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TREATMENT OPTIONS FOR PATIENTS WITH MARBURG VIRUS

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Annotation: Marburg virus, a member of the family *Filoviridae* and genus *Marburgvirus*, is a zoonotic virus that is initially transmitted from animals to humans. Both Marburg virus and ebola virus belong to the *Filoviridae* family of viruses and have the capacity to cause outbreaks with high fatality rates. The animal reservoir in nature for the Marburg virus is the African fruit bat (i.e., *Rousettus aegyptiacus*). Marburg virus is clinically similar to ebola virus and can lead to Marburg virus disease (MVD), formerly known as Marburg hemorrhagic fever. MVD is a rare and severe hemorrhagic fever affecting both humans and non-human primates. Marburg virus was first discovered in 1967, following two large simultaneous Marburg outbreaks in Marburg and Frankfurt in Germany and in Belgrade, Serbia. The initial outbreak was associated with laboratory work using African green monkeys imported from Uganda. Subsequent outbreaks and sporadic cases were later observed in Angola, the Democratic Republic of the Congo, Kenya, South Africa, and Uganda.

Key words: Marburg, virus, infection, filoviridae, marburgvirus.

According to the World Health Organization, Marburg virus is typically transmitted to people from fruit bats through a variety of mechanisms. Infected fruit bats can spread Marburg virus to other animals (e.g., monkeys) directly or indirectly, such as through food products contaminated by fruit bats (e.g., figs, mangoes, and dates). Marburg virus infection can occur in humans after prolonged exposure to environments inhabited by African fruit bats, such as mines or caves; close contact with an infected animal; contact with an infected animal's body fluids, such as saliva, feces, and urine; and through contaminated food products.

Person-to-person spread of Marburg virus is most common within families, amongst caregivers of Marburg-infected individuals, and in healthcare settings. Infected humans can spread Marburg virus to other humans through exchange of blood or body fluids (e.g., respiratory droplets, urine, sweat, saliva, semen, feces, vomit, and breast milk) through broken skin or mucous membranes. Marburg virus can also persist in the eyes and testes of individuals who have recovered from MVD. However, there is no evidence that Marburg virus can spread through contact with vaginal fluids in those assigned female at birth who have recovered from MVD. In pregnant individuals, Marburg virus can persist in the placenta, amniotic fluid, and breast milk.

Marburg virus may also spread between humans through objects contaminated with body fluids, such as clothing, bedding, and utensils. Health workers may become infected with Marburg virus through contaminated medical equipment. Burial ceremonies involving direct contact with a

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deceased body infected with Marburg virus may also contribute to transmission of the virus as individuals remain infectious as long as their blood contains the virus. Individuals at risk of Marburg virus infection include those that have had close contact with *Rousettus aegyptiacus* African fruit bats or their secretions, such as travelers visiting caves or mines inhabited by infected bats in endemic regions of Africa. Individuals already suffering from MVD or non-human primates infected with Marburg virus may also put individuals at risk of Marburg virus infection. Individuals at highest risk of Marburg virus infection include family members and/or hospital staff members that experience prolonged exposure to individuals infected with Marburg virus, particularly if appropriate infection prevention and control measures are not followed. Additional individuals at risk include those practicing in certain occupations where exposure to Marburg virus is a possibility, such as veterinarians or laboratory workers that handle non-human primates from Africa.

At present, there is no vaccine to offer protection against Marburg virus or limit spread from individuals with MVD. Prevention strategies against the spread of MVD focus on risk reduction and contact tracing. Risk reduction methods include reducing the risk of bat-to-human transmission of Marburg virus by wearing personal protective equipment (PPE), such as masks, gloves, and eye protection and ensuring frequent hand hygiene when exposed to caves inhabited by fruit bat colonies. Reduction of human-to-human transmission of Marburg virus involves avoiding close physical contact with individuals with suspected or confirmed MVD and wearing PPE as well as ensuring frequent hand hygiene if close contact is required. Human-to-human transmission of MVD may also be reduced by following safe sex practices with male survivors of MVD for at least 12 months from the onset of symptoms or until their semen tests negative twice for Marburg virus. Contact tracing measures include identifying individuals who may have been in contact with someone infected with Marburg virus and monitoring for any signs and symptoms of MVD for 21 days after exposure.

The Marburg virus replicates after entering infected host cells through attachment, endocytosis, and fusion. Once the viral RNA genome of the Marburg virus is inside the infected host cell, it undergoes transcription and replication, after which it is released into the bloodstream where the virus continues to multiply.

Signs and symptoms of Marburg virus infection typically appear 2-21 days after exposure to the virus. Fruit bats infected with Marburg virus do not show obvious signs of illness; however, human and non-human primates infected with Marburg virus may develop serious signs and symptoms.

Early signs and symptoms of MVD are commonly characterized by the sudden onset of fever, chills, headache, sore throat, weakness, and muscle aches. Bloody or nonbloody diarrhea, abdominal pain, nausea, and vomiting may begin three days after the onset of illness. A maculopapular, or raised, rash most commonly on the chest, back, and/or stomach may appear five days after the onset of signs and symptoms. Many individuals may develop severe hemorrhagic signs and symptoms 5-7 days after the onset of illness, such as bruising and bleeding from the eyes, ears, nose, mouth, and/or rectum.

Over time, signs and symptoms may become increasingly severe and may involve chest pain, severe weight loss, confusion, seizures, sustained high fevers, inflammation of one or both testicles (in those assigned male at birth), shock, and multiple organ failure. In fatal cases, death may occur 8-9 days after the onset of symptoms, typically due to severe blood loss and shock.

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Individuals who survive MVD typically undergo a slow recovery as the Marburg virus usually remains in the body for several weeks. Individuals may experience long-term signs and symptoms, such as hair loss, liver inflammation, weakness, fatigue, headaches, and eye and testicular inflammation.

Infection with the Marburg virus is typically diagnosed by a medical professional upon a thorough review of systems and medical history and conduction of a physical examination. Early detection and diagnosis of MVD can be challenging as the early signs and symptoms of MVD are non-specific and difficult to distinguish from other infectious diseases, such as malaria, typhoid fever, shigellosis, meningitis, and other viral hemorrhagic fevers, (e.g., Lassa fever or Ebola). The consequent delay in diagnosis can therefore hinder survival chances and create challenges in controlling transmission and outbreak. Marburg virus is commonly suspected in those who have been exposed to geographic areas where Marburg virus is common, particularly in individuals with a known exposure.

During the early stages of MVD, detection of the virus can be made through throat and nasal swabs, cerebrospinal fluid samples, urine samples, and/or blood samples. Samples collected from individuals with MVD are a biological hazard and should be handled and tested under maximum biological containment conditions.

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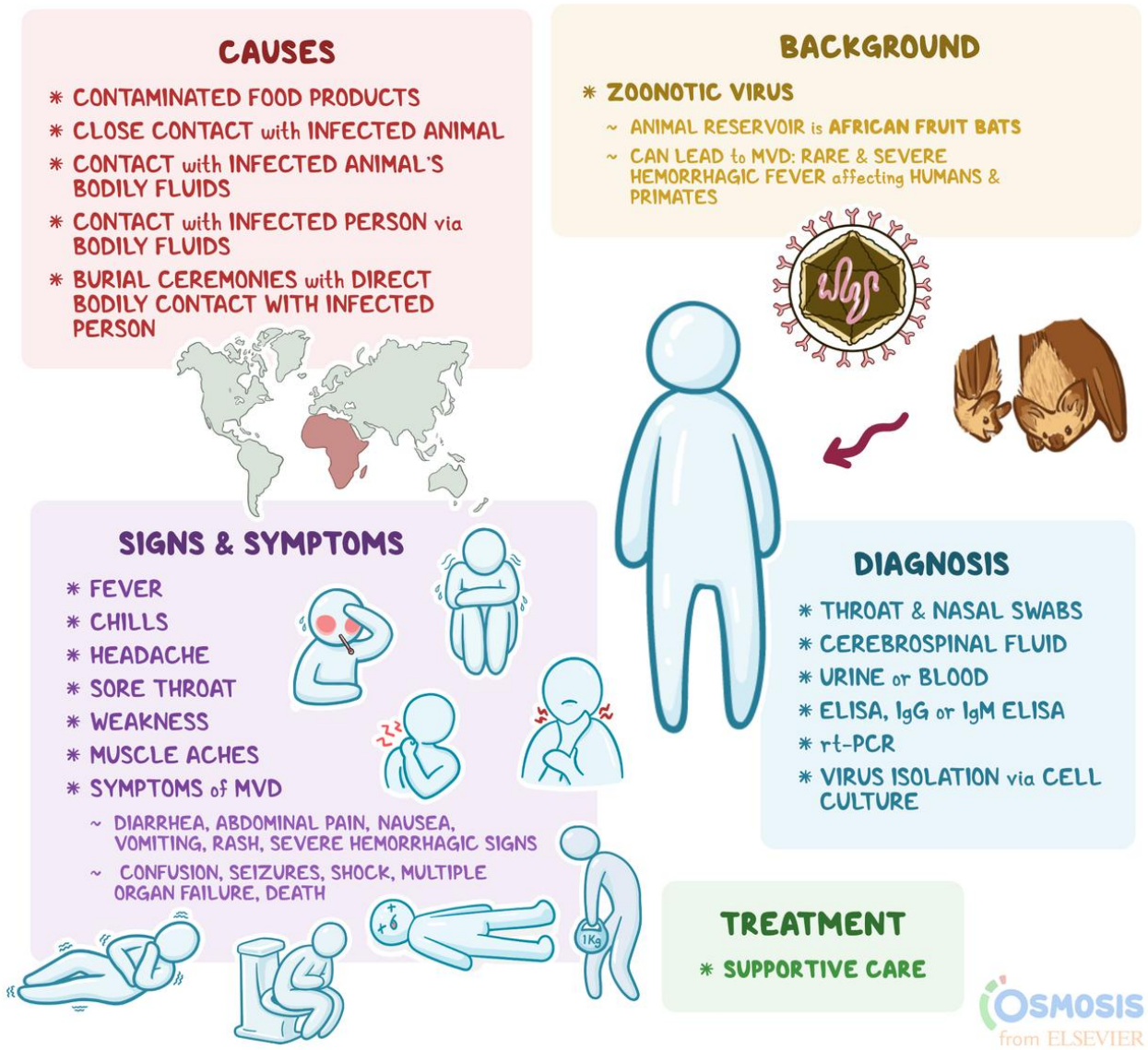

These samples can be analyzed through enzyme-linked immunosorbent assay (i.e., ELISA) testing, reverse transcriptase polymerase chain reaction (RT-PCR), and IgM-capture ELISA to detect antibodies, antigens, and proteins specific to Marburg virus. Virus isolation by cell culture may also be performed in high containment laboratories. IgG-capture ELISA may be done in the later stages of MVD or after recovery to confirm infection. In deceased patients, immunohistochemistry, virus isolation, or PCR of blood and/or tissue specimens may be performed to diagnose prior MVD. The quality, quantity, type, timing of sample collection, and the time needed to transfer samples to the laboratory may all affect the accuracy of laboratory results.

Treatment of Marburg virus infection is limited to supportive care, typically after hospitalization, which includes rest, hydration, oxygen, and treatment of specific symptoms upon onset. Supportive medications include acetaminophen to relieve pain and fevers and dimenhydrinate and/or ondansetron to control nausea and vomiting. Intravenous and/or oral

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fluids may be provided to replace lost fluids, stabilize electrolytes, and maintain blood pressure. Blood transfusions may also be provided to replace lost blood and clotting factors. If other complicated infections develop, appropriate antiviral and/or antibiotic therapies may be indicated.

While there are not currently any approved drug treatments for Marburg virus infection, immunotherapeutic treatments known as monoclonal antibody therapies are currently under development and evaluation for treatment of MVD. Antiviral therapies, such as remdesivier and favipiravir, have been used in clinical studies for Ebola that may also be tested for use in MVD.

Marburg virus is a zoonotic virus that is initially transmitted from animals to humans. The animal reservoir in nature for the Marburg virus are the African fruit bats. Marburg virus replicates after entering infected host cells through attachment, endocytosis, and fusion. Marburg can lead to MVD, which is a rare and severe hemorrhagic fever affecting both humans and non-human primates. Marburg virus infection can occur in humans after close contact with an infected animal or its body fluids and through contaminated food products. Infected humans can then spread Marburg virus to other humans through exchange of blood or body fluids through broken skin or mucous membranes and objects contaminated with body fluids. Early signs and symptoms of MVD typically consist of fever, chills, headache, sore throat, weakness, and muscle aches. As MVD progresses, diarrhea, abdominal pain, nausea, vomiting, rash, and severe hemorrhagic signs and symptoms may also occur. In severe cases, confusion, seizures, shock, multiple organ failure, and death may follow. MVD may be diagnosed using throat and nasal swabs, cerebrospinal fluid samples, urine samples, and/or blood samples. ELISA testing, RT-PCR, IgM and/or IgG capture ELISA, and virus isolation by cell culture may also be used in diagnostic measures. Treatment of Marburg virus is limited to supportive care during hospitalization, which includes rest, hydration, and treatment of specific symptoms as they occur.

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