Angiostrongylus cantonensis Infection in Brown Rats (*Rattus norvegicus*), Atlanta, Georgia, USA, 2019–2022

[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. Guilherme Verocai, a clinical assistant professor at Texas A&M University. We'll be discussing rat lungworm infection in brown rats in Atlanta, Georgia.

Welcome, Dr. Verocai.

[Guilherme Verocai] Hello, Sarah. Thank you, and thanks for having me.

[Sarah Gregory] What's rat lungworm?

[Guilherme Verocai] Rat lungworm is the common name for a parasitic worm or roundworm called *Angiostrongylus cantonensis*, which normally affects the lungs of rodents including the brown and black rat.

[Sarah Gregory] Where did it first originate?

[Guilherme Verocai] This species of parasite was originally described in 1935 (so, almost nine years ago) by a Chinese parasitologist called Chen, who examined parasite specimens collected in rats from Guangzhou (a region in China that was formally known as Canton), and hence the species name—so *cantonensis*, meaning in Latin 'from Canton'. However, it's thought to be naturally distributed throughout various East and Southeast Asian countries.

[Sarah Gregory] When and how was it first discovered in the United States, then?

[Guilherme Verocai] That's an interesting story. The first state in which *Angiostrongylus cantonensis* was found here in the US was Hawaii, and this goes back to late 50's and early 60's. So there was a parasitologist called Lawrence Ash that found *Angiostrongylus* in rats from Honolulu (Oahu Island). And around the same time, there was some human cases of eosinophilic meningitis that were confirmed to be caused by this parasite there in the same island. And after that, of course, this parasite was also found in some other areas of the US or unincorporated territories in the Pacific Ocean, such as Guam and Northern Mariana Islands, and then, later on in several continental states of the US including Florida, Louisiana, Alabama, Texas, Mississippi, and now Georgia.

[Sarah Gregory] How did it get in the United States in the first place? How did it get to Hawaii?

[Guilherme Verocai] So that's another interesting story, or that's where it gets interesting. So it has been hypothesized that this parasite came along with rats or infected rats coming from merchant ships. So with increased movement across continents and globalization and commerce that all this had contributed to introduction of this parasite into new areas, including Hawaii and other areas of the US. However, a parasite might come into a new area and not establish or not stay and become an issue. So we believe that this parasite just happened to find a suitable environment and all the needs for sustaining its lifecycle, including all animal hosts, which we're going to talk about in more detail.

[Sarah Gregory] In your article, you mention definitive, intermediate, and paratenic hosts of this parasite. What do these terms mean and what's the difference between them?

[Guilherme Verocai] In the case of helminths or parasitic roundworms like *Angiostrongylus cantonensis*, we call the sentient host those in which sexual reproduction occurs. So those males and females will mate and shed eggs or larva in the environment. So some parasites have a direct lifecycle, so they only need a single host to complete their lifecycle (so those would be the definitive hosts). But in the case of *Angiostrongylus cantonensis*, they have an indirect lifecycle. So in addition to definitive hosts where sexual reproduction occurs, they also require an intermediate host. So... and the intermediate hosts are those where there's development of larval stages of this parasite. So in the case of *Angiostrongylus cantonensis*, they are using slugs or snails, and within those snails or slugs, the larva... the first-stage larva will grow within a couple weeks, the third-stage larva (which is the infective stage) to the definitive hosts.

And to make it more complicated, there's still the paratenic hosts. Those are the third option, I guess, for *Angiostrongylus cantonensis* and a couple other parasites. But they are not strictly necessary for the completion of the lifecycle of this parasite (or no other parasite). However, those animals may serve as a... like a biological incubator. It will keep the infective larval stage viable for the infection of their definitive host. And usually this happens by carnivorism or prey/predator lifecycle. So for example, in *Angiostrongylus cantonensis*, amphibians or reptiles can act as paratenic hosts. So they're kind of bridging the intermediate hosts and definitive hosts, making the chances of the parasite infecting other tentative hosts higher.

[Sarah Gregory] Adding on to that, what are gastropods?

[Guilherme Verocai] Gastropods... those are snails and slugs. They are simply invertebrate animals within the class Gastropoda within the phylum Mollusca. So they comprise a diverse group of organisms living in terrestrial and aquatic ecosystems, including freshwater and marine environments. And again, those are snails and slugs, as we kind of known since we were kids. So snails will be the ones with an external shell that's visible to us. And slugs, on the other hand, they have actually also a shell, and we often dismiss. So they're like a small, internal shell that's kind of within their mantle, which is a slightly elevated area just behind their head (if you can picture a slug right now).

[Sarah Gregory] I never noticed this before though. I'm trying to imagine what this is.

[Guilherme Verocai] They have a hidden shell.

[Sarah Gregory] Interesting. Okay, explain the lifecycle of this parasite in rats—how they get infected and how the parasite evolves.

[Guilherme Verocai] The rats in this case, which are the definitive hosts, will get infected by ingesting third-stage larva of this parasite. And this third-stage larvae, as I mentioned before, they have to develop within a snail or a slug or a gastropod-intermediate host so the rodent or the rat can just ingest the... eat, pretty much, the snail or the slug which might be infected with this parasite. Or they may ingest the third-stage larva (the infective stage) that might be in the environment or present in food or vegetables, for example. And, as another option, they might ingest a paratenic host, which would be those animals serving as a bridge between the intermediate host or snail or slug and the rats. And within the rats (so that's the infective stage) will start migrating. So they will be ingested. So within the stomach, they will penetrate and start migrating through the body. They will go through a couple organs, especially brain, heart, and lungs.

And the lungs are usually their final spot, their ideal location for them to complete their lifecycle, so that's why they are called lungworms. And within the lungs, then the males and females will mate, and the females will shed some eggs. They will hatch in the lungs and the airways, and then they will be (interestingly enough) cough and swallowed, and those little larvae will travel throughout the gastrointestinal tract of the rat and come out in feces as first-stage larva, which will be the one that may infect the next susceptible snail or slug.

[Sarah Gregory] Good heavens. What makes rats such opportune hosts for so many diseases?

[Guilherme Verocai] That's a tough, loaded question. Overall, I think every single animal species are infected with a plethora of agents of disease, including parasites, bacteria, fungi, viruses. But why rats are opportune hosts for those pathogens that can also infect humans? And I think that's in part because of their lifestyle. So they, for a couple thousands of years (or if not more) they adapted to live in close contact with human beings—so within households or anthropogenically modified areas like cities, urban areas. And just looking for shelter and that food availability that we kind of provide. So within that, I think those pathogens had the chance or enough time to evolve and develop and adapt also to the human hosts. So crossing that species barrier from rodents to humans and often causing disease.

[Sarah Gregory] Then how do people get infected with this lungworm? We're not eating the rats or their feces, I hope.

[Guilherme Verocai] I also hope. So there's a few potential ways of humans to get infected with rat lungworm, so the first being through the ingestion of an infected snail or slug, and that can be accidentally or intentionally, but... especially if those slugs or snails are raw or undercooked. So that is one of the ways. And sometimes, because of the accidental portion—so it could be just within the salad, it was not thoroughly washed, and someone might ingest a snail accidentally or not knowing, for example. So that's one of the ways. And for the third-stage larva (the one that infects the rats or the human beings) may also come out of the snail or slug and survive for some time or not too long, but sometimes in water or just like in foods or old food. And that could be another way of humans getting infected. But it's always by ingestion of a larva that may be outside or within a snail or a slug.

[Sarah Gregory] There's so many reasons to thoroughly wash your greens. Gosh, yikes.

What are some of the symptoms in people if they get infected with it? How would they know?

[Guilherme Verocai] Overall, when we think about rat lungworm infection in humans, we think about neurological disease, because of eosinophilic meningitis, and that's the main symptom that it causes. But initially—so early on after ingestion of the larva, after infection—there might be some abdominal pain, nausea, vomiting. But after that, the larva will keep migrating and go to the central nervous system and causing those neurological signs.

[Sarah Gregory] Is there a treatment or a test for it?

[Guilherme Verocai] Yes. I'll start with the test, because I think we... as a veterinarian or clinician, we're going to think about testing before you decide to treat or not. So diagnosing *Angiostrongylus cantonensis* infection can be difficult in people and in any other animal, partially because there's no readily available diagnostic tests available for commercial labs, for example. But... so you start thinking about the history, of some of those symptoms that I mentioned before, especially central nervous system signs such as headaches or myalgia—so

muscle pain, things like that. And then, to think about that... so there's history of the patient. So did that person travel to an area where this parasite is known to be found? Did the patient also eat raw or undercooked gastropods or those paratenic hosts, like frogs and others in those areas? So... and that will kind of guide, not the testing, but like the thinking of *Angiostrongylus cantonensis* will go higher up in the list of suspicions that may be causing that neurological disease.

So for parasites, usually it doesn't matter if it's in humans or animals, we may also look at the levels of eosinophils, which are immune cells that fight that parasite infection (so it's called eosinophilia). So a higher eosinophilia will also be suggestive of a parasitic infection, and with all that together we might think of, okay, what to test or how to test that animal or human. And again, as a veterinarian, I keep saying animals, but humans are animals, after all. Having said that, there's no commercially available test, but there's a lot of research being done throughout various countries where this parasite is important, including a group at the CDC who developed a molecular diagnostic test capable of detecting parasite DNA in cerebrospinal fluid of human patients with neurological disease, with using eosinophilic meningitis suspected to being infected by *Angiostrongylus cantonensis*. So there are ways, but usually in a reference lab, there's not a rapid test in commercial labs that we can buy easily.

So as far as treatment goes, we do overall think about how the patient is or what needs to be done, and I feel very uncomfortable as an animal doctor and not a human doctor talking about this, but as a parasitologist, I would say that we should include, of course, anthelmintic drugs. Those are, like, a dewormer, pretty much, that will kill the migrating worms. But of course, it's dangerous to kill worms in the central nervous system of people with neurological disease. So while they can be used, there's some debate or controversy in using or not that because, well, there might be bad worms in the meninges of a person and that will trigger an inflammatory reaction that can be also pretty bad. So there's no amazing treatment, though we need to think about likely... think about some anthelmintics like albendazole, corticosteroids, to bring down that potential immune response to the killing of the worm. And again, I'll let the human doctors to... on treatment of humans, but again, it's managing the patient and making sure the person is doing well and being careful with some sequalae or potential issues that may come from treatment.

[Sarah Gregory] Tell us about your study now. What prompted it and what were you looking for?

[Guilherme Verocai] Our study was like a collaborative study among Zoo Atlanta veterinarians, veterinary parasitologists at the University of Georgia, and my lab here at Texas A&M University, which again, focuses on parasitology and special vectorborne and zoonotic parasites. So initially, they were screening rats or rodents in general caught in the zoo premises, and screening broadly to see if they would find a parasite or whatever other potential diseases that could be shared with people and other animals there at the zoo. And the pathologist... actually, they did the postmortem examination, collected tissues for histopathology (stained slides and what not), and they happened to find some worms that resembled the rat lungworm in some tissue cross-sections of lungs, heart, and brain. So then they contacted me to support them, confirming their suspicion using molecular diagnostics. So I received the samples—so there were scrolls of formalin-fixed, paraffin-embedded tissues—and then extracted DNA, amplified DNA via polymerase chain reaction, and sequenced those DNA of this parasite. And with the

results, sequences matched those of *Angiostrongylus cantonensis*, confirming the overall suspicion.

[Sarah Gregory] Is this parasite becoming more widespread in the south?

[Guilherme Verocai] We know that the rat lungworm has been reported from various southern states, including Florida, Louisiana, Alabama, Texas, Mississippi and Georgia, as I mentioned before. And those are the places where the parasite was confirmed through human cases or cases in different animal hosts, including rodents, gastropods, and some of those paratenic hosts. So interestingly enough—and we're talking about a zoological facility here—there are many cases of *Angiostrongylus* and fatal cases of encephalitis due to this parasite in non-human primates kept in zoos. So a lot of those might be tips of the iceberg. We know that those cases are there, and we may confirm diagnostically. But while we cannot confirm that this parasite is actually spreading, we cannot assume that they are absent in some places that they have not been confirmed yet. Also, because of the lack of surveillance... so if we are not looking for something, unless there's a clinical case that we follow through (either human or animal), will not confirm that the parasite is there. So I think there are chances, of course, for spreading or a range expansion, but we just don't know yet at this stage.

[Sarah Gregory] Well after all of this, what did you find?

[Guilherme Verocai] Well, we could confirm that *Angiostrongylus cantonensis* (rat lungworm) was present in those rats caught at Zoo Atlanta, and this is a novel area or geographic area in which this parasite is present.

[Sarah Gregory] Was there anything in particular that surprised you?

[Guilherme Verocai] The fact of finding this parasite of public health importance in a new area in the United States and in an urban area like Atlanta, it's surprising and concerning because people and animals might be at risk of infection. And another interesting but not necessarily surprising finding was that we confirmed infection in rats from a couple subsequent years (2019, 21, and 22). So that suggests the parasite is established there in that area, and it's potentially cycling within the premise of the zoo. So it's not an isolated finding, but it suggests that it is established and it's happening right there.

[Sarah Gregory] Based on what you just said, how big a threat is rat lungworm to people and other animals in the Atlanta area?

[Guilherme Verocai] Currently, we do not know how common this parasite is in rats from Atlanta area or if it's present in other areas of Georgia, but I do not believe that the risk to or the threat to humans or companion animals is very high at this stage because, again, the presence of the parasite means risk. But again, if people are taking the risk or exposing themselves by eating raw or undercooked snails, that's another step that plays into the actual risk of infection. One thing, however, that concerns me is that there are non-human primates that are of conservation importance maintained in those zoological facilities, and there are several reports of disease or fatal infection by *Angiostrongylus cantonensis* in non-human primates from zoos across the southern US. So for them, I think the risk of infection is relatively high if the parasite is present there, because they might be just eating snails or slugs in their premises. And again, there's no washing or telling the monkey to not eat a snail or a slug that will prevent that, so that's a challenge.

[Sarah Gregory] That is a challenge. A lot of these diseases are becoming more and more challenges to wildlife and zoological wildlife.

What do you consider the main public health implications of your findings?

[Guilherme Verocai] As I mentioned, so just the simple finding of the zoonotic parasite in a new area which was never found before already poses a level of risk to humans and other susceptible animals. So there is zoonotic concern and public health implications, but again, we need to know more what needs to be done or how common and how widespread it is and understand better the epidemiology of this parasite in this area, then act with education or bring in information on prevention. But again, often we're very reactive instead of proactive, waiting for the problem to happen in humans to then act upon it.

[Sarah Gregory] So right now, do we have any concrete ways to reduce the spread of it?

[Guilherme Verocai] Well, because it's a parasite with an indirect and complex lifecycle, there are probably many ways to reduce its spread or bring down prevalence or outcome or transmission. And it's like find, pretty much, to a point in the lifecycle. So for example, so pest control, targeting brown and black rat populations in an urban area or around the household. That would already directly infect transmission, because there could be many black rats who get infected to begin with. And again, all the other ways for humans to avoid infection are listed in the CDC. So it of course includes several practices like educating people that are living in endemic areas, tell them not to ingest raw or undercooked snails and slugs and other potential paratenic hosts like lizards and frogs and shrimp, make sure that they are washing thoroughly their vegetables, and things like that.

[Sarah Gregory] What additional research would you like to see done on this parasite?

[Guilherme Verocai] I can see substantial gaps in our knowledge around *Angiostrongylus cantonensis* in the continental United States, especially. So I think a first step would be to better characterize its current range, so we can have a theory or a real-time track a potential range expansion, instead of just assuming that it is expanding. Maybe it was there, and we just never found it before. And to look overall, like sampling and testing rodents and gastropods from across various states, it would be beneficial to be a first thing to do in a larger scale, I guess. But at a more focused or local scale, like perhaps in the Atlanta area, like understand what biological and environmental factors may be contributing to the establishment and transmission of the parasite—which snails or slugs are involved in the lifecycle, where are they present, where the risk truly exists—so therefore, we could understand or find some relevant target or intervention to mitigate infection of people and animals.

[Sarah Gregory] Tell us about your job and what you do and what you enjoy most about it.

[Guilherme Verocai] As you said, I'm a clinical assistant professor here at Texas A&M University School of Veterinary Medicine. My job is pretty diverse, so it can be divided in three main areas, which the first one would be teaching and mentoring undergrads, professionals, veterinary students and graduate students. Second would be diagnostic service in parasitology, so I'm a director of the veterinary parasitology diagnostic lab here at the university. So that's a handful already. And the third pillar would be research, so mainly focusing on advancing diagnostic tools for detection of parasitic infections in various animal species, including companion animals, livestock, wildlife, including those that potentially are shared with humans.

So what I enjoy the most... I think as a veterinarian and a parasitologist, I think since I studied parasites in vet school, I got caught or infected with parasites, I guess. So they are so diverse and complex. So that's the first thing. So they are so different. There are so many weird cases that we come across here diagnostically or on the research side. So there's never a dull moment. We have parasites of whales to wild bison, or rats to rhinos, and again, everything in between—dogs, cats, llamas, alpacas, cattle, or horses. So really, it is very different and diverse, so I enjoy that. And at the same time, trying to figure out what those parasites are, where they are, and how to better diagnose them and treat them. I'm also passing my knowledge, interacting with students from diverse backgrounds, and hopefully some of them will care about parasites enough to study parasites and be the next parasitologist in an academic institution.

[Sarah Gregory] Well, it's a field that definitely needs expanding, I think.

Between bad bacteria, parasites, viruses, fungi—which all seem to be increasing rapidly—what worries you the most?

[Guilherme Verocai] Pragmatically, I think all of them worry me equally, so I would be worried about all of them. But as a parasitologist, I have to use this to call for the parasites. So parasites tend to be ignored in comparison to viruses and bacteria, partially because they may not cause a disease outbreak, or usually they're not a high mortality. But they are an insidious, chronic problem that we have in human health, animal health, and what not. So in the human side, though, parasites, even in the United States, they will affect the most vulnerable communities—think about the US, but also globally in developing countries. So there's kind of less of an urge to act, and that bothers me quite a bit.

And so, yeah, we pretty much... I think we cannot ignore the parasites just because they are not necessarily or many of them are not killing people as a virus would. But I think being proactive—so better understanding of their epidemiology, where they are, distribution—searching for new and better ways to diagnose and treat the infections, etcetera, that would be much better than just being reactive. So they are usually neglected as part of human and veterinary medicine.

[Sarah Gregory] Last month, we had the EID article about the brain worm the woman got from the python in Australia that was all over the news and I did a podcast about it. That hopefully put parasites a little bit more on the map.

[Guilherme Verocai] Yes, that was an unusual case, for sure, and unique enough. But again, there are more relevant and more common parasites infecting people as we speak (more than a one-off case). But again, whatever brings some attention and show that parasites matter and are important and are worth studying.

[Sarah Gregory] Well, thank you very much for talking with me today, Dr. Verocai.

[Guilherme Verocai] Thank you, Sarah. It was my pleasure. Hopefully I'll get some people excited about parasites.

[Sarah Gregory] One more thing on my ever-growing list of things to be—I don't know if excited is the right word—but concerned about.

And thanks for joining me out there. You can read the October 2023 article, *Angiostrongylus cantonensis* Infection in Brown Rats (*Rattus norvegicus*), Atlanta, Georgia, USA, 2019–2022, online at cdc.gov/eid.

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

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