

# Influence of Landscape Patterns on Exposure to Lassa Fever Virus, Guinea

*[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. Miles Carroll, the professor of emerging viruses at the Pandemic Sciences Institute at Oxford University in the United Kingdom. We'll be discussing the influence of landscape patterns on exposure to Lassa fever virus in Guinea.

Welcome, Dr. Carroll.

[Miles Carroll] Thank you for having me on your podcast.

[Sarah Gregory] Let's start with Lassa fever. What is it?

[Miles Carroll] Lassa fever is an acute and often fatal viral disease, occurring primarily in West Africa, and it is usually acquired from infected rats.

[Sarah Gregory] So is West Africa where it is endemic?

[Miles Carroll] Correct. Primarily in the countries of Liberia, Sierra Leone, Nigeria, and Republic of Guinea.

[Sarah Gregory] What are the signs and symptoms?

[Miles Carroll] Usually after a few days after infection, typical symptoms are headache, sore throat, muscle pain, chest pain, and then progress into nausea and vomiting, diarrhea, and abdominal pain. So not that dissimilar to the early symptoms of Ebola virus disease. But in severe cases, you also get facial swelling and fluid in the lung cavity and hemorrhaging from mucus membranes, which result in a drop in blood pressure. And up to 20% of hospitalized cases are actually fatal.

[Sarah Gregory] So it is pretty dangerous.

[Miles Carroll] It certainly is, but there's many infections are actually asymptomatic or have mild symptoms. So for these cases, they never have been reported because the patient isn't showing symptoms. But when you do show symptoms, it can be extremely dangerous and fatal.

[Sarah Gregory] Do we know how many people get it globally annually and how many people die from it?

[Miles Carroll] It's pretty hard to get those numbers because many people are never actually diagnosed, even fatal cases, because these cases occur in countries where they haven't got great public health services and haven't got great diagnostics to support and identify the infectious agent. However, estimates of annual human cases of Lassa fever infections in West Africa are estimated to be up to 100,000, and associated deaths are about 5,000. But these are all based on epidemiological studies that were performed in 1987 in Sierra Leone. And so, they're modeled on that data. So characterizing the distribution and transmission intensities of Lassa fever in endemic areas is essential to be able to improve on those estimates so we can get an accurate picture of the real threat of the virus.

[Sarah Gregory] Is there a treatment for it?

[Miles Carroll] A lot of cases in severe virus infections, there's a number of licensed products that are thrown at patients in the hope to try to reduce symptoms and increase survivability. But there are no known antiviral drugs that actually work against Lassa fever that have actually been shown in a randomized study to actually have any benefit. And there's no licensed vaccine, either.

[Sarah Gregory] Your study is about Guinea particularly. Why there?

[Miles Carroll] Back to the beginning of the West Africa Ebola epidemic, which started, we think, in 2013 but really started going in 2014, I deployed with a group of scientists from what was called Public Health England Porton Down to provide diagnostic support to MSF, who had just set up a treatment center up in the prefect of Guéckédou (a forested region of Guinea), which is the epicenter of the Ebola outbreak. So that's why we carry on a program of research looking at the immunity to Ebola in survivors, and this project is associated with the work we're doing looking at potential spillover events in the bushmeat hunter population in that region of Guinea.

[Sarah Gregory] So we already talked about this a little bit, and you said there's no real good numbers about how many people get it every year, but are you able to be more specific in Guinea itself? Or is that still a number you're not entirely sure of?

[Miles Carroll] It's a number we're not entirely sure of. We do see every year isolated cases of about two or three or four Lassa fevers that get physically diagnosed by molecular tests, and they usually are...result in fatal outcomes.

[Sarah Gregory] What were you looking for particularly when you went ahead with this study, adding onto your other work?

[Miles Carroll] As I said before, there is a significant lack of data (positive data) on the true burden of disease of Lassa fever in West Africa. What we were trying to do is to improve on that by looking at the antibody response to Lassa fever (i.e., the footprint that the virus leaves behind) and to try to improve the accuracy of how many people are physically infected, and also what is the contribution of the landscape changes in the forested region on the incidence of Lassa fever.

[Sarah Gregory] Tell us about those varying landscapes of Guinea and their effect on Lassa fever cases.

[Miles Carroll] So our study was looking at two regions of Guinea. One is the lowland region of the Atlantic Coast, which is a shrub-type of ecology. And also in the north...well actually, it's the southwest of the country...southeast of the country, sorry, there's a significant forest that straddles the border of Guinea, Sierra Leone, and Liberia. And so, with those two different landscapes, we could ask the question: "Is Lassa fever more prevalent in a forested region or in an unforested region that is mainly agriculture as well?". So that's why we were lucky enough to have those two cohorts of serum on those different groups of people. And we found that the data suggests that 60% of the population (the forested region)—and these are adults; we didn't look at children—were actually antibody positive, while less than 10% were antibody positive in the Atlantic Coastal region.

[Sarah Gregory] Speaking of antibody positive, can people get this more than once?

[Miles Carroll] That is an unknown. The theory is that if you've had it once, then you would be protected against reinfection. But that's not known 100%. But that's the theory.

[Sarah Gregory] So let's go back to the landscape. It's changing in Guinea, right? Why and what's happening there?

[Miles Carroll] In the forested region, you have relatively sparsely populated groupings and villages that have developed local farming practices around a village hub. And these villages have grown, so then more land is being cleared for planting rice, etcetera. So the punctuated closed forest canopy, it's certainly becoming more open.

[Sarah Gregory] Why is it important for us to know about these landscape differences and how they impact the disease?

[Miles Carroll] If we know the landscape is changing and we know it's associated with an increase incidence of disease, then we can flag this as a danger for increased spillover, not just of Lassa fever, but also other what we call "high-consequence" or emerging viruses—i.e., those viruses where there's no therapeutics, no vaccines, and they have a high case fatality rate. And they could be the source of the next outbreak or epidemic, as we saw with Ebola in West Africa.

[Sarah Gregory] Rats seem to play a significant role in the spread of Lassa fever. Tell us about their role and what kinds of rats we are talking about, here.

[Miles Carroll] The specific type of rat is the Natal multimammate rat, and it's considered the main natural reservoir of Lassa fever. It's a commensal rodent and agricultural pest actually in the region. And they do live in close proximity to houses...to the dwellings and the villages. So that's definitely an issue that these are the rats that carry the virus, and they have a high association with humans.

[Sarah Gregory] But how do they infect humans? Is it bites or fleas or urine...droppings? What's passing it?

[Miles Carroll] Yeah, the rats have the virus. They don't seem to get too sick with it, and so they carry on feeding. They eat the food that's in the house. They will urinate and excrete on that food, some of that will become aerosolized to some extent as well. And so, the villagers (the householders) will become infected through eating their food stuff, or through aerosolized rodent urine and droppings.

[Sarah Gregory] How did you go about this study? What kinds of samples did you take and from whom?

[Miles Carroll] As I mentioned previously, the samples that were in the forested region were from a mixture of bushmeat hunters and local villagers. And the samples that came from the Atlantic Coast were part of a vaccine study for Ebola vaccine development. And the lead scientist on the ground was actually my former PhD student, a local Guinean scientist called Joseph Akoi Bore. So after...I met him during the Ebola outbreak (he worked in our diagnostic unit), and when I was meeting and discussing with him, he shared he wanted to do a PhD. So we created this project as part of his PhD program, which he finished actually a couple of years back, and we're still working with him in the forested region on other seroepidemiology studies.

[Sarah Gregory] When we say samples (taking samples from people), what kind of samples? Flesh? Blood? Hair?

[Miles Carroll] These are venous blood samples taken from volunteers that were through the sensitization of the village, explained to them why we want...we'd like to take blood samples of

volunteers and explained the relevance of the study. And in many cases, we would go back to the village and explain what we found.

[Sarah Gregory] Always when human samples are used, there's some ethics involved. So give us a brief rundown on the ethics and the approval process needed when you take these samples?

[Miles Carroll] Yes. Abiding by the ethical standards is extremely high on our agenda. And for doing the work in Guinea, you have to present your protocol to the research ethics committee that's in Conakry after approval, then you obviously negotiate material transfer agreement. If the...as much of the research we would do in Guinea, but sometimes a sample has to be taken out for enhanced analysis. And then we need to actually get a research ethics permission from our host university in the UK as well.

[Sarah Gregory] Tell us who your partners and collaborators and funders were? I understand there's some very high-level people involved in this.

[Miles Carroll] So this was, as most successful research is, part of an international collaboration. First has to be recognized the support (both physically and scientifically) from the Guinean government Ministry of Health and the scientists that are part of the publication, but also working with the World Health Organization, colleagues at the Bernhard Nocht Institute of Virology in Germany, as well as London School of Hygiene Tropical Medicine and my former host organization, now called the UK Health Security Agency. And importantly, you can't do any research without funding, and that was made possible by the US Food and Drug Administration, who have been funding my programs of work over the last five years, but primarily focused on Ebola vaccine development and licensure.

[Sarah Gregory] Going back to the study, when all was said and done, what did you find?

[Miles Carroll] We found that there was a significant difference in the level of seropositives in the Atlantic Coast, compared that was down to 10%. But there was a really high positive response in the bushmeat hunter and village community in the forested region in the prefect of Guéckédou and Macenta. And that to us was a major surprise because the incidence of severe disease is relatively low, but the actual burden of disease was revealed to be much higher than we initially thought.

[Sarah Gregory] These were surprises. Were there any others?

[Miles Carroll] Yes. One of our collaborators, Kimberly Fornace, she specializes in looking at the relationship to the incidence of disease and how the landscape has changed. And I mentioned a little bit before that in the village...in the forested region, these villages have a local farming economy, if you like. They have actually taken more and more land to clear to support their populations. And what Kim found was that the villages where there's more clearances, there was a higher incidence of Lassa seropositive cases, which suggests that the more that you expand your population, probably the more rats that you are attracting in and increasing the incidence of zoonotic spillover from the rat to the villagers.

[Sarah Gregory] What were the challenges? And were there limitations?

[Miles Carroll] The challenges are, when showing that the local Guinean authorities are on board with you, we always include...well, this is, like I said, that we're part of the PhD project of the Guinean scientists. So that was great to illustrate that we were training Guineans in this area of

research which will help support future outbreak response in Guinea. So then, like I said, you have to get all the paperwork in place to ensure that you're not breaking any rules.

[Sarah Gregory] What do you think is the most important takeaway from your study?

[Miles Carroll] So the most important takeaway, I think, is that Lassa fever incidence is much higher than we had expected, and we initially thought and that this human impact on landscape, it seems to be directly linked to this increase incidence in zoonotic spillover in the forested region. And there's multiple examples of how human activities on the environment and also climate change is increasing the incidence of zoonotic spillover. And that's probably why there's a lot more reports of outbreaks of these emerging viruses that are exceptionally fatal.

[Sarah Gregory] Talking about climate changes, do you think they will continue to worsen diseases in, not just this, but all kinds of diseases?

[Miles Carroll] Certainly. I mean, it isn't just my work, there's many scientists in the field that are looking at the relationship to the changing environment and the increase incidence of zoonotic spillover (those viruses are reservoired in animals that spillover to human population). And the more that...forest clearings that we do, the more likely that humans are going to come into contact with animals. As the temperature changes, the vectors that carry some of these viruses, be it a tick or a mosquito, the range that they can exist means that they can actually carry that pathogen and infect humans in areas that currently don't support that vector. So you're looking at an increased incidence of the infection.

[Sarah Gregory] This may be a bit out of your purview, but are there any immediate practical things that can be done to stall the impact?

[Miles Carroll] If you're looking at trying to reduce forest clearance, you could work with the local farming community to improve their current practices to increase the yield from the land that they have cleared, which may be one way to prevent or the need to clear more forest areas.

[Sarah Gregory] Are there future studies that you'd suggest on Lassa fever?

[Miles Carroll] Our study was based on looking at the antibody response to a certain protein within the virus (what we call the nucleoprotein). So we don't have the sequence of the virus infecting these people, but we think the footprint left behind (the antibody's to the nucleoprotein) indicates an effect with Lassa fever. But we can't be 100% sure, because we haven't actually sequenced the virus that infected them in the first place. So what would be a good thing is a broader sampling of the rodent population to actually sequence the virus that's actually infecting them to ensure that it is the virus we think it is (Lassa fever), or it could be a variant of Lassa fever. So the more knowledge we have of the animal population (what they are infected with), that would give us more insight to what's actually infecting humans.

[Sarah Gregory] Well, Dr. Carroll, on a final note, tell us about yourself—your job and what intrigues you most. Institute of Pandemic Sciences sounds incredibly relevant to the world.

[Miles Carroll] Yes. So I class myself as a virologist, I did my postdoctoral training at the National Institutes of Health on poxviruses, actually. So the monkeypox pandemic (recent pandemic) has been a great interest of mine, as well. But I also work on recombinant vaccines, as well as emerging viruses. So my past job for the last 14 years was head of research at the UK government high containment facility in Porton Down. But a couple of years ago, I had the opportunity to concentrate more on my research, and I moved into academia and then started the

role as a researcher in the Pandemic Sciences Institute at the University of Oxford. And so, the Pandemic Sciences Institute was really born from the realization that Oxford and many collaborators throughout the world, when we work together, we can do things pretty effectively—for example, the vaccine developed in Oxford, a lot of structural biology work on SARS-CoV-2, and also therapeutics. And so, the Pandemic Sciences Institute is bringing together virologists, immunologists, vaccinologists, clinical trialists, modelers, as well as ethics into one essential hub. So we're all in one place across the universe...across the university, sorry, to make this work more efficiently. But it's a very outward-looking institute as well. So...and we've got a conference on 10th to the 11th of July on pandemic sciences that we obviously want to publicize and get as many international people to attend as possible.

[Sarah Gregory] Where will that be held?

[Miles Carroll] It will be held in Oxford on the 10th–11th of July this year.

[Sarah Gregory] At Oxford University, okay, good to know. Well, thank you so much for taking the time to talk with me today, Dr. Carroll.

[Miles Carroll] Thank you very much for having me.

[Sarah Gregory] And thanks for joining me out there. You can read the February 2023 article, *Influence of Landscape Patterns on Exposure to Lassa Fever Virus, Guinea*, online at [cdc.gov/eid](https://www.cdc.gov/eid).

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

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