Position Statement

September 2024

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Ebola Virus

Background

Ebola viruses (EBOV) are members of a group (or genus) of viruses, four of which can cause Ebola disease (EBOD) in humans. The most well-known species is *Orthoebolavirus zairense* (EBOV; formerly *Zaire ebolavirus*), identified in 1976 in the Democratic Republic of the Congo (DRC). The associated illness caused by EBOV is referred to as Ebola virus disease (EVD).

EBOD is a serious acute illness. The average case fatality rate is approximately 50% but may vary from 25–90% depending on the level of available supportive care and the patient's immune response.

EBOD is a zoonosis. Although not proven, fruit bats are thought to be the most likely natural Ebola virus hosts with non-human primates and other animals serving as intermediate hosts. The increase in the number of outbreaks of EBOD in the last 20 years is likely due to the closer proximity of human habitats to Ebola reservoirs as well as deforestation and climate change. The exact mechanism of *Orthoebolavirus* spillover from animals to humans has not been elucidated, but once this has occurred inter-human transmission is through direct (or indirect, e.g. soiled bedding) contact with the blood and body fluids of an infected individual. The virus is geographically restricted to the endemic areas where its host species reside. Occasional cases have been reported outside Africa – these are usually healthcare/laboratory acquired or associated infections.

Since 1976 there have been over 20 recorded outbreaks of EBOD, mainly in Central Africa; DRC (2022, 2021, 2018–2020, 2017, 2014, 2012), Uganda (2022, 2011, 2012), Republic of Congo (2005), Sudan (2004), all within approximately 10 degrees N and S of the equator. The DRC continues to be the most frequently affected country, having had five outbreaks declared between May 2020 and September 2022 alone, involving the North Kivu and Equateur provinces. The North Kivu region of the DRC was the area afflicted with the largest ever DRC outbreak from 2018 to 2020.

Outbreaks can be sporadic and unpredictable. Earlier outbreaks were largely contained and controlled because they occurred either in less populated areas where isolation of infected individuals was possible or, for individual cases imported into countries with developed healthcare systems, full isolation of the patients was possible. The West African EVD outbreak in 2013–2016 however, which centred on Sierra Leone, Guinea and Liberia, has been the largest outbreak to date, with 28,000 cases and 11,000 deaths. The global response, providing multinational support and intervention, ultimately brought an end to the epidemic and provided further insights into EVD. Although another EVD outbreak was declared in Guinea on 14 February 2021, it was declared over by June 2021. More recently, the Ugandan Sudan Virus Disease (SVD) outbreak caused by *Orthoebolavirus sudanense* (SUDV) was first announced in September 2022 and declared over by 13 January 2023 included 142 confirmed cases and 55 deaths (case fatality ratio 38.7%).

Countries affected by Ebola virus are shown in the GDRI and any associated Change Notifications.

Modes of transmission

Although transfusion-transmission is theoretically possible, at this time there have been no reports of cases in affected countries. It is assumed an infected and infectious donor would be symptomatic and thus unlikely to donate, however, asymptomatic infections have been described. Depending on the assay used and the extent of exposure, EBOV IgG has been detected in 2.5%–45.9% of contacts in EVD seroprevalence studies.

Transmission is seen frequently within families, within hospitals, and during some mortuary rituals where contact among individuals becomes more likely. Exposure to infected patients and their body fluids puts healthcare workers at a high risk of infection unless appropriate procedures are followed. Data from trials on the use of antivirals (e.g. monoclonal antibody therapies) and vaccines for both pre- and post-exposure prophylaxis has led to recommendations for their use in outbreak settings.

Several cases of sexual transmission have been reported. Ebola virus nucleic acid can persist in semen after recovery from EVD and is an important mode of transmission in the convalescent period. Indeed, transmission of EBOV due to persistence in body fluids such as semen has been described as a cause of 'flare-ups' and clusters of EVD. For example, genomic studies of the Guinea EVD outbreak in 2021 suggested the source of resurgent virus was a survivor from the 2013–2016 West African outbreak, a concerning interval for viral latency of five years. Recrudescence and relapse of infection due to persistence of EBOV RNA at immune privileged sites (e.g. the central nervous system) has also been described. Furthermore, recent studies have shown serological evidence of reactivation in one-third to one-half of recovered individuals. The implication for onward transmission under these circumstances is unclear and has led to the need for precautionary deferrals of potentially at-risk donors.

Transmission through food (with the possible exception of bush meat) and water does not occur. Outside of controlled laboratory experiments, spread of Ebola via aerosols has not been clearly described.

Management and prevention of EBOD

EBOD is mostly managed with good supportive care.

Most evidence on therapeutics and vaccination exists for EBOV. The Pamoja Tulinde Maisha (PALM) randomised controlled trial (RCT) in 2019, compared ZMapp with three other agents (remdesivir, REGN-EB3 and mAb114) and led WHO to recommend EBOV-specific therapeutics in patients with EVD (2022). This included a strong recommendation for treatment with mAb114 or REGN-EB3 for patients with confirmed EVD. Of note, they issued a conditional recommendation against treatment with remdesivir and ZMapp in these guidelines.

In 2021, the Strategic Advisory Group of Experts on Immunization (SAGE) recommended using ERVEBO in ring vaccination during outbreaks of EBOV, as it confers protection after one dose. A second two-dose vaccine (Zabdeno/Mvabea), given 50 days apart, is recommended for preventive vaccination in areas at lower risk for EVD (or areas neighbouring an outbreak). ERVEBO was shown to be safe and effective during clinical trials and has likely played an important role in limiting Ebola morbidity and mortality. In a study conducted in Ebola treatment facilities in DRC, 56% of unvaccinated patients died from Ebola, compared with 25% of patients vaccinated before symptom onset.

Therapies and vaccines for other species of *Orthoebolavirus* are in phase 2 studies, including for SUDV.

Blood and safety measures

Although countries with EBOD outbreaks are generally not major tourist destinations, travel to and within these countries does occur, and there may be some migration to the UK and other European countries. EBOD outbreaks, excepting any potential person-to-person transmission in a healthcare setting when an infected individual has been moved to a non-affected country for treatment, have been identified only in countries that are also malarious. Therefore, all individuals who have been in affected areas will be excluded from blood or tissue donation for at least four months after their return to the UK under current UK donor/donation malaria guidelines. Individuals who have ever been infected with Ebola virus are permanently excluded from donating, except for those who are donating immune (convalescent) plasma for therapeutic use in patients with EBOD. Potential blood donors who are contacts of those who have been infected with Ebola will be excluded for six months from last contact. Data to suggest that some *Orthoebolavirus* species can be found in privileged sites in survivors, and which could potentially lead to transmission resulted in the Advisory Committee for Dangerous Pathogens (ACDP) updating their EBOD guidance. In response, the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) updated guidance for deferral of potential tissue and cell donors who had been in contact with an infected individual, was under investigation for EBOD or who has been in contact with an individual that was present in an area during an active outbreak, implementing a precautionary permanent deferral. This deferral is currently under review and the advice will be updated accordingly. A permanent deferral of blood donors who have ever been a sexual contact of an EBOD survivor is advised, because relapsed disease in the survivor creates a risk of onward transmission even after a significant interval of recovery.

Ebola serology could be used to identify risk (asymptomatic individuals who could present as donors and sexual contacts of asymptomatic individuals) but reliable CE-marked Ebola serology assays for blood donor screening are not available. Recent modelling data suggests a decline in antibody reactivity (even if there is periodic restimulation, as mentioned above) in the six months to two years post-recovery. In one study 3% (4/117) of previously affected individuals did not have detectable circulating Ebola virus specific antibodies. Due to the introduction of vaccines in high-risk populations, serological assays would need to distinguish vaccinated from naturally immune individuals and be able to detect all species. Therefore, serological testing of donors for Ebola virus specific antibodies is not employed as a blood/tissue safety measure at this time.

Convalescent (immune) plasma

As with many viral infections, those who recover from EBOD develop antibodies which then may confer a degree of protection against further exposure to the same Ebola virus species. One of the Ebola treatment approaches has been the infusion of plasma from recently infected and recovered individuals: convalescent or immune plasma. In theory, the antibodies present in the plasma would neutralise virus circulating in an infected individual, helping to reduce viral load and consequently reduce the load on the individual's immune system, with the overall aim of helping to ensure recovery. Individuals who have been laboratory-proven to have been recently infected and recovered from EBOD may be eligible to donate convalescent (immune) plasma for use in the treatment of individuals with EBOD. Sensitive and specific IgG capture and competitive enzyme immunoassays have been used to identify potential high titre convalescent plasma donors 'in the field'.

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