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# Ebola virus: Ancient virus on a recent outbreak

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**ABSTRACT**

Ebola virus a very old virus, in reference with the WHO bulletin in 1978 the first cases of ebola virus were reported in 1976 in Zaire, as per the reports 280 deaths and 38 serologically confirmed survivors were recorded. The first onset of symptoms were observed in 5 days after receiving an injection of chloroquine for presumptive malaria, the patient actually had a reoccurrence of his malaria symptoms and was treated for so at yambuku Mission Hospital. Within one week several other patients who received injection for the treatment at YMH also suffered from Ebola hemorrhagic fever, and all the cases which were reported had received injection at the hospital or had close contact with the affected person.

## Reported Cases

Ebola virus a very old virus, in reference with the WHO bulletin in 1978 [1] the first cases of ebola virus were reported in 1976 in Zaire, as per the reports 280 deaths and 38 serologically confirmed survivors were recorded. The first onset of symptoms were observed in 5 days after receiving an injection of chloroquine for presumptive malaria, the patient actually had a reoccurrence of his malaria symptoms and was treated for so at yambuku Mission Hospital. Within one week several other patients who received injection for the treatment at YMH also suffered from Ebola hemorrhagic fever [2-10] and all the cases which were reported had received injection at the hospital or had close contact with the affected person.

The virus was so epidemic that the hospital was closed within first four weeks when the symptoms first appeared as 11 of the total 17 staff who nursed the infected patients also died of the disease [11,12]. All ages of both the sexes were affected, mostly women of the age group between 15-29 years of the age had highest incidence of the disease [13-19].

The disease was actually caused by a virus that is morphologically similar to Marburg virus, but immunologically distinct. Marburg virus disease was first identified in 1967 in Yugoslavia and was transmitted from infected monkeys from Uganda [20-28]. Both Ebola virus and Marburg virus causes highly fatal disease and both come from the same family “Filoviridae”. Both the diseases are very rare but can cause dramatic out breaks with high fatality rate [29-35].

## Causative Agent

The causative agent of ebola virus was first isolated from the blood of 8-10 suspected cases using Vero cell cultures [36-45]. The vero cell lines were derived from the kidney of a normal, adult, African green monkey. Currently, the Vero cell line is used to produce only one U.S. licensed viral vaccine that is poliovirus vaccine. However "The Center for Biologics Evaluation and Research" (CBER) is one Center within the Food and Drug Administration, an Agency within the United States Government's Department of Health and Human Services (HHS), had received proposals either in pre-IND or under IND (Investigational New Drug Application) to use Vero cells to produce many other viral vaccines, including live viral vaccines [46-70]. Except the polio vaccine all other licensed vaccines are produced in diploid cell strains. Diploid cultures have a finite lifespan Normal human cells, such as human skin fibroblasts, are one example of diploid cells [71-90]. Continuous cell lines are immortalized cell lines with an infinite lifespan [91-95]. These usually either come from tumor tissue or have been deliberately immortalized or transformed. However, many rodent cell lines spontaneously transform [96-100].

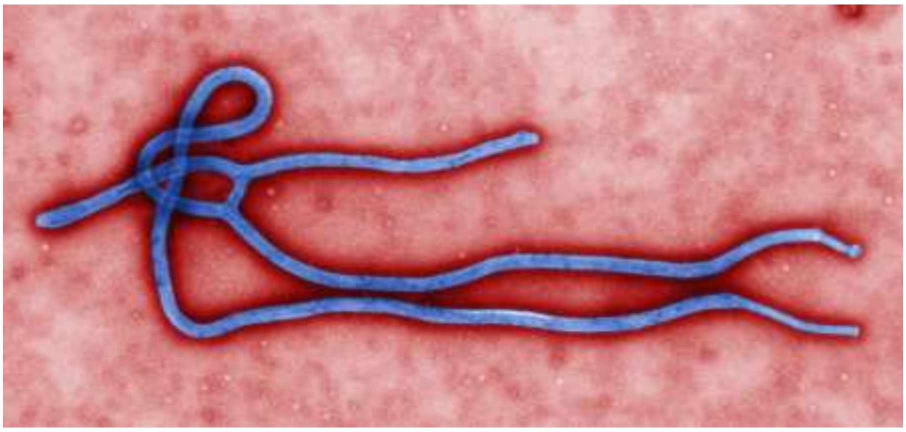

Figure 1: Ebola virus

## CONCLUSION

The virus replicates only inside the living cells of other organisms. The virus changes its protein sequence oftenly and become resistant to antibiotics which makes it difficult to control when the disease is epidemic . The ebola virus which has been epidemic in the recent 2014, 2015 cases reported may be same virus reported in Zaire in 1976 and the cases reported on 6th October, 1979 in southern sudan is yet to be known.

## REFERENCES

1. Mohamed A Daw and Abdallah El-Bouzedi. Viral Haemorrhagic Fever in North Africa; an Evolving Emergency. J Clin Exp Pathol. 2015;5:215.
2. http://whqlibdoc.who.int/bulletin/1978/Vol56-No2/bulletin_1978_56%282%29_271-293.pdf
3. Shittu RO et al. Awareness, Knowledge and Misconceptions about Ebola Virus Disease (EVD) in a Family Practice Setting in Nigeria, West Africa. J Antivir Antiretrovir. 2015; 7: 010-014.
4. http://www.who.int/ihr/global_alert/en/
5. Weltman JK. Identification of Invariant Peptide Domains within Ebola Virus Glycoprotein GP1, 2. J Med Microb Diagn. 2015; 4: 176.
6. Sticklen M. Plantipharma Technology: Production of Antibodies, Anti-HIV, Anti-Ebola Virus, Anti-End-Stage Metastatic Melanoma and Other Recombinant Biotech Drugs in Crops. J Adv Crop Sci Tech. 2014; 2: e120.
7. Wiwanitkit V. Is it Sufficient for the Present Emerging 2014 Africa Ebola Virus Infection Outbreak. J Clin Case Rep. 2014; 4: e137.

8. Adams RE and Boscarino JA. Stress and well-being in the aftermath of the World Trade Center attack: The continuing effects of a communitywide disaster. Journal of Community Psychology. 2005; 33: 175-190.
9. Kimani S et al. Ebola Outbreak: Knowledge to Act. Occup Med Health Aff. 2014;2:184.
10. Joshi RM. Ebola Virus Disease (EVD): An Unprecedented Major Outbreak in West Africa. Clin Microbial. 2014;3:e119.
11. Lebea P. Biosecurity and Biodefense: Lessons from Ebola Virus Outbreak. 2014;5:e112.
12. Cenciarelli O. Biological Emergency Management: The Case of Ebola 2014 and the Air Transportation Involvement. J Microb Biochem Technol. 2014; 6: 247-253.
13. Richardson JS et al. Evaluation of Different Strategies for Post-Exposure Treatment of Ebola Virus Infection in Rodents. J Bioterr Biodef. 2011;S1:007.
14. Bagchi P et al. Pharmaco-Informatics: Homology Modelling of the Target Protein (GP1, 2) for Ebola Hemorrhagic Fever and Predicting an Ayurvedic Remediation of the Disease. J Proteomics Bioinform. 2009; 2:287-294.
15. Basler CF and Amarasinghe GK. Evasion of interferon responses by Ebola and Marburg viruses. J Interferon Cytokine Res. 2009;29:511-520.
16. Wilson JA et al. Ebola virus: the search for vaccines and treatments. Cell Mol Life Sci. 2009;58: 1826-41.
17. Geisbert TW et al. Vesicular stomatitis virus-based vaccines protect nonhuman primates against aerosol challenge with Ebola and Marburg viruses. Vaccine. 2008;26:6894-6900.
18. Hart MK. Vaccine research efforts for filoviruses. Int J Parasitol. 2013;33:583- 595.
19. Xu L et al. Immunization for Ebola virus infection. Nat Med. 1998;4:37-42.
20. Swenson DL et al. Virus-like particles exhibit potential as a pan-filovirus vaccine for both Ebola and Marburg viral infections Vaccine. 2005;23:3033-3042.
21. Warfield KL et al. Ebola virus-like particles protect from lethal Ebola virus infection. Proc Natl Acad Sci USA. 2003;100:15889-15994.
22. Warfield KL et al. Induction of humoral and CD8+ T cell responses are required for protection against lethal Ebola virus infection. J Immunol. 2005;175:1184-1191.
23. Kelly LW et al. Ebola viruslike particle-based vaccine protects nonhuman primates against lethal Ebola virus challenge. J Infect Dis 196 Suppl. 2003;2: s430-s437.
24. Feldmann H et al. Effective post-exposure treatment of Ebola infection. PLoS Pathog. 2007;3:e2.
25. Garbutt M et al. Properties of replication-competent vesicular stomatitis virus vectors expressing glycoproteins of filoviruses and arenaviruses. J Virol. 2004;78:5458-5465.
26. Geisbert T W et al. Single-injection vaccine protects nonhuman primates against infection with marburg virus and three species of ebola virus. J Virol. 2009;83:7296-7304.
27. Jones SM et al. Live attenuated recombinant vaccine protects nonhuman primates against Ebola and Marburg viruses. Nat Med. 2005;11:786-790.
28. Qiu X et al. Mucosal immunization of cynomolgus macaques with the VSVDeltaG/ZEBOVGP vaccine stimulates strong ebola GP-specific immune responses. PLoS One. 2009;4:e5547.
29. Bukreyev A et al. Successful topical respiratory tract immunization of primates against Ebola virus. J Virol. 2007;81:6379-6388.
30. Bukreyev A et al. A single intranasal inoculation with a paramyxovirus-vectored vaccine protects guinea pigs against a lethal-dose Ebola virus challenge. J Virol. 2006;80:2267-2279.
31. Yang L et al. A paramyxovirus-vectored intranasal vaccine against Ebola virus is immunogenic in vector-immune animals. Virology. 2008;377:255-264.
32. Geisbert T W et al. Evaluation in nonhuman primates of vaccines against Ebola virus. Emerg Infect Dis. 2002;8:503-507.

33. Geisbert T W and P B Jahrling. Towards a vaccine against Ebola virus. Expert Rev Vaccines. 2003;2:777-789.
34. Geisbert T W et al. Postexposure protection of non-human primates against a lethal Ebola virus challenge with RNA interference: a proof-of-concept study. Lancet. 2010;375:1896-1905.
35. Geisbert T W et al. Treatment of Ebola virus infection with a recombinant inhibitor of factor VIIa/ tissue factor: a study in rhesus monkeys. Lancet. 2003;362:1953-1958.
36. Bray M and T W Geisbert. Ebola virus: the role of macrophages and dendritic cells in the pathogenesis of Ebola hemorrhagic fever. Int J Biochem Cell Biol. 2005;37:1560-1566.
37. Gupta M et al. Monocyte-derived human macrophages and peripheral blood mononuclear cells infected with ebola virus secrete MIP-1alpha and TNF-alpha and inhibit poly-IC-induced IFN-alpha in vitro. Virology. 2001;284:20-25.
38. Bosio C M et al. Ebola and Marburg viruses replicate in monocyte-derived dendritic cells without inducing the production of cytokines and full maturation. J Infect Dis. 2003;188:1630-1638.
39. Mahanty S et al. Cutting edge: impairment of dendritic cells and adaptive immunity by Ebola and Lassa viruses. J Immunol. 2003;170:2797-2801.
40. Chang T H et al. Ebola Zaire virus blocks type I interferon production by exploiting the host SUMO modification machinery. PLoS Pathog. 2009;5:e1000493.
41. Prins K C et al. Ebola virus protein VP35 impairs the function of interferon regulatory factor-activating kinases IKKepsilon and TBK-1. J Virol. 2009;83:3069-3077.
42. Reid SP et al. Ebola virus VP24 binds karyopherin alpha1 and blocks STAT1 nuclear accumulation. J Virol. 2006;80:5156-5167.
43. Jahrling PB et al. Evaluation of immune globulin and recombinant interferon-alpha2b for treatment of experimental Ebola virus infections. J Infect Dis. 1999;179:224-234.
44. Bray M et al. Treatment of lethal Ebola virus infection in mice with a single dose of an S-adenosyl-L-homocysteine hydrolase inhibitor. Antiviral Res. 2000;45:135-147.
45. Kumaki Y et al. Singledose intranasal administration with mDEF201 (adenovirus vectored mouse interferon-alpha) confers protection from mortality in a lethal SARS-CoV BALB/c mouse model. Antiviral Res. 2011;89:75-82.
46. Julander J G et al. Treatment of yellow fever virus with an adenovirus-vectored interferon, DEF201, in a hamster model. Antimicrob Agents Chemother. 2011;55:2067-2073.
47. Richardson JS et al. Enhanced protection against Ebola virus mediated by an improved adenovirusbased vaccine. PLoS One. 2009;4:e5308.
48. Tatsis N H C Ertl. Adenoviruses as vaccine vectors. Mol Ther. 2004;10:616- 629.
49. Desy O et al. Immunosuppressive effect of isopropanol: down-regulation of cytokine production results from the alteration of discrete transcriptional pathways in activated lymphocytes. J Immunol. 2008;181:2348-2355.
50. Loomans C J et al. Differentiation of bone marrow-derived endothelial progenitor cells is shifted into a proinflammatory phenotype by hyperglycemia. Mol Med. 2009;15:152-159.
51. Yamauchi K et al. Azithromycin suppresses interleukin-12p40 expression in lipopolysaccharide and interferongamma stimulated macrophages. Int J Biol Sci. 2009;5:667-678.
52. Brassard D L et al. Interferon-alpha as an immunotherapeutic protein. J Leukoc Biol. 2002;71:565-581.
53. Hensley S E, Giles-Davis W, McCoy KC, Weninger W, Ertl HC (2005) Dendritic cell maturation, but not CD8+ T cell induction, is dependent on type I IFN signaling during vaccination with adenovirus vectors. J Immunol 175: 6032- 6041.
54. Reddy K R et al. Efficacy and safety of pegylated (40-kd) interferon alpha-2a compared with interferon alpha-2a in noncirrhotic patients with chronic hepatitis C. Hepatology. 2001;33:433-438.

55. Mueller S N et al. Immunization with live attenuated influenza viruses that express altered NS1 proteins results in potent and protective memory CD8+ T-cell responses. J Virol. 2010;84:1847-1855.
56. Gao G et al. High throughput creation of recombinant adenovirus vectors by direct cloning, green-white selection and I-Sce I-mediated rescue of circular adenovirus plasmids in 293 cells. Gene Ther. 2003;10: 1926-1930.
57. Kobinger G P et al. Chimpanzee adenovirus vaccine protects against Zaire Ebola virus. Virology. 2006;346:394-401.
58. Wu J Q et al. Preand post-exposure protection against Western equine encephalitis virus after single inoculation with adenovirus vector expressing interferon alpha. Virology. 2007;369:206-213.
59. Bray M et al. A mouse model for evaluation of prophylaxis and therapy of Ebola hemorrhagic fever. J Infect Dis. 1998;178:651-661.
60. Connolly B M et al. Pathogenesis of experimental Ebola virus infection in guinea pigs. J Infect Dis. 1999;179:203-217.
61. Nakayama E et al. Enzyme-linked immunosorbent assay for the detection of filovirus speciesspecific antibodies. Clin Vaccine Immunol. 2010;17:1723-1728.
62. Rao M et al. Cytotoxic T lymphocytes to Ebola Zaire virus are induced in mice by immunization with liposomes containing lipid A. Vaccine. 1999;17:2991-2998.
63. Baron RC et al. Ebola virus disease in southern Sudan: hospital dissemination and intrafamilial spread. Bulletin of the World Health Organization. 1983;61:997-1003.
64. World Health Organization. Viral haemorrhagic fever in imported monkeys. Weekly Epidemiological Record. 1992;67:183.
65. Georges AJ et al. Ebola hemorrhagic fever outbreaks in Gabon, 1994-1997: epidemiologic and health control issues. Journal of Infectious Diseases. 1999;179:S65-75.
66. Le Guenno B et al. Isolation and partial characterisation of a new strain of Ebola virus. Lancet. 1995;345:1271-1274.
67. Khan AS et al. The Reemergence of Ebola Hemorrhagic Fever, Democratic Republic of the Congo, 1995. Journal of Infectious Diseases. 1999;179:S76-S86.
68. World Health Organization. Ebola haemorrhagic fever - South Africa. Weekly Epidemiological Record. 1996;71:359.
69. Rollin PE et al. Isolated cases of Ebola (subtype Reston) virus among quarantined non-human primates recently imported from the Philippines to the United States. Journal of Infectious Diseases. 1999;179:S108-S114.
70. Miranda ME et al. Epidemiology of Ebola (subtype Reston) virus in the Philippines, 1996. Journal of Infectious Diseases. 1999;179:S115-S119.
71. Feldmann H et al. Ebola virus: from discovery to vaccine. Nat Rev Immunol. 2003;3:677-685.
72. Kuhn JH et al. Proposal for a revised taxonomy of the family Filoviridae: classification, names of taxa and viruses, and virus abbreviations. Arch Virol. 2010;155:2083-2103.
73. Feldmann H and Klenk HD. Filoviruses. In: Medical Microbiology. (4thedn), Baron S, edt. University of Texas Medical Branch at Galveston, Galveston,1196. TX, USA.
74. World Health Organization (WHO) Media Center: Ebola virus disease. Fact sheet NÂ° 103.
75. Reed Z. A Historical Perspective and Review of the Evidence to Support Fruit Bats as the Natural Reservoir for Ebola Viruses. Georgia State University, USA, Public Health Theses. 2012;241.
76. Centers for Disease Control and Prevention (CDC) Viral haemorrhagic fevers (VSFs). Filoviridae
77. Groseth A et al. The ecology of Ebola virus. Trends Microbiol. 2007;15:408-416.
78. Leroy EM et al. Fruit bats as reservoirs of Ebola virus. Nature. 2005;438:575-576.
79. Negredo A et al. Discovery of an ebolavirus-like filovirus in europe. PLoS Pathog. 2011;7:e1002304.

80. Feldmann H and Geisbert TW. Ebola haemorrhagic fever. Lancet. 2011;377:849-862.
81. Johnson E et al. Lethal experimental infections of rhesus monkeys by aerosolized Ebola virus. Int J Exp Pathol. 1995;76:227-236.
82. Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) Infection Control for Viral Haemorrhagic Fevers in the African Health Care Setting. Centers for Disease Control and Prevention, Atlanta, USA. 1998;1-198.
83. Centers for Disease Control and Prevention (CDC) Ebola Hemorrhagic Fever Information Packet. Special Pathogens Branch. 2009.
84. Sanchez A etal. â€œFiloviridae: Marburg and Ebola Viruses,â€☐ In Fields Virology 5th edition. Knipe DM, Howley PM (Eds.). Lippincott-Williams & Wilkins, Philadelphia. 2007;1409-1448.
85. Approved List of Biological Agents. Advisory Committee on Dangerous Pathogens (ACDP). Health and Safety Executive (HSE), UK. 2004.
86. Buzard GS et al. Multi-platform comparison of ten commercial master mixes for probe-based real-time polymerase chain reaction detection of bioterrorism threat agents for surge preparedness. Forensic Sci Int. 2012;223:292-297.
87. Lazarus A and Decker CF. Plague. Respir Care Clin N Am. 2004;10:83-98.
88. Jaax NK et al. Lethal experimental infection of rhesus monkeys with Ebola-Zaire (Mayinga) virus by the oral and conjunctival route of exposure. Arch Pathol Lab Med. 1996;120:140-155.
89. Cenciarelli O et al. Bioweapons and Bioterrorism: a review of History and Biological Agents. Defence S&T Technical Bullettin. 2013;6:111-129.
90. http://whqlibdoc.who.int/bulletin/1978/Vol56-No2/bulletin_1978_56%282%29_247-270.pdf
91. http://whqlibdoc.who.int/bulletin/1983/Vol61-No6/bulletin_1983_61%286%29_997-1003.pdf
92. European Centre for Disease Prevention and Control (ECDC) (2009) Technical Report - Risk Assessment Guidelines for Infectious Diseases transmitted on Aircraft (RAGIDA). ECDC, Stockholm, Sweden.
93. European Centre for Disease Prevention and Control (ECDC) (2010) Guidance - Risk Assessment Guidelines for Diseases transmitted on Aircraft (RAGIDA). PART 2: Operational guidelines for assisting in the evaluation of risk for transmission by disease. ECDC, II Edition, Stockholm, Sweden
94. World Health Organization (WHO) (2009) Guide to hygiene and sanitation in aviation. World Health Organization. WHO Press, 3rd Edition, Geneve, Switzerland
95. Kenyon TA etal. Transmission of multidrug-resistant Mycobacterium tuberculosis during a long airplane flight. N Engl J Med. 1996;334:933-938.
96. Olsen SJ et al. Transmission of the severe acute respiratory syndrome on aircraft. N Engl J Med. 2013;349: 2416-2422.
97. European Centre for Disease Prevention and Control (ECDC) (2014) Updated 8 April. Outbreak of Ebola virus disease in West Africa. ECDC, Stockholm.
98. Albarino CG et al. Genomic analysis of filoviruses associated with four viral hemorrhagic fever outbreaks in Uganda and the Democratic Republic of the Congo in 2012. Virology. 2013;442:97
99. ShittuRO et al. Awareness, Knowledge and Misconceptions about Ebola Virus Disease (EVD) in a Family Practice Setting in Nigeria, West Africa. J Antivir Antiretrovir. 2015;7:010-014.
100. Bagchi P, et al. Pharmaco-Informatics: Homology Modelling of the Target Protein (GP1, 2) for Ebola Hemorrhagic Fever and Predicting an Ayurvedic Remediation of the Disease. J Proteomics Bioinform. 2009;2:287-294