Ebola Virus Ecology

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(See the article by Leroy et al., on pages 1895–9.)

It has been nearly 30 years since Ebola virus was identified during 2 outbreaks in the Democratic Republic of Congo (DRC) and Sudan [1, 2], and it has been closer to 40 years since Marburg virus, the first identified member of the filovirus family, was discovered [3, 4]. Despite investigators’ considerable effort, the ecology of the filoviruses remains arguably as obscure today as it was after these first outbreaks. The article by Leroy et al. [5] makes a small step toward a better understanding of this ecology. Their study supports what many have suspected: that the filoviruses circulate widely in the central African rain forests and that they can infect humans and many nonhuman primates, including some previously undocumented members, such as mandrills and baboons (previously infected only in the laboratory). Although the recent outbreaks of Ebola in chimpanzees, apparently primarily with lethal disease, and the Republic of Congo. Despite the

strain and its virulence remain unclear. We have known since the original Marburg outbreak that filoviruses could infect primates, because Marburg virus was first discovered in infected Cercopithecus aethiops monkeys shipped from Uganda [7]. We also know that Marburg infections in humans have been seen from central to southern Africa and are possibly ongoing in eastern DRC [8–12], but we know virtually nothing of the ecology of the Marburg or Ebola strains in that or any other geographic area.

In 1990, the scientific world was surprised by the appearance of another member of the filovirus family, this one occurring in the United States, in Reston, VA, in infected cynomolgous monkeys from the Philippines. The tenuous evidence that we have suggests that this less-pathogenic filovirus is from the dense rain forests of the infected animals’ country of origin [13]. Unlike the other members of its family, Reston virus causes no disease in humans [14], and careful laboratory studies that used virus seed free of contamination by simian hemorrhagic-fever virus demonstrated that Reston virus, compared with the lethal African filoviruses, caused milder or no disease in primates [15, 16].

The geographic distribution of the filoviruses is far from distinct. Previously, we knew only that these viruses originate in tropical rain forests near the equator, where they can infect monkeys and humans, apparently primarily with lethal disease. Leroy et al. found that infection rates in chimpanzees in Cameroon was 12.9% and inferred that the infections were caused by the same virus strain that circulates in forest areas farther east and south, where human and nonhuman-primate outbreaks of Ebola have been occurring with regularity in recent years. The Cameroon forest is also on the same latitude as southern Sudan, where the less-virulent Sudan strain of Ebola virus circulates. We do know that some humans with high-titer antibody to Ebola virus survive infection during known outbreaks or single infections [17–22]. The Cameroon chimpanzees might, therefore, be survivors of an unknown local or regional epizootic. It is also plausible, however, that, as in the Philippines, a less-virulent member of the filovirus family is circulating in Cameroon, a situation that would account for the lack of local human cases and/or observed epizootics.

Antibodies to Ebola and Marburg viruses have been found in humans living in the same geographic areas of Africa. Antibodies to Ebola and Marburg viruses do not cross-react in any test, but no published results of antibody assays have yet distinguished between antibodies to any of the known Ebola virus strains, regardless of their origin or pathogenicity. The data presented in the Leroy et al. article are based on assays using only antigens from the Zaire strain of the Ebola virus, previously confined to the DRC, Gabon, and the Republic of Congo. Despite the
improved specificity of the ELISA assays used in the Leroy et al. study, no antigens specific to other Ebola virus strains were included in the assay, so it is impossible to say with certainty that a given reaction reflects infection with a particular Ebola virus strain—rather than with a related virus, known or unknown—or even with some confounding antigen. The odds of finding other filoviruses in this vast, remote, and highly biodiverse geographic area are high, and diagnosis of human or primate symptomatic disease in specific areas may not be sufficient to allow one to delineate the ecological range of each virus. Perhaps Cameroon is a good place to start a geographic survey of filovirus ranges.

Thus, until the ecologies of the Ebola virus strains are determined through careful investigations defining their distributions and possibly their primary reservoir, data based solely on antibody assays are insufficient to determine the distribution of these viruses. Some novel experiments have been conducted on potential reservoirs of filoviruses [23], but neither these nor extensive ecological studies at several sites have led to the identification of the primary reservoir, which remains elusive. We do know that the Sudan strain of the Ebola virus, which is closely related to the Zaire strain, infects humans in southern Sudan (adjacent to both the area in northern DRC with Ebola outbreaks and to regions in the DRC and Uganda with Marburg outbreaks), but we have no data on the ecological distribution of the Zaire or Sudan strain or on nonhuman-primate infections [24]. What Leroy et al. do confirm is that Ebola viruses circulate in the forests of central Africa, even in areas where human cases (not necessarily infections) or epizootics have not been observed. However, the identities of the filoviruses that circulate in the entire equatorial region remain an important—and, in my view, an open—question.

Leroy et al. conclude that their data best support a multiple-introduction hypothesis for the Zaire strain of the Ebola virus. This hypothesis supports the idea that infections in humans and nonhuman primates are less rare than we had thought but that they must originate from ecological foci that we cannot identify. Another acceptable hypothesis is that there are multiple point sources for infection but that the ranges and origins of the viruses are unknown.

The study by Leroy et al. reminds us of the challenge of understanding the ecological origin of filovirus infections in humans and nonhuman primates in the wild. In Africa, the resources available in Gabon are unparalleled for providing opportunities for studies of the ecology of the filoviruses. Cautiously interpreted serological studies in nonhuman primates, such as that by Leroy et al., along with virological studies and more-extensive human epidemiological studies, are likely to be the key to the eventual understanding of the ecology of the filoviruses.

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