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

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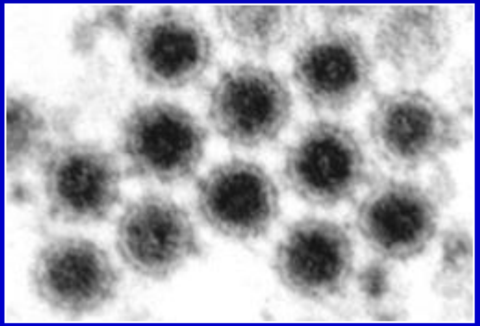

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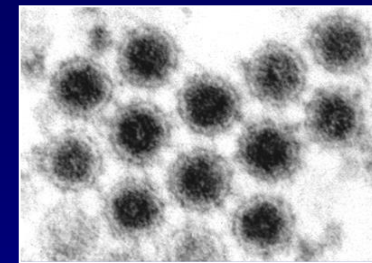
Eastern Equine Encephalitis



- 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

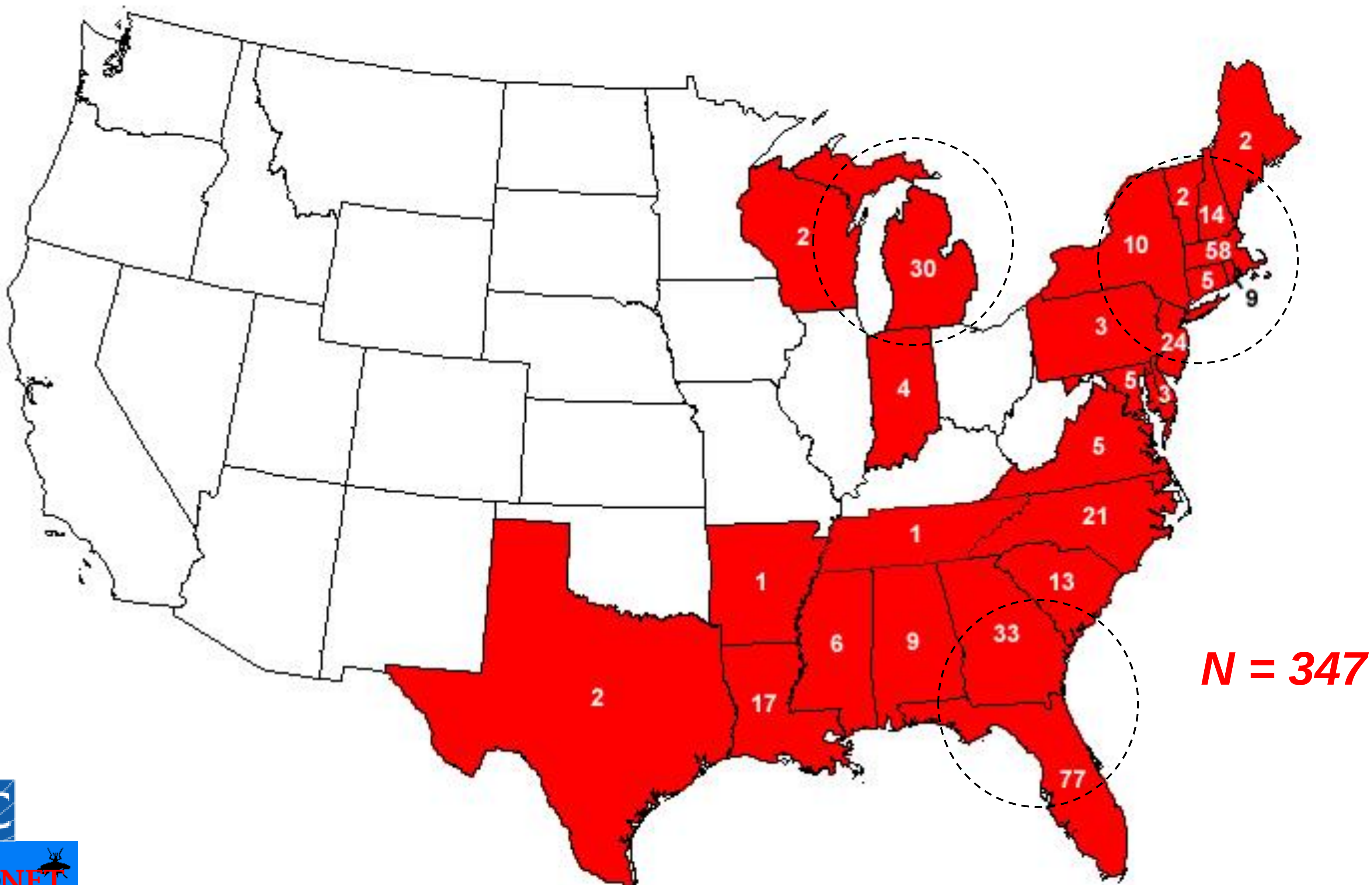
  - Culiseta melanura
  - Culiseta morsitans
  } *Role as "bridge vectors" unresolved*

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

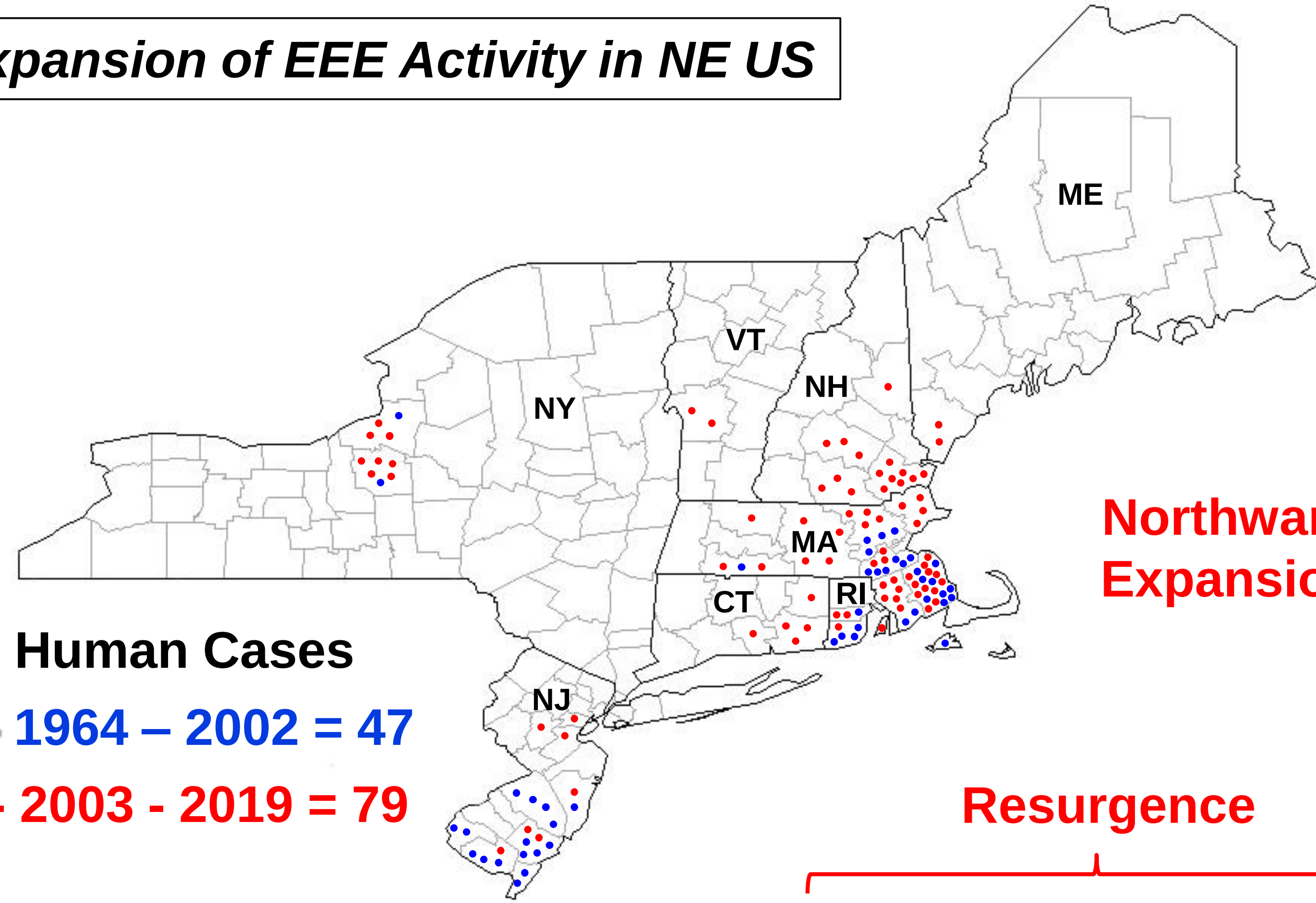
Human Cases of EEE in the United States 1964 - 2019

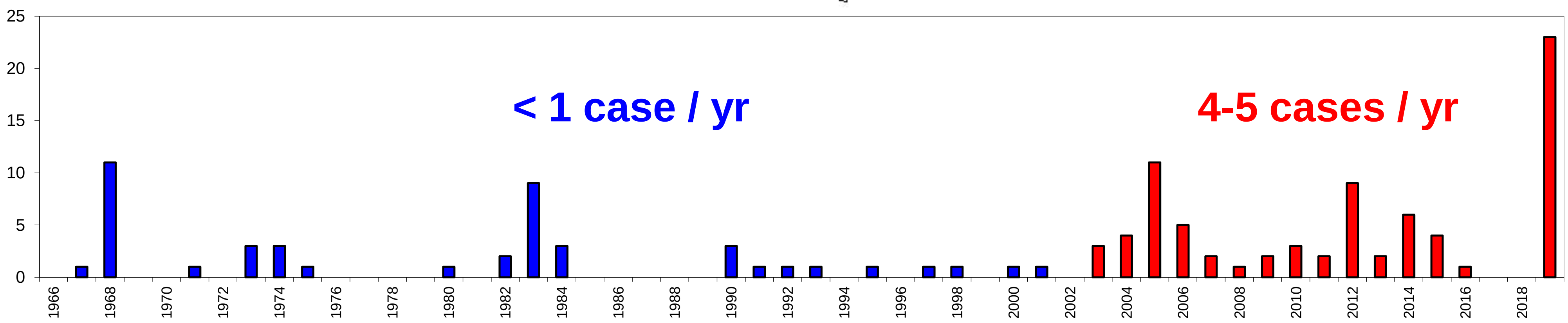


CDC
ArboNET

Resurgence and Expansion of EEE Activity in NE US

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

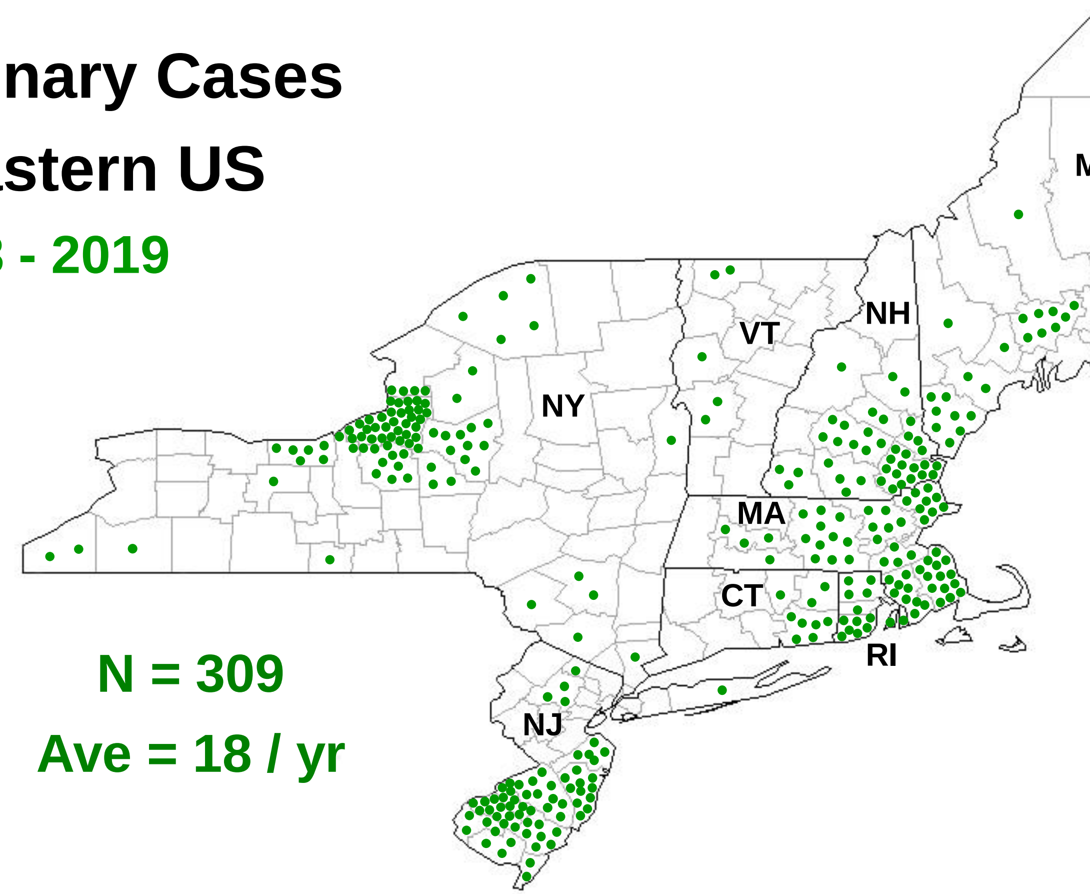




Armstrong & Andreadis NE J Med 2013

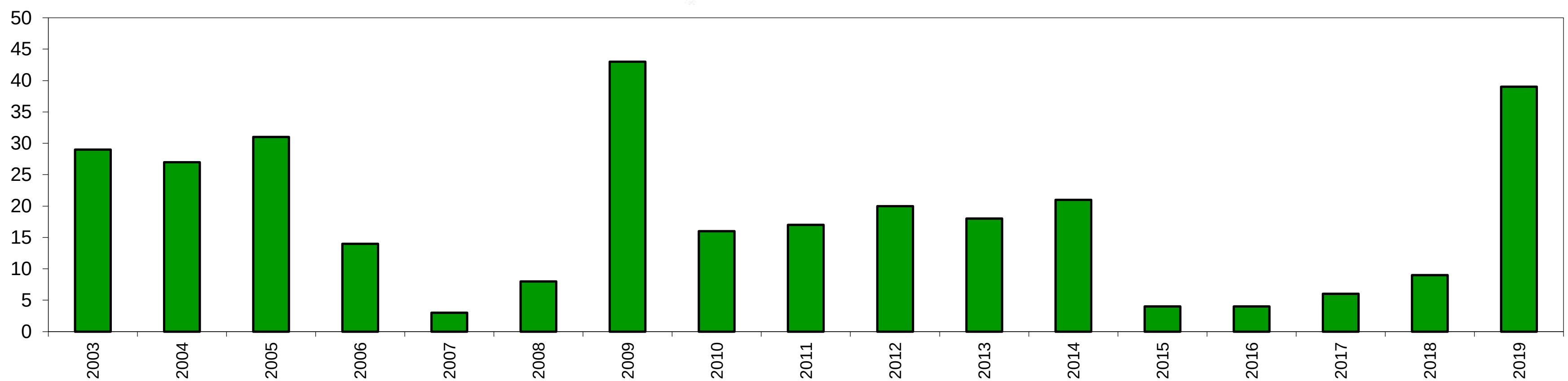
EEE Veterinary Cases
Northeastern US

2003 - 2019

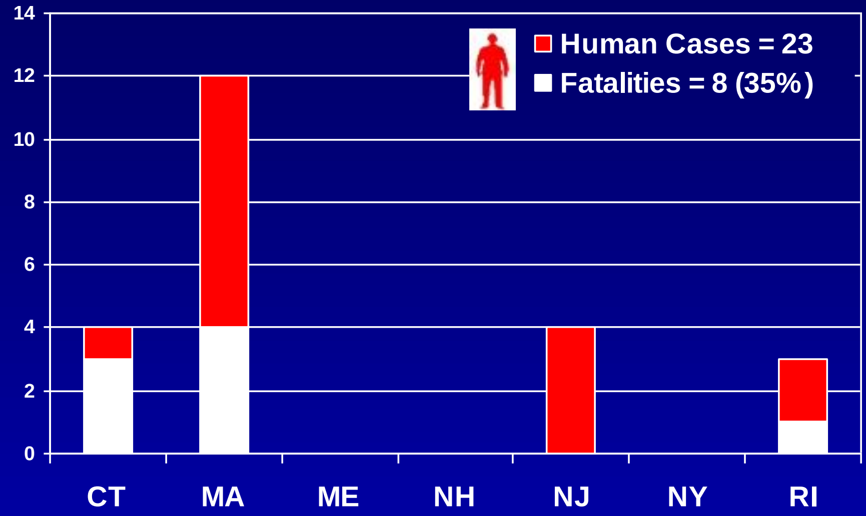


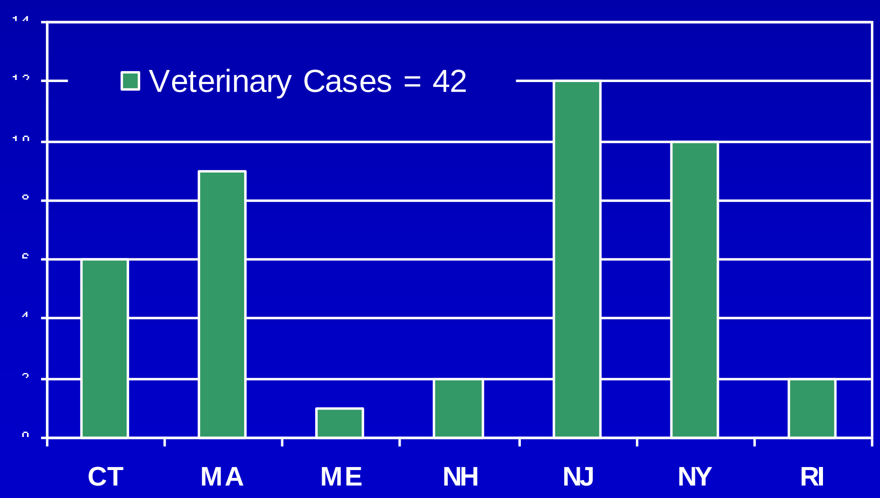
N = 309

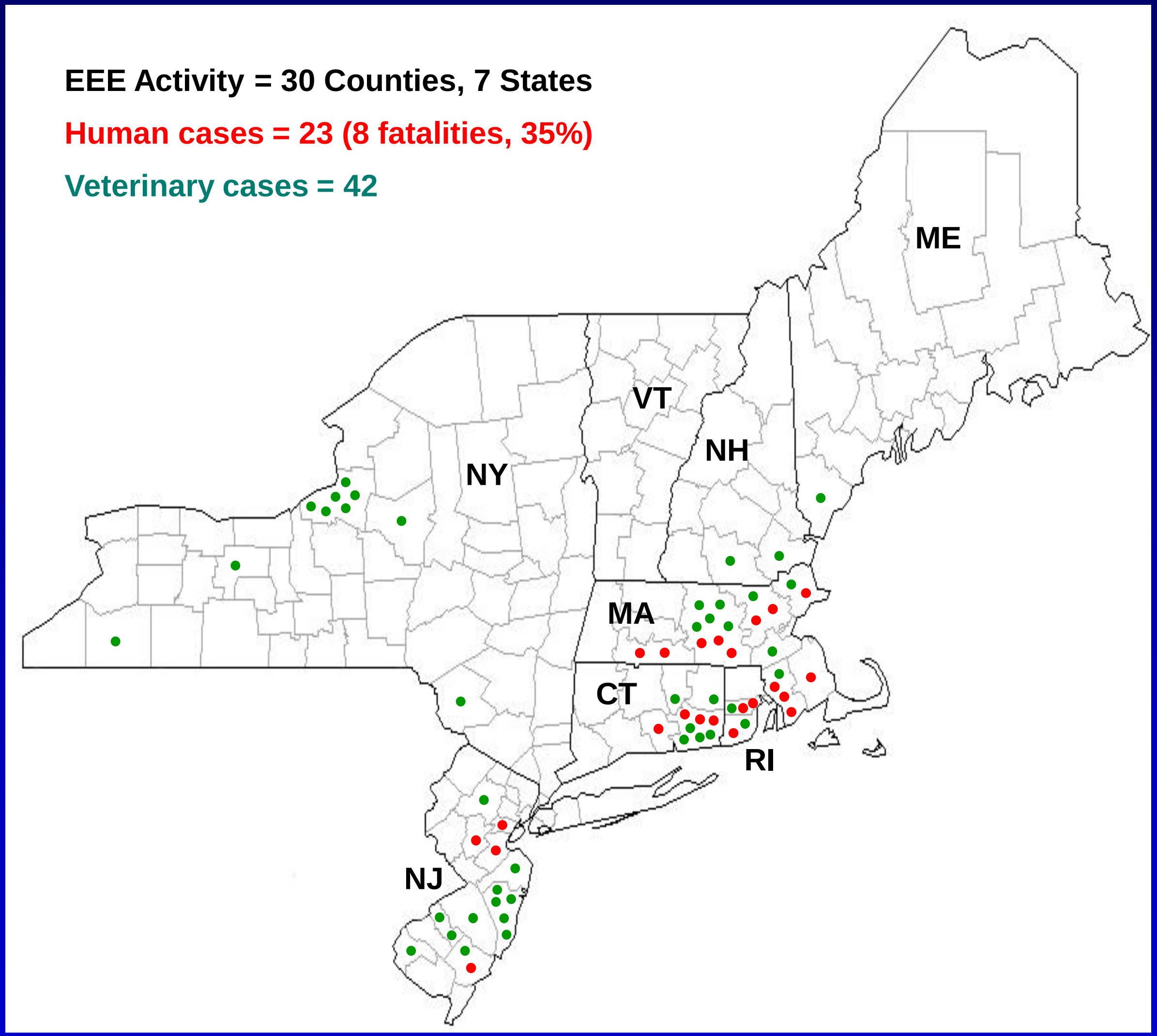
Ave = 18 / yr



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







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

  Resulting in:
  - 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

Historical Risk Factors for EEE in the Northeastern US

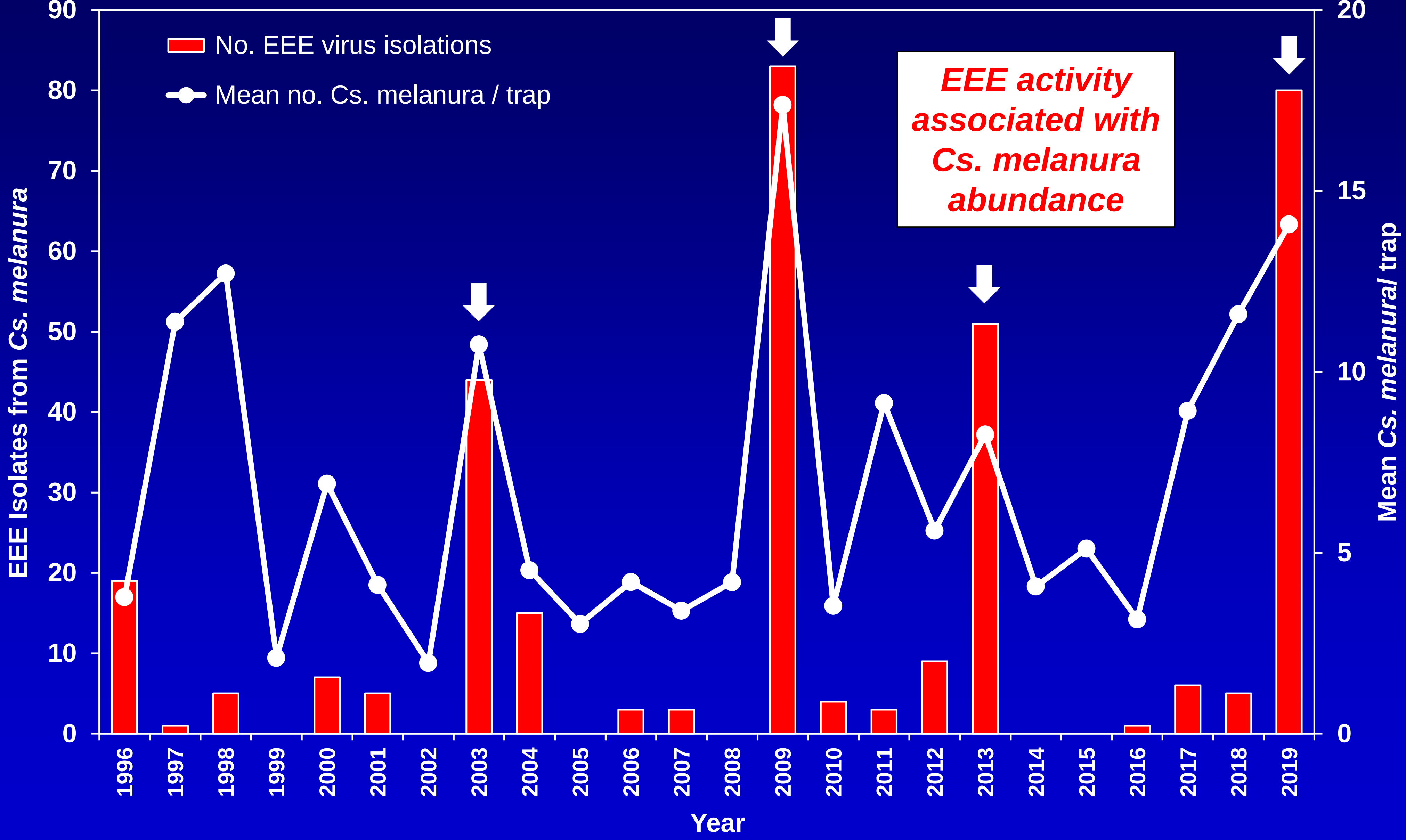
Pre-Season

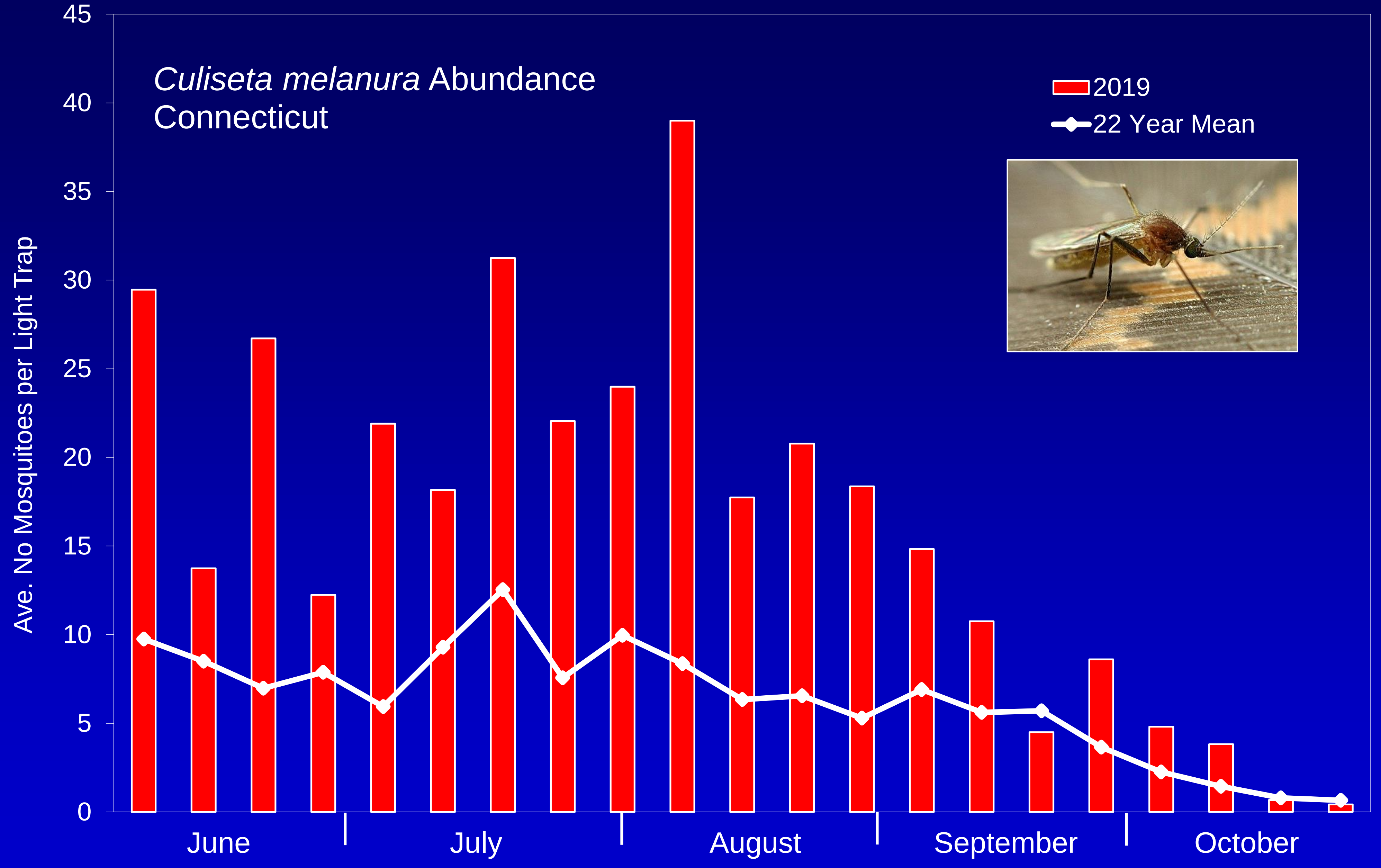
- Significant EEE activity in the previous year
- ✔ Mild winters with insulating snow cover
- ✔ High water table in enzootic swamps
- ✔ Above average rainfall in the prior fall/winter and spring

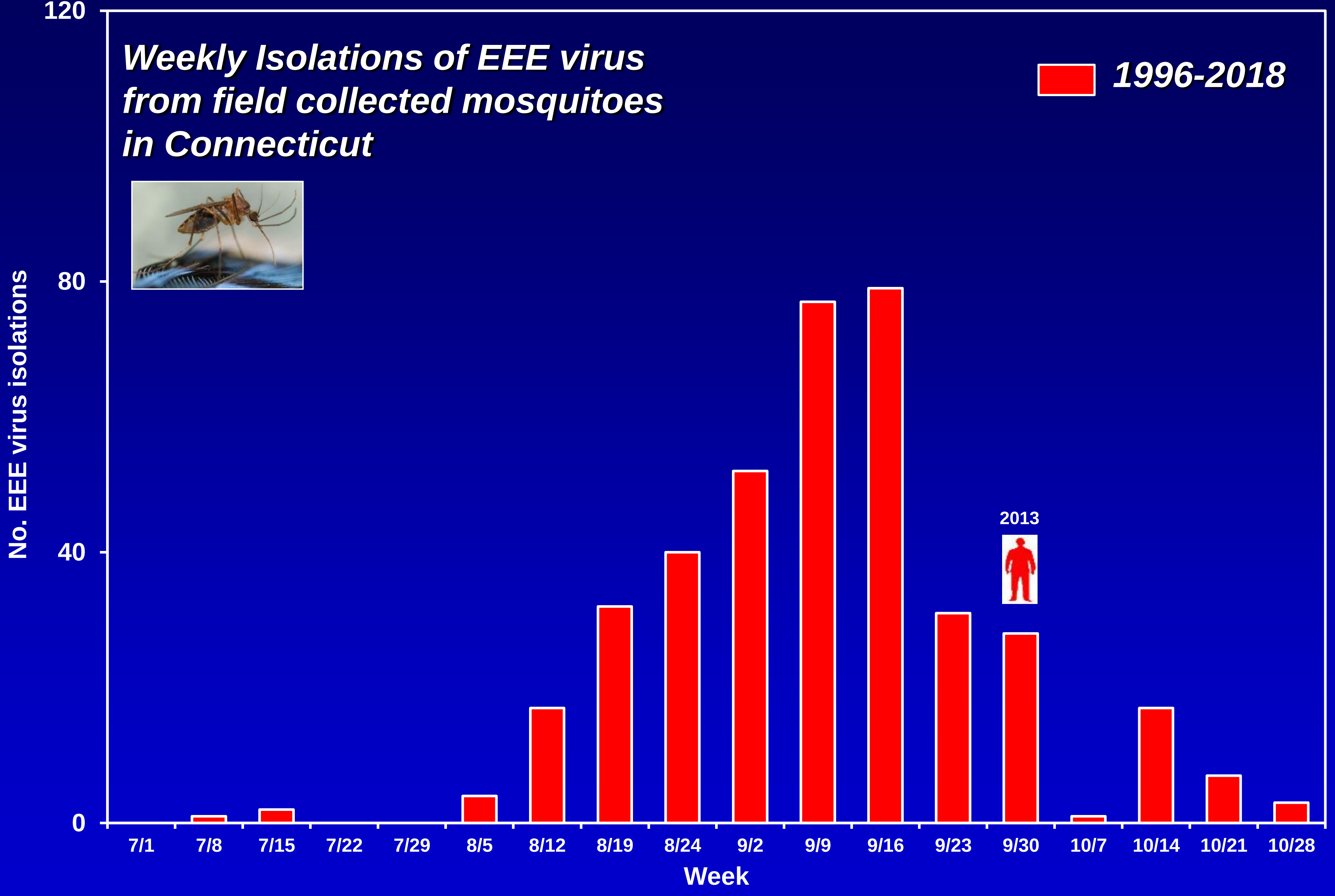
In-Season

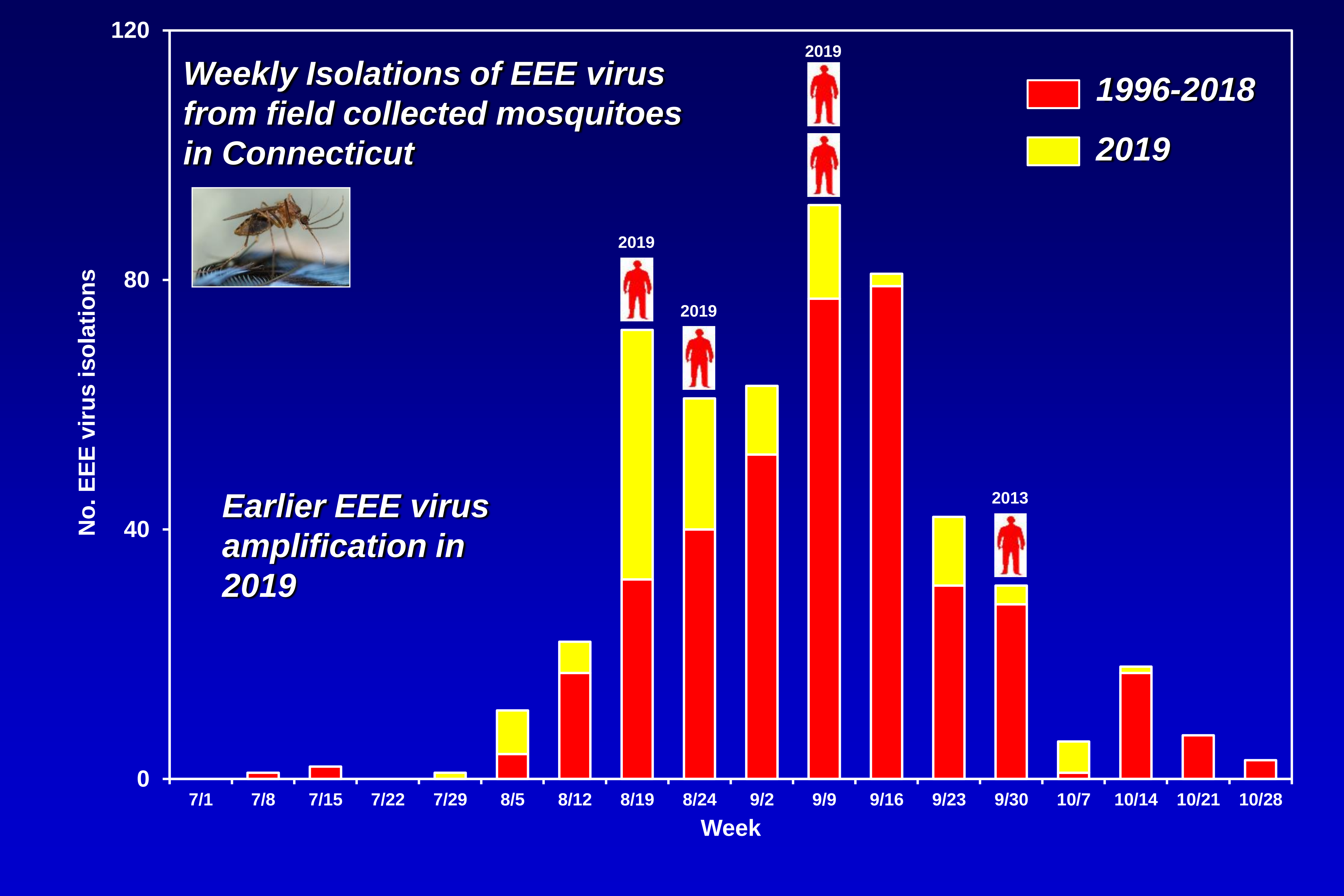
- ✔ Above average *Culiseta melanura* populations
- ✔ EEE virus isolations from mosquitoes in June or early July
- ✔ Isolations of EEE virus from a mammal-biting mosquitoes – *Cq. perturbans*
- ✔ Numerous EEE isolations > 30 – 50
- ✔ High MIR in *Culiseta melanura* >1:1000
- ✔ EEE activity beyond traditional areas
- ✔ Early and above average equine cases
- ✔ Infection of a human prior to August

EEE isolations and abundance of *Cs. melanura* – Connecticut, 1996-2019




Culiseta melanura Abundance
Connecticut
2019
22 Year Mean
Ave. No Mosquitoes per Light Trap
45
40
35
30
25
20
15
10
5
0
June
July
August
September
October


Weekly Isolations of EEE virus
from field collected mosquitoes
in Connecticut
1996-2018
2013
No. EEE virus isolations
120
80
40
0
7/1
7/8
7/15
7/22
7/29
8/5
8/12
8/19
8/24
9/2
9/9
9/16
9/23
9/30
10/7
10/14
10/21
10/28
Week

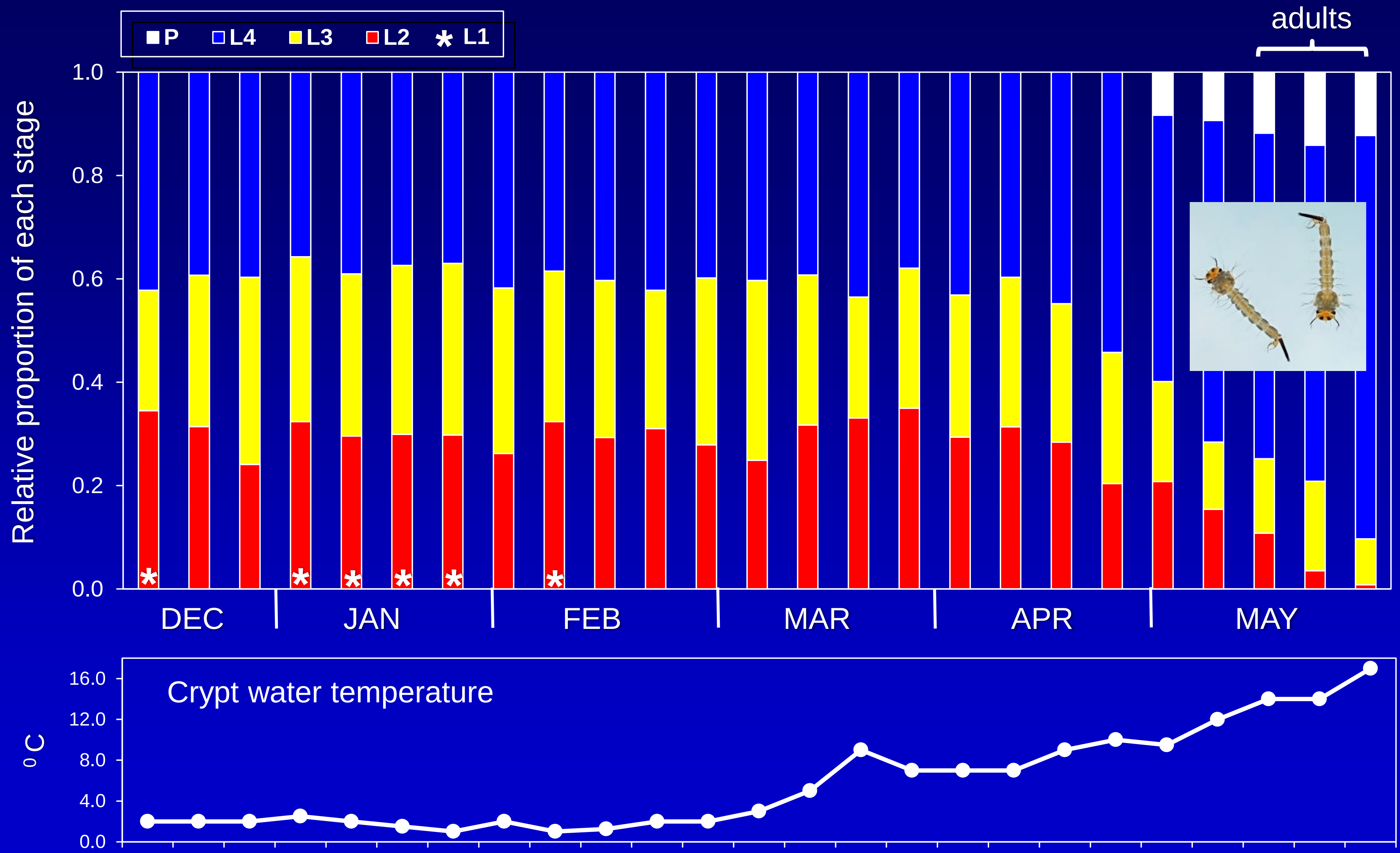


Weekly Isolations of EEE virus from field collected mosquitoes in Connecticut
1996-2018
2019
Earlier EEE virus amplification in 2019
No. EEE virus isolations
120
80
40
0
2019
2019
2019
2013
7/1
7/8
7/15
7/22
7/29
8/5
8/12
8/19
8/24
9/2
9/9
9/16
9/23
9/30
10/7
10/14
10/21
10/28
Week

Culiseta melanura

- **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)

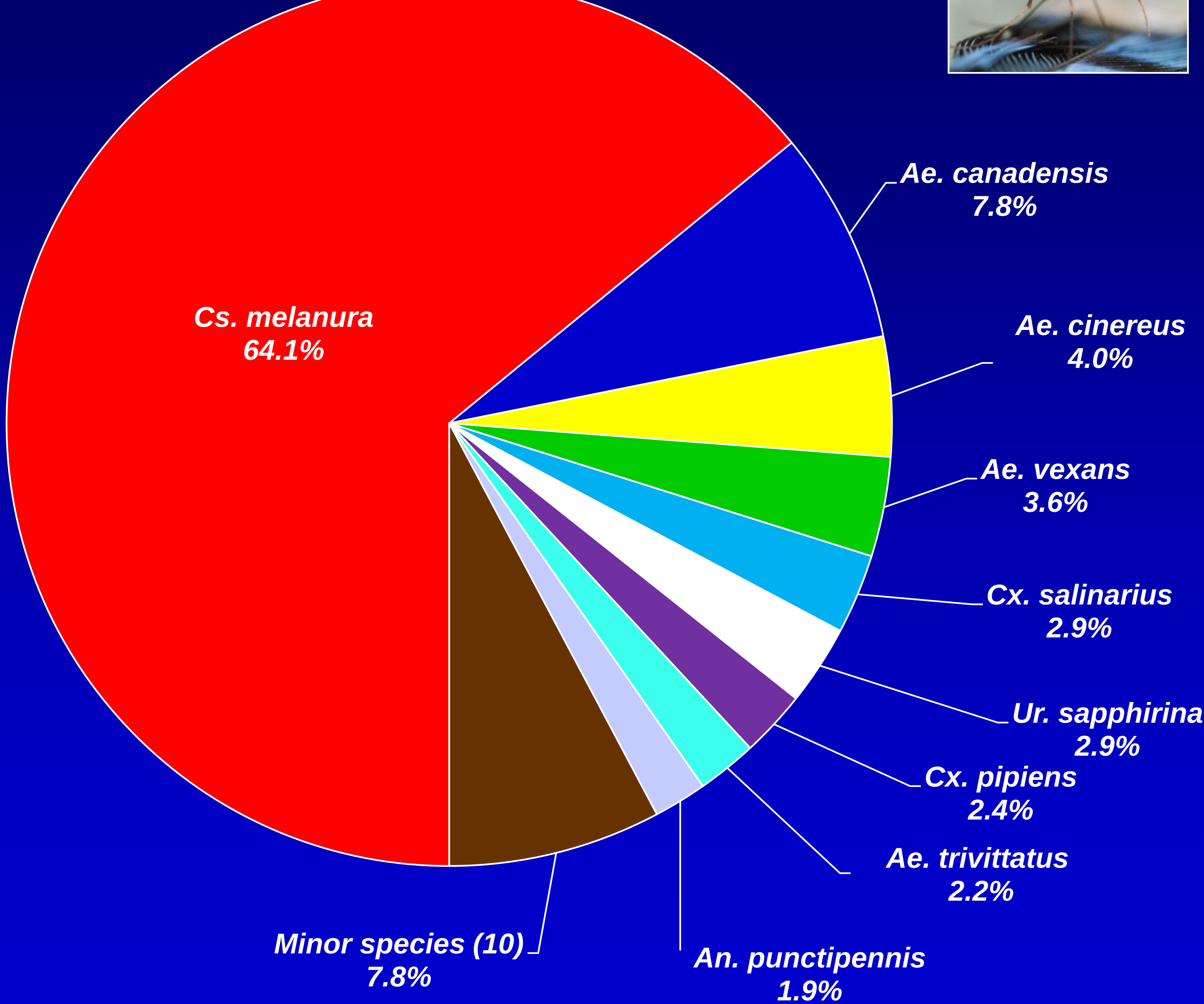
Phenology of Overwintering Development of *Cs. melanura*



Andreadis et al JAMCA 2012

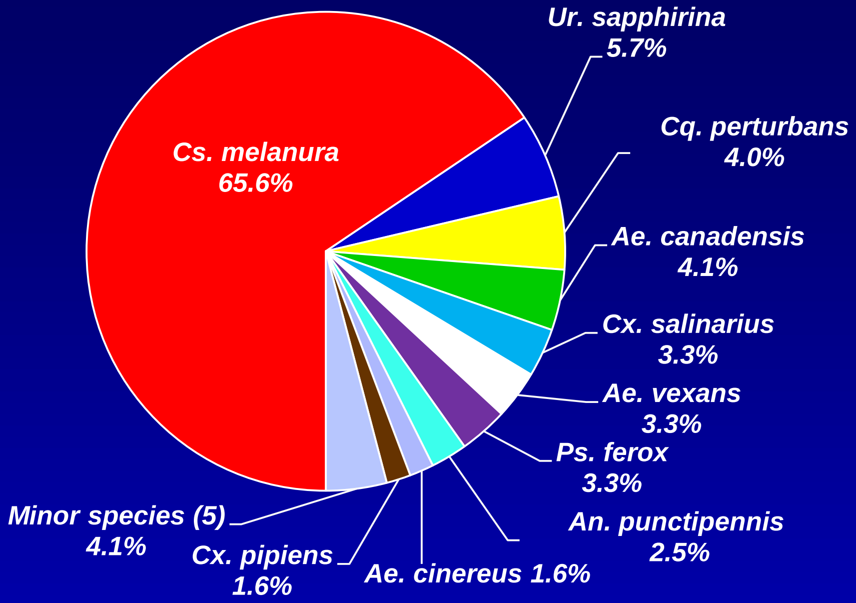
EEE Virus Isolations from Mosquitoes in Connecticut 1996 - 2018

Species (n = 19)	***No.***
Cs. melanura	264
Ae. canadensis	32
Ae. cinereus	18
Ae. vexans	15
Cx. salinarius	12
Ur. sapphirina	12
Cx. pipiens	10
Ae. trivittatus	9
An. punctipennis	8
Ae. cantator	5
Cs. morsitans	5
Cq. perturbans	4
Others (7 species)	18

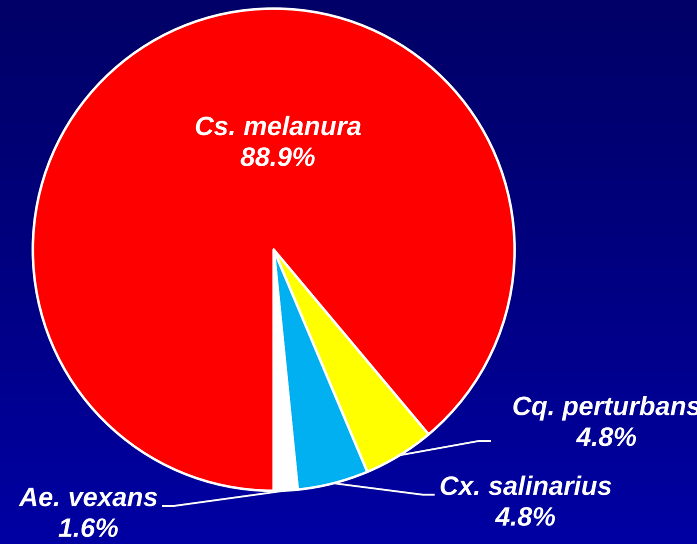


EEE Virus Detections from Mosquitoes in CT, MA, NJ and NY - 2019

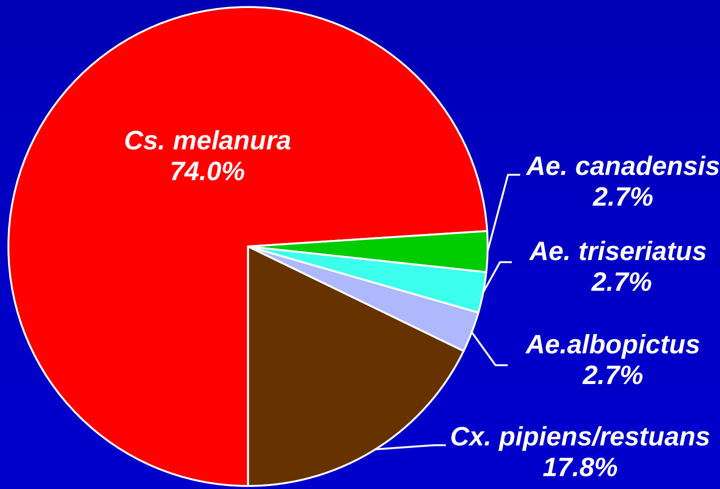
Connecticut



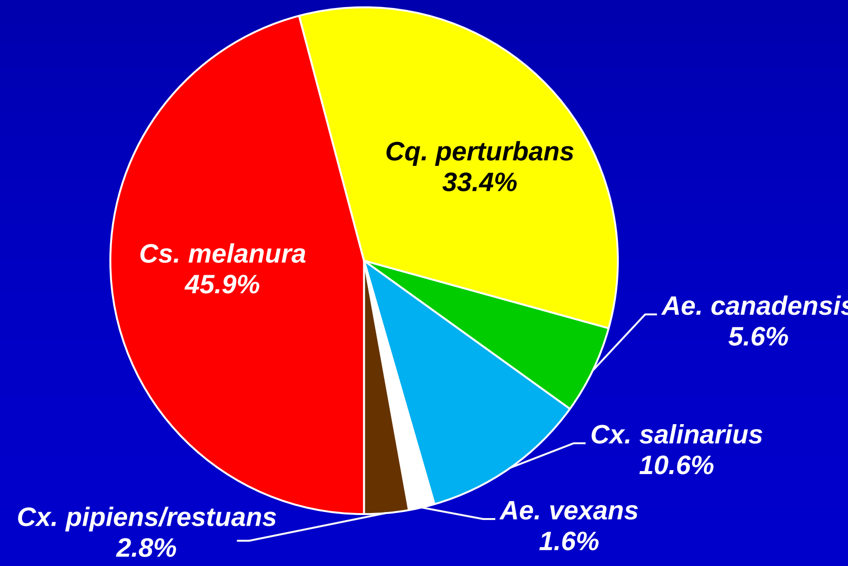
New York



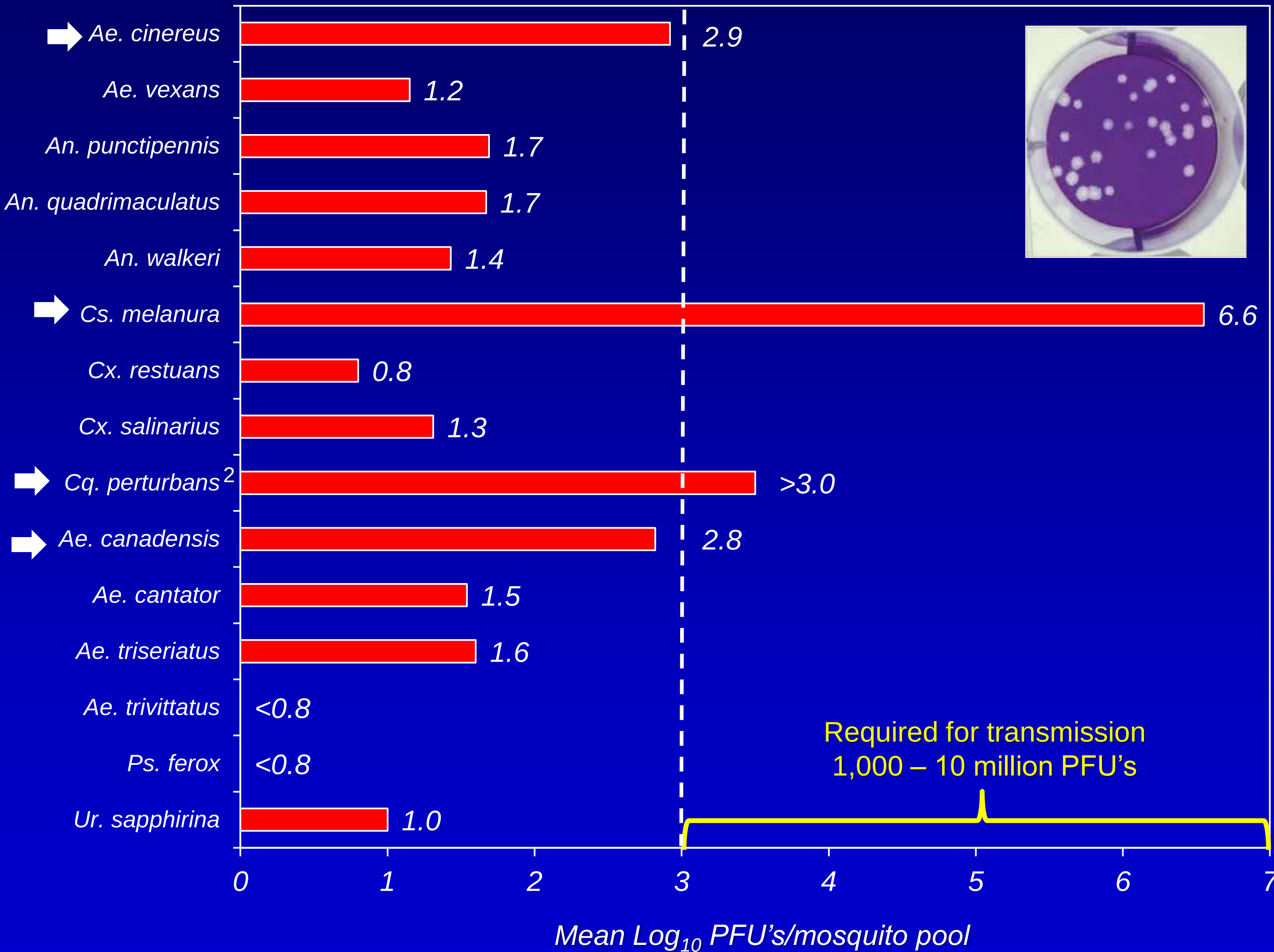
New Jersey



Massachusetts



Mean EEE Virus Titers in Field-Collected Mosquitoes by Plaque Assay [1]

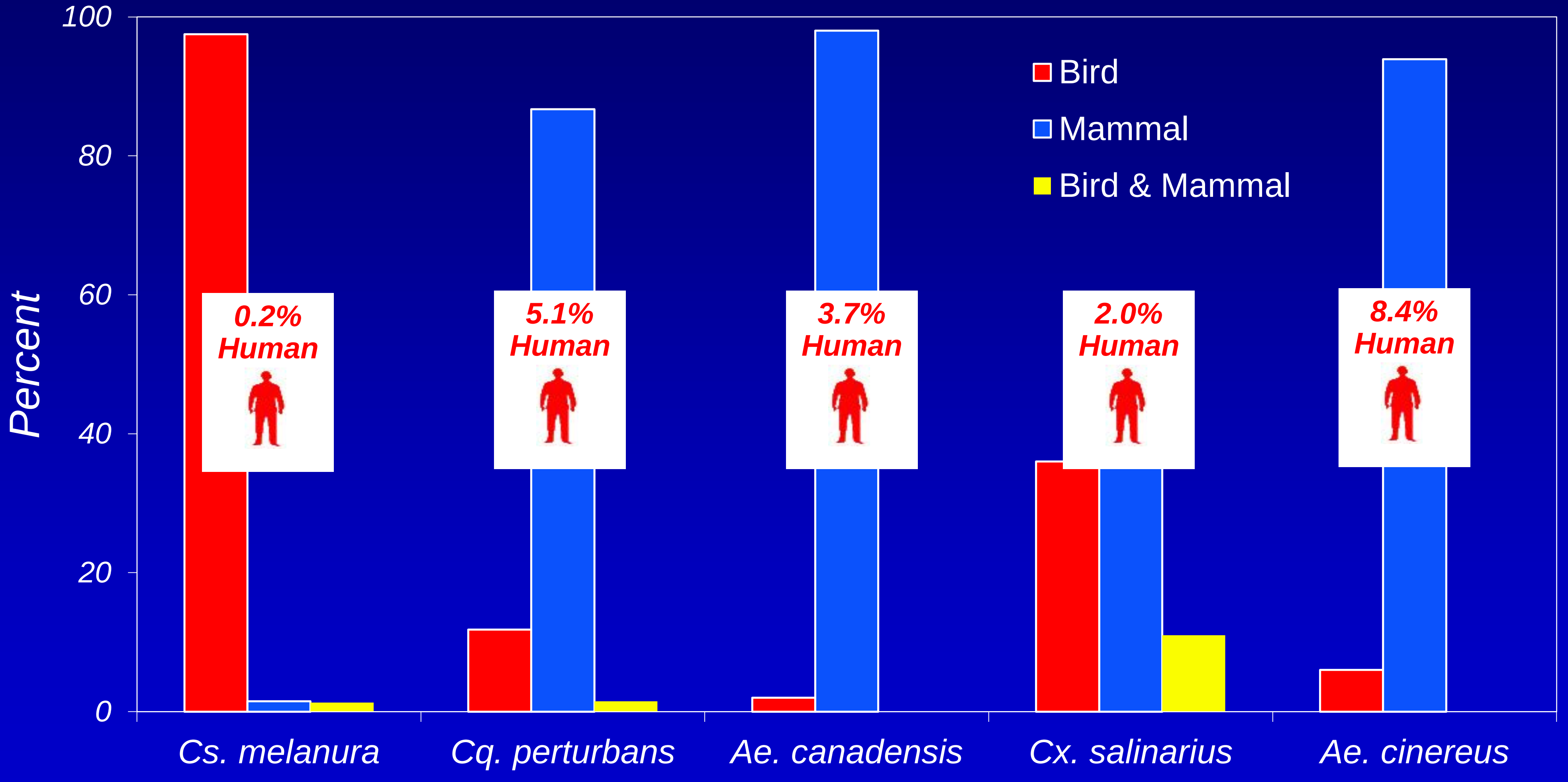


- There are major differences in the quantity of virus found in EEE virus-positive, field-collected mosquitoes
- *Cs. melanura* appears to be the only species in which virus titers are sufficiently high enough to support efficient transmission
- Other species include *Ae. cinereus, Cq. perturbans, Ae. canadensis*
- Important to consider virus titers when implicating other mosquito vectors

[1] Armstrong & Andreadis EID 2010

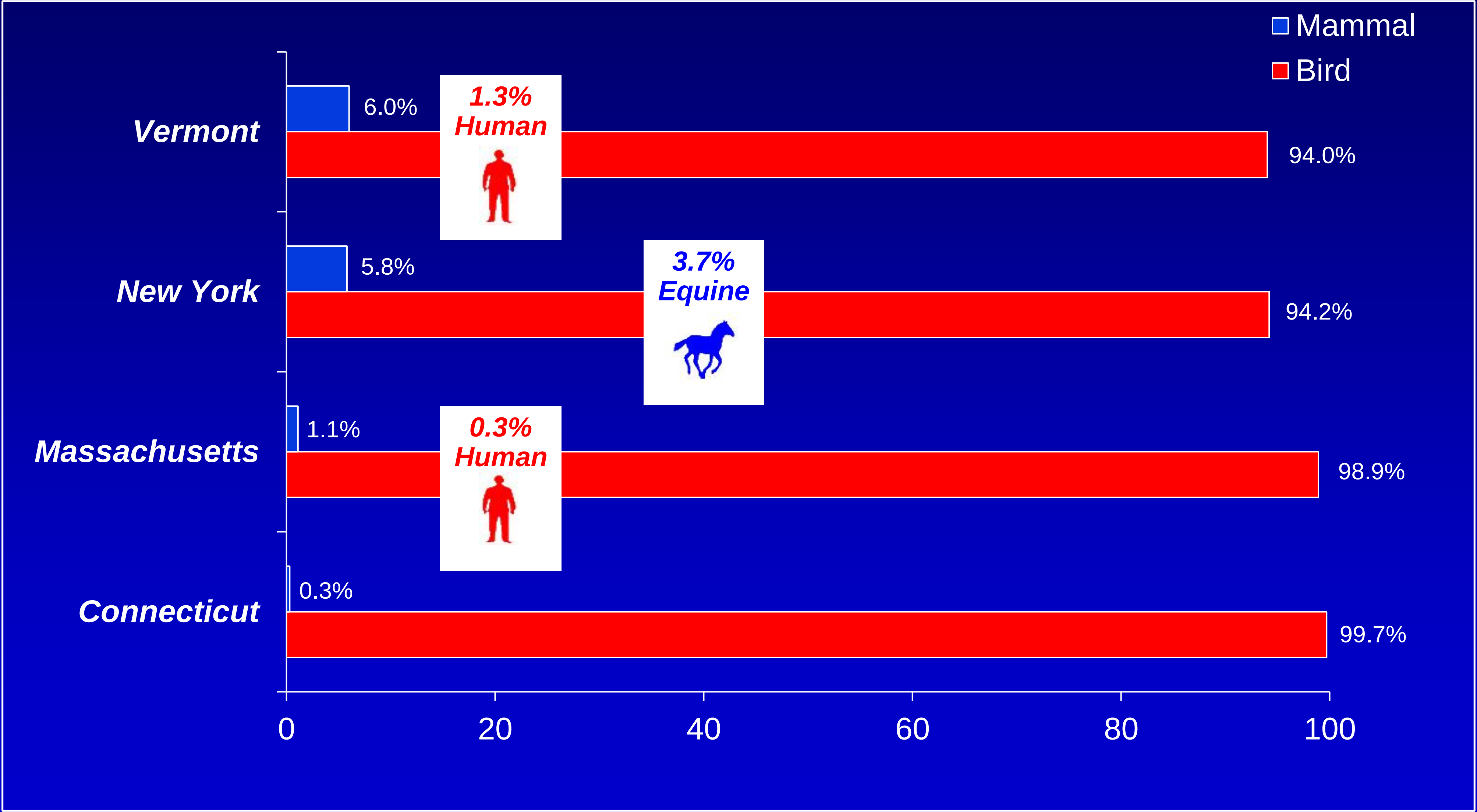
[2] Nasci & Mitchell JAMCA 1996

Host Feeding Patterns of *Culiseta melanura* and Potential Bridge Vectors of EEE in the Northeastern US (CT, MA, NY, VT)

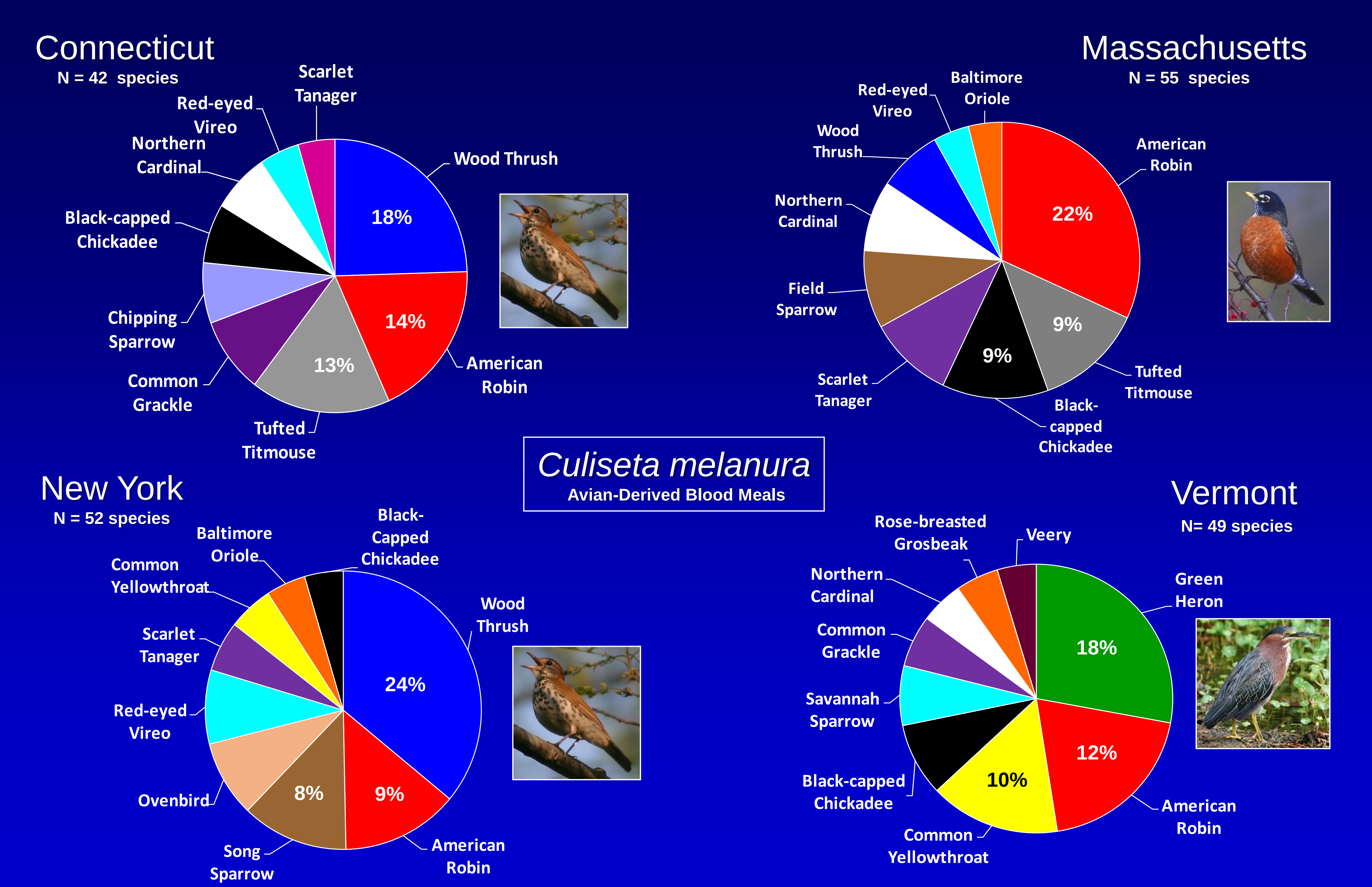


Molaei & Andreadis EID 2006, Molaei et al AJTMH 2006, JME 2008, VBZD 2013

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

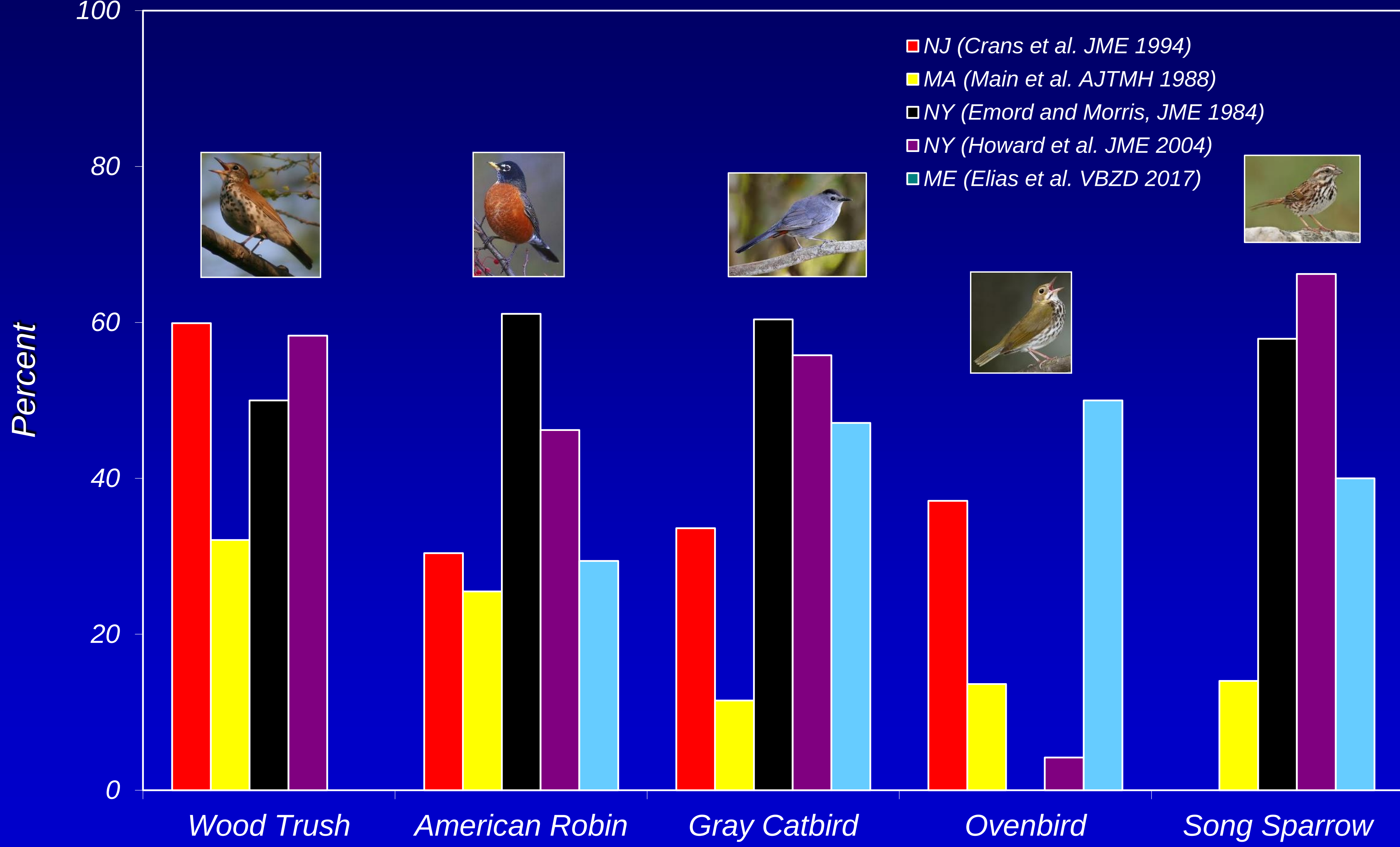


Molaei & Andreadis EID 2006, Molaei et al AJTMH 2006, JME 2008, VBZD 2013



Molaei & Andreadis EID 2006, Molaei et al AJTMH 2006, JME 2008, VBZD 2013

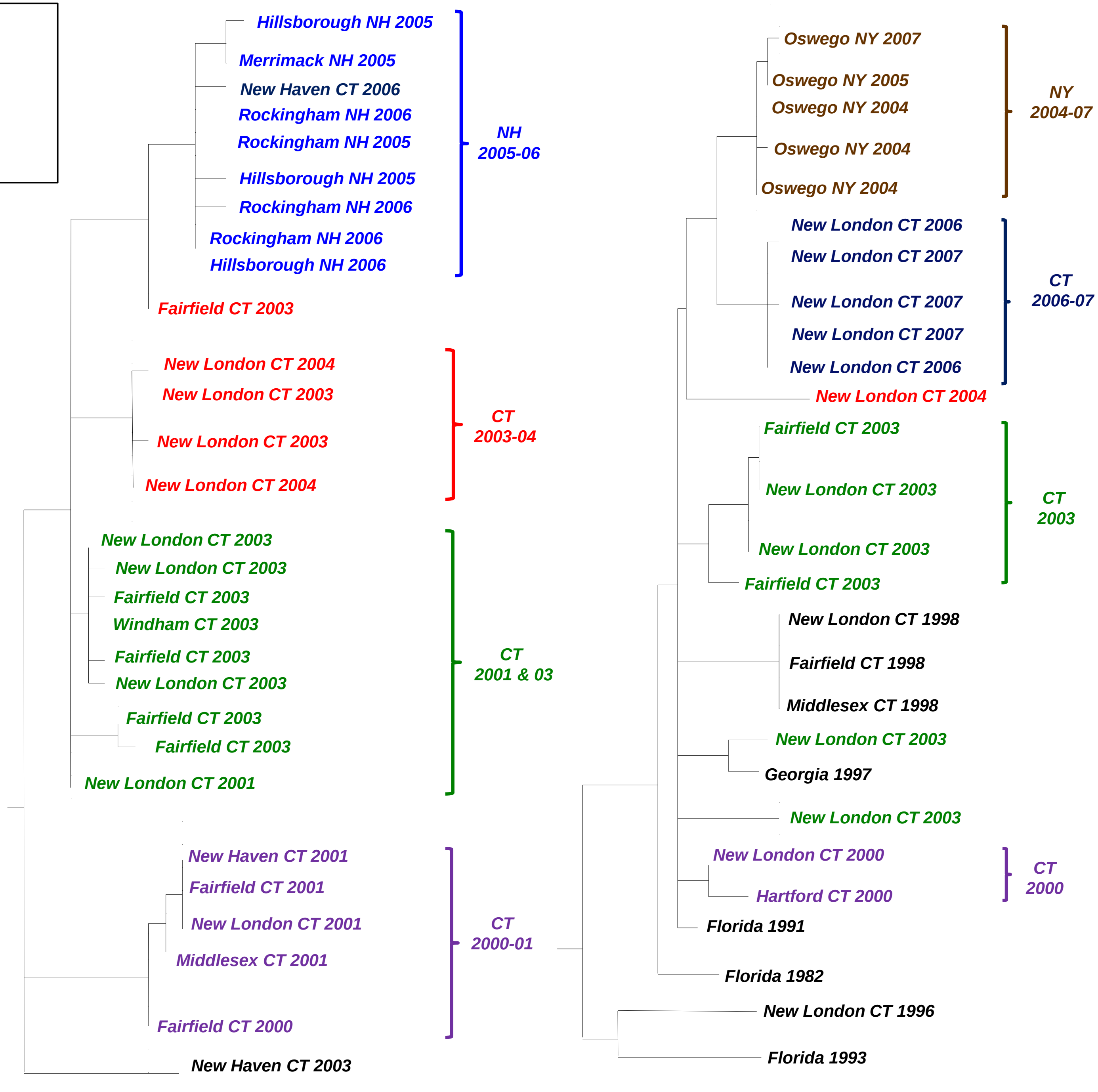
EEE Antibody Prevalence in Wild Birds: Regional Comparisons



Tracking Eastern Equine Encephalitis Virus Perpetuation in the Northeastern United States by Phylogenetic Analysis

PM Armstrong, TG Andreadis, JF Anderson, JW Stull, CN Mores.
2008. *Am. J. Trop. Med. Hyg.*

- 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

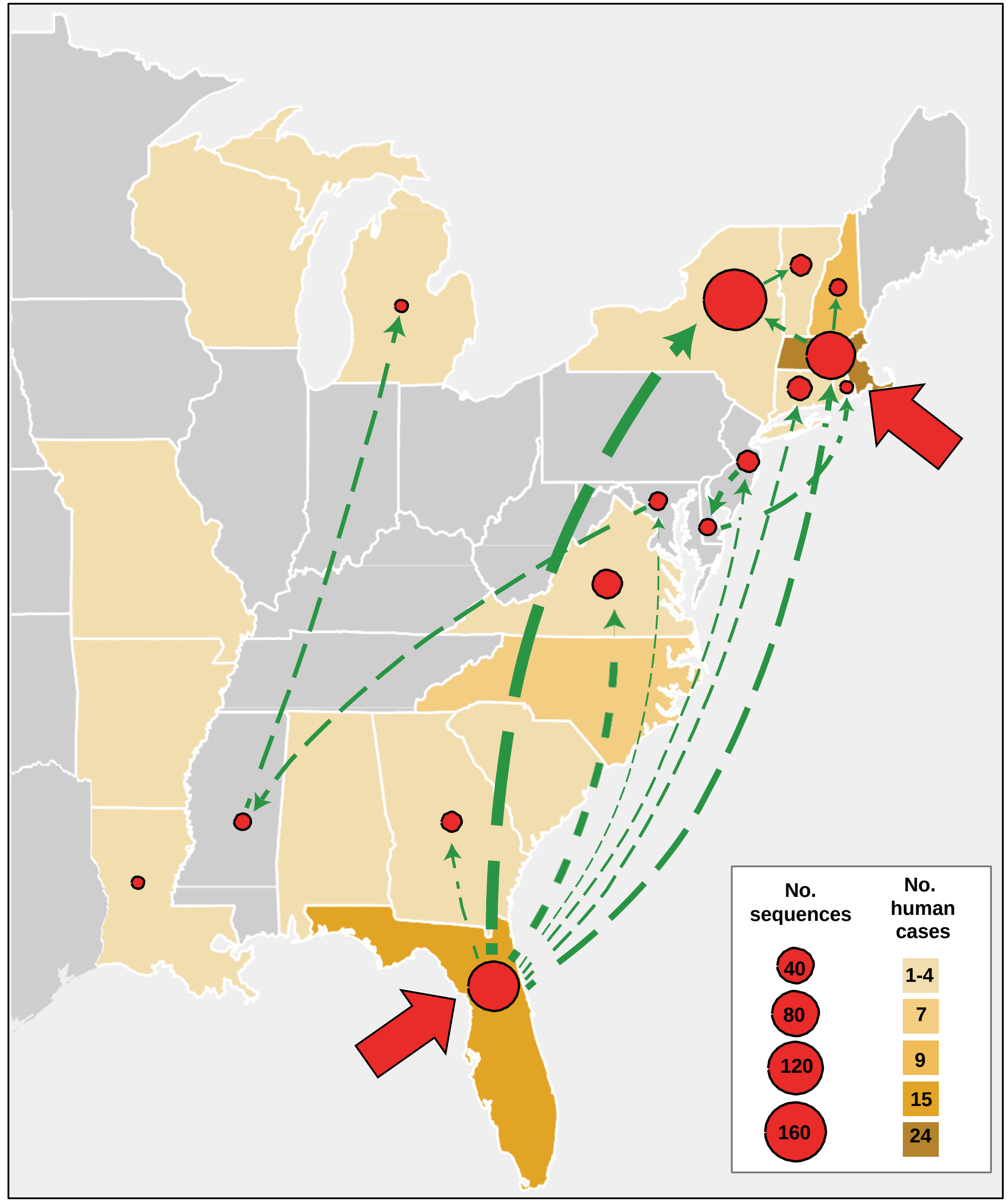


Journal of Virololgy 92 (12), 2018, 1-18.

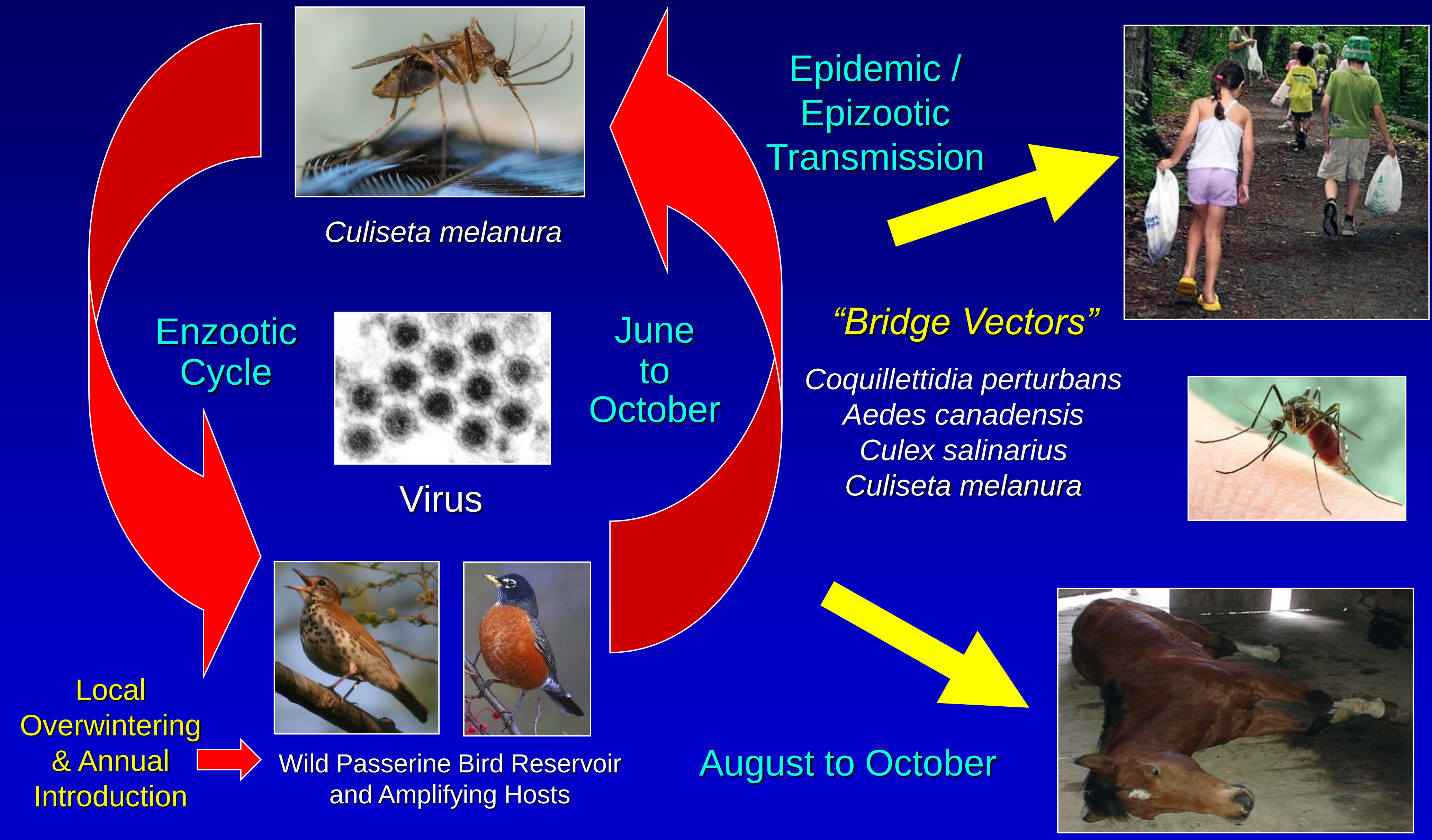
Large-Scale Complete-Genome Sequencing and Phylodynamic Analysis of Eastern Equine Encephalitis Virus Reveals Source-Sink Transmission Dynamics in the United States

Tan et al. (19 authors)

- 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

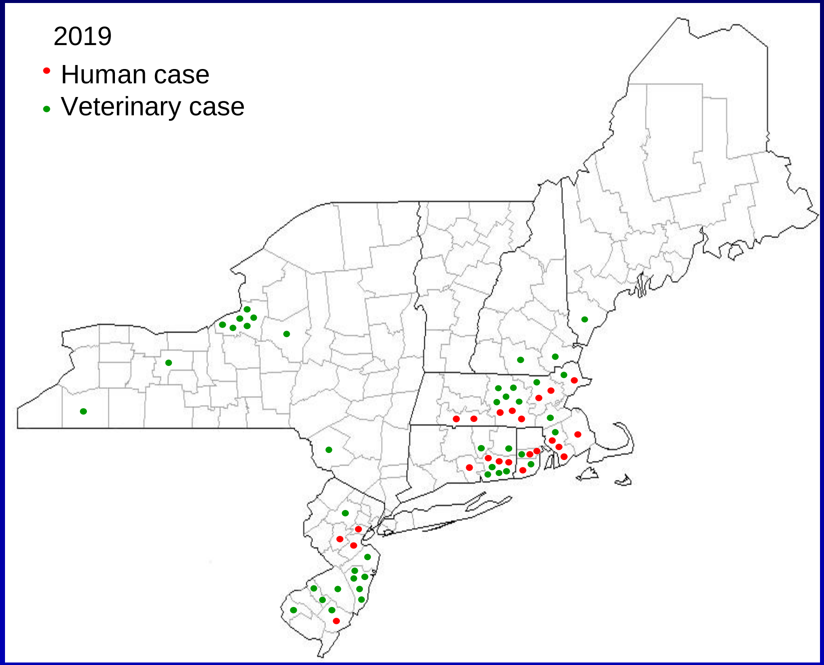


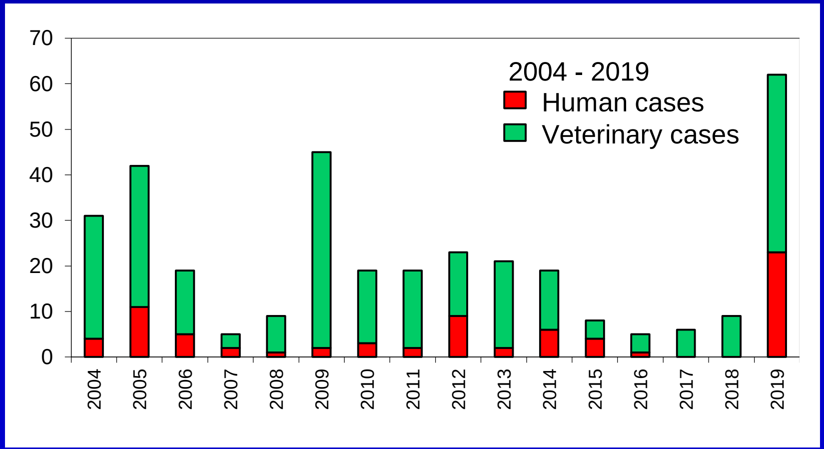
Northeastern US EEE Virus Transmission Cycle



Expectations for 2020

- 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?





Research – Surveillance Priorities

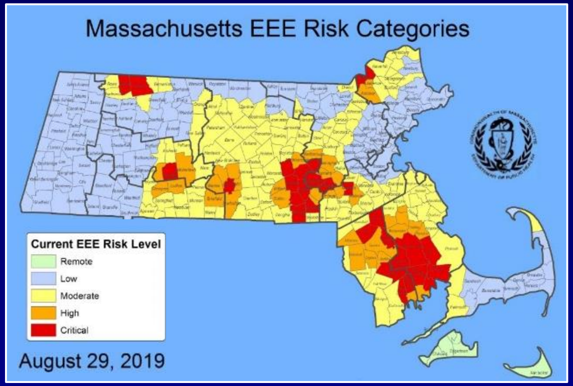
- Human serosurvey - human exposure ?
  - EEE antibodies detected in 0.7% of persons with no history of encephalitis after 1955 outbreak in Massachusetts (Feemster et al NEJM 1958)
  - Inapparent infections ranged from 3.1% to 7.6% after the 1959 outbreak in New Jersey (Goldfield et al. Am J Epidem 1968)

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

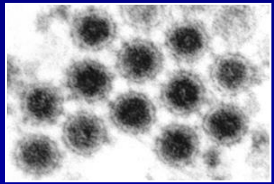
- Screening larvae for virus – overwintering
  - One reported isolation of EEE virus from *Cs. melanura* larvae (Philbrook et al CDC Tech Rep 1961)
  - Never been duplicated or confirmed
- Pre-season treatment of *Cs. melanura* breeding sites
  - Methoprene has been shown to be an effective larvicide 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

FIGHT THE BITE

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”

NORTHEAST REGIONAL CENTER FOR EXCELLENCE IN VECTOR-BORNE DISEASES

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