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Equine Protozoal Myeloencephalitis

Avery Warschauer Brickson, DVM[†] and Axel Sondhof, DVM^{††}

Disease

Equine protozoal myeloencephalitis (EPM) is a neurologic disease of horses caused by the apicomplexan protozoa *Sarcocystis neurona*, an organism which is thought to be genetically identical to *Sarcocystis falcatula*.¹ *Sarcocystis neurona* has a two-host life cycle which is perpetuated when a carnivore or an omnivore consumes the flesh of an infected intermediate host containing sarcocysts (the encysted stages of the parasite).² The opossum is the primary host of the parasite, while birds are intermediate hosts; the horse is merely an aberrant, dead-end host.¹

Mature parasites live in the intestinal tract of the opossum and the sporocysts are passed in its feces.^{1,2} These sporocysts can survive in the environment for up to a year or more.² Birds then consume the parasite via fecally contaminated food or water.³ The parasite penetrates the intestine and divides asexually in the vascular endothelium.³ The resulting merozoites eventually travel through the blood stream to the skeletal muscle. Once there, they develop into sarcocysts, ready to be consumed by predator or scavenger and to complete their life cycle in the intestine.³

When a horse consumes water or feed which is contaminated with sporocysts, the sporozoites penetrate the intestine and enter the blood stream to replicate in the endothelial cells of the blood vessels. However, instead of localizing in skeletal muscle, the parasites penetrate the damaged blood vessels of the blood-brain barrier, enter the neurons, and reproduce asexually in the CNS tissues.⁴ The inflammatory response that the horse mounts against the replicating parasite along with the parasite itself



The clinical signs of Equine Protozoal Myeloencephalitis may vary greatly from case to case.

causes progressive damage to the neural tissues, leading to the clinical signs associated with neurologic disease. The incubation period of the disease is extremely variable and stress may increase the likelihood of developing clinical disease.^{2,5}

Incidence and Prevalence

Sarcocystis neurona is not contagious from horse to horse since schizonts (the product of asexual reproduction) are not infective and sarcocysts do not develop in equine central nervous system tissue.⁴ EPM occurs in horses throughout the western hemisphere (since there are no opossums in the eastern hemisphere).² EPM demonstrates no sex or age predilection as compared to other neurological diseases.⁵ Current studies suggest a trend of decreasing risk from younger to older horses.⁵ In addition, Warmbloods, Thoroughbreds, and Standardbreds may be

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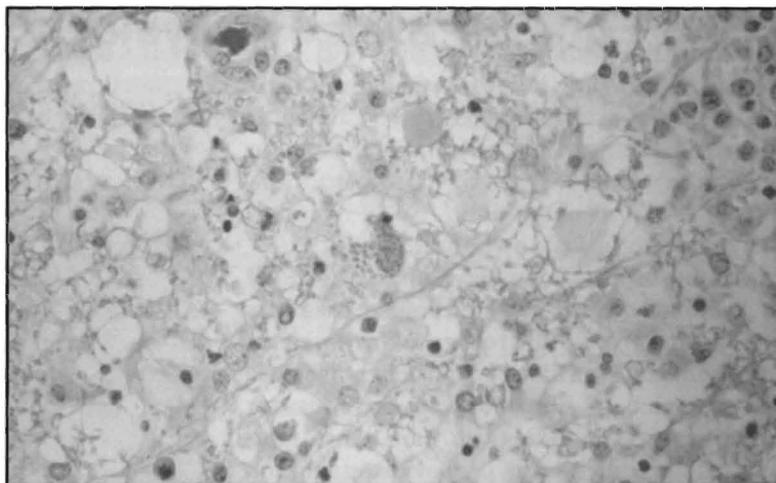
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at a higher risk of disease.⁵ At least one recent study suggests that horses who are frequently re-exposed to the parasite may actually develop some degree of protective immunity; more extensive research in this area may lead to the development of an EPM vaccine.⁶

Clinical Signs

The clinical signs of EPM vary tremendously from case to case. Neurologic signs may show characteristics of brain, brainstem and/or spinal cord disease and may appear focal or multifocal.⁴ Onset of the disease may be acute or insidious and may take as few as 28 days to as long as two years.⁶ Clinical signs may include, but are not limited to, abnormal upper airway function, unusual lameness or gait abnormality with abnormal hoof wear, weakness, focal or asymmetric muscle atrophy, ataxia, spasticity, decreased proprioception, areas of hypalgesia or complete sensory loss and depression.^{3,4} Cranial nerve signs such as a head tilt, facial nerve paralysis, and difficulty swallowing may also be observed.⁴ Neurologic symptoms of EPM are almost always asymmetric. This asymmetry makes distinguishing EPM from other neurologic diseases of the horse easier. Other CNS disease such as cervical vertebral malformation, myelopathy, and Equine herpes virus myelitis often present with symmetric neurologic signs.⁴ In addition, most horses that are infected with EPM have normal bloodwork.⁴

The disease is progressive and can be fatal if left untreated. The course of the disease is highly variable, and in some cases, the condition of the horse may appear to stabilize and remain static for a period of time.⁴ An infected horse may develop pain and lameness secondary to asymmetric neurologic signs as it attempts to compensate for the instability. A horse may have a luxating patella on the affected side due to muscle weakness that was not previously present.



An aggregate of merozoites typical of *Sarcocystis falculata* is present in the center. In addition, changes in the spinal cord include axonal degeneration and gliosis.

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Very early in the course of the disease, a conscientious rider or handler may detect slight changes in performance such as "clumsiness" or imbalances never felt or seen before. As the disease progresses, an infected horse may sustain various injuries resulting from difficulties rising to a standing position after lying down.

Diagnosis and Necropsy Findings

Many factors should be considered when diagnosing EPM including sensitivity and specificity of every test. Test sensitivity is defined as the proportion of diseased animals that actually test positive.⁷ On the other hand, test specificity is defined as the proportion of non-diseased animals that actually test negative.⁷ Sensitivity and specificity are fixed characteristics of each individual test and do not change according to the disease prevalence within a population. Test information can not be effectively applied without understanding the positive and negative predictive values which change for each test depending upon the disease prevalence within the tested population. The positive predictive value is defined as the proportion of animals testing positive that are truly diseased.⁷ The negative predictive value is defined as the proportion of animals testing negative that are not diseased.⁷ In addition, one must consider the stage or severity of disease in each particular horse involved. Finally, one must also

look at the prevalence of disease in each geographic area.

Two tests are typically used when diagnosing EPM. Western immunoblotting is used to test for antibodies to EPM in either serum or cerebral spinal fluid (CSF). It is well known that testing for serum antibodies against *Sarcocystis neurona* is of limited value when diagnosing EPM because positive serum indicates an immune response due to exposure only.² Instead, diagnosis should be made from a clean sample of CSF. A clean sample means that the CSF has not been contaminated with blood or blood components. This contamination can occur as a result of a compromised blood-brain barrier with leakage of blood proteins (including antibodies into the CSF) or as a result of blood contamination during tap procedure. The potential for contamination and false positive results of Western immunoblotting analysis has prompted the development of CSF indices that can be used to determine if blood contamination of the CSF sample has occurred. The indices compare blood levels of IgG and albumin with the CSF levels of IgG and albumin.⁸ The albumin quotient (AQ) is equal to 100 times the concentration of albumin in the CSF divided by the concentration of albumin in the serum.⁴ A value of 2.0 or greater suggests leakage of the blood-brain barrier has occurred. The IgG index is equal to the serum albumin concentration divided by the CSF albumin concentration and multiplying that quantity

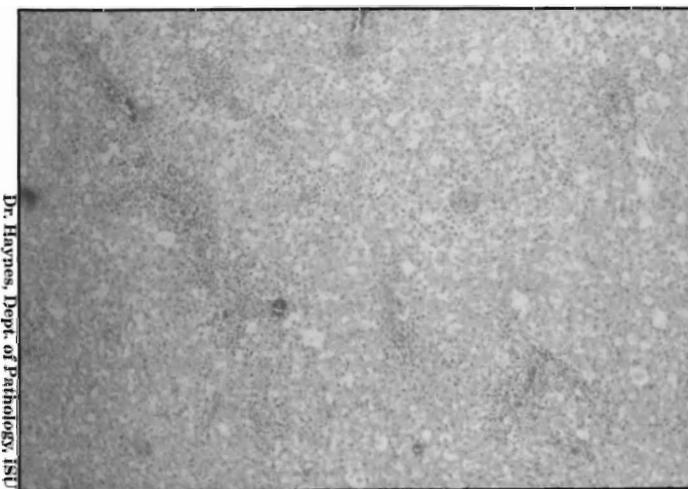
by the quotient of the IgG concentration in the CSF divided by the serum IgG concentration.⁴ A value greater than 0.3 is considered abnormally elevated.⁴ Increased AQ coupled with increased IgG index indicates increased blood-brain permeability or increased production of intrathecal antibody.⁴ Increased AQ with a normal IgG index indicates increased blood-brain barrier permeability, while a normal AQ with an increased IgG index indicates increased intrathecal antibody production.⁴ These indices are essential to determine the validity of test results when using Western blot analysis of CSF.

The second EPM diagnostic test is the polymerase chain reaction (PCR). PCR detects ribosomal RNA of the organism present in the CSF.⁴ It is often used to back up results of Western immunoblotting analysis. When using Western Blot analysis to test for antibody to *Sarcocystis neurona* in CSF from a population in an area of low prevalence, the positive predictive value is very low⁷ since very few clinically normal horses have EPM compared to horses that show neurologic signs; therefore, Western blot analysis of CSF fluid obtained from clinically normal horses is *not* a reliable method of determining whether or not a horse has EPM.⁷ PCR can confirm that a horse may be in the very early signs of the disease.

Necropsy findings can range from microscopic to grossly visible lesions.⁴ The lesions, characterized by mild to severe necrosis and suppurative myelo-encephalitis with mononuclear and giant cell infiltration,⁴ are often multifocal but always confined to the CNS.⁴

Treatment

Standard treatment for EPM includes at least twelve weeks of a combination of potentiated sulfonamides at 15 - 20 mg/kg orally BID and pyrimethamine at 1mg/kg SID.⁹ If a horse with EPM does not respond in 30 days, a systematic increase of medication dos-



White matter of spinal cord. Note the axonal degeneration, necrosis, and gliosis. In addition, there are several perivascular cuffs of lymphocytes, plasma cells and gitter cells.

ages is suggested every 30 days, keeping in mind the mechanism of action of the aforementioned drugs.⁹ More research is needed to understand how to safely implement increased dosages into a treatment program.

The use of these drugs is intended to produce a sequential blockade of folic acid metabolism in the parasite; therefore, folic acid deficiency anemia (+/-thrombocytopenia or neutropenia) can be an adverse effect of the treatment.⁴ To prevent this possible complication, folic acid supplementation (along with vitamin E) has been recommended in addition to regular complete blood counts at two-week intervals.⁴ The organism cannot use preformed folic acid while the horse can.⁴

Recent studies have shown pregnant mares that have been treated for EPM with sulfonamides, pyrimethamine, folic acid, and vitamin E have been known to produce foals with congenital defects such as bone marrow aplasia and hypoplasia, renal nephrosis or hypoplasia, and skin lesions.¹⁰ For this reason, dietary folic acid supplements are not currently recommended for pregnant mares. In addition, these drugs may cause reduced spermatogenesis in stallions.⁹

Two recently introduced drugs, Diclazuril® and Toltrazuril®, are being considered in the treatment of EPM. Both are triazine-based agents¹¹ that appear to have a very low toxicity in mammals, are well-absorbed orally, have long plasma half-lives, and are toxic against *Sarcocystis neurona*.¹² These drugs are currently being extensively tested, researched, and show a great deal of potential in the future treatment of EPM.

Finally, anti-inflammatory agents may be used (especially in acute cases) such as dimethyl sulphoxide, flunixin meglumine, and phenylbutazone.⁴ Corticosteroids are not recommended; however, short-term use (1-3 days) may be necessary in a severely debilitated animal.²

Treatment appears to result in recovery of approximately 60% of the cases and greater than 60% of the cases appear to respond to therapy.⁹ The duration of treatment beyond 60 to 90 days is dependent upon the regression of clinical signs and the point at which the CSF no longer remains positive. Although some horses remain CSF positive with the Western blot for a year or

more, continuation of the treatment for 30 days after clinical improvement has ceased is generally recommended.² It is important to avoid periodic or intermittent treatment, as this may lead to parasite resistance.⁹ Failure to respond to continuous treatment generally necessitates euthanasia.⁴

Conclusion

Our knowledge of EPM grows daily, and the speed at which we are learning about this disease is remarkable. However, EPM presents the equine practitioner with a monumental challenge: Keeping up with the constant flow of new information and sorting out what is valid will allow faster, more effective diagnosis and treatment and will decrease the loss of horses' lives and careers to this disease.◆

References

1. Oliver JE, Lorenz MD, Kornegay JN. Equine protozoal myeloencephalomyelitis. *Handbook of Veterinary Neurology*. 3rd ed. Philadelphia: W. B. Saunders Company, 1997; 140-141.
2. Granstrom DE. EPM Seminar. *The horse* 1995;XII(No. 11):14-23.
3. Granstrom, DE: Equine protozoal myeloencephalitis. *Equine Biondiagnostics, Inc. Technical Bulletin* 1995:1-2.
4. Reed SM, Saville WJA. Equine protozoal encephalomyelitis. *AAEP Proceedings* 1996; 42:75-79.
5. Saville WJA, Reed SM, Granstrom DE, et al. Some epidemiologic aspects of equine protozoal myeloencephalitis. *AAEP Proceedings* 1997; 43:6-7.
6. Saville WJA, Reed SM, Granstrom DE, et al. Response of horses exposed to *Sarcocystis neurona* when monitored biweekly. *AAEP Proceedings* 1997; 43: 8-9.
7. Morley PS, Saville WJA. Equine protozoal myeloencephalitis: what does a positive test mean? *AAEP Proceedings* 1997; 43:1-5.
8. Andrews FM, Latimer F, Grubbs 5, et al. CSF indices after repeated spinal taps in horses diagnosed with equine protozoal myeloencephalitis. *AAEP Proceedings* 1997; 43:10-12.
9. Saville WJA. Immunodiagnosis of EPM. Unpublished Information 1997.
10. Toribio RE, Bain Fr, Mrad DR, et al. Congenital defects in newborn foals of mares treated for equine protozoal myeloencephalitis during pregnancy. *JAVMA* 1 998; 21 2:697-701.
11. Granstrom DE, McCrillis 5, Wulff-Strobel C, et al. Diclazuril and equine protozoal myeloencephalitis. *AAEP Proceedings* 1997; 43:13-14.
12. Tobin T, Dirikolu L, Harkins JD, et al. Preliminary pharmacokinetics of diclazuril and toltrazuril in the horse. *AAEP Proceedings* 1997; 43:15-16.