

NEWSLETTER 2018, Volume 3



Quote of the season: - "If DNA sequencing can be used to confirm Lyme disease in a dead man frozen 5000 years ago, why are we not trying to use the same technology to diagnose Lyme disease on those still walking?" Sin Lee 2018 <u>http://www.dnalymetest.com/</u>

And to inspire us: - "Where does our power lie and how do we school ourselves to use it in the service of what we believe?" Audre Lorde in *A* Burst *of* Light: *and* Other Essays

Highlights...

Scroll down to see these features and more!

- Report from the state on tick activities 2018
- Federal Tick-Borne Disease Working Group
- Latest numbers of tick-borne diseases reported in North Carolina
- Lone Star ticks found to be effective for Bourbon virus, another new tickborne disease
- Lyme disease in horses
- Patent application for a handheld arthropod detection device
- CDC report on Lyme disease in Hispanics
- The Longhorned or Bush tick, native to East Asia, now established in parts of the US
- Length of tick attachment and likelihood of pathogen transmission
- Free paper on persister cells

State Vector-Borne Disease Working Group 2018 Meeting Schedule

Tentative 2018 VBWG meeting dates: July 27 and Nov 9 (Check with us before going to confirm date as they occasionally change.) **Location:** Office of the Chief Medical Examiner Photo ID required. 4312 District Drive, Raleigh, NC 27607

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

The 2018 letters the State Department of Public Health issues every year to medical providers regarding Lyme disease and Rickettsial diseases such as RMSF are on the Home Page of our website 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"

Go to: <u>www.cdc.gov/lyme/healthcare/index.html</u>. (The links below in a clip of the website are not active.) Scroll down and find "Case Definition and Report Forms". See the gray box with "Note" containing the disclaimer.

Case Definition and Report Forms

- Lyme Disease Surveillance Case Definition (revised Jan 2017)
- Lyme Disease Surveillance Case Report Form 🟂 [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 15 August 2017.

Final numbers for 2016 from the CDC

The CDC has released 2016 final numbers for Lyme disease. *Case numbers are no longer available by week.* The entire table can be seen at: wonder.cdc.gov/nndss/static/2016/annual/2016-table2i.html. (Ignore the column labeled 'Listeriosis.') Another link for Lyme disease stats is: www.cdc.gov/lyme/stats/index.html.

Reporting Area	Listeriosis	Total	Confirmed	Probable
United States	786	36,429	26,203	10,226
South Atlantic	158	4,736	3,197	1,539
Delaware	2	506	391	115
District of Columbia	1	103	66	37
Florida	43	216	132	84
Georgia	21	4	4	_
Maryland	• 23	1,866	1,274	592
North Carolina	23	272	32	240
South Carolina	17	51	25	26
Virginia	23	1,350	976	374
West Virginia	5	368	297	71
East South Central	29	97	41	56
Alabama	8	38	17	21
Kentucky	3	33	16	17
Mississippi	6	1	1	_
Tennessee	12	25	7	18

TABLE 2i. Reported cases of notifiable diseases, by region and reporting area - United States and U.S. territories, 2016

Report from the state on tick activities 2018

Currently, the state of North Carolina does not test ticks for Powassan (POW) or any other tick-borne illness. We do have contracts with a university partner that collects and identifies ticks in five of the 100 North Carolina counties in order to determine the distribution of Ixodes ticks. Those ticks are then sent to partners at CDC, where they are tested for Borrelia and Rickettsia species. The CDC does not test for POW because the test for POW requires a different panel and a different preservation method.

In early 2017 we partnered with the Virginia Department of Public Health to drag and test ticks for POW. Those ticks were also sent to CDC to be tested and came back negative for POW. We hope in the future that North Carolina can develop the capacity to test ticks for tick borne illness at the State Lab of Public Health. At the moment all of our testing, which is limited, is run through CDC.

Federal Tick-Borne Disease Working Group

Agenda for meeting Feb 12, 2018

http://www.hhs.gov/ash/advisory-committees/tickbornedisease/meetings/index.html

Description of Duties

The Working Group shall have the following responsibilities:

(A) Not later than two years after the date of enactment of the authorizing legislation, develop or update a summary of:

- (1) ongoing tick-borne disease research, including research related to causes, prevention, treatment, surveillance, diagnosis, diagnostics, duration of illness, and intervention for individuals with tick-borne diseases;
- (2) advances made pursuant to such research;
- (3) federal activities related to tick-borne diseases, including:
 - (a) epidemiological activities related to tick-borne diseases; and
 - (b) basic, clinical, and translational tick-borne disease research related to the pathogenesis, prevention, diagnosis, and treatment of tick-borne diseases.
- (4) gaps in tick-borne disease research described in clause 3b;
- (5) the Working Group's meetings; and the comments received by the Working Group.
- (B) Make recommendations to the Secretary regarding any appropriate changes or improvements to such activities and research; and
- (C) Solicit input from States, localities, and non-governmental entities, including organizations representing patients, health care providers, researchers, and industry regarding scientific advances, research questions, surveillance activities, and emerging strains in species of pathogenic organisms.

Subcommittee reports released May 10, 2018. The Tick-Borne Disease Working Group (Working Group) is required to submit a report on its activities and any recommendations to the HHS Secretary and Congress every two years. The first report is due December 2018.

The six subcommittees of the Working Group prepared reports to inform the Working Group and its 14 voting members. These reports offer insights into gaps, opportunities and potential actions to be considered by the Working Group for the report to Congress and HHS Secretary. <u>http://www.hhs.gov/ash/advisory-committees/tickbornedisease/reports/index.html</u>

Report of the Access to Care Services and Support to Patients Subcommittee Report of the Disease Vectors, Surveillance, and Prevention Subcommittee Report of the Other Tick-Borne Diseases and Co-Infections Subcommittee Report of the Pathogenesis, Transmission and Treatment Subcommittee Report of the Testing and Diagnostics Subcommittee Report of the Vaccine and Therapeutics Subcommittee

CDC study recently released: North Carolina No. 12 in the US for tick-borne diseases

A new report from the agency reveals that diseases transmitted through the bites of blood-feeding ticks, mosquitoes, and fleas are a "growing public health problem" in the United States.

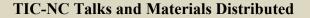
Reported cases of what are called vector-borne diseases have more than tripled nationwide, growing from 27,388 cases reported in 2004 to a whopping 96,075 cases reported in 2016, according to the new Vital Signs report published by the CDC on Tuesday.

In North Carolina, between 2004 and 2016, there were 9,075 tick-borne disease cases, according to CDC data. According to the data, **North Carolina was No. 12 in the U.S. for tick-borne diseases**, which occur throughout the country but predominate in the eastern parts of the country and along the Pacific Coast. www.cnn.com/2018/05/01/health/ticks-mosquito-borne-diseases-cdc-study/index.html patch.com/north-carolina/charlotte/tick-borne-diseases-rise-nc-elsewhere-us-cdc

	Total cases by year of report 2014 Preliminary	2015 F inal	2016 Final
Disease	Confirmed + Probable (Confirmed/Probable/ Suspected)	(Probable/Confirme/Sus- pected)	(Probable/ Confirmed)
Lyme disease	170 (27/143/86)	192/38/46	274/32
Rickettsioses	496 (10/486/278)	454/5/130	682/10
Ehrlichioses	73 (11/62/31)	58/16/18	61/10
Anaplasmoses	12 (0/12/12)	15/4/3	16/1

NC TBIs 2014-2016, probable/confirmed- Final numbers

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.



Brochures/booklets:

- Haw River Spice Bush Spring Walk by the Friends of State Parks – Lower Haw River State Natural Area UNC Health Expo
- Veterinary Practices—1,200 booklets across the southeast

Hanging Rock State Park (thanks to a volunteer) Alpha-gal Symposium, Pittsboro, May 30

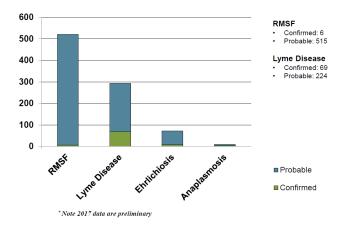
Talks: Fearrington Community-- Fearrington Cares North Carolina Park Rangers Tick Workshop

Report from the state Vector-borne Disease Work Group meeting

April 16, 2018. The state Vector-borne Disease Working Group Meeting was held at the Office of the Chief Medical Examiner. Preliminary data on mosquito and tick-borne diseases for 2017 were presented.

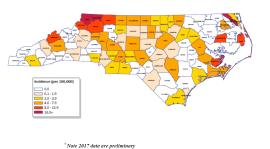
Data presented by the state *Vector-borne Disease Working Group*, April 16, 2018 NC State Lab of Public Health

Tick Borne Illness in 2017

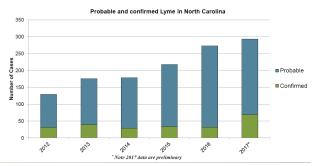


North Carolina Lyme disease data

Incidence of Confirmed and Probable Cases of Lyme in North Carolina (2017)*



Probable and confirmed cases of Lyme are increasing.



TIC-NC Activities

TIC-NC and NC State Parks collaborated on their first annual symposium on Ticks, Tick Diseases and Allergies in March of 2018. Through these efforts there will be increased tick signage in state parks and increased programming for the public to promote tick bite prevention and awareness of ticks and tick diseases. *Thank you, Brian Bockhahn, Regional Education Specialist, North Carolina State Parks.*



TIC-NC member Janet Dooley worked on and presented a proclamation from the

mayor designating May as Tick-borne Disease Awareness Month to the Asheville City Council on May 15, 2018. She also presented materials including ILADS Psychiatric Lyme brochures, the new book *LYME, the First Epidemic of Climate Change* by Mary Beth Pfeiffer, a copy of the video "A Ticking Time Bomb," and Tick Warning signs for the parks. Thank you, Janet!

North Carolina and South

Article in the Salisbury, NC Post about a woman with Lyme disease

Watch out for ticks: Lyme disease often misdiagnosed

Andrea Stallings suffered with a puzzling illness for several years that made her leave her nursing job for employment that allowed her to work from home. Eventually Stallings was determined to have contracted Lyme disease, a bacteria that is transmitted by ticks. Tuesday, May 22, 2018, in Salisbury, N.C. JON C. LAKEY / SALISBURY POST

www.salisburypost.com/2018/05/26/watch-out-for-ticks-lyme-disease-often-misdiagnosed/

Ed note: There are several points in the article that are not accurate. We do not know of evidence that the Lyme disease bacteria "invades the mitochondria." The most common appearance of the so-called target or bull's eye rash is solid red. A person can get this rash from the Lone Star tick, a different tick than the one that transmits classic Lyme disease. That infection is called STARI and is treated in the same way as Lyme disease. Always keep any tick found biting. Tape it firmly on a card or calendar, noting the date and place on the body. Watch for symptoms for 30 days. If you see your provider take the tick with you. This can help with diagnosis.

Alpha-gal syndrome possibly related to Rickettsia in Lone Star ticks

Characterizing the Geographic Distribution of the Alpha-gal Syndrome: Relevance to Lone Star Ticks (Amblyomma americanum) and Rickettsia

RATIONALE: Allergic reactions in patients with IgE to galactose-alpha-1, 3-galactose, known as alpha-gal syndrome (AS), are well recognized in the southeastern USA. The original recognition of the relevance of *A.americanum* tick bites came from the apparent similar area of Rocky Mountain Spotted Fever (RMSF) cases. However, severe cases of RMSF are rare in this area, and in addition *Rickettsia rickettsii* is uncommonly identified in humans or *A.americanum*.

METHODS: Using a modified snowball design, we interviewed ~100 allergists starting in areas with high prevalence of AS. The questionnaire related to the number of confirmed cases, the response to an avoidance diet and the relationship to tick bites. The incidence of AS was compared to recent publications from the CDC describing the geographic distribution of *A.americanum* and tick-borne infections.

RESULTS: Large numbers of cases, i.e. 50-200, were reported by many allergists in the southeast, but also in Long Island, NY and to a lesser extent in northern Minnesota. The CDC reported high prevalence of RMSF in the southeast as late as 2015, however abundant evidence now suggests that spotted fever group Rickettsia (SFG), but not RMSF, are the culprit. The established range of *A.americanum* largely corresponds with the incidence of AS, but the agreement is stronger when also considering incidence of tick-borne organisms such as SFG or Ehrlichia.

CONCLUSIONS: The geographic relationship between the established range of *A.americanum* and incidence of AS is strong. However, the possibility exists that alpha-gal sensitization relates to a Rickettsia in the context of tick saliva.

TAE Platts-Mills, et al. Journal of Allergy and ..., 2018, J Allergy Clin Immun 141:2 www.jacionline.org/article/S0091-6749(17)32370-9/pdf

22% of small mammals in this study were positive for the Lyme disease bacteria

Borrelia burgdorferi in small mammal reservoirs in Kentucky, a traditionally non-endemic state for Lyme disease

The incidence of tick-borne zoonoses such as Lyme disease has steadily increased in the southeastern United States. Southeastern states accounted for 1500 of over 28,000 confirmed cases of Lyme disease reported in the United States during 2015. *Borrelia burgdorferi*, the etiologic agent of Lyme disease, is maintained in small mammal reservoirs and vectored to new hosts by ixodid ticks. This study



examined ecological relationships of the *B. burgdorferi*/vector/reservoir system in order to understand the dynamics of Lyme disease risk in Kentucky. Small mammals were captured using live traps from November 2014 to October 2015. Ticks were removed and blood and tissue collected from small mammals were screened for *B. burgdorferi* DNA by PCR with primers specific to the OspA gene. Prevalence of *B. burgdorferi* (21.8%) in Kentucky small mammals was comparable to the lowest recorded prevalence in regions where Lyme disease is endemic. Moreover, infestation of small mammals by *Ixodes scapularis*, the primary vector of *B. burgdorferi*, was rare, while *Dermacentor variabilis* comprised the majority of ticks collected. These findings provide ecological insight into the relative paucity of Lyme disease in Kentucky. Buchholz et al. <u>Parasitol Res.</u> 2018 Feb 7. https://www.ncbi.nlm.nih.gov/pubmed/29417273

DD National Section DD

More evidence that the lone star tick is the vector of the Bourbon virus 2018

Surveillance for Tick-Borne Viruses Near the Location of a Fatal Human Case of Bourbon Virus (Family *Orthomyxoviridae*: Genus *Thogotovirus*) in Eastern Kansas, 2015

Bourbon virus (Family Orthomyxoviridae: Genus Thogotovirus) was first isolated from a human casepatient residing in Bourbon County, Kansas, who subsequently died. Before becoming ill in late spring of 2014, the patient reported several tick bites. In response, we initiated tick surveillance in Bourbon County and adjacent southern Linn County during spring and summer of 2015. We collected 20,639 host-seeking ticks representing four species from 12 sites. Amblyomma americanum (L.) (Acari: Ixodidae) and Dermacentor variabilis (Say) (Acari: Ixodidae) accounted for nearly all ticks collected (99.99%). Three tick pools, all composed of adult A. americanum ticks collected in Bourbon County, were virus positive. Two pools were Heartland virus (Family Bunyaviridae: Genus Phlebovirus) positive, and one was Bourbon virus positive. The Bourbon virus positive tick pool was composed of five adult females collected on a private recreational property on June 5. Detection of Bourbon virus in the abundant and aggressive human-biting tick A. americanum in Bourbon County supports the contention that A. americanum is a vector of Bourbon virus to humans. The current data combined with virus detections in Missouri suggest that Bourbon virus is transmitted to humans by A. americanum ticks, including both the nymphal and adult stages, that ticks of this species become infected as either larvae, nymphs or both, perhaps by feeding on viremic vertebrate hosts, by cofeeding with infected ticks, or both, and that Bourbon virus is transstadially transmitted. Multiple detections of Heartland virus and Bourbon virus in A. americanum ticks suggest that these viruses share important components of their transmission cycles. Savage, et al. Journal of Medical Entomology, tjx251, https://doi.org/10.1093/jme/tjx251

New test for multiple tick-borne diseases

A multiplex serologic platform for diagnosis of tick-borne diseases

Tick-borne diseases are the most common vector-borne diseases in the United States, with serology being the primary method of diagnosis. We developed the first multiplex, array-based assay for serodiagnosis of tick-borne diseases called the TBD-Serochip. The TBD-Serochip was designed to discriminate antibody responses to 8 major tick-borne pathogens present in the United States, including Anaplasma phagocytophilum, Babesia microti, Borrelia burgdorferi, Borrelia miyamotoi, Ehrlichia chafeensis, Rickettsia rickettsii, Heartland virus and Powassan virus. Each assay contains approximately 170,000 12-mer linear peptides that tile along the protein sequence of the major antigens from each agent with 11 amino acid overlap. This permits accurate identification of a wide range of specific immunodominant IgG and IgM epitopes that can then be used to enhance diagnostic accuracy and integrate differential diagnosis into a single assay. To test the performance of the TBD-Serochip, we examined sera from patients with confirmed Lyme disease, babesiosis, anaplasmosis, and Powassan virus disease. We identified a wide range of specific discriminatory epitopes that facilitated accurate diagnosis of each disease. We also identified previously undiagnosed infections. Our results indicate that the TBD-Serochip is a promising tool for a differential diagnosis not available with currently employed serologic assays for TBDs. Tokarz et al. Scientific Reports volume 8, Article number: 3158(2018), https://www.nature.com/articles/s41598-018-21349-2

Lyme disease in horses

Borrelia burgdorferi Infection and Lyme Disease in North American Horses: A Consensus Statement

Borrelia burgdorferi infection is common in horses living in Lyme endemic areas and the geographic range for exposure is increasing. Morbidity after *B. burgdorferi* infection in horses is unknown. Documented, naturally occurring syndromes attributed to *B. burgdorferi* infection in horses include neuroborreliosis, uveitis, and cutaneous pseudolymphoma. Although other clinical signs such as lameness and stiffness are reported in horses, these are often not well documented. Diagnosis of Lyme disease is based on exposure to *B. burgdorferi*, cytology or histopathology of infected fluid or tissue and antigen detection. Treatment of Lyme disease in horses is similar to treatment of humans or small animals but treatment success might not be the same because of species differences in antimicrobial bioavailability and duration of infection before initiation of treatment. There are no approved equine label Lyme vaccines but there is strong evidence that proper vaccination could prevent infection in horses. Divers et al. (2018), *Borrelia burgdorferi* Infection and Lyme Disease in North American Horses: A Consensus Statement. J Vet Intern Med. https://www.ncbi.nlm.nih.gov/pubmed/29469222. Consensus Statements of the American College of Veterinary Internal Medicine (ACVIM) provide the veterinary community with up-to-date information on the pathophysiology, diagnosis, and treatment of clinically important animal diseases. The ACVIM Board of Regents oversees selection of relevant topics, identification of panel members with the expertise to draft the statements.

Lyme Disease in Hispanics, United States, 2000–2013

Hispanics comprise a growing portion of the US population and might have distinct risk factors for tick-borne diseases. Outdoor workers in LD-endemic areas have increased odds of occupational exposure to ticks and a rate of LD seropositivity substantially higher than that of the general population. In the United States, Hispanics comprise 43.6% of grounds maintenance workers and 43.4% of workers in the farming, fishing, and forestry industries, potentially placing this population at greater risk for LD from occupational exposures. During 2000-2013, a total of 5,473 Lyme disease cases were reported among Hispanics through national surveillance. Hispanics were more likely than non-Hispanics to have signs of disseminated infection and onset during fall months. Nelson et al. Lyme Disease in Hispanics, United States, 2000–2013. *Emerging Infectious Diseases, 22*(3), 522-525. 2016. wwwnc.cdc.gov/eid/article/22/3/15-1273_article_

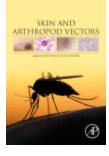
Early Disseminated Lyme Disease Causing False-Positive Serology for Primary Epstein-Barr Virus Infection: Report of 2 Cases

False-positive serology for Lyme disease was reported in patients with acute infectious mononucleosis. Here we describe 2 patients with early disseminated Lyme disease who were misdiagnosed with infectious mononucleosis based on false-positive tests for primary Epstein-Barr virus infection. Paveltic and Marques, 2017 *Clinical Infectious Diseases*, 65:336–337 <u>doi.org/10.1093/cid/cix298</u>

International & General Section

Tick Saliva and Its Role in Pathogen Transmission

Ticks are major vectors of pathogens affecting both humans and animals worldwide and surpass all other arthropods in the variety of microorganisms—including viruses, bacteria, and parasites (protozoa and helminths)—they are able to transmit. They are strict hematophagous arthropods and pool feeders, ingesting all the fluids that are exuded into the wound generated by the bite. For most tick-borne pathogens (TBP), transmission occurs via the saliva injected alternately with blood uptake



during the tick bite. This saliva is secreted by the tick salivary glands, which are implicated in several other functions that are essential to tick biology and development. Saliva is an essential bio-fluid for ticks, which dampens host defenses and facilitates the flow of blood to assure adequate feeding. It exhibits cytolytic, vasodilator, anticoagulant, anti-inflammatory, and immunosuppressive activities that, in addition, to underpinning blood feeding, provide a favorable context for transmission, survival, and propagation of TBP. Bonnet et al. Abstract from Chapter 5 in Skin and Arthropod Vectors 2018, pp 121–191. https://www.sciencedirect.com/science/article/pii/B9780128114360000058

Chapter 1: Genotyping Strains of Lyme Disease Agents Directly from Ticks, Blood, or Tissue. Alan G. Barbour and Vanessa J. Cook

Abstract. The tick-borne spirochetes that cause Lyme disease in North America and Eurasia display strong linkage disequilibrium between certain chromosomal and plasmid loci within each three major geographic areas of their distribution. For strain typing for epidemiologic and ecologic purposes, the commonly used genotypes based on a single locus are the spacer between the 16S–23S ribosomal RNA and the ospC gene of a plasmid. A simple genotyping scheme based on the two loci allows for discrimination between strains representing all the areas of distribution. The methods presented here are meant for genotyping directly from ticks and from blood and tissue samples from vertebrates.

The name "Borreliella" has been proposed [1] and formally accepted [2] for a new genus comprising all species of Lyme disease agents as well as closely-related species that are not associated with human disease. The genus name Borreliella replaces the term "Borrelia burgdorferi sensu lato" that has been used to distinguish this coherent clade from an equally coherent clade of relapsing fever species, which retain the genus name Borrelia on the basis of priority. The family name for the genera Borrelia and Borreliella is Borreliaceae.

References

1. Adeolu M, Gupta RS (2014) A phylogenomic and molecular marker based proposal for the division of the genus Borrelia into two genera: the emended genus Borrelia containing only the members of the relapsing fever Borrelia, and the genus Borreliella gen. nov. containing the members of the Lyme disease Borrelia (Borrelia burgdorferi sensu lato complex). Antonie Van Leeuwenhoek 105 (6):1049–1072. doi:10.1007/s10482-014- 0164-x

2. Oren A, Garrity GM (2015) List of new names and new combinations previously effectively, but not validly, published. Int J Syst Evol Microbiol 65(7):2017–2025

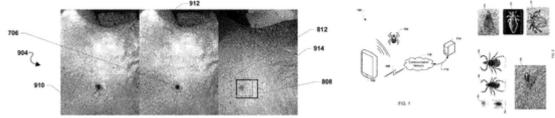
In: Utpal Pal and Ozlem Buyuktanir (eds.), Borrelia burgdorferi: Methods and Protocols, Methods in Molecular Biology, vol. 1690, DOI 10.1007/978-1-4939-7383-5_1, © Springer Science+Business Media LLC 2018

The Longhorned tick now established in New Jersey and West Virginia

Last August, a species of tick native to East Asia that causes diseases in livestock and humans mysteriously showed up on a farm in New Jersey. Now the New Jersey Department of Agriculture says that the *Haemaphysalis longicornis*, which is also known as the Longhorned tick or bush tick, has survived the winter and "has possibly become established in the state." www.countryliving.com/life/a20051995/east-asia-tick-found-in-new-jersey/

Patent application for Handheld arthropod detection device

Various embodiments include systems and methods of arthropod detection using an electronic arthropod detection device. A processor of an electronic arthropod detection device may scan a surface or a subject using the electronic arthropod detection device and capture at least one image while scanning the surface or the subject using the electronic arthropod detection device. The processor may determine whether the at least one image includes a region of interest (ROI) corresponding to an arthropod and provide an identification area of the at least one image to an object detection model in response to detected procedure in response to receiving a result from the object detection model that indicates that an arthropod is detected within the identification area of the at least one image. Diamond et al. Patent #2017-08-09US15673389, Status: 2018-02-15 US20180046872A1 Application



Rocky Mountain spotted fever confirmed in another state in Brazil

Confirming *Rickettsia rickettsii* as the etiological agent of lethal spotted fever group rickettsiosis in human patients from Espírito Santo state, Brazil

Although Espírito Santo state is considered an endemic area for Brazilian spotted fever (BSF) with related lethal cases, it also constitutes the only state of southeastern Brazil that currently lacks a specific confirmation of the specific rickettsial agent. In an attempt to a species level confirmation of the etiological agent of fatal rickettsiosis cases in Espírito Santo state, in this study we tested human sera obtained between 2015 to 2017 by means of qPCR and subsequent conventional PCR protocols targeting *gltA* (citrate synthase) and *ompA* (190-kDA outer membrane protein) rickettsial genes. All samples were found to contain rickettsial DNA through the citrate synthase qPCR protocol. By conventional PCR, rickettsial *gltA* and *ompA* specific DNA fragments were detected in 25% (one sample) and 50% (2 samples) of the screened sera, respectively. Obtained consensuses for each gene partial sequences were 100% identical to *Rickettsia rickettsii gltA* and *ompA* genes. The present study confirms for the first time *R. rickettsii* as the etiological agent of a lethal spotted fever group rickettsiosis in human patients from Espírito Santo state. Ticks and Tick-borne Diseases, Faccini-Martínez et al. https://doi.org/10.1016/j.ttbdis.2018.01.005

Tick Paralysis

Introduction

Tick paralysis is an uncommon, noninfectious, neurologic syndrome characterized by acute ataxia progressing to ascending paralysis. It is caused by the salivary neurotoxin of several species of tick. Clinical findings are similar to and often confused with Guillain-Barre syndrome. Most human cases of tick paralysis occur in North America and Australia. If recognized early and treated promptly, complete recovery is expected with tick removal and supportive care alone. Untreated, it can advance to respiratory failure and death. It is important for healthcare workers to be familiar with this relatively rare but readily treatable cause of acute motor weakness and to maintain a high index of suspicion to avoid delays in diagnosis and treatment. Tick paralysis should be considered in all cases of acute ataxia, especially in children. Simon and McKinney. StatPearls [Internet]. Last Update: November 27, 2017. For entire article see: www.ncbi.nlm.nih.gov/books/NBK470478/.

Review article on the probability of transmission resulting in host infection by black-legged ticks: 24 to 72 h after nymphal attachment, transmission is higher when multiple infected ticks feed together

Pathogen transmission in relation to duration of attachment by Ixodes scapularis ticks

The blacklegged tick, *Ixodes scapularis*, is the primary vector to humans in the eastern United States of the deer tick virus lineage of Powassan virus (Powassan virus disease); the protozoan parasite *Babesia microti* (babesiosis); and multiple bacterial disease agents including *Anaplasma phagocytophilum* (anaplasmosis), *Borrelia burgdorferi* and *Borrelia mayonii* (Lyme disease), *Borrelia miyamotoi* (relapsing fever-like illness, named *Borrelia miyamotoi* disease), and *Ehrlichia muris eauclairensis* (a minor causative agent of ehrlichiosis).



With the notable exception of Powassan virus, which can be transmitted within minutes after attachment by an infected tick, there is no doubt that the risk of transmission of other *I. scapularis*-borne pathogens, including Lyme disease spirochetes, increases with the length of time (number of days) infected ticks are allowed to remain attached.

This review summarizes data from experimental transmission studies to reinforce the important disease-prevention message that regular (at least daily) tick checks and prompt tick removal has strong potential to reduce the risk of transmission of *I. scapularis*-borne bacterial and parasitic pathogens from infected attached ticks. The most likely scenario for human exposure to an *I. scapularis*-borne pathogen is the bite by a single infected tick. However, recent reviews have failed to make a clear distinction between data based on transmission studies where experimental hosts were fed upon by a single versus multiple infected ticks.

A summary of data from experimental studies on transmission of Lyme disease spirochetes (*Bo. burgdorferi* and *Bo. mayonii*) by *I. scapularis* nymphs indicates that the probability of transmission resulting in host infection, at time points from 24 to 72 h after nymphal attachment, is higher when multiple infected ticks feed together as compared to feeding by a single infected tick. In the specific context of risk for human infection, the most relevant experimental studies therefore are those where the probability of pathogen transmission at a given point in time after attachment was determined using a single infected tick.

The minimum duration of attachment by single infected *I. scapularis* nymphs required for transmission to result in host infection is poorly defined for most pathogens, but experimental studies have shown that Powassan virus can be transmitted within 15 min of tick attachment and both *A. phagocytophilum* and *Bo. miyamotoi* within the first 24 h of attachment. There is no experimental evidence for transmission of Lyme disease spirochetes by single infected *I. scapularis* nymphs to result in host infection when ticks are attached for only 24 h (despite exposure of nearly 90 experimental rodent hosts across multiple studies) but the probability of transmission resulting in host infection appears to increase to approximately 10% by 48 h and reach 70% by 72 h for *Bo. burgdorferi*. Caveats to the results from experimental transmission studies, including specific circumstances (such as reattachment of previously partially fed infected ticks) that may lead to more rapid transmission are discussed. Eisen, TTD, <u>doi.org/10.1016/j.ttbdis.2018.01.002</u>

Recently recognized pathogen in the Rickettsia family: *Candidatus* Neoehrlichia Mikurensis (No common name, known as CNM)

Candidatus Neoehrlichia Mikurensis—Recent Insights and Future Perspectives on Clinical Cases, Vectors, and Reservoirs in Europe

Ticks are among the most important vectors of pathogens concerning animal and human health worldwide. *Candidatus* Neoehrlichia mikurensis (CNM) is a recently discovered intracellular bacterium of the order *Rickettsiales* associated with human clinical cases. In this review, we give an overview on the current knowledge of CNM in connection with diagnosis, clinical cases, and treatment and discuss the newest developments in the knowledge on potential vectors and reservoirs.

Small mammals and in particular rodents seem to be the most likely reservoir hosts for CNM in Europe. Ticks may be competent vectors in which the pathogen is transstadially transmitted. In both, vectors and reservoirs, vertical transmission is controversially discussed. Some recent studies suggested that CNM may be rather rodent- than tick-associated. As regards clinical cases, mainly immunosuppressed persons are affected but evidence of contact to CNM has also been established in some healthy people. Many other aspects such as important life history traits of CNM remain unknown and neglected in both research and diagnosis.

CNM is a highly interesting tick-borne and rodent-associated pathogen that under the right preconditions can cause severe disease in human beings. The cultivation of this intracellular bacterium of the order *Rickettsiales* seems to be the most pressing task to tackle in the future research on this pathogen. Obiegala & Silaghi, Curr Clin Micro Rpt (2018). https://doi.org/10.1007/s40588-018-0085-y

And a Chilean version-

"*Candidatus* Neoehrlichia chilensis" sp. nov.: Molecular detection and characterization of a novel Anaplasmataceae in wild rodents from Valdivia, southern Chile

This study aimed to screen wild rodents from southern Chile, for the presence of Anaplasmatacea. Spleen samples from 33 wild rodents trapped in Valdivia Province were screened by conventional PCR (cPCR), targeting the Anaplasmataceae 16S rRNA gene (16S). Positive samples were further evaluated, targeting a larger 16S fragment, *groEL* operon, and *gltA*gene, followed by sequencing and phylogenetic analysis. Anaplasmataceae DNA was detected in 15% (five of 33) of the tested rodents (*Abrothrix* sp. [four of five] and *Mus musculus* [one of five]). Analysis of sequenced products based on the 16S gene revealed high similarity with "*Ca*. Neoehrlichia mikurensis," "*Ca*. Neoehrlichia lotoris" and "*Ca*. Neoehrlichia arcana" (97.8%–98.6%). A lower similarity was observed with *Candidatus* Neoehrlichia *groEL* (89.7%-92%) and *gltA* (79.5%–79.9%) loci. According to the *16SrRNA*, *groEL* and *gltA* phylogenetic analyses, two closely related genotypes of "*Candidatus* Neoehrlichia" spp. from Chile were observed, which clustered together in a separate clade from other species in this genus. This study suggests the presence of two genotypes of a novel species of "*Candidatus* Neoehrlichia," proposed as "*Candidatus* Neoehrlichia chilensis," circulating in rodents from Chile. This is the first report of "*Ca*. Neoehrlichia" species in rodents from America. Müller et al. Transbound Emerg Dis. 2018;00:1–6. <u>https://doi.org/10.1111/tbed.12815</u>.

6% of a group of Swedish blood donors had evidence of sub-clinical Lyme disease

Subclinical Lyme borreliosis is common in south-eastern Sweden and may be distinguished from Lyme neuroborreliosis by sex, age and specific immune marker patterns Abstract



Determinants of a subclinical course of Lyme borreliosis (LB) remain largely unknown. The aim of this study was to assess the extent, sex and age profiles of subclinical *Borrelia*sero conversion in a LB endemic area in Sweden and to map blood cellular *Borrelia*-specific immune marker patterns in individuals with a previous subclinical LB course compared with patients previously diagnosed with Lyme neuroborreliosis (LNB).

A large group of 1113 healthy blood donors was screened for multiple IgG anti-*Borrelia* antibodies and asked to complete a health inquiry regarding previous LB. An extensive panel of immune markers was analysed in the supernatants

after stimulation using multiplex bead arrays, and *Borrelia*-specific secretion was determined by subtracting the spontaneous secretion.

A total of 125/1113 blood donors reported previous clinical LB. In contrast, 66 donors denied previous LB but showed multiple IgG anti-*Borrelia* antibodies; these were defined as subclinical subjects, of whom 60 were available for further studies. The subclinical subjects consisted of significantly more men and had a younger age compared with the LNB patients ($p \le 0.01$). Discriminant analysis revealed a distinct pattern of sex, age and PBMC *B. garinii*-specific levels of IL-10, IL-17A and CCL20 discriminating subclinical subjects from LNB patients.

This study confirms that subclinical *Borrelia* seroconversion is common in south-eastern Sweden. The findings further suggest that male sex, younger age together with *B. gariniii* induced levels of IL-10, IL-17A and CCL20 may be associated with a subclinical course. Ekerfelt, et al. Ticks and Tick-borne Diseases. 2018 <u>10.1016/j.ttbdis.2018.02.011</u>

Persister Cells

Identification of Genes Involved in Bacteriostatic Antibiotic-Induced Persister Formation

Persister cells are metabolically quiescent multi-drug tolerant fraction of a genetically sensitive bacterial population and are thought to be responsible for relapse of many persistent infections.

Persisters can be formed naturally in the stationary phase culture, and also can be induced by bacteriostatic antibiotics. However, the molecular basis of bacteriostatic antibiotic induced persister formation is unknown... Cui et al. Front. Microbiol. March 2018.

If you want to know more about persister cells, the entire paper is free of charge at: <u>http://www.frontiersin.org/articles/10.3389/fmicb.2018.00413/full</u>

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