



## MARBURG VIRUS DISEASE

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**Abstract:** Marburg virus disease is a highly virulent disease that causes haemorrhagic fever, with a fatality ratio of up to 88%. Marburg virus disease is a severe illness of humans and non-human primates caused by either of the two marburgviruses, Marburg virus (MARV) and Ravn virus (RAVV) MVD is a viral hemorrhagic fever (VHF). There are currently no Food and Drug Administration-approved vaccines for the prevention of MVD.

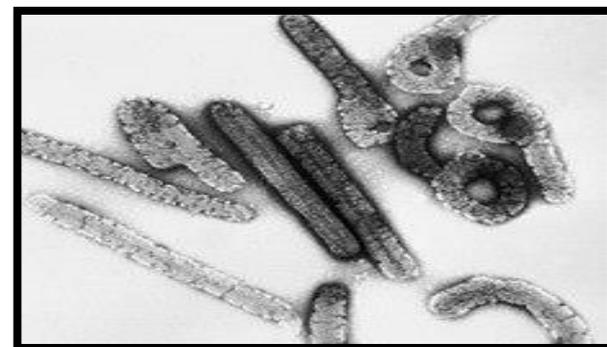
**Index Terms** - Marburg Virus, Haemorrhagic Fever, Fatality, Secretions, Incubation

### Introduction:

Marburg virus disease is a highly virulent disease that causes haemorrhagic fever, with a fatality ratio of up to 88%. It is in the same family as the virus that causes Ebola virus disease. Human infection with Marburg virus disease initially results from prolonged exposure to mines or caves inhabited by Rousettus bat colonies. Once an individual is infected with the virus, Marburg can spread 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.

### Incidence:

Two large outbreaks that occurred simultaneously in Marburg and Frankfurt in Germany, and in Belgrade, Serbia, in 1967, led to the initial recognition of the disease. The outbreak was associated with laboratory work using African green monkeys (*Cercopithecus aethiops*) imported from Uganda. Subsequently, outbreaks and sporadic cases have been reported in Angola, Democratic Republic of the Congo, Kenya, South Africa (in a person with recent travel history to Zimbabwe) and Uganda. In 2008, two independent cases were reported in travellers who visited a cave inhabited by Rousettus bat colonies in Uganda.



## Causative agent:

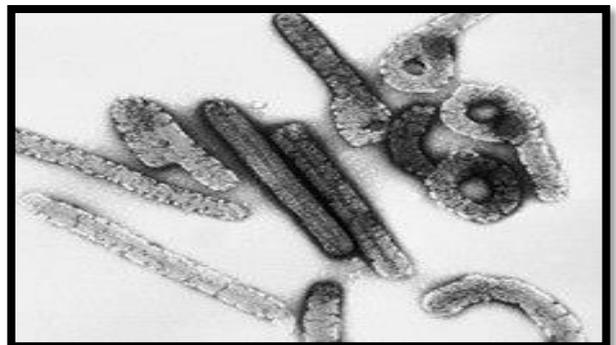
**Marburg virus disease (MVD; formerly Marburg hemorrhagic fever)** is a severe illness of humans and non-human primates caused by either of the two marburgviruses, Marburg virus (MARV) and Ravn virus (RAVV) MVD is a viral hemorrhagic fever (VHF).

## Signs and symptoms

Illness caused by Marburg virus begins abruptly, with high fever, severe headache and severe malaise. Muscle aches and pains are a common feature. Severe watery diarrhoea, abdominal pain and cramping, nausea and vomiting can begin on the third day. Diarrhoea can persist for a week. The appearance of patients at this phase has been described as showing “ghost-like” drawn features, deep-set eyes, expressionless faces and extreme lethargy. A non-itchy rash has been noted between 2 and 7 days after the onset of symptoms. Many patients develop severe haemorrhagic manifestations within 7 days, and fatal cases usually have bleeding, often from multiple areas. Fresh blood in vomitus and faeces is often accompanied by bleeding from the nose, gums and vagina. Spontaneous bleeding at venepuncture sites (where intravenous access is obtained to give fluids or obtain blood samples) can be particularly troublesome. During the severe phase of illness, patients have sustained high fevers. Involvement of the central nervous system can result in confusion, irritability and aggression. Orchitis (inflammation of the testicles) has been reported occasionally in the late phase (15 days). In fatal cases, death usually occurs between 8 and 9 days after onset, usually preceded by severe blood loss and shock.

## Clinical phases of Marburg Hemorrhagic Fever:

1. **Incubation:** 2–21 days, averaging 5–9 days.
2. **Generalization Phase:** Day 1 up to Day 5 from onset of clinical symptoms. MHF presents with a high fever 104 °F (~40°C) and a sudden, severe headache, with accompanying chills, fatigue, nausea, vomiting, diarrhea, pharyngitis, maculopapular rash, abdominal pain, conjunctivitis, & malaise.
3. **Early Organ Phase:** Day 5 up to Day 13. Symptoms include prostration, dyspnea, edema, conjunctival injection, viral exanthema, and CNS symptoms, including encephalitis, confusion, delirium, apathy, and aggression. Hemorrhagic symptoms typically occur late and herald the end of the early organ phase, leading either to eventual recovery or worsening & death. Symptoms include bloody stools, ecchymoses, blood leakage from venipuncture sites, mucosal & visceral hemorrhaging, and possibly hematemesis.
4. **Late Organ Phase:** Day 13 up to Day 21+. Symptoms bifurcate into two constellations for survivors & fatal cases. Survivors will enter a **convalescence phase**, experiencing myalgia, fibromyalgia, hepatitis, asthenia, ocular symptoms, & psychosis. Fatal cases continue to deteriorate, experiencing continued fever, obtundation, coma, convulsions, diffuse coagulopathy, metabolic disturbances, shock and death, with death typically occurring between Days 8 and 16.



## Diagnosis:

It can be difficult to clinically distinguish Marburg virus disease (MVD) from other infectious diseases such as malaria, typhoid fever, shigellosis, meningitis and other viral haemorrhagic fevers. Confirmation that symptoms are caused by Marburg virus infection are made using the following diagnostic methods:

- Antibody enzyme-linked immunosorbent assay (ELISA);
- Antigen detection tests;
- Serum neutralization tests;
- Reverse-transcriptase polymerase chain reaction (RT-PCR) assay; and
- Virus isolation by cell culture.

Samples collected from patients are an extreme biohazard risk and laboratory testing on non-inactivated samples need to be conducted under maximum biological containment conditions. All biological specimens must be packaged using the triple packaging system when transported nationally and internationally.

## Prevention

There are currently no Food and Drug Administration-approved vaccines for the prevention of MVD. Many candidate vaccines have been developed and tested in various animal models. Of those, the most promising ones are DNA vaccines<sup>1</sup> or based on Venezuelan equine encephalitis virus replicons, vesicular stomatitis Indiana virus (VSIV) or filovirus-like particles (VLPs) as all of these candidates could protect nonhuman primates from marburgvirus-induced disease. DNA vaccines have entered clinical trials. Marburgviruses are highly infectious, but not very contagious. Importantly, and contrary to popular belief, marburgviruses do not get transmitted by aerosol during natural MVD outbreaks. Due to the absence of an approved vaccine, prevention of MVD therefore relies predominantly on behavior modification, proper personal protective equipment, and sterilization/disinfection.

### • Endemic zones

The natural maintenance hosts of marburg viruses remain to be identified unequivocally. However, the isolation of both MARV and RAVV from bats and the association of several MVD outbreaks with bat-infested mines or caves strongly suggests that bats are involved in marburg virus transmission to humans. Avoidance of contact with bats and abstaining from visits to caves is highly recommended, but may not be possible for those working in mines or people dependent on bats as a food source.

### • During outbreaks

Since marburgviruses are not spreading via aerosol, the most straightforward prevention method during MVD outbreaks is to avoid direct (skin-to-skin) contact with patients, their excretions and body fluids, or possibly contaminated materials and utensils. Patients ought to be isolated but still have the right to be visited by family members. Medical staff should be trained and apply strict barrier nursing techniques (disposable face mask, gloves, goggles, and a gown at all times). Traditional burial rituals, especially those requiring embalming of bodies, ought to be discouraged or modified, ideally with the help of local traditional healers.

- **In the laboratory**

Marburgviruses are World Health Organization Risk Group 4 Pathogens, requiring Biosafety Level 4-equivalent containment,<sup>[53]</sup> laboratory researchers have to be properly trained in BSL-4 practices and wear proper personal protective equipment.

## Treatment

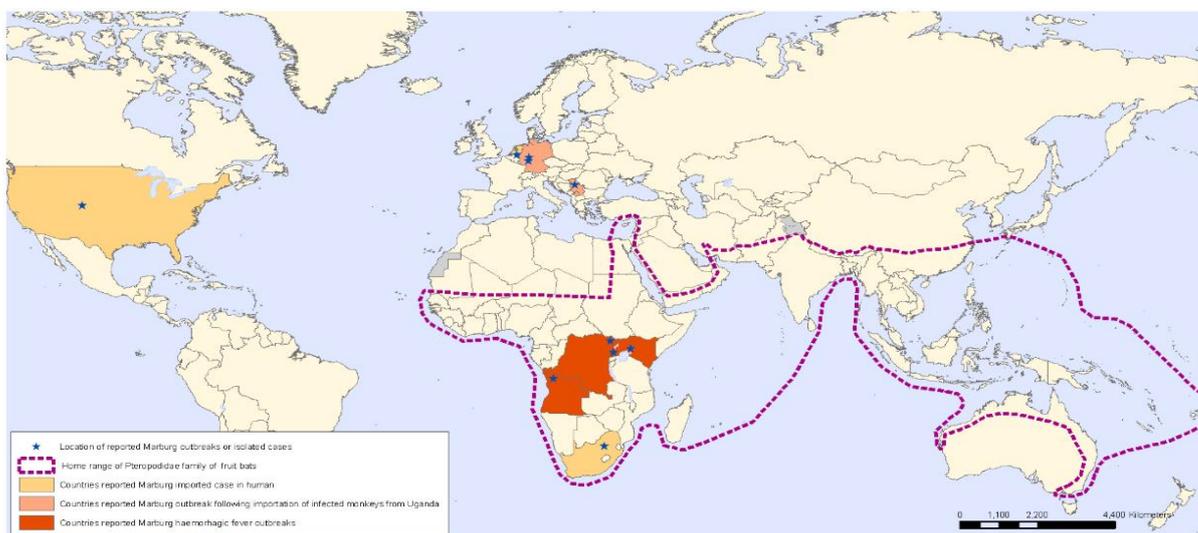
There is as yet no proven treatment available for Marburg virus disease. However, a range of potential treatments including blood products, immune therapies and drug therapies are currently being evaluated. Supportive care – rehydration with oral or intravenous fluids – and treatment of specific symptoms improves survival.

There is currently no effective marburgvirus-specific therapy for MVD. Treatment is primarily supportive in nature and includes minimizing invasive procedures, balancing fluids and electrolytes to counter dehydration, administration of anticoagulants early in infection to prevent or control disseminated intravascular coagulation, administration of procoagulants late in infection to control hemorrhaging, maintaining oxygen levels, pain management, and administration of antibiotics or antimycotics to treat secondary infections. Experimentally, recombinant vesicular stomatitis Indiana virus (VSIV) expressing the glycoprotein of MARV has been used successfully in nonhuman primate models as post-exposure prophylaxis. Experimental therapeutic regimens relying on antisense technology have shown promise, with phosphorodiamidate morpholino oligomers (PMOs) targeting the MARV genome. New therapies from Sarepta and Tekmira have also been successfully used in humans as well as primates.

## Prognosis

Prognosis is generally poor. If a patient survives, recovery may be prompt and complete, or protracted with sequelae, such as orchitis, hepatitis, uveitis, parotitis, desquamation or alopecia. Importantly, MARV is known to be able to persist in some survivors and to either reactivate and cause a secondary bout of MVD or to be transmitted via sperm, causing secondary cases of infection and disease.

## Epidemiology



## Geographic distribution of Marburgh haemorrhagic fever outbreaks

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