Less common in NC
- Vectors are primarily nocturnal
- EEE has high CFR

Mosquito-borne Disease: Travel

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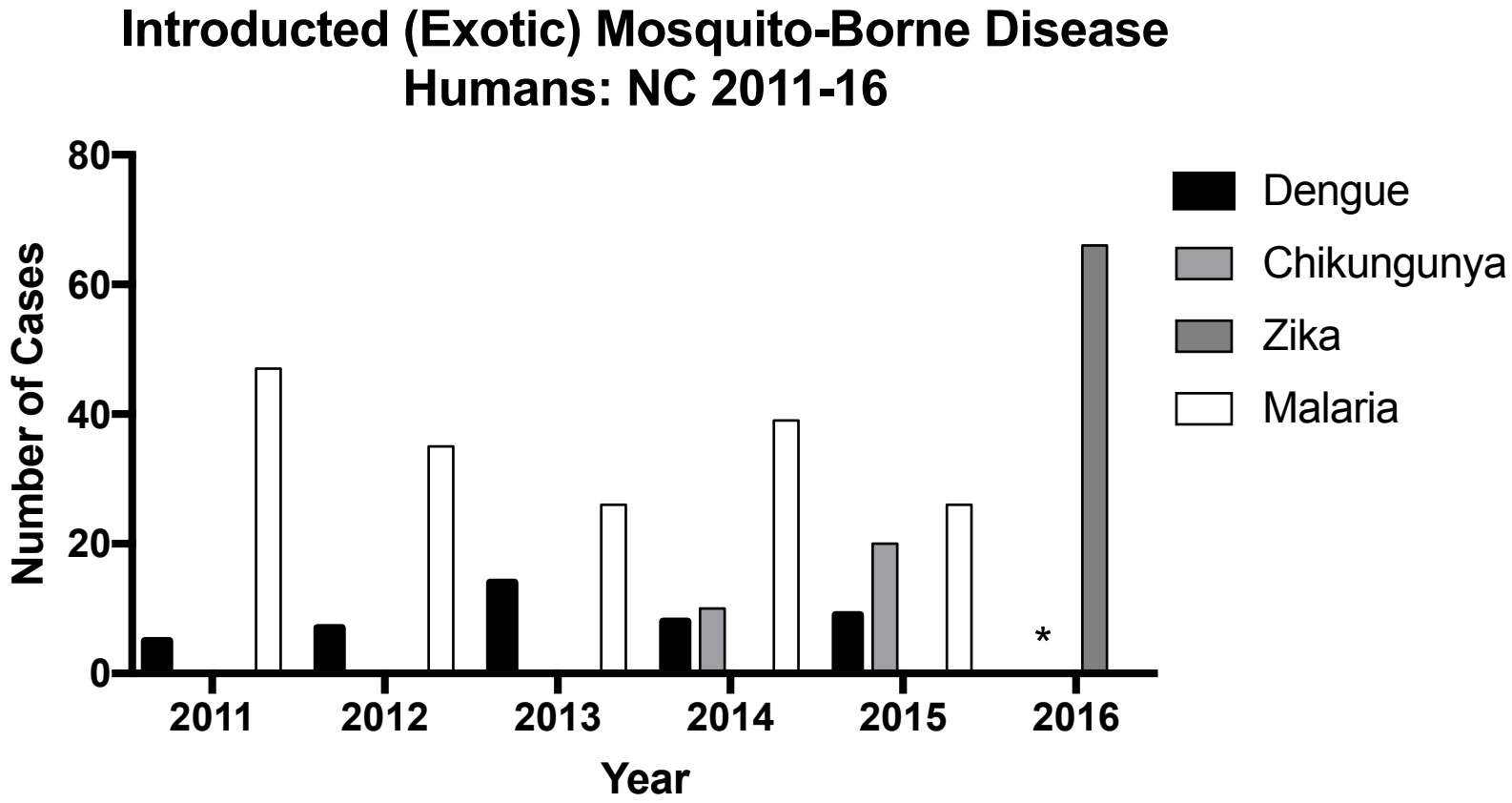
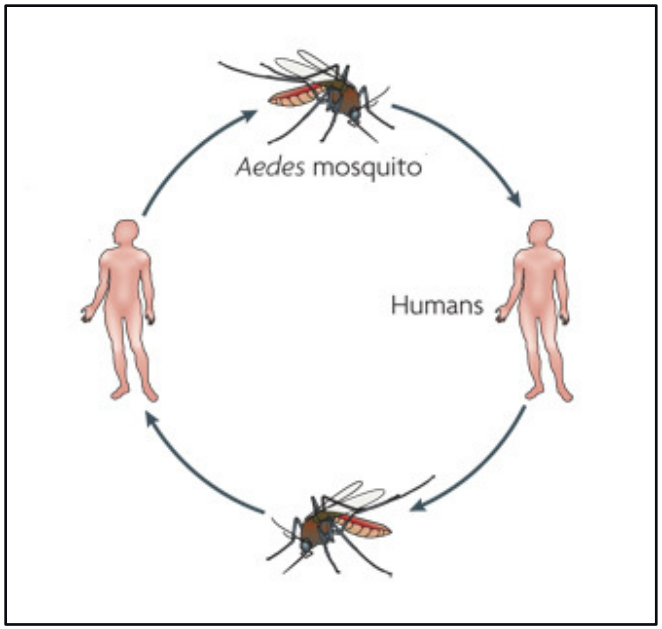
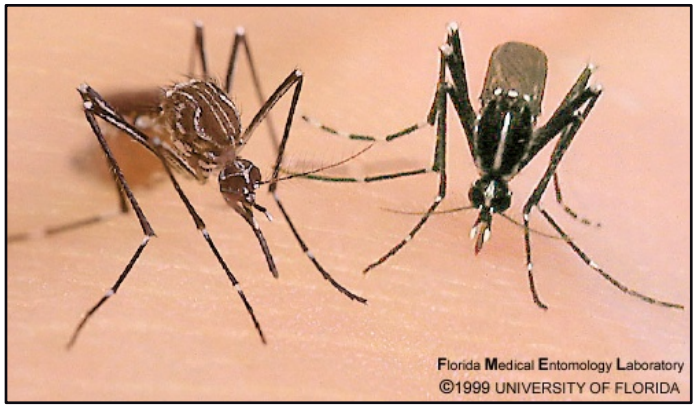


*DEN/CHIK/Malaria Data Not Currently Available

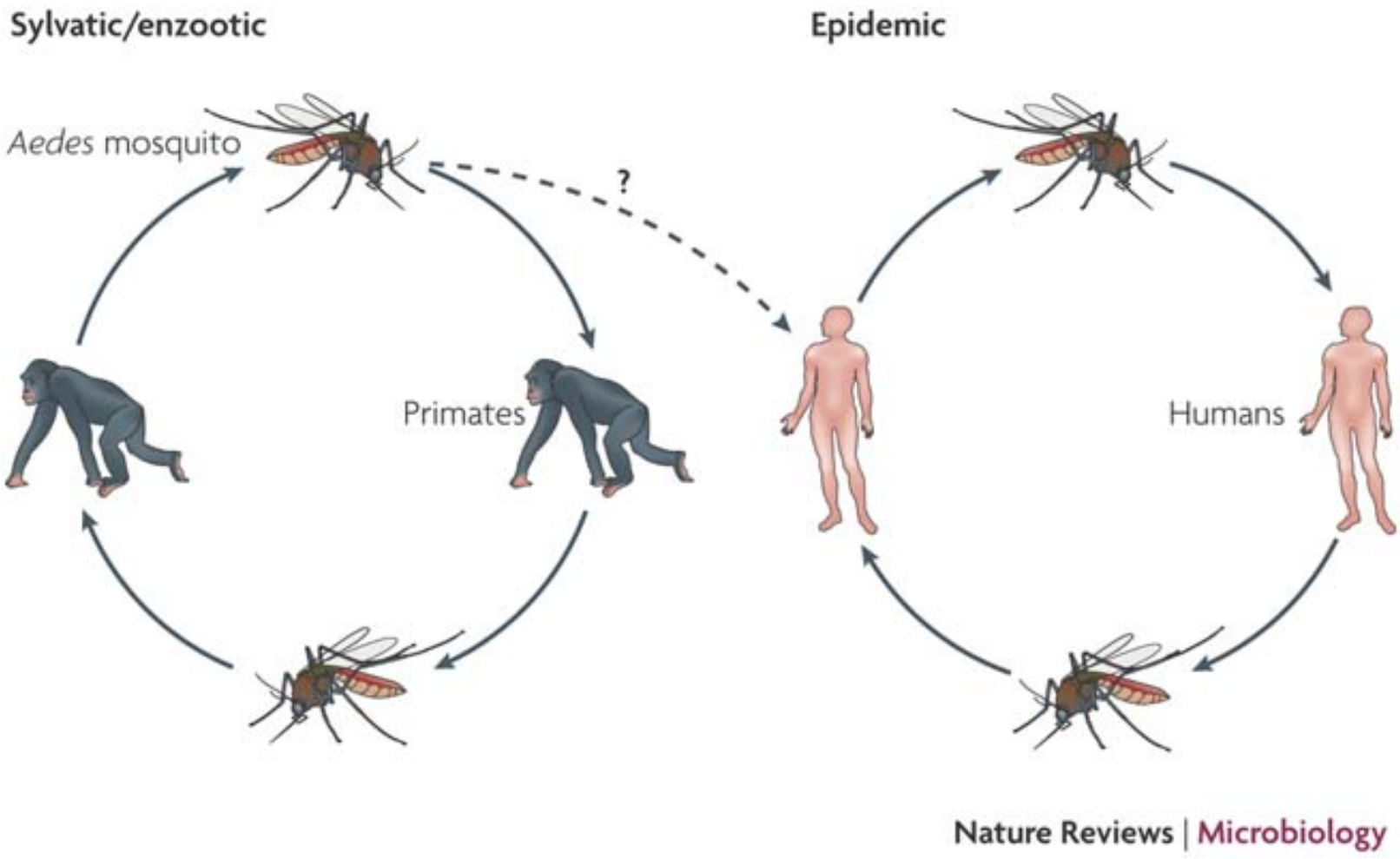
Anthroponotic Arboviruses

- **Epidemic Transmission**
  - Human-Mosquito-Human
- **CHIKv: Alphavirus**
- **Dengue: Flavivirus**
- **Zika: Flavivirus**
- **Peridomestic Transmission:**
  - *Aedes* mosquitoes
    - *Aedes aegypti*
    - *Aedes albopictus*



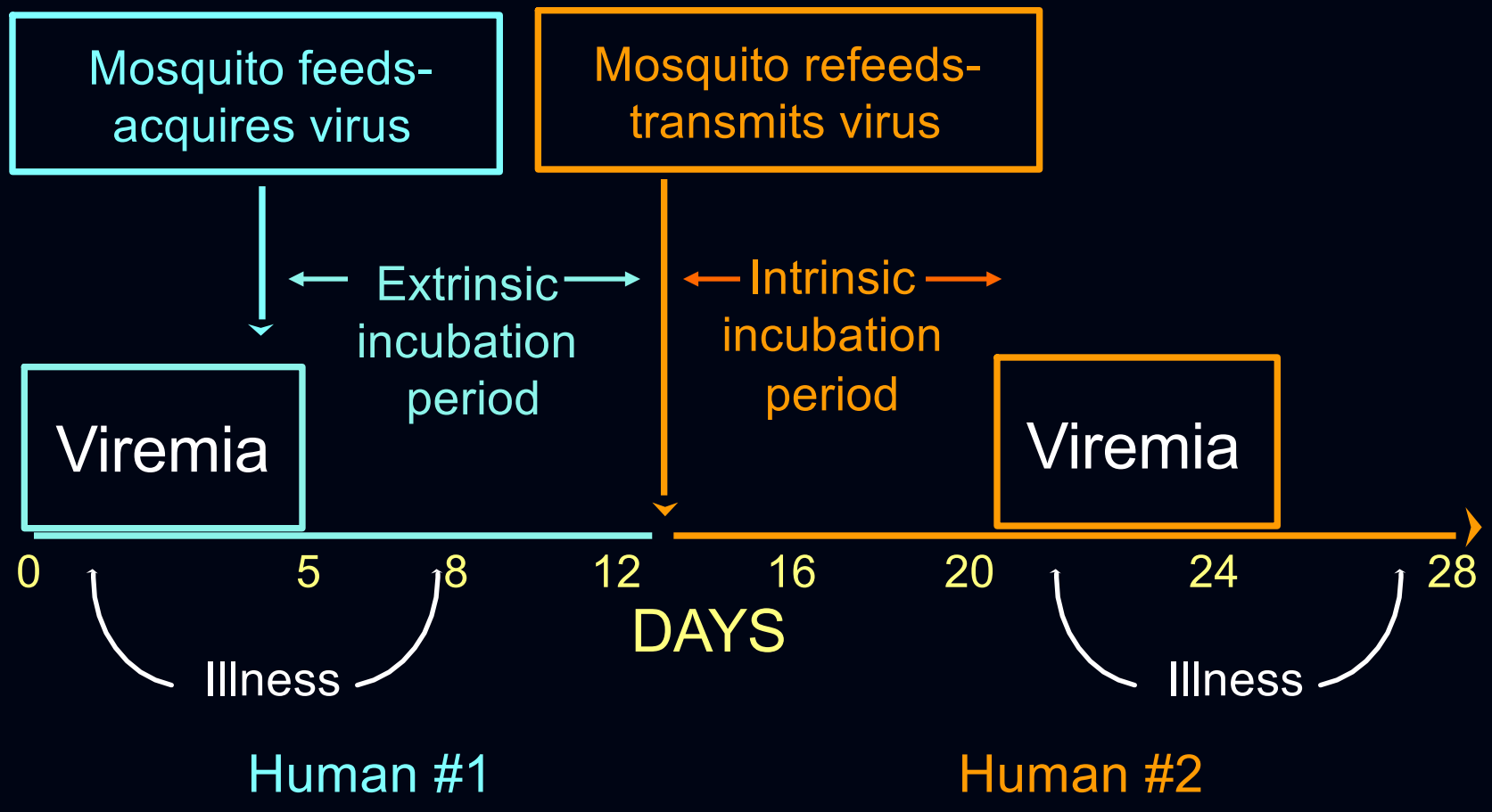


Anthroponotic Arboviruses



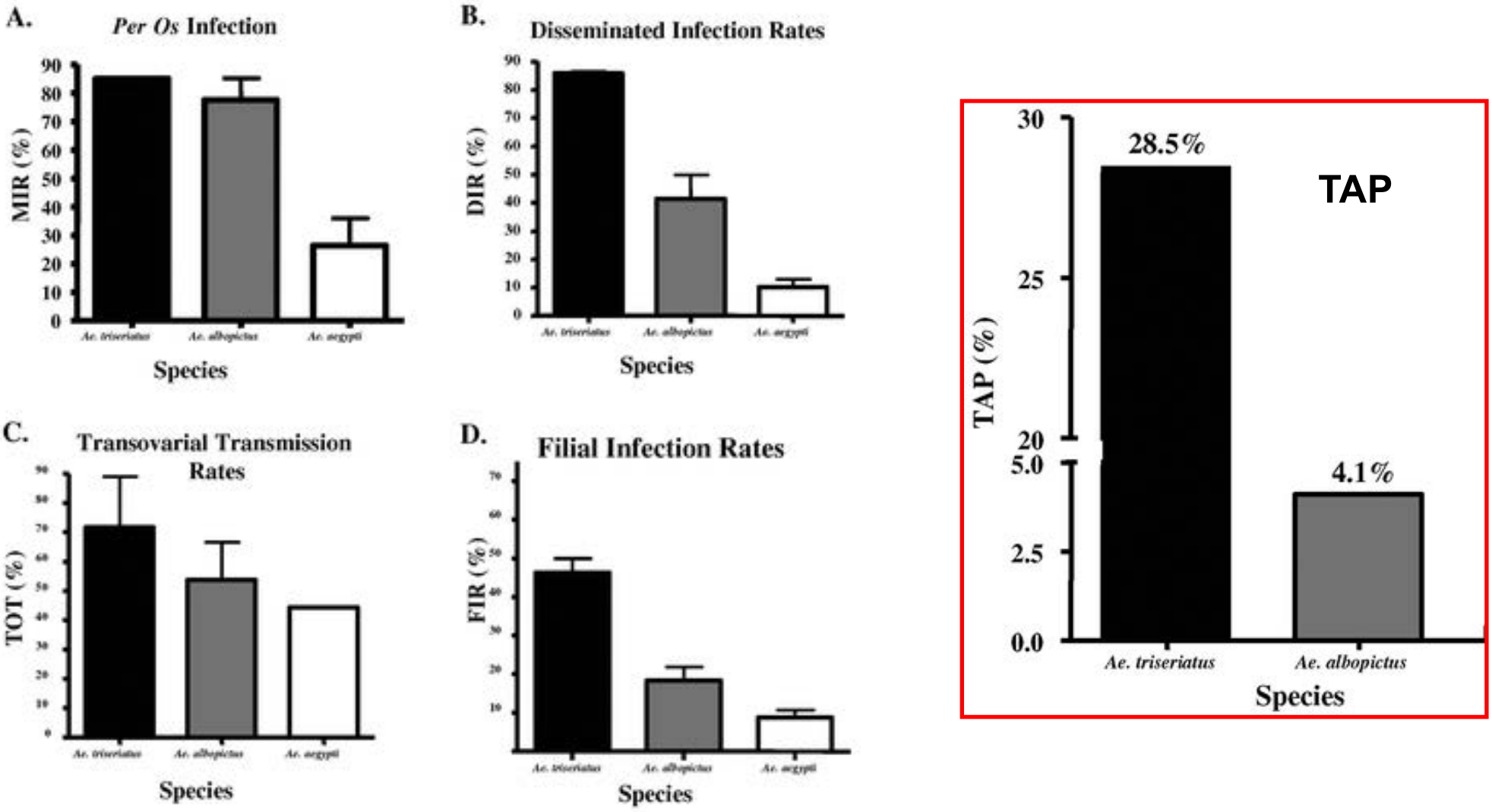
Dengue, Chikungunya, and Zika viruses: Identical Epidemic Vectors

Epidemic Transmission



Consider these transmission dynamics in the context of laboratory diagnostics

Transmission Amplification Potential



Hughes MT et al. Comparative potential of *Aedes triseriatus*, *Aedes albopictus*, and *Aedes aegypti* (Diptera: Culicidae) to transovarially transmit La Crosse virus. J Med Entomol. 2006 Jul;43(4):757-61.

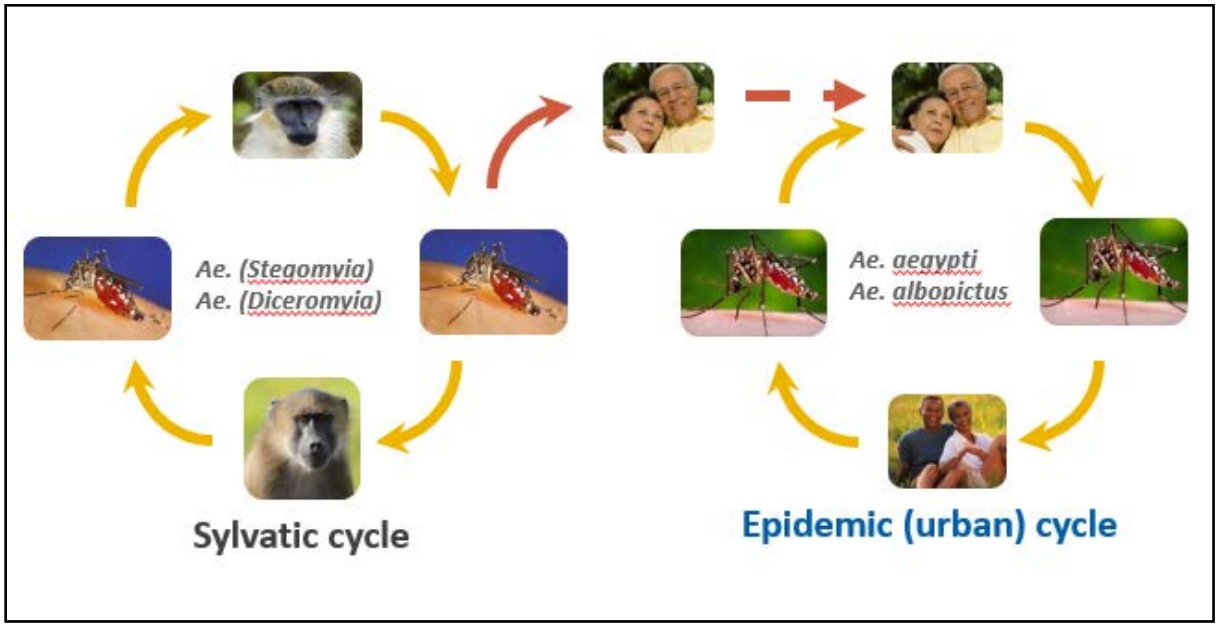
Vectorial Capacity

$$C = \frac{ma^2\,(P^n)V}{(-\ln P)}$$

ma = bites per human per day (biting rate)
P = probability of daily survival
n = extrinsic incubation period
V = vector competence (innate transmission efficiency)

Zika Virus

- **Flavivirus named after Zika forest, Uganda**
  - Isolated in 1947 (*Rhesus*) and 1948 (*Ae. africanus*)
  - Global travel has resulted in the introduction of this virus into Europe, Americas, Pacific Islands, etc.



Selected images from H. Savage/John Paul Mutebi (CDC)

Probable non-vector-borne transmission of Zika virus, Colorado, USA.

Foy BD, Kobylinski KC, Chilson Foy JL, Blitvich BJ, Travassos da Rosa A, Haddow AD, Lanciotti RS, Tesh RB. *Emerg Infect Dis.* 2011 May;17(5):880-2.

Zika Infection

Western Carolina University

Transmission

- Mosquito-borne
- Mother to child
- Sex
- Blood Transfusion
- Lab Exposure

Theoretical:
-Organ or tissue transplant
-Breast Milk (Viral RNA detected)

Yap Island Outbreak: 2007

Symptoms	N (n=31)	%
Macular or papular rash	28	90%
Subjective fever	20	65%
Arthralgia	20	65%
Conjunctivitis	17	55%
Myalgia	15	48%
Headache	14	45%
Retro-orbital pain	12	39%
Edema	6	19%
Vomiting	3	10%

Duffy M. N Engl J Med 2009

Infection Rates: 73% (95% CI: 68-77)
Symptomatic Rate: 18% (95% CI: 10-27)

French Polynesia: 2013

- **1st Reported hospitalization from Zika**
  - Guillian-Barré syndrome (GBS)
  - Case-Control Study:
    - 98% GBS cases with Zika IgM
- **Perinatal transmission described**
- **No microcephaly noted at the time**
  - Microcephaly noted in retrospective analysis

Besnard M, et al. . Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014. Euro Surveill. 2014 Apr 3;19(13)
Cao-Lormeau VM, et al. Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. *Lancet*. 2016 Feb 29.
Cauchemez S, et al. Association between Zika virus and microcephaly in French Polynesia, 2013-15: a retrospective study. *Lancet*. 2016 Mar 15.

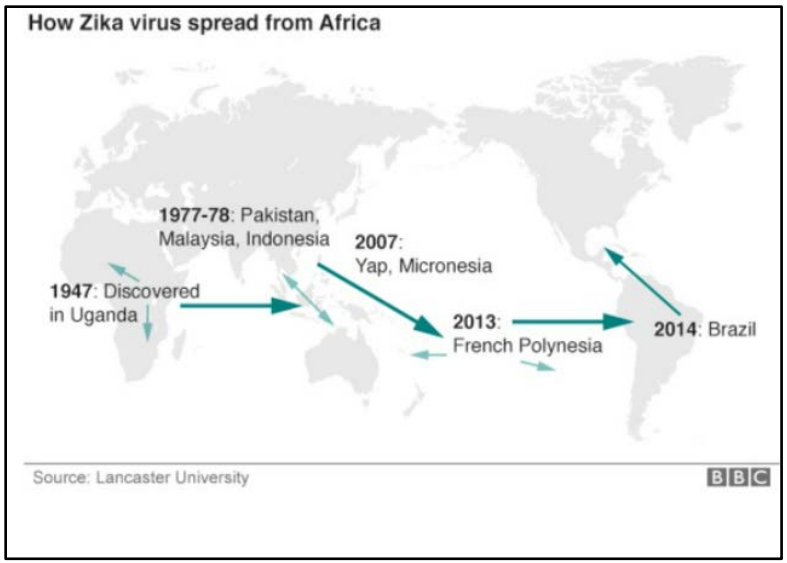
Microcephaly Evidence

- **Epidemiology:**
  - Chronologically/spatially associated with Zika
  - Virus Isolation:
    - Amniotic fluid of infants with microcephaly
    - Brain of fetuses with microcephaly
- **IgM Antibodies**
  - In microcephalic babies (Brazil)
  - Not maternal antibodies

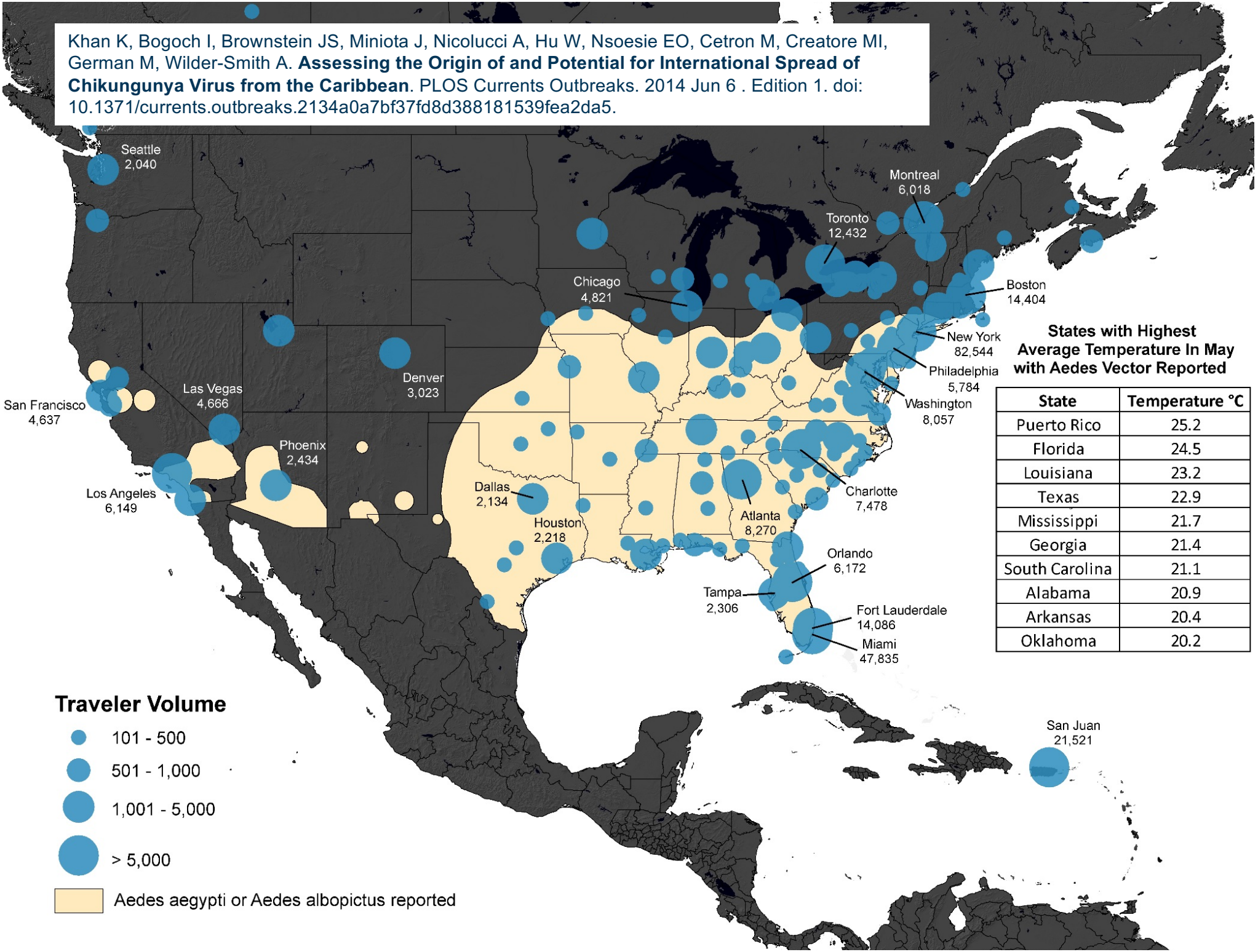
Evidence of microcephaly risk from Zika infection during pregnancy is major concern.

Rapid Spread in New World

- Completely immunologically naïve population
- Environmental/ecological conditions
- Presence of both known epidemic vectors
- Insufficient/unavailable public health response
- High viremias/duration of viremia



Khan K, Bogoch I, Brownstein JS, Miniota J, Nicolucci A, Hu W, Nsoesie EO, Cetron M, Creatore MI, German M, Wilder-Smith A. **Assessing the Origin of and Potential for International Spread of Chikungunya Virus from the Caribbean**. PLOS Currents Outbreaks. 2014 Jun 6 . Edition 1. doi: 10.1371/currents.outbreaks.2134a0a7bf37fd8d388181539fea2da5.



States with Highest Average Temperature In May with Aedes Vector Reported

State	Temperature °C
Puerto Rico	25.2
Florida	24.5
Louisiana	23.2
Texas	22.9
Mississippi	21.7
Georgia	21.4
South Carolina	21.1
Alabama	20.9
Arkansas	20.4
Oklahoma	20.2

Zika Vectors

- ***Aedes aegypti***
  - Very closely associated with people
  - Does not depend greatly on vegetation
  - Indoor/outdoor (resting, biting, oviposition)
  - Urban/suburban/rural areas
  - Greater resistance to desiccation
  - Main DEN/CHIK/Zika vector

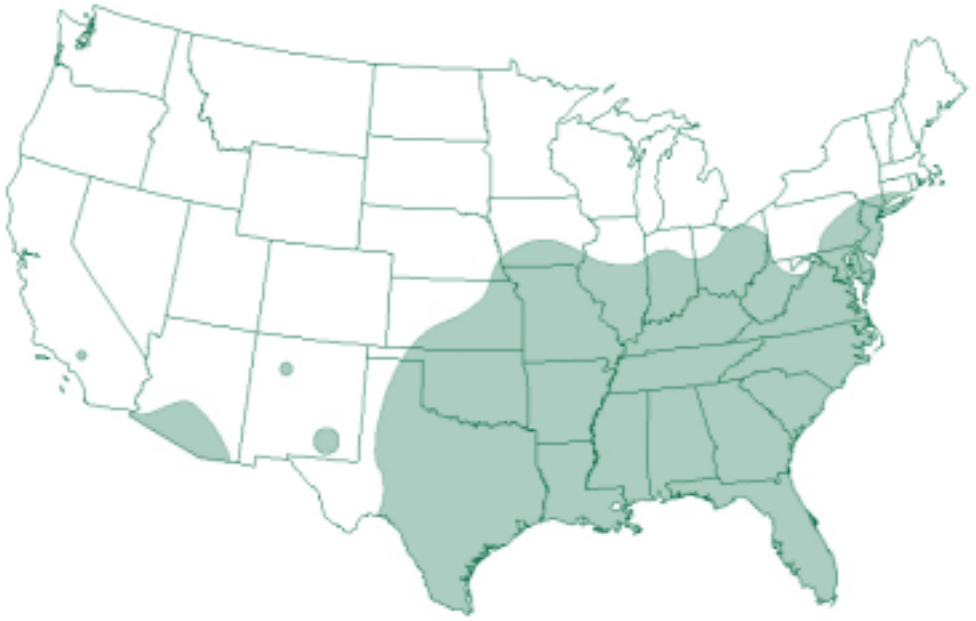
- ***Aedes albopictus***
  - Less dependent on people
  - Rests in/near vegetation
  - Outdoor mosquito
  - Suburban/rural areas
  - Greater cold hardiness
  - In some areas, may be main DEN vector

Both: Container Inhabiting

Adapted from R. Barrera (DB/CDC)

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

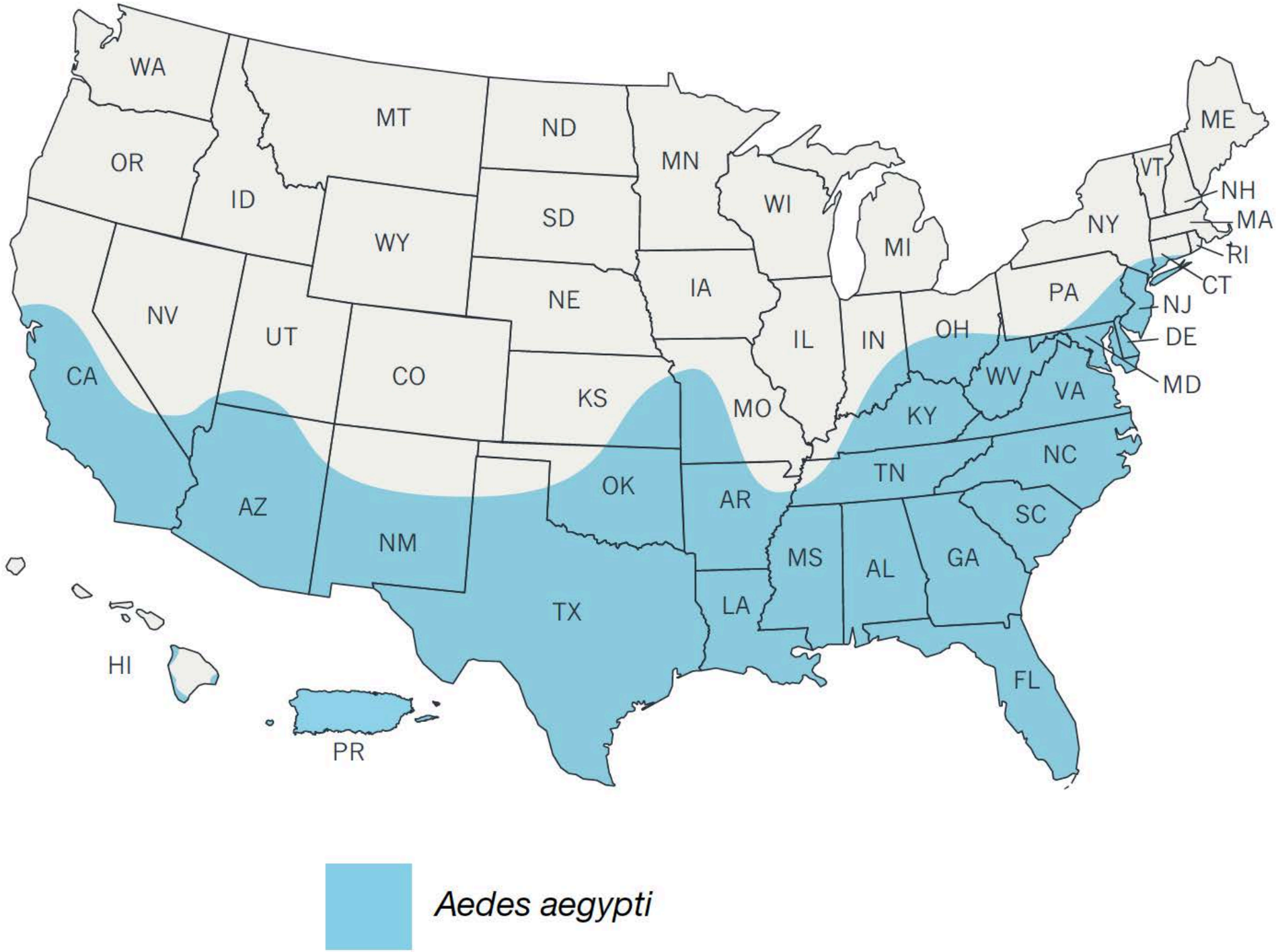
Aedes aegypti



Aedes albopictus

Slide from H. Savage (CDC)

"Estimated Potential Range of *Aedes aegypti*"



NC Ovitrap Survey
(May-Oct 2016)

Western Carolina University

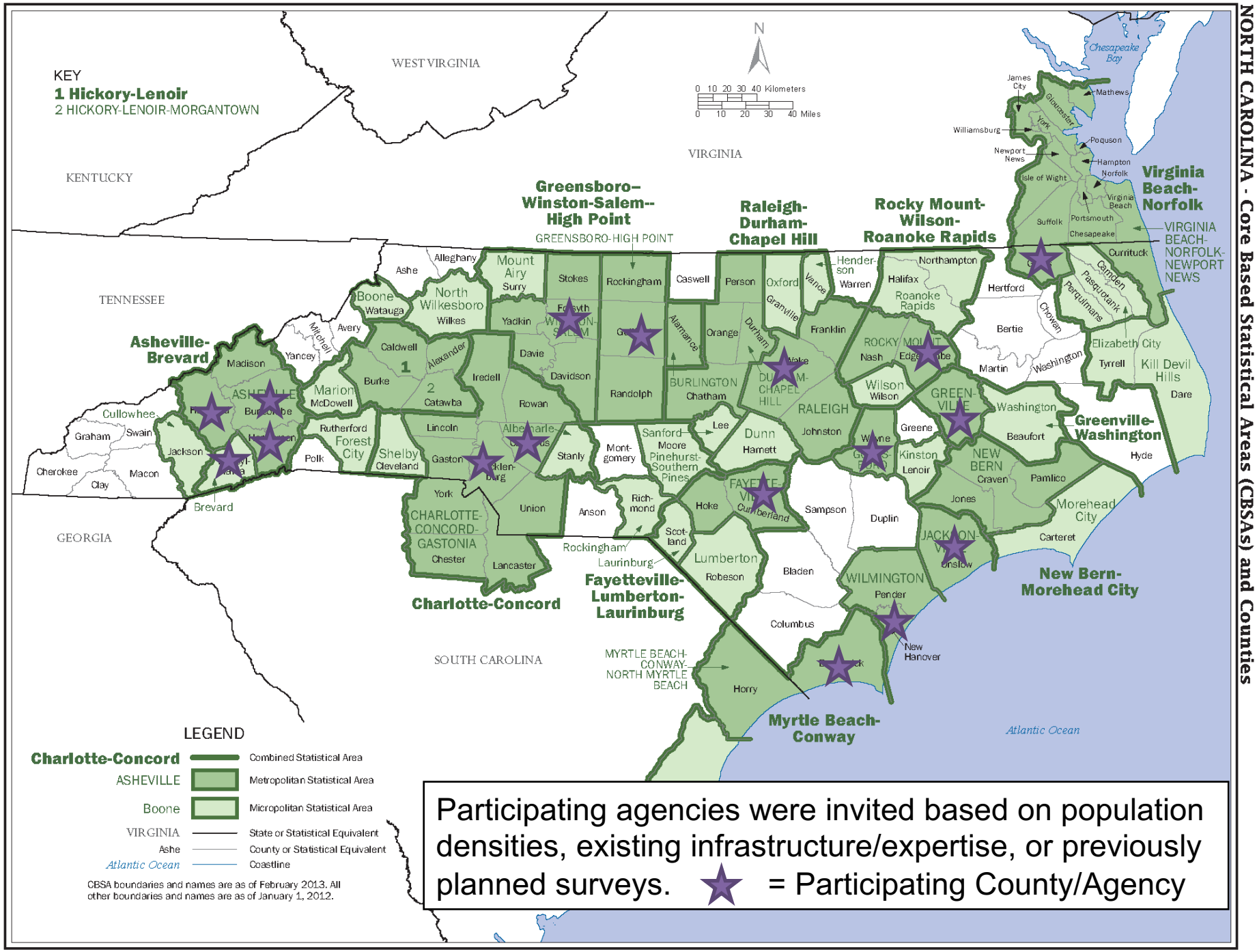
Ovitrap Collections: Container-inhabiting *Aedes* eggs will be collected using “ovitraps”. Weekly or bi-weekly collections sent to the university labs for hatching and identification.

Ovitraps
(“egg traps”)

Aedes eggs
(magnified)

U.S. DEPARTMENT OF COMMERCE Economics and Statistics Administration U.S. Census Bureau

NORTH CAROLINA - Core Based Statistical Areas (CBSAs) and Counties



A metro area contains a core urban area of 50,000 or more population. Each metro area consists of one or more counties and includes the counties containing the core urban area, as well as any adjacent counties that have a high degree of social and economic integration (as measured by commuting to work) with the urban core.

2016 Ovitrap Participants

- **Western Carolina University (Byrd)**
  - Buncombe, Henderson, Haywood, Transylvania, Mecklenburg, Cabarrus
- **East Carolina University (Richards)**
  - Brunswick, Onslow, New Hanover, Pitt, Gates, Currituck, (DOD: Camp Lejeune, SJAFB)
- **North Carolina State University (Reiskind)**
  - Edgecombe, Wake, Forsyth, Guilford, Cumberland

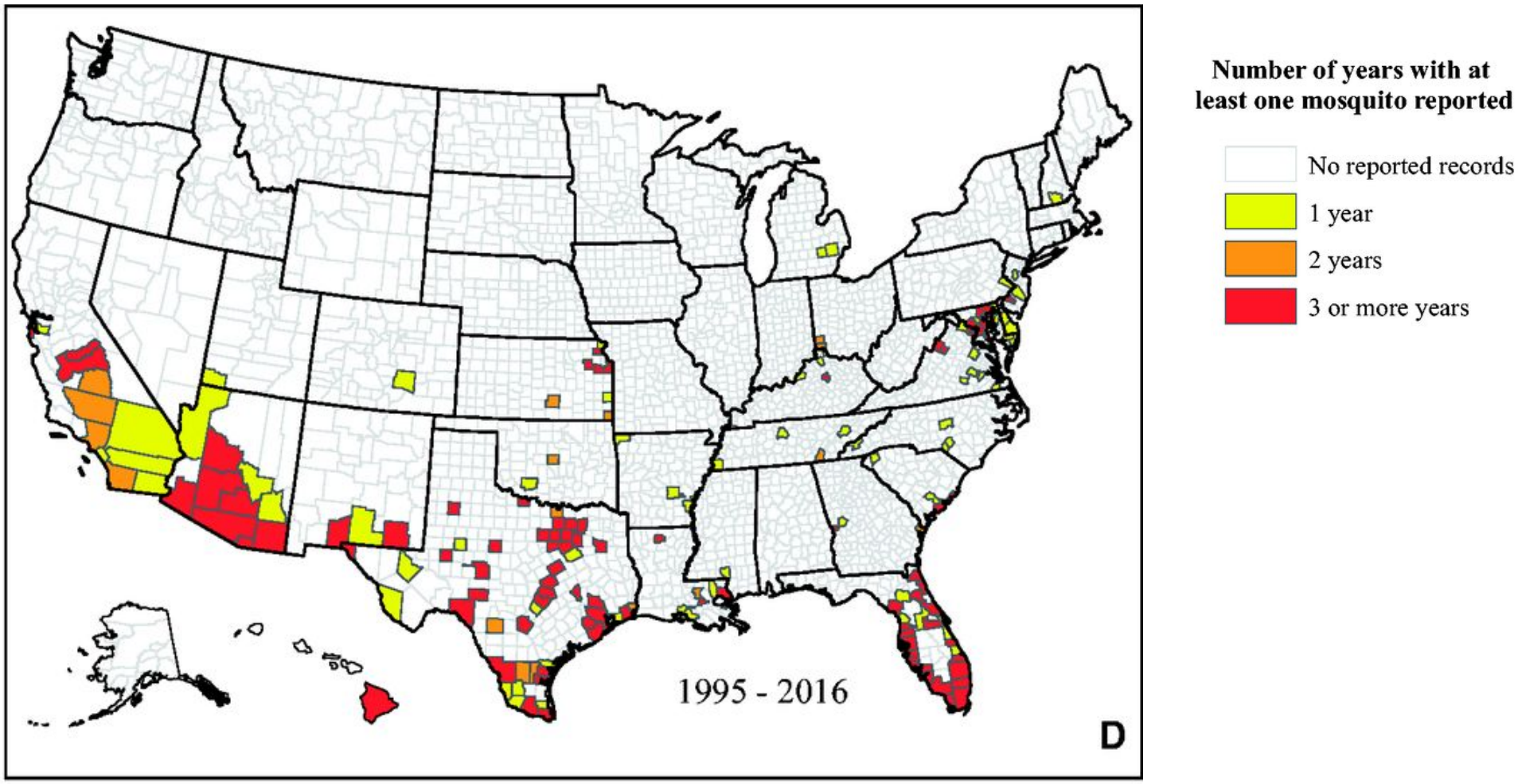
Ovitrap Results (10/2016)

University	Eggs	Identified	*Ae. albopictus*	*Ae. triseriatus*	*Ae. japonicus*	*Ae. aegypti*
ECU	88,556	15,904	14,922	719	263	0
NCSU	123,164	24,699	22,370	1,584	745	0
WCU	66,482	21,975	13,272	4,475	4,228	0
Totals	278,202	62,637	50,564 (80.7%)	6,778 (10.8%)	5,236 (8.4%)	0

To date, more than 278,202 *Aedes spp*. eggs have been received by the universities and 62,637 mosquitoes have been identified to species by microscopy. At present, no *Aedes aegypti* have been identified in the submissions. More than 99.9% of the ovitrap collections are represented by 3 species: 80.7% (n=50,564) of the identified *Aedes* are *Aedes albopictus*, 10.8% (n=6,778) are *Aedes triseriatus*, and 8.4% (n=5,236) are *Aedes japonicus*. The percentages of *Aedes japonicus* and *Aedes triseriatus* vary regionally, but *Aedes albopictus* is the primary container inhabiting *Aedes* in the participating counties according to the ovitrap data. Temporal trends and relative abundance data will be assessed both regionally and at a county level for publication and distribution in Dec 2016.

Preliminary Data

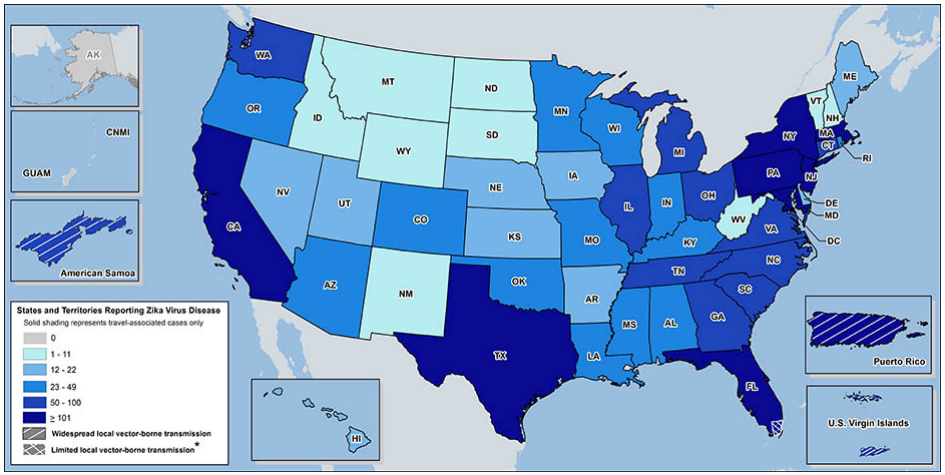
Aedes aegypti (Reported Occurrence by County: 1995-2016)



Hahn MB, Eisen RJ, Eisen L, Boegler KA, Moore CG, McAllister J, Savage HM, Mutebi JP. Reported Distribution of *Aedes (Stegomyia) aegypti* and *Aedes (Stegomyia) albopictus* in the United States, 1995-2016 (Diptera: Culicidae). J Med Entomol. 2016(June)

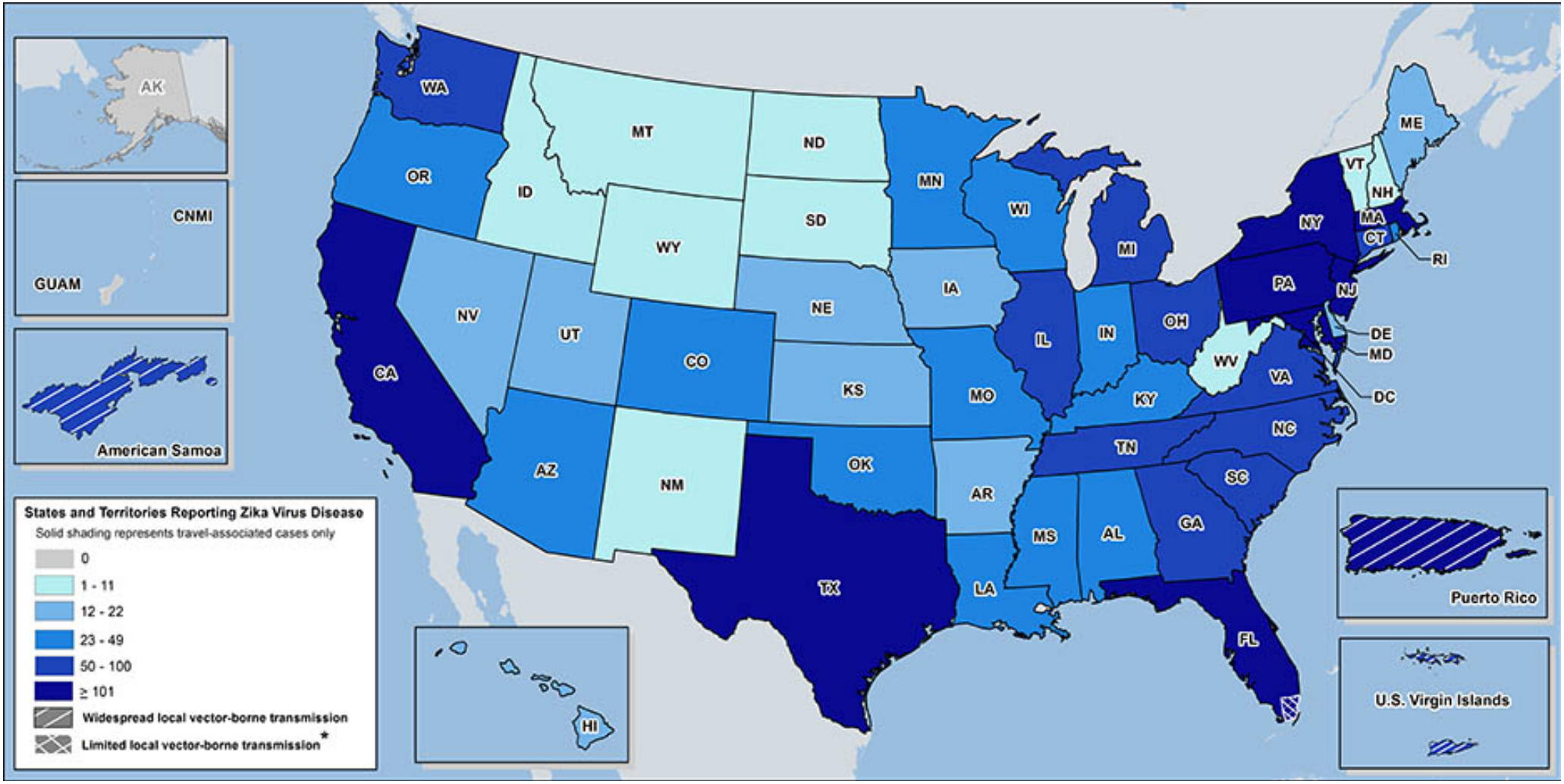
Zika in US: Oct. 26

- **Travel-associated virus disease cases**
  - 3,951 (US Total)
  - 72 (North Carolina)
- **Locally acquired vector-borne cases**
  - 139 (FL)
  - None (NC)
- **Infections in pregnancy**
  - 953
- **Other:**
  - Sexually transmitted: 33
  - Guillain-Barré: 13



Zika in US (Oct. 26th)

Western Carolina University



Challenges Ahead….

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- **Majority of cases are asymptomatic**
- **Importance of Zika STIs?**
  - Non-vector local transmission
  - Pregnancy/Microcephaly
- **Diagnostic limitations**
  - Cross reactivity
  - Delays
- **Limited state-wide mosquito control capacity**

NC Zika Response (Vector)

Western Carolina University

- **ICS: Zika Preparedness (DHHS)**
- **Recruit Public Health Entomology Expertise**
  - University Vector Biologists/PH Entomologists
    - PHPR: Contract Entomologists
  - Recruit & Hire PH Entomologist
    - NC DHHS Permanent Employee (DPH/CDB)
- **Determine and map presence of Zika vectors**
  - Initial Survey 2016 (PHPR/EH)
  - University and Local HD

NC Zika Response (Vector)

Western Carolina University

- **Respond to viremic cases**
  - "Public Health Entomology Response Team"
  - Assess entomologic and environmental risks at viremic case residences (DHHS/PH Ento/LHDs)
- **Aid to County**
  - Ebola Response
  - State (170K) /Federal ELC (100K) Funds
    - Set up 10 regional surveillance hubs through AA
    - In Progress
- **Leverage Additional Federal Funding (Supp. ELC)**

Mike Doyle (DHHS)

Michael S. Doyle
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Final Notes:

- **For all mosquito-borne diseases in NC:**
  - "Prevention is the Cure"
  - No specific treatments/cure
  - Avoid mosquito bites:
    - Wear insect repellent
    - Cover up!
    - Use air conditioning if available
    - Repair and use window/door screens
  - Source reduction (eliminate larval habitats)
    - "Tip or Toss" containers around house

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