Features of the disease and managing an outbreak.

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Equine Herpesvirus Myeloencephalopathy

Equine herpesvirus 1 (EHV-1) is an important pathogen of horses of all ages that causes abortion in mares, early neonatal disease in foals, and respiratory disease in young horses. The neurological form of EHV-1 (myeloencephalopathy), first described in Norway in 1966, is considered uncommon. Equine herpesvirus-4 (EHV4) has also been associated with abortions and myeloencephalopathy in horses. EHV-1 myeloencephalopathy, defined as an acute and progressive neurologic disorder of horses, more often affects adults than foals. Several outbreaks of EHV-1 myeloencephalopathy were recorded in the United States in 2003.

Etiology: There are five known equine herpesviruses, three are alphaherpesviruses (EHV-1, EHV-3, EHV-4) and two are gammaherpesviruses (EHV-2, EHV-5). Only EHV-1 and EHV-4 have been associated with neurological disease.

Epidemiology: EHV-1 and EHV-4 are enzootic in the equine population. Seroprevalence for EHV-4 is higher than for EHV-1. Infection primarily occurs via the respiratory tract. The neurological form of EHV-1 is rare. EHV-1 mostly causes abortion, neonatal mortality, and neurological disease, while EHV-4 is associated with respiratory disease. Since these are herpesviruses, recrudescence of latent infections is important, and it may explain the occurrence of the disease in closed populations. Spread of the virus is by inhalation or ingestion of viral particles from aerosols, nasal and ocular discharges, from aborted fetuses, and in feces of young animals. The virus remains infective in the environment for up to 2 weeks. The myeloencephalopathic form of EHV-1 has worldwide distribution. In general the neurological disease occurs in association with respiratory disease and abortion, although it also occurs in animals with no previous history of EHV-1 infection. EHV-1 myeloencephalopathy occurs as individual cases or as outbreaks and it has been observed in horses of any age, however, it is infrequent in foals. EHV-1 affects all breeds of horses and other equidae, and it has been reported in a zebra. There is no report that EHV-1 affects mules and donkeys.

Several outbreaks of EHV-1 myeloencephalopathy were recorded in several parts of the United States in 2003. Those outbreaks were unique because of the high morbidity rate. In an outbreak in Ohio for example, of 135 stabled horses, over 46 developed neurological disease. New horses entered the stable one month earlier, and 5-8 days later some horses develop fever, with occasional cough and nasal discharge. Around 5 days after the fever some horses became ataxic and recumbent. Of the 46 affected horses, 14 died or were euthanized. All horses were vaccinated for EHV-1.

Pathogenesis: The pathogenesis of the respiratory and reproductive forms of EHV-1 is not discussed. Following ingestion or inhalation of EHV-1, infective viral particles replicate in the nasopharyngeal epithelium and cells of the lymphoreticular system. Subsequent systemic viral migration occurs via infected mononuclear cells. In the CNS, the vascular endothelium is the primary site of viral infection. The development of neurological signs is the result of vasculitis and thrombosis of arterioles in the brain and spinal cord. The decreased blood flow and abnormal vascular integrity results in hemorrhages, edema, necrosis, and hypoxia, affecting primarily the white matter, but also the gray matter. This description on the pathogenesis of EHV-1 myeloencephalopathy is based on histopathological changes as well as from the unsuccessful isolation of EHV-1 from the neural tissue. It also has been proposed that the ability of EHV-1 to induce neurological disease is the result of endotheliotropism rather than a

neurotropism; however, there is some evidence suggesting that some strains of EHV-1 are neurotropic. In the CNS, the trigeminal ganglia are considered important sites for maintaining the virus in a latent stage, in particular after a recent infection.

The lack of explanation for some horses to develop neurological disease while others do not is suggestive of the presence of different strains of EHV-1. Viral isolation and DNA sequencing of viral isolates from the 2003 U.S. outbreaks suggest the existence of a neurotropic strain of EHV-1.

The severity of the neurological clinical signs appears to be influenced by age, sex, and immunity against EHV-1.

Clinical signs: Neurological signs in general occur 5-10 days after infection. Some animals develop fever, nasal discharge, inappetence, and limb edema 1-2 weeks before they develop neurological signs, while other horses just develop neurological disease. Even is the affected animal has no history of respiratory disease or abortion, often times there is a history of other animals being affected in the farm. Fever is not a consistent finding as affected horses may be hyper-, normo-, or hypothermic depending on the clinical condition. These horses in general develop an acute and progressive symmetric spinal ataxia associated with paresis, indicating white matter dysfunction. Tail and anal tone are weak, and urinary incontinence is also common. The disease can also be asymmetric with hemiparesis or affecting one limb. Most lesions are in the spinal cord although lesions on peripheral nerves have been documented. Hindlimbs are more commonly affected than forelimbs. On neurological examination, these horses have conscious and unconscious proprioceptive deficits. There is spinal ataxia, toe dragging, knuckling, circumduction, pivoting, and spasticity. Severely affected horses also have weakness, paralysis, paraplegia, or tetraplegia. Perineal analgesia or hypalgesia may be noted. Spinal reflexes may be normal or increased. These horses often remain alert unless there are secondary infections or involvement of the brain. Behavioral changes and cranial nerve dysfunction resulting in facial nerve paralysis, nystagmus, strabismus, head tilt, and dysphagia have been reported. Signs of colic may be present, and rectal examination often reveals fecal retention and urinary bladder distension. Urine dibbling may be present, resulting in scalding of the perineum and legs. Because these horses often require bladder catheterization, cystitis is a common complication. Paraphimosis, repeated erections, and vulvar flaccidity may also be present.

Diagnosis: The differential diagnosis for EHV-1 myeloencephalopathy includes West Nile virus encephalomyelitis, equine protozoal myeloencephalitis (EPM), cervical vertebral instability and cervical stenotic myelopathy (wobbler), CNS trauma, rabies, Eastern-Western-Venezuelan

encephalitides, parasite migration, equine degenerative myelopathy (EDM), botulism, meningitis, CNS abscessation, cauda equina neuritis, and intoxication. The clinical history is important to rule out many of these conditions. The presence of animals with history of respiratory disease and abortion is important. Collection and evaluation of the cerebrospinal fluid (CSF) is necessary for ante-mortem diagnosis. These horses often times have a xanthochromic CSF with increased protein concentrations. Isolation of EHV-1 from the CSF, respiratory tract, or buffy coat and/or a four-fold increase in serum neutralizing antibodies to EHV-1 (1-3 weeks apart) is highly suggestive of the disease; however, in most cases a final diagnosis is not reached.

Additional testing includes PCR, immunofluorescent testing of the brain/spinal cord, and ELISA for viral particles.

Pathological findings: Macroscopic lesions in general include hemorrhages in the meninges, brain, spinal cord, and occasionally in the in the spinal nerve roots and cauda equina. Areas of malacia may be present. Microscopically, there is severe multifocal vasculitis, thrombosis, congestion, gray and white matter degeneration, and axonal swelling.

Prognosis: The prognosis of EHV-1 myeloencephalopathy depends on the progression of the disease and whether or not the animal is recumbent. Horses with a rapid progression of the clinical signs or recumbent have a poor prognosis because of the severity of the CNS lesions, the development of decubital ulcers, cystitis, gastrointestinal and respiratory disease, and other of secondary infections. Before electing for euthanasia, however, it is important to consider that some recumbent horses may recover with proper care.

Treatment: An important rule in cases suspected of having an EHV-1 infection is isolation followed by a strict infectious disease protocol. Based on our experience at The Ohio State University, it is our policy that any horse with neurological signs and fever/respiratory disease gets isolated upon arrival. We encourage horses to remain standing. In recumbent animals, is important to maintain them in a sternal position with frequent rolling (4-8 times a day) to avoid decubital ulcers. Maintaining a good caloric and water intake is necessary. Because these horses may develop large colon impactions and fecal retention, laxatives such as mineral oil, bran mashed, and psyllium are indicated. Placing a feeding nasogastric tube may be necessary to provide feeding gruels, water, and electrolytes. Intravenous fluids may also be administered. Manual emptying of the bladder can be accomplished by applying pressure through the rectum or by urinary catheterization. Bladder catheterization should be performed under aseptic conditions with the tubing attached to a closed and sterile collection bag or container. Most of the catheterized horses develop cystitis which can be complicated by bladder necrosis, bladder rupture, nephritis, and sepsis. Manual evacuation of the rectum and administration of enemas may be necessary. Since there is evidence that hemorrhages and edema develop from vasculitis, which may be immune-mediated, the use of corticosteroids is recommended. The

most frequent used drugs are dexamethasone (0.05- 0.25 mg/kg, IV or IM/ once daily) and prednisolone (1-2 mg/kg/day). Dimethyl sulfoxide (DMSO) (1.0 g/kg, IV, once a day for 3 days in a 10% solution) has been advocated for many years. In addition, we also recommend the use of non-steroidal anti-inflammatory drugs, preferable flunixin meglumine (1.0 mg/kg, IV, twice a day). Since these animals are a high risk for developing cystitis as well as other secondary bacterial infections, broad spectrum antimicrobials are highly indicated. Sulfonamides or penicillin G in combination with gentamicin are the most common drugs used. In the Ohio outbreak in 2003, few horses were also treated with the anti-viral drug valacyclovir.

Control and prevention: Isolation of horses with fever and respiratory disease, as well as mares that have aborted is very important in preventing the spread of the disease. Fetuses and fetal membranes should be collected in sealed containers for diagnosis. Bedding and dirt exposed should be disposed of or burnt, and other areas and equipment should be disinfected. Do not vaccinate horses that have been exposed. Unexposed horses should be vaccinated. Exposed horses should also be isolated for 3-4 weeks and kept under close observation for the development of signs of the disease.