Prevention of Equine Protozoal Myeloencephalitis (EPM)

William J. A. Saville, DVM, Diplomate ACVIM, PhD, Stephen M. Reed, DVM, Diplomate ACVIM; and J. P. Dubey, MVSc, PhD

Numerous intermediate hosts that can complete the life cycle of *S. neurona* have been identified. A significant number of these hosts are killed on US freeways providing ample food sources for the opossum, leading to subsequent contamination of the environment. Prevention of equine protozoal myeloencephalitis should involve many factors but an important part of any prevention program should include management changes, which eliminate these as a source of infection for the definitive host. Authors’ addresses: Department of Veterinary Preventive Medicine, 1920 Coffey Road, Columbus, Ohio 43210-1092 (Saville); Department of Large Animal Clinical Sciences, 601 Vernon Tharp Dr., Columbus, OH 43210-1089 (Reed); United States Department of Agriculture, Parasite Biology, Epidemiology and Systematics Laboratory, Building 1001, Beltsville, MD 20705-2350 (Dubey). © 2002 AAEP.

1. Introduction
Equine protozoal myeloencephalitis (EPM) is one of the most important neurologic diseases in the horse. ¹ Prevention of the disease has been paramount in the mind of veterinarians as well as horse owners; however, it may be much more difficult than anyone imagined. As we learn more about the disease, we find that wildlife management, risk-factor manipulation, prophylactic medications, and possibly vaccination may all be mechanisms utilisable for prevention of EPM.

2. Definitive host
Although the disease has received much publicity, scientific knowledge has been sorely lacking regarding pathophysiology of the disease and the mechanisms by which the parasite has been maintained in nature. In the last 15 mo, tremendous strides have been made in solving the life cycle of this organism. Knowledge regarding the life cycle may be utilized as one major modality in the prevention of EPM. Original research in the mid-1990s led to the discovery of the opossum (Didelphis virginiana) as the definitive host for *Sarcocystis neurona*, the primary parasite that causes EPM in horses. ² Most *Sarcocystis* spp. have a predator-prey life cycle, which allows the parasite to cycle in nature and to perpetuate itself.³ Having solved the definitive host equation, this discovery led to erroneous conclusions that the parasite had a bird-opossum life cycle.⁴ It took several years before this was rectified when the opossum turned out to be the host of at least three *Sarcocystis* spp.⁵ However, this did not help to elucidate the prey arm or intermediate host of the *S. neurona* life cycle.

3. Intermediate hosts
Cat
Completion of the life cycle for *S. neurona* was first accomplished in a laboratory setting by using the
domestic house cat (*Felis domesticus*) as the intermediate host species. Laboratory-raised cats were fed *S. neurona* sporocysts leading to development of sarcocysts in the cat’s muscle. Cat muscle infected with sarcocysts was subsequently fed to laboratory-raised opossums, which led to excretion of *S. neurona* sporocysts. These laboratory-derived sporocysts were then fed to IFN-γ KO mice resulting in encephalitis. Sporocysts were also fed to ponies which developed neurologic deficits and seroconverted in developed neurologic deficits. Sporocysts were also fed to ponies which developed neurologic deficits and seroconverted in both serum and cerebrospinal fluid to antibodies to *S. neurona*. Subsequent work by the same research group examined exposure rates of barn and feral cats to *S. neurona* in the state of Ohio. Horse farms were targeted where horses had cases of EPM, there were resident cats and the farms were in sylvatic areas, hence wildlife present. Exposure rates of cats to *S. neurona* were high (40%) on these premises. Another subset of cats that were presented to a mobile spay and neuter clinic were sampled and those cats had a much lower (10%) exposure rate. Further corroboration has been published where feral cat muscle fed to laboratory-raised opossums resulted in *S. neurona* sporocyst production. These studies suggest that the domestic house cat does play a role in transmission of *S. neurona* in nature and therefore likely has an impact on EPM in the horse. The extent to which the cat is involved needs to be determined before we understand how big a role it may play in the life cycle of *S. neurona*.

**Armadillo**

Following publication of the cat as the intermediate host, a natural intermediate host with high levels of exposure to *S. neurona* was reported; the nine-banded armadillo (*Dasypus novemcinctus*). Sarcocystis-infected muscles from road-killed armadillos were fed to laboratory-raised opossums leading to shedding of *S. neurona* sporocysts infective for a 2-mo-old Arabian foal. Oral inoculating the foal with 5 × 10⁶ sporocysts from the opossums fed armadillo muscle resulted in neurologic deficits in the foal with *S. neurona* antibodies in the CSF. All 19 wild-caught armadillos had detectable *S. neurona* antibodies in their serum. This fact coupled with the production of sporocysts after feeding sarcocyst-infected muscle from road-killed armadillos is strongly suggestive that the nine-banded armadillo is a natural intermediate host for *S. neurona*. Further work also needs to be done to determine the extent of their involvement.

**Skunk**

Subsequent to the cat and armadillo discoveries, a third species was determined to be a laboratory intermediate host for *S. neurona*. Sporocysts from opossums fed to a laboratory-raised striped skunk (*Mephitis mephitis*) resulted in sarcocyst development. Muscles from the infected skunks were fed to laboratory-raised opossums which produced sporocysts that were subsequently fed to IFN-γ KO mice and a naïve pony foal. Both the foal and the mice developed *S. neurona* antibodies and the mice developed encephalitis. Earlier, there was a report that the only species of wildlife examined at the time with *S. neurona* antibodies was the striped skunk. Completion of the life cycle with the striped skunk along with reports of *S. neurona* antibodies in wild skunks is also suggestive that the striped skunk may very well be a natural as well as a laboratory intermediate host.

**Raccoon**

Another more recent natural intermediate host to complete the life cycle of *S. neurona* is the raccoon (*Procyon lotor*). In that study, it was demonstrated that the raccoon is naturally infected with *S. neurona* after feeding wild-caught raccoon tongue muscle to naive opossums leading to production of sporocysts infective for ponies, horses, and IFN-γ KO mice. Another recent study has demonstrated the presence of antibodies to *S. neurona* in 58.6% of wild raccoons from 4 different states. This high seroprevalence rate in raccoons is similar to the exposure rate in horses. This finding of high exposure rates in combination with the feeding of wild-caught raccoon muscle to produce sporocysts makes for a compelling argument that the raccoon is an ideal intermediate host in the life cycle of *S. neurona*.

**Sea Otter**

The latest intermediate host to complete the life cycle of *S. neurona* so far is the sea otter (*Enhydra lutris*). The role of the sea otter in the contamination of the environment with *S. neurona* sporocysts is likely limited; however, what it does demonstrate is that the number of natural intermediate hosts may be numerous and thus make prevention of contamination of the environment difficult; hence, prevention of EPM.

### 3. Prevention

The opossum is a scavenger by nature and will eat anything (omnivorous). Several studies have demonstrated the presence of domestic cat, raccoon, and striped skunk in the stomach contents of the opossum. Most conclude that the presence of the larger mammals was likely the result of eating carrion. In addition, based on these early reports, it appears that these are not the preferred diet of the opossum, which may be the reason why early reports have determined that 20% or less of the opossums excrete *S. neurona* sporocysts. The fact that these mammals would not be considered prey likely resulted in a different direction being studied with regard to the true intermediate hosts involved in this life cycle.

Based on the eating habits of the opossum, prevention of EPM becomes problematic due to the excess of road-kill on highways across the United States.
States. The opossum will scavenge carrion to survive if other more preferred types of food are not available. Cleanup of road-kill of four of the above-named species in particular, would help to solve some of the EPM problems as each of these species are able to complete the life cycle of *S. neurona*. However, given the fact that 4 species that complete the life cycle have been discovered in the last 12–15 mo, it seems likely that more species are involved in completing the life cycle and will add to the excretion of sporocysts to contaminate the environment. Preventing access of opossums to the farm or ranch environment is also difficult, particularly if food and water are in short supply. Even if hay and grain are kept stored in opossum-proof facilities, there is still no protection of grass pastures from contamination with *S. neurona* sporocysts. Encouragement of horse owners to pick up dead species and keep them from being eaten by opossums is one method of prevention; however, the effort to do this seems problematic.

Recent publications describing risk factors for EPM have delineated a few measures that could be manipulated to reduce the incidence of the disease. Research from Ohio suggests that risk factors for the disease include age of the horse, occupation of the horse, season of the year, presence of woods on the premises, presence of opossums, lack of feed security, health events before diagnosis, and previous cases of EPM being diagnosed on the farm. The horse factors are very difficult to manipulate, however, efforts to improve the immune status of the horse may be warranted. Unfortunately, the highest risk occupations are racing and showing of horses. This involves transport of horses to racetracks and show events and transport has been determined to be a risk factor for the disease as well. Other than stopping the transport of horses, which is very unlikely, improvement of immune status while in transit may be a solution. The presence of woods and opossums on the property corroborate the finding that the opossum is the definitive host and is contaminating the environment; therefore, preventing opossum access to property, or at least the horse feed, is important in prevention. Unfortunately, removal of woods from the premises,
while removing the opossum habitat, would not likely solve the problem as the opossum has learned to adapt very well. Both the Ohio and the NAHMS studies (involving horses from 28 states across the U.S.) found an increased risk for EPM in the fall of the year.26,27 The reason for this finding was that a lot of the major horse competitions were in the fall, which also involved transport.28 However, it is related to the change in the opossum diet in the fall, as research has determined that the carrion involves a much higher percentage of the opossum diet at that time.21

A vaccine has been developed for EPM prevention. This is a killed vaccine using S. neurona meronts. This vaccine is conditionally licensed for use in horses, however, there is as yet no clinical evidence and little research data indicating that the vaccine is efficacious. There is a longitudinal study in progress at the present time involving several universities and private practices that may help in determining if the vaccine has any efficacy in prevention of EPM. Recently there has been some evidence that suggests there are triazene derivative medications that will prevent S. neurona in IFN-γ/KO mice.29 The medication used was diclazuril, a herbicide that has been used in several species in other countries as a coccidiostat in both poultry and swine.29 Diclazuril has been used to treat horses that are diagnosed with EPM.30 Perhaps this medication as well as other similar compounds may be developed as preventive therapy in the top dress of horse rations.

Conclusion

Although we have made enormous strides in understanding the life cycle of S. neurona (Fig. 1), we have only a few good suggestions regarding prevention of the disease. Notwithstanding this, it is apparent that prevention of EPM should be centered around the wildlife involved in the transmission of the parasite. It is not the live wildlife that are the problem when considering the intermediate host as a cause of the disease. As far as we know, the majority of the intermediate hosts involved only play a role when they are killed or die due to disease. Therefore, picking up dead skunks, raccoons, armadillos, or cats on your property and disposing of the carcasses to prevent opossums from eating them, may prevent many sporocysts from contaminating the environment and hence reduce the incidence of the disease. Manipulation of risk factors that are involved in the disease may also help. It remains to be seen whether the vaccine or other preventive therapies will be useful in the future.

References


