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Patient Zero Believed to Be Sole Source of Ebola Outbreak

By pinpointing the virus's source, a new report validates steps health care workers are taking to battle the disease

August 28, 2014 | By Dina Fine Maron |

One glaring fact from the latest report on the Ebola outbreak is that five of the many study authors are dead, killed by the disease that is roiling west Africa. The new analysis, published in the August 29 issue of *Science*, reveals that the current Ebola outbreak stemmed from an earlier initial leap from the wild into humans, rather than the virus repeatedly jumping from a natural reservoir—perhaps infected animals—to humans. By essentially sketching out a high-tech molecular family tree, researchers concluded that the virus spreading in Sierra Leone and nearby countries is the descendent of an original Ebola viral jump, and not new versions of the pathogen that are being repeatedly introduced into the human population. That means the public health response to this outbreak—which focuses on tracking and treating those who have been exposed to people with Ebola, rather than attempting to keep people away from potential animal carriers—has been the right strategy.

Study author Augustine Goba, pictured above, diagnosed the first case of Ebola in Sierra Leone. *Photo courtesy of Stephen Gire*

That conclusion comes from a sweeping analysis of 99 Ebola virus genome sequences that comprise some 70 percent of the Ebola patients diagnosed in Sierra Leone in late May to mid-June. The virus samples were extracted from the blood of 78 patients early in Sierra Leone's outbreak. And the work indicates that the first case of the disease in that country stemmed from the burial of a traditional healer who had previously treated Ebola patients in Guinea. Subsequently, 13 additional women who attended the burial developed Ebola viral disease.

This work cannot yet help researchers understand what the original source of the infection was earlier this year—whether it was infected meat or an encounter with an infected fruit bat or something else altogether. Earlier work published in the *The New England Journal of Medicine* showed that the Ebola virus responsible for the current outbreak is related to the Zaire strain of the virus, but it still remains unknown how the pathogen made the leap into humans. This new information, however, does confirm that the current outbreak agent originated from the 1976 Ebola strain instead of a co-evolved strain of the virus, which was a concern early in the outbreak.

The study provides a reference point for how this strain of the virus compares with those in other outbreaks. Unsurprisingly, the virus has changed significantly as it ages—as most viruses do—with more than 300 mutations that differentiate it from other Ebola outbreaks since the 1970s. And just how quickly the virus mutates is also readily apparent; 55 small changes have occurred, compared with reference sequences taken from Ebola viruses in Guinea just a few months earlier.

On the virus mutation spectrum, Ebola has a relatively slow mutation rate compared with influenza and HIV, but its mutations still develop faster than those of the smallpox virus. Still, the longer the pathogen goes unchecked means that it will continue to accumulate mutations, some of which could prove more problematic and make it potentially more lethal or easily transmitted among humans. Yet exactly how any of these current alterations—some of which involve changes in amino acids—may prove problematic for humans has not been identified. The new sequencing work could help public health experts understand how to control the current outbreak by revealing how well diagnostics and potential therapies may match up with the genetic makeup of the viral strain. When a new drug is created, for example, it is typically screened against all the available sequences of the virus it aims to treat.

Study author Stephen Gire, an Ebola research scientist at Harvard University, says one of the most important points raised in the paper is that unlike sequencing efforts in most prior outbreaks, his team was able to sequence many viruses fast enough to help inform the current outbreak response efforts—allowing the genomes to act as a reference to measure potential therapies against as well as confirming the virus is spreading from human to human instead of from other sources. Still, there are limitations to the data. Because the sequencing was just of the viruses in Sierra Leone over a three-week period this spring, "We're really not getting a full picture of the outbreak in west Africa, and that information, I think, is vital to understanding this outbreak as a whole," Gire says.

Yet, the effort does provide valuable insights into the current outbreak. "I am absolutely entranced by this work," says William Schaffner, an expert in infectious diseases at Vanderbilt University. The work provides "powerful evidence that once the virus was introduced into the human population subsequent transmission was human to human, and this is not from repeated introductions from the wild," he says. If the virus had come from more than one natural reservoir it would be detectable in the genome sequences, adds Christopher Mores, associate director of Louisiana State University's Center for Experimental Infectious Disease Research. "If we were seeing introductions from other outbreak zones or more likely another natural reservoir—animals—we would expect to see a pre-outbreak signature coming in again and again." Gire notes that, "exposure to animal reservoirs will always be an area of concern, and education on how to properly handle bushmeat and to stay clear of already dead animals is important in disease prevention, but our data does show that human-to-human transmission is the driver of this outbreak."

Since the current Ebola outbreak was first reported to WHO in March more than 1,500 people have died in Guinea, Liberia, Nigeria and Sierra Leone, including more than 120 health workers. "In many cases medical staff are at risk because no protective equipment is available—not even gloves and face masks. Even in dedicated Ebola wards, personal protective equipment is often scarce or not being properly used," WHO said in a statement.

The report in *Science* represents a collaboration between health care workers from Harvard University and Kenema Government Hospital in Sierra Leone, among other institutions. The five deceased study authors, from the group of 58 authors, were all from Sierra Leone and included three nurses, a physician and a hematologist who worked part-time in an Ebola lab. It remains unknown if the study authors contracted Ebola on the job or from ill family or community members.

To date, there is no current Ebola vaccine or proven drug treatment. The National Institutes of Health expect to begin a clinical trial in humans for one potential Ebola vaccine early next week. Initial results indicating whether the drug proves safe and sparks an immune response should be available in November. And another vaccine will undergo clinical trials in Canada. Meanwhile, no drug treatment has proved effective to assist Ebola patients. Although one experimental drug, ZMapp, was given to a handful of patients (including the two U.S. American aid workers)—some of them died and there is no way to tell if the drug helped, hurt or had no effect.

The current epidemic only underscores how little focus has been on the necessity of a strong global health infrastructure and making global health security a priority in individual countries, says Anthony Fauci, executive director of the U.S. National Institute of Allergy and Infectious Diseases. "If there was a health care infrastructure in those countries of rapidly responding—identifying and isolating cases and providing adequate medical care and doing the proper contact tracing—then this epidemic might well have been put under control a long time ago."

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