Reflections on the Ecology and Epidemiology of Eastern Equine Encephalitis in the Northeastern United States

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**Eastern Equine Encephalitis**

- Most pathogenic arthropod-borne virus in North America (Alphavirus: Togaviridae, SSRNA)
  - ~ 6-7 human cases / year
  - 40% case fatality rate
  - Neurological impairment in survivors (35%)
  - No commercial vaccine or effective treatment

- Activity is most common in and around freshwater hardwood swamps – highly focal

- Perpetuates in an enzootic cycle involving wild Passeriformes birds and ornithophilic mosquitoes

- Principal enzootic vectors in the northeastern US
  - *Culiseta melanura*
  - *Culiseta morsitans*  
    - Role as “bridge vectors” unresolved
Key EEE Historical Events – Northeastern US

• 1831 - First equine outbreak of EEE virus in Massachusetts - “horses dying of a brain disease”
• 1933 - First isolation of EEE virus from horse brain during an outbreak in coastal areas of Delaware, Maryland, New Jersey and Virginia
• 1934 - Mosquitoes first incriminated as potential vectors in a series of vector competence studies with species of Aedes, Culex and Coquillettidia
• 1935 - Birds considered as reservoir hosts; 1950 - first isolation of EEE made from a wild bird
• 1938 - The first human cases confirmed – 35 (25 fatal) human cases, > 300 horse cases in Massachusetts; 38 horse cases in Connecticut
• 1938 - Shown that virus could cause of encephalitis in wild and domestic pheasants in Connecticut
• 1949 - First isolation of EEE virus from mosquitoes – Cq. perturbans
• 1951 - First isolation of EEE virus from Culiseta melanura
• 1959 - Major outbreak in New Jersey – 33 human cases
• 1971 - EEE discovered in Central New York – 1st human case
Human Cases of EEE in the United States 1964 - 2019

N = 347
Resurgence and Expansion of EEE Activity in NE US

- 1964 to 2002 – sporadic outbreaks with no apparent pattern
- 2003 – resurgence and expansion

Human Cases
- 1964 – 2002 = 47
- 2003 - 2019 = 79

< 1 case / yr
4-5 cases / yr

Armstrong & Andreadis NE J Med 2013
EEE Veterinary Cases
Northeastern US
2003 - 2019

N = 309
Ave = 18 / yr

ArboNET
Human and Veterinary Cases of EEE in the Northeastern US - 2019

EEE Activity = 30 Counties, 7 States
Human cases = 23 (8 fatalities, 35%)
Veterinary cases = 42
Factors Contributing to the Resurgence of EEE in the Northeastern US

- Reforestation and wetland restoration – by mid 1800’s much of the forests in the northeastern US were stripped and cedar swamps were destroyed

- Increased habitat for *Culiseta melanura*
- Proliferation of wetland roosting sites for birds (e.g. robins, wood thrush)

- Suburban development near critical wetland mosquito habitat
- Increasingly expose people to the threat of EEE infection

- Changes in average temperatures and precipitation events related to climate change
- Milder winters
- Warmer summers
- Extremes in both precipitation and drought
- Enhance overwintering survival
- Extend transmission season
- Accelerate generation time
- Increase frequency of blood feeding
- Accelerate virus replication within mosquito
- Allow mosquitoes to extend northward range

Komar & Speilman NY Acad Sci 1994
Pre-Season

- Significant EEE activity in the previous year
- Mild winters with insulating snow cover
- High water table in enzootic swamps
- Above average rainfall in the prior fall/winter and spring

In-Season

- Above average *Culiseta melanura* populations
- EEE virus isolations from mosquitoes in June or early July
- Isolations of EEE virus from a mammal-biting mosquitoes – *Cq. perturbans*
- Numerous EEE isolations > 30 – 50
- High MIR in *Culiseta melanura* >1:1000
- EEE activity beyond traditional areas
- Early and above average equine cases
- Infection of a human prior to August
<table>
<thead>
<tr>
<th>Year</th>
<th>No. EEE virus isolations</th>
<th>Mean no. Cs. melanura / trap</th>
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<tbody>
<tr>
<td>1996</td>
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<td>2019</td>
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</table>
Ave. No Mosquitoes per Light Trap

Culiseta melanura Abundance
Connecticut

- **June**
- **July**
- **August**
- **September**
- **October**

**2019**

**22 Year Mean**
Weekly Isolations of EEE virus from field collected mosquitoes in Connecticut

No. EEE virus isolations

Week
Weekly Isolations of EEE virus from field collected mosquitoes in Connecticut

Earlier EEE virus amplification in 2019
**Habitat**: Densely wooded freshwater swamps (red maple and white cedar) and sphagnum bogs

**Development**: Develop in subterranean “crypts” in deep shaded cavities under tree roots

**Seasonal Distribution**: mid-May – October

**Feeding Preference**: Primarily birds with occasional feeding on mammals including humans

**Number of Generations**: 2-3 per year

**Adult Flight Range**: > 2 miles

**Overwintering Stage**: Larvae (all instars)
Phenology of Overwintering Development of *Cs. melanura*

Andreadis et al. *JAMCA* 2012
### EEE Virus Isolations from Mosquitoes in Connecticut 1996 - 2018

#### Species (n = 19) and No.

<table>
<thead>
<tr>
<th>Species</th>
<th>No.</th>
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<tbody>
<tr>
<td><em>Cs. melanura</em></td>
<td>264</td>
</tr>
<tr>
<td><em>Ae. canadensis</em></td>
<td>32</td>
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<tr>
<td><em>Ae. cinereus</em></td>
<td>18</td>
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<tr>
<td><em>Ae. vexans</em></td>
<td>15</td>
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<tr>
<td><em>Cx. salinarius</em></td>
<td>12</td>
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<tr>
<td><em>Ur. sapphirina</em></td>
<td>12</td>
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<tr>
<td><em>Cx. pipiens</em></td>
<td>10</td>
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<tr>
<td><em>Ae. trivittatus</em></td>
<td>9</td>
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<tr>
<td><em>An. punctipennis</em></td>
<td>8</td>
</tr>
<tr>
<td><em>Ae. cantator</em></td>
<td>5</td>
</tr>
<tr>
<td><em>Cs. morsitans</em></td>
<td>5</td>
</tr>
<tr>
<td><em>Cq. perturbans</em></td>
<td>4</td>
</tr>
<tr>
<td>Others (7 species)</td>
<td>18</td>
</tr>
</tbody>
</table>

#### Species Distribution

- **Cs. melanura**: 64.1%
- **Ae. canadensis**: 7.8%
- **Ae. cinereus**: 4.0%
- **Ae. vexans**: 3.6%
- **Cx. salinarius**: 2.9%
- **Ur. sapphirina**: 2.9%
- **Cx. pipiens**: 2.4%
- **Ae. trivittatus**: 2.2%
- **An. punctipennis**: 1.9%
- **Minor species (10)**: 7.8%
EEE Virus Detections from Mosquitoes in CT, MA, NJ and NY - 2019

**Connecticut**

- *C. melanura*: 65.6%
- *Ur. sapphirina*: 5.7%
- *Cq. perturbans*: 4.0%
- *Ae. canadensis*: 4.1%
- *Cx. salinarius*: 3.3%
- *Ae. vexans*: 3.3%
- *Ps. ferox*: 3.3%
- *An. punctipennis*: 2.5%
- *Cx. pipiens*: 1.6%
- *Ae. cinereus*: 1.6%
- Minor species (5): 4.1%

**New York**

- *C. melanura*: 88.9%
- *Cq. perturbans*: 4.8%
- *Ae. vexans*: 1.6%
- *Cx. salinarius*: 4.8%
- *Ae. albopticus*: 2.7%
- *Ae. triseriatus*: 2.7%
- *Ae. canadensis*: 1.6%
- *Cx. pipiens/restuans*: 17.8%
- *Cq. perturbans*: 33.4%

**Massachusetts**

- *C. melanura*: 45.9%
- *Cq. perturbans*: 4.8%
- *Ae. albopticus*: 2.7%
- *Ae. canadensis*: 5.6%
- *Ae. triseriatus*: 2.7%
- *Ae. vexans*: 1.6%
- *Cx. pipiens/restuans*: 2.8%
- *Cx. salinarius*: 10.6%
- *Cq. perturbans*: 33.4%
There are major differences in the quantity of virus found in EEE virus-positive, field-collected mosquitoes.

- **Cs. melanura** appears to be the only species in which virus titers are sufficiently high enough to support efficient transmission.

- Other species include *Ae. cinereus*, *Cq. perturbans*, *Ae. canadensis*.

- Important to consider virus titers when implicating other mosquito vectors.

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1 Armstrong & Andreadis EID 2010
2 Nasci & Mitchell JAMCA 1996
Host Feeding Patterns of *Culiseta melanura* and Potential Bridge Vectors of EEE in the Northeastern US (CT, MA, NY, VT)

![Bar chart showing host feeding patterns of *Culiseta melanura* and potential bridge vectors of EEE in the Northeastern US (CT, MA, NY, VT).](chart)

- **Cs. melanura**: 0.2% Human
- **Cq. perturbans**: 5.1% Human
- **Ae. canadensis**: 3.7% Human
- **Cx. salinarius**: 2.0% Human
- **Ae. cinereus**: 8.4% Human

Proportion of Avian and Mammalian Derived Blood Meals in *Culiseta melanura* populations in the Northeastern US

<table>
<thead>
<tr>
<th>Location</th>
<th>Mammal</th>
<th>Bird</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vermont</td>
<td>6.0%</td>
<td>94.0%</td>
</tr>
<tr>
<td>New York</td>
<td>5.8%</td>
<td>94.2%</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>1.1%</td>
<td>98.9%</td>
</tr>
<tr>
<td>Connecticut</td>
<td>0.3%</td>
<td>99.7%</td>
</tr>
</tbody>
</table>

Wood Thrush
American Robin
Tufted Titmouse
Common Grackle
Chipping Sparrow
Black-capped Chickadee
Northern Cardinal
Red-eyed Vireo
Scarlet Tanager
Common Yellowthroat
Baltimore Oriole
Black-capped Chickadee
Veery
Green Heron

Connecticut
N = 42 species
18%
14%
13%

New York
N = 52 species
24%
8%
9%

Massachusetts
N = 55 species
22%
9%
9%

Vermont
N = 49 species
18%
10%
12%

Culiseta melanura
Avian-Derived Blood Meals

EEE Antibody Prevalence in Wild Birds: Regional Comparisons

Wood Trush
American Robin
Gray Catbird
Ovenbird
Song Sparrow

NJ (Crans et al. JME 1994)
MA (Main et al. AJTMH 1988)
NY (Emord and Morris, JME 1984)
NY (Howard et al. JME 2004)
ME (Elias et al. VBZD 2017)
• EEE viruses group into temporally discrete genetically diverse clades by year - suggests separate annual introduction events into the region
  − Migrating viremic birds

• Some strains persist into 2nd year - provides evidence for local overwintering
  − Vertical transmission in mosquitoes (Philbrook et al. CDC TR 1961)
  − Recrudescence in chronically infected birds (Crans et al. JME 1994)
  − Reptiles or amphibians (?)

• Support for both hypotheses
Sequenced complete genomes of 433 EEEV strains collected within the U.S. from 1934 to 2014

EEEV evolves relatively slowly and that transmission is enzootic in Florida, characterized by higher genetic diversity and long-term local persistence

EEEV in CT, MA and NY were characterized by lower genetic diversity, multiple introductions, and shorter local persistence

Supports a source-sink model in which FL is the major source of EEEV
Northeastern US EEE Virus Transmission Cycle

Enzootic Cycle

Virus

Culiseta melanura

June to October

Coquillettidia perturbans
Aedes canadensis
Culex salinarius
Culiseta melanura

“Bridge Vectors”

Epidemic / Epizootic Transmission

Local Overwintering & Annual Introduction

Wild Passerine Bird Reservoir and Amplifying Hosts

August to October

Wild Passerine Bird Reservoir

June to October

Culiseta melanura

Overwintering & Annual Introduction
• High likelihood that the EEE virus will reemerge
  - EEE usually persists after a major outbreak
  - Have consistently experienced equine and/or human cases every year since 2004

• Unlikely that we will experience as high a level of EEE virus activity
  - Herd immunity in reservoir birds – dampen enzootic transmission

• Remains to be seen how widespread activity will be
  - Will we see further expansion into NH, ME and VT?
Human serosurvey - human exposure?
- EEE antibodies detected in 0.7% of persons with no history of encephalitis after 1955 outbreak in Massachusetts (Feemster et al. NEJM 1958)
- Inapparent infections ranged from 3.1% to 7.6% after the 1959 outbreak in New Jersey (Goldfield et al. Am J Epidem 1968)

Identification of *Cs. melanura* breeding sites in newly recognized foci of human and animal infection

Screening larvae for virus – overwintering
- One reported isolation of EEE virus from *Cs. melanura* larvae (Philbrook et al. CDC Tech Rep 1961)
- Never been duplicated or confirmed

Pre-season treatment of *Cs. melanura* breeding sites
- Methoprene has been shown to be an effective larvicide when applied by fixed wing aircraft (Woodrow et al. JAMCA 1995)

Enhanced mosquito surveillance – in season
EEE Challenges and Issues

1. Risk assessment and communication
   - How do best assess human risk and communicate it to the public
   - Analysis and interpretation of surveillance findings
   - Triggers for response

2. Sharing samples for genetic analysis and validation
   - Virus availability – virus isolation vs PCR detection

3. Delays in laboratory diagnosis of human infection
   - Concerns with commercial labs – serology and false negatives

4. Prevention and control
   - Personal protective measures – effectiveness?
   - Preseason preemptive treatments of *Cs. melanura* breeding sites with larvicides
   - Truck-mounted and aerial adulticides – how do we evaluate effectiveness
   - Difficulties with public acceptance – environmental issues
   - Delays in implementation and high costs
   - What level of control is needed to reduce human risk of infection
Questions?

Alexander Skochkov "Old Mosquito"