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

- Food, Space, Breeding sites
- Weather and Climate
- Weather and Climate
- Food, Space, Breeding sites

Vertebrate Host

- Virus

Vector

- Virus
- Eggs
- Pupae
- Larvae
- Terrestrial Aquatic

Primary or Accessory Vector

Incidental hosts
12 yo with Headache, Vomiting, and Inappropriate Combativeness after eating at Wendy’s

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

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
  – Trivitattus virus

✓ Three segments
✓ Single-stranded RNA
✓ Spherical or oval
✓ Enveloped
La Crosse Encephalitis in Children

- 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.**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>MEAN VALUE ±SD</th>
<th>RANGE</th>
<th>REMARKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrospinal fluid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White-cell count (per mm³)</td>
<td>130±151</td>
<td>2–867</td>
<td>&lt;200/mm³ in most cases</td>
</tr>
<tr>
<td>Differential count (% lymphocytes)</td>
<td>—</td>
<td>2–100</td>
<td>Predominance of lymphocytes</td>
</tr>
<tr>
<td>Red-cell count (per mm³)</td>
<td>71±213</td>
<td>0–1500</td>
<td>Elevated (≥20/mm³) in 25%</td>
</tr>
<tr>
<td>Glucose (mg/dl)*</td>
<td>75±20</td>
<td>37–149</td>
<td>Normal</td>
</tr>
<tr>
<td>Protein (mg/dl)</td>
<td>37±15</td>
<td>10–85</td>
<td>Rarely elevated</td>
</tr>
<tr>
<td>Peripheral blood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White-cell count (per mm³)</td>
<td>15,700±5900</td>
<td>6800–49,700</td>
<td>Usually elevated (&gt;15,000/mm³)</td>
</tr>
<tr>
<td>Differential count (% polymorphonuclear leukocytes)</td>
<td>—</td>
<td>17–94</td>
<td>Predominance of polymorphonuclear leukocytes</td>
</tr>
</tbody>
</table>

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 ± 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

<table>
<thead>
<tr>
<th></th>
<th>WBC</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>22 mo</td>
<td></td>
<td>14.9</td>
<td>Na</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSF</td>
<td>WBC</td>
<td>DIFF</td>
<td>Protein</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/7</td>
<td>132</td>
<td>55N, 33L</td>
<td>33</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Misc</td>
<td>-HSV</td>
<td>-ENTERO</td>
<td></td>
<td>-CX</td>
<td></td>
</tr>
<tr>
<td>30 mo</td>
<td></td>
<td>16.1</td>
<td>Na</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSF</td>
<td>WBC</td>
<td>DIFF</td>
<td>Protein</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/24</td>
<td>177</td>
<td>5S,80L</td>
<td>34</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Misc</td>
<td>-HSV</td>
<td>-ENTERO</td>
<td></td>
<td>-CX</td>
<td></td>
</tr>
</tbody>
</table>
California serogroup (CAL) virus activity reported to ArboNET, by state, United States, 2010

as of October 19, 2010

63 US cases
14 NC

*These jurisdictions may have also reported non-human CAL virus activity.
California Serogroup Virus Neuroinvasive Disease
Average Annual Incidence by County, 1996-2008

Incidence per 100,000 population
- < 0.1
- 0.1 - 0.9
- >= 1.00
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

<table>
<thead>
<tr>
<th>Serum</th>
<th>WBC</th>
<th>10.2</th>
<th>Na</th>
<th>124</th>
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</thead>
<tbody>
<tr>
<td>CSF</td>
<td>WBC</td>
<td>DIFF</td>
<td>Protein</td>
<td>Glucose</td>
</tr>
<tr>
<td>3/25</td>
<td>268</td>
<td>80N, 8L</td>
<td>156</td>
<td>43</td>
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<tr>
<td>4/10</td>
<td>20</td>
<td>59N, 28L</td>
<td>104</td>
<td>50</td>
</tr>
<tr>
<td>4/13</td>
<td>13</td>
<td>35N, 49L</td>
<td>88</td>
<td>43</td>
</tr>
<tr>
<td>Misc</td>
<td>-HSV</td>
<td>-ENTERO</td>
<td>-CRYPTO</td>
<td>-MTB</td>
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<tr>
<td>-JC</td>
<td>-EBV</td>
<td>-CMV</td>
<td>-VZV</td>
<td>-VDRL</td>
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</table>
The mosquitoes that spread LACV are most active during the daytime.

Aedes triseriatus

Transmission cycle of LACV

Mosquito vector

Dead-end host

Amplifying 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

<table>
<thead>
<tr>
<th></th>
<th>WBC</th>
<th>CSF</th>
<th>WBC</th>
<th>DIFF</th>
<th>Protein</th>
<th>Glucose</th>
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<tbody>
<tr>
<td>Swain</td>
<td>11.9</td>
<td>Na</td>
<td>133</td>
<td></td>
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<tr>
<td>CSF</td>
<td>WBC</td>
<td>DIFF</td>
<td>Protein</td>
<td>Glucose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/2</td>
<td>73</td>
<td>57S, 35L</td>
<td>81</td>
<td>65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Misc</td>
<td>-HSV</td>
<td>-RPR</td>
<td>-CX</td>
<td></td>
<td></td>
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<tr>
<td>Cherokee</td>
<td>WBC</td>
<td>16.8</td>
<td>Na</td>
<td>124</td>
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<td></td>
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<tr>
<td>CSF</td>
<td>WBC</td>
<td>DIFF</td>
<td>Protein</td>
<td>Glucose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8/9</td>
<td>56</td>
<td>30S, 56L</td>
<td>45</td>
<td>60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Misc</td>
<td>-HSV</td>
<td>-Crypt</td>
<td>-CX</td>
<td></td>
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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)

<table>
<thead>
<tr>
<th>COUNTY</th>
<th>1998</th>
<th>1999</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>Total</th>
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<tbody>
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<td>Buncombe</td>
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<td>1</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td>8</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>4</td>
<td>34</td>
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<tr>
<td>Haywood</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
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<td>26</td>
</tr>
<tr>
<td>Jackson</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>22</td>
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<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>8</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>22</td>
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<tr>
<td>Swain</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>1</td>
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<td>16</td>
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<td>Henderson</td>
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<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Total</td>
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<td>32</td>
<td>18</td>
<td>10</td>
<td>7</td>
<td>16</td>
<td>165</td>
</tr>
</tbody>
</table>
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*

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

* 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

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

589 cases
West Nile virus (WNV) neuroinvasive disease incidence reported to ArboNET, by state, United States, 2010

as of November 30, 2010

Per 100,000 Population*

0.00
0.01 - 0.24
0.25 - 0.49
0.50 - 0.99
>= 1.00

*Scales are different for state and county incidence maps

375 cases
41 deaths
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

8 cases

*These jurisdictions may have also reported non-human SLEV activity.
St. Louis Encephalitis Virus Neuroinvasive Disease Cases Reported by State, 1964-2009

[Map showing the distribution of cases across the United States with numbers indicating the number of cases in each state.]
Transmission cycle of SLEV

*Cx pipiens*, *Cx quinquefasciatus*

*Cx nigripalpus*, *Cx tarsalis*

Mosquito vector

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

La Crosse Virus in *Aedes albopictus*

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