Jamestown Canyon Virus Revisited: Are We Neglecting and Under Recognized Mosquito-Borne Disease

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• Mosquito-borne *Orthobunyavirus* (ss-RNA) found throughout much of temperate North America
• First isolated in 1961 from *Culiseta inornata* in CO
• Human cases are comparatively rare but appear to be on the rise (166 cases from 2004 – 2018)
• Mostly in Midwestern and Northeastern states
• Sero-prevalence = 6.7% - 48.2% - “Under Recognized”
• Causes acute febrile illness, fever, meningitis, or meningoencephalitis
• Infects a variety of free ranging ungulates - deer, moose, bison, elk (sero-prevalence: 21% in CT, 77% in WI)
• White-tailed deer recognized as principal amplification hosts (experimental infections and prevalence of Ab)
• Isolated from 26 mosquito species, mostly boreal *Aedes*
• Vertically transmitted in mosquitoes
Clinical manifestations of patients with JCV disease

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>83%</td>
</tr>
<tr>
<td>General weakness</td>
<td>70%</td>
</tr>
<tr>
<td>Headache</td>
<td>66%</td>
</tr>
<tr>
<td>Nausea</td>
<td>37%</td>
</tr>
<tr>
<td>Neck rigidity</td>
<td>30%</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>23%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>16%</td>
</tr>
<tr>
<td>Photophobia</td>
<td>13%</td>
</tr>
<tr>
<td>Tremors</td>
<td>13%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>13%</td>
</tr>
<tr>
<td>Seizures</td>
<td>6%</td>
</tr>
</tbody>
</table>

N = 30

Probable cases vs. Confirmed cases

Month of illness onset

- July: 8 cases
- August: 6 cases
- September: 4 cases
- June: 4 cases
- May: 3 cases
- April: 1 case
- March: 1 case
- February: 1 case
- January: 1 case
- October: 1 case
- November: 1 case
- December: 1 case

**Characteristics of patients with JCV disease**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Range</td>
<td>10-84 yrs.</td>
</tr>
<tr>
<td>Median Age</td>
<td>54 yrs.</td>
</tr>
<tr>
<td>Males</td>
<td>56%</td>
</tr>
<tr>
<td>Outdoor exposure</td>
<td>73%</td>
</tr>
<tr>
<td>History of mosquito bite</td>
<td>56%</td>
</tr>
<tr>
<td>No travel out of state</td>
<td>80%</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>47%</td>
</tr>
<tr>
<td>Neuroinvasive</td>
<td>50%</td>
</tr>
<tr>
<td>Fatality</td>
<td>3%</td>
</tr>
</tbody>
</table>

N = 30
Median age = 54 yrs

![Bar chart showing age distribution and probable vs. confirmed cases]
Examine the spatial and temporal patterns of Jamestown Canyon virus activity in the Connecticut as a function of:

- Vector mosquito abundance and distribution with identification of key vectors
- Land use characteristics
  - Agriculture/Grass
  - Forest
  - Developed
  - Wetland
- Distribution and abundance of white-tailed deer, *Odocoileus virginianus*, reservoir vertebrate host
  - Exponential increase with reforestation throughout the northeastern US since 1900
Mosquito Collection and Arbovirus Isolation Methods

- Data gleaned from our State-wide Mosquito/Arbovirus Surveillance Program
- 20 year period: 1997 to 2017
- Conducted from June - October
- 92 permanent trapping stations (trap weekly)
- CO₂-baited CDC light trap and gravid traps
- Mosquitoes identified to species (45 species)
- Pooled by species and site (Maximum of 50)
- Virus isolation in Vero cell cultures (BSL 3)
- Virus identification by real time PCR or RT-PCR
Jamestown Canyon Virus – Spatial Geographic Distribution

- Virus detected in 84 of 91 sites (92%) 1997-2017
- Equally distributed throughout urban, suburban and rural locales
- No significant association with any land cover categories ($r = 0.17$)
- No significant relationship to white-tailed deer abundance
• 478 virus isolations from 25 of 45 (55%) mosquito species collected

• Mostly Aedes and Anopheles

• 5 species incriminated as most important vectors based on:
  - Number of years detected
  - Number of sites detected
  - Number of virus isolations

• Aedes canadensis*
• Aedes cantator
• Aedes abserratus
• Anopheles punctipennis*
• Aedes aurifer

* Competent lab vector
Among the most abundant and widely distributed species in the state

Larvae develop in a variety of freshwater habitats
- Temporary leaf-lined pools in wooded areas
- Roadside ditches
- Vernal pools in open fields
- Permanent swamps

Univoltine – peak populations in June - July

Feed on a variety of animals but mostly mammals (98%) including humans (Molaei et al JME 2008)

White-tailed deer - 95% of mammalian blood meals

Competent vector of JCV (Heard et al JAMCA 1991)
Jamestown Canyon Virus – Yearly Activity 1997 - 2017

- Consistently detected every year
- Infection rates range from 0.05 - 0.36 (MLE/1000) mean = 0.16
- Yearly virus activity is directly related to overall mosquito abundance
Jamestown Canyon Virus – Seasonal Prevalence

- Infected mosquitoes detected from June through September
- Virus isolations parallel overall mosquito abundance
- Greatest number of virus isolations: mid-June through mid-July
- Correspondingly high infection rates (MLE) during same time (0.5)
- Consistent with vertical transmission

Andreadis et al. VBZD 8: 2008
• Sequenced 56 JCV isolates from Connecticut 1966 - 2006
• Analysis of nucleotide sequences from the S segment (nucleocapsid) (maximum likelihood)
• Two Major Lineages in Connecticut
  - Lineage A 1966 - 2006
  - Lineages B1 and B2 1998 - 2004
• Lineages did not group by year of isolation or mosquito species
• Very little change over time
Distribution of Jamestown Canyon Virus Lineages in Connecticut

- Geographically structured
  - Lineage A (west)
  - Lineage B (east)
- Both lineages in some sites
- Long term maintenance of local populations of JCV suggests local overwintering and persistence of virus
- JCV appears to be evolving slowly by random mutation (genetic drift)
- No evidence for genetic reassortment among lineages A and B (genetic shift)
Summary

- JCV is widely distributed in CT and consistently amplifies each year
- Activity occurs from June to September with peak from late June through mid July
- Activity is a function of mosquito abundance
- Vectors are largely univoltine woodland species
- *Aedes canadensis* appears to be principal vector
- The virus is very stable suggesting local overwintering in mosquitoes via transovarial transmission with long term persistence
- Human exposure is likely to be moderate to high
- Clinicians should consider JCV infection in differential diagnosis when an arboviral infection is suspected to be causing febrile neurological illness and WNV testing is inconclusive or negative
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Questions?

Alexander Skochkov “Old Mosquito”