

Marburg Virus

Disease Agent:

- Marburg virus (MARV)

Disease Agent Characteristics:

- Family: *Filoviridae*; Genus: *Marburgvirus*, Species: *Lake Victoria 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 790-860 nm in length
- 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 minutes; infectivity greatly reduced or destroyed by UV light and gamma irradiation, lipid solvents, β-propiolactone, formaldehyde, sodium hypochlorite, and phenolic disinfectants

Disease Names:

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

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical; viremia is a feature of symptomatic infection with this agent. 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

Background:

- 1967: Initially described in Marburg (Germany) and 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
- 1975-1982: six cases in Zimbabwe, South Africa, and Kenya in travelers and health-care workers
- 1998: 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%)

- Classified among the highest priority for bioterrorism agents by the CDC (Category A)

Common Human Exposure Routes:

- Original cases resulted from extremely close contact with monkey blood or cell cultures.
- Body fluids, 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.

Likelihood of Secondary Transmission:

- In the original outbreak, 6 of 31 infections observed among health-care workers represented secondary transmission. They were associated with blood and body fluid (possibly vomit, urine, and stools) exposures. 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.

At-Risk Populations:

- Humans in contact with Marburg infected sick persons, dead primates, infected tissues, or cell cultures.
- A threat as a bioterrorist weapon for populations not previously considered being at risk

Vector and Reservoir Involved:

- Suspected to be a zoonosis with incidental transmission to humans. Given the high and rapid death rate that occurs in primates following infection, consideration of this population as a viable reservoir for the disease seems implausible.
- Reservoir is still unknown; bats are considered a leading contender.

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.

Survival/Persistence in Blood Products:

- Unknown

Transmission by Blood Transfusion:

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

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 Congo, and Angola, revealed prevalence rates ranging from 0 to 3.2%.

Incubation Period:

- 3-9 days (range: 2-19 days); transmission by nonpercutaneous routes does not appear to occur during the incubation period.

Likelihood of Clinical Disease:

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

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 (somnia, 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 because of multiorgan dysfunction and disseminated intravascular coagulation.

Severity of Clinical Disease:

- High

Mortality:

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

Chronic Carriage:

- No

Treatment Available/Efficacious:

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

Agent-Specific Screening Question(s):

- No specific question is in use; however, current geographic deferrals for malaria and group O HIV 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.

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening tests exist.
- In the US, assays are available only at CDC or the US Army Research Institute of Infectious Diseases (USAMRIID). Confirmatory tests need to be performed.
- EIA (IgG using recombinant nucleoprotein antigens), 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.

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 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 and group O HIV is expected to be longer than what might be recommended for donors from Marburg endemic areas who have clinically recovered from their disease.

Impact on Blood Availability:

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

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

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 could not be relied upon.
- Animal studies suggest that lymphocytes are nonpermissive to infection, unlike monocytes.

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.

Other Prevention Measures:

- None

Other Comments:

- There is no evidence that convalescent plasma, purified IgG, or human monoclonal antibodies might be useful, based on studies with Ebola.
- All six Marburg virus strains (Musoke, Ratayczak, Popp, Voegelé, Ozolin, and Marburg Ravn) are considered to be pathogenic.
- 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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