# Presenter Disclosure Information

**Alfred DeMaria, Jr., M.D.**

<table>
<thead>
<tr>
<th>Consultant</th>
<th>No relevant conflicts of interest to declare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grant Research/Support</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Speaker’s Bureau</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Major Stockholder</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Other Financial or Material Interest</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
</tbody>
</table>

No recommendations for off-label use of drugs or devices.
Coverage

- Ticks

- Mosquitoes

- Flys, fleas and mites less important in North America, and not covered
Vectorborne Diseases

- Need reservoir – human or other species
- Need competent vector
  - Usually particular to the infecting organism
- Infectious agent has life cycle in vertebrate host and vector
  - Not acting as a needle and syringe
- Seasonality related to weather and climate
## Mosquitoes Versus Ticks

### Mosquitoes
- **Insects**
  - 3 body parts (head, thorax, abdomen)
  - Antennae
  - 6 legs
  - Wings (can fly)
- Siphons blood from vessels
- Feeds to reproduce
- Multiple life stages

### Ticks
- **Arachnids**
  - One body part
  - No antennae
  - 8 legs (except earliest stage)
    - Can’t jump
  - No wings (can’t fly)
- Injures, slurps blood
- Feeds to develop and reproduce
- Multiple life stages
Tickborne Diseases in North America

**Ixodes scapularis, I. pacificus**
- Lyme Borreliosis (*Borrelia burgdorferi*)
- Babesiosis (*Babesia microti, Babesia duncani, Babesia sp. WA-1 and MO-1*)
- Anaplasmosis (HGE – *Anaplasma phagocytophilum*)
- *Borrelia miyamotoi*

**Amblyomma americanum**
- Ehrlichiosis (HME - *Ehrlichia chaffeensis*)
- Southern, tick associated rash illness (STARI, Master’s disease)

**Dermacentor andersoni, D. variabilis**
- Tularemia (*Francisella tularensis*)
- Rocky Mountain spotted fever (*Rickettsia rickettsii*)
- Colorado tick fever (group A *Coltivirus*)

**Ornithodoros sp.**
- Relapsing fever (*Borellia sp.*)

**Ixodes cookei (? I. scapularis)**
- Powassan virus encephalitis

Tick paralysis (tick neurotoxin)
Ixodes scapularis
1. Engorged females lay eggs

2. Larvae hatch and feed

3. Nymphs attach & feed on small mammals and birds

4. Adults seek medium to large mammalian hosts, primarily deer

5. Adult ticks active on warm days winter with second peak of activity in spring
Factors Associated with Increasing Risk of Lyme other Tickborne Diseases

- Increased deer population
- Increased black-legged tick population
- Fragmented forest environment
  - Increased white-footed mouse population
  - Increased risk of mouse infection
  - Expansion of habitat
  - Loss of biodiversity
- More people exposed to “ticky” habitat
Reported Cases of Lyme Disease—United States, 2011
Number of Confirmed Cases of Lyme Disease Reported in Massachusetts By Year, 1997-2012

(as of May 21, 2013)

MDPH Office of Integrated Surveillance and Informatics Services
Confirmed Lyme disease cases by age and sex--United States, 2001-2010
Number of Confirmed Lyme Disease Cases Reported in Massachusetts, by Month of Onset, 2011

Number of Confirmed Cases

Month of Diagnosis

JAN  FEB  MAR  APR  MAY  JUN  JUL  AUG  SEP  OCT  NOV  DEC

MDPH Office of Integrated Surveillance and Informatics Services
Maximum Pause Length : 13.9 sec.
Chronic Lyme Disease

- Chronic neurological and musculoskeletal symptoms of chronic Lyme disease are well described
- Post-Lyme disease chronic symptoms are a subject of intense and acrimonious controversy
  - Conflicting treatment studies and questions
  - Conflicting treatment guidelines
Chronic Neurologic Manifestations of Lyme Disease
Logigian, Kaplan and Steere, NEJM 1990 323:1438-44.

Figure 1. Interval between the Onset of Lyme Disease and the Occurrence of Encephalopathy, Polyneuropathy, or Leukoencephalitis and the Duration of These Complications in the 25 Patients in Whom the Onset of Infection Could Be Determined. Chronic neurologic abnormalities began 1 month to 14 years after the onset of disease and lasted from 3 months to 14 years.

Table 2. Signs and Symptoms of Chronic Neurologic Abnormalities.

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>No. of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
<td>24 (89)</td>
</tr>
<tr>
<td>Memory loss</td>
<td>22 (81)</td>
</tr>
<tr>
<td>Depression</td>
<td>10 (37)</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>8 (30)</td>
</tr>
<tr>
<td>Irritability</td>
<td>7 (26)</td>
</tr>
<tr>
<td>Difficulty finding words</td>
<td>5 (19)</td>
</tr>
<tr>
<td>Polyneuropathy</td>
<td>19 (70)</td>
</tr>
<tr>
<td>Spinal or radicular pain</td>
<td>11 (41)</td>
</tr>
<tr>
<td>Distal paresthesia</td>
<td>7 (26)</td>
</tr>
<tr>
<td>Sensory loss</td>
<td>12 (44)</td>
</tr>
<tr>
<td>Lower-motor-neuron weakness</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Ankle hyporeflexia</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Leukoencephalitis</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Upper-motor-neuron weakness</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Hyperreflexia</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Increased muscle tone</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Other symptoms</td>
<td>27 (100)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>20 (74)</td>
</tr>
<tr>
<td>Headache</td>
<td>13 (48)</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>4 (15)</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>4 (15)</td>
</tr>
</tbody>
</table>
### The Long-Term Outcome of Lyme Disease


<table>
<thead>
<tr>
<th>Current Symptoms</th>
<th>Lyme Disease (n = 38)</th>
<th>Controls (n = 43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequent arthralgias*, n (%)</td>
<td>23 (61)</td>
<td>7 (16)</td>
</tr>
<tr>
<td>Myalgias, n (%)</td>
<td>3 (8)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Numbness, tingling, or burning pain in an extremity†, n (%)</td>
<td>6 (16)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Coordination difficulties†, n (%)</td>
<td>6 (16)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Seizures, n (%)</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Unusual fatigue‡, n (%)</td>
<td>10 (26)</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Persistent depression</td>
<td>3 (8)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Concentration difficulties‡, n (%)†</td>
<td>6 (16)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Emotional lability§, n (%)</td>
<td>7 (18)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Difficulty sleeping‖, n (%)</td>
<td>18 (47)</td>
<td>7 (16)</td>
</tr>
<tr>
<td>Short Form 36 score‡, mean (SD)</td>
<td>23.8 (15.2)</td>
<td>18.0 (15.6)</td>
</tr>
</tbody>
</table>

* P < 0.0001.
† P = 0.03.
‡ P = 0.04
§ P = 0.05.
‖ P = 0.003.
Diagnosis of Lyme Disease

- **Clinical**
  - Signs and symptoms
  - Non-specific tests: ESR, ALT/AST, CSF

- **Laboratory**
  - Two-tiered, EIA or IFA and Western blot
  - Isolation of *Borellia burgdorferi* (modified Barbour-Stoenner-Kelly medium)
  - Polymerase chain reaction (PCR, real time PCR)
  - Antigen tests (OSPA, OSPB, flagellin, etc.)
## Recommended Treatment of Lyme Disease

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage for adults</th>
<th>Dosage for children</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preferred oral regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>500 mg 3 times per day&lt;sup&gt;a&lt;/sup&gt;</td>
<td>50 mg/kg per day in 3 divided doses (maximum, 500 mg per dose)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100 mg twice per day&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Not recommended for children aged &lt;8 years</td>
</tr>
<tr>
<td>Cefuroxime axetil</td>
<td>500 mg twice per day</td>
<td>30 mg/kg per day in 2 divided doses (maximum, 500 mg per dose)</td>
</tr>
<tr>
<td><strong>Alternative oral regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selected macrolides&lt;sup&gt;c&lt;/sup&gt;</td>
<td>For recommended dosing regimens, see footnote d in table 3</td>
<td>For recommended dosing regimens, see footnote in table 3</td>
</tr>
<tr>
<td><strong>Preferred parenteral regimen</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>2 g intravenously once per day</td>
<td>50–75 mg/kg intravenously per day in a single dose (maximum, 2 g)</td>
</tr>
<tr>
<td><strong>Alternative parenteral regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>2 g intravenously every 8 h&lt;sup&gt;d&lt;/sup&gt;</td>
<td>150–200 mg/kg per day intravenously in 3–4 divided doses (maximum, 6 g per day)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Penicillin G</td>
<td>18–24 million U per day intravenously, divided every 4 h&lt;sup&gt;d&lt;/sup&gt;</td>
<td>200,000–400,000 U/kg per day divided every 4 h&lt;sup&gt;d&lt;/sup&gt; (not to exceed 18–24 million U per day)</td>
</tr>
</tbody>
</table>

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<sup>a</sup> Although a higher dosage given twice per day might be equally as effective, in view of the absence of data on efficacy, twice-daily administration is not recommended.

<sup>b</sup> Tetracyclines are relatively contraindicated in pregnant or lactating women and in children <8 years of age.

<sup>c</sup> Because of their lower efficacy, macrolides are reserved for patients who are unable to take or who are intolerant of tetracyclines, penicillins, and cephalosporins.

<sup>d</sup> Dosage should be reduced for patients with impaired renal function.
Erythema Migrans at the Site of an *Ixodes scapularis* Tick Bite in 482 Subjects


<table>
<thead>
<tr>
<th>TICK STAGE AND ENGORGEMENT STATUS</th>
<th>DOXYCYCLINE GROUP (N=235)</th>
<th>PLACEBO GROUP (N=247)</th>
<th>P VALUE*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nymphal</td>
<td>1/124 (0.8)</td>
<td>8/142 (5.6)</td>
<td>&lt;0.04</td>
</tr>
<tr>
<td>Partially engorged</td>
<td>1/78 (1.3)</td>
<td>8/81 (9.9)</td>
<td>0.03</td>
</tr>
<tr>
<td>Unfed (flat)</td>
<td>0/43</td>
<td>0/59</td>
<td>1.00</td>
</tr>
<tr>
<td>Adult female</td>
<td>0/100</td>
<td>0/97</td>
<td>1.00</td>
</tr>
<tr>
<td>Partially engorged</td>
<td>0/28</td>
<td>0/36</td>
<td>1.00</td>
</tr>
<tr>
<td>Unfed (flat)</td>
<td>0/66</td>
<td>0/57</td>
<td>1.00</td>
</tr>
<tr>
<td>Larval</td>
<td>0/10</td>
<td>0/8</td>
<td>1.00</td>
</tr>
<tr>
<td>Adult male</td>
<td>0/1</td>
<td>0/0</td>
<td>1.00</td>
</tr>
<tr>
<td>All</td>
<td>1/235 (0.4)</td>
<td>8/247 (3.2)</td>
<td>&lt;0.04</td>
</tr>
</tbody>
</table>

*P values were derived by the two-tailed Fisher’s exact test.

Adverse events: 30 versus 11%

87% (25-98%) protective re EM
Prophylaxis Recommendations

Single dose 200 mg doxycycline

- Within 72 hours of discovery of attached tick
  - Lyme disease endemic
  - Obviously engorged tick
  - Attached >36 hours

- No recommendation for children
- Must always counsel about erythema migrans and symptoms
Humans are dead-end hosts
Subsequent transmission occurring from ticks feeding on infected persons is rare.

Human-to-human transmission is possible through blood transfusions.
Babesiosis

- “Nantucket fever”
- Parasite, *Babesia microti* and other species
- Invades red blood cells

**Signs and symptoms**

- Usually none (therefore may donate blood)
- Those at risk develop fever (often high), chills and anemia

**Risk factors**
- Lack of spleen
- Immune deficiency
- Age (very young, very old)
Confirmed and Probable Babesiosis in Massachusetts

(as of May 21, 2013)

MDPH Office of Integrated Surveillance and Informatics Services
Babesiosis: Treatment

- Atovaquone plus azithromycin or clindamycin plus quinine

- Severely ill patients with high parasitemia and asplenic patients with life-threatening illness should be considered for exchange transfusion
Confirmed and Probable Anaplasmosis Reported in Massachusetts

(as of May 21, 2013)

MDPH Office of Integrated Surveillance and Informatics Services
Anaplasmosis

- Incubation period is 1 to 2 weeks
- Mild signs or none at all
- Fever, headache, muscle aches, chills, sweating, nausea, and vomiting
- More severe complications are associated with older age, diabetes, immunocompromise, delayed treatment
# Treatment of Anaplasmosis

<table>
<thead>
<tr>
<th>AGE CATEGORY</th>
<th>DRUG</th>
<th>DOSAGE</th>
<th>MAXIMUM</th>
<th>DURATION (DAYS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>Doxycycline</td>
<td>100 mg twice per day orally or IV</td>
<td>N/A</td>
<td>10</td>
</tr>
<tr>
<td>Children</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 years of age or older</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>moderate illness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td>4 mg/kg per day orally or IV in 2 divided doses</td>
<td>100 mg per dose</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Children</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>less than 8 years of age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>severe illness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>without Lyme disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td>4 mg/kg per day orally or IV in 2 divided doses</td>
<td>100 mg per dose</td>
<td>4-5 OR approx. 3 days after resolution of fever</td>
<td></td>
</tr>
<tr>
<td>Children</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>less than 8 years of age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>severe illness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>with Lyme disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td>4 mg/kg per day given orally or IV in 2 divided doses</td>
<td>100 mg per dose</td>
<td>4-5</td>
<td></td>
</tr>
<tr>
<td>Followed By</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>50 mg per day in 3 divided doses</td>
<td>500 mg per dose</td>
<td>to complete a 14 day total course of antibiotic therapy</td>
<td></td>
</tr>
<tr>
<td>or</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefuroxime axetil</td>
<td>30 mg/kg per day in 2 divided doses</td>
<td>500 mg per dose</td>
<td>to complete a 14 day total course of antibiotic therapy</td>
<td></td>
</tr>
</tbody>
</table>
Human Monocytic Ehrlichiosis (HME)

- *Ehrlichia chaffeensis*
- Transmitted primarily by *Amblyomma americanum* (lone star tick) – sometimes other ticks
- Southern, South-Central and Atlantic states
- Fever, headache, malaise and myalgia
- Rash – petechial to maculopapular
- Thrombocytopenia, leukopenia, elevated transaminases
Rocky Mountain Spotted Fever

- Transmitted by wood and dog ticks (*Dermacentor* sp.)
- Incubation period is 5-7 days
- Fever, severe headache, myalgia, confusion, photophobia, nausea, vomiting and anorexia
- In ~80% of cases, a maculopapular rash on the extremities will appear 3-5 days after fever onset and rapidly spread to the trunk
- The characteristic petechial rash is usually not seen until the sixth day or later
Tularemia

- *Francisella tularensis* - non-motile, facultative, Gram-negative, coccobacillus
- Intracellular pathogen
- Usually zoonotic – ticks (*Dermacentor*), biting flies, direct contact, fleas, inhalation, ingestion of meat, other food and water
- Prevalence in wild rabbits may be up to 1%
- Immune animals may clear ticks of infection
- Transovarian transmission in ticks
Reported cases of tularemia -- United States, 2000-2008

One dot placed randomly within county of residence of each reported case
Tularemia: Treatment

- **Treatment**
  - streptomycin or gentamicin
  - tetracycline and chloramphenicol active, but associated with relapses
  - Jarish-Herxheimer-like reactions
  - death rate 4% or less with treatment

- **Vaccine**
  - IND (live, attenuated)
  - Need CMI response
Powassan Virus

- North American flavivirus
- Transmitted by *Ixodes cookei*, but other ticks also implicated
- High seroprevalence in burrowing mammals in New England
- Rare disease in humans – but severe illness associated with marked neurological sequelae and 10-15% case-fatality rate
- Increased recognition with increased evaluation of encephalitis because of WNV
- Related virus isolated from *I. scapularis* by Telford, et al
DEER TICK
Ixodes scapularis

AMERICAN DOG TICK
Dermacentor variabilis

Massachusetts Department of Public Health
Division of Epidemiology and Immunization
617-983-6800
www.state.ma.us/dph
Design courtesy of Cape Cod Cooperative Extension
DEET

- Never use more than 30%
  - Raises likelihood of adverse event
  - Doesn’t offer significant added benefit
- Not for children <2 months old
- Effectiveness time varies with temperature, perspiration and water exposure

<table>
<thead>
<tr>
<th>DEET%:</th>
<th>Protection time in hours:</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.75%</td>
<td>1 ½</td>
</tr>
<tr>
<td>6.65%</td>
<td>2</td>
</tr>
<tr>
<td>20%</td>
<td>4</td>
</tr>
<tr>
<td>23.8%</td>
<td>5</td>
</tr>
</tbody>
</table>
Tick Management Handbook

An integrated guide for homeowners, pest control operators, and public health officials for the prevention of tick-associated disease

Revised Edition

Prepared by:

Kirby C. Stafford III, Ph.D.
Vice Director, Chief Entomologist
Connecticut Agricultural Experiment Station, New Haven

Support for printing this revised edition provided by
The Connecticut Agricultural Experiment Station
The Connecticut General Assembly

Bulletin No. 1010
Ticks

Did you know?
- Ticks are arachnids, relatives of spiders.
- Ticks live in wooded areas, brushy fields, and around your home.
- Ticks survive by eating blood from their hosts.
- Ticks can pass infections from one host to the next including humans.

Avoiding ticks
- On people
- On pets
- In the yard

All about ticks
- Geographic distribution
- Tick life cycle and hosts
- Diseases transmitted by ticks

If you've been bitten by a tick, what should you do?
- Removing a tick
- Symptoms of tickborne illness

Resources
Free Webinar CME course: Recognizing and Treating Tick-Borne Diseases

Notable tickborne diseases
- Anaplasmosis
- Babesiosis
- Ehrlichiosis
- Lyme disease
- Rocky Mountain spotted fever
- Other spotted fevers
- Southern Tick-Associated Rash Illness
- Other tickborne diseases
Mosquitoborne Diseases in North America

- In North America viral diseases
- Endemic diseases order of incidence, in U.S., in 2011
  - West Nile virus (WNV)
  - LaCrosse (LAC) virus
  - St. Louis encephalitis (SLE) virus
  - Eastern equine encephalitis (EEE) virus
  - Jamestown Canyon virus (JCV)
  - Western equine encephalitis (WEE) virus

- Emerging threats
  - Dengue
  - Yellow fever
EEE & WNV Encephalitis Cycle
also SLE
La Crosse Virus Cycle in North Central U.S.

Spring
- Amplification
  - Small vertebrates
  - Woodland Aedes spp. (A. triseriatus, A. vexans, A. canadensis, others?)

Fall
- Aedes species
- Local winter reservoirs
- Transovarian transmission in A. triseriatus, ? other species
- Vertebrate reservoir?

Dead end hosts: humans and other large mammals

Known portion of cycle
Speculative portion of cycle
Yellow Fever Virus Cycles in Tropical America

Urban Cycle:
- Humans ➔ Aedes spp. Mosquitoes ➔ Humans

Jungle Cycle (sylvatic):
- Humans ➔ Monkeys ➔ Haemagogus spp. Mosquitoes ➔ Monkeys
Outbreak of Encephalitis in Man Due to the Eastern Virus of Equine Encephalomyelitis

ROY F. FEEMSTER, M.D., Dr.P.H., F.A.P.H.A.
Director of the Division of Communicable Diseases of the Massachusetts Department of Public Health, Boston, Mass.

About the middle of August, 1938, cases of encephalomyelitis in horses were recognized in Massachusetts and it was soon ascertained that an epidemic of considerable proportions existed. On August 12 a child from Brockton died of encephalitis, and when a second child from the same city died on August 30 a rumor spread that the two had been victims of the disease prevalent among horses.

On September 1, the Massachusetts All five of these cases occurred within 15 miles of each other, the nearest being 20 miles southeast of Boston. An interesting coincidence was that they had occurred in essentially the same area as the equine disease. Because of this fact and also on the chance that this was just the beginning of an outbreak similar to the one at St. Louis, the department arranged for virus studies on any fatal cases that might occur. Over the Labor Day week and
Massachusetts 1970-2012

Human EEE and EEEV Mosquito Isolates

Human Outbreak Cycle 1938-2006, mean 13 years (7-19)

Aerial spray

1973-75
1990
2006  2010  2012

Human Cases
Mosquito EEE Isolations
Eastern Equine Encephalitis Virus

- *Alphavirus* genus, family *Togaviridae*
- First isolated in 1933
- First human case confirmed by isolation from brain tissue in 1938
- *Culiseta melanura* is primary enzootic vector
- *Aedes vexans, Aedes canadensis, Coquillettidia perturbans* are putative bridge vectors
- Passerine birds are primary amplifying hosts
Eastern Equine Encephalitis
Clinical Course

- Abrupt onset fever, chills, headache, muscle aches, nausea and vomiting
- Progressive disorientation, discoordination
- Seizures, coma
- ~30-50% mortality
- ~80% residual neurological deficits
Magnetic resonance images (MRIs) and computed tomography (CT) neuroradiographs showing lesions in brains of 3 children with eastern equine encephalitis. Silverman, et al. EID 2013; 19: 194-201.
Association of Length of Prodrome with Clinical Outcome in Children with Eastern Equine Encephalitis

\[ p = 0.002 \]
EEE Activity in the U.S
(as of October 30, 2012)

CDC
West Nile Virus

- Isolated from woman with fever, West Nile region, Northern Province, Uganda, 1937
- First epidemic described: Israel, 1950
- Multiple strains, widely endemic - Middle East, Africa, Asia, Europe, Australia, and now North America
- Broad range of hosts: birds, mammals
- Human infection common in endemic areas
West Nile Virus
New York City, 1999

- First appearance in North America, Summer of 1999
- 62 confirmed and probable cases, 7 deaths
- Serosurveys suggest widespread, unrecognized, human infection
- Severe disease and deaths in birds and horses
West Nile Virus Infection
Human Disease

- Incubation period 5 to 15 days
- Headache, sore throat, fatigue, myalgia, arthralgia, fever (moderate to high), conjunctivitis, lymphadenopathy
- Rash (roseolar) more common than with other flaviviruses
- Muscle weakness, often profound
- Aseptic meningitis, encephalitis, meningoencephalitis
- Myocarditis, hepatitis, pancreatitis
- Mild and sub-clinical infection very common, age-related severity
## WNV Encephalitis/Infection and Clinical/Sub-Clinical Ratios

<table>
<thead>
<tr>
<th>Area</th>
<th>Year(s)</th>
<th>Encephalitis/Infection</th>
<th>Clinical/Sub-Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Israel</td>
<td>1950s</td>
<td>1:100</td>
<td>-</td>
</tr>
<tr>
<td>Romania</td>
<td>1996</td>
<td>1:331</td>
<td>-</td>
</tr>
<tr>
<td>Czechland</td>
<td>1997</td>
<td>-</td>
<td>1:1.6</td>
</tr>
<tr>
<td>NYC</td>
<td>1999</td>
<td>1:139</td>
<td>1:4.8</td>
</tr>
<tr>
<td>Staten Island</td>
<td>2000</td>
<td>1:157</td>
<td></td>
</tr>
<tr>
<td>Suffolk Co., NY</td>
<td>2000</td>
<td>1:&gt;:121</td>
<td></td>
</tr>
</tbody>
</table>
West Nile virus (WNV) Activity
United States, 2012
West Nile Virus
Laboratory Confirmation

- WNV isolation (virus identified by IFA, neutralization, RT-PCR or sequencing)
- RT-PCR using multiple primers
- Captured WNV antigen
- IgM by capture EIA
- IgG by EIA, HI or neutralization test
- Identification of WNV antigen or genome in tissue
West Nile Virus
Emerged Issues

- Transfusion and organ transplant transmission
- Intra-utero/congenital infection
- Breast milk
- Occupational exposure/transmission
- Acute flaccid paralysis
# WNV Acute Flaccid Paralysis Versus Guillain-Barré Syndrome

<table>
<thead>
<tr>
<th>GBS</th>
<th>WNV-AFP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follows infection/syndrome</td>
<td>Acute phase of infection</td>
</tr>
<tr>
<td>Fever, leukocytosis absent</td>
<td>Fever, leukocytosis present</td>
</tr>
<tr>
<td>Concurrent encephalopathy absent</td>
<td>Concurrent encephalopathy frequent</td>
</tr>
<tr>
<td>Symmetric usually</td>
<td>Asymmetric generally</td>
</tr>
<tr>
<td>Sensory change/paresthesia</td>
<td>No sensory component</td>
</tr>
<tr>
<td>CSF without cells, protein elevated</td>
<td>CSF with cells and elevated protein</td>
</tr>
<tr>
<td>EMG/NCS consistent with demyelination</td>
<td>EMG/NCS consistent with pure motor deficit</td>
</tr>
<tr>
<td>Treated with IVIG, anticoagulation,</td>
<td>GBS treatment would be detrimental</td>
</tr>
<tr>
<td>plasmapheresis, high dose steroids</td>
<td></td>
</tr>
</tbody>
</table>
St. Louis Encephalitis Virus Neuroinvasive Disease Cases Reported by State, 1964-2010
St. Louis Encephalitis Virus Neuroinvasive Disease* Cases Reported by Year, 1964-2010

* Neuroinvasive disease includes cases reported as encephalitis, meningoencephalitis, or meningitis.
California Serogroup Virus Neuroinvasive Disease Cases Reported by State, 1964-2010
Percent of Human WNV and EEE Cases in Massachusetts, 2001-2012, by Age Group

California sero-group/LAC

SLE
Prevention

- **Reduce mosquito exposure**
  - Window and door screens
  - Mosquito netting
  - Staying indoors at peak mosquito times

- **Reduce mosquito bites**
  - Clothing
  - Repellents
    - DEET (N-N-diethyl-meta-toluamide)
    - Picaridin
    - Oil of lemon eucalyptus
    - Permethrin

- **Reduce mosquitoes**
  - Reduce standing water
  - Mosquito control
    - Reducing breeding environment
    - Larviciding
    - Adulticiding
What’s Next in Mosquitoes?

**Togaviruses**
- Eastern equine
- Western equine
- Venezuelan
- Chikungunya
- Sindbis
- Ross River

**Flaviviruses**
- West Nile
- St. Louis
- Dengue
- Yellow fever
- Japanese
- Murray Valley

**Bunyaviruses**
- California group (LaCrosse, Jamestown Canyon, etc.)
- Cache Valley
- Tensaw
- Rift Valley
- Other?

Colors:
- Blue: Here, now
- Red: Could come
- Black: Unlikely
Aedes aegypti
Dengue fever

**Febrile phase**
- sudden-onset fever
- headache
- mouth and nose bleeding
- muscle and joint pains
- vomiting
- rash
- diarrhea

**Critical phase**
- hypotension
- pleural effusion
- ascites
- gastrointestinal bleeding

**Recovery phase**
- altered level of consciousness
- seizures
- itching
- slow heart rate
DENGUE ± WARNING SIGNS

CRITERIA FOR DENGUE ± WARNING SIGNS

Probable dengue
- live in/travel to dengue endemic area
- Fever and 2 of the following criteria:
  - Nausea, vomiting
  - Rash
  - Aches and pains
  - Tourniquet test positive
  - Leukopenia
  - Any warning sign

Laboratory-confirmed dengue
- (important when no sign of plasma leakage)

Warning signs*
- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy, restlessness
- Liver enlargement >2 cm
- Laboratory: increase in HCT concurrent with rapid decrease in platelet count

* (requiring strict observation and medical intervention)

CRITERIA FOR SEVERE DENGUE

Severe plasma leakage
- leading to:
  - Shock (DSS)
  - Fluid accumulation with respiratory distress

Severe bleeding
- as evaluated by clinician

Severe organ involvement
- Liver: AST or ALT >=1000
- CNS: Impaired consciousness
- Heart and other organs

SEVERE DENGUE

1. Severe plasma leakage
2. Severe haemorrhage
3. Severe organ impairment
Yellow Fever

- Flavivirus
- Most infections asymptomatic
- Incubation period for symptoms is 3-6 days
- Acute onset of fever, chills, headache, back pain, myalgias, nausea and vomiting, and weakness
- In 15% of symptomatic cases, recurrent high fever, with potential for jaundice, hemorrhage, shock and multi-organ failure
Areas with Yellow Fever
Aedes albopictus
Distribution of *Aedes albopictus* the Asian Tiger Mosquito

Chikungunya

- Alphavirus – similar to Sindbis, Mayaro
- Many competent mosquito vectors
- Epidemic polyarthritis
- Rash follows arthritis
- Mild hemorrhagic manifestations
- Imported cases in the United States
- Question of potential transmission in the United States
Chikungunya: Origins and Introductions
Can it really be bug season already?

Warm winter may draw them out

By Doyle Rice
USA TODAY

One of the USA’s warmest winters in years could lead to a bug bonanza over the next few weeks, as beetles, ants, termites, wasps and other insects come out much earlier than average.

“Even things like mosquitoes might come out earlier,” says Rutgers entomologist George Hamilton, who says the pests typically don’t appear until late April.

In some places, the onslaught has already begun: “We’re seeing insects out there that we don’t usually see this time of year,” says Missy Henriksen of the National Pest Management Association, who listed such annoyances as stink bugs and box elder bugs.

“Several states have even reported tick sightings, which is especially worrisome as people head outdoors to enjoy the weather and are unprepared for tick encounters,” she says.

The widespread warmth could have an impact on insects across much of the country, Hamilton says.

Several cities, including Chicago, New York and Washington, are on track to have one of their top 10 warmest winters on record, according to The Weather Channel data.

The biggest impact isn’t on the number of insects, Hamilton says, but on when we’ll see the insects appearing.

“Many insects hibernate during the cold months, but as this winter has been anything but typical, they may be emerging from their hiding places much earlier than we expect,” Henriksen says.

Bugs survive the cold with strategies such as slowing down their metabolism and respiration. With the warmer temperatures, many are forced out early in search of food.

One key for the insects is that if they come out early, the flowers and plants they feed on must also bloom equally early. “They have to be synchronized with what they’re feeding upon,” reports entomologist David Denlinger of Ohio State University. Insects such as honeybees could die, he says, if the flowers aren’t also out.

This isn’t a concern for insects like mosquitoes that feed on human or animal blood. Along the Gulf Coast, the mild winter, combined with tropical storms last year, will likely lead to a banner year for mosquitoes.

Contributing: The Associated Press