

Rabies Across Borders

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

[Sarah Gregory] Today, I'm talking with Dr. Roman Biek, in Glasgow, about rabies crossing the U.S. border into Canada. Welcome Dr. Biek.

[Roman Biek] Hello. Thanks for having me on your program.

[Sarah Gregory] So, borders are geopolitical constructs. How is it possible to contain rabies at a border?

[Roman Biek] Rabies is a virus transmitted by animals and, at least in North America, that essentially means wildlife. So, you're right that wild animals like raccoons will pay no attention to a national border. Following a major outbreak of rabies in raccoons across Eastern United States during the 1980s and 90s, raccoon rabies was threatening to spread into Canada, and because rabies is a dangerous zoonosis, Canada, of course, wanted to prevent rabies from entering its territory.

The border happens to run across some natural barriers, such as the Great Lakes and the St. Lawrence river, and we would expect that those would limit the movement of infected raccoons but they wouldn't ultimately prevent it. So to prevent the virus from crossing the border, government agencies on both sides implemented oral vaccination campaigns for raccoons. And this was largely successful, but on a few occasions the virus still spilled over onto Canadian territory.

[Sarah Gregory] Frankly, orally vaccinating raccoons at the border boggles my mind. How is this accomplished?

[Roman Biek] By using a range of different approaches. One is to drop baits containing the vaccine, and this was done from airplanes or vehicles and can be done across larger areas. Millions of baits are actually distributed in this way in the U.S. each year and this has allowed raccoon rabies to be contained within the area currently affected and to prevent it from spreading further west and northwards. The baits are covered in a fishmeal as an attractant, and when the raccoon finds the bait, it's likely to consume it and in doing so, it takes up the vaccine and thus becomes immunized.

Another approach is to live-trap raccoons, and then to vaccinate them, and release them again. And this was done in parts of Canada that were thought to be at the highest risk of raccoon rabies entering and crossing the border.

[Sarah Gregory] Would you give us a timeline for this vaccination program?

[Roman Biek] The oral vaccination campaign started in the 1990s—the mid-1990s-- and continues to this day. And without this, safe to say, raccoon rabies would affect a much larger area and cause a much greater public health burden than it currently does.

[Sarah Gregory] So what happened, why were there raccoon rabies virus outbreaks in Canada?

[Roman Biek] Well, vaccination will never reach the entire population, so not all raccoons will encounter a bait or eat enough of it to become vaccinated. Individuals can also wander in from

outside the vaccinated area. The percentage of animals vaccinated does not have to be 100 percent for the vaccine barrier to be effective, but even if coverage is high, there's always a possibility that the virus breaks through. So, in our study, we looked at six instances in which raccoon rabies caused outbreaks in Canada over the last two decades, and that happened in Ontario, Quebec, and in New Brunswick.

[Sarah Gregory] Would you explain the whole-genome phylogeography to us, please?

[Roman Biek] Sure. The first part, whole genome, simply refers to the virus. So we have been able to obtain sequence data from viruses, and rabies virus specifically, for quite some time now but only recently has it become technically feasible to sequence entire genomes, or at least for large numbers of samples we can do that now. And sequencing entire genomes allows us to detect very small genetic differences between the sampled viruses—very few mutations. And where previously all viruses within an outbreak would have looked genetically more or less the same, we can see in whole genome data that some of these viruses clearly cluster together, genetically, whereas others are more distinct. And so these differences come about because rabies virus continues to accumulate new mutations all the time, like other RNA viruses do too, and this happens even over the course of a single outbreak. So, to visualize these differences, we built a genealogy or a phylogenetic tree of our rabies genomes. And this is pretty much like constructing the genealogy of someone's family history. So you can think of it as reconstructing the ancestral history of these rabies viruses circulating within raccoons along the U.S.-Canada border.

And the second part of phylogeography is what we can do with these phylogenetic trees, or genealogies, once we've obtained them. So, the phylogeography bit—the 'phylo' refers to the trees and 'geography' to the geographic area over which we took our samples. So, by looking at genetic differences in the virus that are distributed across space, we see clusters of closely related viruses in one area or viruses from another nearby area that look genetically slightly different, and from that we can learn how rabies has spread across the landscape. Ultimately, this can give us important epidemiological information, such as whether an outbreak was caused by a single introduction of the virus across the border or by more than one.

[Sarah Gregory] So you used whole-genome phylogeography to learn about this outbreak and what was causing it?

[Roman Biek] Yes. We looked at these six occasions in which raccoon rabies emerged on Canadian territory. We wanted to know whether we could learn general lessons about how these outbreaks occurred—were they caused by introductions of virus circulating right adjacent to the border or viruses introduced from very different areas? Has the virus crossed the border more than once? Did transmission across the border occur in both directions or in just one? So, for this we obtained whole genome data from over 250 rabies viruses sampled over more than thirty years along the U.S.-Canada border. So, not just samples from the Canadian outbreaks, but also viruses from the U.S. side so to put the outbreak data into context.

[Sarah Gregory] Ontario, Quebec, and New Brunswick were sites of outbreaks. Would you tell a little about these areas were affected?

[Roman Biek] For each of these three provinces, we had data from two distinct outbreaks. Apart from New Brunswick, where the same area was affected in both cases, the outbreaks occurred at

different places along the border. And these outbreaks varied substantially in size, between one and several hundred recorded cases, and also in duration. In some cases, it was over within weeks and in others the outbreak lasted for six years.

[Sarah Gregory] What are some of the obstacles to the vaccination program working along the Quebec border?

[Roman Biek] The U.S. border with Quebec is a long one and does not involve many natural barriers to raccoon movement, compared to Ontario, for example, where the border runs along some of the Great Lakes and the St Lawrence river. So, it is a stretch of the border that will be harder to protect against rabies incursions.

One noticeable result of our analysis was that the 2006-2009 outbreak in Quebec showed patterns that were different from any of the other five outbreaks we looked at. We could see from our genetic data, very clearly, that there had been at least four independent introductions of the virus from Vermont into Quebec during that period and there was also virus flow back into Vermont. So, this indicates that the vaccinated area was relatively permeable to rabies transmission during that time.

[Sarah Gregory] Dr. Biek, please tell us, generally, why these breaches of vaccination corridor occurred? I understand you found local and long distance translocations of the virus.

[Roman Biek] For the case in Quebec, we can only speculate that vaccine coverage in the raccoon population at the time might not have been as high as assumed, maybe because of higher raccoon populations or lower vaccine uptake. We can certainly say that the virus strains responsible were the local ones circulating just south of the border. So this is not the case of an infected animal from somewhere far outside the vaccine corridor carrying the virus across into Canada.

But in other cases, specifically one of the Ontario outbreaks, we have evidence for exactly that type of scenario—the single introduction of a virus that came from a very far distance. The virus responsible for the outbreak was so different from any of the ones circulating near the border that we suspect it came from several hundred kilometers away, for this particular Ontario outbreak, and such a distance is actually beyond what we could expect a raccoon to move naturally, so there might have been some human involvement in this, actually. And there are anecdotal stories about raccoons inadvertently hitching rides on garbage trucks, for example.

[Sarah Gregory] From a public health perspective, what's needed to contain these cross-border outbreaks—more surveillance, different vaccines, more collaboration between countries?

[Roman Biek] It's worth emphasizing that, for the most part, the vaccine corridor is working really well. There's no question that without it, outbreaks would have occurred much more frequently than those six breaches over the past 20 years, so it's important that these measures continue. The long-distance translocation event that led to one of the Ontario outbreaks also illustrates that there will be cases where the vaccine corridor won't be able to offer protection because animals might occasionally cross it by other means. So good surveillance systems are important for picking up those unusual cases of emergence in areas where you wouldn't expect it.

But surveillance is equally important to catch new outbreaks in those areas along the border where they are most likely to occur, and to catch those outbreaks early. The earlier it happens and the outbreak is identified, the smaller the number of raccoons already infected, and that means that less resources will be required to control the outbreak. So ultimately, I would say surveillance really is the key. There are new oral vaccines that have been tested and that might bring further improvements. And with respect to collaboration, I can say that, in our case, collaboration between U.S. and Canadian officials has really been excellent. We would not have been able to do our study if the state and provincial departments hadn't collected all those data and samples over multiple decades and also if they hadn't been so open about sharing them. Often, these departments are not given the resources specifically dedicated to these kinds of activities. But without collecting and archiving samples and data long-term, we really lose the opportunity to learn from past events about how we can improve what we do about rabies control. And the need for allocating sufficient resources for adequate surveillance and sample archiving is really an issue that applies not only to North America, but to many areas around the world. Many of these areas also experience similar challenges of rabies spreading into areas previously free of rabies, whether the spread happens through wildlife or dogs, so we hope that our work will help others to successfully tackle the problem of transboundary spread and since doing this will be an important part of reducing the burden of rabies worldwide and hopefully to ultimately eliminate it.

[Sarah Gregory] Thank you so much for talking to me today, Dr. Biek. I've been talking with Dr. Roman Biek about his September 2017 article, Processes Underlying Rabies Virus Incursions across US–Canada Border as Revealed by Whole-Genome Phylogeography. Listeners can read the article online at cdc.gov/eid.

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

[Announcer] For the most accurate health information, visit cdc.gov or call 1-800-CDC-INFO.