infections usually follow either outdoor activities resulting in tick bites or consumption of raw (unpasteurized) milk from infected goats or, less commonly, from other infected animals (cows, sheep). Milk seems to represent the main transmission route for louping ill viruses, which cause disease only very rarely. The western/European subtype viruses are transmitted mainly by *Ixodes ricinus* from Scandinavia to the Ural Mountains. (Ural-)Siberian viruses are transmitted predominantly by *Ixodes persulcatus* from Europe across the Ural Mountains to the Pacific Ocean; louping ill viruses seem to be confined primarily to Great Britain. Several thousand infections with tick-borne encephalitis virus are recorded each year among people of all ages. Human tick-borne viral encephalitis occurs between April and October, with a peak in June and July.

Western/European viruses classically caused bimodal disease. After an incubation period of 7–14 days, the illness begins with a *fever–myalgia phase* (arthralgia, fever, headaches, myalgia, nausea) that lasts for 2–4 days and is thought to correlate with viremia. A subsequent remission for several days is followed by the recurrence of fever and the onset of meningeal signs. The *CNS phase* (7–10 days before onset of improvement) varies from mild aseptic meningitis, which is more common among younger patients, to severe (meningo-)encephalitis with coma, seizures, tremors, and motor signs. Spinal and medullary involvement can lead to typical limb-girdle paralysis and respiratory paralysis. Most patients with western/European virus infections recover (lethality rate, 1%), and only a minority of patients have significant deficits. However, the lethality rate from (Ural-)Siberian virus infections reaches 7–8%.

Infections with Far Eastern viruses generally run a more abrupt course. The encephalitic syndrome caused by these viruses sometimes begins without a remission from the fever–myalgia phase and has more severe manifestations than the western/European syndrome. The lethality rate is high (20–40%), and major sequelae—most notably, lower motor neuron paralyses of the proximal muscles of the extremities, trunk, and neck—are common, developing in approximately one-half of patients. Thrombocytopenia sometimes develops during the initial febrile illness, resembling the early hemorrhagic phase of some other tick-borne flavivirus infections, such as Kyasanur Forest disease. In the early stage of the illness, virus may be isolated from the blood. In the CNS phase, IgM antibodies are detectable in serum and/or CSF.

Diagnosis of tick-borne viral encephalitis primarily relies on serology and detection of viral genomes by RT-PCR. There is no specific therapy for infection. However, effective alum-adjuvanted, formalin-inactivated virus vaccines are produced in Austria, Germany, and Russia in chicken embryo cells (FSME-Immun® and Encepur®). Two doses of the Austrian vaccine separated by an interval of 1–3 months appear to be effective in the field, and antibody responses are similar when vaccine is given on days 0 and 14. Because rare cases of postvaccination Guillain-Barré syndrome have been reported, vaccination should be reserved for persons likely to experience rural exposure in an endemic area during the season of transmission. Cross-neutralization for the western/European and Far Eastern variants has been established, but there are no published field studies on cross-protection among formalin-inactivated vaccines.

Because 0.2–4% of ticks in endemic areas may be infected, the use of immunoglobulin prophylaxis of tick-borne viral encephalitis has been raised. Prompt administration of high-titered specific antibody preparations should probably be undertaken, although no controlled data are available to prove the efficacy of this measure. Immunoglobulins should be considered because of the risk of antibody-mediated enhancement of infection or antigen–antibody complex deposition in tissues.

WEST NILE VIRUS INFECTION West Nile virus is now the primary cause of arboviral encephalitis in the United States. In 2012, 2873 cases of neuroinvasive disease (e.g., meningitis, encephalitis, acute flaccid paralysis), with 270 deaths, and 2801 cases of non-neuroinvasive infection were reported. West Nile virus was initially described as being transmitted among wild birds by *Culex* mosquitoes in Africa, Asia, and southern Europe. In addition, the virus has been implicated in severe and fatal hepatic necrosis in Africa. West Nile virus was introduced into New York City in 1999 and subsequently spread to other areas of the northeastern United States, causing die-offs among crows, exotic zoo birds, and other birds. The virus has continued to spread and is now found in almost all states as well as in Canada, Mexico, South America, and the Caribbean islands. *C. pipiens* remains the major vector in the northeastern United States, but several other *Culex* species and *A. albopictus* are also involved. Jays compete with crows and other corvids as amplifiers and lethal targets in other areas of the country.

West Nile virus is a common cause of febrile disease without CNS involvement (incubation period, 3–14 days), but it occasionally causes aseptic meningitis and severe encephalitis, particularly among the elderly. The fever–myalgia syndrome caused by West Nile virus differs from that caused by other viruses in terms of the frequent—rather than occasional—appearance of a maculopapular rash concentrated on the trunk (especially in children) and the development of lymphadenopathy. Back pain, fatigue, headache, myalgia, retroorbital pain, sore throat, nausea and vomiting, and arthralgia (but not arthritis) are common accompaniments that may persist for several weeks. Encephalitis, sequelae, and death are all more common among elderly, diabetic, and hypertensive patients and among patients with previous CNS insults. In addition to the more severe motor and cognitive sequelae, milder findings may include tremor, slight abnormalities in motor skills, and loss of executive functions. Intense clinical interest and the availability of laboratory diagnostic methods have made it possible to define a number of unusual clinical features. Such features include chorioretinitis, flaccid paralysis with histologic lesions resembling poliomyelitis, and initial presentation with fever and focal neurologic deficits in the absence of diffuse encephalitis. Immunosuppressed patients may have fulminant courses or develop persistent CNS infection. Virus transmission through both transplantation and blood transfusion has necessitated screening of blood and organ donors by nucleic acid–based tests. Occasionally, pregnant women infect their fetuses with West Nile virus.

Rhabdoviruses: Chandipura Virus Infection Chandipura virus seems to be an emerging and increasingly important human virus in India, where it is transmitted among hedgehogs by mosquitoes and sandflies. In humans, the disease begins as an influenza-like illness, with fever, headache, abdominal pain, nausea, and vomiting; these manifestations are followed by neurologic impairment and infection-related or autoimmune-mediated encephalitis. Chandipura virus infection is characterized by high lethality in children. Several hundred cases of infection are recorded in India every year. Infections with other arthropod-borne rhabdoviruses (Isfahan, Piry, vesicular stomatitis Indiana, vesicular stomatitis New Jersey) may imitate the early febrile stage of Chandipura virus infection.

Togaviruses • *EASTERN EQUINE ENCEPHALITIS* This disease is encountered primarily in swampy foci along the eastern coast of the United States, with a few inland foci as far removed as Michigan. Infected humans present for medical care from June through October. During this period, the bird–*Culiseta* mosquito cycle spills over into other mosquitoes such as *Aedes sollicitans* or *Aedes vexans*, which are more likely to feed on mammals. There is concern over the potential role of the introduced anthropophilic mosquito species *A. albopictus*, which has been found to be infected with eastern equine encephalitis virus and is an effective experimental vector in the laboratory. Horses are a common target for the virus. Contact with unvaccinated horses may be associated with human disease, but horses probably do not play a significant role in amplification of the virus.

Eastern equine encephalitis is one of the most destructive of the arboviral diseases, with a sudden onset after an incubation period of ~5–10 days, rapid progression, 50–75% lethality, and frequent sequelae in survivors. This severity is reflected in the extensive necrotic lesions and polymorphonuclear infiltrates found at postmortem examination of the brain. Acute polymorphonuclear CSF pleocytosis, often occurring during the first 1–3 days of disease, is another indication of severity. In addition, leukocytosis with a left shift is a common feature. A formalin-inactivated vaccine has been used to protect laboratory workers but is not generally available or applicable.