International International Journal of Health Science & Biomedicine (IJHSB)

EPICGLOBE PUBLISHER

RESEARCH ARTICLE OPEN ACCESS

Review of Marbug Hemorrhagic Fever Disease

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Citation: Artin Badparva (2025) The prevalence of gene mutation in Cystic Fibrosis (CF) in Children medical center Tehran from 1395-1400. Int. J. Health Sci. Biomed. 2(5):1-8.

Received Date: 2025-09-1, **Accepted Date:** 2025-09-19, **Published Date:** 2025-09-30

Keywords: Marburg Virus; Pathogenicity; Virulence; Transmission Dynamics; Epidemiology; Cellular Tropism; Human T-Cell Lymphotropic Virus; Ebola Virus Malady

Abstract

Marburg hemorrhagic fever (MHF) is a serious and often fatal viral disease caused by the Marburg virus, which belongs to the Filoviridae family. Since it first emerged in 1967, MHF has been linked to high mortality rates, and recent outbreaks have underscored the critical need for a thorough understanding and effective response strategies. This updated review consolidates current knowledge about MHF, emphasizing its epidemiology, clinical manifestations, pathogenesis, and recent advancements in treatment and prevention. Recent epidemiological data show that MHF outbreaks are mainly concentrated in sub-Saharan Africa, where fruit bats serve as the primary reservoir for Zoonotic transmission. The clinical presentation of MHF typically begins with a sudden onset of fever, severe headache, and gastrointestinal bleeding, which can result in multi-organ failure. Understanding the disease's underlying path physiological mechanisms is essential for developing effective therapeutic interventions. Although there are no specific antiviral treatments approved for MHF, supportive care is the foundation of management. Recent research has investigated potential therapeutic options, such as monoclonal antibodies and antiviral agents, which have shown promise in both preclinical and clinical studies. Furthermore, vaccine development is advancing, with several candidates now entering clinical trials. This review highlights the critical need for continuous surveillance, research, and public health preparedness to reduce the impact of Marburg hemorrhagic fever. Strengthening international collaboration and investing in healthcare infrastructure are vital for effectively responding to future outbreaks and safeguarding global health.

Introduction

MARV (Marburg virus) is a highly pathogenic virus that has caused several deadly outbreaks. Originally identified in Europe, it has predominantly been reported in African countries. Due to its potential for widespread transmission and the high mortality rate associated with MARV infections, the National Institute of Allergy and Infectious Diseases has designated it as a priority pathogen. MVD (Marburg virus disease) is an acute and often fatal illness that can lead to symptoms such as hemorrhagic fever, liver failure, infections of the brain and spleen, kidney damage, and coagulation disorders in both humans and nonhuman primates .The Marburg virus (MARV) belongs to the Marburg virus genus within the Filoviridae family and the Mononegavirales order. This family includes the Marburg virus. Both the Ebola virus and the Marburg virus are members of the Filoviridae family and have caused severe outbreaks of hemorrhagic fever for over four decades. The genomes of the viruses encode seven distinct proteins, which show no significant similarity to any known macromolecules. Additionally, the Marburg virus and Ebola virus demonstrate notable differences in their protein homology. The person-to-person transmission of the Marburg virus is comparable to that of Ebola viruses but the latter is better defined [1]. Despite extensive research efforts, the natural reservoirs of the Marburg virus (MARV) remain unknown due to its sporadic occurrence. However recent studies have provided valuable

insights into the mechanisms of virus transmission and the identification of potential hosts. The largest recorded outbreak of Marburg Virus Disease (MVD) occurred in 2005, resulting in 200 to 270 cases and highlighting it as a significant global health concern [2]. Despite the challenges posed by this virus, extensive research efforts have provided valuable insights into its sources and transmission processes. Studies have identified Rousettusaegyptiacus bats as the primary natural hosts for the Marburg virus, while other bat species, including Hipposideroscamphoratus, can also act as sources of infection [3]. The cellular pathology associated with Marburg virus infections involves endothelial cell lysis caused by the filovirus in human umbilical vein endothelial cells. The diffuse transmembrane glycoprotein likely contributes to the cytotoxicity and attachment of virions to target cells. Postmortem human observations have revealed diffuse antigens present in the endothelial cells of multiple limbs. However, widespread damage to these cells may not be immediately evident in the final stages of experimental Marburg virus (MARV) infections in nonhuman primates [2]. The processes underlying disease progression during failovers infections remain poorly understood. Interestingly, virus particles have been found to enter the lymphatic vessels or vascular system directly through small lesions at the onset of infection. The primary organ tropism, which includes lymph nodes, spleen, and liver, may be due to direct access of these diffuse particles to non-penetrating macrophages, without breaching the cell or tissue barrier [4]. Future studies are needed to better understand the complexities of MARV pathogenesis and transmission. The pan-tropism observed in filoviruses infections, which often emerges late in the disease progression, is not yet fully understood [5]. One potential mechanism for virus dissemination and localized tissue destruction involves the elimination of circulating infectious cells, including monocytes. This process necessitates the involvement of excretory cells and endothelial cells and is typically mediated by cytokines and chemokines [6]. However, there is currently no experimental evidence demonstrating the infection or activity of monocytes by filoviruses. Further research is needed to clarify the mechanisms underlying the pan-tropic behavior of filoviruses [1].

Historical Prevalence and Epidemiology of the Disease

A thorough understanding of the historical prevalence and epidemiology of the Marburg virus is critical for developing effective universal health strategies and interventions to prevent future outbreaks. The first recorded outbreak of the Marburg virus (MARV) occurred in 1967 in Marburg, Germany, where scientists were conducting experiments with tissue samples from monkeys collected in East Africa as part of efforts to develop a polio vaccine. During this outbreak, additional cases were reported in Frankfurt, Germany, and Yugoslavia. Using electron microscopy on infected guinea pig plasma, researchers identified the virus and named it "Marburg virus [7]."The next documented outbreak of MARV took place in 1975 in South Africa, infecting three individuals. The first patient contracted the virus while traveling to Zimbabwe, and it was subsequently transmitted person-to-person to a companion and a nurse [3]. Between 1975 and 1985, another outbreak was reported in an East African country, where a man became infected after visiting a cave. A doctor also contracted the virus while treating this patient [7]. A smaller outbreak occurred in Kenya between 1987 and 1995, leading to the discovery of a new strain of the virus [8]. The epizootic of this virus has been characterized by widespread outbreaks in various geographic regions. Between 1980 and 1986, a single case of this virus was reported in a young boy who had explored the same cave in the East African country just days before [8]. The Marburg virus has caused significant outbreaks, notably in the coldest inhabited region of Russia from 1988 to 1998, and in West Africa between 1998 and 2005, resulting in 158 deaths [9]. This outbreak began among young gold miners in South Africa and spread to the nearby city of Wide, where at least nine genetically distinct strains of the Marburg virus were identified [7]. Another severe outbreak occurred in northwestern Angola from 2004 to 2006, following the death of a hospital staff member. This outbreak led to 257 confirmed cases and 228 fatalities, yielding an alarming 89% mortality rate [5]. Genetic studies revealed similarities between the strains involved in the Angolan outbreak and those from earlier occurrences of the virus [10].These events underscore the persistent threat posed by filoviruses and highlight the need for ongoing research into their pathogenesis and the development of effective countermeasures. Since the major outbreak in Angola, there have been no reports of similarly large outbreaks, however, sporadic cases and smaller outbreaks have occurred globally. In 2007, four miners in Uganda's Kamansanga District contracted the virus during mining operations, leading to two additional cases in the United States and the Netherlands. The American patient survived, while the Dutch patient succumbed to the virus. Both individuals had contracted the virus while visiting the Maramagambo Forest Python Cave in Uganda. Subsequently; three additional outbreaks were reported in Uganda. The first occurred in the Kastone zone of western Uganda between 2011 and 2012, lasting three to four weeks and affecting approximately 13 to 15 individuals, four of whom died. The genome sequence from the 2012 Ugandan outbreak was found to be similar to previously identified strains. These outbreaks underscore the ongoing threat posed by filoviruses and the necessity for continued surveillance and research efforts to develop effective interventions against these pathogenic viruses. Following the 2012 outbreak, there were additional sporadic cases and small outbreaks of the Marburg virus. In 2014, an outbreak occurred in Uganda's capital, Kampala, where a health surveillance worker contracted the virus and died shortly thereafter. The viral genome shared similarities with a previously identified strain of the Marburg virus from a type of fruit bat in a region connecting northeast Africa to the Middle East. Another outbreak took place in the Kween zone of Uganda in 2017, where four members of a single family were infected with the Marburg virus, and only one survived. The genome sequence from this outbreak also resembled previously identified strains, however, therapeutic findings related to this incident remain insufficient, and intensive research is ongoing. A recent outbreak was declared in Guinea in August 2021, concluding in September 2021, involving one man who contracted the virus and subsequently died. Unfortunately, no information about the specific strain of the Marburg virus involved in this outbreak has been released. Regarding 2023, the last reported case occurred on April 11, 2023, with the second negative PCR test conducted on April 19, 2023. All cases were reported from the Bukoba district in the Kagera region of northern Tanzania. Among the confirmed cases, three individuals recovered, while six deaths were recorded, resulting in a case fatality rate of 67% (CFR). Of the six deaths, five were confirmed cases, and one was deemed probable. The ages of those affected ranged from 1 to 60 years, with a median age of 33 to 35 years, and males were the most affected group (n=6, 67%). Six of the cases were close relatives of the index case, and two were healthcare workers who provided medical care to the infected individuals.

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These sporadic outbreaks highlight the challenges of managing filoviruses transmissions and emphasize the ongoing need for enhanced surveillance and research efforts to understand transmission dynamics, pathogenesis, and the potential for future outbreaks.

Genome and Structure of the Marburg Virus

The EBOV (Ebola virus) and MARV (Marburg virus) belong to the Filoviridae family, which is characterized by enveloped, negative-stranded RNA genomes and unique filamentous structures. Ebola virus particles have a uniform diameter of 80 nm, but their lengths can vary significantly, ranging from 795 to 828 nm. The filoviruses genome is composed of seven genes arranged in the following order: 3' leader, nucleoprotein (NP), virion protein 35 (VP35), VP40, glycoprotein (GP), VP30, VP24, and RNA-dependent RNA polymerase (L) - 5' trailer. With the exception of the glycoprotein gene, all genes encode structural proteins and are monocistronic.Within the virion particles, the RNA genome is enclosed by nucleoprotein, forming the internal rib nucleoprotein complex. This complex associates with RNA polymerase, VP35, and VP30 to create the functional transcriptase-replicase complex. In addition to their structural roles, the proteins of the rib nucleoprotein complex, including VP35 and VP40, have additional functions in filoviruses infections. Specifically, VP35 acts as an interferon antagonist, while VP40 serves as a matrix protein involved in viral assembly.The glycoprotein is the only protein present on the viral membrane, consisting of two disulfide-linked fragments, GP1 and GP2, arranged in a trimetric structure. Notably, the Ebola virus produces a soluble glycoprotein, the principal product of the GP gene, which is secreted in large quantities from infected cells. Filoviruses possess a distinctive structure characterized by a non-linear, negative-sense RNA genome that contains unique genes arranged in the order 3'-NP-VP35-VP40-GP-VP30-VP24-L-5'. This genome features high conservation of replication and transcription signals, along with long non-coding regions that play a crucial role in viral replication. These features differentiate filoviruses from other Mononegavirales and contribute to their Pathogenicity. In the Marburg virus genome, long non-coding regions contain elements that are vital for replication and transcription. With the exception of two genes, all other genes are separated by 4 to 97 nucleotides through long intergenic regions. The transcription stop signal from the VP24 gene and the transcription start signal from the VP30 gene share a five-nucleotide overlapping sequence, UAAUU. All seven genes in the Marburg virus genome are monocistronic, encoding distinct structural proteins responsible for various functions during viral replication: NP,

VP35, VP40, GP, VP30, VP24, and L.The genome is encapsulated by a nucleocapsid complex composed of NP, VP35, VP30, and L. NP acts as the primary nucleocapsid protein, forming a helical structure that interacts with VP35 to establish a complex with L, which functions as the RNA-dependent RNA polymerase, with VP35 serving as a polymerase cofactor. All four nucleocapsid proteins play essential roles in the replication and transcription of the viral genome. Additionally, the Marburg virus features a host-derived membrane layer enriched with glycoproteins, which are crucial for binding to host cells. The inner structure of the virion is formed by VP40, which mediates budding and interaction with the matrix and nucleocapsid. VP24 interacts with NP and other cellular membranes, contributing to the release of progeny virions from infected cells.

Trauma Causadopelo Marburg virus

The Marburg virus typically enters the body through broken skin, damaging various cells and tissues, which leads to Marburg pyrexia. The most severe manifestations of Marburg pyrexia include fluid imbalances, coagulation complications, shock, and multiorgan failure. Experimental studies in monkeys have shown that the Marburg virus primarily targets immune system cells that engulf debris, foreign substances, microbes, and cancer cells-a process known as xenophagy. White blood cells, part of the immune system and classified as agranulocytes, range in size from 15 to 25 microns (occasionally up to 30 or 40 microns). These cells are typically round or oval, with nuclei that can be lobular, kidney-shaped, or twisted, and may exhibit depressions or a horseshoe shape. Special macrophages located in the liver also play a role in this immune response. Antigen-presenting cells, another type of immune cell, process and present antigens to resting lymphocytes during the primary immune response and to memory lymphocytes during the secondary response. When the Marburg virus infects mononuclear phagocytic cells, such as monocytes and macrophages, it disrupts cellular functions and damages secondary targets, including the thin layer of cells lining blood and lymphatic vessels. This layer is crucial as it separates blood or lymph fluid from the underlying tissues and the vessel's inner channel. Additionally, the activity of macrophages and monocytes leads to the release of cytokines and pro-inflammatory mediators, contributing to the development of shock, which is a primary complication in Marburg pyrexia. These path physiological processes underscore the importance of early diagnosis and aggressive supportive care to slow disease progression and reduce mortality rates associated with Marburg virus infection.

The Impact of Marburg Virus Trauma on Humans

Comprehensive therapeutic studies on Marburg virus (MARV) trauma in humans are limited due to the rural settings where outbreaks often occur and the insufficient collection of evidence and trauma data from patients. Current therapeutic findings primarily derive from data related to the initial outbreak in Germany, followed by subsequent outbreaks in South Africa and smaller outbreaks in other parts of Africa. Experiments on cultured cells from MARV-infected patients have shown significant adaptive immune responses, characterized by an initial increase in immune cells. Additionally, examination of serum samples from infected patients revealed IgG reactivity to the viral proteins NP and GP with two patients demonstrating significant neutralizing antibody titers. However, these neutralizing antibody titers gradually decreased, falling below detectable levels by 27 months post-infection. At the organ level, the Marburg virus typically targets the adrenal glands, liver, and lymphoid tissues in infected patients. Autopsies conducted on patients infected with Ravn virus, a close relative of MARV, revealed multiple pathological effects, including swelling of the kidneys, heart, brain, and lymphoid tissues, as well

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as bleeding in soft tissues and mucosa. These findings underscore the need for ongoing research to better understand the pathogenesis of MARV in humans and to develop effective interventions to prevent and treat Marburg hemorrhagic fever. Proving ground analyses have shown that MARV exhibits hepatotropic properties, suggesting that the hepatic asialoglycoprotein receptor may facilitate Marburg virus infections. Necrosis of liver parenchymal cells disrupts the reticuloendothelial system and can elevate liver enzyme levels associated with MARV infection. Infection of other organs can lead to various symptoms, including proteinuria due to renal dysfunction, cardiac and pulmonary hemorrhages, scrotal pain, and necrosis of the testes and ovaries. The trauma model of MARV hemorrhagic fever in humans indicates that the virus primarily targets dendritic cells, monocytes, liver parenchymal cells, adrenal cortex cells, and various lymphoid tissues. Infection of dendritic cells results in suboptimal T-lymphocyte stimulation, leading to lymphocyte apoptosis and subsequent immune suppression. This process increases the levels of cytokines and chemokines, resulting in shock and multiple organ damage. These path physiological mechanisms emphasize the complexity of Marburg virus infections and highlight the necessity for ongoing research to enhance our understanding of the virus's pathogenesis and to develop effective treatments for Marburg hemorrhagic fever. Infection of macrophages or monocytes by Marburg virus leads to uncontrolled cytokine and chemokines activity, which can further damage T lymphocytes and endothelial cells. Infection of endothelial cells increases blood vessel permeability and can lead to diffuse intravascular coagulation, resulting in bleeding. Systemic proliferation may also arise from MARV infection of endothelial cells. Infection of parenchymal cells in the liver can reduce coagulation factors, potentially leading to bleeding later in the disease progression. Adrenal cortical cell infection by the Marburg virus can cause metabolic disturbances and irregular blood pressure, with bleeding occurring later in the illness. Infection of lymphoid tissues, particularly the spleen and lymph nodes, can result in tissue necrosis and impaired adaptive immune function, ultimately causing shock and damage to lymphatic organs. At the cellular level, antigen-presenting cells play a critical role in the immune system by processing and presenting antigens to resting lymphocytes during the primary response, and to memory lymphocytes during the secondary response. These cells also ingest cellular debris, foreign substances, microbes, cancer cells, and anything lacking proteins specific to healthy body cells in a process known as xenophagy. They are primary targets for Marburg virus entry. These findings were confirmed through the identification of virions and virus-associated antigens using immunohistochemical tests and electron microscopy during the 1987 outbreak in Kenya, as well as through observations of diffuse infections in macaque macrophages based on peripheral blood smear results. These path physiological processes underscore the importance of early detection and effective treatment to mitigate severe outcomes associated with Marburg hemorrhagic fever (Francis, et al., 2025).Flow cytometry studies have shown that Marburg virus (MARV) infection of dendritic cells leads to suppression of the innate immune response and abnormalities in lymphocyte activation. Additionally, macrophage infections increase the production of pro-inflammatory cytokines, such as TNF-α (tumor necrosis factor-alpha), which can induce bystander apoptosis in lymphocyte populations, resulting in immunosuppressant and lymphopenia. Upon stimulation, MARV-infected macrophages release the virus and trigger the production of additional cytokines and chemokines. These path physiological processes contribute to the development of shock and multiple organ damage in Marburg hemorrhagic fever, highlighting the need for effective interventions to manage cytokine storms that often occur in widespread infections.

The Impact of Marburg Virus on Animals

Marburg virus (MARV) has been observed affecting various animal species, including baboons and several types of non-human primates such as rhesus monkeys, common monkeys, crab-eating macaques, Saimiri cebids, and Chlorocebusaethiops. In these animal models, MARV infects Kupffer cells, monocytes, dendritic cells, macrophages, and types of white blood cells that produce antibodies, including natural killer cells and phagocytes, which can engulf and destroy microorganisms, ingest foreign material, and remove dead cells. Without widespread infection, a decrease in natural killer cells and CD4 and CD8 T-lymphocytes typically occurs due to cell death by apoptosis. In humanized mouse models infected with MARV, the virus shows increased virulence and primarily targets macrophages, which are critical components of the immune system that develop from stem cells in the bone marrow, as well as natural killer cells and phagocytes. In the MARV-Ravn-incompatible wild-type mouse model, the infection leads to acute illness, liver enlargement and necrosis, splenomegaly, and depletion of lymphocyte populations. In contrast, the MARV-Ravn-adapted mouse model displays distinct symptoms, including reduced physical activity, weight loss and wrinkled fur 3 to 4 days post-infection, with mortality occurring within 5 to 7 days. Guinea pigs typically exhibit mild fever when infected with the host-adapted variant of MARV. These findings underscore the complex pathogenesis of MARV in animals and highlight the need for ongoing research to better understand the virus's Pathogenicity and develop effective interventions for managing Marburg hemorrhagic fever in both animals and humans. Successive passages of guinea pigs infected with MARV can lead to severe conditions in these animals. One of the initial studies using a guinea pig model demonstrated that 100% of the guinea pigs inoculated with MARV died 7 to 9 days post-infection after receiving eight complete blood transfusions. This model was used to explore the effects of the Angolan strain of MARV, revealing that MARV infections can lead to lymphopenia, a condition characterized by a deficiency of white blood cells, as well as infections in the kidneys, liver, spleen, and lungs. The effects of Marburg virus in guinea pigs appear similar to those observed in mice and humans. Furthermore, extensive vaccination studies have been conducted in guinea pigs. One study testing a triatomic replication-competent vesicular stomatitis virus-based candidate vaccine showed 100% protection against MARV infection. The Syrian golden hamster model typically exhibits no symptoms when infected with wild-type strains of Marburg virus. However, rodent models with Signal Transducer and Activator of Transcription 2 (STAT2) deficiency show liver and spleen infections, neutrophil leukocytosis, and increased production of pro-inflammatory cytokines. These findings highlight the critical role of animal models

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in understanding the pathogenesis of Marburg hemorrhagic fever and developing effective interventions for the disease. The effects of the Marburg virus in guinea pigs resemble those observed in mice and humans. Extensive vaccination studies have been conducted using guinea pigs, with one study of a triatomic replication-competent vesicular stomatitis virus-based candidate vaccine demonstrating 100% protection against MARV infection. In contrast, the Syrian golden hamster model typically shows no symptoms when infected with wild-type strains of the Marburg virus. However, rodent models with Signal Transducer and Activator of Transcription 2 (STAT2) deficiency exhibit liver and spleen infections, neutrophil leukocytosis, and increased production of pro-inflammatory cytokines. These findings underscore the critical role of animal models in understanding the pathogenesis of Marburg hemorrhagic fever and in developing effective interventions for the disease. In non-human primates (NHPs), Marburg infection commonly leads to lymphocytosis in the early stages and progresses to leukocytosis and thrombocytopenia within 5-6 days due to elevated neutrophil levels. The virus subsequently infects the adrenal glands, liver cells, and lymphoid tissue. In the later stages, it targets the endothelium of various organs, with diffuse antigens detectable in multiple tissues, including the kidneys, liver, spleen, and adrenal glands. These path physiological processes highlight the complexity of MARV infections in animals and emphasize the importance of using animal models to understand the disease's pathogenesis and to develop effective interventions for managing Marburg hemorrhagic fever in both animals and humans. After 2 to 6 days of infection with the Marburg virus, typical clinical signs include diarrhea, anorexia, fever, rash, and bleeding. Viremia typically occurs on the third day, with the highest viral titer usually observed around 8 days post-infection. However, a recent experiment in mice showed that MARV did not cause disease or induce Viremia in these animals. Despite positive serological results for MARV infection and the production of neutralizing antibodies, the mice did not develop clinical disease. These findings suggest that further research is needed to understand the differences in disease manifestation between animal models and humans. Additional studies in ferrets may contribute to our understanding of the various processes that lead to differences in disease severity and enhancing our knowledge of Marburg hemorrhagic fever. Such research emphasizes the importance of continued efforts to develop effective interventions to manage the disease and prevent its spread.

Debarment and Control

Given the recent cases of Marburg Virus Disease (MVD) reported in Ghana and its prevalence in previous years, there is an urgent need to develop effective vaccines and treatments for this devastating disease. Since the Marburg virus (MARV) can only be handled in biosafety level 4 (BSL-4) facilities, very few laboratories possess the necessary capabilities for research and therapeutic development against this deadly virus. Strengthening research facilities with advanced labs for handling MARV is therefore critical. The lessons learned from the SARS-CoV-2 pandemic highlight the importance of the One Health approach, which recognizes the interdependence of environmental, animal, and human health. This approach emphasizes the need for collaborative efforts to prevent and control diseases shared between humans and animals, such as MVD. Proactive measures, such as enhancing surveillance and early detection systems, implementing appropriate containment and control strategies, and investing in research and development, can help mitigate the impact of MVD outbreaks and prevent future epidemics. To address the threat of Marburg Virus Disease, rapid, multidisciplinary action is required to identify and contain cases before they can spread, as seen in other regions and countries. In light of the ongoing COVID-19 pandemic and the rising cases of monkey pox, there is an urgent need for effective treatments and vaccines against this deadly virus. Although no specific treatment or vaccine currently exists for MVD, therapies such as cardiac glycosides, antipyretics, and steroids are already being prescribed, and various drugs are under investigation. Recent studies suggest that remdesivir may be effective against the Marburg virus in Macacafascicularis models, while cholesterol-conjugated fusion inhibitors have also shown promise. Other potential treatments include 4-(amino methyl) benzamide, BCX4430, favipiravir, alloprene small molecules, monoclonal antibodies, and cytokines. Several efforts have been made to develop a suitable vaccine and treatment regimen for MVD, with matrix proteins GP and VP40 identified as the most antigenic proteins for creating new chimeric subunit vaccines. Recent discoveries of inhibitory compounds such as FC-10696 and AVI-7288 have shown potential for suppressing MARV exit and serving as post-exposure prophylaxis, respectively. Additionally, various experiments have been conducted on rodents and non-human primate models to test vaccine efficacy against MARV. Integrating these research efforts with proactive surveillance, early detection, and effective containment measures can help mitigate the impact of MVD outbreaks and prevent future epidemics To date, few vaccines have been tested for human use against the Marburg virus. Among these, the cAd3 vaccine, a chimpanzee adenovirus serotype 3 vector encoding wild-type GP, is currently undergoing a phase 1 clinical trial for human use. In-hospital supportive care is essential for managing MVD, focusing on maintaining the patient's electrolytes, fluids, oxygen levels, and blood pressure, replacing lost blood and clotting factors, and treating any secondary infections. The scarcity of MARV samples, low case numbers, and limited research interest may explain the current lack of effective treatments and vaccines for this deadly virus. Analysis of research topic distribution has identified several clusters where MARV, Ebola, infection, human health, outbreaks, disease, and vaccines are significantly present. The first paper on the Marburg virus was published in 1962, and a highly cited paper discussing vaccination against Ebola and Marburg viruses was accepted by Nature Medicine in 2005.Vaccine candidates formulated with glycoprotein's from the Ebola virus (EBOV) or Marburg virus (MARV) and expressed in attenuated recombinant virus vectors have shown both safety and high efficacy in non-human primates. While researchers are actively working to develop effective interventions against MARV, it is crucial to recognize that certain aspects of the virus and its related diseases are still not well understood. Thus, ongoing research is essential to identify new therapeutic targets and to create effective preventive measures against MARV.

Detection of Diffuse Antigens with Labeled Antibodies

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Direct observation of diffuse antigen localization is often essential in various research and diagnostic contexts. This can be accomplished by using antibodies that are labeled, bound, or conjugated with a dye, which allows visualization under either a conventional or electron microscope. Two common labeling methods for antibodies suitable for light microscopy include using a fluorescein dye that emits visible fluorescence when excited by UV light, or conjugating antibodies with peroxidase followed by the addition of hydrogen peroxide and diaminobenzidine to produce a dark brown precipitate. Labeled antibodies are invaluable tools in studying diffuse pathogenesis, enabling researchers to trace contagion pathways and examine how viruses transition within zymotic cells. They also function as rapid diagnostic tools, allowing for the detection of small amounts of fluorescein-labeled or peroxidase-labeled biochemicals against suspected viruses, resulting in staining or fluorescence of zymotic cells. Overall, the use of labeled antibodies is a critical aspect of diffuse detection and characterization, providing insights into the mechanisms of diffuse contagions and assisting in the development of effective interventions against these maladies. Labeling antibodies is a powerful technique that facilitates the observation of diffuse antigen distribution within zymotic cells. The distribution patterns often reveal characteristic features, such as nuclear or cytoplasmic localization and diffuse or localized distribution, which can aid in diffuse detection. Antibodies can be labeled with large molecules or particles that are visible under an electron microscope, such as ferritin or colloidal gold, allowing precise observation of diffuse antigen distribution in zymotic cells. This technique is particularly significant for studies focusing on the synthesis, assembly, and localization of virus protein components. Since the 19th century, antibodies have been utilized for the treatment and prevention of diffuse contagions. However, the full potential of passive immunization for infectious diseases remains untapped. The development of efficient methods to isolate broad and potent neutralizing human monoclonal antibodies has enabled the generation of antibodies with remarkable capabilities. These advancements have opened exciting avenues in antibody-based therapies. A notable breakthrough is the discovery of modifications in the IgG Fc region that extend the half-life of antibodies in humans by three months or more suggesting that antibodies could become crucial tools in managing future diffuse epidemics. Antibodies targeting members of various diffuse families that cause severe diseases in humans have been isolated, with much currently undergoing therapeutic development. The COVID-19 pandemic has accelerated research efforts, leading to the rapid creation of monoclonal antibody therapies targeting SARS-CoV-2, the virus responsible for COVID-19. Broad and potent neutralizing antibodies also serve as important research reagents for identifying. protective epitopes, which can be engineered into active vaccines using structure-based reverse vaccinology. This approach involves analyzing the three-dimensional structures of diffuse proteins and utilizing this information to design vaccines that provoke an immune response against specific diffuse epitopes. Thus, broad and potent neutralizing antibodies can guide vaccine development by identifying these protective targets. In summary, the use of antibodies for therapeutic and prophylactic purposes holds significant promise in combating diffuse maladies, and ongoing research in this field is likely to lead to important advancements in the years ahead.

Proteins encoded by diffusion located on cell surfaces

The presence of antigenic markers on the surface of zymotic cells is a common characteristic of viral infections. In enveloped viruses, these markers are typically part of the diffuse envelope, whereas in non-enveloped viruses, they may consist of key non-structural or structural proteins. These proteins signal to the immune system that the cells are infected. Membrane-associated RING-CH (MARCH) family proteins, which are RING finger E3 ubiquity ligases, are known to down regulate cell membrane proteins. Among these, MARCH 8 has emerged as a novel anti-diffuse factor that inhibits the envelope glycoprotein's of HIV-1 and vesicular stomatitis virus G by removing them from the cell surface, thus reducing their incorporation into virions. Identifying and characterizing such anti-diffuse factors provides important insights into the mechanisms of diffuse pathogenesis and host defense against viral infections. MARCH 8 reduces viral infectivity through two distinct mechanisms, one of which involves the degradation of various transmembrane proteins by ubiquitin ligases. These proteins include a wide range of abbreviations, such as adaptor protein, apolipoprotein, B-cell receptor-associated protein 31, bone marrow stromal cell antigen 2, cadherin-1, clathrin-independent endocytosis, envelope glycoprotein in retroviridae, endosomal sorting complexes required for transport, hepatitis C virus, hepatocyte growth factor-regulated tyrosine kinase substrate, interferons, interleukin-1 receptor accessory protein, intraluminal vesicles late endosomes, membrane-associated RING-CH 8, mitochondrial anti-diffuse signaling protein, monocyte-derived macrophages, major histocompatibility complex, murine leukemia virus, multivesicular bodies, the capsid of a virus with enclosed nucleic acid, nuclear dot protein 52 kDa, neural precursor cell expressed developmentally downregulated protein 4, natural killer cells, nonstructural protein 2, porcine epidemic diarrhea virus, plasma membrane, recycling endosomes, severe acute respiratory syndrome coronavirus, transferrin receptor, trans-Golgi network, TNF-related apoptosis-inducing ligand receptor 1, vacuolar protein sorting 4, and vesicular stomatitis virus G.

The Role of Shark Proteins and the Komodo Dragon Genome in Developing New Treatments for the Marburg Virus

The Marburg virus is a highly pathogenic filovirus that leads to severe hemorrhagic fever with high mortality rates in humans. Current treatment options are limited, with no widely available approved vaccines or specific antiviral therapies, highlighting the need for innovative approaches. Recent zoological research has examined shark proteins and the Komodo dragon genome, revealing their unique immunological adaptations, especially in innate immunity and antimicrobial peptides. These findings may provide novel strategies for combating viral infections such as Marburg. In the sections below, we will explore the potential of shark-derived antibodies and Komodo dragon antimicrobial peptides in antiviral research, backed by recent zoological discoveries.

Shark Proteins: The Antiviral Potential of Nan bodies

Sharks, particularly species like the nurse shark (Galeocerdocuvier)

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and the bamboo shark (Chiloscylliumplagiosum), produce unique immunoglobulin new antigen receptors (IgNARs), also known as variable new antigen receptor (VNAR) antibodies or anybodies. These single-domain antibodies are smaller, more stable, and capable of binding to specific epitopes with high affinity, making them promising candidates for therapeutic development. A 2023 study published in Nature Communications found that nurse sharks immunized with the SARS-CoV-2 spike protein receptor-binding domain (RBD) produced IgNARs that target two distinct conserved epitopes on the viral spike protein. These shark-derived antibodies (ShAbs) exhibited strong neutralization against various SARS-CoV-2 variants, including Omicron, and offered protection in a transgenic mouse model. Additionally, the study emphasized the ShAbs' capacity to cross-neutralize related corona viruses, such as SARS-CoV-1, owing to their high affinity and stability. In 2024, further research optimized shark nanobodies against SARS-CoV-2, confirming specific binding to the RBD and suggesting their potential as a platform for developing cross-reactive antiviral therapies.

Relevance to the Marburg Virus

The Marburg virus uses its glycoprotein (GP) to attach to host cell receptors, such as Niemann-Pick C1 (NPC1), enabling viral entry. The high specificity and stability of shark nanobodies can be utilized to target conserved regions of the Marburg virus GP, potentially blocking the virus from entering host cells. The ability of shark antibodies (ShAbs) to neutralize various viral variants, as demonstrated with SARS-CoV-2, indicates they could be engineered to recognize Marburg virus epitopes, providing a novel therapeutic approach. Furthermore, the small size of VNARs enhances tissue penetration and allows for potential delivery through inhalation or other methods, which could be crucial for treating hemorrhagic fevers where rapid systemic spread occurs.

The Komodo Dragon Genome: Antimicrobial Peptides and Immune Adaptations

The Komodo dragon (Varanuskomodoensis), the largest living lizard, possesses a robust immune system that is well-suited to its diet, which is rich in carrion, and its exposure to pathogenic bacteria found in its saliva. A 2019 study published in BMC Genomics sequenced the Komodo dragons genome, identifying 17,213 predicted genes, particularly focusing on antimicrobial host-defense peptides such as defensins and cathelicidins. These peptides are essential components of innate immunity, which is thought to play a more significant role in reptiles than in mammals. The study highlighted several cathelicidin genes, including Cathelicidin2_VARKO and Cathelicidin4.1_VARKO, which encode peptides that exhibit strong antimicrobial activity against bacteria and potentially other pathogens. Additionally, another 2019 study in Nature Ecology & Evolution further examined the Komodo dragon genome, uncovering adaptations in cardiovascular, muscular, and chemosensory systems. Notably, this study found evidence of positive selection in pathways associated with hemostasis, which may help counteract the anticoagulant effects of the dragon's venomous saliva. These adaptations indicate that Komodo dragons have developed mechanisms to withstand the systemic effects of their own venom and bacterial exposure, which could provide insights for antiviral strategies.

Relevance to the Marburg Virus:

The Marburg virus leads to severe coagulopathy and immune dysregulation, resulting in hemorrhagic symptoms and immune suppression. Investigating the antimicrobial peptides from Komodo dragons, particularly cathelicidins, may reveal their potential to modulate immune responses or inhibit viral replication. For example, cathelicidins have demonstrated antiviral activity against enveloped viruses by disrupting viral membranes and enhancing innate immune responses. Since Marburg is an enveloped virus, these peptides could potentially target its lipid envelope. Furthermore, the hemostatic adaptations found in the Komodo dragon genome may inspire the development of peptide-based therapies to stabilize blood clotting in patients infected with Marburg, thereby addressing the virus's hemorrhagic effects.

Proposed Therapeutic Approaches for Marburg Virus

Two primary therapeutic strategies can be proposed based on the immunological properties of shark proteins and Komodo dragon peptides:

Shark Nanobody-Based Antivirals: VNARs derived from sharks could be engineered to specifically target the glycoprotein (GP) of the Marburg virus, thereby preventing the virus from entering host cells. The effectiveness of shark antibodies (ShAbs) against various SARS-CoV-2 variants indicates that a similar strategy may work for Marburg, especially given the conserved nature of filovirus glycoproteins. Preclinical studies could involve immunizing sharks with Marburg GP to generate specific VNARs, followed by in vitro and in vivo testing to evaluate their neutralization efficacy. Additionally, the stability of VNARs makes them ideal for use in resource-limited settings, where Marburg outbreaks frequently occur.

Omodo Dragon Peptide-Based Immunomodulators: Cathelicidins and defensins from the Komodo dragon could. be synthesized or expressed recombinantly to evaluate their antiviral and immunomodulatory effects against the Marburg virus. These peptides may enhance innate immune responses in infected patients, potentially decreasing viral load and alleviating immune dysregulation. Furthermore, peptides derived from hemostatic pathways could be investigated to address Marburg-induced coagulopathy, providing a dual therapeutic strategy.

Rationale and Future Directions

The exploration of shark proteins and Komodo dragon peptides is motivated by their evolutionary adaptations to extreme environments, which have equipped them with unique immunological tools. Sharks, as ancient vertebrates, have developed a highly effective adaptive immune system that produces versatile and resilient nanobodies. In contrast, Komodo dragons, which inhabit bacterially rich environments, have evolved powerful innate immune defenses that may be repurposed for antiviral applications Although no studies have directly linked these biological systems to the treatment of the Marburg virus, their proven efficacy against other pathogens

Citation: Artin Badparva (2025) Review of Marbug Hemorrhagic Fever Disease. Int. J. Health Sci. Biomed. 2(5):1-8.

such as SARS-CoV-2 for shark nanobodies and various bacteria for Komodo peptides provides a solid foundation for hypothesis-driven research.

Future research should prioritize:

- **In Vitro Studies:** Evaluate the binding and neutralization of shark nanobodies against the Marburg virus glycoprotein (GP) in cell culture models.
- **Peptide Screening:** Evaluate the antiviral activity of Komodo dragon cathelicidins and defensins against the Marburg virus using enveloped virus models.
- **In Vivo Models:** Utilize animal models, such as nonhuman primates, to evaluate the efficacy and safety of these biologics for treating Marburg virus infection.
- **Synthetic Biology:** Develop synthetic analogs of these proteins and peptides to enhance their stability, specificity, and scalability for clinical applications.

Conclusion

The rising threat of Marburg virus outbreaks, marked by high mortality rates and diagnostic difficulties, is exacerbated by the increasing emergence of zoonotic viruses due to human encroachment and climate change. This situation highlights the urgent need for robust surveillance, rapid diagnostics, and effective infection control measures, especially in remote African regions where outbreaks are most common. At the same time, the unique immunological properties of shark nanobodies (VNARs) and Komodo dragon antimicrobial peptides present a promising opportunity for developing innovative therapies. Their high-affinity binding and broad-spectrum antiviral potential can help meet the urgent demand for treatments against the Marburg virus. By integrating improved surveillance systems with insights from cross-species biology, we can enhance our preparedness for emerging infectious diseases and leverage biodiversity-driven innovations to transform medical countermeasures, ensuring a proactive and resilient response to global health threats.

References

1. Marzi (2023) SARS-CoV-2. Further research on shark-derived nanobodies against. journal of Nanobiotechnology.
2. Wenjun Z, Guodong L, Wenguang C, Shihua H, Anders L, et al. (2022) A cloned recombinant vesicular stomatitis virus-vectored Marburg vaccine, PHV01, protects Guinea pigs from lethal Marburg virus disease 10: 1004.
3. Pingray V, Klein K, Alonso JP, Belizan M, Babinska M, et al. (2025) A core outcome set for maternal and neonatal health research and surveillance of emerging and ongoing epidemic threats (MNH-EPI-COS): a modified Delphi-based international consensus. 80:103025.
4. Sekwadi P, Smith AM, Maruma W, Mongologa G, Tsele G, et al. (2024) A prolonged outbreak of enteric fever associated with illegal miners in the City of Matlosana, South Africa. Open Forum Infectious Diseases 11: ofae118.
5. Feng B, Li C, Zhang Z, Huang Y, Liu B, et al. (2025) A shark-derived broadly neutralizing nanobody targeting a highly conserved epitope on the S2 domain of sarbecoviruses. Journal of Nanobiotechnology 23: 110.
6. Amagai R, Takahashi T, Terui H, Fujimura T, Yamasaki K, et al. (2023) An antimicrobial peptide cathelicidin passes mainly scavenger receptors. International Journal of Molecular Science 24: 875.
7. Khan SS, Luqman S (2025) Antimicrobial plant peptides: structure, classification, mechanism and therapeutic potential. Current Topics in Medicinal Chemistry 25: 3103-3156.
8. Jakobsen J, Barbesgaard M, Støen MA (2025) Beyond contracts: supply chains and dynamics of incorporation among classes of capital in the aftermath of global outbreaks of avian flu. Journal of Agrarian Change 25.
9. Srivastava S, Sharma D, Kumar S, Sharma A, Rijal R, et al. (2023) Emergence of Marburg virus: a global perspective on fatal outbreaks and clinical challenges. Frontiers in microbiology 14:1239079.
10. Musafiri S, Siddig EE, Nkuranga JB, Rukundo A, Mpunga T, et al. (2025) Emerging Strategies and Progress in the Medical Management of Marburg Virus Disease. Pathogens 14: 322.

Citation: Artin Badparva (2025) Review of Marbug Hemorrhagic Fever Disease. Int. J. Health Sci. Biomed. 2(5):1-8.