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EBOLA'S LOST WARD

A hospital in Sierra Leone has struggled to continue its research amid the worst Ebola outbreak in history.

BY ERIKA CHECK HAYDEN

Robert Garry had a bad feeling about the tin roof teetering above his head. It was June, and he and a colleague, Sheik Humarr Khan, were surveying a makeshift shelter that was to serve as a temporary Ebola ward for Kenema Government Hospital in Sierra Leone. They could see that the only thing holding the metal sheets to a 5-metre-tall wooden frame was a handful of thin, twisted wires.

Half an hour later, at a meeting in the main hospital building, the men were interrupted by a tremendous crash. As the sound reverberated through the hospital grounds, Garry and Khan rushed back outside to see what had seemed inevitable: the precarious structure had collapsed.

It was an omen of things to come. In less than a month, the hospital's operations would topple under the weight of the worst Ebola outbreak in history. The wards were overwhelmed with

patients and Khan, an infectious-disease physician at Kenema, and many of his staff were among those fighting for their lives.

The epidemic has killed more than 2,600 people since it began in December 2013, and it could infect tens of thousands more by the end of this year, according to the World Health Organization (WHO). Three countries — Guinea, Liberia and Sierra Leone — have been the epicentre, struggling with weak health systems and a wholly inadequate global aid response, even after the WHO declared the epidemic an international public-health emergency in early August (see *Nature* <http://doi.org/vsc>; 2014).

Khan and his team came to the fight against Ebola armed with experience battling another virus: Lassa, which like Ebola causes a life-threatening illness that sometimes results in haemorrhagic fever. But Lassa has much more predictable annual infection cycles. Along with Garry, a virologist at Tulane University in New Orleans, Louisiana,

One of the general wards at Kenema Government Hospital was abandoned by staff and patients owing to fears over Ebola.

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For a video about some of the people involved, see: go.nature.com/kaln6

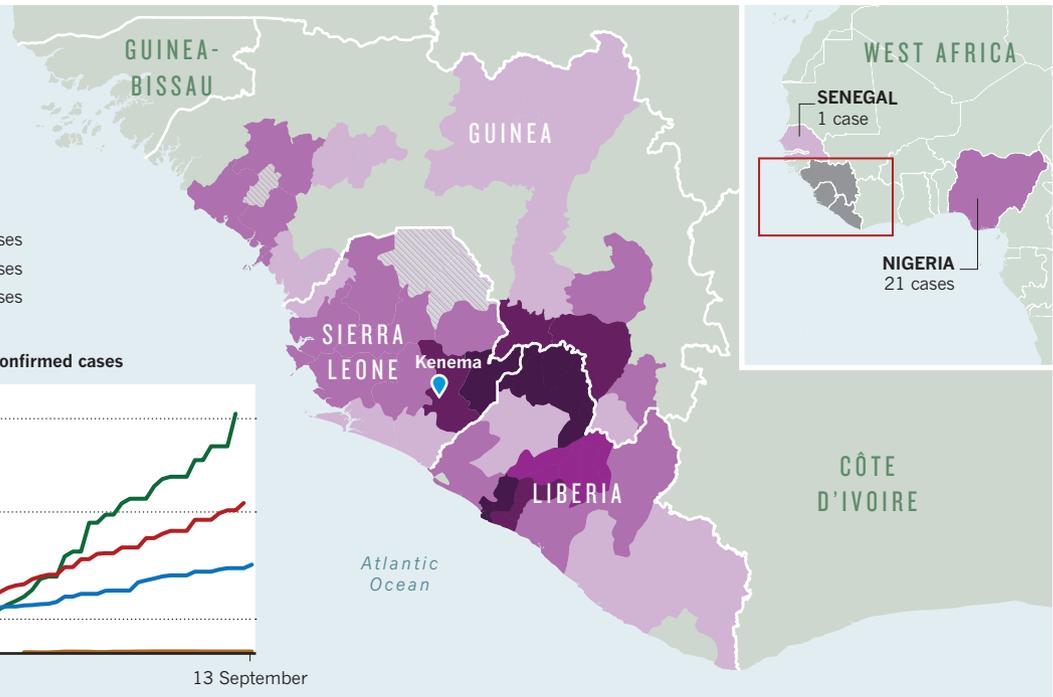
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EBOLA'S EPICENTRE

Since Guinea saw the first confirmed case of Ebola in March, the number of people who have become infected has climbed steadily. Kenema Government Hospital identified Sierra Leone's first case in May.



Cumulative suspected, probable and confirmed cases



and an international team of scientists, Khan had spent the better part of a decade building a Lassa treatment and research programme at Kenema, including a dedicated ward and a modern diagnostic laboratory. The ward they were adding was the next step in their arsenal against the disease.

But before it could be completed, the Lassa lab diagnosed Sierra Leone's first case of Ebola. Hundreds more followed. And a medical facility that had been set up to study one disease suddenly found itself overwhelmed by another.

Researchers worked hard to study the disease that was filling the wards — to trace its path into and through the country. But the outbreak consumed the hospital, and research was put on hold. It became clear that even if science could inform the outbreak response, the much more pressing need was for health resources and humanitarian aid.

“There’s a question of research’s role here,” says Pardis Sabeti, a computational geneticist at the Broad Institute in Cambridge, Massachusetts, who has worked with the Kenema team since 2008. Too frustrated to stand on the sidelines, she and other US researchers called for more aid to be sent to Kenema, but found the response painfully slow. “Our friends needed support and every international organization we turned to was stretched too thin.”

A SHINING EXAMPLE

Khan knew the risks of working on haemorrhagic fevers: he became the lead Lassa doctor at Kenema after his predecessor died of the disease. Lassa infects 300,000 to 500,000 people a year and kills between 5,000 and 20,000 of those.

The hospital in Kenema had been treating patients in its Lassa ward for decades, even struggling through a bloody civil war that lasted from 1991 to 2002. Its expertise made it an ideal nucleus for a group called the Viral Haemorrhagic Fever Consortium, which started in 2010 and included scientists from Kenema, Tulane and other partners in West Africa and the United States.

One of the main obstacles that doctors faced was diagnosing diseases quickly enough to treat them; after the war, no lab in Africa had the technology to detect Lassa in a patient’s blood. So in 2005, Kenema

built a lab and developed a diagnostic test. Sabeti, one of the founding members, began to sequence samples to understand how the disease spread through West Africa.

In May, Sabeti, Khan and Garry met in Nigeria to celebrate an enormous step forward for their work. In October, the World Bank and the US National Institutes of Health had funded a Centre for Genomics of Infectious Disease led by a collaborator in Ogun State, Nigeria, and the institute was hosting its inaugural meeting. The centre would use genetic technologies to study microbes in West Africa; it would soon acquire the first high-throughput sequencer in the region, mean-

ing that Kenema would no longer have to send samples of Lassa and other viruses overseas for in-depth sequencing. The partnership was becoming a shining example of scientific collaboration on the continent, building infrastructure and experience from within rather than importing it all from abroad.

Everyone was buoyed by the news, and by the progress in Sierra Leone, where, with a grant from the US Navy, Kenema was building its new Lassa ward. The ward would have 48 beds — almost double the capacity of the current

ward. It would have air conditioning to help nurses and doctors, who often had to wear stifling protective gear in oppressive equatorial heat. And it would be safer, with features such as a tiled floor and a drainage system, so that a worker could clean it out just by hosing it down. People with haemorrhagic fevers shed the virus in their blood, vomit, diarrhoea, sweat and tears. In the old Lassa ward, with its concrete floors, staff risked infection every time they slogged through the waste with a broom.

But the team knew that trouble was coming. When Guinea, to the north, notified the WHO about its Ebola cases in March (see ‘Ebola’s epicentre’), Garry predicted that Kenema would be next. He and Sabeti shipped trunks of protective gear to Kenema. Researchers from Sabeti’s lab travelled there with the genetic probes needed to diagnose Ebola.

In May, the first cases arrived. A woman turned up with a fever, and was bleeding heavily after a miscarriage. She and 13 others had become infected at the funeral of a traditional healer who had been treating Ebola victims in neighbouring Guinea. On 25 May, Augustine Goba, head of the Lassa diagnostic lab, confirmed that these people had brought the virus into Sierra Leone. They were admitted to Kenema’s Lassa ward.

“Our friends needed support and every international organization we turned to was stretched too thin.”



ERICA OLLMANN SAPHIRE

Pardis Sabeti (centre) worked with nurses at Kenema Government Hospital to study Lassa virus, but switched to studying Ebola once the outbreak began.

Garry flew in right away to help make sure that the Kenema staff were prepared. They needed to swap out their usual gowns and masks for Tyvek 'bunny' suits that cover the whole body in a waterproof barrier. Garry also made sure that the technicians were collecting, decontaminating and packing blood samples from patients after they had been used in diagnosis, so that Sabeti could sequence the DNA at the Broad Institute.

At first, the patients arrived slowly — too slowly. In early June, workers tracing the contacts of infected individuals could see that there were many more people who were potentially infected than there were in the hospital. But Ebola had never before come to West Africa, and people were spreading the disease without knowing it, simply by caring for the sick and burying the dead. Whole villages would be wiped out.

Khan suspected that Kenema would soon see a wave of cases, so he ordered the construction of the new, temporary ward. (After the first structure collapsed, workers rebuilt it with a shorter, sturdier roof). His prediction was right: by the end of June, the old Lassa ward was overwhelmed and suspect cases were being admitted to the temporary one. Patients began to flood in from all over eastern Sierra Leone. Everyone was sending patients to Kenema Government Hospital; there was nowhere else to go.

Supplies and staff were thin on the ground: Médecins Sans Frontières (MSF) and other aid groups were already stretched beyond capacity treating patients in Guinea and Liberia. The WHO had sent some staff to Kenema in June, but supplies were dwindling, and Khan was often the only doctor in charge of treating 80 people. He felt alone and afraid for his life. But he continued to care for his patients as best he could. "If I refuse to treat them, who would treat me?" he told his sister.

A DEADLY CHAIN OF EVENTS

Back in Cambridge, Sabeti was analysing data from the samples that Garry had shipped out of Kenema. Her group now had 99 Ebola virus samples from the first 78 patients in the country's outbreak. The researchers were performing in-depth genetic sequencing to track the way the virus mutated as it passed from person to person. No one had ever gathered these kinds of data on an outbreak while it was unfolding.

Important information was already emerging — for instance, that the whole outbreak could be traced to a single event in which an animal, probably a bat, transmitted the virus to a human. They also saw that the virus had accumulated hundreds of mutations since separating from an ancestral Ebola virus in Central Africa a decade ago (see *Nature* <http://doi.org/vsd;2014>).

It is the sort of work that could eventually change the way in which outbreaks are fought, says Anthony Fauci, head of the US National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Maryland, which funded the work. "We would normally come out with an analysis like this two years after an outbreak is over," he says. "To be able to do this is just extraordinary."

Sabeti's team released its data as quickly as it could, by 31 July. Among the first users were researchers who had been developing experimental drugs and vaccines for Ebola. These include the antibody cocktail ZMapp, which has since been given to seven individuals, not all of whom have survived, and a NIAID vaccine that entered human trials in early September. None of the mutations seen in the virus so far would render these products less effective, although some affect regions of the virus that are targeted by current diagnostic tests.

Sabeti was in close contact with Khan throughout, and knew that the situation in Kenema was deteriorating fast. "He was concerned, and he was sort of still by himself, and not really getting the support he needed," Sabeti says.

In late June, a feverish local chief was admitted to a private ward in Kenema that lacked the infection-control measures used in the Lassa ward. That started a deadly chain reaction: he infected five staff members, including a pregnant nurse. A midwife, Mbalu Fonnies, who was also the chief Lassa nurse, worked with three others to deliver the nurse's stillborn baby. She and the other nurses were all infected, almost certainly during the delivery. They all died.

Fonnies's death on 21 July and the deaths of other senior nurses snapped a thread that had kept the hospital together. 'Aunty Mbalu' had been treating Lassa at Kenema for 25 years — throughout the civil war — and had survived a Lassa infection herself. Now she was gone.

"A lot of these people spent a good part of their childhoods hiding out in the bush from the rebels."



Mbalu Fonnies (left), Veronica Koroma and Sheik Humarr Khan all worked to treat Ebola patients at Kenema General Hospital. Fonnies and Khan have since died from the disease.

The next day, while in a lab meeting, Sabetti glanced at her e-mail and saw that there was a message about Khan. She opened it immediately: Khan had Ebola. “I just broke down and started bawling,” she says.

Sabetti felt helpless. She wanted to do something — anything. So she wrote a white paper urging US officials to commit more supplies and money to fighting the outbreak, and sent it to Broad Institute director Eric Lander and other members of a board of science advisers to the US president. She and Garry had already travelled to Washington DC to ask health officials and Congress to send more aid; Garry had asked officials to send experimental vaccines and medicines.

Now they urged doctors from MSF and the WHO to treat Khan with ZMapp. But the doctors feared that if something went wrong, it would undermine the already-fragile public trust in them, so they decided not to do it.

With Khan now very ill, the Kenema hospital was on the verge of collapse. There were too many patients and too few staff to treat them, and supplies were dwindling. Fearing for their lives and feeling ill-equipped to do their jobs, the remaining nurses and lab technicians went on strike. The hospital as a whole had virtually shut down, except for its Ebola ward.

Tulane physician Daniel Bausch was working in the Ebola ward around that time. One day, he went into the ward with a WHO worker. “There were 50 patients and no nurses or other health workers in there. My first reaction was, we just need to close this centre. We can’t say this offers any care.” Still, they soldiered on, knowing full well that Kenema was a place of last resort for patients, who would only spread the disease if released.

Meanwhile, hearing rumours that Ebola was a hoax or a conspiracy, people from the surrounding city attacked the hospital, throwing rocks at the building. Police used tear gas to drive the rioters away.

On 29 July, Sabetti received a second e-mail from an epidemiologist in Sierra Leone. The message simply read: “Dr. Khan is gone.”

LASSA LOOMING

The period after Khan’s death was the nadir of the outbreak in Kenema. The loss of its leader and of so many others was devastating. “It completely demoralized the community. It has completely torn them apart,” says Joseph Fair, a virologist who has been working in Sierra Leone since 2004 and advised the country on its response to the current outbreak. Sabetti and her team were also shocked. “We loved that man,” Sabetti says.

By the time the paper on the sequencing of the first 78 cases was

published (S. K. Gire *et al. Science* **345**, 1369–1372; 2014), on 28 August, six of its authors, including Khan and Fonnies, had died.

But by then, help had started to arrive. Workers from the WHO and MSF began to restock supplies of protective equipment. The International Committee of the Red Cross began building a treatment centre just outside Kenema. Kenema is still treating roughly 50 Ebola patients, but it is trying to wind down that work and reopen its general wards.

But with all the attention now on Ebola, physicians who work in Kenema are concerned about Lassa. The peak Lassa season, November to April (J. G. Shaffer *et al. PLoS Negl. Trop. Dis.* **8**, e2748; 2014), is approaching, and of the hospital’s original 36 specialized Lassa staff, 11 have now been infected and 6 have died. Surveillance staff, doctors, nurses, drivers, cleaners and lab technicians have all lost their lives to Ebola. New trainees and the remaining staff — including Ebola survivors — are stepping up to treat the cases that do arrive. But the hospital is seeing fewer Lassa patients than it would have expected for this time of year. “We think the patients are reluctant to come in,” says Garry. “That’s not good.”

Garry still hopes to make Kenema a centre of excellence for Lassa research by training African staff to carry out clinical trials on the best ways to track, diagnose and treat the disease. And the haemorrhagic-fever consortium plans to name the new ward after Khan when it is finally completed. The goal is to outfit it with a high-throughput genetic sequencer so that researchers there can study the circulating viruses all the time, and perhaps detect the next outbreak, of Ebola or otherwise, before it grows out of control. Garry has faith in Kenema’s survivors. “A lot of these people spent a good part of their childhoods hiding out in the bush from the rebels,” Garry says, thinking back to the days of civil war. “You’re talking about a very resilient group of individuals.”

Sabetti, Garry and their colleagues are now preparing for the next step in their research: sequencing samples from every Ebola patient seen at Kenema since 18 June. They hope that the data will reveal whether the virus is continuing to mutate at the same rate and in the same genetic regions as before, and whether the mutations seen in the current outbreak made different circulating viruses more or less able to transmit between people and cause death. The data will also tell a more personal story, revealing the precise path taken by the virus as it infected Khan, Auntie Mbalu and so many of their colleagues. They, too, are represented in the samples. ■

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