TPWKY	This is Exactly Right.
Brian Allan	My name is Brian Allan, I'm an Associate Professor in the Department of Entomology at the University of Illinois and I study the ecology of ticks and tick-borne diseases. And I got into this line of work as a result of my first experience with Lyme disease which was both my first research experience with Lyme disease but also my first experience with contracting Lyme disease. So I was fortunate the summer after my senior year of college to get a research internship at the Cary Institute of Ecosystem Studies in upstate New York and I was funded to study the ecology of Lyme disease. This was the summer of 2000. So I had this summer internship and a lot of what it involved was traveling to different Lyme disease hotspots and collecting ticks in those locations.
	And so of course in the course of that work I was pretty diligent about protecting myself against tick bites but the infection rate in ticks in that area is incredibly high and so that point in the summer at least one tick got through my defenses and I came down with Lyme disease. So that was my first brush with the illness as well as with studying the biology of the disease. I don't believe I ever found the one that got me, so I just came down with the symptoms. Despite wearing protective clothing I was typically removing at least one tick per day. And so for the most part I was probably removing those ticks before I could be exposed to the Lyme pathogen but yeah, I just came down with the Lyme symptoms and it came on like a freight train.
	So I first woke up feeling the arthritic pain in my joints and a little bit of a fever. And I'd been spending the summer studying Lyme disease so I was really quite confident in my self-diagnosis. So I went straight to a physician and in that part of the U.S. the second you report symptoms in the summertime that even remotely approximate Lyme disease, they treat you with antibiotics. And so I was feeling better within 24 hours. I got better quite quickly. And then I eventually got the bullseye rash but it was about a week later, I was already recovered at that point, back out doing fieldwork, collecting more ticks.
	So in that lab I was unfortunately the only person to get Lyme disease that summer. There were probably about 20 or 25 students and this was a research group working on Lyme disease and so the mantra of the research group was 'don't get Lyme disease' right? Like everybody was supposed to take these preventative measure really seriously and so I felt it was disappointing that I was the one person who got Lyme disease that summer. And then of course everybody wanted to see the bullseye rash and so for the week that that rash was on the back of knee I couldn't get down the hall without somebody asking to stop and look at it which was just this constant reminder that I'd failed to prevent myself from getting Lyme disease while collecting ticks.
	And I haven't had any tick-borne disease since, so I've been bitten by hundreds if not thousands of ticks since then but it made me all that much more cautious. During the course of doing fieldwork on ticks I'll check myself multiple times a day, don't just trust in my clothing and repellents to get the job done. Cause tick checks really are the best strategy for preventing tick-borne disease.
TPWKY	(This Podcast Will Kill You intro theme)
Erin Welsh	Hi, I'm Erin Welsh.
Erin Allmann Updyke	And I'm Erin Allmann Updyke.
Erin Welsh	And this is This Podcast Will Kill You.

Erin Allmann Updyke	And it's our final episode of the season.
Erin Welsh	It is and you know what, guys? It's gonna be okay.
Erin Allmann Updyke	We'll all get through this time.
Erin Welsh	Yeah. We're gonna miss it as much as you do.
Erin Allmann Updyke	It's true.
Erin Welsh	Actually yeah, it really is.
Erin Allmann Updyke	It really is.
Erin Welsh	So we have to take a break though because there are a number of really important and cool and exciting things happening. Erin, what's going on? What's going on with you?
Erin Allmann Updyke	So with me what's going is by the time this episode comes out I will have birthed a baby human.
Erin Welsh	A baby human?
Erin Allmann Updyke	A baby human! Yeah so I'll be doing that during our break until we come back for Season 3, trying to keep that baby human alive outside of my body, that's the new challenge. What will you be doing, Erin?
Erin Welsh	I will be moving across the Atlantic actually within a couple of weeks after this episode airs I will be moving all of the stuff that I brought with me over to Europe back to the U.S.
Erin Allmann Updyke	Woo-woo!
Erin Welsh	Which means we'll be in the same place recording for once.
Erin Allmann Updyke	Oh my gosh. I am so thrilled. I can't even express my emotions.
Erin Welsh	Me too. And it's not gonna be a long wait until Season 3 starts, it's only til the end of October and don't worry, we've got plenty of stuff that we're working on during our break.
Erin Allmann Updyke	Yep.
Erin Welsh	Including crossover episodes.
Erin Allmann Updyke	Yep.
Erin Welsh	Including we're working on merch.
Erin Allmann Updyke	Yeah!

Erin Welsh	More merch. I know that you all have requested different t-shirts and stuff like that and guess what? We want to bring them to you.
Erin Allmann Updyke	Yeah we do. So we're working on that. So make sure if you don't already to follow us on Twitter @TPWKY and/or on Instagram and Facebook @thispodcastwillkillyou so that you stay up to date with what we're doing in the meantime. And make sure you click that subscribe button so that when we come back for Season 3 at the end of October you won't miss a single episode.
Erin Welsh	So this week as you may have guessed we are talking about the much requested-
Erin Allmann Updyke	Much requested.
Erin Welsh	Lyme borreliosis.
Erin Allmann Updyke	Lyme disease everybody! We've gotten more requests for this than I think any other disease.
Erin Welsh	Yeah I think so too. And you just heard from our incredible, wonderful, supportive, kind-
Erin Allmann Updyke	Fantastic, tall. That was weird.
Erin Welsh	Very tall. He is very tall though. (laughs) PhD advisor Dr. Brian Allan.
Erin Allmann Updyke	The one and only, folks.
Erin Welsh	The one and only.
Erin Allmann Updyke	Hope you give him a round of applause wherever you're listening to this because we've mentioned him before, we haven't ever had him on the pod, we're thrilled that he's here to give us not only our firsthand account but also some insight into the current research on the ecology of Lyme disease later in this episode.
Erin Welsh	Yes. Brian, thanks for coming on. And also so many people during their PhDs, one of the sources of stress or complaint or frustration is their advisors and that conflict between student and advisor and it was never the case with Brian.
Erin Allmann Updyke	Yeah.
Erin Welsh	And it's amazing how much that paved the way for an as pleasant as could be PhD experience. Brian, you're the best. Anyone who wants to work on disease ecology please contact Brian Allan. He's the best.
Erin Allmann Updyke	Yeah give him an email. I mean he's so the best that he let two of his grad students start a podcast during the last year of their PhDs. That's pretty...I mean I feel like that speaks for itself.
Erin Welsh	I mean to be fair he called it a blog for like four months.
Erin Allmann Updyke	He did. (laughs) Still not sure that he'll ever listen to this, I don't know if he knows how.
Erin Welsh	He will, he will. (laughs)

Erin Allmann Updyke	Anyways. Okay.
Erin Welsh	On to more important things.
Erin Allmann Updyke	The most important things in fact.
Erin Welsh	Quarantini time?
Erin Allmann Updyke	It's quarantini time. What are we drinking this week, Erin?
Erin Welsh	We are drinking The Dilution Effect.
Erin Allmann Updyke	This is such a good name for this drink, you'll just have to wait until the history section to find out why. It's a really great name.
Erin Welsh	I'm pretty stoked about it. What is in The Dilution Effect?
Erin Allmann Updyke	The Dilution Effect, it's essentially a Lime Rickey which was our first name for this quarantini.
Erin Welsh	Which is also a great name.
Erin Allmann Updyke	It's also a great name. This is gin, lime juice, sugar, chunks of lime, and club soda. It's pretty straightforward.
Erin Welsh	And?
Erin Allmann Updyke	And of course-
Erin Welsh	And a beautiful plump cherry. Pop that sucker in there so that it's like a fully engorged tick full of blood, just waiting to be popped.
Erin Allmann Updyke	Your blood just gooing out of it.
Erin Welsh	Yeah.
Erin Allmann Updyke	It's lovely. It's a very delicious drink and we will post the recipe for that quarantini along with our nonalcoholic placeborita on all of our social media channels as well as our website thispodcastwillkillyou.com. All right, that's fun.
Erin Welsh	All right, we're there. We're in the mood.
Erin Allmann Updyke	We're in the mood.
Erin Welsh	Let's start this.
Erin Allmann Updyke	Let's get into the biology of Lyme disease, shall we?
Erin Welsh	I think we shall.

Erin Allmann Updyke	Okay.
Erin Welsh	Do we need a break?
Erin Allmann Updyke	We'll take a quick break.
TPWKY	(transition theme)
Erin Allmann Updyke	So Lyme disease is a bit of a doozy.
Erin Welsh	Yeah.
Erin Allmann Updyke	This is the longest pages of notes I've ever had, so.
Erin Welsh	Oh my god, really?
Erin Allmann Updyke	Yeah.
Erin Welsh	Longer than vaccines?
Erin Allmann Updyke	Maybe not longer than vaccines but that was two episodes so it doesn't really count.
Erin Welsh	Okay.
Erin Allmann Updyke	Okay. So Lyme disease. People have been requesting this for a very long time and it's probably because this is something that many of our listeners or their friends may have had in the past if you live in the U.S. or in Europe or in Canada or even in parts of Asia, which I didn't realize that Lyme disease was quite so widespread.
Erin Welsh	It's global, baby.
Erin Allmann Updyke	Global disease. Lyme disease is the most common tick-borne disease diagnosed in both the U.S. and Europe and I'm pretty sure in Canada as well and the most common vector-borne disease in the United States.
Erin Welsh	Yes. It's a big one.
Erin Allmann Updyke	I also can't kind of believe that this is the first time we've ever covered a tick-borne disease on this podcast.
Erin Welsh	Yeah. I have noticed that and I think it's surprising and not surprising at the same time. It also won't be the last one that we cover.
Erin Allmann Updyke	Definitely not, there's a lot of really, really interesting tick-borne diseases out there. So get excited. Okay I'm not gonna talk about the life cycle or the ecology of ticks because you're going to do that. Am I right, Erin?
Erin Welsh	I'm gonna attempt that.

Erin Allmann Updyke	You're gonna do a great job. So we'll just jump right into when humans get infected essentially. So Lyme disease is a disease that's caused by bacteria, specifically little spirochete bacteria which means they're adorable little corkscrew-shaped little creatures which also makes them very hard to find because they're very thin and spindly, so when you try and stain for them the way that we stain for other bacteria they're really difficult to find on stains. And I'm saying bacteria plural on purpose because we're not just talking about a single species, this disease is very much more complicated than that. Most commonly Lyme disease is caused by the bacterium Borrelia burgdorferi in the U.S. and in Canada as well as in Europe. However in Europe Lyme can also be caused by two other species of Borrelia, Borrelia afzelii and Borrelia garinii. Am I saying those right?
Erin Welsh	I always hear 'afzeli' but...
Erin Allmann Updyke	Oh, 'afzeli'?
Erin Welsh	Yeah.
Erin Allmann Updyke	That's actually probably right, yeah.
Erin Welsh	And also there are a couple other ones that are newly discovered as well but let's just call it the Borrelia group in Europe and the Borrelia group in North America, the Borrelia group in Asia.
Erin Allmann Updyke	Yes. There you go. Yes. There's many other species as well. So on top of that they're transmitted by multiple different tick species across their range. So we've got multiple tick species, multiple bacterial species, one multifaceted disease. Ooh, okay.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	This is complicated.
Erin Allmann Updyke	All right. So how do humans get infected? That's the first question we have to answer. So when you encounter an infected tick and it bites you, it's not like a mosquito, it doesn't just feed on your for like 10 seconds and barf its whole salivary glands into you right away. Ticks take their time. They burrow their face into you and after some time of being attached they will then start spitting the contents of their salivary glands into you and transmitting the disease. So that's how you get infected. You get bit by a tick, it stays on for long enough to spit its contents into you and now these little spirochetes are free underneath your skin.
Erin Welsh	Did you know though that Lyme disease, so Borrelia, the tick needs to be attached for a lot longer than for something like tick-borne encephalitis which is just instantaneous?
Erin Allmann Updyke	Yeah. Is it just like it's deeper in their salivary glands or something? It takes them longer to get it up and out or what?
Erin Welsh	I don't know. I think maybe it's something like that, maybe it's something about the feeding process itself or where exactly, yeah. I don't know.
Erin Allmann Updyke	Yeah but in general they have to be attached for at least 24-36 hours before you're at risk of getting infected with Lyme disease.

Erin Welsh	Tick checks are important.
Erin Allmann Updyke	Tick checks, check your bod. And your friend's bod for ticks.
Erin Welsh	There are several country songs about this.
Erin Allmann Updyke	(laughs) Should we get permission to play one?
Erin Welsh	(singing) I'd like to check you for ticks.
Erin Allmann Updyke	(laughs) Okay.
Erin Welsh	I just played one.
Erin Allmann Updyke	There we go. Okay so now your infected. You have little spirochete bacteria underneath your skin, spiraling their way through your skin tissue, maybe making their way into your bloodstream. And here's where we run into our first set of complications when it comes to Lyme disease. We don't have a really great handle on what Borrelia does once it's in your body or exactly where it goes which can make it difficult if you're trying to find the actual bacterium in someone's bloodstream for example which is how we usually test for infections, right. We take your blood and we look for stuff in it or we take some of their bodily fluid and we look for bacteria in it.
	Borrelia are kind of hard to find and we don't know exactly where they go. What we do know is that as they're making their way through your body, they stimulate a massive immune response on your part. So your body knows that these spirochetes are there and really starts attacking them. So what that means is that most of the symptoms that we'll talk about are not caused by the bacterium directly but by your immune system's response to the bacterium. Cool?
Erin Welsh	Right, right.
Erin Allmann Updyke	Cool. Okay. So that's the easy part.
Erin Welsh	Uh oh.
Erin Allmann Updyke	Now we'll move into the harder part.
Erin Welsh	Oh yay.

Erin Allmann Updyke	Lyme disease, we can't get that far into this episode without talking about the fact that there's a lot of controversy I guess you'd call it around Lyme disease. There's a lot of misconceptions and a lot of miscommunications and a lot of angry yelling when it comes to Lyme disease. And this has led to a lot of mistrust between the medical community and patient advocacy groups and a lot of people not feeling very heard or seen by physicians. So while full disclaimer, we don't have all of the answers when it comes to Lyme disease, there are still some gray areas, there is a lot that we do know. So while this is a complex disease, what we're gonna do for you is try and break down the scientific data that we have as it currently stands. So what I wanna do is first talk about the symptoms and how we diagnose and treat Lyme and then I'll try and address some of the specific misconceptions and controversies surrounding Lyme disease. That sound good?
Erin Welsh	Yeah. Sounds great.
Erin Allmann Updyke	Okay. So the first thing to know about Lyme is that there are actually three different stages of Lyme disease. Early localized, early disseminated, and late Lyme disease. Those are the three main stages. As you can imagine early localized Lyme starts the earliest after exposure and it's characterized by a very, very specific type of rash called erythema migrans.
Erin Welsh	EM.
Erin Allmann Updyke	EM, baby. Erythema means redness and migrans is to migrate. So this is a red rash, it's not itchy, it's not usually painful at all. It's usually round or at least roundish and often it has an area of what they call central clearing, so there's a part towards the middle that's less red than the edges which are more red. And then sometimes right in the center you'll get some serious inflammation or necrosis even where the tissue starts to die right in the middle.
Erin Welsh	Bullseye.
Erin Allmann Updyke	Yeah, this is what we call the bullseye rash. It really doesn't look like an actual bullseye all that often but it is a very distinctive rash, this sort of red margin and then it's more clear in the center. And while it can be confused for something like cellulitis or something like that, in general this is not painful at all. And it also slowly grows over time which is why it's called erythema migrans, it's like it migrates. This rash doesn't have to happen where you got bit from the tick. So it's not like the tick bite is in the center of the rash or anything like that, it can happen anywhere on the body. Most often it happens in the armpits, the groin, or the back of the knee. Don't ask why.
Erin Welsh	Really?
Erin Allmann Updyke	Don't ask me why. (laughs)
Erin Welsh	Well hold on but armpits, groin, and the back of the knee. So at least in the armpits and the groin there are lymph nodes.
Erin Allmann Updyke	Back of the knee too. There's tons of lymph nodes in the back of the knee.
Erin Welsh	Really? In the back of the knee.
Erin Allmann Updyke	Yeah.
Erin Welsh	So I wonder if it has something to do with that.

Erin Allmann Updyke	Yeah, it absolutely could. That actually probably has a lot to do with it. Okay. So this early localized form of the disease begins within usually a few days of exposure although it can take up to a month after exposure for this rash to first appear. And this rash, you could have only this rash and that could be the only symptom that you have of Lyme disease. But very often you might have some other very nonspecific symptoms. Things like a mild fever, nothing bonkers high or anything, just a low-grade fever, generalized weakness and muscle aches, arthralgias or joint pain are pretty often associated with Lyme disease, and then things like headache, stiff neck, maybe you have some swelling of lymph nodes all around. What you don't see are things like respiratory symptoms or couch or anything like that. Okay so two important things about EM, this rash specifically. It's estimated that 80% of patients actually have this rash. 80%.
Erin Welsh	Wow, that's higher than I thought.
Erin Allmann Updyke	That's literally what I wrote. That is way higher than I thought.
Erin Welsh	I thought it was 60%.
Erin Allmann Updyke	Yeah it's more common. And my guess is that this is 80% of people who are actually diagnosed with Lyme. So it might be lower in people who end up not getting diagnosed or something like that. But it's estimated that that EM rash happens in 80% of patients and EM doesn't happen in basically any other disease except for something called STARI which is Southern Tick-Associated Rash Illness, the lamest name for an illness of all time.
Erin Welsh	Okay.
Erin Allmann Updyke	And I'm not gonna talk about it. It's another beast entirely that we don't know a lot about but it causes this same rash, it's transmitted by a different tick, it's in different geographic areas. Okay?
Erin Welsh	Which tick? Amblyomma americanum?
Erin Allmann Updyke	Erin, I don't remember. I'm sorry. Maybe it's the lone star, is that Amblyomma?
Erin Welsh	Amblyomma americanum, yeah.
Erin Allmann Updyke	Yeah, I think it might be that one. It's in the south. Okay so what that means is if you come into a doctor's office with this EM rash, you've got Lyme. Done. Especially and hopefully this true, you have some kind of way that you've potentially been exposed to ticks even if you never found a tick on your body, right. Like you've been outside in an area where ticks could potentially exist.
Erin Welsh	Right.

Erin Allmann Updyke	Okay. But what's important is that at this stage testing is often negative and we'll talk more later about why that is. But at this point if you see that rash, that's Lyme and it can be treated as such. Okay. That's early localized disease. Second stage is early disseminated Lyme disease which is similar in that it's an early manifestation, usually again within a week to several months. But someone may or may not have ever had the specific symptoms of early localized disease. It's basically just you can think of it as a little bit more severe down the scale of Lyme disease where now in addition to potentially having multiple of these EM rashes, early disseminated disease is characterized by like neurologic symptoms, so that means that the bacteria or the inflammation has reached your nervous system, especially things like meningitis are very common which we've talked about before, that's inflammation of the lining of your nervous system. That shows up with things like headache and stiff neck. You can get nerve palsies which is nerve - what's the word - paralysis, especially one of the kind of classic symptoms is bilateral facial nerve palsy.
Erin Welsh	Oh.
Erin Allmann Updyke	So bilateral Bell's palsy. Both of your facial nerves get paralyzed essentially. But it can happen to any other nerves, it's not only your facial nerves but it is very common to happen in cranial nerves where you'll have cranial nerves that get paralyzed. You can also get nerve pain or end up with something even more serious like encephalomyelitis which is inflammation of the brain and spinal cord both. So those are sort of more serious manifestations and they're also more rare manifestations of Lyme.
Erin Welsh	Okay.
Erin Allmann Updyke	The other common presentation at this stage of Lyme disease, the early disseminated stage, is what's called Lyme carditis which 'card' as in cardio like your heart means that there are heart manifestations. The most common is called heart block which means that the conduction system of your heart is no longer working properly so that then your heart can't beat properly. This is a pretty serious illness that can happen as a part of Lyme disease. You also can get myopericarditis which is inflammation of the muscle tissue itself, so not the conduction system but the muscle tissue and the lining of your heart, the surrounding of your heart. So there's a lot of different ways that Lyme disease can affect and all of this is part of early disseminated Lyme disease. Cool?
Erin Welsh	That's super cool. Well super fascinating.
Erin Allmann Updyke	You mean terrible? Yeah.
Erin Welsh	Are you gonna give me some numbers on what percentage of people this happens to?
Erin Allmann Updyke	It's a good question. I don't have exact numbers.
Erin Welsh	Okay.
Erin Allmann Updyke	Yeah. I mean we'll talk about how many people get diagnosed in general, I don't know what the breakdown generally is between how many people are diagnosed early localized vs early disseminated vs late except to say that the vast majority of people are diagnosed at some point in the early stages, so whether it's early localized or early disseminated. And honestly it's a little wishy washy the window between those, right? It's really just if you have these serious nerve or heart manifestations then we're gonna call that disseminated whereas if the symptoms are less severe, just like fever and joint pains, they'll probably call that early localized. And if you have multiple vs a single of the bullseye rash.

Erin Welsh	And so how does this play into the actual microbiology of the bacterium itself? Like what is it doing inside your body? Where is it going? How is it actually causing these neurological symptoms? You're throwing your hands up.
Erin Allmann Updyke	I'm throwing my hands up in the air cause it's a great question. It's really unclear. And like I said it seems as though many of the manifestations of Lyme are caused by inflammation, so our body's response to the spirochete.
Erin Welsh	Right.
Erin Allmann Updyke	But we don't really know where the spirochete is going. I mean obviously it's attacking our heart and it's attacking our nerves. How exactly it's doing that isn't entirely clear. There's a lot that we don't know about Lyme.
Erin Welsh	Yeah, there really is.
Erin Allmann Updyke	There really is. Yeah.
Erin Welsh	There's a lot that we do know.
Erin Allmann Updyke	There's a lot that we do know and we'll keep talking to tell you all those things. So generally by the time that somebody presents with some of these more severe symptoms, that generally means that they have been infected long enough, that their body has started to make antibodies against the bacterium. So that means that now we can actually test for Lyme disease. In the early localized stage when you just have just the bullseye rash and maybe a fever, you haven't started to make enough antibodies to be able to test for whether or not you're infected with Lyme. But by this stage you have. So now we can check your blood and find evidence of the fact that you've been exposed. Cause like I said before, since we don't know exactly where the spirochete is going, if it does hang out in your bloodstream it makes itself really hard to find. We don't have a lot of good tests to look for the bacterium itself, so the way that we tell that someone has been infected with the Lyme spirochete, with Borrelia, is that we look for antibodies against Borrelia.
Erin Welsh	Okay. So the antibody test is the primary-
Erin Allmann Updyke	Yes, seropositive.
Erin Welsh	Seropositive test would be the only way.
Erin Allmann Updyke	Pretty much, yeah. There are some others but they're not as good. And one thing I wanna address even though I said I was gonna address misconceptions later, let's start with one right now. There's a lot of I think misinformation about whether or not these serological tests are reliable and obviously no tests that we have in all of medicine is 100% perfect, I don't think there's a single one that's 100% sensitive and specific, maybe there is and someone's gonna yell at me for saying that. But a test that has a really high sensitivity will accurately identify everyone with the disease, they won't miss a lot of people. So you end up with a lot less falsely negative people. Does that make sense?
Erin Welsh	Yes.

Erin Allmann Updyke	A highly specific test means that if you got a positive, it's definitely just that disease that you're testing for. So you end up with a lot less false positives with a highly specific test but you might miss some positives with a highly specific test. Does that make sense?
Erin Welsh	Yes. So you want a test to be highly sensitive over highly specific.
Erin Allmann Updyke	Potentially, depending on the scenario. And in this scenario yes, you'd probably want a test that's highly sensitive cause that means that we're not gonna be missing any cases of Lyme.
Erin Welsh	Yeah.
Erin Allmann Updyke	We might accidentally diagnose people with Lyme that actually don't have it, that are falsely positive, but we won't miss anyone and say, 'Oh don't worry, you don't have Lyme' when they actually do.
Erin Welsh	Right.
Erin Allmann Updyke	With a highly sensitive test. So early on in like an early localized stage of the disease, these tests, these serological tests are not very sensitive. They're maybe like 40%, 45% sensitive. However as the stages progress, so as time goes on, they are between 90-99% sensitive and they're also pretty dang specific as well. So these are actually very good serological tests. So what that means is if someone has been tested especially after a certain period of time and tests negative, it's very, very, very unlikely that they had Lyme disease. Does that make sense?
Erin Welsh	Makes sense.
Erin Allmann Updyke	All right. So glad we cleared up that first misconception. Okay. We have one more stage of Lyme disease and that is late Lyme disease. So this is something that happens if someone who was exposed to Lyme disease was never treated and it generally happens between a few months to even a few years after exposure, again if someone was never treated for Lyme. The most common feature of late Lyme disease is arthritis especially in a few large joints, so not like all of your joints but not just one but a few large joints. But it also can present with encephalopathy which means mental status changes, so something like mild memory loss or feeling fuzzy, not feeling like yourself. And what's scary about this one is it's usually really subtle, it's not like full on all of a sudden you can't remember anything, it's just little brain shifts which sounds just so insidious and yucky.
Erin Welsh	Yeah.
Erin Allmann Updyke	And you also could have polyneuropathy, so nerve pain. And then because we're talking about in some cases different species of Borrelia in Europe, there's actually a few different manifestations of both the early disseminated and the late disseminated that are more common in Europe and a lot of them are sort of skin manifestations, so like weird blue-colored lesions that slowly enlarge and then the veins stay distended.
Erin Welsh	What?
Erin Allmann Updyke	Yeah, it's called acrodermatitis chronica atrophicans.
Erin Welsh	That's very interesting and strange. Okay.

Erin Allmann Updyke	So those skin manifestations are mostly due to Borrelia afzelii infection specifically. So late Lyme disease is actually the type that was first characterized which is cool, I didn't know that. But these days it's fairly uncommon because most people have some kind of early symptoms and are able to be diagnosed and treated. But if somebody never was, like maybe they just had a rash and very mild symptoms and never noticed the rash cause it was in a weird spot, then it is possible that they could present for the very first time with symptoms of late Lyme disease. But this is diagnosed in exactly the same way as early disseminated where we look for antibodies in your blood. Cool?
Erin Welsh	Okay.
Erin Allmann Updyke	Okay. So how do we treat it?
Erin Welsh	So question though. Active infection vs residual inflammation processes...
Erin Allmann Updyke	Let's talk about it. (laughs) That's a long convo so let's first talk about how we can treat it, then we can talk about what might happen after we treat it.
Erin Welsh	Okay.
Erin Allmann Updyke	So most people who present with signs and symptoms of early disease, whether early localized or disseminated will need between 10-21 days of oral antibiotics. It's usually doxycycline which is a pretty standard antibiotic, there are some others that people use as well. And so current recommendations are between 10-21 days for early disease. Now if you have certain neurologic or cardiac or more complicated manifestations that may require IV antibiotics for up to a month or so and the same is true for some people with arthritis or arthritic manifestations of Lyme. They might require longer courses or IV antibiotics. And about 10% of people in the U. S. who present with severe joint symptoms don't seem to respond very well to that first round of antibiotics and may require a second round.
	There is not a ton of evidence so far for antibiotic resistance for Borrelia but obviously antibiotic resistance is a huge issue in general so that's a concern for every bacterial disease. Most people if they present with either early localized or early disseminated symptoms will recover completely, most of the time within 20 days which is still a very long time. 20 days to be sick and feeling miserable? Like that's still a really long time.
Erin Welsh	Yeah, yeah.
Erin Allmann Updyke	And in some cases it can actually take up to 6 months, so it's not that you're on antibiotics for 6 months but it might take you up to 6 months or more before you're actually feeling all the way better.
Erin Welsh	100%, yeah.
Erin Allmann Updyke	Yeah. Which is miserable especially with some of these symptoms like joint pain, muscle pain, fatigue, like this can make it really difficult to function like a human in the society that we currently live in.
Erin Welsh	Yeah.

Erin Allmann Updyke	Now several studies have shown in addition to this that even though most people recover completely, between 11-15% of people who are treated for Lyme will report persistent symptoms, so lasting longer than 6 months. Symptoms like fatigue, myalgia so muscle pain, and difficulties with concentration and memory. So it makes sense, it's a logical jump to think that hey, I got sick with Lyme and I felt like crap and I got treated with antibiotics but I'm still miserable, that must mean I need more treatment, right, the antibiotics didn't work. But this is where Lyme gets a little tricky. For some people these persistent symptoms after treatment for Lyme disease have led to a diagnosis of chronic Lyme disease. This is a really controversial term and it's not one that currently has a definition in the medical community, it's not a recognized disease in the medical community. This is in part because the notion of a chronic Lyme disease implies a chronic or prolonged infection with Borrelia burgdorferi, the spirochete bacterium that causes Lyme, right? However there is no good evidence in people with these persistent symptoms of persistent infection with the Lyme bacterium.
Erin Welsh	Right.
Erin Allmann Updyke	Okay. So while there have been a few animal models that suggest that small amounts of the spirochete might persist in certain tissues, these studies don't translate well to human disease for a couple of reasons. One, this is as you'll hear later a wildlife disease so it's very reasonable to think when we're studying it in rodents that the spirochete might behave very differently than it does in humans.
Erin Welsh	Particularly in its reservoir hosts.
Erin Allmann Updyke	Exactly, which are small rodents that are very commonly used for animal testing. Additionally a lot of the persistent symptoms, most of the persistent symptoms that we see are subjective. They're things like arthritis and fatigue. Animals can't tell you if they're feeling those feelings the way that humans can so it's really difficult to even understand how that might translate from an animal model to a human. However in studies of humans with persistent symptoms after treatment for Lyme disease there is no good evidence of chronic infection with Borrelia. So they've tested for trying to find the actual bacterium in various tissues, blood, skin tissue, joint aspirates especially so if you're having joint pain and it's caused by a bacterial infection you would expect to find bacteria in the joint fluid and there's no good evidence that after treatment you still find those bacteria.
Erin Welsh	So they've tried to culture it and nothing has happened.
Erin Allmann Updyke	Yes, yeah. Exactly. Which means that chronic or long term antibiotic use is not beneficial for people suffering from these symptoms. There have been multiple studies which have shown no benefit of long term antibiotic use compared to a placebo. And in some cases they have shown more harm than good can come from long term antibiotic use cause antibiotics are not without their own risks.
Erin Welsh	Like what?

Erin Allmann Updyke	Like antibiotic resistance, clearing out your own microbiome, right, disrupting your natural gut flora and things which can lead to secondary infections, and then antibiotics also have a number of nonspecific effects. So they can be bad for your live, they can be bad for other organs, they're not overall drugs that you want to take unless you really have to. But the problem is people are still suffering and in some cases they might have been through a lot of testing and different drugs and who knows what else to try and get relief for their symptoms. And honestly there's likely no shortage of doctors who are crappy listeners and just ignore or downplay or don't take seriously these kind of subjective complaints. And I think that's in large part where so much of the frustration between people suffering from these symptoms and the medical community has come from, it's not feeling heard.
	So the question then is what is actually causing these symptoms in people who have evidence of having had Lyme disease and were treated but are still miserable? There is some evidence that these symptoms may be caused by autoimmune or inflammatory type reactions much in the way that rheumatic heart disease can be a manifestation following an infection with a bacteria called Strep. pyogenes or the way people can get Guillain-Barre syndrome after an infection with campylobacter.
Erin Welsh	Right. This is like a common theme in infections.
Erin Allmann Updyke	Exactly. Yeah this isn't a phenomenon that's unique to Lyme to think that maybe what's happening here is some kind of autoimmune or inflammatory reaction after treatment for Lyme bacteria. And in fact some people with these persistent symptoms, especially the joint-type symptoms respond well to NSAIDs, nonsteroidal anti-inflammatories like ibuprofen or to joint injections with steroids or in some cases to anti-rheumatic treatments, these are things that we would normally give to someone with something like rheumatoid arthritis or lupus.
	This is evidence suggesting in favor of the idea that these post-treatment Lyme symptoms are indeed related to autoimmune or inflammatory disease, not persistent infection. And the issue too is that we don't have a good handle on what Borrelia is doing precisely inside of our bodies in the first place and we definitely don't have a good handle on what antigens it might be that we potentially could be making antibodies against that then lead to this sort of autoimmune type flare up. So because we don't have a good handle on what's going on, that can be really frustrating cause it means that we don't have very directed therapies, right. It's just like try ibuprofen, see if that helps kind of a thing.
Erin Welsh	Yeah and it's very unsatisfying.
Erin Allmann Updyke	Yeah. There's also a few other issues at play here and that is that so for one thing there are actually pretty high rates of coinfection both in the ticks and then it can be passed onto humans, so there's coinfection between Borrelia and other tick-borne illnesses many of which don't respond to the same antibiotics as Lyme. So Anaplasma which is one tick-borne disease that a tick could be coinfected with and could therefore co-infect you with is, that's treated with doxycycline. But Babesia and tick-borne viruses, these things don't respond to the antibiotics that we use to treat Lyme so it's also possible that somebody could be adequately treated for Lyme but have another underlying infection that is untreated.
Erin Welsh	Yeah.

Erin Allmann Updyke	But the thing I do wanna stress in addition to what you said Erin that it's not like these symptoms aren't really and we know that post-treatment symptoms can occur for a number of people, the thing that I do wanna point out is that there also have been people treated for Lyme with these Lyme-type symptoms who don't have any evidence of a Lyme infection. And I think that those people sometimes get grouped into this chronic Lyme or post-treatment Lyme. And like we talked about earlier in terms of diagnosing Lyme, while the tests that we have to diagnose Lyme aren't perfect, they're actually pretty good as long as you're testing late in the course of disease.
Erin Welsh	Hypothetically speaking let's say that somebody was infected with Borrelia.
Erin Allmann Updyke	Yes.
Erin Welsh	They're going to test negative up until a certain point?
Erin Allmann Updyke	Yeah until their body starts making antibodies against Borrelia.
Erin Welsh	Right.
Erin Allmann Updyke	Then they will test negative on that serological test. But after a week or two if you test them again they would be positive.
Erin Welsh	And then for the rest of their lives would they test positive?
Erin Allmann Updyke	Pretty much, yeah. And so that is something that you can't tell if the infection is necessarily an active infection vs you had it 10 years ago or something like that. So if someone tested positive with symptoms and had never been treated for Lyme, they should be treated for Lyme, right? But if they test positive but they've been treated for Lyme, that's just residual antibodies, it doesn't mean they have an active infection.
Erin Welsh	Gotcha.
Erin Allmann Updyke	Although there's some nuance to that because there are early antibodies and then there are late antibodies but you can tell if you got reinfected for example, but that's a different story. Cause that's also possible.
Erin Welsh	It happened to Brian.
Erin Allmann Updyke	Yeah, it did. (laughs) That's basically Lyme in a nutshell.
Erin Welsh	In a tick shell?
Erin Allmann Updyke	In a tick shell. Do you need a break?
Erin Welsh	I think I need a break.
Erin Allmann Updyke	I need a break.
TPWKY	(transition theme)

Erin Welsh	For many people a walk in the park is no longer just a walk in the park. It feels like taking a gamble with your or your family's health on the line. Multi-day treks, short hikes, picnics, gardening, all of this formerly innocuous activities are now or at least they should be accompanied by a full body screen for a tiny hitchhiking arthropod, a tick check. And if such a critter is found, panic mode might set in as you frantically search for tweezers to rip this invader from your flesh. At this point if Google fails to give you satisfactory answers about the odds of you coming down with an infection or if you are simply spurred into action by the horror-inducing headlines that flash across your screen, you may schedule a doctor's appointment to confirm or assuage your fears. And that's if you spot the tick in the first place. For many people if not most the horror only comes afterwards when your body starts to tell you something is wrong. And the source of this wrongness? The even tinier hitchhiker hidden inside the tiny tick hitchhiker, Borrelia burgdorferi.
Erin Allmann Updyke	(laughs) That makes it sound so cute.
Erin Welsh	I mean it is kinda cute.
Erin Allmann Updyke	It is.
Erin Welsh	Ticks are cute, that's my opinion.
Erin Allmann Updyke	That's your opinion.
Erin Welsh	If you don't believe me look up Amblyomma gemma, it's a genuinely beautiful tick.
Erin Allmann Updyke	Yes it's beautiful in its coloration and stuff but it's not any less creepy and awful just because it's pretty.
Erin Welsh	No and I will be the first to admit that as a person who studied ticks for the last 6 or 7 years, okay. They are creepy and I don't like finding them on my body.
Erin Allmann Updyke	(laughs) They're so creepy.
Erin Welsh	This fear of Lyme, this paranoia that surrounds tick bite, these aren't deeply rooted things going back millennia. More of a 'ew, get this thing off of me' maybe but not sort of the instant panic and fear that I think now is a lot more prevalent. And that's because Lyme borreliosis is a recent emerging infectious disease and it's not one of the most common vector-borne diseases worldwide.
Erin Allmann Updyke	Wow.
Erin Welsh	And it's one that had surged in prevalence in the decades since it was given its name. And so I'll go into some of the ideas as to how and why it seems to have spread so rapidly but first let's trace Lyme back to its roots as I usually do.
Erin Allmann Updyke	Yes! Our favorite thing.
Erin Welsh	Always. While the fear of Lyme borreliosis only goes back a few decades, the disease itself and certainly the pathogen goes back a lot farther, goes back a lot further.
Erin Allmann Updyke	(laughs) Sorry that was so dorky.

Erin Welsh	Farther and further are very different things.
Erin Allmann Updyke	I know but I wouldn't have done it correctly.
Erin Welsh	Oh god. The history of Borrelia burgdorferi and Lyme borreliosis are separate chapters of the same story so I'll start at the beginning. Okay. The first chapter: Pathogen. As you mentioned, Lyme borreliosis can be caused by a number of different species of Borrelia and that depends on where in the world you are. It could be Borrelia burgdorferi sensu stricto, Borrelia afzelii, Borrelia garinii, Borrelia spielmanii, and many others with more being described all the time. And this diversity of Borrelia species causing infection in humans and the existence of multiple strains within a species point towards this being a very old group of bacteria and that's supported by genomic research. So by comparing the Borrelias found in infected people and infected ticks from all over the world and then overlaying that with the geographic location of the infection, researchers could point out not just how long the bacteria have been around but also when they went from point A to point B and just what those points A and B are.
Erin Allmann Updyke	Awesome.
Erin Welsh	So here's a general disclaimer that this is an area of active research so conclusions aren't necessarily firm and that's probably something I should just say as a blanket statement for this entire section.
Erin Allmann Updyke	For sure, yeah.
Erin Welsh	But a few things do stand out in this research. Okay so we have a bunch of Borrelia species that cause disease in humans, some of which are only found in North America and some of which are only found in Europe or Asia and some that are found in both places. Those that are just found in Europe are likely of European origin, pretty simple. And those that are found in North America, likely North American origin. But what about Borrelia burgdorferi sensu stricto which is found in both places? There's not a super clear story here but it seems moderately more likely that this species originated in Europe and then was introduced to North America several times. And how that happened is still a bit of a mystery since humans are considered a dead end host for the disease which means that it's extremely unlikely that an uninfected larva will feed on a human infected with Borrelia and then become infected itself and then able to introduce the disease into the ecosystem.
Erin Allmann Updyke	I don't think that I knew that.
Erin Welsh	Yeah they don't contribute to the disease cycle.
Erin Allmann Updyke	Wow, yeah. I mean that makes a lot of sense but I never really thought about... Like if it was something like West Nile it's like obviously humans are dead end but with Lyme I never really thought about it.
Erin Welsh	Yeah.
Erin Allmann Updyke	Great job disease ecologists.
Erin Welsh	Yeah I mean but that makes it more confusing cause if you imagine the human migrations to North America it's unlikely that that would be the source of infection there.

Erin Allmann Updyke	Right.
Erin Welsh	So then maybe what about something like birds?
Erin Allmann Updyke	Okay.
Erin Welsh	But apparently there aren't very many bird species that migrate east to west, so it's more north to south generally speaking. So maybe some sea birds could do the trick but that really hasn't been fully investigated. Okay so still some questions there but that does seem to be multiple introductions from Europe to North America. But what's the time scale that I'm talking about here? When is all of this taking place? Over thousands and thousands of years.
Erin Allmann Updyke	What?
Erin Welsh	Oh yeah. One study I read puts the most recent common ancestor of Borrelia burgdorferi at 60,000 years ago.
Erin Allmann Updyke	Whoa!
Erin Welsh	Yeah. And other stories agree that the bacterium existed in North America in pre-Columbian times.
Erin Allmann Updyke	Wow.
Erin Welsh	Okay so it's gonna get really cool because I was very thrilled to read this. What about any physical evidence of Borrelia Burgdorferi's ancientness?
Erin Allmann Updyke	Yeah.
Erin Welsh	Is that the word, ancientness?
Erin Allmann Updyke	For sure that's the word.
Erin Welsh	Okay good. Well here there are a couple of cool findings. Have you ever heard of the Tyrolean Iceman?
Erin Allmann Updyke	Erin, no. I haven't. (laughs)
Erin Welsh	Okay yeah, I didn't either. (laughs) He was found in 1991 in the Italian alps and was estimated to be about 5300 years old.
Erin Allmann Updyke	Okay.
Erin Welsh	He had brown eyes, type O blood, lactose intolerance, and an increased risk for coronary heart disease and probably died a violent death judging from the arrowhead that was lodged into his shoulder.
Erin Allmann Updyke	Okay.
Erin Welsh	Oh and also he probably had Lyme borreliosis.

Erin Allmann Updyke	Oh and also.
Erin Welsh	And also. The researchers who analyzed his genome for all of those traits that I just listed also looked for bacteria and they found evidence for infection with Borrelia Burgdorferi.
Erin Allmann Updyke	What?
Erin Welsh	5300 years before the cluster of juvenile rheumatoid arthritis cases in Lyme, Connecticut.
Erin Allmann Updyke	Wow.
Erin Welsh	Okay.
Erin Allmann Updyke	That's very cool.
Erin Welsh	That's very cool.
Erin Allmann Updyke	We haven't had like an ice mummy or anything in a while on this show so it's very exciting.
Erin Welsh	I know, back to our roots, yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	Okay, what else? Researchers have also tested museum specimens of mice and ticks for evidence of Borrelia infection and in Germany an Ixodes ricinus tick from 1884 tested positive for Borrelia and several Ixodes scapularis ticks from Long Island, New York collected in the 1940s were also found to carry the bacterium.
Erin Allmann Updyke	Cool.
Erin Welsh	A couple of white-footed mice from Massachusetts that died or were collected in 1894 also tested positive for Borrelia.
Erin Allmann Updyke	In Massachusetts, okay.
Erin Welsh	Okay so my goal for this chapter of the story, the pathogen chapter, was to show you that these bacterial species have been around and widespread, multiple continents, for millennia and so are likely to have caused disease in humans throughout that time. But like I said the story of Borrelia and the story of Lyme borreliosis are two separate chapters in the same story. So when did humans first recognize borreliosis as a disease?
Erin Allmann Updyke	Yeah.
Erin Welsh	Spoiler alert: it wasn't in Lyme, Connecticut in the 1970s.
Erin Allmann Updyke	Ooh.
Erin Welsh	It wasn't in the 1900s at all.

Erin Allmann Updyke	Ooh!
Erin Welsh	Or in North America.
Erin Allmann Updyke	What?
Erin Welsh	Yeah.
Erin Allmann Updyke	Okay, keep going.
Erin Welsh	Okay. Chapter Two: The Disease. The story of Lyme starts in Lyme, Connecticut in the U.S. in the 1970s, right?
Erin Allmann Updyke	No, you just said it doesn't. (laughs)
Erin Welsh	Correct. That was my leading question. Glad you're paying attention. But that's the story that I'm guessing most people in North America are more familiar with. But it's really only part of the story and it's definitely not the beginning. The disease that we know as Lyme disease was actually first described 92 years before it was given that name.
Erin Allmann Updyke	Whoa so that's the 1800s.
Erin Welsh	Yes.
Erin Allmann Updyke	Way to go, math.
Erin Welsh	In the late 1800s a German physician noticed that several people were presenting with a chronic skin disorder and he named it acrodermatitis chronica atrophicans.
Erin Allmann Updyke	Yeah! We talked about that.
Erin Welsh	We did. And his description didn't fade into obscurity. Throughout Europe, physicians were finding people that had this rash and by the early 1910s it was proposed that this rash was caused by a tick bite.
Erin Allmann Updyke	Wow.
Erin Welsh	It just goes way back, yeah.
Erin Allmann Updyke	That's amazing.
Erin Welsh	Yeah. Okay so the rash might be a pretty easy one to spot and then associate with a tick bite but what about the neurological or arthritic symptoms? Those were also described long before Lyme disease had been coined as a name.
Erin Allmann Updyke	Wow.

Erin Welsh	In 1922 two French neurologists published a case study of someone with borrelial infection of the central nervous system and the link between the rash and the neurological symptoms was made in 1930, again by a German doctor. Right after WWII when antibiotics started to be widely used a Swedish doctor named Arvid Afzelius which sounds like a name from Harry Potter, right?
Erin Allmann Updyke	It does, yeah.
Erin Welsh	And also is yeah, as I could see your little light bulb turned on, is where the causative agent of Lyme borreliosis in Northern Europe got its name, Borrelia afzelii. So Afzelius treated dozens of his patients that had the characteristic rash and followed up with them for two years and found that 70% had fully recovered.
Erin Allmann Updyke	Once he treated them with antibiotics?
Erin Welsh	Yeah with penicillin.
Erin Allmann Updyke	Fabulous.
Erin Welsh	Over the next few decades leading up to the discovery of the cluster of cases in Lyme, Connecticut researchers and physicians, most of them European, continued to work on getting the full picture of this disease. They had described its chronic rash and linked it to persistent neurological symptoms, they had concluded it was infectious, mostly likely bacterial because of how it responded to antibiotics and they thought it was most likely tick-borne. So the only thing missing was the bacterial agent itself. So this all had been done almost 100 years before-
Erin Allmann Updyke	That's amazing.
Erin Welsh	Yeah, yeah. Okay so let's head to Lyme, Connecticut in the 1970s. In the small affluent town of about 2000 people, neighbors began to talk. Something strange was happening to the kids of Lyme. Several had been diagnosed with something called juvenile rheumatoid - I cannot say that quickly - juvenile rheumatoid arthritis. It's like a tongue twister.
Erin Allmann Updyke	(laughs) It feels like me trying to say Giardia, just saying.
Erin Welsh	Yeah. (laughs) There we go. Oh how the turntables...
Erin Allmann Updyke	Yes.
Erin Welsh	So juvenile rheumatoid arthritis is an autoimmune condition where your joints become damaged and inflamed when your white blood cells attack the healthy tissues there. And so as with a lot of other autoimmune diseases it's not super clear on what causes the self-attack. It's a painful condition but it had been well described for quite a while. So what was strange about these particular cases in Lyme? And simply it was the number of them. Only about 1 in 50,000 or 1 in 75,000 children are diagnosed with JRA so when there were several in a town of 2000 it threw up some red flags. Researchers at Yale were notified of these cases and they concluded that there was a statistical cluster in Lyme and that there was probably something going on in the town to have caused this sudden rise in juvenile rheumatoid arthritis. Could it be an environmental contaminant? Outbreak of some food-borne illness?
Erin Allmann Updyke	Perhaps.

Erin Welsh	Or a new infectious disease?
Erin Allmann Updyke	Ooh.
Erin Welsh	The first two were pretty quickly ruled out and so that left infectious agent. It was time to talk to the patients to see if there was anything else linking them. It turned out that these kids all had a skin rash just a couple of weeks before developing the joint pain and arthritis so they suspected the two were linked. The researchers began tracking new people who came in with similar skin rashes and found that several later also developed joint pain. At the same time other researchers were doing some deep dives into old literature where they found some articles from the late 1800s describing the same thing.
Erin Allmann Updyke	Ooh.
Erin Welsh	The link between this disease that had been previously described in Europe and this new disease wasn't solid by their eyes and so researchers gave this new one a new name, Lyme disease, to indicate where it was found even though shortly after that first Lyme cluster was investigated a bunch more kids all over New England were found to have this condition. By the late 1970s the Yale researchers had put together a pretty compelling case that this disease was caused by a bacterium transmitted by a tick bite.
Erin Allmann Updyke	Wow.
Erin Welsh	The only thing missing were the two smoking guns which were the bacterium and the tick. But they didn't have long to wait because at the same time - this is a lot of things happening all at the same time - the same time that these researchers were tracking their cases, other researchers were looking at ticks around that same area but for different reasons. They had been looking for the tick species that transmits Rickettsia rickettsii, the causative agent of Rocky Mountain spotted fever. But they had much more success finding a different tick, Ixodes scapularis, in the New England area. They thought maybe this also carried the Rickettsia responsible for Rocky Mountain spotted fever and so they sent them to Willy Burgdorfer's lab for testing.
Erin Allmann Updyke	Willy Burgdorfer!
Erin Welsh	There we go. Willy didn't find Rickettsia rickettsii but he did find another type of bacterium called a spirochete. And this wasn't like one or two ticks with the bacterium, this was an infection prevalence of about 60%.
Erin Allmann Updyke	Wow!
Erin Welsh	Very high. So maybe, he thought, that this could be the Lyme bacterium. So his lab cultured it, they tested it on lab animals, and they found that it caused a Lyme-like disease. And they named it Borrelia burgdorferi to honor the key discoverer.
Erin Allmann Updyke	Willy.

Erin Welsh	Willy. So now that the causative agent and arthropod vector had been identified, work could start on the medical side of things using antibiotics to treat the disease and also on the ecological side things, understanding what animals and habitats led to the transmission of the disease so that people could actually try to start controlling or preventing its spread. This also meant that researchers could test for it in tick and human and animal samples which is when they finally concluded that what they had on their hands was not a new disease at all, not even a newly described one strictly speaking because there was a match between the North American and European cases. The Borrelias were found all over. So what was happening? Were we witnessing the emergence of a brand new disease on two continents simultaneously? The answer is yes and no.
Erin Allmann Updyke	Oh.
Erin Welsh	Lyme disease definitely fits the definition of an emerging disease because it's something that is increasing rapidly in a period of time in new geographic areas and increasing in prevalence. But as we know this certainly was not a new pathogen or a new disease. So what led to the sudden uptick in cases? 'Uptick', I didn't even realize, 'uptick'.
Erin Allmann Updyke	Oh that's a good one. (laughs)
Erin Welsh	And would it ever stop? So to answer these questions let's talk ecology.
Erin Allmann Updyke	Yes!
Erin Welsh	Here we go.
Erin Allmann Updyke	That was really a beautiful intro just to be able to talk about the ecology of Lyme.
Erin Welsh	Why thank you, thank you so much.
Erin Allmann Updyke	Yes, it's very nicely done.
Erin Welsh	Okay. Chapter Three: Ecology. I might be biased but I feel that as a field disease ecology owes a lot to Lyme disease because in many ways the ecological complexity of that disease system made researchers look at it not just from the perspective of an entomologist studying tick biology or an epidemiologist studying exposure patterns or a microbiologist studying Borrelia burgdorferi strain diversity.
Erin Allmann Updyke	Yeah.
Erin Welsh	They had to look at it from all of those perspectives, tossing in species interactions and the impact of environmental variables and many other things just to get a glimpse into how infection happened.
Erin Allmann Updyke	Yeah, I agree.
Erin Welsh	But even though the Lyme disease system is complicated and a lot of different factors are at work, that doesn't mean that it's impossible to understand. So let's work our way upward. I wanna start with the system itself, introducing the pathogen, tick, and hosts and then talk about the timing of Lyme disease emergence, so why it started popping up when it did.

Erin Allmann Updyke	Awesome.
Erin Welsh	Okay. So for Lyme disease we have three players to consider. The tick, the pathogen, and the host. Let's start with the tick. Ticks are obligate ectoparasites which basically just means that they need hosts to survive and they live on the outside of their hosts, spending most of their lives in the environment. A tick starts its life as a little egg waiting patiently in the environment until conditions are just right for it to hatch into a larva and start looking for an animal to feed on. Borrelia isn't transmitted from a mother tick to her offspring, so all of these larval ticks are free from Borrelia infection.
Erin Allmann Updyke	Yeah.
Erin Welsh	If you are bitten by a larval tick it is extraordinarily unlikely that you will get Lyme borreliosis from it.
Erin Allmann Updyke	That's important.
Erin Welsh	There are other things you can get of course like Rocky Mountain spotted fever but we won't go into that on this episode.
Erin Allmann Updyke	That's a different episode.
Erin Welsh	Yes. So anyway this larva is an innocent, well most likely an innocent uninfected little parasite.
Erin Allmann Updyke	It's still sucking your blood but you know.
Erin Welsh	It's still sucking your blood but you know it needs you to survive.
Erin Allmann Updyke	Yeah. Poor guy.
Erin Welsh	Well yeah. So this little larva, all it's looking for is a host. Let's say that that host that it finds is a white-footed mouse if we're in the U.S. or a bank vole if we're in Finland for instance. Both of these animals are notoriously good at being infected with Borrelia so if that larva has a nice, juicy meal on one of those guys, it's going to fall off completely sated and utterly infected with Borrelia. Ticks only feed one time during each of their life stages so that little engorged larva is going to just chill out in the environment until it molts into the next stage which is called a nymph.
	Now this nymph is the one you're gonna wanna watch out for. Lyme disease researchers often use the density of infected nymphs, so like how many nymphs on average are infected in a certain area like 100 square meters as a measure of disease risk. And that's because nymphs can be infected, unlike larvae, are more numerous in the environment compared to adults, and are more likely to bite humans. We'll post a picture but also do yourself a favor and look up the size differences of larva, nymph, and adult.
Erin Allmann Updyke	Yeah.
Erin Welsh	Just to inform yourself. Larvae have six legs, nymphs and adults have eight legs.
Erin Allmann Updyke	Yeah. The larvae of Ixodes scapularis are so tiny I feel like you won't even see them, period.

Erin Welsh	They're super tiny.
Erin Allmann Updyke	They're so small.
Erin Welsh	They're very difficult when you're drag sampling.
Erin Allmann Updyke	Yeah.
Erin Welsh	Like, my eyes. Okay.
Erin Allmann Updyke	Okay. So continue.
Erin Welsh	Anyway. So it's usually one of these nymphs then, one of these little creeps that responsible for making you sick. If that infected nymph bites say another mouse or a bank vole rather than a human it will pass on the Borrelia while it's feeding, leading to another infected rodent or host and another full and happy tick which is still infected, it doesn't lose the infection over its life. That nymph again chills in the environment, eventually molting into a male or adult female tick. These adult ticks tend to be a bit pickier in their tastes, choosing larger hosts like deer over rodents or humans although that still does occasionally happen. Once on this larger host a love story ensues. The male and female lock eyes over their shared blood meal, gazing at each other through the strands of tawny deer fur until they're both full and they can have their moment.
Erin Allmann Updyke	(laughs) Oh dear.
Erin Welsh	Yeah. Oh deer! (laughs)
Erin Allmann Updyke	I can't.
Erin Welsh	I know, I'm sorry.
Erin Allmann Updyke	Don't be sorry, I love it.
Erin Welsh	I'm the dorkiest. Okay good. After their moment they drop off the host, the female lays eggs and then dies and the cycle starts anew. Pretty simple. Eggs hatch into larvae, larvae feed on a host and turn into nymphs, nymphs feed on a host and turn into adults, adults feed on a host, mate, lay eggs, and die. Boom.
Erin Allmann Updyke	Rapid fire.
Erin Welsh	Yeah, there you go. There is nothing new about the way that ticks carry out this life cycle. They have been doing it for millennia. Nor is there anything new about the bacteria themselves, as we've learned, they're ancient. So that begs the question why now? What has been happening in the past 50 years to lead to the emergence of what is now the most common tick-borne disease in the northern hemisphere? The answer does not lie in conspiracy theories but bioweapons. Surprise, surprise. It's simply in the ecology of the system and to me it's much more interesting, not to mention actually based on facts, than a wild America-centric story created to sell books and headlines.
Erin Allmann Updyke	Yeah.

Erin Welsh	In the interest of not overgeneralizing, I'm going to concentrate on the North American emergence of the pathogen which does have some parallels to what happened in Europe. Okay so before Columbus came over and started the devastation of the people and land of North America, the Lyme bacterium probably existed in the same cycle that it does today. The many large forests allowed for higher populations of hosts like deer and mice that could support the ticks and the pathogens, then after colonization the woods turned into a resource which was used almost to the point of exhaustion. Deer and other large mammals, the hosts that are great for producing more ticks, were hunted until their numbers dwindled and tick populations probably also dropped a bit. Patches of forest with deer and ticks remained in places such as Long Island and some islands off Massachusetts where Borrelia probably also hid out.
	The mid 20th century saw a big reversal of fortune for deer and forests. Large areas were reforested and deer populations were being reintroduced everywhere. At the same time, the human population was growing and they had to have somewhere to live. This led to the suburbs, neighborhoods being built right next to or in place of forests. The barrier between humans and deer or just humans and other wildlife species shrank as this suburban spread continued. With all of these deer, the ticks now had ample hosts to feed on which meant that the chances of a human encountering a tick was much more likely. These things set the stage for the seemingly sudden reappearance of Lyme disease even though we know it's been around a lot longer.
	But it's not a simple equation of more deer equals more Lyme disease, so don't go blaming the deer. It's probably more of a threshold thing. An area might need just a few deer to keep tick populations plentiful. And notice that I'm also just talking about deer and ticks, not deer and Borrelia and that's because there's a key element to the Lyme disease system that makes it a whole lot more complex than just more hosts equals more disease. Because not all hosts, #notallhosts - I won't do that, no.
Erin Allmann Updyke	(laughs) Please do that. #notallhosts. I love it.
Erin Welsh	Are equally good at being infected with Borrelia. In disease ecology terms we would say that hosts vary in their reservoir competence. Deer, not so good. White-footed mice and bank voles? Fantastic.
Erin Allmann Updyke	Excellent.
Erin Welsh	Western fence lizards? Terrible.
Erin Allmann Updyke	Worst.
Erin Welsh	Opossums? Terrible.
Erin Allmann Updyke	Horrible.
Erin Welsh	Eastern chipmunks? Great.
Erin Allmann Updyke	Beautiful.
Erin Welsh	So there's a lot of variation depending on the host species and it's a spectrum.
Erin Allmann Updyke	Yeah. Those terms by the way were beautiful at being a host for Borrelia aka horrible for humans.

Erin Welsh	Right. So western fence lizards being terrible at being reservoirs.
Erin Allmann Updyke	Yes.
Erin Welsh	So remember that a larval tick turns into an infected nymph by feeding on an infected host. If the host that that larva feeds on is a good reservoir like a white-footed mouse, meaning that that mouse is probably chock full of Borrelia, the tick will probably become infected because chances are that host is infected. But if the host of choice is a poor reservoir like a western fence lizard, that lizard is probably uninfected and so the tick probably won't become infected. So it's not just about the number of hosts that are present in an area, it's about which hosts are present and in what proportions.
Erin Allmann Updyke	Yeah. This is just so exciting.
Erin Welsh	Ecology is beautiful, yeah.
Erin Allmann Updyke	We haven't done such like a deep ecology episode before and this is just really exciting.
Erin Welsh	It's really exciting and also I think so crucial in understanding the patterns of Lyme disease and how it works.
Erin Allmann Updyke	Right. It totally is, yeah.
Erin Welsh	And there's just so many pieces to this puzzle, it's fascinating.
Erin Allmann Updyke	Yeah, yeah.
Erin Welsh	So as a general rule the newly forested regions and the forest fragments created by suburbs and development in general, they tend to be species poor and the species that are there are predictable. Guess what? They're often great reservoirs meaning highly infected like the white-footed mice, or important for tick populations like white-tailed deer. White-tailed deer are great at living in urban or suburban areas.
Erin Allmann Updyke	Yeah, they're very well adapted to the destruction that we've caused.
Erin Welsh	Yeah, yeah. And in these areas the ticks are much more likely to feed on a host that is a good reservoir and the prevalence of Borrelia will likely climb and climb and the density of infected nymphs will be high. These areas are often the closest to humans where people live or picnic or garden or simply go for a walk. In larger, more undisturbed areas with higher biodiversity there are more species there and a larval tick has many different hosts to choose from and some of these hosts are going to be less likely to be infected. In these more intact biodiverse forests, the density of infected nymphs is likely lower than in those forest fragments. So this idea, the idea that higher biodiversity reduces disease spread is called the dilution effect. The dilution effect is definitely a controversial or at least contentious issue in disease ecology.
Erin Allmann Updyke	Oh my god, yeah.

Erin Welsh	Yeah. There is this ongoing debate about whether biodiversity leads to lower disease, so the dilution effect, or increased disease in humans called the amplification effect. And the unexciting answer I would say to what is actually happening is that both can happen, it just depends, it's ecology.
Erin Allmann Updyke	Yeah.
Erin Welsh	It depends on the disease system, the location, the scale, the time frame, so many things. But in the case of Lyme disease there are many studies that show that the dilution effect is likely what's happening in eastern North America. So in those forest fragments when you have low biodiversity, the hosts that tend to be there, the hosts that the ticks are feeding on are likely infected and great at being infected and that causes a higher disease risk for humans.
Erin Allmann Updyke	Right.
Erin Welsh	One more reason for people to care about biodiversity and stopping habitat loss.
Erin Allmann Updyke	Yeah.
Erin Welsh	Okay so now that you know what a beautifully complex ecology that Lyme disease has, let's talk about the bioweapon conspiracy theory that's been in the news lately.
Erin Allmann Updyke	Oh I just love it.
Erin Welsh	Well hopefully now that I've talked about the history and the ecology you'll agree that this conspiracy makes no sense and has no basis in fact. I've heard different and read different variations of this conspiracy but the basic story is that in an attempt to make bioweapons the U.S. government either cooked up Borrelia burgdorferi and purposely infected ticks with it and released those ticks or just infected and released ticks with Borrelia burgdorferi. This seemingly sudden emergence and spread of Lyme disease over the past 50 years in North America is because of this bioweapon experiment gone wrong according to the conspiracy theory. Okay so this idea doesn't make sense for a number of reasons. Here are just a few. Number one, ticks would make terrible bioweapons.
Erin Allmann Updyke	Yeah.
Erin Welsh	They're high maintenance!
Erin Allmann Updyke	That's the thing that really, really grinds my gears is like if you're gonna make a bioweapon-
Erin Welsh	You wouldn't want it to be a vector.
Erin Allmann Updyke	Absolutely not.
Erin Welsh	No.
Erin Allmann Updyke	Absolutely not. Especially not Borrelia in ticks which have to be attached for at least 24-36 hours to even cause infection.
Erin Welsh	Yep, yep.

Erin Allmann Updyke	Oh gosh.
Erin Welsh	Also ticks are high maintenance, they need a lot of things like right environmental conditions, the appropriate hosts in high enough densities, and then they would still have to bite someone.
Erin Allmann Updyke	Yeah.
Erin Welsh	It doesn't make any sense.
Erin Allmann Updyke	No.
Erin Welsh	Okay, moving on. Number two, Lyme disease isn't fatal. Bioweapons programs tend to focus on the diseases that will actually kill you and are not curable, so what would the purpose be of releasing a disease that is fully treatable with antibiotics?
Erin Allmann Updyke	And has a very, very, very, very low fatality rate even when untreated, though it has chronic symptoms for sure if it's untreated.
Erin Welsh	Yes, right.
Erin Allmann Updyke	It's very low fatality rate.
Erin Welsh	That's often not causing chronic symptoms in a population who are unlucky enough to get bitten by a tick is not often the goal of bioweapons programs. Number three, Lyme disease certainly wasn't cooked up in a lab.
Erin Allmann Updyke	Yeah.
Erin Welsh	It's been around for millennia as we know. A lot of the bioweapon conspiracy theories lean heavily on the sudden emergence of the cluster of cases in Lyme, Connecticut. But how many of them talk about the person in 1970 in central Wisconsin that was described as having erythema migrans after a tick bite he got while grouse hunting?
Erin Allmann Updyke	Ooh.
Erin Welsh	The doctor who treated him guessed that it was caused by a spirochete bacterium so he treated it with penicillin.
Erin Allmann Updyke	Okay wait, that's awesome.
Erin Welsh	Right?
Erin Allmann Updyke	Yeah.
Erin Welsh	Right.
Erin Allmann Updyke	That guy doesn't get enough cred.
Erin Welsh	I know. And how many of these conspiracy books or articles mention the presence of Lyme disease in Europe? Where it was described and treated long before the Lyme cluster.

Erin Allmann Updyke	Our hands are up in the air, you guys.
Erin Welsh	They're up in the air. Yeah. Even if ticks were purposely infected and released it wouldn't be enough to explain the sudden global increase in the disease. This is a very American-centric conspiracy theory that has no support from Lyme borreliosis researchers, no support whatsoever. My personal conspiracy theory about this conspiracy theory is that the people who are promoting it are not willing to accept the role that humans have played in the wide scale environmental change including climate change that has set the stage for Lyme borreliosis emergence.
Erin Allmann Updyke	Which is so funny, like let's blame just this small group of people instead of all of humanity.
Erin Welsh	Yeah. It's kind of classic.
Erin Allmann Updyke	Yeah, totally.
Erin Welsh	Okay. So anyway the answer to any ecological question about Lyme disease could start with 'it depends'. How will climate change impact the spread of Lyme disease? It depends. It depends on the scale of your question, neighborhood, county, state, country. It depends on what climate change projections you're looking at, depends on the animals in a region. What we do know is that it will change as the climate changes. And there are so many different aspects of the Lyme disease system that need to be examined before we can understand enough about what's going on in a region to make any predictions. The biology of the pathogen and the tick, the environmental conditions affecting tick survival, the types of host species that are there, the human behavior leading to exposure, all of these things interact.
	And this complexity I think has contributed a lot to the controversies surrounding the disease as well as the frustrations of people who feel as if they're being lied to or at the very least ignored. I talked in this section about the history of the pathogen and the history of Lyme disease but I'd didn't really touch on how Lyme disease has been perceived in the medical community since being discovered which is a big part of its history and I think it's something that's really important to talk about. Because Lyme disease is a very controversial issue and it's important to examine why that controversy exists. When a new disease shows up it can take a while before anyone recognizes it as something new and then even longer before there's a treatment for it. And if you've listened to this podcast before, that probably sounds really familiar.
Erin Allmann Updyke	Yeah.
Erin Welsh	In Lyme that journey towards pathogen discovery was relatively quick after the cluster of juvenile rheumatoid arthritis cases in Lyme, Connecticut was identified. But then figuring out how to describe Lyme disease as an infection took a little bit longer because of the wide variety of symptoms it can cause. And then figuring out what might be happening long after the Borrelia are gone and no longer causing an active infection was even trickier and people are still trying to puzzle that out.
Erin Allmann Updyke	Yeah, definitely.

Erin Welsh	In the beginning even recognizing that there could be autoimmune symptoms triggered by Borrelia took time. Back in the mid 1990s the Infectious Disease Society of America did not do a great job of acknowledging people who were suffering and seeking help and some people on the receiving end of that didn't respond well either, making death threats or verbally attacking researchers. It really happened, yeah.
Erin Allmann Updyke	Just chaos.
Erin Welsh	And this clash, this chaos kind of set the tone for what is unfortunately still a big part of the Lyme disease conversation today. Since then we have come a long way in what we know about how the disease works. And Erin, I think you did a really good job talking about long term antibiotic use and how it won't actually help someone who does not have an active Borrelia infection and how it can actually hurt them. And I feel like a lot of this controversy is because the terminology that we use and the science that we have based it on is still being developed. We know so much more now than we did 20 or even 10 years ago but it takes time for that information and in particular that terminology and the science behind it to trickle down to physicians and also to people who aren't in any medical field whatsoever.
Erin Allmann Updyke	Yeah.
Erin Welsh	And in a way it's not that surprising then that Lyme disease would have led to such controversy because you really need a huge foundation of knowledge to understand the ecology of the system as well as the biology of the pathogen which is something we're still grappling with. It's an incredibly complex disease and even though we know a lot, there's still a lot that we don't know. And this lack of knowledge is a really common theme in a lot of chronic or autoimmune diseases that don't have a very clear pathology or a treatment that we figured out yet, especially those with subjective symptoms that we can't quantify well. The more mysterious a disease is the more we don't understand it, the more gray areas that end up surrounding it.
	And that's especially the case when we're dealing with as I mentioned these nonspecific subjective symptoms of disease. In our last episode on cystic fibrosis I talked a bit about language and disease and how it's so hard to know what someone means when they say they're tired or when they're in pain or when their brain is foggy because those are things that might feel different to each person.
Erin Allmann Updyke	Right.
Erin Welsh	And so I think that can make them be more easily dismissed.
Erin Allmann Updyke	Definitely.
Erin Welsh	But at the same time you know yourself and your baseline in a way that no one else can which means you would probably know when things are beyond normal. And so then being told, 'No, this is normal, this is just normal wear and tear,' that must be incredibly frustrating.
Erin Allmann Updyke	Yeah.
Erin Welsh	When you go to a physician because you have something wrong with you but you don't know what that is, I feel like you have two basic expectations. One, the doctor will be able to tell you what's wrong with you, and two they will be able to help you get better or at least try. And I think these are reasonable expectations because over our lives we go to the doctor and we get treated. This is sort of the situation that we have experienced all of our lives.

Erin Allmann Updyke	Right, that's the norm.
Erin Welsh	Yeah, that's what we expect and that has made us have trust and confidence in our physicians and the medical establishment as a whole. So then when you're told, 'We don't know what's wrong with you' or 'You've been treated so your symptoms should've gone away' or 'We can't find anything wrong with you' it's no wonder that it feels like you're being dismissed or outright ignored. Not having a diagnosis sucks because that feels hopeless.
Erin Allmann Updyke	Yeah, it really does. And I can only imagine how frustrating that must be for physicians as well because there is so little you can do for your patients if you can't figure out what's wrong, right?
Erin Welsh	Right.
Erin Allmann Updyke	And that's often what happens in a lot of these chronic illnesses, not only in Lyme disease. And I think that part of the problem has become that in some cases a diagnosis of Lyme disease has been made based on exclusion. And Lyme disease is not and should not be a diagnosis of exclusion, it shouldn't be that just because we can't figure out what else is going on to cause your symptoms that we then call it Lyme disease. That's what a diagnosis of exclusion is, 'Well we've tested for everything that we can think of and we can't find what's going on, so you have Lyme disease.' That's not accurate for Lyme because contrary to some of the information on the internet, we actually can diagnose Lyme.
	So by diagnosing somebody with Lyme disease based on these exclusion criteria alone without laboratory confirmation, it can actually make it a lot harder for people who have had confirmed diagnoses of Lyme and who are still suffering from these post-treatment symptoms, cause I think it conflates these groups and makes it really hard for us to even study from a scientific perspective what's going on so that we can develop better treatments.
Erin Welsh	Yeah, that's a really good point. Yeah the whole thing is a very complex disease and as such it has led to really complex issues.
Erin Allmann Updyke	Big time.
Erin Welsh	But what we need to talk about next Erin, I think, is the scope of this.
Erin Allmann Updyke	Yeah. Okay.
Erin Welsh	What is actually going on in the world of Lyme both in terms of epidemiology and also some maybe medical advancements. Maybe what's some cool, cutting edge ecological research?
Erin Allmann Updyke	Ooh, let's find out. But maybe we need a breather first.
Erin Welsh	I think so, let's take a breather.
Erin Allmann Updyke	I think so too.
TPWKY	(transition theme)
Erin Allmann Updyke	So let's talk about the epidemiology of Lyme borreliosis. In the U.S. in 2017 there were 42,000 cases reported.

Erin Welsh	Wow.
Erin Allmann Updyke	That's a lot more than I expected and it's estimated that the actual number is probably closer to 300,000.
Erin Welsh	Yeah I've seen that number widely quoted.
Erin Allmann Updyke	Yeah.
Erin Welsh	It's a big number.
Erin Allmann Updyke	It's a huge number. And Lyme is a reportable disease, so those 42,000 cases that were reported, those are all the people who were basically treated for Lyme disease essentially.
Erin Welsh	Right.
Erin Allmann Updyke	So it's estimated that there's a lot more people who never get seen and therefore never get reported or treated.
Erin Welsh	Okay. Do we know what proportion of people can clear the infection without being treated?
Erin Allmann Updyke	Good question. No idea. No clue. But I mean based on if we're estimating that 300,000 cases are happening every year and only 42,000 people are getting treatment, I would say it's probably pretty high.
Erin Welsh	Right.
Erin Allmann Updyke	Right, I would guess that for a large proportion of people it's a relatively self-limiting disease.
Erin Welsh	Okay.
Erin Allmann Updyke	But that's a guess. Don't quote me on it please. In Europe there's not great aggregate data in general. So you can go country by country but that's a lot to do. So in a paper from 2016 they estimated that there was probably around 235,000 cases annually across Western Europe.
Erin Welsh	Wow.
Erin Allmann Updyke	Yeah, that seems low compared to the estimates for the numbers in the U.S. but I don't know. In the UK there's an estimated 3000 cases annually.
Erin Welsh	Okay.
Erin Allmann Updyke	And then in places like Germany, Austria, and Sweden the numbers are quite a bit higher than 3000 though I don't have the exact numbers.
Erin Welsh	I noticed you left out Finland.
Erin Allmann Updyke	I did, I didn't find good numbers on Finland.

Erin Welsh	What? There's plenty of good numbers.
Erin Allmann Updyke	Google it, Erin. This is my favorite because...okay listen. In Canada Lyme is the most prevalent tick-borne disease, most prevalent vector-borne disease right, in Canada. Guess how many cases there were in 2015 in Canada, that huge amount of country?
Erin Welsh	Okay if there were 300,000 in the U.S. let's say 50,000.
Erin Allmann Updyke	917. (laughs)
Erin Welsh	What?
Erin Allmann Updyke	There were 917 cases reported in Canada in 2015. However that is a crap ton more than in 2009 when only 144 cases were reported in all of Canada.
Erin Welsh	Wow.
Erin Allmann Updyke	Isn't that fascinating?
Erin Welsh	And so that increase is a factor of both the tick vector spreading northwards because of climate change and also diagnostic and people reading articles and saying, 'I'm gonna go get treated or go talk to a doctor.'
Erin Allmann Updyke	Yeah. So first let me say that the disease has been reported in other places as well. It's in Japan and Korea and it's well established in China but we don't have numbers for those areas. But overall there's across the globe hundreds of thousands of cases and the vast majority go undiagnosed. Okay. But like you said the geographic distribution and the overall case numbers are going up so what is it that's driving these increases in prevalence? Probably diagnostics is a huge part of it, we're getting better at recognizing and diagnosing Lyme disease than we were 20 years ago, especially in realizing that it is spreading geographically, that means that people are looking for it in wider areas than they would have been before. So somewhere in the Midwest 20 years ago people might have been like, 'No, no, there is no Lyme disease here, it's only on the East coast.'
Erin Welsh	Right.
Erin Allmann Updyke	But now we know it's actually much more widespread than that.
Erin Welsh	I remember seeing at a conference a few years ago a map of state by state prevalence of Lyme and Kentucky was 0. And I was like oh that's weird, it's surrounded by Tennessee which has a bunch, it's surrounded by Indiana, by Ohio, by Virginia or West Virginia, all these places that were prevalent with Lyme disease. And I asked the presenter, I was like why is Kentucky like a hole there? Why is there no Lyme in Kentucky? And he was like, 'Oh no one's looked there. They're probably all over there.' And I'm like oh, okay.
Erin Allmann Updyke	Yeah. (laughs) Just no one has looked yet, yeah.
Erin Welsh	No one has looked in the ticks for Borrelia, yeah. I'm sure they have now.

Erin Allmann Updyke	There's also the issue of if somebody is diagnosed with Lyme, let's say in Florida, did they actually get infected with Lyme in Florida or did they get infected when they were on vacation somewhere else? And so where do you report that as being a case, in Florida or where they got it?
Erin Welsh	Right.
Erin Allmann Updyke	So it does get really complicated when we're looking at especially geographic reports of the disease. But that's one reason that we're probably seeing increases is just getting better at recognizing it. But the tick is spreading and the disease is also spreading. So the real question is why is it that we are seeing this increase in spread not only in the U.S. but across the globe? And I'm not gonna answer that question for you because we have with us today someone with a lot more knowledge on the subject who can tell us about the ways that we interact with our environment and the effect that ecology, climate change, etc, forest fragmentation, urbanization, all of these awesome big picture questions, what do they have to do with the increase in Lyme disease. So let's ask our favorite-
Erin Welsh	Our favorite advisor in the whole world, Dr. Brian Allan.
Erin Allmann Updyke	Take it away.
Brian Allan	Lyme disease is amazing because it's received a huge amount of attention from ecologists and epidemiologists, it's arguably the most prevalent vector-borne disease in North America, the economic and health impacts are enormous. And so despite the amount of attention it's received, we're still making new discoveries in the ecology of Lyme disease and so it's been really a productive system from a biological standpoint. What it has told us about the role of infectious agents in ecological communities and the way humans can disrupt ecological communities and influence their risk of exposure to a tick-borne disease, Lyme disease has been just really illuminating.
	There is this intersection between the applied and basic research when it comes to Lyme disease because it's this human health problem and so I think one of the big areas going forward it going to be just understanding why does Lyme disease continue to grow both in incidence and the number of people who are reported getting Lyme disease every year but also the spatial distribution is expanding as well. And so the tick is spreading, the pathogen is spreading. That is biologically an interesting problem because we don't fully understand mechanistically how that's happening, so we don't think that these ticks are capable of any kind of significant dispersal on their own nor does the pathogen, right, the pathogen is either residing in the tick or it's residing in one of the animal hosts, one of the vertebrate hosts.
	So it must be some movements of wildlife facilitated by humans or influenced by humans that's allowing the tick and the pathogen to spread to new areas. And so the frontiers I think will include how does climate change influence the spread of tick and pathogen but also how do humans modify their landscapes in ways that can affect the distribution of a Lyme disease system as well. Another really interesting aspect of this is that Lyme disease was really the big tick-borne disease on our radar initially because it was causing so many cased but through the study of the biology or ecology of Lyme disease, we've discovered that there are a number of other pathogens that are transmitted by this particular species of tick, the black-legged tick.

It also shined the spotlight that there are other ticks In North America and other diseases associated with them as well. So there's probably at least 15 tick-borne diseases that occur in North America that are associated with several different tick species. And they're all biologically somewhat different from each other and so how much does what we know about the biology of Lyme disease, which we understand really well at this point, how much does that apply to these other tick-borne agents vs how much are these all idiosyncratic. And similar levels of effort need to be put into studying each of these tick-borne diseases to understand their biology and their control.

Erin Welsh

So what do you think is going on in terms of the spread of the ticks and the pathogens? How are these ticks and pathogens getting from point A to point B? And how is that different depending on where you're looking? I mean if you look at North America in the northeast that might be different than if you look in the west or if you look in Europe and other places. What do you think, are there any general rules here?

Brian Allan

So there's been a lot of research looking at what wildlife hosts might be involved in the dispersal of both the ticks and the pathogens and it creates a really interesting landscape that probably suggests there will be major differences among the tick-borne diseases in terms of how they spread through the landscape. So for example there's been impressive research on the role of migratory songbirds in the dispersal of ticks and pathogens and it's not I think something people typically think about when they think about songbird migrations that you have these birds flying overhead. And the typical tick burden per bird, by which I mean how many ticks are on each individual animal, is not that many. We've captured birds here in Illinois and one or two or maybe three ticks is the typical number of ticks per bird. But when you have millions of birds flying overhead, you actually have millions of ticks flying overhead as well.

And so you have the timing of the spring and the fall migrations and to what extent that aligns with the timing of the different stages in the ticks life cycle can determine which tick life stages are being dispersed and in which direction. And then some of those birds are also capable of transmitting the Lyme pathogen to ticks and others are not. And so under some scenarios you can have a tick being dispersed without the pathogen which that tick is then annoying or a nuisance but it's not much of a health risk vs ticks being dispersed with the pathogen. And then you can even have the scenario where you have infected animals dispersing the pathogen without the tick and then if they arrive some place where the ticks are established then they can be bitten and start the cycle there. And so you actually have a number of different pathways by which you can have the spread of either the tick or the pathogen, or the tick and the pathogen. So that's pretty cool.

Some of the work from the northeast indicates that Lyme disease is spreading faster than another tick-borne agent, the one that causes babesiosis in humans, and that's because of the wildlife hosts that are what we refer to as the reservoirs for the pathogens that cause those illnesses. And in the case of babesiosis it's mostly small mammals that don't disperse long distances and so babesiosis is spreading slowly whereas Lyme disease can be carried by wildlife that travel much further distances and so Lyme disease is spreading faster. The extent to which climate change as one from of human environmental change will impact these processes in part depends on the timing of when wildlife migrate, the timing of the tick life cycle. And so that's an area where there's a lot of active research going on trying to project into the future what can we expect for the distribution of tick-borne disease under environmental change.

Erin Welsh

So with all this information and research about invasion and how ticks and the pathogens spread into new areas, is there any ecological research being done on how to use this information to actually control the disease itself? Are there any interesting bits of research in that arena?

Brian Allan	There are but I would argue both are important. And so just knowing where these diseases are occurring is actually one of the most useful pieces of information we can provide because a surprising extent of the public health effort against tick-borne diseases like Lyme disease still depends on good biological information on where risk is high and where risk is low. And that helps physicians understand when a patient comes in describing symptoms that could potentially apply to a number of different illnesses, one of the chances that they might be looking at Lyme disease vs something else. And we still are really lacking for good distribution information, so that's actually been a big focus these last few years. A push from the CDC is to try to get better distribution maps for the ticks and the pathogens so that we can really keep the public health community updated on where these occur. But there are interventions and control measures that have been proposed. Their efficacy is also an ongoing area of study.
	So technology that was developed several decades ago but hasn't seen that widespread deployment is different types of - traps is not quite the right word but something that brings wildlife in to get a reward, like a feeding station and then they get a pesticide applied to them when they come in for the bait. And so there are versions of these for deer which treat deer against ticks, there are also versions that can be used for mice and some of the other small mammals that are these critical hosts for the Lyme pathogen. And so there are challenges in the deployment of those over large spatial scales but it's possible that in areas that are particularly high risk or where we're seeing a lot of human cases, those could be adequately deployed.
	Another controversy in the ecology of Lyme disease is how critical is deer population size and that has been a focus of Lyme disease research for a long time but it's a surprisingly tough question to answer. And so if you have high deer population density, will that always equate high Lyme disease risk? The data suggests not always. And so in the context of deer management this often comes up. And so some communities engage in deer management no necessarily just because of Lyme disease, it can be also because of vehicle collisions and other concerns. But Lyme disease particularly in areas where it's endemic is often proposed as a reason. And so another area where there's ongoing research is to address to what extent do these deer management programs also manage Lyme disease risk.
	So there are things communities can do. I think educating the public about the level of risk and then from what I've seen from the public health literature is that getting people to engage in preventative measures is still one of the most effective things the scientific community can do. And so if we can get people to take precautions at an individual level that probably will do more to reduce Lyme disease cases than just about any other strategy.
Erin Welsh	I have a question that I think you probably get asked all the time cause I have been asked it frequently. Why do ticks matter? Why can't we just kill them all? What would happen? I wanna hear your take on this.
Brian Allan	Yeah, this is also probably the most frequent question I receive and not just from the public, sometimes from other scientists as well. And so I usually have a couple responses I give to that question. First is that from nature's perspective there isn't good or bad, these are organisms that are occupying an open ecological niche and parasitism is one of the most common strategies in nature. There's many species on earth that have adopted a parasitic strategy because it works. And so nature doesn't think in terms of good or bad. We find ticks a nuisance and they make us sick so we have a very negative perception of ticks, understandably so.

	And from the perspective of ecosystems I've seen the argument made and I've seen some data that supports this that in the absence of predators, one can expect an increase in the abundance of parasites. And so there's actually a really interesting paper that came out a few years ago showing that the extirpation of the gray wolf from North America probably released Lyme disease, caused an increase in deer populations and also indirectly and increase in the populations of small mammals and as a result that might have set the stage for the emergence of Lyme disease. And so in the absence of top predators, top carnivores, in ecosystems what you may see emerge in their place are an abundance of parasites. And so this all in some ways may be consequences of the way humans have modified the ecosystems in which we live.
Erin Allmann Updyke	I have a question. So you have been directly impacted by Lyme disease and yet still study ticks constantly. What are your favorite and least favorite parts of studying ticks and tick ecology?
Brian Allan	I love that question. I'll start with my favorite part. So to be the most interesting thing about studying ticks is that most tick species, or many tick species anyway, will feed on a wide diversity of different wildlife hosts. And so by studying ticks I get to study many different organisms, not just ticks. And so I bill myself as a tick biologist and that's served me well but I really do find it interesting the way ticks connect many of the organisms within the ecosystem in which they occur. And so I am able to study a much greater diversity of wildlife as a result of working on ticks.
	Least favorite part? You know I hear from a lot of people who are suffering from serious illness including people who haven't been able to get the treatment they need to feel better. And I feel bad for people who are suffering from long term illness from tick-borne disease and I'm not a physician, I'm not really able to offer them anything other than my sympathy. And I hope through the research I do I can make things better for people who haven't yet been exposed to tick-borne disease but it is heartbreaking sometimes to hear people's stories. Some people are very sick, very debilitated from things like Lyme disease.
TPWKY	(transition theme)
Erin Welsh	That was fantastic, it was so much fun to talk with Brian.
Erin Allmann Updyke	It was so great.
Erin Welsh	Oh, Brian.
Erin Allmann Updyke	I can't believe it took us two full seasons to get him on the show!
Erin Welsh	I think we were just waiting for the right moment.
Erin Allmann Updyke	This was the right moment.
Erin Welsh	This was the right moment. Thanks Brian, for everything.
Erin Allmann Updyke	Thank you for literally the last 6 years of our life.
Erin Welsh	Yes. So Erin, there's more medical things though, right? Like can you tell me any updates on the medical side of Lyme? Is there a vaccine in the works? Why do dogs get vaccines?

Erin Allmann Updyke	Great questions. Yeah so there is a vaccine for dogs, you can get it for your dogs, I think for your cats as well. I got it for my dog because she runs around and gets bit by ticks even though she's on tick prevention and things like that. Why not, might as well. There used to be a vaccine for humans.
Erin Welsh	Used to be.
Erin Allmann Updyke	Used to be. It was relatively effective from what I can tell.
Erin Welsh	What is relatively effective?
Erin Allmann Updyke	I'm not sure exactly what the effectiveness was but it was like more than 50% effective.
Erin Welsh	Okay.
Erin Allmann Updyke	Meaning that more than 50% of people, if you gave them this vaccine, would mount a response and then not get infected with the Lyme pathogen.
Erin Welsh	Okay.
Erin Allmann Updyke	But there was a theoretical fear raised that giving this vaccine would increase the risk of Lyme arthritis because it's very likely that Lyme arthritis is an autoimmune response and not directly caused by the pathogen. So this is not an unreasonable idea that maybe giving a killed version of this bacteria in some way would activate that same sort of immune response. There wasn't any actually evidence in any clinical trials that this happened but after that idea was raised there was like no market for the vaccine and the manufacturers weren't making any money so they stopped making it.
Erin Welsh	That's it.
Erin Allmann Updyke	That's it.
Erin Welsh	So it didn't become unlicensed or anything like that?
Erin Allmann Updyke	I think so much time has passed that it's no longer a licensed vaccine, it's no longer available for humans. So there is no humans Lyme vaccine. I think that's hilarious.
Erin Welsh	So then are there any research groups that are working on a vaccine or anything like that?
Erin Allmann Updyke	There probably are, I've had a hard time finding them. So there's like things that you can find on different Lyme vaccine patents and things like that. Let me check clinicaltrials.gov really quickly actually. So there was a paper that came out in 2017 that was analyzing the past Lyme vaccines that have existed and kind of trying to guide the way for further vaccine development. But yeah, it's really interesting. Lyme vaccine used to exist, maybe it will again.
Erin Welsh	Do you know why it was not highly effective? Does it have something to do with the strain diversity of Lyme? And was it only Borrelia burgdorferi?
Erin Allmann Updyke	I think it was only Borrelia burgdorferi, I think it was pretty effective though. "Reduced new infections in vaccinated adults by nearly 80%".

Erin Welsh	80%.
Erin Allmann Updyke	So yeah, it was almost 80% effective. But then they withdrew sales. Ooh, this is a great paper, I will post this. 'Lyme Vaccine: A Cautionary Tale'.
Erin Welsh	I'm curious, I'd like to read that.
Erin Allmann Updyke	Yeah. We didn't touch at all in the polio really about the pacific coast side of Lyme disease and the ticks that transmit there and the hosts that are there are entirely different than on the northeast coast. And if you wanna hear more about that I would recommend an episode of Ologies that features none other than Dr. Andrea Swei who's fantastic. And she talks a lot about her research on Lyme disease on the pacific coast. So if people are interested they should definitely check out that episode of Ologies. That's all.
Erin Welsh	Yeah, that's a good recommendation. So that's it on the medical side of things.
Erin Allmann Updyke	That's it on the medical side of things. I had fun with this episode.
Erin Welsh	I did too. Tick-borne diseases and vector-borne diseases are fascinating because of how complex they are and it's a little bit daunting to try to learn each new system and all of the different terminology, reservoir competence and tick hosts and blah, blah, blah. But I think it's just such an amazing thing to try to tease apart all of these strands and that's ecology.
Erin Allmann Updyke	Yeah.
Erin Welsh	Like this is disease ecology at its most beautiful.
Erin Allmann Updyke	Yeah, I agree. So, sources?
Erin Welsh	Sources. Okay so I read a few different books and a bunch of articles for this. One book that I definitely wanna shout out is called 'Lyme disease: the ecology of a complex system' and this is by Rick Ostfeld.
Erin Allmann Updyke	Rick!
Erin Welsh	And he is the most knowledgeable Lyme disease person I think, he has been doing Lyme disease research and has teased apart of much of the ecology. So this is a really well written, understandable, and fact-based book. In David Quammen's 'Spillover' there's a great chapter on Lyme disease called The Deer, The Parrot, And The Kid Next Door. Super fun. And then a bunch of papers and I'll post them all. I do wanna point out that there are some books out there that are not reliable and that present a lot of nonscientific information that's not based on fact or on the research that has wide consensus among Lyme researchers. And this is a real problem because what some of these books do is use scientific language and they use interviews with scientists to bolster whatever arguments they're trying to portray or whatever story they're trying to sell. And this makes finding reliable information very difficult.
Erin Allmann Updyke	Yeah.
Erin Welsh	And I read a few of these books because I wanted to explore this realm. And I am going to list them here as a way of saying hey, these are some that are not reliable.

Erin Allmann Updyke	Yeah.
Erin Welsh	One is called 'Lyme: The First Epidemic of Climate Change' by Mary Beth Pfeiffer and the other is called 'Lab 257' and that's by Michael C. Carroll. And I found in both of these books what seemed to be a lack of understanding of the Lyme disease system which made me doubt the credibility of the rest of the books.
Erin Allmann Updyke	Yeah. I think that's really important because it's hard enough to find good information out there. You expect that if it's a book it's legit.
Erin Welsh	Right.
Erin Allmann Updyke	Yeah.
Erin Welsh	And the thing that we need to remember is that there is no peer review process for publishing nonscientific books the way there is for these journals which have to go through pretty rigorous screening of the study design, of the interpretation of the analysis, all of these things.
Erin Allmann Updyke	Right. And even then they're sometimes wrong. And so with books there's not even a screening. (laughs)
Erin Welsh	No, this is a realm that can be very tricky to then know where to find the right information or correct information.
Erin Allmann Updyke	Yah, absolutely. Cool. I have several really great articles. One really, really great one that I really enjoyed by John Halperin that's addressing a lot of the common misconceptions about Lyme disease. That's the title, 'Common misconceptions about Lyme disease.'
Erin Welsh	Wonderful.
Erin Allmann Updyke	It was published in 2013. And then there are several other reviews that I found that are super comprehensive and really easy to read if you want some just really good info about Lyme disease in general. So we will post the links to these sources as always on our website thispodcastwillkillyou.com. You can find every source that we cite from every single one of our episodes. And yeah.
Erin Welsh	We would like to thank Brian once again.
Erin Allmann Updyke	Yes.
Erin Welsh	For coming onto the podcast, we really appreciate it. It was so much fun.
Erin Allmann Updyke	It was so fun to have you. We'd like to thank Bloodmobile for the music for this episode and all of our episodes. You can find a link to his music on our website.
Erin Welsh	And also we'd like to thank you for listening to us and for so many of you who suggested Lyme disease. And also for being patient as this is our final episode of this season but we will be back in just a few short weeks.
Erin Allmann Updyke	Thank you so much for allowing us to make two whole seasons of this podcast and listening to it.

Erin Welsh	And then a third one.
Erin Allmann Updyke	And then a third one! Don't worry, it's coming.
Erin Welsh	It's coming.
Erin Allmann Updyke	We just have some things to take care of in the meantime.
Erin Welsh	Yeah.
Erin Allmann Updyke	Okay?
Erin Welsh	Okay.
Erin Allmann Updyke	With that-
Erin Welsh	Wash your hands!
Erin Allmann Updyke	You filthy, beautiful animals.
Erin Welsh	And check yourself for ticks.
Erin Allmann Updyke	Do a tick check.