

South African doctors move quickly to contain new virus

Four people died after they were infected by a new strain of Old World arenavirus. The rapid response of the investigating team was crucial in halting the outbreak in southern Africa and calming public fears. Claire Keeton reports.

When a microbiologist at a private laboratory requested assistance in a case of suspected viral haemorrhagic fever (VHF), alarm bells started ringing at the National Institute for Communicable Diseases (NICD) in South Africa.

Dr Lucille Blumberg, head of the epidemiology division at the institute, said her team noted that the doctor who had treated this potential VHF patient, an adult male, had also treated a woman safari agent from Zambia. The woman had been suffering from fever, vomiting and diarrhoea, followed by rash, liver dysfunction and convulsions. On 12 September, she was evacuated in critical condition to a private clinic in Johannesburg. A day after being admitted, she died.

It transpired that the suspected VHF case was a male paramedic who had become ill on 21 September, nine days after caring for the safari agent during her evacuation from Zambia. He died on 2 October.

Blumberg's fears of a disease outbreak were heightened when a third case, a nurse who had treated the safari agent at the Johannesburg clinic, was admitted to hospital on 30 September. Five days later, she too was dead.

"I thought there was something very wrong, something going on," said Blumberg, "and then on Thursday night we heard about the nurse who had been admitted."

Two further cases were identified in October. One had cleaned the hospital room occupied by the safari agent, the index case in this outbreak. The cleaner died on 6 October. The fifth case was a nurse who had cared for the paramedic (case number two). This nurse was treated with ribavirin, which has been effective in patients with Lassa fever, and she has since made a good recovery. She was the only one of the five to receive this treatment because the virus had been identified by the time she became ill.

All patients initially had non-specific flu-like illness. Symptoms included

fever, headache and muscle pain. The illness increased in severity over a week, with the patients developing diarrhoea and pharyngitis. A rapid deterioration, with respiratory distress, neurological signs and circulatory collapse were terminal features in all four patients who died.

Blumberg's fears that "something was very wrong" were borne out when the cause of the outbreak was found to be a distinct new strain of Old World arenavirus. This was established in tests done by the special pathogens unit (SPU) of the NICD at the National Health Laboratory Service in Sandringham, South Africa, the infectious diseases pathology branch of the Centers for Disease Control and Prevention (CDC) in Atlanta, USA, and Columbia University in New York.

The new strain, which was isolated by SPU head Dr Janusz Paweska, is a distant relative of two Old World arenaviruses known to be pathogenic for humans: Lassa virus, which is common in western Africa, and lymphocytic choriomeningitis (LCM) virus, which

can be found worldwide. But neither LCM virus nor Lassa fever virus has ever been found in southern Africa. The newly discovered virus is now the third Old World arenavirus species known to cause a severe and frequently fatal infection in humans.

Arenaviruses are broadly divided into two groups: New World arenaviruses, found in the Americas; and Old World arenaviruses, found in Africa. Both are associated with rodents and have co-evolved with them. Rodents are common in village houses in western Africa and therefore human exposure to the virus can be frequent.

That the outbreak has been contained to five people speaks volumes for the work of the provincial outbreak response teams in partnership with the NICD, which was formed in 2002 to gather intelligence on communicable diseases and provide expertise throughout the southern Africa region.

Its epidemiology team was alerted to the problem early, while the SPU – a WHO Collaborating Centre for the research and diagnosis of VHF's



Dr Janusz Paweska, head of the special pathogens unit (SPU), at the National Institute for Communicable Diseases (NICD) in South Africa – the only biosafety level 4 laboratory in Africa.

SPU, NICD

and other viruses – was able to help identify this new species of Old World arenavirus. This swift identification of the virus led to the successful treatment of the fifth case and containment of the outbreak through close monitoring of the victims' contacts.

Blumberg said the successful outcome had been the result of strong teamwork within NICD and with its various partners, as well as a measure of luck. "It was serendipitous that the same doctor treated both of the first two victims," she said.

The experience had also emphasized the need for extensive testing and gathering of case details. "What was important in the whole story was that the physician treating the second case (the paramedic) also treated the first index patient, whom he had originally diagnosed as having 'tick-bite fever'. Nevertheless, he knew of a link between the two cases and sent off blood from the second case (paramedic) for viral haemorrhagic fevers testing," Blumberg said, adding: "You never say 'never'. A disease might not normally be seen in a geographical area, but you should never rule it out."

Paweska said his team was under "high and constant" pressure from many quarters to find answers quickly amid much media and public anxiety.

"Identifying an agent that is causing an outbreak of great public health concern is important for a number of reasons; it allows for streaming down diagnostic tests for laboratory case confirmation, implementation of appropriate containment, treatment and hospital infection control measures," Paweska said, adding: "It also helps in calming public fears and anxiety when

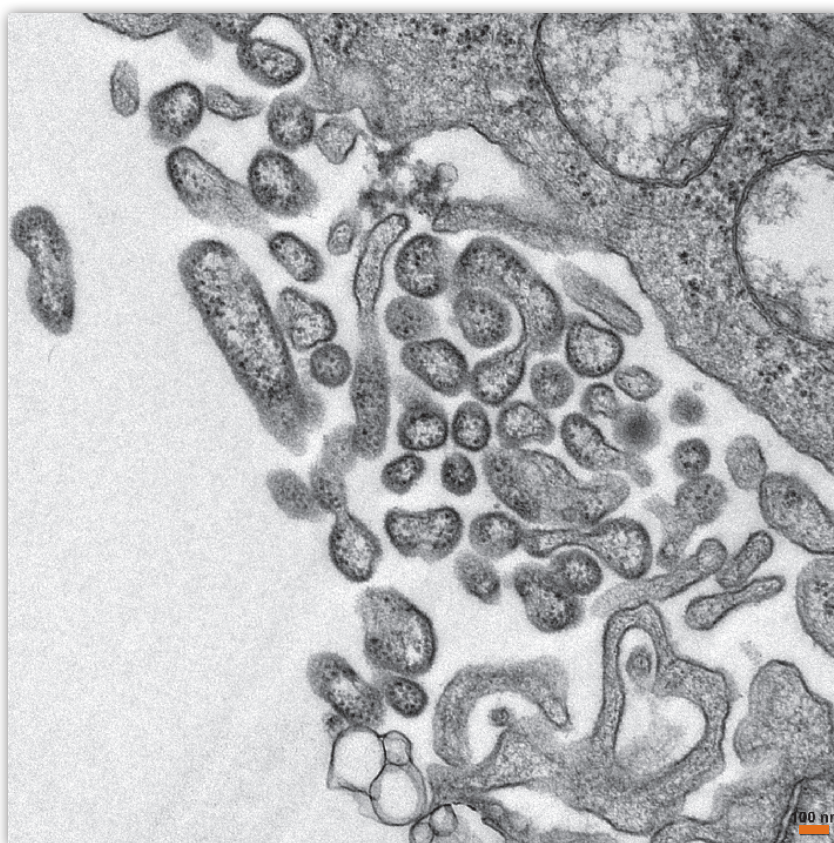


Image of arenavirus particles with their typically sandy appearance, from which they get their name *arena* meaning "sand" in Latin. Bar 100 nanometres.

scientists can show what is causing a disease."

When the paramedic died (case number two), a strong connection was made with the safari agent (index case). "We started thinking of a link to prove it. But it was difficult as we had only one single collection of blood sample from him," he said, explaining that by the time the sample was taken the disease agent may not have been present in the bloodstream any more. "Even when the virus has been cleared from the bloodstream, it can still replicate or traces of it can be found in other tissues."

Paweska continued: "At this stage we thought it was most likely a viral haemorrhagic fever. A number of tests were set up, including those for Ebola, Marburg, Lassa, Rift Valley fever and Crimean Congo haemorrhagic fever, but they yielded negative results. It was quite puzzling. When the next cases were identified it was obvious we were dealing with a cluster of hospital infections."

It became crucial to obtain liver, skin and muscle biopsies. Subsequent analysis of sequencing data of these samples generated at the SPU, CDC

and Columbia University in New York indicated that the outbreak was caused by a unique Old World arenavirus. SPU is the only biosafety level 4 laboratory in Africa – the highest level of laboratory safety that is required for work with extremely dangerous pathogens.

"Taking biopsies during this outbreak was pivotal to the successful recognition of the outbreak, virus isolation and identification – a milestone in this investigation," Paweska said. "I wonder where we'd be now if we had not done it – still fishing around probably."

Paweska said that he and his colleagues in Zambia are discussing how to name the virus. In the past arenaviruses were often named after the places where they originated, but today scientists feel it is unfair to stigmatize these places with a disease name.

"We can no longer call it the Zambia, Lusaka or Johannesburg virus. One has to give this virus a neutral name but still reflecting its origin, for example using a very old name of a region or location, which is not in common public use." ■

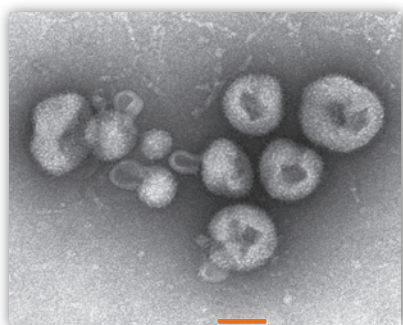


Image of arenavirus particles obtained from infected cells. The distinctive grainy appearance and surface projections are typical for arenaviruses. Bar 100 nanometres.