Joint UKBTS Professional Advisory Committee ([1])

Position Statement

Ebola virus

May 2022

Approved by: Standing Advisory Committee on Transfusion Transmitted Infections

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Background

Ebola viruses (EBOV) are members of a group (or genus) of viruses that cause Ebola disease (EBOD), of which the most well-known is *Ebolavirus* (EBOV; formerly *Zaire ebola virus*). EBOV was first identified in 1976 in what the Democratic Republic of the Congo. The associated illness is referred to as Ebola virus disease (EVD).

EVD 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.

EVD 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. Transmission of Ebola virus from animal reservoirs to humans was previously uncommon, and the increase in the number of outbreaks of EVD 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 EBOV spill over 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 EVD, mainly in Central Africa (Democratic Republic of the Congo 2021, 2018-2020, 2017, 2014, 2012), Uganda (2011, 2012), Republic of Congo (2005), Sudan (2004). The most recent outbreak in the North Kivu region of the DRC (7th February-3rd May 2021), was the area afflicted with the largest ever DRC outbreak from 2018 to 2020.

Outbreaks can be sporadic and unpredictable, but they have been occurring with increasing frequency in the last decade. 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 2013-16 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 multi-national support and intervention ultimately brought an end to the epidemic and provided further insights into

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EVD. Although another EVD outbreak was declared in Guinea on February 14th 2021, it was declared over by June 2021.

Modes of Transmission

Although transfusion-transmission is theoretically possible, at this time there have not been any 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 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. As data emerges on the use of e.g. monoclonal therapies and vaccines for both pre- and post-exposure prophylaxis the burden of EVD in HCW will hopefully decline in the future. 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 in regions where active transmission was thought to have ceased. 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 5 years. Recrudescence and relapse of infection due to persistence of EBOV RNA at immune-privileged sites (e.g. the central nervous system) has been described. Furthermore, recent studies have shown serological evidence of reactivation in one-third to one-half of recovered individuals. Post recovery sub-clinical antigenic stimulation was observed at a high frequency in the investigation of antibody responses of convalescent plasma donors from the West African 2013-2016 outbreak. The implication for onward transmission under these circumstances is unclear. 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 is very rare.

Management of EVD

EVD is mostly managed with good supportive care. The major antigenic target of EBOV vaccines is the glycoprotein GP. Ervebo® or rVSV∆G-ZEBOV-GP (live-attenuated recombinant vesiculo stomatitis virus) vaccine when utilised in a 'ring' vaccination strategy resulted in complete protection against EVD 10 days (or more) after vaccination if contacts of EVD cases were vaccinated 'immediately'. The vaccine was approved by the FDA and European Commission for use in the 2018 DRC EVD outbreak, again contacts and secondary contacts were vaccinated. The WHO reported an estimated efficacy of 97.5% from the DRC data. Ervebo has been granted marketing authorisation by the European Commission and prequalification from WHO. A two-dose combination vaccine Zabdeno® (d26.ZEBOV,

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monovalent vaccine expressing the EBOV glycoprotein active against *Zaire ebolavirus*) AND Mvabea® (MVA-BN-Filo-EBOV, Sudan, Marburg and Tai Forest virus antigenic targets), were approved for use in the recent DRC outbreak, with evidence of 'durable immunity' in persons >/= 1 year of age. The vaccine, administered as separate doses received a marketing authorisation under 'exceptional circumstances' from the EMA, for the prevention of disease caused by *Zaire ebolavirus* in individuals ≥1 year of age. Studies evaluating the use of anti-viral therapies include the PALM and MEURI trials which commenced in the DRC August 2018. Investigators reported a statistically higher probability of survival in the Ansuvimanb (formerly known as MAb114, a monoclonal antibody from an EVD survivor) and/or REGN-EB3 (a triple murine monoclonal antibody cocktail) arms compared to the ZMapp (triple humanised monoclonal antibody cocktail targeting 3 glycoprotein epitopes) or Remdesivir arms. REGN-EB3 is now FDA-approved for the treatment of Zaire EBOV. Potential EVD therapies are still the subject of ongoing research and development.

Blood and Tissue Safety Measures

Although countries with Ebola virus 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. Ebola virus 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 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 EVD. 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 EBOV can be found in privileged sites in survivors, and which could potentially lead to EVD transmission resulted in the Advisory Committee for Dangerous Pathogens (ACDP) updating their EBOV guidance. In response SaBTO updated guidance for deferral of potential tissue and cell donors who had been in contact with an infected individual, was under investigation for EBOV or who has been in contact with an individual that was present in an area during an active outbreak, implementing a precautionary permanent deferral. Similarly, a permanent deferral of blood donors who have ever been a sexual contact of an EVD survivor is advised, because relapsed EVD in the survivor creates a risk of onward transmission even after a significant interval of recovery.

Ebola serology could be useful 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 currently available. Recent modelling data would suggest a decline in antibody reactivity (even if there is periodic restimulation, as mentioned above) in the 6 months to 2 years post-recovery and 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. Therefore, serological testing of donors for Ebolavirus 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 EVD develop antibodies which then may confer a degree of protection against further exposure to Ebola virus. 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 EVD may be eligible to donate immune/convalescent plasma for use in the treatment of individuals with EVD. Sensitive and specific immunoglobulin G capture and competitive enzyme immunoassays have been used to identify potential high titre CP donors 'in the field'.

Countries affected by Ebola virus are shown in the Geographical Disease Risk Index (GDRI) and any associated Change Notifications.

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