TICKS: IT'S MORE THAN JUST LYME DISEASE

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Center for Vector Biology & Zoonotic Diseases
CT Agricultural Experiment Station
New Haven, CT

CEHA
November 1, 2019
Widespread and difficult to control, diseases from mosquito, tick, and flea bites are major causes of sickness and death worldwide. The growing number and spread of these diseases pose an increasing risk in the U.S. The report found that the nation needs to be better prepared to face this public health threat.
DISCOVERY OF TICKBORNE PATHOGENS AS CAUSES OF HUMAN DISEASE BY YEAR, 1909-1959

- **Amblyomma spp.**
- **Dermacentor spp.**
- **Ixodes spp.**
- **Ornithodoros spp.**

**Borrelia hermsii** (tick-borne relapsing fever)
- 1920

**Borrelia turicatae** (tick-borne relapsing fever)
- 1900

**Rickettsia rickettsii** (Rocky Mountain spotted fever)
- 1930

**Francisella tularensis** (tularemia)
- 1940

**Borrelia parkeri** (tick-borne relapsing fever)
- 1950

**Colorado tick fever virus** (Colorado tick fever disease)
- 1960

**Powassan virus** (Powassan encephalitis)
- 1955

- Year represents when tickborne pathogen was recognized as cause of human disease.

Adapted from slide by Ben Beard CDC-Division Vector-Borne Diseases
DISCOVERY OF TICKBORNE PATHOGENS HAS ACCELERATED, 1960-2016

- **Amblyomma spp.**
- **Dermacentor spp.**
- **Ixodes spp.**

**Ehrlichia chaffeensis** (ehrlichiosis) - 1960

- **Babesia microti** (babesiosis) - 1960
- **Borrelia burgdorferi** (Lyme disease) - 1980
- **Anaplasma phagocytophilum** (anaplasmiosis) - 1990
- **Rickettsia parkeri** (rickettsiosis) - 2000
- **Rickettsia philipii** (Pacific Coast tick fever) - 2020
- **Heartland virus** (Heartland virus disease) - 2020
- **Borrelia mayonii** (Lyme disease) - 2010
- **Borrelia miyamotoi** (B. miyamotoi disease) - 2015
- **Ehrlichia muris** (ehrlichiosis) - 2015

- Year represents when tickborne pathogen was recognized as cause of human disease.

Adapted from slide by Ben Beard CDC-Division Vector-Borne Diseases
TOTAL TICK-BORNE DISEASE CASES, UNITED STATES, 2004–2017


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Majority of Reported Vector-Borne Diseases are Spread by Ticks

Lyme disease (68%) 42,743
Other tickborne Diseases (27%)
Mosquito- or flea-borne diseases (5%)

Diagnosed cases Prob. ~430,000

Cases of Nationally Notifiable Vector-borne Diseases Reported in the U.S., 2017

N= 62,399 cases
LYME DISEASE CASE DISTRIBUTION – 19 YEAR TREND

1996

2017

430,000 cases of Lyme disease

TICK-ASSOCIATED DISEASES HUMANS IN THE U.S.

- Anaplasmosis
- Babesiosis
- Lyme disease (*Borrelia burgdorferi*)
- *Borrelia miyamotoi* infection
- *Borrelia mayonii* n. sp.
- Bourbon virus
- Colorado Tick Fever
- Ehrlichiosis (*E. chaffeensis, E. ewingii*)
  - *E. muris* subsp. *eauclairensis*
- Heartland virus infection
- Red meat allergy
- Southern Tick-Associated Rash Illness
- Spotted Fever Group Rickettsia
- Tick-borne relapsing fever
- Powassan virus infection
- Tick paralysis (toxin)
- Tularemia
There are over 900 tick species worldwide of which ~ 10% act as vectors of human and domestic animal pathogens. There are around 100 species in the U.S. Only about 20 or so are of major public health or veterinary importance.
At least 16 species of ticks known (11 in NJ, 30 in NY State)
3 species commonly bite humans
4 species can transmit disease pathogens

Blacklegged Tick
*Ixodes scapularis*

American Dog Tick
*Dermacentor variabilis*

Lone Star Tick
*Amblyomma americanum*

Woodchuck Tick
*Ixodes cookei*

Others from humans in Connecticut include *I. dentatus, R. sanguineus*
THREE-HOST TICK LIFE-CYCLE

Kirby Stafford, CT Agricultural Experiment Station
Lone star ticks on deer

Blacklegged Tick
1,000-2,000 eggs

Lone Star Tick
1,000-8,000 eggs; avg. 3,000

Larvae hatching from egg mass
Female tick
White-footed mouse, birds
Eastern chipmunk & shrews
SEASONAL ACTIVITY OF *IXODES SCAPULARIS*

- **Nymphs**
- **Adults**
- **Larvae**

Chart showing relative activity over the seasons from January to December.
LYME DISEASE BY MONTH OF ONSET, CONNECTICUT, 2016
WITH SEASONAL ACTIVITY IXODES SCAPULARIS

[Graph showing the number of cases for nymphs, adults, and larvae by month.]

* Numbers and cases reflect changes in the reporting systems and the national surveillance case definition.

Connecticut Department of Public Health
LYME DISEASE RISK

Data: Stamford Health Department
1989-2000, n = 4551 records and 2001, n = 266 records
AGE DISTRIBUTION FOR LYME DISEASE

Confirmed Lyme disease cases by age and sex—United States, 2001-2017

Lyme Disease Incidence by Ten Year Age Groups, Connecticut, 2018*

Confirmed Lyme disease cases U.S., 2001-2017

*Numbers will not reflect changes to the reporting process and the external surveillance system definitions.
Lyme Disease Cases Statewide by Case Status, Connecticut, 1991 – 2018


Connecticut Department of Public Health

DPH Keeping Connecticut Healthy
Ixodes scapularis (Blacklegged Tick) N = 3,491 (80.0%)

Dermacentor variabilis (American Dog Tick) N = 725 (16.6%)

Amblyomma americanum (Lone Star Tick) N = 138 (3.2%)

Other tick species N = 8 (0.02%) incl.
3 I. cookei
1 A. maculatum
1 D. andersoni
1 H. longicornis
1 R. sanguineus

Total ticks submitted for identification N = 4,362

Data courtesy Dr. Goudarz Molaei
### Tick Testing Results, 2015-2018

#### Tick Testing Laboratory

**Nymph & Adult *Ixodes scapularis***

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. ticks tested</td>
<td>2,503</td>
<td>2,235</td>
<td>4,458</td>
<td>3,273</td>
</tr>
<tr>
<td>Uninfected</td>
<td>53.7%</td>
<td>64.7%</td>
<td>40.0%</td>
<td>41.4%</td>
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<tr>
<td><em>Borrelia burgdorferi</em></td>
<td>31.5%</td>
<td>28.8%</td>
<td>32.0%</td>
<td>38.3%</td>
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<tr>
<td><em>Babesia microti</em></td>
<td>11.0%</td>
<td>7.4%</td>
<td>6.0%</td>
<td>9.5%</td>
</tr>
<tr>
<td><em>Anaplasma phagocytophilum</em></td>
<td>4.9%</td>
<td>4.6%</td>
<td>7.0%</td>
<td>12.0%</td>
</tr>
<tr>
<td><em>Borrelia + Babesia</em></td>
<td>4.1%</td>
<td>2.8%</td>
<td>3.1%</td>
<td>5.0%</td>
</tr>
<tr>
<td><em>Borrelia + Anaplasma</em></td>
<td>1.9%</td>
<td>1.8%</td>
<td>3.7%</td>
<td>6.6%</td>
</tr>
<tr>
<td><em>Babesia + Anaplasma</em></td>
<td>0.1%</td>
<td>0.0%</td>
<td>0.5%</td>
<td>1.4%</td>
</tr>
<tr>
<td><em>Borrelia + Babesia + Anaplasma</em></td>
<td>0.2%</td>
<td>0.2%</td>
<td>0.4%</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

Data courtesy Dr. Goudarz Molaei, CAES (available on CAES website)
POWASSAN VIRUS

Powassan (POW) Disease

- First described in 1958 in Powassan, Ontario
- Agent: Powassan virus (POWV), flavivirus closely related to West Nile virus (WNV)
  - Lineage II strain (“deer tick virus”), vector: *Ixodes scapularis*
  - Lineage I strain (prototype virus), vector: *Ixodes cookei*

The four cases in 2019 in CT were in Ridgefield, New Canaan, New Preston, and Newton with 1 fatality

Number of cases reported in US 2009-2018
LONE STAR TICK
AMBLYOMMA AMERICANUM

95% tick bites in southeastern U.S.

- Bourbon virus
- Ehrlichiosis
  - Ehrichia chaffeensis
  - Ehrichia ewingii
  - Panola Mountain ehrlichia
- Heartland virus infection
- Southern Tick-Associated Rash Illness (STARI)
- Spotted Fever Group Rickettsia
- Tularemia
- Red Meat Allergy (alpha-gal syndrome)
MINIMUM TEMPERATURE FACTOR
NORTHERN DISTRIBUTION LONE STAR TICK?


“NOAA data shows that in every Northeast state except Pennsylvania, the temperatures of the winter months of December through February have risen by 2 degrees Celsius since 1895-1896”
Departures shown are based on the 20th century mean (1901-2000).
SUBMISSIONS TO CAES-TTL, 1996-2017

No. of Ticks Submitted

Year

No. Ticks (In-state)

No. Ticks (Out-of-State)

CAES
The Connecticut Agricultural Experiment Station
Putting Science to Work for Society since 1875
Ticks discovered on white-tailed deer on 27 June 2017 at Manresa Island, a peninsula in South Norwalk by a DEEP EnvCon Officer and confirmed as lone star ticks by Dr. Kirby Stafford 28 June 2017

Active infestation seems limited to that site
Ticks placed in vials in tick “pots” buried in the ground in randomized block design with Hobo data loggers. Four treatment combinations:
Leaf and snow removal (LRSR)
No leaf removal and snow removal (NLRSR)
Leaf removal and no snow removal (LRNSR)
No leaf and no snow removal (NLRNSR)

Example one month Hobo data
January-2017

Degrees F
Min of LRNSR

Day
1-3-17 1-9-17 1-13-17
Overwintering survival adult lone star ticks 2016-2017
Connecticut 32-83%

Overwintering survival adult lone star ticks 2017-2018
Connecticut 47-73%

Overwintering survival adult lone star ticks 2018-2019
Connecticut 37-78%
Overwintering survival adult lone star ticks 2016-2017
Maine 2-13%

Overwintering survival adult lone star ticks 2017-2018
Maine 11-73%

Overwintering survival adult lone star ticks 2018-2019
Maine 4-18% (Males)
New Jersey announced the discovery of an East Asian tick, also known as a longhorned tick, *Haemaphysalis longicornis*, on sheep at a farm in Hunterdon County on 9 Nov 2017. The East Asian tick is considered a serious pest to livestock including cattle, horses, sheep, and goats. It can attack humans, pets and wildlife and is a known vector for a number of human and animal pathogens. It has been detected in at least 9 states and is abundant in NJ and parts of the NYC area.
COUNTIES AND COUNTY EQUIVALENTS* WHERE HAEMAPHYSALIS LONGICORNIS HAS BEEN REPORTED (N = 63) — UNITED STATES, AS OF MAY 9, 2019

• From August 2017 to September 10, 2019, reported from twelve U.S. states (Arkansas, Connecticut, Delaware, Kentucky, Maryland, New Jersey, New York, North Carolina, Pennsylvania, Tennessee, Virginia, and West Virginia)
• Documented in 82 counties or county equivalents
• Known distribution is expanding as surveillance efforts increase

Source: National Haemaphysalis longicornis Situation Report, US Department of Agriculture, September 10, 2019
From NEVBD Webinar November 19, 2018 with Dr. Allen C.G. Heath, Dr. Andrea Egizi, and Dr. Richard Falco

Asian Longhorned Tick: Where Found in NY So Far, October 2018 (Note: no farms!)
TWO NYMPHS ASIAN LONGHORNED TICK DETECTED IN CT 2018

WCSU discovers first specimen of exotic tick in Connecticut

DANBURY, Conn. — Western Connecticut State University researchers have found the first Asian longhorned tick in Connecticut. The invasive species can harm livestock and, where it originates in Asia, can carry deadly diseases. So far the tick is not known to be a danger to humans in the U.S.

Brittany Schappach, a recent WCSU biology department graduate who works as a research assistant for the WCSU Tickborne Disease Prevention Laboratory, collected the tick, Haemaphysalis longicornis, on July 3 during weekly tick monitoring for the lab.

Brittany Schappach collects ticks.

East Asian longhorned tick, Haemaphysalis longicornis
(Photos by Kitty Prapayotin-Riveros (The CAES))

Tick Testing Laboratory at The Connecticut Agricultural Experiment Station Reports the First Evidence of Human Biting by the Exotic East Asian Longhorned Tick in the State

New Haven, CT — The Tick Testing Laboratory at The Connecticut Agricultural Experiment Station (CAES) is reporting the first evidence of human biting by the exotic east Asian longhorned tick, Haemaphysalis longicornis in a resident from Fairfield County. The longhorned tick is an invasive species.

One Asian longhorned tick nymph was collected in Fairfield County in 2019.
Integrated Tick Management

- Education and behavior change
- Personal protection measures
- Landscape modifications
- Chemical control
  - Synthetic insecticides
  - Botanicals, “natural” compounds
- Biological control
- Host reduction or exclusion
- Host-targeted acaricides
- Host-targeted vaccines

Kirby Stafford
Barnstable Co. Coop. Ext.

Skip Wieseburger

CAES
The Connecticut Agricultural Experiment Station
Putting Science to Work for Society since 1873
Most ticks require high humidity and cover (canopy)

New England has 240,000 miles of stone walls
Forest land covers nearly 60% (1.9 million acres) of the CT's total land area.
TICK SAMPLING

Worst job in science: Tick collecting

Tick Dragger
Popular Science November 2004

©National Geographic

CAES

The Connecticut Agricultural Experiment Station
Paving Science to Work for Society since 1875
DISTRIBUTION IXODES SCAPULARIS ON RESIDENTIAL LAWNS

- 0-1 m: 68%
- 1-3 m: 13.8%
- > 3 m: 18.2%

Residential Landscape Management
Higher tick counts associated with exotic invasive forest understory than native forest understory or open understory forests in Maine. Reduction and long-term management barberry significantly reduced abundance infected ticks


Ticks and a greater infection with some associated disease pathogens have been found where invasive plants like Japanese barberry and amur honeysuckle is reported invasive. Removal honeysuckle decreased deer activity and numbers of *Ehrlichia* infected ticks

SPRAYING

Carbamate Pyrethroids Biopesticides

Microbial Biochemical, i.e., natural occurring substances, including plant extracts

Photographs: Kirby Stafford
<table>
<thead>
<tr>
<th>Acaricide</th>
<th>Application</th>
<th>reduction nymphs*</th>
<th>Time evaluation</th>
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<tbody>
<tr>
<td>Bifenthrin</td>
<td>Spray</td>
<td>45-100%</td>
<td>1-6 wks</td>
</tr>
<tr>
<td>Cyfluthrin</td>
<td>Spray</td>
<td>88-100%</td>
<td>2-8 wks</td>
</tr>
<tr>
<td>Cyfluthrin</td>
<td>Granules</td>
<td>87-97%</td>
<td>1-8 wks</td>
</tr>
<tr>
<td>Deltamethrin</td>
<td>Granules</td>
<td>87-100%</td>
<td>1-5 wks</td>
</tr>
<tr>
<td>Carbaryl</td>
<td>Spray</td>
<td>43-93%</td>
<td>2-13 wks</td>
</tr>
<tr>
<td>Carbaryl</td>
<td>Granules</td>
<td>46-96%</td>
<td>1 wk-3 mo</td>
</tr>
<tr>
<td>Rosemary, etc.*</td>
<td>Spray (low, 2x) (IC2)</td>
<td>73-95%</td>
<td>1-5 wks</td>
</tr>
<tr>
<td>Rosemary, etc.*</td>
<td>Spray (high) (IC2)</td>
<td>100%</td>
<td>1-2 wks</td>
</tr>
<tr>
<td>Garlic</td>
<td>Mosquito Barrier</td>
<td>37-59% repellency</td>
<td>1-2 wks</td>
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<tr>
<td>Pyrethrum, thyme oil, etc.**</td>
<td>EcoPCO</td>
<td>99.6% KD 72% residual</td>
<td>NA</td>
</tr>
<tr>
<td>Cedar oil**</td>
<td>Cedarcide &amp; Tick Kills</td>
<td>5.0-5.9% KD</td>
<td>0-8.5% residual</td>
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<tr>
<td>Cedar oil ***</td>
<td>Cedar Safe</td>
<td>31-40%</td>
<td>2 wks</td>
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</table>

**MET52® EC BIOINSECTICIDE**

- *Metarhizium anisopliae* Strain52
  Novozymes Biologicals, Inc.
  Monsanto BioAg™ Inc.
- Registered in all states
- 53-74% control original trials
- 71-85% control current trials

Non-refrigerated formulation
Label rate: 2-3 fl. oz. per 1,000 ft²
4 gallons water per 1,000 ft²
Apply 4-8 week intervals

*M. anisopliae* on female *I. scapularis*
*(Photo: Stafford)*

balEnce™ biopesticide control of flies, *Beauveria bassiana* (Terregena Inc.)
SUMMARY ISSUES “NATURAL” PRODUCTS

- No or limited efficacy data, especially under real world field conditions.
- Exempted from testing for toxicity, some may be toxic at higher doses, irritants, or allergens.
- Variable composition of essential oils depending on source plant species (may or may not be known or released by manufacturer), extraction method, etc.
- Volatility and lack of persistence, requiring frequent applications.
- Efficacy oil vs. specific components of the plant extract or oil Laboratory (topical, direct spray) vs. field evaluations (i.e., residual activity - ticks under leaf litter). Nootkatone under EPA review under name NootkaShield™ from Evolva.
- Formulation may make a huge difference as activity likely due to synergism or interaction multiple ingredients.
HOST-TARGETED TICK CONTROL
Rodent Reservoirs
White-footed Mice
Eastern Chipmunk

Treatment

Entry Points
Non-Toxic Food blocks
Wick with 3 mls Fipronil 0.7%

80-84%

20-30%

White-tailed Deer

1. Exclusion
2. Reduction
3. Treatment

RTV - Vaccine
Deer reduced 40-54/km² to 0-9/km² (ca. 122 to 13.2 deer/mi²) (≥ 87%)
76% reduction in tick abundance
80% reduction in resident-reported cases of Lyme disease
Densities of 5.1 deer/km² (13/mi²) significantly reduced the number of infected ticks and human risk of contracting Lyme disease
Integrated Control of Nymphal *Ixodes scapularis*: Effectiveness of White-Tailed Deer Reduction, the Entomopathogenic Fungus *Metarhizium anisopliae*, and Fipronil-Based Rodent Bait Boxes

Scott C. Williams, Kirby C. Stafford, III, Goudarz Molaei, and Megan A. Linske

Vector-Borne and Zoonotic Diseases 18: 55-64 (2018)

Integrated control of juvenile *Ixodes scapularis* parasitizing *Peromyscus leucopus* in residential settings in Connecticut, United States

Scott C. Williams, Eliza A.H. Little, Kirby C. Stafford, III, Goudarz Molaei, Megan A. Linske

Ticks and Tick-Borne Diseases 9: 1310-1316 (2018)

**Four 1-mi² neighborhoods**

1. Control (n = 12 residences)
2. Deer removal only (n = 8)
3. Met 52 + Bait box (n = 13)
4. Deer removal, Met 52, Bait box (n = 5)
The combination of fipronil-based bait boxes and broadcast application of *M. anisopliae* had the most impact of any treatment combination; questing nymphs were reduced 78–95% within each year and *Borrelia burgdorferi*-infected questing nymphal *I. scapularis* encounter potential was reduced by 66% as compared with no treatment in the third year of the study.
Scott Williams, Megan Linske, Kirby Stafford with Michael Short and Heidi Stuber

<table>
<thead>
<tr>
<th>Neighborhood</th>
<th>4-poster</th>
<th>Bait Box</th>
<th>Met52</th>
<th>No. 4-poster locations</th>
<th>No. tick sampling properties</th>
<th>No. rodent sampling properties</th>
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<tr>
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<td>7</td>
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<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>83</td>
<td>63</td>
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</tbody>
</table>

Summer 2017 Baseline Year Sampling
Spring 2018 deployment 4-posters
Summer 2018 full implementation of treatments with spraying Met52 (*M. anisopliae*) and fipronil bait boxes.
Fall 2018 2nd deployment 4-posters
Summer 2019 full implementation
WHERE DO WE GO FROM HERE?

- The number of ticks, increasing distribution, and spread of associated diseases pose an increasing public health and veterinary risk in the U.S.
- There are many tools available for killing ticks, but impact on disease largely unclear or unproven, few options available or utilized by homeowners
- How define and support individual and community-wide interventions
- In the absence of a human vaccine, safe, cost-effective and effective prevention tools & Integrated Tick Management data badly needed
Valneva Reports Positive Phase I Interim Results for Its Lyme Vaccine Candidate VLA15

Phase I study (VLA15-101) primary endpoint met

- No safety concerns associated with VLA15 in any treatment group

Encouraging immunogenicity with VLA15

- VLA15 is immunogenic in all doses and formulations tested
- Good OspA-specific IgG antibody responses against all OspA serotypes

VLA15-201 is the first of two planned, parallel Phase 2 studies. It is a randomized, observer-blind, placebo controlled trial conducted at trial sites in the US and Europe. The complete Phase 2 study is expected to be approximately two years in duration with interim data (primary endpoint) expected mid-2020.

The charter for the Tick-Borne Disease Working Group was approved by the Secretary of Health and Human Services on August 10, 2017, marking the official establishment of the Working Group within HHS. The Working Group was authorized by Congress for a total of six years from the date that the Act became law.

The charter defines how the Working Group is structured and functions in response to the charge provided by the 21st Century Cures Act, and is renewed every two years in accordance with Federal advisory committee guidelines. The current charter expires August 10, 2021.
From red-bugs and bed-bugs, from sand-flies and land-flies, Mosquitoes, gallinippers and fleas, From hog-ticks and dog-ticks, from hen-lice and men-lice, We pray thee, good Lord, give us ease.

An old prayer, circa 1856