viruses) also cause human disease. Transovarial transmission is a strong component of transmission of the California serogroup viruses in *Aedes* and *Ochlerotatus* mosquitoes. The mosquito vector of La Crosse virus is *Ochlerotatus triseriatus*. In addition to transovarial transmission, acquisition through feeding on viremic chipmunks and other mammals as well as venereal transmission can result in infection of this mosquito. *O. triseriatus* breeds in sites such as tree holes and abandoned tires and bites during daylight hours. The habits of this mosquito correlate with the risk factors for human cases: recreation in forested areas, residence at a forest's edge, and the presence of water-containing abandoned tires around the home. Intensive environmental modification based on these findings has reduced the incidence of disease in a highly endemic area in the U.S. Midwest.

Most humans are infected from July through September. The Asian tiger mosquito (*A. albopictus*) efficiently transmits La Crosse virus to mice and also transmits the agent transovarially in the laboratory; this aggressive anthropophilic mosquito has the capacity to urbanize, and its possible impact on transmission of virus to humans is of concern. The prevalence of antibody to La Crosse virus in humans is ≥20% in endemic areas, a figure indicating that infection is common but often asymptomatic. CNS disease has been recognized primarily in children <15 years of age.

The illness from La Crosse virus varies from aseptic meningitis accompanied by confusion to severe and occasionally fatal encephalitis (lethality rate, <0.5%). The incubation period is ~3–7 days. Although there may be prodromal symptoms/signs, the onset of CNS disease is sudden, with fever, headache, and lethargy often joined by nausea and vomiting, convulsions (in one-half of patients), and coma (in one-third of patients). Focal seizures, hemiparesis, tremor, aphasia, chorea, Babinski signs, and other evidence of significant neurologic dysfunction are common, but residual disease is not. Approximately 10% of patients have recurrent seizures in the succeeding months. Other serious sequelae of La Crosse virus infection are rare, although a decrease in scholastic standing in children has been reported and mild personality change has occasionally been suggested.

The blood leukocyte count is commonly elevated in patients with La Crosse virus infection, sometimes reaching 20,000/μL, and is usually accompanied by a left shift. CSF leukocyte counts are typically 30–500/μL with a mononuclear cell predominance (although 25–90% of cells are polymorphonuclear in some patients). The blood protein concentration is normal or slightly increased, and the glucose concentration is normal. Specific virologic diagnosis based on IgM-capture assays of serum and CSF is efficient. The only human anatomic site from which virus has been isolated is the brain.

Treatment is supportive over a 1- to 2-week acute phase during which status epilepticus, cerebral edema, and inappropriate secretion of antidiuretic hormone are important concerns. A phase 2B clinical trial of IV ribavirin in children with La Crosse virus infection was discontinued during dose escalation because of adverse effects.

Jamestown Canyon virus has been implicated in several cases of encephalitis in adults, usually with a significant respiratory illness at onset. Human infection with this virus has been documented in New York, Wisconsin, Ohio, Michigan, Ontario, and other areas of North America where the vector mosquito, *Aedes stimulans*, feeds on its main host, the white-tailed deer. Tahyña virus can be found in central Europe, Russia, China, and Africa. The virus is a prominent cause of febrile disease but can also cause pharyngitis, pulmonary syndromes, aseptic meningitis, or meningoencephalitis.

Flaviviruses The most important flavivirus encephalitides are Japanese encephalitis, St. Louis encephalitis, tick-borne encephalitis, and West Nile virus infection. Australian encephalitis (Murray Valley encephalitis) and Rocio virus infection resemble Japanese encephalitis but are documented only occasionally in Australia and Brazil, respectively. Powassan virus has caused ~50 cases of often-severe disease (lethality rate, ~10%), frequently occurring among children in eastern Canada and the United States. Usutu virus has caused only individual cases of human infection, but such infections may be underdiagnosed.

JAPANESE ENCEPHALITIS Japanese encephalitis is the most important viral encephalitis in Asia. Each year 35,000–50,000 cases and more than 15,000 deaths are reported. Japanese encephalitis virus is found throughout Asia, including far eastern Russia, Japan, China, India, Pakistan, and southeastern Asia, and causes occasional epidemics on western Pacific islands. The virus has been detected in the Torres Strait islands, and five human encephalitis cases have been identified on the nearby Australian mainland. The virus is particularly common in areas where irrigated rice fields attract the natural avian vertebrate hosts and provide abundant breeding sites for mosquitoes such as *Culex tritaeniorhynchus*, which transmit the virus to humans. Additional amplification by pigs, which suffer abortion, and horses, which develop encephalitis, may be significant as well. Vaccination of these additional amplifying hosts may reduce the transmission of the virus.

Clinical signs of Japanese encephalitis emerge after an incubation period of 5–15 days and range from an unspecific febrile presentation (nausea, vomiting, diarrhea, cough) to aseptic meningitis, meningoencephalitis, acute flaccid paralysis, and severe encephalitis. Common findings are cerebellar signs, cranial nerve palsies, and cognitive and speech impairments. A Parkinsonian presentation and seizures are typical in severe cases. Effective vaccines are available. Vaccination is indicated for summer travelers to rural Asia, where the risk of acquiring Japanese encephalitis is considered to be about 1 per 5000 to 1 per 20,000 travelers per week if travel duration exceeds 3 weeks. Usually two intramuscular doses of the vaccine are given 28 days apart, with the second dose administered at least 1 week prior to travel.

ST. LOUIS ENCEPHALITIS St. Louis encephalitis virus is transmitted between mosquitoes and birds. This virus causes a low-level endemic infection among rural residents of the western and central United States, where *Culex tarsalis* is the vector (see "Western Equine Encephalitis," below). The more urbanized mosquitoes *Culex pipiens* and *Culex quinquefasciatus* have been responsible for epidemics resulting in hundreds or even thousands of cases in cities of the central and eastern United States. Most cases occur in June through October. The urban mosquitoes breed in accumulations of stagnant water and sewage with high organic content and readily feed on humans in and around houses at dusk. The elimination of open sewers and trash-filled drainage systems is expensive and may not be possible, but screening of houses and implementation of personal protective measures may be an effective approach to the prevention of infection. The rural mosquito vector is most active at dusk and outdoors; its bites can be avoided by modification of activities and use of repellents.

Disease severity increases with age. St. Louis encephalitis virus infections that result in aseptic meningitis or mild encephalitis are concentrated among children and young adults, while severe and fatal cases primarily affect the elderly. Infection rates are similar in all age groups; thus the greater susceptibility of older persons to disease is a biologic consequence of aging. St. Louis encephalitis has an abrupt onset after an incubation period of 4–21 days, sometimes following a prodrome, and begins with fever, lethargy, confusion, and headache. In addition, nuchal rigidity, hypotonia, hyperreflexia, myoclonus, and tremors are common. Severe cases can include cranial nerve palsies, hemiparesis, and seizures. Patients often report dysuria and may have viral antigen in urine as well as pyuria. The overall rate of lethality is generally ~7% but may reach 20% among patients >60 years of age. Recovery is slow. Emotional lability, difficulties with concentration and memory, asthenia, and tremors are commonly prolonged in older convalescent patients. The CSF of patients with St. Louis encephalitis usually contains tens to hundreds of leukocytes, with a lymphocytic predominance and a left shift. The CSF glucose concentration is normal in these patients.

TICK-BORNE VIRAL ENCEPHALITIS Tick-borne encephalitis viruses are currently subdivided into four groups: the western/European subtype (previously called central European encephalitis virus), the (Ural-) Siberian subtype (previously called Russian spring-summer encephalitis virus), the Far Eastern subtype, and the louping ill subtype (previously called louping ill virus or, in Japan, Negishi virus). Small mammals and grouse, deer, and sheep are the vertebrate amplifiers for these viruses, which are transmitted by ticks. The risk of infection varies by geographic area and can be highly localized within a given area; human