



HEALTH ZONE *EPM*

EPM Treatment, Testing Options Reviewed

BY ERICA LARSEN
STEPHANIE CHURCH PHOTOS

One of the most common equine neurologic diseases—equine protozoal myeloencephalitis, or EPM—is also one of the most difficult diseases to diagnose. Further, with only three FDA-approved treatment options, treating EPM can be quite a

EPM is the most common equine neurologic disease in North America

challenge as well.

At the 2013 Western Veterinary Conference, held Feb. 17-21 in Las Vegas, Nev., Dr. Laurie Beard, associate clinical professor at Kansas State University's College of Veterinary Medicine, reviewed the current diagnostic and treatment options for veterinary attendees.

Beard said that EPM is the most common equine neurologic disease in North America, and it affects horses of all ages, breeds, and disciplines. It is a progressive (increasing in extent and severity) and potentially fatal neurologic disease caused by protozoal (single cell) microorganisms—most commonly



For neurological conditions, the veterinarian should evaluate the overall mental activity of the horse

Sarcocystis neurona and less commonly *Neospora hughesi*—that cause inflammation in the brain and/or spinal cord. Clinical signs of disease vary widely, she said, and include:

- Ataxia (incoordination), ranging from mild to severe, depending on disease status;
- Muscle atrophy;

- Lameness, ranging from mild to severe;
- Head tilting; and
- In severe cases, recumbency (the inability to stand or rise).

In many cases, EPM clinical signs are asymmetric, meaning one side of the horse's body is more severely affected than the other.

EPM AT A GLANCE: THE MUST-KNOW FACTS

Potentially, any horse living in an area with a opossum population is at risk to develop equine protozoal myeloencephalitis (EPM). In general, EPM is not specific to a certain age, breed, gender, or discipline. However, there are studies showing an increased incidence among racing (Thoroughbred and Standardbred) and western performance horses. This could be due to career-related stresses. Other risk factors include living in proximity to a wooded area; living on a farm where other horses have been diagnosed with EPM; and concurrent exposure to stressful events including travel, relocation, heavy training, or recent illness or injury.

There is no vaccine on the market to prevent EPM, so management prac-

tices must be implemented to reduce the risk of exposure, including:

- Protecting feed/water sources from opossums to avoid contamination with *S. neurona* sporocysts;
- Reducing exposure to areas inhabited by opossums;
- Reducing stress to avoid suppressing the immune system;

The key to successful treatment and recovery is early detection and aggressive therapy. Veterinary involvement is essential to help rule out other neurologic diseases that can mimic EPM.

Horses should be monitored closely for the signs of EPM, including:

- Incoordination;
- Asymmetric muscle atrophy;
- Weakness;

- Head tilt, ear droop;
- Difficulty swallowing;
- Lameness;
- Behavior change;
- Unexplained decrease in horse's performance.

Therapy includes administration of an FDA-approved anti-protozoal product for a sufficient length of time. Protazil™, a pelleted formulation of diclazuril, is the newest FDA-approved EPM treatment.

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By Dr. Wendy Vaala, senior equine technical services veterinarian for Merck Animal Health

TRIAGING ACUTE NEUROLOGIC EMERGENCIES

A horse owner's day can go from great to horrific in a matter of seconds if he or she arrives at the barn to find their charge either staggering around the field or completely unable to rise. A prompt call to the veterinarian is warranted in these scenarios, but what should an owner expect when the veterinarian arrives?

Dr. Amelia S. Munsterman, a clinical lecturer in equine emergency and critical care at the Auburn University College of Veterinary Medicine, reviewed the steps in triaging acute neurologic emergencies at the 2013 Western Veterinary Conference, held Feb. 17-21 in Las Vegas, Nev.

"Neurologic emergencies are a challenge for the veterinarian as well as the horse owner," Munsterman said. She noted several diagnostic hurdles veterinarians typically encounter when dealing with an acutely neurologic horse:

- **The fight or flight temperament:** The horse's fight or flight temperament can make them somewhat unpredictable when they're sick or injured, which can increase the risk of injury to themselves and to the people trying to help them.
- **Imaging limitations:** A veterinarian's ability to identifying internal abnormalities via imaging modalities such as MRI or CT scan is limited in large patients such as horses. Therefore, they must apply other diagnostic modalities.
- **Specialized testing:** Tests for infectious diseases must be submitted to an outside laboratory and the results might not be available for days.
- **Risk of infection:** Munsterman stressed that veterinarians should consider rabies as a differential diagnosis for any

horse presenting with neurologic signs. This means all people in contact with the horse should wear gloves and the number of people working with the animal should be limited to reduce the risk of human infection with this zoonotic disease.

A veterinarian should have several goals when triaging a neurologic horse, Munsterman said:

- Identify if the nervous system is involved;
- Rule out or identify problems involving other body systems;
- Provide a list of differential diagnoses and discuss any risks and potential expenses with the owner early;
- Initiate supportive care and treatment; and
- Facilitate referral to a clinic or hospital, if needed.

Step one to achieving these goals is to examine the horse.

Examining the Acutely Neurologic Horse

Munsterman explained that the initial examination of a neurologic horse generally isn't easy; these horses are often severely ataxic (incoordinated) or recumbent (unable to rise), or they could be hyperexcitable (excessively reactive to stimuli), all of which complicate physical examinations.

Nonetheless, she said, it's crucial to be "as thorough as possible, considering the situation." She noted that findings during the physical examination can help veterinarians narrow the long list of differential diagnoses.

She first said veterinarians should evaluate the horse's overall mentation, making note of whether the animal seems confused, hyperexcitable, or dull. He or she should also identify stupor (meaning

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The veterinarian should also perform a tail pull to determine how weak a horse is in its back end

Beard also noted that disease prevalence generally correlates with opossum (*S. neurona*'s definitive host and the animal that passes EPM-causing organisms on to horses) populations in specific geographic regions.

Current Diagnostic Options

When it comes to diagnosing EPM, Beard noted a few key points that veterinarians should consider:

- First, she said, perform a thorough neurologic examination and rule out as many differential diagnoses as possible prior to testing.
- She recommended only testing horses that have clinical signs of neurologic disease. "No test is 100% accurate," she said. "When you test a group of animals with a very low prev-



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Watching a horse turn and move in a circle allows the veterinarian to look for problems such as ataxia or leg swinging

absence of disease (i.e., normal horses), the positive predictive value—meaning that a positive test is really a true positive—is very low. However, if you test a group of animals with a higher preva-

lence of disease (i.e., horses with neurologic disease) the positive predictive value (the positive test result is really a true positive) of that test increases.”

- Consider performing multiple

tests; Beard says this will increase the sensitivity of the test (or increase the chance of finding a positive test result) but can decrease specificity (an increased chance of a false positive).

Commonly used EPM diagnostic test options include:

- Western blot: The first commercially available EPM test was the Western blot. It's still used today and essentially gives practitioners a yes or no answer as to whether a horse has developed antibodies against EPM's causative agents. Beard said when the Western blot test is run on cerebrospinal fluid, it's sensitive to blood contamination, potentially leading to false positive results. This test can be (and often is) performed with a blood sample, as well, she said.

- IFAT: A newer and commonly used diagnostic test is the immunofluorescent antibody test, or IFAT. The IFAT identifies the immune response to *S. neurona's* and *N. hughesi's* surface antigens (SAG) and produces a quantifying number (referred to as a quantitative test), or titer, that expresses the concentration of antibodies circulating in the horse's blood. This test is most successful when used on a blood

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the horse only responds to intense stimuli) and any coma or seizure activity, Munsterman said. She noted that seizure activity could be as subtle as focal muscle twitching or as major as a “grand mal” event.

Next, she said the veterinarian should examine the cranial nerves. The cranial nerves control the facial muscles and certain specialized activities of the head (such as sight, smell, and hearing), and veterinarians test these nerves’ function by evaluating the horse’s response to a quick hand movement toward the eye (i.e., whether he flinches).

If the horse is standing, Munsterman said veterinarians should evaluate his posture at rest, looking at the horse’s head and neck position and noting any head tilts or fasciculations (twitches). Munsterman said the practitioner should also evaluate head and neck movement (for instance, does moving the head and neck cause increased muscle tremors?) and note any abnormalities. Also, he

or she should check for nystagmus (rapid, involuntary, rhythmic eye movements that are often indicative of central nervous system dysfunction).

After the head and neck, Munsterman said veterinarians should evaluate the rest of the horse’s body position and assess the horse’s stance and trunk position, noting abnormal stances and any muscle atrophy. It’s also important to determine whether the horse can feel sensations along his neck and body; if they can, it indicates nerves from their spinal column are still functioning, Munsterman said.

Additionally, she stressed the importance of evaluating the horse’s tail and anus. She cautioned that if there’s little tail tone and the horse cannot feel sensations on his tail or anus, he likely won’t be able to defecate normally and will need additional supportive care.

Evaluating a severely ataxic or recumbent horse’s gait can be challenging or even impossible, Munsterman said, but there are evaluation options even for these patients. For recumbent horses, the

veterinarian can assess limb strength and sensitivity, reflexes, and whether the horse can retract or extend his limbs. He or she should flip the recumbent horse over and examine both sides.

If a gait evaluation can be carried out, Munsterman said the veterinarian should assess the horse at a walk and a trot (if possible), watching for abnormalities including a swaying trunk, increased pelvic limb strides, “waving” limbs before placement, crossing limbs, and stepping on feet. Next, the veterinarian should observe the horse circling, backing, and going up and down hills or curbs; any deviations from normal should be noted. The veterinarian should also perform a tail pull to determine how weak a horse is in his hind end, she said.

After a thorough examination, Munsterman said veterinarians should be able to start localizing lesions based on clinical signs. For example, brain stem lesions can present with weakness, ataxia, cranial nerve deficits, and altered mentation. Cer-

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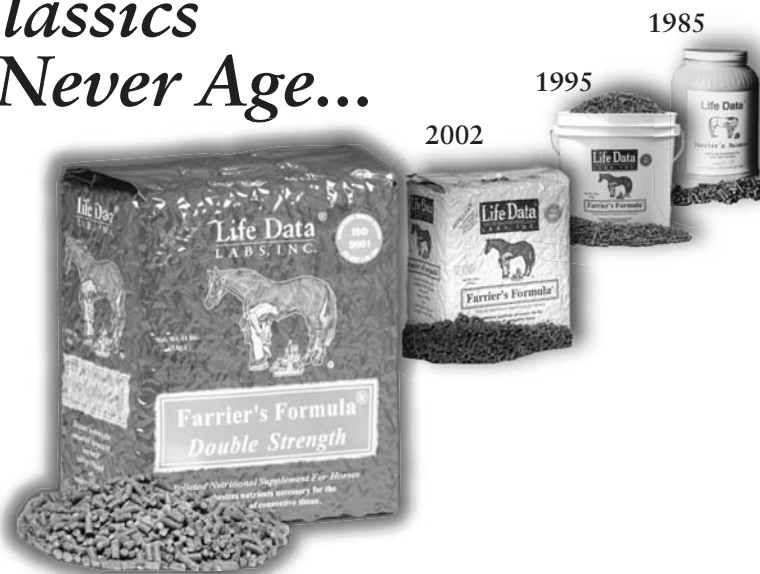
Marketed as Protazil, diclazuril is sold as an alfalfa pellet

sample, Beard said. “If all you have is a blood sample, it is the test I would pick,” she said. “This test is still useful for CSF (cerebrospinal fluid) as well.”

- SAG-1 ELISA: Another quantitative test uses an enzyme-linked immunosorbent assay format (ELISA) to measure the antibody response to the surface antigen SAG-1. Some strains of the *S. neurona* organism do not contain this surface antigen, generating false negative results.

- SAG-2, 3, and 4 ELISA: Finally, Beard discussed the newest EPM diagnostic test, which measures anti-

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bodies to the *S. neurona* surface antigens SAG-2, SAG-3, and SAG-4 in blood and CSF. This test focuses on the ratio of titers in blood compared to CSF and is generally considered positive when the ratio (as calculated by the laboratory that carries out the test) totals less than 100, she said. This test appears to have a good sensitivity and specificity, Beard said.

“There’s no perfect test—there will al-

ways be false positives and negatives,” Beard said. Thus, she recommended veterinarians retest horses if they’re not satisfied with initial results.

Treatment Options

The three FDA-approved EPM treatments—ponazuril, diclazuril, and sulfadiazine and pyrimethamine—all report 60%-70% success rates, said Beard.

- Ponazuril (marketed as Marquis) is

available in paste form, she said. The recommended dose is 5 milligrams per kilogram (mg/kg) of body weight daily for a minimum of 28 days. Some veterinarians believe that combining ponazuril with a small oral dose of dimethyl sulfoxide (commonly known as DMSO) could help increase ponazuril’s bioavailability (the amount of drug that actually reaches systemic circulation), Beard said.

- Diclazuril (marketed as Protazil) is sold as an alfalfa pellet; the recommended dose is 1 mg/kg daily for a minimum of 28 days.

- Sulfadiazine and pyrimethamine (marketed as Re-Balance) has recently been made available again after a span of being commercially unavailable. The recommended dose of the oral suspension is 15 mg/kg of sulfadiazine and 1 mg/kg of pyrimethamine once daily for a minimum of three to six months.

Beard said some veterinarians use adjunct therapeutic options including non-steroidal anti-inflammatory drugs, natural vitamin E, and immunostimulators in addition the FDA-approved treatment options.

Prognosis

The severity and progression of clinical signs are the most important prognostic indicators, Beard said.

“Horses that present with severe ataxia (and have a) rapid progression to recumbency have a very poor prognosis,” she said. “The prognosis in horses with mild to moderate clinical signs is usually considered good, with the majority of horses making a significant improvement in clinical signs.”

She cautioned that a relapse of clinical signs can be an ongoing problem in some cases.

Take-Home Message

EPM remains a diagnostic challenge for veterinarians due to its extremely variable clinical signs and the current diagnostic tests available. Despite that, many mildly to moderately affected horses recover with treatment. **BH**

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EPM is a result of infection of the CNS by the parasite *Sarcocystis neurona* and less commonly *Neospora hughesi*. Most diagnostic tests available are based on testing for antibodies against *S. neurona* in either the serum or CSF.

Commercially, there are 3 EPM test formats: western blot (WB), IFA and ELISA, the last two generating a quantitative titer. EDS lab performs the

standard western blot and SAG 2,3,4 ELISA test for *S. neurona* and an ELISA for *N. hughesi*. Serum testing is useful to confirm exposure to these parasites, absence of serum antibodies can serve as a rule out for EPM. CSF testing is used to determine production of antibodies in the central nervous system. However, due to normal diffusion of antibodies across the blood brain barrier, EDS uses the novel approach of determining the ratio of serum antibody to CSF antibody. A ratio of ≤ 100 is highly predictive of active infection with assay sensitivity of 93% and specificity of 83%. Additionally, if blood contamination of the CSF is present a specific index can be performed to determine whether the CSF antibodies measured are of CNS origin. Contact EDS at (859) 288-5255 or www.equinediagnosticsolutions.com

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vical spine deficits, on the other hand, cause neurologic deficits in all four limbs. Munsterman reviewed some different localizations and related clinical signs with veterinary attendees.

Narrowing Down a Diagnosis

After the physical examination it's time for veterinarians to narrow down the list of differential diagnoses, Munsterman said. The list of differentials for acute onset neurologic deficits is long and includes the following disorders:

- Trauma or injury (the No. 1 cause, Munsterman said);
- Infectious disease (including Eastern, Western, and Venezuelan equine encephalitis; West Nile virus; equine herpesvirus; rabies; and equine protozoal myeloencephalitis [EPM], etc.);
- Bacterial meningitis (which Munsterman said is quite rare);
- Polyneuritis equi (or cauda equine syndrome; this progressive disorder involves a loss of function of the nerves of the tail and, most commonly, the anus and is not treatable);
- Equine degenerative myelopathy;
- Cervical vertebral stenotic myelopathy, or wobbler syndrome;
- Electrolyte disorders;
- Toxin ingestion; and
- Hepatic encephalopathy.

Based on physical examination findings and an understanding of the disorder, the veterinarian can piece the puzzle together to formulate a short list of possible diagnoses. Based on that list, the veterinarian can select diagnostic testing options and move forward with treatment.

Early Treatment

Because diagnostic test results can take days to come in, Munsterman said it's important to start treating the patient as soon as possible. This largely surrounds providing the horse with any supportive care he needs to counteract physiologic and/or metabolic disorders.

While some less severely affected horses can be treated in the field, veterinarians often refer severely affected horses to a clinic. "The daily care and physical needs of the equine neurologic patient are the primary reason many horses are referred," Munsterman said. "It is difficult for owners, especially on a farm, to logistically provide for an animal that weighs over 1,000 pounds."

Regardless of where the horse is treated, she recommended starting the patient on an EPM treatment if that is even remotely suspected, along with non-steroidal anti-inflammatory drugs (NSAIDs) to help manage any pain and inflammation. She also noted that adjunct therapies such as intravenous dimethylsulfoxide (DMSO) administration and natural vitamin E supplementation might help some horses afflicted with neurologic disease.

Supportive care includes ensuring the horse's nutritional needs are satisfied and that they can urinate and defecate or regularly empty their bladder and rectum. Recumbent horses develop pressure sores over time and should be flipped every three to four hours, Munsterman said. If horses will tolerate it, use a sling can to help them remain upright, reducing the risk of pneumonia and pressure sores, she added.

Munsterman reminded, "Horses with acute neurologic signs should be considered biohazards until test results return, both to humans (i.e., rabies) as well as other horses (i.e., neurologic equine herpesvirus)."

Once test results arrive, the veterinarian should discuss the best steps to take moving forward.

Take-Home Message

"The overall outcome for acute neurologic injuries can be improved by prompt and aggressive care," Munsterman concluded. She stressed that veterinarians should never withhold or delay treatment due to the lack of a specific diagnosis.



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