




Epidemiology and Clinical Impact of West Nile in Texas

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Pediatrics

Emerging Arboviruses in Texas:

- **Dengue**
  - First recognized outbreak of dengue-like illness in 1895-1896: more than 16,000 cases in Austin area*
  - 1922: more than 500,000 cases ("Galveston outbreak")*
- **St. Louis encephalitis virus**
  - First identified in 1933, first recognized outbreak in Texas in 1964
- **West Nile virus**
  - Introduced to US in 1999 and Texas in 2002
- **Chikungunya virus**
  - 1st locally acquired case reported 2016
- **Zika virus**
  - 1st locally acquired case reported 2016

*Beaumier et al. Current Tropical Medicine Reports, 2014

West Nile Virus

- Natural transmission → mosquito vector
  - Houston: *Culex quinquefasciatus*
  - Birds are reservoir host

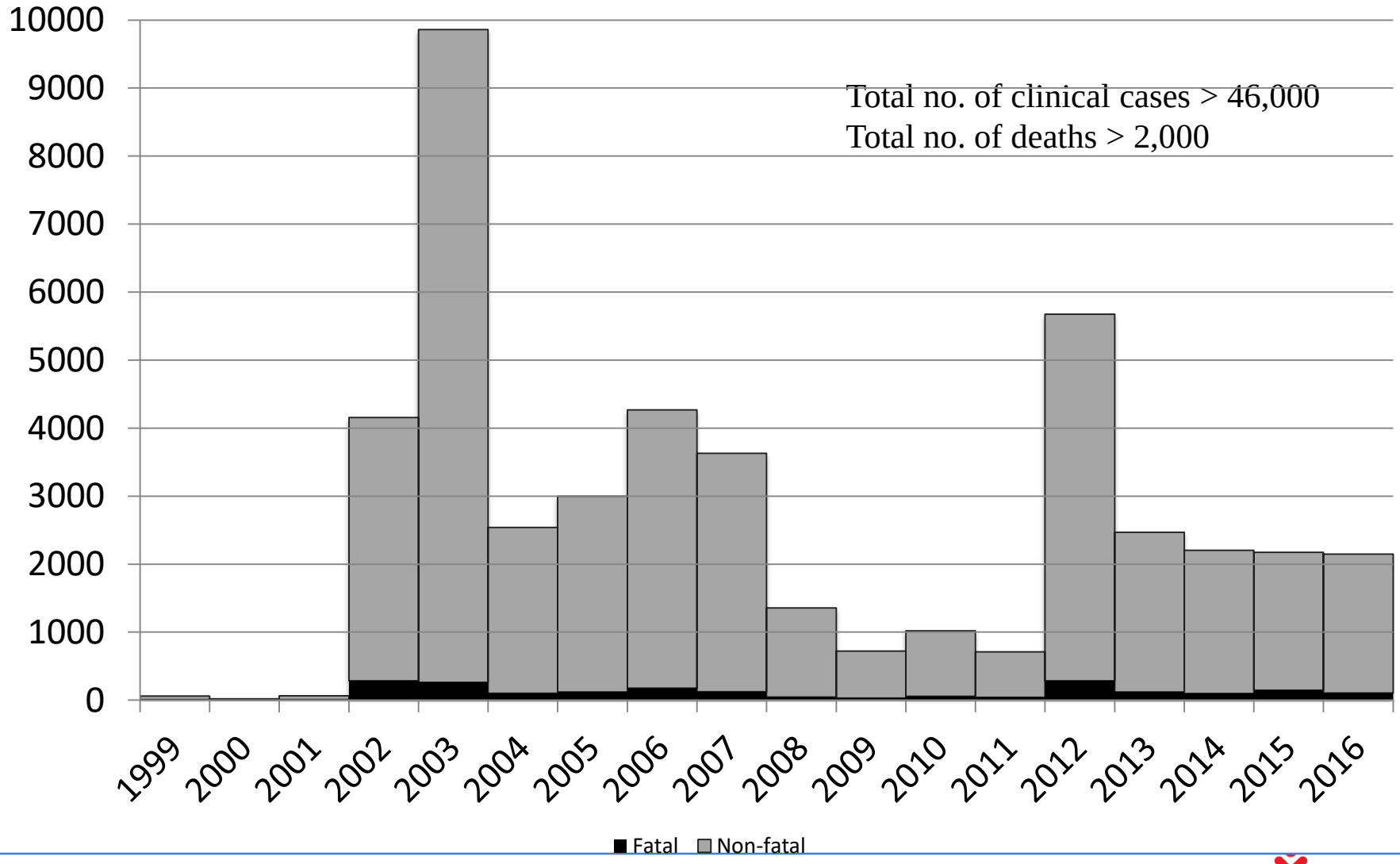
- Newly discovered means of transmission with WNV in humans (2002)
  - Transplant
  - Transfusion
  - Transplacental
  - Breastfeeding
  - Laboratory acquired
  - Sexual?

West Nile Virus
Clinical Features in Humans

- Incubation 2 to 15 days
- ~ 80% infected persons asymptomatic
- ~ 20% infected persons flu-like symptoms
- < 1% (1 out of 150) “neuroinvasive disease”
  - WNM: Meningitis
  - WNE: Encephalitis or meningoencephalitis
  - Acute flaccid paralysis
  - 10 % case fatality ratio for those with severe disease

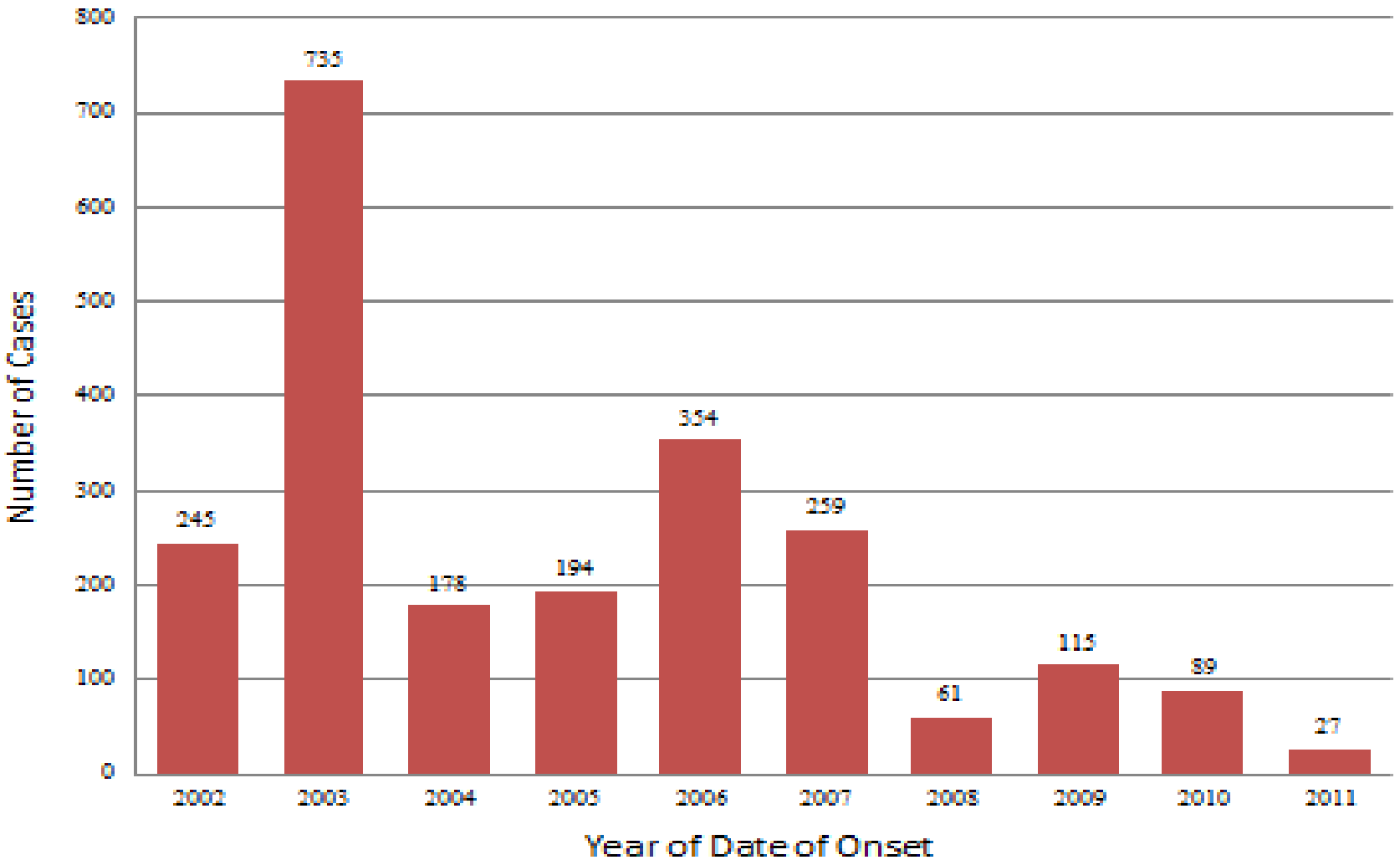
West Nile Virus

Clinical Cases by Year, 1999-2016

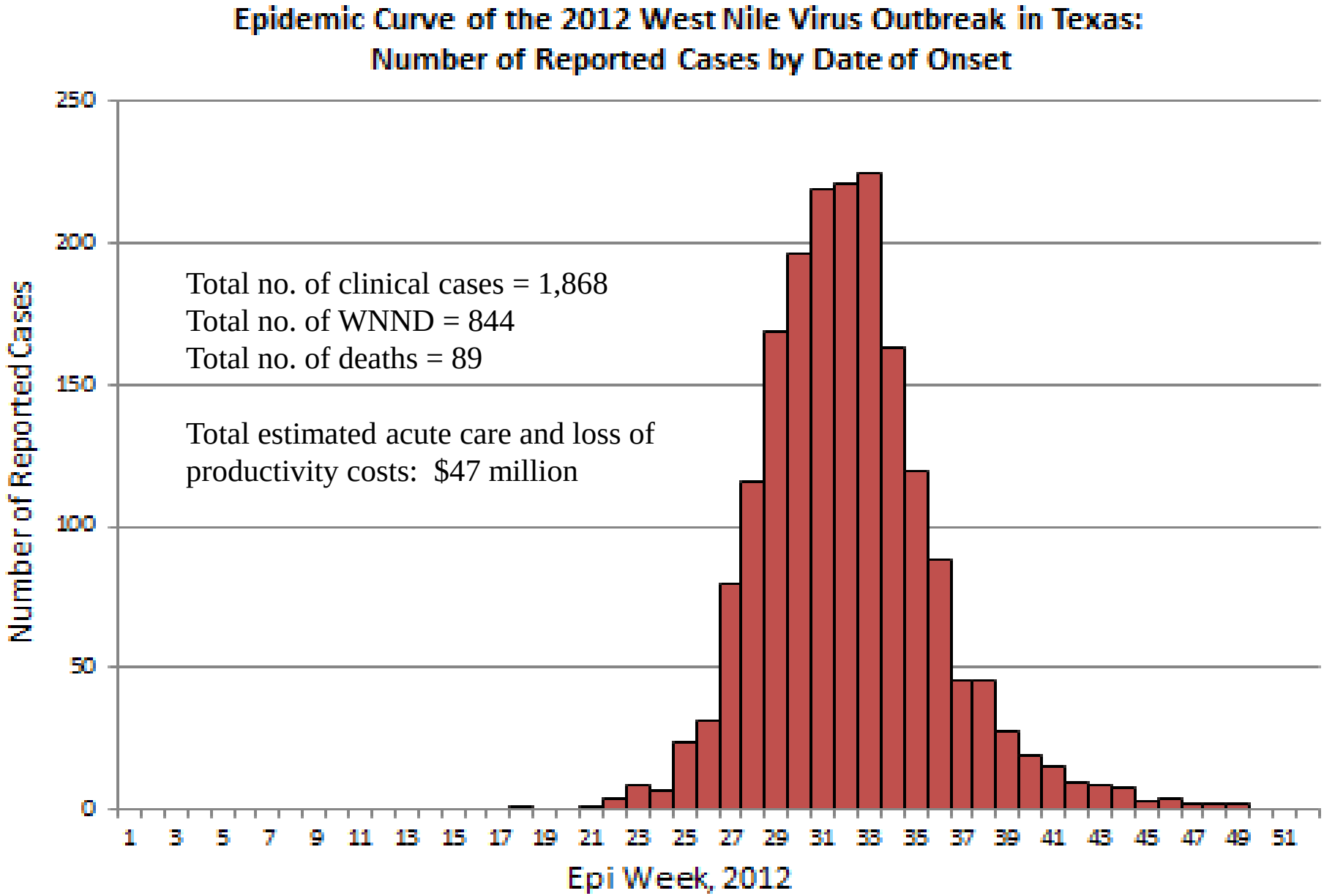


Montgomery and Murray, Expert Rev. Anti Infect. Ther., 2015.

Decade of WNV Transmission in Texas

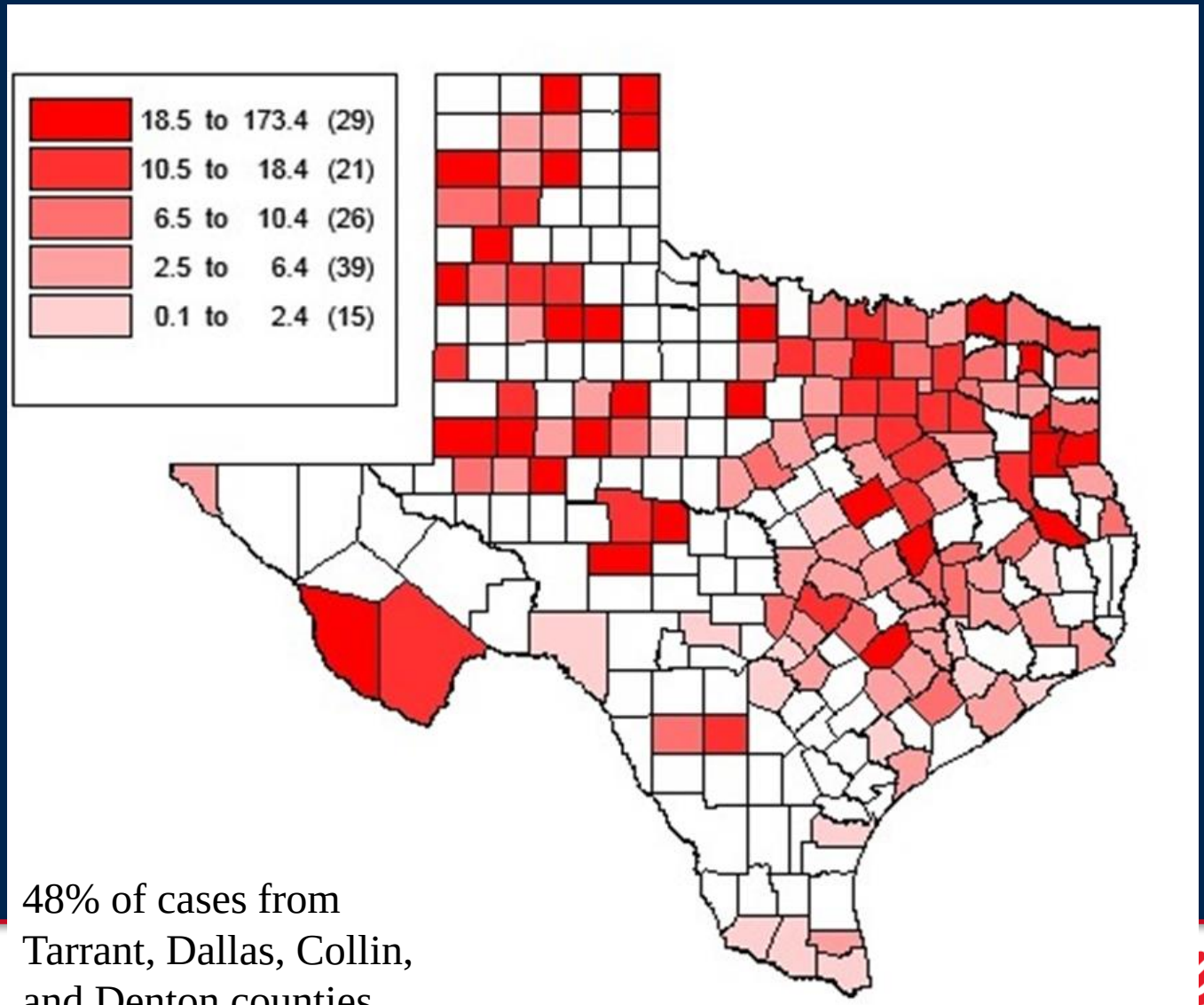


Nolan et al. *Emerging Infectious Diseases*, 2013



Murray et al., *Emerging Infect Diseases*, Nov. 2013

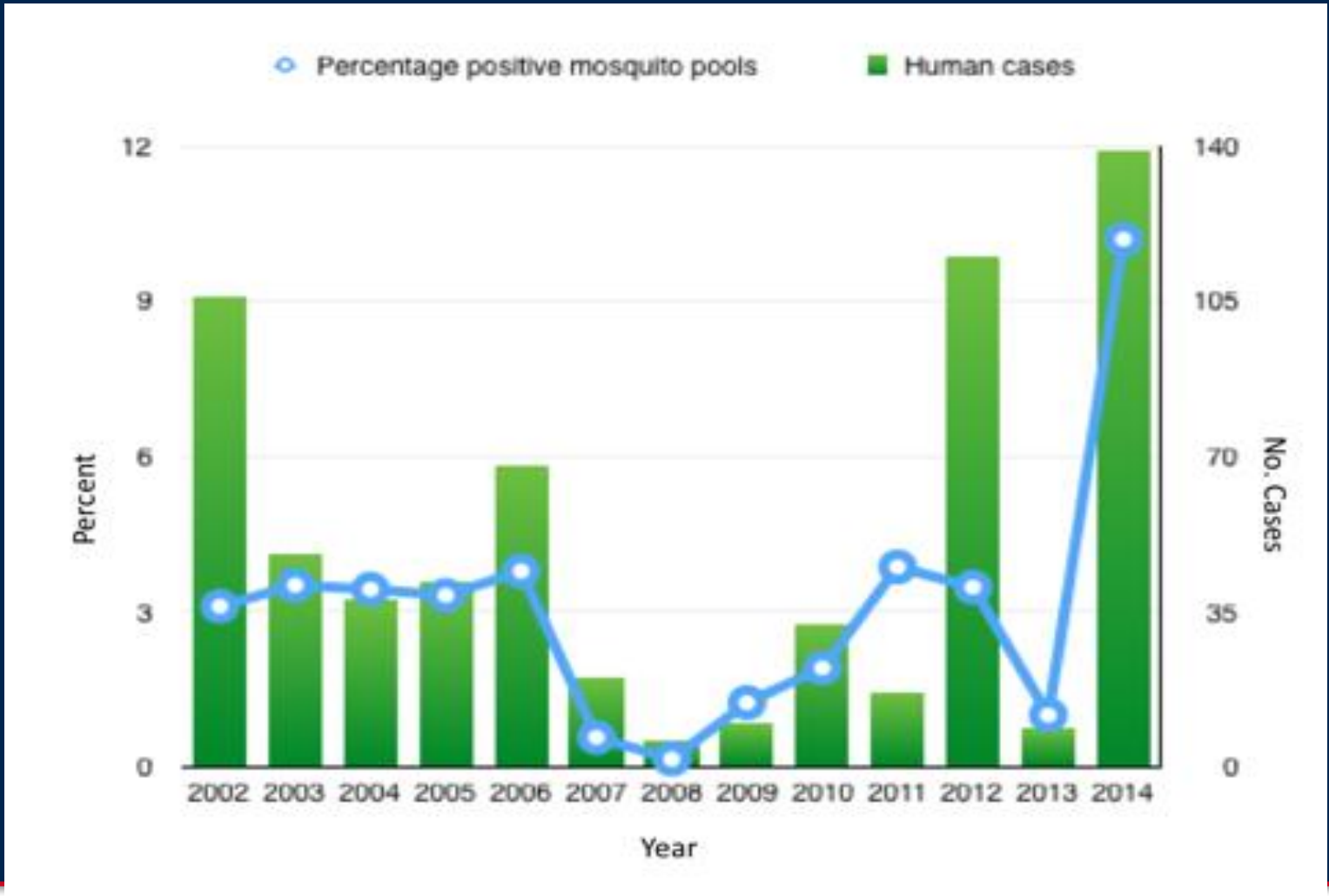
WNV Incidence per 100,000 population in 2012



48% of cases from Tarrant, Dallas, Collin, and Denton counties

Murray et al., EID 2013

Houston 2014 WNV Outbreak



Martinez et al., in press, *Emerging Infectious Diseases*

Pediatrics

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2018 Activity as of mid-September

Study Methods

- Study initiated in 2002 following introduction to Houston
- Cases of WNV identified through local surveillance
- Medical chart abstractions completed on all cases (n=302)
- Cases invited to enroll in 10 year prospective, longitudinal cohort study, 267 cases currently enrolled
  - Interviews and blood draws q. 6 mos
  - Subjective symptoms
  - Objective measurements: CES-D, Barthel Index, MMSE
  - Other studies using the cohort: risk factors for encephalitis and death, clinical predictors for death, genetic susceptibility, immune functioning

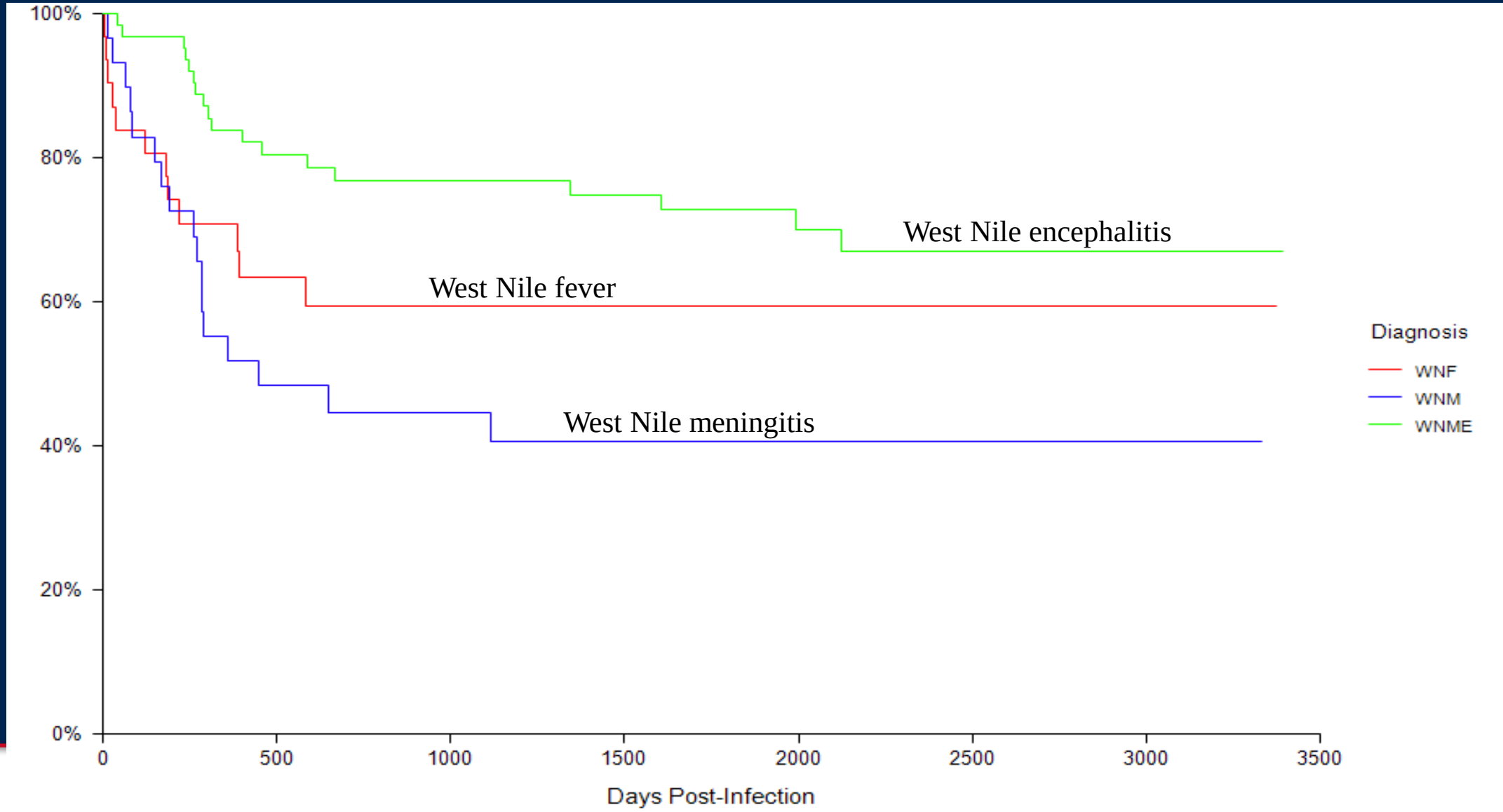
Sequelae following Infection

- 1 year: 60.1%
- 2 years: 46.4%
- 3 years: 40.6%
- 4 years: 38.9%
- 5 years: 41.9%

- Most commonly reported sequelae: depression/personality change, weakness, fatigue, difficulty walking, blurred vision, paralysis, memory loss, confusion, headaches, tremors

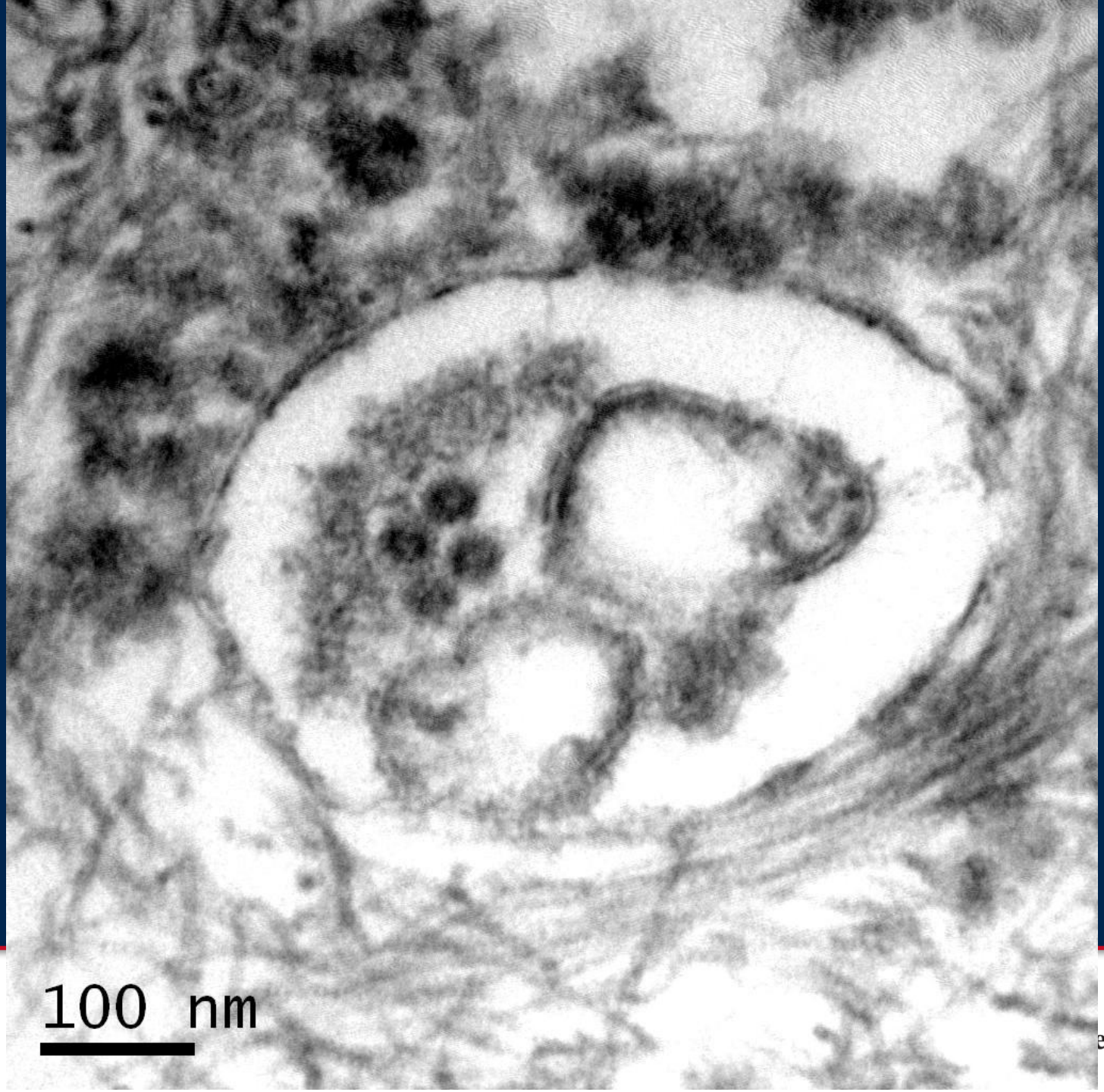
- Depression: 31% new onset depression; 75% have CES-D scores indicative of clinical depression. Can continue up to 8 yrs (Murray et al, EID 2007 and Nolan et al, J Clin Psych 2012)

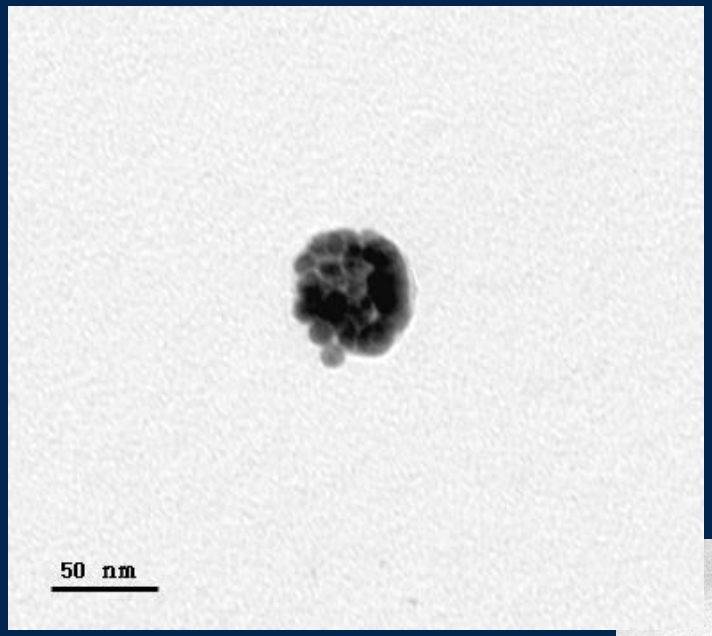
Kaplan-Meier Survival Curve: Percentage of Study Participants Continuing to Report West-Nile Virus-related Symptoms by Days Post-Infection based on Initial Diagnosis



Murray et al. PLoS One, 2014.

	All WNV participants n=139 (%)	Neuroinvasive WNV n=67 (%)	Mild WNV n=44 (%)	Asymptomatic WNV n=28 (%)
CKD Prevalence				
CKD, All Stages	55 (40)	32 (48)	12 (27)	11 (39)
CKD Stages 3-5	13 (10)	9 (13)	3 (7)	1 (4)
CKD Stage 1-2	42 (30)	23 (34)	9 (20)	10 (36)
CKD Indicators				
Proteinuria	36(26)	21(31)	9(20)	6(21)
Hematuria	32(23)	18(27)	7(16)	7(24)
Anemia	80(60)	40(60)	23(58)	17(63)


100 nm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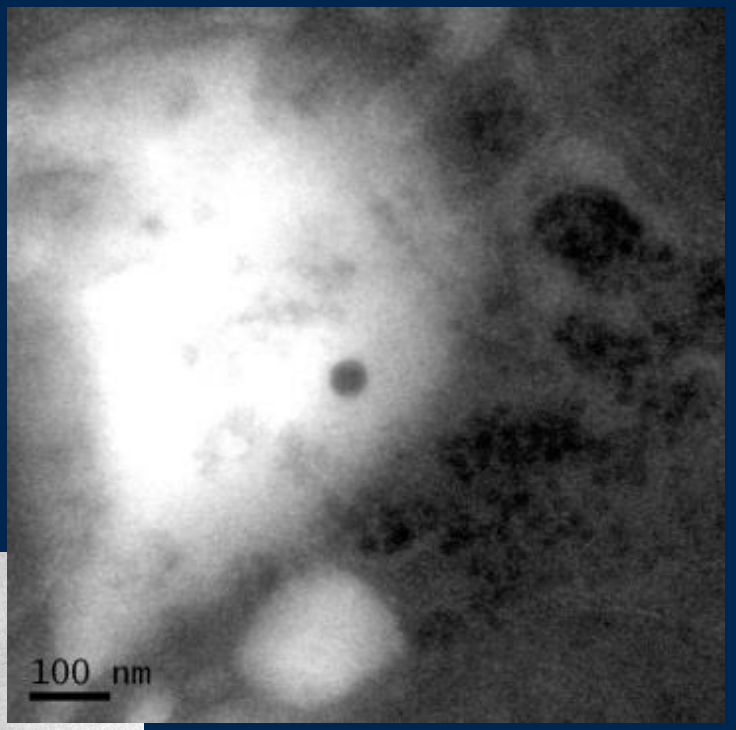
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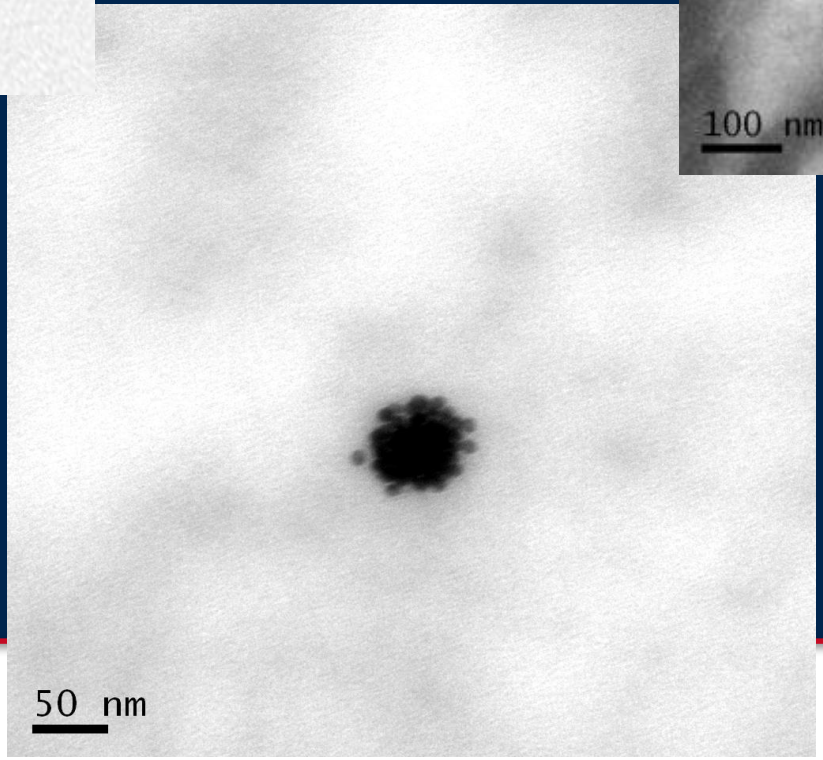

50 nm

West Nile Persistence

- Persistent symptoms, persistent IgM, abnormal cytokine response, progressive kidney disease
  - Persistent infection of kidneys with shedding of viral RNA

- What about CNS persistence?

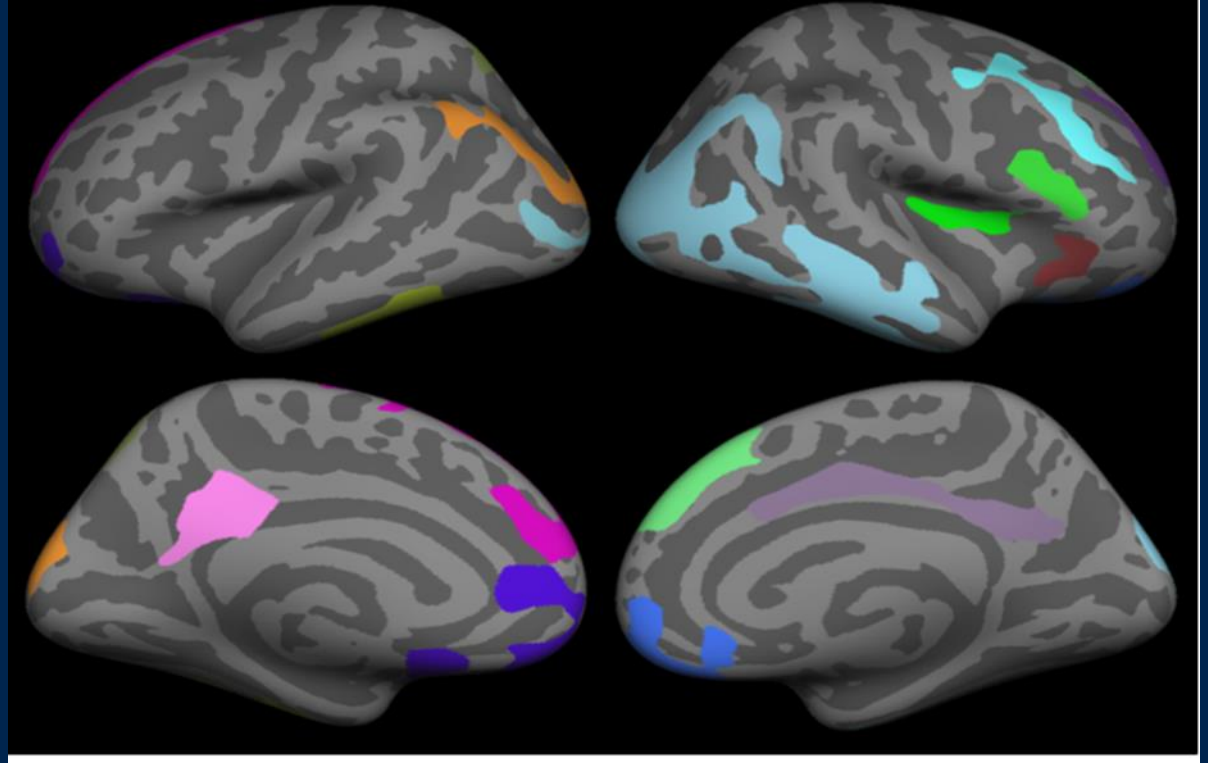
Am. J. Trop. Med. Hyg., 92(5), 2015, pp. 1006–1012
doi:10.4269/ajtmh.14-0616

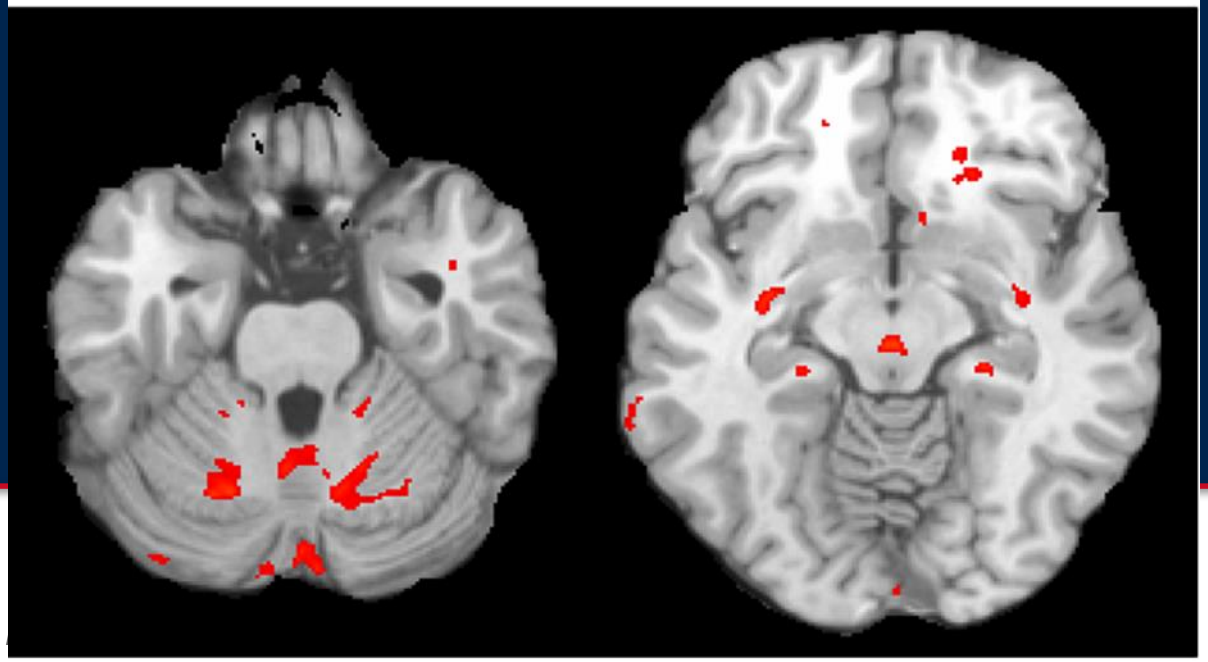
Long-Term Neurological Outcomes in West Nile Virus–Infected Patients: An Observational Study

Jill E. Weatherhead, Vicki E. Miller, Melissa N. Garcia, Rodrigo Hasbun, Lucrecia Salazar, Mazen M. Dimachkie, and Kristy O. Murray*

Baylor College of Medicine, Department of Pediatrics, Houston, Texas; The University of Texas Health Science Center at Houston, Houston, Texas; The University of Kansas Medical Center, Kansas City, Kansas

- 86% of encephalitis cases, 25% of meningitis, and 20% fever cases had abnormal neurological exams after acute infection
- Anomalies: abnormal motor strength, vibratory sensory loss, tandem gait and balance abnormalities, hearing loss, and postural or intention/action tremors
- 63% of encephalitis cases had impaired tandem gait, suggesting vestibular-cerebellar and/or dorsal column dysfunction
- At the time of the second assessment 7 years later, 57% of WNF, 33% of WNM, and 36% of WNE had developed new neurological complications.





•Cortical Thinning:

- posterior cingulate cortex, superior frontal cortex, medial-orbito frontal region, anterior cingulate cortex, inferior frontal cortex, cuneus and para hippocampal region, middle and inferior temporal cortex, supramarginal region, inferior frontal region and insular cortex

•Regional atrophy

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Use of Testing for West Nile Virus and Other Arboviruses

Jakapat Vanichanan, Lucrecia Salazar, Susan H. Wootton, Elizabeth Aguilera, Melissa N. Garcia, Kristy O. Murray, Rodrigo Hasbun

- 751 patients in Houston area diagnosed with meningitis or encephalitis, 2005-2010
  - 281 (37%) were tested for WNV; only 25% of children tested
  - 220/470 (47%) not tested for WNV had onset June-Oct
  - 518 had an unknown etiology (69%)

- Similar study ongoing at TCH: 1,699 meningitis/encephalitis cases diagnosed 2009-2014; 1,192 unknown etiology (70%); only 10% tested for WNV

Vanichanan et al. 2016, *Emerging Infectious Diseases*

Risk of Arboviruses in Houston: the Perfect Storm

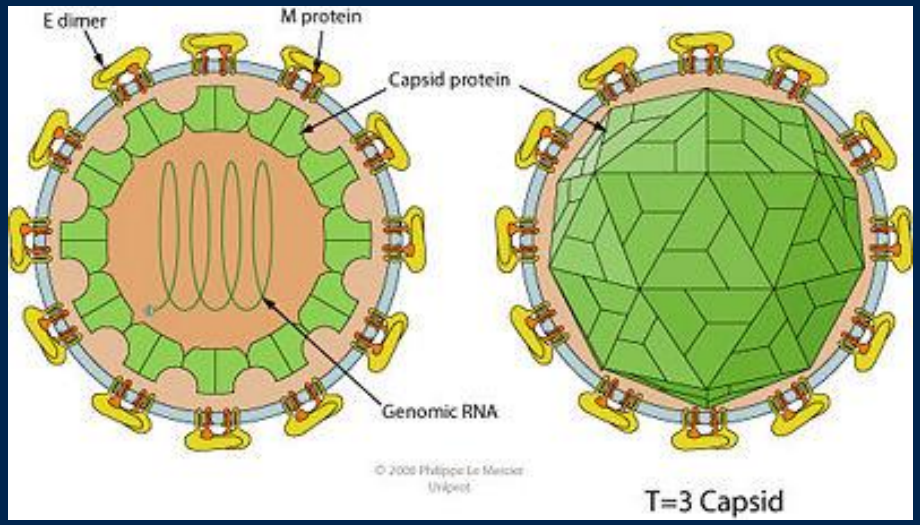
- Proximity to endemic areas
- Vast shipping; both air and ship travel entry points; NAFTA
- High proportion of its ~6 million residents who routinely travel to and from endemic areas
- Dense urban population
- Abundance of *Aedes sp.*
- Mild winters and year-round survival of mosquitoes
- Passive surveillance, lack of diagnostic testing available

What's next?

Zika Virus: an arbovirus and a flavivirus

FLAVIVIRUSES (ss +RNA)

- Dengue Virus
- Yellow Fever Virus
- Japanese Encephalitis Virus
- West Nile Virus
- St. Louis Encephalitis Virus
- Zika Virus

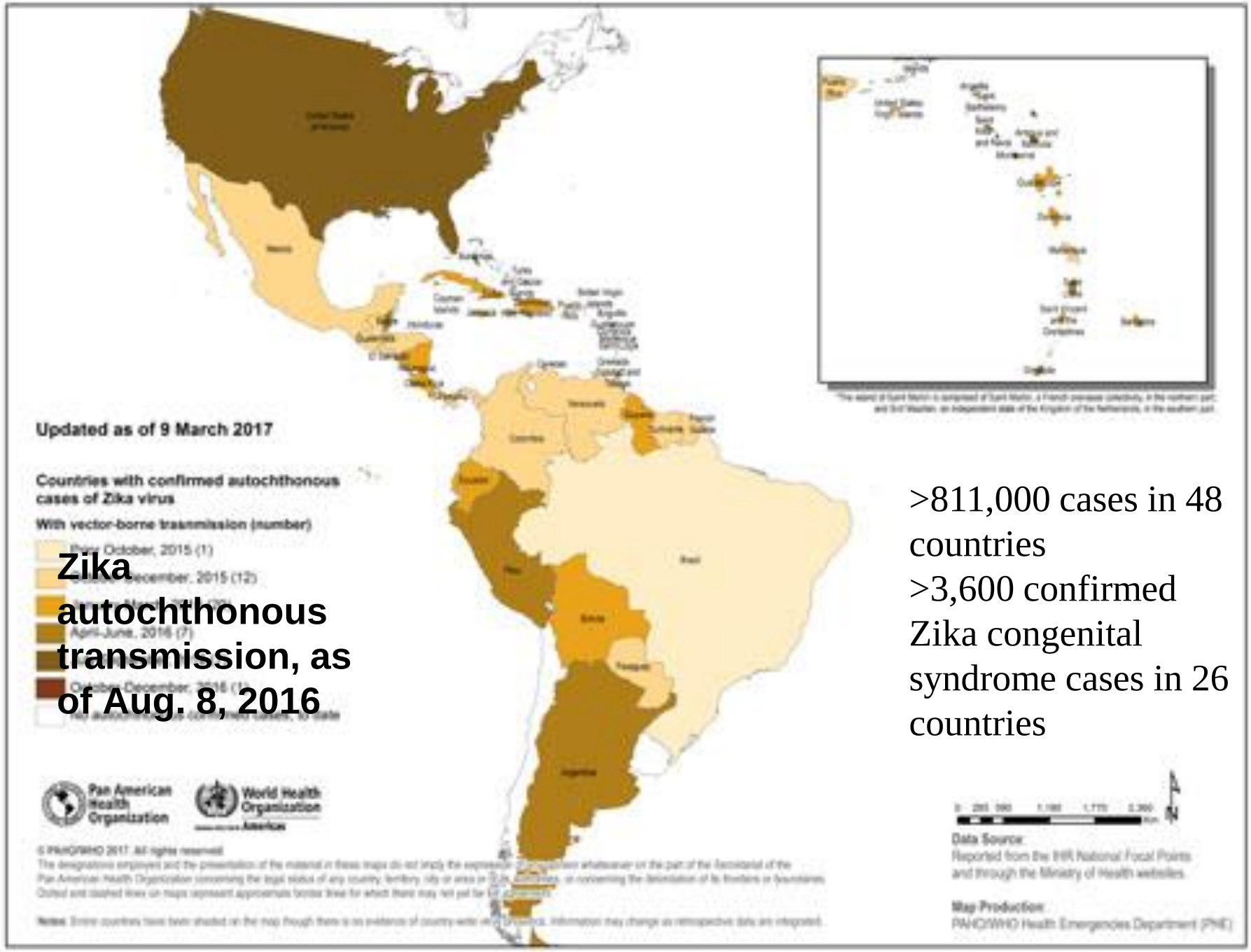


TRANSMITTED BY AEDES MOSQUITOES

- Dengue, Yellow Fever, but NOT WNV

SEXUAL TRANSMISSION

Image source: Swiss Institute of Bioinformatics. Hepacivirus. http://viralzone.expasy.org/viralzone/all_by_species/37.html. Accessed February 3, 2015.



Zika autochthonous transmission, as of Aug. 8, 2016

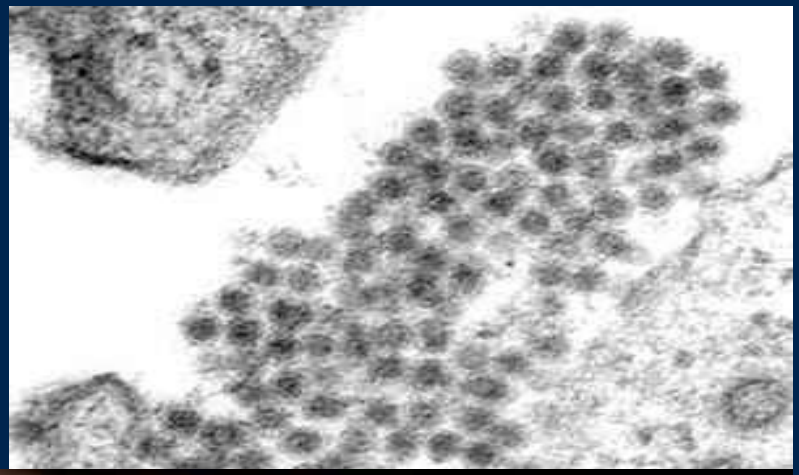
>811,000 cases in 48 countries
>3,600 confirmed Zika congenital syndrome cases in 26 countries

Challenges and Needs

- Best approach to combat Zika?
  - Mosquito bite prevention (Integrated Mosquito Control Management)
  - Educate on sexual transmission risk
  - Surveillance strategies
  - No treatment available…..need a vaccine!!!
- Diagnostic tests to detect exposure
- Research to better understand risks for microcephaly, virus shedding/infectivity, clinical outcomes

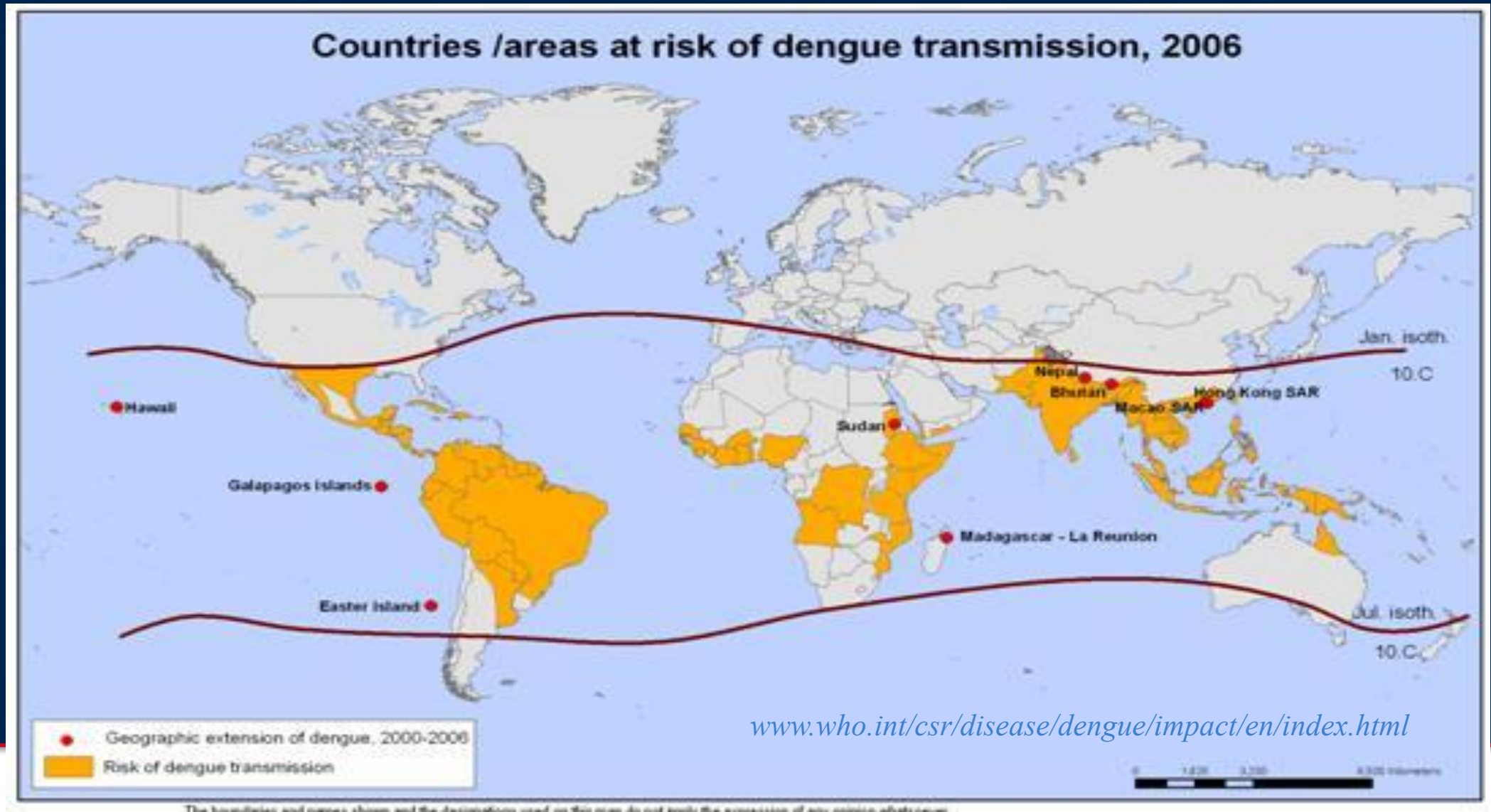
Dengue Virus

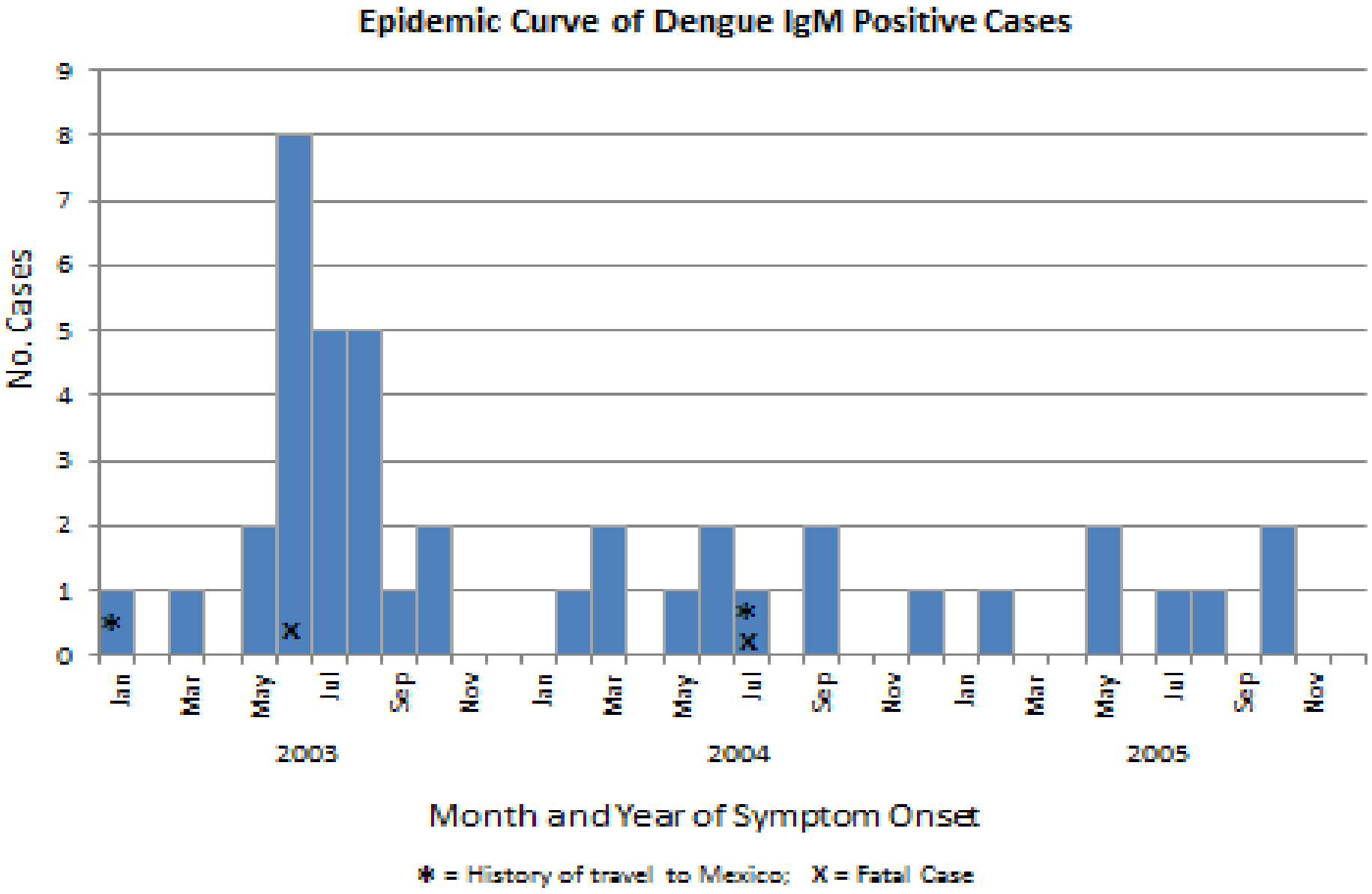
Image: www.stanford.edu/.../virus/flavi/2000/dengue.htm



- Flavivirus
- Four serotypes
  - DEN-1, DEN-2, DEN-3, DEN-4
- Lifelong immunity
- Complicated illness with secondary infection of different serotype
- Three classifications of disease
  - Dengue Fever (DF)
  - Dengue Hemorrhagic Fever (DHF)
  - Dengue Shock Syndrome (DSS)

Epidemiology

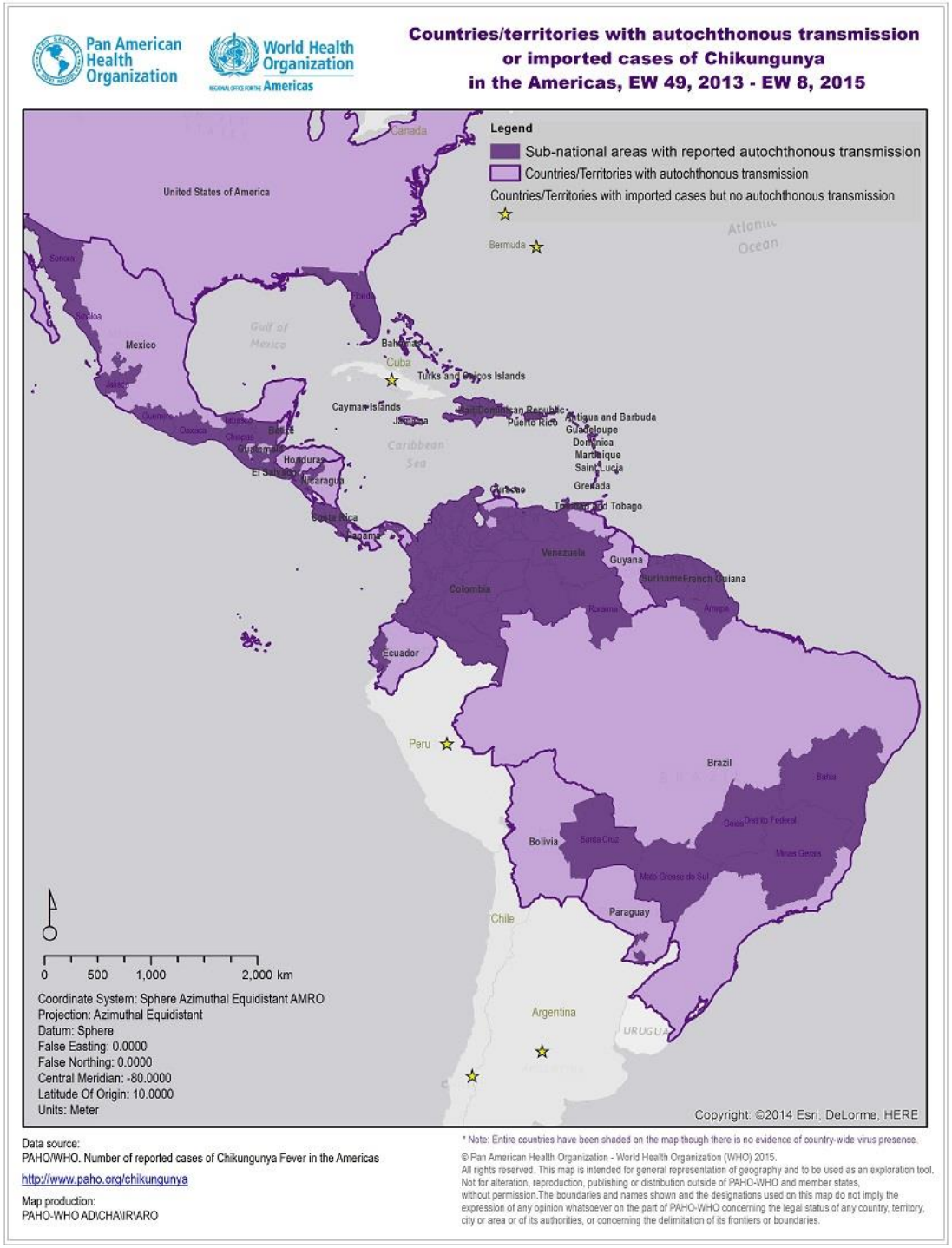



Epidemic Curve of Dengue IgM Positive Cases
No. Cases
0
1
2
3
4
5
6
7
8
9
Jan
Mar
May
Jul
Sep
Nov
Jan
Mar
May
Jul
Sep
Nov
Jan
Mar
May
Jul
Sep
Nov
2003
2004
2005
Month and Year of Symptom Onset
* = History of travel to Mexico; X = Fatal Case

Chikungunya

- Vector: *Aedes* species mosquitoes

- "that which bends up"
  - Fever, headache, fatigue, rash, nausea, vomiting, muscle pain, severe joint pain
  - Fatality rare



Introduced Western Hemisphere in 2013

By 2015:
44 countries/territories reporting autochthonous cases

> 1.25 million cases reported in Western Hemisphere

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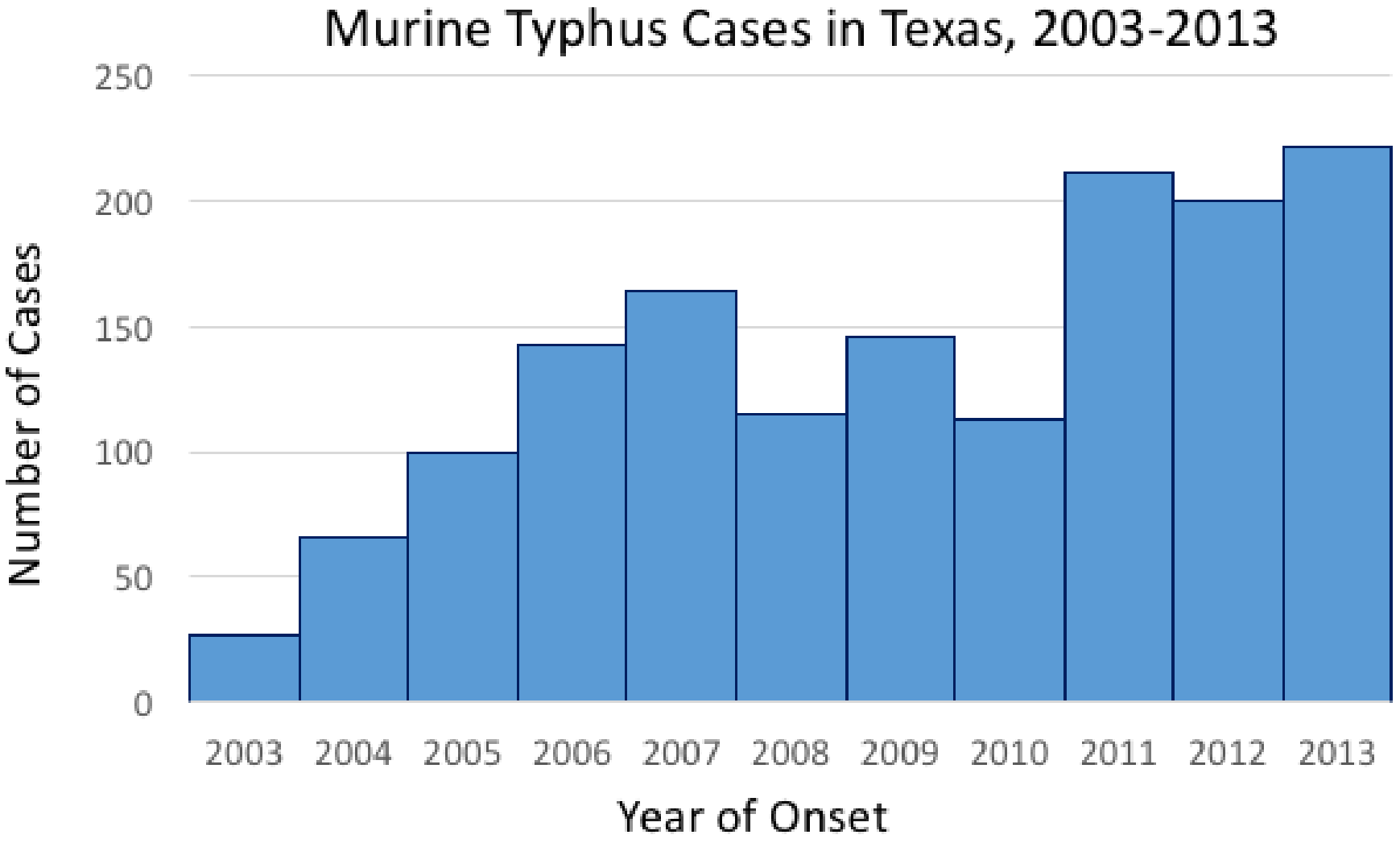
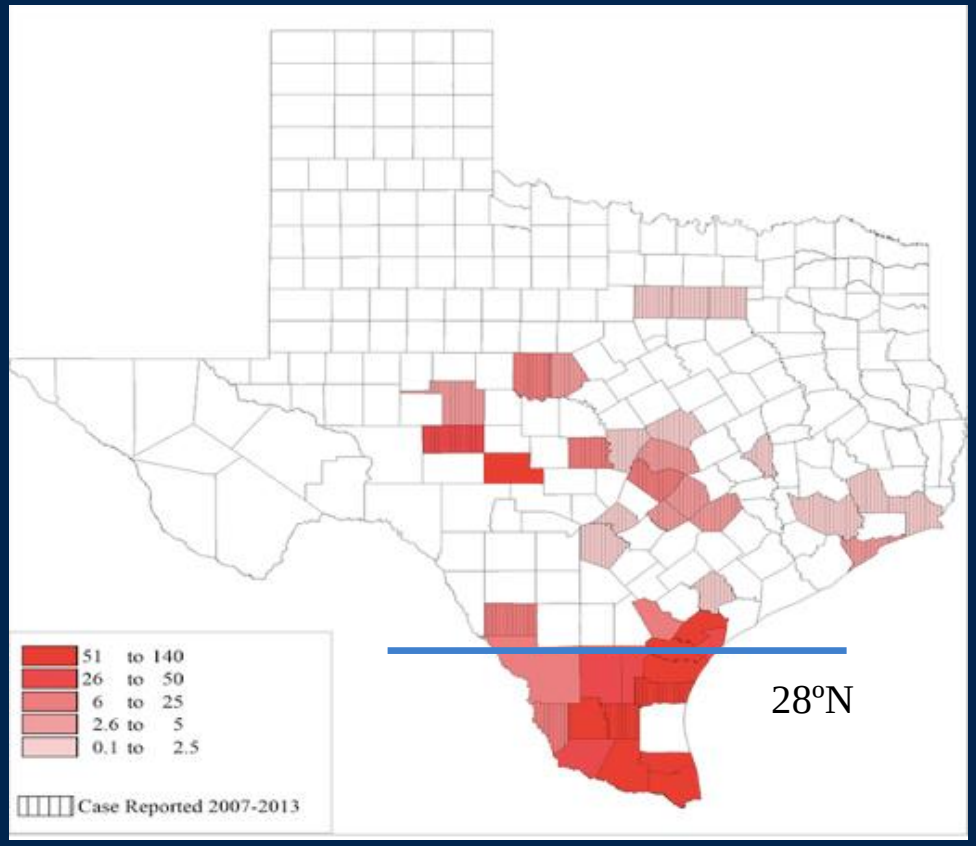
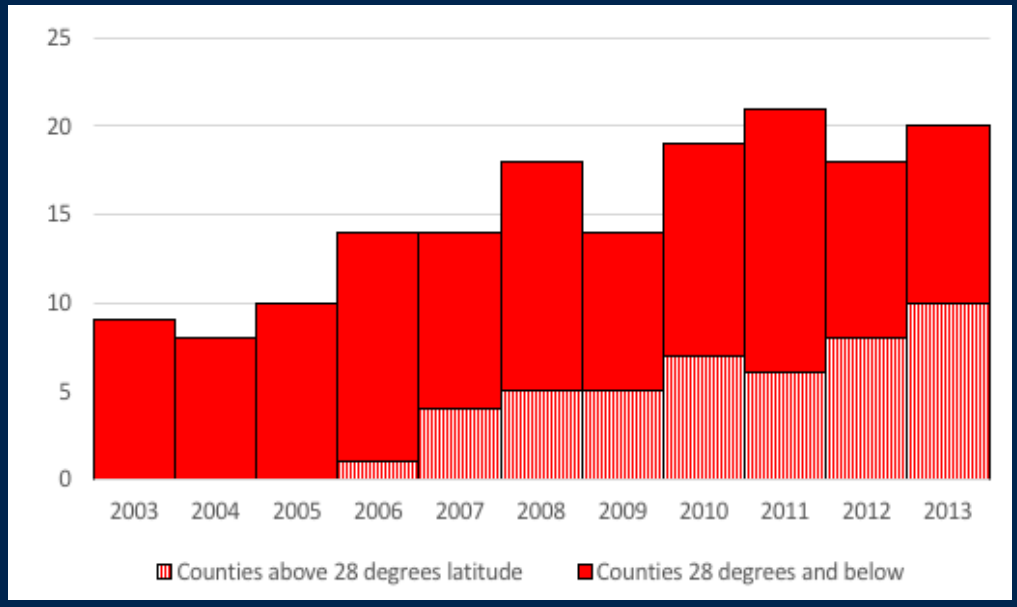

Murine Typhus Cases in Texas, 2003-2013
Number of Cases
250
200
150
100
50
0
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
Year of Onset

Geographic Distribution

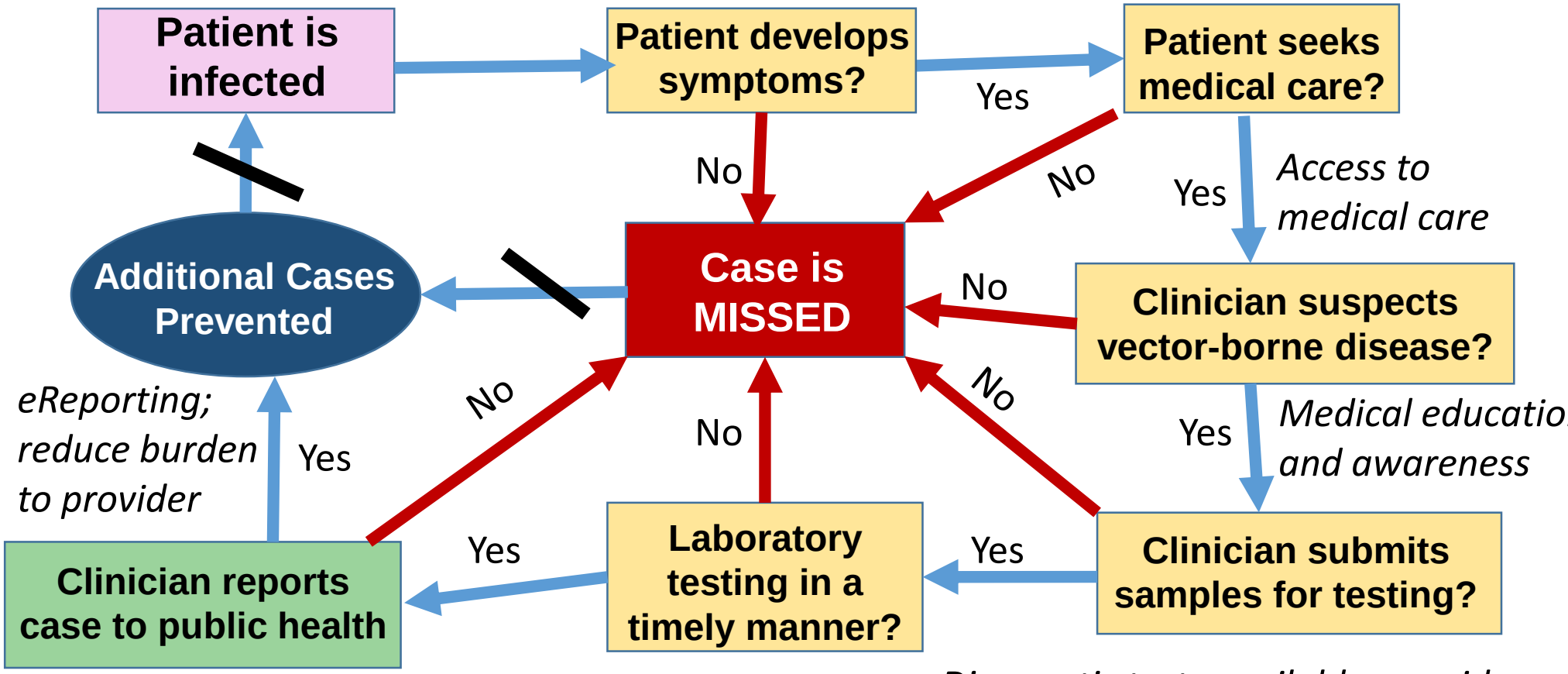




Prevention of Emerging Vector-borne Diseases

- Surveillance, surveillance, surveillance
  - Humans (active + “enhanced” passive), sentinel species, mosquitoes
  - Multidisciplinary “One Health” approach is critical
- Public education
- Prevention of bites
- Vaccine, diagnostic, and therapeutic development
- Did I mention surveillance?

Barriers to Public Health Surveillance



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- City of Houston Health Dept: Raouf Arafat, Salma Khuwaja, Cynthia Turner
- Harris Co. PHES: Umair Shah, Cindy Kilborn, Diana Martinez, Rudy Bueno, Martin Reyna
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Thanks!