INFECTIOUS DISEASE

Genomes reveal start of Ebola outbreak

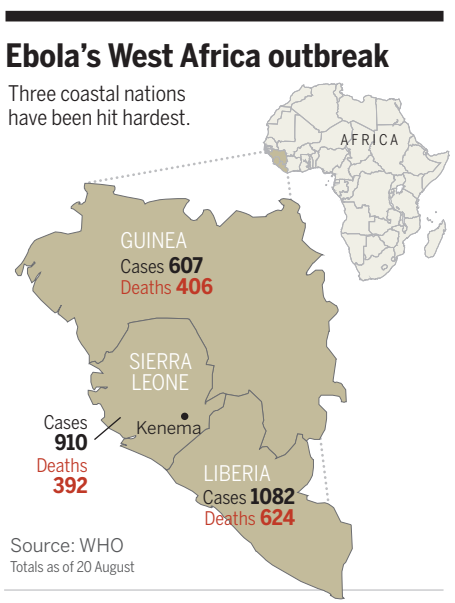
Viral sequences demonstrate how the disease spread in Sierra Leone

By **Gretchen Vogel**

When the young woman arrived at the Kenema Government Hospital in Sierra Leone in late May, she had high fever and had just miscarried. The hospital suspected she had contracted Lassa fever, because the viral disease is endemic in the region and often causes miscarriages. But Ebola virus disease, another hemorrhagic fever illness, had been spreading in neighboring Guinea for months, so when she began bleeding profusely, staff tested her for that virus as well. The results were positive, making her the first confirmed case of Ebola in Sierra Leone.

Volunteers in protective gear bury a victim of Ebola in Kenema.

PHOTO: MOHAMMED ELSHAMY/ANADOLU AGENCY/GETTY IMAGES



The young woman, who eventually recovered, is now at the heart of a tragic but potentially important research tale. In a paper online this week in *Science* (http://scim.ag/sgire), a collaboration led by Stephen Gire and Pardis Sabeti of Harvard University and the Broad Institute in Cambridge, Massachusetts, report sequencing and analyzing the genomes of Ebola virus samples from 78 people in Sierra Leone who were diagnosed with Ebola between late May and mid-June, including the young woman who came to Kenema's hospital. The 99 complete sequences—some patients were sampled more than once—provide insights into how the virus is changing during the outbreak, which could help improve current diagnostic tests and, in the long term, guide researchers working on vaccines and treatments.

The study, however, also highlights the unrelenting toll the outbreak has taken on health workers on the front lines. More than 50 co-authors from four countries helped collect and analyze the viral sequences. Five of them contracted Ebola virus disease themselves and died.

That first diagnosed case in Sierra Leone infected no one at the hospital, says Robert Garry, a virologist at Tulane University in New Orleans, Louisiana, who works with the Kenema hospital's Lassa fever research center and is also a co-author on the paper. But a team from the ministry of health was immediately dispatched to the woman's home village to find out where and how she had been infected. They learned that she had attended the recent funeral of a traditional healer—an herbalist—who had been treating Ebola patients from across the nearby border with Guinea.

The team found 13 more people who were infected, all women who had attended the burial. It was those mourners who largely sparked Sierra Leone's outbreak, which has sickened more than 900 and killed more than 390 people. Blood samples from 12 of those mourners and other infected people have allowed Gire, Sabeti, and their colleagues to track how the virus changed as it spread. "It is the first time that the real evolution of the Ebola virus can be observed in humans," says Sylvain Baize of the Institut Pasteur in Lyon, France, who sequenced some of the first Ebola virus samples from patients in Guinea, where the current outbreak originated, but who was not involved in this project.

The genomic data also shed new light on how the virus—officially called EBOV—ended up in West Africa. EBOV, one of five ebolaviruses known to infect humans, has caused at least 12 outbreaks in Central Africa and Gabon since 1976. Until this year, though, it had never been identified in West Africa.

Some researchers theorized, based on early sequencing data, that EBOV had circulated for decades, undetected, in animals in the region. But the new analysis, strengthened by the unprecedented number of genomes, supports another theory: that the virus spread, via animal hosts, from Central Africa within the last decade. Researchers aren't sure which animal to blame, but fruit bats are their leading suspects (*Science*, 11 April, p. 140). At least one fruit bat species known to carry ebolavirus has a population range that stretches from Central Africa across to Guinea.

Gire, Sabeti, and their colleagues found that in the current outbreak the virus's genome is changing fairly quickly, including in regions that are key for the accuracy of the PCR-based diagnostic tests. It will be important to keep track of such changes, Gire says, so that tests can be updated if necessary. Vaccines and antibody-based treatments—such

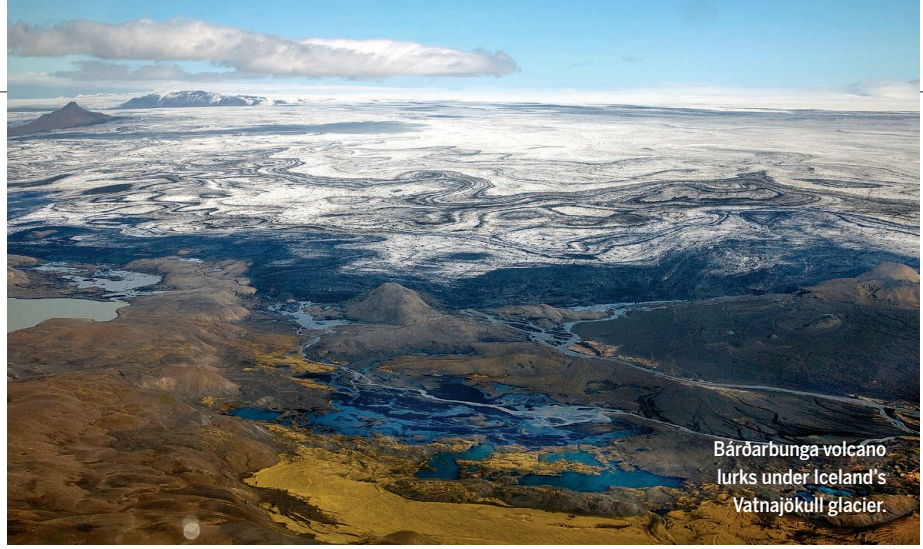
as the ZMapp drug that was used in a handful of patients—could also be affected by the kinds of changes the researchers identified. (Sabeti says ZMapp researchers contacted her about the new sequences her group had posted online.)

The analysis reveals that the outbreak in Sierra Leone was sparked by at least two distinct viruses, introduced from Guinea at about the same time. It is unclear whether the herbalist was infected with both variants, or whether perhaps another funeral attendee was independently infected. One Ebola virus lineage disappears from patient samples taken later in the outbreak, while a third lineage appears. That lineage—tied to a nurse who was traveling to reach a hospital but died along the way—seems to have originated when one of the lineages present at the funeral gained a new mutation. This third lineage was spread, Garry says, via a truck driver who transported the nurse, as well as others who cared for her in the town where she died.

Further studies of the differences between the various Ebola lineages might link such mutations to the virus's behavior—how lethal it is, and how easily it spreads, for example. "The paper shows the unrealized potential of what these methods could do," says Roman Biek, who studies the evolution and ecology of infectious diseases at the University of Glasgow in the United Kingdom.

Missing from the sequencing analysis are Ebola samples from people infected in Liberia and Guinea. Stephan Günther of the Bernhard Nocht Institute for Tropical Medicine in Hamburg, Germany, says he has samples from Guinea in his lab, waiting to be sequenced once he and colleagues can find the time. (This week Günther was in Nigeria, tracing contacts of an Ebola patient there, who was infected by a traveler from Liberia.) Researchers in Liberia have also collected samples, but are focused on attempting to slow the epidemic there, where it is spreading in the densely populated capital and shows no signs of slowing down. (Congo is also on high alert as Ebola has popped up in a remote region in the northwest of the country. As *Science* went to press, it was not clear which ebolavirus is causing that outbreak.)

Sabeti, who with her colleagues posted the virus sequences in a public database as soon as they were generated, says she hopes this work and the tragedy that befell her coauthors and other health care workers will inspire other researchers to make their data public quickly, in both this outbreak and future epidemics. "We've got to crowdsource the epidemic," she says. "The more information you get into hands of people who can help, the more likely you are to come up with a solution." ■



Bárðarbunga volcano lurks under Iceland's Vatnajökull glacier.

PHOTO: © EGGERT NORÐDAHL/DEMOTIX/CORBIS

ICELAND

As volcano rumbles, scientists plan for aviation alerts

Ash sensors ready to deploy on ground, planes

By **Carolyn Gramling**

After 2 weeks of seismic grumbling, Iceland's Bárðarbunga volcano was holding scientists—and the aviation industry—in suspense this week. Buried beneath the island's giant Vatnajökull glacier, under 100 to 400 meters of ice, the volcano had yet to erupt as *Science* went to press. But scientists at the Icelandic Meteorological Office (IMO) in Reykjavík, seasoned by back-to-back eruptions at Eyjafjallajökull in 2010 and Grímsvötn in 2011 that produced large ash clouds and caused costly air traffic snarls over northern Europe, are better prepared than before to monitor ash and assess its threat to aircraft.

"One of the criticisms of the 2010 incident was that there were a lot of model forecasts," but few observations, says Fred Prata, an atmospheric scientist at Nicarnica Aviation in Kjeller, Norway. Airlines thought flights were disrupted unnecessarily and "were a bit critical of the scientists," Prata says.

In August 2011, at the urging of Iceland's government, IMO began devoting more resources to volcano hazards. IMO and the University of Iceland are leading a European Union–funded research program, FUTUREVOLC, that has brought new monitoring capabilities. "We have installed new seismic stations, [and] an experimental type of new water chemistry that … can look for chlorine, fluorine, sulfur, and other species indicative of volcanic activity," says IMO atmospheric volcanologist Melissa Pfeffer. If there's an explosive eruption, "we have a lot more instrumentation that will go into the field."

In July, as part of FUTUREVOLC, Prata's team delivered three ground-based infrared cameras to Iceland that can detect silicate particles in volcanic ash. Prata and Nicarnica also tested a plane-mounted sensor, the Airborne Volcanic Object Imaging Detector (AVOID) last October: The team released a tonne of ash, scooped from a deposit in Iceland, over France's Bay of Biscay and flew an Airbus airplane fitted with AVOID behind the cloud. The sensor, which uses multispectral cameras to distinguish silicate from ice particles, detected the ash from 60 kilometers away. If Bárðarbunga erupts, Prata says, the team could deploy another AVOID unit in 36 to 72 hours. They are also gearing up to equip partnering airline easyJet with removable ash sensors for future eruptions.

At press time, alarm over Bárðarbunga was subsiding. IMO scientists briefly raised the aviation alert to red on 23 August, when they saw seismic tremors—small, continuous earthquakes thought to be generated when lava encounters ice—followed by rapid seismic swarms. They interpreted this as a likely eruption under the ice—but testing and reconnaissance revealed no meltwater surges, cracks in the ice, or telltale gases, Pfeffer says.

Most current seismic activity is at the tip of a magma intrusion, or dyke, extending tens of kilometers north from the caldera, beyond the edge of the glacier. If magma reaches the surface there, less water interaction would mean a less explosive eruption, Pfeffer says. But the magma could still erupt beneath the glacier. Scientists are standing by. ■