Press release: Innovative genomics tool guides response to Lassa fever outbreak

For the first time during an ongoing Lassa fever outbreak, scientists have used rapid, portable genomic sequencing technology to identify viruses without prior knowledge of the cause of disease. This enabled researchers to allay fears and direct the public health interventions to limit the spread of the virus and help to protect more people from disease.

The research, conducted during the 2018 Lassa fever epidemic in Nigeria, was carried out by scientists from Public Health England (PHE) (UK), the Bernhard Nocht Institute for Tropical Medicine (BNITM) (Germany) and Irrua Specialist Teaching Hospital (ISTH) (Nigeria), in collaboration with the Nigeria Center for Disease Control (NCDC) and the World Health Organization (WHO). It was published in the journal ‘Science’ on 3 January 2019.

Lassa fever is caused by a virus carried in the urine or faeces of infected rats. The virus causes fever, weakness, muscle pain and seizures, and is frequently fatal. The Lassa virus occurs endemically in West Africa and while it regularly causes small outbreaks, an outbreak of the virus in the area in early 2018 led to 376 confirmed cases within a few months, more than the combined total for the 3 previous years.

The sudden upsurge in cases raised concerns that a new, highly transmissible form of the virus had evolved, able to pass from person to person more effectively than previous strains.

In order to better understand the reasons for the heightened number of cases, the NCDC, together with the WHO, commissioned the research team to analyse patient samples to understand if the virus had an increased transmission potential. The research builds on work that was carried out by PHE and BNITM during the 2014 to 2016 Ebola outbreak.

The team, working at the ISTH in Irrua, Nigeria, used Oxford Nanopore Technology‘s portable device to rapidly sequence the genetic code of 120 virus samples. Traditionally, genomic assays used in the field required researchers to look at one genetic marker or virus strain at a time. However, this time they used a different approach, in combination with DNA sequencing, and known as metagenomics, which enabled the team to test for multiple different variations of Lassa virus genome, which is known to be highly diverse – speeding up the process of identifying the strains responsible for causing illness in this outbreak.

The approach gives insights into the genetic material of an entire virus population at a specific point in time. The researchers found that the strains in the samples weren’t all closely related, suggesting that there wasn’t a single source of the virus that then spread from person to person.

Instead, there were lots of different strains, suggesting multiple different instances of contraction from rodents. These early, rapid results allowed teams on the ground to continue focusing the public health response on community engagement around rodent control, environmental sanitation and safe food storage rather than shifting to solely focusing on addressing person to person spread.

The analysis revealed a great deal of diversity and indicated mixing with Lassa virus strains of the previous year’s outbreaks.

Explaining the results, Professor Stephan Günther, Head of the Virology Department at BNITM, said:

> By using this technology to look at the Lassa virus family tree and comparing samples from this outbreak to those from previous years, we were able to exclude human-to-human transmission as the reason for the surge in cases.
>
> Instead, a frequent transmission from animals to humans seems to be the cause of the high case numbers.

Professor Miles Carroll, Head of Research and Development of the National Infection Service at Public Health England, said:

> Viruses are constantly changing, becoming more or less infectious and deadly over time. By studying their genetic code, we can better understand where the virus has come from and how it spreads.
>
> Our previous tools to probe viral genomes took over a month to provide insights. Now, we can view results in as little as one day and in a field situation, guiding the public health interventions we deliver and ensuring we can act fast to stop more people becoming ill.
>
> Human-to-human transmission of viruses is something we always want to avoid, but in this instance, the evidence indicated that we also needed to act in other areas for maximum impact.

The Chief Medical Director of ISTH, Prof Sylvanus Okogbenin, said:

> The result of the sequencing reassured managing clinicians in ISTH, the main centre for the diagnosis and treatment of Lassa fever in Nigeria. I’d like to congratulate the team for the feat. The institution is very willing to collaborate further to ensure that on-site sequencing is a regular feature of its institute of Lassa fever research and control.

Dr Chikwe Ihekweazu the Director General of NCDC added:

> The results from this study, which were made available to NCDC as they became available, were critical in enabling us to provide answers to questions during the outbreak and focus response measures appropriately.
>
> We are proud that all the sequencing was done onsite in ISTH, and will work with our partners to increase capacity for metagenomics in Nigeria.

The real-time, portable DNA sequencing technology used in this study has applications beyond Lassa fever. By being able to look at lots of different pathogen sequences in one go, the technology could be applied to previously unknown pathogens. This is important because international health agencies have predicted that an unknown ‘Pathogen X’ could cause the next major outbreak.

This new technology has the potential to enable scientists on the ground during an outbreak to rapidly study the pathogen genome without necessarily knowing what it is they are looking for.

About Bernhard Nocht Institute for Tropical Medicine (BNITM)

BNITM is Germany’s largest institution for research, services and training in the field of tropical diseases and emerging infections. The current scientific focus is on malaria, haemorrhagic fever viruses, immunology, epidemiology, clinical research of tropical infections and mechanism of transmission of viruses by mosquitoes. To study highly pathogenic viruses and infected insects, the institute is equipped with laboratories of the highest biosafety levels (BSL4) and a BSL3 insectary.

BNITM comprises the National Reference Centre for Tropical Pathogens and the WHO Collaborating Centre for Arbovirus and Haemorrhagic Fever Reference and Research. Together with the Ghanaian Ministry of Health and the University of Kumasi, it runs a modern research and training centre in the West African rainforest, which is also available to external research groups.

About PHE

PHE will continue to work with NCDC to strengthen their capacity to detect and respond to similar events in the future through the UK Aid funded IHR Strengthening Project.

About Nigeria Centre for Disease Control (NCDC)

NCDC was established in the year 2011 in response to the challenges of public health emergencies and to enhance Nigeria’s preparedness and response to epidemics through prevention, detection, and control of communicable diseases. Its core mandate is to detect, investigate, prevent and control diseases of national and international public health importance.