Tick-Borne Infections Council of North Carolina, Inc.

NEWSLETTER 2021, Volume 1

Quote: - **[T]he duration of time until diagnosis [of Lyme disease] was delayed due to issues that have arisen because of the COVID-19 pandemic.**
Gary Wormser et al. www.sciencedirect.com/science/article/abs/pii/S0732889320306039?via=ihub

Highlights…

- **Latest NC tick data, the State Department of Public Health**
- **North Carolina, ticks, and climate change**
- **Lyme Disease and COVID-19: Risk for Mix-up and Delay**
- **Learn about alpha gal via a Podcast from UNC Drs. Falk and Cummins**
- **Northern and southern black-legged ticks meeting in North Carolina**
- **Soft bodied tick found in New Jersey (not previously in the eastern US)**
- **FDA approves GMO pork safe for people with alpha-gal allergy**
- **Alpha gal (red meat allergy) with only GI symptoms**
- **Novel *Rickettsia* species infecting dogs**
- **COVID-19 leads to confusion with tickborne infections**
- **Enhanced mass spectrometry may be a new tool for studying tick-borne infections**
- **Delay in doxycycline may be associated with severe ehrlichiosis**
- **Scientists identify protein that protects against Lyme**

Special notice:

COVID-19 vs. Tick-Borne Diseases: How to Tell the Difference

People are getting outside more due to the pandemic. The link below is to an article from New York but is pertinent to NC. We would add that here *ticks are active all year*, so even in the winter on a warmer day it is possible to contract a tickborne infection (TBI).

Second, knowledge or evidence of a tick bite is not as easy as this article would imply. Many people that contract a TBI have no knowledge or easy to see evidence of a tick bite on their skin.

Third, respiratory symptoms of Covid-19 may not occur immediately or can be minimal. This can delay seeking medical care, adding to the risk of a late diagnosis of TBIs because of overlapping diagnostic symptoms.

There are cases now reported in the medical literature of late treatment for TBIs due to this confusion. See special Covid-19/Tickborne Disease Section below.

In addition, we at TIC-NC are aware of at least two. (Comments from the newsletter editor- M. Herman-Giddens) https://healthmatters.nyp.org/how-to-protect-yourself-from-ticks/

The State of NC has no meetings scheduled for the Vector-Borne Working Group so far.

Location:
Office of the Chief Medical Examiner
4312 District Drive
Raleigh, NC 27607

Photo ID required.

Link to **Letter to Medical Providers from the State Department of Public Health - Annual Update on Diagnosis and Surveillance for Tick-borne diseases**
Please see link to the letter on our website home page: www.tic-nc.org

From the CDC

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"

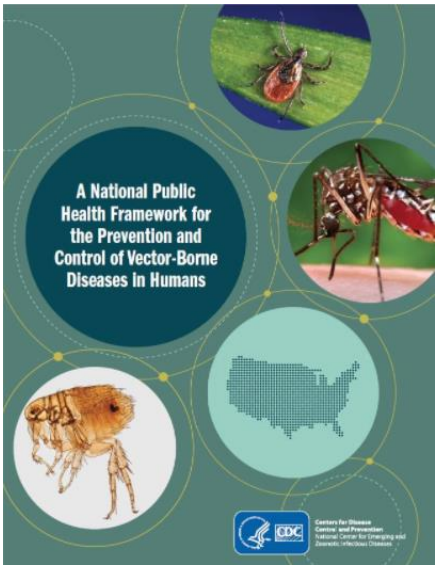
Case Definition and Report Forms

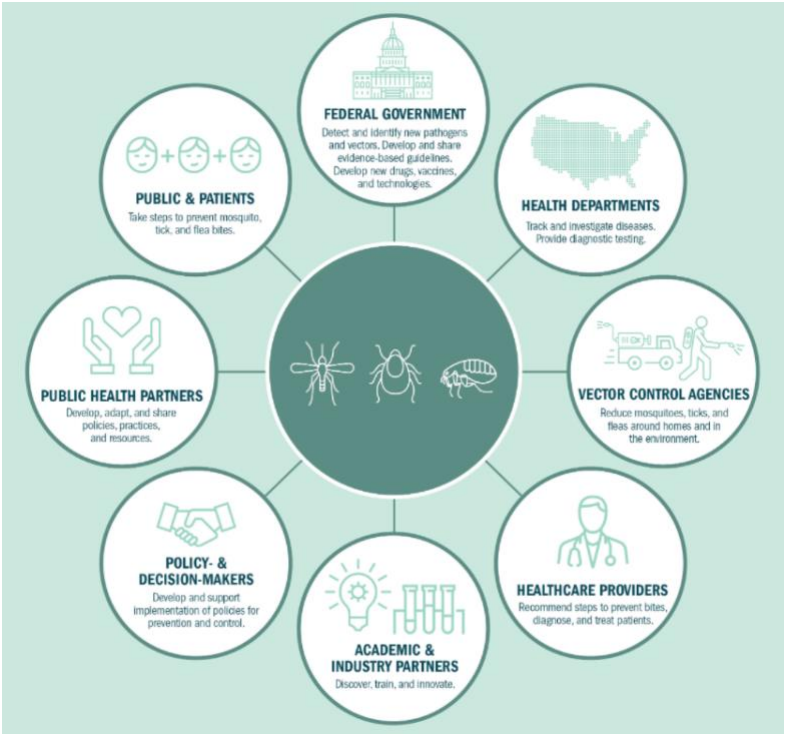
- Lyme Disease Surveillance Case Definition (revised Jan 2017)
- Lyme Disease Surveillance Case Report FormCdc-pdf PDF – 2 pages] (for public health officials' use)

> **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.

The CDC has recently collaborated with five federal departments (Health and Human Services, Agriculture, Defense, Homeland Security, Interior) and the EPA to develop and publish **a joint national framework** outlining federal activities necessary to detect, prevent, and control vector-borne diseases in humans in the US. The framework outlines five essential goals to protect people from illness, suffering, and death due to vector-borne diseases. Read more about the coordinated approach and strategic priorities outlined in this framework by visiting https://www.cdc.gov/ncezid/dvbd/framework.html.





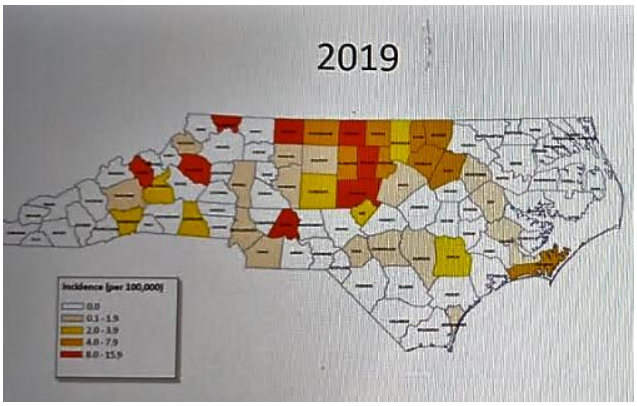
Resources

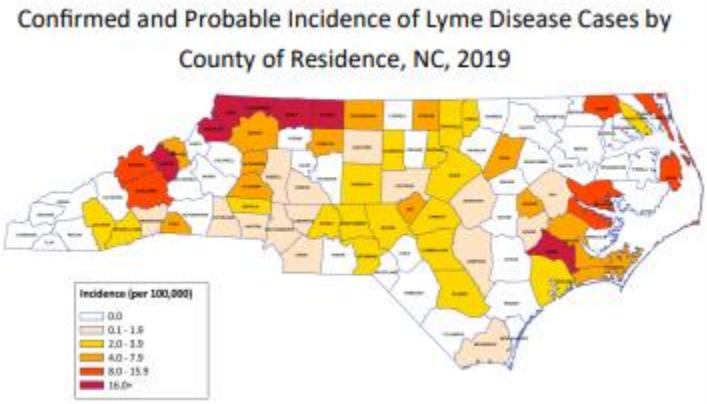
- A National Public Health Framework for the Prevention and Control of Vector-Borne Diseases in Humans pdf icon[PDF – 16 pages]
- National Framework fact sheet pdf icon[PDF – 2 pages]

State tick research and/or reports

The 2019 tick bone disease surveillance summaries are now complete. You can view them at the bottom of the NC DHHS Epi Section Facts & Figures page, under Vector-borne Disease section: https://epi.dph.ncdhhs.gov/cd/figures.html.

Ehrlichiosis incidence per county





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.

TIC-NC Talks and Materials Distributed

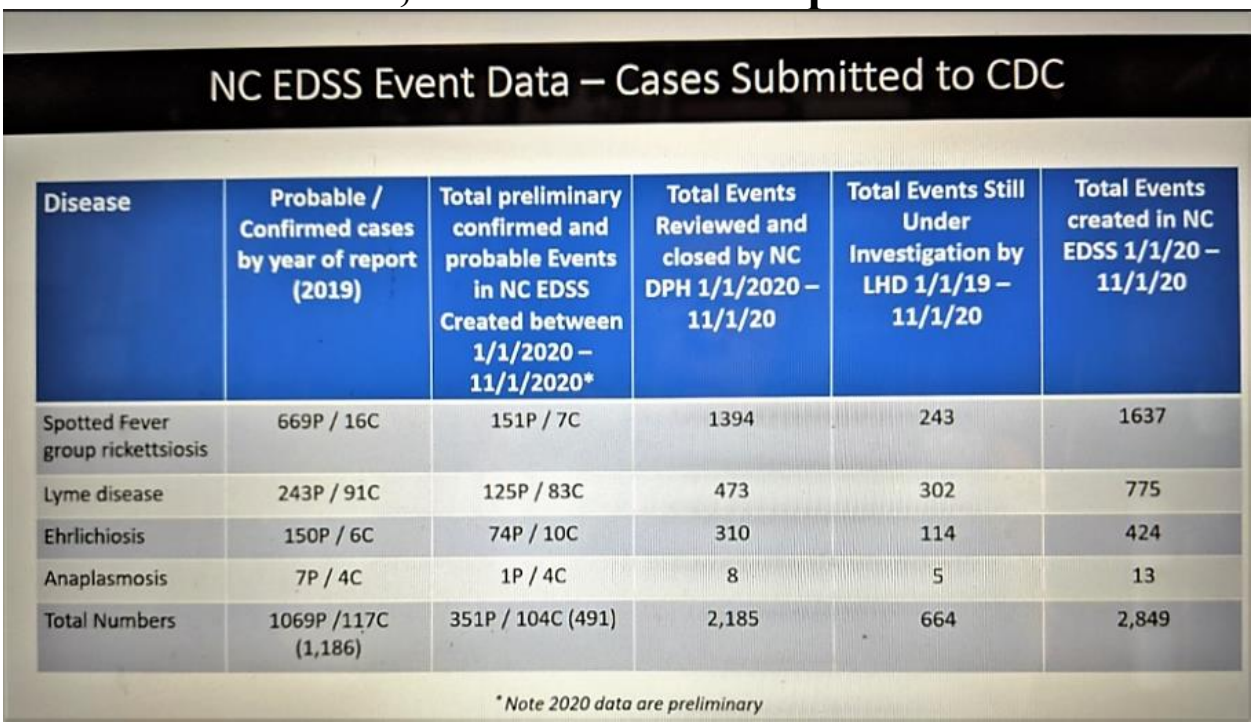
Brochures/booklets:

- **Winston-Salem**
- **Asheville**

Talks:

- **Marcia E Herman Giddens presented: "D**n Ticks: What's New" at the North Carolina Mosquito and Vector-borne Disease Control Annual Meeting, via Zoom, November 5, 2020**
- **NC Vegetative Management Annual Meeting via Zoom, December 9, 2020**

NC TBIs 2019 final, 2020 to November probable/confirmed



NC EDSS Event Data – Cases Submitted to CDC

Disease	Probable / Confirmed cases by year of report (2019)	Total preliminary confirmed and probable Events in NC EDSS Created between 1/1/2020 – 11/1/2020*	Total Events Reviewed and closed by NC DPH 1/1/2020 – 11/1/20	Total Events Still Under Investigation by LHD 1/1/19 – 11/1/20	Total Events created in NC EDSS 1/1/20 – 11/1/20
Spotted Fever group rickettsiosis	669P / 16C	151P / 7C	1394	243	1637
Lyme disease	243P / 91C	125P / 83C	473	302	775
Ehrlichiosis	150P / 6C	74P / 10C	310	114	424
Anaplasmosis	7P / 4C	1P / 4C	8	5	13
Total Numbers	1069P /117C (1,186)	351P / 104C (491)	2,185	664	2,849

*Note 2020 data are preliminary

Special notice: The Infectious Disease Society of America's updated Lyme disease guidelines are out. Long awaited. They do not appear much different than those from 14 years ago.

"The scope of this guideline includes prevention of Lyme disease, and the diagnosis and treatment of Lyme disease presenting as erythema migrans, Lyme disease complicated by neurologic, cardiac, and rheumatologic manifestations, Eurasian manifestations of Lyme disease, and Lyme disease complicated by coinfection with other tick-borne pathogens." Entire document at www.idsociety.org/practice-guideline/lyme-disease/.

And, the IDSA Babesiosis Guidelines

Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA): 2020 Guideline on Diagnosis and Management of Babesiosis
Clinical Infectious Diseases, ciaa1216, https://doi.org/10.1093/cid/ciaa1216
https://www.idsociety.org/practice-guideline/babesiosis/ 11.30.2020.

ᚕᚕ TIC-NC Activities ᚕᚕ

Volunteer's Corner

Kudos to our volunteer Janey Dooley from a fan:

> Mms Dooley, My name is R__ and I live here in Asheville. Thank you for your relentless pursuit of tick-borne illness awareness. I have a new appreciation, as I have been battling it all Summer. I've faced all the usual challenges of delayed diagnosis, and resistance from medical professionals to take it seriously. You made an impression on a nurse friend of mine at Mission who told me about your work.
> *Ed- Ms. Dooley regularly promotes and distributes our materials in Buncombe County. Thank you, Janet!*

COVID-19/Tickborne Disease Section

Negative impact of the COVID-19 pandemic on the timely diagnosis of tick-borne infections

We describe 3 adult patients who did not have COVID-19 but instead had a treatable tick-borne infection. In each case, however, the duration of time until diagnosis was delayed due to issues that have arisen because of the COVID-19 pandemic. These issues need to be addressed to preserve patient well-being. Wormser et al. https://doi.org/10.1016/j.diagmicrobio.2020.115226.

Murine typhus mistaken for COVID-19 in a young man

Fever is a widely recognized presenting symptom of COVID-19. Consequently, other febrile illnesses may be difficult to distinguish from COVID-19—leading to delays in diagnosis and treatment. One such illness is murine typhus, a flea-borne illness with worldwide distribution caused by *Rickettsia typhi*. It often presents with fever, headache and myalgia, all of which have been commonly reported with COVID-19. Although the disease is usually mild with a good prognosis, there have been reports of severe illness and death. I present a case of murine typhus in a young male who had 2 weeks of headaches and daily fevers during the COVID-19 pandemic. He was ultimately tested for murine typhus when his occupation as a dog trainer was queried, and he experienced resolution of symptoms after treatment with doxycycline. During this pandemic, clinicians must be vigilant of other febrile illnesses whose symptoms overlap with COVID-19. Pate HM. BMJ Case Rep. 2020; doi: 10.1136/bcr-2020-239471.

ᴎᴎ North Carolina and South ᴎᴎ

Vector-borne Diseases and Climate Change
North Carolina's Policy Should Promote Regional Resilience

- From 2004-2018, tick-borne pathogens were responsible for more than 90% of reportable human VBD cases in North Carolina.

- Temperatures across North Carolina have warmed about 1°F since record-keeping began, and the most recent decade has been the warmest on record.

- Climate change resilience should be interwoven with community resilience and public health practice. Article includes five suggestions.
  Byrd et al. 2020. Entire article free of charge at www.ncmedicaljournal.com/content/81/5/324.full

Lyme Disease in the Era of COVID-19: A Delayed Diagnosis and Risk for Complications

We describe a patient with fever and myalgia who did not have COVID-19 but instead had Lyme disease. We propose that the cooccurrence of COVID-19 and Lyme disease during the spring of 2020 resulted in a delayed diagnosis of Lyme disease due to COVID-19 pandemic-related changes in healthcare workflow and diagnostic reasoning. This delayed diagnosis of Lyme disease in the patient we describe resulted in disseminated infection and sixth nerve palsy. We present the use of telemedicine to aid in the diagnosis of Lyme disease and to provide prompt access to diagnosis and care during the ongoing COVID-19 pandemic and in the future. Novak CB et al. Case Reports in Infectious Diseases Volume 2021.
https://scholar.google.com/scholar?q=Novak+CB+et+al.+Case+Reports+in+Infectious+Diseases+Volume+2021&hl=en&as_sdt=0&as_vis=1&oi=scholart.

Learn about alpha gal via a Podcast from UNC Drs. Falk and Cummins

Podcast with UNC Med. Department chair, Dr. Ron Falk, and Dr. Scott Cummins – the physician scientist working on alpha gal. https://www.med.unc.edu/medicine/news/chairs-corner/podcast/alpha-gal/.

Northern and southern blacklegged (deer) ticks are genetically distinct with different histories and Lyme spirochete infection rates

Lyme borreliosis (LB) is the archetypal emerging zoonosis and is dependent on transmission by ticks in the genus *Ixodes*. Understanding the origin, maintenance, and spread of these ticks contributes much to our understanding of the spread of LB and other disease agents borne by these ticks. We collected 1232 *Ixodes scapularis* ticks from 17 east coast sites ranging from New Hampshire to Florida and used mtDNA, three nuclear genetic loci, and incorporated Bayesian analyses to resolve geographically distinct tick populations and compare their demographic histories.

A sparse, stable, and genetically diverse population of ticks in the Southeastern US, that is rarely infected with the agent of LB is genetically distinct from an abundant, expanding, and comparatively uniform population in the Northeast, where epidemic LB now constitutes the most important vector-borne disease in the United States. The contrasting geography and demography of tick populations, interpreted in the context of the geological history of the region, suggests that during the last glacial period such ticks occupied distinct refugia, with only the northern-most site of refuge giving rise to those ticks and pathogens now fueling the epidemic. Xu G, et al. *Sci Rep* **10,** 10289 (2020). https://doi.org/10.1038/s41598-020-67259-0.

A Comparison of Tick Collection Materials and Methods in Southeastern Virginia

In field studies of tick ecology, observed patterns may be biased by sampling methods. Results can vary by species, life stage, and habitat, and understanding these biases will improve comparisons of data across studies as well as assessment of human disease risk. A direct comparison of flagging versus dragging was conducted in southeastern Virginia. Transects were surveyed over a 6-wk period to identify differences in species and life stage collected, as well as differences between corduroy and denim material and inspection method for drags.

Flagging collected more *Ixodes affinis* Neumann (Acari: Ixodidae) adults and *Amblyomma americanum* L. (Acari: Ixodidae) adults than dragging. Ground inspection was more efficient than tree inspection for collection of *I. affinis* adults, with no significant difference in inspection method for any other species or life stage. Corduroy was found to be more effective than denim in collecting nymphal *A. americanum*, although this may be an artifact of three large samples for corduroy collection of these ticks. There was no significant difference in *Ixodes scapularis* Say (Acari: Ixodidae) collection in any comparison.

Dragging, tree inspection, and denim were not found to be more efficient in any scenario. This is the first comparison of flagging and dragging conducted in the southeastern United States. The community composition of ticks in this region greatly differs from regions where studies of these commonly used sampling techniques have been conducted. As the distributions of ticks continue to change over time, it will be important to evaluate best practices annually. Espada et al. *Journal of Medical Entomology*, tjaa207, https://doi.org/10.1093/jme/tjaa207.

One of the samples used in this study came off a dog from Raleigh area that had not been out of the state . . .

Novel *Rickettsia* species infecting dogs, United States.

In the United States, tickborne *Rickettsia parkeri*, *R. philipii* (*Rickettsia* 364D), and *R. rickettsii*, causative agents of Rocky Mountain spotted fever (RMSF), are well-documented human spotted fever group (SFG) rickettsioses. *R. rickettsii* is the only known cause of SFG rickettsioses in dogs. The extent to which other SFG *Rickettsia* are pathogenic in dogs is unclear; however, SFG *Rickettsia* seroprevalence is high among dogs in the United States and Mexico. The increased *R. rickettsii* seroprevalence in humans in the United States during the past decade has been attributed to SFG *Rickettsia* cross-reactivity.

We report 3 dogs with febrile illness located in different US states. Samples from the dogs were *R. rickettsii* seroreactive. Identical *Rickettsia* DNA gene sequences were obtained from each dog's blood specimen and used to investigate *Rickettsia* spp.

Based on serologic cross-reactivity, presence of *ompA*, and phylogenetic tree analysis, the new *Rickettsia* sp. is an SFG *Rickettsia*, phylogenetically related to human pathogenic *R. heilongjiangensis* and *R. massiliae*, with only 95% identity to each. Thus, we report a previously unknown and unique *Rickettsia* sp. with clinical significance for dogs and potentially humans. Because this novel *Rickettsia* cross-reacts with *R. rickettsia* on IFA, it could be underdiagnosed and more geographically widespread. Studies aimed at identifying the tick vector, potential animal reservoirs, and prevalence are ongoing. These 3 canine rickettsioses cases underscore the value of dogs as sentinels for emerging tickborne pathogens. Wilson JM, et al. Emerg Infect Dis. 2020 https://wwwnc.cdc.gov/eid/article/26/12/20-0272_article.

◘◘ National Section ◘◘

FDA approves GMO pork safe for people with alpha-gal allergy

Frankenswine: Hypoallergenic Pigs Win FDA Nod — Engineered to be safe for people with "alpha-gal" reactions

Medpage Today: Barbecue can return to the menu for individuals with "alpha-gal" syndrome -- severe allergic reactions to the alpha-galactose saccharide found in red meat -- with FDA approval Monday of pigs engineered to lack an enzyme considered key to the condition.

Developed by a company called Revivicor, the "GalSafe" pigs might also have therapeutic potential as sources of xenograft organs and tissues, the FDA said. Another example the agency offered was heparin "free of detectable alpha-gal sugar."

The decision represents the FDA's first approval of "intentional genomic alteration" (IGA) in an animal that may be used both for food and medical use, the agency said. However, any use of the animals for xenotransplant or other therapeutic applications must undergo a separate regulatory review; at this point, only meat for the dining table has the agency's OK.

It's not the first genetically engineered food animal, though -- that honor belongs to AquaBounty's salmon with a growth hormone gene and certain regulatory elements added from other species.

In both cases, the FDA determined that foods derived from the modified creatures posed no more risk to humans or the environment than their unmodified counterparts.

In the case of Revivicor's swine, the agency said, "conditions under which GalSafe pigs will be kept are far more stringent than those for conventionally farmed pigs. Additionally, no animal safety concerns were noted for GalSafe pigs beyond those that would be expected in well-managed, commercial swine operations."

The specific alteration in the pigs is to delete the gene for alpha-1,3-galactosyltransferase, which attaches alpha-galactose sugars to cell surfaces.

Alpha-gal syndrome appears to originate with bites from certain tick species. People thus sensitized then develop allergic reactions to foods containing alpha-galactose, such as beef, lamb, and other red meats, in addition to pork. Although considered rare, it's also believed to be responsible for up to half of anaphylactic reactions with no obvious trigger.

At least initially, Revivicor plans to sell pork from its GalSafe herd only via mail order, not in supermarkets, the FDA said. By John Gever, Managing Editor, MedPage Today December 14, 2020.

Recurring Gastrointestinal Symptoms as a Novel Presentation of Alpha-Gal Allergy

…There are no case reports of adults with abdominal pain as the sole symptom of this allergy…The first alpha-gal allergy to mammalian meat was documented in 2006 and it is still not fully understood. It is proposed that remnant alpha-gal from previous mammalian blood meals are transmitted to humans through the saliva of *Amblyomma americanum* (lone star tick), which is endemic to the southwest region of the United States…

It is crucial to obtain a good clinical history and recognize that recurrent abdominal pain, nausea or vomiting may be the only presentation especially given that the current mean time to diagnosis is 7.1 years. Diagnosis is made with blood work assessing IgE levels to beef, pork, and lamb… Given the risk of anaphylaxis, prescription of an epinephrine pen and elimination of mammalian meat is the only treatment. D'Souza M & Lania M. The American Journal of Gastroenterology: https://journals.lww.com/ajg/Fulltext/2020/10001/S3011_Recurring_Gastrointestinal_Symptoms_as_a.3010.aspx

A delay in doxycycline may be a significant factor associated with severe ehrlichiosis

Assessment of Risk Factors and Outcomes of Severe Ehrlichiosis Infection
Key Points
Question What risk factors are associated with severe ehrlichiosis?

Findings This cross-sectional study including 155 patients identified a delay in doxycycline therapy as a significant factor associated with severe ehrlichiosis. Documentation of tick exposure was independently associated with a decreased need for intensive care unit admission, and a change toward a decreased need for intensive care unit admission among immunosuppressed persons was identified.

Meaning In this study, delay in initiation of empirical doxycycline therapy appears to be a risk factor for severe ehrlichiosis; education focused on early recognition and treatment may decrease morbidity associated with this infection. Kuriakose K, et al.. JAMA Netw Open. 2020;3(11):e2025577..
Paper is free of charge.

Focus on Lyme Scientific Conference on the Immune Response

The Focus on Lyme Scientific Conference brings together the brightest minds in Lyme disease to share the latest in research and treatment. We create a collaborative environment that includes researchers, clinicians and top advocacy groups.

At this year's Focus on Lyme Scientific Conference, our focus was on research related to the immune response to Borrelia, and how it can contribute to the clinical disease experienced by many Lyme disease patients.

Monica Embers, PhD
Assistant Professor, Tulane National Primate Research Center

Holly Ahern, MS, MT(ASCP)
Professor of Microbiology, State University New York Adirondack & Focus On Lyme's Scientific Advisor

Neal Woodbury

Professor and Director, School of Molecular Sciences Chief Science Officer, Arizona State University

Tim Haystead, PhD
Duke University School of Medicine

Bennett Nemser
Steven and Alexandra Cohen Foundation

Mark J. Soloski, PhD
Johns Hopkins School of Medicine

Link to YouTube for the conference: https://www.focusonlyme.org/

Elevated Infections of Lyme Disease Patients with *Cryptosporidium parvum*

We report for the first time a relationship between clinical cases of Lyme disease diagnosed in a US patient population in a Virginia clinical facility and intestinal infections with *Cryptosporidium parvum* identified from fecal samples collected from the same patients tested in an Arizona Parasitology Center (PCI). Infections with *C. parvum* in the populations of Lyme disease patients were at a considerably higher prevalence rate than in the general non-Lyme US population. *Bartonella*, *Babesia*, *Ehrlichia*, and *Borrelia* co-infections with the Lyme disease have been well established. All these infections are resident in the *Ixodes* tick vector system and can be transmitted to human *via* tick bite. Infections with *C. parvum*, however, are transmitted by the water/food vehicle and not by tick bites and therefore do not lend themselves to the tick bite transmission pattern.

This is the first such report involving a relationship between two pathologies with very different epidemiology. Our findings are more similar to the reported association between HIV-AIDS and *Cryptosporidium* infections as both conditions can often be associated with the fecal contamination *via* certain sexual practices. Our report addresses 456 cases studied for Lyme disease and *C. parvum* infections by sex and age tested in the same facility. Amin OM, Rubtsova NY (2020) J Bacteriol Parasitol. 11:380. DOI:10.35248/2155-9597.20.11.380.

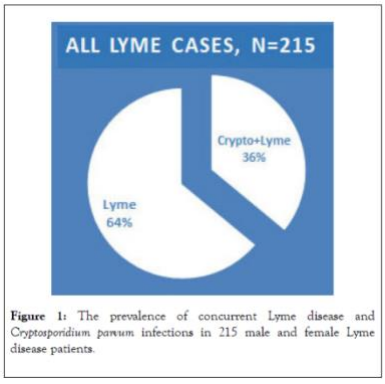


Figure 1: The prevalence of concurrent Lyme disease and *Cryptosporidium parvum* infections in 215 male and female Lyme disease patients.

Tick-Borne-Associated Illnesses in the Pediatric Intensive Care Unit

When unrecognized and antibiotic delay occurs, Lyme disease, Rocky Mountain–spotted fever, babesiosis, and human ehrlichiosis and anaplasmosis can result in multiorgan system dysfunction and potentially death. This review focuses on the early recognition, evaluation, and stabilization of the rare life-threatening sequelae seen in tick-borne illnesses that require admission in the pediatric intensive care unit. Lessner & Krawiec, Journal of Pediatric Infectious Diseases, DOI: 10.1055/s-0040-1717149.

First Record of *Carios kelleyi* (Acari: Ixodida: Argasidae) in New Jersey, United States and Implications for Public Health

The soft tick *Carios kelleyi* (Cooley and Kohls), a parasite of bats known to occur in at least 29 of the 48 conterminous U.S. states, is here reported from New Jersey for the first time, based on larvae collected from big brown bats, *Eptesicus fuscus*. Although thought to be widespread in North America, the ecology of *C. kelleyi* is not well understood, despite reports of this species feeding on humans and its consequent potential as a disease vector. The association of *C. kelleyi* with bat species that regularly roost in human-made structures, such as attics and barns, and recent isolations from this tick of pathogens capable of infecting humans, companion animals, and livestock underscore the need for further studies of these bat ectoparasites.

- Found in 29 states
- First time in NJ
- infected with a novel spotted fever *Rickettsia*,
- novel relapsing fever-related *Borrelia*
- *Bartonella henselae*
- a novel relapsing fever spirochete, identified as *Borrelia johnsonii* (in tick in Iowa)
- one WS pt + by PCR of 7,000 for *B. johnsonii*

Occi et al, *Journal of Medical Entomology,* XX(X), 2020, 1–4, doi: 10.1093/jme/tjaa189.

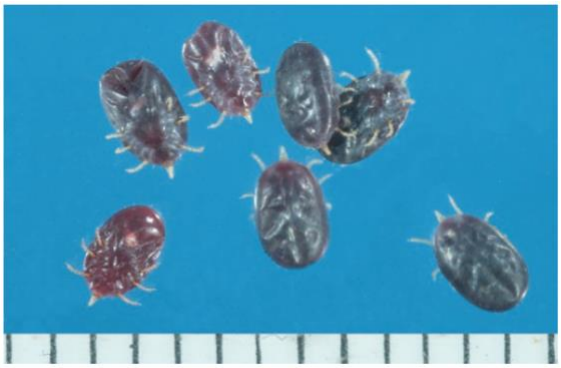


Fig. 1. Mix of dorsal and ventral views of a group of *Carios kelleyi* larvae obtained from New Jersey big brown bats. Notice all specimens are blood-engorged. The scale is in millimeters.

"Take-away" lesson-- carditis can be the presenting manifestation of Lyme disease in pediatric patients

Chest palpitations in a teenager as an unusual presentation of Lyme disease: case report

The incidence of Lyme disease (LD) in North America has increased substantially in the past two decades… The patient was a 16-year-old male who presented with the main concerns of acute onset of palpitations and chest pain. An important clinical finding was *Erythema migrans* (EM) on physical exam… The primary diagnoses were LD with associated Lyme carditis, based on the finding of 1st degree atrioventricular heart block (AVB) and positive IgM and IgG antibodies to *Borrelia burgdorferi*... The hospital course was further remarkable for transition to 2nd degree heart block and transient episodes of complete heart block. A normal sinus rhythm and PR interval were restored after antibiotic therapy and the primary outcome was that of an uneventful recovery.

Lyme carditis occurs in < 5% of LD cases, but the "take-away" lesson of this case is that carditis can be the presenting manifestation of *B. burgdorferi* infection in pediatric patients. Any patient with suspected Lyme carditis manifesting cardiac symptoms such as syncope, chest pain, or EKG changes should be admitted for parenteral antibiotic therapy and cardiac monitoring. The

most common manifestation of Lyme carditis is AVB. AVB may manifest as first-degree block, or may present as high-grade second or third-degree block… With the rising incidence of LD, providers must maintain a high level of suspicion in order to promptly diagnose and treat Lyme carditis. Myers et al. *BMC Infect Dis* **20,** 730 (2020). https://doi.org/10.1186/s12879-020-05438-0.

Global Warming Has Brown Dog Ticks Jumping from Dogs to Humans

MONDAY, Nov. 16, 2020 (HealthDay News) -- Climate change could increase people's risk of getting dangerous diseases from ticks, researchers warn.

The investigators conducted tests with brown dog ticks that carry the bacteria that cause the deadly disease Rocky Mountain spotted fever (RMSF) and found the ticks are much more likely to prefer feeding on the blood of people than dogs when temperatures rise.

Brown dog ticks are found throughout the continental United States. Previous research has suggested they may be more aggressive toward humans in hot weather.

The findings were presented Nov. 16 at a virtual meeting of the American Society of Tropical Medicine and Hygiene (ASTMH). Research presented at meetings should be considered preliminary until published in a peer-reviewed journal.

… "We found that when temperatures rose from about 74 to 100 degrees Fahrenheit, brown dog ticks that carry the disease were 2.5 times more likely to prefer humans over dogs," Backus said in a society news release.

"Climate change is moving so quickly that it is critical to keep pace with the many ways it may alter and intensify the risk of a wide range of infectious diseases so we are better prepared to diagnose, treat and prevent them," Breman added in the news release.

Frantic About Residential Tick Management? This Film Series is Just for You

Our team at the Western Connecticut State University Tickborne Disease Prevention Laboratory and the Ridgefield Connecticut Department of Health sought to clear up confusion about residential tick management, specifically surrounding backyard acaricide use. Studies show that one well-timed application of a pyrethroid-based acaricide to targeted areas of one's backyard is effective for managing nymphal blacklegged ticks. We wondered how we could convey evidence-based information about safe and judicious acaricide use in an engaging way that could also be shared online and via social media. Studies have shown that short, story-based narrative films with engaging characters and humor can effectively communicate health information. So, the *Spray Safe, Play Safe* film series was born, and so was Fran Tick. In October, my colleagues and I published a report in the *Journal of Medical Entomology* that shares results from an evaluation we conducted on the films' effectiveness in increasing homeowner confidence in backyard tick management. We posted the *Spray Safe, Play Safe* films

(see full series of films in the video below) to a project-dedicated website, www.spraysafeplaysafe.org/, and to YouTube.

International & General Section

Photo of Lyme disease spirochetes in the gut of a black-legged tick nymph

Interactions Between Ticks and Lyme Disease Spirochetes

Borrelia burgdorferi sensu lato causes Lyme borreliosis in a variety of animals and humans. These atypical bacterial pathogens are maintained in a complex enzootic life cycle that primarily involves a vertebrate host and Ixodes spp. ticks. In the Northeastern United States, I. scapularis is the main vector, while wild rodents serve as the mammalian reservoir host. As B. burgdorferi is transmitted only by I. scapularis and closely related ticks, the spirochete-tick interactions are thought to be highly specific…

This review will focus on the past discoveries and future challenges that are relevant to our understanding of the molecular interactions between B. burgdorferi and Ixodes ticks. This information will not only impact scientific advancements in the research of tick transmitted infections but will also contribute to the development of novel preventive measures that interfere with the B. burgdorferi life cycle. Utpal P et al. Curr. Issues Mol. Biol. 42: 113-144. DOI: https://doi.org/10.21775/cimb.042.113

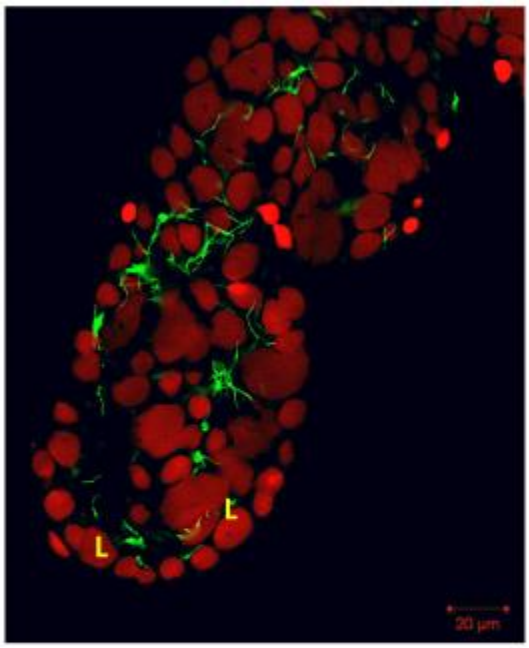


Figure 1. Colonized *B. burgdorferi* within the gut diverticulum of a nymphal *I. scapularis*. The gut of an unfed nymphal *I. scapularis* tick was dissected and processed for confocal immunofluorescence microscopy, as detailed (Pal et al., 2004a). The image shows a portion of the gut diverticulum, where tick nuclei (red) were labeled with propidium iodide, and spirochetes towards the luminal side (green) were detected using FITC-labeled anti-*B. burgdorferi* antibodies. L, Lumen of the gut, Bar = 20 µm.

The Platelet Fraction Is a Novel Reservoir to Detect Lyme Borrelia in Blood

To diagnose Lyme disease, a patient's blood is tested for antibodies that develop as part of the immune response. This can lead to cases being missed or inadequately treated. An ideal test would directly detect the Lyme disease bacteria, Borrelia, to provide better clinical guidance. In

this study, we aimed to improve the methods currently used to find Borrelia in human blood and identified two opportunities for optimization.

We demonstrate that the container most commonly used to collect blood (EDTA) decreases Borrelia's ability to grow, and we identify a superior alternative (citrate). Additionally, using experimentally infected blood, we show that Borrelia is highly concentrated in the platelet fraction, making it an ideal candidate for direct detection. These results lay the foundation for diagnostic test development, which could improve patient outcomes. Sanderson et al. Biology 2020, 9, 366; doi:10.3390/biology9110366

Scientists identify protein that protects against Lyme

A human secretome library screen reveals a role for Peptidoglycan Recognition Protein 1 in Lyme borreliosis

Lyme disease, the most common vector-borne illness in North America, is caused by the spirochete *Borrelia burgdorferi*. Infection begins in the skin following a tick bite and can spread to the hearts, joints, nervous system, and other organs. Diverse host responses influence the level of *B. burgdorferi* infection in mice and humans.

For the study, the Yale team expressed more than 1,000 human genes in yeast and analyzed their interactions with 36 samples of B. burgdorferi. They found that one protein, Peptidoglycan Recognition Protein 1 (PGLYRP1), acts like an early warning signal to the immune system when exposed to the bacteria. When exposed to the Lyme spirochete, mice lacking PGLYRP1 had much higher levels of B. burgdorferi than mice with the protein and showed signs of immune system dysfunction, the researchers report.

Fikrig and his colleagues are also investigating whether people with higher levels of PGLYRP1 may be less susceptible to infection by B. burgdorferi, which would help explain why some infected individuals have better outcomes. Gupta A et al. PLoS Pathogens, doi.org/10.1371/journal.ppat.1009030

Enhanced mass spectrometry may be a new tool for studying tick-borne pathogen infections

Evaluation of pathogen specific urinary peptides in tick-borne illnesses

Mass spectrometry enhanced by nanotechnology can achieve previously unattainable sensitivity for characterizing urinary pathogen-derived peptides. We utilized mass spectrometry enhanced by affinity hydrogel particles (analytical sensitivity = 2.5 pg/mL) to study tick pathogen-specific proteins shed in the urine of patients with (1) erythema migrans rash and acute symptoms, (2) post treatment Lyme disease syndrome (PTLDS), and (3) clinical suspicion of tick-borne illnesses (TBI).

Targeted pathogens were Borrelia, Babesia, Anaplasma, Rickettsia, Ehrlichia, Bartonella, Francisella, Powassan virus, tick-borne encephalitis virus, and Colorado tick fever virus. Specificity was defined by 100% amino acid sequence identity with tick-borne pathogen proteins, evolutionary taxonomic verification for related pathogens, and no identity with human or other organisms. Using a cut off of two pathogen peptides, 9/10 acute Lyme Borreliosis patients resulted positive, while we identified zero false positive in 250 controls.

Two or more pathogen peptides were identified in 40% of samples from PTLDS and TBI patients (categories 2 and 3 above, n = 59/148). Collectively, 279 distinct unique tick-borne pathogen derived peptides were identified. The number of pathogen specific peptides was directly correlated with presence or absence of symptoms reported by patients (ordinal regression pseudo-$R^2 = 0.392$, $p = 0.010$). Enhanced mass spectrometry is a new tool for studying tick-borne pathogen infections. Magni, R, *et al.* Evaluation of pathogen specific urinary peptides in tick-borne illnesses. *Sci Rep* **10,** 19340 (2020). https://doi.org/10.1038/s41598-020-75051-3

Metabolic Response in Patients with Post-Treatment Lyme Disease Symptoms/Syndrome

Post-treatment Lyme disease symptoms/syndrome (PTLDS) occurs in approximately 10% of Lyme disease patients following antibiotic treatment. Biomarkers or specific clinical symptoms to identify PTLDS patients do not currently exist and the PTLDS classification is based on the report of persistent, subjective symptoms for ≥ 6 months following antibiotic treatment for Lyme disease.

Untargeted liquid chromatography-mass spectrometry metabolomics was used to determine longitudinal metabolic responses and biosignatures in PTLDS and clinically cured non-PTLDS Lyme patients. Evaluation of biosignatures included: 1) defining altered classes of metabolites; 2) elastic net regularization to define metabolites that most strongly defined PTLDS and non-PTLDS patients at different timepoints; 3) changes in the longitudinal abundance of metabolites; 4) linear discriminant analysis to evaluate robustness in a second patient cohort.

This study determined that observable metabolic differences exist between PTLDS and non-PTLDS patients at multiple timepoints. The metabolites with differential abundance included those from glycerophospholipid, bile acid and acylcarnitine metabolism. Distinct longitudinal patterns of metabolite abundance indicated a greater metabolic variability in PTLDS vs non-PTLDS patients. Small numbers of metabolites (6-40) could be used to define PTLDS vs. non-PTLDS patients at defined time points, and the findings were validated in a second cohort of PTLDS and non-PTLDS patients.

These data provide evidence that an objective metabolite-based measurement can distinguish patients with PTLDS and help understand the underlying biochemistry of PTLDS.
Fitzgerald BL, et al. *Clinical Infectious Diseases*, https://doi.org/10.1093/cid/ciaa1455.

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