Tick-Borne Infections Council of North Carolina, Inc.

NEWSLETTER 2020, Volume 1

Quote: –The dream of a one-size-fits-all approach to Lyme-plus has collapsed under the weight of so much complexity: an expanding group of infections; variations in human biology; and the specter of climate change spreading ticks far beyond disease zones on maps. Cookie-cutter treatments recommended by some doctors could never fix all this. But under the banner of personalized medicine and with a raft of funding from non-profits and the government alike, researchers are seeking answers and the biomedical tools to bring sick patients back from the brink. These scientists need our support, not our scorn. –Pamela Weintraub, health and psychology editor, Aeon | www.nbcnews.com/think/opinion/lyme-disease-emergency-instead-feeding-hype-we-must-support-science-ncna1062611

Highlights…

- **Pathogenic Borrelia, Ehrlichia, and Rickettsia species in the north and north-central Florida**
- **Diagnosis and management of patients with the α-Gal syndrome**
- **Historical account of the discovery of the Lyme disease agent**
- **Analysis of findings on risk of tick bites**
- **CDC finds the new Asian longhorned tick is unlikely, if at all, to transmit Lyme disease in the US**
- **Long-Term persistence of Borrelia burgdorferi antigens**
- **25% of black-legged tick nymphs infected with Lyme in eastern Pennsylvania**
- **Sleep quality in well-defined Lyme disease**
- **Blacklegged ticks in Pittsburgh's parks are highly infected with the Lyme disease bacteria**

- **Tick-borne infections other than Lyme disease increased dramatically from 2010-2016**
- **Can dogs get red meat allergy?**
- **Lyme disease case numbers higher in northern Mongolia**
- **Tick bite to heart failure; Ehrlichial myocarditis**
- **As many as 11% of Latino outdoor workers in a New York state county are positive for Lyme disease**
- **Eye involvement in tick-borne diseases**
- **Disease transmission time after tick attachment for Lyme disease**
- **Two more deaths from Lyme disease infecting the heart**

State Vector-Borne Disease Working Group 2019 Meeting Schedule

2020 VBWG meeting dates are not yet set.

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

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. Please see the home page of our website to access.
www.tic-nc.org

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 14 September 2019.

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

CDC: Lyme disease and maternal transmission to fetus- change of language on website under "other ways to get Lyme disease:" www.cdc.gov/lyme/transmission/index.html

"Untreated Lyme disease during pregnancy can lead to infection of the placenta. Spread from mother to fetus is possible but rare. Fortunately, with appropriate antibiotic treatment, there is no increased risk of adverse birth outcomes. There are no published studies assessing developmental outcomes of children whose mothers acquired Lyme disease during pregnancy."

https://www.niaid.nih.gov/sites/default/files/NIH-Strategic-Plan-Tick-borne-Disease-Research-2019.pdf

State tick research and/or reports

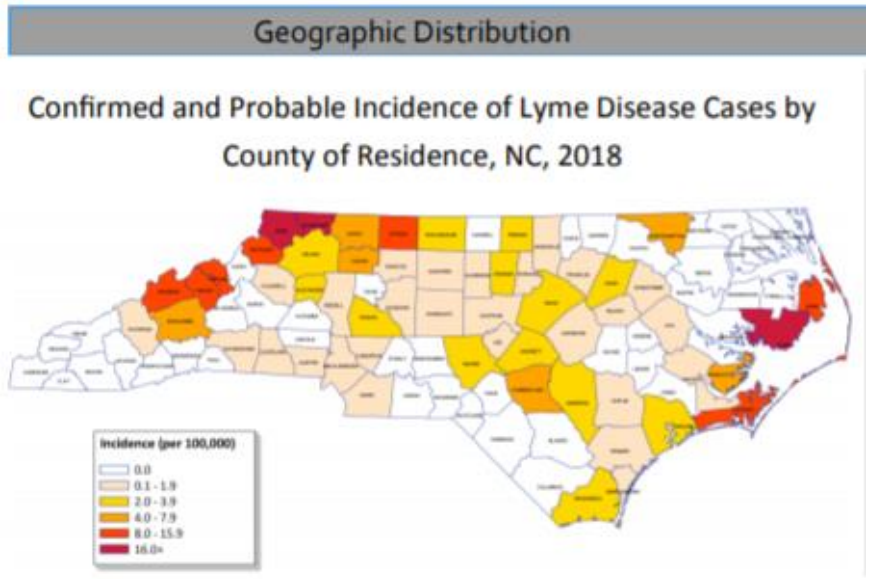
NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

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

… 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 was 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.

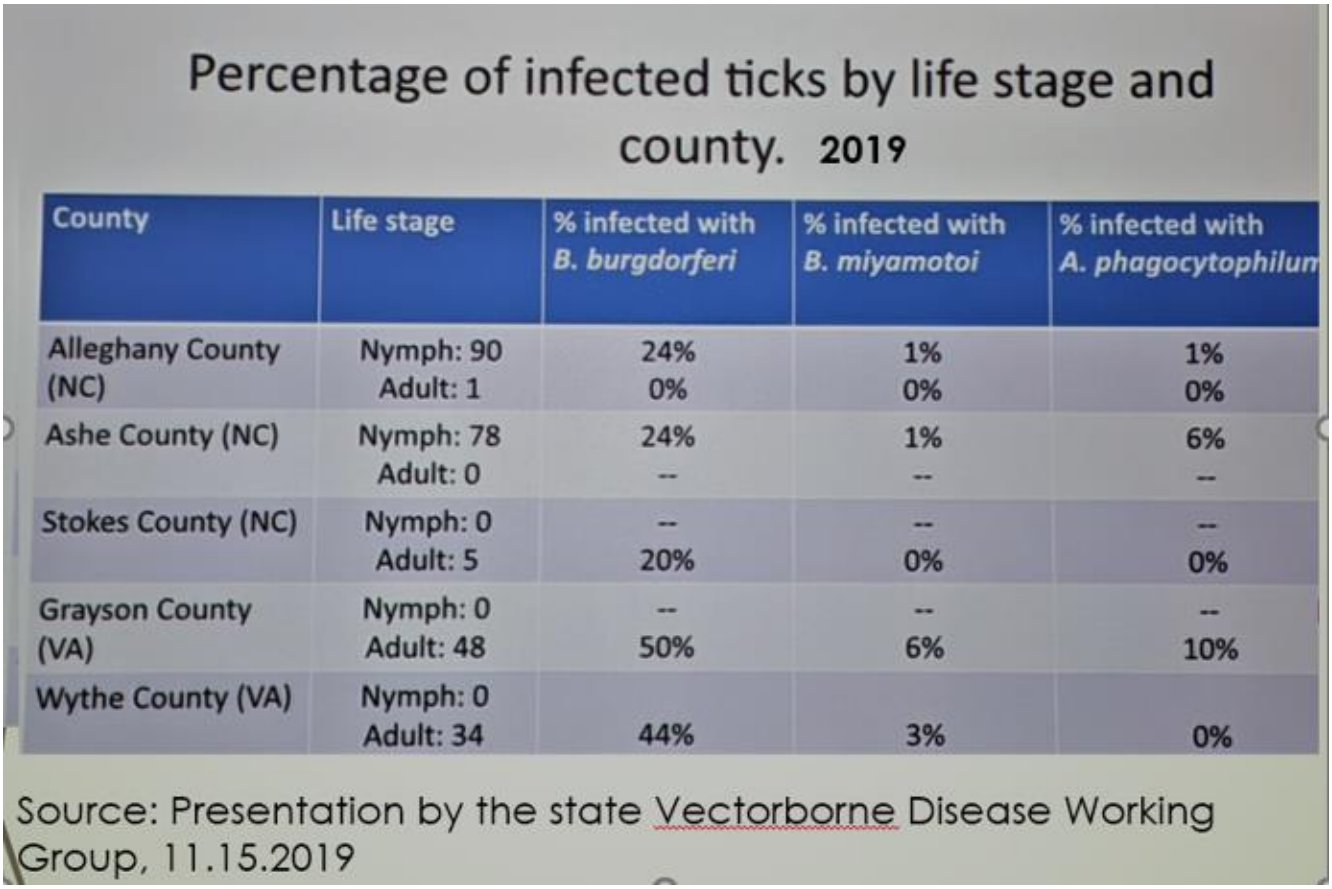
1.Shapiro, ED. N Engl J Med 2014;370:1724-31. DOI: 10.1056/NEJMcp1314325 Although reputed to have a bull's-eye appearance, approximately two thirds of single erythema migrans lesions either are uniformly erythematous or have enhanced central erythema without clearing around it.

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.

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 or Vectorborne Disease Work Group meeting, November 15, 2019

North Carolina Public Health along with help from the CDC and several state universities are conducting studies on Lyme disease. See clips from the Workgroup presentation in November below. The corner of the state bordering Tennessee and Virginia is becoming a hotspot for Lyme disease.

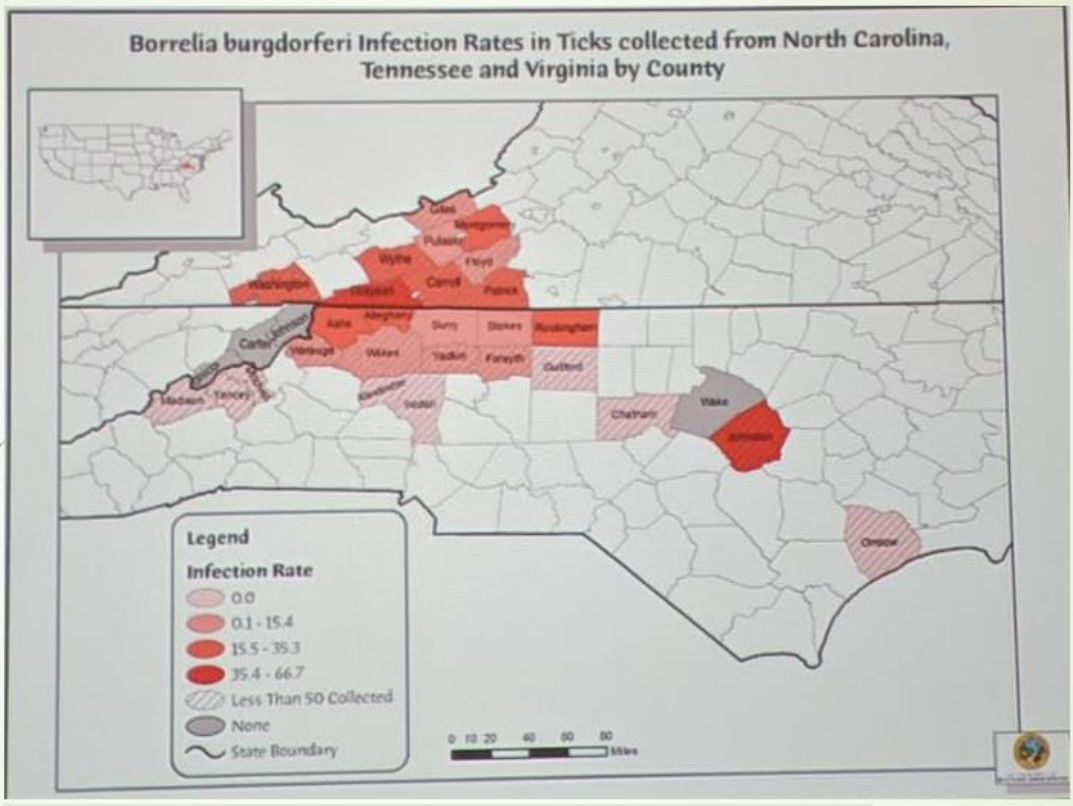


Percentage of infected ticks by life stage and county. 2019

County	Life stage	% infected with *B. burgdorferi*	% infected with *B. miyamotoi*	% infected with *A. phagocytophilum*
Alleghany County (NC)	Nymph: 90 Adult: 1	24% 0%	1% 0%	1% 0%
Ashe County (NC)	Nymph: 78 Adult: 0	24% --	1% --	6% --
Stokes County (NC)	Nymph: 0 Adult: 5	-- 20%	-- 0%	-- 0%
Grayson County (VA)	Nymph: 0 Adult: 48	-- 50%	-- 6%	-- 10%
Wythe County (VA)	Nymph: 0 Adult: 34	44%	3%	0%

Source: Presentation by the state Vectorborne Disease Working Group, 11.15.2019

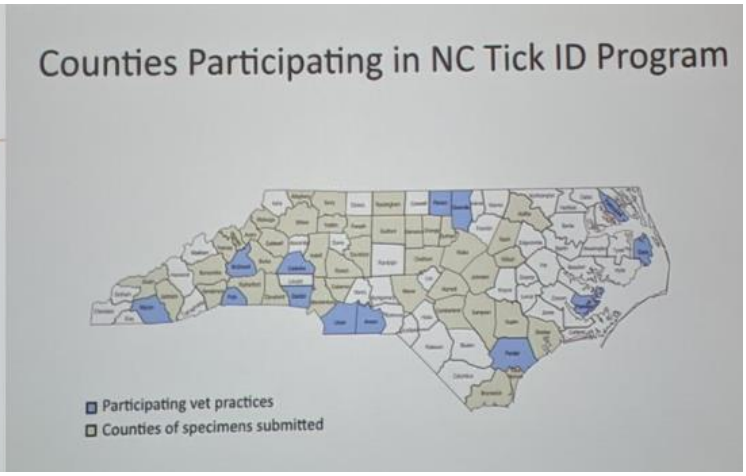
2018-2019 Research by the NC universities and CDC



Source: Presentation by the state Vectorborne Disease Working Group, 11.15.2019

North Carolina Tick Identification Program

- Surveillance program began in July 2018
  - Describe diversity and distribution of ticks across North Carolina
  - 48 counties participating
  - 118 practices participating
- Program expansion
  - Land surveyors
  - SLPH rabies submissions
  - General public (2020)



NC TBIs 2017 final, 2018 to November probable/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

-TIC-NC Talks and Materials Distributed

Brochures/booklets:

Turtle Island Preserve Asheville

Surrey County Department of Agriculture representative

Physician in Marion who was unaware of tick-borne diseases in North Carolina by Asheville volunteer, Janet

Asheville volunteer, Rick, sent booklets to all 100 state Departments of Education

Talks:

North Carolina Mosquito and Vector Control Association, Carolina Beach, December 2019

ᵡᵡ North Carolina and South ᵡᵡ

Hispanics less likely to be familiar with tick-borne risks

Knowledge and prevention of tick-borne diseases among Hispanic and non-Hispanic residents of Maryland and Virginia

Tick-borne diseases (TBDs) such as Lyme disease (LD), babesiosis, ehrlichiosis and Rocky Mountain spotted fever cause substantial morbidity and even mortality in the USA. Data indicate that Hispanic populations may be at greater risk for occupational exposure to ticks and disseminated LD; however, information on knowledge and practices of Hispanic populations regarding TBDs is limited.

We surveyed 153 Hispanic and 153 non-Hispanic residents of Maryland and Virginia to assess awareness of TBDs, prevention practices and risk of tick encounters. Hispanic respondents were less likely than non-Hispanics to report familiarity with LD symptoms (21% vs. 53%, $p < 0.001$) and correctly identify ticks as vectors of LD (40% vs. 85%, $p < 0.001$). Although there was no significant difference in overall proportion of respondents who routinely take one or more preventive measures to prevent tick bites (59% vs. 61%, $p = 0.65$), Hispanics were more likely to report showering after coming indoors (36% vs. 25%, $p = 0.04$) but less likely to conduct daily tick checks compared with non-Hispanics (17% vs. 35%, $p < 0.001$). History of tick bite or finding a tick crawling on oneself or a household member in the past year did not significantly differ between Hispanics and non-Hispanics (19% vs. 24%, $p = 0.26$).

Notably, after controlling for Hispanic/non-Hispanic ethnicity, primary language (English vs. Spanish) was a significant predictor of whether an individual had knowledge of LD symptoms, correctly identified ticks as vectors for LD and performed daily tick checks. These results provide guidance for future development of more targeted and effective TBD prevention education for both Hispanic and non-Hispanic communities. Hu et al. Zoonoses and Public Health. doi.org/10.1111/zph.12627

Pathogenic Borrelia, Ehrlichia, and Rickettsia species were all detected in the North and North-Central Florida

A Survey of Tick-Borne Bacterial Pathogens in Florida

Within the past three decades, new bacterial etiological agents of tick-borne disease have been discovered in the southeastern U.S., and the number of reported tick-borne pathogen infections has increased. In Florida, few systematic studies have been conducted to determine the presence of tick-borne bacterial pathogens.

This investigation examined the distribution and presence of tick-borne bacterial pathogens in Florida. Ticks were collected by flagging at 41 field sites, spanning the climatic regions of mainland Florida. DNA was extracted individually from 1608 ticks and screened for Anaplasma, Borrelia, Ehrlichia and Rickettsia using conventional PCR and primers that amplified multiple species for each genus. PCR positive samples were Sanger sequenced.

Four species of ticks were collected: Amblyomma americanum, Amblyomma maculatum, Dermacentor variabilis, and Ixodes scapularis. Within these ticks, six bacterial species were identified: Borrelia burgdorferi, Borrelia lonestari, Ehrlichia ewingii, Rickettsia amblyommatis, Rickettsia andeanae, Rickettsia parkeri, and Rickettsia endosymbionts. Pathogenic Borrelia, Ehrlichia, and Rickettsia species were all detected in the North and North-Central Florida counties; however, we found only moderate concordance between the distribution of ticks infected with pathogenic bacteria and human cases of tick-borne diseases in Florida. Given the diversity and numerous bacterial species detected in ticks in Florida, further investigations should be conducted to identify regional hotspots of tick-borne pathogens. De Jesus et al. Insects 2019, 10, 297; doi:10.3390/insects10090297.

Habitat amount, quality, and fragmentation associated with prevalence of the tick-borne pathogen *Ehrlichia chaffeensis* and occupancy dynamics of its vector, *Amblyomma americanum*

We collected nymphal ticks from 130 plots in southeastern Virginia, U.S., for 5 years and tested for *E. chaffeensis* via targeted PCR. We derived metrics of landscape context from Landsat data and related these to pathogen prevalence and tick turnover using hierarchical Bayesian models.

Landscape context was associated with both pathogen prevalence and tick turnover. Pathogen prevalence was negatively associated with total forest landcover, coniferous forest landcover, and forest edge density. Tick turnover was positively associated with coniferous landcover and with an interaction between total forest landcover and edge. This interaction was such that turnover was predicted to be lowest in small contiguous forests, and highest in small fragmented forests.

Landscape context affects *E. chaffeensis* prevalence and occupancy dynamics of its tick host, though these processes appear decoupled. We hypothesize that pathogen prevalence may be more driven by reservoir host movement and social behavior and tick dynamics are more driven by host population density. Simpson et al. Landscape Ecol. doi.org/10.1007/s10980-019-00898-5.

Diagnosis and management of patients with the α-Gal syndrome

The α-Gal syndrome has many novel features that are relevant to diagnosis and management. In most cases the diagnosis can be made on a history of delayed allergic reactions to red meat and the blood test for IgE to the oligosaccharide galactose-α-1,3-galactose (α-Gal). In general, the diagnosis also dictates the primary treatment, i.e. – avoiding mammalian meat and also dairy in some cases. In the USA the lone star tick is the primary cause of this disease but different ticks are responsible in other countries. Blood levels of IgE to α-Gal often drop in patients who avoid recurrent tick bites, but the rate of decline is variable. Similarly, the delay before reactions is variable and the severity of the allergic reactions is not predicted by the delay or the titer of specific IgE.

Some mammalian-derived products are only relevant to select patient groups, such as heart valves, gelatin-based plasma expanders, and pancreatic enzymes. A minority of cases may benefit from avoiding a wide range of products that are prepared with mammalian–derived constituents, such as gelatin. This review focuses on the nature of the syndrome, common challenges in diagnosis and

management, and also gaps in our current knowledge that would benefit from additional investigation. Platts-Mills et al. The Journal of Allergy and Clinical Immunology: In Practice. doi.org/10.1016/j.jaip.2019.09.017.

Trends in canine seroprevalence to *Borrelia burgdorferi* and *Anaplasma* spp. in the eastern USA, 2010–2017

Conclusions. As expected, seroprevalence continued to increase in regions where Lyme borreliosis and anaplasmosis are more newly endemic. However, the declining seroprevalence evident in other areas was not anticipated. Although the reasons for the decreasing trends are not clear, our finding may reflect shifting ecologic factors that have resulted in decreased infection risk or the combined positive influence of canine vaccination, tick control, and routine testing of dogs in regions where these infections have long been endemic. Analysis of trends in canine test results for tick-borne infections continues to be a valuable tool to understand relative geographical and temporal risk for these zoonotic agents.

…States with an *increasing* trend included three in the Northeast (Maine, New York, and Pennsylvania), 3 in the Southeast (North Carolina, South Carolina, and West Virginia), and two in the Midwest (Iowa and Michigan). Dewage, et al. Parasites Vectors (2019) 12: 476. https://doi.org/10.1186/s13071-019-3735-x. Entire article free of charge.

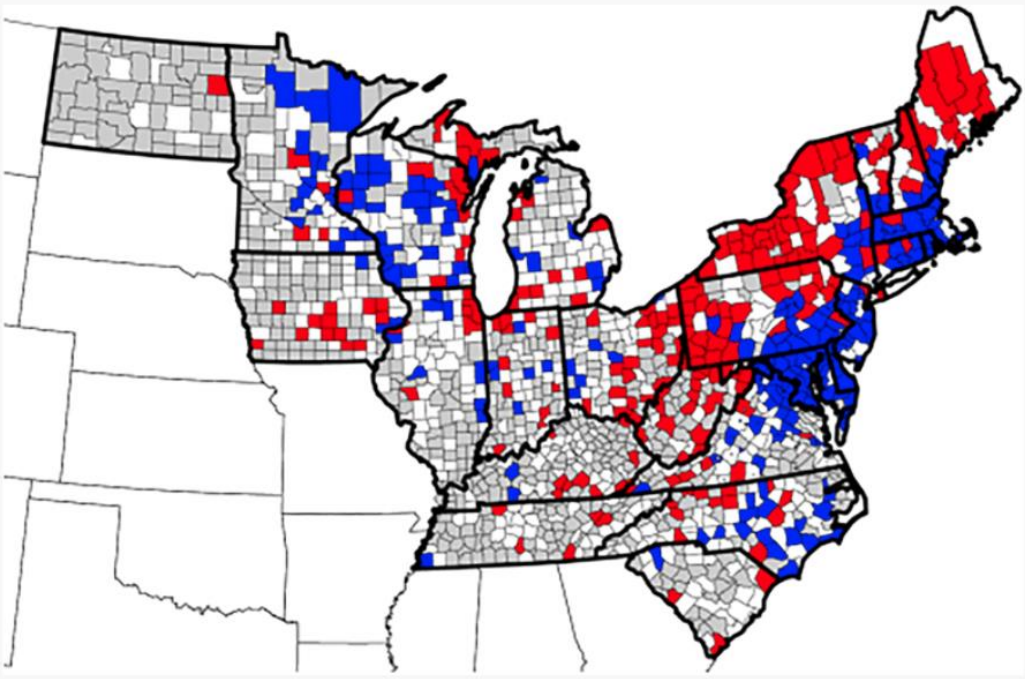


Fig. 3
County trends in seroprevalence for antibodies to *Borrelia burgdorferi*, 2010–2017. Trends evident included decreasing (blue), increasing (red), and no significant change (white). Counties for which adequate data were not available are shown in gray

Discovery of the Lyme Disease Agent

A detailed first-hand account of the events leading up to the discovery of the Lyme disease agent has been lacking. Nearly 40 years have elapsed since the discovery of the organism that was named *Borrelia burgdorferi*. There are thousands of articles in the scientific and medical literature on this organism and the disease that it causes. In the interval since the organism's discovery, however, misconceptions have arisen regarding not only the disease but the discovery itself. Accordingly, with this paper, we aim to fill in the details of this episode in medical history with a joint introduction, first-person accounts by the two authors, a summary of contemporaneous events, and concluding comments.

The history of the discovery of the Lyme disease agent has threads originating in different places in the United States. Studies on Long Island, NY, provided the epidemiological thread of studies on rickettsial diseases and babesiosis, linking the latter with the cutaneous manifestation of Lyme disease, now known as erythema migrans. The Long Island thread intersected Montana's Rocky Mountain Laboratories thread of studies on a relapsing fever *Borrelia* and its cultivation and expertise in vector biology. This intersection made possible the discovery of the spirochete and its recovery from patients. This paper stresses that what may seem to have been an individual scientific discovery is actually the product of several threads coming together and is attributable to more people than appreciated. Barbour and Benach, mBio. Entire paper free of charge at doi: 10.1128/mBio.02166-19.

***TIC - NC editor Marcia E. Herman-Giddens note:** From the recent paper "Discovery of the Lyme Disease Agent," https://mbio.asm.org/content/mbio/10/5/e02166-19.full.pdf

Interesting sentence in the paragraph below from the paper by Benach and Barbour. So, it turns out the ubiquitous and possibly infamous B31 strain of Borrelia burgdorferi was actually the more numerous strain from the original culture which turns out to be three strains, hence the 3 in the moniker for this strain. It is interesting to reflect on how selecting this one strain from the beginning instead of examining the complexities and effects of having several might have affected the course of history with regard to Lyme disease.

> "The population of spirochetes that eventually grew out of the 10 3 dilution free of contamination was subsequently cloned by limiting dilution. The lab name for this clonal population was "B31," which signified the first isolate of the 3 B's of Burgdorfer, Benach, and Barbour. This stuck as the official name for the type strain of the species. We recently determined that the original uncloned isolate from the midguts of a set of ticks was (unsurprisingly given the high prevalence of infection in ticks and the strain diversity of B. burgdorferi) a mixture of two different strains of B. burgdorferi. What was designated B31 was the more numerous of the two, thus its selection in pure culture by serial dilution. However, there was also a strain of the OspC N genotype that was recovered from the blood of a mouse that had been inoculated with the uncloned population."

Analysis of findings on risk of tick bites from numerous papers from 1984 – 2018: landscape-related tick control measures tended to *increase* risk

Risk Factors for Bites and Diseases Associated with Black-legged Ticks

The emergence and spread of Lyme disease and other infections associated with black-legged ticks is causing a public health crisis. No human vaccines are currently available, and both diagnosis and treatment are sometimes ineffectual, leading to advocacy for self-directed preventative measures. These recommendations are widely communicated to the public, but there is limited evidence for their efficacy.

We undertook a systematic review and mixed-effects meta-regression analysis of factors purported to increase or decrease risk of black-legged tick bites and tick-borne disease. Published articles used in the study spanned the years 1984–2018.

Variables associated with *increased probability of tick-borne disease*, with odds ratios significantly greater than 1, included:

1. deer abundance
2. high density of nymph-stage black-legged ticks
3. landscapes with interspersed herbaceous and forested habitat
4. low human population density
5. gardens
6. cat ownership
7. race

Contrary to recommendations, use of landscape-related tick control measures, such as clearing brush, trimming branches, and having a dry barrier between lawn and woods, tended to *increase risk*. Pet ownership increased bite risk. Bite risk was highest for children aged 5 years or less, with a secondary peak in persons aged 50–70 years. Although some widely disseminated recommendations are supported by the research analyzed, others require further evaluation. Additional research is also needed to understand the mechanisms underlying significant relationships. Fischhoff et al. Am J Epidemiol. 2019;188(9):1742-1750. (Ed. note: italics and numbered list by ed.)

As many as 11% of Latino outdoor workers in a New York State County are positive for Lyme disease

High Seroprevalence and Seroconversion Rate of *Borrelia burgdorferi* Infection Among Hispanic/Latino Immigrant Workers in Eastern Suffolk County, New York: A Longitudinal-Based Study

Lyme disease, caused by *Borrelia burgdorferi*, continues to be the most commonly reported vector-borne disease in the United States (US) affecting the public health and the economy. Suffolk County, New York (NY) has one of the highest incidences in NY State affecting primarily the Hispanic/Latino population working in gardening, landscaping, and agriculture (field workers). However, there is a paucity of research among this population. Thus, the aim of this longitudinal study was to assess the current seroprevalence and seroconversion of the *Borrelia burgdorferi* infection and its risk factors such as sociodemographic, symptoms, tick encounter, and use of the Fatigue Severity Scale, associated with seropositivity in the Hispanic/Latino immigrant worker population of Eastern Suffolk County.

Recruitment of participants was based on several towns of this County. Following signed informed consent, participants completed a questionnaire and had their blood drawn. Samples were tested using the conventional 2-tiered serological testing for Borreliosis.

Between June 2016 and October 2018, 660 (83.5%) completed Visit 1; 58.8% of them completed elementary school or less, and 56.7% reported earning = or <$20,000 annually, 344 were field workers, from which, 82.3% and 55.2% were male and from Guatemala, respectively. The overall seroprevalence was 7.2% (48/660) but was significantly higher among gardener/Landscapers (11.5%) having an adjusted odds ratio (OR) = 2.02 with a CI = 1.02–4.03. Another significant risk factor was experiencing fevers after a tick-bite (Adjusted OR: 2.08, CI:1.42–5.63). 2.7% (8/292) seroconverted and were gardener/landscaper.

Several barriers to healthcare access, health literacy, and prevention were identified. Gardening/landscaping has an occupational risk in this population. Efforts to educate about tick-borne infections and preventive methods such as vaccinations are warranted for this population. Vilcarromero et al. Open Forum Infect Dis. 10.1093/ofid/ofz360.1509

CDC finds the new Asian longhorned tick is unlikely, if at all, to transmit Lyme disease in the US

Failure of the Asian longhorned tick, *Haemaphysalis longicornis*, to serve as an experimental vector of the Lyme disease spirochete, *Borrelia burgdorferi* sensu stricto

The invasive, human-biting Asian longhorned tick, *Haemaphysalis longicornis*, was detected in New Jersey in the eastern United States in August of 2017 and by November of 2018 this tick had been recorded from 45 counties across 9 states, primarily along the Eastern Seaboard. The establishment of *H. longicornis* in the United States has raised the questions of how commonly it will bite humans and which native pathogens may naturally infect this tick. There also is a need for experimental vector competence studies with native pathogens to determine if *H. longicornis* can acquire a given pathogen while feeding, pass it transstadially, and then transmit the pathogen in the next life stage. In this experimental study, we evaluated the vector competence of a population of *H. longicornis* originating from the United States (New York) for a native isolate (B31) of the Lyme disease spirochete, *Borrelia burgdorferi* sensu stricto (s.s.).

In agreement with a previous experimental study on the vector competence of *H. longicornis* for *Borrelia garinii*, we found that uninfected *H. longicornis* larvae could acquire *B. burgdorferi* s.s. while feeding on infected *Mus musculus* mice (infection prevalence >50% in freshly fed larvae) but that the infection was lost during the molt to the nymphal stage. None of 520 tested molted nymphs were found to be infected, indicating that transstadial passage of *B. burgdorferi* s.s. is absent or rare in *H. longicornis*; and based on the potential error associated with the number of nymphs testing negative in this study, we estimate that the upper 95% limit for infection prevalence was 0.73%.

An *Ixodes scapularis* process control showed both effective acquisition of *B. burgdorferi* s.s. from infected mice by uninfected larvae and transstadial passage to the nymphal stage (infection prevalence of 80–82% for both freshly fed larvae and molted nymphs). We also observed that although *H. longicornis* larvae could be compelled to feed on mice by placing the ticks within feeding capsules, attachment and feeding success was minimal (<0.5%) when larvae were placed freely on the fur of the mice. We conclude that *H. longicornis* is unlikely to contribute more than minimally, if at all, to transmission of Lyme disease spirochetes in the United States. Nicole E.Breuner et al. Ticks and Tick-borne Diseases, doi.org/10.1016/j.ttbdis.2019.101311

Tick Bite Risk and Tick-Borne Disease Perceptions of School District Administrators in the Mid-Atlantic United States

We surveyed school administrators to determine the perception of risk of tick encounters and tick control methods implemented on school campuses in the mid-Atlantic.

Responses from Pennsylvania and New Jersey districts indicate school district administrators had knowledge of Lyme disease and blacklegged ticks, but knowledge of other tick species and tick-borne diseases was limited. Overall, the results suggest that targeted communication of educational information regarding ticks and tick control to school districts could encourage increased participation in organized tick control or other preventative measures.

Overall, respondents were aware of ticks and Lyme disease, but were not aware or had limited awareness of many other tick-borne diseases, and how tick bite risk could be reduced. Targeted communication of educational information regarding ticks and tick control to school districts could provide a framework for reducing tick-borne disease risk in mid-Atlantic school districts. Machtinger et al. J of School Health, doi.org/10.1111/josh.12835.

Tick-borne infections other than Lyme disease increased dramatically from 2010-2016 according to Quest Diagnostics

Laboratory Blood-Based Testing for Non-Lyme Disease Tick-Borne Infections at a National Reference Laboratory: A Seven-Year Experience

We evaluated trends in non-Lyme disease tick-borne disease (NLTBI) testing at a national reference laboratory.

Testing data performed at Quest Diagnostics during 2010 to 2016 were analyzed nationally and at the state level.

Testing and positivity for most NLTBIs increased dramatically from 2010 through 2016 based on testing from a large reference laboratory. The number of positive cases, though not as stringent as criteria for public health reporting, generally exceeds that reported by the Centers for Disease Control and Prevention. The frequency of NLTBI in the US is seasonal but testing activity and positive test results are observed throughout all months of the year. Positive results for NLTBI testing mostly originated from a limited number of states, indicating the geographic concentration and distribution of NLTBIs reported in this study. This report provides an important complementary source of data to best understand trends in and spread of NLTBI. https://academic.oup.com/ajcp/article/152/1/91/5461358

Two more deaths from Lyme disease infecting the heart

Fatal Lyme Carditis in New England: Two Case Reports | LETTERS |22 OCTOBER 2019

Lyme disease is the most common vector-borne disease in the United States, and it is hyperendemic in the Northeast (1). In the United States, the spirochete *Borrelia burgdorferi* causes Lyme disease and is transmitted by the bite of an infected black-legged tick. Carditis is a rare manifestation that can usually be treated successfully with a short course of antibiotics (2). However, it can present with many

symptoms, and its severity can change rapidly and unpredictably (3). Death can occur when Lyme carditis is untreated. Before this report, only 9 fatal cases were reported... Marx et al. Annals of Internal Medicine. Full report at https://annals.org/aim/article-abstract/2753436/fatal-lyme-carditis-new-england-two-case-reports

Sleep quality in well-defined Lyme disease: a clinical cohort study in Maryland

The primary objective of this study is to examine and quantify sleep quality among patients with early LD during the acute and convalescent periods, including among the subset who met criteria for PTLDS. Methods: This paper draws from a clinical cohort study of participants with early LD (n = 122) and a subcohort of individuals who later met criteria for PTLDS (n = 6). Participants were followed for 1 year after antibiotic treatment.

Participants with early LD experienced poor sleep quality, which is associated with typical LD symptoms of pain and fatigue. In the subset of patients who developed PTLDS, sleep quality remains affected for up to 1 year post-treatment and is commonly associated with pain. Sleep quality should be considered in the clinical picture for LD and PTLDS. Weinstein et al. Sleep Research Society. doi: 10.1093/sleep/zsy035. Entire paper free of charge.

The Long-Term Persistence of Borrelia burgdorferi Antigens and DNA in the Tissues of a Patient with Lyme Disease

Whether Borrelia burgdorferi, the causative agent of Lyme disease, can persist for long periods in the human body has been a controversial question. The objective of this study was to see if we could find B. burgdorferi in a Lyme disease patient after a long clinical course and after long-term antibiotic treatment. Therefore, we investigated the potential presence of B. burgdorferi antigens and DNA in human autopsy tissues from a well-documented serum-, PCR-, and culture-positive Lyme disease patient, a 53-year-old female from northern Westchester County in the lower Hudson Valley Region of New York State, who had received extensive antibiotic treatments over the course of her 16-year-long illness. We also asked what form the organism might take, with special interest in the recently found antibiotic-resistant aggregate form, biofilm. We also examined the host tissues for the presence of inflammatory markers such as CD3+ T lymphocytes.

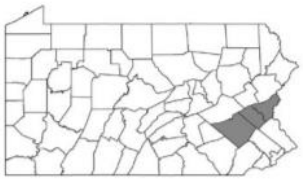
Autopsy tissue sections of the brain, heart, kidney, and liver were analyzed by histological and immunohistochemical methods (IHC), confocal microscopy, fluorescent in situ hybridization (FISH), polymerase chain reaction (PCR), and whole-genome sequencing (WGS)/metagenomics. We found significant pathological changes, including borrelial spirochetal clusters, in all of the organs using IHC combined with confocal microscopy. The aggregates contained a well-established biofilm marker, alginate, on their surfaces, suggesting they are true biofilm.

We found B. burgdorferi DNA by FISH, polymerase chain reaction (PCR), and an independent verification by WGS/metagenomics, which resulted in the detection of B. burgdorferi sensu stricto specific DNA sequences. IHC analyses showed significant numbers of infiltrating CD3+ T lymphocytes present next to B. burgdorferi biofilms. In summary, we provide several lines of evidence that suggest that B. burgdorferi can persist in the human body, not only in the spirochetal but also in the antibiotic-resistant biofilm form, even after long-term antibiotic treatment. The presence of infiltrating lymphocytes in the vicinity of B. burgdorferi biofilms suggests that the organism in biofilm form might trigger chronic inflammation. Sapi et al. Antibiotics 2019, 8, 183; doi:10.3390/antibiotics8040183. Entire paper free of charge.

Almost 25% of black-legged tick nymphs infected with the Lyme disease bacteria in eastern Pennsylvania

A 4-Yr Survey of the Range of Ticks and Tick-Borne Pathogens in the Lehigh Valley Region of Eastern Pennsylvania

Questing ticks were surveyed by dragging in forested habitats within the Lehigh Valley region of eastern Pennsylvania for four consecutive summers (2015–2018). A high level of inter-annual variation was found in the density of blacklegged tick nymphs, Ixodes scapularis Say, with a high density of host-seeking nymphs (DON) in summer 2015 and 2017 and a relatively low DON in summer 2016 and 2018. Very few American dog ticks (Dermacentor variabilis Say) and Ixodes cookei Packard were collected. Lone star ticks (Amblyomma americanum L.) and longhorned ticks (Haemaphysalis longicornis Neumann) were not represented among the 6,398 ticks collected. For tick-borne pathogen surveillance, DNA samples from 1,721 I. scapularis nymphs were prepared from specimens collected in summers 2015–2017 and screened using qPCR, high resolution melting analysis, and DNA sequencing when necessary.



The overall 3-yr nymphal infection prevalence of Borrelia burgdorferi was 24.8%, Borrelia miyamotoi was 0.3%, Anaplasma phagocytophilum variant-ha was 0.8%, and Babesia microti was 2.8%. Prevalence of coinfection with B. burgdorferi and B. microti as well as B. burgdorferi and A. phagocytophilum variant-ha were significantly higher than would be expected by independent infection. B. burgdorferi nymphal infection prevalence is similar to what other studies have found in the Hudson Valley region of New York, but levels of B. microti and A. phagocytophilum variant-ha nymphal infection prevalence are relatively lower. This study reinforces the urgent need for continued tick and pathogen surveillance in the Lehigh Valley region. Edwards et al. Journal of Medical Entomology, 2019, 10.1093/jme/tjz043

Blacklegged ticks in Pittsburgh's parks are highly infected with the Lyme disease bacteria

Lyme Disease Risk of Exposure to Blacklegged Ticks (Acari: Ixodidae) Infected with *Borrelia burgdorferi* (Spirochaetales: Spirochaetaceae) in Pittsburgh Regional Parks

… Although Lyme disease risk has been studied in residential and recreational settings across rural to urban landscapes including metropolitan areas, risk within U.S. cities has not been adequately evaluated despite the presence of natural and undeveloped public parkland where visitors could be exposed to *B. burgdorferi*-infected *I. scapularis*.

We studied the occurrence of *I. scapularis* and infection prevalence of *B. burgdorferi* in four insular regional parks within the city of Pittsburgh to assess Lyme disease risk of exposure to infected adults and nymphs. We found that the density of *I. scapularis* adults (1.16 ± 0.21 ticks/100 m^2) and nymphs (3.42 ± 0.45 ticks/100 m^2), infection prevalence of *B. burgdorferi* in adults (51.9%) and nymphs (19.3%), and density of infected adults (0.06 ticks/100 m^2) and nymphs (0.66 ticks/100 m^2) are as high in these city parks as nonurban residential and recreational areas in the highly endemic coastal Northeast.

These findings emphasize the need to reconsider, assess, and manage Lyme disease risk in greenspaces within cities, especially in high Lyme disease incidence states. Simmons et al. *Journal of Medical Entomology*, tjz140, https://doi.org/10.1093/jme/tjz140.

The eye and tick-borne disease in the United States

Tick-borne diseases are increasing in incidence and geographic distribution. Several diseases endemic to the United States have ophthalmic manifestations, including the most common tick-borne disease, Lyme borreliosis. As ocular complaints may lead a patient to seek medical evaluation, it is important to be aware of the systemic and ophthalmic manifestations of tick-borne diseases in order to make the correct diagnosis.

Vision-threatening ophthalmic manifestations are relatively common in Lyme disease and Rocky Mountain spotted fever. Ocular involvement is rare in babesiosis, tick-borne relapsing fever, Powassan encephalitis, ehrlichiosis, anaplasmosis, and Colorado tick fever. There are clear guidelines for diagnosis and treatment of Lyme disease; however, confusion and misinformation among the general public as well as controversy about chronic or late-stage Lyme disease can impact the evaluation of ophthalmic disease. Furthermore, there are many gaps in our knowledge regarding the pathophysiology of ocular borreliosis although it seems likely that Lyme uveitis is rare in the United States.
Sathiamoorthia & Smith, Curr Opin Ophthalmol 2016, 27:530–537.

Advancing the Science of Tick and Tick-Borne Disease Surveillance in the United States

Globally, vector-borne diseases are an increasing public health burden; in the United States, tick-borne diseases have tripled in the last three years. The United States Centers for Disease Control and Prevention (CDC) recognizes the need for resilience to the increasing vector-borne disease burden and has called for increased partnerships and sustained networks to identify and respond to the most pressing challenges that face vector-borne disease management, including increased surveillance.
To increase applied research, develop communities of practice, and enhance workforce development, the CDC has created five regional Centers of Excellence in Vector-borne Disease. These Centers are a partnership of public health agencies, vector control groups, academic institutions, and industries….
Wisely & Glass. Insects 2019, 10, 361.

•The Northeast Regional COE at **Cornell** University
•The Pacific Southwest COE at the **University of California**, **Davis and Riverside**
•The Southeastern Regional COE at the **University of Florida**
•The Western Gulf COE at the **University of Texas Medical Branch in Galveston**
•The Midwest COE at the **University of Wisconsin, Madison**

Can dogs get red meat allergy? A European study that involves their species.

Tick Bites Induce Anti-α-Gal Antibodies in Dogs

Due to the functional inactivation of the gene encoding for the enzyme that is involved in the oligosaccharide galactose-α-1,3-galactose (α-Gal) synthesis, humans and Old-World primates are able to produce a large amount of antibodies against the glycan epitope. Apart from being involved in the hyperacute organ rejection in humans, anti-α-Gal antibodies have shown a protective effect against some pathogenic agents and an implication in the recently recognized tick-induced mammalian meat allergy. Conversely, non-primate mammals, including dogs, have the ability to synthetize α-Gal and, thus, their immune system is not expected to naturally generate the antibodies toward this self-antigen molecule.

However, in the current study, we detected specific IgG, IgM, and IgE antibodies to α-Gal in sera of clinically healthy dogs by an indirect enzyme-linked immunosorbent assay (ELISA) for the first time. Furthermore, in a tick infestation experiment, we showed that bites of Ixodes ricinus induce the immune response to α-Gal in dogs and that the resulting antibodies (IgM) might be protective against Anaplasma phagocytophilum.

These findings may help lead to a better understanding of the underlying mechanisms involved in mammalian meat allergy and tick-host-pathogen interactions, but they also open up the question about the possibility that dogs could develop an allergy to mammalian meat after tick bites, similar to that in humans. Hodži et al. Vaccines 2019, 7, 114; doi:10.3390/vaccines7030114. Article free of charge.

Compassion and Health Care: A Discussion with the Dalai Lama

The calling to be a physician has historically been driven by compassion— that is, the desire to relieve the suffering of others. However, the current health care delivery system in the United States has increasingly limited the ability of physicians to express compassion as they are afforded little time for meaningful interaction with their patients. One of the authors (R.S.) draws on his current focus on developing personalized, proactive, and patient-driven models of care to argue that patient engagement plays a critical role in achieving favorable outcomes.

Believing that compassion is key for establishing the physician–patient relationship needed to foster patient engagement, R.S. sought the advice of one of the world's most recognized thought leaders on this topic, His Holiness the 14th Dalai Lama. This Invited Commentary describes the meeting between the two authors, the Dalai Lama's thoughts about compassion, and his challenge to bring attention to the importance of compassion in medical education, practice, and research. R. Snyderman, MD, Tenzin Gyatso, the 14th Dalai Lama, Academic Medicine, Vol. 94, No. 8. Entire article at: journals.lww.com/academicmedicine/Fulltext/2019/08000/Compassion_and_Health_Care__A_Discussion_With_the.9.aspx

Borrelia seroprevalence among blood donors in Southeast Brazil

Serological evidence of *Borrelia* circulation among blood donors in the São Paulo state, Brazil

There is evidence that *Borrelia* spirochetes are circulating in Brazil; however, there are no studies that characterise these bacteria and investigate their seroprevalence in the Brazilian population. Such a situation, combined with a recent outbreak of tick-borne Rocky Mountain spotted fever in the São Paulo state demonstrates the increasing role of ticks as arthropod vectors in Brazil.

For the purpose of the study, 452 blood donors from Ribeirão Preto city, São Paulo state were tested using anti-*Borrelia* immunoglobulin G (IgG) assay. The positive results were also confirmed by Western blot for anti-borrelia IgM/IgG.

The anti-*Borrelia* IgG enzyme-linked immunosorbent assay (ELISA) showed nine positive and nine borderline reactive samples, giving a total seroprevalence of 2·0% of anti-*Borrelia* IgG among Brazilian blood donors. The confirmation of the seropositive and borderline samples by Borrelia Western blot was demonstrated by IgG-positive results in 16 samples (a seroprevalence of 3.5%). Anti-*Borrelia* IgM antibodies were also detected in one sample.

Our results demonstrate that *Borrelia*-like spirochetes may be circulating among blood donors from the São Paulo State and that the ticks have an important epidemiological role as vectors of bacterial infections in this Brazilian region. These results not only alert us to possible actions that might be undertaken in order to completely characterise the aetiological agents of Lyme-like syndromes in Brazil but also the possible impact that these bacterial agents might have on haemotherapy practices. Slavov et al. https://doi.org/10.1111/tme.12627 Transfusion Medicine Volume 29, Issue 5

Lyme disease cases highest in northern Mongolia

Geographic Range of Lyme Borreliosis in Mongolia

In Asia, *Borrelia garinii, B. afzelii*, and *B. bavariensis* are transmitted by *Ixodes persulcatus* ticks and clinically present with a wide range of neurological and arthritic symptoms. This report aims to provide details on the geographic distribution of suspected cases of Lyme borreliosis (LB), reported to local Mongolian hospitals between 2007 and 2017.

This report examines 150 reported cases of suspected LB from 13 aimags (provinces) in Mongolia from April 2007 to August 2017, including date and location of infection, method of diagnosis (indirect immunofluorescent assay and/or enzyme-linked immunosorbent assay test), frequency of specific symptoms, and case demographics. Information was gathered through collaboration with the National Center of Communicable Disease and the National Center for Zoonotic Diseases.

Zavkhan and Selenge, located in northern Mongolia, had the highest percentage of reported suspected cases, with 25% and 20%, respectively. Ages ranged from 1 to 78 years, with a mean age of 26 years, however, 37% of individuals were younger than 10. More than twice as many women sought treatment as men, and the distribution of men who sought treatment was skewed toward children and the elderly. Most frequently reported symptoms include fever, rash, headache, and enlarged lymph glands. Furthermore, peak months of tick bite and treatment seeking occurred between April and June.

Based on these preliminary findings, syndromic surveillance should be expanded across northern Mongolia, with LB considered in differential diagnosis for patients reporting a recent tick bite. Frinken et al. Vector-Borne and Zoonotic Diseases. doi.org/10.1089/vbz.2018.2421.

From Tick Bite to Heart Failure; Ehrlichial Myocarditis

Cardiac involvement in myocarditis induced by Human Monocytic Ehrlichiosis (HME) infection is an incredibly uncommon complication with sparsely available literature. Also, this case highlights the importance of early recognition as a first step in management.
A 58-year-old woman presented to the emergency department (ED) with altered mental status and difficulty breathing. She had been having intermittent weakness and fever over the preceding month. Her husband reported that he had noticed a rash over her extremity. She had a history of multiple tick exposures from a recent outdoors excursion. In the ED, the patient was found to be hypotensive and hypoxic. She was intubated and was started on vasopressors.

Following the identification of E. chafeensis on PCR, both vancomycin and cefepime were stopped and only Doxycycline was continued. Her respiratory status improved and on hospital day 8 she was able to be extubated. However, the patient kept having frequent pre-mature ventricular contractions and multiple episodes of NSVT. There was a high suspicion for myocarditis. ... [Numerous studies and procedures were performed.]

...An implantable cardioverter-defibrillator was implanted for primary prevention of sudden cardiac death. The patient is now 12 months after her initial hospitalization and has had 2 admissions for acute heart failure exacerbation.

…A suspicion for ehrlichiosis induced myocarditis should be maintained in endemic areas, especially during the summer months. Of the four published case reports which discuss cardiac manifestations of ehrlichiosis, only two patients received Doxycycline therapy early enough to have a favorable outcome and survive. Almaddah et al. doi.org/10.1016/j.cjco.2019.09.003.

Lyme borreliosis: a review of data on transmission time after tick attachment

Lyme borreliosis is increasing rapidly in many parts of the world and is the most commonly occurring vector-borne disease in Europe and the USA…. Transmission to humans is incidental and can occur during visits to a vector habitat, when host mammals and their associated ticks migrate into the urban environment, or when companion animals bring ticks into areas of human habitation.

It is frequently stated that the risk of infection is very low if the tick is removed within 24-48 hours, with some claims that there is no risk if an attached tick is removed within 24 hours or 48 hours.

A literature review has determined that in animal models, transmission can occur in <16 hours, and the minimum attachment time for transmission of infection has never been established. Mechanisms for early transmission of spirochetes have been proposed based on their presence in different organs of the tick. Studies have found systemic infection and the presence of spirochetes in the tick salivary glands prior to feeding, which could result in cases of rapid transmission. Also, there is evidence that spirochete transmission times and virulence depend upon the tick and Borrelia species. These factors

support anecdotal evidence that Borrelia infection can occur in humans within a short time after tick attachment. Cook M. Int J Gen Med. 2014, doi: 10.2147/IJGM.S73791.

Chronic post-concussive syndrome and Lyme disease prevalence

The prevalence of Lyme disease and associated co-infections in people with a chronic post-concussive syndrome

There is increasing awareness that Lyme borreliosis (LB) and traumatic brain injury (TBI) may cause mental health symptoms…. We have identified an alarming number of individuals suffering from post-concussion syndrome (PCS) that are refractory to care and that have serologically tested positive for Lyme disease.
A single-center retrospective review of patient charts that were symptomatic a minimum of one year after a TBI that were tested for Lyme disease to ascertain if there was a relationship. 217 PCS patient records (93 females with a mean age of 34 years, 120 males with a mean age of 40 years and 4 individuals with unknown gender) were included in the review. 38% had a positive Western Blot Igenex IgM…. There was statistical and substantive significance between individuals with chronic PCS having a positive Western Blot Igenex IgM. Males were more likely to have a positive Western Blot Igenex IgM than females. Azzolino et al. Psychiatria Danubina, 2019; Vol. 31, Suppl. 3, pp 299–307 Conference paper. Canadian Cardiovascular Society volume 1, issue 6

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* The editor of the TIC-NC newsletters is our scientific advisor, Marcia E. Herman-Giddens

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