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

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

- Anaplasmosis
- Ehrlichiosis
- Babesiosis

![Graph showing reported cases of Lyme disease from 1991 to 2015](chart.png)
LYME DISEASE LIFE CYCLE

Nymphs primarily transmit to people

BLACKLEGGED TICK
Ixodes scapularis
TIMING OF LYME DISEASE IN THE YEAR

The diagram shows the number of cases of Lyme disease by onset week. The x-axis represents the onset week, and the y-axis represents the number of cases. Two categories are shown: confirmed and probable cases. The data peaks in the middle of the year, with a significant increase in cases from May to August.
LYME DISEASE EXPANDING IN U.S.

Reported Distribution of Blacklegged Tick

Reported cases of Lyme Disease

Eisen and Eisen. Trends in Parasitol. 2018
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
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.

Test dogs for Lyme antibodies

Identify asymptomatic vs symptomatic* Lyme disease cases

Analyze Cell Types in Blood

*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)

- 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

Total=209
LYME AND ANAPLASMA MOST COMMON TICK DISEASE EXPOSURES IN SPRINGER SPANIELS

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*.

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

- 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:

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

- The CD94hi NK subset has greater capacity to produce IFNγ than the CD94lo subset. (Yu et al., 2009; 2010)
NKT cells from asymptomatic Lyme Disease dogs better able to kill infected cells?

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

- IL-21 is known to enhance NKT cell cytotoxicity. (Ngai 2018)
“Inflamatory” 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.
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.
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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Collaborating hunting dog kennels and owners

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