and myalgia. Lymphocytic choriomeningitis virus is transmitted to humans from the common house mouse (*Mus musculus*) by aerosols of excreta and secreta. The virus is maintained in the mouse mainly by vertical transmission from infected dams. The vertically infected mouse remains viremic and sheds virus for life, with high concentrations of virus in all tissues. Infected colonies of pet hamsters also can serve as a link to humans. Infections among scientists and animal caretakers can occur because the virus is widely used in immunology laboratories as a model of T cell function and can silently infect cell cultures and passaged tumor lines. In addition, patients may have a history of residence in rodent-infested housing or other exposure to rodents. An antibody prevalence of ~5–10% has been reported among adults from Argentina, Germany, and the United States.

Lymphocytic choriomeningitis/meningoencephalitis differs from the general syndrome of fever and myalgia in that the onset is gradual. Conditions occasionally associated with the disease are orchitis, transient alopecia, arthritis, pharyngitis, cough, and maculopapular rash. An estimated one-fourth of patients (or fewer) experience a febrile phase of 3–6 days. After a brief remission, many develop renewed fever accompanied by severe headache, nausea and vomiting, and meningeal signs lasting for ~1 week (the CNS phase). These patients virtually always recover fully, as do the rare patients with clear-cut signs of encephalitis. Recovery may be delayed by transient hydrocephalus. During the initial febrile phase, leukopenia and thrombocytopenia are common, and virus can usually be isolated from blood. During the CNS phase, the virus may be found in the CSF, and antibodies are present in the blood. The pathogenesis of lymphocytic choriomeningitis/meningoencephalitis is thought to resemble that following direct intracranial inoculation of the virus into adult mice. The onset of the immune response leads to T cell–mediated immunopathologic meningitis. During the meningeal phase, CSF mononuclear-cell counts range from the hundreds to the low thousands per microliter, and hypoglycorrhachia is found in one-third of patients.

IgM-capture ELISA, immunochemistry, and RT-PCR are used in the diagnosis of lymphocytic choriomeningitis/meningoencephalitis. IgM-capture ELISA of serum and CSF usually yields positive results; RT-PCR assays have been developed for probing CSF. Because patients who have fulminant infections transmitted by recent organ transplantation do not mount an immune response, immunohistochemistry or RT-PCR is required for diagnosis. Infection should be suspected in acutely ill febrile patients with marked leukopenia and thrombocytopenia. In patients with aseptic meningitis, any of the following suggests lymphocytic choriomeningitis/meningoencephalitis: a well-marked febrile prodrome, adult age, occurrence in the autumn, low CSF glucose levels, or CSF mononuclear-cell counts of >1000/μL. In pregnant women, infection may lead to fetal invasion with consequent congenital hydrocephalus and chorioretinitis. Because the maternal infection may be mild, causing only a short febrile illness, antibodies to the virus should be sought in both the mother and the fetus under suspicious circumstances, particularly in TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and HIV)–negative neonatal hydrocephalus.

Bunyaviruses Numerous bunyaviruses cause fever and myalgia. Many of these viruses cause individual infections and usually do not result in epidemics—e.g., the viruses of the orthobunyavirus Anopheles A serogroup (e.g., Tacaiuma virus), Bwamba serogroup (Bwamba virus, Pongola virus), Guama serogroup (Catu virus, Guama virus), Nyando serogroup (Nyando virus), and Wyeomyia serogroup (Wyeomyia virus); the unclassified bunyavirus Tataguine virus; the phlebovirus Bhanja complex (Bhanja virus, Heartland virus) and Candiru complex (Alenquer, Candiru, Escharate, Maldonado, Morumbi, and Serra Norte viruses); the hantavirus Choclo virus; and the Dugbe and Nairobi sheep disease nairoviruses. In the relevant orthobunyaviral Bunyamwera serogroup (Bunyamwera, Batai, Cache Valley, Fort Sherman, Germiston, Guaroa, Ilesha, Ngari, Shokwe, and Xingu viruses), Ngari virus recently has been implicated in a large epidemic in Africa.

ORTHOBUNYAVIRUS GROUP C SEROGROUP Apeú, Caraparú, Itaquí, Madrid, Marituba, Murutucú, Nepuyo, Oriboca, Ossa, Restan, and Zungarococha viruses are among the most common causes of arboviral infection in humans entering South American jungles. These viruses cause acute febrile disease and are transmitted by mosquitoes in neotropical forests.

ORTHOBUNYAVIRUS SIMBU SEROGROUP Oropouche virus is transmitted in Central and South America by a biting midge, *Culicoides paraensis*, which often breeds to high density in cacao husks and other vegetable detritus found in towns and cities. Explosive epidemics involving thousands of patients have been reported from several towns in Brazil and Peru. Rash and aseptic meningitis have been detected in a number of patients. Iquitos virus, a recently discovered reassortant and close relative of Oropouche virus, causes disease that is easily mistaken for Oropouche virus disease; its overall epidemiologic significance remains to be determined.

PHLEBOVIRUS SANDFLY FEVER SEROGROUP A previous designation for sandfly fever, "3-day fever," instructively describes the brief debilitating course associated with this essentially benign infection. There is neither a rash nor CNS involvement, and complete recovery is the rule. Sandfly fever is caused by at least six distinct phleboviruses of the phlebovirus sandfly fever serocomplex (Chagres virus, sandfly fever Cyprus virus, sandfly fever Naples virus, sandfly fever Sicilian virus, sandfly fever Turkey virus, and Toscana virus). Sandfly fever Naples virus, sandfly fever Sicilian virus, and Toscana viruses are the most important human pathogens of this group. *Phlebotomus* sandflies transmit the viruses, probably among small mammals, and infect humans by bites. Female sandflies may be infected by the oral route as they take a blood meal and may transmit the virus to offspring when they lay their eggs after a second blood meal. This prominent transovarial transmission confounds virus control.

Sandfly fever is found in the circum-Mediterranean area, extending to the east through the Balkans into parts of China as well as into western Asia. Chagres virus is endemic in Panama. Sandflies are found in both rural and urban settings and are known for their short flight ranges and their small sizes; the latter enables them to penetrate standard mosquito screens and netting. Epidemics have been described in the wake of natural disasters and wars. After World War II, extensive spraying in parts of Europe to control malaria greatly reduced sandfly populations and sandfly fever Naples virus transmission; the incidence of sandfly fever continues to be low.

A common pattern of disease in endemic areas consists of high attack rates among travelers and military personnel and little or no disease in the local population, who are protected after childhood infection. Toscana virus infection is common during the summer among rural residents and vacationers, particularly in Italy, Spain, and Portugal; a number of cases have been identified in travelers returning to Germany and Scandinavia. The disease may manifest as an uncomplicated febrile illness but is often associated with aseptic meningitis, with virus isolated from the CSF.

Punta Toro virus is a phlebovirus that is not part of the sandfly fever serocomplex but that, like the members of this complex, is transmitted by sandflies. Punta Toro virus causes a sandfly fever–like disease in the Latin American tropical forest, where the vectors rest on tree buttresses. Epidemics have not been reported, but antibody prevalence among inhabitants of villages in endemic areas indicates a cumulative lifetime exposure rate of >50%.

Flaviviruses The most clinically important flaviviruses that cause the fever and myalgia syndrome are dengue viruses 1–4. In fact, dengue is probably the most important arthropod-borne viral disease worldwide, with 50–100 million infections occurring per year. Year-round transmission of dengue viruses 1–4 occurs between latitudes of 25°N and 25°S, but seasonal forays of the viruses into the United States and Europe have been documented. All four viruses have *A. aegypti* as their principal vector. Through increasing spread of mosquitoes throughout the tropics and subtropics and international travel of infected humans, large areas of the world have become vulnerable to the introduction of dengue viruses. Thus, dengue and severe dengue (see "Viral Hemorrhagic Fevers," below) are becoming increasingly common. For instance, conditions favorable to dengue virus 1–4 transmission via