



Down on the Farm

by HEATHER SMITH THOMAS

Equine Protozoal Myeloencephalitis (EPM) is one of the most common causes of neurological problems in horses; the protozoa that cause this disease invade the brain and spinal cord and affect the nerves that control the horse's movements. There are still some things we don't know about EPM, and research is ongoing to find better ways to diagnose, treat and prevent it.

Dr. Nicola Pusterla, U.C. Davis (Associate Professor, Diplomate ACVIM) says EPM was probably the most important neurological disease in horses in North America, until West Nile Virus (WNV) appeared, and at that point EPM lost some of its research urgency. Now we are seeing fewer cases of WNV, so there is renewed interest in EPM.

"There are probably some regional differences, but about 10 percent of our neurological case load here at U.C. Davis is diagnosed as EPM. Some of the newest developments have occurred in diagnosis and treatment, and also in the investigations of animals that can harbor or spread the protozoal organisms," says Pusterla.

"We are also recognizing a second organism (besides *Sarcocystis neurona*) that causes EPM. The disease can also be caused by another protozoan, *Neospora hughesi*. This organism has been recognized for many years but was thought to be just a disease seen in the western U.S. We have now learned that it is more widespread," he says.

Test For EPM

There are several diagnostic tests for EPM. "The oldest one is the Western Blot, which is qualitative, and gives a positive or negative result. However, this Western immunoblot test only checks for *S. neurona*. There have been additional tests used, including the ELISA and indirect immunofluorescence antibody test (IFAT). The latter was developed and validated here at U.C. Davis. The IFAT has the advantage of testing for both organisms; it is actually two tests. With a mathematical model the researchers have also determined probability of disease

EPM Update

based on the titer (antibody level in serum and cerebrospinal fluid)," explains Pusterla. In a neurologic horse, the higher the antibody titer is, the more likely you are dealing with EPM.



An EPM horse with ataxia and abnormal stance

Spinal taps are still used in diagnosis. "In horses showing neurological signs, if we find very high titers that give us a high probability of disease (80 to 90 percent) there is not a lot of benefit from doing a spinal tap. We usually assume the horse has EPM. But if we get low titers, with the probability of disease somewhere between 30 to 60 percent, then it is worthwhile to do the spinal tap," he explains.

"We've had a few incidences in which the sample sent in had undetectable antibodies in the blood and high levels of antibodies in the cerebrospinal fluid. We would have missed them if we hadn't done the CSF test. If the diagnostic work that you perform doesn't match the clinical impression, then you need to pursue it farther, rather than just ruling out EPM because the test was negative. If you still suspect that the horse might have EPM, it's worthwhile to check by doing a

spinal tap. It mainly helps rule out other diseases that can be tested via the cerebral-spinal fluid," he says, but it can also point toward EPM on occasion.

"The test that was developed at U.C. Davis is now becoming very popular. We are also seeing more sample submission from the Midwest and the East Coast and get to recognize more cases of *Neospora hughesi* so we now know that this is not just a disease of the western states," he says.

Dr. Sharon Witonsky, Associate Professor (Large Animal Clinical Sciences) at Virginia-Maryland Regional, is involved with EPM research and says that researchers led by Dr. Dan Howe at Gluck Research Center, University of Kentucky, are working with some of the surface antigens of *Sarcocystis neurona*, looking at the specificity and sensitivity of those proteins for detecting EPM. This may eventually lead to a better test.

“Here in our research in Virginia, we are looking at the immune system’s response to infection, trying to better define what is happening with the immune responses in horses who develop EPM. It does look there are some differences in the ability of some of the antigen-presenting cells from EPM-affected horses to respond to the infection,” says Witonsky. Many horses are exposed to EPM and develop antibodies, and most of them handle it without developing EPM. A few, however, cannot seem to deal with the infection and end up with EPM.

“This is a very challenging disease. It’s important to try to diagnose cases as early as possible, but there are obvious limitations with the tests available. There are no perfect tests yet, due to the nature of this disease,” she says.

Treatment

“There is one new drug coming out soon,” says Pusterla. Currently the only FDA-approved medication for EPM is ponazuril—marketed in paste form as Marquis. Diclazuril, a related drug, has also gained FDA approval.

“Diclazuril will be marketed as an anti-protazoal drug in pelleted form (to add to feed). This would help with ease of administration,” he says. This would give horse owners another treatment option.

The diclazuril in pellet form will have an advantage in that it could be used for prevention of EPM (perhaps fed at low dose for long periods) as well as treatment. “I haven’t seen any studies coming out on this, but it is definitely something people will consider. It will be labeled for use in prevention. EPM is always easier to prevent than to treat, however, so some people may use it for this, especially in animals at high risk. This would include young animals in stressful situations or high levels of competition,” he says. This drug is supposed to be on the market later this year.

Dr. Rob MacKay, University of Florida, published an article in 2006, in which he suggested that if we can treat cases earlier in the disease process, their overall prognosis for full recovery is better. This is a neurologic disease and damage done to the central nervous system may not heal as well as other tissues. If a horse has EPM there may be some residual impairments even after recovering from the infection.

Horse owners should try to intervene as early as possible. When in doubt as to a lameness or incoordination problem,

they should have the horse checked by a veterinarian. If clinical signs point toward EPM, the horse should be assessed and tested, and treatment started as soon as possible if it looks like EPM.

Prevention

For a while there was a vaccine available for EPM, made by Fort Dodge under a conditional license. “They were not able to prove efficacy because they had a hard time establishing an animal model. Once a vaccine has been approved under a conditional license, then the company has to show progress, and they were unable to do this. It doesn’t mean the vaccine wasn’t working, it just means

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that they were faced with some technical issues,” he says. Currently there is no vaccine available.

There is work being done toward a vaccine, however. Dr. Siobhan Ellison (the President of Pathogenes Inc., a company in Florida that is working to develop an EPM vaccine) has published a paper in the *Canadian Journal of Veterinary Medicine*, describing a model of infection in which she used her new vaccine (utilizing SnSAG-1, one of the surface proteins of *Sarcocystis neurona*), which appeared to be effective. She compared a group of vaccinated horses with a group of unvaccinated horses, using her model of infection. She has plans for a larger efficacy study, now that she has proven her model.

Protozoal diseases, in general, are a challenge in regard to creating effective vaccines. “There are a lot of technical issues,” says Pusterla. “Also, we have to think about where we want to halt the organism. Do we want to stop entrance to the body at the level of the gut? Do we want to stop the protozoa while they are still moving around in the body (because we still don’t know how they get into the central nervous system), or are we going to try to prevent establishment of a latent stage?” he asks.

It is still being debated whether the horse is a dead-end host or an intermediate host. Most of the time horses seem to be a dead-end host. The organism usually doesn’t have a dormant stage in horses, but there is also evidence that this sometimes happens. The protozoan can form a cyst and become dormant in certain animals. We are still seeking to

understand some of the fundamentals and the parasitology of this disease.

“Some scientists have concerns that there may be some SnSAG-1 negative strains—some *Sarcocystis neurona* strains that don’t express the protein that’s in the vaccine,” says Witonsky. “Thus the vaccine might only protect against some of these strains, and its effectiveness would depend on whether there is any cross-protection between the different antigens of the different strains,” she explains. This particular vaccine would also not protect against *Neospora hughesi*, the other protozoan that can cause EPM in horses.

“The problem with generating a vaccine is that it would be limited, with our present diagnostic tests—which rely on antigen detection,” says Pusterla. “The tests all rely on indirect assessment of exposure, using measurement of antibody titers. Most of the vaccines use whole or parts of organisms and the tests won’t allow us to differentiate between an animal who is vaccinated and one who has been naturally exposed. So what would we then use as a test to see if



A filly with facial paralysis

the animal has EPM, because vaccine failure will still occur,” he explains. “Treatment is still the best diagnosis. If the horse responds to treatment, then you know it had the disease.”

Regarding prevention, the main strategy is to try to keep wildlife away from horse feed or feeding areas. “We can’t eliminate the wildlife, but we can try to keep them from sharing the feeding and storage areas,” says Pusterla. “This means covering horse feeds, using no-climb fence, halting interaction of wildlife (mainly opossums) and horses, etc.” It’s an on-going battle. 🐾

Research On Neospora-Caused EPM

Pusterla has been doing a lot of work on *Neospora hughesi* (the other protozoan that caused EPM in horses), trying to determine the route of transmission. “A closely related organism called *Neospora caninum* causes abortion in cattle and has a huge economic impact on the livestock industry. In cattle, there are two routes of transmission. One is horizontal—going to cattle from the definitive host (dogs or wild canines). But the most efficient way the organism is transmitted in cattle is vertically, from the dam to the offspring during gestation. There can be different outcomes, depending on the stage of gestation when the fetus is exposed. Infection of the fetus can cause abortion or the birth of a persistently infected animal, depending on the immune stage of the fetus when infection occurs,” he explains.

He was suspicious that this mode of transmission also occurs in horses—from dam to fetus. “I have been working with a herd that included two mares who tested serologically positive to *Neospora hughesi*. Every one of their offspring that we’ve tested shows evidence of vertical transmission. It definitely happens in horses as well as in cattle. Once they are congenitally infected, they can pass the disease to their progeny. If it’s a filly and she’s bred after she grows up, she can transmit EPM to her offspring,” he says.

“People often don’t think about this when horses are moved around the country,” says Pusterla. Even though neospora infections were thought to occur mainly in the western part of the U.S. it’s not uncommon to see horses from the West sent to the East, so infection with neospora can now be found in horses anywhere in the country. 🐾