



Targeting Lyme Disease and other tick borne diseases in dogs: research update

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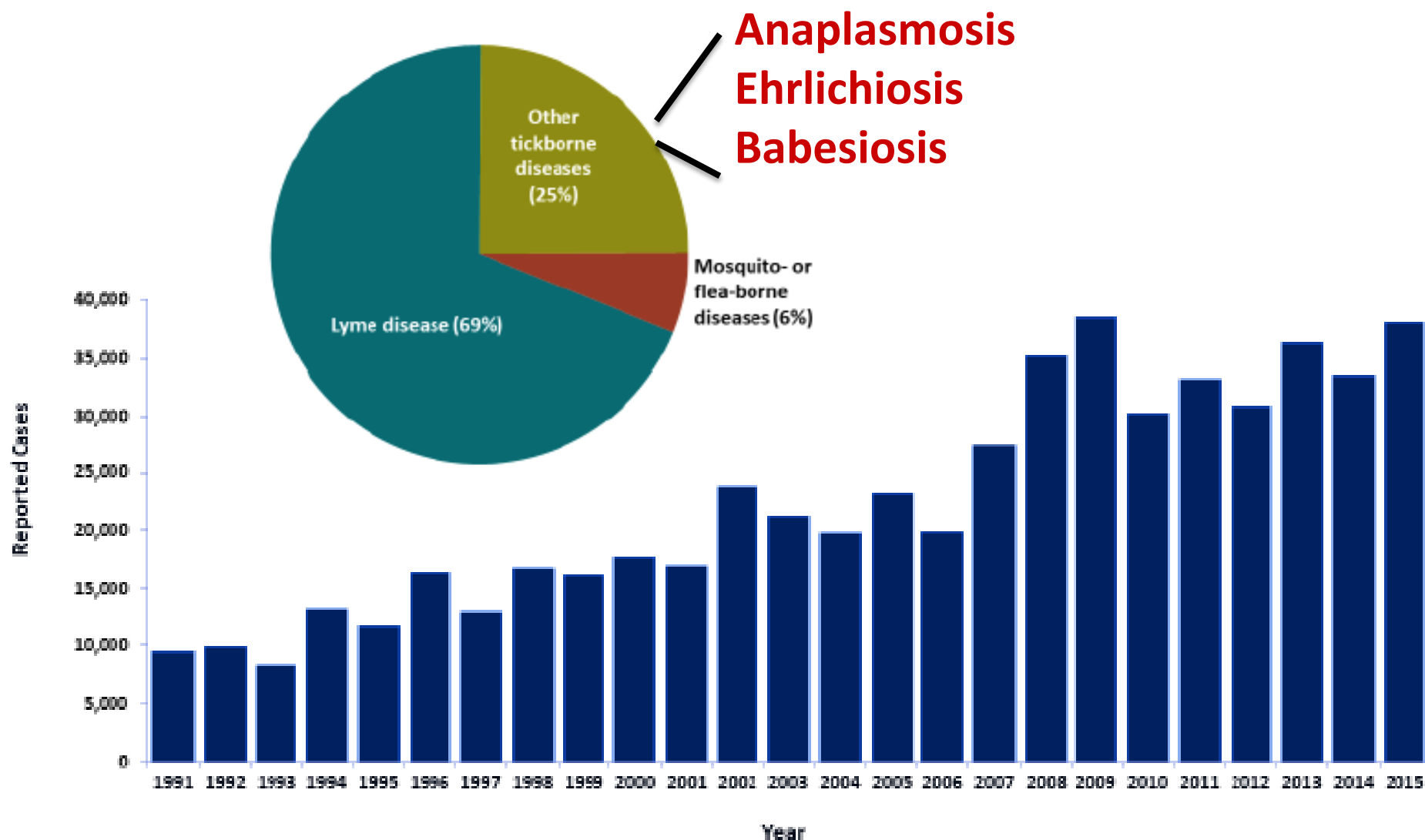
ESSFTA Meeting, April 26th

University of Iowa

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LYME DISEASE MOST COMMON VECTOR-BORNE DISEASE IN U.S. PEOPLE



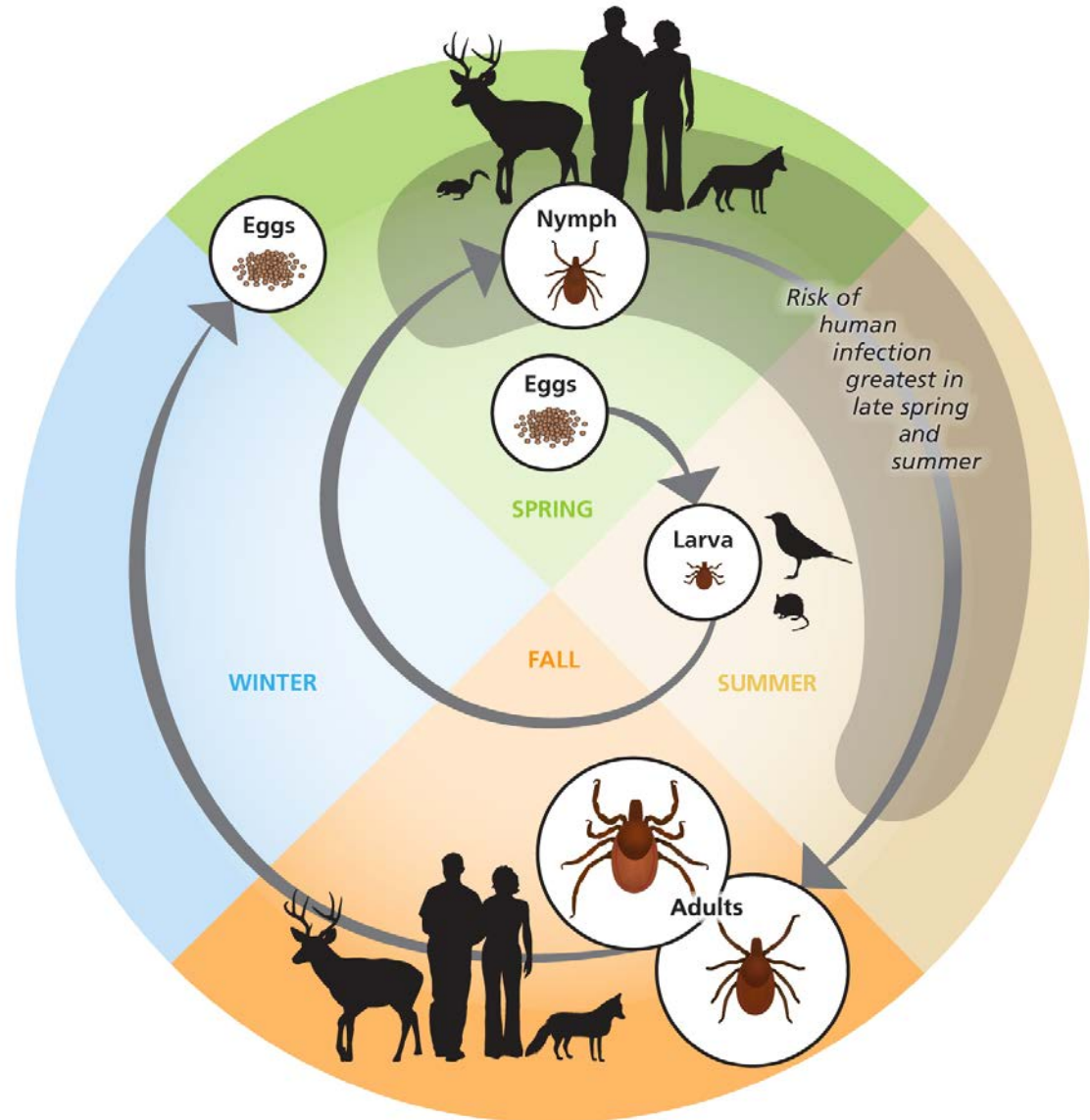


LYME DISEASE LIFE CYCLE

Nymphs primarily transmit to people

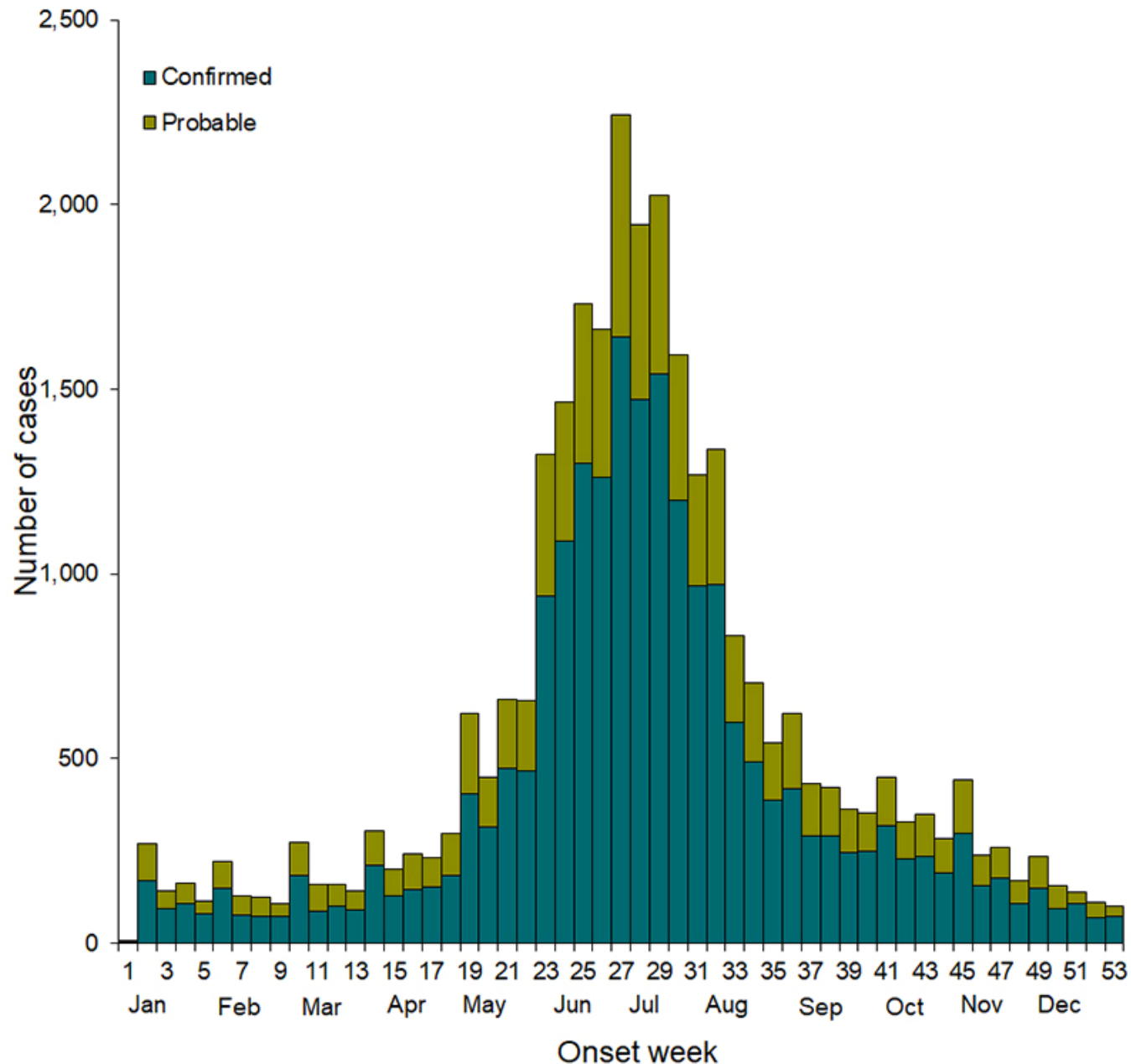


BLACKLEGGED TICK
Ixodes scapularis



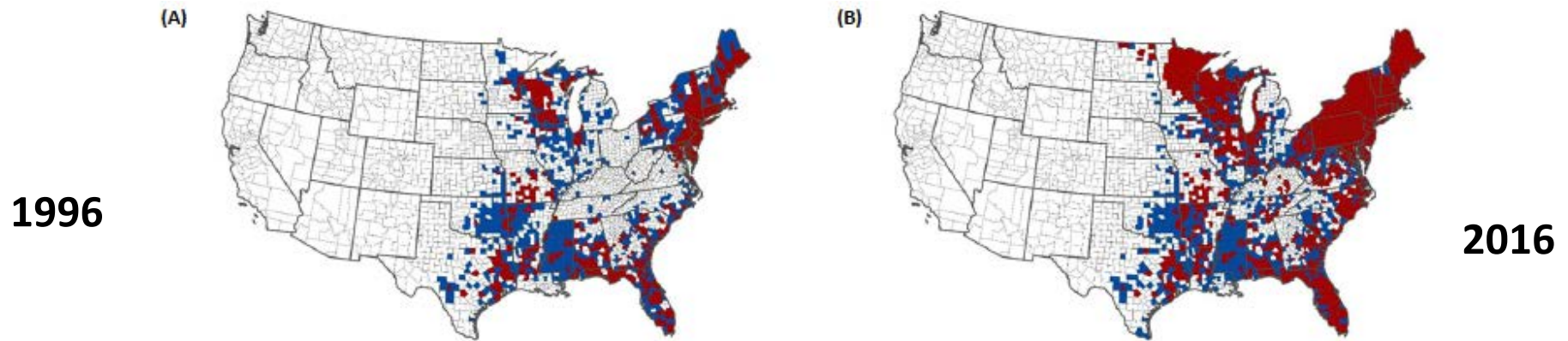


TIMING OF LYME DISEASE IN THE YEAR

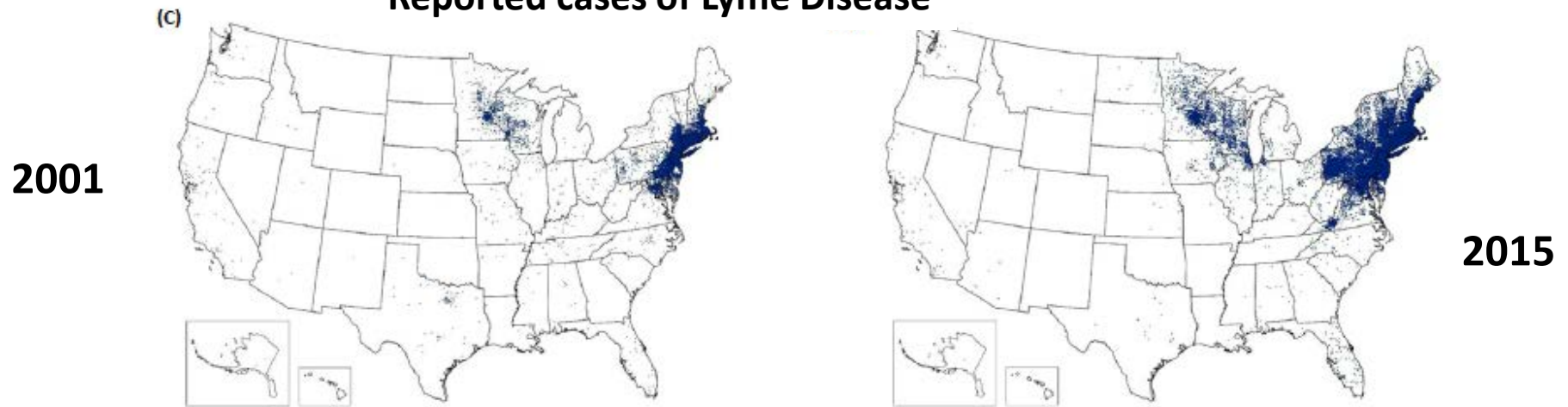


LYME DISEASE EXPANDING IN U.S.

Reported Distribution of Blacklegged Tick



Reported cases of Lyme Disease



Trends in Parasitology

LYME DISEASE

Borrelia burgdorferi bacteria

Clinical Manifestations

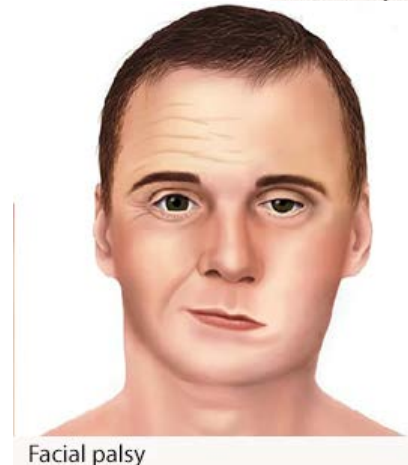
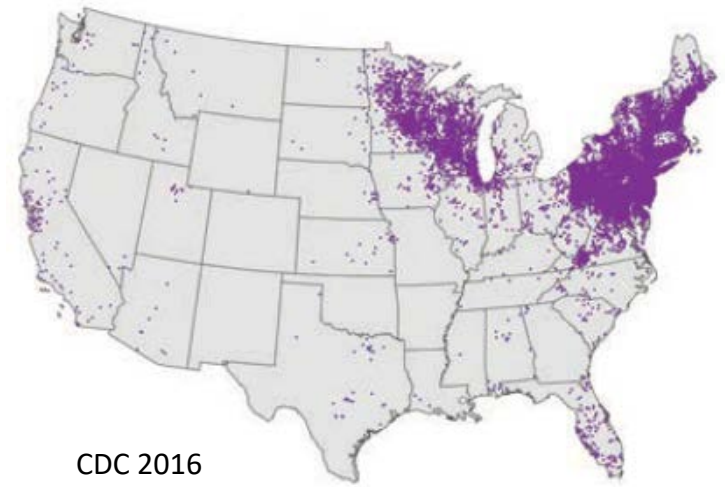
- 3-30 days post tick bite
 - *Erythema migrans* rash (70-80% of patients)
- days-months post tick bite
 - Facial paralysis
 - Asymmetric arthritis/joint swelling
 - Blockage of heart muscle
 - Nervous system effects

Transmission

- Blacklegged aka Deer tick

Risk Factors

- Owning pets increases owner tick exposure
- Co-infection with *Anaplasma* or *Babesia* can present with more severe symptoms



OTHER COMMON TICK-BORNE INFECTIONS

ANAPLASMOSIS – *Anaplasma* bacteria

- Can cause anemia
- Transmission: Blacklegged tick aka Deer tick, blood transfusion
- Risk Factors: age, immunosuppression, delayed diagnosis and treatment



EHRLICHIOSIS – *Ehrlichia* bacteria

- Can cause fatal anemia
- Transmission: Lone Star tick, Blacklegged tick aka Deer tick, blood transfusion
- Risk Factors: age <10 or ≥70 years, immunosuppression



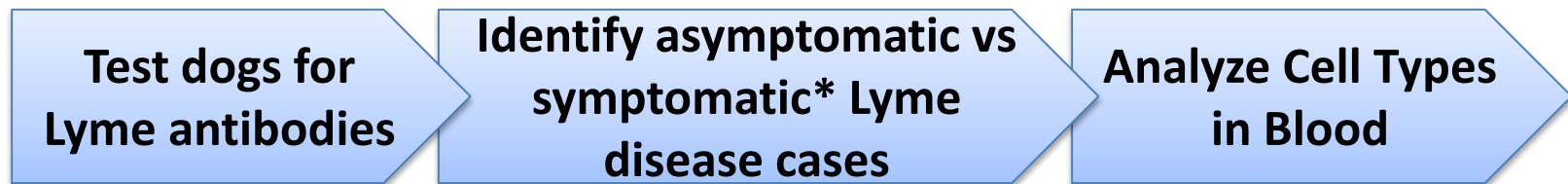
BABESIOSIS – *Babesia* parasites

- Human infection ranges from asymptomatic to severe anemia
- Transmission: Blacklegged tick aka Deer tick, blood transfusion, rare cases of congenital transmission
- Risk Factors: Immunosuppression, Advanced age



RESEARCH STUDY: *“Cellular mechanisms of inflammation during canine tick-borne diseases”*

- Immune responses and disease outcomes are very similar in people and dogs, studying canine disease can also teach us about human disease.
- Study Research Question: What immune cell types are increased during asymptomatic vs. symptomatic vs. treated Lyme Disease in canines?
- Ultimate Goal: Identify molecules produced by these cells that can be targeted by drugs to alter the course of tick-borne disease in dogs.

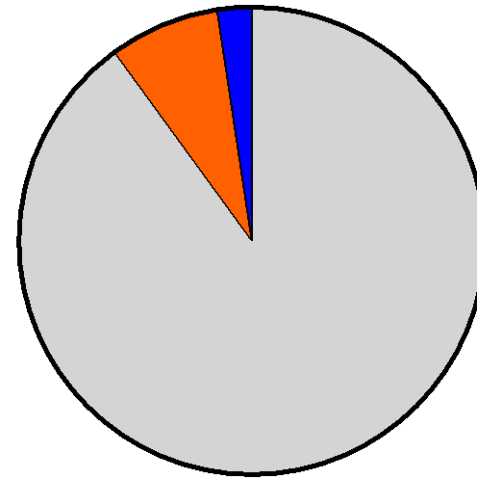


*Symptomatic Lyme disease cases were administered Doxycycline and blood drawn when possible




10% of FIELD TRIAL SPRINGER SPANIELS EXPOSED TO TICK-BORNE INFECTIONS



**% Field Trial English Springer Spaniels
positive for tick-borne infection
(2018 results)**



Total=209

-  89.95% Negative for tick-borne diseases
-  7.66% Positive for 1 tick-borne infection
-  2.39% Positive for 2 or more tick-borne infections

LYME AND ANAPLASMA MOST COMMON TICK DISEASE EXPOSURES IN SPRINGER SPANIELS

Field Trial English Springer Spaniels exposed to
Borrelia, *Anaplasma*, or *Ehrlichia*
(2018 results)

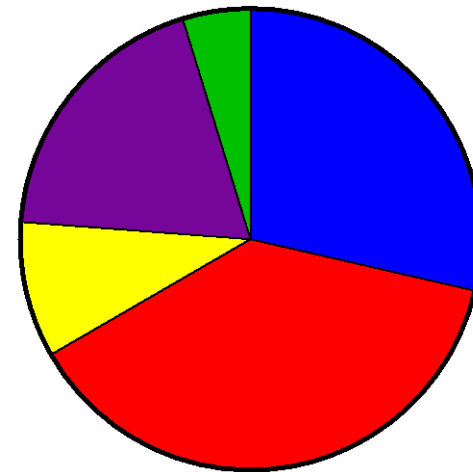
Lyme Disease exposure across the US:

- pet dogs: 5.0%,
- Springer Spaniels: 5.3%

Anaplasma exposure across the US:

- pet dogs: 5.7%,
- Springer Spaniels: 6.2%

~25% of Springer Spaniels exposed to tick-borne pathogens were co-exposed to both Lyme Disease and *Anaplasma*.



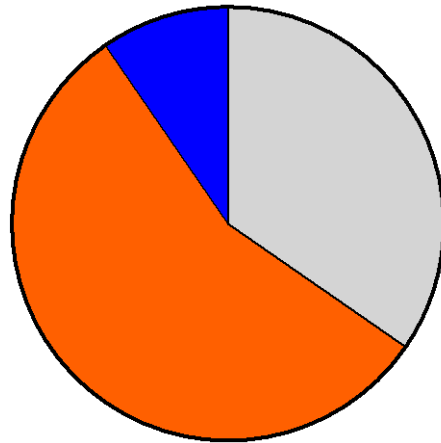
Total=21

- 28.57% Lyme Disease
- 38.10% Anaplasmosis
- 9.52% Ehrlichiosis
- 19.05% Lyme Disease and Anaplasmosis
- 4.76% Lyme Disease, Anaplasmosis, and Ehrlichiosis

based on a rapid diagnostic test (IDEXX 4Dx Snap Test)

Hunting and Sporting dogs included in the study:

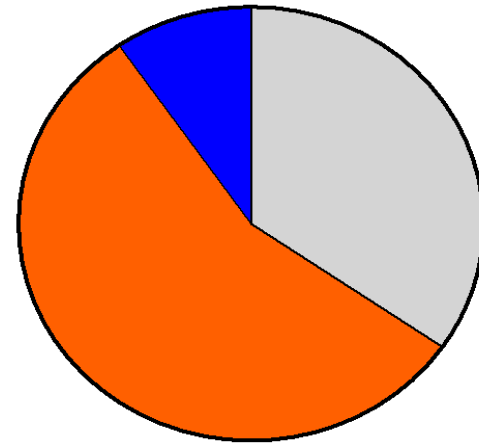
Rate of tick-borne infection
exposure of dogs included in study



Total=156

- 34.62% Negative for tick-borne infections
- 55.77% Positive for 1 tick-borne infection
- 9.62% Positive for 2 or more tick-borne infections

Rate of tick-borne infection
exposure of dogs included in study



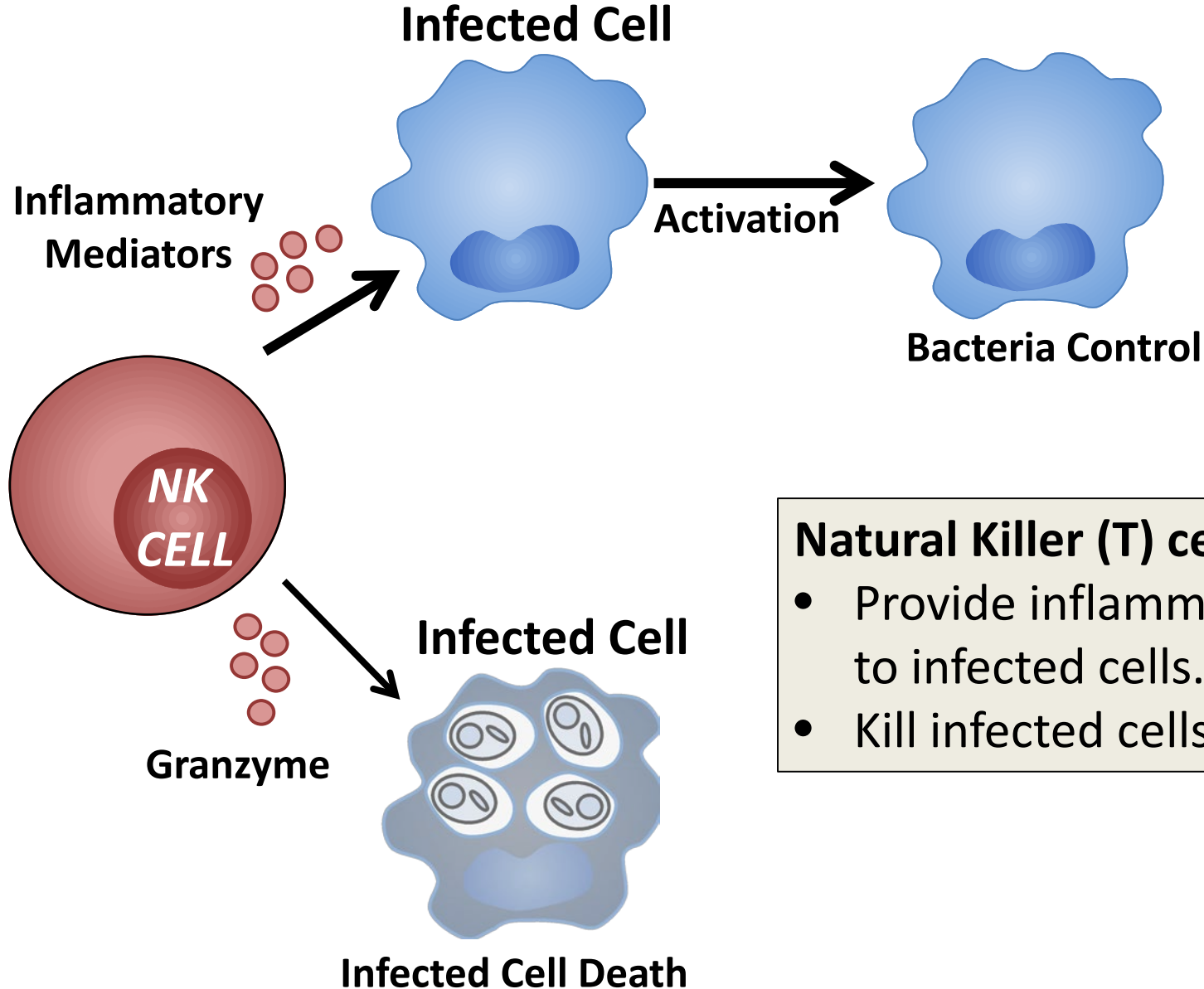
Total=156

- 34.62% Negative for tick-borne infections
- 55.77% Positive for 1 tick-borne infection
- 9.62% Positive for 2 or more tick-borne infections

Includes Springer Spaniels and Fox Hounds



Natural Killer (T) cells during infection



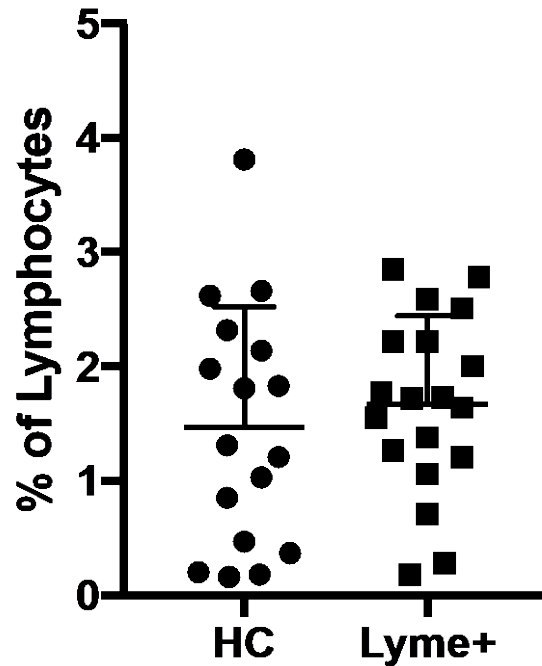
Natural Killer (T) cells:

- Provide inflammatory signals to infected cells.
- Kill infected cells directly.

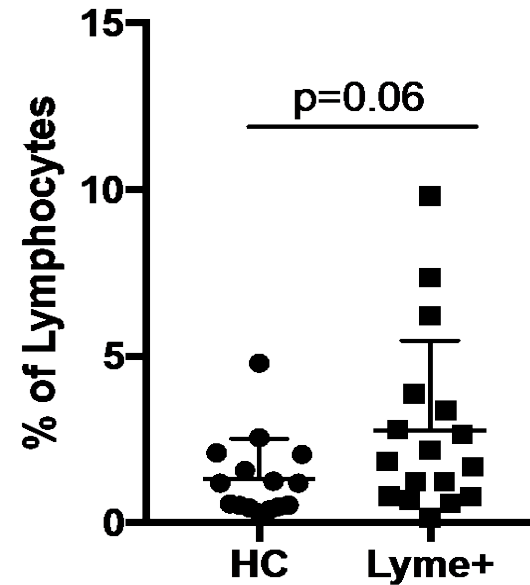


Natural Killer T cells increased in dogs exposed to Lyme Disease

Natural Killer Cells



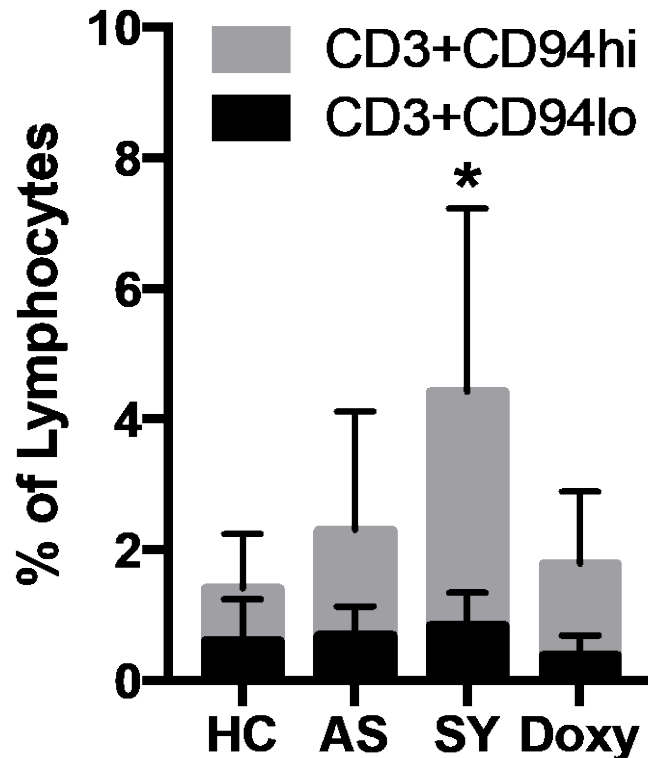
Natural Killer T Cells



CD3	T cell/NKT cell marker
CD94	NK/NKT cell marker

NKT cells inflammatory during Lyme Disease and less likely to kill infected cells

Natural Killer T Cells

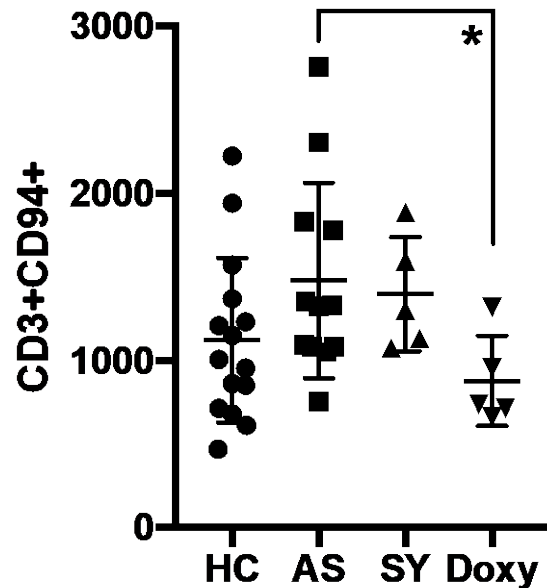


- The CD94hi NK subset has greater capacity to produce IFN γ than the CD94lo subset. (Yu et al., 2009; 2010)

CD3	T cell/NKT cell marker
CD94	NK/NKT cell marker

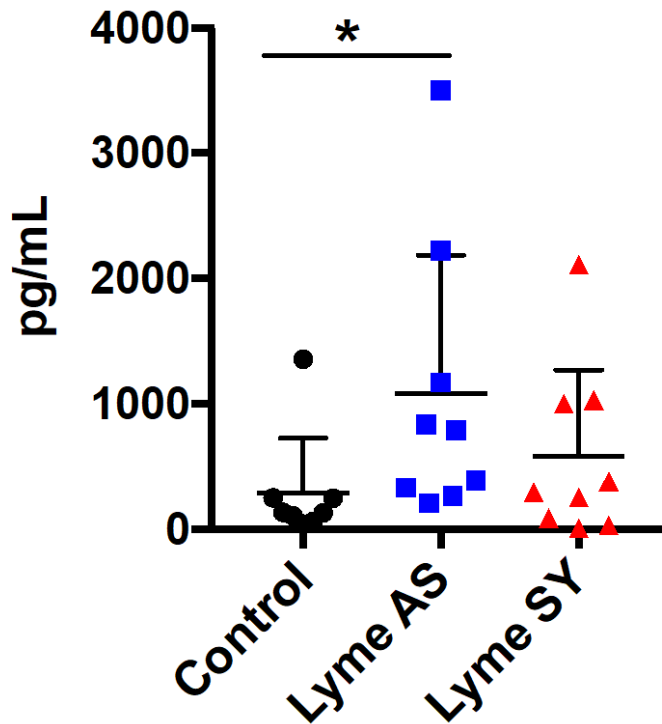
NKT cells from asymptomatic Lyme Disease dogs better able to kill infected cells?

NKT cell Granzyme Expression



- Granzymes are used by NKT cells to kill infected (or “target”) cells.

Serum IL-21 Concentration



- IL-21 is known to enhance NKT cell cytotoxicity. (Ngai 2018)

Conclusions and Next Steps...

“Inflammatory” NKT cells associated with symptomatic Lyme Disease.

- Too much inflammation causes symptoms?
- Next: Measure inflammation markers (cytokines) made by these cells during different disease stages and after treatment.

“Killer” phenotype NKT cells associated with asymptomatic canine Lyme Disease.

- This type of activation helps control bacteria infection?
- Next: Are cells from asymptomatic Lyme Disease dogs better at killing infected cells?

***Anaplasma* co-exposure is common in dogs with Lyme Disease.**

- What are the effects of *Anaplasma* co-infection on Lyme Disease immune responses in these dogs?
- Next: Collect more samples from co-exposed dogs to compare.

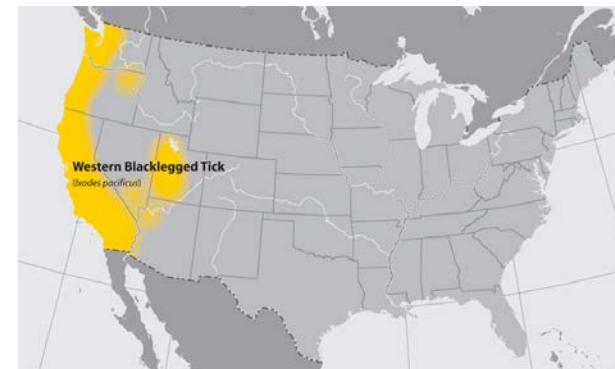
***Anaplasma* alone also common.**

- Is this because these dogs were vaccinated against Lyme disease and would have been also Lyme disease positive if not vaccinated?
- Next: Perform an analysis to see if *Anaplasma* alone dogs have higher vax rate.

OVERLAPPING DISTRIBUTION OF DISEASE CAUSING TICK SPECIES



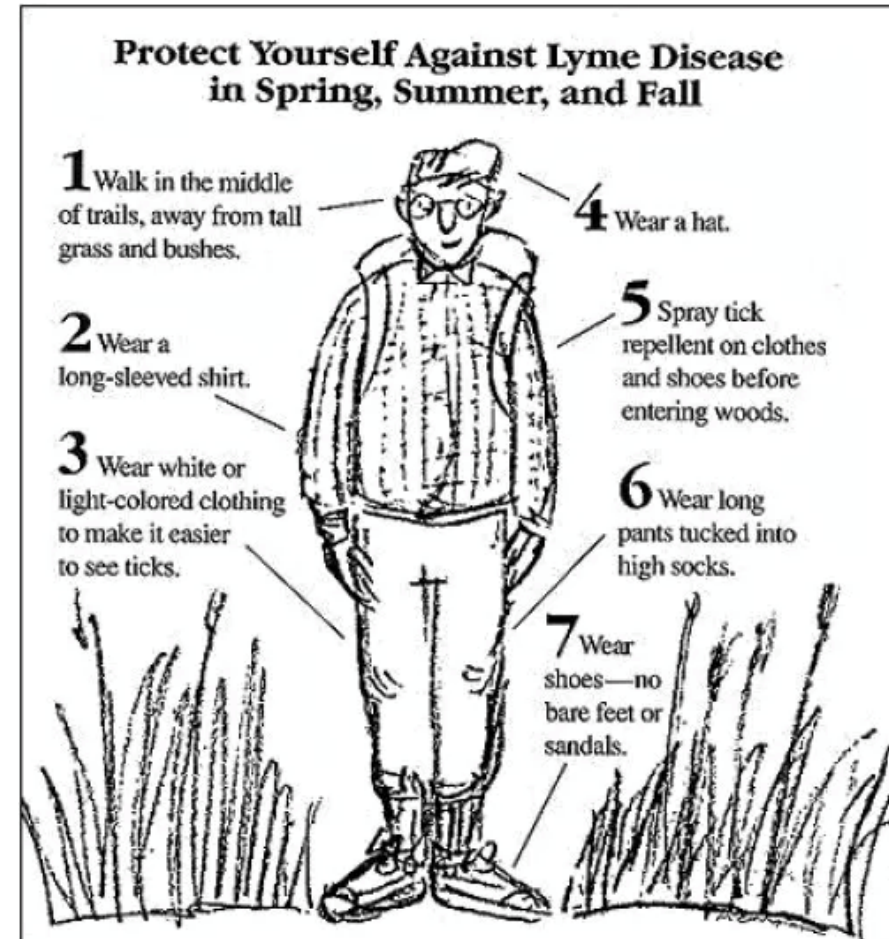
- Humans and animals, living in areas inhabited by multiple tick species can be at risk of contracting multiple tick-borne infections simultaneously.
- As tick distributions expand, the potential for new pathogen combinations to occur in ticks and us increases.



PREVENTION AND CONTROL OF TICK-BORNE INFECTIONS

Reduce Tick Exposure

- Smart clothing choices if going into tick environments
- Insect repellents, permethrin-treated clothing
- Ecto-parasiticide medication for pets/dogs
- Manual tick checks with help and wash well after visiting tick environments



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