Tick-Borne Infections Council of North Carolina, Inc.

NEWSLETTER 2019, Volume 6

Quote: - The CDC disclaimer states:
"A surveillance case definition is a set of uniform criteria used to define a disease for public health surveillance. Surveillance case definitions enable public health officials to classify and count cases consistently across reporting jurisdictions. Surveillance case definitions are not intended to be used by healthcare providers for making a clinical diagnosis or determining how to meet an individual patient's health needs." July 2019

Highlights…

- **In Memoriam: Senator Kay Hagan has died from Powassan virus**
- **Frequent prescribed fires can reduce risk of tick-borne diseases**
- **Rhesus monkey brains and neurological Lyme disease**
- **Unusual drug to treat long-term Lyme disease being studied**
- **Survey: The staggering cost of Lyme disease**
- **Lyme disease infection induces bone loss in mice**
- **New technologies for Lyme diagnostics being investigated**
- **Seed ticks (lone star larvae) in New England**
- **Persistence of *Babesia microti* Infection in Humans**
- **MyLymeData Patient Registry Analysis**
- **Laboratory-confirmed Lyme disease rose in England and Wales over 3 years**
- **Tularemia: what do we know and not know?**
- **Ticks in Sweden affect recreation choices**

State Vector-Borne Disease Working Group 2019 Meeting Schedule

There are no further meetings in 2019.

Location:
Office of the Chief Medical Examiner Photo ID required.
4312 District Drive
Raleigh, NC 27607

In Memoriam: Senator Kay Hagan died October 28, 2019 from Powassan virus

Kay Hagan, a former senator from North Carolina who served one term in Washington, died at her home in Greensboro, N.C. She was 66. Her husband, Charles T. Hagan III, said she died of complications from a type of encephalitis, or brain inflammation, caused by the rare Powassan virus. The virus is transmitted to humans by blacklegged ticks. Mr. Hagan thinks she picked up the tick during a 2016 late November hike in northern Virginia. The New York Times article on her death is at: www.nytimes.com/2019/10/28/us/politics/kay-hagan-dead.html?

NC Health news article related to Hagan's death

TIC-NC is included in the discussion. Marcia E. Herman-Giddens was interviewed for the article. Entire article at: https://www.northcarolinahealthnews.org/2019/11/05/virus-from-tick-that-killed-former-sen-hagan-has-never-been-detected-in-n-c/

Some of the data shared for the article:
Source: epi.dph.ncdhhs.gov/cd/diseases/ticks.html
Reports are available at that link for disease incident summaries over five years, 2013 – 2018. Be aware that the cases reported and accepted as a report (many are screened out) represent the "tip of the iceberg" as far as the actual numbers go. The "probable" and "confirmed" case numbers are included in the accounts. Each disease has complicated criteria for meeting these definitions.
Some clinicians still do not realize that **Lyme disease** can be acquired in North Carolina. Case numbers for Lyme disease have been reported for many years. It is widely spread over the state but the hotspot now is the northwest corner of the state.

Spotted fever rickettsiosis (includes Rocky Mountains spotted fever) – 2013 to 2018 total 2,887.
Yearly average = about 600 cases
Ehrlichiosis – 2013 to 2018 –413 cases. Yearly average = 83
Lyme disease – 2013 two 2018 1381 cases. Yearly average = 276

Cases are reported by county of residence so a case does not always mean the person acquired the disease in their county or even the state. There have been no known reported cases of Powassan virus thus far in NC. Virginia has had at least one so it is probably a matter of time before we have it in NC. The vector tick for Powassan, the black-legged tick, is widely distributed across the state. Not all tick diseases and conditions are required to be reported.

North Carolina has six species of ticks that bite humans. All except the Asian longhorned are described on our website. Five species are known to transmit diseases to humans. The most recent tick is the

invasive Asian longhorned. It is not yet known whether it may transmit human pathogens in the future. To date, all longhorned ticks tested for pathogens have been negative. Fortunately, not all ticks are infected with human pathogens. See our website www.TIC-NC.org for more information.

The following tick-borne infections are known to be in ticks in North Carolina:

- Spotted fever rickettsiosis which includes Rocky Mountains spotted fever
- Lyme disease
- Borrelia miyamotoi
- Rickettsia parkeri (no common name)
- Southern tick associated rash illness (STARI)
- Ehrlichiosis
- Tularemia
- Anaplasma
- Heartland virus

Tick-borne conditions in North Carolina:

- Red meat allergy (also called alpha-gal)
- Tick paralysis
  (Bourbon virus and babesiosis are possibly in North Carolina but have not yet been officially identified.)

Link to Letter to Medical Providers from the State Department of Public Health on Lyme Disease and Rickettsial Diseases

The state has started issuing only one letter, accessible on our website at: http://tic-nc.org/wp-content/uploads/2019/06/TBD_memo_2019.pdf

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

- Lyme Disease Surveillance Case Definition (revised Jan 2017)
- Lyme Disease Surveillance Case Report FormCdc-pdf PDF – 2 pages] (for public health officials' use)

  Note: Surveillance case definitions establish uniform criteria for disease reporting and should not be used as the sole criteria for establishing clinical diagnoses, determining the standard of care necessary for a particular patient, setting guidelines for quality assurance, or providing standards for reimbursement.

  Accessed and copied 22 September 2019. https://www.cdc.gov/lyme/stats/forms.html

CDC: The Emerging Issues in Tickborne Diseases webinar, presented June 13, 2019, is now online.

State tick research and/or reports

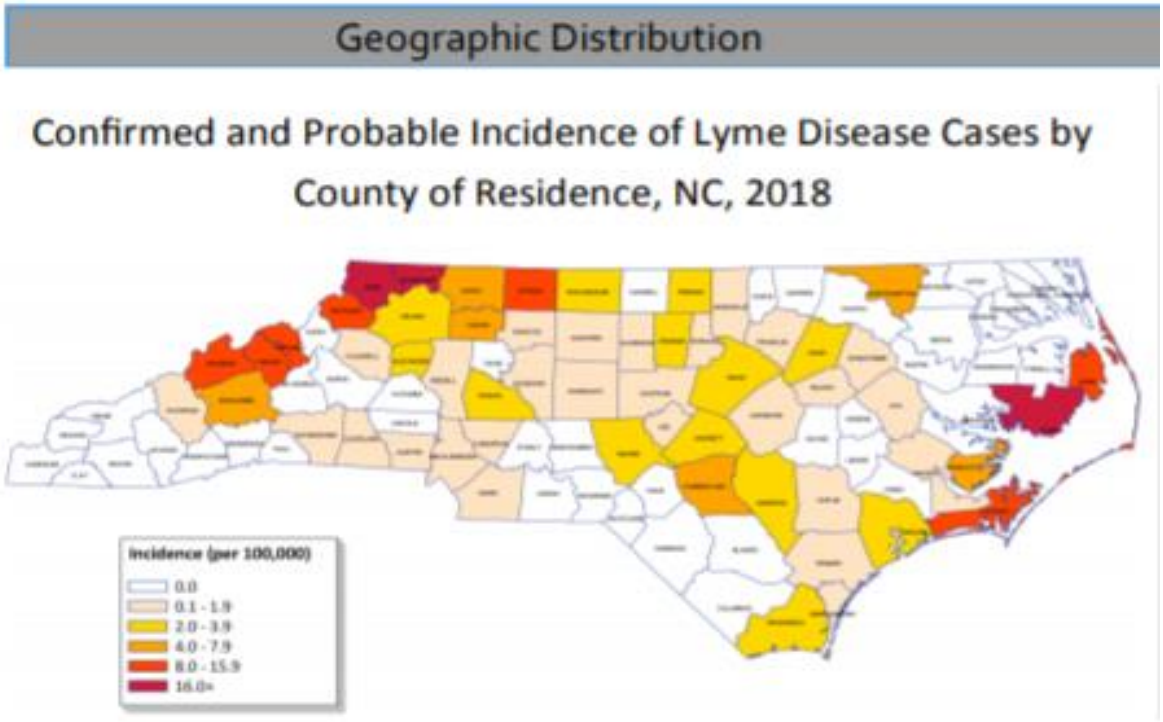
NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

ROY COOPER • Governor
MANDY COHEN, MD, MPH • Secretary
BETH LOVETTE • Interim Director, Division of Public Health

Developed by the North Carolina Division of Public Health, Communicable Disease Branch

Lyme Disease Surveillance Summary from 2013—2018

… North Carolina In the state of North Carolina, the number of confirmed and probable cases of Lyme disease has increased over the past five years. The highest incidence of Lyme disease in 2018 is clustered to the northwestern portion of the state, particularly in Ashe, Alleghany, Surry, Watauga, Wilkes, and Madison counties. The 5-year average incidence rate of Lyme disease in North Carolina between 2013-2017 was 2.30 confirmed and probable cases per 100,000 residents… .



For entire report see: epi.ncpublichealth.info/cd/lyme/LymeSurveillanceSummary2018.pdf
Ed note: This report fails to state that (1) most EM rashes from Lyme disease are solid red or red in the center and paler red toward the edge. They usually do *not* present as the so-called typical target or bull's eye lesion. This report also fails to state that (2) during the first few weeks of infection, whether or not the person has an erythema migrans rash, *the test is expected to be negative*. And, that if symptoms have been present for 30 days or less the provider may treat the patient and follow up with a convalescent serum.

1.Shapiro, ED. N Engl J Med 2014;370:1724-31. DOI: 10.1056/NEJMcp1314325 Although reputed to have a bull's-eye appearance, approximately two thirds of single erythema migrans lesions either are uniformly erythematous or have enhanced central erythema without clearing around it.

2. www.cdc.gov/lyme/diagnosistesting/labtest/twostep/index.html. Excerpted: Or in cases where the patient has had symptoms for less than or equal to 30 days, the provider may treat the patient and follow up with a convalescent serum. www.cdc.gov/lyme/faq/index.html. Excerpted: During the first few weeks of infection, such as when a patient has an erythema migrans rash, the test is expected to be negative.

NC TBIs 2017 final, 2018 probable/confirmed *C=confirmed*

Disease	Total Cases/Confirmed cases by year of report 2017†	Total preliminary confirmed and probable Events in NCEDSS created between 1/1/2018 - 8/9/2018*	Total Events Reviewed and closed by NC DPH 1/1/17 - 8/9/2018	Total Events Still Under Investigation by LHD 1/1/18 - 8/9/2018	Total Events created in NCEDSS 1/1/18 - 8/9/2018
Lyme Disease	298/71C	81/35C	530	102	632
RMSF	521/6C	418/6C	2039	282	2321
Ehrlichiosis	72/18C	51/8C	192	18	210
Anaplasmosis	10/4C	9/4C	29	4	33

* *Note 2018 data are preliminary*

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.

Report from the State Vector-Borne Disease Working Group meeting

NC TBIs 2017 final, 2018 to November probable/confirmed *C=confirmed*

NC EDSS Event Data – Cases Submitted to CDC

Disease	Total Cases / Confirmed Cases by year of report 2017	Total preliminary confirmed and probable Events in NC EDSS Created between 1/1/2018 – 11/13/2018*	Total Events Reviewed and closed by NC DPH 1/1/18 – 11/13/18	Total Events Still Under Investigation by LHD 1/1/18 – 11/13/18	Total Events created in NC EDSS 1/1/18 – 11/13/18
Lyme Disease	298/71C	177/51C	736	110	836
RMSF	521/6C	419/10C	2016	346	2362
Ehrlichiosis	72/18C	86/14C	331	54	398
Anaplasmosis	10/4C	4/0C	22	1	23

TIC-NC Activities

Volunteer Corner

Tami McGraw of Chatham County was part of a panel of guests at the commissioners North Carolina Food Safety held August 28 at the state fairgrounds. She spoke about alpha gal and distributed TIC-NC materials. Tami has also distributed materials to various places around Chatham County, especially veterinary clinics. Thank you, Tami!

TIC-NC Talks and Materials Distributed

Brochures/booklets/folletos:
Asheville area:
- **Several officers at the Court House**
- **A person at the Clerk of Deeds**
- **Ingles grocery store bulletin boards**
- **Dollar Store clerks**

Alamance County Piedmont Health Clinic
Northwood High School Chatham County
Pittsboro Animal Supply
Samantha's Pupusas
Ixtapa Mexican Restaurant

Talks:
- **Piedmont Health Clinics Inservice**

ᴎᴎ North Carolina and South ᴎᴎ

The CDC has created a new interactive RMSF training module to help healthcare providers recognize and diagnose RMSF. www.cdc.gov/rmsf/training/hcp/

We, at TIC-NC, are concerned that lone star ticks (Amblyomma americanum) are NOT included in the list of vectors for Rocky Mountain spotted fever. Even though they are uncommon vectors for RMSF, they can and have vectored the disease. This has occurred in NC. Lone stars are common and aggressive biters. In addition to their presence in the south, lone stars are now as far north as Maine and as far west as Nebraska. We have communicated our concern to the CDC and, to date, they have stated they have no plans to include lone stars as vectors even though research has shown that they are.

Frequent Prescribed Fires Can Reduce Risk of Tick-borne Diseases | Fires conducted in NW Florida and SW Georgia

Recently, a two-year study found that long-term prescribed fires significantly reduced tick abundance at sites with varying burn regimes (burned surrounded by burned areas [BB], burned surrounded by unburned areas [BUB], and unburned surrounded by burned areas [UBB]). In the current study, these ticks were tested for pathogens to more directly investigate the impacts of long-term prescribed burning on human disease risk.

A total of 5,103 ticks (4,607Amblyomma americanum, 76 Amblyomma maculatum, 383 Ixodes scapularis, two Ixodes brunneus, and 35 Dermacentor variabilis) were tested for Borrelia spp., Rickettsia spp., Ehrlichia spp., and Anaplasma phagocytophilum. Long-term prescribed fire did not significantly impact pathogen prevalence except that A. americanum from burned habitats had significantly lower prevalence of Rickettsia (8.7% and 4.6% for BUB and UBB sites, respectively) compared to ticks from control sites (unburned, surrounded by unburned [UBUB]) (14.6%).

However, during the warm season (spring/summer), encounter rates with ticks infected with pathogenic bacteria was significantly lower (98%) at burned sites than at UBUB sites. Thus, despite there being no differences in pathogen prevalence between burned and UBUB sites, risk of pathogen transmission is lower at sites subjected to long-term burning due to lower encounter rates with infected ticks. Gleim et al. Scientific Reports 2019 | doi.org/10.1038/s41598-019-46377-4

Standardized Ixodid Tick Survey in Mainland Florida

A statewide survey of questing ixodid ticks in mainland Florida was developed consistent with U.S. CDC standards to maximize the amount of epidemiologic and environmental data gathered. Survey sites were stratified by climatic zones and proportional to recognized land cover categories. A total of 560 transects on 41 sites within the state were sampled repeatedly by flagging between 2015 and 2018.

Four tick species were collected; Amblyomma americanum, Amblyomma maculatum, Ixodes scapularis and Dermacentor variabilis. All species were more commonly found in northern and central regions of the state than in southern and western regions. Adult I. scapularis were active from autumn through spring and complementary to adult A. americanum and D. variabilis. Standardized survey

methods help reduce sampling biases and better characterize risk from the species surveyed. However, differences in the attractiveness of collection methods for different tick species makes cross-species comparisons a continuing challenge. Glass et al. Insects, doi:10.3390/insects10080235.

Link for entomology activists from Entomology Today, a project of the Entomological Society of America

15 Ways to Get Involved at the State or Local Level

1. Attend town, city, or county council meetings. You don't have to attend every one, but stay informed and show up especially when important issues come up.

2. Write a letter to the editor. Or write an op-ed. Last week here at *Entomology Today*, my fellow entomologist and science advocate Helen Spafford, Ph.D., offered advice on getting your perspectives published.

3. Follow your legislators on social media to stay informed on current issues. This is a great way to track their activities and communicate with them remotely in real time. Yes, you can tweet at them!

4. Invite your legislators on a tour of your workplace. More about this later. The next post in our series on entomology advocacy will share suggestions for earning a visit from your legislators and making it count.

5. Track your legislators' voting records on sites such as Ballotpedia.org **or** OnTheIssues.org**.** If you approve of their vote on a given issue, it can't hurt to reach out to thank them. Much of the correspondence they receive from constituents is negative, so sending a positive message can help you foster a good relationship and act as positive reinforcement for "good behavior."

6. Show up to legislators' coffee hours, breakfasts, and other informal town halls. This can be a less-daunting approach than meeting at their legislative office, and it still gives you valuable face-time with decision-makers.

7. Attend a school board meeting. Don't have kids? Don't let that hold you back—everyone benefits from working toward ensuring that the students in your community are getting a top-notch education.

8. Plan a trip to the state capitol to discuss a particular issue. If possible, go as a group and show up in matching T-shirts (see photo at the top of this post). Don't underestimate the impact of demonstrating that you are a group unified for a common purpose.

9. Make yourself known as a go-to expert. After introducing yourself to a legislator or other politician, offer your availability as an authority on any entomology-related issue. Most politicians do not have a science advisor on staff, and many of them would be grateful to have access to one. Make sure to be responsive and non-confrontational in this role.

10. Join a committee, commission, task force, or working group. These groups often lack willing participants with the necessary background to make scientifically sound recommendations and could benefit greatly from your expertise.

11. Focus on local issues to foster greater connection. Local issues will resonate more strongly and are less likely to have controversy or partisanship associated with them, compared to issues on the national stage.

12. Practice your elevator pitch. It's vital to deliver a summary of your research in a concise and easily understood manner. Relatively few legislators and legislative staff have a science background, so remember to avoid jargon and stick to the main points. They are usually pressed for time; don't be surprised if they tune out after a few minutes' discussion, which is why it's important to start with the most important information you want to convey.

13. Circulate a petition. As every periodical cicada knows, there's strength in numbers. A petition demonstrates that a particular issue is important not just to you but to the broader community. By itself, a petition drive may not be a strong tactic, but in concert with other action items on this list it can help to get across an important idea.

14. Contact neighbors. Chances are, if you've made it this far down this list, you're already more involved in the process than many of your friends and neighbors are. Reach out to them to encourage them to follow your lead, particularly on quick, actionable items that can act as a "gateway" into greater advocacy efforts down the road.

15. Call your legislators to voice your opinion on issues. Calling is considered more impactful than email. Phone-shy? Don't worry, these calls typically take less than a minute. Simply give your name and say that you are a constituent (you may be prompted for ZIP code or full address), then briefly explain why you are calling. Legislative staff will probably take down your comment without asking for additional detail.
Entire document at: entomologytoday.org/2019/08/01/15-ways-advocate-entomology-local-state-level/

◘◘ National Section ◘◘

Clinical trials: Study looking at the use of an unusual drug to treat chronic/post treatment Lyme disease

Disulfiram: A Test of Symptom Reduction Among Patients with Previously Treated Lyme

Brief Summary:
Approximately 10-20% of patients experience ongoing symptoms despite having received standard antibiotic therapy for Lyme disease. Possible explanations for persistent symptoms include persistent infection and/or post-infectious causes. Recent in vitro studies indicate that disulfiram is effective at killing both the actively replicating and the more quiescent persister forms of Borrelia burgdorferi, the microbe that causes Lyme Disease. In this study, the investigators are examining the safety of disulfiram among patients with post-treatment Lyme disease symptoms. The investigators are also conducting a preliminary investigation regarding the relative benefit of 4 vs 8 weeks of treatment with disulfiram. clinicaltrials.gov/ct2/show/NCT03891667

Survey: The staggering cost of Lyme disease

MILPITAS, Calif., July 10, 2019 /PRNewswire/ -- Nearly 36 percent of patients with a tick-borne disease spent more than $10,000 on tests, treatments, appointments, and other costs associated with their disease, a new IGeneX survey found.

The survey analyzed the cases of 198 patients from 2018 and 2019 who were tested by IGeneX, a leading testing lab in California. Researchers sought to determine how long it took for patients to obtain a proper diagnosis, how many doctors they had visited, and how much financial impact they had ultimately incurred. According to the survey:

- 45% of patients needed more than three years to obtain the proper diagnosis
- 65% of patients were forced to quit a job or cut back on their hours due to their symptoms
- 24% of patients saw more than ten doctors before receiving a proper diagnosis
- 86% of patients suffer from long-term side effects from not having been diagnosed sooner

Entire story at: finance.yahoo.com/news/staggering-cost-lyme-disease-other-123600606.html

Human Seroprevalence of Tick-Borne *Anaplasma phagocytophilum*, *Borrelia burgdorferi*, and *Rickettsia* Species in Northern California

There is a paucity of data on human exposure to tick-borne pathogens in the western United States. This study reports prevalence of antibodies against three clinically important tick-borne pathogens (*Borrelia burgdorferi*, *Anaplasma phagocytophilum*, and *Rickettsia* spp.) among 249 people in five counties in northern California. Individuals from Humboldt County were recruited and answered a questionnaire to assess risk of exposure to tick-borne pathogens. Samples from other counties were obtained from a blood bank and were anonymized.

Seventeen (6.8%) samples were seropositive for antibodies against at least one pathogen: five for *A. phagocytophilum*, eight for *B. burgdorferi*, and four for *Rickettsia* spp. Women and people aged 26–35 had higher seroprevalence compared to other demographic groups. Santa Cruz County had no seropositive individuals, northern Central Valley counties had three seropositive individuals (all against *A. phagocytophilum*), and Humboldt County had 14 (all three pathogens), a significant, four-fold elevated risk of exposure.

The Humboldt County questionnaire revealed that a bird feeder in the yard was statistically associated with exposure to ticks, and lifetime number of tick bites was associated with increasing age, time watching wildlife, and time hiking. Three-quarters of respondents were concerned about tick-associated disease, 81.0% reported experiencing tick bites, and 39.0% of those bitten reported a tick-borne disease symptom, including skin lesions (76.4%), muscle aches (49.1%), joint pain (25.5%), or fever (23.6%).

Despite high levels of concern, many individuals who had been bitten by a tick were not tested for a tick-borne pathogen, including those with consistent symptoms. We highlight the need for further research and dissemination of information to residents and physicians in Northern California regarding tick-associated disease, so that appropriate medical attention can be rapidly sought and administered.
Pascoe et al. Vector-Borne and Zoonotic Diseases, doi.org/10.1089/vbz.2019.2489.

Stanford Weighs in on Lyme Disease

In Stand4Lyme Foundation's video, scientists tackle the Lyme disease Epidemic. Experts address the serious consequences of Lyme and tick-borne diseases, an increasing source of morbidity and mortality worldwide. Stand4Lyme makes a clear business case for pharmaceutical support and federal research funding to develop reliable diagnostic tools and accessible effective medical treatment. The goal of this video is to help educate all stakeholders from a scientific perspective and garner increased government support and funding. This is a 47 minute video from October 2018.
https://www.youtube.com/watch?v=0a3sBmleRQo&feature=youtu.be

Visiting New England next summer? Watch out for seed ticks (lone star larvae)!

Early Questing by Lone Star Tick Larvae, New York and Massachusetts, USA, 2018

Subtropical lone star tick larvae typically emerge in late summer. We found clusters of host-seeking lone star tick larvae during early June 2018 in New York and Massachusetts, USA. Invasion and persistence of this tick in more northern locations may have been promoted by adaptation to an accelerated life cycle. Telford, S. R., Buchthal, J., & Elias, P. (2019 *Emerging Infectious Diseases*, *25*(8), 1592-1593. https://dx.doi.org/10.3201/eid2508.181293.

Persistence of *Babesia microti* Infection in Humans

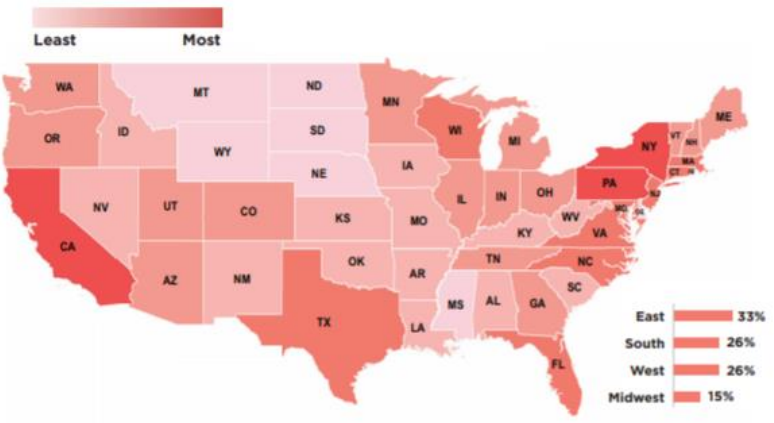
Persistent infection is a characteristic feature of babesiosis, a worldwide, emerging tick-borne disease caused by members of the genus *Babesia*. Persistence of *Babesia* infection in reservoir hosts increases the probability of survival and transmission of these pathogens. Laboratory tools to detect *Babesia* in red blood cells include microscopic detection using peripheral blood smears, nucleic acid detection (polymerase chain reaction and transcription mediated amplification), antigen detection, and antibody detection.

Babesia microti, the major cause of human babesiosis, can asymptomatically infect immunocompetent individuals for up to two years. Chronically infected blood donors may transmit the pathogen to another person through blood transfusion. Transfusion-transmitted babesiosis causes severe complications and death in about a fifth of cases. Immunocompromised patients, including those with asplenia, HIV/AIDS, malignancy, or on immunosuppressive drugs, often experience severe disease that may relapse up to two years later despite anti-*Babesia* therapy.

Persistent *Babesia* infection is promoted by *Babesia* immune evasive strategies and impaired host immune mechanisms. The health burden of persistent and recrudescent babesiosis can be minimized by development of novel therapeutic measures, such as new anti-parasitic drugs or drug combinations, improved anti-parasitic drug duration strategies, or immunoglobulin preparations; and novel preventive approaches, including early detection methods, tick-avoidance, and blood donor screening. Bloch et al. *Pathogens* **2019**, *8*(3), 102; https://doi.org/10.3390/pathogens8030102. Entire paper free of charge.

Highlights of MyLymeData Patient Registry Analysis of Phase 1 Data (November 2015-2016)

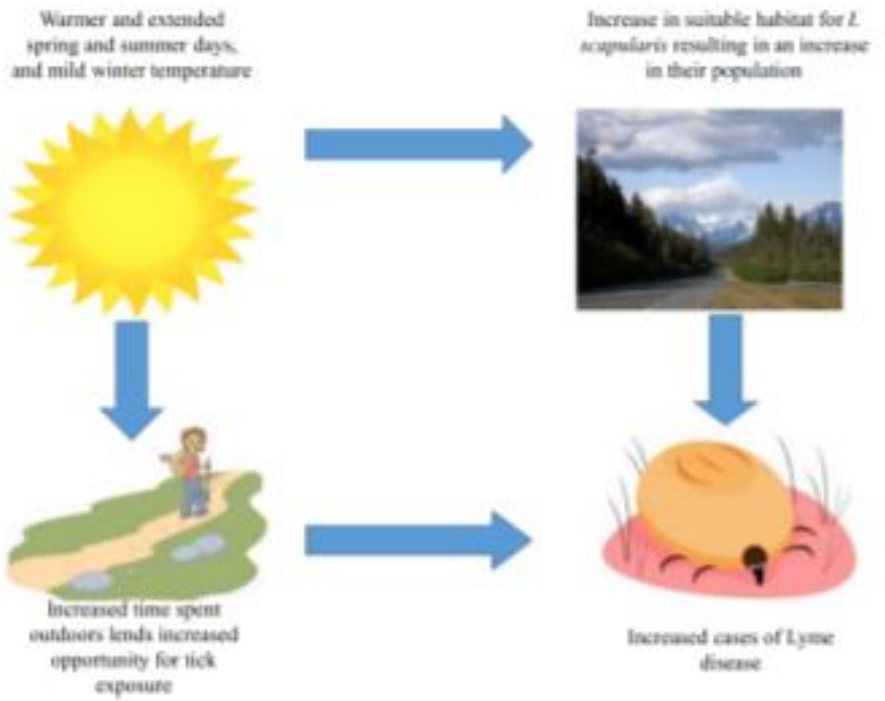
MyLymeData is a patient registry and research platform that was developed and launched by LymeDisease.org in 2015. It uses big data research tools that allow patients to quickly and privately pool their data to determine which treatments work best. The registry includes patients enrolled from every state. This map reflects patients enrolled in the registry from November 2015 to November 2017.



Lyme disease is caused by the spirochete Borrelia burgdorferi and is transmitted primarily by tick bite. It is the most common vector-borne disease in the United States. The Centers for Disease Control and Prevention (CDC) estimates that 300,000 cases of Lyme disease occur annually. Patients diagnosed and treated early generally respond well to treatment. However, treatment failures ranging from 10-35% have been reported in early disease and higher rates are reported for late disease.
Very little research has been conducted regarding how best to treat patients who do not respond to short-term 78% of diagnosis supported by serology 51% >3 years to diagnosis 89% willing to participate in research 70% not diagnosed until late stage (> 6 months) 60% diagnosed with co-infection 53% saw >5 clinicians 72% misdiagnosed before Lyme diagnosis 12,000+ enrolled to date treatment approaches or who are not diagnosed early.

MyLymeData was developed to accelerate research in Lyme disease by providing observational data and serving as a research platform for more traditional studies. Most of the patients in MyLymeData (79%) identify their current stage of illness as late (16%) or chronic Lyme disease (61%). The majority of patients in the registry report were diagnosed late (70%), when treatment success is much more difficult to achieve. Fewer than 13% of patients in the registry were diagnosed within the critical first month. Johnson, Lorraine (2019): 2019 Chart Book -- MyLymeData Registry. (Phase 1 April 27, 2017. Sample 3,903). doi.org/10.6084/m9.figshare.7849244. Report at: www.lymedisease.org/2019-mylymedata-highlights.pdf.

The effects of multiyear and seasonal weather factors on incidence of Lyme disease and its vector in New York State



• Lyme disease incidence has increased and has spread northward from coastal regions over time in New York State.
• The proportion of Lyme disease was higher among those aged 0–10 years and 40–50 years. • Mild winter temperatures, extended spring, and warmer summer days appear to increase Lyme disease cases.
• Biologically relevant weather indicators in the index and previous year were used as unique tools in Lyme disease research.
• Males and residents living in Hudson Valley had higher proportions of Lyme disease.
Science of the Total Environment 665 (2019) 1182–1188, Lin et al. |doi.org/10.1016/j.scitotenv.2019.02.123 0048-9697. The entire paper free of charge.

Knowledge, Attitudes, and Behaviors Regarding Tick-borne Disease Prevention in Endemic Areas

As part of a TickNET collaboration during 2016-2017, printed invitations were mailed via the post office to 27,029 households requesting participation in an online survey regarding knowledge of TBD, risk perceptions, and prevention behaviors. Prevention behaviors included tick checks, showering/bathing, insect repellents, pet tick control, and chemical or natural pesticide use on residential properties.

Overall, 1883 (7%) persons completed the survey. Participants reported using preventive behaviors most of the time or always as follows: pet tick control (83%), tick checks (58%), showering/bathing (42%), insect repellent (31%), and chemical (23%) or natural (15%) pesticides on property. Self-rated knowledge of LD, perceived prevalence of LD, perceived severity of LD, and perceived likelihood of contracting LD or another TBD were significantly ($p < 0.05$) associated with performing a tick check. Female gender and perceived prevalence of LD were significantly associated with applying insect repellent. Perceived prevalence of LD was significantly associated with showering or bathing, insect repellents, and pet tick control. Income ≥ $100,000 was significantly associated with applying a chemical or natural pesticide to one's property. A majority of respondents (84%) reported that they were very likely or somewhat likely to get a LD vaccine if one were available.

Few behaviors (tick checks and pet tick control) were reported to be practiced by more than half of the respondents living in LD endemic areas. Perceived prevalence of LD was the only factor associated with performing most of the prevention behaviors (tick checks, showering/bathing, use of insect repellents, and pet tick control). Use of chemical or natural pesticides appears to be driven by income. Greater efforts are needed to encourage use of prevention behaviors in endemic areas, and this may be facilitated by increasing awareness of local prevalence. Niesobecki et al, Ticks and Tick-borne Diseases. Open access, https://doi.org/10.1016/j.ttbdis.2019.07.008.

Borrelia miyamotoi infection leads to cross-reactive antibodies to the C6 peptide in mice and men

A widely used test for serodiagnosis of Lyme borreliosis is an EIA based on the C6 peptide of the *B. burgdorferi* sl VlsE protein…. We show that infection with *B. miyamotoi* leads to cross-reactive antibodies to the C6-peptide. Since BMD and Lyme borreliosis are found in the same geographical locations, caution should be used when relying solely on C6-reactivity testing. We propose that a positive C6 EIA with negative immunoblot, especially in patients with fever several weeks after a tick bite, warrants further testing for *B. miyamotoi*. Koetsveld et al. Clinical Microbiology and Infection, https://doi.org/10.1016/j.cmi.2019.07.026.

Molecular Testing of Serial Blood Specimens from Patients with Early Lyme Disease during Treatment Reveals Changing Coinfection with Mixtures of Borrelia burgdorferi Genotypes

Borrelia burgdorferi is the etiological agent of Lyme disease. In the current study, we used direct-detection PCR and electrospray ionization mass spectrometry to monitor and genotype B. burgdorferi isolates from serially collected whole blood specimens from patients clinically diagnosed with early Lyme disease before and during 21 days of antibiotic therapy. B. burgdorferi isolates were detected up

to 3 weeks after the initiation of antibiotic treatment, with ratios of coinfecting B. burgdorferi genotypes changing over time. Mosel et al. Antimicrob Agents Chemother 63:e00237-19. doi.org/10.1128/AAC.00237-19.

International & General Section

First evidence that the Lyme disease infection induces bone loss in mice

The Lyme disease pathogen Borrelia burgdorferi infects murine bone and induces trabecular bone loss

Lyme disease is caused by members of the Borrelia burgdorferi sensu lato species complex. Arthritis is a well-known late-stage pathology of Lyme disease, but the effects of B. burgdorferi infection on bone at sites other than articular surfaces are largely unknown. In this study, we investigated whether B. burgdorferi infection affects bone health in mice. In mice inoculated with B. burgdorferi or vehicle (mock infection), we measured the presence of B. burgdorferi DNA in bones, bone mineral density (BMD), bone formation rates, biomechanical properties, cellular composition, and two- and three-dimensional features of bone microarchitecture. B. burgdorferi DNA was detected in bone.

In the long bones, increasing B. burgdorferi DNA copy number correlated with reductions in areal and trabecular volumetric BMDs. Trabecular regions of femora exhibited significant, copy number-correlated microarchitectural disruption, but BMD, microarchitectural, and biomechanical properties of cortical bone were not affected. Bone loss in tibiae was not due to increased osteoclast numbers or bone-resorbing surface area, but it was associated with reduced osteoblast numbers, implying that bone loss in long bones was due to impaired bone building. Osteoid-producing and mineralization activities of existing osteoblasts were unaffected by infection.

Therefore, deterioration of trabecular bone was not dependent on inhibition of osteoblast function but was more likely caused by blockade of osteoblastogenesis, reduced osteoblast survival, and/or induction of osteoblast death. Together, these data represent the first evidence that B. burgdorferi infection induces bone loss in mice and suggest that this phenotype results from inhibition of bone building rather than increased bone resorption. Tang, et al. Infect Immun 85:e00781-16. https://doi.org/10.1128/IAI.00781-16.

Steroid Use in Lyme Disease-Associated Facial Palsy Is Associated with Worse Long-Term Outcomes

The purpose of this study was to determine whether differences in long-term facial function outcomes following acute Lyme disease-associated facial palsy (LDFP) exist between patients who received antibiotic monotherapy (MT); dual-therapy (DT) with antibiotics and corticosteroids; and triple therapy (TT) with antibiotics, corticosteroids, and antivirals.

All patients with a prior diagnosis of unilateral LDFP who presented to our center between 2002 and 2015 were retrospectively assessed for inclusion. Two blinded experts graded static, dynamic, and synkinesis parameters of facial functions using standardized video documentation of facial function. An association between corticosteroid use in acute LDFP and worse long-term facial function outcomes has been demonstrated. Care should be taken in differentiating viral or idiopathic facial palsy (e.g., Bell palsy) from LDFP. Jowett et al. Laryngoscope, 127:1451-1458, 2017.

Ticks and Tularemia: Do We Know What We Don't Know?

Francisella tularensis, the causative agent of the zoonotic disease tularemia, is characterized by high morbidity and mortality rates in over 190 different mammalian species, including humans. Based on its low infectious dose, multiple routes of infection, and ability to induce rapid and lethal disease, F. tularensis has been recognized as a severe public health threat—being designated as a NIH Category A Priority Pathogen and a CDC Tier 1 Select Agent.

Despite concerns over its use as a bioweapon, most U.S. tularemia cases are tick-mediated and ticks are believed to be the major environmental reservoir for F. tularensis in the U.S. The American dog tick (Dermacentor variabilis) has been reported to be the primary tick vector for F. tularensis, but the lone star tick (Amblyomma americanum) and other tick species also have been shown to harbor F. tularensis. This review highlights what is known, not known, and is debated, about the roles of different tick species as environmental reservoirs and transmission vectors for a variety of F. tularensis genotypes/strains. Zellner and Huntley, Front. Cell. Infect. Microbiol. 9:146. doi: 10.3389/fcimb.2019.00146. Open access.

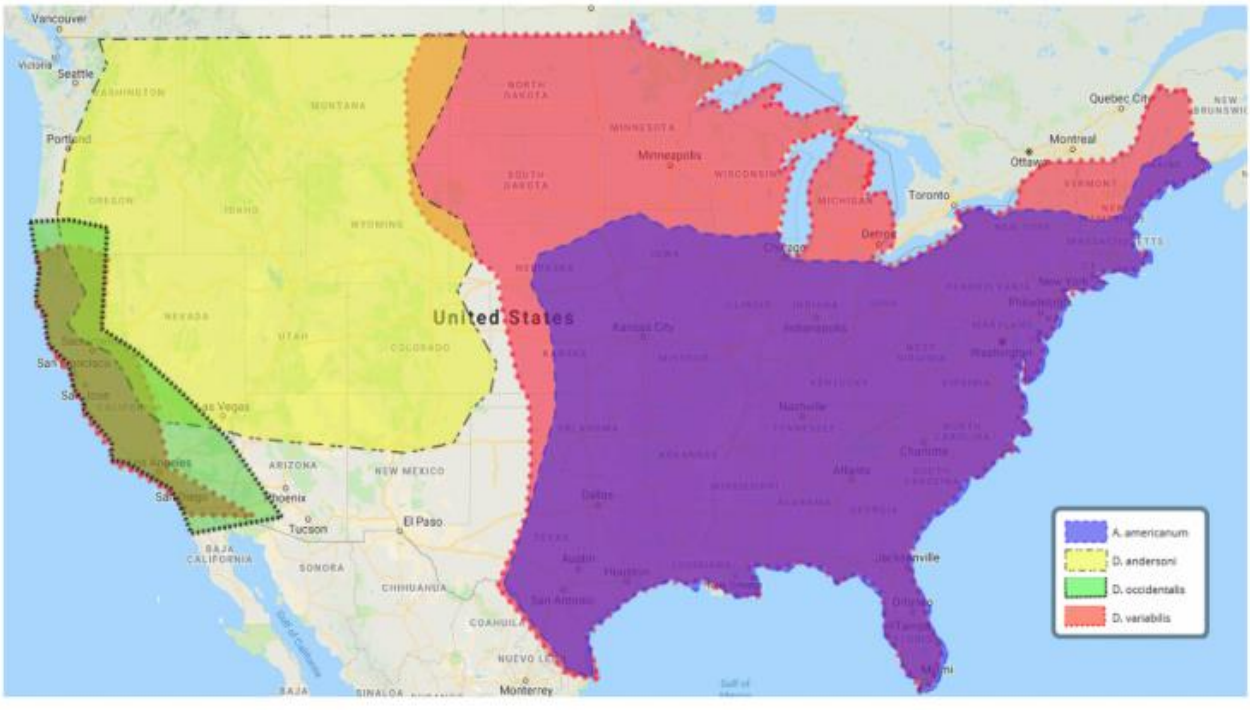


FIGURE 1 | U.S. geographic distribution of ticks associated with human tularemia. Data adapted from the Centers for Disease Control and Prevention, https://www.cdc.gov/ticks/geographic__distribution.html.

Choices for recreation in Sweden are influenced by prevalence of ticks and incident of Lyme disease

Valuation when baselines are changing: Tick-borne disease risk and recreational choice

> Understanding how changes in baseline risk influence preferences for risk reduction is important when valuing the welfare effects of environmental change, including the spread of disease. We conduct a survey-based choice experiment among respondents residing in areas with different prevalence of ticks and incidence of Lyme borreliosis (LB) and tick-borne encephalitis (TBE) in Sweden. Respondents face a trade-off between risk and travel cost when choosing between visiting recreational areas differing in prevalence of ticks and disease incidence.
>
> Our study indicates that the presence of ticks and the associated risk of tick-borne diseases significantly influence the choice of recreational area and have substantial welfare effects. The mean willingness to pay (WTP) per trip to avoid areas with different levels of ticks, LB risk and TBE risk ranges from 12 – 78 EUR. The WTP for risk reduction is significantly lower among respondents residing in risk areas compared to respondents in emerging risk areas. Explanations for these differences in WTP for risk reduction between groups with different baseline risks include differences in reference point utility, knowledge and learning, leading to adaptation of behaviour and preferences. Slunge et al. Resource and Energy Economics, doi.org/10.1016/j.reseneeco.2019.101119

Incidence of laboratory-confirmed Lyme disease rose significantly in England and Wales over 3 years

The demographics and geographic distribution of laboratory-confirmed Lyme disease cases in England and Wales (2013–2016): an ecological study

Public Health England's national Lyme disease testing laboratory routinely collected laboratory surveillance data and tested 3986 laboratory-confirmed cases of Lyme disease between 2013 and 2016.

In England and Wales, the incidence of laboratory-confirmed Lyme disease rose significantly over the study period from 1.62 cases per 100 000 in 2013 to 1.95 cases per 100 000 in 2016. There was a bimodal age distribution (with peaks at 6–10 and 61–65 years age bands) with a predominance of male patients. A significant clustering of areas with high Lyme disease incidence was located in southern England. An association was found between disease incidence and socioeconomic status, based on the patient's resident postcode, with more cases found in less deprived areas. Cases were disproportionately found in rural areas compared with the national population distribution.

Conclusions These results suggest that Lyme disease patients originate from areas with higher socioeconomic status and disproportionately in rural areas. Identification of the Lyme disease hotspots in southern England, alongside the socio-demographics described, will enable a targeted approach to public health interventions and messages. Tullock et al. BMJ Open, dx.doi.org/10.1136/bmjopen-2018-028064.

Rhesus monkey brains provide a way to look at the basis of neurological Lyme disease

Rhesus Brain Transcriptomic Landscape in an *ex vivo* Model of the Interaction of Live *Borrelia Burgdorferi* With Frontal Cortex Tissue Explants

Lyme neuroborreliosis (LNB) is the most dangerous manifestation of Lyme disease caused by the spirochete *Borrelia burgdorferi* which can reach the central nervous system most commonly presenting with lymphocytic meningitis; however, the molecular basis for neuroborreliosis is still poorly understood.

We incubated explants from the frontal cortex of three rhesus brains with medium alone or medium with added live *Borrelia burgdorferi* for 6, 12, and 24 h and isolated RNA from each group was used for RNA sequencing with further bioinformatic analysis. Transcriptomic differences between the *ex vivo* model of live *Borrelia burgdorferi* with rhesus frontal cortex tissue explants and the controls during the progression of the infection were identified. A total of 2249, 1064, and 420 genes were significantly altered, of which 80.7, 52.9, and 19.8% were upregulated and 19.3, 47.1, 80.2% were downregulated at 6, 12, and 24 h, respectively. Gene ontology and KEGG pathway analyses revealed various pathways related to immune and inflammatory responses during the spirochete infection were enriched which is suggested to have a causal role in the pathogenesis of neurological Lyme disease. Moreover, we propose that the overexpressed FOLR2 which was demonstrated by the real-time PCR and western blotting could play a key role in neuroinflammation of the neuroborreliosis based on PPI analysis for the first time.

To our knowledge, this is the first study to provide comprehensive information regarding the transcriptomic signatures that occur in the frontal cortex of the brain upon exposure to *Borrelia burgdorferi*, and suggest that FOLR2 is a promising target that is associated with neuroinflammation and may represent a new diagnostic or therapeutic marker in LNB. Ding et al. Front. Neurosci., 28 June 2019 | https://doi.org/10.3389/fnins.2019.00651. Entire paper free of charge.

Ed. note: Transcriptomics is the study of the transcriptome—the complete set of RNA transcripts that are produced by the genome, under specific circumstances or in a specific cell—using high-throughput methods, such as microarray analysis. The transcriptome is the set of all RNA molecules in one cell or a population of cells.

New technologies for Lyme diagnostics being investigated

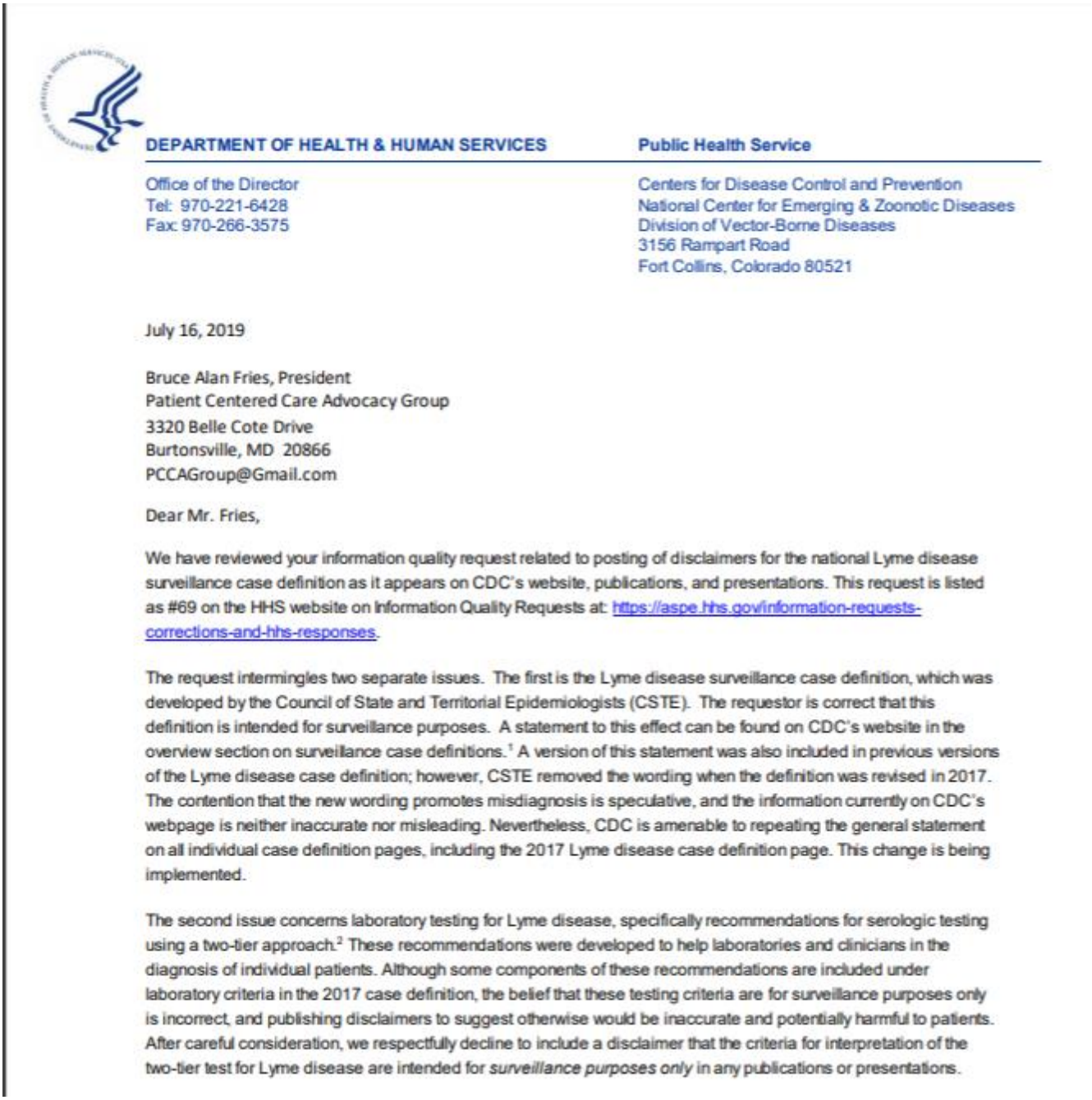
QIAGEN and DiaSorin collaborate on novel QuantiFERON-based test for earlier detection

Very technical. The companies plan multi-site clinical validations during the 2020 Lyme disease season, with regulatory submissions expected at the end of the same year in the United States and Europe. The QuantiFERON technology comes in two components: the QuantiFERON sample collection component with the proprietary assay stimulus/initiation and QuantiFERON read-out component to measure the signal created by the stimulus. The QuantiFERON read-out component of the assay will be run on DiaSorin's widely used LIAISON family of fully automated analyzers and both components will be designed for use on these platforms. Entire report: corporate.qiagen.com/newsroom/press-releases/2019/20190605_DiaSorin_QFT_Lyme?sc_lang=en.

CDC Agrees to Add Disclaimer to Lyme Disease Case Definition

Washington, DC – WEBWIRE – Monday, July 22, 2019 | www.webwire.com/ViewPressRel.asp?

The Centers for Disease Control and Prevention (CDC) has agreed to add a disclaimer to the surveillance case definition for Lyme disease that it is "*not intended to be used by healthcare providers for making a clinical diagnosis or determining how to meet an individual patient's health needs."*



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July 16, 2019

Bruce Alan Fries, President
Patient Centered Care Advocacy Group
3320 Belle Cote Drive
Burtonsville, MD 20866
PCCAGroup@Gmail.com

Dear Mr. Fries,

We have reviewed your information quality request related to posting of disclaimers for the national Lyme disease surveillance case definition as it appears on CDC's website, publications, and presentations. This request is listed as #69 on the HHS website on Information Quality Requests at: https://aspe.hhs.gov/information-requests-corrections-and-hhs-responses.

The request intermingles two separate issues. The first is the Lyme disease surveillance case definition, which was developed by the Council of State and Territorial Epidemiologists (CSTE). The requestor is correct that this definition is intended for surveillance purposes. A statement to this effect can be found on CDC's website in the overview section on surveillance case definitions.[1] A version of this statement was also included in previous versions of the Lyme disease case definition; however, CSTE removed the wording when the definition was revised in 2017. The contention that the new wording promotes misdiagnosis is speculative, and the information currently on CDC's webpage is neither inaccurate nor misleading. Nevertheless, CDC is amenable to repeating the general statement on all individual case definition pages, including the 2017 Lyme disease case definition page. This change is being implemented.

The second issue concerns laboratory testing for Lyme disease, specifically recommendations for serologic testing using a two-tier approach.[2] These recommendations were developed to help laboratories and clinicians in the diagnosis of individual patients. Although some components of these recommendations are included under laboratory criteria in the 2017 case definition, the belief that these testing criteria are for surveillance purposes only is incorrect, and publishing disclaimers to suggest otherwise would be inaccurate and potentially harmful to patients. After careful consideration, we respectfully decline to include a disclaimer that the criteria for interpretation of the two-tier test for Lyme disease are intended for *surveillance purposes only* in any publications or presentations.

If you wish to appeal this response to your request for a correction, you may send a written hard copy or electronic request for reconsideration within 30 days of receipt of the agency's decision. The appeal must state the reasons why the agency response is insufficient or inadequate. You must attach a copy of the original request and the agency's response to it. Clearly mark the appeal with the words, "Information Quality Appeal," and send the appeal by mail to CDC/ATSDR, Attn: Mailstop H21-8 (attn.: Office of Science Quality); 1600 Clifton Road, N.E., Atlanta, GA 30333 or by e-mail to InfoQuality@cdc.gov.

Best Regards,

/S/

Lyle Petersen, MD, MPH
Director, Division of Vector-Borne Diseases
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention

References

1. Nationally Notifiable Diseases Surveillance System (NNDSS). Case Definitions for Current and Historical Conditions. Available at: https://wwwn.cdc.gov/nndss/conditions/

2. Notice to Readers Recommendations for Test Performance and Interpretation from the Second National Conference on Serologic Diagnosis of Lyme Disease. Morb Mort Weekly Rep (MMWR) 1995; 44:590-591. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/00038469.htm

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