

Rat Hepatitis E Virus in Norway Rats, Ontario, Canada, 2018–2021

[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. Sarah Robinson, a postdoctoral researcher at the University of Guelph. We'll be discussing hepatitis E virus in Norway rats in Ontario, Canada.

Welcome, Dr. Robinson.

[Sarah Robinson] Thank you very much. Good morning.

[Sarah Gregory] Most people have especially heard about hepatitis A, B, and C. But what is hepatitis E and how is it different than the other strains? And is there a D?

[Sarah Robinson] Yes, hepatitis B, C, and D (there is a hepatitis D). Now, hepatitis E is a liver disease as well as the other hepatitis strains, and it's caused by hepatitis E virus or HEV. And hepatitis E is unique because it can have different clinical signs and patterns of disease depending on where the infection is acquired because of the different species and genotypes of the virus that are circulating in different parts of the world. So hepatitis B, C, and D are transmitted from person to person through contact with infected blood, for example, whereas with HEV, yes we have the virus circulating in people, but we also have documented ongoing zoonotic transmission, which is transmission from animals to people.

[Sarah Gregory] When and how was it first detected?

[Sarah Robinson] Hepatitis E was first recognized as a disease during an epidemic of hepatitis in India in 1978, where other types of hepatitis (so, A and B at that time) had been ruled out. The virus itself (HEV) was identified later on in 1983 following a similar epidemic as in India in a Soviet military camp in Afghanistan, and Dr. Balayan actually volunteered to ingesting pooled stool extracts from presumed cases and then identified virus-like particles by immune electron microscopy.

[Sarah Gregory] Wow. Like something out of *Contagion*, he actually ingested it himself.

[Sarah Robinson] Yes, he did.

[Sarah Gregory] What animals are known to carry it?

[Sarah Robinson] HEV variants have been reported in many animal species, so different animals can carry different species and genotypes of HEV. So hepatitis E in people is mainly caused by the species *Paslahepevirus balayani* genotypes 1 to 4. So genotypes 1 and 2 circulate in people, whereas genotypes 3 and 4 are zoonotic, with pigs as the main animal host. But animal reservoirs of genotypes 3 and 4 include a number of domestic wild animals, including wild boar, deer, and rabbits. And then there is rat HEV, which is the species *Rocahepevirus rattii* genotype C1, and it's genetically highly divergent from other HEVs and a number of rodent species can carry rat HEV.

[Sarah Gregory] How is this virus then transmitted from animals to people?

[Sarah Robinson] So HEV can be transmitted in a number of ways through direct contact with an infected animal, if an environment is contaminated with animal feces which carried the virus, as well as foodborne transmission from eating undercooked pork, venison, and wild boar meats.

[Sarah Gregory] What are the signs that someone is infected with HEV?

[Sarah Robinson] Symptoms of hepatitis E are similar to other types of viral hepatitis, like those you mentioned earlier. So we have fatigue, low appetite, stomach pain, nausea, vomiting, fever, as well as jaundice. However, in many people, the infection can cause no symptoms. In immunocompromised patients, we can see chronic infection which could lead to liver failure. There can also be signs outside the liver, such as neurological, renal, and pancreatic complications. So there can be diverse clinical presentation.

[Sarah Gregory] Clearly, it can be pretty serious. Are there any other things we need to know about?

[Sarah Robinson] Yeah. Usually, HEV infection does cause a self-limiting acute illness, and most people recover fully without complications. However, some infections can be severe or even fatal in rare cases. As I mentioned, it can be chronic especially in patients that are immunocompromised, and pregnant women are most likely to experience severe illness.

[Sarah Gregory] Would that affect their infants?

[Sarah Robinson] Yes. I believe in pregnant women, generally, if an infection is identified, they are hospitalized just to be safe and to monitor symptoms.

[Sarah Gregory] Since it's a virus, there's no medicine for it, right?

[Sarah Robinson] Yeah, that's correct. There's no specific medicine or antiviral therapy for hepatitis E, so really, it's only supportive therapy to help relieve those symptoms that are associated with the disease. So usually, it will resolve without treatment but hospitalization for that supportive therapy may be necessary in some severe cases.

[Sarah Gregory] Do the hepatitis A or B vaccines protect a person from HEV?

[Sarah Robinson] No, and there's no approved vaccine for hepatitis E currently available in the US or in Canada, so the best protection really wouldn't be relying on vaccines for other types of hepatitis, but it would be prevention, which would really depend on the species and genotype of HEV. So as I mentioned, for *Paslahepevirus balayani* genotype 1 and 2, that prevention would really ensure safe drinking water because of how it's transmitted for those genotypes 3 and 4 (which are zoonotic); safe food practices when eating pork, deer, or wild boar; and then for rat HEV, the potential method of transmission from rats or other rodents isn't well understood, but avoiding close contact with rodents or contaminated environments.

[Sarah Gregory] In which parts of the world is it mostly found?

[Sarah Robinson] In developing countries, hepatitis E is widespread and causes large outbreaks in areas with inadequate water supply and poor sanitation. So in these countries, the virus circulates in people and is transmitted by the fecal-oral route through contaminated drinking water. So that's where it's mostly found.

[Sarah Gregory] How common is it?

[Sarah Robinson] Well, I believe the WHO approximates about 20 million HEV infections each year. But out of those, there will be 3 million infections that actually cause clinical disease. So it is found worldwide, but the hepatitis E disease is most common in East and South Asia.

[Sarah Gregory] But cases of hepatitis E are starting to appear in industrialized countries. How did it get into these countries in the first place? Is it travel? Animal trade? Something else?

[Sarah Robinson] Yeah. Many of these cases are in people who have traveled to a developing country where hepatitis E is endemic, which historically we thought hepatitis E cases were restricted to travelers returning from these areas. However, sporadic cases of locally acquired zoonotic HEV are increasingly reported in industrialized countries and that's where different genotypes of the virus are being transmitted from animals to people, primarily through foodborne transmission after eating uncooked or undercooked pork or deer meat.

[Sarah Gregory] You studied HEV in Norway rats in Canada. What's going on there? Is this virus becoming more of a concern?

[Sarah Robinson] Yeah. Rats are a natural host of HEV variants in the species *Rocaehepevirus rattii* genotype C1, which I mentioned we call rat HEV. So rat HEV was detected in the feces of wild Norway rats in Germany in 2010 for the first time. And since then, it has been identified in Norway rats from the US, China, Vietnam, various countries in Europe. But the occurrence of the virus in Norway rats in Canada was unknown. There's also been cases in people. So there was one case of hepatitis E caused by rat HEV in a Canadian, however the infection was acquired in Central Africa. So wanting to understand the occurrence of HEV in Norway rats in our own country, particularly in Ontario, and given that this is thought to be perhaps an emerging disease in people, that prompted us to study the virus here.

[Sarah Gregory] Why specifically in Norway rats? What about other rats?

[Sarah Robinson] Norway rats were the focus of my PhD research at the University of Guelph. They're adaptable and tenacious animals. They're common in cities, living in close proximity to humans, and that close proximity provides the opportunity for transmission of pathogens. So the actual risk of these pathogens for people is likely low in Canada, but with rapid urbanization and population growth, their importance is expected to increase as more people come into contact with urban rats. And our urban rats here in Canada, particularly in Ontario, tend to be the Norway rat as opposed to other species of rats (like black rats). I also just find rats fascinating beyond a zoonotic disease perspective. Despite living so closely to them for centuries, particularly in urban areas, there's still a lot we just don't know about them.

[Sarah Gregory] Rats are so great. I love rats. It is a shame that they have so many diseases.

[Sarah Robinson] I'm glad you think so. I think they get a bit of a bad rep and they're generally considered a pest, but they are fascinating creatures, for sure.

[Sarah Gregory] Can it affect other species of rats and other rodents like mice? It's not just Norway rats because there's something biological about them, it's more about where they are and how many of them there are, is that right?

[Sarah Robinson] Yes. So rat HEV is found in other rodents, including other species of rats as well as mice, and in addition, actually shrews, ferrets, and mink as well.

[Sarah Gregory] You mentioned the foodborne route. Talk to us a little bit about that and other ways to catch it besides from rodents.

[Sarah Robinson] So foodborne transmission is for the *Paslahepevirus balayani* genotypes 3 and 4 species and genotype of HEV. But for rat HEV, transmission from rats to humans, although suggested, the exact course and route of transmission is unclear. So studies conducted in both

Spain and Hong Kong have reported similarity between viral sequences in people and in rodents in the same geographic area, suggesting that HEV may be transmitted through direct or indirect contact with rodents. However, in most of these cases, the patients don't report contact with rodents. So there's additional research that needs to be done to fully understand this.

[Sarah Gregory] Clarify for us here—is there a difference between human hepatitis E and rat hepatitis E?

[Sarah Robinson] There are different species and genotypes of hepatitis E virus that are transmitted in different ways. So hepatitis E that is transmitted from person to person is spread fecal-orally, as mentioned, through contaminated drinking water, whereas hepatitis E from rat HEV (which is a different species of HEV) is thought to be transmitted from rats to humans.

[Sarah Gregory] Besides your love of rats, what prompted you to do this study and what questions were you looking to answer?

[Sarah Robinson] Recently, there have been cases of acute hepatitis caused by rat HEV in Hong Kong, Spain, and Canada. So given the potential risk of transmission from rats to humans and hepatitis E as an emerging infectious disease, we wanted to investigate HEV in rats here in Ontario. We wanted to know if the virus was present in Norway rats in this region, and if it was, were there any associations between season, land use, year of collection, and particularly rat characteristics such as sexual maturity and body condition.

[Sarah Gregory] Take a moment here and tell us about your study and how it was conducted.

[Sarah Robinson] Happy to. Rat carcasses were submitted for the study through collaborations with pest control professionals working in the southern Ontario region. These rats were frozen and shipped to the University of Guelph, where we performed full necropsies, recording rat characteristic data and collecting liver samples for HEV testing. In total, we studied 372 Norway rats submitted from 161 unique locations across southern Ontario, collected between November 2018 and June 2021.

[Sarah Gregory] What did you find?

[Sarah Robinson] Of the rats that we tested, 5.6 percent were positive for HEV. These positive rats were from 16 distinct locations in seven cities or towns across the region, including three major cities: Toronto, Hamilton, and Windsor. We also found that the odds of HEV infection were significantly higher in sexually mature rats.

[Sarah Gregory] Based on these findings, why do you think that infection was more likely to be found in sexually mature rats?

[Sarah Robinson] That's an excellent question. So this finding was actually in contrast to previous studies of rats which found no association with age and infection status, but this may have been due to differences in how age classes can be identified. So also, there haven't been that many studies looking at these associations. And in our study, infection may have been more likely in sexually mature rats due to cumulative exposure to the virus, leading to increased risk of infection over time. Also, behaviors in sexually mature rats such as exploratory and aggressive behaviors, those could increase transmission as well.

[Sarah Gregory] What are the public health implications of your study?

[Sarah Robinson] Our study provides further evidence that rat HEV has a broad geographic distribution globally and may be endemic in Norway rats. Taken with the recent cases of rat HEV reported in people, there is a need for continued research to further understand rat HEV in Norway rats and the potential public health risk, especially given that we're not quite sure about the source and route of transmission in some of these human cases.

[Sarah Gregory] And along those lines, what future research do you think is needed?

[Sarah Robinson] I think future research is really needed to investigate that transmission, to understand to potential for rat to human transmission and all the associated public health risks, but also related to the diagnostics. Hepatitis E caused by rat HEV might be underreported in people due to cases with mild or no symptoms, limited awareness of the disease, but also diagnostic testing for HEV that may not detect rat HEV.

[Sarah Gregory] Dr. Robinson, tell us about your job and what you like most about it.

[Sarah Robinson] I'm a veterinarian and researcher, and I'm currently doing work with the University of Guelph as well as a postdoctoral fellow at the Pacific Institute on Pathogens, Pandemics, and Society at Simon Fraser University. I conduct interdisciplinary research related to wildlife health and disease and One Health, which is an integrated approach with the goal of sustainably optimizing the health of not just people, but people, animals, and ecosystems. And really what I enjoy most, it's hard to pick just one thing, but it's the collaborative nature of my work—working with diverse people from diverse backgrounds, partnering with groups not only within academia, but in government and in communities. This allows me to learn constantly about new fields of research, new approaches, and allows me to tackle those challenging and complex problems in innovative ways.

[Sarah Gregory] With all that research, out of all of the zoonotic diseases out there, what worries you the most?

[Sarah Robinson] That's a tough question. I don't think I could name one zoonotic disease specifically, but I would say those zoonotic pathogens that are likely to be affected by climate change. So climate change can lead to the spread of zoonotic hosts and vectors, it can alter host-pathogen dynamics. So we may see significant and complex changes in the global distribution and prevalence of many zoonotic diseases as climate change advances.

[Sarah Gregory] I just read an article yesterday that said we're losing the battle with mosquitoes. How do you feel about that?

[Sarah Robinson] Yes, particularly vectorborne diseases I think worry me as they're related to climate change because temperature changes, moisture changes, humidity changes, all those can affect those vectors like mosquitoes. So we might see a larger distribution of those vectorborne diseases as mosquitoes can spread to different areas. We can see vectorborne diseases, mosquito-borne diseases, in areas that previously didn't have them. So that is worrisome, especially we're already seeing climate change effects with summer in particular, and also wildfires. Really, we just...we have predictions, we have signs that things are changing already. So we need to take action and we need to take action now.

[Sarah Gregory] Totally agree. Malaria is back after all these years.

Well, anyway, thank you so much for taking the time to talk with me today, Dr. Robinson.

[Sarah Robinson] Oh, thank you very much.

[Sarah Gregory] And thanks for joining me out there. You can read the September 2023 article, Rat Hepatitis E Virus in Norway Rats, Ontario, Canada, 2018–2021, online at [cdc.gov/eid](https://www.cdc.gov/eid).

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

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