

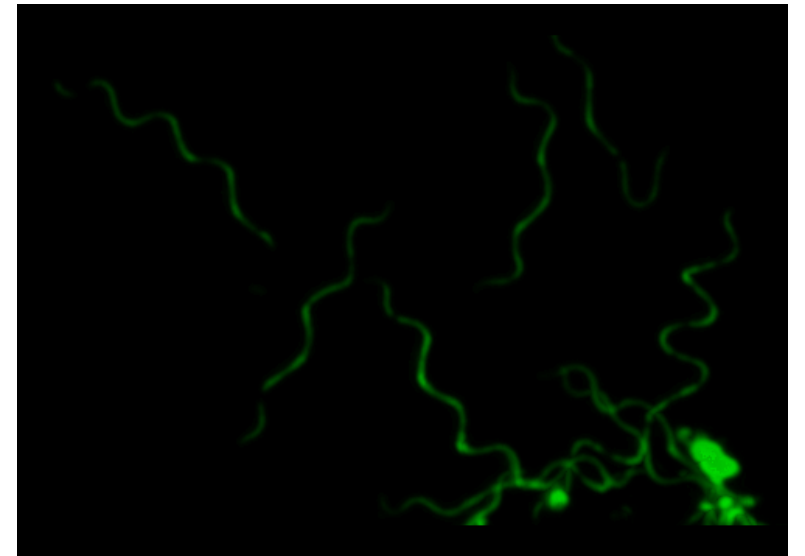
Tick-borne diseases: An emerging public health threat

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Environmental Health and Medicine

- Educates students about the intersection of human health and the environment
 - Analysis, prevention and mitigation of potential environmental hazards (biological, chemical or physical)
- Required professional internship in environmental health



Outline

- The Ticks
- Bacterial diseases
- Protozoal diseases
- Viral diseases
- Borreliosis
 - Lyme
 - Relapsing Fever
- Prevention

off the mark.com by Mark Parisi



Tick Host Seeking (Questing)

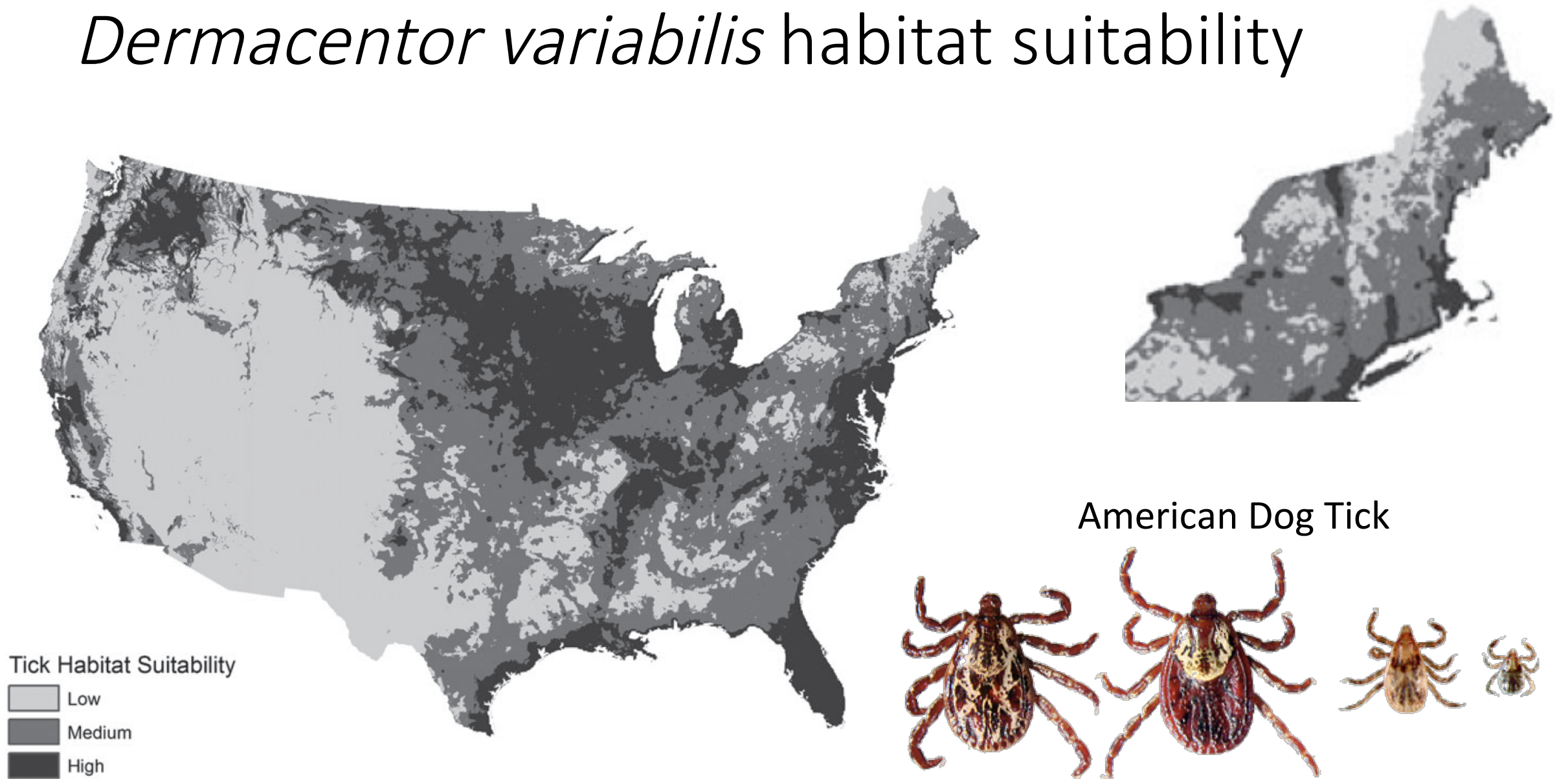
- Ambush strategy
 - Ticks crawl up the stems of grass or perch on the edges of leaves on the ground in a typical posture with the front legs extended, especially in response to a host passing by
- Active strategy
 - Hunter/Assassin ticks
 - Ticks shelter under the ground of their habitats, and emerge to attack hosts when these animals appear nearby
 - They crawl (or run) across distances of many meters to attack and feed on animals resting nearby

Tick Host Seeking Cues

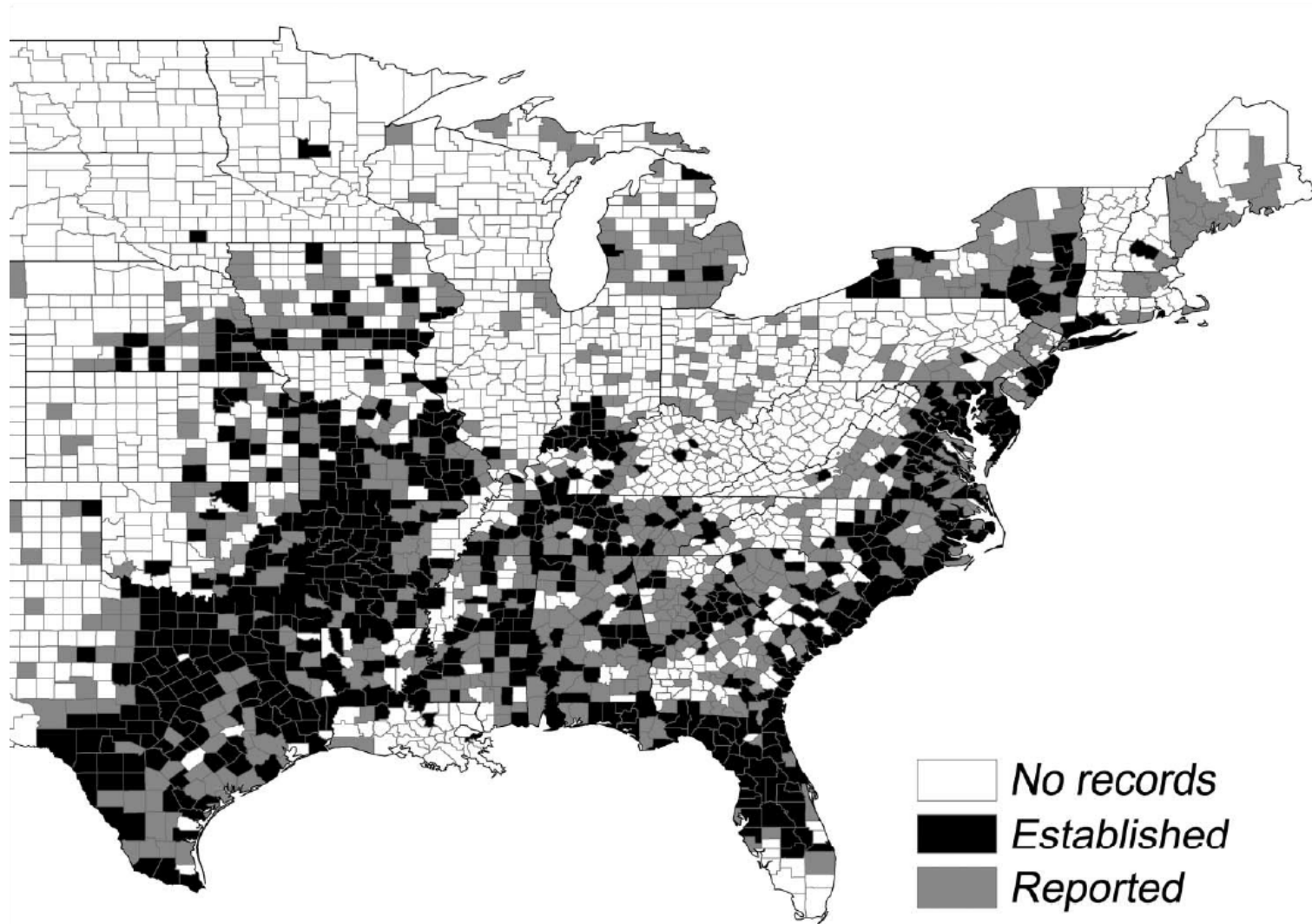
- Odorants and CO₂
 - Animal Breath, Ammonia, Butyric & Lactic Acid
- Radiant Heat
- Vibrations
- Some ticks respond to host sound
 - Feeding cattle & barking dogs
- Tick emitted pheromones



Dermacentor variabilis habitat suitability



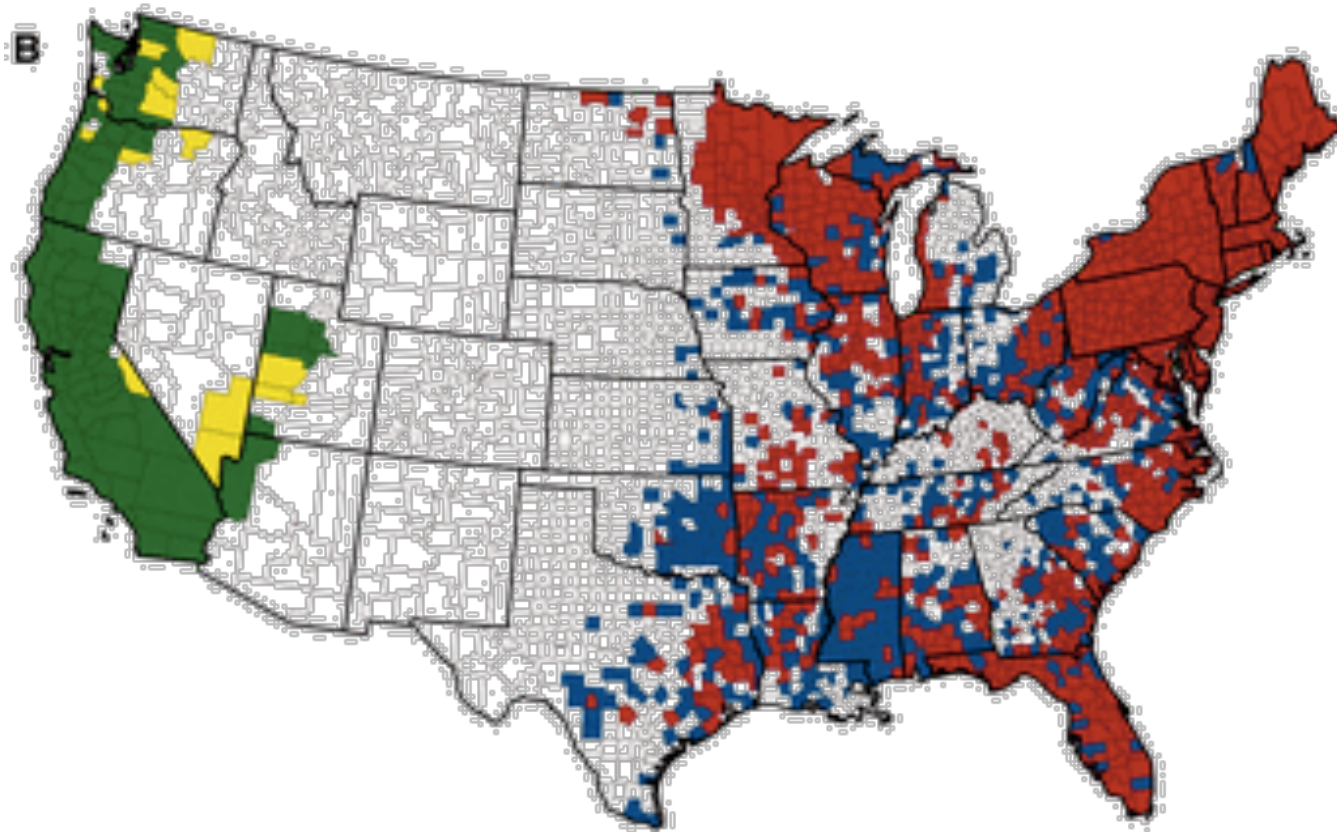
Amblyomma americanum distribution



Lone Star Tick



Ixodes scapularis distribution



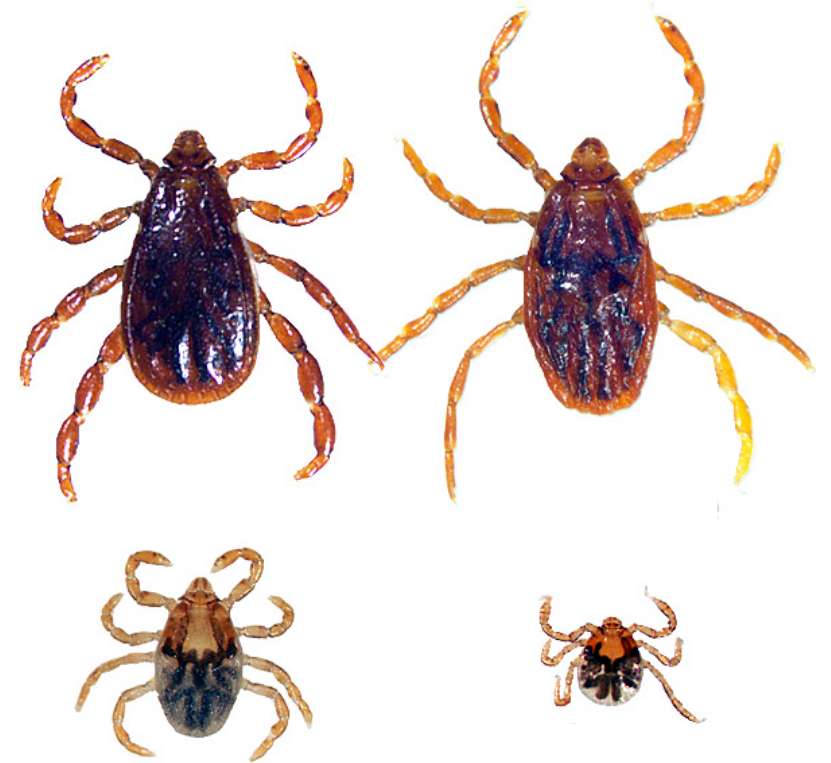
Black-Legged Tick



Rhipicephalus sanguineus distribution



Brown Dog Tick



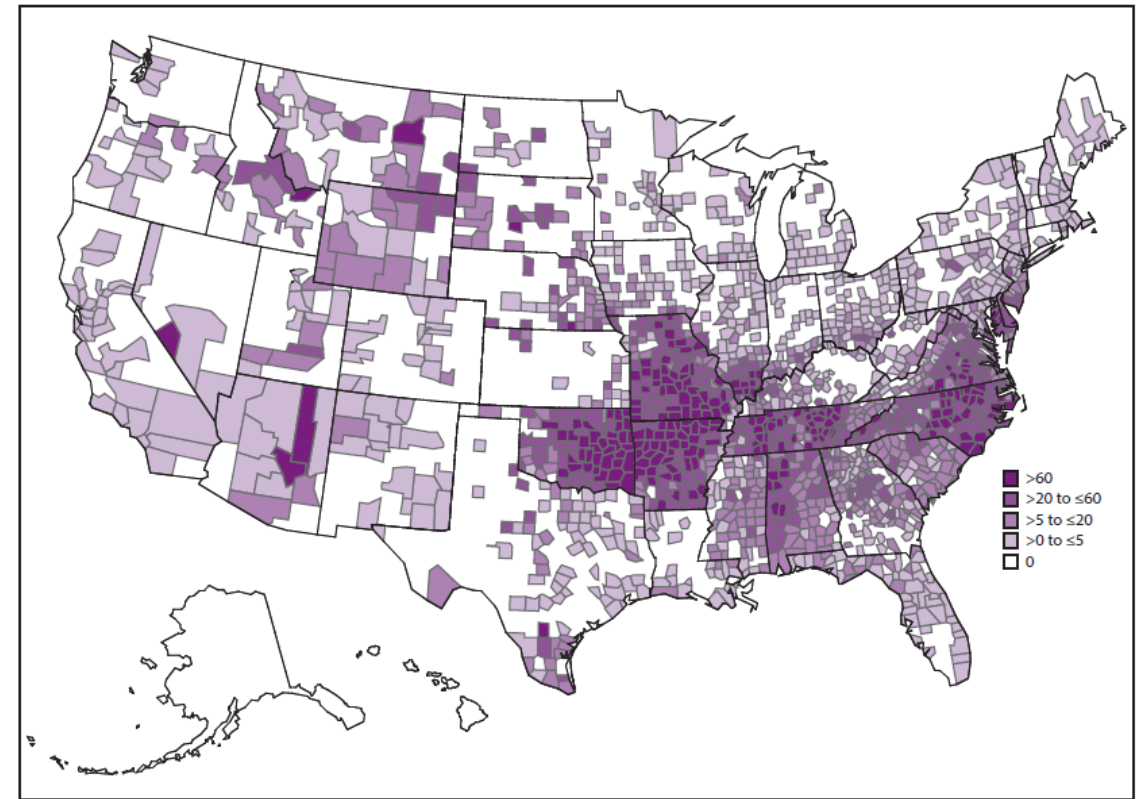
General tick-borne (TB) illness symptoms

- Fever
- Malaise
- Muscle Pain
- Fatigue
- Headache
- Confusion
- Chills
- Nausea and vomiting



Spotted Fever Group Rickettsiosis (SFGR)

- Low prevalence ($>0.01\%$) in wild ticks (RMSF)
- Rocky Mountain Spotted Fever
 - American Dog Tick
 - Brown Dog Tick
- Tidewater Spotted Fever
 - Gulf Coast Tick
- *Rickettsia amblyommii*
 - Lone Star Tick
- Diagnostic tests cross react among the Rickettsiae
- General tick-borne disease symptoms



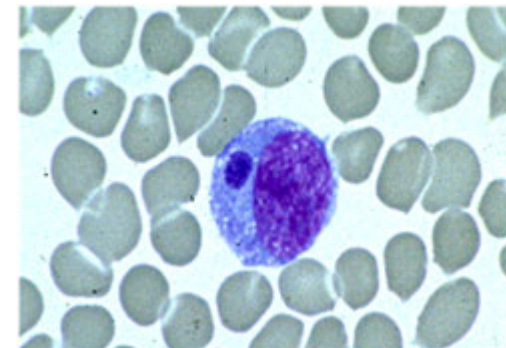
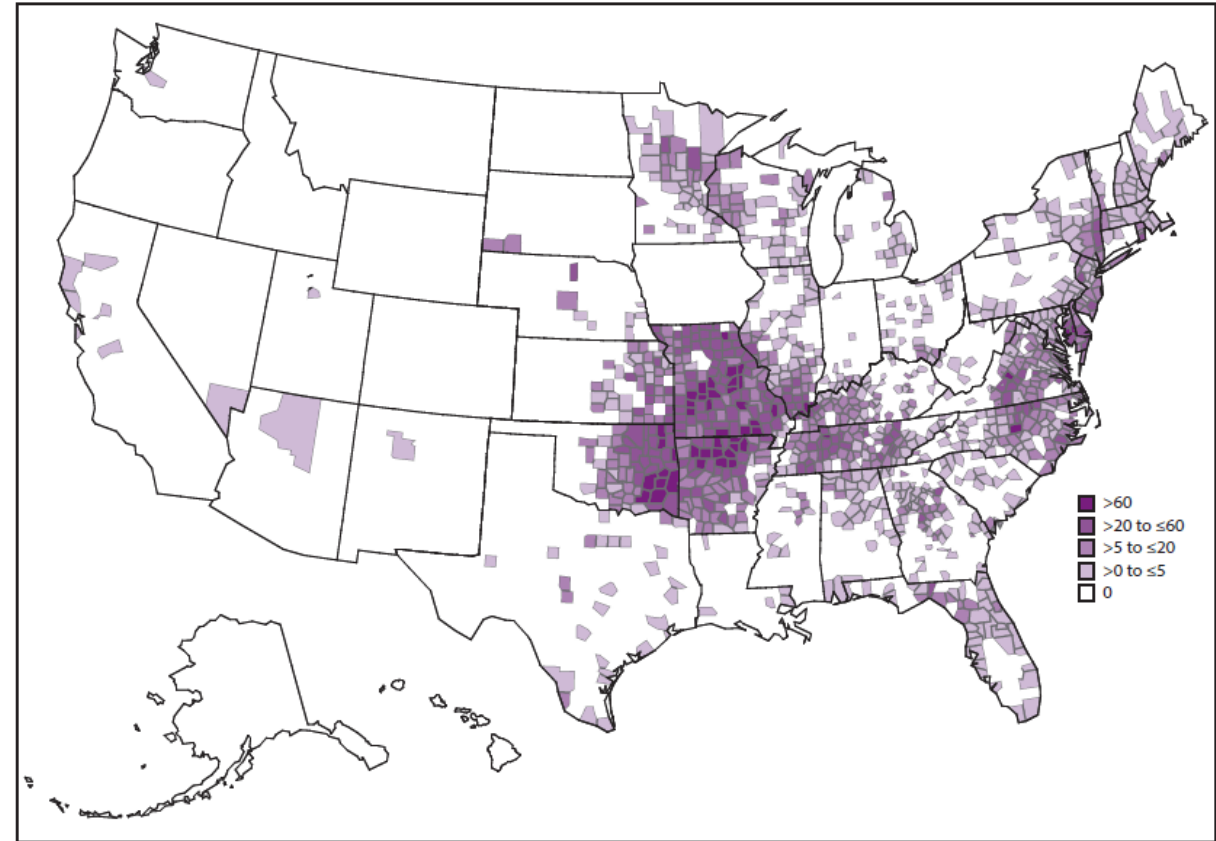
Rocky Mountain Spotted Fever

- Bacteria: *Rickettsia rickettsii*
- Transovarially maintained by ticks
- 3-12 day incubation period
- Fever, headache, nausea
- 90% of patients develop a Rash (2-5 days after fever)
- Rash starts on extremities and migrates to trunk
- Late symptoms include neurological complication, tissue necrosis and multiple organ failure
- Recovery rapid if treated early
 - 5-10% case fatality rate



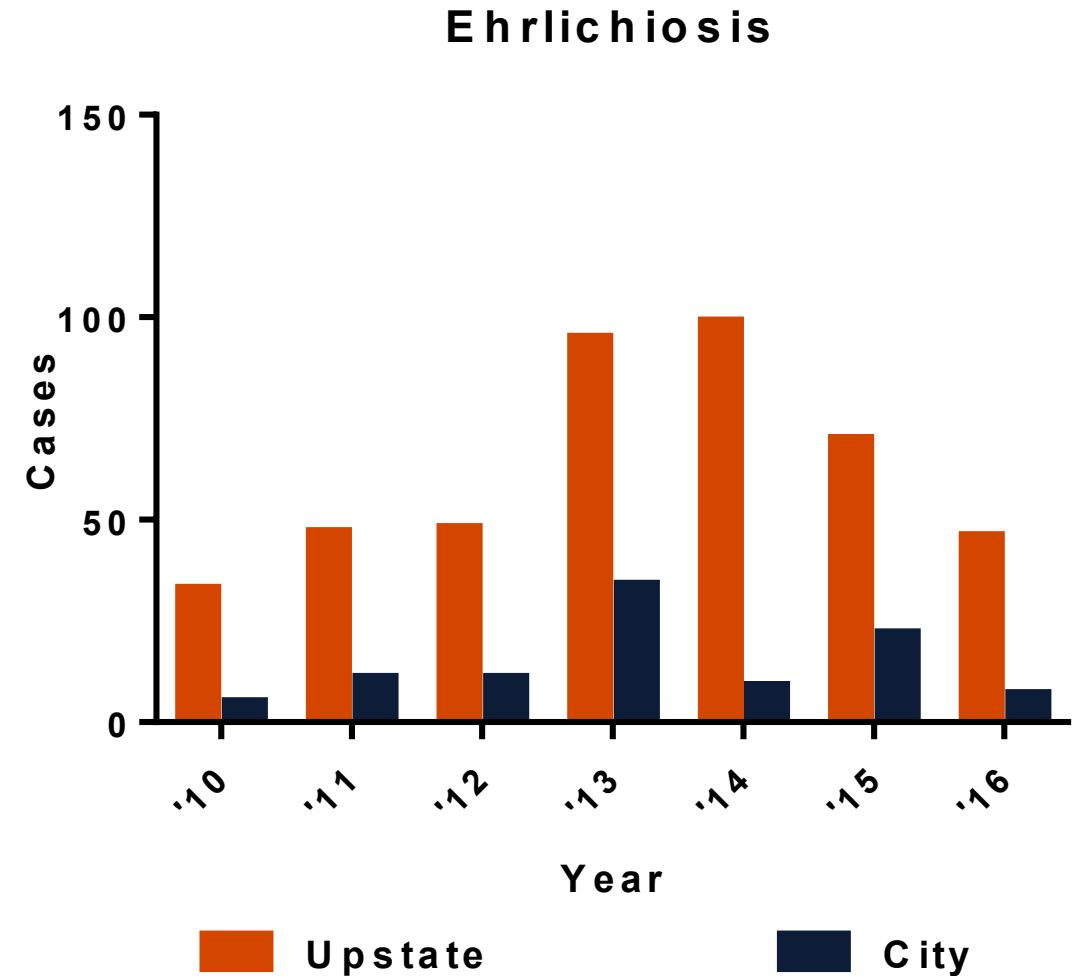
Ehrlichiosis

- *Ehrlichia chaffeensis*
 - Lone Star Tick
 - White-tailed deer are the main reservoir
 - Often associated with monocytes
- *E. ewingii*
 - Lone Star Tick
 - Often associated with granulocytes
- *E. muris*-like
 - Black-legged tick
 - 69 cases in Minnesota/Wisconsin (2013)



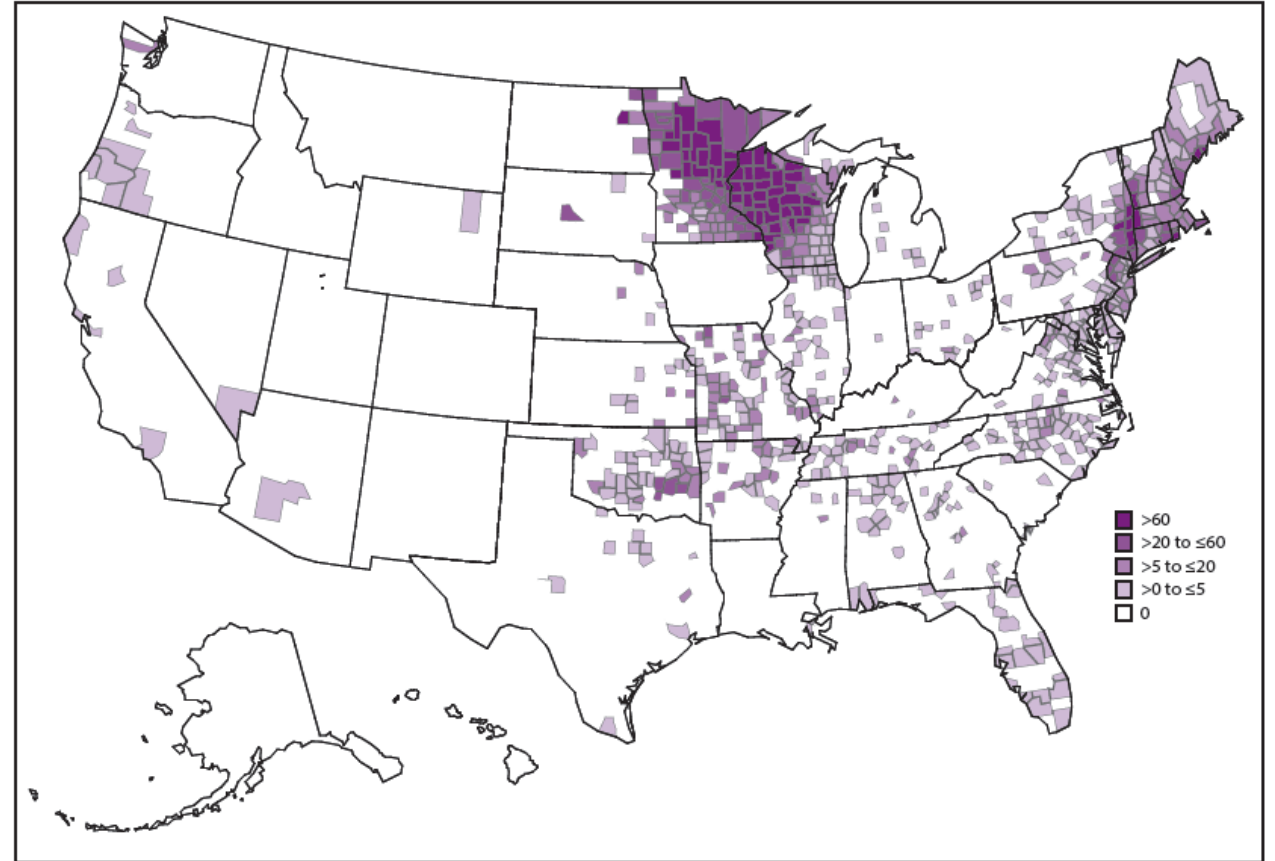
Ehrlichiosis

- General TB illness
- *E. chaffeensis*
 - 5-14 day incubation period
 - Variable pattern rash in 30% of adults, 60% of children
 - Rash onset 5 days after illness onset
 - Case fatality rate is 1-3%
- *E. ewingii*
 - Rash is rare
- *E. muris*-like
 - Rash in 12% of patients
- Less than 15% of patients have Antibody titers in the first week
 - Titers develop 7-10 days



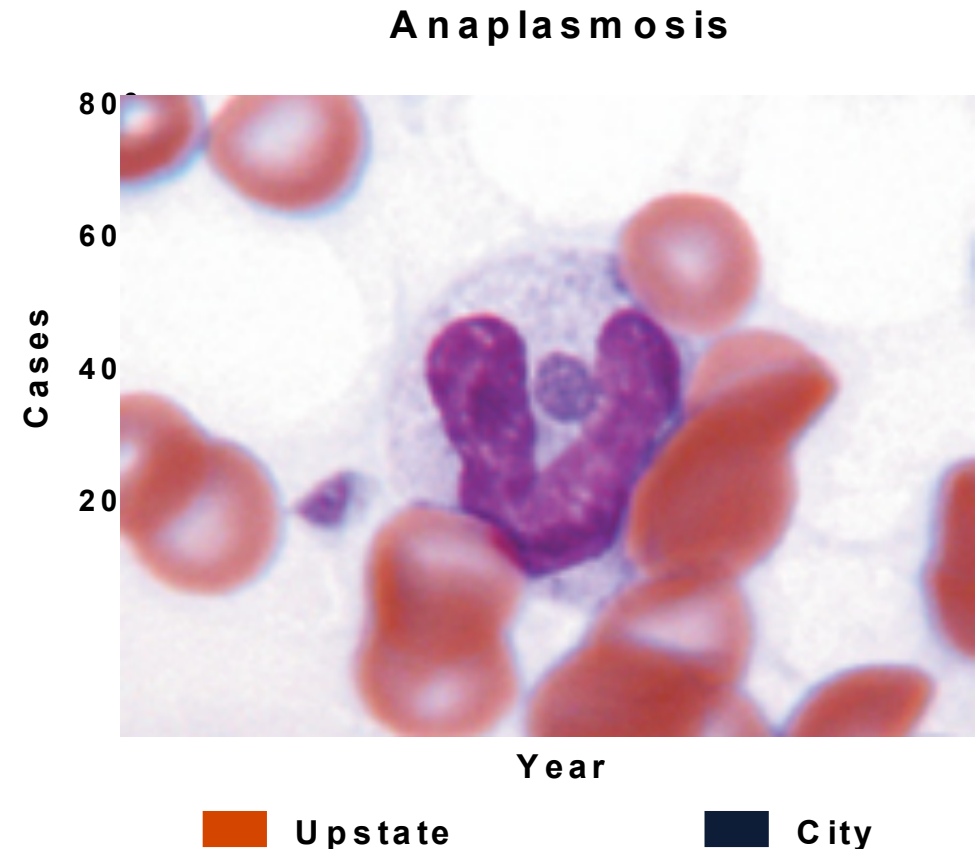
Anaplasmosis

- *Anaplasma phagocytophilum*
 - Vector = Black-Legged Tick (*I. scapularis*)
 - Reservoirs = White-footed mouse, Chipmunks and shrews
- Symptoms= General TB illness
- Severe Disease
 - Breathing difficulty
 - Hemorrhage
 - Renal failure
 - Neurological problems
- >1% case fatality rate



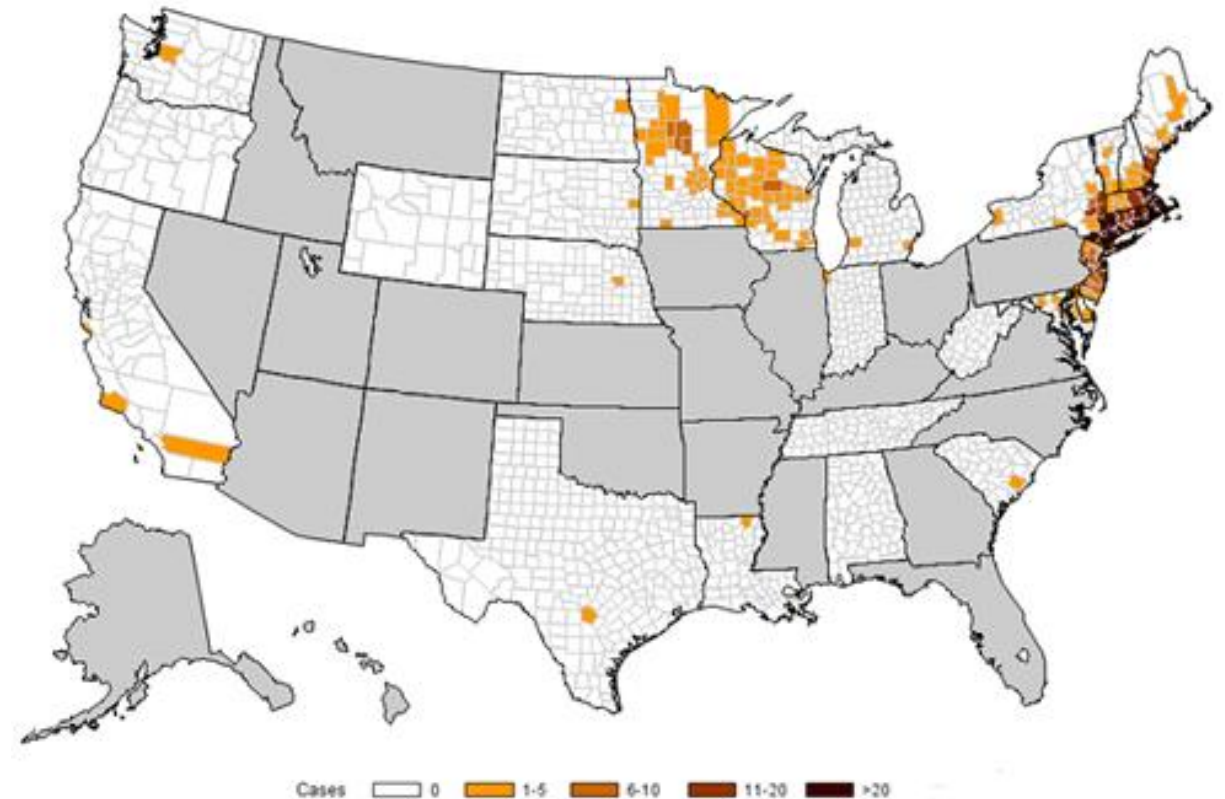
Anaplasmosis cont.

- Detectable antibodies 7-10 days post-infection
- Peripheral blood smears may reveal morulae in granulocyte WBC (20% patients)
- Gold standard= indirect Immunofluorescence assay (IFA)
 - Paired serum samples showing a significant increase in Ab titer



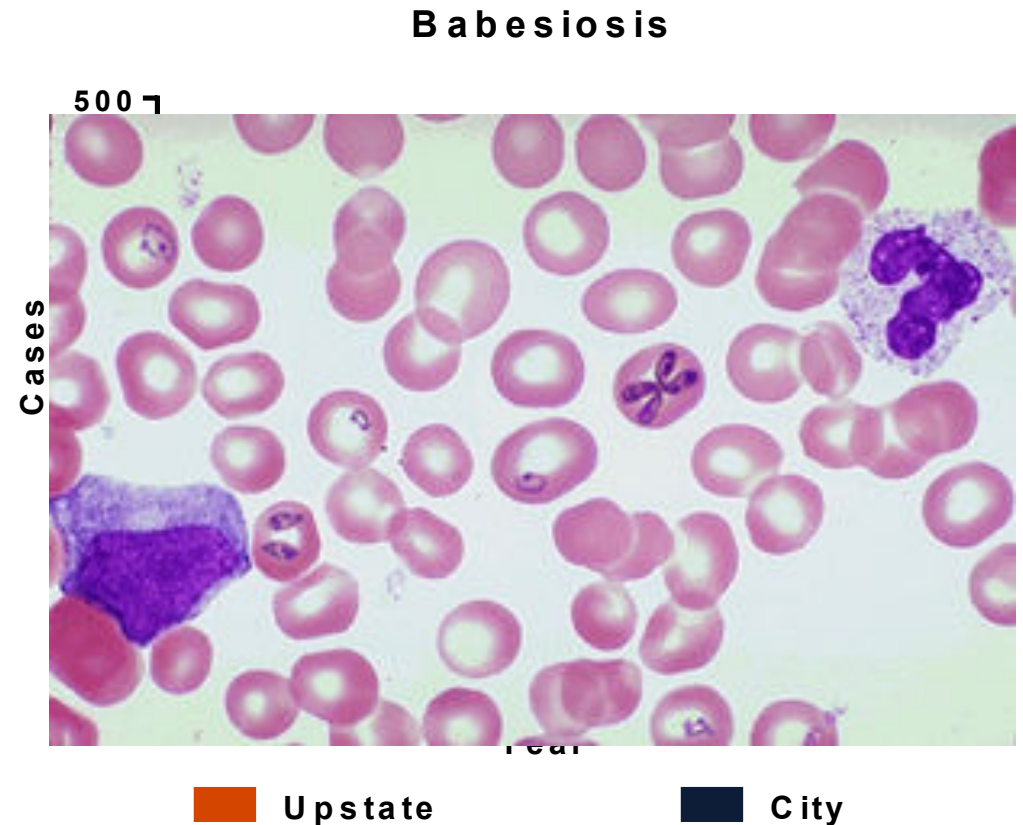
Babesiosis

- Intraerythrocytic protozoan
 - *Babesia microti*
- First infectious agent to be described as an arthropod-borne pathogen
- White-footed mouse (*Peromyscus leucopus*)
- Black-Legged Tick (*I. scapularis*)
 - 1-20% infection prevalence



Babesiosis

- General TB illness
- Severe illness = Hemolytic anemia
- Life-threatening in immunocompromised patients
- Diagnosis is via blood smear
 - PCR and serology (4 fold Ab titer increase)
- Death in up to 10% of patients hospitalized



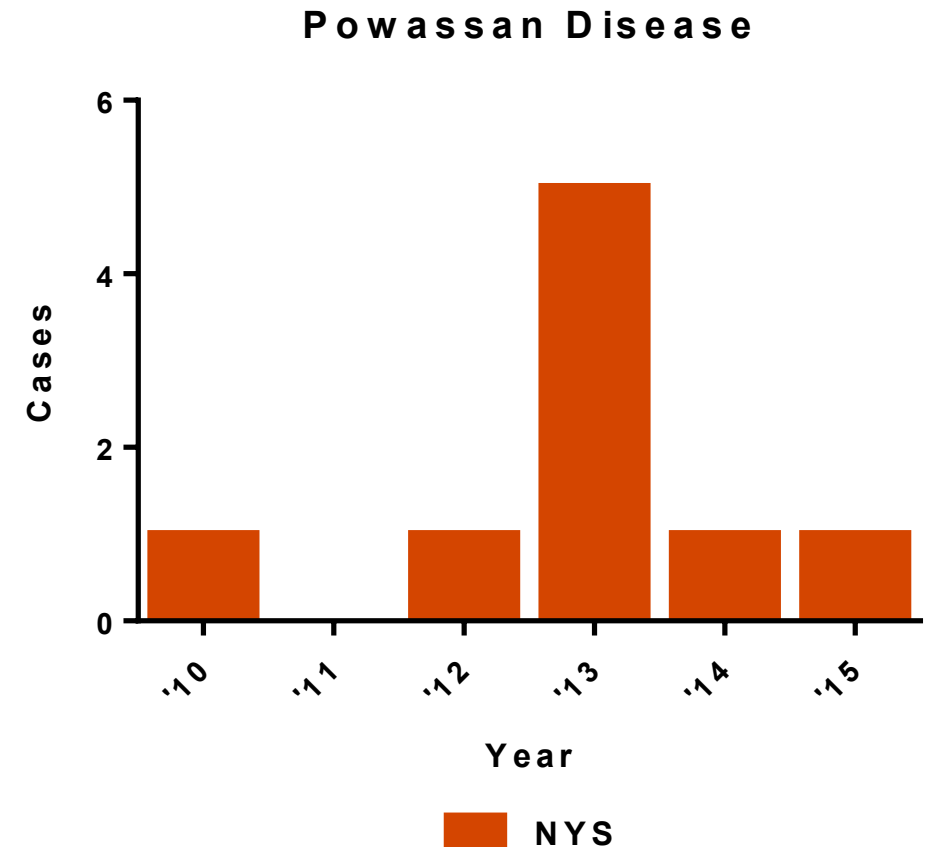
Powassan Disease

- Flavivirus
- Powassan virus
 - Groundhog Tick (*Ixodes cookei*)
 - 60 cases in the US over the past 10 years
- Deer Tick Virus
 - Black Legged Tick (*I. scapularis*)
 - Experimentally shown to be transmitted within 15 mins of tick bite
- Infection rates in NY ticks
 - 0-4%



Powassan Disease

- Reservoirs are small to medium sized animals
 - Groundhogs, skunk & white footed mice
 - Chipmunks, shrews, red squirrel
- Many people are asymptomatic
- Incubation period 1 week to 1 month
- Symptoms include fever, headache, vomiting, malaise, confusion
- POW can affect the CNS and cause encephalitis, meningitis
 - 50% of survivors report permanent neurological symptoms
 - Case fatality rate is 10%

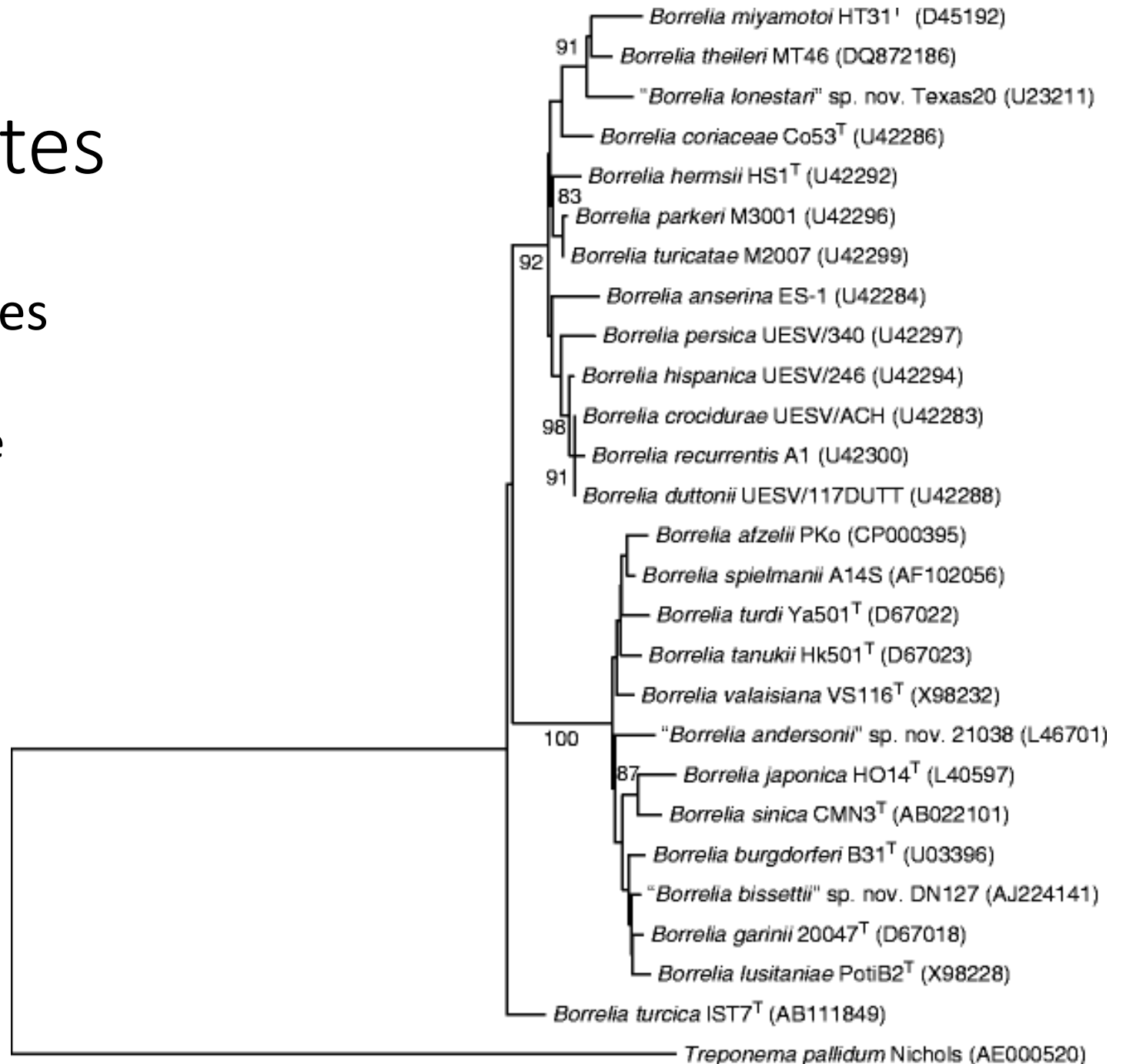


Other Tick borne viruses

- Bourbon Virus
 - One fatal case in Kentucky
 - Associated with a tick bite (unknown species)
- Heartland Virus
 - Lone Star Tick (*A. americanum*)
 - 8 cases in Missouri & Tennessee
- Both diseases have occurred in patients over 50 years of age
- General TB illness symptoms
 - Discovered by reverse transcriptase PCR & next generation sequencing after ruling out other tick borne diseases

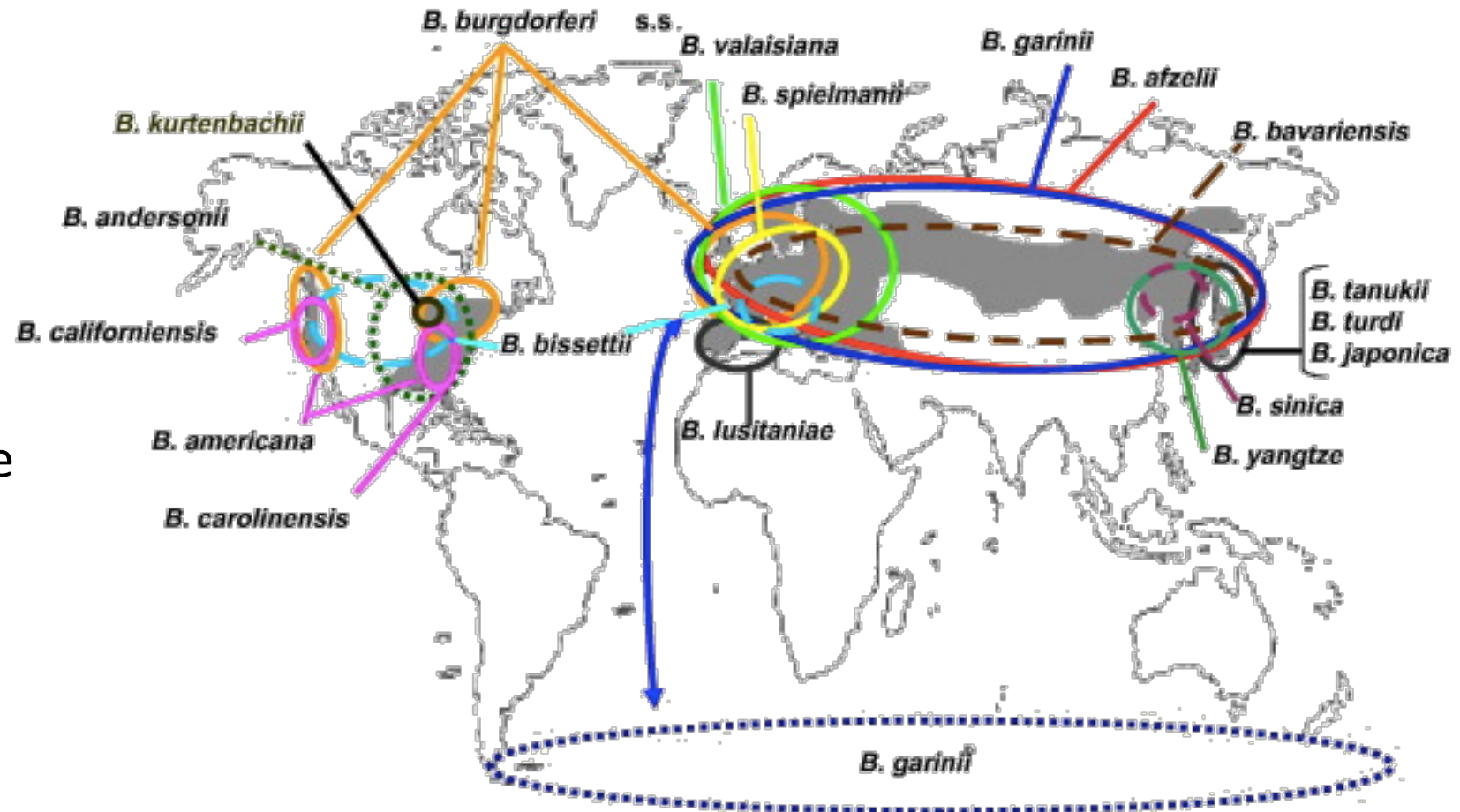
Borrelia spirochetes

- 2 major genetic complexes
 - Lyme Borreliae
 - Relapsing Fever Borreliae



Lyme *Borrelia* (*B. burgdorferi* sensu lato)

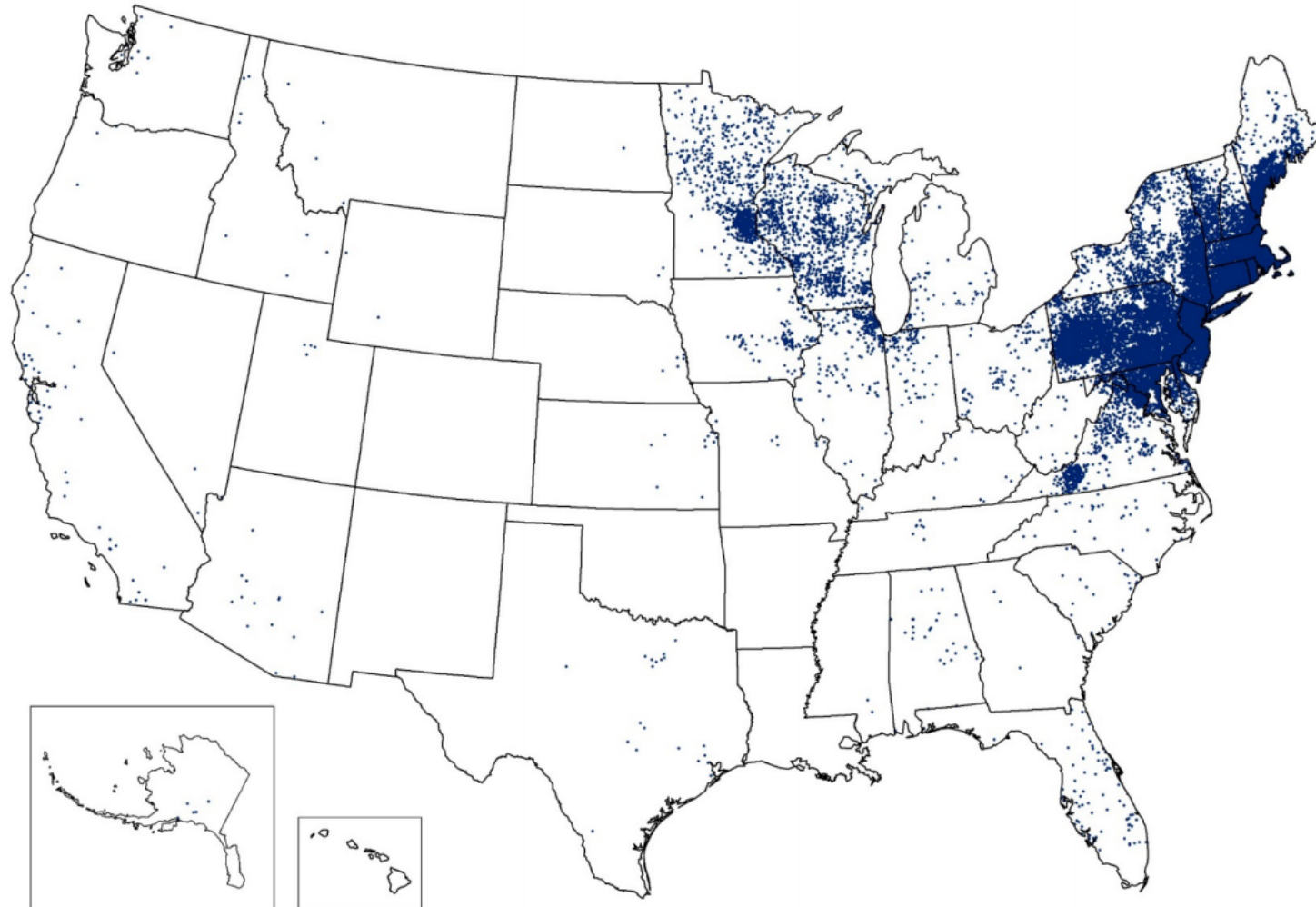
- ~21 species
 - 8 in the US
- 10 have been associated with human disease
 - 4 species responsible for the majority of human cases



Distribution of Lyme Disease

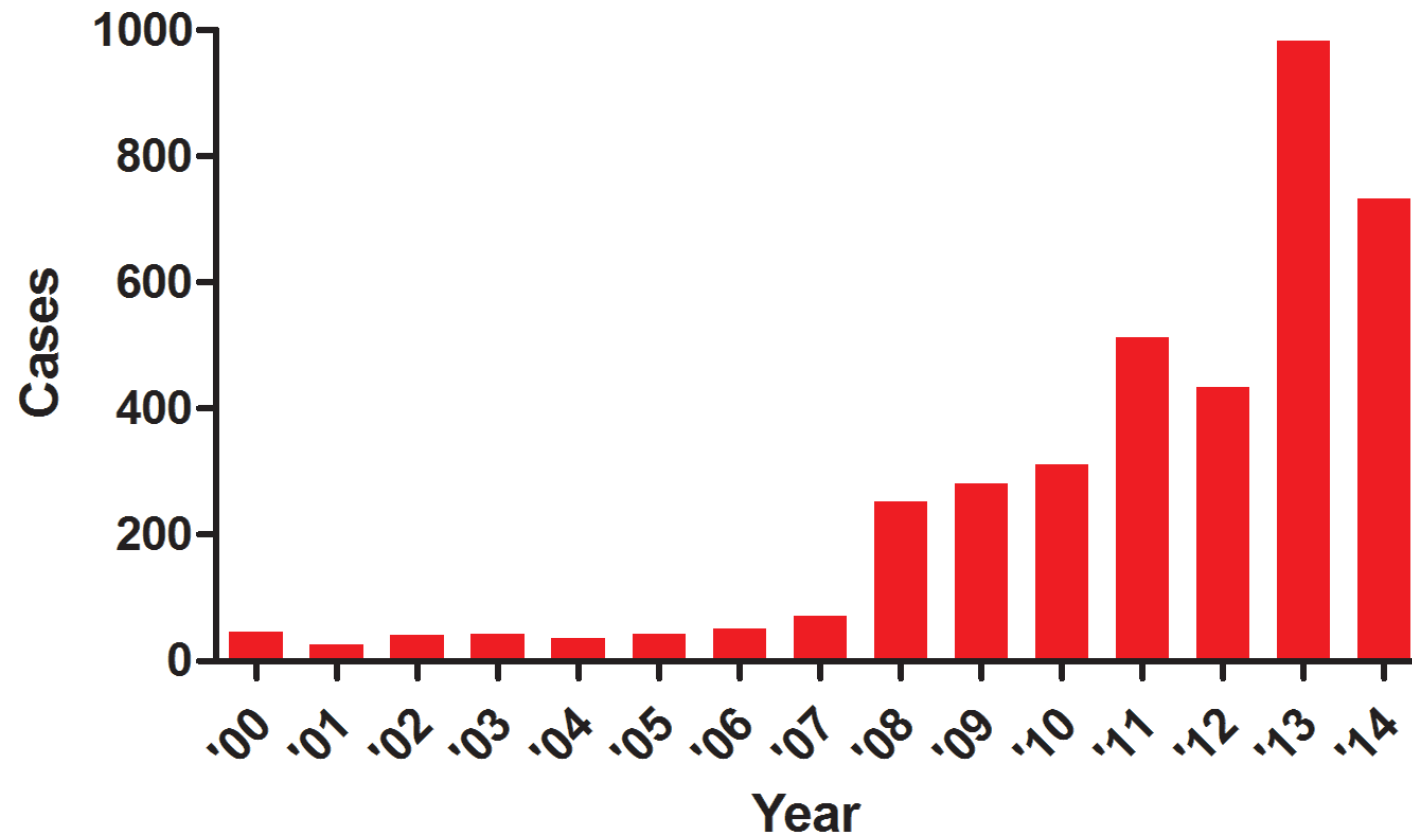
- Worldwide in temperate zones
- Most common tick-borne disease in the World
 - Widespread in North America
 - 300,000 cases estimated yearly
 - Cases reported in 48 states, to date
 - Northeast, from Massachusetts to Virginia
 - North-central states, especially Wisconsin and Minnesota
 - West Coast, particularly northern California
 - Europe, Northern Asia
 - Endemic
 - Most countries don't keep case numbers

Reported cases of Lyme disease, 2014



1 dot placed randomly within county of residence for each confirmed case

Lyme Cases in Central Region of NYS



Lyme Disease in the US

- Most common disease agent:
 - *Borrelia burgdorferi* sensu stricto
- Four additional species have been detected in human clinical samples
 - *B. mayonii*, *B. americana*, *B. andersoni*, *B. bissettii*
 - Very understudied

Reservoir Hosts of *B. burgdorferi*

- Wild rodents and birds
 - Mice
 - White-footed (*Peromyscus leucopus*)
 - Cotton (*P. gossypinus*)
 - Deer (*P. maniculatus*)
 - Shrews:
 - Least (*Cryptotis parva*)
 - Short-tailed (*Blarina* spp),
 - Long tailed (*Sorex* spp.)
 - Rats
 - Wood (*Neotoma* spp)
 - Cotton (*Sigmodon* spp)
 - Squirrels (*Sciurus* spp)
 - Passerine birds



Clinical Lyme Disease

- Early Stage
 - Characteristic skin rash, erythema migrans
 - Usually develops ~7 days after tick bite
- Chronic disseminated disease:
 - Arthritis in 60% of patients in the US



Solid



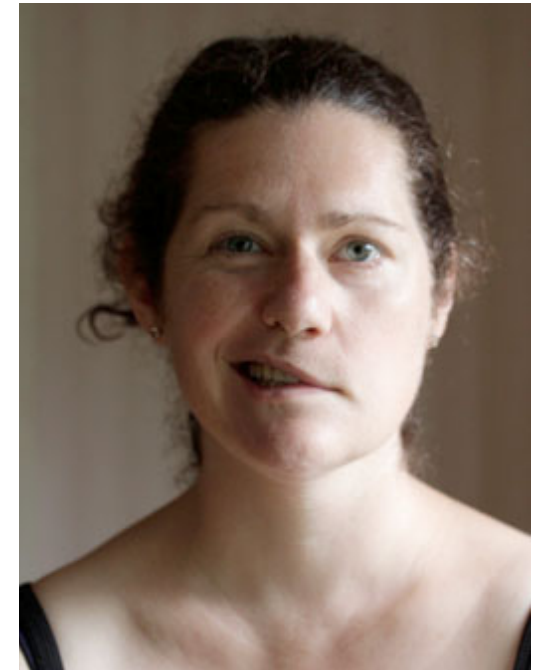
Multiple



Target

Clinical Lyme Disease

- Disseminated disease
- Major Joint Arthritis
- Cardiac
 - 3rd degree Heart Block
- Neurological
 - Bells Palsy
 - Meningitis



Symptoms after treatment

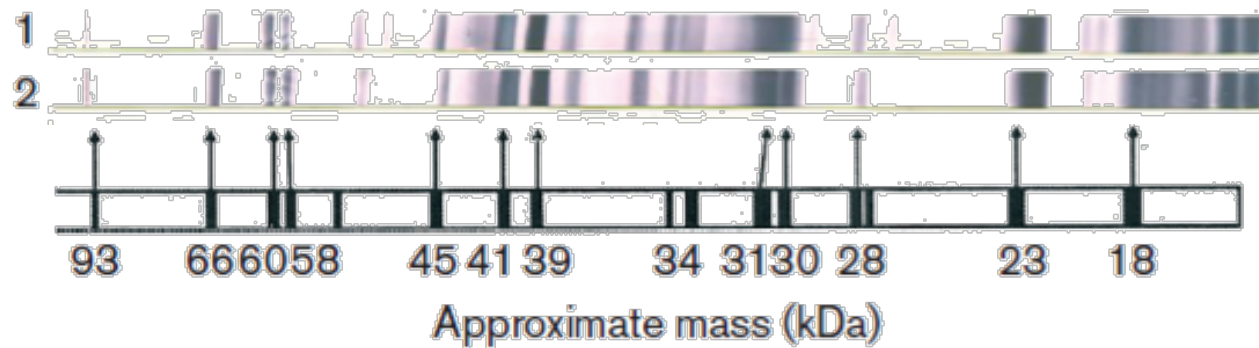
- Post Treatment Lyme Disease Syndrome (PTLDS)
 - Lingering Symptoms after Antibiotic treatment (up to 6 months)
 - Possible residual damage and or immune response
- Chronic Lyme
 - Highly controversial
 - Symptoms last years after treatment
 - Lingering infection?, Re-Infection?

Diagnosis of Lyme Disease

- Early disease is difficult to diagnose
 - Clinical signs
 - History of tick bite in endemic area
 - Serologic testing (Two-Tier Test)
 - Whole Cell ELISA & IgG or IgM Western Blots (depending on length of symptoms)
 - False negatives possible in early stages
 - Not recommended for patients without symptoms of Lyme disease or with only erythema migrans

Efficacy of Two Tier Test

- Disease Stages
 - EM (29-40%)
 - Stage 2 (42-87%)
 - Stage 3 (97-100%)
- Acute Disease (Single EM)
 - 1 week (9%)
 - 2-3 weeks (33%)
 - 4 weeks (86%)



Borrelia mayonii

- 11 years 100,545 patient samples tested (PCR)
- 2012-2014 9197 samples for the upper Midwest
 - Minnesota, Wisconsin and North Dakota
 - 102 positive for *B. burgdorferi*
 - 6 positive for *B. mayonii*
- Vector= Black-Legged Tick (*I. scapularis*)
- Similar signs as Lyme Disease and:
 - Nausea and vomiting
 - Diffuse rashes
- Higher concentration of Bacteria in Blood (10^5 - 10^6 per mL)
- Whereas >50% of Lyme cases with EM have detectable DNA in blood

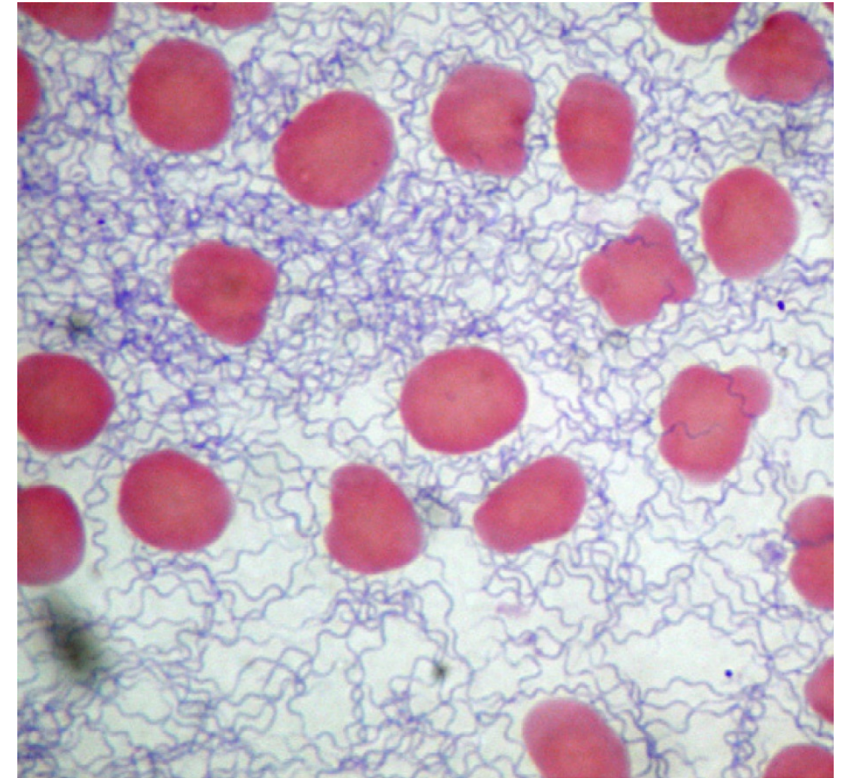
Relapsing Fever Borrelia

- Similar morphology to Lyme Borrelia
- Occur in large numbers in Bloodstream
 - Unlike more tissue tropic Lyme *Borrelia*
- Genetically distinct from Lyme *Borrelia*
- 1857 David Livingstone recorded fever associated with soft tick bites during African explorations
- Once a “Hot” Disease
 - Robert Koch
 - Charles Nicolle
 - Joseph Everett Dutton



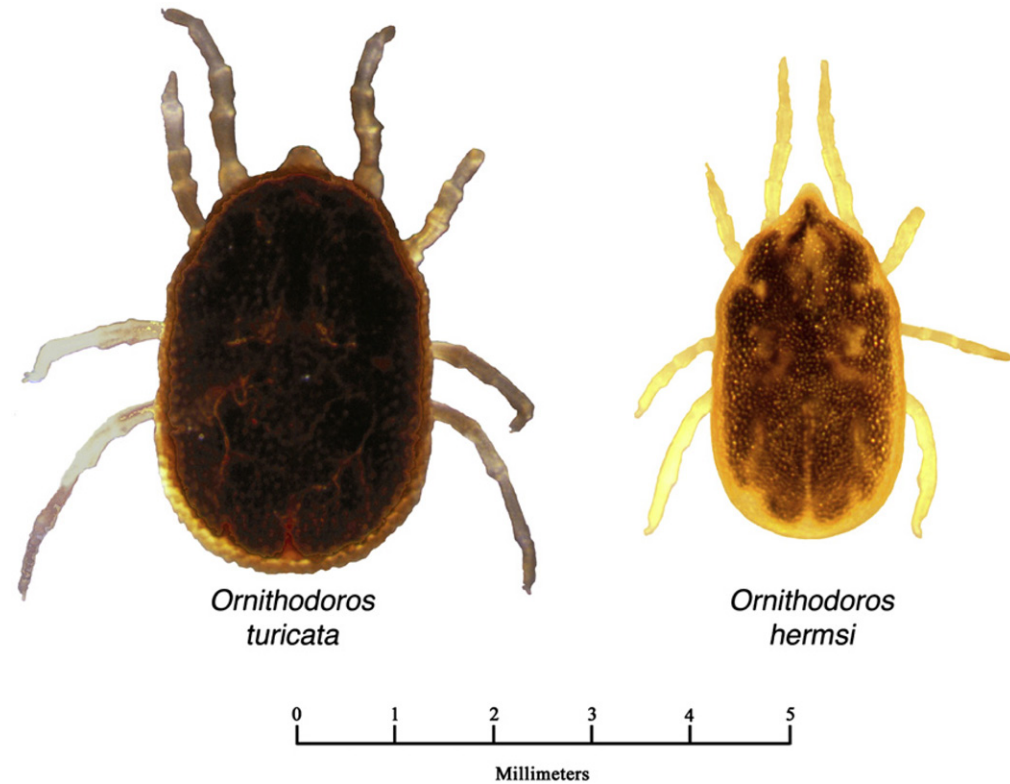
Tick-borne relapsing fever (TBRF)

- Caused by *Borrelia* spirochetes
- Soft tick-borne relapsing fever
 - *B. hermsii*, *B. parkerii*, and *B. turicatae*
- Hard tick-borne relapsing fever
 - *B. miyamotoi*, *B. lonestari*



TBRF vectors in the US

- Argasid Ticks
 - “Soft Tick”
- Fast feeders
 - 5-60 mins
- Can live up to 10 years
- Take many blood meals
 - Females lay eggs after bloodmeal
- Transovarially transmitted (Some...)
- Rodent reservoirs



Ecology of TBRF

- TBRF is endemic in the western US, southern British Columbia, plateau regions of Mexico, Central and South America, the Mediterranean, Central Asia, and much of Africa
- First epidemic recognized in U.S. in 1915 in Colorado
- First case was actually in 1905 in New Yorker traveling to TX
 - Now in 14 states
 - Most recent cases and outbreaks have occurred in rustic cabin or vacation home settings at higher elevations (> 8,000 feet) in coniferous forests in the western US

Borrelia miyamotoi

- First detected in ticks in 1994
- Associated with Human illness in 2011
- Peak detection August-September
 - Suggesting the possibility of larval *I. scapularis* transmission
- Acute febrile illness
 - Fever and Headache
 - Fever reoccurrence 4-10% of patients
 - Rash was observed in 8% of American patients (none described as EM)
- Treatment
 - Doxycycline, amoxicillin, and ceftriaxone

B. miyamotoi

- Diagnosis by PCR and DNA sequencing
- Antibody test (GlpQ)
- PCR positivity in 1% of suspected tick borne illness patients in NE (n=11,515)
- Prevalence may be as high as *Babesia* and *Anaplasma* infections
- New York Black-Legged Ticks
 - Dutchess Co. 0.56%
 - Suffolk Co. 1.1%
 - Westchester Co. 6.8%

α -Gal Allergy (Red Meat Allergy)

- Cetuximab
 - Drug used to treat metastatic colorectal cancer, non-small cell lung cancer & head and neck cancer
 - Certain geographic regions have a high rate of anaphylactic reactions to cetuximab upon the first exposure to the medication (1% in the NE versus up to 20% in SE)
- Drug is produced in mice and contains the α -Gal carbohydrate (as do all mammalian cells, minus the primates)
- Epidemiologically linked to the bite of the lone star tick



α -Gal Allergy (Red Meat Allergy)

- Patients experiencing this allergy report intense itching, swelling, and/or develop hives at 3 – 6 hours after eating red meat, i.e. beef, lamb, pork, venison
- Can be severe enough to lead to hospitalization



Treatment of Tick-borne Diseases

- Recognition of symptoms post tick exposure
 - Flu like symptoms
- Recognition of tick-borne infection by physician
 - SAVE THE TICK!
- Short course of Antibiotics (Doxycycline)
- Antiprotozoals
- Definitive care & supportive measures for viral and late stage manifestation

Prevention of Lyme Disease (and other TBDs)

- Tick avoidance
- No vaccine available
 - Although some are in development
- Prophylactic antibiotic treatment
 - People in endemic areas who are bitten by *Ixodes* ticks
 - Controversial
 - Benefit vs. risk of allergic reaction
 - May be warranted if risk of infection following bite is high enough

**PREVENT
LYME
DISEASE!**

- **WEAR REPELLENT**
- **CHECK FOR TICKS DAILY**
- **SHOWER SOON AFTER
BEING OUTDOORS**
- **CALL YOUR DOCTOR IF YOU
GET A FEVER OR RASH**



For more information:
www.cdc.gov



Tick Removal



Prevention of Tick-borne diseases

- Proper Clothing



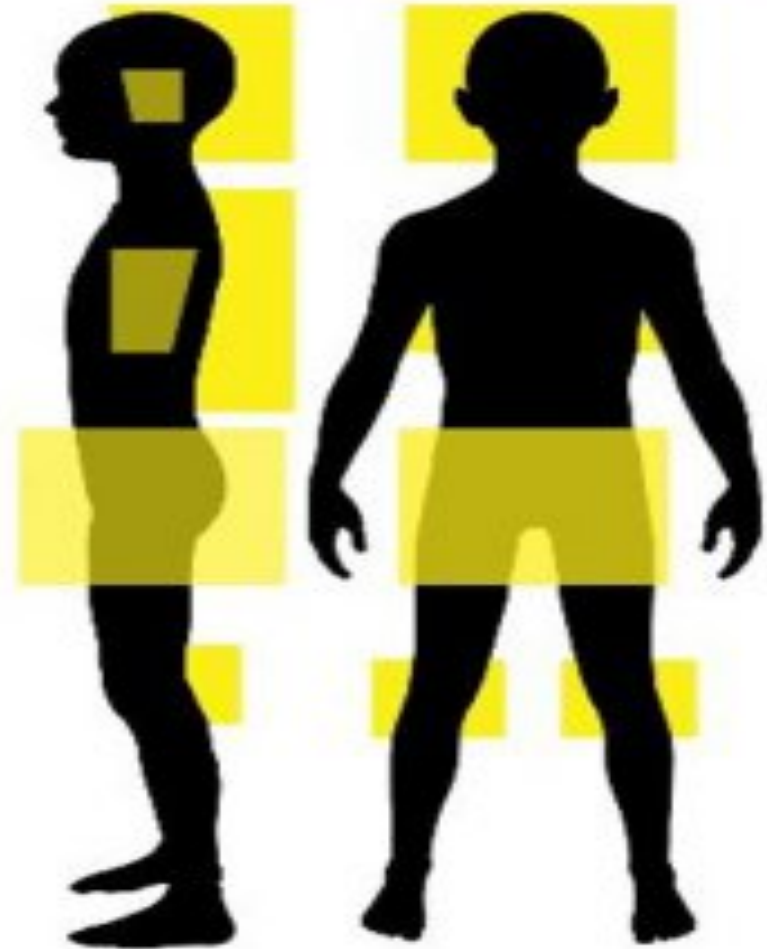
Prevention of Tick-borne diseases

- Proper Clothing
- Personal Acaricides



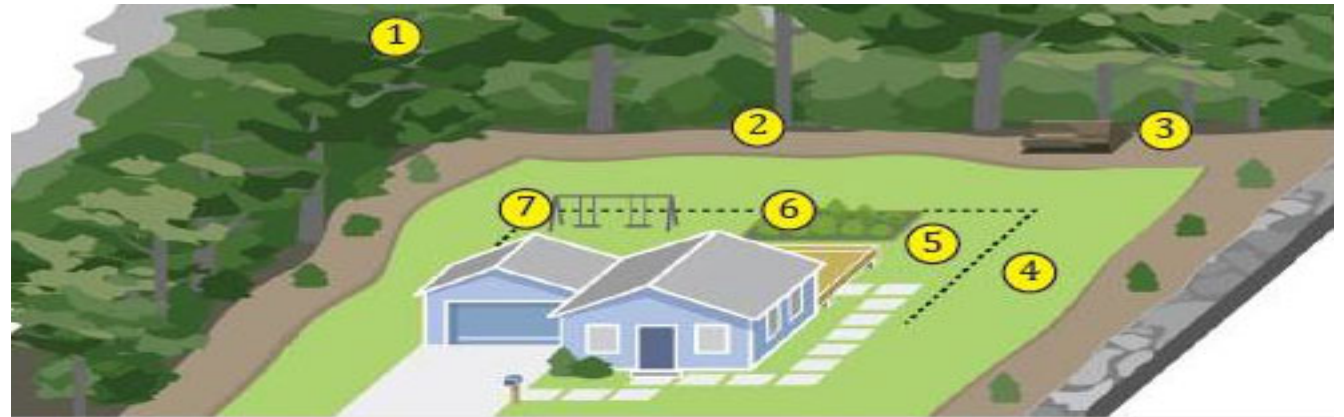
Prevention of Tick-borne diseases

- Proper Clothing
- Personal Acaricides
- Tick Checks



Prevention of Tick-borne diseases

- Proper Clothing
- Personal Acaricides
- Tick Checks
- Yard Landscaping



1	Tick zone	Avoid areas with forest and brush where deer, rodents, and ticks are common.
2	Wood chip barrier	Use a 3 ft. barrier of wood chips or rock to separate the "tick zone" and rock walls from the lawn.
3	Wood pile	Keep wood piles on the wood chip barrier, away from the home.
4	Tick migration zone	Maintain a 9 ft. barrier of lawn between the wood chips and areas such as patios, gardens, and play sets.
5	Tick safe zone	Enjoy daily living activities such as gardening and outdoor play inside this perimeter.
6	Gardens	Plant deer resistant crops. If desired, an 8-ft. fence can keep deer out of the yard.
7	Play sets	Keep play sets in the "tick safe zone" in sunny areas where ticks have difficulty surviving.

Based on a diagram by K. Stafford, Connecticut Agricultural Experiment Station

References

- Bacon, Biggerstaff et al. 2003. Journal of Infectious Diseases, 187, 1187-1199
- Agüero-Rosenfeld, Wang et al. 2005. Clinical Microbiology Reviews, 34, 1-9
- Branda, Linskey et al. 2011, Clinical Infectious Diseases, 53 (6), 541-547
- Branda, Strle et al. 2013, Clinical Infectious Diseases, 57 (3), 333-340
- Commins, S. P., Satinover, S. M. et al. (2009). Journal of Allergy and Clinical Immunology, 123(2), 426-433.
- Wormser, Nowakowski et al. 2008, Clinical Vaccine Immunology, 15 (10), 1519-1522
- Wormser, Pritt 2015. Infectious Disease Clinics of North America, 29, 371-381
- Vannier et al. 2015. Infectious Disease Clinics of North America, 29, 357-370
- James et al. 2015, Medical and Veterinary Entomology, 29, 178-188
- Springer et al. 2014. Journal of Medical Entomology, 51 (2), 342-351
- Bakken and Dumler. Infectious Disease Clinics of North America, 29, 341-355
- Kosoy et al. 2015. Emerging Infectious Diseases, 21 (5), 760-764
- Pritt et al. 2016. The Lancet Infectious Diseases, 16 (5), 556-564
- CDC website

Questions?



STARI

Southern Tick-Associated Rash Illness

- Vector=Lone Star Tick (*A. americanum*)
- Rash indistinguishable from Lyme EM
 - Evidence for and against disseminated clinical signs
- Unknown Etiology
 - Possible pathogen
 - Possible allergic reaction
- Has been documented in the Northeast

