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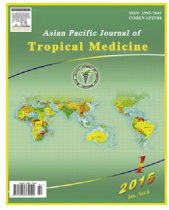

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An update on the 2014 Ebola outbreak in western Africa

Haaris A. Shiwani[1], Rebabonye B. Pharithi[2], Barkat Khan[2], Christian Binoun-A Egom[3], Peter Kruzliak[4], Vincent Maher[2], Emmanuel Eroume-A Egom[1,2,5]✉

[1]*Department of Clinical Medicine, Education Division, Trinity College Dublin, The University of Dublin, Dublin, Ireland*

[2]*Department of Cardiology, The Adelaide and Meath Hospital Dublin, Incorporating the National Children Hospital, Tallaght, Dublin, 24, Ireland*

[3]*University of Ndjamena, Faculty of Medicine, Ndjamena, Chad*

[4]*International Clinical Research Center, St. Anne's University Hospital and Masaryk University, Brno, Czech Republic*

[5]*Egom Clinical and Translational Research Services, Dartmouth, NS, Canada*

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ABSTRACT

The recent Ebola outbreak in Western Africa was the most devastating outbreak witnessed in recent times. There have been remarkable local and international efforts to control the crisis. Ebola Virus Disease is the focus of immense research activity. The progression of events in the region has been evolving swiftly and it is of paramount importance to the medical community to be acquainted with the situation. Over 28 000 people were inflicted with the condition, over 11 000 have died. Novel data has emerged regarding modes of transmission, providing rationale for recent flare-ups. Similarly, studies on survivors are elucidating the later stages of the disease recovery process. Novel techniques for diagnosis are also discussed. Finally, the current research regarding treatment and vaccine development is reviewed, particularly the implementation of rVSV-ZEBOV vaccination programs.

1. Introduction

The recent Ebola outbreak in Western Africa was the most devastating outbreak witnessed in recent times. The declaration of an international health emergency took place on the 8th of August 2014 [1]. In March of 2014, the first case of Ebola was confirmed in Guinea, Africa. By May, Liberia and Sierra Leone had cases of the condition, and by July the virus had spread to Nigeria and Senegal. In October, the disease touched Mali [2]. The outbreaks in Nigeria, Liberia, Sierra Leone and Guinea were officially declared over on 19th October 2014, 9th May 2015, 7th November 2015 and 29th December 2015, respectively [1,2]. On the 29th of March 2016, the WHO Director-General declared, during the 9th Emergency Committee meeting, that the outbreak was no longer a Public Health Emergency of International Concern [3]. In June 2016, Guinea and Liberia were declared to be free of transmission [4,5].

In the aftermath of the crisis which unfolded in Western Africa, it is now of interest to the medical community to assess where we stand today. What has happened since the media attention has dissipated? Can we forget about Ebola? What has been done to prevent future disasters of such catastrophic proportions? This review intends to update the reader on one of the worst medical emergencies of the modern era, particularly elaborating on (1) the latest epidemiological data, (2) recent studies (on survivors) which explicate the modes of viral transmission as well as the effects of the disease after recovery, (3) advances in treatment and prevention, and (iv) the future outlook of Ebola.

2. Epidemiology

Since its first occurrence in 1976, five different subtypes of Ebola virus have been identified across several areas of Africa. Evidence suggests that the Ebola virus tends to break out in

First author: Haaris A. Shiwani, Department of Clinical Medicine, Education Division, Trinity College Dublin, The University of Dublin, Dublin, Ireland.

✉Corresponding author: Emmanuel Eroume-A Egom, MD, Ph.D, M.Sc, MRCP, Egom Clinical and Translational Research Services, Dartmouth, NS, Canada.
Tel: +1 353(0)14142112
Fax: +1 353(0)14143052
E-mail: egomemmanuel@gmail.com

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small villages that are in close proximity to or are perhaps located in tropical rainforests [6]. As it was the case for all previous Ebola outbreaks, which all began in Africa, the most recent epidemic started in the West African nation of Guinea in late 2013 and was confirmed by the World Health Organization in March 2014 [6].

The Centres for Disease Control and Prevention has reported extensive data regarding the scale of the crisis [7]. Among the most heavily inflicted countries within Africa–Sierra Leone, Liberia and Guinea – there have been a total of 28616 cases reported (14124, 10678 and 3814 cases, respectively), resulting in 11310 deaths (3956, 4810 and 2544, respectively). As of the 13th of April 2016, 7 other countries have also reported cases of the disease. Nigeria, Mali, the United States, Senegal, Spain, the United Kingdom and Italy have encountered a total of 36 cases (20, 8, 4, 1, 1, 1 and 1 cases, respectively). Of the 36 cases, there were 8 deaths in Nigeria, 6 in Mali and 1 in the United States. Eight hundred and eighty one healthcare workers were infected during this tragedy and 513 died due to the disease. The healthcare workforce in Liberia, Sierra Leone and Guinea was reduced by 8%, 7% and 1%, respectively [8]. In Sierra Leone, consequently, there was a drastic 23% reduction in the delivery of health care services [8].

After the end of the initial outbreak, there have been a relatively low number of new cases that have re-emerged, all of which were rapidly and efficiently controlled [9]. Initially, in March 2015, 1 case was reported in Liberia, where 192 contacts were identified and sexual transmission was suspected. In June 2015, Liberia encountered 7 cases, with 126 identified contacts. August 2015 saw 6 cases emerge in Sierra Leone, with 840 contacts and sexual transmission suspected. Additionally, 1 case was reported in Sierra Leone in September 2015, with 780 identified contacts. In November, Liberia once again had 3 new cases of the condition being reported, with 165 contacts. In January 2016, Sierra Leone was challenged with a further 2 cases with over 150 contacts. Finally, March 2016 saw both Liberia and Guinea affected with 13 new cases and over 1200 contacts identified with a suspicion of sexual transmission.

In the most severely affected countries, services have been established in order to accommodate survivors of the disease, e.g. MSF survivor clinics [10]. From August to November 2014, an EBOV outbreak unrelated to that in the West of Africa emerged in the Democratic Republic of Congo, with 66 cases reported, resulting in 49 deaths (74%). The initial case was reported on August 24th in a pregnant woman involved in the dissection of a bush animal [11].

3. Pathogenesis and transmission

Epidemics of Ebola virus disease are generally thought to begin when an individual becomes infected through contact with the meat or body fluids of an infected animal [6]. Once the individual becomes ill or dies, the virus then spreads to others who come into direct contact with the infected individual's blood, skin, or other body fluids [6]. However, it should be noted that for any large-scale human transmittance to occur, there must be a direct contact of mucous membranes, or broken skin with bloody or bodily fluids of an infected person [6]. Such transmission can involve any contact by the form of blood or bodily fluids including but not limited to urine, saliva, sweat, faeces, vomitus, breast milk, and semen, as well as via contaminated objects like needles and syringes [6]. It has become evident, by the repeated re-emergence of the Ebola virus disease, that periods of transmission persist even when there are no active cases of the disease present. This phenomenon can be attributed to human to human transmission, rather than the animal to human transmission that led to the initial appearance of the disease in humans. After a patient recovers from Ebola virus disease, the virus can survive in organs where there is relative protection from the immune system – sites of immune privilege [12]. Infectious Ebola virus has been identified in the following survivors' body fluids or tissue: cerebrospinal fluid, breast milk, seminal fluid, vaginal fluids, gastrointestinal (rectal swab, faeces, saliva, vomitus), urine, lower respiratory tract (alveoli), eye (aqueous humour, tears, conjunctivae), and other (skin, sweat, placenta, cord blood and amniotic fluid) for extended periods of time after onset of the illness, as highlighted in Figure 1 [13]. Survivors facing neurological or ocular symptoms after recovery from Ebola may still harbour replicating EBOV [13]. This persistence may explain the re-emergences of the disease that have occurred, particularly in settings of sexual transmission. One case of a survivor of EVD showed the presence of EBOV RNA in a semen sample by RT-PCR assay at 175 days after there was a negative serum EBOV [14]. A contact of this survivor contracted the disease and subsequently died following unprotected intercourse in a period after the survivor had recovered from the acute illness [14]. Data from the PREVAIL III trial demonstrated that in 97 (male) survivors of Ebola virus disease, viral RNA was detected in 37% of patients, with 18 months being the longest gap between active disease and detection [15]. It has been elucidated that although there have been no cases to indicate airborne transmission of the virus, studies have shown that small-particle viral aerosols can be a route of infection in rodents [16]. Thus, extensive exposure to aerosolised virus by healthcare workers may pose a risk.

4. Complications of Ebola virus infection

After the outbreak, many researchers have extensively followed-up survivors of the disease. Numerous complications have been identified in survivors including but not limited to arthralgia, myalgia, depression and anxiety, uveitis, vision loss, hearing Loss, paraesthesia, and concentration, mood and memory disturbances [17–19].

5. Diagnosis

Although there are no approved specific therapies for Ebola virus disease, it is essential to make the diagnosis as early as possible, in order to initiate supportive measures before the development of irreversible shock and to institute infection control procedures [6]. The methods of diagnosis used in the recent outbreak include Antigen-capture ELISA (Enzyme Linked ImmunoSorbent Assay) testing, Immunoglobulin (Ig) M ELISA, PCR, Virus Isolation, Serum IgM, IgG, and Immunohistochemistry [20]. These methods were effective; however, there is relative room for improvement, particularly in optimising speed, sensitivity and cost effectiveness. Several novel techniques are in the process of development, and recent evidence suggests that they may provide some advantages over existing methods. Optofluidic nanoplasmonic biosensor,

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