Tick-Borne Infections Council of North Carolina, Inc.

NEWSLETTER 2023, Volume 3

Free Screening of Lyme Documentary *The Quiet Epidemic* in Durham Next Month (November 14)

There will be a special, free screening of the award-winning documentary feature film *The Quiet Epidemic* at the Carolina Theater of Durham on Tuesday, November 14, at 7:00 PM. This event is hosted by Denise Spector in honor of the beloved Dr. Neil Spector, who is one of the main subjects of the film. You can watch the film's trailer here.

The post-screening discussion will feature Bill Rawls, MD (local Lyme-literate healthcare provider), David Alcorta, Ph.D. (Research scientist, Duke University), Ed Breitschwerdt, DVM (Infectious diseases expert, NC State University), and **TIC-NC**'s own Scientific Adviser Marcia Herman-Giddens, PA, MPH, DrPH (UNC Chapel Hill). The panel will be moderated by the film's co-directors Lindsay Keys and Winslow Crane-Murdoch.

This event is free to attend with an RSVP on Eventbrite.

See more about the film under the TIC-NC Activities section.

Highlights

- **20%-30% of black-legged ticks in Ashe County, NC are infected with Lyme disease bacteria**
- **NC study showing tick bites as a factor in alpha-gal allergy**

- **Pfizer Vaccine Report**
- **Fatal Case of Heartland Virus Disease- W Va/Maryland area**
- **Trends in Reported Babesiosis Cases — United States, 2011–2019**
- **Chronic Gastrointestinal Symptoms in Children from Alpha-gal**
- **White-tailed Deer Serum Kills the Lyme Disease Spirochete**
- **New York State Tick Blitz: harnessing community-based science**
- **Citizen Science Informs How Missourians Interact With Ticks**
- **Germany: Twelve times more cases of Lyme disease than official incidence**
- **From 2010-2018 more than 34,000 persons positive for alpha-gal**
- **Remission of paralysis from mixed tick-borne disease with long-term antibiotics and more**
- **Nomenclature for Human Infections Caused by Relapsing Fever *Borrelia***
- **Spotted fever group rickettsiae and *Anaplasma phagocytophilum* in *Borrelia burgdorferi sensu lato* seropositive individuals with or without Lyme disease**
- **Detection of *Ehrlichia muris eauclairensis* in Blacklegged Ticks in MA**
- **Portable immunosensor provides sensitive and rapid detection of *Borrelia burgdorferi* antigen in spiked blood**
- **Lone star ticks infected with Bourbon virus in New Jersey, USA**
- **Powassan virus persistence after acute infection**
- **Unexpected behavior: Adult blacklegged ticks found to be active in the summertime in Mississippi**

Link to Notice to Medical Providers from the State Department of Public Health on Lyme Disease and Rickettsial Diseases: "Annual Update on Diagnosis and Surveillance for Tickborne Diseases"

The state has started issuing only one letter. Please see the homepage of our website to access. www.tic-nc.org.
To look at the (state) NCDHHS's tick data, go to epi.dph.ncdhhs.gov/cd/diseases/ticks.html.

Case data for Lyme disease according to the CDC for North Carolina The CDC:

NC had 344 cases of reported Lyme disease in 2019.
NC had 264 cases of reported Lyme disease in 2020.
https://www.cdc.gov/lyme/datasurveillance/surveillance-data.html
Links to access Lyme and other tick-borne infections data from the CDC.
https://www.cdc.gov/lyme/datasurveillance/surveillance-data.html
Annual incidence. https://www.cdc.gov/lyme/datasurveillance/surveillance-data.html
https://wonder.cdc.gov/nndss/nndss_annual_tables_menu.asp
https://www.cdc.gov/lyme/datasurveillance/maps-recent.html
As of November 1, 2022, 2019 is the latest year for which there is Lyme disease data.
CDC: "More recent case counts are not publicly available at this time." (Accessed Nov 1, 2022.)

Where To Find CDC Case Definitions and their Statement that the Surveillance Case Definitions Are "not to be used as the sole criteria for establishing critical diagnosis"

Case Definition and Report Forms

The surveillance definition of Lyme disease was revised in January 2022.

See https://www.cste.org/resource/resmgr/ps/ps2021/21-ID-05_Lyme_Disease.pdf for the rationale behind the changes.

- ndc.services.cdc.gov/case-definitions/lyme-disease-2022/
- www.cdc.gov/lyme/resources/lymediseasecasereportform.pdf (for public health officials' use)
- **Note from the CDC:** *The categorical labels used here to stratify laboratory evidence are intended to support the standardization of case classifications for public health surveillance. The categorical labels should not be used to interpret the utility or validity of any laboratory test methodology.* Accessed and copied Nov16, 2022 at https://ndc.services.cdc.gov/case-definitions/lyme-disease-2022/

The surveillance definition of Rocky Mountain spotted fever/spotted fever rickettsiosis *was revised* in 2020.

- ndc.services.cdc.gov/case-definitions/spotted-fever-rickettsiosis-2020/

The Southeast Regional Center of Excellence in Vector-Borne Disease (SECVBD) will continue its vital work for another five years, thanks to renewed funding from the Centers for Disease Control and Prevention (CDC). See TIC-NC Newsletter Vol 2, 2023 for more details.
https://physician-news.umiamihealth.org/cdc-renews-funding-for-study-of-vector-borne-diseases/.

National Institutes of Health 2023:
https://www.nih.gov/news-events/news-releases/nih-awards-will-fund-post-treatment-lyme-disease-syndrome-research.

State tick research and/or reports

The 2019 tick borne disease surveillance summaries are now complete. You can view them at the bottom of the NC DHHS Epi Section Facts & Figures page, under Vector.

- https://epi.dph.ncdhhs.gov/cd/vector/LymeSurveillanceSummary2020.pdf
- https://epi.dph.ncdhhs.gov/cd/vector/SpottedFeverGroupRickettsiosisSurveillanceSummary2020.pdf

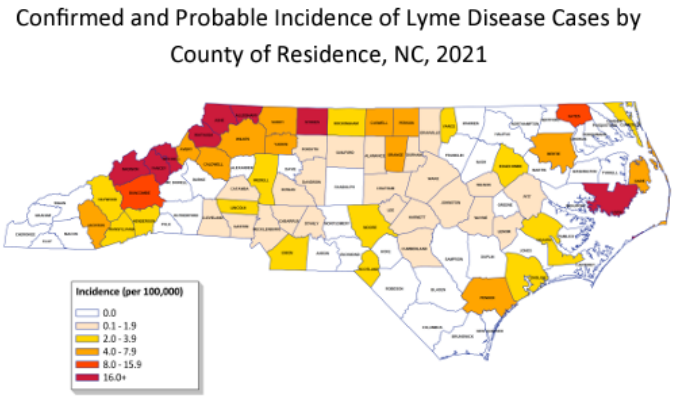
Note: By the *former* CDC definition, six counties had confirmed cases of Lyme disease in two persons who had not traveled out of the county for 30 days after their tick exposure. **Therefore, these counties were endemic for Lyme disease by the former CDC definition: Wake, Guilford, Haywood, Alleghany, Buncombe, and Wilkes.** Counties with one case of locally acquired Lyme disease were: Cleveland (2008), Wilson (2009), Pitt (2009), Carteret (2009), Gates (2011), Perquimans (2011), Rowan (2013), Union (2013), Caldwell (2013), Franklin (2014), Stanley (2014), Duplin 2014.

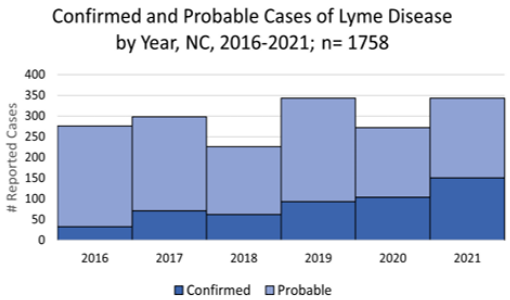
Vectorborne Disease Working Group (VBWG) meeting dates for 2023: None announced.

This group has not met since the beginning of the pandemic in 2020.

State tick research and/or reports

The 2021 tick-borne disease surveillance summaries are now complete. You can view them at the bottom of the NC DHHS Epi Section Facts & Figures page, under Vector
epi.dph.ncdhhs.gov/cd/lyme/LymeSurveillanceSummary2021.pdf





Note: Map is for 2021 only.

TIC-NC Activities

We are happy to announce a new volunteer for the western part of NC. Welcome to Sharon Stacy in **Boone**! She will start by distributing our booklets at her children's school.

TIC-NC Talks and Materials Distributed

Booklets:

Boone- school
-thanks to Janet Dooley
Pittsboro- AG Fest
Juneteenth County Fairgrounds
-thanks to Jennifer Platt
Hawbridge School Earth Day
-thanks to Jennifer Platt
Haw River bridge parking area
-thanks to TIC-NC

MORE ABOUT *THE QUIET EPIDEMIC* film

After years of living with mysterious symptoms, a young girl from Brooklyn and a Duke University scientist are diagnosed with a disease said to not exist: Chronic Lyme disease. *The Quiet Epidemic* follows their search for answers, which lands them in the middle of a medical controversy. What begins as a patient story evolves into an investigation into the history of Lyme disease, dating back to its discovery in 1975.

The Quiet Epidemic premiered at the prestigious Hot Docs Canadian International Documentary Festival in Toronto in Spring 2022, where it was voted into the Top 20 out of 200+ films. It has since been featured in 20 additional festivals (Hamptons Int'l Film Festival, DOC NYC, Woodstock Film Festival, Mill Valley Film Festival) and won five festival awards. *The Quiet Epidemic* qualified for the 2022 Academy Awards and had a successful limited theatrical run in early 2023.

North Carolina and the South

Dissertation from UNC-Greensboro that finds ~20%-30% of black-legged ticks in Ashe County, NC are infected with the Lyme disease bacteria

Role of topographic corridors and small mammals in facilitating the spread of Lyme disease from southwestern Virginia to northwestern North Carolina.
A Dissertation Submitted to the Faculty of The Graduate School at The University of North Carolina at Greensboro in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy

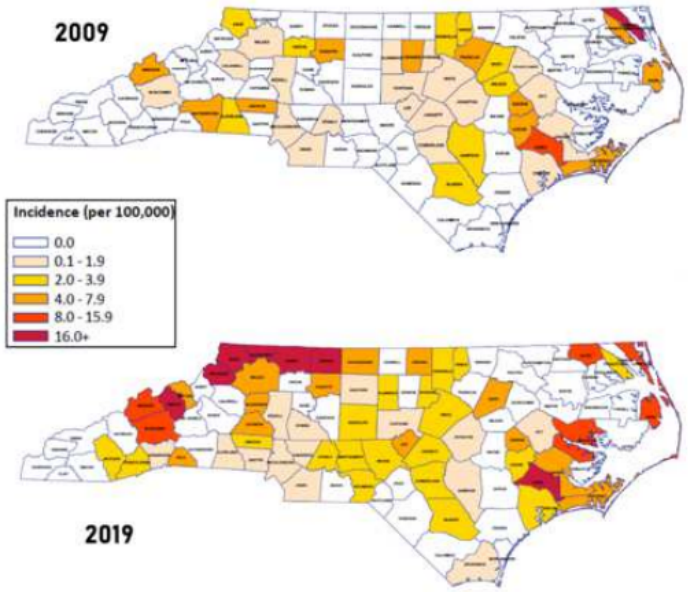
Lyme disease (LD) cases in Virginia are expanding southward into North Carolina. Recent studies have shown that the disease is following the southern Appalachian and Piedmont Mountain ranges, possibly because they provide suitable psychrophilic environments comparable to what is experienced in the Northeast. Although LD cases are rising in the New River Valley, there is little information on the vector and pathogen components associated with the rising cases in this area. Also, the role of geographic features along the path of the southward descent that may be facilitating the spread of the disease is unknown.

This study investigated the role of the New River as a potential corridor that may be facilitating Lyme disease spread from southwestern Virginia to northwestern North Carolina. Ixodes scapularis ticks were collected along the New River from Pulaski County in Virginia to Burke County in North Carolina, and at corresponding sites along the western Piedmont region from Bedford County in Virginia to Iredell County in North Carolina. A representative number of the collected ticks were screened for Borrelia burgdorferi to determine infection rates.

The results indicated that Alleghany County in North Carolina and its neighboring Ashe County were the current spots of peaked I. scapularis abundance and B. burgdorferi infection. The results indicated a hump-shaped north to-south distribution of the I. scapularis ticks as well as their B. burgdorferi infection rates. Noninfected I. scapularis ticks were detected further south than B. burgdorferi-infected I. scapularis, suggesting that the tick-first invasion mechanism is occurring. Higher densities of I. scapularis nymphs were found in the New River region compared to western Piedmont and had spread 23 further south along the New River compared to western Piedmont. Overall, the New River is facilitating the southward spread of I. scapularis and B. burgdorferi into western North Carolina.

GARSHONG, REUBEN AKWEI. Ph.D. (2022) Directed by Dr. Gideon Wasserberg. 152 pp.

Figure 6. Maps of 2009 and 2019 of LD cases in North Carolina showing a shift in the geographical distribution of confirmed and probable LD cases from a more eastern-central distribution to a clear cluster in northwestern counties of North Carolina (NC Division of Public Health, 2019).



NC study showing tick bites as a factor in alpha-gal allergy

Tick bite as a risk factor for alpha-gal–specific immunoglobulin E antibodies and development of alpha-gal syndrome

The disaccharide galactose-α-1,3-galactose (alpha-gal) is expressed in mammals other than humans, apes, and old-world monkeys. In humans, elevated immunoglobulin E (IgE) antibodies specific for alpha-gal can result in allergic hypersensitivity known as alpha-gal syndrome (AGS). Case reports and series suggest that tick bites can induce alpha-gal–specific IgE (sIgE) antibodies.

We conducted a case-control study comparing patients with AGS from a North Carolina allergy clinic with controls who were patients at a nearby internal medicine clinic. Cases and controls were administered a questionnaire to obtain information about demographics, home environment, outdoor activities, and recollection of tick bite. Serum samples taken at the time of enrollment were tested for total IgE, alpha-gal sIgE, and antibodies to other tick-borne pathogens.

The patients with AGS were more likely to recall finding a tick on themselves (odds ratio [OR], 11.20; 95% confidence interval [CI], 4.97-25.15), live near wooded forest (OR, 2.27; 95% CI, 0.92-5.55), and spend 17 or more hours per week outdoors in wooded areas (OR, 5.58; 95% CI, 2.56-12.19). The patients with AGS were also more likely to report 4 or more tick bites (OR, 33.05; 95% CI, 9.92-155.12) and reactions at the site of tick bites (OR, 7.93; 95% CI, 3.74-16.80). Furthermore, elevated alpha-gal sIgE level was observed in 33% of the controls and was associated with tick exposure in the controls (OR, 4.25; 95% CI, 2.21-8.18).

The results define tick bite as a risk factor for AGS and elevated alpha-gal sIgE level. Kersh GJ, et al. Annals of Allergy, Asthma, and Immunology, doi.org/10.1016.j.anai.2022.11.021.

Fatal Case of Heartland Virus Disease Acquired in the Mid-Atlantic Region, United States

Heartland virus (HRTV) disease is an emerging tickborne illness in the midwestern and southern United States. We describe a reported fatal case of HRTV infection in the Maryland and Virginia region, states not widely recognized to have human HRTV disease cases. The range of HRTV could be expanding in the United States. Liu S, et al. Emerg Infect Dis, doi: 10.3201/eid2905.221488.

Ticks and Tick-Borne Pathogens in Recreational Greenspaces in North Central Florida, USA

Tick-borne infections are an increasing medical and veterinary concern in the southeastern United States, but there is limited understanding of how recreational greenspaces influence the hazard of pathogen transmission. This study aimed to estimate the potential human and

companion animal encounter risk with different questing tick species, and the bacterial or protozoal agents they carry in recreational greenspaces.
We collected ticks bimonthly along trails and designated recreational areas in 17 publicly accessible greenspaces, in and around Gainesville, Florida, USA. We collected *Amblyomma americanum*, *Ixodes scapularis*, *Amblyomma maculatum*, *Dermacentor variabilis*, *Ixodes affinis*, and *Haemaphysalis leporispalustris*. Across the six tick species collected, we detected 18 species of bacteria or protozoa within the *Babesia*, *Borrelia*, *Cytauxzoon*, *Cryptoplasma (Allocryptoplasma)*, *Ehrlichia*, *Hepatozoon*, *Rickettsia*, and *Theileria* genera, including pathogens of medical or veterinary importance.

While tick abundance and associated microorganism prevalence and richness were the greatest in natural habitats surrounded by forests, we found both ticks and pathogenic microorganisms in manicured groundcover. This relationship is important for public health and awareness, because it suggests that the probability of encountering an infected tick is measurable and substantial even on closely manicured turf or gravel, if the surrounding landcover is undeveloped. The presence of medically important ticks and pathogenic microorganisms in recreational greenspaces indicates that public education efforts regarding ticks and tick-borne diseases are warranted in this region of the United States. Bhosale CR, et al. *Microorganisms* 2023, *11*(3), 756; https://doi.org/10.3390/microorganisms11030756.

From 2010-2018 more than 34,000 persons positive for alpha-gal

Diagnostic testing for galactose-alpha-1,3-galactose, United States, 2010 to 2018

Background: Alpha-gal syndrome (AGS) is an emerging immunoglobulin E (IgE)-mediated allergy to galactose-alpha-1,3-galactose (alpha-gal). The geographic distribution and burden of AGS in the United States are unknown.

Objective: To characterize alpha-gal IgE testing patterns and describe the trends and distribution from 2010 to 2018 in the United States.

Methods: This retrospective analysis included all persons tested for alpha-gal IgE antibodies by Viracor-IBT Laboratories (Lee's Summit, Missouri), the primary site of testing in the United States. Data included age and sex of person tested, specimen state of origin, collection date, and result value; persons with at least 1 positive test result (≥0.1 kU/L) were compared with negatives. Proportions tested and with positive test results were calculated using the US Census population estimates.

Results: Overall, 122,068 specimens from 105,674 persons were tested for alpha-gal IgE during July 1, 2010, to December 31, 2018. Nearly one-third (34,256, 32.4%) had at least 1 positive result. The number of persons receiving positive test results increased 6-fold from 1110 in 2011 to 7798 in 2018. Of those receiving positive test results, mean [SD] age was 46.9 (19.8) years; men were more likely to test positive than women (43.3% vs 26.0%). Arkansas, Virginia, Kentucky, Oklahoma, and Missouri had the highest number of persons who were tested and had a positive result per 100,000 population.

Conclusion: More than 34,000 persons, most presumably symptomatic, have received positive test results for IgE antibodies to alpha-gal, suggesting AGS is an increasingly recognized public health problem. The geographic distribution of persons who tested positive is consistent with exposure to Amblyomma americanum ticks. Binder AM, et al. Ann Allergy Asthma Immuno, doi: 10.1016/j.anai.2020.12.019.

Nomenclature for Human Infections Caused by Relapsing Fever *Borrelia*

To the Editor: Vazquez et al. report a convincing case of relapsing fever caused by *Borrelia lonestari* bacteria (*1*). This discovery highlights an existing problem with the nomenclature for relapsing fever.

Tick-borne relapsing fever (TBRF) is the name given to illness caused by several genospecies of relapsing fever *Borrelia* bacteria, all of which are transmitted by argasid (soft) ticks (*2*). The limitations of this term became apparent after discovery of *B. miyamotoi*, a related genospecies that is transmitted by ixodid (hard) ticks and causes illness that differs epidemiologically from traditional TBRF (*3*). Consequently, 3 terms are used in the scientific literature to describe *B. miyamotoi* infections: *Borrelia miyamotoi* disease, hard tick–borne relapsing fever, and hard tick relapsing fever (*3*,*4*). In the interest of standard nomenclature, it is worth considering objectively the relative merits of each term.

The term *Borrelia miyamotoi* disease (BMD) is problematic because it is species specific and cannot accommodate the discovery of related pathogens transmitted by ixodid ticks, including potentially *B. lonestari* (*1*,*3*). Disease names are most serviceable as umbrella terms that exist above the species level (e.g., Lyme disease, shigellosis).

The term hard tick–borne relapsing fever has a different problem, a grammatical one. The word hard rightly modifies tick, not tick-borne, which is a mode of transmission. This problem is solved by shortening to hard tick relapsing fever. The suffix "-borne" is not essential for clarity, as demonstrated by other established names (e.g., sand fly fever, Colorado tick fever) (*2*).

In the absence of a formal nomenclature decision by the World Health Organization, the following terms are consistent with precedent, epidemiologically useful, linguistically sensible replacements for TBRF: hard tick relapsing fever (HTRF) for illness caused by relapsing fever–clade *Borrelia* transmitted by ixodid ticks, and its congener, soft tick relapsing fever (STRF), for related agents transmitted by argasid ticks. Mead, PS. (2023). *Emerging Infectious Diseases*, *29*(5), 1084. https://doi.org/10.3201/eid2905.230195.

Lone star ticks (Acari: Ixodidae) infected with Bourbon virus in New Jersey, USA

Lone star ticks (*Amblyomma americanum* L.) are expanding within the northeast United States, a region historically focused on *Ixodes scapularis*-transmitted diseases. In Monmouth County, NJ, the shift has been dramatic, and lone star ticks now vastly outnumber blacklegged ticks. As a result, there is an enhanced need to focus on the potential health risks of *A. americanum*-transmitted pathogens, such as the emerging Heartland (HRTV) and Bourbon (BRBV) viruses.

We screened 1,205 nymphal lone star ticks for HRTV and BRBV using RT-qPCR assays and detected BRBV in 3 ticks collected in Monmouth County, NJ, in 2021. Additionally, we sequenced a complete BRBV genome from a single infected specimen, finding 99.4% identity with human pathogenic isolates from the eastern-central United States.

Our results have important public health implications for a region only recently becoming aware of public health risks posed by lone star ticks. Of note, we report successful detection of viral RNA in samples that were stored and intended for DNA preservation, for example, kept in ethanol at room temperature, which may reduce barriers for public health agencies seeking to expand their tick testing to include viruses. Egizi A, et al. *Journal of Medical Entomology*, doi.org/10.1093/jme/tjad052.

Chronic Gastrointestinal Symptoms in Children from Alpha-gal

Non-anaphylactic Variant of Alpha-gal Syndrome as an Etiology for Chronic Gastrointestinal Symptoms in Children

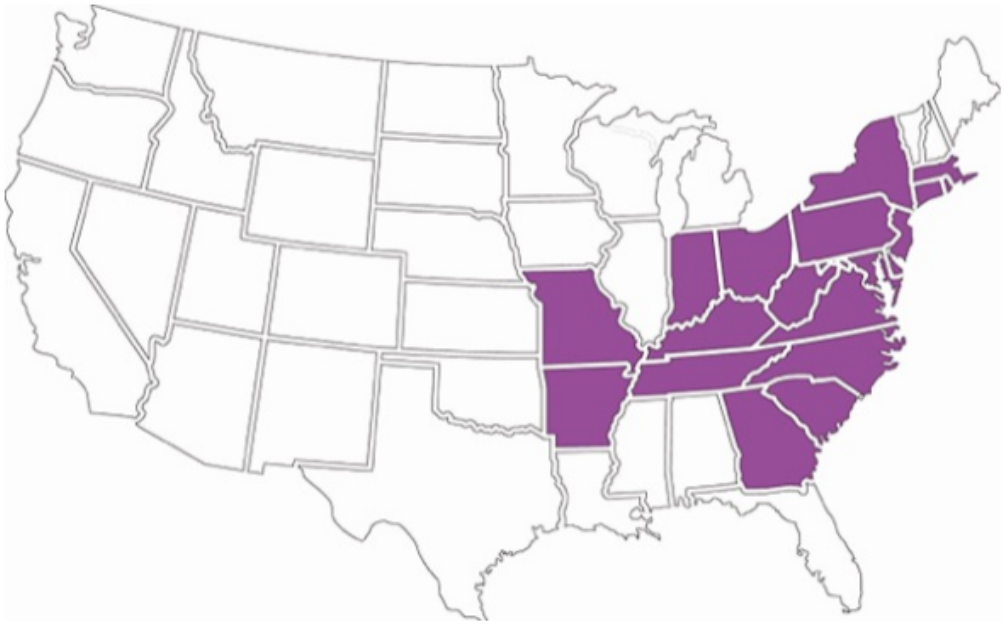
We report 3 pediatric patients who present with only non-anaphylactic symptoms of alpha-gal syndrome. This report highlights the necessity of not discounting alpha-gal syndrome from a differential diagnosis for patients with recurrent gastrointestinal distress and emesis after consuming mammalian meat, even in the absence of an anaphylactic reaction. Glynn D, et al. The Journal of Pediatrics, doi.org/10.1016/j.jpeds.

Asian Longhorn tick distribution

New Tick in Town

The Asian longhorned tick causes the loss of millions of dollars in agricultural revenue to cattle producers worldwide, and has been found in the United States, according to Maria Diuk-Wasser, PhD, a professor of ecology, evolution and environmental biology at Columbia University, in New York City.

Originally found in eastern Russia and the Australasian region, this tick was first found in the United States in 2017 in New Jersey. It has since reached the mid-Atlantic, New England and Midwestern regions of the United States, and now has been discovered in northern Missouri.



Where the Asian longhorned tick has been reported in the U.S., 2023. Source: CDC

Unexpected behavior: Adult blacklegged ticks found to be active in the summertime in Mississippi

Anomalous phenology of *Ixodes scapularis* (Ixodida: Ixodidae) in Mississippi

The blacklegged tick, *Ixodes scapularis* Say, is one of the most important vectors of tick-borne disease agents in North America. Accordingly, it is crucial to know this species local composition, abundance, and seasonality (phenology) to help prevent tick-borne illnesses. The phenology of adult *I. scapularis* is reported in the scientific literature from October through May. Data from previous research in Mississippi have all supported this time frame for adult blacklegged tick activity. However, in this study, we report a collection of 13 *I. scapularis* from 9 widely separated areas in Mississippi during the summer and early fall of 2022 (June, July, and September). These findings are remarkable, even enigmatic, and should prompt further investigation. Goddard J, et al. *Journal of Medical Entomology*, 22023, tjad081, https://doi.org/10.1093/jme/tjad081.

National Section

Valneva and Pfizer Report Positive Pediatric and Adolescent Phase 2 Booster Results for Lyme Disease Vaccine Candidate

- *Strong immune response shown in both children and adolescents one month after booster dose (month 19) in VLA15-221 study*
- *Previously observed high anamnestic antibody response in adults confirmed*
- *VLA15 well-tolerated in all age groups following booster dose*

Saint-Herblain (France) & New York, September 7, 2023 – Valneva SE (Nasdaq: VALN; Euronext Paris: VLA) and Pfizer Inc. (NYSE: PFE) announced today positive pediatric and adolescent immunogenicity and safety data for their Lyme disease vaccine candidate, VLA15, when given as a booster.
https://www.pfizer.com/news/announcements/valneva-and-pfizer-report-positive-pediatric-and-adolescent-phase-2-booster.

Remission of paralysis from mixed tick-borne disease with long-term antibiotics and more

Complete Remission in Paralytic Late Tick-Borne Neurological Disease Comprising Mixed Involvement of *Borrelia, Babesia, Anaplasma*, and *Bartonella*: Use of Long-Term Treatments with Antibiotics and Antiparasitics in a Series of 10 Cases

This study aimed to demonstrate that severe neurological motor deficits in the context of late tick-borne disease with mixed microorganism involvement are eligible for long-term combined antibiotic/antiparasitic treatments.

The inclusion criteria were: 1. neurological limb paralysis with a disability score >4 according to the EDSS Kurtzke disability scale; 2. serological tests pointing to an involvement of the main tick-borne microorganisms *Borrelia burgdorferi* s.l., *Babesia*, *Anaplasma*, and *Bartonella*; 3. a general disease for more than 6 months with fatigue, pain and subjective cognitive deficit. The patients were administered long-term treatments with repeated cycles (at least three) of 35-day IV ceftriaxone and repeated oral regimens of azithromycin–doxycycline and azithromycin–doxycycline–rifampicin. For *Babesia*, repeated courses of atovaquone–azithromycin were administered.

Ten patients had intractable or severe motor deficits before treatment in the context of *Borrelia* (two cases) *Borrelia–Babesia* (four cases), *Borrelia–Babesia–Anaplasma* (two cases), *Borrelia–Babesia–Anaplasma–Bartonella* (one case) and *Babesia–Anaplasma* (one case). For several months, five had been in wheelchairs, and four had been walking with sticks. Seven patients out of 10 (70%) showed complete remission after a mean active treatment duration of

20.1 + 6.6 months, with a mean number of 4 ceftriaxone cycles. Three patients showed an initial remission but suffered secondary antibiotic/antiparasitic-resistant motor recurrences.

Among the nine patients with *Borrelia* serologic positivity, treatments obtained complete remission in seven cases (77%). The findings of this ten-case series suggest the usefulness of long-term antibiotic/antiparasitic treatments in patients with severe late tick-borne neurological deficits with highly significant elements of tick-borne involvement. Trouillas P, Franck M. *Antibiotics* 2023, *12*(6), 1021; https://doi.org/10.3390/antibiotics12061021.

Blacklegged tick was first detected in Maine in the 1980s, now abundant in coastal areas

A citizen science approach to investigate the distribution, abundance, and pathogen infection of vector ticks through active surveillance

Tick-borne disease poses a growing public health burden in the United States and understanding the patterns of presence and density of infected vector ticks is key to developing and implementing effective public health management strategies. Citizen science has emerged as a highly effective means to generate data sets on the geographical distribution of tick species. But to date, nearly all citizen science studies of ticks are 'passive surveillance' programs in which researchers accept reports of ticks, together with either physical specimens or digital images, found opportunistically on people, pets, and livestock from community members for species identification and in some cases also tick-borne pathogen detection…

In this study, we engaged citizen scientists in 'active surveillance' of host-seeking ticks, training volunteers to actively collect ticks on their woodland properties in an emergent region of tick-borne disease in the state of Maine, USA. We developed volunteer recruitment strategies, materials to train volunteers in data collection methods, field data collection protocols based on techniques used by professional scientists, and a variety of incentives to promote volunteer retention and satisfaction with their experiences, and we communicated research findings to participants.

A total of 125 volunteers in 2020 and 181 volunteers in 2021 collected 7,246 ticks in southern and coastal Maine, including the American dog tick (Dermacentor variabilis, 4,023 specimens), the blacklegged tick (Ixodes scapularis, 3,092 specimens), and the rabbit tick (Haemaphysalis leporispalustris, 102 specimens). We demonstrated the feasibility of citizen scientists collecting ticks using active surveillance methods and found that volunteers were motivated to participate largely by their interest in the scientific problem and a desire to learn about ticks on their properties. Ballman ES, et al. Ticks and Tick-borne Diseases, https://doi.org/10.1016/j.ttbdis.2023.102144.

Detection of *Ehrlichia muris eauclairensis* in Blacklegged Ticks (*Ixodes scapularis*) and White-Footed Mice (*Peromyscus leucopus*) in Massachusetts

In 2011, *Ehrlichia muris eauclairensis* (EME) was described as a human pathogen spread by the blacklegged tick, *Ixodes scapularis*. Until very recently, its reported distribution was limited to the upper midwestern United States, mainly in Minnesota and Wisconsin. In this study, we report the detection of EME DNA in 4 of 16,146 human biting *I. scapularis* ticks submitted from Massachusetts to a passive tick surveillance program.

Active tick surveillance yielded evidence of EME local transmission in the northeastern United States through detection of EME DNA in 2 of 461 host-seeking *I. scapularis* nymphs, and in 2 white-footed mice (*Peromyscus leucopus*) of 491 rodent samples collected in the National Ecological Observatory Network (NEON) Harvard Forest site in Massachusetts. Xu G, et al. Vector Borne Zoonotic Dis, doi: 10.1089/vbz.2022.0098.

White-Tailed Deer Serum Kills the Lyme Disease Spirochete, *Borrelia burgdorferi*

Borrelia burgdorferi is a human pathogen vectored by *Ixodes* ticks and maintained in nature by a suite of competent vertebrate reservoirs. White-tailed deer (WTD) are considered to be noncompetent reservoirs for *B. burgdorferi*. Sera from other deer species have been found to be borreliacidal, and similar mechanisms could explain the lack of reservoir competence of WTD. Therefore, we determined whether WTD serum can kill *B. burgdorferi.* Using an *in vitro* serum sensitivity assay and subculturing of spirochetes, we demonstrated that WTD serum effectively kills *B. burgdorferi*. The borreliacidal activity of WTD serum likely contributes to the inability of WTD to efficiently harbor and transmit *B. burgdorferi*. Rich SM, et al. Vector-Borne and Zoonotic Diseases, doi.org/10.1089/vbz.2022.0095.

Trends in Reported Babesiosis Cases — United States, 2011–2019

During 2011–2019, U.S. babesiosis incidence significantly increased in northeastern states. Three states (Maine, New Hampshire, and Vermont) that were not considered to have endemic babesiosis had significantly increasing incidences and reported case counts similar to or higher than those in the seven states with known endemic transmission. Swanson M, et al. Morb Mortal Wkly Rep 2023;72:273–277. DOI: http://dx.doi.org/10.15585/mmwr.mm7211a1.

New York State Tick Blitz: Harnessing community-based science to understand range expansion of ticks

Ticks and tick-borne diseases are an immense public health burden in New York State (NYS), United States. Tick species and associated pathogens are expanding into new areas, shifting threats to human, and animal health across the state. For example, the invasive

tick, *Haemaphysalis longicornis* Neumann (Acari: Ixodidae), was first detected in the United States in 2017 and has since been identified in 17 states, including NYS. In addition, *Amblyomma americanum* (L.) (Acari: Ixodidae) is a native tick thought to be reestablishing historical populations in NYS.

We implemented a community-based science project called the "NYS Tick Blitz" to determine the distribution of *A. americanum* and *H. longicornis* in NYS. Community volunteers were recruited, provided with education, training, and materials to conduct active tick sampling during a 2-wk period in June 2021. Fifty-nine volunteers sampled 164 sites across 15 counties, for a total of 179 separate collection events and 3,759 ticks collected. The most frequently collected species was *H. longicornis*, followed by *Dermacentor variabilis* Say (Acari: Ixodidae), *Ixodes scapularis* Say (Acari: Ixodidae), and *A. americanum*, respectively. Through the NYS Tick Blitz collections, *H. longicornis* was identified for the first time in Putnam County.

We conducted pooled pathogen testing on a subset of specimens, with the highest rates of infection detected for pathogens transmitted by *I. scapularis*, including *Borrelia burgdorferi*, *Anaplasma phagocytophilum*, and *Babesia microti*. Most participants who completed a follow-up survey (n = 23, 71.9%) were promoters of the NYS Tick Blitz and 50% (n = 15) reported that they enjoyed participating in meaningful science. Foley N, et al. *Journal of Medical Entomology*, tjad039, https://doi.org/10.1093/jme/tjad039.

Two Insects, Two Bites, One Patient: A Lyme Disease and Jamestown Canyon Co-infection

Lyme disease (LD) is the most common tick-borne illness across the United States, caused by the bacterium Borrelia burgdorferi sensu lato and transmitted to humans by the bite of infected Ixodes ticks. Jamestown Canyon Virus (JCV) is an emerging mosquito-borne pathogen found mostly in the upper Midwest and Northeastern United States. Co-infection between these two pathogens has not been previously reported since it would require the host to be bitten by the two infected vectors at the same time.

We report a 36-yearold man who presented with erythema migrans and meningitis. While erythema migrans is a pathognomonic sign of early localized Lyme disease, Lyme meningitis does not occur in this stage but in the early disseminated stage. Furthermore, CSF tests were not supportive of neuroborreliosis, and the patient was ultimately diagnosed with JCV meningitis. We review JCV infection, LD, and this first reported co-infection to illustrate the complex interaction between different vectors and pathogens and to emphasize the importance of considering co-infection in people who live in vector-endemic areas. Weiler EN, et al. *Cureus*, doi: 10.7759/cureus.40222.

Overcoming the Challenges of Lyme Disease Diagnosis: The Role of Phage-based Testing

Preprint, not peer reviewed as of yet.
Tick-borne diseases are a growing concern worldwide, affecting both human and animal populations. Ticks are known to harbor a wide range of pathogens and are considered one of the most important vectors of disease. Lyme disease, caused by Borrelia burgdorferi sensu lato, is the most common tick-borne disease in the US and Europe.

However, accurate diagnosis of Lyme disease can be challenging due to the complex immune evasion strategies employed by Borrelia species and the limitations of existing diagnostic tests. To address this issue, researchers are exploring novel approaches, including the use of bacteriophages as diagnostic tools. Bacteriophages are highly specific and offer advantages over traditional methods for detecting bacteria, including Borrelia. In particular, the use of multicopy bacteriophages as molecular markers for Borrelia detection is a promising approach that may provide greater sensitivity than targeting single-copy bacterial genes. Nonetheless, the task of identifying trace amounts of bacteriophages in blood samples necessitates attention, and scientists are devising innovative techniques to surmount this hurdle.

In summary, employing bacteriophages as a diagnostic tool for tick-borne diseases, such as Lyme disease, by specifically targeting free circulating bacteriophages in blood samples, offers significant potential for enhancing patient outcomes and public health. Jia SJ et al. Preprints.org 2023. doi.org/10.20944/preprints202306.0816.v1Copy.

Citizen Science Informs How Missourians Interact with Ticks

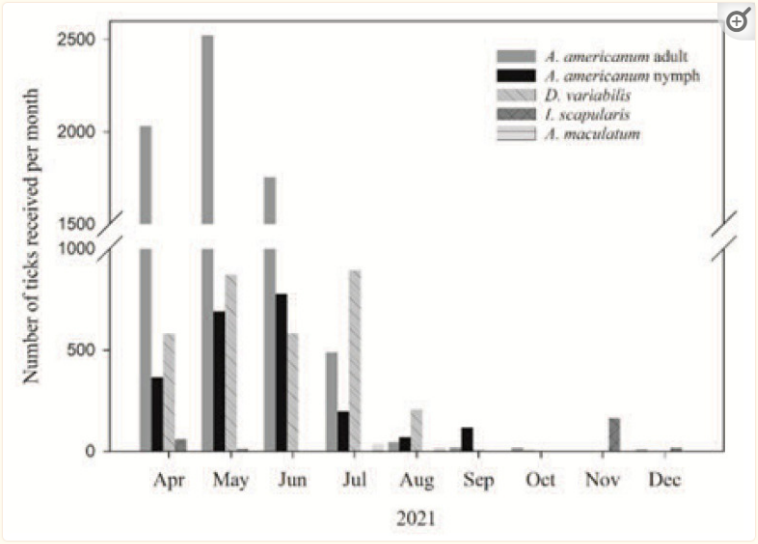


Figure 2

Seasonality of monthly tick submissions by tick species.

Understanding which tick species Missourians interact with and where exposures occur can help prevent and diagnose tickborne diseases. A statewide survey of ticks and tickborne pathogens was conducted using citizen science. Missourians submitted 12,819 ticks from April–December 2021. In total, 71% of ticks were Amblyomma americanum, and 89% were collected from a person or a pet. These preliminary data provide tick distributions at the county level and identify patterns of direct tick exposure to humans. Hudman et al. Mo Med. 2023 Mar-Apr; 120(2): 121–127.

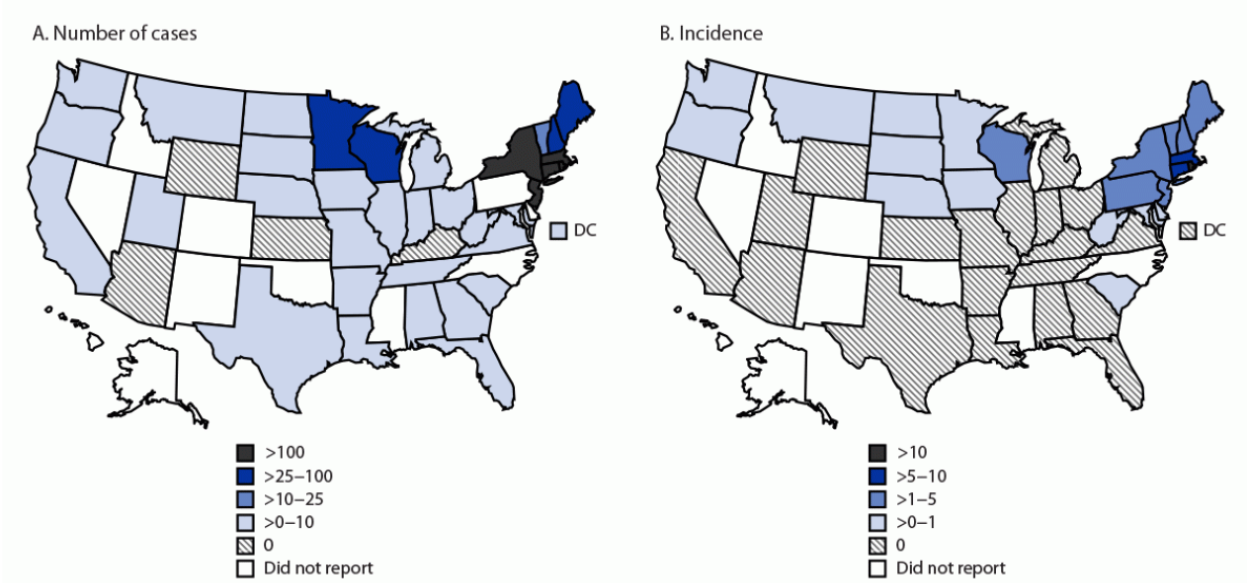
Understanding Habitats and Environmental Conditions of White-Tailed Deer

Population Density and Public Health Data to Aid in Assessing Human Tick-Borne Disease Risk

The extent of tick-borne diseases (TBDs) in the United States is largely unknown and underreported. Equitable diagnostic and treatment options may vary by geographic location. Triangulating multi-modal data sources informed by a One Health approach provides robust proxies for human TBD risk. Using data from the Indiana Department of Natural Resources collected from hunters during the white-tailed deer (*Odocoileus virginianus*) hunting season and other sources, we employ a mixed-methods approach based on thematic mapping and mixed effects modelling to determine if deer population density aligns with official disease data at the county level from (1) positive canine serological reports for, anaplasmosis, and Lyme Disease (LD); (2) positive human cases of ehrlichiosis, anaplasmosis, LD, and Spotted Fever rickettsioses; and (3) tick infectivity.

We propose the need for multimodal data analysis using a variety of potential proxies to better estimate disease risk and inform public health policy and practice. We find similar spatial distributions between deer population density and human and canine TBDs in northeastern and southern Indiana, which are rural and mixed geographic areas. Overall, LD is more prevalent in the northwest, central-western, and southeastern counties, while ehrlichiosis is more common in the southern counties. These findings hold true across humans, canines, and deer. Maxwell SP, et al. *Microorganisms* 2023, *11*(4), 865; https://doi.org/10.3390/microorganisms11040865.

FIGURE. Average number of reported babesiosis cases (A)* and average babesiosis incidence (B),† by state — United States, 2011–2019



Spotted fever group rickettsiae and *Anaplasma phagocytophilum* in *Borrelia burgdorferi sensu lato* seropositive individuals with or without Lyme disease: A retrospective analysis

The *Ixodes ricinus* tick is the main vector of *Borrelia burgdorferi* and tick-borne encephalitis virus in Switzerland. Spotted fever group Rickettsiae (SFG) and *Anaplasma phagocytophilum* have been detected in Swiss ticks, however, information about the extent and clinical presentation of these infections in humans is scant.

Indirect fluorescent antibody tests for SFG rickettsiae and *Anaplasma phagocytophilum* were performed on serum samples of 121 *Borrelia burgdorferi* seropositive patients with and without Lyme disease and 43 negative controls.

Out of 121 *Borrelia burgdorferi* seropositive individuals, 65 (53.7%) were seropositive for IgG and 15 (12.4%) for IgM antibodies to SFG rickettsiae. IgM antibodies were detected more frequently in early-than in late-stage of Lyme disease (12 out of 51 and 2 out of 49; respectively; $p = 0.0078$). Significantly higher IgG antibody titers against SFG rickettsiae were found in patients with late-stage compared to patients with early-stage Lyme disease (mean titer 1:261 and 1:129, respectively; $p = 0.038$). This difference was even more pronounced in patients with acrodermatitis chronica atrophicans compared to patients with early stage of Lyme disease (mean titer 1:337 and 1:129, respectively; $p = 0.009$).

In patients presenting with fatigue, headache and myalgia, the prevalence of IgG antibodies against SFG rickettsiae was significantly higher (7 out of 11; 63.6%) than in *Borrelia burgdorferi* seropositive individuals without clinical illness (1 out of 10; 10%; $p = 0.024$). IgG antibodies to *Anaplasma phagocytophilum* were detected in 12 out of 121 individuals (9.9%), no IgM antibodies were found.

Infections with SFG rickettsiae and *Anaplasma phagocytophilum* are underdiagnosed and should be ruled out after a tick bite. Further studies are needed to elucidate the possible causative role of SFG rickettsiae for myalgia, headache and long-lasting fatigue after a tick bite and to determine the necessity for an antibiotic treatment. Kosak L, et al. New Microbes and New Infections, doi.org/10.1016/j.nmni.2023.101139.

A portable immunosensor provides sensitive and rapid detection of *Borrelia burgdorferi* antigen in spiked blood

There are no assays for detecting *B. burgdorferi* antigen in blood of infected Lyme disease individuals. Here, we provide proof-of-principle evidence that we can quantify *B. burgdorferi* antigen in spiked blood using a portable smartphone-based fluorescence microscope that measures immunoagglutination on a paper microfluidic chip.

We targeted *B. burgdorferi* OspA to develop a working prototype and added examples of two antigens (OspC and VlsE) that have diagnostic value for discrimination of Lyme disease stage.

Using an extensively validated monoclonal antibody to OspA (LA-2), detection of OspA antigen had a broad linear range up to 100 pg/mL in 1% blood and the limit of detection (LOD) was 100 fg/mL (= 10 pg/mL in undiluted blood), which was 1000 times lower than our target of 10 ng/mL. Analysis of the two other targets was done using polyclonal and monoclonal antibodies. OspC antigen was detected at LOD 100 pg/mL (= 10 ng/mL of undiluted blood) and VlsE antigen was detected at LOD 1–10 pg/mL (= 0.1–1 ng/mL of undiluted blood).

The method is accurate and was performed in 20 min from sample to answer. When optimized for detecting several *B. burgdorferi* antigens, this assay may differentiate active from past infections and facilitate diagnosis of Lyme disease in the initial weeks of infection, when antibody presence is typically below the threshold to be detected by serologic methods. Kim S, Samanta K, Nguyen BT, *et al. Sci Rep* **13**, 7546 (2023). https://doi.org/10.1038/s41598-023-34108-9.

Powassan virus persistence after acute infection

Survivors of Powassan encephalitis often have persistent neurological disease. A new mouse model replicates some elements of the human disease and demonstrates the presence of viral RNA in the brain as well as myelitis more than 2 mo after the acute infection. The related tick-borne encephalitis and West Nile Neuroinvasive Disease (WNND) also have common neurological sequelae, and models for these better-studied diseases provide evidence for prolonged virus, RNA, and inflammation in some cases, in addition to damage from the acute encephalitic disease. A better understanding of the biological basis for persistent signs and symptoms after Powassan encephalitis, currently a rare disease, could benefit from further studies of the more prevalent flaviviral encephalitides. Telford SR & Piantadosi AL. mBio, 2023, doi: 10.1128/mbio.00712-23.

International Section

Neoehrlichia mikurensis in Danish immunocompromised patients: a retrospective cohort study

The tick-borne bacterium, *Neoehrlichia mikurensis (N. mikurensis)* can cause severe febrile illness and thromboembolic complications in immunocompromised individuals. We investigated the presence of *N. mikurensis* DNA in retrospectively collected plasma from a well-characterized cohort of Danish immunocompromised patients.

Plasma samples from 239 patients with immune dysfunction related to hematological or rheumatological disease or due to immunosuppressive therapy, were retrieved from a transdisciplinary biobank (PERSIMUNE) at Rigshospitalet, Copenhagen, Denmark. Serving as

immunocompetent controls, plasma samples from 192 blood donors were included. All samples were collected between 2015 and 2019. Real-time PCR targeting the *groEL* gene was used to detect *N. mikurensis* DNA. Sequencing was used for confirmation. *Borrelia burgdorferi* sensu lato IgG antibodies were detected by ELISA as a proxy of tick exposure. Prevalence was compared using Fisher's exact test.

Neoehrlichia mikurensis DNA was detected in 3/239 (1.3%, 95% confidence interval (CI): 0.3 – 3.6%) patients, all of whom primarily had a hematological disease. Follow-up samples of these patients were negative. *N. mikurensis* DNA was not detected in any of the blood donor samples. IgG antibodies against *B. burgdorferi* s.l. were detected with similar prevalence in immunocompromised patients and blood donors, i.e., 18/239 (7.5%, 95% CI: 4.8–11.5%) and 11/192 (5.7%, 95%: CI 3.2–10.0%).

In this study, patients with *N. mikurensis* were not identified by clinical indication and *N. mikurensis* may therefore be underdiagnosed in Danish patients. Further investigations are needed to explore the clinical significance and implications of this infection. Gynthersen RMM, et al. Ann Clin Microbiol Antimicrob. 2023 Mar 20;22(1):20. doi: 10.1186/s12941-023-00571-5.

Mild Infections with Multiple Spotted Fever Grouped *Rickettsia* Species among Forest Rangers with Tick Bites

Tick-borne rickettsiae are increasingly recognized to cause human infections; however, a complete clinical spectrum is lacking. Thus, surveillance study was conducted among forest rangers with tick bites to describe the clinical manifestations.

One hundred fifty-nine blood samples were obtained from individuals bitten by ticks and 780 tick samples collected in the same endemic region were examined for the presence of *Rickettsia*. Serum samples were tested for IgM and IgG antibodies against *R. heilongjiangensis*.

Twenty-five (15.7%) individuals were shown to be infected with 5 *Rickettsia* species, including 14 *Candidatus* Rickettsia tarasevichiae (CRT), 8 *R. raoultii*, 1 *R. felis*, 1 *R. heilongjiangensis*, and 1 *R. massiliae*. Five individuals (1 CRT, 1 *R. heilongjiangensis*, and 3 *R. raoultii*) had mild illnesses; the other 20 individuals were asymptomatic. CRT was present in 38.4% (274/713) of *I. persulcatus* and 6.4% (3/47) of *Hae. concinna*. *R. raoultii* was demonstrated in 30.0% (6/20) of *D. silvarum* and 14.9% (7/17) of *Hae. concinna*. *R. heilongjiangensis* was detected in 9.5% (2/21) of *D. silvarum* and 0.3% (2/713) of *I. persulcatus*.

The clinical manifestations of these rickettsioses were non-specific and differed from traditional features, thus supporting the necessity of wider investigations involving individuals with tick bites to develop an early differential diagnosis. Yong-Xiang Wu, et al. Zoonoses. doi:10.15212/ZOONOSES-2023-0010.

Germany: Twelve times more cases of Lyme disease than official incidence

Estimated number of symptomatic Lyme borreliosis cases in Germany in 2021 after adjusting for under-ascertainment

As a model for European countries that conduct LB surveillance, we sought to estimate the population-based incidence of symptomatic LB after adjusting for under-ascertainment.

Estimating seroprevalence-derived under-ascertainment relies on data from seroprevalence studies, public health surveillance, and published literature. The number of symptomatic LB cases in states that conduct LB surveillance was estimated from studies reporting the seroprevalence of antibodies against *Borrelia burgdorferi* sensu lato, the proportion of LB cases that are asymptomatic, and the duration of antibody detection. The number of estimated incident symptomatic LB cases was compared with the number of surveillance-reported LB cases to derive under-ascertainment multipliers. The multipliers were applied to the number of 2021 surveillance-reported LB cases to estimate the population-based incidence of symptomatic LB in Germany.

Adjusting for seroprevalence-based under-ascertainment multipliers, the estimated number of symptomatic LB cases in states that conducted surveillance was 129,870 (408 per 100,000 population) in 2021. As there were 11,051 surveillance-reported cases in 2021 in these states, these data indicate there were 12 symptomatic LB cases for every surveillance-reported LB case.

We demonstrate that symptomatic LB is underdetected in Germany and that this seroprevalence-based approach can be applied elsewhere in Europe where requisite data are available. Nationwide expansion of LB surveillance would further elucidate the true LB disease burden in Germany and could support targeted disease prevention efforts to address the high LB disease burden. Olsen JF, et al. Vector Borne Zoonotic Dis, 10.1089/vbz.2022.0051.

Citizen Science on Lyme Borreliosis in Spain Reveals Disease-Associated Risk Factors and Control Interventions

Lyme borreliosis (LB) caused by *Borrelia burgdorferi sensu* lato complex spirochetes is one of the tick-borne diseases with high prevalence and social/economic burden in the United States, Spain, and other European countries. The objective is to address limited information available about the incidence, prevalence, and symptoms of LB, current prevention, and treatment interventions that are not adequately focused and thus not very effective against this disease.

To address these limitations, in this study, we used a citizen science approach to evaluate the LB-associated risks and implementation of control interventions in Spain. A total of 405 participants in the survey were included in the analysis. Responses to the questionnaire were received during January—July 2022. The questionnaire contained qualitative and quantitative questions. Homogeneity among binary variables was analyzed using a Fisher's exact test.

Despite limitations of the study associated with response to the questionnaire and information on tick species, the results evidenced the effect of factors such as age, gender, tick bites, disease clinical signs, comorbidities such as alpha-gal syndrome, health care services, and treatment effectiveness affecting LB.

The main conclusions of the study highlight the need for better surveillance of tick infestations, pathogen infection, and diagnosis of LB and related comorbidities. To advance in disease prevention, diagnosis, and treatment, new interventions need to be developed and implemented in both public and private health care services. Providing access to these results to the society, health care system, and scientists is important to further advance in disease surveillance, diagnosis, control, and prevention. La Fuente et al. Vector-Borne and Zoonotic Diseases, https://doi.org/10.1089/vbz.2023.0016.

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Tick-Borne Infections Council of North Carolina is a non-profit 501(c)3 organization formed to improve the recognition, treatment, control, and understanding of tick-borne diseases in North Carolina. We are an all-volunteer organization and appreciate donations.

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