

Eastern Equine Encephalomyelitis, Western Equine Encephalomyelitis and Venezuelan Equine Encephalomyelitis

Sleeping Sickness

Eastern Equine Encephalomyelitis (EEE) –Eastern Equine Encephalitis, Eastern Encephalitis

Western Equine Encephalomyelitis (WEE) –Western Equine Encephalitis

Venezuelan Equine Encephalomyelitis (VEE) –Peste Loca, Venezuelan Equine Encephalitis, Venezuelan Equine Fever

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Importance

Eastern, Western, and Venezuelan equine encephalomyelitis are mosquito-borne, viral infections that can cause severe encephalitis in horses and humans. Some of these viruses also cause disease occasionally in other mammals and birds. No specific treatment is available, and depending on the virus and host, the case fatality rate may be as high as 90%. As a result of vaccination, severe Eastern (EEE) and Western (WEE) equine encephalomyelitis epidemics no longer occur regularly in the U.S., but sporadic cases and small outbreaks are still seen. Epidemic Venezuelan equine encephalomyelitis (VEE) viruses continue to emerge periodically in South America, and sweep through equine and human populations. One two-year VEE epidemic, which began in 1969, extended from South America to the southern U.S., and caused an estimated 38,000-50,000 cases in equids. Epidemic VEE viruses are also potential bioterrorist weapons.

Etiology

Eastern, Western and Venezuelan equine encephalomyelitis result from infection by the respectively named viruses in the genus *Alphavirus* (family *Togaviridae*). In the human literature, the disease is usually called Eastern, Western or Venezuelan equine encephalitis rather than encephalomyelitis.

Eastern equine encephalomyelitis virus

The numerous isolates of the Eastern equine encephalomyelitis virus (EEEV) can be grouped into two variants. The variant found in North America is more pathogenic than the variant that occurs in South and Central America.

Western equine encephalomyelitis viruses

The Western equine encephalomyelitis virus (WEEV) is closely related to some other alphaviruses including Sindbis, Ft. Morgan Aura and Highlands J viruses; however, these viruses are considered to be distinct species. Only WEEV is considered in this factsheet, but some related viruses have also been associated with disease.

Venezuelan equine encephalomyelitis viruses

The Venezuelan equine encephalomyelitis complex contains at least six viral subtypes, I to VI. Subtype I, the Venezuelan equine encephalomyelitis virus (VEEV), is divided into five antigenic variants or serovars, AB to F. Some of the other five subtypes also have official species names; subtype II is known as Everglades virus, subtype III as Mucambo virus, and subtype IV as Pixuna virus.

VEE complex viruses are divided into epizootic (or epidemic) and enzootic (or endemic) groups. The epizootic viruses, which are amplified in equines and are responsible for most epidemics, are found in VEEV subtypes I-AB and I-C. The remaining viruses, including VEEV I-D, VEEV I-E and variants in subtypes II-VI are enzootic (sylvatic) subtypes. These viruses are generally found in limited geographic areas, where they usually occur in natural cycles between rodents and mosquitoes. The enzootic subtypes are typically nonpathogenic for horses, and are not amplified in this host; however, in 1993 an enzootic I-E variant was responsible for an outbreak of VEE among horses in Mexico.

Geographic Distribution

The Western, Eastern and Venezuelan encephalomyelitis viruses occur in North, Central and South America.

WEEV has been isolated from Argentina to western Canada. In the U.S., this virus is found west of the Mississippi. The North American EEEV variant occurs in eastern Canada and all U.S. states east of the Mississippi. It has also been isolated from Arkansas, Minnesota, South Dakota and Texas. The South American variant occurs in parts of Central and South America, particularly along the Gulf coast. Most isolates in the Caribbean belong to the North American EEEV group, but the South American variant can also be found.

Epizootic VEE viruses (VEEV I-AB and I-C) are found in South and Central America. Most VEE epidemics occur in northern and western South America, but

some may spread into adjacent countries, including the U.S. Enzootic VEE viruses have been found in Mexico, parts of the U.S., and South and Central America.

Transmission

Eastern and Western equine encephalomyelitis

Eastern and Western encephalomyelitis viruses normally cycle in bird populations, and are transmitted mainly by mosquitoes. Neither virus can survive outside the host.

EEEV occurs regularly in birds and mosquitoes in some wetlands. How this virus overwinters is unknown, but several mechanisms, including persistence in reptiles and vertical transmission in mosquitoes, have been suggested. Although EEEV can be isolated from more than 25 species of mosquitoes, the most important vector in this enzootic cycle is *Culiseta melanura*, a mosquito that primarily feeds on birds. During some years, EEEV is transmitted to mammalian hosts by bridge vectors, mosquitoes that feed on both birds and mammals. Bridge vectors for EEEV include *Coquilletidia perturbans* and members of the genera *Aedes*, *Ochlerotatus* and *Culex*. EEEV can also be found in the introduced species *Aedes albopictus* (the Asian tiger mosquito), and limited evidence suggests this mosquito might be a particularly efficient vector. In addition, EEEV can occur in chicken lice, chicken mites (Dermanyssidae) and assassin bugs; chicken mites can transmit the virus experimentally. Horses, humans and other mammals are generally considered to be incidental (dead end) hosts, but some horses develop a transient viremia greater than the minimal titer to infect a mosquito. Horses might be able to temporarily amplify EEEV where equine and mosquito populations are concentrated. In birds, EEEV is occasionally spread by non-arthropod-borne routes. During outbreaks of disease in game birds, infections are introduced by mosquitoes but spread in the flock mainly by feather picking and cannibalism. In humans, this virus may be able to cross the placenta.

WEEV primarily cycles between passerine birds and culicine mosquitoes, with a variety of mammals as incidental hosts. *Culex tarsalis* appears to be the most important vector; other significant vectors include *Aedes melanimon*, *Aedes dorsalis* and *Aedes campestris*. WEEV can also cycle between the mosquito *A. melanimon* and blacktail jackrabbits (*Lepus californicus*), probably after infection from the bird/mosquito cycle. Horses infected with this virus do not develop a significant viremia, and are true dead-end hosts. It is possible that WEEV overwinters in reptiles. Infections have been reported in snakes, frogs, and tortoises, and experimentally infected garter snakes could transmit WEEV to mosquitoes. Vertical transmission or other mechanisms might also be responsible for overwintering. In humans, WEEV can cross the placenta, and congenitally infected infants have been reported.

Venezuelan equine encephalomyelitis

Enzootic VEE viruses usually cycle between mosquitoes in the genus *Culex* and sylvatic rodents or marsupials. Birds are involved in a few cycles. Humans and horses are incidental (dead end) hosts for the enzootic subtypes.

The natural host for the epizootic VEE subtypes, between epidemics, is unknown. It is possible that these subtypes emerge from enzootic viruses. Horses are the main amplifiers for epizootic VEEV during outbreaks. Other mammals do not seem to be epidemiologically significant in transmission, although sufficient viremia to infect mosquitoes has been reported in humans and the occasional cases in cattle and pigs. Many species of mosquitoes and other hematogenous insects can transmit epizootic VEEV. Efficient vectors include arthropods in the genera *Aedes*, *Anopheles*, *Culex*, *Mansonia*, *Psorophora* and possibly *Ochlerotatus*. Blackflies may be important mechanical vectors for epizootic strains during some outbreaks. Mites can also transmit these viruses mechanically. Ticks including *Amblyomma cajennense* and *Hyalomma truncatum* can be infected by both enzootic and epizootic VEEV strains.

Horses can shed epizootic VEEV in body fluids, and some authorities suggest that these viruses might be spread occasionally by direct contact or via aerosols. However, natural transmission between horses or from horses to humans has not been reported. In some cases, people have been infected by exposure to aerosolized debris from the cages of infected laboratory rodents, or after laboratory accidents. Person-to-person transmission has not been reported; however, VEEV can be found in pharyngeal secretions in humans and is stable when aerosolized. It can also cross the placenta in pregnant women.

Disinfection

EEE and WEE viruses do not persist in the environment, but VEEV may be found in dried blood and exudates. All three alphaviruses are susceptible to many common disinfectants including 1% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde and formaldehyde. They can also be destroyed by moist or dry heat, as well as by drying.

Infections in Humans

Incubation Period

Although sources vary, the incubation period can be 1 to 6 days for VEE, and is usually 5 to 10 days for WEE or EEE.

Clinical Signs

Eastern equine encephalomyelitis

Eastern equine encephalitis usually begins abruptly, with fever, chills, myalgia and arthralgia. This prodrome

is often but not always followed within a few days by neurologic signs. The symptoms of encephalitis may include headache, irritability, focal neurologic deficits, neck stiffness, confusion, somnolence or stupor, disorientation, tremors, seizures and paralysis. Some patients enter a coma. Abdominal pain, vomiting and diarrhea may also be seen. Children sometimes develop generalized edema, facial edema or periorbital edema, together with paralysis. A biphasic illness, with apparent recovery from the prodromal illness before the onset of encephalitis, may also be seen in young patients. In infants, central nervous system (CNS) disease can occur suddenly, without prodromal signs. The mortality rate for EEE encephalitis is high, and permanent brain damage, often severe, occurs in many survivors. However, people who do not develop neurologic signs usually recover completely after an illness of 1 to 2 weeks. Subclinical infections also occur.

Western equine encephalomyelitis

Western equine encephalitis resembles EEE but is usually asymptomatic or mild in adults, with nonspecific signs of illness and few deaths. The symptoms usually appear abruptly and may include fever, chills, headache, nausea, vomiting, anorexia and malaise. Respiratory signs are occasionally seen. Many adults do not develop other symptoms, but in more severe cases, neurologic symptoms similar to EEE can develop within several days. Patients who recover from encephalitis can have fatigue, headaches, irritability or tremors for up to two years. Although most adults recover completely, permanent neurological damage is possible. More severe disease can be seen in children, particularly infants under a year of age. Permanent, severe neurological damage occurs most often in infants under three months. Although other sequelae are uncommon in children over a year of age, persistent seizures develop in 25-33% of children who have convulsions during their illness.

Venezuelan equine encephalomyelitis

In humans, VEE is usually an acute, often mild, systemic illness. The clinical signs may include fever, chills, generalized malaise, severe headache, photophobia and myalgia particularly in the legs and lumbosacral region. Coughing, sore throat, nausea, vomiting and diarrhea may also be seen. Approximately 4% of children develop mild to severe encephalitis; neurologic disease occurs in less than 1% of symptomatic adults. VEE usually resolves within two weeks, with acute symptoms subsiding after 4 to 6 days, and deaths are rare. In pregnant women, this disease can affect the fetus; fetal encephalitis, placental damage, abortion/ stillbirth or severe congenital neurologic anomalies may be seen. Infections caused by enzootic VEE strains may be less virulent than those caused by epizootic viruses.

Communicability

WEE and EEE viruses are not found in the blood or cerebrospinal fluid (CSF) after the symptoms appear, and only low titers develop during the viremic phase. Humans do not transmit these viruses to mosquitoes, and person-to-person transmission is not seen. Person-to-person transmission is theoretically possible for VEE, but it has not been reported in natural cases. Humans with VEE can infect mosquitoes for approximately 72 hours. All three viruses seem to be able to cross the placenta in pregnant women.

Diagnostic Tests

Eastern, Western and Venezuelan equine encephalitis are often diagnosed by serology. Under some circumstances, these diseases can also be diagnosed by virus isolation, or by the detection of antigens or nucleic acids in tissues and body fluids.

EEEV is difficult to find in blood or CSF, but it can sometimes be detected in serum during the prodromal stage. At autopsy, this virus can be found in the brain and other tissues. EEEV can be isolated in A549 and MRC-5 cell cultures. Viral antigens may be identified in cultures by immunofluorescence or enzyme-linked immunosorbent assay (ELISA), and viral RNA can be detected with nucleic acid hybridization or reverse transcription polymerase chain reaction assay (RT-PCR). Some laboratories may also identify the virus directly in tissues by RT-PCR. A definitive diagnosis can be made by serology if specific IgM is found in rapid tests such as the ELISA, or if there is greater than a fourfold increase between paired titers in the hemagglutinin inhibition, immunofluorescence, virus neutralization or complement fixation tests. A single high titer may be used for presumptive identification.

WEEV is also difficult to find in the blood or CSF, but can be found in brain and other tissues at autopsy. Throat swabs are occasionally positive. WEEV can be isolated in embryonated eggs (Vero cell plaque assay) or mice. The identification of the virus in cultures, detection of nucleic acids by RT-PCR, and serologic testing is similar to EEEV.

VEEV can be isolated from blood, CSF or throat swabs. During the febrile stage of the illness, antigen-capture ELISAs can often detect VEEV antigens in the blood. This test is generally not useful during the encephalitic stage. Diagnosis of this infection by virus isolation, serology or RT-PCR is similar to EEE and WEE.

Treatment

Treatment consists of supportive care. Mechanical ventilation, as well as other measures, may be necessary in some cases. The efficacy of antiviral drugs such as ribavirin is currently unknown.

Control

Measures to prevent mosquito bites, including the use of repellants and protective clothing (i.e. long pants and long-sleeved shirts) can reduce the risk of infection. Permethrin can also be applied to clothing to discourage bites. Outdoor exposure should be limited at times when mosquitoes are active, especially during outbreaks. Mosquito abatement programs such as habitat modification and/or the application of larvicides or adulticides reduce the risk of human infection. Improved irrigation management has decreased vector populations in California, where a primary mosquito vector for WEEV is associated with irrigation systems. Cases in horses can provide an early warning for human disease. Surveillance programs in birds (including sentinel chickens) are also helpful in predicting EEE outbreaks. Controlling epizootic VEE in horses can help prevent human infections.

Precautions should be taken to prevent exposure to body fluids when performing necropsies on horses. Containment level 3 is required for work with EEEV, WEEV or VEEV in the laboratory. Investigational vaccines may be available for people at high risk of infection. In the U.S., these vaccines are distributed by U.S. Army Special Immunizations Program. Access to the investigational VEE vaccine has become highly restricted for civilians; however, a new, genetically engineered vaccine is in development.

Morbidity and Mortality

Eastern equine encephalomyelitis

In North America, the annual incidence of EEE varies from 0 to 36 cases, with an average of seven cases per year. Most cases are seen in people over 55 and children younger than 15. The ratio of encephalitis to asymptomatic infection or nonspecific illness may be as high as 1:17 in children, and as low as 1:40 in adults. During one outbreak in New Jersey, the ratio of apparent to inapparent infection was 1:23, or one clinical case per 1000 population. Clinical cases of EEE are often severe. Estimates of the case fatality rate vary from 30% to 70% (survival has improved in recent years), and permanent neurologic deficits can occur in survivors. Only 10% of patients are estimated to recover fully, and many survivors with severe impairment die within a few years. Permanent neurologic damage and death are particularly common in children.

Western equine encephalomyelitis

The annual incidence of WEE is highly variable. Between 1955 and 1984, an average of 34 confirmed cases were reported annually in the U.S., with a range of 0 to 172. From 1964 to 1992, an average of 22 cases were reported each year. However, severe epidemics were reported in the past, with more than 3000 cases in the U.S. and Canada in 1941, and 375 confirmed cases and nine

deaths reported in California in 1952. Overall, the case:infection ratio is estimated to be approximately 1:1000 in adults, 1:58 in children from 1 to 4 years of age, and 1:1 in infants up to a year of age.

WEE is usually much milder than EEE, with an overall case fatality rate of 3-4%; however, during the 1941 epidemic, the case fatality rate was 8-15%. Most infections in adults are asymptomatic or mild, and neurologic disease is not seen. Infections in children (particularly infants under one year of age) and the elderly can be severe. Approximately 5-30% of young patients, and 56% of infants under a month of age, have permanent neurologic damage. With the exception of seizures, serious sequelae are uncommon in children over a year of age.

Venezuelan equine encephalomyelitis

VEE can be widespread in human populations during epidemics; more than 10% of the population in an area may be affected. Between epidemics, sporadic cases of VEE are caused by enzootic viruses. Humans are highly susceptible to VEE; approximately 90-100% of exposed individuals become infected, and nearly 100% develop clinical signs. However, most infections are mild. Less than 1% of adults develop encephalitis, with approximately 10% of these cases ending in death; the overall case fatality rate in adults is less than 1%. Very young or elderly patients are more likely to develop severe infections. Encephalitis, with a case fatality rate of 35%, occurs in approximately 4% of children less than 15 years of age. More severe disease, with a higher incidence of neurologic signs, might occur in both children and adults after a biological attack with aerosolized virus.

Infections in Animals

Species Affected

Equine encephalomyelitis viruses primarily cause disease in equids, but infections or clinical cases are occasionally seen in other animals.

Eastern equine encephalomyelitis

Birds are the principal reservoir hosts for EEEV. Most infections in birds appear to be asymptomatic; however, disease has been reported in chukar partridges, pheasants, egrets, glossy ibises (*Plegadis falcinellus*), rock doves, house sparrows, psittacine birds, ratites (emus, ostriches), African penguins and whooping cranes.

This virus mainly causes disease in horses, but occasional cases of encephalitis have also been reported in sheep, cattle, deer, South American camelids (llamas and alpacas) and pigs. In addition, infections have been seen in dogs, goats, bats and small mammals including rodents, as well as reptiles and amphibians. Experimental infections have been reported in a variety of species including rabbits, calves and swine.

Western equine encephalomyelitis

Birds are the usual reservoir hosts for WEEV, but this virus can also cycle in jackrabbit populations. WEEV causes disease in horses and some species of birds such as emus. Asymptomatic infections have been reported in some wild mammals including squirrels, as well as snakes, frogs, and tortoises.

Venezuelan equine encephalomyelitis

Rodents are usually the natural hosts for enzootic VEE viruses, but birds are involved in a few cycles. The maintenance host for epizootic VEEV between outbreaks is unknown; during epidemics, these viruses are amplified mainly in equids.

Epidemic VEE viruses can cause serious disease in horses, mules, burros, donkeys and zebras. During epizootics, fatal cases have also been reported in domesticated rabbits, dogs, goats and sheep. Cattle, pigs, bats and opossums can also be infected. Experimental infections have been reported in non-human primates, guinea pigs, mice and hamsters; some isolates are fatal for laboratory rodents, although they are usually asymptomatic in their normal rodent hosts.

Incubation Period

The incubation period for WEE or EEE is five to 14 days. The first symptoms of VEE can occur one to five days after infection, but neurologic signs usually appear in approximately five days.

Clinical Signs

Eastern and Western equine encephalomyelitis in horses

Eastern and Western equine encephalomyelitis are very similar in horses, although the course of EEE may be shorter. The initial clinical signs include fever, anorexia and depression. In severe cases, this prodromal stage is followed by encephalitis; altered mentation, hypersensitivity to stimuli, involuntary muscle movements, impaired vision, aimless wandering, head pressing, circling, an inability to swallow, ataxia, paresis, paralysis and convulsions may be seen. Periods of excitement or intense pruritus can also occur. Laterally recumbent animals sometimes have a characteristic “paddling” motion. In addition, some animals may develop diarrhea or constipation, or have significant weight loss. Some affected horses die, particularly when infected with EEE, within a few days. Horses that recover from encephalitis have a high incidence of residual deficits. Both EEE and WEE also cause asymptomatic infections or mild disease without neurologic signs.

Venezuelan equine encephalomyelitis in horses

Enzootic VEE viruses usually infect horses subclinically or cause only mild symptoms. Epizootic subtypes may cause a syndrome resembling EEE and

WEE; in this form, a febrile prodrome with depression, tachycardia, and inappetence is followed by neurologic signs. Weakness and ataxia may be seen early, and can be followed by overt neurologic signs such as muscle spasms, incoordination, aimless wandering, head pressing, chewing movements, incoordination, loss of reflexes, circling and convulsions. Paddling can occur in laterally recumbent animals. Some animals also have diarrhea and colic. Death can occur within hours after the onset of neurologic signs or after protracted disease accompanied by dehydration and extreme weight loss. Sudden death is also reported. Animals that recover may have permanent neurologic signs. Alternatively, epizootic strains of VEE may cause generalized acute febrile disease without neurologic signs. The symptoms may include fever, weakness, depression, anorexia, colic and diarrhea. Asymptomatic infections also occur.

Equine encephalomyelitis viruses in other mammals

Neurologic disease caused by EEEV has been reported in llamas, alpacas, deer, sheep, cattle and pigs. In EEEV-infected llamas and alpacas, the symptoms have included fever, lethargy, ataxia, vestibular signs, cranial nerve deficits, twitching of the head and neck, torticollis, recumbency, opisthotonos and seizures. Symptoms reported in EEEV-infected deer include emaciation, dyspnea, excessive salivation, and neurological signs such as confusion, ataxia, head tilt, circling and blindness. Some infected deer lost their natural fear of humans. EEE was recently reported in a young sheep with initial clinical signs of fever and front limb incoordination, gradually progressing to forelimb and hindlimb paralysis with muscle fasciculation and paddling. This animal remained alert and maintained a good appetite until it was euthanized.

Fatal VEE has been reported in various mammals including rabbits, goats, dogs and sheep during epizootics. Some VEE viruses also kill laboratory rodents including hamsters, guinea pigs and mice; however, natural reservoir hosts for enzootic strains usually remain asymptomatic. Experimentally infected, nonhuman primates develop a nonspecific febrile illness similar to human disease.

Western and Eastern equine encephalomyelitis viruses in birds

Western and Eastern equine encephalomyelitis virus infections are asymptomatic in most species of birds, but serious or fatal infections can occur in some species.

EEE outbreaks have been reported in several avian species, with symptoms ranging from neurological signs to hemorrhagic enteritis. In pheasants, the symptoms may include fever, depression, weakness, profuse diarrhea, and neurological signs such as incoordination, circling, tremors, and partial or complete paralysis of the legs. In the late stages of the disease, the birds cannot stand but can still move their wings. Chukar partridges infected with EEEV

are dull and listless, and are typically found with ruffled feathers, sitting on their hocks with the beak on the ground. Whooping cranes may have lethargy, ataxia and paresis of the legs and neck. In a colony of African penguins, the early symptoms included anorexia, mild lethargy and intermittent vomiting, and were followed by persistent regurgitation, mild diarrhea, ataxia, and seizures, as well as voluminous diarrhea in a few birds. Some birds became recumbent. Most penguins recovered, but subtle, intermittent ataxia persisted in some.

This virus can also cause disease without obvious neurologic signs in some species of birds. EEEV-infected raptors develop hemorrhagic enteritis; the characteristic clinical signs include depression, diarrhea (which may be blood-stained) and regurgitation. Bloody diarrhea and vomiting of bloodstained material may be seen in the final stage. The onset of disease is usually rapid in this species, and the mortality rate is high. EEEV can also cause depression, somnolence, decreased egg production and death in turkeys. Experimentally infected, two-week-old chickens developed severe depression and somnolence, followed by abdominal distention and growth retardation. Some of these chickens died. In contrast, infections are usually asymptomatic in adult chickens. EEEV has also been isolated from psittacine birds with viral serositis.

WEE has been linked less often with disease in birds. In emus, WEEV can cause mild to severe disease, with symptoms of anorexia, lethargy, weight loss, watery diarrhea, and neurological signs including gait abnormalities, somnolence, muscle tremors, head tilt and paralysis. Lateral recumbency with paddling has been reported. Some infections have been fatal; some birds died during the illness, while sudden death was reported in others. In turkeys, WEEV can cause a drop in egg production, with an increase in the number of shell-less and small, pale eggs.

Communicability

Hosts that develop viremia sufficient to infect mosquitoes include some species of birds infected with WEEV, EEEV or a few enzootic strains of VEEV; rodents infected with enzootic strains of VEE viruses; horses infected with epizootic VEEV and possibly EEEV; jackrabbits infected with WEEV; and possibly reptiles infected with EEEV or WEEV. Some sources suggest that VEEV-infected cattle and pigs may also be able to transmit the virus to mosquitoes.

Direct transmission of EEEV has been seen only in birds. Game birds can spread this virus by feather picking and cannibalism. Infected emus also shed EEEV in secretions and excretions. VEEV can be found in the body fluids of horses, and transmission by direct contact or aerosols is theoretically possible in this species. However, natural transmission of VEEV between horses or from horses to humans has not been seen. Infected laboratory rodents can also shed this virus, and people

have been infected after exposure to aerosolized debris from cages. There is no evidence that WEEV is contagious in any species.

Post Mortem Lesions

The gross lesions of equine encephalitis are usually nonspecific. Horses with VEE may have no lesions in the CNS or there may be extensive necrosis with hemorrhages. Necrotic foci are sometimes seen in the pancreas, liver and heart of horses infected with this virus, but in general, the extracranial lesions are too variable to be diagnostically useful. Congestion of the brain and meninges is found in some cases of EEE and WEE. Antemortem trauma can result in ecchymotic hemorrhages with any of the three viruses. Most birds affected by EEE or WEE have encephalitis, but hemorrhagic enteritis with multiple petechiae on the viscera is reported in EEE-infected emus.

Microscopic analysis of the brain tissue is often diagnostic. The typical lesion is severe inflammation of the gray matter; neuronal degeneration, infiltration by inflammatory cells, gliosis, perivascular cuffing and hemorrhages may be seen. WEE, EEE and VEE sometimes differ in the location and pattern of the lesions in the brain.

Diagnostic Tests

Eastern and Western equine encephalomyelitis

In horses, Eastern and Western equine encephalomyelitis can be diagnosed by serology. Commonly used tests include virus neutralization (the plaque reduction neutralization or PRN test), hemagglutination inhibition, ELISA and complement fixation. A definitive diagnosis usually requires a fourfold rise in titer in paired samples. The identification of specific IgM in the ELISA is also useful. A presumptive diagnosis may be obtained with a single sample, particularly when a combination of serologic tests is used. Cross-reactions can occur between EEE and WEE antibodies in the complement fixation and hemagglutination inhibition tests; however, these viruses can be differentiated by virus neutralization or antigen-capture ELISA.

In horses, EEE may also be diagnosed by virus isolation. This virus can usually be recovered from the brain of infected horses; other tissues such as the liver or spleen may be positive. Virus isolation from herd mates can be helpful, as viremia usually occurs early in the infection. Virus isolation is rarely successful in WEE-infected animals. EEE and WEE viruses can be isolated in newborn mice, embryonating chicken eggs, newly hatched chicks or cell cultures including primary chicken or duck embryo fibroblasts, African green monkey kidney (Vero), rabbit kidney (RK-13), and baby hamster kidney (BHK-21) cells. Virus identity can be confirmed by the detection of antigens with immunofluorescence, ELISA

or virus neutralization tests, or by the detection of nucleic acids with nucleic acid hybridization or RT-PCR. At necropsy, EEEV or WEEV may be found in tissues, particularly the brain, with immunohistochemistry, ELISA or RT-PCR.

Similar tests can be used to diagnose EEE infections in other mammals. Clinical EEE or WEE is relatively difficult to diagnose in birds. Avian infections are usually diagnosed by virus isolation, but serology (hemagglutination inhibition), immunohistochemistry to detect viral antigens in the brain, or RT-PCR can also be helpful.

Venezuelan equine encephalomyelitis

VEE can be diagnosed by virus isolation or serology. VEEV can often be recovered from the blood during the early, febrile stage of disease, but animals with neurologic signs are not usually viremic. This virus is sometimes isolated from the brain at necropsy; however, if the illness is prolonged, it may disappear from the CNS before death. VEEV is also found occasionally in the pancreas or other tissues. VEE viruses can be isolated in guinea pigs, hamsters, mice, embryonated chicken eggs or cell lines including Vero, RK-13, BHK-21 and duck or chicken embryo fibroblasts. These viruses can be identified by complement fixation, hemagglutination inhibition, virus neutralization or immunofluorescence assays. Subtypes can be characterized by immunofluorescence, differential virus neutralization (PRN) tests or nucleic acid sequencing.

VEE can also be diagnosed by serology. Serologic tests include virus neutralization, complement fixation, hemagglutination inhibition and ELISAs. Definitive diagnosis requires a fourfold increase in paired titers. Because antibodies develop early in this disease, a fourfold rise may not be seen in horses with encephalitis. In this case, paired samples taken from febrile herd mates may be helpful. In horses not recently vaccinated with a live virus, specific IgM in the ELISA test also suggests exposure. Cross-reactions can occur between VEE, EEE and WEE viruses in the hemagglutination inhibition test. Some animals infected with epizootic VEEV may have pre-existing antibodies to enzootic variants of VEE.

Treatment

There is no specific treatment for WEE, EEE or VEE. Supportive care including fluid therapy, electrolytes, anticonvulsants, anti-inflammatory therapy and good nursing can be helpful. During one outbreak in penguins, adult birds recovered with intensive supportive care including nutritional support via orogastric intubation, metoclopramide to decrease regurgitation, anticonvulsants, and fluids. Mild to severe residual signs may be seen in treated animals that recover; the severity of the sequelae varies with the virus and host species.

Control

Equine vaccines are available for EEE, WEE and VEE in some countries. Some birds are also vaccinated

for EEE. Where they are available, live attenuated VEE vaccines are more effective in preventing or controlling epizootic VEE than inactivated multivalent vaccines. The risk of infection can also be reduced by housing horses in screened barns, particularly during the hours of high mosquito activity. Repellents and fans can be helpful.

Because equids are the primary amplifiers for epizootic VEEV, these outbreaks are controlled by movement controls on equids, mosquito control measures in the environment, and vaccination of equids.

Morbidity and Mortality

Eastern and Western equine encephalomyelitis

WEE is reported more often than EEE. Of 2620 cases of encephalitis with specific diagnoses between 1956 and 1970, 2015 were caused by WEEV and 605 by EEEV. Before vaccines were developed for these diseases, outbreaks occurred regularly in the U.S. and Canada. These epidemics varied in severity; however, one WEE outbreak in 1937-38 affected more than 350,000 horses and mules in the U.S. and Canada, and a 1947 EEE outbreak killed an estimated 12,000 horses in Louisiana. Currently, WEE tends to occur as sporadic cases of encephalitis in horses, scattered over a wide area. Clinical cases of EEE are usually more clustered. Occasional EEE epidemics are still seen, particularly in the southern U.S., where the long mosquito season may outlast the short duration of immunity from vaccination.

The case fatality rate for EEE can be as high as 90% in horses with encephalitis. WEE is more likely to be asymptomatic or mild; the case fatality rate is usually 20-30%, although 50% of clinically affected equids died in the 1930 outbreak. EEE infections in other mammals such as sheep, cattle, pigs and South American camelids are reported only sporadically. One study reported that alpacas and llamas had a case fatality rate of 89%. The morbidity and mortality rates from EEE in white-tailed deer are unknown; asymptomatic infections were reported in Georgia, but several affected deer were recently seen in Michigan.

EEE can also cause significant morbidity and mortality in some birds. The case fatality rate in EEEV-infected pheasants is 5-75%. In emus, the morbidity rate was 76% in one outbreak, and the case fatality rate was 87%. High mortality has also been reported in EEEV-infected whooping cranes and glossy ibises. Experimentally infected bobwhite quail and white-throated sparrows usually survive, but mortality rates can be higher in red-winged blackbirds, house sparrows, cowbirds, and grackles. In one penguin colony, the prevalence of infection was 64%, and 93% of clinically affected birds recovered with intensive supportive care. Clinical disease is reported less often in WEEV-infected birds. The morbidity rate in eight flocks of WEEV-infected emus varied from 15% to 50%, and approximately 9% of the birds died.

Venezuelan equine encephalomyelitis

VEE epidemics typically begin in horses, with human cases developing weeks later. Unlike EEE and WEE outbreaks, which usually end with the first freeze, VEE epidemics can last for several years. Epizootic subtypes of VEE can cause significant morbidity and mortality in equids; the infection rate can be as high as 90%, and the morbidity rate varies from 10-40% in some areas to 50-100% in others. The case fatality rate in horses is 38-90%. Fatal infections have also been reported in goats, rabbits, dogs and sheep during epizootics, as well as in laboratory rodents infected with some isolates.

Most enzootic VEE subtypes do not result in serious disease or deaths in horses, but limited outbreaks of encephalitis have been reported with some variants.

Internet Resources

- Centers for Disease Control and Prevention (CDC)
Information on Arboviral Encephalitides.
<http://www.cdc.gov/ncidod/dvbid/arbtor/arbdet.htm>
- Food and Agriculture Organization of the United Nations (FAO). Manual for the Recognition of Exotic Diseases of Livestock
<http://www.spc.int/rahs/>
- Public Health Agency of Canada, Material Safety Data Sheets
<http://www.phac-aspc.gc.ca/msds-ftss/index.html>
- Medical Microbiology
<http://www.gsbs.utmb.edu/microbook>
- The Merck Manual
<http://www.merck.com/pubs/mmanual/>
- The Merck Veterinary Manual
<http://www.merckvetmanual.com/mvm/index.jsp>
- United States Animal Health Association.
Foreign Animal Diseases
http://www.vet.uga.edu/vpp/gray_book02/fad/index.php
- World Organization for Animal Health (OIE)
<http://www.oie.int>
- Office International des Epizooties (OIE). Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/eng/normes/mmanual/a_summry.htm
- OIE Terrestrial Animal Health Code
http://www.oie.int/eng/normes/mcode/A_summry.htm

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*Link defunct as of 2007