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The Effects of Climate Change on the Transmission of Lyme Disease

Schuyler Hedican, Katherine Kistler, and Iveth Martinez Granados

Abstract

Lyme disease currently affects approximately 300,000 people annually in the United States, but climate change threatens to increase this number. Rising temperatures, humidity, and levels of rainfall are impacting the relationship and interactions between the bacterium that causes Lyme disease (*Borrelia burgdorferi*), its vectors, and associated hosts. Climate change models predict a northward expansion of these disease-carrying vectors and hosts into new territories in North America, as formerly unsuitable territories become more hospitable, most notably in Canada. Human exposure to the bacteria through the bite of an infected tick can lead to the characteristic symptoms of Lyme disease, such as a skin rash, fever, headache, chills and in severe cases encephalitis and polyneuropathy. Therefore, this public health concern will also expand to new populations and better mitigation strategies will be necessary.

Introduction

Lyme disease is a major health concern, as it is the most prevalent vector-borne disease in the United States. Between 1982 and 2005, over 100,000 cases of Lyme disease were reported in the United States (Brownstein et al., 2005). Now, the number of cases is closer to 300,000 per year in the United States (CDC, 2021). Symptoms, including a skin rash, headache, fever, and chills, arise after a person is infected with the bacterium that causes the disease, *Borrelia burgdorferi*. Severe cases, or even mild cases that are left untreated, can lead to neurological issues, such as encephalitis and polyneuropathy (Shapiro, 2014). Lyme disease was first identified in 1883, but the spirochete bacterium was not confirmed as the cause of Lyme disease until 1981 (Ward & Brown, 2004). It was discovered that, "Lyme borreliosis agents are vigorously motile, corkscrew-shaped bacteria that belong to the eubacterial phylum of spirochetes" (Steere et al., 2004). However, the bacterium itself is not the only component involved in terms of human risk of developing Lyme disease.

The disease-causing bacteria are transmitted to humans through the bite of an infected host vector. The most common vectors for Lyme disease are ixodid ticks, such as the deer tick (*Ixodes scapularis*), also called the black-legged tick (Huang et al., 2019). To lessen the risk for developing Lyme disease, ticks need to be removed from a person within 48 hours of becoming attached (Ward & Brown, 2004). The ticks transmit the bacterial pathogen through their saliva while feeding. The longer a tick stays attached to a host to feed, the greater the probability of transmission to that host. About 50% of infected ticks can transmit the bacteria within 48 hours, whereas almost 100% can transmit the bacteria within 72 hours after attachment (Ward & Brown, 2004). Once infected, symptoms can be tracked according to three clinical stages. During the stage of early localized disease, a skin rash called erythema migrans is common, occurring in approximately 90% of Lyme disease cases in the United States (Shapiro, 2014). This skin lesion can expand over time, spreading up to a foot in diameter and typically appears within 7 to 14 days after infection. However, this rash can still appear at the site of the tick bite anywhere between 3 to 30 days post infection. Manifestations of the early disseminated disease stage include cranial nerve paralysis or meningitis, swelling of a protective membrane surrounding the brain. While extremely rare, especially in children, encephalitis and polyneuropathy may manifest in late Lyme disease (Shapiro, 2014). Other potential symptoms include neck stiffness, fatigue, joint pain, muscle pain, swollen lymph nodes, irregular heartbeat, numbness, and tingling in the extremities (Alexandria W, 2016). A doctor's examination is required to diagnose a patient as having the disease, and blood tests can be performed to detect infection. For example, an ELISA (enzyme-linked immunosorbent assay) test and a Western blot test both check to see if the body has started to produce against *Borrelia burgdorferi.* Furthermore, a Western blot test splits the proteins in a patient's blood and compares that pattern to patterns of blood proteins in known cases. The combinations of these two tests are said to be 99.9% accurate (SHC, 2017). Because of the severity of the disease, along with its elevated risk of exposure in certain geographical regions, Lyme disease is considered a public health concern in North America.

Different geographical locations have varying levels of exposure risk due to the presence or absence of the tick vectors. The blacklegged tick, *Ixodes scapularis*, is the predominant vector for Lyme disease and is common to the northeastern and midwestern regions of the United States. The Western blacklegged tick, *Ixodes pacificus*, is also capable of transmitting the disease bacteria but is more commonly found in the western United States, along the Pacific coast (Ward & Brown, 2004). Because of the range differences for the vectors, most Lyme disease cases have come from the eastern and midwestern regions of the United States, where *Ixodes scapularis* is present. From 1992 to 2007, 95% of Lyme disease cases in the United States came from just 13 states: Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Virginia, and Wisconsin (Monaghan et al., 2015). The sheer presence or absence of ticks does not necessarily define the risk of disease transmission.

The spread of the disease-causing bacteria also depends on the tick vector's ability to progress through its life cycle. The life cycle of ixodid ticks lasts two years and a bloodmeal is needed at every stage. White-footed mice are the most common food source for ticks in the nymphal and larval stages (Ward & Brown, 2004). The specific host organism varies geographically, but the spread of Lyme disease occurs when the ticks feed on any host organism infected with the *Borrelia burgdorferi* bacteria. Once the ticks take up the bacteria, they are then able to transmit it to other organisms during future bloodmeal bites. The most common stage for humans to become infected occurs when the ticks are in the nymphal stage, after taking up the bacteria during the first bloodmeal of their life cycle (Ward & Brown, 2004). In all, there is a delicate relationship between host and vector interactions that influences the spread of Lyme disease.

However, climate change is causing changes in those relationships, which means an increased risk of human exposure to the disease-carrying vectors in certain places. Rising temperatures, humidity levels, and rainfall are changing the environmental hospitable quality for the survival of these ticks and hosts. Because of this, the vectors and hosts will either adapt over time or physically relocate to regions that are more suitable for their survival. Research is showing that such relocation is already happening. Current data is showing not only is the spread of Lyme disease regulated spatially, but it is also regulated temporally.

Transmission of Lyme disease is highly seasonal. Symptoms are usually first noticed in the springtime, and most cases are diagnosed and reported in the summer (Monaghan et al., 2015). This timing is also related to the increased risk of exposure that comes when humans are around nymphal *Ixodes scapularis* ticks, which is the most common stage for human infection (Tran et al., 2021). However, climate change is affecting the seasonality of these ticks. As mentioned, temperature, humidity, and rainfall are good predictors of spatial distribution of *I. scapularis* ticks. These factors are also good predictors of their temporal distribution. More specifically, greenhouse gases are leading to an earlier onset of transmission from ticks and human reports of Lyme disease symptoms. This is because increasing concentrations of greenhouse gases are leading to rising temperatures during the winter and spring months, which correspond to critical behaviors in the life cycle of *Ixodes scapularis* ticks (Monaghan et al., 2015). The study by Monaghan et al. (2015) notes that an earlier onset of Lyme disease season is positively associated with the observed increases in temperature, increases in humidity, and decreases in rainfall amounts during the preceding winter and spring months. Tick vectors prefer moist environments with minimal sunlight (Ward & Brown, 2014). So, increases in humidity and temperature in months that are usually colder and drier, are encouraging tick activity sooner. Climate models predict temperatures in the United States will have increased 1.5-5.5°C by the end of the 21st century, especially compared to the 0.8°C seen over the 20th century. The models used in this study predict that Lyme disease season onset will begin, on average, 0.4-0.5 weeks earlier between the years 2025-2040. This onset will then shift to 0.7-1.9 weeks earlier between the years 2065-2080 (Monaghan et al., 2015). Earlier onset of tick seasonality suggests a longer timeframe of heightened human exposure and without effective mitigation strategies, more cases of Lyme disease are likely to occur as a result.

In order to combat the spread of Lyme disease in the age of climate change, it is important to understand how or why the bacterium, hosts, and vectors associated with the disease are relocating in the way they are. This information can then be used to help educate the general public on the severity of climate change's impact on the transmission of Lyme disease and what precautions should be taken.

Status of Understanding

As the "vector" in the "vector-borne" Lyme disease, where the ticks are determines what human populations are exposed and at higher risk for developing the disease. Populations of vectors and their hosts have fluctuated over time. In the 1800s, tick and deer populations were essentially wiped out due to overhunting and heavy deforestation that was intended to clear tracts for agricultural use. The introduction of natural resource regulating institutions throughout the early and mid-1900s allowed deer populations to recover (Webb, 2016). Into the early 2000s, reforestation in the eastern United States, large-scale farming in the Midwest, abandoned farms left to grow wild in the Northeast, and more restrictions on hunting overall contributed to the resurgence of deer, ticks, and Lyme disease (Ward & Brown, 2004). To demonstrate this, in 1900, there were approximately 500,000 deer in North America. By the early 2000s, deer populations were close to 30,000,000 in North America (Ward & Brown, 2004). Current projections suggest that climate change is expected to continue to increase deer populations (Weiskopf et al., 2019).

More presently, Tran et al. (2021) investigated how the presence of *Ixodes scapularis* nymphs practically tripled between 2008 and 2018 in New York alone. Through flagging and dragging sampling, these researchers collected and counted the number of nymphs found in flannel or canvas nets that were drug across 532 different wooded sampling locations in various counties throughout the state. When they started in 2008, the number of counties with a presence of *I. scapularis* nymphs was around 33%. By 2018, that number increased to around 90%. More specifically, the abundance of vector nymphs stayed at high levels in eastern New York over the course of the study, whereas counties in Northern and Western New York saw levels that went from undetectable or barely detectable to high levels similar to those in the eastern counties. Lastly, the number of Lyme disease cases stemming from each county mimicked the nymphal abundance levels in that county. In other words, there were more cases of Lyme disease that came from counties with higher abundances of the tick vector (Tran et al., 2021). This is an important observation, because it emphasizes the benefit that can come from monitoring and controlling the populations of the tick vectors.

Researchers have been tracking how tick populations have been moving over time, from the past until the present. Based on those data, they can also make predictions as to where the ticks will expand their presence to in the future. Climate change will continue to have a major impact on that distribution. Of particular concern is the impact from increasing greenhouse gases and sulfate aerosols. As illustrated in Figure 2 of their published article titled “Effect of climate change on Lyme Disease Risk in North America,” Brownstein et al. (2005) predicted an overall decrease of 12% in areas with suitable climate for tick vectors in North America in the 2020s. During this time period, there is expected to be more retraction than expansion at 24.7% and 12.8%, respectively (Brownstein et al., 2005). A larger percentage of retraction could translate to putting less people at risk of exposure to the tick vectors and Lyme disease bacteria. However, most of this retraction is focused in the Midwest, and most of the expansion is focused in southern Canada. The overall retraction trend does not last for long though. In the 2050s, the trend of decreasing suitability is reversed to an increase in suitability of 10.3%. Extension into Canada shows an additional 49.8% in suitability. By the 2080s, suitable areas in the United States increase by 68.9%, while Canada sees an increase up to 213% (Brownstein et al., 2005). Expanding ranges of tick suitability could mean putting more people at higher risk of exposure to the tick vectors and Lyme disease bacteria. Of interesting note is the predictions for a few of the southern U.S. states. By the 2080s, the southern United States will see an overall reduction in suitability for *Ixodes scapularis* ticks. The temperature increases will cause environmental conditions to become too unfavorable for their survival, considering the majority of the tick life cycle happens off-host. Analyzing the effect of increasing greenhouse gas concentration and its link to increasing temperatures, Texas, Mississippi, and Florida are predicted to become uninhabitable for these ticks by the 2080s (Brownstein et al., 2005). Although the models used in the study show suitability ranges are predicted to change, the study does not mention the impact on the overall population of *Ixodes scapularis* ticks over time.

The survivability factor for these tick vectors is related to their life cycle and necessary interactions with other nearby organisms. Ticks have a life cycle that spans two years and requires three different hosts to complete, as illustrated in Figure 2 of "A framework for incorporating the prevention of Lyme disease transmission into the landscape planning and design process" (Ward & Brown, 2004). A bloodmeal is required at the larval, nymphal, and adult stages. The ticks begin as eggs that hatch sometime in the summer, usually the months of July or August. Transovarial transmission of *Borrelia burgdorferi* is low, which means infected mothers do not pass on the bacteria to their offspring. In other words, the newly hatched ticks are pathogen-free. Soon after hatching, larvae begin to quest, seeking out hosts to feed on for their first bloodmeal. White-footed mice and other small mammals are common food sources at this stage. Those small mammals can act as reservoir hosts of the *Borrelia burgdorferi* bacteria, harboring the bacteria without ill effects (Ward & Brown, 2004). When the ticks attach and feed, they can take up the bacteria as well and can then transmit it to other organisms in subsequent feedings. After this first meal, the larval ticks drop from the host back to the ground and molt into nymphs (Kurokawa et al., 2020).

Months later, in late May to early June of the following year, the new nymphs emerge after molting and begin seeking their next host sometime in the late spring to early summer window. Again, this bloodmeal usually comes from a small mammal, such as the white-footed mouse. However, if humans are going to be exposed to the Lyme disease bacteria, it is during this nymphal stage, when they become inadvertent hosts for a bloodmeal. At this point, nymphs are smaller than adult ticks, so humans are more likely to overlook them, whether on the body or in the environment. This risk to humans is exacerbated by the fact that this stage of the tick life cycle corresponds to when humans spend more time outside. After this second feeding, the nymphal tick drops to the ground and molts again (Ward & Brown, 2004). This time, the tick will emerge as an adult.

In October and November of the same year, these now-adult ticks begin host seeking. As winters become warmer, there are an increasing number of days where the adult ticks can continue seeking hosts in this season. Before, colder temperatures required more conservation of energy and less time questing. Mostly feeding on white-tailed deer and other medium and large-sized mammals, the purpose of this bloodmeal is to make it to the reproductive stage, where an adult female tick can they lay her eggs to continue the tick population. After attaching and feeding on this host, the adult tick once again drops to the ground to prepare for laying eggs and finishing her life cycle. In May, female ticks lay hundreds to thousands of eggs, which will hatch into larvae, starting the life cycles of the next generation of tick vectors that will be capable of transmitting the Lyme disease bacteria (Ward & Brown, 2004).

As mentioned, a factor that determines tick distribution is survivability in a certain region. *Ixodes scapularis* are taxonomically classified as part of the Ixodidae family of the phylum of Arthropoda. Synapomorphies, or characteristics unique to this phylum, include their chitin exoskeletons and inability to regulate their own body temperature. Having a hard exoskeleton without dermal pores makes homeostasis difficult to maintain for these ticks. In regard to climate change and increasing temperatures, this means ticks are more prone to overheating in summer months with temperatures outside of their survivable range, coupled with the need to rehydrate and lower their temperatures in the soil more frequently. Therefore, they have a strong thermal sensitivity and preference. Within this physiological perspective is the idea that tick development is related to temperature, as well. Previous studies have demonstrated that consistent temperatures above 4°C and below 32°C are "critical for molting and reproductive output of *I. scapularis*" (Fieler et al., 2021). With exposure to temperatures that are too high, the ticks risk overheating. Elevated temperatures also lead to a decrease in questing activity, the behavior of ticks when they go out into vegetation and wait for passing hosts to attach to. Ticks have to rehydrate more frequently when temperatures are warmer and drier. Rehydration takes place in the soil, away from potential hosts, thus lowering the probability of actually finding a host. However, during warmer temperatures, humans are outside wearing fewer layers of clothing. This leads to a higher potential for exposure and disease transmission directly from ticks to humans (Fieler et al., 2021). On the other hand, with exposure to temperatures that are too cold, the ticks can freeze. Dehydration can also occur under these conditions. When a tick responds to these stressors, a large energy expense is required, which can only be replenished when the tick finds a new host and gets its next bloodmeal (Fieler et al., 2021). Therefore, it is beneficial for the ticks to live in regions that do not deplete their energy levels.

The Fieler et al. (2021) study also found that *Ixodes scapularis* ticks have a much narrower range of survivable temperatures compared to the five other larval ticks involved in the study. *Ixodes scapularis* larvae had a higher lower lethal temperature (LLT) and a lower upper lethal temperature (ULT). That means *I. scapularis* larvae cannot survive in as cold or as warm of temperatures as the other tick larvae can. Putting the LLT and ULT together, the thermal tolerance of *I. scapularis* larvae was found to be between 15°C and 41°C. Adult ticks can survive in slightly cooler and warmer temperatures, but there is a risk of overwintering at the larval stage

(Fieler et al., 2021). The authors suggest that this narrower range can be explained because higher abundances of *I. scapularis* larvae are found in the mid-summer months and the larval stage for these ticks is not adapted to cold exposure (Fieler et al., 2021). It is also worth noting that proteins tend to denature around 45°C. Therefore, *Ixodes scapularis* larvae can survive fairly warm temperatures, but this study shows there is a limit to how much heat they can tolerate or even prefer. When given the choice, *I. scapularis* larvae preferred a temperature around 20°C. This conclusion was based on how much time the larval ticks spent in a clear, plastic tube that was heated on one end to 43°C, cooled to 0°C on the other end, and around 24°C in the middle. If the ticks can find environments that are closer to their thermal preference, they will be able to be active for longer periods of time. As temperatures continue to increase due to climate change, ticks have an increased amount of time for their seasonality, where temperatures fall within their survivability range.

To give a metabolic perspective, the researchers also investigated how O_2 consumption in larval ticks changes in response to temperature changes. Metabolic rate is important because it signals proper functioning and regulation, as opposed to an organism being under distress. The researchers found *Ixodes scapularis* larvae had no metabolic rate at or below 0°C, as well as at or above 50°C. The highest metabolic rate occurred at 30°C (Fieler et al., 2021). The observed metabolic rates are related to the ticks' inability to regulate their own body temperatures independently from the environment. They cannot maintain homeostasis under conditions outside of this range, so lower metabolic rates show the tick is in a state of starvation and is trying to conserve energy. It would not be beneficial for the tick to be tapping into its energy sources too much when not actively questing, trying to find a host for its bloodmeal. Again, these findings emphasize the existence of a thermal survivability threshold for the tick vectors.

Knowing what regions maintain conditions within this threshold can function as a clue for what populations are at higher risk of exposure to the Lyme disease bacteria. Even if temperatures are within the tolerance range for these ticks, that does not necessarily guarantee higher transmission rates of Lyme disease.

As the main reservoir host involved in the transmission of Lyme disease, harboring the *Borrelia burgdorferi* bacteria, how climate change is impacting the distribution of white-footed mice is also a key factor. Looking at the life cycle of the tick host vector, white-footed mice (*Peromyscus leucopus*) are an important host for *Ixodes scapularis* nymphs and larvae. Winter is the hardest season for these mice, as snow and colder temperatures make it more difficult to find food and regulate internal processes, including the reproductive system (Roy-Dufresne et al., 2013). Because of this, white-footed mice are also increasing their distribution to locations with warmer winters, in an effort to increase survival.

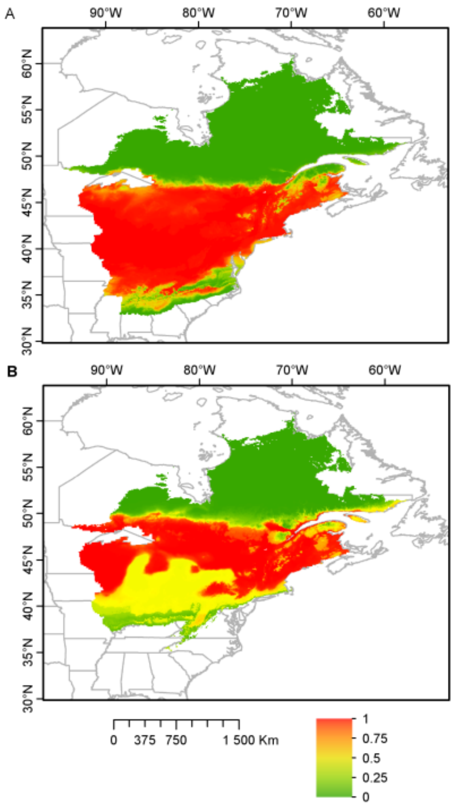

Figure 2. Current predicted (A) and future projected (B) distribution of the white-footed mouse modeled in BIOMOD. The projected distribution for 2050 was modeled with a change in climate under the A2 greenhouse gas emissions scenario from the IPCC [45] (WGS 1984 World Mercator). Models for gas emissions scenarios A1b and B1 are provided in Figure S1. The occurrence probability of the white-footed mouse is lowest in green and highest in red.
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Figure 1. Current predicted (A) and future projected (B) distribution of the white-footed mouse modeled in BIOMOD. The projected distribution for 2050 was modeled with a change in climate under the A2 greenhouse gas emissions scenario from the IPCC (WGS 1984 World Mercator). The occurrence probability of the white-footed mice is lowest in green and highest in red. Figure and caption from Roy-Dufresne et al. (2013). (CC BY 3.0)

Figure 1 shows the current and projected (2050s) distribution of the white-footed mouse in response to climate change. While not including the entire distribution of white-footed mice in the United States, these models focus on regions east of the Mississippi River, where most white-footed mice that will be impacted by climate change are located. The red represents higher densities of white-footed mouse, whereas the green represents less-occupied regions (Roy-Dufresne et al., 2013). Based on these models, there is a clear, northward expansion of white-footed mice, with a significant increase in density happening in southern Canada. The exact reason white-footed mice are predicted to decrease their distribution in southern regions is not entirely clear, but warmer winters in northern regions will allow for higher survival rates for white-footed mice (Bednar, 2012). Knowing where these reservoir hosts are in relation to the tick vectors helps determine the risk of Lyme disease transmission. In order for the ticks to be able to transmit the disease to humans, they must pick it up from a reservoir host, such as the white-footed mouse or other small mammal. Although less common, ground-dwelling birds, such as the common yellowthroat (*Geothlypis trichas*), are other possible reservoir hosts (Huang et al., 2019; Voordouw et al., 2015). If the populations of reservoir hosts and tick vectors are redistributing in similar patterns, they maintain a high probability of interaction. With these interactions comes a higher risk of human infection, as risk of infection depends on the presence of ticks and mice. But there is still another factor to consider when analyzing how climate change will impact the spread of Lyme disease.

The distribution of white-tailed deer (*Odocoileus virginianus*) also affects the transmission of Lyme disease. While white-tailed deer are incompetent hosts for the Lyme disease bacteria, meaning they cannot become infected by *Borrelia burgdorferi*, they do play a central role as key reproductive hosts for the tick vector, *Ixodes scapularis*. As reproductive hosts, they are the source of the bloodmeal required for mating to occur and for adult females before they lay their eggs (Huang et al., 2019). Therefore, knowing where white-tailed deer are changing in distribution in response to climate change, is also of significant importance. In fact, these deer also have the potential to reduce the spread of Lyme disease, given their incompetence as hosts for the bacteria. A ‘dilution effect’ can occur if deer are chosen as hosts for tick vectors in the nymphal or larval stage instead of white-footed mice. While less common, avoiding reservoir hosts for this meal and instead choosing incompetent hosts means fewer ticks become infected with the bacterial pathogen and thus less transmission to humans. On the one hand, a large number of deer initially means more adult ticks can mate and have offspring, leading to an overall larger tick population. However, for nymphs, more deer means a larger potential for bites on an incompetent host, decreasing tick infection and disease transmission. Therefore, predicting the spread of Lyme disease does not depend solely on the number of tick vectors in a given area. Larger populations of infected mice and other competent hosts for nymphal ticks to feed on, as well as an increased tick population due to deer aiding in reproduction, increases the overall probability of Lyme disease transmission (Huang et al., 2019). Limiting the distribution overlap among *Ixodes scapularis* tick vectors, *Peromyscus leucopus* mice reservoir hosts, and *Odocoileus virginianus* deer populations can consequently lower disease transmission and risk to humans.

White-tailed deer distributions are also predicted to be affected by climate change. Their distribution is mainly affected by the severity of a region's winter climate. Like white-footed mice, white-tailed deer are impacted by cold temperatures and depth of snow. More specifically, white-tailed deer have been found to have a lower thermal tolerance limit of around -7°C (Weiskopf et al., 2019). Temperatures below this limit lead to decreased survivability from physiological disruptions. Snow depth and rainfall reduce maternal body condition and reproductive success since cold temperatures are associated with higher metabolic costs for thermoregulation. Warmer winter weather and increased rainfall in the spring and autumn lead to higher success in reproduction. Matching with the trends of climate change, "warmer, shorter winters, with less snow, and wetter springs may increase the range and population size of white-tailed deer in North America" (Weiskopf et al., 2019). If a region can sustain a large-enough deer population to outweigh the transmission of *Borrelia burgdorferi* from mice to ticks, a dilution effect could take place. However, if deer relocate to regions where their role as an incompetent host cannot outweigh the transmission of *Borrelia burgdorferi* from mice to ticks, then humans will likely experience greater risk of exposure to Lyme disease.

Gaps in Understanding

Overall, most researchers agree that rising temperatures from climate change are leading to northward expansion of *Ixodes scapularis* tick vectors. There are also numerous studies, including the Huang et al. (2019), Roy-Dufresne et al. (2013), and Weiskopf et al. (2019) studies mentioned earlier, showing northward expansion of white-footed mice and white-tailed deer. All of these factors, individually and collectively, are predicted to increase human cases of Lyme disease. However, there are a few points that remain unclear. Much is unknown about how infectivity of the bacterium is responding to climate change. Most of the research focuses on how the hosts and vectors of Lyme disease are responding to climate change. In regard to the tick vectors, the molecular and physiological response of *Ixodes scapularis* to temperature still has room for specificity. Studies, such as Fieler et al. (2021), show that ticks do not survive outside of a certain temperature range but do not point to what exactly goes wrong. Additionally, many studies point out climate change's impact on the seasonality of the tick vectors, leading to earlier onsets as time goes on. Since the tick life cycle lasts two years, there is an opportunity to investigate how temperature changes will impact the duration of seasonality of ticks in the fall. A few studies also make reference to ticks and hosts preferring warmer temperatures and that being a main driver of their redistribution patterns (Brownstein et al, 2005; Monaghan et al., 2015; Roy-Dufresne et al, 2013; Tran et al., 2021). However, if temperatures continue to increase at alarming rates, it would be interesting to know if there could ever be a point where temperatures get so hot, yet still tolerable to humans, that the ticks will die or go extinct and thus have the potential for the disease to no longer be in circulation.

Adaptation and mitigation

Transmission of the Lyme disease bacterium to humans occurs through the bite of an infected tick vector. Most of this spread occurs in northeastern, mid Atlantic, and north-central United States during spring and summer months. The blacklegged tick (or deer tick, *Ixodes scapularis*) spreads the disease in these regions. Ticks can attach to any part of the human body and are often found in hard areas, like the groin, armpits, and scalp. For the Lyme disease bacterium to be transmitted, the tick must be attached for 36-48 hours (Sotsky, 2017). Most humans get infected from bites of immature ticks called nymphs. Nymphs are tiny (<2mm) and feed during the spring and summer months. They play a key role in transmission because of their small size and short feeding time (Hajdušek et al., 2013). Adult ticks can also transmit Lyme disease bacteria but are more likely to be discovered and removed before they have the time to transmit the bacteria because of their larger size. It also helps that these ticks are more active during the cooler months of the year (CDC, 2020). Increasing awareness and education on the importance of intentionally checking for ticks can reduce the spread of Lyme disease. Parents or guardians should specifically know to check for their children for ticks under their arms, around their ears, inside belly button, behind the knees and other crevices of the body. One of the most important places to check is the hair, as it is where ticks can hide and go undetected. A simple recommendation is to increase advertisement of the educational brochures, posters, and other documents the CDC has on Lyme disease can help educate the communities, especially those in high-risk areas, on how to prevent Lyme disease.

The impact of climate change on one aspect of the relationship amongst the bacterium, its hosts, and vectors will inevitably affect the others and lead to changing rates of Lyme disease transmission. *Ixodes scapularis* ticks have a narrow range of survivable temperatures. Therefore, when temperatures become too high, they will relocate to areas that are more suitable for their survival. Northward translocation will introduce the vector and the disease into previously unaffected areas (Fieler et al., 2021). Studies predict tick expansion into regions of Canada that were previously uninhabited by these ticks (Brownstein et al., 2005). Transmission of Lyme disease also depends on the presence of hosts. White-tailed deer, a predominant host for *Ixodes scapularis* ticks, are said to be incompetent hosts for bacterial infection. While these deer contribute to increasing the population of *I. scapularis* ticks, they can also help reduce the spread of the disease itself, since they cannot become infected (Huang et al., 2019). Climate change models predict populations of these deer will also expand northward (Weiskopf et al., 2019). However, white-footed mice, important reservoir hosts, are also showing northward expansion trends in response to climate change. Because the distribution changes are similar across the predominant hosts and vectors, Lyme disease will continue to be of high risk. However, the specific populations at high risk will change.

Transmission

There is no research or evidence that Lyme disease can be transmitted from person-to-person through physical touch like kissing or having sex with someone who has Lyme disease. However, during pregnancy, untreated Lyme disease can lead to infection of the placenta. The spread from mother to fetus is possible but rare. Currently, there are no published studies addressing the development or outcomes of children whose mothers acquire Lyme disease during pregnancy (CDC, 2020). Additionally, blood transfusion scientists have found that the Lyme disease bacterium can live in the blood that is being donated. So, if an individual is still being treated for Lyme disease, they should not donate blood, unless they have completed their antibiotic treatment and are considered okay to donate blood (CDC, 2020).

As for contact with pets, dogs can get Lyme disease, but there is no evidence that they spread the disease to their owners. However, there is a possibility that they can bring infected ticks into one's home or yard. One solution is to use tick control products on pets, to prevent them from bringing ticks into homes (CDC, 2020). When eating meat, there is no risk of Lyme disease infection from squirrel meat or venison. Once again, there is still a potential that hunting will bring infected ticks into the home, putting people in close contact with them at a higher risk (CDC, 2020). While it is important to be aware of which ticks can act as vectors of Lyme disease, not all ticks carry the *Borrelia burgdorferi* bacteria.

General mitigation

There are a few general mitigation strategies that can be used to minimize the transmission of Lyme disease. One of those involves implementing personal protective behaviors. Personal protective behaviors, as its name suggests, refer to actions the general public can take when high exposure to the tick vectors is anticipated. One of these behaviors includes wearing protective clothing. Long sleeves, long pants, and other layers cover exposed skin and prevent ticks from attaching directly into the skin. Using tick repellents can also help keep ticks off of the skin. Lastly, intentionally checking for ticks after spending time outside in areas where ticks are common can reduce the risk of overlooking small ticks, especially ticks at the nymphal stage (Bhate & Schwartz, 2011). These mitigation strategies are aimed at individuals, but there are larger-scale strategies, as well.

Environmental control is a way to reduce populations of *Ixodes scapularis* ticks. One method of environmental control is the removal of leaf litter. Proper removal of leaf litter from personal property and public land removes a common site for tick eggs, nymphs, and larvae. However, this removal method requires large amounts of manual labor and time to be systematic and effective. Another method of environmental control is to use acaricides, which are pesticides used to get rid of ticks and mites (Bhate & Schwartz, 2011). Because acaricides are synthetic chemicals and can damage the environment, their use is controversial.

Current research is investigating environmentally friendly alternatives to reduce the spread of Lyme disease. One such way is through biocontrol with an entomopathogenic fungus that kills or disables any tick it infects. Specifically, this fungus strain, *Metarhizium anisopliae* strain F52, is pathogenic to *Ixodes scapularis* nymphs. If introduced properly, populations of infected ticks could be reduced significantly. In their study, researchers Bharadwaj & Stafford suggest an application of this fungus at the end of June and early July "provided significant control in the second half of the nymphal season," whereas a preemptive application before the seasonality of ticks in early May was not effective in killing *Ixodes scapularis* (2010).

Clinical mitigation

If infection does occur, there are clinical mitigation strategies to reduce the overall severity and symptoms. When left untreated, the body can experience arthritis or other severe symptoms. In other words, getting treated right away is important. Antibiotics are most effective right after the stage of infection. Lyme disease can usually be successfully treated with 3-4 weeks of antibiotic therapy. Doxycycline is one example of an antibiotic used to treat Lyme disease. After a tick bite, a single dosage of doxycycline can help with the rash caused by Lyme disease. Although, only one study has investigated the effectiveness of such a low dosage

(Cameron, 2017). Amoxicillin is another antibiotic that has the potential to reduce the severity of Lyme disease. This antibiotic is used in dogs to treat bacterial infections and works by preventing bacteria from producing the proteins that allow them to grow. Amoxicillin can treat the infection within a few days (Vetinfo).

Although Lyme disease is intensively studied, no vaccine is currently available to prevent infection (Hajdušek et al., 2013). According to CDC guidelines, there is presently no Lyme disease vaccine available. LYMERix® was the only vaccination formerly offered in the United States but was withdrawn from the market in 2002 due to a lack of consumer demand. Sales for LYMERix declined from about 1.5 million doses in 1999 to a projected 10,000 doses in 2002. Although there is no vaccine to treat Lyme disease today, two potential vaccines being investigated (GSK-SKB and Pasteur Merieux Conaught) were found to be between 49 and 68 percent effective in preventing Lyme disease after two injections (NIH, 2018). There is no associated explanation on why the effectiveness of these vaccines is low. The duration of the protective immunity generated in response to the vaccines is also not known.

Stopping the bacterial infection in rodents could potentially prevent the transmission of the bacteria to the ticks that depend on them. Rodents are a major reservoir host for Lyme disease, so scientists have been looking at ways to prevent them from getting infected with *B. burgdorferi* in the first place. This reservoir is the habitat for the infectious agent to live and multiply, which is a problem because this is their way to survive and be transmitted to a host. The NIAID (National Institute of Allergy and Infectious Diseases) has funded research of potential reservoir vaccines in reducing Lyme disease in humans (NIH, 2018). These vaccines could be given to white-footed mice or other rodent reservoir hosts in the form of an oral "bait", as "scientists are working to grow rice plants that contain vaccine elements that could eventually be fed to rodent populations, thus blocking the transmission cycle of the disease from rodents to ticks to people" (NIH, 2018). The NIAID supports significant research efforts focused on human vaccination against Lyme disease as well. These researchers have identified tick proteins that facilitate transmission of Lyme disease bacteria or that enhance survival of those bacteria in vertebrate hosts. Studies are ongoing to see if vaccines specially targeting some of these proteins may be used as a strategy or an "anti-tick vaccine" in the future (NIH, 2018). For a vaccine, such as a Lyme disease vaccine, to get approval for administration, it must first go through the FDA. Then, the CDC will take over and work with the Advisory Committee on Immunization Practices (ACIP) to develop recommendations on how the community can benefit from this vaccine (CDC, 2021).

Recommendations

The order in which future research is conducted can have profound effects on mitigating the transmission or symptoms of Lyme disease. Developing an effective and safe vaccine is of extreme importance. Next, developing an effective acaricide to reduce the tick vector population that also minimizes its own environmental impact would be extremely beneficial. Additionally, developing more reliable ways to test for active infections would reduce misdiagnoses and could lead to more effective treatments for Lyme disease. As for the general public, it will continue to be in their best interest to dress according to the risk of exposure in the surrounding area, as well as to stay educated on the current distribution of the tick vectors. Limiting time in areas with large populations of white-footed mice or white-tailed deer can also be a good general rule to follow.

Overall, climate change is expected to change the distribution of key hosts and vectors that are responsible for transmitting the Lyme disease bacteria. These movements are predicted to occur mostly in the northward direction, as warming temperatures and milder winters allow the vectors and hosts to survive in these locations. Staying aware of where the vectors and hosts are present, as well as what human populations are at high risk of exposure, can limit transmission from tick vectors to humans. Additionally, environmental control and biocontrol are also promising in terms of reducing human exposure to the tick vectors. But if infection does occur, hopefully more-advanced methods for clinical alleviation of symptoms can help reduce the severity of the disease soon, along with a vaccine to prevent infection altogether.

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