

28 | MARBURG VIRUS

28.1 | Disease agent

- Marburg virus (MARV)

28.2 | Disease agent characteristics

- Family: *Filoviridae*; Genus: *Marburgvirus*, Species: *Marburg marburgvirus*.
- Virion morphology and size: Enveloped, helical, cross-striated nucleocapsid symmetry, with filamentous or pleomorphic virions that are flexible with extensive branching, 80 nm in diameter and up to 14,000 nm in length (peak infectivity measured to be 790–860 nm).
- Nucleic acid: Linear, negative-sense, single-stranded RNA, ~19.1 kb in length.
- Physicochemical properties: Stable at room temperature and can resist desiccation; inactivated at 60°C for 30 min; infectivity greatly reduced or destroyed by UV light and gamma irradiation, lipid solvents, β -propiolactone, formaldehyde, sodium hypochlorite, and phenolic disinfectants.

28.3 | Disease names

- Marburg hemorrhagic fever (MHF)
- Marburg virus disease
- Durba syndrome

28.4 | Priority level

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical; in symptomatic cases, viremia is a feature of infectivity. Asymptomatic viremia has been neither well studied nor sought aggressively, so there are few or no data to make a critical assessment of risk.
- Public perception and/or regulatory concern regarding blood safety: Very low/Absent
- Public concern regarding disease agent: Low; Moderate in West Africa

28.5 | Background

- First identified in 1967 in Marburg and Frankfurt (Germany) and later in Belgrade (former Yugoslavia), when African green monkeys (*Cercopithecus aethiops*) were brought from Uganda for use in vaccine

production and biomedical research resulting in transmission from monkeys to 31 humans with seven deaths (23%).

- 1975–1982: Six cases in Zimbabwe, South Africa, and Kenya in travelers and health-care workers
- 1998–2000: Large outbreak in Africa (Democratic Republic of Congo, in the Watsa/Durba region), linked to gold mining activity, with 154 cases and 128 deaths (83%)
- October 2004–November 2005 (last outbreak): Angola (Northern province of Uige) with more than 370 cases and 320 deaths (86%)
- 2007–2017: several small outbreaks in Uganda resulted in two infections exported to the United States and the Netherlands.
- Since 2021, at least two deadly outbreaks of MARV have occurred in Guinea and Ghana to the time of these revisions (2023).
- Classified among the highest priority for bioterrorism agents by the CDC (Category A)

28.6 | Common human exposure routes

- Original cases resulted from close contact with monkey blood or cell cultures.
- Body fluids from humans, including those from skin or mucous membranes, are infectious. Risk exists from parenteral inoculation with contaminated needles and syringes.
- Sexual transmission is theoretically possible but unconfirmed. Nucleic acid has been detected in semen for many weeks after clinical recovery.
- MARV is present in infected human alveoli and in aerosol particles. This could lead to human transmission by the aerosol route but is considered to be inefficient.
- Infectivity seems to be higher during the patient's hemorrhagic phase.

28.7 | Likelihood of secondary transmission

- In the original outbreak, 6 of 31 infections observed among healthcare workers represented secondary transmission. They were associated with blood and body fluid (possibly vomit, urine, and stools). In one study, the secondary attack rate was estimated as 23% for family members sleeping in the same room with the patient versus 81% for those providing direct care.
- MARV remains viable for 4–5 days in dried blood.

28.8 | At-risk populations

- Humans in direct contact with MARV-infected sick persons or cadavers, dead primates (e.g., necropsies), infected tissues and organs, or cell cultures.
- A threat as a bioterrorist weapon for populations not previously considered being at risk.

28.9 | Vector and reservoir involved

- Suspected to be a zoonosis with incidental transmission to humans. Given the high and rapid death rate that occurs in nonhuman primates following infection, consideration of this population as a viable reservoir for the disease seems implausible.
- Other reservoirs are still unknown; cave-dwelling fruit bats are considered possible.

28.10 | Blood phase

- Virus has been demonstrated by antigen detection, culture, and NAT in blood from patients in the 2004–2005 Angolan outbreak.
- MARV was cultured from the anterior chamber of the eye aspirated 80 days after onset of illness and up to 3 months from the semen of recovered patients.
- Virus does not undergo significant early replication in the blood and, instead, replicates in organs such as the liver and spleen. The virus begins to accumulate in the blood only after significant replication has already occurred in those organs, making viremia an indicator of infection only after initial stages have become established.

28.11 | Survival/persistence in blood products

- Unknown

28.12 | Transmission by blood transfusion

- Never documented.
- Transmission has occurred following contact with the blood and body fluids of clinical cases.

28.13 | Cases/frequency in population

- All age groups are susceptible, although pediatric cases are uncommon under the age of 5.

- Several IFA seroprevalence studies in individuals (not blood donors) from drier areas of tropical Africa, particularly Uganda, Zimbabwe, Democratic Republic of the Congo, and Angola, revealed prevalence rates ranging from 0 to 3.2%.
- Seroprevalence study of 809 blood donors in the Republic of the Congo in 2011 found 0.5% (4 in 809) were IgG antibody positive for MARV without any identified risk factors.

28.14 | Incubation period

- 4–10 days (range: 2–21 days); transmission by non-percutaneous routes does not appear to occur during the incubation period.

28.15 | Likelihood of clinical disease

- High.
- In one study, no serologic evidence for asymptomatic or mild infection was found.

28.16 | Primary disease symptoms

- Nonspecific, with abrupt fever, myalgia, headache, nausea, vomiting, abdominal pain, diarrhea, chest pain, cough, pharyngitis, conjunctival injection, jaundice, lymphadenopathy, and pancreatitis.
- CNS involvement occurs in a subsequent phase (somnolence, delirium, coma) followed by wasting and bleeding manifestations (petechiae, mucous membrane hemorrhages, ecchymoses, particularly around punctures) in 50% of cases.
- After 14 days, the patient either markedly improves or dies with multiorgan dysfunction and disseminated intravascular coagulation.

28.17 | Severity of clinical disease

- High

28.18 | Mortality

- Mortality is ~25% (Marburg outbreak, 1967) to higher than 80% (Democratic Republic of the Congo and Angola outbreaks in 1998 and 2004–2005, respectively).

28.19 | Chronic carriage

- Not recognized

28.20 | Treatment available/efficacious

- No specific therapy is available; treatment should be supportive (intravenous fluid replacement, analgesics, and standard nursing care).

28.21 | Agent-specific screening question(s)

- No specific question is in use; however, current geographic deferrals for malaria would exclude at-risk populations from endemic sub-Saharan Africa if an asymptomatic viremic interval exists.
- Not indicated because transfusion transmission has not been demonstrated
- No sensitive or specific question is feasible.
- Under circumstances of a bioterrorism threat, the need for and potential effectiveness of specific donor screening questions would need to be addressed.

28.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening tests exist.
- In the United States, assays are available only at CDC or the US Army Research Institute of Infectious Diseases (USAMRIID). Confirmatory tests need to be performed.
- *Marburg marburgvirus* is included on the FDA-approved diagnostic BioFire PCR Defense Warrior Panel. This FilmArray panel is manufactured solely for the use by the US Department of Defense (DoD) laboratories and laboratories designated by the DoD.
- EIA, IFA, western blot, real-time RT-PCR, and Vero cell cultures; molecular methods, though available in several labs, still require interlaboratory validation.
- In outbreaks, the diagnosis is often made with immunoperoxidase staining of formalin-fixed biopsies from sick or deceased persons. Coinfection with malaria is common, so this should be ruled out by proper laboratory tests.

28.23 | Currently recommended donor deferral period

- No FDA Guidance or AABB Standard exists for patients previously diagnosed with MHF or persons who have had contact with the blood of infected non-human primates or patients.
- There are insufficient data to make recommendations regarding an indefinite or other deferral period.
- The deferral interval due to geographic risk for malaria is expected to be longer than what might be recommended for donors from Marburg endemic areas during outbreaks or who have recovered from their disease.

28.24 | Impact on blood availability

- Agent-specific screening question(s): Not applicable; in response to a bioterrorism threat, impact of a local deferral could be significant.
- Laboratory test(s) available: Not applicable

28.25 | Impact on blood safety

- Agent-specific screening question(s): Not applicable; unknown impact in response to a bioterrorism threat
- Laboratory test(s) available: Not applicable

28.26 | Leukoreduction efficacy

- Leukoreduction might reduce virus levels because monocytes appear to support replication. However, it also is likely that the virus is circulating free in plasma, and leukoreduction cannot be relied upon.

28.27 | Pathogen reduction efficacy for plasma derivatives

- Multiple pathogen reduction steps used in the fractionation process have been shown to be robust in removal of enveloped viruses.

28.28 | Other prevention measures

- None

28.29 | Other comments

- There is no evidence that convalescent plasma, purified IgG, or human monoclonal antibodies might be useful, based on studies with Ebola.
- No serological cross-reactivity is observed with Ebola virus, the other important pathogenic filovirus.
- Category A bioterrorism agent that requires Biosafety Level 4 (BSL-4) containment

SUGGESTED READING

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