

Marburg Virus Disease (MVD)

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ABSTRACT

The Marburg virus illness is a zoonotic disease that has caused several outbreaks. In humans, it has the potential to cause serious sickness and death. It was initially detected in 1967 after an outbreak in Marburg and Frankfurt, Germany, following the importation of sick monkeys from Uganda. Global Marburg virus data were evaluated, covering epidemiology, reservoir host, Clinique, diagnosis, transmission, and prevention. It is a terrible and typically deadly disease produced by the same virus that causes the Ebola virus sickness. The death rate ranges from 25% during the initial outbreak in a laboratory in 1967 to more than 80% between 1998 and 2000 in the Democratic Republic of the Congo during the 2005 outbreak in Angola. This virus's natural reservoir is *Rousettus Egyptianus*. The discovery of this virus's natural reservoir should encourage the creation of public health measures and preventative campaigns to limit the appearance and onset of prospective outbreaks of hemorrhagic fever.

Keywords

Marburg virus, Filovirus, Ebola virus, Antiviral therapy, Antiviral countermeasure, Vaccine, pathogens.

I. INTRODUCTION

This is the first in a planned series on the treatment of very dangerous communicable infections that may necessitate specialised infection control methods but lack licenced countermeasures. Marburg virus disease (MVD) is an uncommon but severe hemorrhagic illness that affects humans and nonhuman primates. It is caused by an infection with Marburg virus or Ravn virus, both of which belong to the genus Marburgvirus. Marburg viruses are zoonotic (or animal-borne) RNA viruses of the viral family Filoviridae. Ebolaviruses, also known as Filoviruses, are genetically separate yet closely related to Marburg viruses.

Marburg virus was initially identified in 1967, when simultaneous outbreaks of hemorrhagic fever occurred in labs in Marburg and Frankfurt, Germany, as well as Belgrade, Yugoslavia (now Serbia). Thirty-one persons were ill, beginning with laboratory staff and progressing through medical personnel and family members who had cared for them. There were seven deaths recorded. The first persons sick were exposed to Ugandan imported african green monkeys or their tissues while performing study. One more instance was diagnosed retrospectively.

DEFINITION

Marburg virus disease (MVD) is an uncommon but severe hemorrhagic illness that affects humans and nonhuman primates. It is caused by an infection with Marburg virus or Ravn virus, both of which belong to the genus Marburgvirus. Marburg viruses are zoonotic (or animal-borne) RNA viruses of the viral family filoviridae.

- Ebolaviruses, commonly known as filoviruses, are genetically separate yet closely related to Marburg viruses.



INCIDENCE

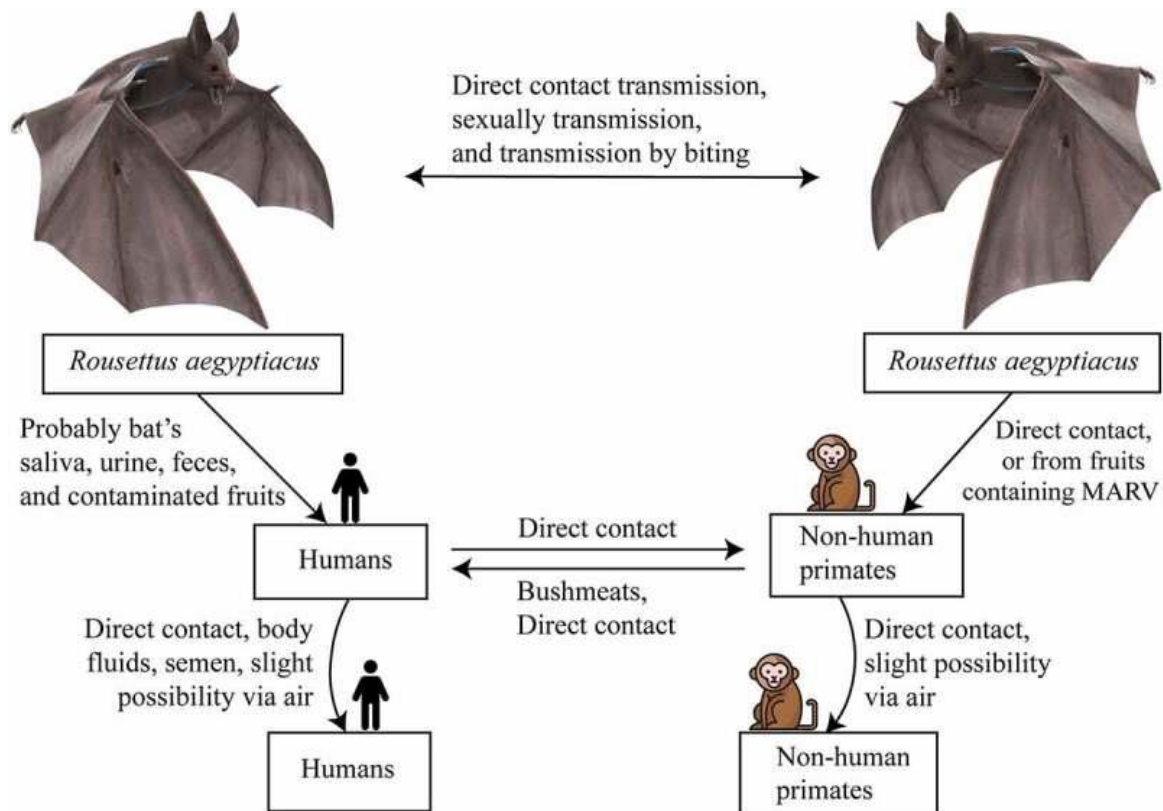
- Marburg virus is the causal agent of Marburg virus disease (MVD), which has a case-fatality ratio of up to 88%. Marburg viral illness was first identified in 1967, following epidemics in Marburg, Frankfurt, and Belgrade, Germany, as well as Belgrade, Serbia.
- On February 13, 2023, government officials in Equatorial Guinea reported a Marburg virus illness epidemic. The Ministry of Health first reported one confirmed case and many suspect cases in Ebebiyin, kie-ntem province, in the country's northeast.
- Tanzanian government officials confirmed the country's first ever epidemic of Marburg virus sickness on March 21, 2023. The instances have been documented in the country's northwest kagera region.

CAUSES

It is caused by an infection with Marburg virus or Ravn virus, both of which belong to the genus *Marburgvirus*. Marburg viruses are zoonotic (or animal-borne) RNA viruses of the viral family *filoviridae*.

TRANSMISSION

- Marburg spreads through human-to-human transmission via direct contact (through broken skin or mucous membranes) with the blood, secretions, organs, or other bodily fluids of infected people, and with surfaces and materials (e.g. Bedding, clothing) contaminated with these fluids.
- Health-care personnel have regularly become infected while treating patients with suspected or confirmed MVD.
- This has occurred due to close contact with patients when infection control protocols are not rigorously followed.
- Transmission via contaminated injection equipment or needle-stick injuries is related with more severe illness, quicker deterioration, and, presumably, a greater death rate.
- Burial rites involving intimate touch with the deceased's body can potentially contribute to the spread of Marburg.
- People are contagious as long as the virus is present in their blood.



PATHOPHYSIOLOGY

Virus primarily targets dendritic cells, monocytes, parenchyma cells at a liver, adrenocortical cells, and several lymphoid tissues.

Poor stimulating condition of t lymphocyte that causes lymphocyte apoptotic condition.

cytokines/chemokines is increased, which leads to shock as well as multiorgan damaging occurrence.

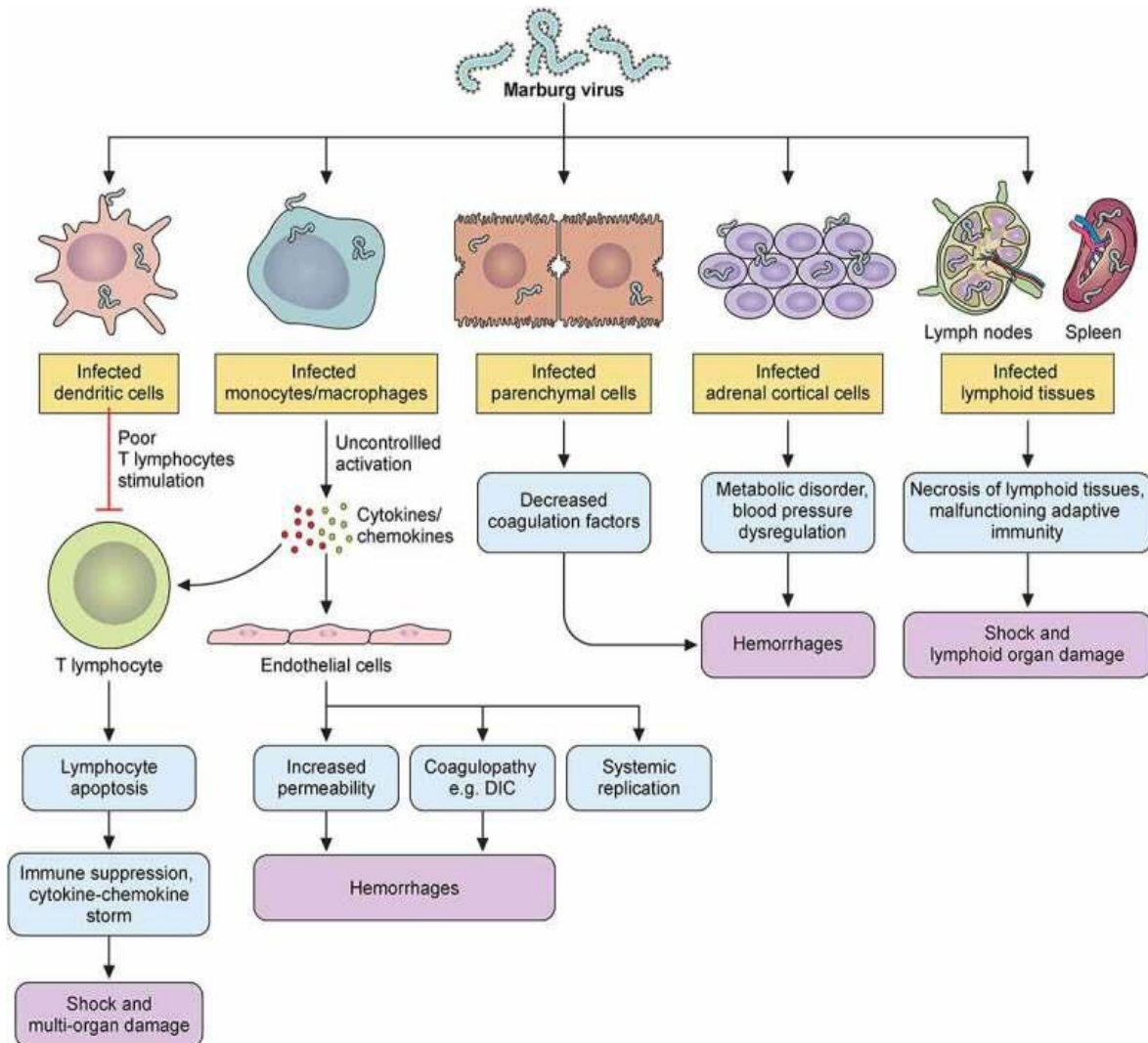
Uncontrolled cytokines/chemokines activation, and they continue the damaging of t-lymphocyte and endothelial cell.

Endothelial cell infection causes increase of blood vessels permeability and DIC, while both occurrences lead to hemorrhages

Systemic replication, infection in endothelial cells and Parenchymal cell in liver can decrease coagulation factors, and these occurrences can cause hemorrhages.

Marv infection the on lymphoid tissues of lymphatic system, especially lymph nodes and spleen infections lead to tissue necrosis and malfunctioning adaptive immunity.

Shock and lymphoid organ damage can occur in the later stage.



SYMPTOMS

The incubation period (interval from infection to onset of symptoms) varies from 2 to 21 days.

- The illness caused by the Marburg virus begins rapidly, with a high temperature, severe headache, and severe malaise.
- Muscle aches and pains are a typical symptom.
- On the third day, severe watery diarrhoea, abdominal discomfort and cramping, nausea, and vomiting might occur.
- Diarrhoea can last up to a week.
- Patients at this stage have been characterised as having "ghost-like" drawn features, deep-set eyes, expressionless faces, and profound lethargy.
- Non-itchy rash was observed in most patients between 2 and 7 days following the beginning of symptoms in the 1967 European epidemic.
- Many patients acquire severe haemorrhagic symptoms between 5 and 7 days, and fatal cases typically have some sort of bleeding, often from numerous sites.
- Fresh blood in vomitus and faeces is sometimes followed by bleeding from the nose, gums, and vagina. Spontaneous bleeding at venepuncture sites (where intravenous access is established to administer fluids or take blood samples) can be especially bothersome.
- Patients have had high fevers throughout the severe phase of the disease. Involvement with the central nervous system can cause confusion, irritation, and violence.
- Orchitis (inflammation of one or both testicles) has been described on rare occasions in the late stage of illness (15 days).

- Death occurs most frequently between 8 and 9 days following symptom start, and is generally preceded by substantial blood loss.

DIAGNOSTIC EVALUATION

Clinically, MVD can be difficult to identify from other infectious disorders such as malaria, typhoid fever, shigellosis, meningitis, and other viral hemorrhagic fevers. The following diagnostic procedures are used to confirm that the symptoms are due by Marburg virus infection:

- Antibody-capture enzyme-linked immunosorbent assay (ELISA) testing
- Serum Neutralisation test;
- Reverse transcriptase polymerase chain reaction (RT-PCR) assay;
- Electron microscopy; and
- Virus isolation by cell culture.

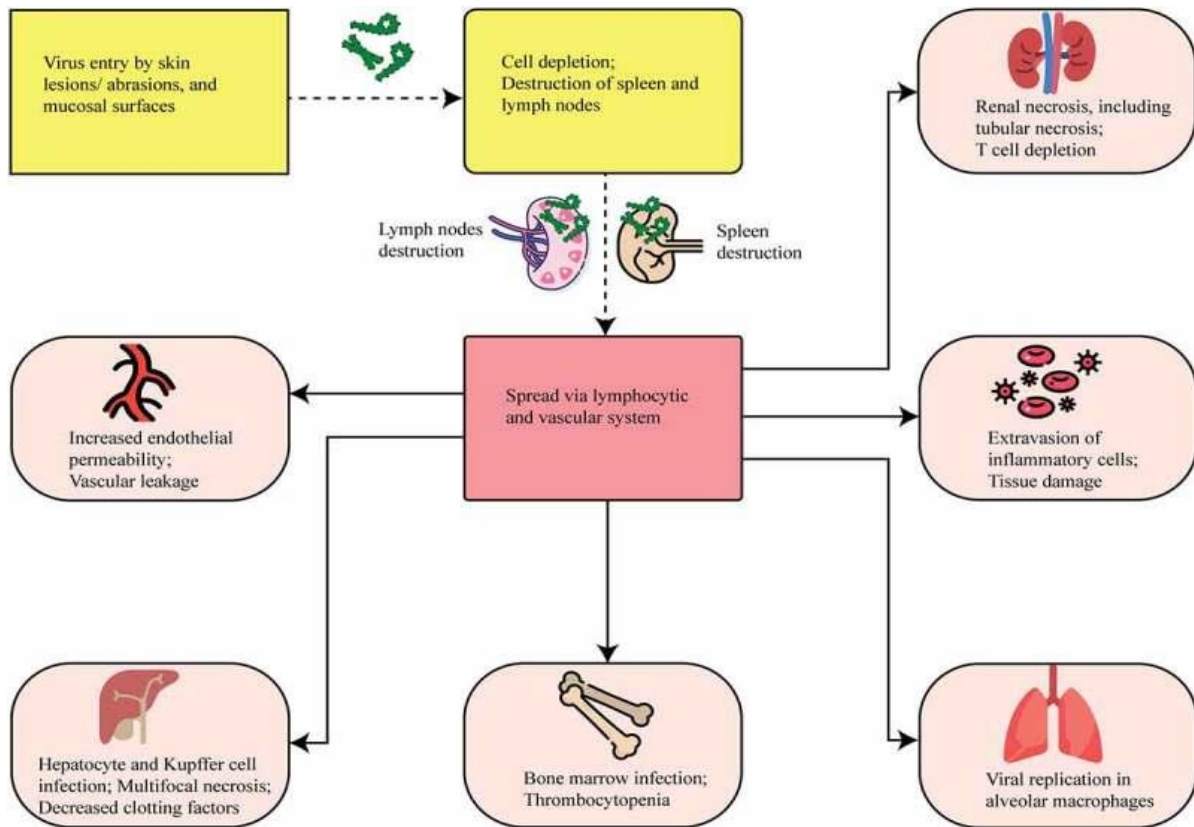
Patient samples provide a severe biohazard risk; laboratory testing on non-inactivated samples should be performed under maximal biological containment settings. When transported domestically or internationally, all biological specimens should be wrapped utilising the triple packing technique.

TREATMENT AND VACCINES

- There are currently no licensed vaccinations or antiviral therapies for MVD.
- Supportive therapy, such as rehydration with oral or intravenous fluids
- There are monoclonal antibodies in development, as well as antivirals such as **Remdesivir** and **favipiravir**.
- The ema approved zabdeno and Mvabea marketing authorization in May 2020.
- The Mvabea virus comprises the vaccinia Ankara bavarian nordic virus, which has been modified to generate four proteins from the zaire ebolavirus and three additional viruses in the same family (filoviridae).
- Although the vaccine has the potential to protect against MVD.

Marburg virus in animals

- *Rousettus aegyptiacus* bats are thought to be natural hosts for Marburg virus. There is no visible illness in the fruit bats. As a result, the geographic distribution of Marburg virus may overlap with that of *rousettus* bats.
- African green monkeys (*cercopithecus aethiops*) transported from Uganda were the source of infection for humans during the first Marburg epidemic.
- Experiments in pigs with several ebola viruses have shown that pigs are vulnerable to filovirus infection and shed the virus.
- Pigs should thus be considered as a possible amplifier host during MVD epidemics.
- Precautionary measures are needed in pig farms in africa to avoid pigs becoming infected through contact with fruit bats. Such infection could potentially amplify the virus and cause or contribute to MVD outbreaks.



PREVENTION AND CONTROL

- Effective outbreak control requires a variety of actions, including case management, surveillance and contact tracing, a strong laboratory service, safe and respectful funerals, and societal mobilisation.
- Community involvement is critical to successfully suppressing epidemics.
- Raising knowledge of risk factors for Marburg infection and precautionary actions that persons may do is an effective strategy to decrease human transmission.

RISK REDUCTION MESSAGING SHOULD FOCUS ON SEVERAL FACTORS

- **Reducing the risk of bat-to-human transmission**
 - As a result of extended exposure to mines or caves inhabited by fruit bat colonies. People should wear gloves and other suitable protective clothes (including masks) when working or doing research in mines or caverns inhabited by fruit bat colonies. During outbreaks, all animal products (blood and meat) should be properly boiled before eating.
- **Reducing the risk of human-to-human transmission in the community**
 - As a result of direct or close contact with infected individuals, particularly their bodily fluids. Close physical contact with Marburg patients should be avoided. When caring for unwell patients at home, gloves and adequate personal protective equipment should be used. Hand cleaning should be done on a regular basis after visiting sick relatives in the hospital or caring for ailing people at home.
- **Communities affected by Marburg**
 - Make efforts to ensure that the populace is adequately educated, both about the nature of the illness and about the essential outbreak control measures.
- **Outbreak containment measures**
 - Must include prompt, safe, and dignified burial of the deceased, identifying people who may have been in contact with someone infected with Marburg and monitoring their health for 21 days, separating the healthy from the sick to prevent further spread, providing care to confirmed patients, and maintaining good hygiene and a clean environment.

- **Reducing the risk of possible sexual transmission**
 - Safer sex and hygiene for 12 months from the beginning of symptoms or until their semen tests negative for Marburg virus twice.
 - Avoiding contact with bodily fluids and cleaning with soap and water
 - Who does not advocate isolation of male or female convalescent patients whose blood has tested negative for Marburg virus

- **Controlling infection in healthcare settings**
 - Regardless of the patient's suspected diagnosis, healthcare staff should always take normal measures when caring for them. Basic hand hygiene, respiratory hygiene, the use of personal protective equipment (to prevent splashes or other contact with infectious materials), safe injection practises, and safe and respectful burial practises are examples of these.
 - When in close contact (within 1 metre) of patients with MVD, health-care workers should wear face protection (a face shield or a medical mask and goggles), a clean, non-sterile long-sleeved gown and gloves (sterilised).
 - Laboratory workers are also at danger. Samples collected from humans and animals for the examination of Marburg infection should be handled by competent personnel and processed in well-equipped labs.

Marburg viral persistence in people recovering from Marburg virus disease

- Marburg virus has been found to persist in immune-privileged areas of people who have recovered from Marburg virus sickness. These sites include the testicles and the inside of the eye.
- In women who were infected while pregnant, the virus remains in the placenta, amniotic fluid, and foetus.
- In women who were infected while nursing, the virus may remain in breast milk.

WHO Recommends that:

1. Male Marburg survivors should be enrolled in semen testing programmes upon discharge (beginning with counselling) and provided semen testing when emotionally and physically ready, within three months of illness onset. If two consecutive negative test results are obtained, sperm testing should be given.
2. All Marburg survivors and their sexual partners should undergo counselling to guarantee safer sexual practices until their sperm has tested negative for the Marburg virus twice.
3. Condoms should be distributed to survivors.
4. Marburg survivors and their sexual partners should either abstain from all sexual practices or use safer condoms until their sperm has tested negative for the virus twice.
5. Male survivors of Marburg virus sickness should practice safer sexual practices and hygiene for 12 months after symptoms appear or until their sperm tests undetectable (negative) for Marburg virus.
6. Until their sperm has tested undetected (negative) for Marburg twice, survivors should practice good hand and personal hygiene by quickly and completely cleaning with soap and water after any physical contact with sperm, including masturbation.
7. All survivors, their partners, and families should be treated with dignity and compassion.

Reference

- [1]. Aborode AT, et al. Marburg virus amidst COVID-19 pandemic in guinea: fighting within the looming cases. *Int J Health Plann Manage.* 2021. 37 553–555. doi: 10.1002/hpm.3332
- [2]. Amiar S, et al. Lipid-Specific oligomerization of the Marburg virus matrix protein VP40 is regulated by two distinct interfaces for virion assembly. *J Biol Chem.* 2021;296 1–20. doi: 10.1016/j.jbc.2021.100796.
- [3]. Amman BR, Schuh AJ, Albariño CG, et al. Marburg Virus persistence on Fruit as a Plausible Route of Bat to Primate Filovirus Transmission. *Viruses.* 2021;13(12):2394. DOI: 10.3390/v13122394.
- [4]. Coffin KM, Liu J, Warren TK, et al. Persistent Marburg virus infection in the testes of nonhuman primate survivors. *Cell Host Microbe.* 2018;24(3):405–416.e3. DOI: 10.1016/j.chom.2018.08.003.
- [5]. Cooper TK, Sword J, Johnson JC, et al. New insights into Marburg virus disease pathogenesis in the rhesus macaque model. *J Infect Dis.* 2018;218(suppl_5):S423–S433. DOI: 10.1093/infdis/jiy367.
- [6]. Hargreaves A, Brady C, Mellors J, et al. Filovirus neutralising antibodies: mechanisms of action and therapeutic application. *Pathogens.* 2021;10(9):1201. DOI: 10.3390/pathogens10091201.
- [7]. Koehler A, Pfeiffer S, Kolesnikova L, et al. Analysis of the multifunctionality of Marburg virus VP40. *J Gen Virol.* 2018;99(12):1614–1620. DOI: 10.1099/jgv.0.001169.
- [8]. Koch B, Dolnik O, Filzmayer M, et al. FP217 Marburg virus & acute kidney injury. *Nephrol Dialysis Transplantation.* 2018;33(suppl_1):104. DOI: 10.1093/ndt/gfy104.FP217.
- [9]. Roozendaal R, Hendriks J, van Effelerte T, et al. Nonhuman primate to human immunobridging to infer the protective effect of an Ebola virus vaccine candidate. *NPJ Vaccines.* 2020;5(1):112. DOI: 10.1038/s41541-020-00261-9.
- [10]. Shifflett K, Marzi A. Marburg virus pathogenesis – differences and similarities in humans and animal models. *Virol J.* 2019;16(1):165.

- [11]. Schultz MJ, Deen J, von Seidlein L, et al. Remote-Controlled and pulse pressure–Guided fluid treatment for adult patients with viral hemorrhagic fevers. *Am J Trop Med Hyg.* 2021;104(4):1172–1175. DOI: 10.4269/ajtmh.20-1515.
- [12]. Uropean Centre for Disease Prevention and Control hweeesdfdA-E-a-M-p. Ebola and Marburg virus diseases - Annual Epidemiological Report for 2019. 2021. Available at: <https://www.ecdc.europa.eu/sites/default/files/documents/AER-Ebola-and-Marburg-2019.pdf>
- [13]. Wan W, Kolesnikova L, Clarke M, et al. Structure and assembly of the Ebola virus nucleocapsid. *Nature.* 2017;551(7680):394–397. DOI: 10.1038/nature24490.
- [14]. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8986239/figure/f0005/>
- [15]. <https://www.indiatoday.in/health/story/what-is-Marburg-disease-the-outbreak-that-who-has-confirmed-in-equatorial-guinea-2334491-2023-02-14>
- [16]. <https://www.cdc.gov/vhf/Marburg/outbreaks/chronology.html>