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Marburg Virus Disease – A Mini-Review

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ABSTRACT

Marburg virus disease (MVD) is a highly fatal disease caused by the Marburg virus (MARV) which belongs to the family Filoviridae. The disease has been recently reported from Ghana, an African country, and nearly 15 outbreaks of MVD have been reported in the past five decades. Various species of bats viz., *Rousettus aegyptiacus*, *Hipposideros caffer*, and certain Chiroptera act as the natural source of infection. Pathophysiology of the disease reveals severe antiviral suppression due to changes in gene expression and interferon-stimulated gene (ISG) production in the hepatic cells. With the progression of the disease, there may be the development of pain in the abdomen, nausea, vomition, pharyngitis, and diarrhea along with the onset of hemorrhagic manifestations which may lead to the death of a patient. The advent of molecular detection techniques and kits viz., reverse transcription polymerase chain reaction (RT-PCR) kit has greatly aided in the diagnosis of MVD. Identification of the virus in the specimen with great accuracy can be done by whole viral genome sequencing. The use of a combination of MR-186-YTE

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(monoclonal antibody) and an antiviral drug named remdesivir in the NHP model is greatly effective for eliminating MARV. The protective effect of a Vesicular stomatitis virus (VSV) (recombinant) - based vaccine expressing the glycoprotein of MARV has been revealed through animal model studies, other vaccines are also being developed. Proper health education, personal hygiene and precautions by health care workers while handling patients, good laboratory facilities and service along with the establishment of enhanced surveillance systems are the need of the hour to tackle this highly fatal disease. This article presents an overview of different aspects and salient features of MARV / MVD, and prevention and control strategies to be adopted.

1 Introduction

Marburg virus (MARV), a member of the family Filoviridae that also contain the Ebola virus, causes Marburg virus disease (MVD) which is zoonotic in nature as well as a very fatal disease with up to 88 percent case fatality rate (Singh et al. 2017; Asad et al. 2020; WHO 2021; Zhao et al. 2022). There are five distinct lineages of MARV as is revealed by phylogenetic analysis of the data regarding genomic sequences. There has been a reclassification of these lineages into two viruses separately viz., MARV and Ravn virus (RAVV). Initially, the disease was recognized in Germany and Serbia after outbreaks occurred simultaneously in the year 1967. In these cases, the outbreak occurred due to the handling of tissues obtained from African green monkeys (*Chlorocebus aethiops*) imported from Uganda by scientists and technicians in the laboratory who were conducting experiments for producing polio vaccines (Ristanović et al. 2020). There are previous reports of an outbreak of MVD from African countries viz., Democratic Republic of Congo, Angola, Kenya, Uganda, South Africa, Guinea, and also from the USA, Netherlands, Yugoslavia, and Russia. The most recent outbreak has been reported from Ghana in the current year 2022 (July month) (Koundouno et al. 2022; Okonji et al. 2022; Sah et al. 2022; WHO 2022; Hussain 2022; Zhao et al. 2022). MARV being highly contagious can spread very rapidly and is responsible for causing high mortality (Abir et al. 2022).

It is to be noted that most of the outbreaks of MVD have occurred in Africa. MDV is seldom treatable in non-human primates (NHPs) and humans. The disease results in hemorrhagic fever and dysfunctions of organs viz., hepatic failure; infection of brain; spleen, and tissues of the renal system along with problems concerning coagulation (Mehedi et al. 2011; van Paassen et al. 2012). There may be a presence of fresh blood in the vomitus and feces along with frequent bleeding through the nostrils, gums, and vagina. There is an increased risk of venepuncture providing fluids or obtaining blood samples from the patients infected as there may be spontaneous bleeding at the venepuncture site. The involvement of the central nervous system results in confusion, irritability, and aggression in the behavior (WHO 2021). Since widespread MARV outbreaks are unusual, clinical studies may not always generate enough data to adequately evaluate the treatment options for MVD. In light of this, a thorough in-depth disease investigations and analysis may facilitate future medical research and help to improve the therapeutic management of MVD. In this mini-review, we reviewed and collated key data on MARV and the disease it causes (MVD), and counteracting management approaches to tackle this highly virulent virus.

2 Etiology

MARV is an enveloped virus belonging to the Filoviridae family and is having a negative sense, non-segmented RNA genome that is single-stranded. The virus is having a single species viz., *Marburg marburgvirus* which comprises two strains i.e. MARV and Ravn virus (RAVV). The strains are divergent from one another by 20 percent at the amino acid level (Towner et al. 2006; Kortepeter et al. 2020). The nucleocapsid core of MARV is composed of viral protein (VP) 30; VP35; nucleoprotein (NP); and the L-polymerase protein. VP40 and VP24 constitute the viral matrix protein. The viral proteins are transcribed from monocistronic RNA (Martin et al. 2016; Gordon et al. 2019). Morphologically, MARV is filamentous. There are certain variants of MARV like Musoke; Angola and Ci67 out of which the variant Angola is the most pathogenic one (Kortepeter et al. 2020).

3 Transmission

MVD is a zoonotic disease, and the major infection source (natural) of MARV is the *Rousettus aegyptiacus* species of fruit bat. Apart from this, *Hipposideros caffer* along with certain Chiroptera can also act as an infection source. The transmission of strains of MARV from bat to bat can occur in various ways. In a recent study, detection of viral shedding in oral and rectal samples along with urine of bats inoculated with MARV has been reported, and interestingly it has been found that there is the presence of MARV in the blood and oral samples of bats in contact. Thus this study proves the horizontal transmission of the virus from bats infected to in-contact bats (Schuh et al. 2017). Intermediate hosts like NHPs and animals killed for obtaining bushmeat may also act as vectors (primary) of transmission of the virus. It is however possible that the infection may probably be transmitted to humans and NHPs from the secretions (viz., saliva) and excretions (feces

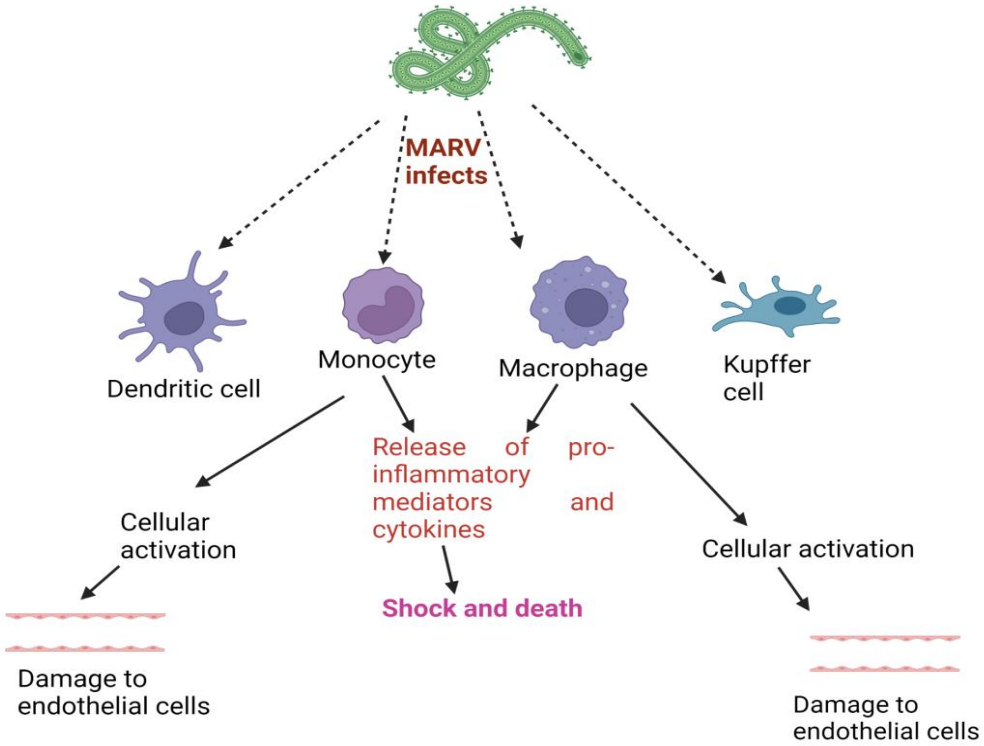

Figure 1 Pathophysiology of Marburg virus (MARV) infection.

and urine) of bats and also from fruits contaminated with MARV (Schuh et al. 2017; Kortepeter et al. 2020; Amman et al. 2021). There may be spread of MARV to humans at the early stages of infection through intermediate animals that are infected. Sexual intercourse may also transmit MVD as already the antigens of MARV have been found in the semen of males infected. Direct contact with blood along with other body fluids viz., urine; feces; tears; breast milk, etc can also facilitate human-to-human transmission. The chances of transmission increase due to the provision of services related to healthcare to the patients infected by MARV, health care workers can be infected, and the handling of corpses of humans inappropriately (Bausch et al. 2003; Kortepeter et al. 2020).

4 Marburg virus disease

The incubation period of the disease varies from 2 days to 3 weeks. Non-specific symptoms like the high rise of temperature; myalgia or arthralgia; malaise and headache appear quickly. There may be an appearance of a maculopapular rash located centrally around the fifth day of MARV infection. As there is a progression of the disease there may be the development of pain in the abdomen; nausea; vomition; pharyngitis and diarrhea. Hemorrhagic manifestations like petechiae and bleeding from mucosa at multiple locations can occur (Miraglia 2019). Severe hemorrhages that prove to be fatal mainly occur in the gastrointestinal tract. It is important to note that during the disease, hemorrhage may not be exhibited in certain patients. Ultimately the patient may die within a few days from the period of onset of clinical signs in fatal cases (Kortepeter et al. 2011; Miraglia 2019). There is a penetration of MARV in the body via broken skin thereby damaging various types of cells and organs. Ultimately there is a development of hemorrhagic fever (Abir et al. 2022). An overview of the pathophysiology of MARV infection is depicted in Figure 1.

5 Diagnosis

MVD should be differentiated from malaria; septicaemia caused by gram-negative organisms; plague; leptospirosis and typhoid (Miraglia 2019). Enzyme-linked immunosorbent assay (ELISA), serum neutralization tests, electron microscopy, virus isolation, and nucleic acid detection methods such as reverse transcriptase polymerase chain reactions (RT-PCR) is used for the diagnosis of MVD (Park et al. 2016; Racsa et al. 2016; Zhao et al. 2022). However, in many areas where MVD outbreaks are most likely to occur, these diagnostic techniques are not readily available (Olejnik et al. 2019; Yu et al., 2022). Biosafety level-4 (BSL-4) facilities are required for the diagnosis and research on MARV. A higher degree of sensitivity, as well as specificity, is obtained by nucleic acid detection methods and with such detection facilities testing can be carried out quickly at the outbreak site (Racsa et al. 2016). The creation of a TaqMan Array card has been done to

screen for outbreaks of acute febrile illness and to use for surveillance purposes. The virus in the specimen can be more accurately identified by sequencing of the full viral genome. Comparison of the full genome of the virus in the specimen with the genome sequences of MARV stored in a database can be done by a microarray assay that uses MARV-specific probes (Miraglia 2019).

6 Treatment and vaccines

No antiviral therapy or vaccine has been approved yet for MVD but supportive care can be given. This includes balancing the levels of fluid and electrolyte; maintaining oxygen level and blood pressure; replacement of blood and clotting factors that are lost due to infection. Attempts have been made to develop efficacious therapies (post-exposure) which include antiviral drugs, antibodies, monoclonal antibodies (mAbs), antiviral small molecules, viral inhibitors-based therapies such as MR-186-YTE (mAb), synthetic anti-VP35 antibody, remdesivir, broad-spectrum nucleoside analogue BCX4430, an inhibitory molecule known as FC-10696a, as well as AVI-7288, host-targeted therapeutics and post-exposure vaccine, recombinant vesicular stomatitis virus vectors (Daddario-DiCaprio et al. 2006; Warren et al. 2014; Cross et al. 2018; Amatya et al., 2019; Cross et al. 2021; Bradfute, 2022; Hickman et al. 2022; Kumari et al. 2022; Zhao et al. 2022). It should be emphasized that if the disease is severe or has progressed to an advanced stage, combined therapy utilizing two direct-acting antiviral (DAA) medications may prove effective, such as remdesivir and a MARV-specific mAb candidate (MR186-YTE) combination therapy was found to more effective (Abir et al. 2022; Hickman et al. 2022; Abir et al. 2022). Besides these, efforts are needed to evaluate the efficacy of herbs, plant metabolites, phytochemicals, immune-boosting nutritional foods, and nutraceuticals as well as novel chemical ligands, antiviral drugs, and broadly neutralizing antibodies, that could be used against MARV / MVD as have been found useful for other important emerging and re-emerging viral pathogens such as SARS-CoV-2, filoviruses including Ebola virus, Zika virus and others (Fu et al. 2016; Dhama et al. 2018a; Dhama et al. 2018b; Tiwari et al. 2018; Zhang et al. 2018; Anand et al. 2021; Calder 2022; Saied et al. 2022).

Investigations have been carried out regarding the potential use of various vaccines against MARV infection. For instance, testing in animal models has revealed the protective effect of a Vesicular stomatitis virus (VSV) (recombinant) based vaccine that expresses the glycoprotein (GP) of MARV (rVSVΔG-MARV-GP) (Marzi et al. 2021). MVA-BN-Filo is another vaccine candidate that contains the antigens of both Ebola and Marburg virus, found to have a potential protective effect against both viruses (Anywaine et al. 2022). Progress has been made in the development of vaccines based on recombinant glycoproteins of filoviruses viz., Ebola virus (EBOV) and Sudan virus (SUDV) along with MARV, for designing monovalent MARV vaccine, monovalent SUDV vaccine, and bivalent formulations. Such a subunit (recombinant) vaccine platform can thereby help in developing multivalent vaccine candidates for protecting against filoviruses while retaining their safety and efficacy (Lehrer et al. 2021). Few other vaccines being tried include multi-epitope vaccine, proteome-based vaccine exploiting computational methods, virus-like particles (VLP), adenoviral vector-based multi-filovirus vaccine, r-protein based filovirus multivalent vaccine, and rVSV-based vesiculovax vector vaccine (rVSV-N4CT1-MARV-GP), and efforts are being made for effective platform designing of preventive MVD vaccines (Reynolds and Marzi 2017; Hasan et al. 2019; Suschak and Schmaljohn 2019; Dulin et al. 2021; Lehrer et al. 2021; Sami et al. 2021; Longini et al. 2022; Sebastian et al. 2020; Soltan et al. 2022; Woolsey et al. 2022; Zhao et al. 2022). Another candidate vaccine (recombinant VSV/ rVSV-based) known as PHV01 has been tested in the guinea pig model for confirming the efficacy (protective effects) against MVD (Zhu et al. 2022).

7 Prevention and control

Effective epidemic control requires many interrelated factors to come together, including case management, strengthening surveillance and tracking, contact tracing, as well as well equipped laboratory facilities, safe and dignified funerals, community mobilization, education, and awareness enhancing of public on the risk factors for catching MARV infection and precautionary measures to be adopted along with adhering to strict standards of hygiene and cleanliness (Aborode et al. 2022; Abir et al. 2022). To avoid MVD it is recommended to avoid contact with NHPs as well as fruit bats, especially in the African setting and outbreaks region. There is a necessity to set up an advanced system of surveillance for interrupting the transmission chain of MARV as a part of a key control strategy by limiting the animal-human interface, following early diagnosis and immediate implementation of mitigation strategies and proactive prevention and control measures. Humans should avoid being too much closeness to fruit bats in mines and caves, and follow personal safety precautions, to lessen the risk of disease transmission. During epidemics, it is crucial that all animal products, including blood and meat, be cooked properly (Baby et al. 2022). Utmost care is required to prevent transmission from human to human by avoiding contact (direct/ close) with people having the symptoms of MVD, especially the contact with body fluid of infected individuals should be avoided. At the hospital, the health care personnel must take care of the ill patients by wearing gloves and personal protective equipment appropriately. After a visit is made to the health care facilities to visit patients, the hands should be washed and sanitized immediately. The use of condoms

is essential for both male and female to reduce any probable chances of possible MARV transmission through sexual contact. The WHO recommends that male survivors of MVD practice safer sex and hygiene for a year or until their semen twice tests negative for the virus (Mehedi et al. 2011; WHO 2021; Wirsiy et al. 2021; WHO 2022). Of note, seeing the rising cases of monkeypox in several countries, now declared a public health emergency of international concern, due attention also needs to be given to MVD which is also presently considered a neglected / rare disease, and high efforts are required to strengthen research, enhance surveillance and develop effective vaccines and therapeutics to counter MVD (Abir et al. 2022; Chakraborty et al. 2022; Sah et al. 2022).

Conclusion & Future perspectives

It is possible to improve the care of patients and reduce death rates, by having a better knowledge of the clinical course as well as the pathology of MVD. Progress has been shown in the field of laboratory diagnosis of the disease and the precision of various diagnostic tests to detect the disease has increased over time. Evaluation of therapeutic compounds as well as vaccines having various mechanisms of action and versatile composition is on the way to reaching any conclusive treatment options and developing vaccines to tackle this deadly virus. Treatment, as well as prevention of MVD, is possible to some extent with some of these compounds and vaccines. However vivid studies are essential to know the exact mechanisms involved in the development of MARV infection (pathogenesis) upon exposure to reservoir animals. Along with this sound knowledge of the mechanism involved in the development of asymptomatic infection is also essential. Trials (clinical) should be carried out in more numbers as far as treatment and vaccination are concerned to earn the approval of the Food and Drug Administration (FDA). High global efforts are required by epidemiologists, diagnosticians, researchers, medicos, veterinarians, health care experts, and health agencies in a coordinated manner so that mankind can get prepared to tackle MVD more efficiently and avoid any probable dangers of global health concerns.

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References

Abir, M. H., Rahman, T., Das, A., Etu, S. N., et al. (2022). Pathogenicity and virulence of Marburg virus. *Virulence*, *13*(1), 609-633. DOI:10.1080/21505594.2022.2054760

Aborode, A. T., Wireko, A. A., Bel-Nono, K. N., Quarshie, L. S., Allison, M., & Bello, M. A. (2022). Marburg virus amidst COVID-19 pandemic in Guinea: Fighting within the looming cases. *The International Journal of Health Planning and Management*, *37*(1), 553-555. DOI: 10.1002/hpm.3332

Amatya, P., Wagner, N., Chen, G., Luthra, P., et al. (2019). Inhibition of Marburg virus RNA synthesis by a synthetic anti-VP35 antibody. *ACS Infectious Diseases*, *5*(8):1385-1396. doi: 10.1021/acsinfecdis.9b00091.

Amman, B. R., Schuh, A. J., Albariño, C. G., & Towner, J. S. (2021). Marburg virus persistence on fruit as a plausible route of bat to primate filovirus transmission. *Viruses*, *13*(12), 2394. DOI: 10.3390/v13122394

Anand, A.V., Balamuralikrishnan, B., Kaviya, M., Bharathi, K., et al. (2021). Medicinal plants, phytochemicals, and herbs to combat viral pathogens including SARS-CoV-2. *Molecules*. *26*(6):1775. doi: 10.3390/molecules26061775.

Anywaine, Z., Barry, H., Anzala, O., Mutua, G., et al. (2022). Safety and immunogenicity of 2-dose heterologous Ad26.ZEBOV, MVA-BN-Filo Ebola vaccination in children and adolescents in Africa: A randomised, placebo-controlled, multicentre Phase II clinical trial. *PLOS Medicine*, *19*(1), e1003865. DOI: 10.1371/journal.pmed.1003865

Asad, A., Aamir, A., Qureshi, N. E., Bhimani, S., et al. (2020). Past and current advances in Marburg virus disease: a review. *Infez Med*, *28*(3):332-345.

Baby, B., Rajalakshmi R., Nair, M. M., & Roshni, P. R. (2022). Sagacious perceptive on Marburg virus foregrounding the recent findings: A critical review. *Infectious Disorders Drug Targets*. DOI: 10.2174/1871526522666220510103618.

Bausch, D. G., Borchert, M., Grein, T., Roth, C., et al. (2003). Risk factors for Marburg hemorrhagic fever, Democratic Republic of the Congo. *Emerging Infectious Diseases*, *9*(12), 1531-1537. DOI: 10.3201/eid0912.030355

Bradfute, S. B. (2022). The discovery and development of novel treatment strategies for filoviruses. *Expert Opinion on Drug Discovery*, *17*(2):139-149. doi: 10.1080/17460441.2022.2013800.

Calder, P. C. (2022). Foods to deliver immune-supporting nutrients. *Current Opinion in Food Science*, *43*, 136-145. doi: 10.1016/j.cofs.2021.12.006.

Chakraborty, S., Chandran, D., Mohapatra, R. K., Alagawany, M., et al. (2022). Clinical management, antiviral drugs and immunotherapeutics for treating monkeypox. An update on current knowledge and futuristic prospects. *International Journal of Surgery*, *106847*. doi: 10.1016/j.ijsu.2022.106847.

Cross, R. W., Bornholdt, Z. A., Prasad, A. N., Borisevich, V., et al. (2021). Combination therapy protects macaques against advanced Marburg virus disease. *Nature Communications*, *12*(1), 1891. DOI: 10.1038/s41467-021-22132-0

Cross, R. W., Mire, C. E., Feldmann, H., & Geisbert, T. W. (2018). Post-exposure treatments for Ebola and Marburg virus infections. *Nature Reviews Drug Discovery*, *17*(6), 413-434. DOI: 10.1038/nrd.2017.251

Daddario-DiCaprio, K. M., Geisbert, T. W., Ströher, U., Geisbert, J. B., et al. (2006). Postexposure protection against Marburg haemorrhagic fever with recombinant vesicular stomatitis virus vectors in non-human primates: an efficacy assessment. *The Lancet*, *367*(9520), 1399-1404. DOI: 10.1016/S0140-6736(06)68546-2

Dhama, K., Karthik, K., Khandia, R., Munjal, A., et al. (2018b). Medicinal and Therapeutic Potential of Herbs and Plant Metabolites / Extracts Countering Viral Pathogens - Current Knowledge and Future Prospects. *Current Drug Metabolism*, *19*(3), 236-263. doi: 10.2174/1389200219666180129145252.

Dhama, K., Karthik, K., Khandia, R., Chakraborty, S., et al. (2018a). Advances in designing and developing vaccines, drugs, and therapies to counter *Ebola* virus. *Frontiers in Immunology*, *9*, 1803. doi: 10.3389/fimmu.2018.01803.

Dulin, N., Spanier, A., Merino, K., Hutter, J. N. , Waterman, P. E., Lee, C., & Hamer, M. J. (2021). Systematic review of Marburg virus vaccine nonhuman primate studies and human clinical trials. *Vaccine*, *39*(2), 202-208. doi: 10.1016/j.vaccine.2020.11.042.

Fu, X., Wang, Z., Li, L., Dong, S., et al. (2016). Novel chemical ligands to Ebola virus and Marburg virus nucleoproteins identified by combining affinity mass spectrometry and metabolomics approaches. *Scientific Reports*, *6*, 29680. doi: 10.1038/srep29680.

Gordon, T. B., Hayward, J. A., Marsh, G. A., Baker, M. L., & Tachedjian, G. (2019). Host and viral proteins modulating Ebola and Marburg virus egress. *Viruses*, *11*(1), 25. DOI: 10.3390/v11010025

Hasan, M., Azim, K. F., Begum, A., Khan, N.A., et al. (2019). Vaccinomics strategy for developing a unique multi-epitope monovalent vaccine against Marburg marburgvirus. *Infection, Genetics and Evolution*, *70*, 140-157. doi: 10.1016/j.meegid.2019.03.003.

Hickman, M. R., Saunders, D. L., Bigger, C. A., Kane, C. D., & Iversen, P. L. (2022). The development of broad-spectrum antiviral medical countermeasures to treat viral hemorrhagic fevers caused by natural or weaponized virus infections. *PLoS Neglected Tropical Diseases*, *16*(3), e0010220. DOI: 10.1371/journal.pntd.0010220.

Hussain, Z. (2022). Ghana declares its first outbreak of Marburg virus disease after two deaths. *British Medical Journal* , *378*, o1797. doi: 10.1136/bmj.o1797.

Kortepeter, M. G., Bausch, D. G., & Bray, M. (2011). Basic clinical and laboratory features of filoviral hemorrhagic fever. *The Journal of Infectious Diseases*, *204*(3), S810-S816. DOI: 10.1093/infdis/jir299

Kortepeter, M. G., Dierberg, K., Shenoy, E. S., Cieslak, T. J., & Medical Countermeasures Working Group of the National Ebola Training and Education Center's (NETEC) Special Pathogens Research Network (SPRN). (2020). Marburg virus disease: A summary for clinicians. *International Journal of Infectious Diseases*, *99*, 233-242. DOI: 10.1016/j.ijid.2020.07.042

Koundouno, F.R., Kafetzopoulou, L.E., Faye, M., Renevey, A., et al. (2022). Detection of Marburg virus disease in Guinea. *The New England Journal of Medicine*, *386*(26), 2528-2530. DOI: 10.1056/NEJMc2120183

Kumari, M., & Subbarao, N. (2022). A hybrid resampling algorithms SMOTE and ENN based deep learning models for identification of Marburg virus inhibitors. *Future Medicinal Chemistry*, *14*(10):701-715. doi: 10.4155/fmc-2021-0290.

Lehrer, A. T., Chuang, E., Namekar, M., Williams, C. A., et al. (2021). Recombinant protein filovirus vaccines protect cynomolgus macaques from Ebola, Sudan, and Marburg viruses. *Frontiers in Immunology*, *12*, 703986. DOI: 10.3389/fimmu.2021.703986

Longini, I. M., Yang, Y., Fleming, T.R., Muñoz-Fontela, C., et al. (2022). A platform trial design for preventive vaccines against Marburg virus and other emerging infectious disease threats.

Clinical Trials, *22*, 17407745221110880. doi: 10.1177/17407745221110880.

Martin, B., Hoenen, T., Canard, B., & Decroly, E. (2016). Filovirus proteins for antiviral drug discovery: A structure/function analysis of surface glycoproteins and virus entry. *Antiviral Research*, *135*, 1-14. DOI: 10.1016/j.antiviral.2016.09.001

Marzi, A., Jankeel, A., Menicucci, A. R., Callison, J., et al. (2021). Single dose of a VSV-based vaccine rapidly protects macaques from Marburg virus disease. *Frontiers in Immunology*, *12*, 774026. DOI: 10.3389/fimmu.2021.774026

Mehedi, M., Groseth, A., Feldmann, H., & Ebihara, H. (2011). Clinical aspects of Marburg hemorrhagic fever. *Future Virology*, *6*(9), 1091-1106. DOI: 10.2217/fvl.11.79

Miraglia, C. M. (2019). Marburgviruses: An update. *Laboratory Medicine*, *50*(1), 16-28. DOI: 10.1093/labmed/lmy046

Okonji, O. C., Okonji, E. F., Mohanan, P., Babar, M. S., et al. (2022). Marburg virus disease outbreak amidst COVID-19 in the Republic of Guinea: A point of contention for the fragile health system? (2022). *Clinical Epidemiology and Global Health*, *13*, 100920. DOI: 10.1016/j.cegh.2021.100920

Olejnik, J., Mühlberger, E., & Hume, A. J. (2019). Recent advances in Marburg virus research, *F1000Research*, *8*, 704. DOI: 10.12688/f1000research.17573.1

Park, S. W., Lee, Y. J., Lee, W. J., Jee, Y., & Choi, W. (2016). One-Step Reverse Transcription-Polymerase Chain Reaction for Ebola and Marburg Viruses. *Osong Public Health and Research Perspectives*, *7*(3), 205-209. DOI: 10.1016/j.phrp.2016.04.004

Racsa, L. D., Kraft, C. S., Olinger, G. G., & Hensley, L. E. (2016). Viral Hemorrhagic Fever Diagnostics. *Clinical Infectious Diseases*, *62*(2), 214-219. DOI: 10.1093/cid/civ792

Reynolds, P., & Marzi, A. (2017). Ebola and Marburg virus vaccines. *Virus genes*, *53*(4), 501–515. https://doi.org/10.1007/s11262-017-1455-x

Ristanović, E. S., Kokoškov, N. S., Crozier, I., Kuhn, J. H., & Gligić, A. S. (2020). A forgotten episode of Marburg Virus disease: Belgrade, Yugoslavia, 1967. *Microbiology and Molecular Biology Reviews*, *84*(2), e00095-19. DOI: 10.1128/MMBR.00095-19

Sah, R., Mohanty, A., Reda, A., Siddiq, A., Mohapatra, R. K., & Dhama, K. (2022). Marburg virus re-emerged in 2022: Recently detected in Ghana, another zoonotic pathogen coming up amid rising cases of monkeypox and ongoing COVID-19 pandemic-Global health concerns and counteracting measures. *Veterinary Quarterly*, *22*:1-9. doi: 10.1080/01652176.2022.2116501.

Saied, A. A., Nascimento, M., do Nascimento Rangel, A. H., Skowron, K., et al. (2022). Transchromosomic bovines-derived broadly neutralizing antibodies as potent biotherapeutics to counter important emerging viral pathogens with a special focus on SARS-CoV-2, MERS-CoV, Ebola, Zika, HIV-1, and influenza A virus. *Journal of medical virology*, *94*(10), 4599–4610. https://doi.org/10.1002/jmv.27907

Sami, S. A., Marma, K. K. S., Mahmud, S., Khan, M. A. N., et al. (2021). Designing of a multi-epitope vaccine against the structural proteins of Marburg virus exploiting the immunoinformatics approach. *ACS Omega*, *6*(47), 32043-32071. doi: 10.1021/acsomega.1c04817.

Schuh, A. J., Amman, B. R., Jones, M. E., Sealy, T. K., et al. (2017). Modelling filovirus maintenance in nature by experimental transmission of Marburg virus between Egyptian rousette bats. *Nature Communications*, *8*, 14446. DOI: 10.1038/ncomms14446.

Sebastian, S., Flaxman, A., Cha, K. M., Ulaszewska, M., et al. (2020). A Multi-Filovirus Vaccine Candidate: Co-Expression of Ebola, Sudan, and Marburg Antigens in a Single Vector. *Vaccines* (Basel), *8*(2), 241. doi: 10.3390/vaccines8020241.

Singh, R. K., Dhama, K., Malik, Y.S., Ramakrishnan, M. A., et al. (2017). Ebola virus - epidemiology, diagnosis, and control: threat to humans, lessons learnt, and preparedness plans - an update on its 40 year's journey. *Veterinary Quarterly*, *37*(1), 98-135. doi: 10.1080/01652176.2017.1309474.

Soltan, M. A., Abdulsahib, W. K., Amer, M., Refaat, A. M., et al. (2022). Mining of Marburg virus proteome for designing an epitope-based vaccine. *Frontiers in Immumnology*, *13*, 907481. doi: 10.3389/fimmu.2022.907481.

Suschak, J. J., & Schmaljohn, C. S. (2019). Vaccines against Ebola virus and Marburg virus: recent advances and promising candidates. *Human Vaccines & Immunotherapeutics*, *15*(10), 2359-2377. doi: 10.1080/21645515.2019.1651140.

Tiwari, R., Latheef, S. K., Ahmed, I., Iqbal, H., et al. (2018). Herbal Immunomodulators - A Remedial Panacea for Designing and Developing Effective Drugs and Medicines: Current Scenario and Future Prospects. *Current drug metabolism*, *19*(3), 264–301. https://doi.org/10.2174/1389200219666180129125436

Towner, J. S., Khristova, M. L., Sealy, T. K., Vincent, M. J., et al. (2006). Marburgvirus genomics and association with a large hemorrhagic fever outbreak in Angola. *Journal of Virology*, *80*(13), 6497-6516. DOI: 10.1128/JVI.00069-06

van Paassen, J., Bauer, M. P., Arbous, M. S., Visser, L. G., et al. (2012). Acute liver failure, multiorgan failure, cerebral oedema,

and activation of proangiogenic and antiangiogenic factors in a case of Marburg haemorrhagic fever. *The Lancet Infectious Diseases*, *12*(8), 635-642. DOI: 10.1016/S1473-3099(12)70018-X

Warren, T. K., Wells, J., Panchal, R. G., Stuthman, K. S., et al. (2014). Protection against filovirus diseases by a novel broad-spectrum nucleoside analogue BCX4430. *Nature*, *508*(7496), 402-405. DOI: 10.1038/nature13027

WHO. (2021). Marburg virus disease. Retrieved from https://www.who.int/news-room/fact-sheets/detail/marburg-virus-disease.

WHO. (2022). Marburg virus- Ghana, 22 July, 2022. Retrieved from https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON402.

Wirsiy, F. S., Ako-Arrey, D. E., Nkfusai, C. N., Yeika, E. V., & Bain, L. E. (2021). Marburg virus disease outbreak in Guinea: a SPIN framework of its transmission and control measures for an exemplary response pattern in West Africa. *The Pan African Medical Journal*, *40*, 143. DOI: 10.11604/pamj.2021.40.143.31709

Woolsey, C., Cross, R. W., Agans, K. N., Borisevich, V., et al. (2022). A highly attenuated Vesiculovax vaccine rapidly protects nonhuman primates against lethal Marburg virus challenge. *PLoS Neglected Tropical Diseases*. *16*(5), e0010433. doi: 10.1371/journal.pntd.0010433

Yu, Z., Wu, H., Huang, Q., & Zhong, Z. (2021). Simultaneous detection of Marburg virus and Ebola virus with TaqMan-based multiplex real-time PCR method. *Journal of Clinical and Laboratory Analysis*, *35*(6), e23786. DOI: 10.1002/jcla.23786.

Zhang, X., Liu, Q., Zhang, N., Li, Q. Q., et al. (2018). Discovery and evolution of aloperine derivatives as novel anti-filovirus agents through targeting entry stage. *European Journal of Medicinal Chemistry*, *149*, 45–55. https://doi.org/10.1016/j.ejmech.2018.02.061

Zhao, F., He, Y., & Lu, H. (2022). Marburg virus disease: A deadly rare virus is coming. *Bioscience Trends*, 10.5582/bst.2022.01333. Advance online publication. https://doi.org/10.5582/bst.2022.01333.

Zhu, W., Liu, G., Cao, W., He, S., et al. (2022). A cloned recombinant vesicular stomatitis virus-vectored Marburg Vaccine, PHV01, protects guinea pigs from lethal Marburg virus disease. *Vaccines (Basel)*, *10*(7), 1004. DOI: 10.3390/vaccines10071004