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# Nigeria's largest Lassa fever outbreak sparked by rats

*Analysis calms fears that the virus had mutated into a super-bug that could move more easily from person to person.*

Amy Maxmen



A health worker arrives at the Institute of Lassa Fever Research and Control in Nigeria with blood samples for testing. Credit: Pius Utomi Ekpei/AFP/Getty

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Rats fuelled the largest outbreak of deadly Lassa fever in Nigeria this year, according to the most extensive and rapid genomic analysis of the Lassa virus conducted thus far.

The study<sup>1</sup>, published on 17 October in the *New England Journal of Medicine*, eases fears that Lassa had mutated into a super-bug that was spreading swiftly between people. Instead, the viral genomes harvested from 220 patients were surprisingly diverse, indicating that most people had not acquired their infections from someone else.

The unprecedented speed of this analysis has helped officials to combat the spread of Lassa fever, and the virus's genetic information will assist researchers as they develop vaccines against the illness. About 514 people fell ill with the disease between January through the end of September, and 134 of them have died.

“Getting whole genome sequences from this number of samples quickly, and at a site of an outbreak, is exciting and important,” says Peter Daszak, the president of EcoHealth Alliance, an organization based in New York City focused on emerging diseases. “This is the way of the future.”

## Viral spread

People can contract Lassa virus from direct contact with the African soft-furred rat (*Mastomys natalensis*) – such as by eating them. And infected rodents can indirectly transmit the virus by salivating or urinating on rice, cassava and other crops stored in barrels or left to dry in the sun. The infection can also pass from person to person through bodily fluids – which is how many health workers contract the virus.

As with Ebola, Lassa causes fevers and can lead to death as a result of internal bleeding. Mortality rates range from 25% to 69% in West Africa.

In February, when the Nigeria Centre for Disease Control (NCDC) reported more cases of Lassa fever than usual, study author Christian Happi – director of the African Center of Excellence for Genomics of Infectious Diseases at Redeemer's University in Osun, Nigeria – began sequencing viral genomes isolated from patients with Lassa fever.

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suggesting that each person was infected by a different lineage of the virus.

The NCDC responded to the preliminary results by prioritizing rat control. “We went to churches to ask pastors to speak with people about preventing contact with rats, especially at night, and keeping food covered,” says Chikwe Ihekweazu, the head of the agency, which is based in Abuja. He also held town meetings and broadcast messages on the radio in local languages.

## Similarities

Happi also shipped blood samples to the Broad Institute of MIT and Harvard in Cambridge, Massachusetts. Together, the researchers analysed 129 virus genomes isolated from patients this year, and 91 others collected from Nigeria between 2015 and 2017. Fewer than 10% were similar enough to indicate that they had probably passed from person to person.

Rather, broadly similar Lassa strains tended to correspond to geographic areas separated by rivers. Lassa viruses collected on the east side of the Niger River, for example, were more like one another than were those on the west bank. The results suggest that the virus has been evolving within rat populations that have been separated by the country's waterways for hundreds of years.

It's unclear why people in Nigeria seem to be encountering rats more often this year. Happi says that more Nigerians might be working in proximity to rodents on farms after the country's economic downturn last year. Or, perhaps last year's crops grew well, prompting rats to multiply.

## Speedy response

Whatever the reason, the virus's genetic diversity is important for vaccine development. Many of the vaccines now being developed include a protein in the Lassa virus that triggers the body's immune system to produce antibodies. But if genetic variation within that protein is large, vaccines based on one strain might not protect against another.

Genetic variation could also thwart diagnostic tests for Lassa that rely on detecting specific

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To avoid that pitfall, Pardis Sabeti, a computational geneticist at the Broad, says her group is exploring a diagnostic tool called SHERLOCK, which is based on CRISPR gene-editing technology. Researchers can program SHERLOCK so that it identifies genetic sequences on the basis of initial studies of the Lassa virus lineages involved in a particular outbreak. “What we’d like to see in the future is that four days after an infection emerges, we learn its genomic sequence and make a diagnostic immediately,” she says.

That kind of speed can also help officials to monitor for mutations in Lassa. “We are always preparing ourselves for the possibility that Lassa virus will pick up a mutation that lets it transmit readily from human to human,” Sabeti says.

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## References

1. Siddle, K.J. *et al.* *N. Engl. J. Med.* <https://doi.org/10.1056/NEJMoa1804498> (2018).

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