is incidental, occurring via bites from mosquitoes that have fed on viremic monkeys. After the identification of *A. aegypti* mosquitoes as vectors of yellow fever, containment strategies were aimed at increased mosquito control. Today, urban yellow fever transmission occurs only in some African cities, but the threat exists in the great cities of South America, where reinfestation by *A. aegypti* has taken place and dengue virus 1–4 transmission by the same mosquito is common. Despite the existence of a highly effective and safe vaccine, several hundred jungle yellow fever cases occur annually in South America, and thousands of jungle and urban cases occur each year in Africa (29,000–60,000 estimated for 2013).

Yellow fever is a typical VHF accompanied by prominent hepatic necrosis. A period of viremia, typically lasting 3 or 4 days, is followed by a period of "intoxication." During the latter phase in severe cases, characteristic jaundice, hemorrhages, black vomit, anuria, and terminal delirium occur, perhaps related in part to extensive hepatic involvement. Blood leukocyte counts may be normal or reduced and are often high in terminal stages. Albuminuria is usually noted and may be marked. As renal function fails in terminal or severe cases, the concentration of blood urea nitrogen rises proportionately. Abnormalities detected in liver function tests range from modest elevations of AST concentrations in mild cases to severe derangement.

Urban yellow fever can be prevented by the control of *A. aegypti*. The continuing sylvatic cycles require vaccination of all visitors to areas of potential transmission with live attenuated variant 17D vaccine virus, which cannot be transmitted by mosquitoes. With few exceptions, reactions to the vaccine are minimal; immunity is provided within 10 days and lasts for at least 25–35 years. An egg allergy mandates caution in vaccine administration. Although there are no documented harmful effects of the vaccine on fetuses, pregnant women should be immunized only if they are definitely at risk of exposure to yellow fever virus. Because vaccination has been associated with several cases of encephalitis in children <6 months of age, it is contraindicated in this age group, nor is it recommended for infants 6–8 months of age unless the risk of exposure is very high. Rare, serious, multisystemic adverse reactions (occasionally fatal) have been reported, particularly affecting the elderly, and risk-to-benefit should be weighed prior to vaccine administration to individuals ≥60 years of age. Nevertheless, the number of deaths of unvaccinated travelers with yellow fever exceeds the number of deaths from vaccination, and a liberal vaccination policy for travelers to involved areas should be pursued. Timely information on changes in yellow fever distribution and yellow fever vaccine requirements can be obtained from the U.S. Centers for Disease Control and Prevention (*http://www.cdc.gov/vaccines/vpd-vac/yf/default.htm*).

234 Ebolavirus and Marburgvirus Infections

Jens H. Kuhn

Several viruses of the family Filoviridae cause severe and frequently fatal viral hemorrhagic fevers in humans. Introduction of filoviruses into human populations is an extremely rare event that most likely occurs by direct or indirect contact with healthy mammalian filovirus hosts or by contact with infected, sick, or deceased nonhuman primates. Filoviruses are highly infectious but not very contagious. Natural human-to-human transmission takes place through direct person-to-person (usually skin-to-skin) contact or exposure to infected bodily fluids and tissues; there is no evidence of such transmission by aerosol or respiratory droplets. Infections progress rapidly from influenza-like to hemorrhagic manifestations and typically culminate in multiple-organ dysfunction syndrome and shock. Treatment of filovirus infections is of necessity entirely supportive because no specific efficacious antiviral agents or vaccines are yet available.

Filoviruses are categorized as World Health Organization (WHO) Risk Group 4 Pathogens. Consequently, all work with material suspected of containing filoviruses should be conducted only in maximal containment (biosafety level 4) laboratories. Experienced personnel handling these viruses must wear appropriate personal protective gear (see "Prevention," below) and follow rigorous standard operating procedures. The proper authorities and WHO reference laboratories should be contacted immediately when filovirus infections are suspected.

ETIOLOGY

The family Filoviridae includes three genera: *Cuevavirus*, *Ebolavirus*, and *Marburgvirus* (Table 234-1 and Fig. 234-1). The available data suggest that the only known cuevavirus, Lloviu virus (LLOV), and one ebolavirus, Reston virus (RESTV), are not pathogenic for humans. The remaining four ebolaviruses—Bundibugyo virus (BDBV), Ebola virus (EBOV), Sudan virus (SUDV), and Taï Forest virus (TAFV)—cause Ebola virus disease (EVD; International Classification of Disease, Tenth Revision [ICD-10], code A98.4). The two marburgviruses, Marburg virus (MARV) and Ravn virus (RAVV), are the etiologic agents of Marburg virus disease (MVD; ICD-10 code A98.3).

Filoviruses have linear, nonsegmented, single-stranded, negative-sense RNA genomes that are ~19 kb in length. These genomes contain six or seven genes that encode the following seven structural proteins: nucleoprotein, polymerase cofactor (VP35), matrix protein (VP40), glycoprotein ($GP_{1,2}$), transcriptional cofactor (VP30), secondary matrix protein (VP24), and RNA-dependent RNA polymerase (L protein). Cuevaviruses and ebolaviruses, but not marburgviruses, also encode three nonstructural proteins of unknown function (sGP, ssGP, and Δ-peptide). Filovirions are unique among human virus particles in that they are predominantly pleomorphic filaments but also assume torus- or 6-like shapes (width, ~80 nm; average length, ≥790 nm). These enveloped virions contain helical ribonucleocapsids and are covered with $GP_{1,2}$ spikes (Fig. 234-2).

TABLE 234-1 FILOVIRUS TAXONOMY

Current Taxonomy and Nomenclature	Previous Taxonomy and Nomenclature
Order Mononegavirales	Order Mononegavirales
Family Filoviridae	Family Filoviridae
Genus *Marburgvirus*	Genus *Marburgvirus*
Species *Marburg marburgvirus*	Species *Lake Victoria marburgvirus*
Virus 1: Marburg virus (MARV)	Virus: Lake Victoria marburgvirus (MARV)
Virus 2: Ravn virus (RAVV)	
Genus *Ebolavirus*	Genus *Ebolavirus*
Species *Taï Forest ebolavirus*	Species *Cote d'Ivoire ebolavirus* [sic[a]]
Virus: Taï Forest virus (TAFV)	Virus: Cote d'Ivoire ebolavirus [sic] (CIEBOV)
Species *Reston ebolavirus*	Species *Reston ebolavirus*
Virus: Reston virus (RESTV)	Virus: Reston ebolavirus (REBOV)
Species *Sudan ebolavirus*	Species *Sudan ebolavirus*
Virus: Sudan virus (SUDV)	Virus: Sudan ebolavirus (SEBOV)
Species *Zaire ebolavirus*	Species *Zaire ebolavirus*
Virus: Ebola virus (EBOV)	Virus: Zaire ebolavirus (ZEBOV)
Species *Bundibugyo ebolavirus*	
Virus: Bundibugyo virus (BDBV)	
Genus *Cuevavirus*	
Species *Lloviu cuevavirus*	
Virus: Lloviu virus (LLOV)	

[a]The correct spelling of the country for which this virus is named is Côte d'Ivoire. The lack of a circumflex in "Cote" in the virus designation produced a false country name. This fact is denoted by "[sic]."