

VENEZUELAN EQUINE ENCEPHALOMYELITIS

(Peste loca, Venezuelan encephalitis, VEE, VE)

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Definition [top](#)

Venezuelan equine encephalomyelitis (VEE) is a zoonotic, mosquito-borne, viral disease affecting both Equidae and humans (6,8). In Equidae, infection may produce an acute, fulminating disease that terminates in death or recovery without development of encephalitic signs, or the more classical disease with progressive clinical encephalitis. In human beings, a flulike syndrome predominates with an accompanying high fever and frontal headache. Human deaths may occur in the young or the aged. A wide variety of hosts and vectors may be infected (5,10,13,15).

Etiology [top](#)

The etiologic agent of VEE is an alphavirus of the family *Togaviridae* (formerly the group A arboviruses). . The virions are 60-75 nm in diameter and have an essential lipid membrane.

Only minor antigenic variations exist among different VEE virus isolates (10,16). Six subtypes (I, II, III, IV, V, and VI) have been identified within the VEE complex. Within subtype I, only two (A/B and C) of the five variants (A/B through F) have been associated with epizootic activity in equines (5,10,13-15). The other variants (I-D through I-F) and subtypes (II through VI) have been associated with nonequine, sylvatic, or enzootic activity. Infection with one variant or vaccination with attenuated virus generally results in production of neutralizing antibodies and cross-protection of variable duration to infection with the other subtypes and variants (13-15).

Host Range [top](#)

A wide variety of laboratory animals are susceptible in varying degrees to both enzootic and epizootic variants of VEE virus (5,10,13,15). In addition, several domestic animals, including cattle, swine, and dogs have serologic and virologic evidence of infection, but generally no clinical sign, during epizootics of VEE. However, with the possible exception of human beings, no evidence exists to date to incriminate any animal species other than Equidae as prime amplifiers of VEE epizootics (5,10,13,15).

Geographic Distribution [top](#)

Venezuelan equine encephalomyelitis was first recognized as a separate disease entity following a major epizootic of encephalitis in Venezuela in 1936 (8,10). From 1936 to 1968, devastating epizootics and epidemics occurred in equines and human beings in Colombia, Ecuador, Peru, and Venezuela (5,10,13,15). In January, 1969 another major epizootic and epidemic of VEE erupted in Ecuador and spread into Peru. In June, 1969, the virus was transported by undetermined means from Ecuador to Guatemala (3). This large scale epizootic and epidemic spread into El Salvador, Honduras, and Nicaragua. In 1970, the epizootic extended into Costa Rica and Mexico and, by 1971, into the United States (5,10,13,15).

Epizootic VEE has not been diagnosed, and epizootic VEE virus variants have not been isolated in the United States since 1971. Twenty years after the last activity in the Western Hemisphere, VEE was reported in 1992-3 and 1995 in outbreaks in horses in Venezuela and in 1993 and 1996 in limited, focal outbreaks in horses in Mexico.

Transmission [top](#)

Sylvatic or Enzootic Cycle

As indicated earlier, variants I-D through I-F and subtypes II through VI of VEE virus are invariably associated with a sylvatic or enzootic cycle in which rodent-mosquito transmission occurs; human beings and horses are only incidentally involved in this cycle. Although sylvatic variants and subtypes are pathogenic for human beings and have caused occasional epidemics with a few deaths, these variants and subtypes are normally nonpathogenic for horses. However, in 1993 and 1996, VEE virus variant I-E was isolated from horses during a focal, limited outbreak in Mexico in areas of sylvatic virus activity. This occasional activity is consistent with previously reported VEE during the mid-1960's in Mexico in which VEE virus variant I-E isolations were made. It is clear that under certain ideal but undefined conditions, sylvatic I-E variant viruses are pathogenic to horses.

Generally, the sylvatic virus tends to cycle in rodents in areas where a highly efficient vector such as *Culex (Melanoconion)* spp. is found (5,10,13-15). Foci of sylvatic virus activity have been identified in Colombia and Panama (subtype I-D); Mexico, Central America, and Panama (subtype I-E); Brazil (subtype I-F); Florida Everglades (subtype II); Brazil and Trinidad (subtype III-A); some Northern Plains states and Surinam (subtype III-B); Brazil (subtype IV); French Guiana (subtype V); and Argentina (subtype VI) (5,10,13,15,16).

Epizootic Cycle

No known epizootic virus variant (I-AB or I-C) has ever been shown to cycle enzootically in rodents. Historically, naturally occurring epizootics of VEE in Equidae have been reported in northern South America since at least the 1920's (10). The original epizootic VEE viral isolate made in Venezuela in 1937 was caused by a strain of variant I-A/B, which was also responsible for the 1969-72 epizootics in Ecuador, Central America, Mexico, and Texas. Epizootics during the 1960's and 1970's and in 1992-3 and 1995 in Colombia and Venezuela were caused by variant I-C. Recent molecular genetic studies of VEE virus isolates indicate very close phylogenetic relationships between epizootic variant I-C isolates and sylvatic variant I-D isolates (11). The results support the hypothesis that epizootic VEE virus variants emerge from sylvatic variant I-D viruses. During epizootics of VEE, many species of mosquitoes and possibly other hematophagous insects are involved in the explosive movement of the outbreak. Horses are the most important amplifiers of VEE virus during epizootics owing to the extremely high viremias that they develop and the large numbers of hematophagous insects that can feed on an animal of such size. Human infections occur tangentially to equine infections, but in spite of moderately high viremia levels, human beings probably do not contribute significantly to the maintenance and movement of an epizootic wave. The maintenance cycle of equine virulent (epizootic) VEE virus during the interepizootic period and the origin of epizootic VEE virus variants are

unknown. Efficient vectors of epizootic VEE include mosquitoes of the genera *Aedes*, *Anopheles*, *Culex*, *Deinocerites*, *Mansonia*, and *Psorophora* (5,10,13,15).

Incubation Period [top](#)

The incubation period from the inoculation of the virus until the febrile response generally is 0.5 to 2 days but may be as long as 5 days, depending on the virus strain or quantity of virus in the inoculum. Typically, detectable viremia occurs concurrently with the onset of fever and persists for 2 to 4 days. Onset of encephalitic signs occurs 4.5 to 5 days after infection at a time when circulating virus is disappearing, neutralizing antibody is first detectable, and body temperature is returning to a normal range (10,14,15)

Clinical Signs [top](#)

In Equidae, VEE virus infection may be expressed as (a) subclinical with no overt signs; (b) moderate and characterized primarily by anorexia, high fever, and depression; (c) severe, but nonfatal, and characterized by anorexia, high fever, stupor, weakness, staggering, blindness, and, occasionally, permanent neurologic sequelae; or (d) fatal, with the same clinical signs (5,7,10,13-15). Not all fatal cases of VEE in Equidae are accompanied by definite neurologic signs. In general, two forms of the disease exist: (a) the fulminating form in which signs of generalized, acute, febrile disease predominate, and (b) the encephalitic form in which the more impressive signs of central nervous system (CNS) involvement usually dominate. An incubation period of 0.5 to 5 days precedes a rise in body temperature to 39-41° C (103-105° F) which is accompanied by a hard, rapid pulse and depression. The onset of VEE virus infection is insidious, with fever, inappetence, and mild excitability being among the earliest clinical signs of disease. Frequently, a rapid progression ensues with depression, weakness, and ataxia followed by overt signs of encephalitis such as muscle spasms, chewing movements, incoordination, and convulsions. Early encephalitic signs include loss of both cutaneous neck reflexes and visual responsiveness; diarrhea and colic may also develop. Some animals may stand quietly in their surroundings whereas others may wander aimlessly or press their heads against solid objects. A braced stance or circling may occur late in the disease. A characteristic paddling motion of the limbs may be observed with lateral recumbency. The course of the disease may be interrupted at any point by recovery or prostration and death. The course of the disease may be rapid with death ensuing within hours after the observation of the first clinical manifestations of encephalitis (during epizootics, reports of sudden death are not uncommon), or more protracted with dehydration and extreme loss of weight occurring before an encephalitic death or recovery.

Gross Lesions [top](#)

The macroscopic appearance of the CNS of horses inoculated with VEE virus varies from no visible lesion to extensive necrosis and hemorrhages. Lesions reported in other tissues have been too variable to be of any diagnostic significance (7,9,10,12,14,15).

Morbidity and Mortality [top](#)

Epizootic VEE due to virus variants I-A/B and I-C may be highly fatal. Estimated case morbidity rates vary from 50 to 100 percent in some areas to 10 to 40 percent in other areas. Mortality rates vary from 50 to 90 percent; infection rates with or without clinical signs may be as high as 90 percent. In most cases, infection with sylvatic or enzootic VEE virus variants I-D, I-E, or I-F, or subtypes II, III, IV, V, and VI is considered to be nonlethal for Equidae. Occasional limited outbreaks of clinical encephalomyelitis in horses from infection with sylvatic variant I-E viruses have been documented and VEE attenuated virus, strain TC-83, has been used effectively to stop recent outbreaks (14,15).

Diagnosis [top](#)

Field Diagnosis [top](#)

A field diagnosis of VEE can rarely be made unless an epizootic of encephalitic disease is in progress and a prior etiologic diagnosis of VEE has been made. Seasonality of the disease and association with large populations of mosquitoes would suggest a diagnosis of arboviral encephalomyelitis. The initial signs of VEE may go undetected. When signs of encephalitis predominate, the disease in equines is indistinguishable from other arboviral equine encephalomyelitides, such as Eastern equine encephalomyelitis (EEE) and Western equine encephalomyelitis (WEE) (3,6,8,13,15). In contrast to EEE or WEE, herd morbidity and mortality with VEE are high (1,5).

Specimens for the Laboratory [top](#)

Specimens for diagnosis are heparinized blood, serum (paired [acute and convalescent] sera if animal survives), and half the brain and piece of pancreas unfixed and a completed set of tissues in 10 percent formalin, if the animal dies.

Laboratory Diagnosis [top](#)

A specific diagnosis can be made only by laboratory procedures, namely, virus isolation or demonstration of a specific rise in hemagglutination-inhibiting or neutralizing antibody with paired (acute and convalescent) sera. Frequently, animals die before a convalescent serum can be obtained. Experimental studies and field experiences have shown that viremia terminates before signs of clinical encephalitis are exhibited by VEE virus-infected equines. In this case, the highest probability of successful viral isolation is obtained by taking sera from other horses with marked elevations of body temperature that are in the vicinity of the encephalitic horse (5,13-15). Virus may also be isolated from brain, pancreas, or whole blood of dead or dying horses, but with a lower frequency of success (7,13,15). Virus is isolated by the intracranial inoculation of suckling mice or in various cell culture systems.

Histopathologic lesions consistent with a diagnosis of VEE are a diffuse necrotizing meningoencephalitis that ranges from a slight perivascular mixed cellular reaction to marked vascular necrosis with hemorrhages, gliosis, and frank neuronal necrosis (9,11). Lesions are usually most severe in the cerebral cortex and become progressively less severe toward the cauda equina. The degree and severity of the CNS lesions vary with the progression and duration of the clinical signs. Necrotic lesions may involve the adrenal cortex, liver, myocardium, and the walls of small and medium blood vessels (7,9-11,14,15).

Differential Diagnosis [top](#)

A variety of diseases may produce signs that resemble one or more of the clinical signs of VEE infection, but since no clinical sign (including encephalitis) is pathognomonic for VEE, an all-inclusive list of differential diagnoses is virtually impossible to provide. A list of the more obvious diseases includes EEE, WEE, and other arboviral encephalomyelitides; African horse sickness; rabies; intoxications; botulism; hepatoencephalopathy; and trauma. During the Texas epizootic, VEE (confirmed) was presumptively diagnosed as equine infectious anemia, colic, or shock, and so any condition that would produce fever and depression, with or without signs of CNS involvement, would need to be considered in the differential diagnosis.

Vaccination [top](#)

An attenuated VEE virus vaccine has been used in many areas of the Americas, both to combat the disease during an epizootic and to administer preventive vaccination in nonepizootic zones where a high risk of infection is present (5,10,12,13,15). Although preexisting neutralizing antibodies to EEE and WEE viruses may interfere with the neutralizing antibody response to VEE virus

vaccination, the interference is not sufficient to affect immunity (4). Simultaneous vaccination with VEE attenuated virus and EEE-WEE inactivated virus produces a VEE neutralizing antibody response equivalent to that produced with the administration of attenuated VEE vaccine alone (4). An inactivated trivalent EEE-VEE-WEE virus vaccine has been shown to immunize equine recipients effectively (2).

Control and Eradication [top](#)

During epizootics, restriction of horse movement between the epizootic zone and noninfected areas is important to control the spread of VEE. Because of the high levels of VEE viremia in Equidae ($>10^{5.5}$ infectious virions/ml of blood), introduction of infected animals into noninfected areas readily establishes new foci of infection. However, control of movement of the equine population is not sufficient to curb the spread of VEE (5,10,13,15).

Mosquito control measures such as aerial spraying with ultralow volumes of insecticides have been instituted during epizootics. Vector control in the absence of other control measures can do little more than slow the spread of VEE and decrease its severity in the human population (5,10,13,15). Physical disruption or insecticide treatment of the aqueous larval habitats also can reduce adult mosquito populations.

For adequate epizootic control, the preceding measures must be accompanied by a large-scale equine immunization program (5,10,13,15).

Owing to the absence of clinical VEE in the United States as well as concerns about seropositivity in vaccinated equines involved in international movement, it has been suggested by veterinary researchers and regulatory personnel that routine vaccination with VEE virus vaccines should be discontinued. However, vaccines should be made available and used during a VEE emergency.

Public Health [top](#)

Human infections resulting from bites of infected mosquitoes occur tangentially to equine infections. Transmission can also occur by exposure to aerosolized infective material. In human beings, a flulike syndrome predominates accompanied by high fever and frontal headache. Human deaths may occur in the young or the aged.

GUIDE TO THE LITERATURE [top](#)

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