

Prevalence of Chagas Disease among Adults, United States

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Caryn Bern, a professor of epidemiology and biostatistics at the University of California, San Francisco School of Medicine. We'll be discussing the prevalence of Chagas disease in adults in the United States.

Welcome, Dr. Bern.

[Caryn Bern] Thank you, Sarah.

[Sarah Gregory] Chagas disease is not one we hear a whole lot about. What is it?

[Caryn Bern] Chagas disease is caused by parasites—a one-celled parasite, a protozoan, so that's like malaria or sleeping sickness. It's a vectorborne parasite, it's carried by an insect vector called a triatomine, and it's also a zoonosis which means it affects non-human animals as well as humans.

[Sarah Gregory] And how is it transmitted?

[Caryn Bern] The transmission cycle basically has three parts. It has the parasite, which is transmitted by the vector to mammals (mammalian infection hosts), and that includes humans. Because it's a zoonosis, that means that many other animals are infected, and humans are not even necessary to the transmission cycle. But what happens is that when the vector takes a blood meal—so, sucks blood from one of these mammalian hosts—it may pick up the parasite if the mammalian host is infected. The parasite then develops inside the vector, and the next time it takes a blood meal, the parasite is actually in the feces (in the stool) of the vector. And in order to take as big a blood meal as possible, it will actually defecate (it will deposit feces) while it's taking the blood meal so that it empties its gut and can take more blood. The parasite is in the feces, and then it can enter through the bite wound. And so, that will complete the cycle. The parasite enters a new host and infects the new host.

[Sarah Gregory] You sent me a video of this process in live action. I mean, a real bug doing this...it was truly horrifying. I sent it around to the rest of the *Emerging Infectious Disease* journal team, and we were all.... goodness.

How common is it in the United States?

[Caryn Bern] When you say, "How common is it?", I think we have to think about the natural cycle in non-human animals and vectors, and then we have to think about what happens in humans. And so, as I said, humans are not necessary to the transmission cycle. And the transmission cycle between non-human mammals (many, many different species of mammal) and the vectors is actually quite common everywhere from about the middle of the United States down to Chile and Argentina. So the Americas, we're talking about the Americas. There's actually a cousin illness in Africa called sleeping sickness (African trypanosomiasis), so the kind of cousins that probably separated tens of millions of years ago. But Chagas disease is only...only has its natural cycle in the Americas. And it's actually quite common.

So common mammalian hosts in the United States include raccoons, various different rodents (especially in the West), possums, and dogs can get infected. We think actually in non-human

mammals that a lot of the infection may occur when the animal eats a bug. Because these are pretty big bugs, they're like an inch long. So it's kind of a mouthful if you're a rodent or even potentially a dog. And that's actually a more efficient way of infecting the mammalian host than what I described with the defecation of the vector, and then the feces has to get into the bite wound or into the eye. It can actually go through the eye (the conjunctiva). Yeah, it sounds really gross, but those of us who work in this field actually find it quite fascinating because it's just a really interesting story about the adaptation of parasites to the vector and to the host.

So what we call enzootic cycle (the cycle in non-human mammals and vectors) occurs, as I said, across the United States and all the way through continental Latin America. And it's fairly common. So in rodents in the west, you may have 20% infection rates of the parasite *Trypanosoma cruzi*. In raccoons in the east, it may also be 25%. Once a vector or mammal becomes infected with a parasite, it's actually lifelong. In humans, if you're treated successfully, then you can get rid of it. But otherwise, that person or dog or raccoon is infected for the rest of their lives. So you can see it's actually quite a big reservoir of infection to maintain the parasite. So it's an adaptive cycle for the parasite.

[Sarah Gregory] Can people get this from other mammals? Could I get this from my dogs?

[Caryn Bern] No, you can't. Actually, having an infected dog is essentially no risk to you, it is a risk to the dog. But the parasite actually needs to go through that cycle within the vector in order to infect its next host. So no. An infected person is not really a risk to another person who is susceptible, with one exception. So it can be transmitted from mother to fetus, and so there is congenital transmission. Although it's the exception rather than the rule. But no, an infected person is no risk to another infected person. An infected dog is no risk to a person.

[Sarah Gregory] Where do we see most cases in people, then, in the United States?

[Caryn Bern] In the United States, there are two sources of the infections that we see, what we call "prevalent infections" (so, existing infections). By far the largest is Latin American immigrants who were infected in their home countries. And that's because the rate of infection is far higher in parts of Latin America than it is in the United States. And then, at a much smaller scale, there are people who become infected in the United States. But those numbers are very small. We're not really very sure, because there hasn't been a lot of study of this, but probably the highest in the southernmost Texas, the southeast, and the southwest. But still, we're talking...locally acquired infections, we're probably talking in the hundreds to thousands, low thousands. Whereas among Latin American immigrants, we have now published a new estimate that there's close to 300,000 infected Latin American immigrants, most of who don't know they have an infection.

[Sarah Gregory] Let me understand this. Other than passing from mother to embryo, people cannot give it to each other. Is that correct?

[Caryn Bern] Essentially, that's true. The exceptions to that would be a blood transfusion or an organ transplant. But this is a parasite that in someone who has chronic infections, which is essentially almost everybody aside from the infants who are born with Chagas disease who are in the acute phase. So in the acute phase, the parasitemia level is high, so there are a fair number of parasites in the blood. But that only lasts one to two months. And after that, the person (or the animal, for that matter) is in the chronic phase, and there are actually very few parasites in the blood. So even through blood transfusion, it's not very common to transmit the parasite from an

infected donor. It looks as though the risk from red cells is very low, for example. And the number of actual transfusion-associated infections, I'd have to look it up to be absolutely sure, but I think it's less than 20 in the United States. Organ transplants, also. Most organ transplants, even from an infected donor, don't transmit. But some of them do. And again, we're talking about a handful over the past 20 years. So in that sense, it can be transmitted from one person to another person, but it actually is a very rare event. But if you're living with someone who's infected... no, you're not at risk from that person.

[Sarah Gregory] How dangerous is it? What kinds of health problems does it lead to? And are there specific gender or populations that are more susceptible, for some reason?

[Caryn Bern] During the acute phase, people may feel ill. They may have a fever, they may have some lymph node enlargement. It's kind of like mono or something like that. And that goes away when the immune system kicks in and controls the parasite. Those acute symptoms go away, most people never realize that what they had was Chagas disease. And then, the person is asymptomatic. And the most common natural history is they're asymptomatic for the rest of their lives. So about 70% of people who have infection never develop symptoms at all, and they never even know that they were infected. But about 20 to 30% of people with the infection will go on to develop heart disease, and that's the main disease (the main syndrome) that's associated with infection with the parasite *Trypanosoma cruzi*. But it generally occurs decades after the original infection.

So someone may be infected as a child in, say, Mexico or El Salvador or Bolivia, which has actually the highest rates in the world, they'll be fine for 20, 30 years. And at the age of 35 or 40, they may develop arrhythmias—they may develop alterations in their heart rhythm and in the conduction system of the heart. That's usually the first thing that occurs. And then, they may not even know about that, or they may know about it. And at that point, they may or may not be diagnosed. And then it may go on to progress to actually congestive heart failure—so, someone who has an enlarged heart, difficulty breathing, and so on. And that usually takes another 10 to 20 years. And so it's a very slow process. And again, as I said, it only occurs in about 20 to 30% of people. In terms of who is more at risk, it appears that males have a higher risk of developing heart disease than females. That's true of most forms of heart disease, not just Chagas disease, and we don't really know why that is.

It also appears that people who are living in an area where they continue to be exposed to the parasite are going to be at higher risk for developing heart disease. So if they've left the area that has a lot of exposure to the parasite, then they may be at lower risk for developing heart disease. But we know that there are plenty of people in the United States who have Chagas heart disease, because there have been studies now in Los Angeles and New York looking at people with heart disease who have risk factors (in other words, they're coming from Latin America). What we find is that up to 10 to 15% of those people in Los Angeles may actually have Chagas heart disease without knowing it—people who have congestive heart failure and are from a Latin American country. So we know this is occurring.

[Sarah Gregory] Is there a test for it? Can I go to my doctor and say, "Okay, I was in Mexico 25 years ago and I got bit all over by some bug. Can you look for this?"...which is true.

[Caryn Bern] Yes. You're actually relatively unlikely to know that you were bitten by triatomines, by these vectors, because they generally do it when you are sleeping and you don't know it. And as we talked about already, it's not the bite that transmits the infection. And

so, the risk to travelers is actually incredibly low. There have been a total of only two reported cases of Chagas disease in travelers from North America who went to Latin America, and one of them was there for 6 months, and the other actually was diagnosed because she realized when her eye swelled up (which is one of the few specific symptoms you can get during the acute phase) that what she had was Chagas disease.

So first of all, first message—the risk to travelers is extremely low. People who are at high risk are actually people who are living in rural housing, usually adobe or mud housing, because the vectors can live in the walls of the house. And so, when I said Bolivia is the place with the very highest prevalence, it's because there are many rural villages in Bolivia where people are still living in adobe housing or what's called tabique, which is actually housing where it's made of poles and then handfuls of mud. And so, when there are lots of cracks in the walls, that's where the vectors can live. And there's a vector in Bolivia that's very well adapted to living in the walls of human dwellings. And so, in those villages, you've got very high rates of infection in people. For you to go to Mexico or Latin America in general and stay for a few weeks and stay in a hotel, your risk is essentially nil. So yes, you could go to your doctor. One of the issues is your doctor may not actually know how to go about diagnosing it, because he or she may not have seen it much (or at all). There is a simple blood test, but it actually takes testing blood by two different tests, and these are called serologic tests. They're not direct tests for the parasite, they test your antibodies to the parasite. And that's actually not an uncommon way of diagnosing many infections. So for example, Lyme disease is diagnosed that way. But you need to get... usually what happens is they will send your blood to one of the standard commercial labs where they will do a single test. If that's negative, that's the end of it. If it's positive, they'll then send serum to the CDC who will do one or two more tests just to make sure, because we want to be very sure that it's not what we call a "false positive". Because you do get false positives on the serological tests.

[Sarah Gregory] For people who do have it, how is it treated (if they know they have it)?

[Caryn Bern] There are two drugs. They are drugs that, for the most part, are not used for other diseases. The one that we use most commonly is called benznidazole, and then the other one is called nifurtimox. And nifurtimox is also used for sleeping sickness. Benznidazole is not used for anything except Chagas disease. These are both FDA-licensed drugs, and those licenses are actually quite recent even though the drugs have been around for 50 years now and have been used in Latin America for 50 years. The problem with the drugs is that, especially in adults, they have a fair number of side effects, and it is quite a long course of treatment (usually 60 days). And so, not everybody can tolerate the drugs. And so, you really need to be treated by a physician with very close follow up, and usually in coordination with physicians who have experience using these drugs. We've actually set up what's called the US Chagas Disease Providers Network, which is a consortium of about 60 physicians and other healthcare providers who have an interest in Chagas disease (and many of us have experience treating Chagas disease). CDC also offers guidance in the use of both the diagnostic tests and the drugs. So your physician can always call CDC to get guidance and to talk to someone who's got some expertise in the treatment of Chagas disease.

[Sarah Gregory] Though rare, 20% or so cases isn't a lot, but if you do have it, it sounds like it is important to catch it early.

[Caryn Bern] Yes, very much so. The earlier in the course of infection that we catch it and treat it, the better the chances are first, that you'll actually cure the disease, and second, that you'll prevent any kind of sequelae...any kind of disease from the infection. Especially this heart disease.

[Sarah Gregory] You used several different data sources to do this analysis. Can you tell us about those?

[Caryn Bern] Sure. So in the past, there's been a couple of estimates of the prevalence of the infection (*Trypanosoma cruzi*) in the United States. And in both cases, this was done using estimates of the number of Latin American immigrants in the United States and the rate of infection in the countries that those Latin American immigrants came from, and those data were coming from. So the census data for the immigrant numbers and data from the World Health Organization for the prevalence of infection in the countries of origin.

So we did something quite similar this time, but we tried to refine it by using a couple of additional data sources. First, we used three different surveys that have been done in US resident populations in Los Angeles, Boston, and the Washington, D.C. area in recent years since the last time these estimates were made. And those we think are probably closer to accurate per US Latin American immigrant populations in terms of the estimates of what the prevalence of infection will be in the immigrant populations to the US, since Chagas disease rates vary quite a bit within countries. And so, it may be that, for example for Mexico, depending on which part of Mexico people are coming from, they may have a higher or a lower rate. So we feel that the prevalence estimates we used are probably a bit more accurate.

But secondly, we were able to make estimates by age. And we did that by using the age-specific prevalence from these surveys that I described, because Chagas disease rates go up with increasing age, in part because it's a lifelong infection (so you're accumulating infections), but also because there's been a lot of effort to control the vector in Latin America. And so, rates of transmission have been going down over the last 30 years. So we wanted to use this age-structured estimates. And then we used something called the American Community Survey. The American Community Survey is part of the US Census, where they do a survey every year of a percent of respondents to the census in order to get much more detailed data. And those data are more detailed in terms of both of where people have come from and also where exactly they are living. And so, that allowed us to make geographic estimates.

And so, we were able to make maps of the United States in order to show where we would estimate that there are more people likely to have Chagas disease based on these geographic locations. The geographic locations are not something you would recognize. They're called public use micro-areas, and the reason they do that is in the American Community Survey is to maintain confidentiality. And so, the PUMAs (the public use micro-areas) each contain about 100,000 people, and you can map those onto a map of the United States. Which is what we did. And if you look at our paper, there's actually an internet link there to our maps, and there are three different maps. There are maps where you can click on an area, you can zoom in, you can see how many cases of Chagas disease we think exist within that PUMA, and we also have percent's... what we estimate to be the prevalence (the percent) of infection among the entire population of that PUMA and among the Latin American-born population of that PUMA.

The results are not that surprising, because if you know something about the demographics of the United States, you know that there are areas that have large percentages of people who are born

in Latin America. They may have come 20 or 30 years ago to the United States, but that was what we based our maps on and our major estimates.

[Sarah Gregory] Okay. Is there more you have to say about why it is important to know these demographic and geographic data?

[Caryn Bern] Yes. So actually, this study grew out of a conversation that we had with some of the people in the US Chagas Disease Providers Network. So we were talking about where we really needed more data and where we needed to try to target through health education for healthcare providers, because we know that one of the issues in the United States is that many healthcare providers... we're not taught about Chagas disease in medical school. And they're not taught about Chagas disease in general in their continuing medical education. And we wanted to try to fill some of those gaps. There are a lot of efforts along these lines.

And so, one of the questions that came up was where should we be targeting these efforts? Where should providers really bear in mind that they may be seeing Chagas disease? So what we wanted to do was to have granular maps so that a physician or another healthcare provider could look at their catchment area and say, "You know what, I should really be looking for Chagas disease in my area". So that was really the kernel that started this whole effort.

[Sarah Gregory] You touched on earlier mothers passing it to embryos or fetuses. Can you tell us a little bit more about that and how that would work?

[Caryn Bern] Sure. So it's probably fetus and not embryo, and it may actually occur at the time of birth. We don't actually know. What we do know is that in studies in places like Bolivia—so, studies that are done in areas that have a lot of Chagas disease—about 5% of births to women who are infected will result in an infection in the infant. It may or may not be picked up at the time of birth, it may be picked up a month later. That's why I say, "could happen" during the birth process, because there's blood that's exchanged during the birth process. The placenta is actually a pretty good barrier to *Trypanosoma cruzi*. The fact that 95% of births to women who are infected do not end up in infection in the infant is actually pretty impressive. It's actually a much lower rate of transmission than, for example, HIV in the days before antiretroviral therapy was used in pregnant women.

One of the problems that we have is that neither of the drugs that we use can be used in pregnant women. There is simply not data to say that they are safe in pregnancy. So we can't treat the woman if she's diagnosed when she's already pregnant. And so, the way that is dealt with in a place like Bolivia is that there are programs where the program mandates that in areas of Bolivia that have a lot of Chagas disease, every woman will be tested for Chagas disease, usually actually during pregnancy or even at the time she comes in to deliver. And then if she's positive by the serological test, they will then look for the parasite in the baby. And ideally, you want to look at the time of birth, you want to look at about one month, and you want to look at nine months (or nine to 12 months). And the reason you need to do that nine to 12 months test is because in the first nine months of life, if you do serological testing, you're picking up the antibody from the mother, because IGG passes the placenta.

So you have to look for the parasite. And the tests for the parasite are not as easy and not as sensitive as serology is. By nine months, usually the maternal antibody has decayed, and you can actually look for the baby's antibody. So you can see it's a pretty complicated program and is fairly difficult to get good follow up rates at nine months. Treatment in infancy is incredibly safe

and almost 100% effective. So we really want to pick it up in the baby, because we know we can cure it in the baby. And then, usually you want to treat the mother after she's finished breast feeding. Because, again, we don't have data to say that it is safe to use it in breast feeding women (although, it probably is). We also know that women who are treated prior to their pregnancy are at least 95% less likely to transmit to their infants. And so, there are a lot of programs in higher income Latin American countries (like Argentina) to try to treat, essentially, all children who are infected before they would even think of becoming...hopefully, before they think of becoming pregnant.

There have actually been a couple of studies in the United States—they're modeling studies, they are cost-benefit studies—that suggest that it really would be cost-beneficial and cost-effective to screen women who have risk factors. But so far, there's no large-scale program, and it is fairly expensive to do this because the rates in young women are quite low, you have to screen a lot of women to pick up an infection.

[Sarah Gregory] Briefly, is there anything else about the study you'd like to tell us?

[Caryn Bern] Yes. I'd like to talk a little bit about the estimates we made for locally acquired infection in the United States. As I mentioned earlier, we know that there is what we call the "enzootic" cycle, so the cycle between non-human mammals and the vectors in the US. And we've got vectors all across the southern half of the United States. And we know that people become infected in the United States, but we think it is quite rare. So we started... in the United States, we started screening the US blood supply in the year 2007. Before that, there had been six or seven locally acquired cases reported between 1955 and 2006. And so, that's one of the reasons we say it's quite rare in the United States. And usually those were picked up because either a vector was found, or the person had acute infection.

Starting in 2007, almost the entire US blood supply was screened for infection using similar serological tests to the ones that I described earlier, where they are looking for antibodies. And over the course of the last 15 years, there have been about 2,400 infections picked up. And about 3/4 of those, at least, were in Latin American immigrants. But about 1/4 of them were not. And there was an estimate that was made by CDC in 2012 that somewhere around 5 1/2 to 7 1/2% of infected donors had locally acquired *Trypanosoma cruzi* infection (so had infection with a parasite that they had picked up somewhere in the United States by contact with a vector). And so based on that, we did a back calculation and came up with a very, very rough estimate. So this estimate is very approximate. It is more of an order of magnitude, relative estimate than a true estimate.

But we estimated that there are about 10,000 infections (infected people) in the United States who acquired infection here in the US. There have been close to 100 (I think about 80) blood donors who were picked up as infected, who have been investigated and the conclusion was this was probably locally acquired. But based on that... those data from the CDC, we think that there are probably about 10,000 infected people. But compared to the 300,000 or so infected immigrants, you can see that there's far more of a disease burden among immigrants than there is among people infected in the United States. On the other hand, it's hard to know who those people are. We think that the rates are probably highest in places like Texas and the Southeast and the Southwest, just because more of the infected donors have been picked up in those areas.

[Sarah Gregory] Are there things that negatively impacted your ability to have the definitive findings you would like?

[Caryn Bern] Well, I'm an epidemiologist, so I always want more data. So I think we would really have liked to have had more surveys of US residents from areas where we think that there's a fair amount of Chagas disease. The other huge gap is that we had almost no data for children. So we based our estimates (the US resident data)... there was, I think, more than 10,000 people who had been surveyed in the three surveys put together, but only 225 children, none of whom were infected. And so, we weren't able to make an estimate of the number of children with Chagas disease in the United States. And because we know that the earlier in the course of infection that a person is treated, the better the outcomes. We really wanted to know about that, because you want to pick up infected children and treat them. But we simply had no data for children. So I'd say that was one of the big gaps, as far as we were concerned. And so, we would really like there to be more of these surveys in places at risk. It would be great to have surveys in areas where we know there have been locally acquired infections to have more data on that...that aspect of it. So I think as an epidemiologist, that's probably not a surprise. I want more data.

[Sarah Gregory] We all want more data, right?

You do some pretty fascinating work. Do you want to tell us about that?

[Caryn Bern] So I've been working on parasitic diseases since I was at CDC. I was at CDC from 1990 to 2011. And starting in 1996, I was in the Division of Parasitic Diseases, as it was called in those days. I think I was already fascinated with parasites, which is why I took the job, but it just became more and more fascinating. And so, I work on Chagas disease, and I also work on a cousin parasite called leishmaniasis. And I've been working on both of those now for more than 20 years. It allows me to work in many different places in the world and learn a lot about different communities. So I've worked in communities in India on leishmaniasis, I've worked in communities in Bolivia on Chagas disease. And for both of them, I think because the transmission cycle is so complex, they both involve a vector and human and non-human hosts, there are always more questions to answer. And for me, as an epidemiologist and a researcher, that keeps me interested. So I'd say, that's basically why I do what I do.

[Sarah Gregory] Well, thank you for what you do and thank you for taking the time to talk with me today, Dr. Bern.

[Caryn Bern] You're very welcome.

[Sarah Gregory] And thanks for joining me out there. You can read the July 2022 article, Updated Estimates and Prevalence of Chagas Disease among Adults, United States, online at [cdc.gov/eid](https://www.cdc.gov/eid).

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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