

Ebola Virus Disease

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Since the discovery of ebola viruses (genus *Ebolavirus*, family *Filoviridae*, order *Mononegavirales*) in 1976, these viruses have continued to emerge unpredictably in humans and susceptible animal populations. To date, five species have been described: *Zaire ebolavirus* (EBOV), *Sudan ebolavirus* (SUDV), *Reston ebolavirus* (RESTV), *Tai Forest ebolavirus* (TAFV), and *Bundibugyo ebolavirus* (BDBV). With the exception of RESTV, all these viruses cause hemorrhagic fever in humans, with the highest case fatality rates reported for EBOV (approximately 90 percent). To date, the only wild nonhuman primates found infected with ebola viruses were African great apes: western lowland gorillas (*Gorilla gorilla gorilla*) and central chimpanzees (*Pan troglodytes troglodytes*) with EBOV and western chimpanzees (*Pan troglodytes verus*) with TAFV. RESTV caused lethal infections in long-tailed macaques (*Macaca fascicularis*) in the Philippines, but thus far these have only been described in captive settings.

Thousands of gorillas and chimpanzees are believed to have died during the EBOV outbreaks in Central Africa over the past decades, though wild populations are hard to monitor and exact population decline estimates vary. Great ape nest estimates in Minkébé, an area known to have experienced an EBOV outbreak but where bushmeat hunting is minimal, suggested a 99 percent decline in nest encounter rate (Walsh et al. 2003). The progression of EBOV infection is hypothesized to be similar between humans and apes, although evidence from great apes is limited; after an incubation period of

between 2 and 21 days, individuals develop high fevers, vomiting, diarrhea, and sometimes internal and external bleeding. The vast majority of human transmission is thought to occur by direct contact with blood or bodily fluids (saliva, mucus, vomit, feces, sweat, tears, breast milk, urine, and semen). Some humans appear to not present symptoms when infected and it is unknown if they are able to spread the virus. The approximately 10 percent antibody detection rate suggested in feces (Reed et al. 2014), along with an approximately 13 percent seroprevalence estimate from wild-born chimpanzees suggests that survival after exposure occurs in great apes as well. Interestingly, this study also detected several other seropositive nonhuman primate samples (*Mandrillus leucophaeus*, *Papio anubis*, *Mandrillus sphinx*, and *Cercopithecus neglectus*), suggesting these species may also survive infections (Leroy et al. 2004a). Recovered humans are thought to be uninfected, though one case of sexual transmission has been confirmed after recovery from infection and the virus has been detected in semen more than six months following recovery (Fischer et al. 2016).

Great apes are hypothesized to transmit the infection to conspecifics by coming into contact with a carcass or via behaviors possibly involving contact with infected body fluids, such as grooming, nursing, and play. Between-group transmission could occur during intergroup encounters and through the emigration of females, particularly following the death of the silverback male in gorillas when a group dissolves. Alternatively, range overlap and the use of shared resources could allow transmission between groups and species, as EBOV viral particles can likely persist for some time, depending on the conditions. Alternatively, repeated spillover events from a reservoir might be responsible for the (relatively) large geographic distribution of outbreaks in great ape populations. Importantly, great ape die-offs have repeatedly been observed concurrently with human outbreaks in Central Africa. A number of human epidemic chains were even traced back to a contact with an infected great ape carcass,

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which then served as an intermediary EBOV amplifier (Leroy et al. 2004b). It should be noted that the largest EBOV epidemic ever, which, as of June 10, 2016 likely infected over 28,600 people, is unlikely to stem from contacts with infected western chimpanzee carcasses. This species is indeed extremely rare in the region where the human outbreak started and absent from the vicinity of the village of the index case (Marí Saéz et al. 2015).

The extreme virulence of ebola viruses observed in human and great ape populations strongly suggests that ebola viruses are not endemic/enzootic pathogens and that other species represent the reservoir. Although all outbreaks observed to date likely had a zoonotic origin, despite intensive efforts, it has only rarely been possible to link many outbreaks to a particular animal reservoir. As a result, the ecology and reservoir of ebola viruses and which factors facilitate zoonotic transmission remain largely unknown. In the search for ebola virus reservoirs, a significant number of species have been sampled, including thousands of individual arthropods and mammals. The best evidence for a reservoir to date comes from fruit bats, where viral RNA was found in 13 specimens of *Epomops franqueti*, *Hypsignathus monstrosus*, and *Myonycteris torquata* collected in Gabon in 2003 (Leroy et al. 2005). On the other hand, researchers were unable to isolate the virus itself and no viral sequences were generated from the huge number of fruit bats captured since. Serological evidence is more abundant but interpretation is also much harder, notably due to potential cross-reactivity. Despite widespread hunting across much of Africa, to date no fruit bat hunter has conclusively been reported as an EBOV index case. Finally, two insectivorous bat species (*Mops condylurus* and *Tadarida pumila*) survived experimental infections with EBOV and *Mops condylurus* was also found to harbor ebola virus-specific antibodies in the wild, suggesting that some insectivorous bats may also play a role in ebola virus ecology. Circumstantial evidence suggests that the spillover event that ignited the West African outbreak involved a two-year-old boy's contact with a high-density colony of insectivorous *Mops condylurus* (Marí Saéz et al. 2015).

Vaccine development has accelerated greatly following the large outbreak of EBOV in West Africa and several candidates have shown great promise. Several of these human vaccines appear to be effective in nonhuman primates, but the main question remaining is how to reach sufficient vaccination coverage given the illusive nature of wild great apes. Vector-based vaccines, in which a benign virus can be modified to display EBOV-specific antigens, can be either replication-competent or replication-deficient; a replication-competent vaccine could in principle be self-spreading, which would facilitate their delivery to wild populations. However, for the latter, key data have to be generated before the question of whether genetically modified organisms should be released into the wild can be discussed. Vaccinating African great apes could enhance long-term survival of great ape populations, while also decreasing human risk of exposure to the virus via contact with carcasses during outbreaks. Whether this is ethical and feasible will require careful consideration.

SEE ALSO: Emerging Infectious Disease; Epidemiology; Epizootiology; Human–Nonhuman Primate Disease Transmission; Zoonoses

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