some countries (see below). Serious adverse effects of human RIG are uncommon. Local pain and low-grade fever may occur.

Two purified inactivated rabies vaccines are available for rabies PEP in the United States. They are highly immunogenic and remarkably safe compared with earlier vaccines. Four 1-mL doses of rabies vaccine should be given IM in the deltoid area. (The anterolateral aspect of the thigh also is acceptable in children.) Gluteal injections, which may not always reach muscle, should not be given and have been associated with rare vaccine failures. Ideally, the first dose should be given as soon as possible after exposure; failing that, it should be given without further delay. The three additional doses should be given on days 3, 7, and 14; a fifth dose on day 28 is no longer recommended. Pregnancy is not a contraindication for immunization. Glucocorticoids and other immunosuppressive medications may interfere with the development of active immunity and should not be administered during PEP unless they are essential. Routine measurement of serum neutralizing antibody titers is not required, but titers should be measured 2–4 weeks after immunization in immunocompromised persons. Local reactions (pain, erythema, edema, and pruritus) and mild systemic reactions (fever, myalgias, headache, and nausea) are common; anti-inflammatory and antipyretic medications may be used, but immunization should not be discontinued. Systemic allergic reactions are uncommon, but anaphylaxis does occur rarely and can be treated with epinephrine and antihistamines. The risk of rabies development should be carefully considered before the decision is made to discontinue vaccination because of an adverse reaction.

Most of the burden of rabies PEP is borne by persons with the fewest resources. In addition to the rabies vaccines discussed above, vaccines grown in either primary cell lines (hamster or dog kidney) or continuous cell lines (Vero cells) are satisfactory and are available in many countries outside the United States. Less expensive vaccines derived from neural tissues are still used in a diminishing number of developing countries; however, these vaccines are associated with serious neuroparalytic complications, including postinfectious encephalomyelitis and Guillain-Barré syndrome. The use of these vaccines should be discontinued as soon as possible, and progress has been made in this regard. Worldwide, >10 million individuals receive postexposure rabies vaccine each year.

If human RIG is unavailable, purified equine RIG can be used in the same manner at a dose of 40 IU/kg. Before the administration of equine RIG, hypersensitivity should be assessed by intradermal testing with a 1:10 dilution. The incidence of anaphylactic reactions and serum sickness has been low with recent equine RIG products.

**Preexposure Rabies Vaccination** Preexposure rabies prophylaxis should be considered for people with an occupational or recreational risk of rabies exposures, including certain travelers to rabies-endemic areas. The primary schedule consists of three doses of rabies vaccine given on days 0, 7, and 21 or 28. Serum neutralizing antibody tests help determine the need for subsequent booster doses. When a previously immunized individual is exposed to rabies, two booster doses of vaccine should be administered on days 0 and 3. Wound care remains essential. As stated above, RIG should not be administered to previously vaccinated persons.

## OTHER RHABDOVIRUSES

### OTHER LYSSAVIRUSES

A growing number of lyssaviruses other than rabies virus have been discovered to infect bat populations in Europe, Africa, Asia, and Australia. Six of these viruses have produced a very small number of cases of a human disease indistinguishable from rabies: European bat lyssaviruses 1 and 2, Australian bat lyssavirus, Irkut virus, and Duvenhage virus. Mokola virus, a lyssavirus that has been isolated from shrews with an unknown reservoir species in Africa, may also produce human disease indistinguishable from rabies.

### VESICULAR STOMATITIS VIRUS

Vesicular stomatitis is a viral disease of cattle, horses, pigs, and some wild mammals. Vesicular stomatitis virus is a member of the genus *Vesiculovirus* in the family Rhabdoviridae. Outbreaks of vesicular stomatitis in horses and cattle occur sporadically in the southwestern United States. The animal infection is associated with severe vesiculation and ulceration of oral tissues, teats, and feet and may be clinically indistinguishable from the more dangerous foot-and-mouth disease. Epidemics are usually seasonal, typically beginning in the late spring, and are probably due to arthropod vectors. Direct animal-to-animal spread can also occur, although the virus cannot penetrate intact skin. Transmission to humans usually results from direct contact with infected animals (particularly cattle) and occasionally follows laboratory exposure. In human disease, early conjunctivitis is followed by an acute influenza-like illness with fever, chills, nausea, vomiting, headache, retrobulbar pain, myalgias, substernal pain, malaise, pharyngitis, and lymphadenitis. Small vesicular lesions may be present on the buccal mucosa or on the fingers. Encephalitis is very rare. The illness usually lasts 3–6 days, with complete recovery. Subclinical infections are common. A serologic diagnosis can be made on the basis of a rise in titer of complement-fixing or neutralizing antibodies. Therapy is symptom-based.



# 233 Arthropod-Borne and Rodent-Borne Virus Infections

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This chapter summarizes the major features of selected arthropod-borne and rodent-borne viruses. Numerous viruses of this category are transmitted in nature among animals without ever infecting humans. Other viruses incidentally infect humans, but only a proportion of these viruses induce human disease. In addition, certain viral agents are regularly introduced into human populations or spread among humans by certain arthropods (specifically, insects and ticks) or by chronically infected rodents. These zoonotic viruses are taxonomically diverse and therefore differ fundamentally from one another in terms of virion morphology, replication strategies, genomic organization, and genome sequence. While a virus's classification in a taxon is enlightening with regard to natural maintenance strategies, sensitivity to antiviral agents, and particular aspects of pathogenesis, the classification does not necessarily predict which clinical signs and symptoms (if any) the virus will cause in humans. Zoonotic viruses are evolving, and "new" zoonotic viruses are regularly discovered. The epizootiology and epidemiology of zoonotic viruses continue to change as a result of environmental alterations affecting vectors, reservoirs, wildlife, livestock, and humans. Zoonotic viruses are most numerous in the tropics but are also found in temperate and even frigid climates. The distribution and seasonal activity of a zoonotic virus may vary, and the rate at which it changes is likely to depend largely on ecologic conditions (e.g., rainfall and temperature), which can affect the density of virus vectors and reservoirs and the development of infection.

Arthropod-borne viruses (arboviruses) infect their vectors after ingestion of a blood meal from a viremic, usually nonhuman vertebrate; some arthropods may also become infected by saliva-activated transmission. The arthropod vectors then develop chronic, systemic infection as the viruses penetrate the gut and spread throughout the body to the salivary glands; such virus dissemination, referred to as *extrinsic incubation*, typically lasts 1–3 weeks in mosquitoes. At this point, if the salivary glands become involved, the arthropod vector is competent to continue the chain of transmission by infecting a vertebrate during a subsequent blood meal. An alternative mechanism for virus maintenance in its arthropod vector is *transovarial transmission*. The arthropod generally is unharmed by the infection, and the natural vertebrate partner usually has only transient viremia with no overt disease.