EBOLA-MARBURG VIRAL DISEASES

(African hemorrhagic fever, Ebola virus hemorrhagic fever, Marburg virus hemorrhagic fever)

DISEASE	ICD-10 CODE
EBOLA HEMORRHAGIC FEVER	ICD-10 A98.4
MARBURG HEMORRHAGIC FEVER	ICD-10 A98.3

1. Clinical features—Severe acute viral illnesses, usually with sudden onset of fever, malaise, myalgia, and headache, followed in most cases by pharyngitis, vomiting, diarrhea, and maculopapular rash. In severe and fatal forms, a hemorrhagic diathesis is often accompanied by hepatic damage, renal failure, central nervous system (CNS) involvement, and terminal shock with multiorgan dysfunction. Laboratory findings usually show lymphopenia, severe thrombocytopenia, and transaminase elevation (AST >ALT), sometimes with hyperamylasemia, elevated creatinine, and blood urea nitrogen levels during the final renal failure phase. Case-fatality rates for Ebola infections in well-studied outbreaks in Africa have ranged from 32% to nearly 88%. In Marburg outbreaks, case-fatality rates have ranged from 22%–90%.

2. Causative agents—Ebola and Marburg viruses are negative stranded RNA viruses in the family *Filoviridae*. Pleomorphic virions with branched, circular, or coiled shapes are frequent on electron microscopy preparation and may reach micrometers in length. Five Ebola virus species have been identified, and viruses in four of these (*Zaire ebolavirus*, *Sudan ebolavirus*, *Taï Forest ebolavirus*, and *Bundibugyo ebolavirus*) have been shown to cause disease in humans. The fifth Ebola species, *Reston ebolavirus*, which originated in the Philippines, causes fatal hemorrhagic disease in nonhuman primates. A single Marburg virus species, *Marburg marburgvirus*, has been identified.

3. Diagnosis—Ebola or Marburg infection can be confirmed by direct detection of virus in blood or tissue samples by virus isolation, conventional or real-time PCR, antigen-detection ELISA, immunohistochemistry on formalin-fixed tissues, or detection of virus-specific IgM antibodies or rising IgG antibody titers. For a proper diagnosis, a combination of laboratory techniques, clinical evaluation and epidemiological investigation is always recommended.

4. Occurrence—Ebola disease was first recognized in 1976. The largest outbreak to date—in Guinea, Liberia, and Sierra Leone—was

ongoing at the time of writing. Significant outbreaks and sporadic or small clusters of cases since 1976 include:

Year	Location	Cases
1976	Democratic Republic of Congo	318 cases, 280 deaths
1976	Sudan	284 cases, 151 deaths
1977	Democratic Republic of Congo	1 fatal case
1979	Sudan	34 cases, 22 deaths
1994	Ivory Coast	1 mild case
1994–1996	Gabon, Republic of South Africa	3 outbreaks (149 cases, 97 deaths); a fatal secondary infection occurred in a nurse in South Africa.
1995	Democratic Republic of Congo	315 cases, 250 deaths
2000–2001	Uganda	425 cases, 224 deaths
2001–2003	Gabon, Republic of Congo	Several outbreaks (300 cases, 254 deaths); high numbers of deaths were simultaneously reported among wild animals in the region, particularly nonhuman primates.
2004	Sudan	17 cases, 7 deaths
2007	Democratic Republic of Congo	264 cases, 187 deaths
2007–2008	Uganda	131 cases, 42 deaths
2008–2009	Democratic Republic of Congo	32 cases, 15 deaths
2011	Uganda	1 fatal case
2012	Uganda	2 outbreaks, 31 cases, 21 deaths
2012	Democratic Republic of Congo	53 cases, 36 deaths
2014	Guinea, Liberia, Sierra Leone	964 cases, 603 deaths (as of 7/12/14)

Antibodies have been found in residents of other areas of sub-Saharan Africa; their relation to the Ebola virus species is unknown. Laboratory infections have been reported in the United Kingdom and Russia.

Reston virus has been isolated from cynomolgus monkeys (*Macaca fascicularis*) imported to the USA in 1989, 1990, and 1996, and to Italy in 1992, all from the same export facility in the Philippines; many of these monkeys died. In the USA in 1989, four animal handlers with daily exposure to these monkeys developed specific antibodies but were asymptomatic. In

2008, Reston virus was isolated from domestic swine experiencing severe disease in the Philippines. Porcine reproductive and respiratory disease syndrome was also present in this pig population. Several animal handlers were asymptomatically infected and developed Ebola antibodies.

Marburg disease was first recognized in laboratory outbreaks in which workers had been exposed to African green monkeys *Chlorocebus tantalus* (formerly *Cercopithecus aethiops*) imported from Uganda, and in outbreaks since then in sub-Saharan Africa:

Year	Location	Cases
1967	Germany, Yugoslavia	31 cases, 7 deaths
1975	South Africa	3 cases, 1 death
1980	Kenya	2 cases, 1 death
1987	Kenya	1 fatal case
1998–2000	Democratic Republic of Congo	≥154 cases, 128 deaths
2005	Angola	252 cases, 227 deaths
2007	Uganda	4 cases, 2 deaths
2008	Netherlands, USA	2 cases among tourists from Netherlands (fatal) and USA after a trip in Uganda
2012	Uganda	23 cases, 15 deaths

5. Reservoir—Forest-dwelling fruit bats are believed to be the reservoir of Ebola viruses, and viral RNA has been detected in 3 bat species in central Africa (*Hypsignathus monstrosus*, *Epomops franqueti*, and *Myonycteris torquata*). Cave-dwelling fruit bats are believed to be the reservoir of Marburg virus, and numerous virus isolates have been acquired from a particular species, *Rousettus aegyptiacus*. Ebola and Marburg viruses have been identified in multiple species of nonhuman primates in which highly lethal outbreaks have occurred, although these are likely incidental hosts and not reservoirs of these viruses. Swine, responsible for the Reston virus epidemic in 2008 in the Philippines, are considered intermediary hosts.

6. Incubation period—Probably 5–15 days for both Ebola and Marburg disease.

7. Transmission—Ebola infection of index cases seems to occur as follows:

- In central Africa, while manipulating infected wild mammals found dead in the rainforest.

- For Reston virus, while handling infected cynomolgus monkeys (through direct contact with their infected blood or fresh organs) or while handling infected pigs (through direct contact with secretions and fresh organs).

Marburg infection of index cases seems to occur when people are in close contact with bats, or spending time in bat-inhabited confined areas, such as caves or mines.

Person-to-person transmission of Ebola and Marburg diseases occurs through direct contact with infected blood, urine, vomiting, diarrhea, secretions, organs, or semen. Risk is highest during the late stages of illness, when the patient is vomiting, having diarrhea, or hemorrhaging, and during funerals with unprotected body preparation. Under natural conditions, airborne transmission among humans has not been documented. Nosocomial infections have been frequent; virtually all patients who have acquired infection from contaminated syringes and needles died. Transmission through semen appears to be rare but has occurred up to 7 weeks after clinical recovery. Risk during the asymptomatic incubation period is negligible. The diseases are not communicable before the febrile phase, and communicability increases with stage of illness, as long as blood and secretions contain virus. For both viruses, the semen may remain infectious for several weeks or months (e.g., Ebola virus was isolated from the seminal fluid on the 61st but not on the 76th day after onset of illness in a laboratory-acquired case).

8. Risk groups—All ages are susceptible. The main human groups at risk are: patients who are injected with contaminated needles and syringes that are not properly sterilized; caregivers in affected communities (often women) and health-care workers handling infected patients, their secretions or excretions; laboratory workers processing clinical specimens or working in research laboratories; people working with wildlife, in particular nonhuman primates in central Africa or bats; people working in bat-inhabited locations, such as mines.

9. Prevention—No vaccines are currently approved for human use. For control measures as well as prevention of infection of patients and hospital and laboratory workers, see Management of Patient subsection in this chapter. In addition: protection of sexual intercourse for 3 months or until semen can be shown to be free of virus.

10. Management of patient—

1) Strict procedures for isolation of patients and their body fluids and excreta must be maintained. Institute immediate strict isolation in a private hospital room away from traffic patterns. Entry of nonessential staff and visitors should be restricted. All

persons entering the patient's room should wear gloves and gowns to prevent contact with contaminated items or environmental surfaces. Face shields or masks (N95 or N99) and eye protection should be worn to prevent contact with blood, other body fluids, secretions (including respiratory droplets), or excretions. The need for additional barriers depends on the potential for fluid contact, as determined by the procedure performed and the presence of clinical symptoms that increase the likelihood of contact with body fluids from the patient. Recourse to a negative pressure room and respiratory protection is desirable. To reduce infectious exposure, laboratory tests should be kept to the minimum necessary for proper diagnosis and patient care and only performed where full infection control measures are correctly implemented. Technicians must be alerted to the nature of the specimens and supervised to ensure application of appropriate specimen inactivation/isolation procedures. Dead bodies should be sealed in leak-proof material and cremated or buried promptly in a sealed casket, while respecting as much as possible religious or cultural burial practices to avoid unnecessary conflicts with affected families and local communities, which may otherwise compromise the outbreak response.

2) Patient's excreta, sputum, blood, and all objects with which the patient has had contact, including needles and syringes as well as laboratory equipment used to carry out tests on blood, must be disinfected with 0.5% sodium hypochlorite solution or 0.5% phenol with detergent, and, as far as possible, effective heating methods—such as autoclaving, incineration, boiling, or irradiation—should be used as appropriate. Laboratory testing must be carried out in special high-containment facilities; if there is no such facility, tests should be kept to a minimum and specimens handled by experienced technicians using all available personal protective equipment, such as gloves, gowns, masks, goggles, and biological safety cabinets. When appropriate, serum may be heat-inactivated at 60°C (140°F) for 1 hour. Thorough terminal disinfection with 0.5% sodium hypochlorite solution or a phenolic compound is adequate; formaldehyde fumigation can be considered.
3) No specific antiviral treatment is available as yet for either Ebola or Marburg disease.

11. Management of contacts and the immediate environment—Identify all close contacts (people living with, caring for, testing laboratory specimens from, or having noncasual contact with the patient) in the 3 weeks after the onset of illness. Establish, at home when practical, close

surveillance of contacts as follows: body temperature checks at least 2 times daily for at least 3 weeks after last exposure. In case of temperature above 38.3°C (101°F), hospitalize immediately in strict isolation facilities while initiating diagnostic testing. Determine patient's place of residence during the 3 weeks prior to onset; search for unreported or undiagnosed cases.

12. Special considerations—Reporting: In many countries, Ebola and Marburg virus infections are reportable as "viral hemorrhagic fever." Suspected cases should be reported to the national health authorities and to a WHO Collaborating Center (Hamburg, Salisbury, Atlanta, Winnipeg, Johannesburg) for diagnostic support. Occurrence of Ebola or Marburg infections likely constitutes an International Health Regulations notifiable event to the World Health Organization. Additionally, isolation of Ebola or Marburg viruses must be reported to the national biosecurity agencies in several countries.

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