

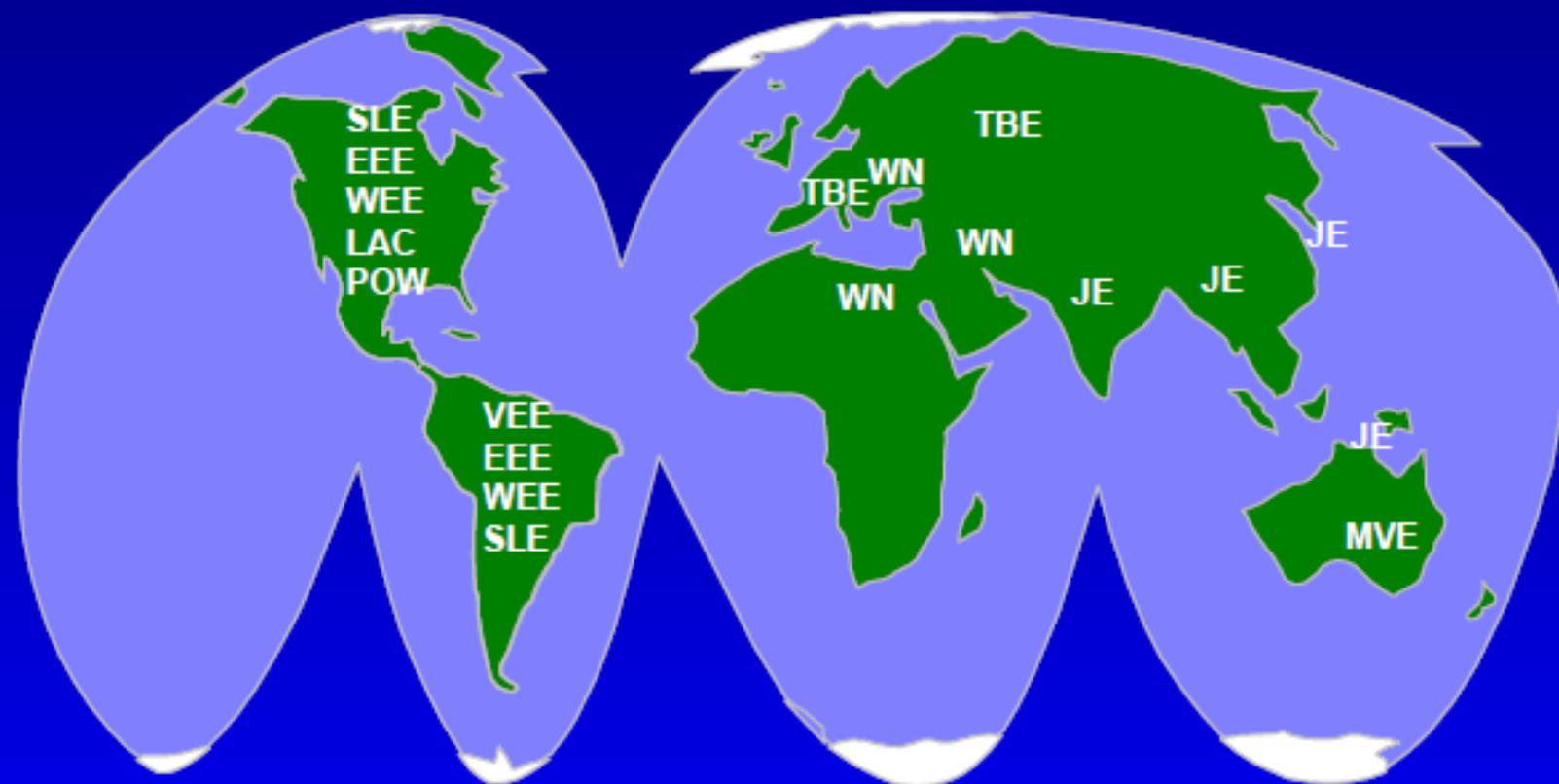
**Mosquito-borne Diseases:  
Epidemiology and Clinical  
Management of La Crosse virus**

**James D Whitehouse, MD, MHS  
Asheville ID Consultants**

# Arthropod-borne Viruses (arboviruses)

- *Bunyaviridae*
  - LaCrosse
  - Rift Valley fever
  - Crimean–Congo
  - Hantavirus
- *Togaviridae*
  - (genus Alphavirus)
  - Western equine encephalitis (WEE)
  - Eastern equine encephalitis (EEE)
  - *Venezuelan equine encephalitis (VEE)*
  - Chikungunya virus
- *Flaviviridae*
  - *West Nile Virus*
  - *St. Louis encephalitis (SLE)*
  - *Dengue virus*
  - *Yellow fever virus*
  - Japanese encephalitis
  - Kunjin
  - Murray Valley encephalitis (MVE)
  - Tick-borne encephalitis
  - Powassan encephalitis

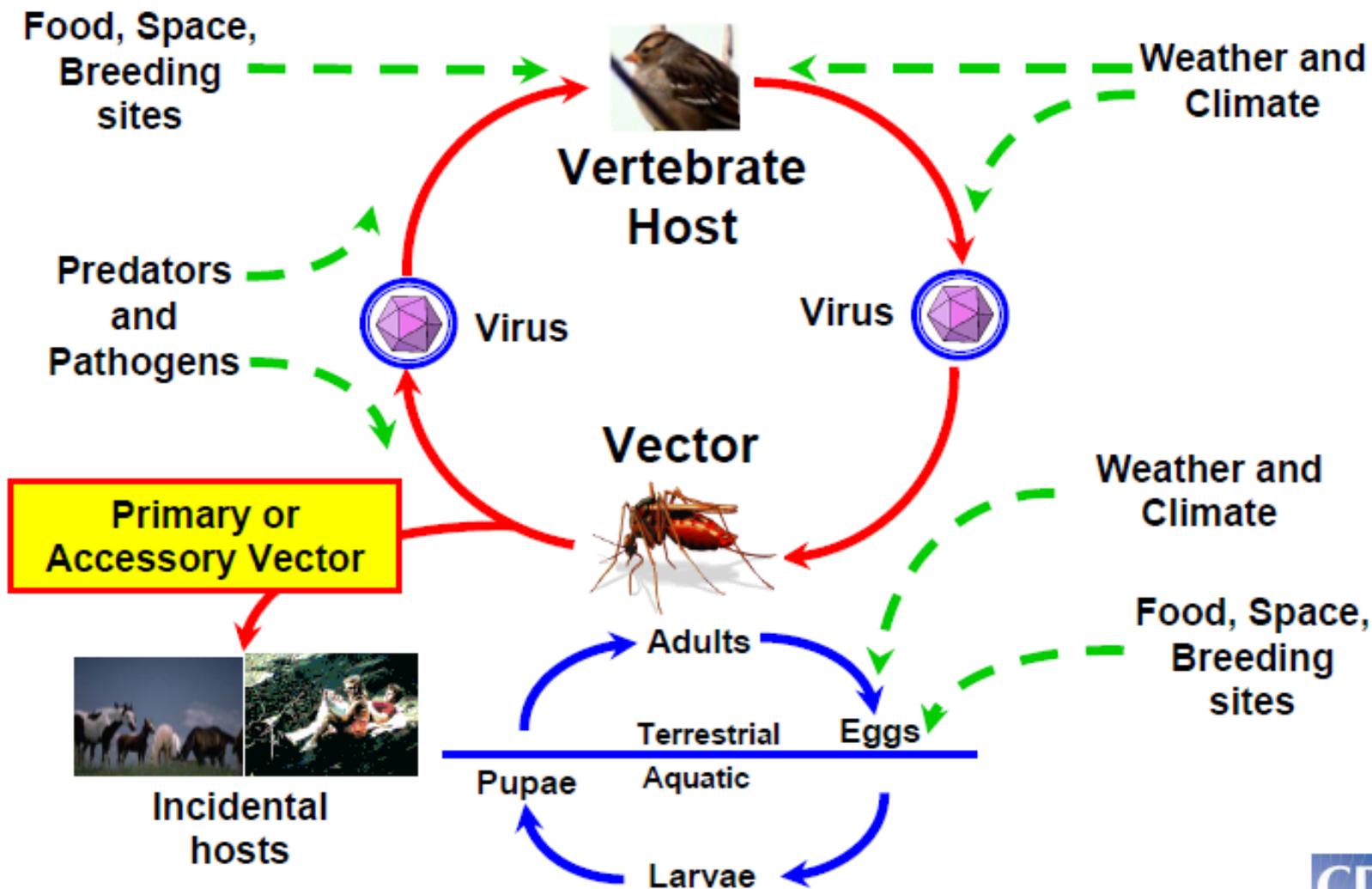
# Worldwide Distribution of Major Arboviral Encephalitides



EEE: Eastern equine encephalitis  
JE: Japanese encephalitis  
LAC: LaCrosse encephalitis  
MVE: Murray Valley encephalitis  
POW: Powassan encephalitis

SLE: St. Louis encephalitis  
TBE: Tick-borne encephalitis  
WEE: Western equine encephalitis  
WN: West Nile encephalitis  
VEE: Venezuelan equine encephalitis

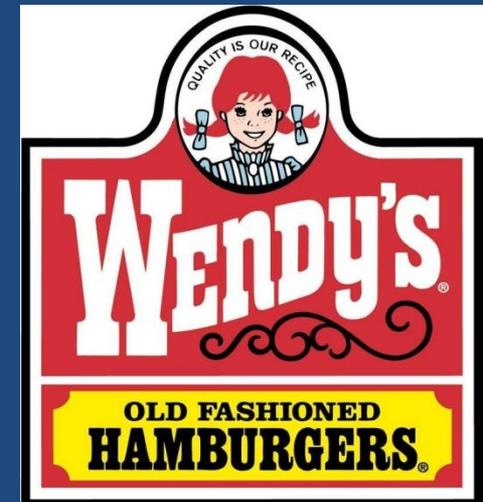
# Arbovirus Transmission Cycle



# 12 yo with Headache, Vomiting, and Inappropriate Combativensness after eating at Wendy's

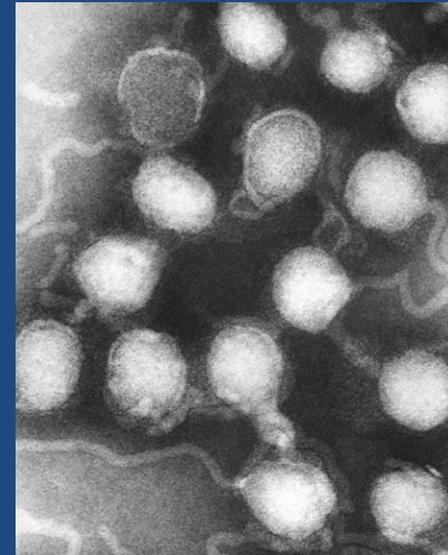
Serum	WBC	14.5	Na	131
CSF	WBC	DIFF	Protein	Glucose
11/14	434	28N, 50L	55	59
11/20	77	4N, 80 L	73	49
Misc	-HSV	-ENTERO	-CRYPTO	-CX

Hospitalized 11/13-18, 11/19-22  
Required Intubation  
Mechanical Ventilation  
Normal CT and MRI  
NC PHE assisted



# La Crosse Encephalitis Virus

- Leading cause of pediatric arboviral encephalitis in the United States
- Bunyaviridae family
- Genus Orthobunyavirus
- California (CAL) serogroup virus
  - LaCrosse virus (LACV)
  - California encephalitis
  - Jamestown Canyon
  - Snowshoe hare virus
  - Trivittatus virus



- ✓ Three segments
- ✓ Single-stranded RNA
- ✓ Spherical or oval
- ✓ Enveloped

# La Crosse Encephalitis in Children

Sex — no. (%)	
Male	90 (71)
Female	37 (29)
Age — no. (%)	
0.5–2 yr	9 (7)
3–5 yr	30 (24)
6–8 yr	42 (33)
9–11 yr	26 (20)
12–14 yr	19 (15)
15 yr	1 (1)
Month of presentation — no. (%)	
June	3 (2)
July	31 (24)
August	38 (30)
September	44 (35)
October	11 (9)
Symptoms on presentation — no. with finding/total no. (%)†	
Headache	105/126 (83)
Fever	107/125 (86)
Vomiting	89/127 (70)
Disorientation	50/119 (42)
Seizures‡	58/127 (46)
Signs on admission — no. with finding/total no. (%)	
Nuchal rigidity	31/120 (26)
Glasgow Coma score ≤12	42/127 (33)
Focal neurologic signs	23/126 (18)

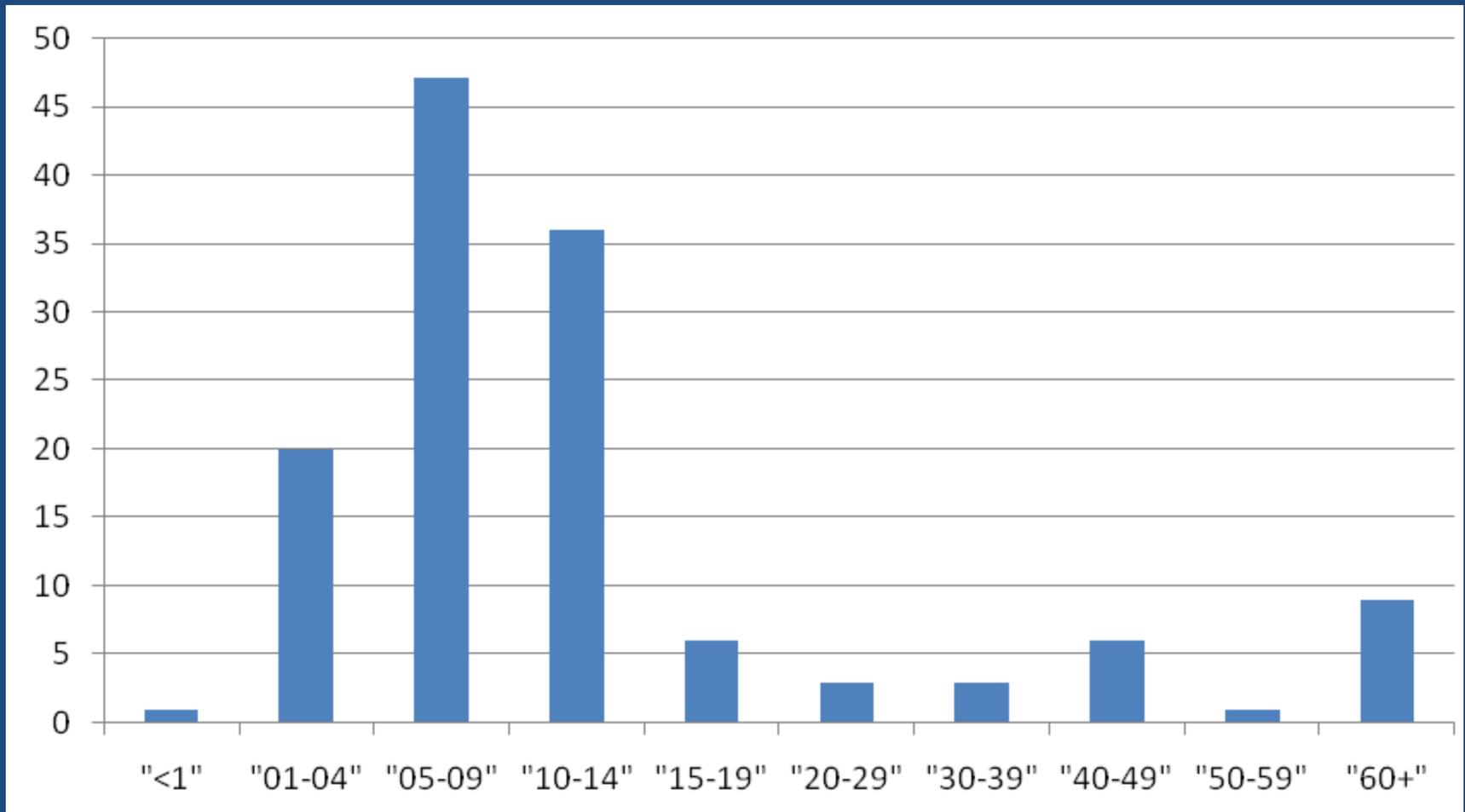
- 127 children
- Seventy-two patients (57 percent) were admitted to the pediatric intensive care unit
- 32 (25 percent) required mechanical ventilation
- 59 patients had abnormal electroencephalography tracings
- At discharge,
  - 15 children (12 percent) had neurologic deficits
  - 36 percent had a full-scale IQ score of 79 or less

# La Crosse Encephalitis in Children

**TABLE 2.** LABORATORY VALUES AT ADMISSION IN PATIENTS WITH LA CROSSE ENCEPHALITIS.

VARIABLE	MEAN VALUE ±SD	RANGE	REMARKS
Cerebrospinal fluid			
White-cell count (per mm <sup>3</sup> )	130±151	2–867	<200/mm <sup>3</sup> in most cases
Differential count (% lymphocytes)	—	2–100	Predominance of lymphocytes
Red-cell count (per mm <sup>3</sup> )	71±213	0–1500	Elevated (≥20/mm <sup>3</sup> ) in 25%
Glucose (mg/dl)*	75±20	37–149	Normal
Protein (mg/dl)	37±15	10–85	Rarely elevated
Peripheral blood			
White-cell count (per mm <sup>3</sup> )	15,700±5900	6800–49,700	Usually elevated (>15,000/mm <sup>3</sup> )
Differential count (% polymorpho- nuclear leukocytes)	—	17–94	Predominance of polymorphonuclear leukocytes

# La Crosse Encephalitis, by Age, NC, 1988-2005



# Economic and Social Impacts of La Crosse in WNC

- 19 (40%) of 47 of all physician-reported LACE cases in NC between 1989 and 2001
- Mean per patient cost of dollar 32,974
  - direct medical costs during acute illness
  - Mean number of nights hospitalized in our study ( $10.9 \pm 11.1$  nights)
- More than half (13 of 25) of the participants in our study claimed that case patients experienced educational sequelae

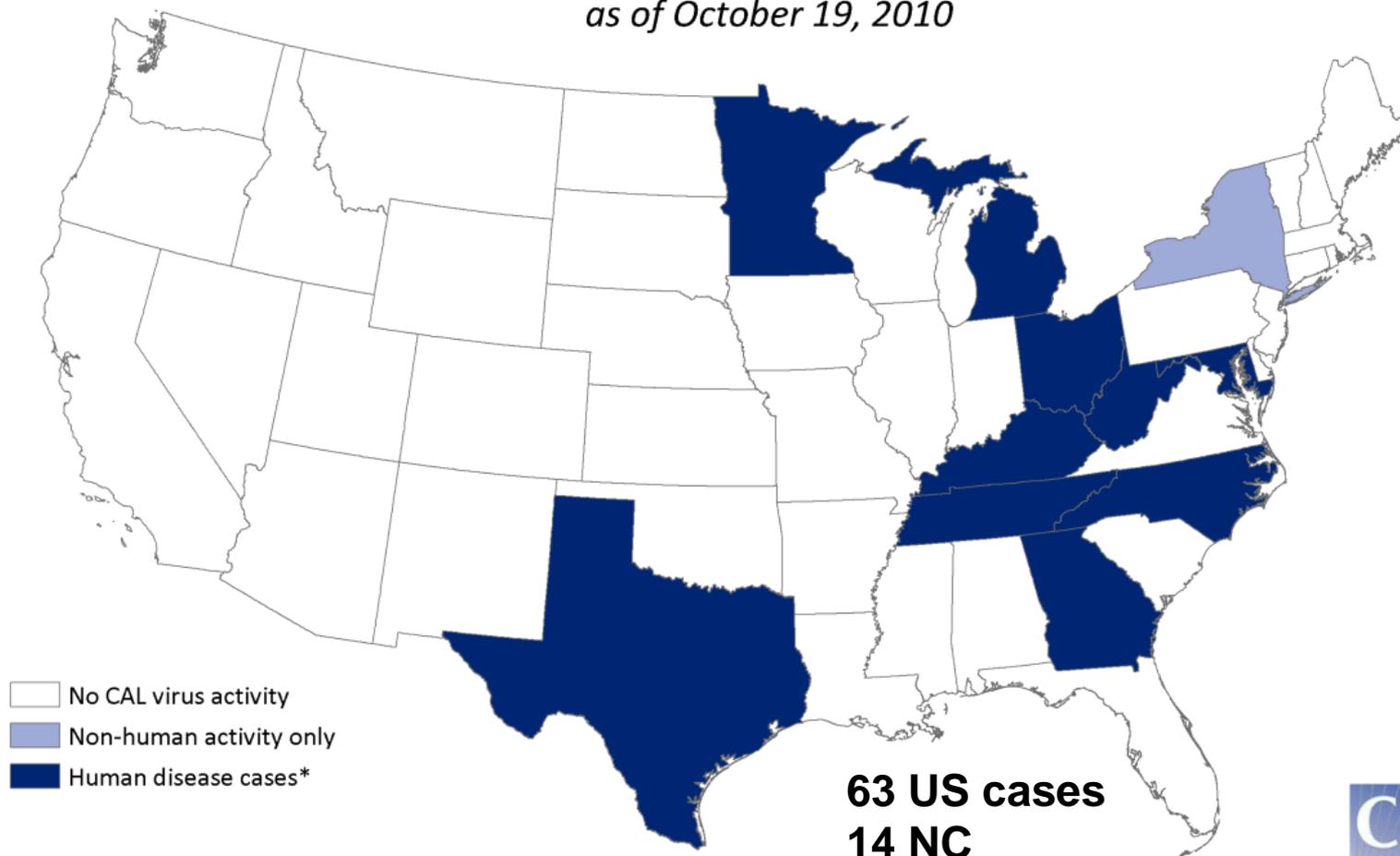
# A Tale of Two Boys from WNC

22 month old boy with Fever, Vomiting, and Seizure

30 month old boy with Fever, Vomiting, and Seizure

<b>22 mo</b>	<b>WBC</b>	<b>14.9</b>	<b>Na</b>	<b>131</b>
CSF	WBC	DIFF	Protein	Glucose
10/7	132	55N, 33L	33	53
Misc	-HSV	-ENTERO		-CX
<b>30 mo</b>	<b>WBC</b>	<b>16.1</b>	<b>Na</b>	<b>123</b>
CSF	WBC	DIFF	Protein	Glucose
10/24	177	5S,80L	34	52
Misc	-HSV	-ENTERO		-CX

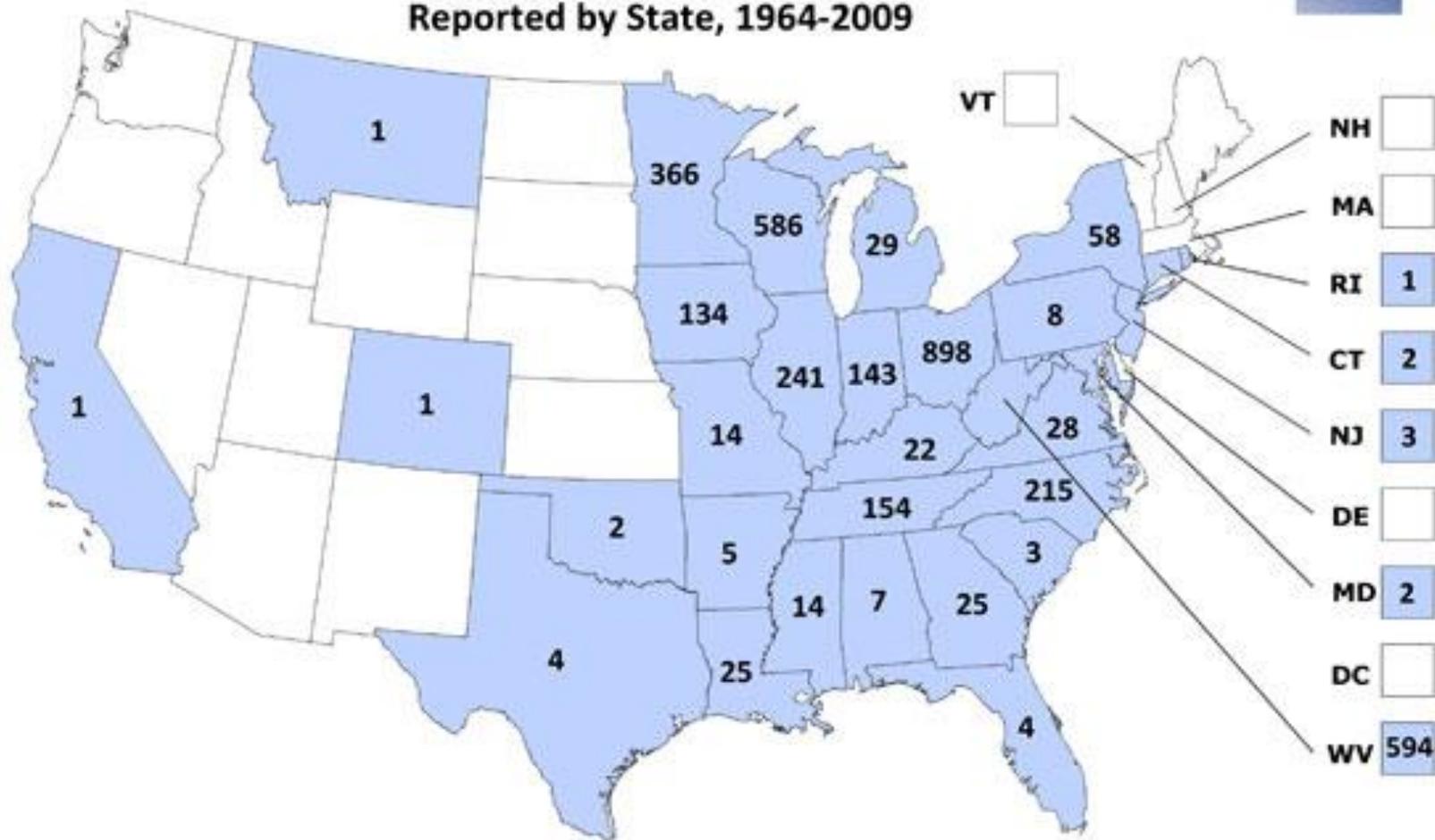
**California serogroup (CAL) virus activity reported to ArboNET, by state, United States, 2010**  
*as of October 19, 2010*



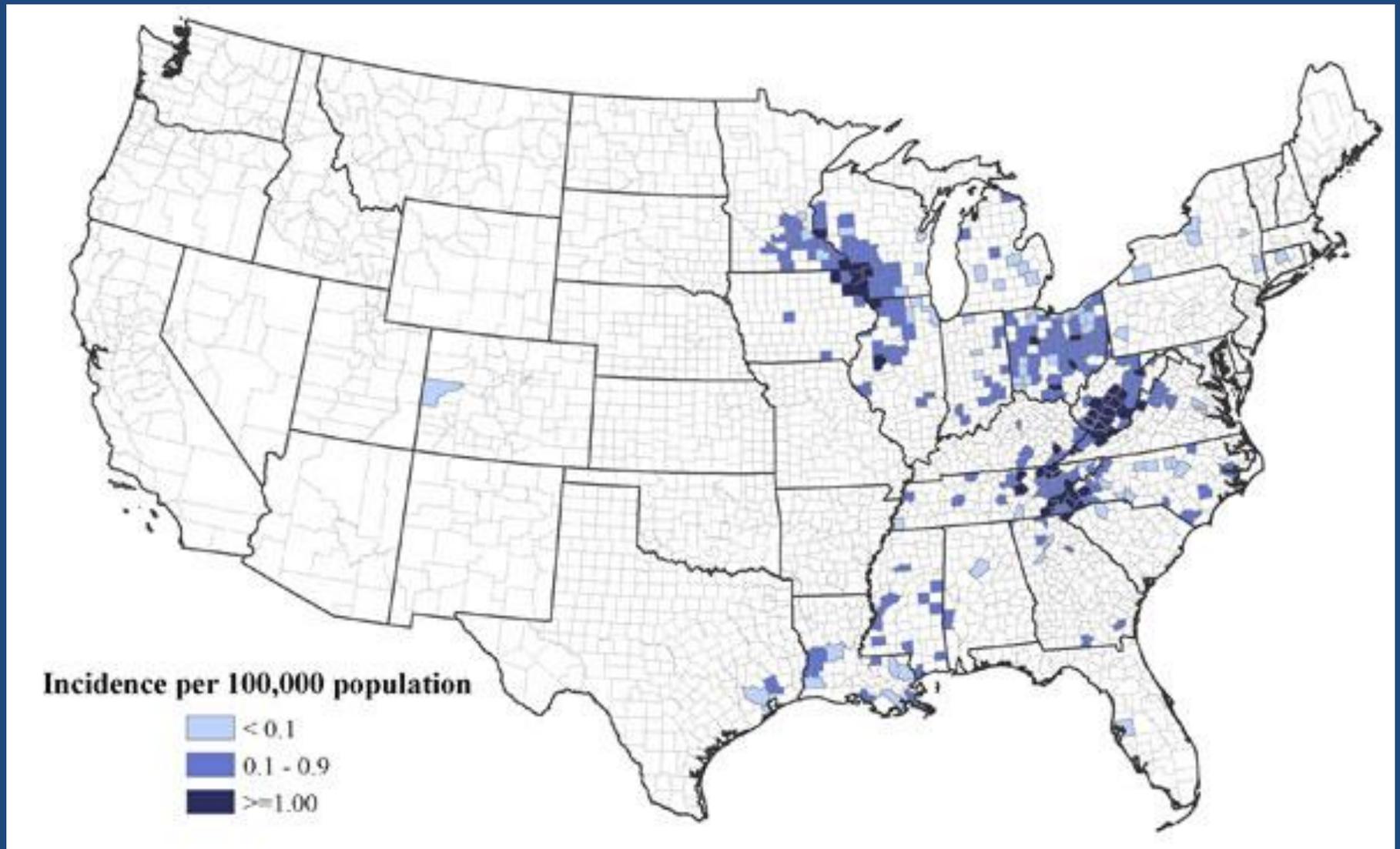
\*These jurisdictions may have also reported non-human CAL virus activity.



# California Serogroup Virus Neuroinvasive Disease Cases Reported by State, 1964-2009

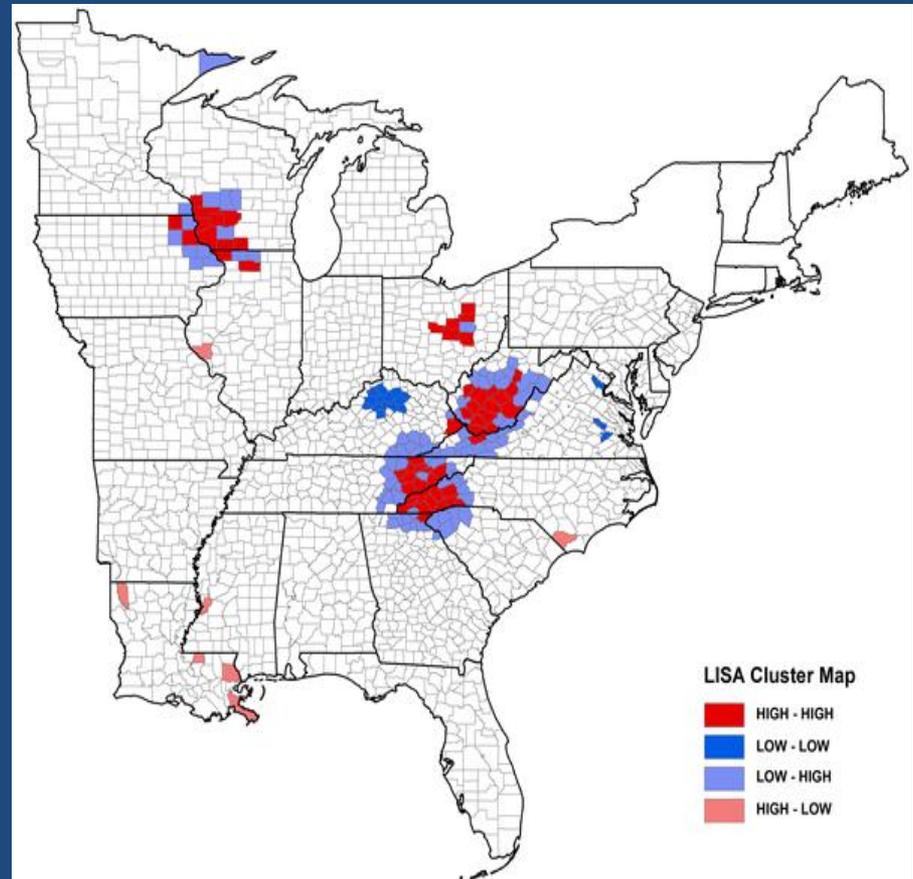


# California Serogroup Virus Neuroinvasive Disease Average Annual Incidence by County, 1996-2008



# La Crosse virus, Eastern United States, 2003-2007

- June, July, August, and September
- 4 states, 74.5 percent of all cases
- Case fatality rate of 1.9 percent



# An Tale Too Early?

74 yo male from Barnardsville with RA on MTX

Found unresponsive in a car

Hospitalized 3/25-30 lethargic, confused, peculiar thoughts

Hospitalized 4/10-15 with fever and ongoing confusion

Serum	WBC	10.2	Na	124
CSF	WBC	DIFF	Protein	Glucose
3/25	268	80N, 8L	156	43
4/10	20	59N, 28L	104	50
4/13	13	35N, 49L	88	43
Misc	-HSV	-ENTERO	-CRYPTO	-MTB
-JC	-EBV	-CMV	-VZV	-VDRL

# Transmission cycle of LACV

*Aedes triseriatus*

Mosquito vector



Amplifying host



Dead-end host

The mosquitoes that spread LACV  
Are most active during the daytime.

# La Crosse Encephalitis Virus

- *Aedes triseriatus*
  - Eastern treehole mosquito
  - Aggressive daytime-biting mosquito
  - Transovarial transmission in mosquito eggs



- Deciduous forest habitats
  - Tires and buckets

# La Crosse Encephalitis Virus

- Vertebrate amplifier host
  - eastern chipmunk, *Tamias striatus*
  - gray squirrel, *Sciurus carolinensis*
  - fox squirrel *Sciurus niger*



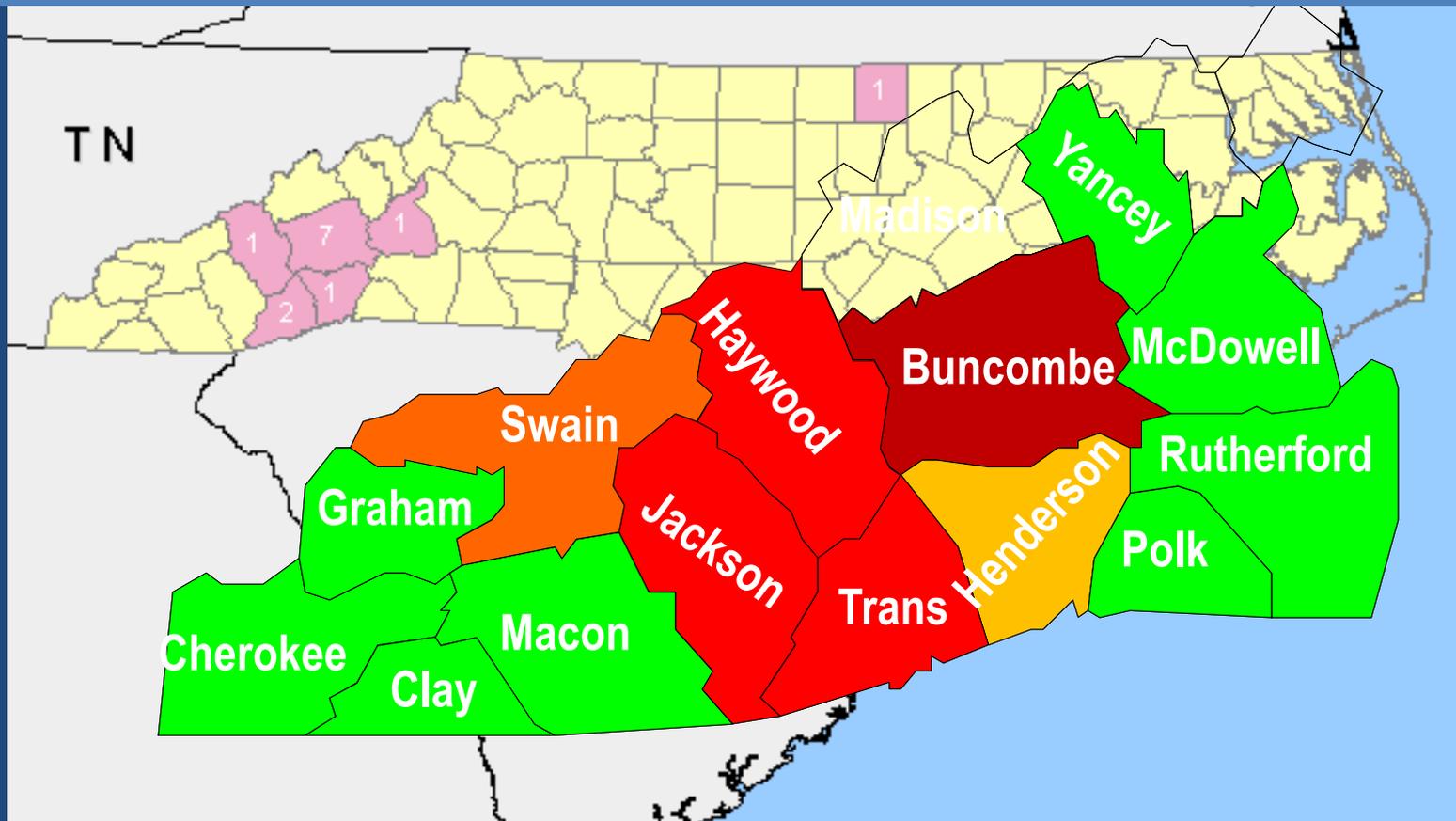
# A Tale of Two Men from WNC

19 yo Swain Co college student with severe headache, lip spasms, and seizure

56 yo Cherokee male with fever, headache, vomiting and progressive confusion

<b>Swain</b>	<b>WBC</b>	<b>11.9</b>	<b>Na</b>	<b>133</b>
CSF	WBC	DIFF	Protein	Glucose
9/2	73	57S, 35L	81	65
Misc	-HSV		-RPR	-CX
<b>Cherokee</b>	<b>WBC</b>	<b>16.8</b>	<b>Na</b>	<b>124</b>
CSF	WBC	DIFF	Protein	Glucose
8/9	56	30S, 56L	45	60
Misc	-HSV		-Crypto	-CX

# Confirmed and Probable LaCrosse Encephalitis Cases by County, NC, 2010 (n=13)



# Confirmed and Probable LaCrosse Encephalitis Cases by County, NC, 1998-2009 (n=165)

COUNTY	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	Total
<b>Buncombe</b>	0	3	1	3	2	5	2	8	4	2	0	4	<b>34</b>
<b>Haywood</b>	1	1	0	0	1	3	3	4	2	4	3	4	<b>26</b>
<b>Jackson</b>	0	1	0	1	3	5	3	4	3	0	0	2	<b>22</b>
<b>Transylvania</b>	0	0	1	0	0	4	0	8	3	3	2	1	<b>22</b>
<b>Swain</b>	1	3	3	2	1	1	1	1	1	0	0	2	<b>16</b>
<b>Henderson</b>	0	1	1	0	1	0	1	3	1	0	0	1	<b>9</b>
<b>Total</b>	<b>4</b>	<b>10</b>	<b>7</b>	<b>9</b>	<b>13</b>	<b>26</b>	<b>13</b>	<b>32</b>	<b>18</b>	<b>10</b>	<b>7</b>	<b>16</b>	<b>165</b>

# La Crosse in WNC

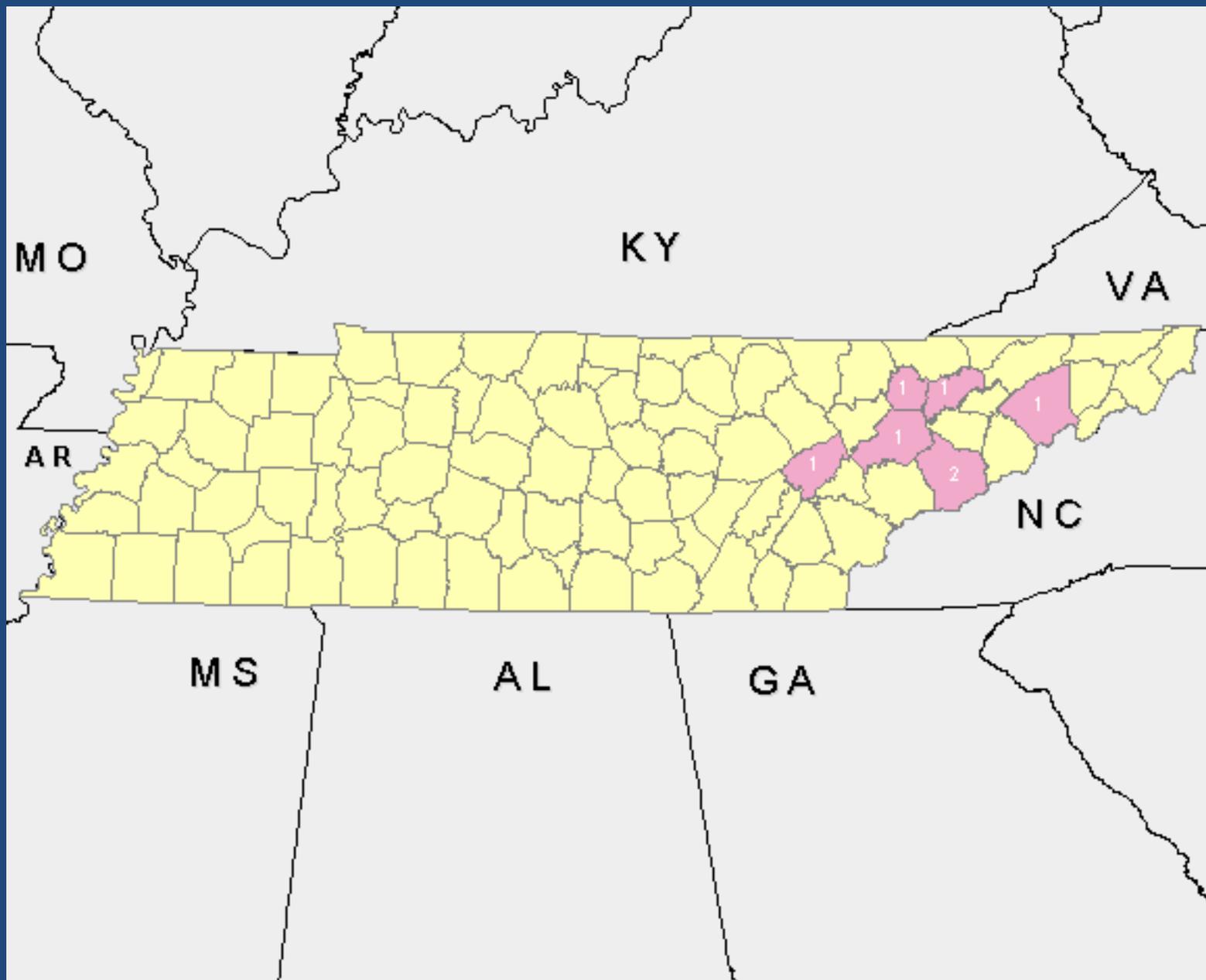
- **Cherokee Indian Reservation area of Jackson and Swain counties**
  - 20.6% seroprevalence on the reservation
  - 4.7% seroprevalence off the reservation
  - 5.5 times more likely to have been exposed to LAC virus
- **Antibody prevalences**
  - 1.8% youngest age group (< 15 years old)
  - 16.7% for the oldest group (75–100 years old)
  - On the Reservation, 53.9% for the oldest group

# La Crosse in WNC

Prevalence of La Crosse virus antibody in blood serum or Nobuto strip samples collected in western North Carolina\*

Location	n	% positive per location	Overall % positive
Cherokee Indian Reservation	311	20.6	6.8
Macon County	36	8.3	0.3
Swain County	175	8.0	1.5
Jackson County	225	4.9	1.2
Haywood County	162	2.5	0.4
Eight additional counties	32	3.0	0.1

\* The county of origin for 66 samples collected off the reservation was missing.



# Treatment and Prevention

- No specific or effective anti-viral treatment for LACV
- Supportive therapy
  - Hospitalization
  - Respiratory support
  - IV fluids
  - Seizure medication
  - Prevention of other nosocomial infections.
- Prevent mosquito bites
  - Use insect repellent
    - DEET
    - Picaridin
  - Wear long sleeves, long pants and socks
  - Avoid peak biting hours
  - Install and repair screens
  - Eliminate mosquito breeding sites

<http://www.epi.state.nc.us/epi/arbovirus/lac.html>

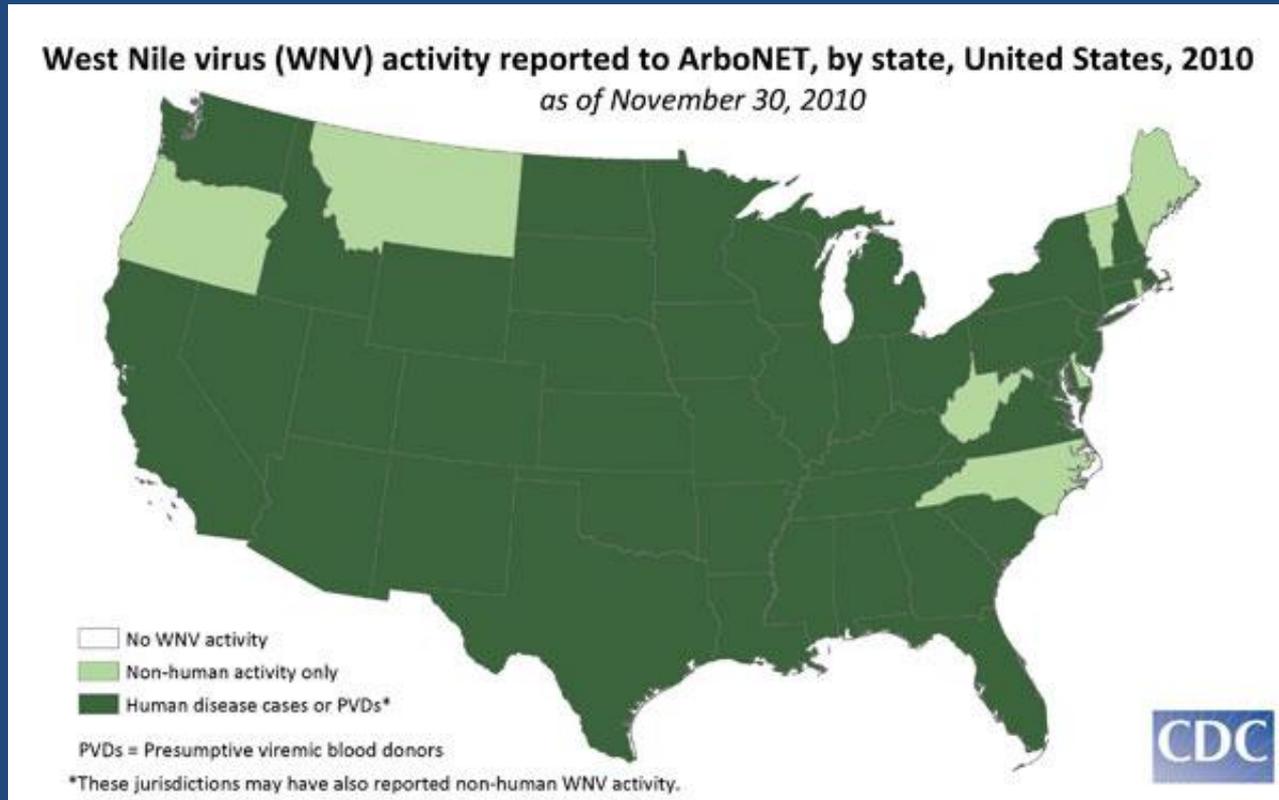
<http://www.epi.state.nc.us/epi/arbovirus/deet.html>

# A Tale of Two Women from WNC

48 yo kayaker seizing while cooking on a riverside  
 74 yo retiree from Lake Toxaway unresponsive on a couch

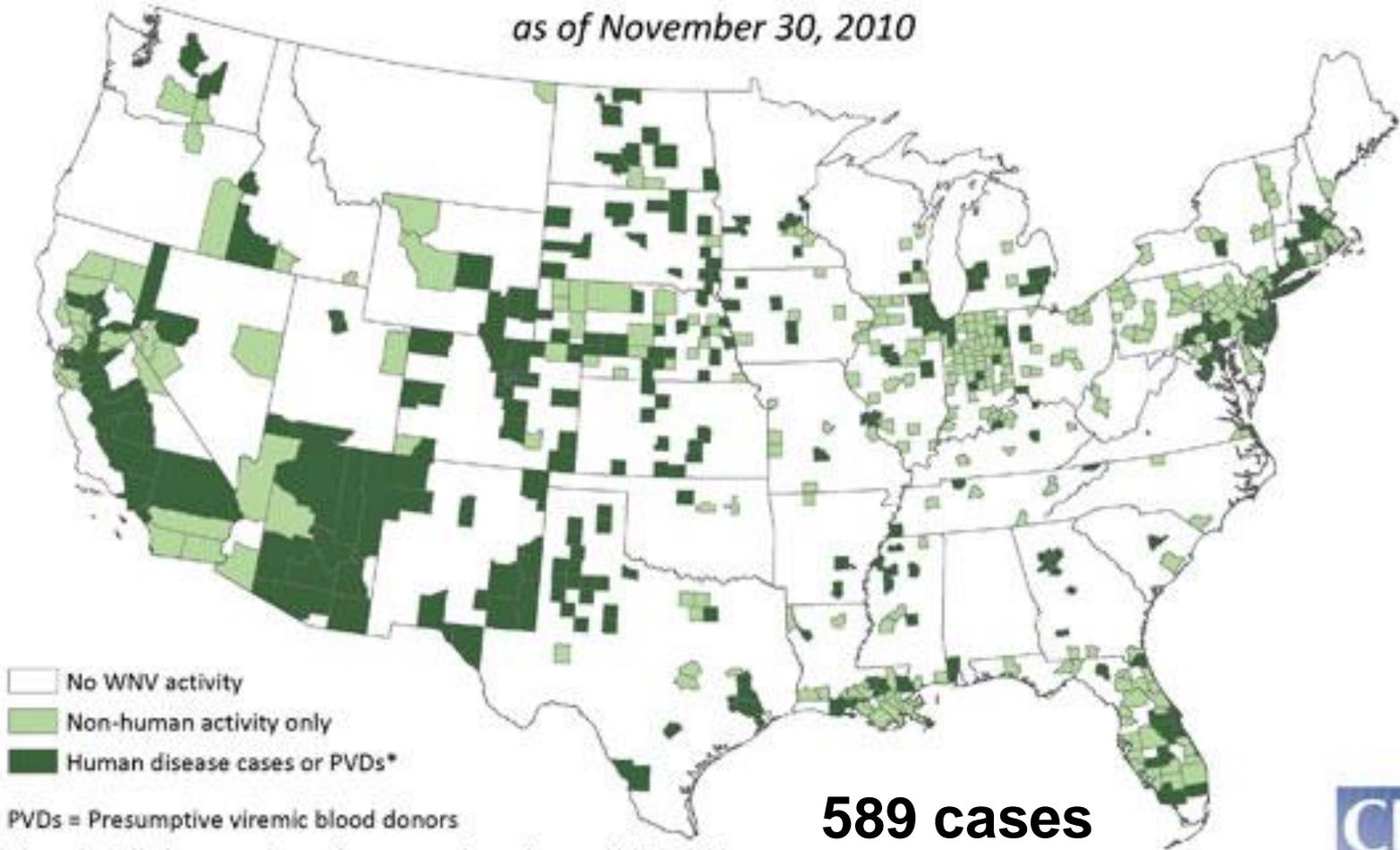
<b>Kayak</b>	<b>WBC</b>	<b>16.6</b>	<b>Na</b>	<b>134</b>
CSF	WBC	DIFF	Protein	Glucose
8/27	171	42S,48L	101	63
Misc	-HSV			-CX
<b>Toxaway</b>	<b>WBC</b>	<b>9.1</b>	<b>Na</b>	<b>122</b>
CSF	WBC	DIFF	Protein	Glucose
9/6	57	14N,67L	52	66
Misc	-HSV	-Enteroc	-Crypto	-CX
-CT/MRI	Carotid	-VZV	-RPR	-VDRL

# West Nile Virus (WNV)



- First isolated in 1937
- Asymptomatic infection and fevers
- Africa, West Asia, and the Middle East
- 1999 metropolitan New York City

**West Nile virus (WNV) activity reported to ArboNET, by county, United States, 2010**  
*as of November 30, 2010*



- No WNV activity
- Non-human activity only
- Human disease cases or PVDs\*

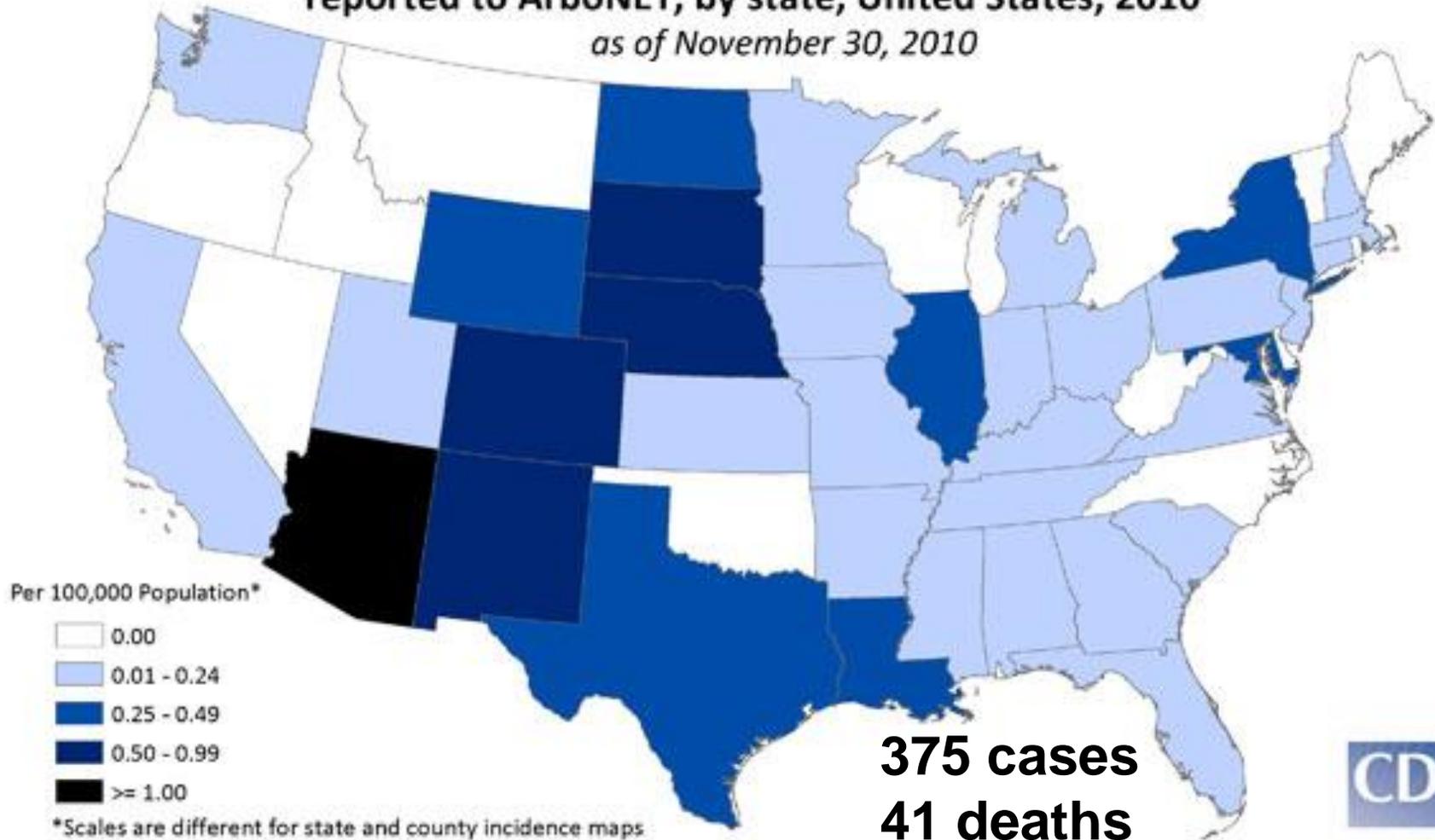
PVDs = Presumptive viremic blood donors

\*These jurisdictions may have also reported non-human WNV activity.

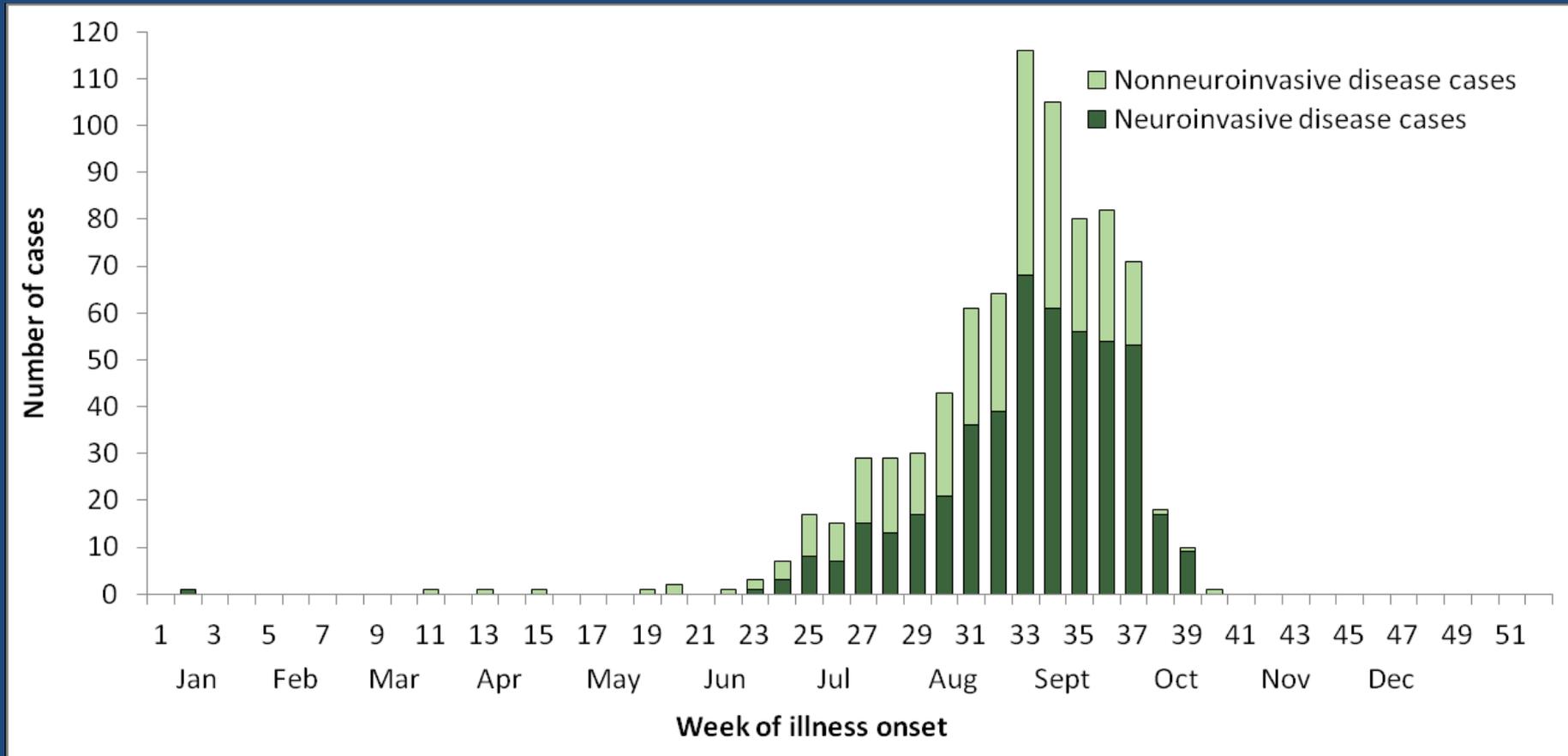
**589 cases**



**West Nile virus (WNV) neuroinvasive disease incidence  
reported to ArboNET, by state, United States, 2010**  
*as of November 30, 2010*

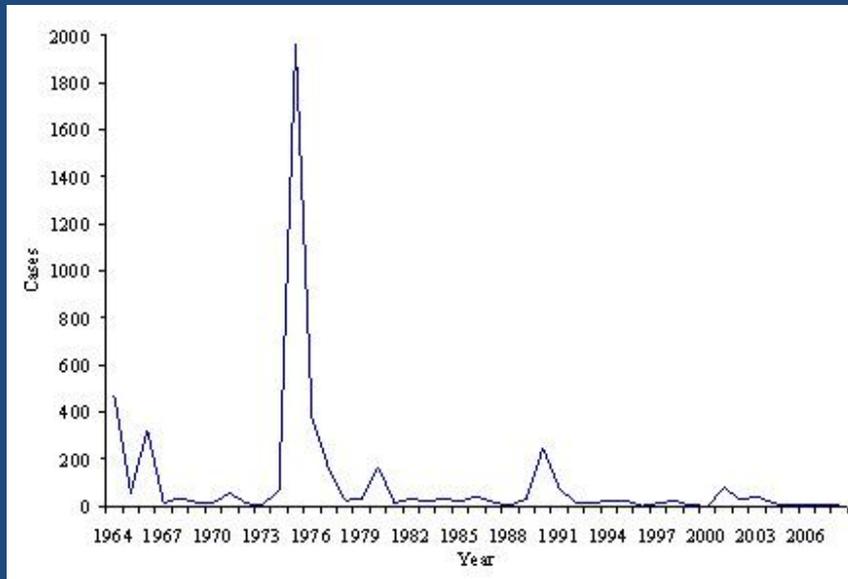


# Human WNV Disease Cases United States, 2010



Less than 1% of infected people develop more severe illness.

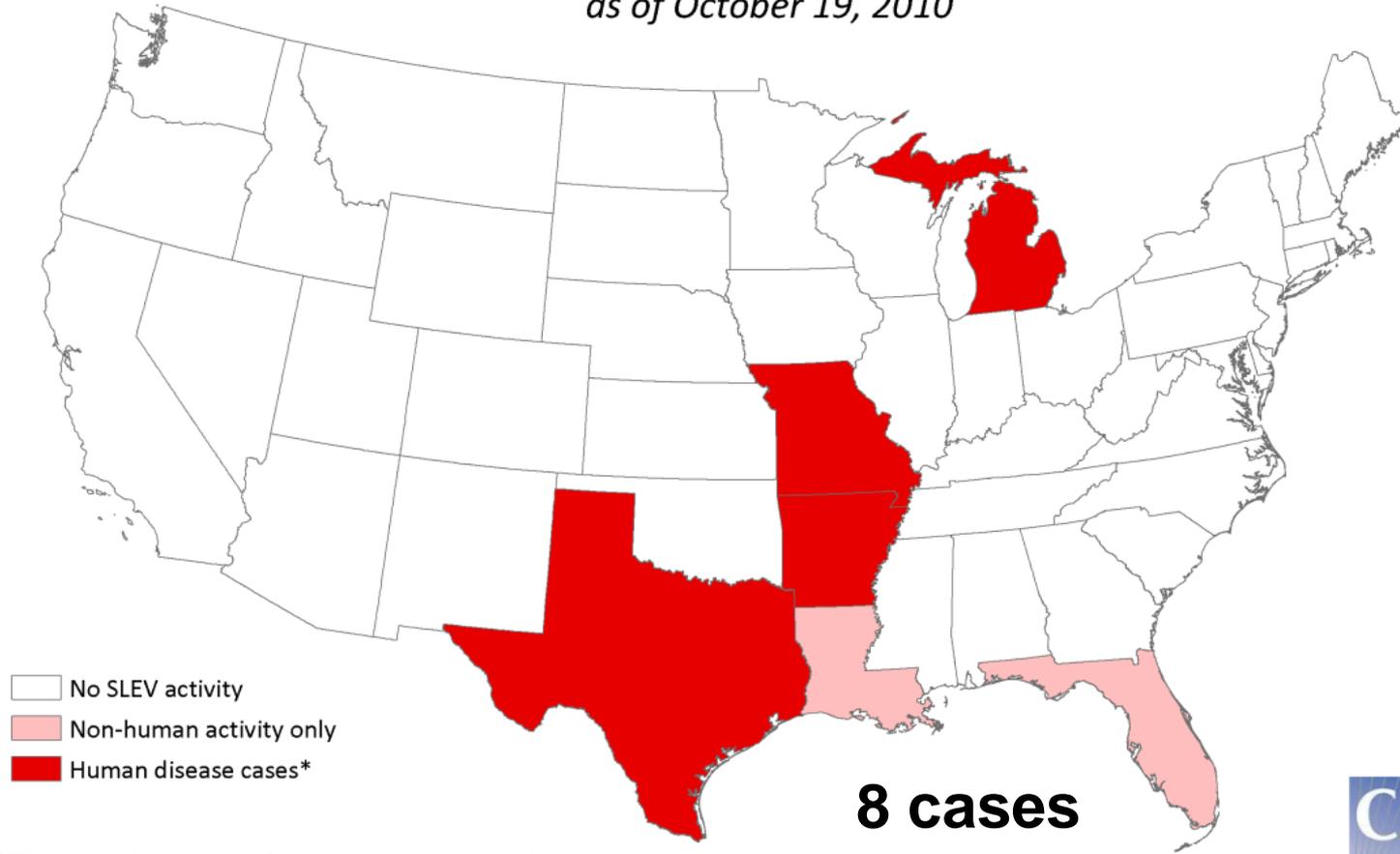
# St. Louis Encephalitis Virus Neuroinvasive Disease Cases



- 1975, 2,000 cases
- Central states in the Ohio-Mississippi River Basin

- Less than 1% of SLE viral infections are clinically apparent
- Milder in children than in adults
- Case-fatality ratio of 5-15 %
- Elderly are at highest risk for severe disease and death

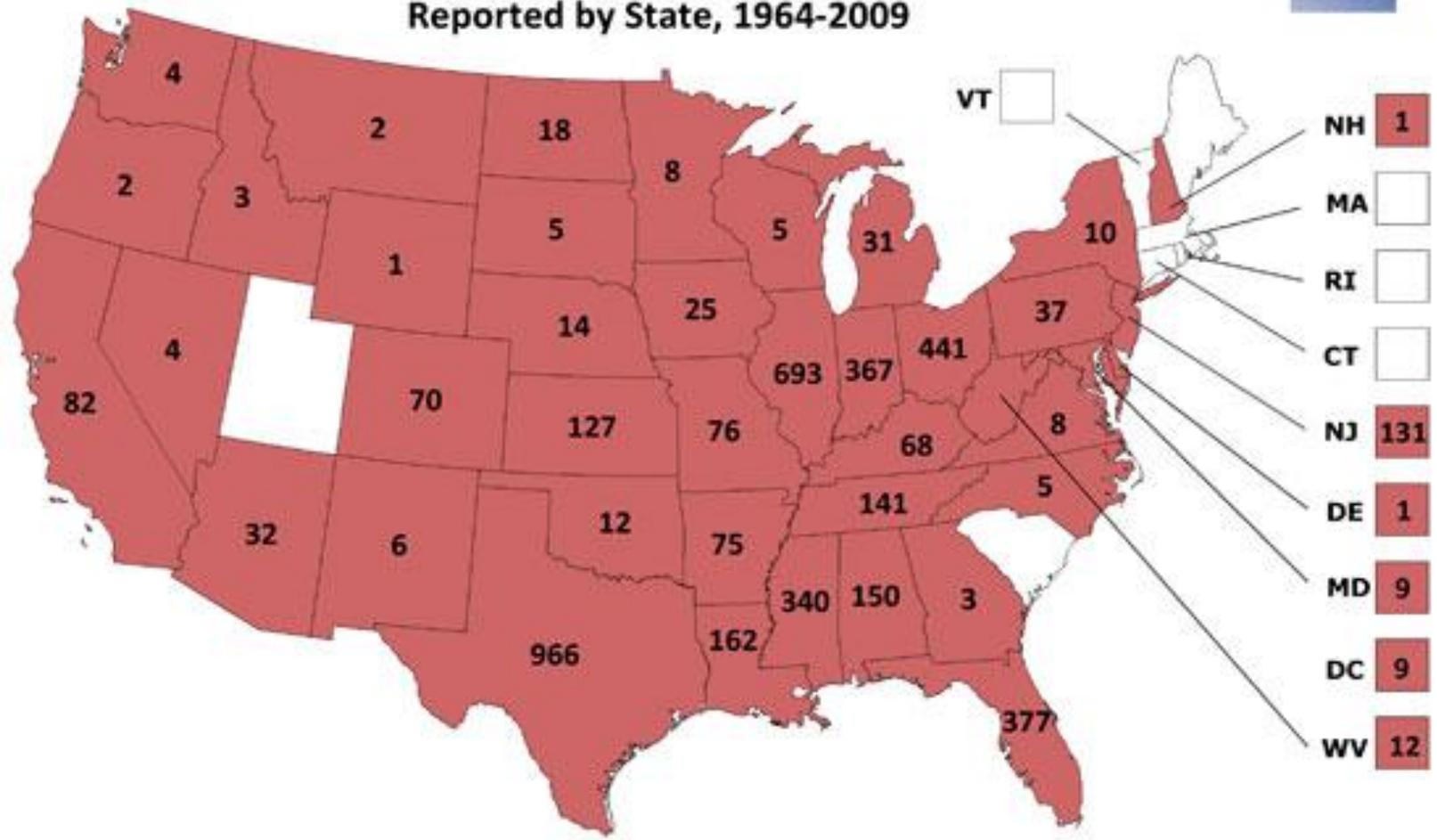
**St. Louis encephalitis virus (SLEV) activity reported to ArboNET, by state, United States, 2010**  
*as of October 19, 2010*



\*These jurisdictions may have also reported non-human SLEV activity.



# St. Louis Encephalitis Virus Neuroinvasive Disease Cases Reported by State, 1964-2009



**Transmission cycle of SLEV**  
*Cx pipiens, Cx quinquefasciatus*  
*Cx nigripalpus, Cx tarsalis*

**Mosquito vector**



**Amplifying host**

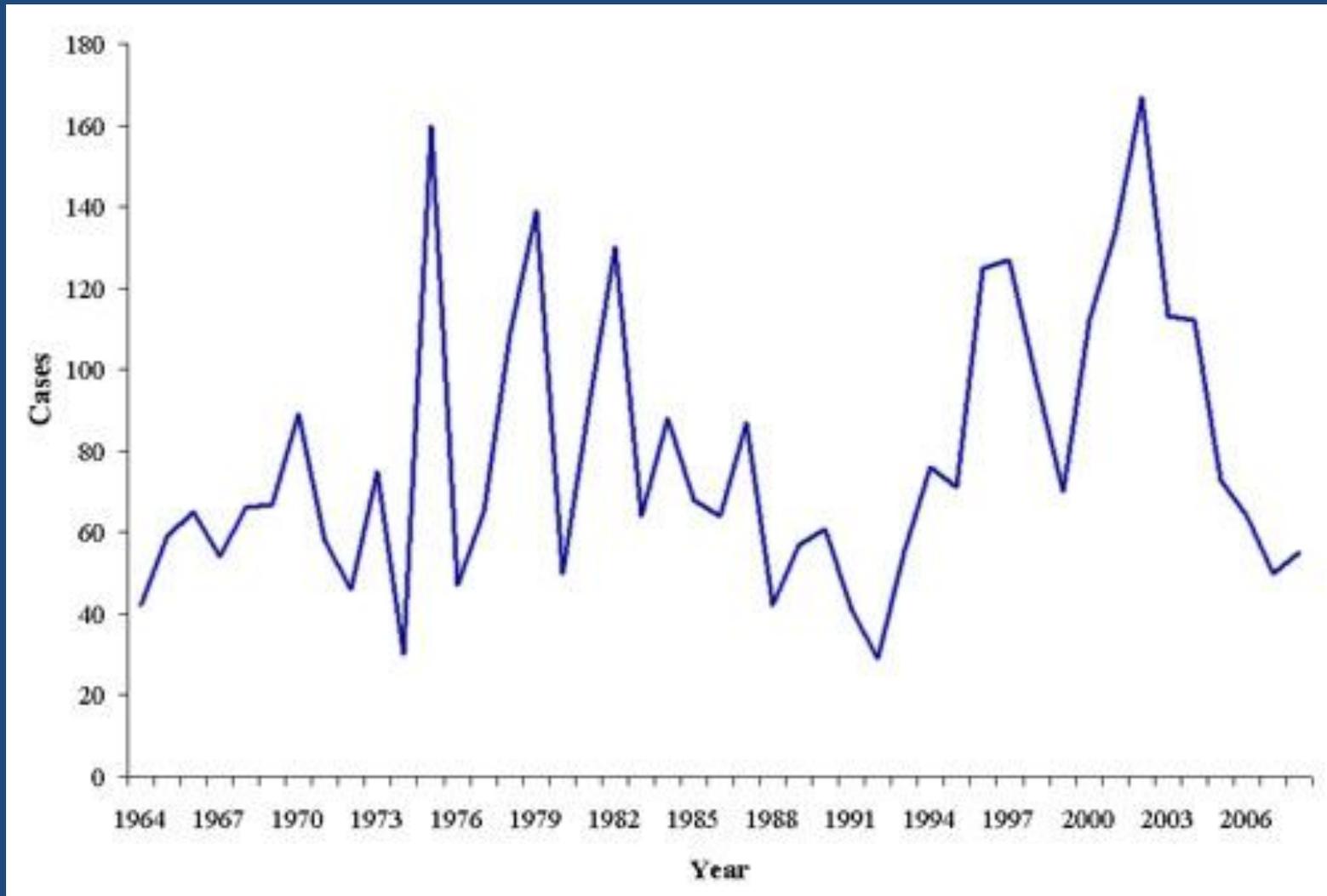


**Dead-end host**

**peridomestic birds**  
**house sparrow, pigeon,**  
**blue jay, and robin**

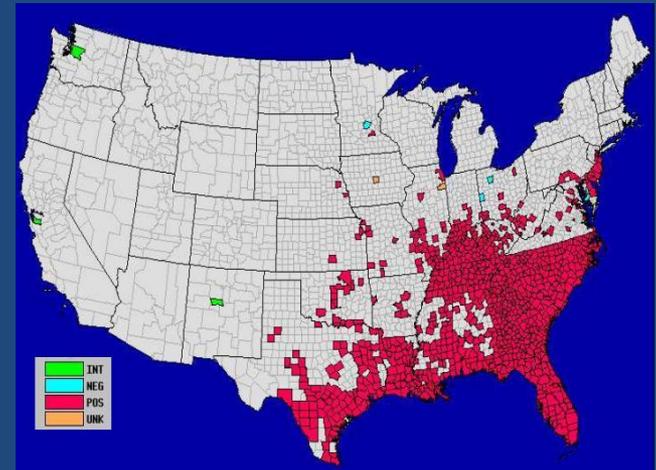


# California Serogroup Virus Neuroinvasive Disease Cases



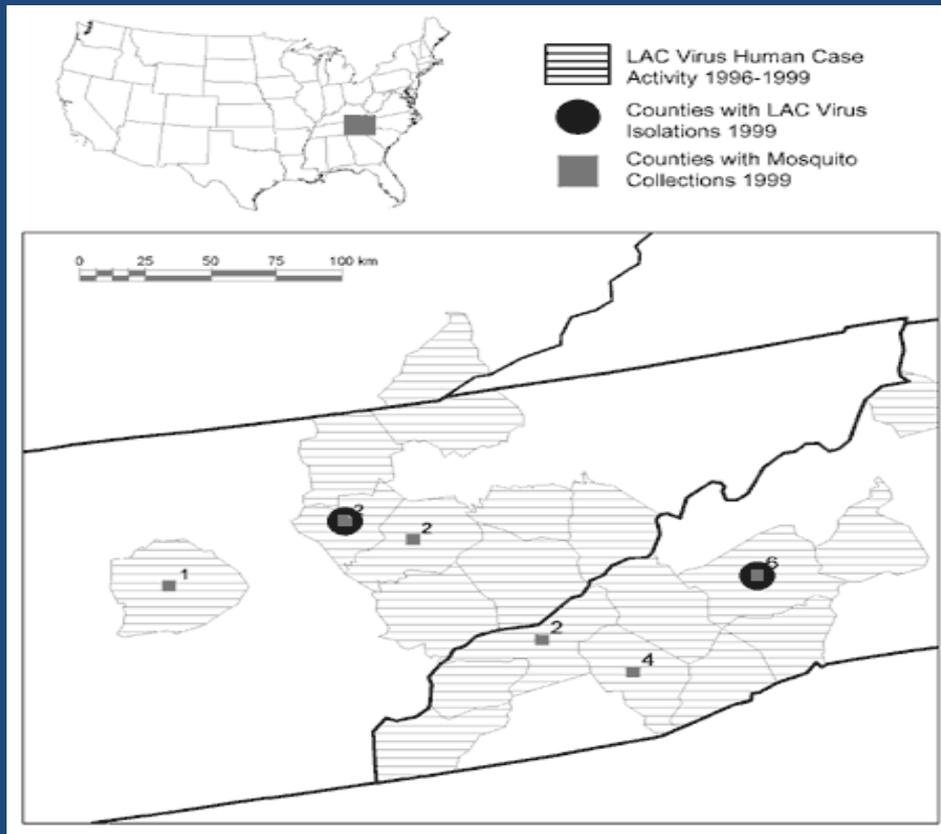
# La Crosse Virus in *Aedes albopictus*

- *Ae. Albopictus*
  - Indigenous to South-east Asia, islands of the Western Pacific and Indian Ocean
  - First discovered in Houston, Texas, in 1985
  - Arrived in the United States in a shipment of used tires from Asia with dormant eggs



Emerg Infect Dis. 2001 Sep-Oct;7(5):807-11.

# La Crosse Virus in *Aedes albopictus*



- Invasive mosquito species
- An opportunistic container-breeder
- Cathartic feeding habits
- Competent vector for at least 22 arboviruses, including LACV