Tick-Borne Infections Council of North Carolina, Inc.

NEWSLETTER 2021, Volume 3

Quote: - By using commercial insurance claims data, we estimated that Lyme disease was diagnosed and treated in ≈476,000 patients in the United States annually during 2010–2018… A previous analysis of insurance claims data for the years 2005–2010 estimated that Lyme disease was diagnosed in ≈329,000 persons annually in the United States. Kugeler KJ, et al. Emerg Infect Dis. 2021. DOI: 10.3201/eid2702.202731.

Highlights…

- **17 NC counties with newly detected presence of blacklegged ticks**
- **Erythema migrans (LD rash) vary by age, sex, duration, and body location**
- **Emerging human babesiosis with "Ground Zero" in North America**
- **Rhabdomyolysis and Organ Failure Due to Ehrlichiosis**
- **CDC estimates almost ½ million cases of Lyme disease a year in US**
- **Tickborne Pathogens after Tick Bite, Austria**
- **Impact of Tick-Borne Diseases on the Bone**
- **Issues with quality of recommendations in Current Infectious Diseases Society of America Guidelines**
- **Fatal anaphylaxis due to alpha-gal syndrome after initial cetuximab**
- **Lone star ticks now in South Dakota**
- **California: Ticks Carrying Disease Found to Be Abundant in Beach Areas Case**

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 evidence easy to see on their skin of a tick bite.

Third, respiratory symptoms in Covid may not always occur quickly so that even several weeks can go by with a person sick from a TBI, not Covid. Sometimes, respiratory symptoms with Covid may be minimal.

There are cases now reported in the medical literature of late treatment for TBIs due to this confusion. 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/

State Vector-borne Disease Working Group

There are no state Vector-borne Disease Working Group meetings planned for 2021 as yet due to the pandemic. They are normally held quarterly at the Office of the Chief Medical Examiner, 4312 District Drive, Raleigh, NC 27607.

There are no reports.

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

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

The state has started issuing only one letter. The most recent is 2019. Please see the home page of our website to access. www.tic-nc.org

From the CDC

New resource: The National Syndromic Surveillance Program (NSSP) is a collaboration between CDC, federal partners, local and state health departments, and academic and private

sector partners. Example of data below. DVBD also recently released a data dashboard showing syndromic surveillance of emergency department visits for tick bites by time, region, age, and sex. Unlike some tickborne disease surveillance data, the dashboard is updated weekly rather than annually. These data can show when people in different parts of the country maybe at highest risk of getting tick bites.
www.cdc.gov/ticks/tickedvisits/

Use of Commercial Claims Data for Evaluating Trends in Lyme Disease Diagnoses, United States, 2010-2018

We evaluated MarketScan, a large commercial insurance claims database, for its potential use as a stable and consistent source of information on Lyme disease diagnoses in the United States. The age, sex, and geographic composition of the enrolled population during 2010–2018 remained proportionally stable, despite fluctuations in the number of enrollees. Annual incidence of Lyme disease diagnoses per 100,000 enrollees ranged from 49 to 88, ≈6–8 times higher than that observed for cases reported through notifiable disease surveillance. Age and sex distributions among Lyme disease diagnoses in MarketScan were similar to those of cases reported through surveillance, but proportionally more diagnoses occurred outside of peak summer months, among female enrollees, and outside high-incidence states. Misdiagnoses, particularly in low-incidence states, may account for some of the observed epidemiologic differences. Commercial claims provide a stable data source to monitor trends in Lyme disease diagnoses, but certain important characteristics warrant further investigation.
https://wwwnc.cdc.gov/eid/article/27/2/20-2728_article

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.

State tick research and/or reports

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

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 meetings

None.

Blacklegged tick data on several NC counties presented at a state Public Health 2020 Zoom meeting.

Note that Ashe and Alleghany Counties now have almost one-quarter of the blacklegged ticks collected there carrying the Lyme disease bacteria.

Percentage of Ixodes ticks infected with pathogens by county:

*Only ticks collected via flagging/dragging were used in this table.

County (# tested)	*Borrelia burgdorferi* (%+)	*Borrelia miyamotoi* (%+)	*Anaplasma phagocytophilum* (%+)
Alleghany (93)	24%	1%	1%
Ashe (81)	23%	1%	6%
Buncombe (39)	15%	1%	0%
Chatham (2)	0%	0%	0%
Johnson (4)	50%	0%	0%
Madison (27)	7%	0%	0%
Mitchell (75)	0%	0%	5%
Onslow (7)	0%	0%	0%
Rockingham (65)	3%	0%	0%
Stokes (8)	13%	0%	0%
Surry (34)	0%	0%	0%
Wake (1)	0%	0%	0%
Watauga (39)	15%	0%	8%
Wilkes (16)	13%	0%	0%
Yadkin (2)	0%	0%	0%
Yancey (48)	0%	0%	0%

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

North Carolina Electronic Disease Surveillance System

TIC-NC Activities

TIC-NC Talks and Materials Distributed

Booklet/Bilingual Folleto distribution:

Dunn, NC. Episcopal Farmworker Ministries & CommWell Health.

Buncombe County Sheriff's Office

Grandfather Mountain Stewardship Foundation 2050 Blowing Rock Hwy, Linville, NC 28646

Julian Price Memorial Park, Milepost, 297 Blue Ridge Pkwy, Blowing Rock, NC 28605

Carolina Hemlocks Recreation Area, 8516 Highway 80 South Burnsville, NC 28714

Black Mountain Campground, 50 Black Mountain Campground Rd. Burnsville, NC 28714

Ayr Mount, St Marys Rd Hillsborough NC 27278

Piedmont Health Farmworker Outreach, Prospect Hill NC 550 Folletos, 140 pointed tweezers

Talks:

NC Dept of Agriculture, Pest Control & Pesticides Division

Radio:

Talked with Frank Graff, PBS, NC, Producer/Director EP SciNC giving information for his blog.

Newspaper:

Asheville Citizen Times referred readers to our website for tick information.

See links to our Booklet and Bilingual Folleto on our Home page: https://tic-nc.org

We have a Chapel Hill high school **volunteer** this summer. Welcome, Hannah Kung! Her first project was developing and sending a questionnaire to 20 outdoor summer camps about the program to protect attendees from ticks including safe tick removal. Only two replied. One had some procedures in place, the other had none. This indicates an area of need.

Janet Dooley, our intrepid **volunteer** has been traveling about her area widely with our booklets and some tick posters. First, the Asheville **Mayor's Office**. A few weeks ago, she got the mayor to make a "Tick-borne Disease Proclamation," then had 100 copies made for distribution. Janet also took the tick safety posters to the mayor's office, and then went on to distribute them to the local fire department, police department, Whole Foods, and Asheville Green Works, a river cleanup group. Later, she visited the Great Smokey Mountains Visitor Center and the Biltmore YMCA pool and their summer camp facility.

Janet wears special shirts she has had made wherever she goes which helps her get into conversations with people about ticks and the risk of tick-borne infections. This shirt says, "1 tick bite can take your life." She has others with other slogans.

Our boardmember, Joanie Alexander, visited Dunn, NC.

I visited the Episcopal Farmworker Ministry and CommWell Health clinic in Dunn to offer our Folletos for distribution to farmworkers and their families. Both sites welcomed the tick-borne infections educational materieals. JA

We have been busy!

ᴎᴎ North Carolina and South ᴎᴎ

Crowd sourced tick images established the largest number of new county reports of the blacklegged tick in North Carolina, Michigan, and Texas: 17 NC counties with newly detected presence of blacklegged ticks

Crowdsourced Tick Image-Informed Updates to U.S. County Records of Three Medically Important Tick Species

Burgeoning cases of tick-borne disease present a significant public health problem in the United States. Passive tick surveillance gained traction as an effective way to collect epidemiologic data, and in particular, photograph-based tick surveillance can complement in-hand tick specimen identification to amass distribution data and related encounter demographics. We compared the Federal Information Processing Standards (FIPS) code of tick photos submitted to a free public identification service (TickSpotters) from 2014 to 2019 to published nationwide county reports for three tick species of medical concern: Ixodes scapularis Say (Ixodida: Ixodidae), Ixodes pacificus Cooley and Kohls (Ixodida: Ixodidae), and Amblyomma americanum Linneaus (Ixodida: Ixodidae).

We tallied the number of TickSpotters submissions for each tick species according to “Reported” or “Established” criteria per county and found that TickSpotters submissions represented more than half of the reported counties of documented occurrence, and potentially identified hundreds of new counties with the occurrence of these species. We detected the largest number of new county reports of I. scapularis presence in Michigan, North Carolina, and Texas. Tick image submissions revealed potentially nine new counties of occurrence for I. pacificus, and we documented the largest increase in new county reports of A. americanum in Kentucky, Illinois, Indiana, and Ohio.

These findings demonstrate the utility of crowdsourced photograph-based tick surveillance as a complement to other tick surveillance strategies in documenting tick distributions on a nationwide scale, its potential for identifying new foci, and its ability to highlight at-risk localities that might benefit from tick-bite prevention education. Kopsco HL, et al. Journal of Medical Entomology, May 2021, doi.org/10.1093/jme/tjab082 Article free of charge.

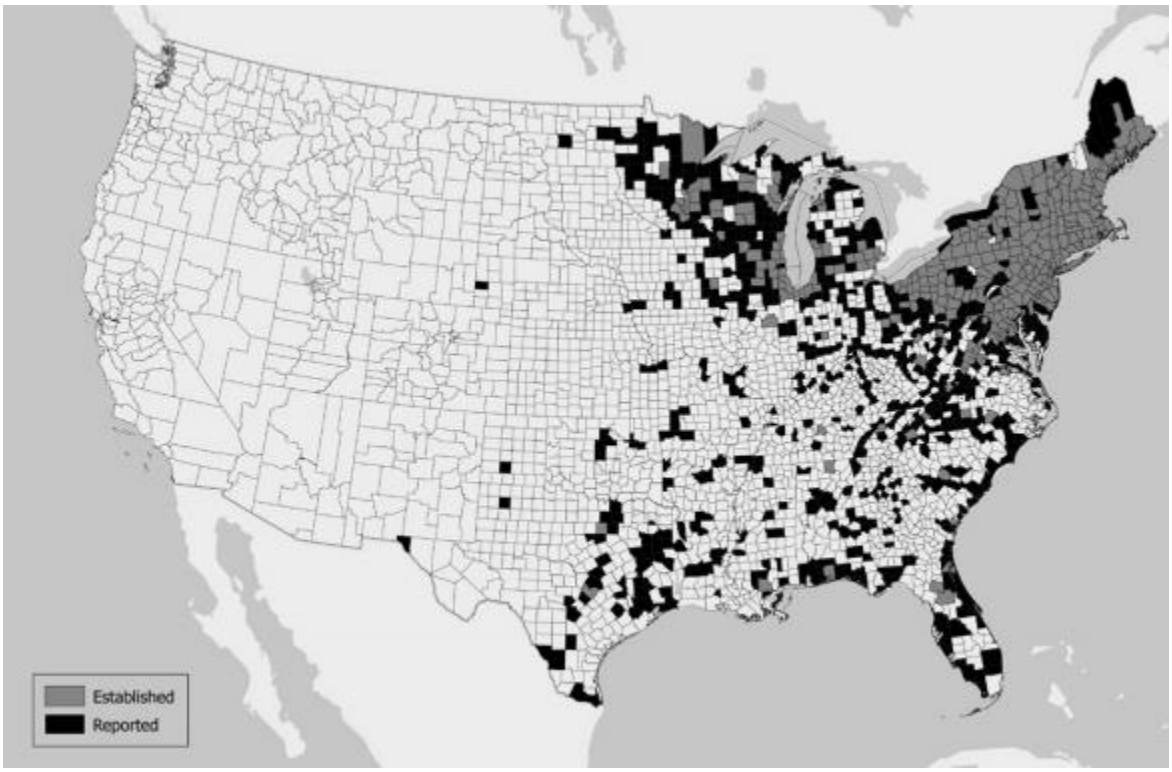

Fig. 2. (a) County-level distribution of Ixodes scapularis as reported to TickSpotters between 2014 and 2019. "Established" is defined as a county with either two life stages present or at least six individual ticks of any life stage. "Reported" is defined as at least one occurrence in a county of any recorded tick stage over the study period (Dennis et al. 1998). (b) Counties of I. scapularis presence identified through TickSpotters submissions that are not represented in Eisen et al. 2016. "Established" is defined as a county with either two life stages present or at least six individual ticks of any life stage, and "Reported" is defined as at least one occurrence in a county of any recorded tick stage over the study period (Dennis et al. 1998).

Lone star tick Rickettsia as a pathogen

Virulence potential of *Rickettsia amblyommatis* for spotted fever pathogenesis in mice

Rickettsia amblyommatis belongs to the spotted fever group of *Rickettsia* and infects *Amblyomma americanum* (Lone Star ticks) for transmission to offspring and mammals. Historically, the geographic range of *A. americanum* was restricted to the southeastern United States. However, recent tick surveys identified the progressive northward invasion of *A. americanum*, contributing to the increased number of patients with febrile illnesses of unknown etiology after a tick bite in the northeastern United States.

While serological evidence strongly suggests that patients are infected with *R. amblyommatis*, the virulence potential of *R. amblyommatis* is not well established. Here, we performed a bioinformatic analysis of three genome sequences of *R. amblyommatis* and identified the presence of multiple putative virulence genes whose products are implicated for spotted fever pathogenesis. Similar to other pathogenic spotted fever rickettsiae, *R. amblyommatis* replicated

intracellularly within the cytoplasm of tissue culture cells. Interestingly, *R. amblyommatis* displayed defective attachment to microvascular endothelial cells.

The attachment defect and slow growth rate of *R. amblyommatis* required relatively high intravenous infectious doses to produce dose-dependent morbidity and mortality in C3H mice. In summary, our results corroborate clinical evidence that *R. amblyommatis* can cause mild disease manifestation in some patients. Yen et al. *Pathogens and Disease*, https://doi.org/10.1093/femspd/ftab024.

Rhabdomyolysis and Multisystem Organ Failure Due to Fulminant Ehrlichiosis Infection

A previously healthy 51-y-old male presented to his local emergency department with subjective fevers, myalgias, dyspnea, and generalized weakness that had been progressive for several weeks. He was initially diagnosed with bilateral pneumonia, septic shock, and rhabdomyolysis requiring transfer to a tertiary care facility. He was treated for sepsis with broad-spectrum antibiotics, steroids, and a fluid bolus before transfer. Once he arrived at the tertiary care facility, he developed respiratory failure requiring intubation and ventilatory support. Ceftriaxone and metronidazole were started in the intensive care unit to cover common causes of community-acquired versus aspiration pneumonia, and doxycycline was included to cover tick-borne disease based on a history of tick exposure from working in his rural yard.
Blood polymerase chain reaction testing later confirmed ehrlichiosis. The patient had a prolonged hospital course requiring ventilatory support and vasopressors, followed by a 4-wk stay in a rehabilitation unit after discharge. Wilderness medical providers should counsel their patients on prevention of tick bites and keep tickborne illness in the differential for acute illness, based on local epidemiology. Overmiller et al. Wilderness & Environmental Medicine 2021, doi.org/10.1016/j.wem.2021.01.009

◘◘ National Section ◘◘

CDC estimates almost ½ million cases of Lyme disease a year in US

Estimating the Frequency of Lyme Disease Diagnoses, United States, 2010–2018

By using commercial insurance claims data, we estimated that Lyme disease was diagnosed and treated in ≈476,000 patients in the United States annually during 2010–2018. Our results underscore the need for accurate diagnosis and improved prevention. Kugeler KJ, et al. (2021). *Emerging Infectious Diseases*, *27*(2), 616-619. https://doi.org/10.3201/eid2702.202731.

Interesting finding from this study of the Lyme disease rash: for every 10-year increase in age, the odds of central clearing decreased 25%

The presenting characteristics of erythema migrans vary by age, sex, duration, and body location

The erythema migrans (EM) skin lesion is often the first clinical sign of Lyme disease. Significant variability in EM presenting characteristics such as shape, color, pattern, and homogeneity, has been reported. We studied associations between these presenting characteristics, as well as whether they were associated with age, sex, EM duration, body location, and initiation of antibiotics.

Fig. 1

Fig. 2

Two hundred and seventy one adult participants with early Lyme disease who had a physician-diagnosed EM skin lesion of ≥ 5 cm in diameter and ≤ 72 h of antibiotic treatment were enrolled. Participant demographics, clinical characteristics, and characteristics of their primary EM lesion were recorded.

After adjusting for potential confounders, EM size increased along with increasing EM duration to a peak of 14 days. Male EM were found to be on average 2.18 cm larger than female EM. The odds of a red (vs blue/red) EM were 65% lower in males compared to females, and were over 3 times as high for EM found on the pelvis, torso, or arm compared to the leg. Age remained a significant predictor of central clearing in adjusted models; for every 10-year increase in age, the odds of central clearing decreased 25%.

Given that EM remains a clinical diagnosis, it is essential that both physicians and the general public are aware of its varied manifestations. Our findings suggest possible patterns within this variability, with implications for prompt diagnosis and treatment initiation, as well as an understanding of the clinical spectrum of EM. Rebman AW et al. *Infection* (2021). https://doi.org/10.1007/s15010-021-01590-0. "Entire article is behind a paywall"

Strength of Recommendation and Quality of Evidence for Recommendations in Current Infectious Diseases Society of America Guidelines

Grading of Recommendations Assessment, Development, and Evaluation (GRADE) is a systematic approach to grading strength of recommendation (SOR) and quality of evidence (QOE) for guideline recommendations. We aimed to assess the relationship between SOR and QOE in current Infectious Diseases Society of America (IDSA) guidelines.
In this cross-sectional analysis, we analyzed the frequency of SOR-QOE pairings, including discordance (defined as strong SOR based on expert opinion, very low, or low QOE) for GRADEd recommendations in IDSA guidelines published since 2010. Data for each recommendation were extracted on SOR, QOE, the domain of disease management (one or more of diagnosis, treatment, prevention, and other categories), and relevance to drug or nondrug treatment.

Seventeen eligible guidelines provided 1042 unique GRADEd recommendations (n = 237, 711, 76, and 73 pertaining to diagnosis, treatment, prevention, and other domains, respectively; n = 574 and 137 pertaining to drug and nondrug treatment). Overall, the most common SOR was strong (71.8%; n = 748) and the most common QOE was low (48.6%; n = 506). Among all strong recommendations, 47.1% (n = 352) demonstrated discordance with QOE. By domain, strong recommendations were discordant in 36.6%, 51.4%, 29.3%, and 58.1% of recommendations pertaining to diagnosis, treatment, prevention, and other domains, respectively. Similarly, 50.7% and 54.0% of strong recommendations related to drug and nondrug treatment were discordant, respectively. We identified 39.6% of discordant recommendations to be consistent with good practice statements, which are recommended to be labeled as such without formal GRADEd designations of SOR or QOE.

Among all IDSA guideline recommendations with strong SOR, approximately half were discordant with QOE, and this frequency varied across strata of domains of disease management.
Miles et al. *Open Forum Infectious Diseases*, Volume 8, Issue 2, February 2021, ofab033, https://doi.org/10.1093/ofid/ofab033

CONCLUSIONS: Approximately half of all strong recommendations in current IDSA guidelines using GRADE methodology from 2010 to 2019 demonstrated discordance between quality of evidence and strength of recommendation, and this frequency varied across domains of disease management.

California: Ticks Carrying Disease Found to Be Abundant in Beach Areas

Examining prevalence and diversity of tick-borne pathogens in questing *Ixodes pacificus* ticks in California.

Tick-borne diseases in California include Lyme disease (caused by *Borrelia burgdorferi*), infections with *Borrelia miyamotoi*, and human granulocytic anaplasmosis (caused by *Anaplasma phagocytophilum*). We surveyed multiple sites and habitats (woodland, grassland,

coastal chaparral) in California to describe spatial patterns of tick-borne pathogen prevalence in western black-legged ticks (*Ixodes pacificus*).

We found that several species of *Borrelia – B. burgdorferi, B. americana* and *B. bissettiae* - were observed in habitats such as coastal chaparral that does not harbor obvious reservoir host candidates. Describing tick-borne pathogen prevalence is strongly influenced by the scale of surveillance: aggregating data from individual sites to match jurisdictional boundaries (e.g., county or state) can lower the reported infection prevalence. Considering multiple pathogen species in the same habitat allows a more cohesive interpretation of local pathogen occurrence. Salkeld DJ, et al. Applied and Environmental Biology, doi.org/10.1128/AEM.00319-21. Paper free of charge.

Lone star ticks now in South Dakota

Tick Surveillance and Pathogen Detection in Eastern South Dakota

Throughout the summers of 2019 and 2020, surveillance efforts were aimed at determining the status of the black-legged tick (*Ixodes scapularis)*, the American dog tick *(Dermacenter variabilis)* and the lone star tick *(Amblyoma americanum)* in Eastern South Dakota. In 2019, tick surveys took place across fourteen locations within eight counties; in 2020, surveillance efforts included 15 locations across 10 counties in Eastern South Dakota.

Tick collection was conducted using a flagging method and each tick was identified in the lab to species, life stage, and sex. A total of 266 ticks of three species was collected over the course of the surveys from mid-May to late-July in 2019.

A total of 259 ticks of three species was collected in 2020. The results reveal new established populations of the lone star tick in Union and Clay Counties in 2019, and further expansion into Yankton County in 2020. Combined with other recent findings, this indicates that the range of *A. americanum* is expanding, possibly due to climate change. Black H. University of South Dakota. https://red.library.usd.edu/idea/283//

International & General Section

Underrecognized Tickborne Illnesses: *Borrelia Miyamotoi* and Powassan Virus

Over the past 2 decades, tickborne disease has been increasingly recognized as a threat to humans as a result of the growing geographic range of ticks. This review describes 2 tickborne diseases, *Borrelia miyamotoi* and Powassan virus, that likely have a significant impact on

humans, yet are underdiagnosed compared to most other tickborne diseases. We performed a literature search from 2015 to 2020. *Borrelia miyamotoi* is a tickborne pathogen that infects and co-infects ticks along with other pathogens, including *Borrelia burgdorferi*.

Because *B miyamotoi* infects the same *Ixodes* ticks as *B burgdorferi*, *B miyamotoi* may cover a similar geographic range. *B miyamotoi* infection may be underdiagnosed for 2 reasons. First, a presumptive treatment approach to Lyme disease may result in *B miyamotoi* infection treatment without identification of the actual cause. Second, the absence of readily available testing and diagnostic criteria makes it difficult to diagnose *B miyamotoi* infection. Powassan virus is a tickborne flavivirus similar to the dengue virus. Powassan virus disease appears to have an asymptomatic or minimally symptomatic presentation in most people but can cause devastating and fatal encephalitis. The Powassan virus may be transmitted in less than 15 min of tick feeding. Powassan virus disease is a difficult diagnosis because testing capabilities are limited and because there may be co-infection with other tickborne pathogens. Della-Giustina et al. Wilderness & Environmental Medicine, April 2021, doi.org/10.1016/j.wem.2021.01.005.

Some islands in Scotland's Highland region that lack woodland coverage have a Lyme disease incidence ≈40 times the national average

Emergence of Lyme Disease on Treeless Islands, Scotland, United Kingdom

Lyme disease is usually associated with forested habitats but has recently emerged on treeless islands in the Western Isles of Scotland. The environmental and human components of Lyme disease risk in open habitats remain unknown. We quantified the environmental hazard and risk factors for human tick bite exposure among treeless islands with low and high Lyme disease incidence in the Western Isles. Millins C, et al. *Emerging Infectious Diseases*, *27*(2), 538-546. https://doi.org/10.3201/eid2702.203862.

Fatal anaphylaxis due to alpha-gal syndrome after initial cetuximab administration: The first forensic case report

Cetuximab is mainly used for the treatment of advanced and metastatic colorectal cancer. Owing to the oligosaccharide galactose-α-1,3-galactose (α-gal) in its heavy chain, cetuximab can induce severe IgE-dependent anaphylaxis. α-Gal is also the antigen responsible for α-gal syndrome, known as mammalian meat allergy. Patients with α-gal syndrome may suffer from cetuximab-induced anaphylaxis at the first administration because of developed α-gal-specific IgE antibodies.

A male patient in his 50s with metastatic colon cancer was receiving chemotherapy involving scheduled cetuximab administration. However, he died soon after the first administration. Forensic autopsy confirmed rectal cancer, metastatic rectal cancer in the liver, and renal cancer. Laboratory blood tests revealed the presence of cetuximab- and beef-specific IgE antibodies before cetuximab administration and an extremely high level of tryptase after administration.

Thus, we determined that the death was caused by cetuximab-induced anaphylaxis due to the preexisting α-gal syndrome. To the best of our knowledge, this is the first autopsy case report in forensic medicine of fatal anaphylaxis after initial cetuximab administration. Wen et al. Legal Medicine. doi.org/10.1016/j.legalmed.2021.101878.

The first reported cases of meat allergy following tick bites in the UK

Allergic reactions frequently involve the production of immunoglobulin E (IgE) antibodies to proteins. However, reactions directed against carbohydrate moieties are increasingly being recognised. Tick bites can contribute to the development of immunoglobulin E to the galactose-1,3-galactose (alpha-gal) moiety on tick salivary proteins. These IgE molecules can cross-react with alpha-gal found in red meats, causing Type I IgE-mediated hypersensitivity reactions to these foods.

We present three cases of delayed reactions to beef, pork and lamb in patients with prior tick bites and in the presence of a positive-specific IgE to alpha-gal. Patients were advised to avoid red meat consumption and to carry emergency treatment in the form of anti-histamines with or without adrenaline autoinjector devices. This is the first published report of red meat allergy caused by tick bites suffered in the UK. Bansal et al. JRSM Open, 2021 Case Report, https://doi.org/10.1177/2054270421996131

A review finds widespread distribution of babesia in humans

Emerging Human Babesiosis with "Ground Zero" in North America

Abstract: The first case of human babesiosis was reported in the literature in 1957. The clinical disease has sporadically occurred as rare case reports in North America and Europe in the subsequent decades. Since the new millennium, especially in the last decade, many more cases have apparently appeared not only in these regions but also in Asia, South America, and Africa. More than 20,000 cases of human babesiosis have been reported in North America alone.

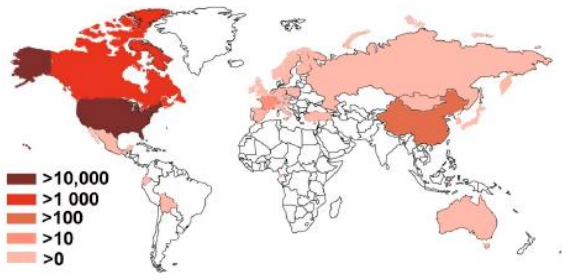

Figure 1. Geographical distribution of human babesiosis. The darker the color, the more numerous cases there are. There are no reported cases in unfilled countries or regions.

In several cross-sectional surveys, exposure to Babesia spp. has been demonstrated within urban and rural human populations with clinical babesiosis reported in both immunocompromised and immunocompetent humans. This review serves to highlight the widespread distribution of these tick-borne pathogens in humans, their tick vectors in readily accessible environments such as parks and recreational areas, and their phylogenetic relationships. Yang et al. Microorganisms, Basel (2021): 440. https://www.mdpi.com/2076-2607/9/2/440.

The Impact of Tick-Borne Diseases on the Bone

Tick-borne infectious diseases can affect many tissues and organs including bone, one of the most multifunctional structures in the human body. There is a scarcity of data regarding the impact of tick-borne pathogens on bone. The aim of this review was to survey existing research literature on this topic.
The search was performed using PubMed and Google Scholar search engines. From our search, we were able to find evidence of eight tick-borne diseases (Anaplasmosis, Ehrlichiosis, Babesiosis, Lyme disease, Bourbon virus disease, Colorado tick fever disease, Tick-borne encephalitis, and Crimean–Congo hemorrhagic fever) affecting the bone.
Pathological bone effects most commonly associated with tick-borne infections were disruption of bone marrow function and bone loss. Most research to date on the effects of tick-borne pathogen infections on bone has been quite preliminary. Further investigation of this topic is warranted. Farooq and Moriarty. Microorganisms 2021, 9, 663. https:// doi.org/10.3390/ microorganisms9030663.

Infections with Tickborne Pathogens after Tick Bite, Austria, 2015–2018

The aim of this prospective study was to assess the risk for tickborne infections after a tick bite. A total of 489 persons bitten by 1,295 ticks were assessed for occurrence of infections with *Borrelia burgdorferi* sensu lato, *Anaplasma phagocytophilum*, *Rickettsia* spp., *Babesia* spp., *Candidatus* Neoehrlichia mikurensis, and relapsing fever borreliae.

B. burgdorferi s.l. infection was found in 25 (5.1%) participants, of whom 15 had erythema migrans. Eleven (2.3%) participants were positive by PCR for *Candidatus* N. mikurensis. One asymptomatic participant infected with *B. miyamotoi* was identified. Full engorgement of the tick (odds ratio 9.52) and confirmation of *B. burgdorferi* s.l. in the tick by PCR (odds ratio 4.39) increased the risk for infection. *Rickettsia helvetica* was highly abundant in ticks but not pathogenic to humans. Knowledge about the outcome of tick bites is crucial because infections with emerging pathogens might be underestimated because of limited laboratory facilities.
Markowicz M, et al. (2021) *Emerging Infectious Diseases*, *27*(4), 1048-1056.
https://dx.doi.org/10.3201/eid2704.203366.

Quantitative multiplexed strategies for human Lyme disease serological testing

Lyme disease, which is primarily caused by infection with the bacterium *Borrelia burgdorferi* in the United States or other *Borrelia* species internationally, presents an ongoing challenge for diagnostics. Serological testing is the primary means of diagnosis but testing approaches differ widely, with varying degrees of sensitivity and specificity. Moreover, there is currently no reliable test to determine disease resolution following treatment.

A distinct challenge in Lyme disease diagnostics is the variable patterns of human immune response to a plurality of antigens presented by *Borrelia* spp. during the infection. Thus, multiplexed testing approaches that capture these patterns and detect serological response against multiple antigens may be the key to prompt, accurate Lyme disease diagnosis.

In this review, current state-of-the-art multiplexed diagnostic approaches are presented and compared with respect to their diagnostic accuracy and their potential for monitoring response to treatment. Chou et al. *Experimental Biology and Medicine*. April 2021. doi:10.1177/15353702211003496.

Proficiency at Tick Identification by Pathologists and Clinicians Is Poor

Prompt accurate identification of tick species is required for appropriate administration of single dose antimicrobial prophylaxis for Lyme disease in selected patients. To determine the proficiency of clinicians at tick identification in the northeastern United States where Lyme disease has its highest incidence, we undertook a survey.

We analyzed the results of a voluntary survey testing proficiency in identifying tick species using high-resolution photographs of ticks.

Only 35% of ticks were correctly identified. Although 60% of respondents could identify a non-engorged adult blacklegged tick, only 34% could correctly identify a partially engorged blacklegged tick. Participants performed even worse at classifying brown dog, American dog, and Lone Star ticks.

Proficiency of tick identification by pathologists and clinicians is poor. Laga AC, et al. The American Journal of Dermatopathology, May 2021. doi: 10.1097/DAD.0000000000001977.

Case showing the importance of clinical evaluation and treatment of Lyme disease

Ceftriaxone and Doxycycline induced Seroconversion in Previously Seronegative Patient with Clinically Suspected Disseminated Lyme Disease: Case Report

We present a case of middle-aged woman whose health problems began 3 months after a registered tick bite in endemic area of Lyme borreliosis. First symptoms included fatigue, chills, cervical lymphadenopathy, neck pain and stiffness. Patient was afebrile. Lyme disease was excluded due to lack of erythema migrans and negative enzyme immunoassay test results for anti-*Borrelia* antibodies.

During the next few months, her condition was getting worse and symptoms were accompanied with brain fog, dizziness, palpitations, irregular menstrual cycles, insomnia, panic attacks, headaches, and muscle aches. This led to multiple medical tests and examinations, but the diagnosis failed to be established. Finally, after occurrence of paresthesia and weakness of leg

muscles, clinical diagnosis of disseminated Lyme borreliosis with nervous system involvement was suspected and antibiotic therapy was initiated.
After the second dose of Ceftriaxone, patient got fever and her condition worsened. However, Ceftriaxone therapy was continued for a total of 5 days and was followed by 4 weeks of doxycycline therapy. Upon completion of antibiotic therapy, high specific anti-*Borrelia* antibodies were detected by Western blot and SeraSpot.

Appearance of anti-*Borrelia* antibodies, in contrast to negative test results performed immediately before the therapy started, indicated seroconversion. 18 months after the therapy, patient was completely without the symptoms. This paper emphasizes importance of clinical evaluation of Lyme disease and shows a unique case of seroconversion in patient with symptoms of disseminated Lyme disease. Seroconversion was likely triggered by release of lipoproteins and other immunogenic molecules from *Borrelia* once the bacterial die-off began due to antibiotic therapy. Zagorac GB & Kezee TG. Infect Chemother 2021 Mar 23. doi: 10.3947/ic.2021.0008.

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