

PACIFIC JOURNAL OF MEDICAL SCIENCES

{Formerly: Medical Sciences Bulletin}

ISSN: 2072 – 1625



Pac. J. Med. Sci. (PJMS)

www.pacjmedsci.com. Email: pacjmedsci@gmail.com.

EDITORIAL

EBOLA IN WEST AFRICA: A CLARION CALL TO ACTION TO AVERT A GLOBAL PANDEMIC

VICTOR J. TEMPLE

M. Sc., Ph. D., C. Biol., M. S. B

Discipline of Biochemistry and Molecular Biology, Division of Basic Medical Sciences,
School of Medicine and Health Sciences, University of Papua New Guinea

Correspondence author: templevictor@gmail.com; templevj@upng.ac.pg

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This special issue of the Pacific Journal of Medical Sciences focuses on the most serious infectious disease pandemic currently ravaging the populations of three West Africa countries – Sierra Leone, Liberia and Guinea. We can no longer afford to be complacent: the virulence of the Ebola virus, coupled with the frightening ease of its transmission in communities and across borders in our “Global Village”, presents a real threat of a global pandemic.

This publication is in response to many requests from our undergraduate and postgraduate medical and health sciences students, as well as from academics and others. Many are overwhelmed by the tsunami wave of information about Ebola in the print, social and news media. Yet, a lot of the information circulating is contradictory, and some is just misinformation.

The objectives of this special issue are to provide some basic information about the causative agent of the current Ebola pandemic and to present the views of experts about the complexity and challenges of dealing with this highly pathogenic virus.

In March 2014, the Ministry of Health (Ministere de la Sante) of the Republic of Guinea officially informed the World Health Organization (WHO) of a rapidly evolving outbreak of Ebola Hemorrhagic fever (EHF) in forested areas of South Eastern Guinea [1, 2]. A total of 49 cases with case fatality of 59.2% were recorded as of 22 March 2014 [2]. The active role of Médecins Sans Frontières, Switzerland (MSF-CH) to treat infected patients was highlighted. The affected districts in Guinea were Guekedou, Macenta, Nzerekore and Kissidougou [2, 3]. The results of the Polymerase Chain Reaction (PCR) analysis of blood samples from seven patients carried out in the Pasteur Institute in Lyon, France, indicated that six samples were positive for Ebola virus. Sequencing of a section of the L-gene showed strong homology with the Zaire Ebolavirus species [2]. This was the confirmation of the outbreak of Ebola Virus Disease (EVD) in West Africa. The WHO later confirmed the spread of the infection to the neighboring countries, Liberia and Sierra Leone [3, 4, 6].

As part of the response to the confirmation of the outbreak and its spread to the neighboring

countries, the WHO release detailed information and directives on the 4 April 2014, stating that [4]:

“..... In coordination with national and regional authorities and technical partners, WHO has deployed experts to help assess and control the situation. Isolation facilities and a mobile laboratory have been established; infection prevention and control and clinical management guidance is being provided; and awareness and education campaigns, social mobilization, and risk communications activities are taking place throughout the affected areas”. “WHO encourages countries to strengthen surveillance, including surveillance for illness compatible with EVD, and to carefully review any unusual patterns, in order to ensure identification and reporting of human infections under the “International Health Regulations-2005” (IHR 2005), and encourages countries to continue national health preparedness actions. WHO does not recommend that any travel or trade restrictions be applied with respect to this event”..... [4]

As stated by the Director General of WHO, the initial response to control the Ebola outbreak was not commensurate with the ferocity of the spread of the disease, especially to major cities, and the high fatality rates in the affected countries [5]. Thus, the current outbreak, with over 21,000 reported cases and over 8,500 fatalities, has been categorized as the largest and most complex Ebola outbreak since the index case of EVD was reported in 1976.

The Ebola virus (EBOV) is the causative agent of EVD or EHF that was first reported in 1976 in two simultaneous outbreaks in Nzara (Sudan) and Yambuku in Zaire, now the Democratic Republic of Congo (DRC) [7 - 10].

The Ebolavirus is in the order Mononegavirales and family Filoviridae (filovirus).

Five distinct species of Ebolavirus have been identified [4, 6, 9].

In 1976, a total of 284 cases of EVD were reported with 53% fatality in Sudan; the virus was identified as Ebola-Sudan (EBO-S or SUDV) [4, 9, 10]. In Zaire, a total of 318 cases were reported with 88% fatality; the virus was identified as Ebola-Zaire (EBO-Z or EBOV) [7 - 10]. In 1989, infected monkeys from Mindanao in the Philippines, imported into Reston, Virginia USA, were identified as the source of the Ebola infection that affected a few people in Reston, but no fatalities were reported [9 - 11]. The virus was identified as Ebola Reston (EBO-R or RESTV). In 1994, a female ethologist was infected with Ebolavirus, while performing necropsy on a dead chimpanzee from the Tai Forest in Cote d'Ivoire; the virus was identified as Ebola Cote d'Ivoire (EBO-CI or TAFV) [9, 10]. An outbreak of Ebola was reported in Bundibugyo district in Western Uganda in 2007; a total of 149 cases were confirmed by the CDC with fatality rate of 25%. The virus was identified as a new Ebola species and was named Bundibugyo ebolavirus (BEBOV or BDBV) [9 - 12].

Since 2000, several outbreaks of Ebola have been reported in Africa; these include the following [9, 10]: In Uganda EBO-S outbreak occurred in 2000 to 2001, 425 cases were confirmed with fatality of 53%; from October 2001 to March 2002, EBO-Z outbreak occurred in

Gabon (65 cases with fatality of 82%) and the Republic of Congo (57 cases with fatality of 75%); in Republic of Congo, EBO-Z outbreaks occurred from December 2002 to April 2003 (143 cases with 89% fatality) and November to December 2003 (35 cases with 83% fatality); Sudan in 2004, EBO-S outbreak with 17 cases and 41% fatality; EBO-Z outbreak in the DRC in 2007 (264 cases with 71% fatality) and from December 2008 to February 2009 (32 cases with 47% fatality); EBO-S outbreak in Uganda from June to October 2012, 11 cases with 36% fatality; in the DRC from June to November 2012, BEBOV outbreak, 36 cases with 36% fatality; in Kibaale district in Uganda, EBO-S outbreak from November 2012 to June 2013, a total of 6 cases with 50% fatality; in the DRC EBO-Z outbreak from August to November 2014, a total of 66 cases with 74% fatality [9, 10].

Three (EBO-S, EBO-Z, BEBOV) of the five species of the Ebolavirus have been associated with the major outbreaks of EVD in various countries in Africa with relatively high fatality rates [4 – 12]. Despite the repeated occurrence of Ebola outbreaks in Africa, including the current unprecedentedly large scale outbreak in West Africa, the primary source of the Ebolavirus is still elusive [4, 6]. Fruit bats are high on the list of possible natural hosts, followed by monkeys, apes and chimpanzees [4 – 8]. Some authors have indicated that pigs might also host the Ebolavirus [13, 14].

Significant progress has been made in elucidating the general and molecular structures of the EBOV [15 – 20]. The genome of the EBOV is a linear negative-sense single stranded RNA {(-) ssRNA} that is encapsulated in a Nucleocapsid (NC). The components of the NC include a Nucleoprotein (NP), Virion Protein 30 (VP30), VP35 and RNA-dependent-RNA-Polymerase (Protein L). The NC is coated in matrix layer made up of matrix proteins VP40 and VP24. This complex is enveloped in a lipid bilayer studded with the major viral Glycoprotein (GP) (Figure 1). The GP forms spikes on the viral envelope that represents the outer surface of the virion; it is involved in the attachment and entry of the virus into the host cell. VP24 and VP40 are the matrix proteins; they play crucial role in maintaining the shape of the virion and are involved in viral reproduction. NP is part of a spiral structure that includes the ssRNA in the center of the virion; VP35 is a minor protein that acts against interferon, which is the natural protein in animal cells that normally functions to destroy viruses. Other virion proteins include VP30, the Transcription activator that triggers Transcription; RNA-dependent-RNA-Polymerase (Protein L) assembles copies of the virion RNA genetic material from positive copies of RNA and transcribes them into messenger RNA in preparation for translation in the host cells.

The EBOV genome, which is about 19 kb in length, encodes seven open reading frames (ORF) and produces 8 major gene products that

have multiple functions [15 – 20]. The diagram in Figure 2 shows the order of the genes in the genome. There are 3 overlaps of genes: the first overlap is between VP35 and VP40; the second is between GP and VP30; and the third – between VP24 and L. The overlaps are limited to the conserved sequence determined for the

Transcriptional signals. Three non-coding sequences are located between VP30 and VP24. The EBOV genome organization can also be represented as:

3'OH-{Leader-untranslated}-{core}-{envelope}-{polymerase}-{Trailer-untranslated}-5'OH.

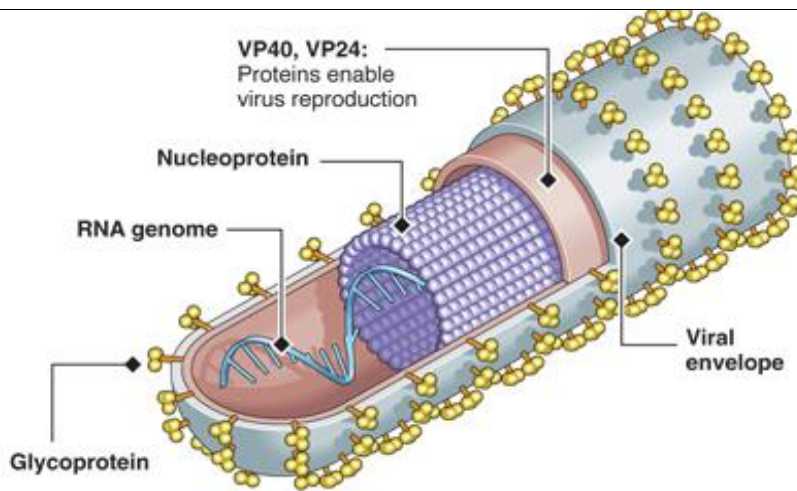


Figure 1: Schematic diagram showing the layers on Ebola virus. (Outermost viral envelope is lipid bilayer acquired from the host cell as the new virus buds off from the cell) [21]

[Credit: www.oxfordhumanists.org/wp-content/uploads/2014/12/Ebola-diagram-simple-and-neat.jpg, www.torontosun.com/2014/07/30/what-you-need-to-know-about-ebola]

VP = Virion Protein

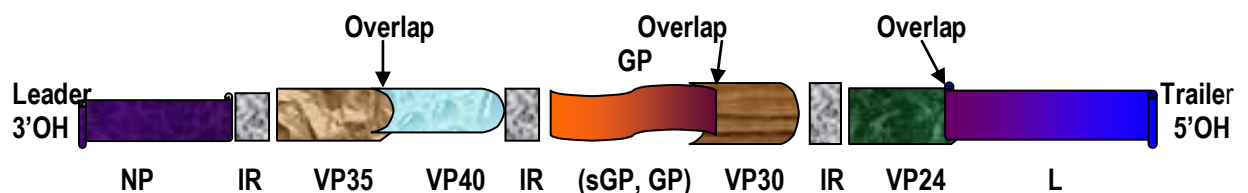


Figure 2: Relative location of genes on Negative-sense Single Stranded RNA {(-) ssRNA} linear genome of the Ebola virus [21].

(IR = Intervening Region, sGP = Soluble Glycoprotein)

Since the index case of EVD was reported about 40 years ago, no appropriate antiviral drugs or vaccines have been developed and approved [4, 6, 21, 22]. One of the major obstacles to scientific research on Ebola is the highly pathogenic nature of the virus. Scientific research work on EBOV must be conducted in high-level containment laboratory, classified as Biosafety Level 4 laboratory [4, 6, 9, 15]. By comparison, scientific research work on the Human Immunodeficiency Virus (HIV) is conducted in Biosafety Level 2 laboratory. Therefore, adequate funding for scientific research on the EBOV is difficult to obtain, which constitutes another major obstacle in the development of appropriate therapy, diagnostic assays and, especially, point-of-care test kits [22].

The global impact of the current Ebola pandemic is a “Clarion call for action” from government and international agencies, philanthropists, major pharmaceutical industries and others to provide the appropriate level of funding required to produce the urgently needed antiviral therapeutics and vaccines to manage the current outbreak and forestall an even more devastating Ebola pandemic. This is significant because the geographical spread of fruit bats is not limited to the African continent; it includes Asia, Australia and America [23, 24].

I wish, on behalf of the Editorial Board of the PJMS, to thank all the distinguished authors that have contributed to the success of this issue by submitting their papers for publication. Our special thanks go to Dr. Ada Igonoh for the paper

“Post Ebola Syndrome”, which is our lead paper in this issue. Dr. Igonoh tells a personal story and raised several questions that need urgent attention by researchers in the medical and social sciences.

We welcome all constructive comments on the papers published in this issue and invite more papers on the Ebola virus and Ebola Virus Disease to be submitted for publication in other issues of this journal.

REFERENCES:

1. www.humanitarianresponse.info/system/files/documents/files/INFO%20FIEVRE%20EBOLA%20GJINEE%2024%20MARS%202014.pdf. Accessed 15 January 2015
2. WHO document: Ebola Hemorrhagic Fever in Guinea (Situation as of 22 March 2014) www.afro.who.int/en/clusters-a-programmes/dpc/epidemic-a-pandemic-alert-and-response/outbreak-news/4063-ebola-virus-disease-in-guinea.html. Accessed 15 January 2015
3. Guinea: Ebola epidemic declared, MSF launches emergency response 22 March 2014 www.msf.org/article/guinea-ebola-epidemic-declared-msf-launches-emergency-response. Accessed, 20 December 2014.
4. WHO document GAR. EVD: background and summary: www.who.int/csr/don/2014_04_ebola/en/: Accessed 20 December 2014.
5. Report by Director-General of WHO www.who.int/dg/speeches/2015/executive-board-ebola/en/ 25 January 2015
6. Ebola (Ebola Virus Disease) CDC document 2015: www.cdc.gov/vhf/ebola/ Accessed 15 January 2015
7. Report of a WHO/International Study Team (1978) Ebola haemorrhagic fever in Sudan, 1976. Bull World Health Organ 56:247–270.
8. Report of an International Commission (1978) Ebola haemorrhagic fever in Zaire, 1976. Bull World Health Organ 56:271–293.

9. Outbreaks Chronology: Ebola Virus Disease: www.cdc.gov/vhf/ebola/outbreaks/history/chronology.html. Accessed 15 January 2015
10. WHO documents Disease outbreak news: Ebola virus disease www.who.int/csr/don/archive/disease/ebola/
11. Ikegami T, Calaor AB, Miranda ME, and Niikura M. Genome structure of Ebola virus subtype Reston: differences among Ebola subtypes Brief Report. Arch Virol. 2001 146: 2021–2027.
12. MacNeil A, Farnon EC, Wamala J, Okware S, Cannon DL, Reed Z, Towner JS, Tappero JW, Lutwama J, Downing R, Nichol ST, Ksiazek TG and Rollin PE. Proportion of Deaths and Clinical Features in Bundibugyo Ebola Virus Infection, Uganda. Emerging Infectious Diseases; www.cdc.gov/eid, Vol. 16, No. 12, December 2010, 1969 – 1972, DOI: 10.3201/eid1612.100627. Accessed 10 December 2014
13. Pan Y, Zhang W, Cui L, Hua X, Wang M and Zeng Q. Reston virus in domestic pigs in China; Arch Virol 159: Issue 5,2014,1129–1132.
14. Weingartl HM, Embury-Hyatt C, Nfon C, Leung A, Smith G, Kobinger G. Transmission of Ebola virus from pigs to non-human primates. Sci Rep. 2012, 2: 811, doi: 10.1038/srep00811. Epub 2012 Nov 15.
15. Ebola Virus resources: www.ncbi.nlm.nih.gov/genome/viruses/variation/ebola/. Accessed 15 January 2015
16. [White JM](#), [Schornberg KL](#). A new player in the puzzle of filovirus entry Nat Rev Microbiol. 2012 Apr 11; 10(5): 317-22. doi: 10.1038/nrmicro2764. Accessed 20 Oct 2014
17. Becquart P, Mahlakoiv T, Nkoghe D and Leroy EM. Identification of continuous human B-cell epitopes in the VP35, VP40, nucleoprotein and glycoprotein of Ebola virus; PloS One. 2014, June 10;9(6):e96360.doi:10.1371/journal.pone.0096360.eCollection 2014. 20 Accessed November 2014
18. Changula K, Yoshida R, Noyori O, Marzi A, Miyamoto H, Ishijima M, Yokoyama A, Kajihara M, Feldmann H, Mweene AS and Takada A. Mapping of conserved and species-specific antibody epitopes on the Ebola virus nucleoprotein. Virus res. 176, 2013; 83–90 doi:10.1016/j.virusres.2013.05.004. Accessed 20 November 2014
19. Dziuban'ska PJ, Derewenda U, Ellena JF, Engelb DA and Derewenda ZS. The structure of the C-terminal domain of the Zaire ebolavirus nucleoprotein Acta Cryst; 2014, D70, 2420–2429 doi:10.1107/S1399004714014710. Accessed 20 November 2014
20. Bharata TAM, Nodab T, Richesa JD, Kraehling V, Kolesnikovac L, Beckerc S, Kawaoka Y and Briggs JAG; Structural dissection of Ebola virus and its assembly determinants using cryo-electron tomography. PNAS, March 13, 2012, vol. 109, no. 11, 4275–4280; www.pnas.org/lookup/suppl/doi:10.1073/pnas.1120453109/-/DCSupplementa. Accessed 20 November 2014
21. What you need to know about Ebola: www.torontosun.com/2014/07/30/what-you-need-to-know-about-ebola Accessed 6 January 2015
22. WHO documents: Ebola vaccines, therapies, diagnostics: www.who.int/csr/disease/ebola/faq-ebola/en/;
23. Medicines, Vaccines WHO Document 2015 www.who.int/medicines/ebola-treatment/en/ Accessed 6 January 2015
24. Olival KJ, Islam A, Yu M, Anthony SJ, Epstein JH, Khan SA, Khan SU, Cramer G, Wang L, Lipkin WI, Luby SP, and Daszak P. Ebola Virus Antibodies in Fruit Bats, Bangladesh. Emerging Infectious Diseases, Vol. 19, No. 2, Feb 2013, 270 – 273 DOI: <http://dx.doi.org/10.3201/eid1902.120524>. wwwnc.cdc.gov/eid/article/19/2/12-0524_article. Accessed 6 January 2015.