TICKS:
IT'S MORE THAN JUST LYME DISEASE

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CEHA
November 1, 2019

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 67
May 1, 2018

Vital Signs: Trends in Reported Vectorborne Disease Cases — United States and Territories, 2004–2016

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.

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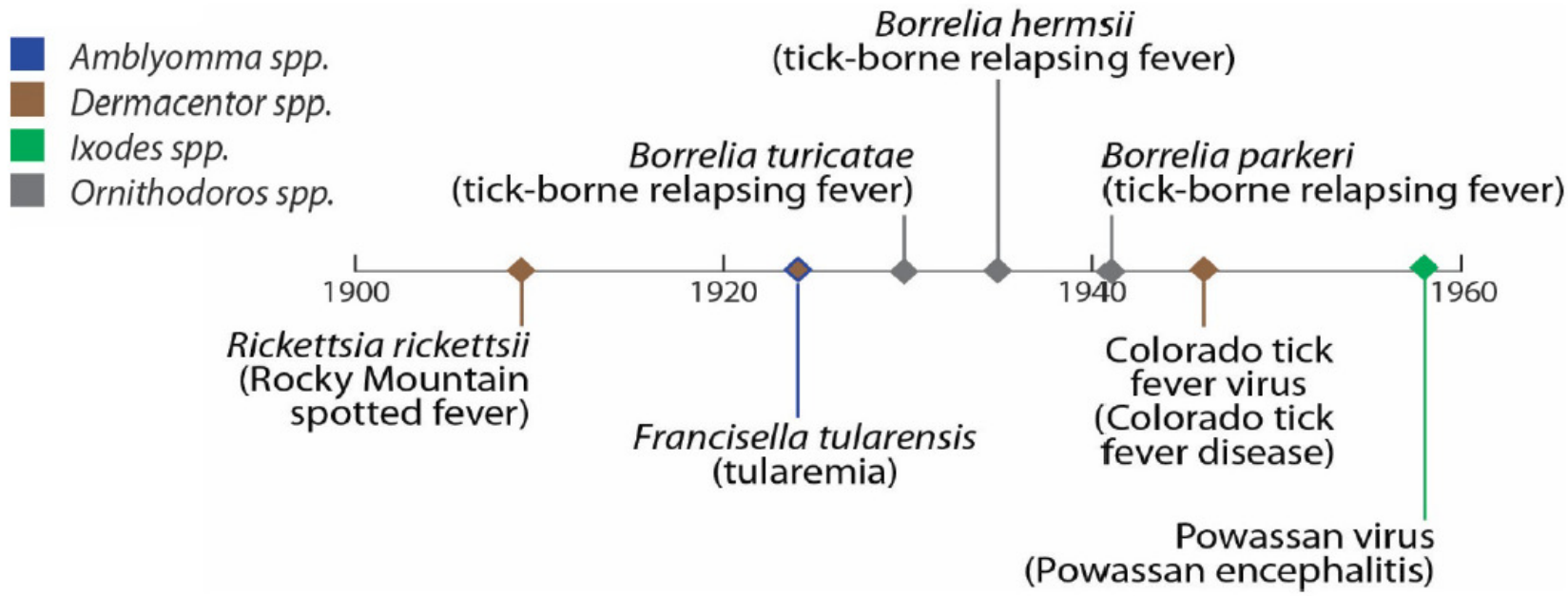
DISCOVERY OF TICKBORNE PATHOGENS AS CAUSES OF HUMAN DISEASE BY YEAR, 1909-1959



- Year represents when tickborne pathogen was recognized as cause of human disease.
- Adapted from: Paddock CD, Lane RS, Staples JE, Labruna MB. 2016. In: Mack A, Editor. Global health impacts of vector-borne diseases: workshop summary. National Academies Press. p. 221-257.

Adapted from slide by Ben Beard CDC-Division Vector-Borne Diseases

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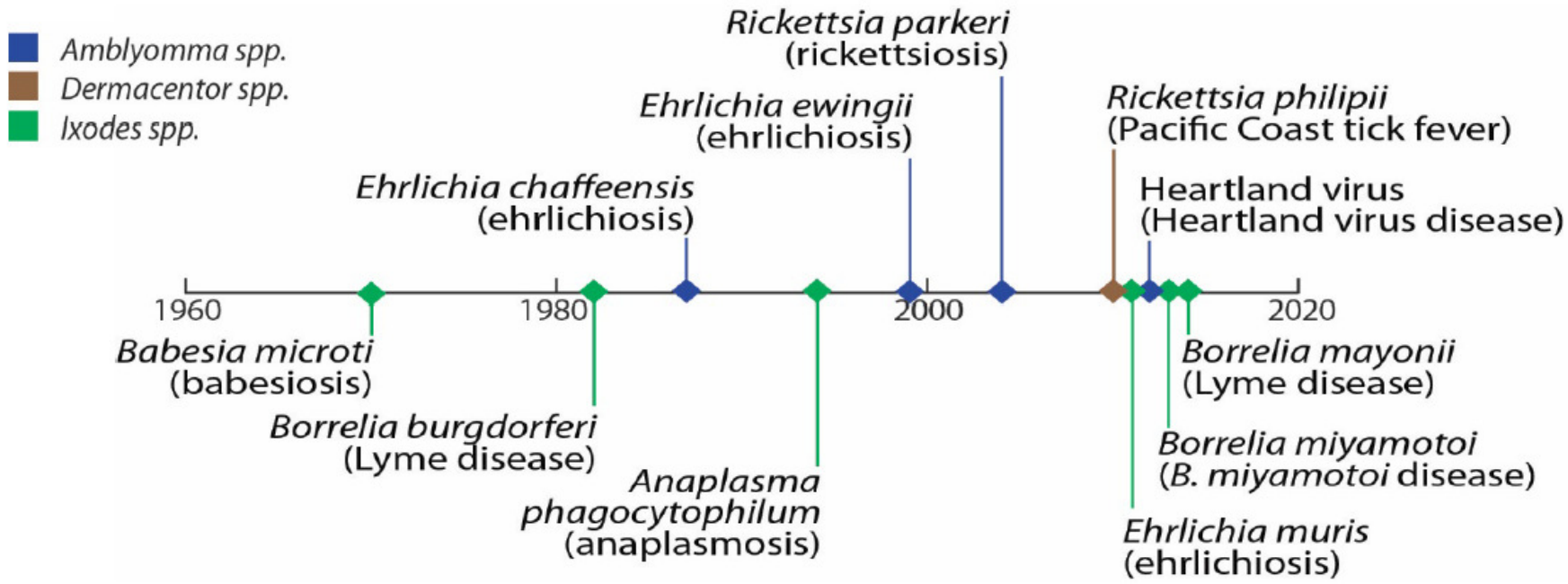
DISCOVERY OF TICKBORNE PATHOGENS HAS ACCELERATED, 1960-2016



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Adapted from slide by Ben Beard CDC-Division Vector-Borne Diseases

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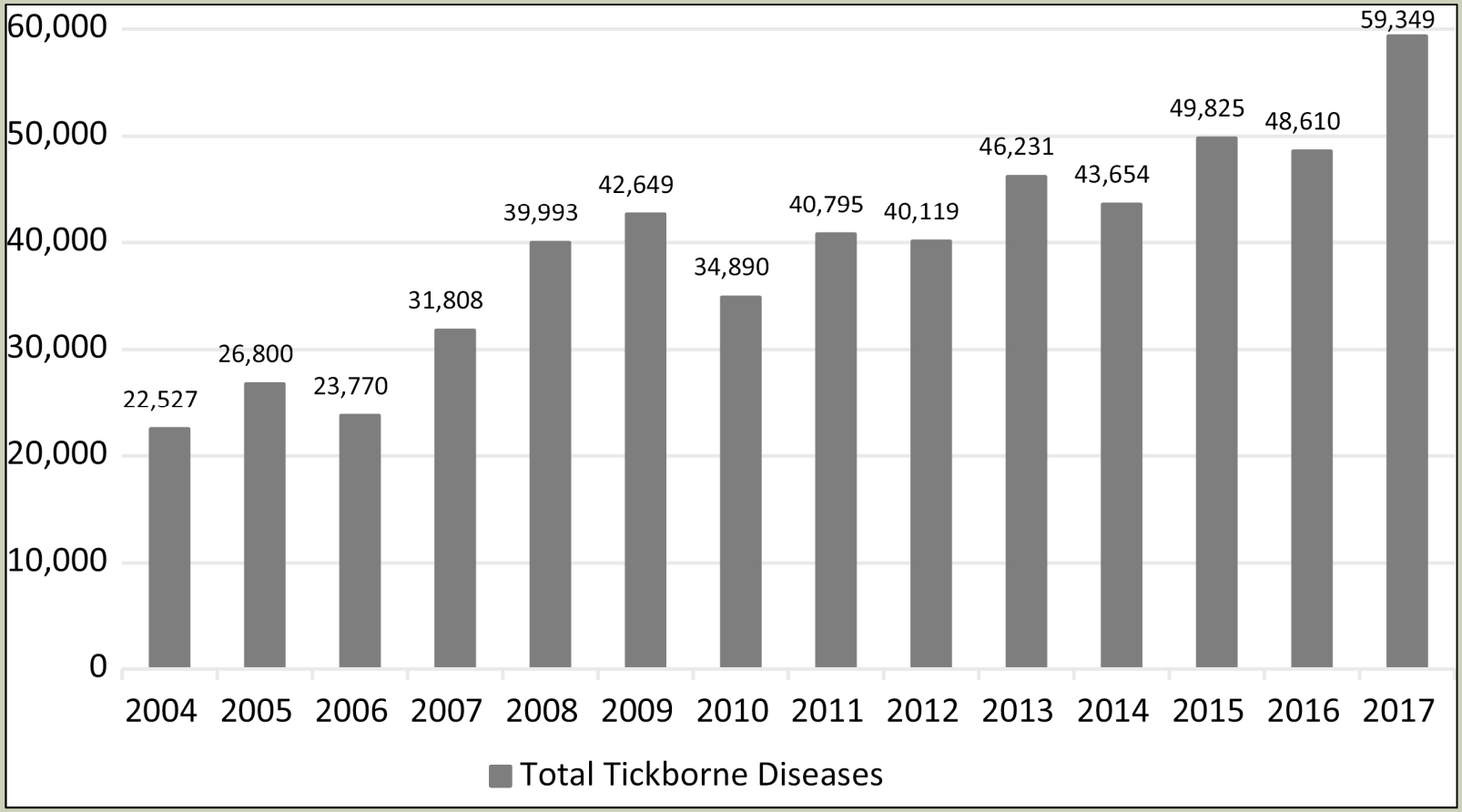
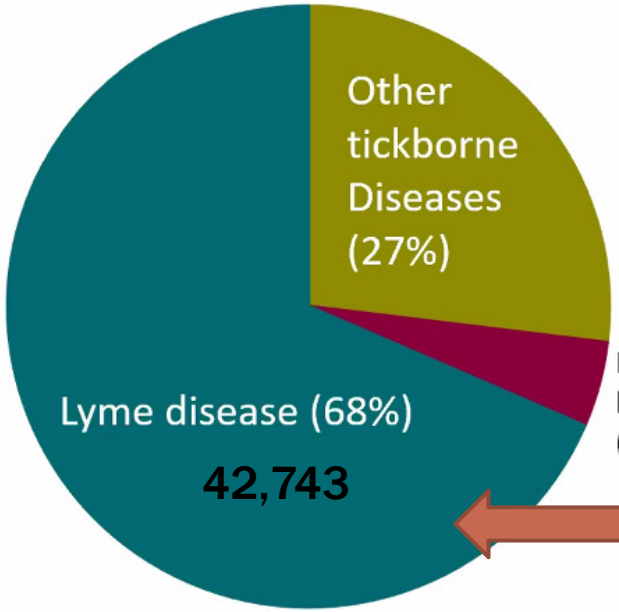
TOTAL TICK-BORNE DISEASE CASES, UNITED STATES, 2004–2017



Journal of Medical Entomology, Volume 56, Issue 5, September 2019, Pages 1199–1203, https://doi.org/10.1093/jme/tjz074

Majority of Reported Vector-Borne Diseases are Spread by Ticks

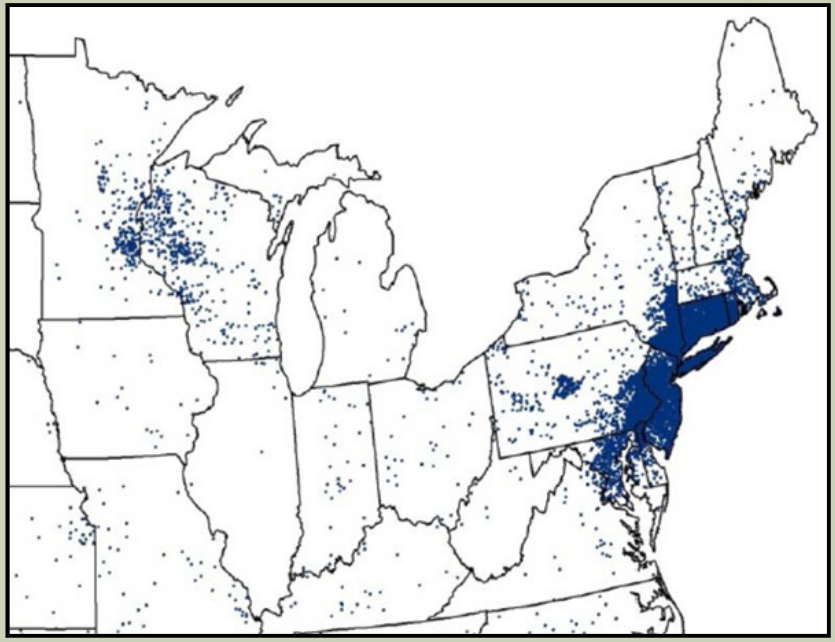


Diagnosed cases
Prob. ~430,000

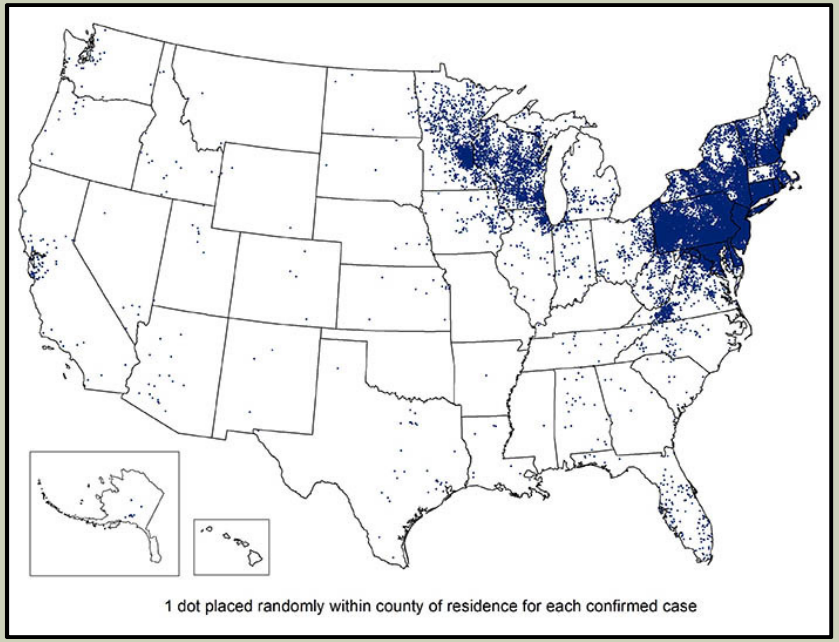
Cases of Nationally Notifiable Vector-borne Diseases Reported in the U.S., 2017

N= 62,399 cases

LYME DISEASE CASE DISTRIBUTION – 19 YEAR TREND



1996



2017

430,000 cases of Lyme disease

http://www.cdc.gov/lyme/stats/maps/interactiveMaps.html

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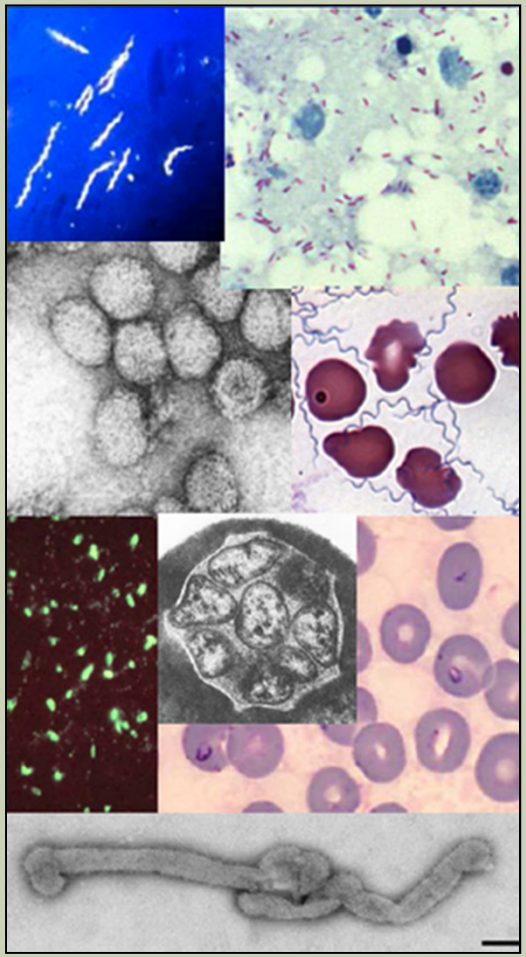
TICK-ASSOCIATED DISEASES HUMANS IN THE U.S.

- 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



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THE TICKS

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

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TICKS IN CONNECTICUT

- 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*

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BLACKLEGGED TICK

IXODES SCAPULARIS

USDA/Scott Bauer

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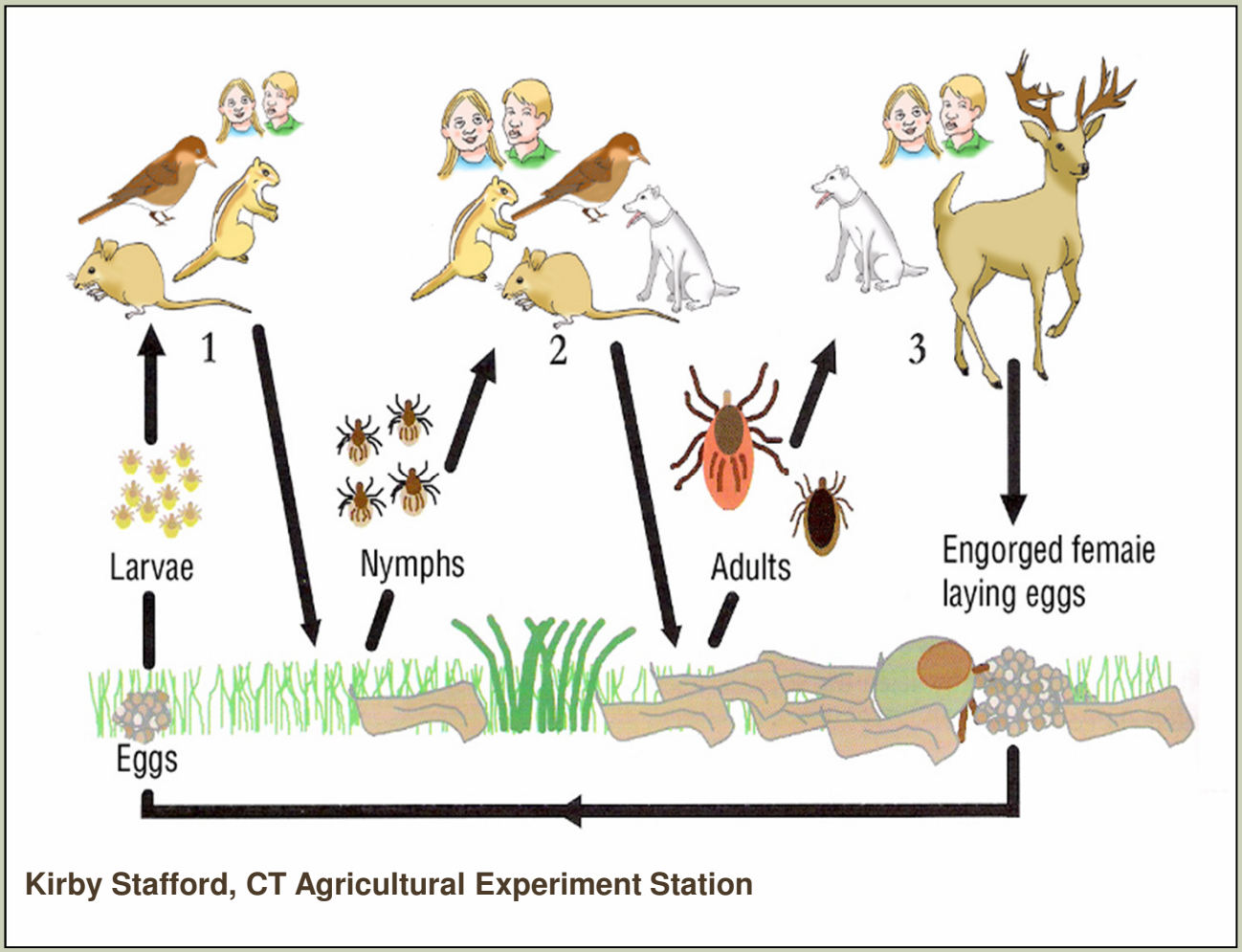
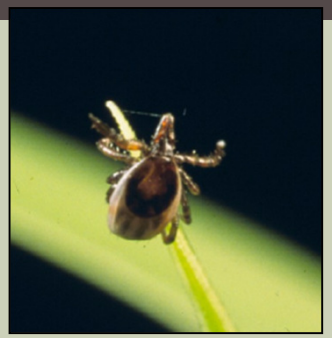
THREE-HOST TICK LIFE-CYCLE



Kirby Stafford, CT Agricultural Experiment Station



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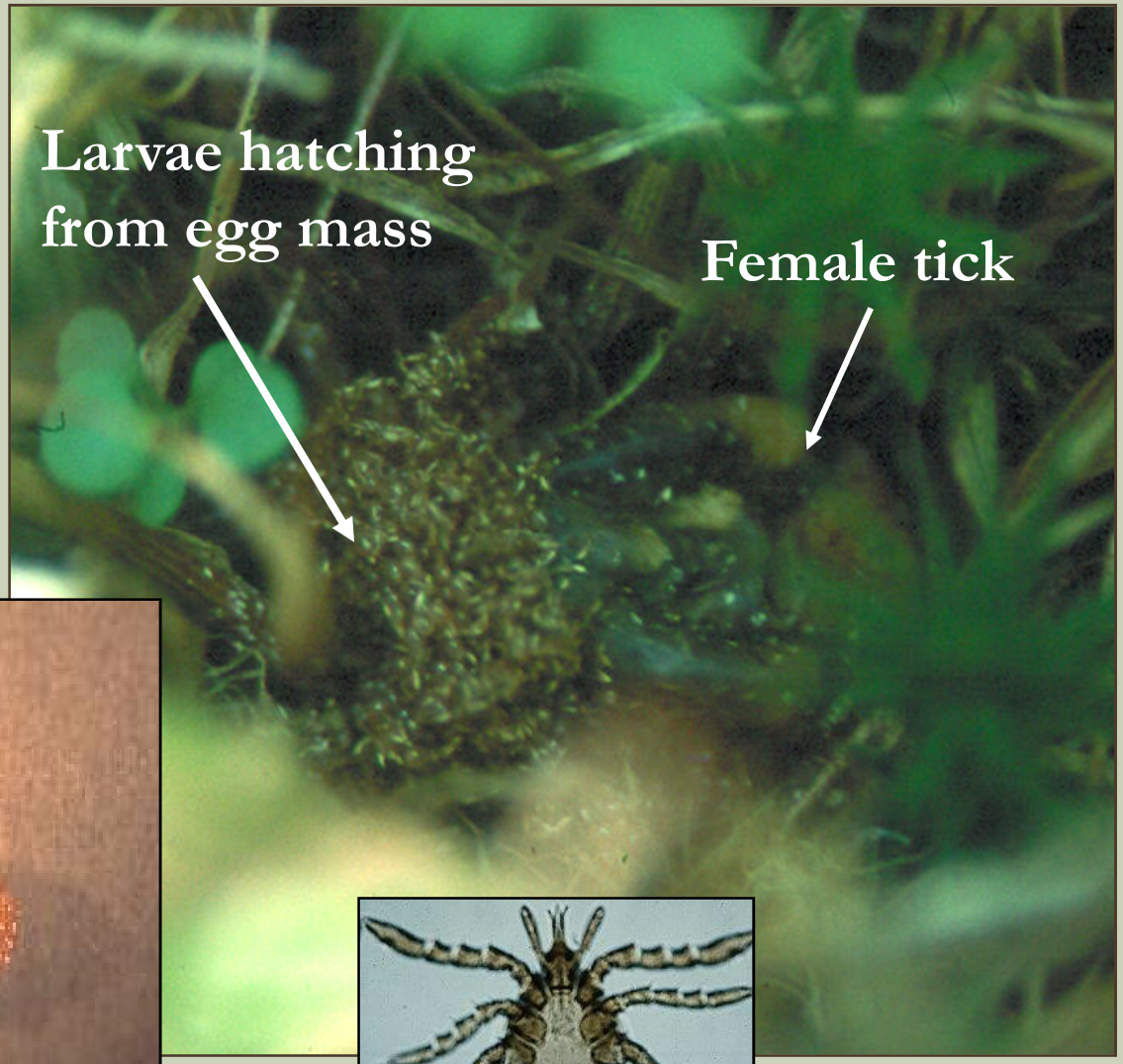
Lone star ticks on deer



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K. Stafford

White-footed mouse, birds
Eastern chipmunk & shrews

J. Occi

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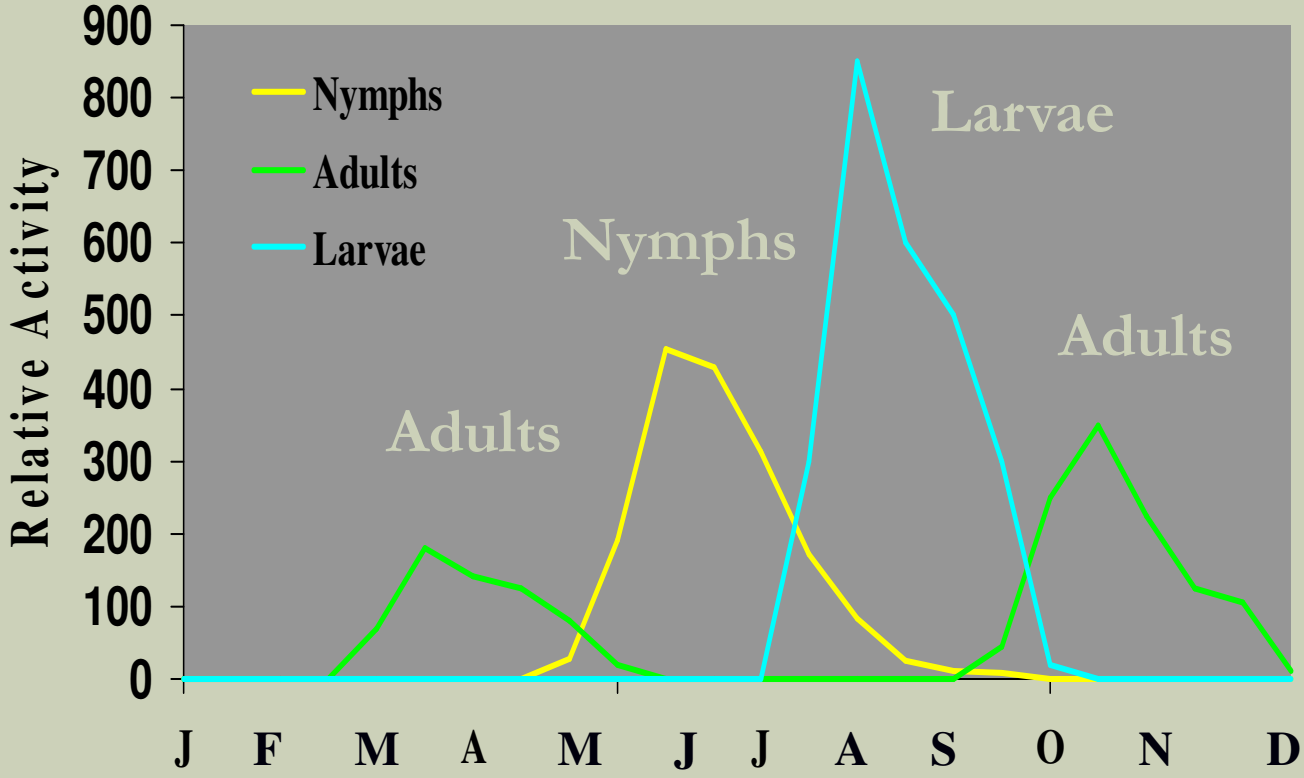
SEASONAL ACTIVITY OF *IXODES SCAPULARIS*



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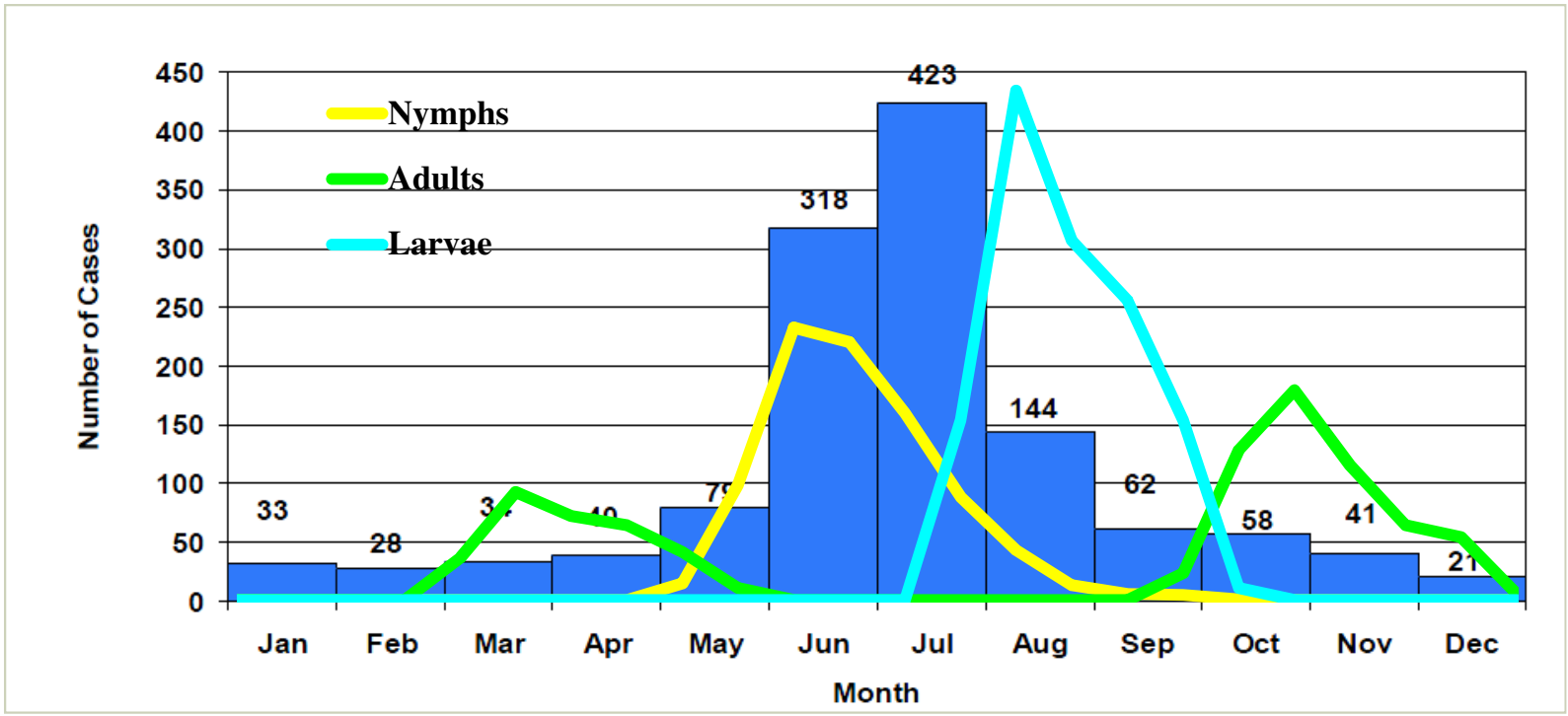
LYME DISEASE BY MONTH OF ONSET, CONNECTICUT, 2016 WITH SEASONAL ACTIVITY *IXODES SCAPULARIS*



DPH Keeping Connecticut Healthy

* Numbers and rates reflect changes in the reporting system and the national surveillance case definition (http://www.cdc.gov/osels/ph_surveillance/nndss/casedef/lyme_disease_current.htm). Surveillance has included physician-reporting (1987-present) and laboratory-reporting (1998-2002, 2006-present) components. The 2008-current data, contains both confirmed and probable cases as defined by the national surveillance case definition.

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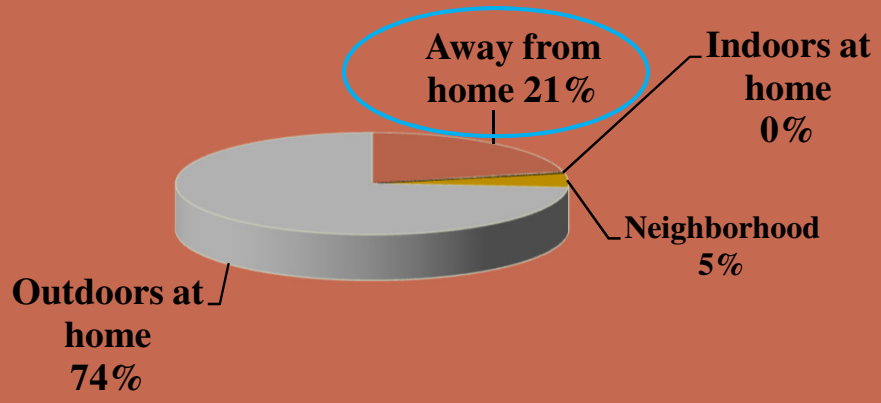

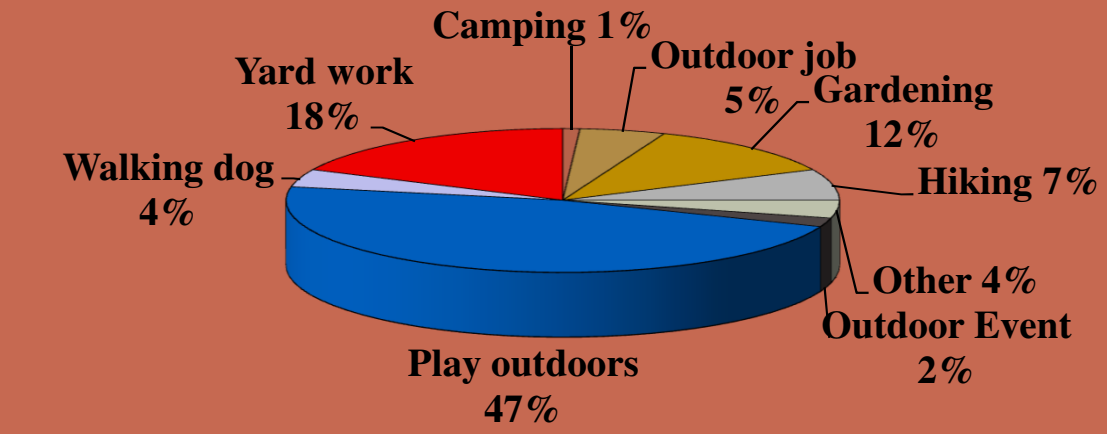

LYME DISEASE RISK

Data: Stamford Health Department
1989-2000, n = 4551 records and 2001, n = 266 records


K. Stafford


Pfizer


Scott Bauer. ARS

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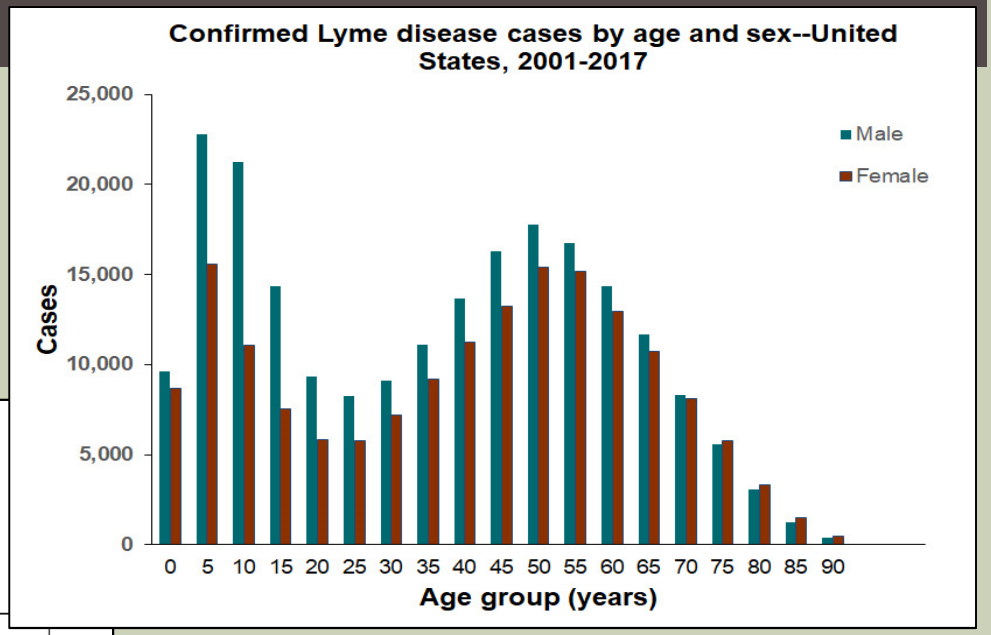
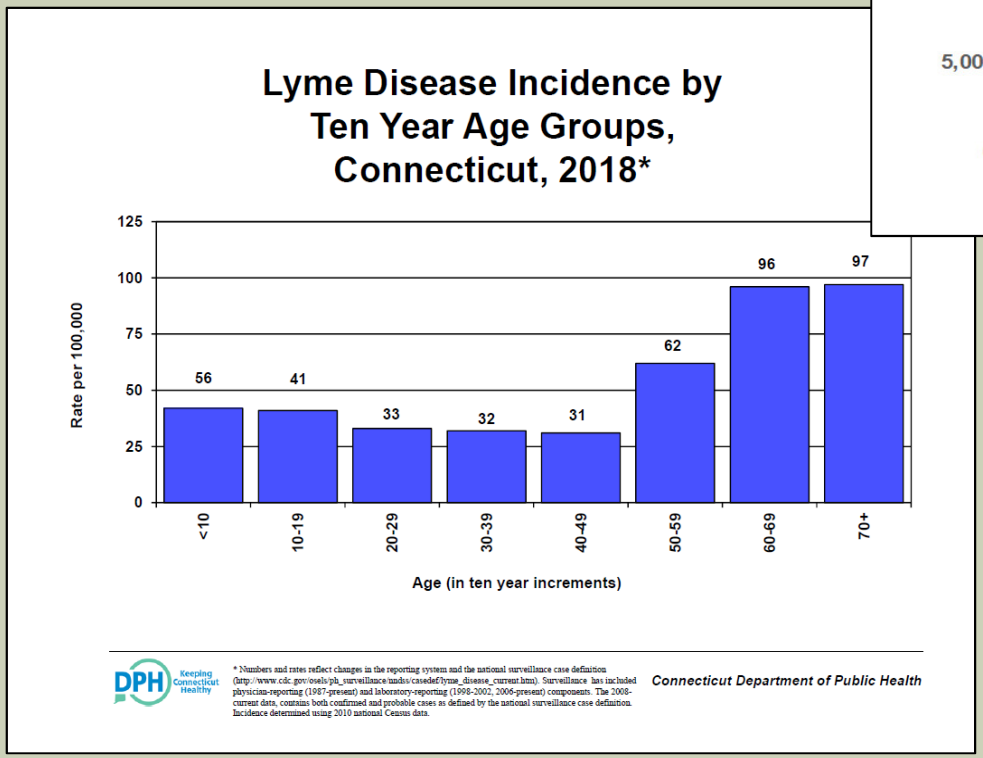
AGE DISTRIBUTION FOR LYME DISEASE



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



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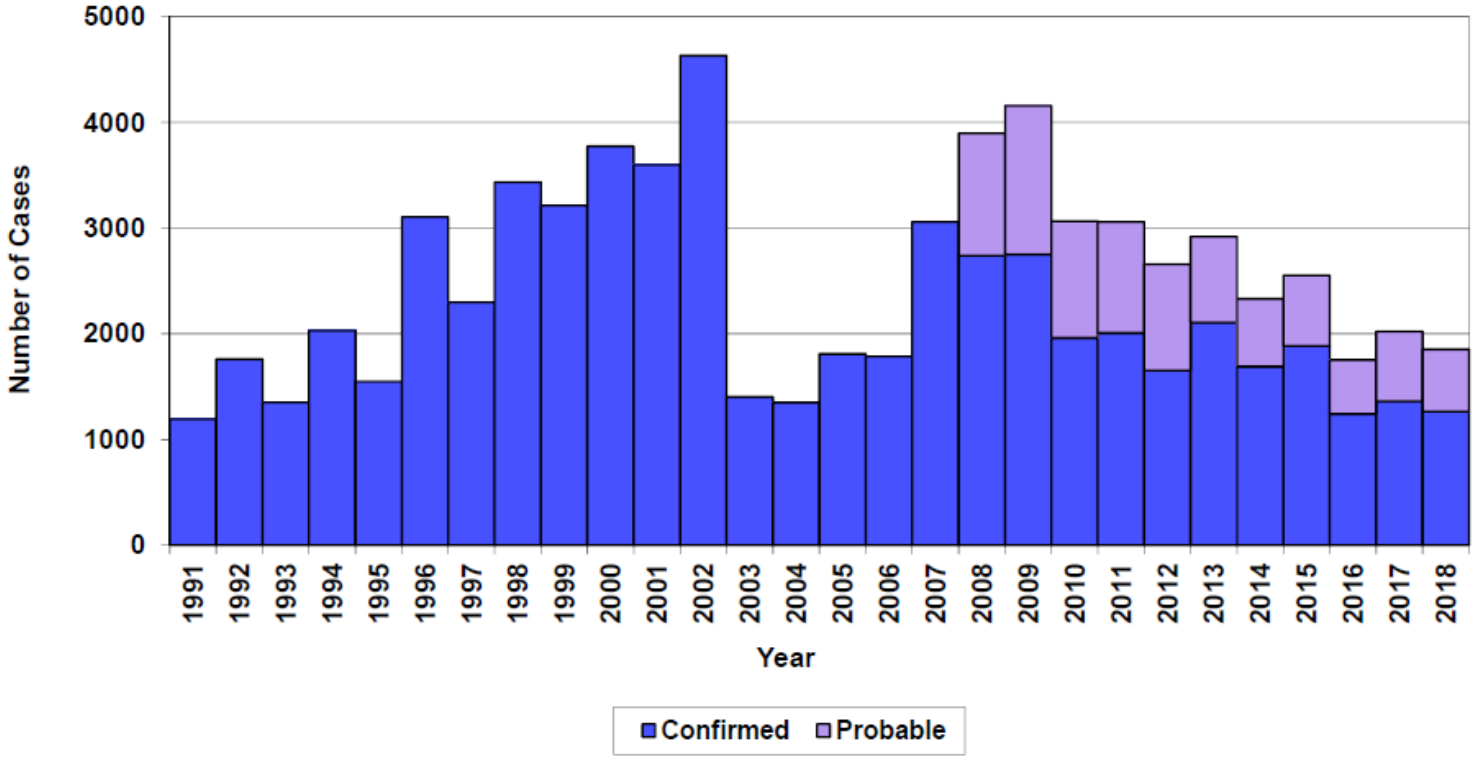
Lyme Disease Cases Statewide by Case Status, Connecticut, 1991 – 2018*



DPH Keeping Connecticut Healthy

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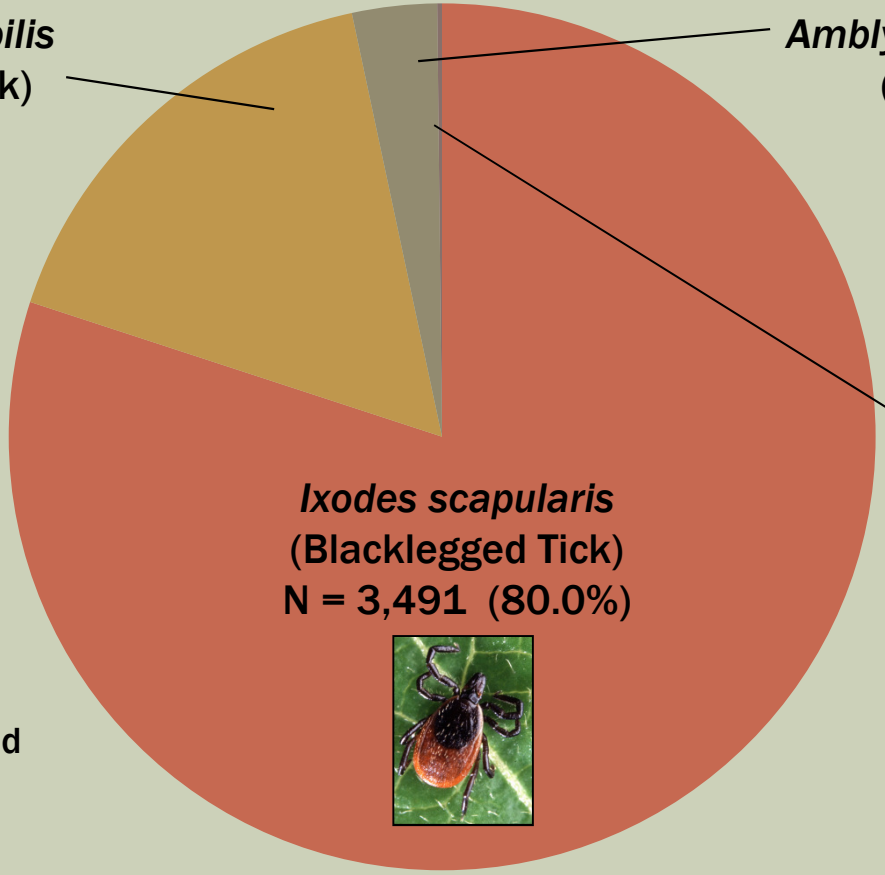
Connecticut Department of Public Health

SPECIES & NUMBER OF TICKS

RECEIVED FOR TESTING 2018



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

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

Ixodes scapularis
(Blacklegged Tick)
N = 3,491 (80.0%)

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

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TICK TESTING RESULTS, 2015-2018

TICK TESTING LABORATORY

Nymph & Adult *Ixodes scapularis*

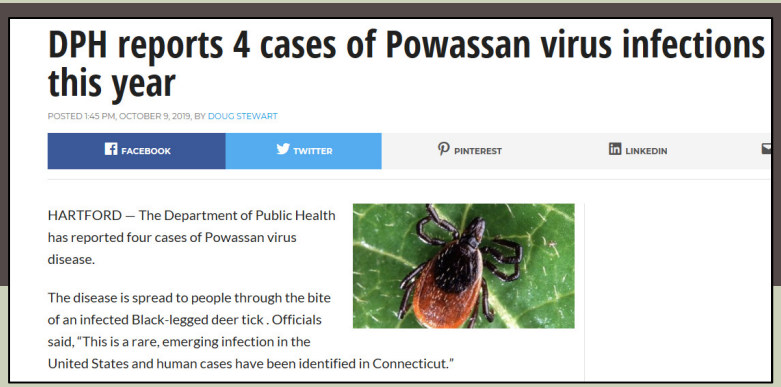
	2015	2016	2017	2018
No. ticks tested	2,503	2,235	4,458	3,273
Uninfected	53.7%	64.7%	40.0%	41.4%
Borrelia burgdorferi	31.5%	28.8%	32.0%	38.3%
Babesia microti	11.0%	7.4%	6.0%	9.5%
Anaplasma phagocytophilum	4.9%	4.6%	7.0%	12.0%
Borrelia + Babesia	4.1%	2.8%	3.1%	5.0%
Borrelia + Anaplasma	1.9%	1.8%	3.7%	6.6%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

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*



DPH reports 4 cases of Powassan virus infections this year

POSTED 1:45 PM, OCTOBER 9, 2019, BY DOUG STEWART

FACEBOOK TWITTER PINTEREST LINKEDIN

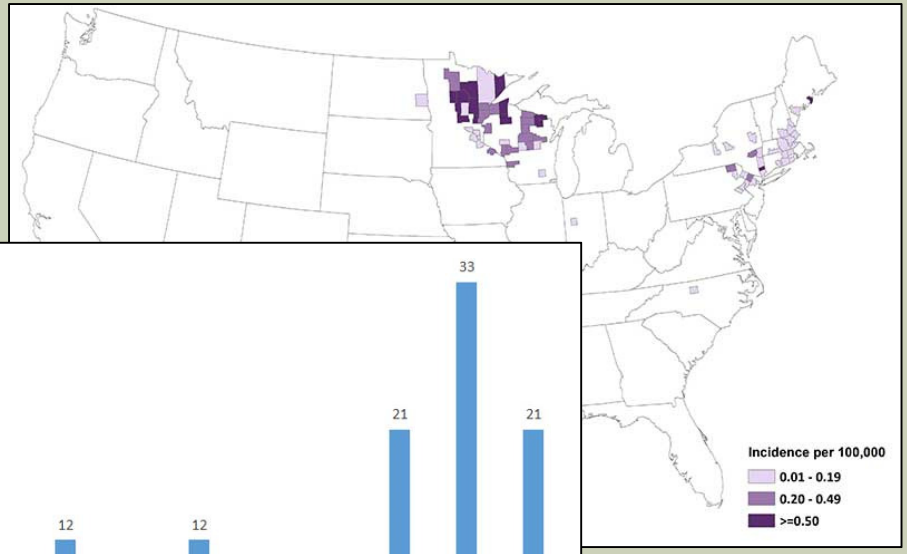
HARTFORD — The Department of Public Health has reported four cases of Powassan virus disease.

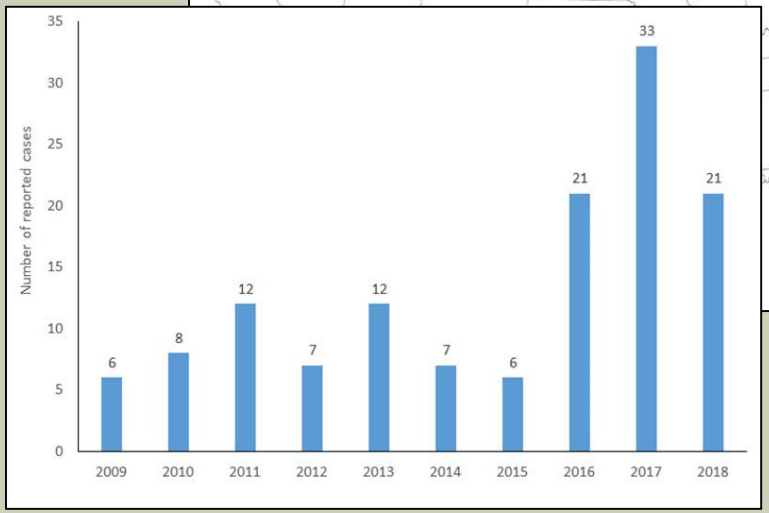
The disease is spread to people through the bite of an infected Black-legged deer tick . Officials said, "This is a rare, emerging infection in the United States and human cases have been identified in Connecticut."

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

Ixodes scapularis
Blacklegged tick

Ixodes cookei
"Woodchuck" tick





Number of cases reported in US 2009-2018

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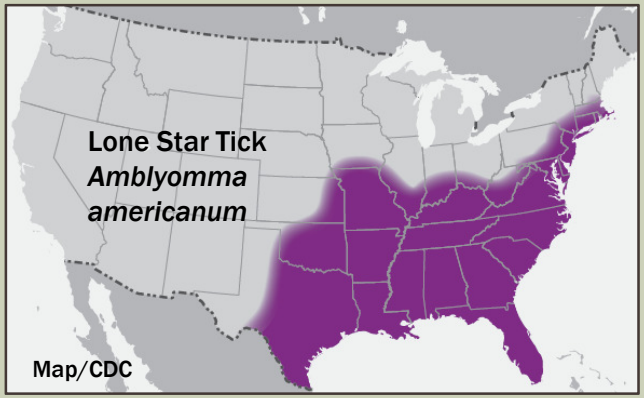
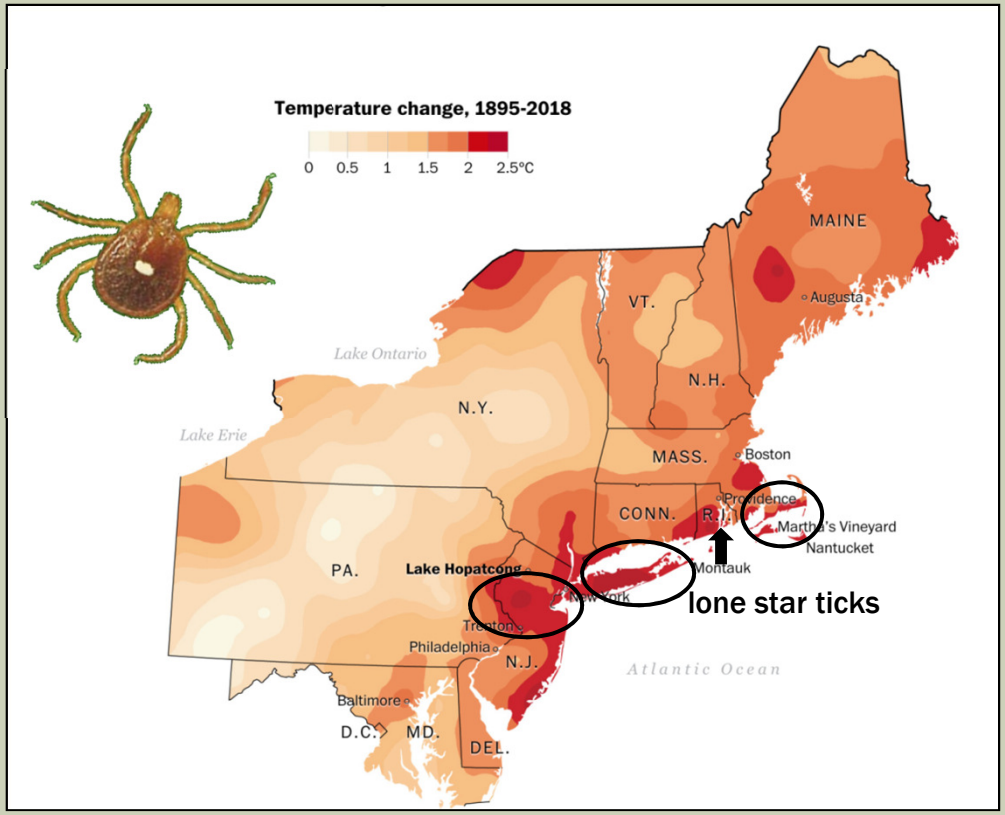
LONE STAR TICK
AMBLYOMMA AMERICANUM



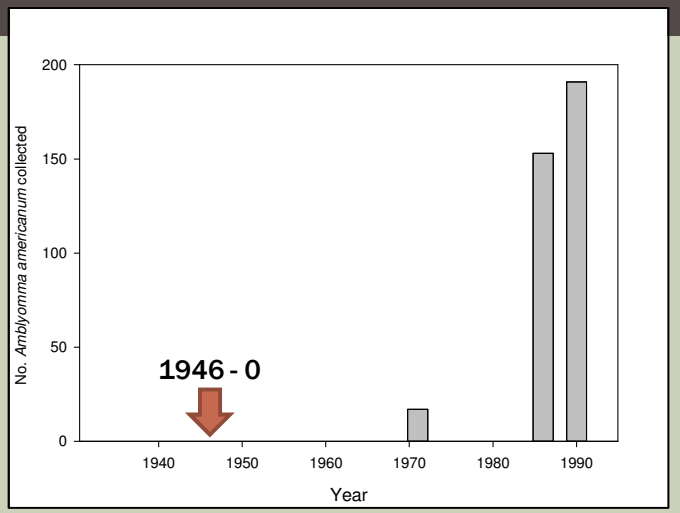
95% tick bites in southeastern U.S.

- Bourbon virus
- Ehrlichiosis
  Ehrichia chaffeensis
  Ehrichia ewingii
  Panola Mountain erhlichia
- 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?



Map from; Steven Mufson, Chris Mooney, Juliet Eilperin, and John Muyskens. 2°C: Beyond the Limit: Extreme climate change has arrived in America. Washington Post, August 13, 2019.



Ginsberg et al. 1991. Increased population densities of *Amblyomma americanum* (Acari: Ixodidae) on Long Island, New York. J. Parasitol. 77(3):493-495

"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"

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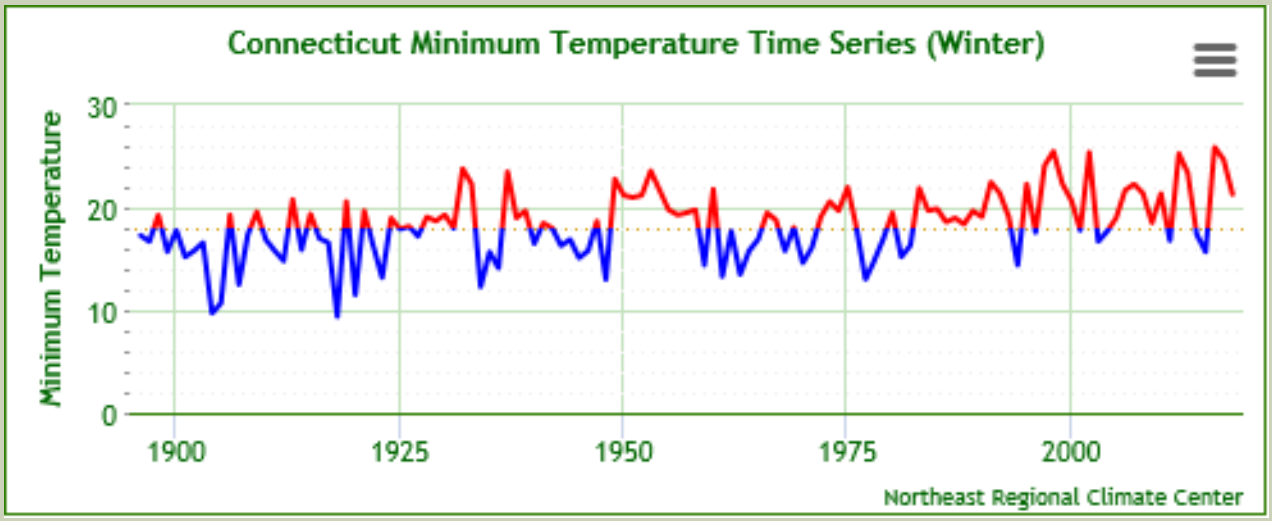
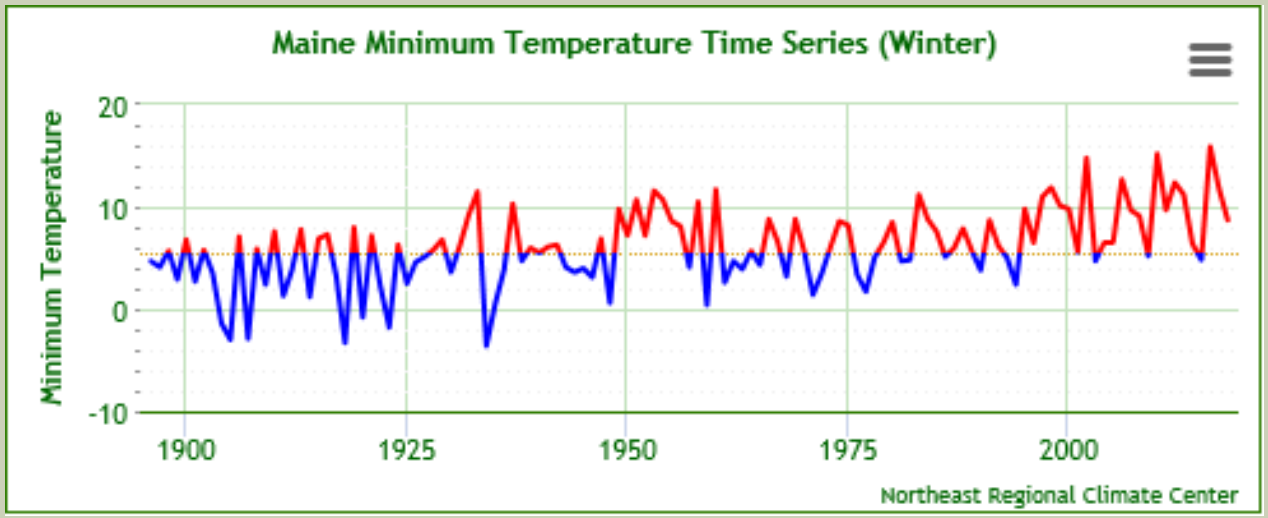
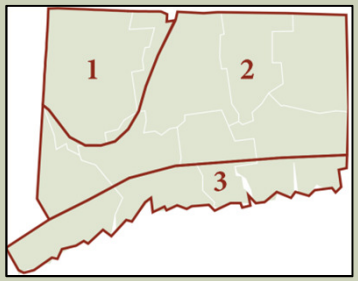
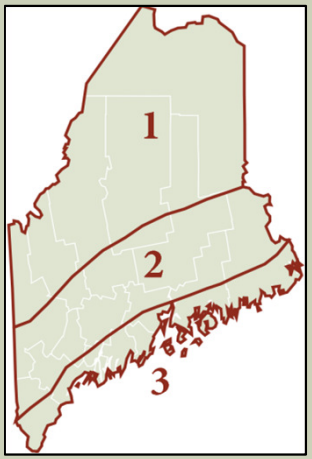
NORTHEAST REGIONAL CLIMATE CENTER



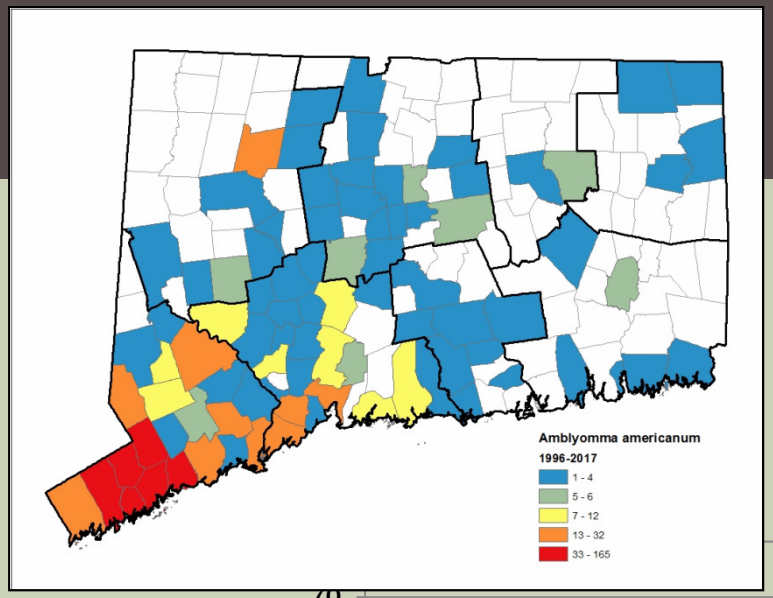


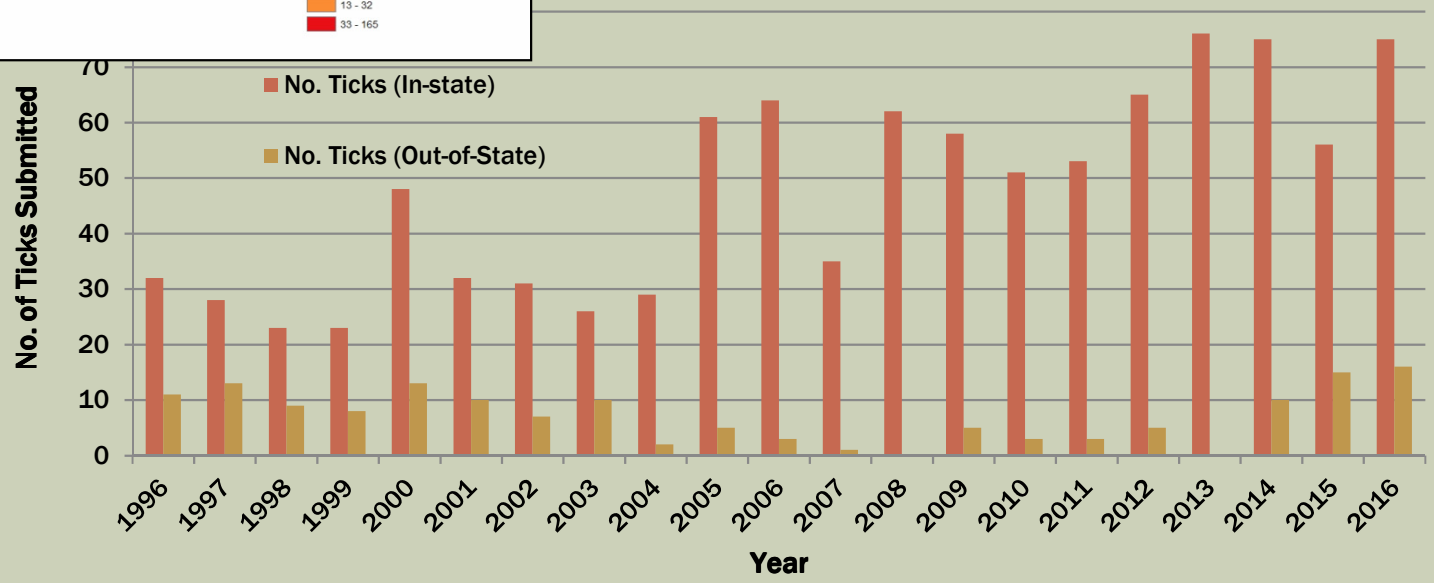
Departures shown are based on the 20th century mean (1901-2000).





SUBMISSIONS TO CAES-TTL, 1996-2017





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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

J. Nivolo/DEEP

K. Stafford/CAES

Active infestation seems limited to that site

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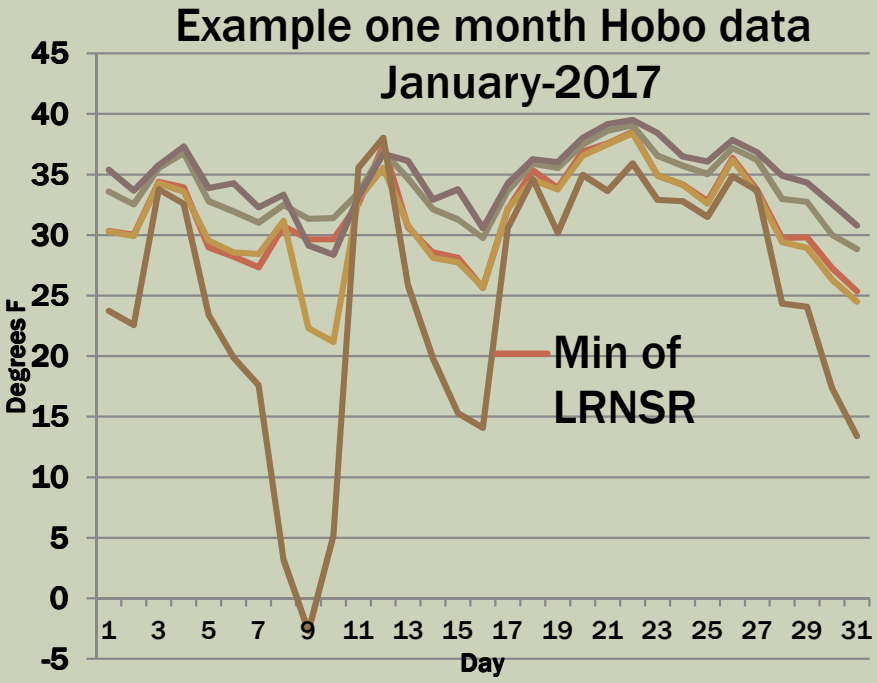
Ticks placed in vials in tick “pots” buried in the ground in randomized block design with Hobo data loggers. Four treatment combinations:

Leaf and snow removal (LRSR)

No leaf removal and snow removal (NLRSR)

Leaf removal and no snow removal (LRNSR)

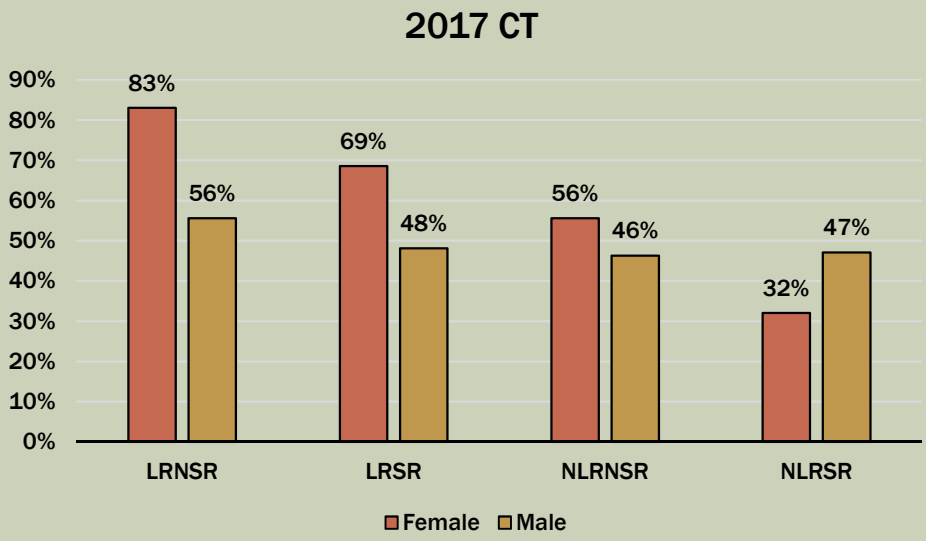
No leaf and no snow removal (NLRNSR)

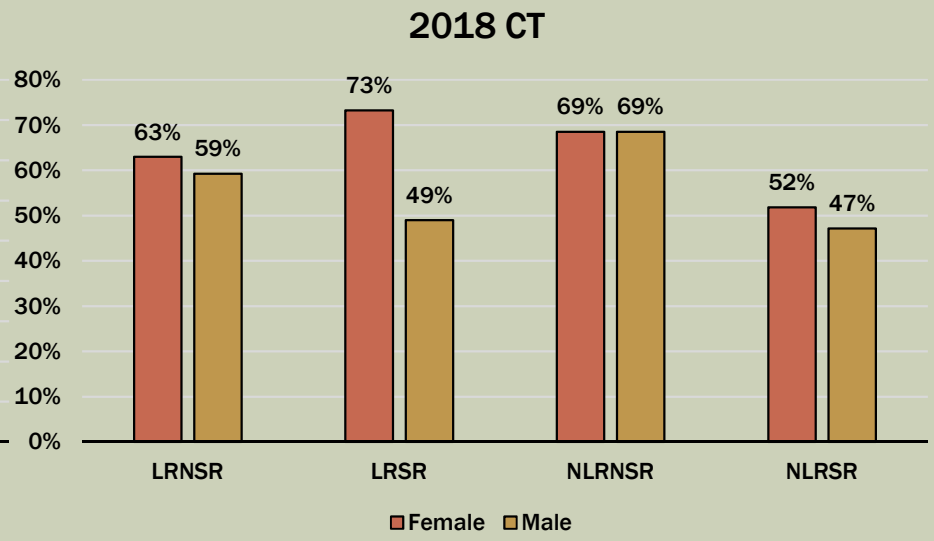


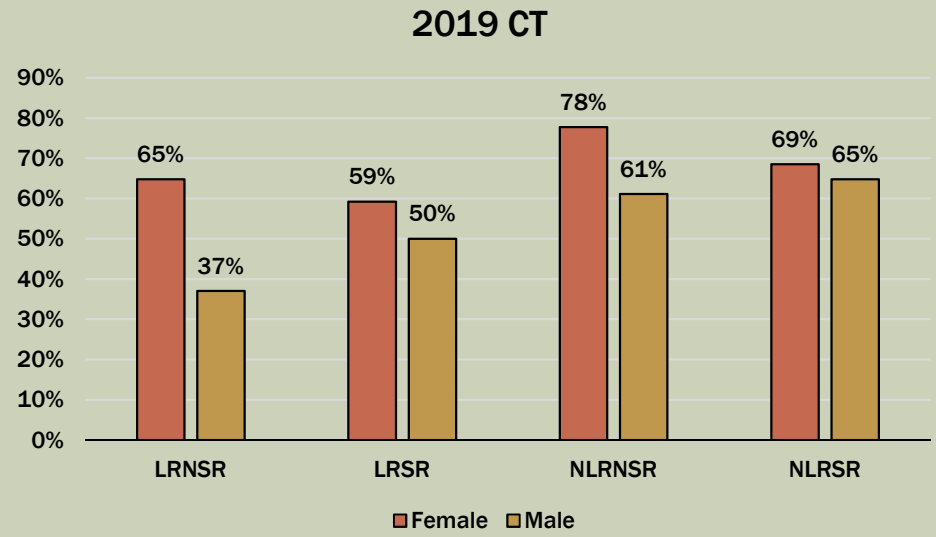
1-9-17

1-13-17

OVERWINTERING SURVIVAL ADULT LONE STAR TICKS - CONNECTICUT







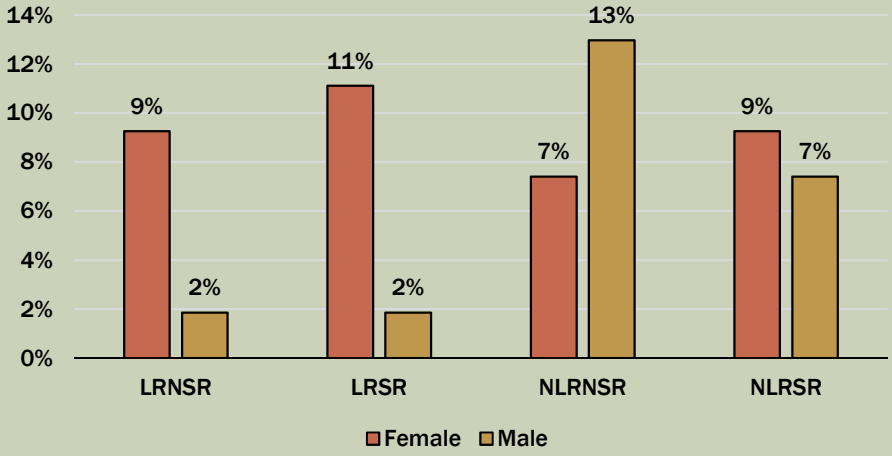
Overwintering survival adult lone star ticks 2016-2017
Connecticut 32-83%

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

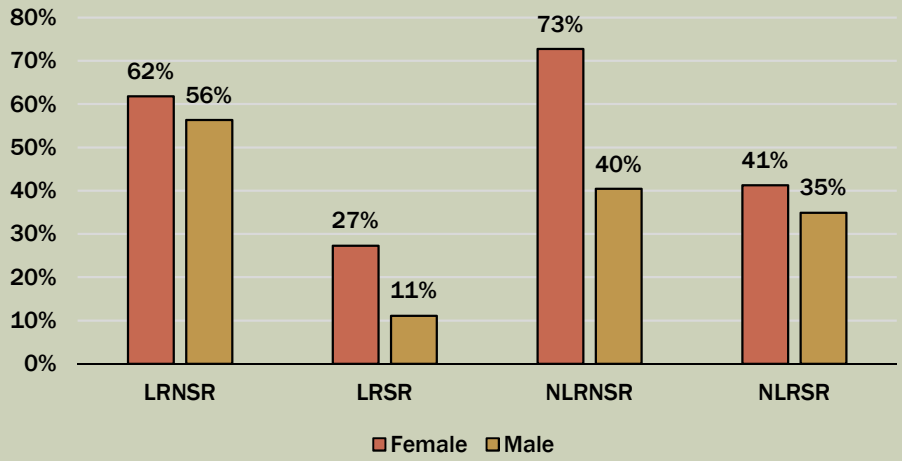
Overwintering survival adult lone star ticks 2018-2019
Connecticut 37-78%

OVERWINTERING SURVIVAL ADULT LONE STAR TICKS - MAINE

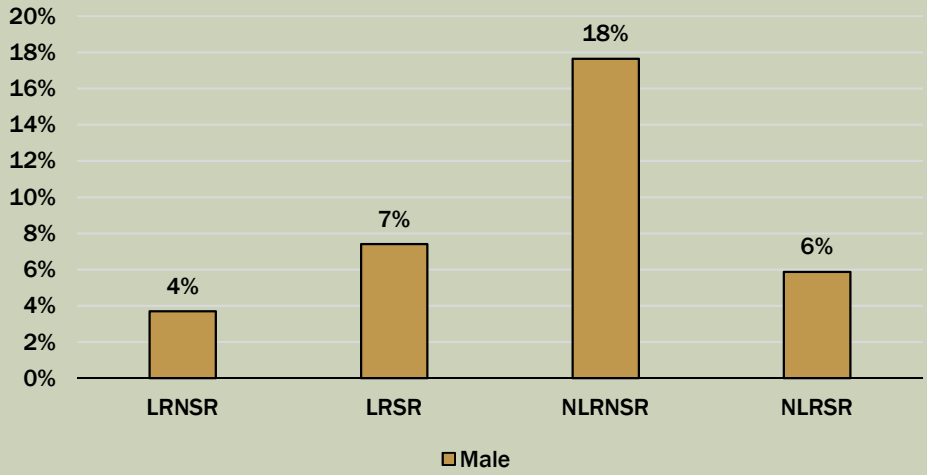
2017 ME



2018 ME



2019 ME (males only)



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)

Asian Longhorned Tick
Haemaphysalis longicornis

Photo credit: Tadhgh Rainey, NJ

James Gathany/Centers for Disease Control and Prevention

THIS PHOTOGRAPH DEPICTS TWO *HAEMAPHYSALIS LONGICORNIS* TICKS, COMMONLY KNOWN AS THE LONGHORNED TICK. THE SMALLER OF THE TWO TICKS ON THE LEFT, IS A NYMPH. THE LARGER TICK IS AN ADULT FEMALE. MALES ARE RARE. THIS TICK CAN REPRODUCE ASEXUALLY.

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

CDC/James Gathany

- 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 equivilants
- Known distribution is expanding as surveillance efforts increase

Source: National *Haemaphysalis longicornis* Situation Report, US Department of Agriculture, September 10, 2019

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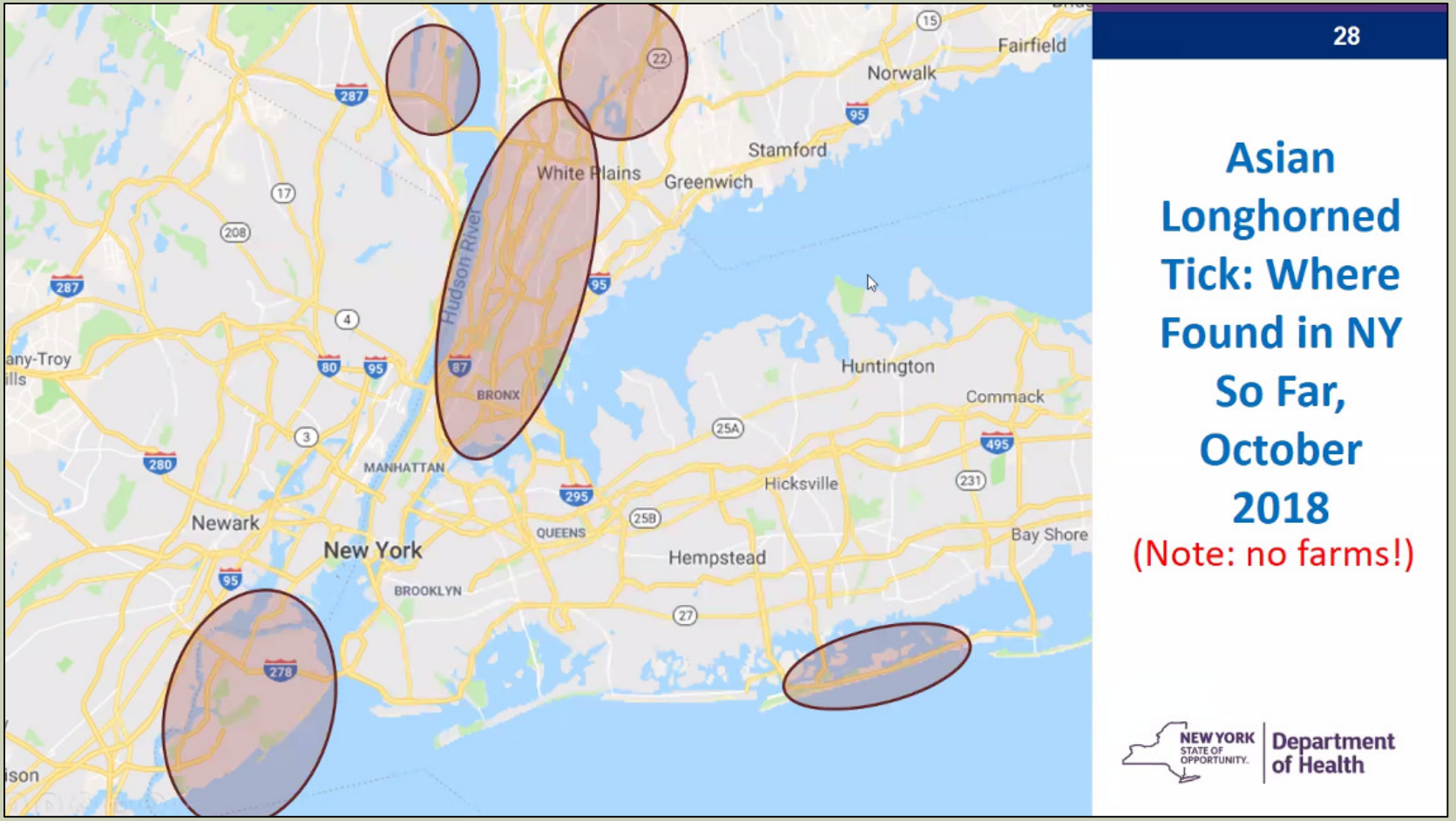


From NEVBD Webinar November 19, 2018 with Dr. Allen C.G. Heath, Dr. Andrea Egizi, and Dr. Richard Falco

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

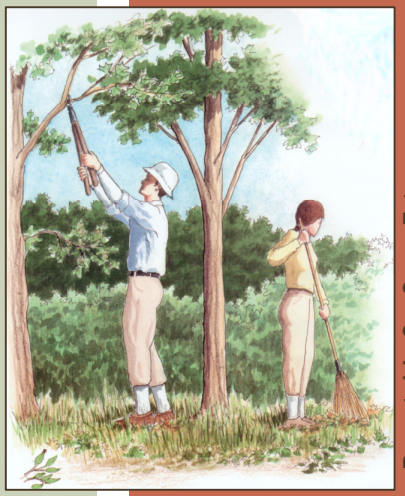
New Haven, CT – The Tick Testing Laboratory at The Connecticut Agricultural Experiment Station (CAES) is reporting the first evidence of human biting by the exotic east Asian longhorned tick, *Haemaphysalis longicornis* in a resident from Fairfield County. The longhorned tick is an invasive species

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 Weisenburger

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LANDSCAPE, INVASIVE PLANTS, AND TICKS

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.

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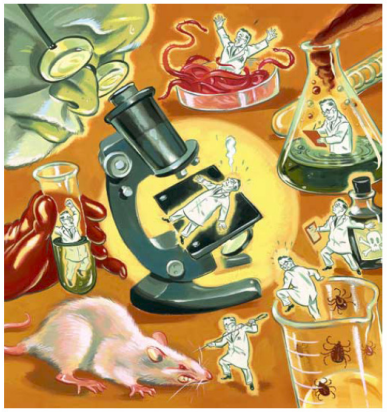
TICK SAMPLING

Worst job in science: Tick collecting



Tick Dragger
Popular Science November 2004

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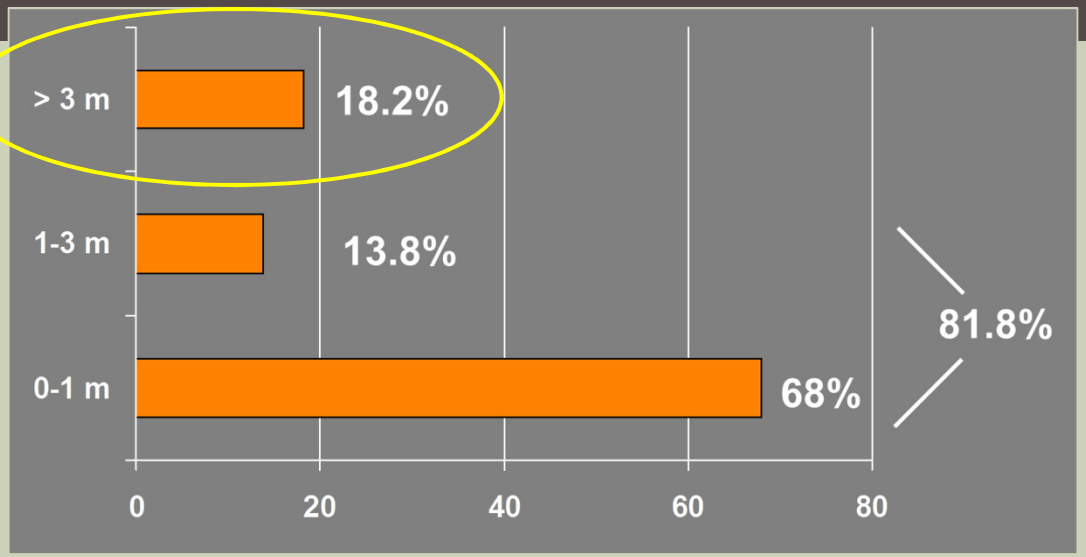
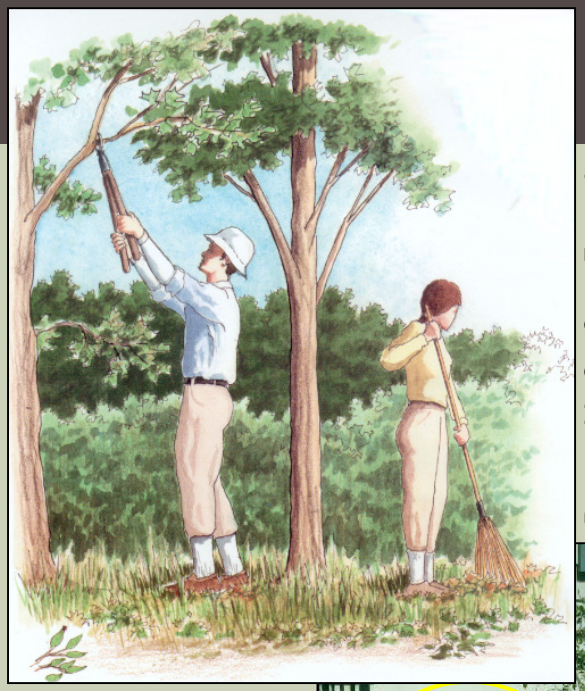
DISTRIBUTION *IXODES SCAPULARIS* ON RESIDENTIAL LAWNS





Barnstable Co. Coop Extension

ALDF

CAES

Stafford. 1993. J. Med. Entomol. 30: 762-771.

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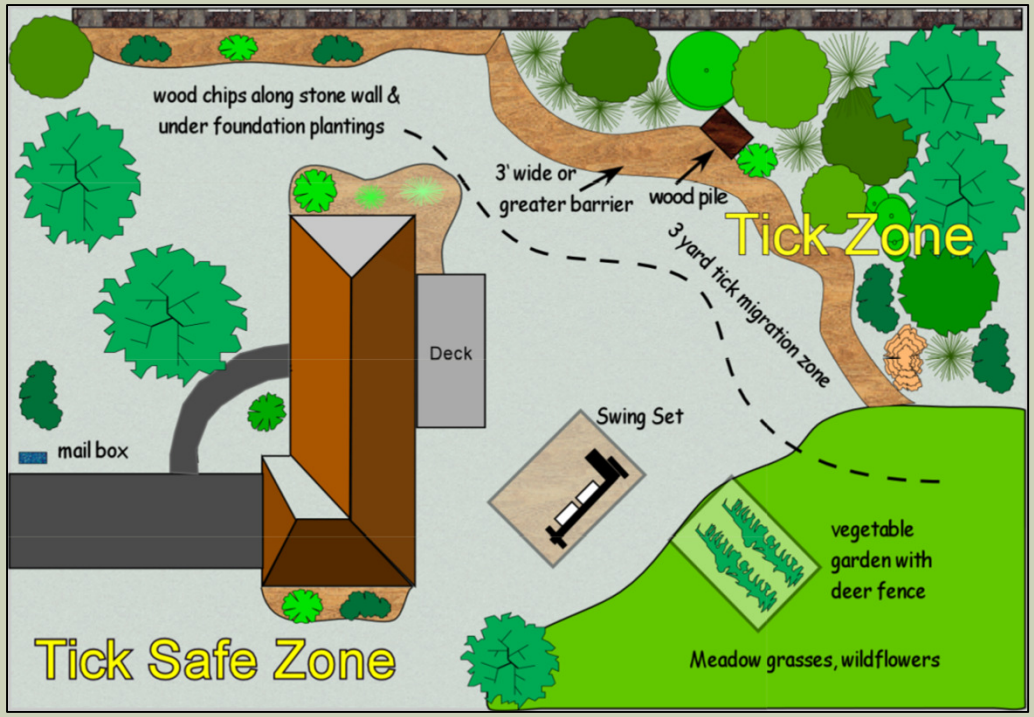
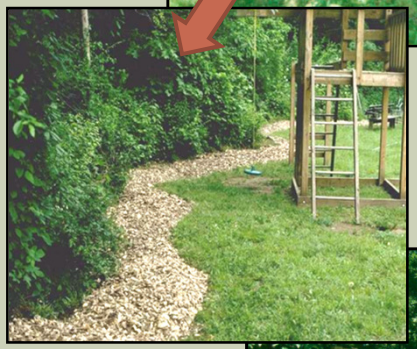
Residential Landscape Management





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INVASIVE PLANTS MAKE GREAT TICK HABITAT

Japanese barberry
Berberis thunbergii

Amur honeysuckle
Lonicera maackii

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

Elias et al. J. Med. Entomol. 2006. 43: 1142-1152
Williams et al. J. Med. Entomol. 2009. 38:977-984
Williams et al. Environ. Entomol. 2010. 39:1911-1921.
Williams et al. Environ. Entomol. 2017. 48:1329-1338.

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

Allan, B. F. et al. 2010. Proc. Nat. Acad. Sci. 107: 18523-18527.

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SPRAYING

Photographs: Kirby Stafford

Carbamate

Pyrethroids

Biopesticides

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

% REDUCTION *IXODES SCAPULARIS* NYMPHS APPLICATION ACARICIDES TO THE ENVIRONMENT

	Acaricide	Application	reduction nymphs*	Time evaluation
Pyrethroids	Bifenthrin	Spray	45-100%	1-6 wks
	Cyfluthrin	Spray	88-100%	2-8 wks
	Cyfluthrin	Granules	87-97%	1-8 wks
	Deltamethrin	Granules	87-100%	1-5 wks
Carbamate	Carbaryl	Spray	43-93%	2-13 wks
	Carbaryl	Granules	46-96%	1 wk-3 mo
25b products	Rosemary, etc.*	Spray (low, 2x) (IC2)	73-95%	1-5 wks
	Rosemary, etc.*	Spray (high) (IC2)	100%	1-2 wks
	Garlic	Mosquito Barrier	37-59% repellency	1-2 wks
	Pyrethrum, thyme oil, etc.**	EcoPCO	99.6% KD 72% residual	NA
	Cedar oil**	Cedarcide & Tick Kills	5.0-5.9% KD	0-8.5% residual
	Cedar oil ***	Cedar Safe	31-40%	2 wks

Eisen, L. and M. C. Dolan. 2016. J. Med. Entomol. 53(3): 1063-1092. *Rosemary, peppermint, wintergreen; **T. Mather (unpublished data), ***Moses Curcura, Suffolk Co. Div. Vector Control

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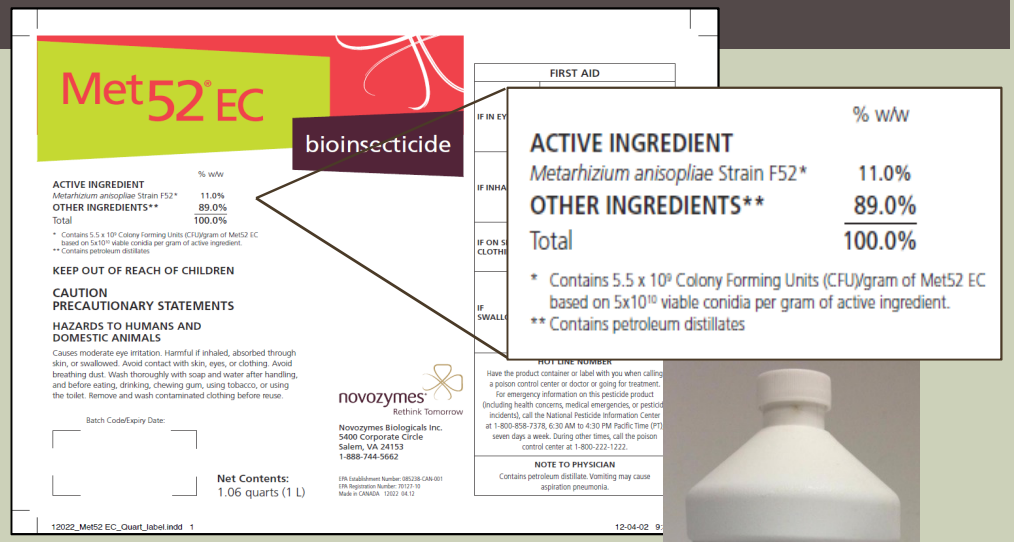
MET52® EC BIOINSECTICIDE

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



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

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

balEnce™ biopesticide control of flies, *Beauveria bassiana* (Terregena Inc.)

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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.**

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Photo by Kirby Stafford

Photo by Skip Weisenburger, The Day

HOST-TARGETED TICK CONTROL

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Rodent Reservoirs

White-footed Mice

Eastern Chipmunk

Treatment

Entry Points

Non-Toxic
Food blocks

Wick with 3 mls
Fipronil 0.7%

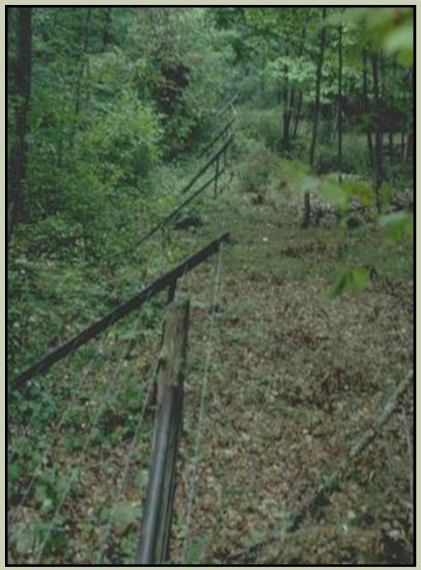
80-84%

20-30%

RTV - Vaccine

White-tailed Deer

1. Exclusion
2. Reduction
3. Treatment



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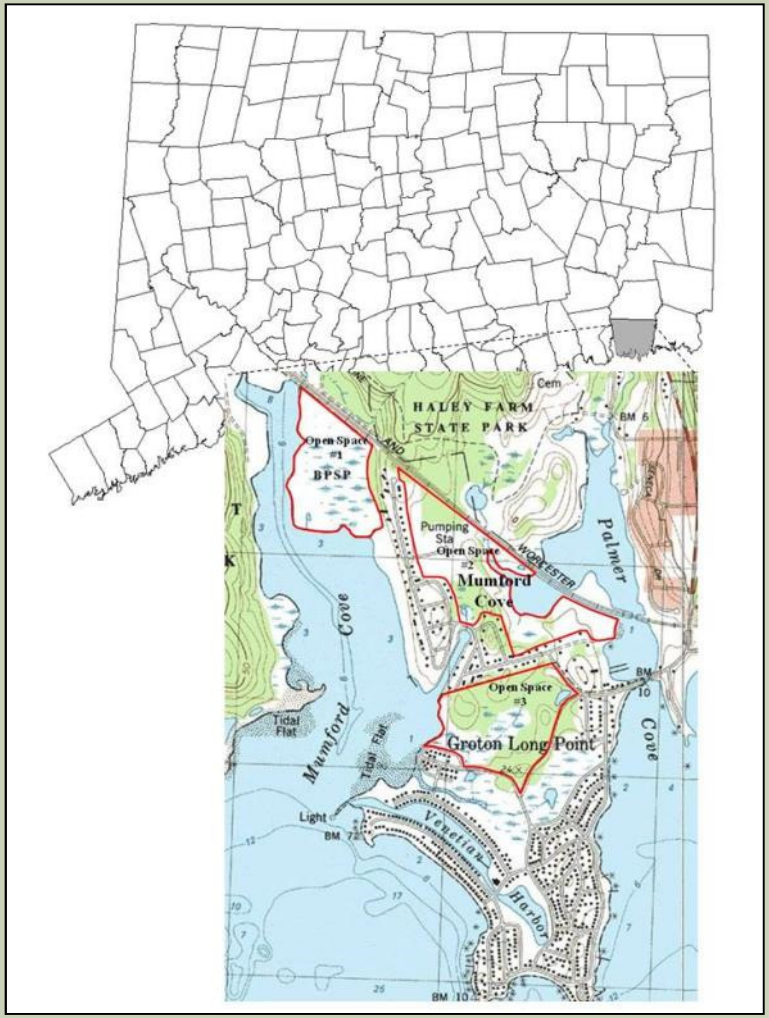
SECTION

The Relationship Between Deer Density, Tick Abundance, and Human Cases of Lyme Disease in a Residential Community

HOWARD J. KILPATRICK,[1,2] ANDREW M. LABONTE,[1] AND KIRBY C. STAFFORD III[1,3]

DEER REDUCTION MUMFORD COVE, CT



Kilpatrick, H. J., A. M. LaBonte, and K. C. Stafford III. 2014. The relationship between deer density, tick abundance, and human cases of Lyme disease in a residential community. J. Med. Entomol. 51: 777-784.

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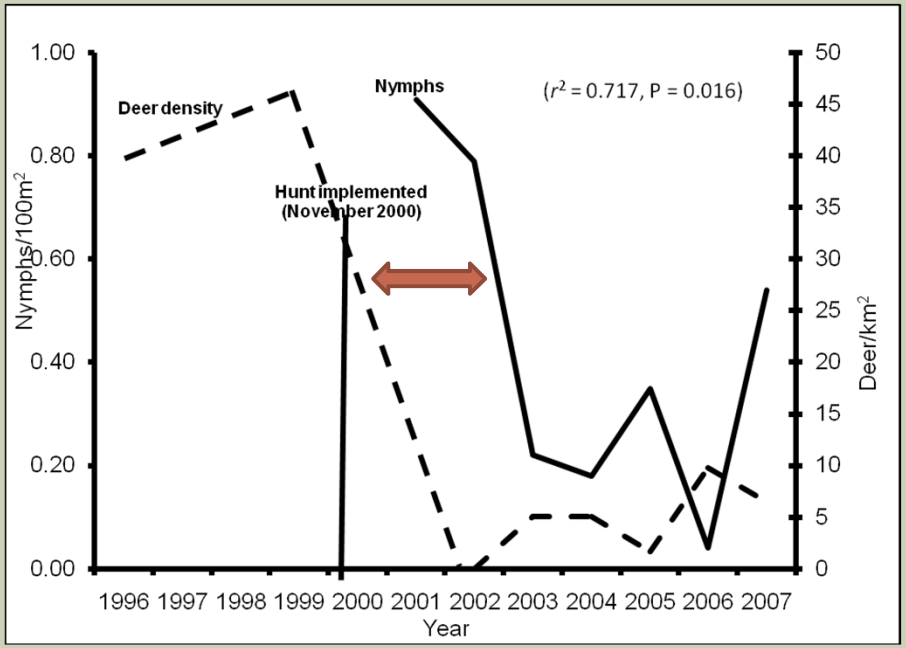
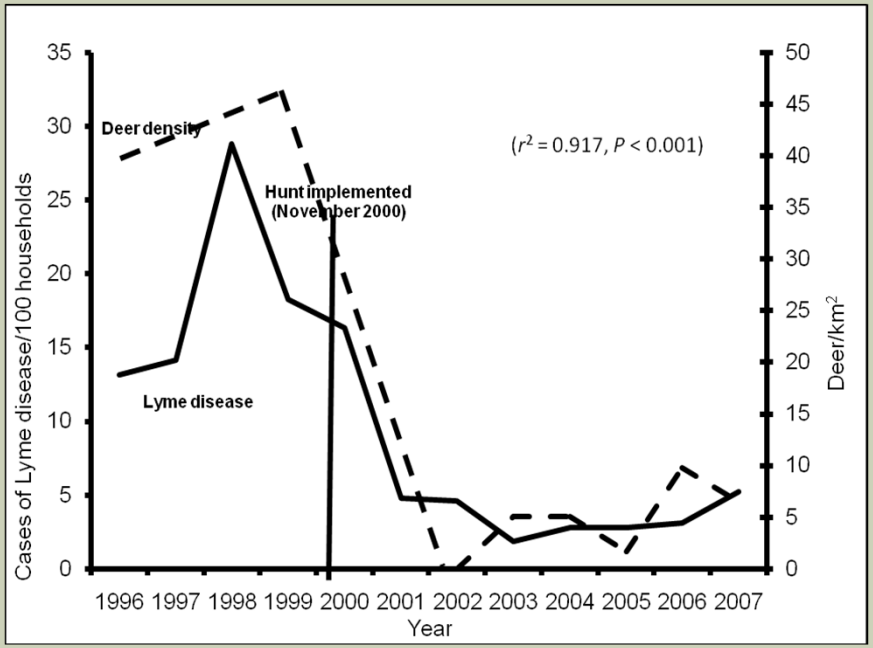
REPORTED CASES OF LYME DISEASE, NYMPHAL TICK DENSITIES, AND DEER DENSITIES IN THE MUMFORD COVE COMMUNITY IN GROTON CONNECTICUT, 1996-2007





- Deer reduced 40-54/km^2 to 0-9/km^2 (ca. 122 to 13.2 deer/mi^2) (≥ 87%)
- 76% reduction in tick abundance
- 80% reduction in resident-reported cases of Lyme disease
- Densities of 5.1 deer/km^2 (13/mi^2) significantly reduced the number of infected ticks and human risk of contracting Lyme disease

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INTEGRATED TICK MANAGEMENT (ITM)

Journal of Integrated Pest Management

Journal of Integrated Pest Management, (2017) 8(1): 28; 1–7
doi: 10.1093/jipm/pmx018
Issue

OXFORD

Integrated Pest Management in Controlling Ticks and Tick-Associated Diseases

Kirby C. Stafford III,[1,3] Scott C. Williams,[1] and Goudarz Molaei[1,2]

Open Access

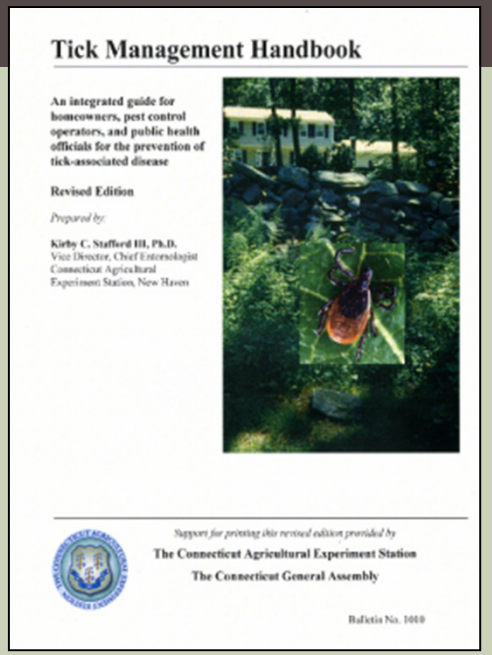
Journal of Integrated Pest Management, (2018 9(1): 12; 1–10
doi: 10.1093/jipm/pmy006
Issues

OXFORD

Review: Application of Tick Control Technologies for Blacklegged, Lone Star, and American Dog Ticks

Alexis White[1] and Holly Gaff[1,2,3]

Open Access



https://portal.ct.gov/CAES

JIPM Collection on Integrated Tick Management
https://academic.oup.com/jipm/pages/integrated_tick_management

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INTEGRATED TICK MGMT – CT (2013-2015)

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,[1] Kirby C. Stafford, III,[1] Goudarz Molaei,[1,2] and Megan A. Linske[1]

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

Original article

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

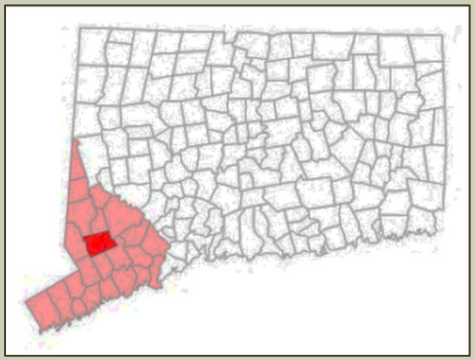
Scott C. Williams[a,*], Eliza A.H. Little[a], Kirby C. Stafford III[a], Goudarz Molaei[a,b], Megan A. Linske[a]

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

Four 1-mi^2 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)

K. Stafford



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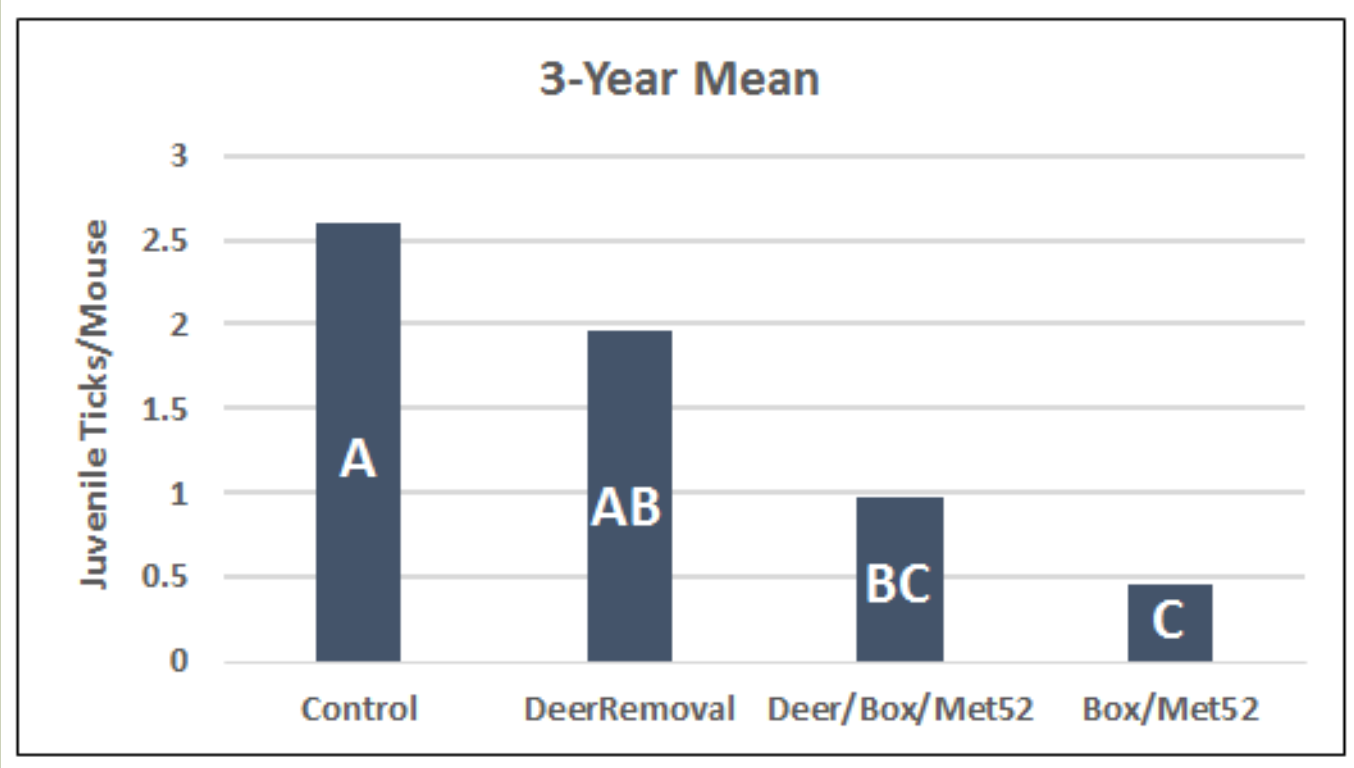
JUVENILE *SCAPULARIS* PARASITIZING CAPTURED *P. LEUCOPUS*

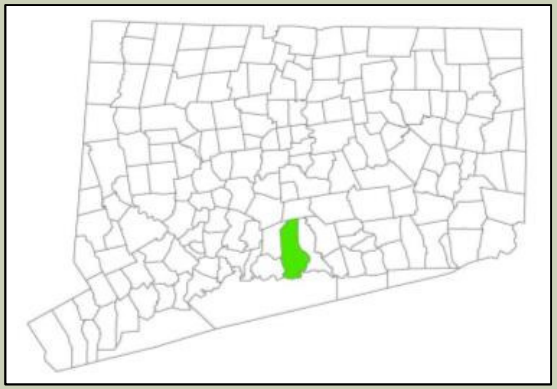


The combination of fipronil-based bait boxes and broadcast application of *M. anisopliae* had the most impact of any treatment combination; questing nymphs were reduced 78–95% within each year and *Borrelia burgdorferi*-infected questing nymphal *I. scapularis* encounter potential was reduced by 66% as compared with no treatment in the third year of the study.

USDA-ARS/CAES ITM (MD & CT)

SUPPRESSION OF VECTOR TICK POPULATIONS IN SUBURBAN LANDSCAPE THROUGH INTEGRATED USE OF HOST-TARGETED AND NON-HOST TARGETED TICK CONTROL MEASURES

Scott Williams, Megan Linske, Kirby Stafford with Michael Short and Heidi Stuber



Neighborhood	4-poster	Bait Box	Met52	No. 4-poster locations	No. tick sampling properties	No. rodent sampling properties
1	No	Yes	Yes	-	10	9
2	Yes	Yes	No	3	12	9
3	Yes	Yes	Yes	3	12	9
4	Yes	Yes	No	3	10	9
5	No	No	No	-	13	9
6	Yes	Yes	Yes	3	13	9
7	No	Yes	Yes	-	13	9
Total					83	63

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

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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 SE
World Trade Center Lyon
Tour Oxygène
10-12 boulevard Marius Vivier Merle
69007 Lyon, *France*

Human Lyme Disease Vaccine

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

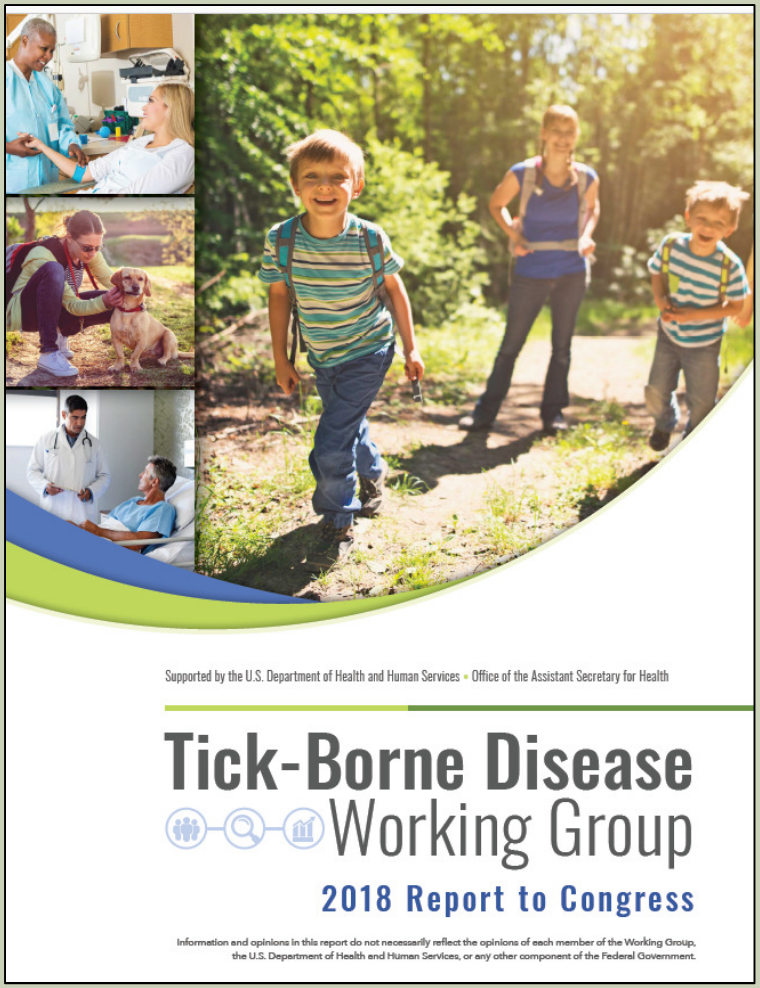
Encouraging immunogenicity with VLA15

- 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.

Source: http://www.valneva.com/en/investors-media/news

TICK-BORNE DISEASE WORKING GROUP



- 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.

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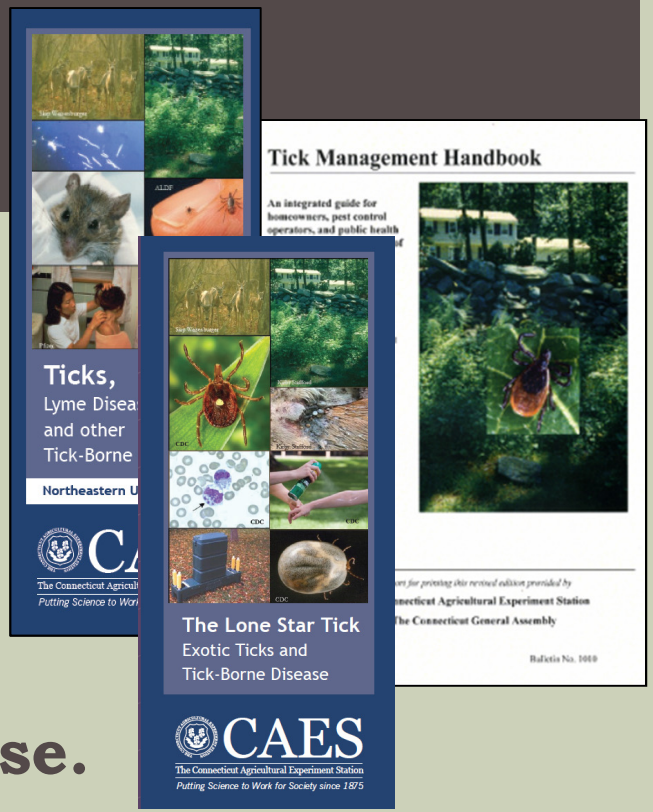
TICKS!



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

Kirby C. Stafford III, Ph.D.
CT Agricultural Experiment Station
123 Huntington Street-Box 1106, New Haven, CT 06504
Ph: (203) 974-8485; Email: Kirby.Stafford@ct.gov