EDITORIAL

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Ebola: Are We Prepared for Recurring Infectious Threats?

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The World Health Organization (WHO) was first notified of a rapidly evolving outbreak of Ebola virus disease (EVD) in Guinea on 23 March 2014. On 8 August 2014, the WHO declared the Ebola epidemic a "public health emergency of international concern". A two-year-old child who died (6 August 2013) in southern Guinea was identified as 'patient zero' of the current Ebola outbreak, which is still raging. As of 21 November 2014, there have been 15,351 reported Ebola cases in eight countries since the outbreak began, with 5,459 reported deaths. The countries affected include Guinea, Liberia, Sierra Leone, Nigeria, Senegal, Mali, Spain, and the US. Transmission remains intense in Guinea, Liberia, and Sierra Leone.[1] Although the overall situation in the affected countries remains critical, there are signs that the disease outbreak is potentially being controlled.

The current EVD outbreak in West Africa is caused by the genus *Ebolavirus* which belongs to the family *Filoviridae*. This is an enveloped, negative-sense single-stranded RNA virus. *Ebolavirus* was first described in 1976 in Zaire (now called the Democratic Republic of the Congo) near the Ebola river, hence the name.[2] There are five identified Ebola virus species, four of which are known to cause disease in human. The virus causing the current outbreak in West Africa Ebola belongs to the Zaire species. Ebola can cause disease in humans and non-human primates (monkeys, gorillas, and chimpanzees). The natural reservoir host of the Ebola virus remains unknown. However, it is believed that the virus is animal-borne and that fruit bats are the most likely reservoir. There has been speculation that the current outbreak of Ebola in West Africa may have been sparked by the handling of bushmeat.

Transmission to humans occurs through exposure of mucous membranes or broken skin to body fluids from an infected animal or human. An infected individual is not contagious until symptoms are present. Symptoms start after an incubation period of two to 21 days. EVD manifests as a sudden onset of non-specific symptoms including fever, headache, muscle and joint pain, asthenia, abdominal pain, anorexia, diarrhea, and vomiting. In severe cases, shock, multi-organ failure, and severe bleeding may follow. The most recent WHO update reported a fatality rate from EVD of 36%.[1]

Healthcare personnel caring for patients infected with Ebola virus must be acquainted with the management of the disease and with the infection control processes specifically designed for the virus. Formation of a specialized, trained Ebola management team, including physicians, nurses, respiratory therapists, and intensive care personnel is an important strategy to optimize clinical care, reduce the risk to healthcare personnel, and streamline communication. Careful implementation of infection control measures requires timely planning and coordination at multiple levels within healthcare facilities: preferably well in advance of caring for patients infected with Ebola.

Clinical management of Ebola infection must be delivered with stringent adherence to infection control protocols specially designed for caring for

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an Ebola infected patient, while assuring the safety of healthcare personnel delivering care.

EVD is primarily transmitted by contact with infected bodily fluids or contaminated objects.[3] The virus has been detected in blood, urine, feces, vomit, sweat, tears, saliva, mucous, breast milk, and semen.[4] Ebola is generally not considered an airborne infection. However, airborne precautions, including use of N95 respirators and placement of patients in negative pressure isolation rooms, offers the theoretical benefit of limiting airborne transmission. The infectious dose for Ebola virus is thought to be low and the viral load in blood increases exponentially as symptoms progress. Healthcare workers have frequently been infected while treating Ebola patients and account for about 10% of infected individuals in the current outbreak.

Centers for Disease Control and Prevention-USA (CDC) and the WHO have issued detailed recommendations for patient isolation, personal protective equipment, sample handling, disposal of waste, and environmental decontamination for dealing with the Ebola outbreak.[5,6] The foundation of protection for healthcare workers is isolation of patients and adherence to infection control protocols. Personal protective equipment must be put on and removed in a systematic method and should be supervised by a trained observer.

In Oman, a practical and scientifically sound contingency laboratory diagnostic plan should be an integral part of hospital preparedness plans for any cases of EVD. Laboratory diagnosis of EVD should only be performed in a certified bio-containment level four laboratory. Such services are not currently available in Oman and samples will be sent to laboratories abroad for testing. Both molecular and serological tests are available for EVD diagnosis with molecular testing using real-time reverse transcription polymerase chain reaction (rRT-PCR) the cornerstone for diagnosing an acute Ebola virus infection. Oman's ministry of health has developed EVD laboratory guidance for handling and processing of clinical samples.[7]

In order to minimize needless exposure to clinical and laboratory staff, blood specimens sent for investigations from patients with suspect EVD should be limited to tests that are critical for their management. Stringent protocols should be in place (preferably tested) to ensure that laboratory workers are trained to process such specimens. CDC has issued guidelines on handling of specimens from suspected EVD cases which stated that laboratory tests can be performed under containment level two conditions providing good laboratory practice is in place and applying enhanced standard and droplet precautions using the appropriate personal protective equipment.[8]

Oman has containment level two laboratories capable of handling specimens safely for routine testing. The use of fully automated closed analysers for biochemistry and haematology testing further minimize exposure to laboratory staff and the environment. However, such systems are not widely available. Therefore, laboratories should ensure that alternative methods are in place such as inactivation of specimens prior to testing, or by implementing point of care testing (POCT). CDC has proposed that POCT can be utilized, and has provided guidance on its use.[9]

Severe Ebola infections are characterized by profound fluid loss, metabolic abnormalities, shock, and organ failure in addition to occasional life-threatening hemorrhages. Intensive supportive care aiming to timely correct and reverse these abnormalities is currently the basis of management in these patients. This approach has been shown to markedly improve the outcome particularly when practiced promptly and aggressively.

Unfortunately, specific and targeted treatment options for patients infected with Ebola virus are currently limited. There are no proven anti-viral agent(s) to treat EVD, although several investigational treatments may be considered. These include convalescent whole blood or plasma infusion, monoclonal antibodies, RNA-based drugs, and small antiviral molecules. The WHO has prioritized convalescent whole blood or plasma infusion, ZMapp (a combination of three monoclonal antibodies), and TKM-Ebola (an interfering RNA molecule used to block expression of two viral replication genes). Additionally, specific antiviral agents (favipiravir-anti influenza, brincidofovir-anti CMV, and adenovirus) may hold promise as Ebola treatment.

There is undoubtedly an urgent need for a safe and effective vaccine against EVD. There are two candidate vaccines currently in Phase I studies. The details of these vaccines are beyond the scope of this editorial.

The current Ebola outbreak is a public health emergency of international concern. This outbreak reinforces the urgent need for nations, including Oman, to be better prepared for coping with emerging infectious diseases through strategic planning and system development including bio-containment and laboratory facilities able to handle these frequently recurring and largely unpredictable outbreaks and epidemics.

"Not a single year passes without [which]...we can tell the world: here is a new disease!"

Rudolf Virchow, 1867 (known for his advancement of public health among many other achievements).[10]

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