

Daisy Hernandez

My name is Daisy Hernandez and I'm an associate professor at Miami University in Ohio and I'm also the author of a book about Chagas disease called 'The Kissing Bug: A True Story of an Insect, a Family, and a Nation's Neglect of a Deadly Disease'. I first learned about Chagas disease when I was about 5 years old. My auntie was diagnosed with Chagas in New York City actually and she was from Colombia where around the time that she was 29, she started to get really seriously sick. And the doctors in Colombia were able to do some exploratory surgery which is how they found out that her large intestine was under some kind of attack. They actually did not diagnose her with Chagas disease, it was in New York City that that happened. And my auntie was very lucky that she was diagnosed and she was able to receive some interventionist kind of treatment at that point.

But she had chronic Chagas disease for the next almost three decades of her life. And so while I was growing up she was in and out of hospitals over the years and sometimes she was in the hospital for one night or two nights and some years she was in the hospital for a month or two. The parasite ended up not only affecting her large intestine but also her esophagus, she had multiple surgeries during these years. And I grew up thinking that Chagas disease was a very rare or unusual illness, I thought my auntie had just been extremely unlucky. And it was not until 2010 when she became very, very ill and actually died from this disease, that was the point at which I started asking questions about Chagas disease.

I think because I had grown up without knowing anyone else who had this disease except my auntie, I thought it was rare and I was really surprised to find out that there are an estimated 300,000 people in the United States who have Chagas disease and they're like my auntie, they're immigrants from South America, Central America, Mexico. And that number was very shocking to me and it made me wonder who these families were. And that's how I ended up starting my book actually was that I wanted to meet other Latinx families in the United States to find out what their experiences with Chagas disease were like and what obstacles they were facing and just how they were navigating the medical system in this country given that as far as I knew was a very neglected disease.

And something that I discovered while working on the book that I did not know about when I was a child was the issue of congenital Chagas disease. I met an incredible woman in the D.C. /Maryland area named Janet who is from South America and her second son was born here in the United States with congenital Chagas. She herself knew about the disease, similar to me she thought that it was an affliction of, actually in her case she thought it was the elderly because she knew her father had Chagas disease, she knew her older sister had Chagas disease. She comes from part of South America where the disease is pretty common but even though it's common she did not know about congenital Chagas disease and her son was born already having cardiac complications due to the disease. I'm happy to share that the baby is now, gosh, now 5 or 6 years old and is doing well. But he was a very unusual case, he ended up being only the second documented case of congenital Chagas disease in the United States and he was unusual just in that he showed symptoms.

Her situation though also really touched me because she herself did not have health insurance, she was not working, she had a toddler and a new baby and she was home and her husband worked in construction and she did qualify for the Affordable Care Act, for Obamacare but she had no signed up for it and it's an additional expense that the family would have to bear. And so she really struggled to actually find a medical provider who could diagnose her, who could work with her. It was a series of obstacles that I kept hearing over the years that I worked on this book while I was talking to both families and medical providers is this constellation of obstacles, not having health insurance, not being fluent in English. Sometime being fluent in English but really struggling to advocate for yourself with a medical provider who doesn't know about the disease and doesn't understand or isn't being proactive.

And also something else which came up often which is that if patients aren't experiencing symptoms, they have so many other things that feel more urgent and are more urgent in some ways in their lives, like in Janet's case she was very concerned about her child's welfare before her own and she was concerned obviously about her family's financial life. She herself has legal residency but is trying to learn English to work toward citizenship. Other families that I interviewed, what felt more urgent in their lives were the immigration status of different family members and job security always comes up. And it becomes easy to actually ignore Chagas disease in a way because they're not having symptoms and it's not the most pressing concern in their lives.

Although I knew about this disease from a very young age, there was a kind of stigma in my family around it. My auntie never wanted anyone to know about this disease, that she had it, she was really afraid I think as an immigrant to be rejected in some way by her coworkers, by this country. She wanted so much I think to be the perfect immigrant turned citizen and in so many ways she was. She got her teaching degree, she taught Spanish in a public school system in New Jersey, she got her master's degree as well, she traveled, she married an incredible man. She had such a wonderful life in so many ways and she didn't want to have this disease and felt like it tarnished.

I think when I was growing up I thought it was very normal that we did not talk about Chagas disease, we did not tell anyone that my auntie had it, we did not mention it, it definitely felt like something that we were supposed to have shame around. And now I look back on that with so much sadness because it was just a lack of information from my own family, it was a lack of information of course in the healthcare community in the United States.

The one sadness that I have is that I do wish my auntie had lived so that I could tell her a lot of what I learned about the disease, you know even the difficult parts of this, even the learning about congenital Chagas, I wish I could've told her that. I wish that I could've told her more about just all these species of this insect, of the triatomine insect. I wish I could have told her about that even though she hated insects, she would not have wanted to probably hear that much detail. But I do wish and I do have sadness that I could have told her because I think that ultimately she died knowing very little about her disease. And so for me, part of working on the book was also a desire that people who have Chagas and their families have a chance to know what they're really facing, you know, so that no one else should have to die without knowing about their own disease and what's happening to their bodies.

TPWKY

(This Podcast Will Kill You intro theme)

Erin Welsh

Thank you so much, Daisy, for taking the time to come on the podcast and chat with us, we really appreciate it.

Erin Allmann Updyke

Yeah, thank you.

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 today we're talking about Chagas disease.

Erin Welsh

Chagas disease.

Erin Allmann Updyke Listen, Erin.

Erin Welsh How do you feel right now?

Erin Allmann Updyke I'm feeling a lot of different feelings, like I'm full of feelings.

Erin Welsh Okay, okay.

Erin Allmann Updyke Listeners, you probably don't know this but I technically did my PhD research on Chagas disease. Technically.

Erin Welsh Technically?

Erin Allmann Updyke Yeah. So I feel like I'm just gonna feel like I didn't do a good job on this no matter what, like I just don't know enough.

Erin Welsh Well first of all you do, you literally have a PhD in different aspects of Chagas disease.

Erin Allmann Updyke Yeah.

Erin Welsh And secondly it's like we say every episode, we are not experts.

Erin Allmann Updyke No, we're not.

Erin Welsh And this is a really big one to cover. Like massive.

Erin Allmann Updyke It is, it's so big. I'm excited about it but it's gonna be big.

Erin Welsh Yeah. But also Erin, you're gonna do a great job, I know it, you always do.

Erin Allmann Updyke Oh Erin, you're so nice.

Erin Welsh I'm serious.

Erin Allmann Updyke I think before we really get into it though it's definitely quarantine time.

Erin Welsh It is, it is. What are we drinking this week?

Erin Allmann Updyke We're drinking The Kiss Goodnight.

Erin Welsh It's called this because Chagas disease is transmitted by what are commonly called or one of the names for them is kissing bugs. And what they do is they feed on you and animals mostly while you're sleeping and they suck your blood. And that's how you get Chagas disease.

Erin Allmann Updyke It sure is. So Erin, what's in The Kiss Goodnight?

Erin Welsh In The Kiss Goodnight is tequila.

Erin Allmann Updyke Of course.

Erin Welsh Cantelope, agave syrup, lime, and orange liqueur.

Erin Allmann Updyke Yum.

Erin Welsh Yeah.

Erin Allmann Updyke That sounds fantastic. We'll post the full recipe for that quarantini as well as our nonalcoholic placeborita on our website thispodcastwillkillyou.com and all of our social media channels.

Erin Welsh Yeah. Other business. Let's see, you can check out our website thispodcastwillkillyou.com, it's got lots of great stuff like transcripts, like the sources for all of our past episodes, it's got links to music, to merch, to our Patreon, to our bookshop.org affiliate account, to Goodreads list and so on. Definitely check out our website. And also remember that you can listen to this episode and all of our past and future episodes on Amazon Music, Apple, Stitcher, or wherever you get your podcasts.

Erin Allmann Updyke Before we get into this episode, speaking of the fact that we are not experts, I have a correction to make. Bartonella was an episode that came out a few episodes ago now. I want to hugely thank multiple listeners that have reached out to help us solve the mystery of cat scratch disease that we were postulating about during that episode. In that episode we were trying to figure out how Bartonella makes it from a cat's blood onto their claws or their teeth and then into our bloodstream after a bite of a scratch. Okay, multiple people have written in. It turns out unsurprisingly when you really think about it, it is largely flea feces that are to blame. So infected flea feces or in some cases just infected cat's blood itself can contaminate a cat's claws during grooming which then can introduce the bacteria via a scratch into our skin or a bite wound, flea feces can contaminate a bite wound, etc. So mystery solved, Erin.

Erin Welsh Flea feces. Say that three times fast.

Erin Allmann Updyke I can't, I couldn't even say it once.

Erin Welsh I also learned with the people who sent in those corrections which was very helpful, thank you, that it's called flea dirt too.

Erin Allmann Updyke Flea dirt.

Erin Welsh Flea dirt. I like it. It's easier to say than flea feces.

Erin Allmann Updyke Yeah but it's also ugh.

Erin Welsh I know, either way ugh.

Erin Allmann Updyke It's gross. But thank you so much honestly, we are not experts, we never get everything 1000% right, so thank you. I appreciate getting to learn from you.

Erin Welsh Yeah. Okay.

Erin Allmann Updyke Okay. With that...

Erin Welsh: Should we get started?

Erin Allmann Updyke: I'm so nervous. Okay, let's take a break and then get into it.

TPWKY: (transition theme)

Erin Allmann Updyke: So Chagas disease. Chagas is a severely neglected tropical disease. Historically very much considered a disease of poverty like many if not all neglected tropical diseases. And like you mentioned up top Erin, it's a vector-borne disease for the most part. It's caused by a protozoan parasite called *Trypanosoma cruzi*, *T. cruzi*. It's a very cute little parasite, looks like of like a comma with wavy flagella. Okay?

Erin Welsh: Okay.

Erin Allmann Updyke: Picture it. It's cute. So *T. cruzi* has a shall we say relatively complex life cycle. So we're gonna go through the life cycle and then from there we can understand the different ways that we as humans can get infected. so we'll start the life cycle in the bug, the insect vector that transmits it. So *T. cruzi* gets picked up during blood feeding by bugs, like you mentioned Erin, called kissing bugs aka triatomines. They have a lot of different names in different countries. Kissing bugs are a type of what's called true bug in the order Hemiptera, okay. Already I'm on tangents. These are blood feeding insects, I think a lot of people might not know what they look like so let me paint you a visual. They're pretty large bugs. The adults are between 3-4 centimeters so a good inch, inch and a half long and they have a flat, oval body with a pointy head and a long, curved proboscis, that's the straw that they use to drink blood. So these are big, honking bugs.

Erin Welsh: They're big.

Erin Allmann Updyke: Right? Like way bigger than ticks, way bigger than mosquitoes, way bigger than most things that bite you.

Erin Welsh: I would say like... Well cockroaches are a whole bunch of different sizes but you know, about the size of your average cockroach.

Erin Allmann Updyke: Yeah like your US house cockroach, definitely. If not bigger.

Erin Welsh: Yeah.

Erin Allmann Updyke: Now both males and females drink blood as do all of the nymphal stages, so these are bugs that have multiple instar stages and they all blood feed. They often have a nest that they stay near but then the adults can fly so they can fly farther from home base to look for blood meals.

Erin Welsh: They have a family nest or individual nest?

Erin Allmann Updyke: Like little families or even multi-generation little families, just like a lot of bugs will often hang out together in a palm tree or whatever.

Erin Welsh: Ooh, that's interesting.

Erin Allmann Updyke: Yeah so like a bunch of nymphs, a bunch of adults, you might find a lot kind of living together.

Erin Welsh: Okay.

Erin Allmann Updyke

Depending on the species but we'll get into that later. So this bug takes a blood meal from someone, picks up a whole bunch of parasites, these parasites travel through the bug's guts, they differentiate, they replicate, and then when that bug gets hungry again and goes to take another blood meal that bug will poop. And in that poop or frass are a whole bunch of parasites. Not unlike the fleas in Bartonella.

Erin Welsh

Hey!

Erin Allmann Updyke

Yeah. And then these parasites that are now pooped onto your skin have to find their way either into that bite wound that the bug just made or some other mucus membrane like your eye or your mouth, etc. And from there they make it into our bloodstream. You look like you have a question, Erin.

Erin Welsh

I do have a question. Okay so they're pooping while they're eating?

Erin Allmann Updyke

Or shortly thereafter.

Erin Welsh

Or shortly after. And so the poop that they're pooping out is from the fresh meal or from the previous meal?

Erin Allmann Updyke

Great question, it's from the previous meal, yeah.

Erin Welsh

And how often do they have to feed?

Erin Allmann Updyke

Great question. Totally varies by species and by life stage. So at least once per nymphal stage and then as adults, like the females have to feed every time that they're going to make a clutch of eggs so it kind of just depends.

Erin Welsh

Okay, gotcha.

Erin Allmann Updyke

Yeah, good questions, Erin. Okay. So now this parasite is inside of us, it made it into our bloodstream. Inside of us these parasites penetrate our cells. They actually can penetrate a pretty wide variety of cells and what cells or what tissue type they infect can then lead to different symptoms of disease. They replicate, they differentiate again inside our cells, they replicate a whole bunch, and then they burst out from our cells to travel through our bloodstream and either infect another cell and start a new replication cycle to just keep going or in the bloodstream they can be picked up by another kissing bug, thus completing their life cycle. So that's just the life cycle of *T. cruzi*.

Erin Welsh

Yeah. I mean it's a complicated one.

Erin Allmann Updyke

Yeah, it's part one of complication.

Erin Welsh

Yeah.

Erin Allmann Updyke

But in my very biased opinion, what's also very important and interesting about the Chagas disease story is how complex the ecology of this disease is. I'm biased but I think listeners will agree once I get into it. So this is one parasite, right, *Trypanosoma cruzi*. But it has like 6 different clades within this species and these different clades vary in terms of virulence, so how sick they make you, and disease manifestations, what tissues they're maybe more likely to infect or how likely they are to cause more chronic disease. And these different clades can vary in geography, they can vary by vector, there's a lot of variation in these different clades of *T. cruzi*. Then there's the vector and I hinted this already. So I said it's a triatomine, a kissing bug. But Erin, is it just one bug?

Erin Welsh

No, Erin, it's many bugs.

Erin Allmann Updyke

It is many bugs.

Erin Welsh

It's a lot, yeah.

Erin Allmann Updyke

So there's like 138 I think, maybe more, species of triatomine. Every one could potentially transmit *Trypanosoma cruzi*. There's at least 3 species that are often cited as being the most important. One in particular, *Triatoma infestans* is a species that's most closely associated with human dwellings. It has adapted to live its entire life cycle within human dwellings, so in walls, in roofs, inside of our homes. So historically that's been the one considered kind of the biggest deal.

But there's a lot of other species in a whole bunch of different genera of triatomine that are capable of and potentially important vectors of Chagas disease. Spoiler, that was like my whole dissertation so I could go on and on. But I think I can pause there, okay. Each of these species has differences in terms of their ecology, so like where they like to live. Do they live in palm trees or do they live under rocks, etc? They have differences in terms of who they like to feed on and like you asked, Erin, how often they feed. They have differences in how long they feed for, how soon after feeding they take a poop and where they take a poop after feeding. It's really, really complicated.

Erin Welsh

Yeah. I mean all of this just kind of serves to underline how difficult this is to control or prevent or to reduce the numbers of.

Erin Allmann Updyke

Absolutely.

Erin Welsh

It's sort of like you have to hit it from so many different angles.

Erin Allmann Updyke

Right.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah. And to throw one last angle on there, Erin, this isn't a human-specific disease, this is a parasite that infects over 150 species of mammal.

Erin Welsh

Right.

Erin Allmann Updyke

All right. So that's a lot, that's really complicated. So we know that. In general this is a group of insects and therefore parasite and disease that was typically considered endemic to the New World, so North, Central, and South America and mostly just the southern part of North America cause it's really restricted to more tropical-type latitudes. But as we'll see when we talk about the clinical picture of disease which I promise I'm about to get to, because of the way that Chagas disease manifests clinically it is a global disease today. It is not limited to South America or even just the Americas.

Erin Welsh

Right.

Erin Allmann Updyke

So let's talk symptoms. In humans Chagas disease has two forms: the acute disease like you get sick shortly after getting infected, and then a chronic disease. This parasite can lay dormant in our bodies for decades, 10, 20, 30 years and then pop up and cause disease very long down the road. So we'll go through those one by one. In the acute phase, honestly Chagas is mostly asymptomatic. And by 'mostly' I mean 90-95% of the time completely asymptomatic. So you get bit, you scratch this parasite into your bloodstream, and you don't know about it at all. If people do have symptoms, so that 5-10% of people that do have symptoms, they're often quite mild and consist of something like maybe some fever, maybe inflammation wherever the parasites entered. And because it's common for the parasites to enter via something like your eye, there's a classic sign that's called Romaña sign which is when one eye, whichever eye the parasites went in from gets really swelling, unilateral swelling of your eye and eyelid. But it could be anywhere, so let's say it happened on your arms then maybe your arm swells up.

Occasionally you might also get some hepatosplenomegaly, one of our favorite TPWKY words, yeah. So that's swelling of your liver and spleen from the parasite and inflammation and immune response associated with it, or swelling of any various lymph nodes. Potentially it can cause things like anemia if it gets more severe. And in very rare instances, like I think usually only 1-5% of the time although one paper I read said 5-10%, it can be a little bit more severe and the specific symptoms depend on which organ is infected severely. So if it's the heart we can see things like myocarditis or pericarditis, inflammation of the heart muscle or lining. Very rarely if it infects the brain you can get meningoencephalitis. And these kind of severe manifestations can be fatal but that's very rare.

Erin Welsh

Can be fatal in the acute phase?

Erin Allmann Updyke

In the acute phase, exactly. Yeah.

Erin Welsh

Okay so why is it the enlargement? Why is there such inflammation? Like what cells are they attacking?

Erin Allmann Updyke

Yeah, good question. They enter into our cells and from what I can tell it's not very specific. So they can enter white blood cells which is probably why we see a lot of hepatosplenomegaly and lymphadenopathy, this is where our white blood cells are congregating. But they can also enter the lining of your heart, they can enter a whole bunch of different tissue types. What makes them either decide or just happen to end up somewhere probably depends on how much parasite you have, like how far they make it before our immune system kicks in, probably depends on how great of an immune response you have to it, probably depends on what specific genotype you were infected with. There's probably a lot of variables that I don't know the full answer to.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah.

Erin Welsh

Okay. So you said 95% are asymptomatic, are there any patterns as to who the 5% are that become symptomatic?

Erin Allmann Updyke

It's a good question. I don't know.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah. Good question.

Erin Welsh

And another question real quick.

Erin Allmann Updyke

Okay.

Erin Welsh

While I have you.

Erin Allmann Updyke

Yeah?

Erin Welsh

Immunity with re-exposure. So you said that your immune system can kind of recognize, take care of it. If someone gets re-exposed, are they immune or can they get reinfected?

Erin Allmann Updyke

Okay let's keep going and I might...

Erin Welsh

Okay. I have a feeling I was jumping the gun.

Erin Allmann Updyke

Yeah. Okay so let's then talk about the chronic phase, okay?

Erin Welsh

Yep, yep.

Erin Allmann Updyke

So the chronic phase is the phase of disease that's more severe. Here's the thing about it. Most people - and when I say 'most' I don't have an exact number but some of the papers I read made it sound like almost all people - if untreated during the acute phase will in fact have some level of chronic infection. But only about 30-40% of those people will actually go on to have any chronic disease as a result of this infection.

Erin Welsh

Okay, okay.

Erin Allmann Updyke

Okay? So for those unlucky 30-40% of people anywhere from 10-30 years after the initial infection which again most of the time is asymptomatic so you never know that you had it, the two most common organs that end up getting infected are the heart and the gastrointestinal tract. And the parasite ends up doing similar things but with very different outcomes since it's heart vs GI tract. Okay. So in the heart often what happens is this parasite and this infection causes an enlargement of the heart, it causes what's called a dilated cardiomyopathy, an enlargement of the heart.

This causes the heart to not be able to conduct electrical impulses properly, that's you heart's one job right, it's to have electrical impulses that all of simultaneously so that your heart contracts in one beautiful thump-thump with enough force to pump blood to the rest of your body. When it gets dilated and those electrical impulses can't transmit, the heart can't contract in sync or it can't contract with enough force or the right timing and synchronization to be able to push your blood forward. So there's a lot of different ways that this can manifest, anything from things like heart block to heart failure to different arrhythmias, just depending on what parts of the heart are most affected and when. But overall the most common cause of death in these individuals is sudden cardiac death because your heart is just all of a sudden not able to pump properly and then you die from sudden cardiac death.

The other organ that's most commonly affected is the GI tract. And same as with the heart, Chagas disease tends to cause enlargement of either the esophagus or the colon, either/or usually. In the esophagus this leads to dysmotility and specifically it leads to something called achalasia which anyone in med school would be like, 'Oh yeah, Chagas disparities, achalasia'. It basically means your esophageal sphincter, the one that lets your food into your stomach, doesn't relax properly and your esophagus gets expanded and then it looks like a bird's beak. So there's a really tight hole where it enters the stomach and then the rest of it is really dilated. Does that make sense? Instead of it being a nice little tube.

Erin Welsh

Okay, yeah.

Erin Allmann Updyke

And so this leads to not being able to swallow properly etc.

Erin Welsh

Ugh, that sounds really difficult.

Erin Allmann Updyke

It's really problematic. It can lead to reflux, it can lead to weight loss cause if you're not able to swallow your food then you're not eating essentially. And a similar thing can happen in the colon. Chagas can lead to what's called megacolon where the entire colon becomes dilated and then isn't able to contract properly to move your digestive food along. So that leads to constipation which is problematic but what's even more worrisome is this dilation can lead to twisting of your bowels which is called volvulus. And that can lead to ischemia because that twisting can then cut off blood flow to the organ.

Erin Welsh

Okay.

Erin Allmann Updyke

Okay. So it's a problematic disease and it's a cause of really chronic disease problems, right. Like megacolon, esophageal dysmotility, heart failure, dilated cardiomyopathy, these are things that happen from a lot of other sources but not this is happening from an infectious disease. So what's going on?

Erin Welsh

Yeah.

Erin Allmann Updyke

Off the bat, Erin, this is a very understudied disease from every possible angle and that's still true for the pathophysiology. So especially in the chronic phase we still don't know the exact details of this pathogenesis, so we don't know exactly what's going on. But we know a few things. So we know that in the acute phase the organ damage, when it happens, is due to direct action of the parasite. So it's parasites causing damage to the tissue from bursting out of our cells. That stimulates an inflammatory response, etc etc. Okay, that's the acute phase. So you think probably similar things are happening in the chronic phase. We know that you asked about who gets chronic disease vs who doesn't. The balance of who gets chronic disease vs just who has infection without ever having disease from it seems to depend a lot on individual balances between our chronic inflammatory response and the parasite infection itself. So like how much is our immune system trying really hard to kill off this parasite vs just tolerating this parasite and coexisting with it?

Erin Welsh

Right.

Erin Allmann Updyke

Okay it gets really complicated because in some areas where transmission has been reduced significantly, so where control efforts have reduced incidence of disease but of course people are still infected, right, cause it's chronic infection, the development of things like cardiomyopathy have actually decreased. There's been a reduction in the development of things like heart disease. So it's thought that maybe there's also some interaction between recurrent exposure to the parasite and increased inflammation.

Erin Welsh

Oh okay. Yeah. So it's like every time let's say you get infected and then your body never sees this again and it's just like okay, well this is just this thing here.

Erin Allmann Updyke

Right.

Erin Welsh

Then if you get continually re-exposed and your immune system keeps waking up and keeps getting inflammation...

Erin Allmann Updyke

Right, exactly.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah. But it does seem to be the case that a lot of the damage is parasite persistence. And that's important because it's not purely an inflammatory or purely an immune response, like the parasite is a really big part of it. Does that make sense?

Erin Welsh

Yeah, yeah.

Erin Allmann Updyke

And it's important when we talk about things like therapeutic vaccines, like this interplay between parasite and immune response. So it's really complicated and we don't know the full answer. I'm gonna throw a little bit more complication in there before I hand it off to you Erin cause it's important to mention that while this is largely a vector-borne disease, vector-borne transmission is the primary route, it is certainly not the only route.

Erin Welsh

Right.

Erin Allmann Updyke

So because this is essentially a blood-borne pathogen this is something that can also be transmitted via blood transfusion or organ transplant but of course that's quite rare and in many places blood is screened for Chagas disease. It can also be a congenital infection. So during pregnancy it can cross the placenta and infect a fetus which can result from anything from spontaneous pregnancy loss to premature birth to a number of different problems in the newborn or in many cases asymptomatic infection but then lifelong infection of the baby.

Erin Welsh

Yeah, it's really bad.

Erin Allmann Updyke

Yeah. And increasingly people are realizing that it's a much bigger problem than had ever been thought before probably just cause nobody had thought to study it.

Erin Welsh

Can I read you a disheartening statistic?

Erin Allmann Updyke

Oh gosh, yeah.

Erin Welsh

So there was a survey in 2008 by the CDC and the American College of Obstetricians and Gynecologists and there was the question can a pregnant person pass *T. cruzi* onto their baby. So again these are obstetricians and gynecologists in the US and 84% of them answered 'I don't know' to that question.

Erin Allmann Updyke

I'm not surprised about that. I can tell you that this absolutely never came up in medical school.

Erin Welsh

Yeah. That's a huge problem.

Erin Allmann Updyke

I mean Chagas came up but not congenital transmission of Chagas.

Erin Welsh

Right but that's like such a big problem.

Erin Allmann Updyke

It's a huge problem, yeah.

Erin Welsh

Oh my gosh. That's frustrating.

Erin Allmann Updyke

Yeah. I know. That's not the end.

Erin Welsh

Yeah.

Erin Allmann Updyke

Chagas has also though rarely been associated with oral transmission. Because this parasite is found in the feces of bugs and a lot of species of triatomine make their little nests in the tops of palm trees there have been a handful of outbreaks of Chagas disease associated with consumption of things like palm fruit juice or other fruits and vegetables that were contaminated with the feces of kissing bugs.

Erin Welsh

I always see acai being called out.

Erin Allmann Updyke

Yeah, acai is I think the most well documented. Yeah. That's a lot, Erin. And there's not any good news in this section. Because there is treatment but in general it's really effective only during the acute phase of the disease, it's much less effective during the chronic phase and you can imagine it's pretty difficult to catch during the acute phase.

Erin Welsh: Yeah. Why is it only effective in the acute phase?

Erin Allmann Updyke: It's a good question, Erin.

Erin Welsh: Okay.

Erin Allmann Updyke: I think if we knew that we might have better drugs.

Erin Welsh: Okay yeah, fair. (laughs)

Erin Allmann Updyke: (laughs) So Erin.

Erin Welsh: Yes.

Erin Allmann Updyke: You think you can tell me a little bit about this little parasite here? I mean it's got a lot going on.

Erin Welsh: It's got a lot going on. Yeah, I'll tell you all about its history. Let's take a quick break first.

TPWKY: (transition theme)

Erin Welsh: I am so excited to talk about the history of Chagas disease because at each step of the way from its evolutionary origins and prehistory to the research leading to its discovery and then a better understanding of disease progression, I was surprised at all of these steps by what I learned.

Erin Allmann Updyke: Ooh fun!

Erin Welsh: I really was. I mean granted I didn't know much about the history of Chagas going into the episode but I think it does stand out for me as a parasite and a disease where things didn't really happen in quite the way you might expect which is definitely something that can be said for its biology as well. It's complicated, you're like, 'I don't know what's going on', you can't really predict things sometimes.

Erin Allmann Updyke: Yeah. Definitely.

Erin Welsh: Yeah. So like always let's start at the beginning which is easier said than done. Until fairly recently, like maybe within the last 10-15 years or so, the origins of *Trypanosoma cruzi* seemed fairly cut and dry or at least as cut and dry as evolutionary origins can be in terms of stuff. You know, it's always being rewritten. It's fine.

Erin Allmann Updyke: Yeah, right.

Erin Welsh: That's how science works. But there was a general consensus that the *Trypanosoma cruzi* clade originated on the southern supercontinent made up of South America, Antarctica, and Australia where they evolved in isolation in early terrestrial mammals. And then when that supercontinent broke up around 40 million years ago the *T. cruzi* clade further diversified in South America. And so if this were the sequence of events that actually happened, we would expect to see a great deal of diversity within *T. cruzi* in South America as well as maybe some evidence of coevolution between mammalian host and parasite with some maybe species-specific strains. However-

Erin Allmann Updyke

However!

Erin Welsh

However there's actually fairly low diversity of the T. cruzi clade in South American mammals, like lower than you would expect if it had been there for 40 million years. And in addition to this, members of the T. cruzi clade also have been found in African and Australian land mammals. So what's going on here?

Erin Allmann Updyke

Yeah.

Erin Welsh

Well it seems most likely that T. cruzi originated elsewhere, likely in Africa where the other major human trypanosome is most prevalent which is T. Brucei which is the causative agent of African sleeping sickness. We should figure out how to pronounce that before we do an episode on that, which we will.

Erin Allmann Updyke

Definitely will.

Erin Welsh

Yeah. So then it originated in Africa and then was brought to South America.

Erin Allmann Updyke

Okay.

Erin Welsh

And this is where I introduce to you the bat seeding hypothesis.

Erin Allmann Updyke

Bat seeding?

Erin Welsh

Bat, yeah.

Erin Allmann Updyke

Okay, okay.

Erin Welsh

This idea basically holds that T. cruzi was brought over to South America from the Old World, likely the African continent, by bats between 7-10 million years ago in several different independent colonization events. And this bat seeding hypothesis has gotten a good deal of support more recently with molecular studies showing that the closest relative to T. cruzi is a South American bat trypanosome that diverged like 6.5-8.5 million years ago. And two other trypanosome species recently described that are related to T. cruzi are found in bats from Mozambique. Yeah. And in addition one genotype of T. cruzi called Tcbat is only found in bats in South America.

Erin Allmann Updyke

Yeah, I knew about that one.

Erin Welsh

Yeah. And that one is closely related to T. cruzi TcI which I'm not gonna get into all the different genotypes and stuff but this is I think a really interesting part of the story.

Erin Allmann Updyke

Yeah.

Erin Welsh

So TcI is mostly associated with opossums and arboreal triatomines.

Erin Allmann Updyke

Yeah. Right.

Erin Welsh: So once these trypanosome-infected bats, infected with *T. cruzi* or some ancestor of *T. cruzi* made it to South America, they were fed on by blood-feeding insects, triatomines, that also took meals from other mammals also living in trees or up high. Right?

Erin Allmann Updyke: In trees. Right, right, right. Makes sense.

Erin Welsh: Like opossums.

Erin Allmann Updyke: Yeah.

Erin Welsh: And so then those opossums were probably some of the first to get infected with *T. cruzi*.

Erin Allmann Updyke: Okay. Yeah, yeah, yeah. Okay.

Erin Welsh: And the ancientness of this relationship might be reflected in the way that the parasite infects those animals.

Erin Allmann Updyke: Ooh!

Erin Welsh: Yeah. I read a paper, actually I think it was mentioned in two that I read cause I was like, 'For real? This is wild.' And these papers reported finding amastigotes which is like-

Erin Allmann Updyke: I know.

Erin Welsh: I know.

Erin Allmann Updyke: I didn't even get into it, Erin.

Erin Welsh: I know. It's a part of the life stage of *T. cruzi*. Yeah.

Erin Allmann Updyke: It's the intracellular part of the life stage.

Erin Welsh: Right, thank you. And so they found amastigotes in the tissues of opossums which is totally what you would expect of mammals susceptible to the parasite, that's where you find them.

Erin Allmann Updyke: Right.

Erin Welsh: And then they found epimastigotes which are found usually only in the insects.

Erin Allmann Updyke: Yeah!

Erin Welsh: They found them multiplying and differentiating in the opossum's anal glands.

Erin Allmann Updyke: What?

Erin Welsh: Yeah. Okay, that I think is fascinating.

Erin Allmann Updyke: I don't even know how to interpret, Erin.

Erin Welsh: Okay so they were able to take those epimastigotes and then complete the infection cycle.

Erin Allmann Updyke: Stop it.

Erin Welsh: Yeah. So opossums might be able to transmit *Trypanosoma cruzi* in their poop.

Erin Allmann Updyke: Stop it.

Erin Welsh: That was my interpretation of this and I think that's what it means.

Erin Allmann Updyke: What?

Erin Welsh: Yeah.

Erin Allmann Updyke: I can't even handle this.

Erin Welsh: I know. And so this paper which was written before the bat seeding hypothesis gained momentum, it suggested that this might have been the earliest route of transmission before the triatomines got involved but it might also have evolved after. In any case this mode of transmission where opossums might be able to transmit through their poop or through the anal gland secretions, this might play a role currently in semi-urban environments or places where the vectors aren't quite as present.

Erin Allmann Updyke: Prevalent, yeah.

Erin Welsh: Yeah.

Erin Allmann Updyke: What?

Erin Welsh: Yeah. My mind was blown.

Erin Allmann Updyke: I just feel really glad that I finished my PhD.

Erin Welsh: (laughs) Before you found that paper?

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah, it's really interesting. I'll definitely put the paper on the website.

Erin Allmann Updyke: I feel like I would've had my hands on a lot more opossum poop or something. Pretty thankful.

Erin Welsh: Yeah, it's super interesting. Okay but once *Trypanosoma cruzi* landed in South America and found its way into opossums, and of course other host mammals followed and the parasite diversified into its current lineages around 1-3 million years ago which seems to be around the same time that the triatomine vectors diversified.

Erin Allmann Updyke: Okay.

Erin Welsh

And then over the past few million years it just continued to spread across South America up through Central America, North America, through primarily animal movement, eggs and nymphs for instance have been found to be carried in bird feathers which I think is interesting. And then later of course human movement would have helped to spread things along too. All right. By the time that humans arrived in South America which was at least 15,000 years ago, *Trypanosoma cruzi* was present in animals across the continent, although to what extent is not quite known since not all habitats might be conducive for the insect vector and whatever susceptible mammal species. But here comes the next 'first we thought it was this, then we realized it was that' moment.

It was originally thought that humans first became exposed to the parasite after the domestication of guinea pigs around 2000 BCE along with other animals that would have attracted the bugs and thus the parasite to human dwellings. Or it was thought that human dwellings built later on and particularly after European invasion would've provided excellent homes for the triatomine vectors. And those things are probably true in that they did increase contact with the bugs but paleoparasitology came along to change the story. The Atacama desert in southern Peru and northern Chile is a desert, so as you would expect it's extremely arid. There's virtually no rainfall and so when a body is buried, it rapidly dehydrates rather than decays or disintegrates and that has left many, many mummified remains in the area. And genetic analysis of these mummies has shown not only the presence of *T. cruzi* but there are actually enough samples to get prevalence estimates.

Erin Allmann Updyke

What?

Erin Welsh

Yeah. So one study from 2003 screened 283 mummies for *T. cruzi* with the mummies dating as old as 9000 years and as young as the 1800s.

Erin Allmann Updyke

Wow.

Erin Welsh

Yeah. Overall the prevalence of *T. cruzi* was 40.6%.

Erin Allmann Updyke

Yeah.

Erin Welsh

Yeah. And that prevalence is actually fairly steady over time, I mean there are a few dips and a few surges and the sample sizes in some of these groups are low and whatever but that's a pretty shockingly high number I think.

Erin Allmann Updyke

Yeah.

Erin Welsh

Nearly 50% of people.

Erin Allmann Updyke

Yeah.

Erin Welsh

And the oldest of these mummies infected was this 9000 year old mummy and that indicated that humans in South America were exposed to the parasite long before domestication of guinea pigs and construction of European-style housing or whatever and that they probably first became infected from the sylvatic cycle of the parasite, so between the wild animals and the bugs. And that was well established by the first human occupation of the area. And it's not just in South America but also in Central and North America that we have evidence of prehistoric infection. The oldest known case in North America for instance is a mummy in South Texas from around 1150 years ago with a megacolon full of feces.

Erin Allmann Updyke

Oh wow.

Erin Welsh

And analysis of these coprolites, cause we love our coprolites, shows that this person - I think this is so fascinating, like you get to see what people ate.

Erin Allmann Updyke

Were eating, oh my gosh.

Erin Welsh

Yeah. This person had ingested fish, snakes, bats, white-footed mouse, pocket gopher, and grasshoppers. And so this led the researchers to suggest that the oral route of transmission might've played a stronger role maybe in that area especially if triatomine bugs were directly ingested.

Erin Allmann Updyke

Yeah.

Erin Welsh

Yeah. So evidence of chronic infection in these prehistoric humans like with this megacolon in Texas has also been found in Peru and in Brazil in the forms of megacolon or cardiac lesions. So it seems pretty clear that humans became infected with *T. cruzi* basically as soon as they arrived in an area where it was circulating in mammals. And since that time the geographic distribution of the parasite, the dominant genotype, the transmission route, the vector species responsible, all of these things likely shifted as human settlement patterns changed, as housing construction changed and materials, and as cultural practices changed as well. But what didn't change and what remains true today is that there continue to be opportunities for infection. So the prevalence estimate that I mentioned in the mummies from the Atacama desert is pretty dang high at 40.6%.

Erin Allmann Updyke

Yeah.

Erin Welsh

And in the more recent mummies tested, like in the last 600 years or so, it was even higher at over 50%.

Erin Allmann Updyke

Whoa.

Erin Welsh

So people had to know about this disease, right?

Erin Allmann Updyke

Wrong.

Erin Welsh

Wrong.

Erin Allmann Updyke

Wrong.

Erin Welsh

Wrong. Yeah. I mean Chagas disease has been called the most neglected of the neglected tropical diseases.

Erin Allmann Updyke

Yeah.

Erin Welsh

And that is due possibly in part to its relative clinical invisibility.

Erin Allmann Updyke

Right.

Erin Welsh: Just like you talked about the acute stage when it is there, it doesn't necessarily have super distinctive signs or symptoms and it's not often severe. And so you just kind of get over it and then you forget about it, right?

Erin Allmann Updyke: Right.

Erin Welsh: And the chronic stage can go unnoticed for a very long time and it can then be attributed to other things or just like heart failure.

Erin Allmann Updyke: Right. Oh you have all these other risk factors for heart failure, you have heart failure. It's a normal kind of heart failure.

Erin Welsh: Right, right. It's not like leishmaniasis with its visible lesions or river blindness with the itching and blindness or dracunculiasis with the actual worm coming out of your foot.

Erin Allmann Updyke: Right.

Erin Welsh: And because of this relative invisibility there don't really seem to be many historical descriptions of Chagas disease prior to its discovery.

Erin Allmann Updyke: I'm not surprised about that.

Erin Welsh: Yeah. The triatomine bugs on the other hand do get some early mentions.

Erin Allmann Updyke: Ooh.

Erin Welsh: I've talked a lot on this podcast about what we can tell from the name of a disease or in this case the vector, the name of the vector. The name itself can tell us what it meant to the people using it, how it was perceived, the number and geographic spread of the names can tell us how widespread the disease was, and it can help trace the history. When did the name first appear? How often was it used? Did it increase in use? Etc. In the case of Chagas disease we don't have historical descriptions of the disease but we do have a long history and a long current list of names for the insect vector.

Erin Allmann Updyke: Oh yeah.

Erin Welsh: We have Vinchuca, a Quechua word meaning 'bug that lets itself fall', chinche, and many other nicknames that mean things like 'barber' or 'sucking blood', 'blood stealer', 'kissing bug', 'bug that dislikes the cold', 'big piercing bug', and so on.

Erin Allmann Updyke: (laughs) I like 'bug that dislikes the cold'.

Erin Welsh: Yeah. (laughs) In one of the chapters I read there's like a giant table showing these different nicknames and where they are used, it's a really, really cool table actually.

Erin Allmann Updyke: Yeah.

Erin Welsh: The most famous description of these bugs though, or at least the one that I saw referenced over and over, comes from none other than Charles Darwin.

Erin Allmann Updyke

What?

Erin Welsh

Yeah, in 1835. Okay. Quote: "At night I experienced an attack (for it deserves no less a name) of the Vinchuca, a species of Reduvius, the great black bug of the Pampas. It is most disgusting to feel soft wingless insects, about an inch long, crawling over one's body. Before sucking they are quite thin, but afterwards they become round and bloated with blood, and in this state are easily crushed."

Erin Allmann Updyke

That's really good but Darwin, the adults have wings.

Erin Welsh

Yeah! Well he wasn't like a famous naturalist or anything, right?

Erin Allmann Updyke

No, just like a minor naturalist.

Erin Welsh

Just minor, yeah. It was a side gig.

Erin Allmann Updyke

Isn't it thought he might have died from complications of Chagas disease?

Erin Welsh

Oh, well, well. Look who's jumping the gun now.

Erin Allmann Updyke

Oh! Look at me go.

Erin Welsh

(laughs) Yeah, so many people have retrospectively diagnosed Darwin with Chagas disease thinking that he was maybe exposed while on the HMS Beagle in like 1834-1835. And it is true that he did become quite sick while in Chile and ended up being bedridden for 7 weeks. And at the time it was thought to be typhoid but no one else on the crew got sick. He eventually recovered but later in his life he complained of palpitations, extreme fatigue, trembling, flatulence, and vomiting. And he was diagnosed first with hypochondriasis.

Erin Allmann Updyke

Are you serious?

Erin Welsh

Yeah. And like a nervous condition or whatever they called it back then.

Erin Allmann Updyke

Wow.

Erin Welsh

And then later with heart failure after experiencing anginal attacks accompanied by extreme exhaustion and digestive disturbances that forced him to abandon his work. But it also might not have been Chagas disease since at least some of these health problems that he complained about he had before he ever went to South America.

Erin Allmann Updyke

Oh.

Erin Welsh

So I mean it's possible.

Erin Allmann Updyke

Who knows?

Erin Welsh: Who knows? And other descriptions of the blood-feeding nature of the bug comes from Agustín Lizárraga, a Peruvian farmer who discovered Machu Picchu in the early 1900s before Hiram Bingham stole all the credit. I just really wanted to throw that in there because I didn't know that Hiram Bingham had stolen all the credit from somebody else but I should've guessed. And then there are some earlier descriptions of the bugs and even some that might hint at the disease by conquistadors although these descriptions I didn't even put in because they're pretty hand-wavy. Like one of them is like, 'Or it could be hemorrhoids.' And I'm like okay well those are kind of different.

Erin Allmann Updyke: (laughs) They are pretty different, yeah.

Erin Welsh: Yeah. All right but I jumped around a bit in time back in here so let's gets reoriented with things.

Erin Allmann Updyke: Okay.

Erin Welsh: Basically by the very early 1900s, although Chagas was probably quite prevalent across part of Central and South America and into North America, it seemed to be unknown entirely as a medical condition.

Erin Allmann Updyke: Wow.

Erin Welsh: But by 1921 all of that would change. Not only would it become well known across the world to infectious disease researchers but its discoverer became famous in his own right, earning both acclaim, he was nominated for a Nobel Prize twice, as well as criticism.

Erin Allmann Updyke: Wow.

Erin Welsh: Okay.

Erin Allmann Updyke: Ooh this is fun, I didn't know this.

Erin Welsh: Yeah, I think this is a very interesting story.

Erin Allmann Updyke: Okay.

Erin Welsh: And I'll get to why and I hope that your mind will be blown just like mine was.

Erin Allmann Updyke: I'm sure.

Erin Welsh: Okay. Carlos Chagas was born on July 9, 1879 on a coffee farm in Minas Gerais, Brazil. His father and two brothers died while Carlos was still young, leaving him to become head of the family. When he was old enough for college his mother urged him to become an engineer but he didn't pass the entrance exams and became very depressed until one of his uncles who was a physician was like, 'Hey, why don't you try for med school?' And so that's what he did. And in his time at med school he focused his work on malaria.

Erin Allmann Updyke: Okay.

Erin Welsh: And after graduating in 1903 he received an invitation from the man who would become his friend and mentor, Oswaldo Cruz.

Erin Allmann Updyke

Oh!

Erin Welsh

Yeah. To work at the Hygiene and Public Health Office monitoring malaria. And Chagas readily took him up on this since he needed a steady income to support his new family, like he had just gotten married, just had a kid. And when Chagas began working there he was not only starting his medical career at a unique time but also at a unique place. So around this time in the early 1900s, germ theory had been fully embraced and many pathogens and parasites had been described and were continuing to be discovered. Tropical medicine as a field was really starting to grow as imperialist countries struggled to develop the countries that they had laid claim to with many people dying of tropical infectious diseases. And for all its imperialist and colonialist beginnings, tropical medicine did mean looking at the whole picture of public health from the life cycle and habitat preferences of a vector to the epidemiological characteristics of a disease to the economic and productivity costs of these infectious diseases. It involved combining applied and basic research with an aim of prevention and control, not just descriptive knowledge building.

Erin Allmann Updyke

Right.

Erin Welsh

And Oswaldo Cruz and the institute he founded which was later to bear his name, the Oswaldo Cruz Institute, encapsulated this and then some. This institute placed the highest importance on the combination of research, education, and assistance. Like other tropical medicine organizations it integrated applied and basic research to solve problems. But unlike the others, Cruz wanted his institute to focus not just on the economic benefits of urban development for the colonialist countries or the big companies but also on the improvement of the lives of Brazilians, of everyone, by preventing infectious disease. And Carlos Chagas picked up this attitude from his mentor and it greatly influenced his career and the way that he viewed medicine. In the words of his son, quote: "For Chagas, science was valid only if it was directed toward the welfare of humanity."

Erin Allmann Updyke

All right.

Erin Welsh

I feel like those are pretty good words.

Erin Allmann Updyke

Yeah. Yeah, they are.

Erin Welsh

His first project under Cruz was to implement a malaria control strategy which was pretty successful in reducing the cases of malaria and also showing that a lot of transmission actually occurred within a home rather than outside as was previously thought.

Erin Allmann Updyke

Yeah.

Erin Welsh

His clinical background as a physician and his research background on vector-borne disease, it perfectly qualified him for this type of work. And soon he was assigned to a new, bigger project. A cross-country railroad to transport agricultural products, the Brazil Central Railroad linking Belo Horizonte to Rio de Janeiro, it was under construction but it kept getting delayed when workers fell ill during malaria outbreaks. Like big, bad outbreaks. In 1907 Chagas was called in to stop the outbreaks using the method that was most commonly employed at the time. Combat the vector, combat the disease. Essentially he was tasked with setting up research stations at the towns along the railroad ahead of the construction to identify potential malaria hotspots and then get rid of the mosquitoes.

Erin Allmann Updyke

Okay, cool.

Erin Welsh

And it was at one of these towns, Lassance, I hope that's how you say it, a small town on the São Francisco River where Chagas heard a chief railroad engineer describe a blood-sucking insect that was infesting the huts in the region and feeding on people while they slept. He called the bug 'the barber bug' since barbers were kind of like surgeons at the time, they did a lot of cutting and whatever. They did. And from this tidbit of information, Chagas pulled off the reverse triple discovery.

Erin Allmann Updyke

What? Reverse triple discovery?

Erin Welsh

Yeah. (laughs) So we've been doing this podcast a while which means we've gone through a heck of a lot of disease discoveries.

Erin Allmann Updyke

Yeah.

Erin Welsh

And it usually goes a little something like this: first a bunch of people get sick and their symptoms are described and classified into one illness.

Erin Allmann Updyke

Right.

Erin Welsh

Second, researchers begin digging around for the causative agent after the rise of germ theory and begin using that as part of diagnosis. And then third is usually when the route of transmission is determined, whether that means arthropod vector or fecal-oral, whatever. But what rarely if ever happens is that sequence in reverse.

Erin Allmann Updyke

I love this, that's fantastic!

Erin Welsh

And that is exactly what Chagas did, the reverse triple discovery.

Erin Allmann Updyke

Wow.

Erin Welsh

All right. I'm gonna read you a quote from Chagas.

Erin Allmann Updyke

Okay.

Erin Welsh

Once we heard of the blood-sucking habits of this insect and of its proliferation in human dwelling places, we became very interested in knowing its exact biology and above all in ascertaining if by any chance it were, as I immediately supposed, a transmitter of any parasite of man or of another vertebrate.

Erin Allmann Updyke

Oh my gracious.

Erin Welsh

So he found these bugs, was shown these bugs, and then was like, 'I'm pretty sure these probably, because they feed on humans, they must transmit a disease.'

Erin Allmann Updyke

Super logical. Honestly he'd been working with malaria mosquitoes forever. He's like, 'Bro, everything that bites you is gonna get you sick somehow, let's be honest.'

Erin Welsh

Exactly. It's like this discovery was the product of his training.

Erin Allmann Updyke

Exactly.

Erin Welsh

His bright mind but also the type of job that he was doing too and the way tropical medicine was being practiced.

Erin Allmann Updyke

Right.

Erin Welsh

It's definitely like of course it happened this way but also oh my gosh, it happened this way?

Erin Allmann Updyke

I know, yeah. Wow. That's cool.

Erin Welsh

It's amazing. So he tested his suspicion of this barber bug as a disease vector by dissecting its hindgut and examining it under the scope where he found trypanosomes. So he gathered up a bunch more bugs, shipped them off to Oswaldo Cruz, and asked him to feed them on monkeys. And he did. They got sick and Chagas then later named his parasite *Trypanosoma cruzi* after his mentor and friend Oswaldo Cruz.

Erin Allmann Updyke

You know what's so interesting Erin is it could've gone so differently, right? He could've found something that transmitted a virus that he never could have figured out or something that only infected humans, so he'd try to feed them on monkeys and it didn't work. Like there are so many ways that this could have not gone the way that it went. But it was like here's an obvious parasite that looks like not so dissimilar to malaria which I'm familiar with, let's feed it on a monkey. Does the monkey get sick? Sure it does, cause any mammal will. Like what?

Erin Welsh

(laughs) I know. I love it.

Erin Allmann Updyke

Yeah.

Erin Welsh

I think it is such a fantastic, fascinating story in the history of medicine.

Erin Allmann Updyke

I love it.

Erin Welsh

It's just so unbelievable but also totally believable.

Erin Allmann Updyke

Yeah, exactly.

Erin Welsh

Just like, what?

Erin Allmann Updyke

That's a good way to describe it. Unbelievable but totally believable.

Erin Welsh

Yeah. (laughs) And so at this point yeah, Chagas had identified a vector and a parasite that was at least somewhat pathogenic to animals or some animals but he still didn't know whether it was a disease of humans. For a couple years after first discovering the trypanosome, he looked for it in animals and humans all over and it took him a while but in 1909 he found it in both. First in a cat and shortly after on April 14th which was declared in 2020 by the WHO as International Chagas Disease Day.

Erin Allmann Updyke

Oh.

Erin Welsh: So on this date he found this parasite in a 2 year old girl named Berenice, the first described case of what would later be known as Chagas disease.

Erin Allmann Updyke: Wow.

Erin Welsh: And Chagas disease was named in fact by Oswaldo Cruz.

Erin Allmann Updyke: Of course it was.

Erin Welsh: Isn't that just really cute? I just think that's really nice.

Erin Allmann Updyke: He's like, 'I'll name the parasite after you.' 'Aw cool, I'll name the disease after you!'

Erin Welsh: (laughs) Yeah. I think it's nice. So Chagas wrote in his famous 1909 publication that Berenice had a swollen liver and spleen, hepatosplenomegaly, and swollen lymph nodes. She was febrile, she was anemic, she had edema and also he found circulating *Trypanosoma cruzi*. In this publication of the acute form of the disease, he also described the morphology of the trypanosome as well as its life cycle and its intermediate and definitive hosts.

Erin Allmann Updyke: Okay.

Erin Welsh: He described his attempts to culture the trypanosome, he described the course of infection, and so on. And over the next couple of years he continued to work on the disease, looking for it in more people in autopsies and better characterizing the acute stage of the disease as well as looking at chronic infection and long term consequences.

Erin Allmann Updyke: He just decided to do that? Or just because of doing autopsies was like...

Erin Welsh: I think probably doing the autopsies kind of led him along.

Erin Allmann Updyke: Yeah.

Erin Welsh: And then he got a researcher involved named Gaspar Vianna who was especially crucial in investigating some of the cardiac impacts specifically.

Erin Allmann Updyke: Okay.

Erin Welsh: But to me it's really impressive that Chagas was like, 'I found the acute stage,' and then was like, 'I wonder if there's a chronic stage to this.'

Erin Allmann Updyke: Yeah, yeah. Like I'm gonna keep going on this.

Erin Welsh: Yeah. And after this publication was released in 1911 which was more thorough about the parasite itself and the disease progression, it was like immediate success and attention for Carlos Chagas. Other researchers throughout South and Central America began looking for and sometimes finding the trypanosome in their areas and Chagas himself was awarded the Schaudinn Prize which was given out only every 4 years for the best work in parasitology and tropical medicine in the world.

Erin Allmann Updyke: Wow.

Erin Welsh

But all the success and acclaim came with an ample supply of haters, as it usually does. German microbiologist Rudolf Kraus took great issue with Chagas' claim that the disease was prevalent all across South America. Kraus, who was working in Argentina, had looked but had been unable to find any trypanosomes in any of the areas that he looked. And attacks also came from members of the Brazilian National Academy of Medicine who undermined his research and tried to discredit him. It's disappointing, I know.

Erin Allmann Updyke

Why? Like why?

Erin Welsh

So I was thinking about like he got in some ways so lucky, like you were saying.

Erin Allmann Updyke

Yeah.

Erin Welsh

There is always, with new discoveries, there is always resistance. There does have to be this sort of ping-ponging of, 'Well wait a second, we need to introduce some healthy skepticism into this.' And so maybe their attacks were way more personal than they needed to be but I do think at the time part of their skepticism or hesitance might have been reasonable considering also the fact that Chagas didn't get it all right in his first go. But I mean who ever does?

Erin Allmann Updyke

Yeah.

Erin Welsh

But he first thought it was the bite of the bug that transmitted the parasite.

Erin Allmann Updyke

Okay. Sorry, pretty reasonable.

Erin Welsh

Very reasonable. And then the French parasitologist Alexandre Brumpt soon realized it was through the feces of triatomines. But the other big thing, the big mistake or false association that Chagas made was that he incorrectly associated the disease with goiters which were really prevalent all across Brazil. Goiters being caused by an iodine deficiency. And so other researchers were finding people with goiters but without trypanosomiasis, they couldn't find the trypanosomes.

Erin Allmann Updyke

Yeah.

Erin Welsh

And so they were like, 'You're seeing something that we're not seeing.'

Erin Allmann Updyke

Yeah.

Erin Welsh

And I feel like the reverse story where those detractors, those haters have been right in other histories of disease where they're like, 'You're not seeing what you're seeing, it must be something else.'

Erin Allmann Updyke

Yeah.

Erin Welsh

Anyways it's the way history is written now.

Erin Allmann Updyke

Yeah.

Erin Welsh: And so some of these haters might have simply been jealous of his quick rise to fame and his ample success but some may not have wanted to recognize that someone not from North America or Europe had made such a monumental discovery.

Erin Allmann Updyke: That was gonna be my guess.

Erin Welsh: Yeah. So like I said earlier, Chagas was nominated two, two times, for the Nobel Prize. And in the second time he was nominated it was 1921, the Nobel Prize wasn't awarded to any scientist that year.

Erin Allmann Updyke: What?

Erin Welsh: And there was no evaluation, there's no record of evaluation of his nomination or his research or whatever by the committee.

Erin Allmann Updyke: What?

Erin Welsh: So it's a little fishy. Yeah apparently there's some drama in those early years about who got the awards and whatever which is unsurprising.

Erin Allmann Updyke: Yeah.

Erin Welsh: But as a result of all this negative press, Chagas disease was all but forgotten about for a short period of time, like a few years. Until physician Salvador Mazza from Argentina began researching the disease. His studies across Argentina which were conducted in the late 1920s found hundreds of cases of Chagas disease where Kraus had found none.

Erin Allmann Updyke: Okay.

Erin Welsh: Yeah. I think in one of the publications Chagas kind of hinted about like, oh well you might not really have the right technique for microscopy or whatever. And Mazza was the first to suggest that the trypanosome could be transmitted through blood transfusions which were slowly improving and becoming more accessible in the 30s and 40s. Mazza's work showing widespread prevalence again kicked things off for Chagas disease research as more and more researchers became aware that it was this tip of the iceberg type of situation. Increasing development, deforestation, and urbanization throughout the mid 20th century led to both this increase in disease prevalence as well as the construction of hospitals where the chronic manifestations of the disease and congenital transmission could be more easily studied, especially as technology improved to actually see what was going on inside, like with your heart and with megacolon and so on. Chagas' son, Evandro, followed somewhat in his father's footsteps and played a big role in uncovering the widespread and hidden nature of the disease. And the little girl, Berenice, Chagas' first Chagas patient-

Erin Allmann Updyke: Yeah.

Erin Welsh: Was found again at the age of 53 still with circulating trypanosomes but no sign of disease.

Erin Allmann Updyke: Oh good!

Erin Welsh: Yeah. She died I think at the age of 73 or 78 maybe, I think 78, with no relation to Chagas disease.

Erin Allmann Updyke

That's pretty good for being born in the early 1900s.

Erin Welsh

Yeah, 1907. Chagas himself became a huge figure in the history of Brazilian public health as the director of the Oswaldo Cruz Institute for 17 years and the head of pandemic influenza campaigns, the head of the Department of Health in Brazil, he discovered pneumocystis pneumonia and created a nursing school. He did a ton of work in his relatively short life, I think he died in his 50s.

Erin Allmann Updyke

Oh my gosh.

Erin Welsh

Oswaldo Cruz died at 44 of kidney disease.

Erin Allmann Updyke

Oh my gracious.

Erin Welsh

Yeah.

Erin Allmann Updyke

There's also a journal named after the institute.

Erin Welsh

Oh yeah, I read a lot of papers from that journal.

Erin Allmann Updyke

Yep.

Erin Welsh

I was like I know you as an institute and a journal, not as a human being.

Erin Allmann Updyke

Yeah.

Erin Welsh

It's fun to learn about you, nice to meet you. But not all Chagas disease researchers were like Chagas, not all of them cared about the wellbeing of the people that they studied. For example in an instance of medicalized torture in Texas, a researcher named Ardzoony Packchianian crushed some kissing bugs and smeared them into the eye of a black man in his 20s who was likely a patient at Austin State Hospital, formerly known as the Texas State Lunatic Asylum, just to study the progression of disease and how long this person would remain with circulating parasites.

Erin Allmann Updyke

What?

Erin Welsh

Yeah. So the person did show symptoms of disease and eventually they recovered and were declared trypanosome-free. But yeah, the study continues to be cited.

Erin Allmann Updyke

What?

Erin Welsh

I know. So Carlos Chagas recognized all the way back in 1909 the public health relevance of American trypanosomiasis but it wasn't until the 1980s that country-wide surveys were conducted using standardized protocols and a reliable estimate of the number of people infected and at risk could be even estimated. And those numbers were often shocking. I'm not gonna go through all of them but I'll throw a few out there. So from 20% in Bolivia to 20% of rural Chile and up to 50% in parts of rural Venezuela. Chagas was a much bigger problem than I think anyone had any idea about.

Erin Allmann Updyke

I feel like that's still true.

Erin Welsh

Yeah, definitely. And around this same time the HIV/AIDS pandemic revealed that *Trypanosoma cruzi* could be reactivated in immunocompromised people and prove to be a huge complication there. And this growing awareness of the enormous problem that Chagas disease poses did help lower the incidence of disease in some places, such as through the Southern Cone Initiative and other pushes for eradication and control. And the existence of the somewhat effective drug that's used, I think it's benznidazole.

Erin Allmann Updyke

That's close to right.

Erin Welsh

Yeah, which was introduced in 1966. These things also helped. But we're still a long way off.

Erin Allmann Updyke

Yeah.

Erin Welsh

But exactly how far off are we, Erin?

Erin Allmann Updyke

Oh, what a good question. Let's get into it right after this break.

TPWKY

(transition theme)

Erin Allmann Updyke

It's interesting, Erin, because despite just how - when you think about it - just how inefficient the transmission cycle really is in terms of trying to get the poop of this bug somewhere near a bite wound. The overall ecology of this disease is so complex with so many different wildlife and domestic mammal species involved. And in humans the infection can persist for so long that this is not only a very difficult disease to control but estimates of incidence and prevalence are also very difficult.

Erin Welsh

Right.

Erin Allmann Updyke

But we'll do our best here.

Erin Welsh

Yeah.

Erin Allmann Updyke

Estimates of incidence, the number of new infections annually, range from 0.1% to 4% of the population in endemic regions, so largely in Central and South America.

Erin Welsh

Wow.

Erin Allmann Updyke

Yeah, which is pretty high in and of itself.

Erin Welsh

Right. I mean if every year 4% of people are getting infected...

Erin Allmann Updyke

Yeah, yeah. But in a lot of places Chagas isn't even a reportable disease everywhere that it's endemic and it's often only diagnosed in the chronic phase and a lot of places don't have registries. So all of these are really just estimates. When we look globally it's estimated that between 6-7 million people worldwide are living with Chagas disease currently. And what I don't know, cause I see your face thinking, is does that mean 6-7 million people living with some amount of illness from Chagas disease or 6-7 million people living with *Trypanosoma cruzi* in their bloodstream?

Erin Welsh

Right.

| | |
|---------------------|---|
| Erin Allmann Updyke | And I imagine because that number is from the World Health Organization that that means people with some amount of disease. |
| Erin Welsh | Okay. |
| Erin Allmann Updyke | Okay. But what's worse than that number, 6-7 million people which is probably an underestimate, that's pretty bad already. But it's estimated that only 1-2% of those people living with Chagas disease have access to treatment. |
| Erin Welsh | I was gonna ask A) what is the treatment for chronic disease? And B) how much does it cost? |
| Erin Allmann Updyke | So once you get to chronic disease, what you're dealing with is whatever your disease manifestation is. So if you have heart failure from Chagas disease, you're treating someone for heart failure, you're not treating them for Chagas disease. |
| Erin Welsh | Right. |
| Erin Allmann Updyke | Right. If you have somebody with megaesophagus, you're treating them for megaesophagus. That's a huge part of the problem, right. |
| Erin Welsh | Right. |
| Erin Allmann Updyke | So you have to be able to find people before they have heart failure from Chagas. And like we've touched on, though historically this is a disease of poverty and of Central and South America and the southern part of the United States, we live in a globalized world and because of global migration this is a global disease. And like you touched on Erin, in non-endemic areas like Europe and much of North America, physician knowledge of the disease is seriously lacking and it's thought that cases are underdiagnosed by like 95% is one of the estimates that I saw. |
| Erin Welsh | That's horrifying but not surprising. |
| Erin Allmann Updyke | Right. Cause again if somebody comes in with heart failure, it's not gonna be the top thing that you think of as someone living in Europe or a lot of North America, like is this the underlying cause of your heart failure. |
| Erin Welsh | Right, yeah. |
| Erin Allmann Updyke | If we look at economics, and you know I don't really love talking about the economic part of it but I think it's important from a public policy perspective, Chagas disease is estimated to have a global economic burden of over 7 billion dollars annually. That's more than rotavirus, that's more than cervical cancer, that's more than Lyme disease. And results in an estimated over 800,000 disability-adjusted life years annually. Okay? |
| Erin Welsh | Yeah. |
| Erin Allmann Updyke | It's a big deal. |
| Erin Welsh | It's a huge one, yeah. |

Erin Allmann Updyke

Huge. So when it comes to research needs there's a lot of them, right. Like I said, there's a lot of parts of this from the ecology to the pathophysiology to treatments to vaccines that we just don't have enough information on. We also just don't have a great handle on prevalence. So there's a lot of room for investigation and luckily there's a lot of incredible people who are researching Chagas disease from every single angle. At this point, as far as I could tell in my research, there aren't any novel therapeutics that have made it very far in the research chain. There are a couple of different avenues for promising vaccine research both in preventative vaccines, so vaccines to help prevent the disease as well as therapeutic vaccines which would be something to help prevent the development of chronic disease. But as far as I could tell, these are all in pretty early stages of development and one of the biggest issues is funding. And then of course people are really starting to realize the impact of non vector-borne transmission routes such as congenital infection.

Erin Welsh

Right.

Erin Allmann Updyke

And how little we know about that. So suffice to say there's a lot of different research needs.

Erin Welsh

Oh yeah.

Erin Allmann Updyke

For that reason we wanted to talk to somebody who has done research on a lot of different aspects of Chagas disease from trying to better understand the dynamics of Chagas here in the US and involves citizen science which is so cool, to really nitty gritty molecular biology to better understand the vectors and the pathogen itself and so much more. So we wanted to talk to someone about all of these lingering questions that we have regarding Chagas. And for that we turned to one of our faves, Dr. Sarah Hamer.

Erin Welsh

All time faves.

Sarah Hamer

I'm Sarah Hamer, I'm an Associate Professor in the College of Veterinary Medicine and Biomedical Sciences at Texas A&M University. I'm a veterinarian and I lead a research lab on the ecology and epidemiology of infectious diseases.

Erin Welsh

Awesome, thank you so much for taking the time to chat today. I'm super excited to hear more about Chagas disease. So in this episode we have so far largely focused on the health impacts of Chagas disease on humans but many different animal species can also become infected with *Trypanosoma cruzi* including both domestic and wild animals. So what can infection with a trypanosome look like in these different animal species? And do some animals tend to be more negatively affected than others?

Sarah Hamer

That's a great question. So I think the first issue is you know this is a generalist parasite that can infect virtually any mammal and it's a generalist vector that will happily feed on lots of different animals, you know domestic, wild. So I think yeah, it makes sense to try to think about how does disease differ depending on the host that's infected. Sadly we don't really know about the impact on a lot of different wildlife species that are infected because it's hard to find them, it's hard to get money to study the clinical outcome or to follow them forward over time, it's hard to do that in nature.

The nice thing is from what we can understand, what we know, disease seems to look similar to what it does in humans. We know the most about the disease outcome in dogs, in nonhuman primates, and in humans just cause that's where the most amount of clinical attention has been paid. So just as we see in infected humans, what we see in these infected animals is that there can be a subpopulation of infected animals that might not ever develop signs of the disease. They might remain asymptomatic for life. So that's a very good thing. But there is some percentage, some unknown percentage of infected animals that will develop disease, usually heart disease, and depending on where the parasite affects the heart, we might see different outward manifestation of the infection.

So just like humans we can see inflammation, fibrosis of the heart depending on exactly where the parasite localizes in the heart. This can lead to acute problems, this can lead to chronic problems in the animal, especially with fibrosis or heart failure, we see sudden death. Often young dogs can die suddenly from this infection. We're working now to try to figure out if there's an infected animal, what are some ways that we can predict the outcome of infection. Is this something we need to be worried about vs is this something that the animal will be able to live with this infection for life and we don't need to be as worried about it.

Erin Welsh

Awesome, yeah. That is really interesting that you might be able to try to figure out who is going to be able to live with this long-term vs those that might not be. And so since some animals can act as reservoirs for *Trypanosoma cruzi*, they can of course have a big impact on the transmission cycle of Chagas disease and then the risk of exposure to humans. So let's start with the domestic side of things. Which domestic animals play a role in the infectious cycle and what does that role look like? And are there some domestic animals that contribute more than others to the risk of exposure for humans?

Sarah Hamer

Yeah, so when we think about domestic animals and Chagas disease, the main domestic animals that come to mind would be our dogs and cats, the most commonly owned pets here in the United States and elsewhere. And both those species can play roles in the ecology and epidemiology of Chagas disease. We know most about dogs, canine Chagas disease has received far more veterinary attention than feline Chagas disease. But what I'd like to start by saying is that there's no evidence that infected dogs or infected cats pose a direct transmission risk to people. So even if you knowingly or unknowingly own a dog that's infected for example, that sort of direct risk, dog to human transmission hasn't been shown.

Instead the role that infected dogs might play is that they could potentially infect kissing bugs that feed on them and then those kissing bugs that are around the home could be a source of infection to other animals or to people. So when we think about domestic animals and their role as a reservoir, by 'reservoir' here we mean that it's an animal that not only gets infected but it gets infected and can kind of sustain that parasite in its body and then serve as a source of infection to another animal or in this case to a vector that's feeding on it. And dogs can certainly play that role. It's actually really hard to figure that out though, it's not as simple as just figuring out if an animal's a reservoir by taking a blood sample and doing a molecular test and yep, the parasite's there, it's a reservoir.

Instead the approach that we've used in our research settings at least to define the role of dogs as reservoirs is that we can sample their blood and then bring that blood to our kissing bug insect colony that we have on campus. And then we can feed the blood from the dogs to clean insects in a very controlled environment. We can monitor those kissing bugs for infection to see if they become infected and will shed the infection in their feces. We can do that days, weeks, or even months after they've been fed this potentially infectious blood meal. So it's through some really neat techniques like that that we can begin to define who are the important reservoirs in domestic environments or in wild environments and that helps us understand the ecology of this disease better.

Erin Welsh

That is fascinating. Oh my gosh, a little colony of clean kissing bugs and then feeding them blood. That's really cool.

Sarah Hamer

Yeah, it's a unique resource that we have for sure. People have mosquito colonies and tick colonies but this kissing bug colony is pretty unique and it's definitely opened the doors for research.

Erin Welsh

Yeah, wow, amazing. Wow. So I wanna ask you a little bit more about some of the research that you do, in particular your incredible citizen science or community science projects and what they have told us so far or what they can tell us about the landscape of Chagas disease risk in Texas.

Sarah Hamer

Yeah. So back in 2013 we started a big community science program where we intended to provide a lot of good material for the public about kissing bugs and about Chagas disease and in return, if members of the public happened to see or find kissing bugs in their home, on their property, in their dog kennels, they could safely collect these insects and then submit them to our lab for part of our research. So this really started out of desperation because we were out doing fieldwork and these insects are really hard to trap using standardized traps, manual fieldwork to find them can be pretty labor intensive.

But we were trapping on these Texas ranches and other areas and the landowners would tell us, 'Oh yeah, I've seen those insects before. I captured a couple of those, I saved them.' They might have them in an old pill jar in the freezer. And so it was really through that that was the start of our community science program. And it's definitely a two-way street, we wanna provide a lot of good info, we do that through our website, through a smartphone app, through printed brochures and outreach seminars that we give. And then in return since 2013 we've received over 8000 kissing bugs from people in 27 different states and they've submitted these insects to our program and we can learn a lot.

And basically at the state level this community science program has replicated what's known of the historic distribution of kissing bug in the United States and has provided just a wealth of great material for our research program. So from the community science program we've learned that on average it's just over 50% infection prevalence of these insects. So of all the insects that we've received from community members that have submitted them to our program, we will dissect them, take their gut material out, do DNA extractions and then try to figure out if they're infected with the parasite or not. And we've found over 50% of the adult insects are infected with *Trypanosoma cruzi*. So pretty high infection prevalence.

And then furthermore we've learned that there's two major genetic variants of the parasite that we find in kissing bugs of the United States and we're kind of mapping out those genetic variants and trying how to figure out if there's different health consequences when people or animals are infected with one type or another. But the most exciting thing I think that we've been able to do with these community science submitted kissing bugs is what's called a blood meal analysis where we can take an individual insect and figure out what has it fed upon, what type of blood meal did it get from what species. And this is really important for not just understanding the ecology of the disease but trying to open the doors for management. Because if we can figure out what types of animals are important for feeding kissing bugs and maintaining their populations, then maybe we could try to manage those species so they have less contact with the vector.

So just a glimpse of some of our data from blood meal analysis of these community science kissing bugs, we find overall about half of them have evidence of feeding on a dog. And that makes sense because we know that a lot of these bugs submitted by the public are actually found in dog kennels or in areas where their dogs sleep, a lot of people submitting bugs will report that they own multiple dogs. So that makes sense. We also find that kissing bugs have fed on cats, chickens, tortoises. A lot of it is depending on the habitat where they're found, whatever the most abundant host is there, that's what they're gonna feed on. Like kissing bugs collected from a chicken coop, they're gonna feed on chickens. But we also get some exciting observations like tigers, that was found from some bugs that were submitted from the local zoo, so it makes sense that that host is available and then the bugs will happily feed on it.

And two of my favorite observations was an elf owl, we found evidence of a kissing bug feeding on the elf owl which is the world's tiniest owl and this was a bug that was collected by a community member from Big Bend National Park where these elf owls will nest, so that was pretty neat. And then a more recent one was our results from blood meal analysis was a peach-faced lovebird and we thought, 'Lovebird?' This isn't a wild species where this insect was submitted from so we wrote back to the submitter and we said, 'We're trying to make sense of this DNA sequence that we got.' And she wrote back immediately and said, 'That's my pet lovebird that I have in a cage in the house.' So this technique can really open our eyes for just how flexible these kissing bugs can be in what they feed on. And this was all enabled by our community science program.

Erin Welsh

That is incredible. 8000, first of all, and also feeding on a tiger? That's so cool, I never would have thought. I was like okay, what is the coolest animal I could think of, like the most surprising animal I could think of in terms of kissing bugs? And a tiger definitely is shocking and very cool.

Sarah Hamer

Yeah and over time it's data like this that will help researchers piece together not just the feeding patterns of the insect but if we can couple that with what animals are infected and what insects are infected, we can just piece together these transmission networks and I think that's gonna be really exciting for opening the doors for management.

Erin Welsh

Yes, absolutely. And so on the note of the fact that these kissing bugs feed so many different species of animal, I kinda wanna shift to now talk about the wildlife and the sylvatic cycle of these bugs. And so humans might not have as much contact with wildlife as they do with domestic animals but many wild animals can still increase the risk of Chagas disease or the prevalence of the trypanosome in certain areas which then might impact the risk to humans. So which wildlife species are considered the most important reservoirs? I know this changes a lot geographically as well but are there some more than others that seem to play the largest role? And I also wanted to kind of ask you about how things like deforestation and land use change is impacting Chagas disease in wildlife and then thus exposure to humans.

Sarah Hamer

So across the southern United States where kissing bugs are endemic, there have been a lot of different infected wild animals that have been identified but in terms of the key species that are most likely playing that role as reservoirs, infecting other kissing bugs and kind of perpetuating this transmission cycle in nature, some of the key species that have emerged include raccoons, opossums, armadillos, woodrats, coyotes, to a lesser extent other rodents or bats. But very little research has been done to really rank their importance to figure out what is the exact wild species that's the most important reservoir in this area or another area.

In terms of your question about land use change and deforestation or other types of land use change that is occurring, of course we know there's some pretty cool and compelling stories from different vector-borne diseases that would say that certain types of deforestation might really increase transmission, for example the Lyme disease system. I think it's a little premature to understand exactly how deforestation or other land use change is likely to impact the ecology of Chagas disease.

These triatomines, they're not just found in sylvatic or natural environments or rural environments, we also regularly find them in urban areas. For example, lots of collections from San Antonio, Dallas, Fort Worth, some of these major urban cores here in the South. They're flexible in where these different kissing bug species can thrive but certainly if we have changes to the landscape like deforestation, that might make that area more or less attractive to the raccoons or the opossums who really can thrive in small forest fragments adjacent to human dwellings. And so maybe if we're changing the landscape in a way that makes it more attractive to some of these medium-sized mammals, then we could have even more of these reservoirs across the landscape that could increase transmission risk. But we can imagine scenarios where the opposite could be true as well.

Erin Welsh

Yeah, it's such a complex system, it's a theme that we've hit on so many times during this episode is that there are just so many moving parts at play and so it makes sense that there's not a clear path forward or a clear prediction as to things like climate change, things like deforestation, land use change, and what impact they'll have.

Sarah Hamer

Yeah.

Erin Welsh

Yeah. So what do you see as the biggest challenges in the control of this disease?

Sarah Hamer

Yes. There are two big, grand challenges that come to mind when I think about the control of Chagas disease. The first is just simply that this is a sylvatic disease and by that we mean it's associated with these vectors that are out in nature interacting with a lot of different members of the wildlife community. We talked about how the insects will happily feed on all different sorts of critters, the parasite can infect virtually any mammal species. So it's sylvatic and it involves a lot of players in the transmission cycle. So it's not as simple, not that it's simple but you know when we think of a different vector-borne disease, human malaria for example, main reservoir would be humans, certain mosquito species. In comparison, here we've got just dozens of species that need to be considered in the management of this disease in nature. So it's sylvatic. The second big challenge that comes to mind is just this relative lack of awareness, lack of medical awareness, lack of veterinary awareness for Chagas disease, *Trypanosoma cruzi*, this is neglected from medical attention, it's neglected from research communities.

And so typically especially when we're thinking about Chagas disease in the United States, it's quick to conclude, 'Oh you know this is a problem elsewhere, this is a problem across Latin America.' But we've got these endemic kissing bugs and we've got endemic infected wildlife and we have spillover transmission to humans and to our domestic animals that are causing big problems. But because there's not more attention, we're not testing more. So we don't have a good understanding of really, especially from the veterinary perspective, how many animals are impacted, what species. What are the impacts for their health? And without those numbers to show just how many animals are impacted, then it's hard to convince big granting agencies to put more money towards this problem. And so I think that the overall lack of awareness is one of the biggest challenges for this disease.

Erin Welsh

Yeah, absolutely. So on that note, could you mention the name of the app and the community science project that you're talking about in case listeners want to get involved or want to find out more about the work that you're doing?

Sarah Hamer

Sure! Our community science website is kissingbug.tamu.edu. And from that website you can learn all about kissing bugs, Chagas disease, wildlife reservoirs, dog infection and so forth. But importantly this is also the portal from which you can contribute your observations and insect specimens to our program. So there's instructions there on how to safely collect these insects and submit them to our program. And the same would be true, our app is available for Apple and Android from the iTunes store and Google Play and you can download that there and it has the same capability as the website.

TPWKY

(transition theme)

Erin Allmann Updyke

Thank you so much Dr. Sarah Hamer for talking with us.

Erin Welsh

It was absolutely thrilling and enlightening and wonderful. And you remain a hero to us.

Erin Allmann Updyke

A true hero.

Erin Welsh

Should we do sources?

Erin Allmann Updyke

We should do sources.

Erin Welsh

Okay. So I'm gonna shout out... I think I have more sources for this than any other episode.

Erin Allmann Updyke

Wow.

Erin Welsh

Yeah. I just couldn't stop. I'm gonna shout out a few. So the first one is 'The Kissing Bug: A True Story of a Family, an Insect, and a Nation's Neglect of a Deadly Disease' by none other than Daisy Hernandez, go check it out. And a couple articles I found super helpful were by Aufderheide et al from 2004, 'A 9,000-year record of Chagas' disease.' By Clément et al 2020, 'Out of Africa: The origins of the protozoan blood parasites of the *Trypanosoma cruzi* clade found in bats from Africa'. And by Steverding from 2014, 'The history of Chagas disease'. And a whole bunch more that I'll post.

Erin Allmann Updyke

I also had probably not as many as you, Erin, but there was a number of really great comprehensive reviews. A couple in *The Lancet*, one in the *New England Journal of Medicine*. There's actually a whole bunch of really nice reviews. We'll post a list of all of our sources from this episode and every single one of our episodes on our website thispodcastwillkillyou.com.

Erin Welsh

Thank you again so much Daisy for taking the time to chat with us, we truly appreciate it.

Erin Allmann Updyke

Yeah, thank you.

Erin Welsh

Thanks to Bloodmobile for providing the music for this episode and all of our episodes.

Erin Allmann Updyke

Thank you to the Exactly Right network of whom we are very proud to be a part.

Erin Welsh

And thank you to you, listeners. We appreciate you so much to keep tuning in episode after episode and listening to us talk on and on about pathogens and parasites and metals and genetic diseases and all of the things.

Erin Allmann Updyke

Yeah. And a special shout out to our patrons, we love you guys.

Erin Welsh

Okay well until next time, wash your hands.

Erin Allmann Updyke

You filthy animals!