



Tick-Borne Infections Council  
of North Carolina, Inc.



## NEWSLETTER 2024, Volume 4

**Quotes:** “The rapid evolution of Lyme disease risk in North Carolina over the past decade poses a substantial threat to public health, especially as many of the most highly impacted areas also experience limited access to health services. Urgent efforts are needed to raise public awareness and educate medical providers in order to prevent excess morbidity.” Neha V. Mokashi, et al., Spatiotemporal patterns of Lyme disease in North Carolina: 2010-2020, *The Lancet Regional*

**New feature:** we now have a summary section for each research update to explain findings for a lay audience and increase accessibility.

### Highlights:

- **Rapid Increase and Seroprevalence of *Borrelia burgdorferi* Antibodies among Dogs, Northwestern North Carolina, USA, 2017-2021**
- **Evidence of Human Bourbon Virus Infections in North Carolina**
- **Alpha-gal Syndrome Presenting as Fibromyalgia in an American Indian Population**
- **Tick-Borne Diseases in America’s National Parks: Observations and Recommendations for Improved Public Health**
- **A Review of Force Health Protection Aspects of Lyme Disease in the U.S. Military**
- **Current and emerging approaches for eliminating *Borrelia burgdorferi* and alleviating persistent Lyme disease symptoms**
- **Global risk dynamics of *Borrelia miyamotoi* in the context of climate change**
- **Tick-Borne Diseases and Pregnancy: A Narrative Review Evaluating Pregnancy Complications Caused by Tick-Borne Diseases**
- **Is Alpha-Gal an Emerging Allergen in Drug Allergy?**
- **Vaccination to Prevent Lyme Disease: A Movement Towards Anti-Tick Approaches**

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## TIC-NC Activities

- More booklets were distributed in the hard-hit Asheville area by our energetic volunteer, Janet Dooley.
- Our scientific advisor, Marcia E. Herman-Giddens, will be giving a presentation, *Keeping Safer from Ticks and Tick Diseases and Conditions* to the organization North Carolina Vegetation Management at their 2024 Annual Meeting on December 4, 2024.
- We are thrilled to welcome the new co-editor of our newsletters, Melody Xiao. Melody is a PhD student at Duke University. Her interests are infectious disease ecology, determinants of zoonotic disease transmission, the human impact on disease dynamics, and improving pandemic prediction systems, all from a One Health context. She believes all living beings have a right to good health and safety. Welcome, Melody!

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## North Carolina and the South

### **Rapid Increase and Seroprevalence of *Borrelia burgdorferi* Antibodies among Dogs, Northwestern North Carolina, USA, 2017-2021**

We evaluated spatial-temporal risk for Lyme disease in northwestern North Carolina, USA, by using individual-level canine *Borrelia burgdorferi* seroprevalence data collected during 2017–2021 at routine veterinary screenings for tickborne diseases. Seroprevalence in dogs increased from 2.2% (47/2,130) in 2017 to 11.2% (339/3,033) in 2021. The percentage of incident seropositivity increased from 2.1% (45/2,130) in 2017 to 7.6% (231/3,033) in 2021. Exploratory geographic analyses found canine seroprevalence shifted from clustered (2017, Moran's I = 0.30) to dispersed (2021, Moran's I = -0.20). Elevation, slope, aspect, and forest land cover density were associated with canine seroprevalence within various household buffer regions in 2017. Slope was associated with seroprevalence at the household level in 2021. Results support the use of individual-level canine seroprevalence data for monitoring human risk for Lyme disease. Establishing sentinel veterinary clinics within Lyme disease–emergent communities might promote prevention and control efforts and provide opportunities for educational and behavioral interventions.

Pretsch, P.K., et al.; *Emerging Infectious Diseases* (2024); <https://doi.org/10.3201/eid3010.240526>

**Summary:** monitoring seroprevalence of *Borrelia burgdorferi* – the causative agent of Lyme disease – in dogs can also tell us about the risk of Lyme disease for humans.

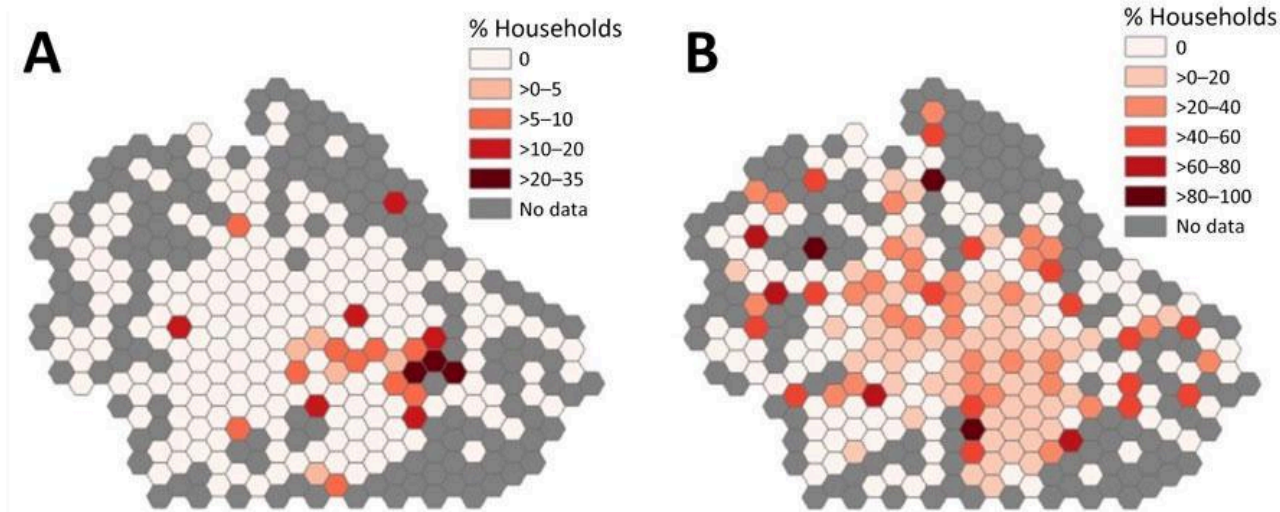


Figure: hexagons indicate percentage of households with dogs positive for *B. burgdorferi* in 2017 (A) and 2021 (B).

## Evidence of Human Bourbon Virus Infections, North Carolina, USA

Bourbon virus is a tickborne virus that can cause human disease. Cases have been reported in Kansas, Oklahoma, and Missouri, USA. We identified Bourbon virus–specific neutralizing antibodies in patients from North Carolina. Bourbon virus infections are likely more common than previously thought, highlighting the need for improved diagnostics and surveillance.

Zychowski, D.L., et al.; *Emerging Infectious Diseases* (2024); <https://doi.org/10.3201/eid3011.240499>

**Summary:** Bourbon virus has been identified for the first time in North Carolina, and more research is needed to gauge the true burden and spread of this disease.

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## National Section

### H.R.9382 – Alpha-gal Allergen Inclusion Act

In August of 2024, Representative Van Drew introduced the Alpha-gal Allergen Inclusion Act (AGAIA), which would amend the Federal Food, Drug, and Cosmetic Act to add alpha-gal to the definition of “major food allergen.” This would require foods, drugs, and cosmetics containing alpha-gal to disclose its presence.

## **Visual dysfunction and sudden onset symptoms leading to early detection of tick-borne infections: A case report**

### **Objectives**

Tick-borne infections frequently impact the visual system; however, their symptoms are commonly misinterpreted as issues related to functional vision disorders, balance, movement, and cognition. Visual symptoms may include blurred vision, double vision, photosensitivity, perception of distorted space, visual strain, headaches during near vision activities, difficulties with balance, dizziness, reduced ability to bring the eyes together (convergence), inability to maintain focus, and inability to tolerate movement in peripheral vision.

### **Case report**

This case report highlights a patient who presented with learning difficulties and behavioral issues. After a comprehensive neuro-optometric evaluation, specific ocular findings were observed, prompting suspicion of tick-borne disease. Subsequent comprehensive blood work for Lyme and associated diseases confirmed a diagnosis of tick-borne infection.

### **Conclusion**

Early detection and diagnosis of tick-borne infections pose significant challenges. Often referred to as “the great mimicker,” these infections frequently result in misdiagnosis or redirection during the medical pursuit of a definitive diagnosis. Failure to diagnose and treat promptly during the acute phase may lead to chronic neurologic progression of the undiagnosed disease.

Sayyed, A.I., Padula, W.V.; *IJID One Health* (2024); <https://doi.org/10.1016/j.ijidoh.2024.100036>

**Summary:** The impact of tick-borne infections on vision is underdiagnosed, as it is often attributed to other causes. This case study details a patient whose visual symptoms were caused by tick-borne infection.

## **Alpha-gal Syndrome Presenting as Fibromyalgia in an American Indian Population**

From January 2021 to January 2024, we studied a total of 301 patients diagnosed with FMS at our Rheumatology service. The diagnosis of FMS was made by applying the 2016 criteria from the American College of Rheumatology.<sup>1</sup> AGS was diagnosed based upon classic historical delayed allergic reactions to non-primate mammalian products including flesh/meat (beef, pork, venison, lamb), medications, personal products, etc., plus an elevated serum level (>0.1 IU/mL) of IgE antibody to alpha-gal.<sup>2</sup>

Of these 301 FMS patients, 33 had concomitant AGS. Their baseline clinical characteristics are shown in Table 1. The main demographic features were: 100% American Indian (AI) race, 90% male gender, age range 25–70 years (mean age 45 years). Only 10 out of the 33 patients were able to remember a tick bite (attached) within the preceding 5-year period. Eleven of the 33 patients had tolerated mammalian flesh for several years following tick exposure before developing FMS and concurrent AGS. On a plant-based nutrition plan and by avoiding exposure to mammalian-meat-derived products, the symptoms of FMS abated completely within 1–3 months in all 33 patients. All 33 patients now carry an epinephrine pen at hand for incidental exposure to the allergen.

Kaushik, P., Suresh, S., and Alexander, C.S.; *Indian Journal of Rheumatology* (2024); <https://doi.org/10.1177/09733698241276710>

**Summary:** This letter to the editor describes the screening of patients diagnosed with fibromyalgia for alpha-gal syndrome, and how lifestyle alterations helped get rid of these patients' symptoms.

## **Exposure of American Black Bears (*Ursus americanus*) to Ticks, Tick-borne Diseases, and Intestinal Parasites in Wisconsin**

We surveyed 159 American black bears (*Ursus americanus*) over a period of three years for the occurrence of ticks, tick-borne diseases, and intestinal parasites in Wisconsin. We collected blood from the bears to test for the presence of antibodies to *Borrelia burgdorferi* (Lyme disease), *Rickettsia rickettsii* (Rocky Mountain spotted fever (RMSF)), *Babesia*, *Ehrlichia*, *Ehrlichia canis*, *Brucella canis*, and *Anaplasma phagocytophilum*. We also examined scat samples for intestinal parasites. We commonly found the tick *Dermacentor variabilis*, but also present the first report of *Rhipicephalus sanguineus* on black bears. We detected antibodies to Lyme disease and RMSF. We detected antibodies to *E. canis* for the first time in a bear and both antibodies to *R. rickettsii* and *A. phagocytophilum* for the first time in a black bear in Wisconsin. No antibodies for *Babesia* or *Br. canis* were detected. We found eggs of the intestinal parasite *Baylascaris transfuga* as well as a low number of *Toxascara leonina* and unknown *Capillaria* species occurrences in the examined feces.

Reichert, N.S., et al.; *Diversity* (2024); <https://doi.org/10.3390/d16090537>

**Summary:** Humans are not the only animals that deal with ticks and tick-borne infections. This paper describes the ticks found on bears and tick-borne pathogens in them, some of which had never been observed before in bears.

## **Tick-Borne Diseases in America's National Parks: Observations and Recommendations for Improved Public Health**

Lyme disease case reports approach nearly half a million annually in the United States, but the true extent of all tick-borne disease cases is largely unknown. Outside of the Northeast, and in areas where Americans enjoy camping, hiking, and back-backing, such as the U.S. National Parks, risk assessment using human disease reports is challenging given the lack of local vs travel-acquired data at the county level. The use of multimodal data sets, including canine serological reports and established tick presence is needed to advance knowledge regarding potential disease risk. This brief report serves as a discussion starter, noting known disease and tick presence while highlighting inconsistencies and patterns for future evaluation.

Maxwell, S.P.; *Zoonotic Diseases* (2024); <https://doi.org/10.3390/zoonoticdis4030019>

**Summary:** The United States' National Parks could potentially be a source of tick bites and tick-borne infections; more research needs to be done to assess the risk they present.

# **A Review of Force Health\* Protection Aspects of Lyme Disease in the U.S. Military**

## **Introduction**

Lyme disease (LD) is an underrated threat to the military that negatively impacts mission readiness. Lyme disease has traditionally been thought to only be a risk in an operational context, where training or deployments are frequently conducted in heavily wooded environments. However, this view diminishes risks posed by many off-duty outdoor recreational activities. Furthermore, although the Army introduced a permethrin factory-treated Army Combat Uniform in 2012, permethrin retention and subsequent protection have been shown to decrease significantly after 3 months of wear. Thus, although LD is a known health risk that threatens unit readiness, beyond using treated uniforms there has been little progress at the unit level to address this threat.

## **Materials and Methods**

Focusing on a narrative review of LD and its impact on U.S. military force health protection, sources included DoD websites and policies, government press releases and information papers from sources like the CDC and FDA, and scholarly peer-reviewed journals with full-text access from the online databases EBSCOhost, MEDLINE, SCOUT, and Google Scholar. Searches included the following key words: LD and military, Army, etiology, epidemiology, incidence, treatments, post-treatment LD, and chronic LD. Articles were selected for review based on the relevance of their abstracts and titles.

## **Results**

Although the incidence of LD appears to be increasing among service members, it is difficult to attribute this increase to military-related duties. Also, despite ongoing LD research specifically conducted and funded by the DoD, there are limited data on the mitigating effects of force education and permethrin-treated uniforms on the LD threat. Therefore, it is reasonable to conclude that LD negatively impacts military readiness and monetary costs diverted from other priorities.

## **Conclusion**

Lyme disease poses a genuine threat to the health and careers of service members and is an often-overlooked disruptor to military operations. Simple, feasible prevention strategies that are tailored to high-risk geographic regions can be emphasized by military units to reduce the incidence of on-duty and off-duty cases. Additionally, there remains a critical need for new preventative and diagnostic measures for LD.

Melanson, V.R., et al.; *Military Medicine* (2024); <https://doi.org/10.1093/milmed/usae415>

\**Force health protection* (FHP) is the practice of preventing injuries and disease to keep the military's strength and capabilities intact. It's a critical priority for the Department of Defense and is intended to ensure that all members of the military are physically and mentally fit to perform their missions.

**Summary:** Lyme disease is a known infectious disease threat to service members. More information on whether military duties affect risk of Lyme disease, and how to protect and diagnose service members, is needed.

## **The Spread of Lone Star Ticks (*Amblyomma americanum*) and Persistence of Blacklegged Ticks (*Ixodes scapularis*) on a Coastal Island in Massachusetts, USA**

When a species expands its geographic range, it may displace similar species in the new region. In the northeastern USA, lone star ticks (*Amblyomma americanum*) have encroached on the range of blacklegged ticks (*Ixodes scapularis*), becoming more numerous in a wide range of habitats. Both species carry human disease agents, and both rely heavily on white-tailed deer (*Odocoileus virginianus*) for reproduction. We used 1265 yard surveys conducted in 2011–2024 to document the timing and pattern of lone star tick establishment on the island of Martha’s Vineyard (MV), Massachusetts. Increases in lone star ticks coincided with new cases of ehrlichiosis and reports of the alpha gal syndrome “red meat” allergy. To provide an index of current tick abundance, we used drag sampling to quantify the numbers of each tick species per kilometer of trail at 14 study sites on eastern MV where both species have coexisted for a decade. Lone star ticks are now ubiquitous at the study sites, while blacklegged ticks are persisting at relatively high levels in the woods. We conclude that the risk of human exposure to pathogens carried by blacklegged ticks remains high and is complemented by additional health risks associated with lone star ticks.

Johnson, R.W., et al.; *Insects* (2024); <https://doi.org/10.3390/insects15090709>

**Summary:** Both blacklegged and lone star ticks are now present in high levels on Martha’s Vineyard which has historically been the territory of blacklegged ticks, which leads to an overlap in the risks associated with both ticks.

## **Neuroborreliosis Presenting as Urinary Retention: Case Report**

Lyme disease is a tick-borne infectious disease caused by the spirochete *Borrelia burgdorferi*. Voiding dysfunction is a rare manifestation of neuroborreliosis with only a few cases reported. Here we describe a case of a 6-year-old male child with an acute urinary retention, paraparesis, and voiding difficulty in whom neuroborreliosis was diagnosed through serologic tests for antibodies, Western blot testing confirmation and intrathecal antibody synthesis. Magnetic resonance imaging (MRI) of the spine led to the diagnosis of acute transverse myelitis and a urodynamic study demonstrated detrusor areflexia. He received a 4-week course of intravenous ceftriaxone (2 g/d). The patient has recovered from the paraparesis but still suffers from a neurogenic bladder.

Ribeiro, Mário, et al.; *Journal of Child Neurology* (2024); <https://doi.org/10.1177/08830738241292843>

**Summary:** Urinary retention – or difficulty emptying the bladder – is a rare symptom of neuroborreliosis, or a systemic infection by *Borrelia* bacteria that affects the central nervous system. In this case study, doctors describe a case of a child experiencing urinary retention from confirmed neuroborreliosis.

## **Modeling spatiotemporal dynamics of *Amblyomma americanum* questing activity in the central Great Plains**

Ticks represent important vectors of a number of bacterial and viral disease agents, owing to their hematophagous nature and their questing behavior (the process in which they seek new hosts). Questing activity is notably seasonal with spatiotemporal dynamics that needs to be understood in detail as part of mediating and mitigating tick-borne disease risk. Models of the geography of tick

questing activity developed to date, however, have ignored the temporal dimensions of that behavior; more fundamentally, they have often not considered the sampling underlying available occurrence data. Here, we have addressed these shortfalls for *Amblyomma americanum*, the most commonly encountered tick in the central Great Plains, via (1) detailed, longitudinal sampling to characterize the spatiotemporal dimensions of tick questing activity; (2) randomization tests to establish in which environmental dimensions a species is manifesting selective use; and (3) modeling methods that include both presence data and absence data, taking fullest advantage of the information available in the data resource. The outcome was a detailed picture of geographic and temporal variation in suitability for the species through the two-year course of this study. Such models that take full advantage of available information will be crucial in understanding the risk of tick-borne disease into the future.

Cobos, M.E., et al.; *PLoS One* (2024); <https://doi.org/10.1371/journal.pone.0304427>

**Summary:** Questing activity – or when ticks search for new hosts to feed on – is associated with seasonality. This study produces a detailed image of questing behavior that can improve understanding of tick-borne disease risk over time.

## **Surveillance of tick-borne pathogens present in ticks (Acari: Ixodidae) removed from companion animals in Louisiana, USA**

Current knowledge of tick distribution and tick-borne pathogen presence across Louisiana is limited. Collaborating with veterinarians across the state, ticks removed from companion animals were recovered and assessed for the presence of zoonotic pathogens. A large number of ticks (n = 959) were removed from companion animals and subsequently screened using qPCR for *Anaplasma phagocytophilum*, *Babesia microti*, *Borrelia burgdorferi*, *Bartonella henselae*, *Ehrlichia chaffeensis*, and spotted fever group *Rickettsia*. Five different tick species, *Ixodes scapularis* (54.5%), *Amblyomma americanum* (18.4%), *Amblyomma maculatum* (12.5%), *Dermacentor variabilis* (11.2%), and *Rhipicephalus sanguineus* (0.3%) from different regions of Louisiana were collected from October 2018 to July 2019. There were 15 PCR-positive ticks for *Rickettsia parkeri* (1.6% prevalence), and four ticks were positive for *Ehrlichia chaffeensis* (0.4% prevalence). This survey identifies ticks and tick-borne pathogens associated with companion animals and areas for future active surveillance.

Valdes, S.M., et al.; *Journal of Medical Entomology* (2024); <https://doi.org/10.1093/jme/tjae122>

**Summary:** Monitoring of the kinds of tick-borne pathogens found in pets can be a useful way to conduct tick-borne disease surveillance and assess human risk of disease.



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## International Section

### **Current and emerging approaches for eliminating *Borrelia burgdorferi* and alleviating persistent Lyme disease symptoms**

Lyme disease is the most prevalent tick-borne infection caused by *Borrelia burgdorferi* bacteria in North America. Other *Borrelia* species are predominately the cause of this disease in Eurasia with some distinct and various overlapping manifestations. Consequently, caution must be exercised when comparing the disease and its manifestations and treatment regimens in North America and Europe. Diagnosis of the early Lyme disease remains difficult using the currently FDA approved serological tests in the absence of a reported tick bite or of erythema migrans in many individuals, non-specific initial symptoms, and the absence of detectable anti-*Borrelia* antibodies in the prepatent period of infection. Furthermore, it is difficult to distinguish persistence of infection and disease versus reinfection in the endemic regions of Lyme disease by serological assays. If early infection remains untreated, spirochetes can disseminate and could affect various organs in the body with a variety of disease manifestations including arthralgias and musculoskeletal pain, neurologic symptoms and anomalies, and acrodermatitis chronica atrophicans (ACA) in Europe. Although most patients recover after antibiotic treatment, an estimated ~10–20% patients in the United States show persistence of symptoms known as post-treatment Lyme disease syndrome (PTLDS). The causes and biomarkers of PTLDS are not well-defined; however, several contributing factors with inconsistent degree of supporting evidence have been suggested. These include antigenic debris, dysregulation of immunological response, bacterial persisters, or combination of these features. This review highlights currently employed treatment approaches describing different antimicrobials used, and vaccine candidates tried to prevent *B. burgdorferi* infection.

Zafar, K., Azuama, O.C., Parveen, N.; *Frontiers in Microbiology* (2024); <https://doi.org/10.3389/fmicb.2024.1459202>

**Summary:** This paper reviews treatments and vaccines that have been tried to reduce the symptoms associated with chronic Lyme disease.

### **Global risk dynamics of *Borrelia miyamotoi* in the context of climate change**

The impact of *Borrelia miyamotoi* on human health, facilitated by the expanding geographical distribution and increasing population of Ixodes ticks, remains obscure in the context of global climate change. We employed multiple models to evaluate the effect of global climate change on the risk of *B. miyamotoi* worldwide across various scenarios. The habitat suitability index of four primary vector tick species for *B. miyamotoi*, including *Ixodes persulcatus*, *Ixodes ricinus*, *Ixodes pacificus* and *Ixodes scapularis*, was projected using a boosted regression tree model, considering multiple shared socio-economic pathway scenarios over various time periods. The modelling analysis reveals that, apart from *I. scapularis*, future global warming will result in a northward shift in the other three vector tick species and a gradual reduction in suitable habitats. Random forest models indicate consistent changes in *B. miyamotoi* and its primary tick species, with potential risk areas shrinking and shifting northward, particularly in the eastern USA, northeastern and northern Europe and northeast Asia. These findings highlight the urgent need for enhanced active surveillance of *B. miyamotoi* infection in primary vector tick species across projected potential risk areas. The effect of climate change on *B.*

miyamotoi distribution might have significant implications for public health decision-making regarding tick-borne pathogens.

Tang, T., et al.; *Environmental Microbiology* (2024); <https://doi.org/10.1111/1462-2920.70000>

**Summary:** When modeling global climate change, *Borrelia miyamotoi* and its primary vectors show changes in their high-risk areas, which may have implications for risk of transmission and public health.

## **Tick-Borne Diseases and Pregnancy: A Narrative Review Evaluating Pregnancy Complications Caused by Tick-Borne Diseases**

Ticks are vectors of public health concern because the pathogens they transmit can cause detrimental diseases in humans. Lyme disease, tick-borne relapsing fever, human granulocytic anaplasmosis, Rocky Mountain spotted fever, tick-borne encephalitis, Crimean-Congo hemorrhagic fever, and babesiosis are some of the most common diseases caused by the pathogens transmitted by ticks. The overlap between human activities and tick habitats is growing, contributing to an increase in tick-borne disease cases. Unfortunately, pregnancy as a risk factor for tick-borne diseases is largely ignored. In this narrative review we use case reports, epidemiological studies, and animal studies to evaluate the maternal, pregnancy, and fetal outcomes caused by Lyme disease, tick-borne relapsing fever, human granulocytic anaplasmosis, Rocky Mountain spotted fever, tick-borne encephalitis, Crimean-Congo hemorrhagic fever, and babesiosis during pregnancy.

Curtis, M.W., Lopez, J.E.; *Tropical Medicine and Infectious Disease* (2024); <https://doi.org/10.3390/tropicalmed9110254>

**Summary:** There is not much information about how pregnancy and tick-borne diseases interact, and more research is needed.

## **Conceptual Framework for Community-Based Prevention of Brown Dog Tick-Associated Rocky Mountain Spotted Fever**

Rocky Mountain spotted fever (RMSF) is a severe tickborne disease that can reach epidemic proportions in communities with certain social and ecologic risk factors. In some areas, the case-fatality rate of brown dog tick-associated RMSF is up to 50%. Because of the spread of brown dog tick-associated RMSF in the southwestern United States and northern Mexico, the disease has the potential to emerge and become endemic in other communities that have large populations of free-roaming dogs, brown dog ticks, limited resources, and low provider awareness of the disease. By using a One Health approach, interdisciplinary teams can identify communities at risk and prevent severe or fatal RMSF in humans before cases occur. We have developed a conceptual framework for RMSF prevention to enable communities to identify their RMSF risk level and implement prevention and control strategies.

Brophy, M.K., et al.; *Emerging Infectious Diseases* (2024); <https://doi.org/10.3201/eid3011.240293>

**Summary:** Prevention and control of Rocky Mountain Spotted Fever in the United States and Mexico can be enhanced by including disease prevention methods among dogs.

## Incidence of hospitalizations related to Lyme disease and other tick-borne diseases using Discharge Abstract Database, Canada, 2009-2021

To estimate rates of hospitalizations for tick-borne diseases (TBDs) in Canada, retrospective analysis was conducted to determine the incidence of patients diagnosed with TBDs during their hospital stay in Canada, and describe demographic characteristics, temporal trends and geographic distributions, from 2009 through 2021. Codes from the International Classification of Diseases, Tenth Revision (ICD-10-CA) were used to capture diagnoses of TBDs in the Discharge Abstract Database (DAD) in Canadian hospitals. From 2009 through 2021, 1,626 patients were diagnosed with TBDs during their hospital stay. Of these, 1,457 were diagnosed with Lyme disease (LD), 162 with other TBDs, and seven were diagnosed with more than one TBD. Annual hospitalization counts for LD showed a significant increase from 50 in 2009 to 259 in 2021 (incidence rate per 100,000 population of 0.1 and 0.7, respectively). Epidemiologic patterns for hospitalized LD cases, including increases and variation in annual incidences, seasonality, demographics and geographic distribution, are consistent with those elucidated in national LD surveillance data. Amongst 162 patients diagnosed with other tick-borne diseases, discharge diagnoses were: rickettsiosis (32.7%), spotted fever due to *rickettsia rickettsii* (23.5%), tularemia (21.0%), babesiosis (8.6%), other tick-borne viral encephalitis (6.2%), tick-borne relapsing fever (4.9%), and Colorado tick fever (0.6%). Annual incidence increased only for rickettsiosis from 3 to 12 patients over the study period. Monitoring the data of hospitalizations using the DAD provided insights into the burden of emerging TBDs, the severity of illnesses and the population most at risk.

Gasmi, S., et al.; *PLoS One* (2024); <https://doi.org/10.1371/journal.pone.0312703>

**Summary:** Monitoring hospital discharge data is a useful way to gauge the burden of tick-borne diseases, the severity of illness, and which populations may be most at risk.

## Understanding *Ixodes ricinus* occurrence in private yards: influence of yard and landscape features

**Background:** Lyme borreliosis is the most frequent zoonotic disease in the northern hemisphere and is transmitted by ticks of the genus *Ixodes*. Although many people are bitten by ticks in private yards, our understanding of the factors associated with their presence in these areas remains limited. To address this gap, we used a citizen science approach to identify the local and landscape features associated with tick presence in yards.

**Methods:** This study was conducted near Nancy, a city in northeastern France, from 2020 to 2022. Citizen scientists collected ticks in their yard on a single event ( $n = 185$ ) and measured 13 yard features. Additionally, we computed 11 features related to the landscape composition and spatial configuration surrounding these yards. Using generalized linear mixed models, we determined the yard and landscape features associated with the presence of ticks and nymphal *Ixodes ricinus* (hereafter nymphs), the life stage, and species that mostly bite humans.

**Results:** Despite a low density, ticks were found in 32% of the yards, including yards in urbanized areas. At the transect level, the likelihood of finding a nymph was nearly three times higher in transects shaded by vegetation compared to those in open areas, with no relationship between nymph occurrence and transect location or grass height. At the yard level, the occurrence of ticks and nymphs was related to both yard and landscape characteristics. Nymph and tick occurrence were more than

twice as high in yards with signs of deer and a wood/brush pile compared to those without these characteristics, and increased with the connectivity of vegetation areas and the percentage of forest areas in the landscape.

**Conclusions:** Our study reveals that private yards across an urbanization gradient are locations of tick exposure with tick presence linked to both yard and landscape factors. These findings emphasize the importance of public awareness regarding tick exposure in yards and provide crucial insights for future public health prevention campaigns.

Mazaleyrat, A., et al.; *International Journal of Health Geography* (2024); <https://doi.org/10.1186/s12942-024-00380-9>

**Summary:** Suburban and urban landscapes have an impact on tick ecology, and a better understanding of this relationship helps us better assess risk of tick-borne disease.

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## Molecular Section

### Is Alpha-Gal an Emerging Allergen in Drug Allergy?

Galactose-alpha-1,3-galactose (alpha-gal) is a ubiquitous singular oligosaccharide and a relevant emergent allergen, first reported in 2008, which caused severe and even fatal allergic reactions to drugs such as the monoclonal antibody cetuximab. This article reviews the literature on drugs containing alpha-gal and on drugs acting such as compounding-factors in alpha-gal allergy and the concomitant risk of anaphylaxis, from the last 15 years.

Martínez-Arcediano, A. et al.; *Curr Treat Options Allergy* (2024); <https://doi.org/10.1007/s40521-024-00371-y>

**Summary:** The lone star tick can cause people to develop an allergy to alpha-gal, a carbohydrate found in most mammals. This can lead to allergic reactions when eating red meats. Many drugs also contain alpha-gal, so we may observe a rise in allergic reactions to drugs as tick bite incidence increases as well.

### Vaccination to Prevent Lyme Disease: A Movement Towards Anti-Tick Approaches

Lyme disease is caused by the spirochete, *Borrelia burgdorferi*, which is transmitted by *Ixodes* spp ticks. The rise in Lyme disease cases since its discovery in the 1970s has reinforced the need for a vaccine. A vaccine based on *B burgdorferi* outer surface protein A (OspA) was approved by the Food and Drug Administration (FDA) several decades ago, but was pulled from the market a few years later, reportedly due to poor sales, despite multiple organizations concluding that it was safe and effective. Newer OspA-based vaccines are being developed and are likely to be available in the coming years. More recently, there has been a push to develop vaccines that target the tick vector instead of the pathogen to inhibit tick feeding and thus prevent transmission of tick-borne pathogens to humans and wildlife reservoirs. This review outlines the history of Lyme disease vaccines and this movement to anti-tick vaccine approaches.

Johnson, E.E., Hart, T.M., Fikrig, E.; *The Journal of Infectious Diseases* (2024); <https://doi.org/10.1093/infdis/jiae202>

**Summary:** While there are vaccines developed and in development against *Borrelia burgdorferi*, which causes Lyme disease, there is a move to develop vaccines that prevent ticks from biting in the first place.

## **Natural selection and recombination at host-interacting lipoprotein loci drive genome diversification of Lyme disease and related bacteria**

Lyme disease (also called Lyme borreliosis in Europe), a condition caused by spirochete bacteria of the genus *Borrelia*, transmitted by hard-bodied *Ixodes* ticks, is currently the most prevalent and rapidly expanding tick-borne disease in the United States and Europe. *Borrelia* interspecies and intraspecies genome comparisons of Lyme disease-related bacteria are essential to reconstruct their evolutionary origins, track epidemiological spread, identify molecular mechanisms of human pathogenicity, and design molecular and ecological approaches to disease prevention, diagnosis, and treatment. These Lyme disease-associated bacteria harbor complex genomes that encode many genes that do not have homologs in other organisms and are distributed across multiple linear and circular plasmids. The functional significance of most of the plasmid-borne genes and the multipartite genome organization itself remains unknown. Here we sequenced, assembled, and analyzed whole genomes of 47 *Borrelia* isolates from around the world, including multiple isolates of the human pathogenic species. Our analysis elucidates the evolutionary origins, historical migration, and sources of genomic variability of these clinically important pathogens. We have developed web-based software tools (BorreliaBase.org) to facilitate dissemination and continued comparative analysis of *Borrelia* genomes to identify determinants of human pathogenicity.

Akther, S., et al.; *mBio* (2024); <https://doi.org/10.1128/mbio.01749-24>

**Summary:** While most of the genetic structure of *Borrelia* species across the world is fairly similar, there is some variation among genes related to infection that can lead to diversification among the genus and variation in its effects on humans.

## ***Rickettsia rickettsii* subsp. *Californica* subsp. Nov., the etiologic agent of Pacific Coast tick fever**

The etiologic agent of Pacific Coast tick fever (PCTF), a moderately severe tickborne illness that resembles Rocky Mountain spotted fever (RMSF), was first isolated in 1966 from specimens of *Dermacentor occidentalis* (the Pacific Coast tick) obtained in California. For several decades, this bacterium was identified ambiguously as the unclassified spotted fever group *Rickettsia* species 364-D, *Rickettsia* 364, or *Rickettsia philipii*. However, none of these epithets satisfied criteria of formal bacterial nomenclature. Data developed from mouse serotyping studies performed 45 years ago, and multi-locus sequence typing several decades later, indicated that this bacterium was similar to, but distinct from isolates of *Rickettsia rickettsii*, the etiological agent of RMSF. We applied an integrative taxonomic approach, combining phenotypic, ecological, and clinical data with whole genome sequencing of 11 contemporary isolates of this pathogen to identify it as a distinct subspecies of *R. rickettsii*, and propose the name *Rickettsia rickettsii* subsp. *californica* subsp. nov.

Paddock, C.D., et al.; *The Journal of Infectious Diseases* (2024); <https://doi.org/10.1093/infdis/jiae512>

**Summary:** Scientists have finally identified the specific agent that causes Pacific Coast tick fever, which has historically been classified alongside other spotted fever *Rickettsia* species but is actually its own subspecies.

## **PCR Detection of *Bartonella* spp. and *Borrelia* spp. DNA in Dry Blood Spot Samples from Human Patients**

Lyme disease is the most commonly reported vector-borne disease in the United States. *Bartonella* constitute an additional zoonotic pathogen whose public health impact and diversity continue to emerge. Rapid, sensitive, and specific detection of these and other vector-borne pathogens remains challenging, especially for patients with persistent infections. This report describes an approach for DNA extraction and PCR testing for the detection of *Bartonella* spp. and *Borrelia* spp. from dry blood spot (DBS) specimens from human patients. The present study included extraction of DNA and PCR testing of DBS samples from 105 patients with poorly defined, chronic symptoms labeled as Lyme-Like Syndromic Illness (LLSI). *Bartonella* spp. DNA was detected in 20/105 (19%) and *Borrelia* spp. DNA was detected in 41/105 (39%) patients with LLSI. Neither group of organisms was detected in DBS samples from 42 healthy control subjects. *Bartonella* spp. 16S–23S rRNA internal transcribed spacer sequences were highly similar to ones previously identified in yellow flies, lone star ticks, a human patient from Florida, mosquitoes in Europe, or *B. apihabitans* and *chladocola* strains from honeybees. These human strains may represent new genetic strains or groups of human pathogenic species of *Bartonella*. The 41 *Borrelia* spp. *flaB* gene sequences obtained from human patients suggested the presence of four different species, including *B. burgdorferi*, *B. americana*, *B. andersonii*, and *B. bissettiae/carolinensis*-like strains. These results suggest that specific aspects of the DBS DNA extraction and PCR approach enabled the detection of *Bartonella* spp. and *Borrelia* spp. DNA from very small amounts of human whole blood from some patients, including specimens stored on filter paper for 17 years.

Clark, K.L., Hartman, S; *Pathogens* (2024); <https://doi.org/10.3390/pathogens13090727>

**Summary:** Diagnosis of tick-borne diseases can be difficult, but PCR from dry blood spots (DBS) can make the process easier given that DBS can yield results from very small amounts of blood and can be stored for many years.



*TIC-NC is grateful for the financial contributions of Insect Shield International, LLC.*



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