Is it really equine protozoal myeloencephalitis? A differential diagnosis is essential when trying to determine if EPM is causing the illness

Identifying the Cause

NEUROLOGICAL ISSUES ARE TRICKY TO DIAGNOSE

By **AMANDA DUCKWORTH**

NEUROLOGIC DISEASES IN horses are often frustrating to accurately diagnose, which in turn can make correct treatment plans complicated to implement. The symptoms, which can include clinical lameness, stumbling, and general incoordination, often overlap across multiple diseases. Among the neurological issues equines are most likely to face are equine herpesvirus myeloencephalopathy (EHM), equine protozoal myeloencephalitis (EPM), and cervical vertebral compressive myelopathy (CVCM), which is commonly referred to as wobbler syndrome.

Because neurologic issues can be hard to pinpoint, the American Association of Equine Practitioners offers the "Neurologic Disease Differential and Diagnostic Flow Chart" on its website, which is reprinted with permission from Cornell University College of Veterinary Medicine (see page 97). The flowchart contains differential diagnoses for acute infectious neurologic disease in adult horses. Ante-mortem and post-mortem diagnostic testing recommendations for each differential are included.

In October 2024, the AAEP published its "Field Diagnostic Guidelines for Infectious Neurologic Disease" to assist practitioners in developing differentials and diagnostic strategies for suspected acute neurologic cases in adult horses.

"Until proven otherwise, practitioners are urged to approach horses with acute-onset neurologic disease cautiously and consider differential diagnoses that are contagious, like Equine Herpesvirus-1, or have public health implications, such as Rabies, West Nile Virus, Eastern Equine Encephalitis, and more," explained the AAEP. "The diagnostic flowchart contained within these guidelines will help practitioners navigate their differential list, sample collection and diagnostic test selection."

There is a vaccine for equine alphaherpesvirus type 1 (EHV-1), which causes EHM, but the virus continues to be an issue. EHM affects the brain and spinal cord, and understanding potential risk factors can help with diagnosis and faster treatment. In May 2024, the Journal of General Virology published "Impact of the host immune response on the development of equine herpesvirus myeloencephalopathy in horses."

"Herpesviruses establish a well-adapted balance with their host's immune system," explained researchers. "Despite this co-evolutionary balance, infections can lead to severe disease including neurological disorders in their natural host. In horses, equine herpesvirus 1 (EHV-1) causes respiratory disease, abortions, neonatal foal death and myeloencephalopathy (EHM) in ~10% of acute infections worldwide. Many aspects of EHM pathogenesis and protection from EHM are still poorly understood. However, it has been shown that the incidence of EHM increases to >70% in female horses >20 years of age."

For the study, researchers used a total of 18 horses, who ranged in age, for an experimental equine EHV-1 model of EHM to identify host-specific factors contributing to EHM. After infection with the neuropathogenic strain EHV-1

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A horse's gait can provide clues if there is neurological impairment

Ab4, both aged mares and yearlings were studied for 21 days post-infection.

"All young horses developed respiratory disease and a bi-phasic fever post-infection, but only 1/9 horses exhibited ataxia," researchers explained. "In contrast, respiratory disease was absent in old mares, but all old mares developed EHM that resulted in euthanasia in 6/9 old mares. Old mares also presented significantly decreased nasal viral shedding but higher viremia coinciding with a single fever peak at the onset of viremia."

The horses were sorted into an EHM group and a non-EHN group during the study. Researchers found the IFN-α levels in nasal secretions of EHM horses were low, while non-EHM horses showed an early upregulation of nasal secretions.

"Moreover, EHM horses showed significantly higher IL-10 levels in nasal secretions, peripheral blood mononuclear cells and CSF and higher serum IgG3/5 antibody titres compared to non-EHM horses," concluded researchers. "These results suggest that protection from EHM depends on timely induction of type 1 IFN and upregulation cytokines and chemokines that are representative of cellular immunity. In contrast, induction of regulatory or TH-2 type immunity appeared to correlate with an increased risk for EHM. It is likely

that future vaccine development for protection from EHM must target shifting this 'at-risk' immunophenotype."

EPM, meanwhile, is inflammation of the brain and spinal cord that is caused by protozoa. It is often contracted via ingesting feed or water contaminated with infected opossum feces. Adding to the complexity of EPM is the fact that many horses based in North America are exposed to the disease-causing organisms, but only a small percentage will develop the disease. There are three Food and Drug Administration approved drugs for EPM, but none are 100% effective. Additionally, a definitive diagnosis of EPM can only be done after a horse dies.

Blood samples can detect antibodies for S. neurona, the primary organism that causes EPM

In August 2025, the Journal of Veterinary Internal Medicine published "Effect of Long-Term Freezing on Indirect Fluorescent Antibody Titers for the Diagnosis of Equine Protozoal Myeloencephalitis."

"The definitive diagnosis of EPM can only be made postmortem, by confirming the presence of protozoal parasites in the central nervous system," explained researchers. "A clinical diagnosis of EPM can be suspected in horses displaying progressive asymmetric focal or multifocal neurological signs of spinal cord disease, multifocal neurogenic muscle atrophy, brain disease, or a combination of these. Acute, subacute, and chronic manifestations can occur; and the exclusion of other neurologic causes further increases the suspicion of EPM in endemic areas or in horses imported from endemic areas.

"Confirming intrathecally-produced antibodies in cerebrospinal fluid (CSF) using validated immunodiagnostic tests on both serum and CSF, such as indirect fluorescent antibody test (IFAT) and S. neurona surface antigen (SnSAG 2/4/3) enzyme-linked immunosorbent assays (ELISAs), is supportive of EPM as the clinical diagnosis."

Researchers wanted to study the effect of long-term storage at -80°C on IFAT against S. neurona and N. hughesi in equine serum and cerebrospinal fluid (CSF). They compared antibody titers across time points during the prospective study of samples stored 6-12, 13-18, and 19-24 months.

"We demonstrated that equine S. neurona and N. hughesi antibodies present in both serum and CSF generally remained within an acceptable variation of 2 dilutions for the different time points when samples were stored at −80°C for up to 24 and 18 months for S. neurona and N. hughesi, respectively," concluded researchers. "However, as freezing storage time increased, antibodies in serum and especially CSF showed increasing variability, with antibodies in CSF becoming undetectable in 26% of the samples upon retesting from baseline titers ranging from 5 to 80. Changes in antibody titers in both serum and CSF resulted in alterations of the calculated serum to CSF ratio in 41% (N = 19/46) of the paired samples. Of these 19, 16 calculated ratios changed to > 64 and 3 changed to ≤ 64.

"The clinical relevance of our findings consists of the identification of alterations in the interpretation of results based on calculated ratios from antibody titers with acceptable variability despite the lack of significant difference. On an individual basis, these results have substantial clinical implications and for research purposes. Therefore, awareness of this finding is essential and raises the question of whether long-term frozen samples should be used for future studies or clinical follow-up."

CVCM, often called wobbler syndrome, is when there is compression of the horse's spinal cord in the cervical region by the vertebrae. It is one of

A veterinarian performs a neurological examination

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the most common noninfectious causes of spinal ataxia in a horse, and it is usually diagnosed by X-rays and/or other advanced imaging techniques. In September 2025, the Equine Veterinary Journal published "Cone beam computed tomographic myelography in horses with cervical vertebral compressive myelopathy."

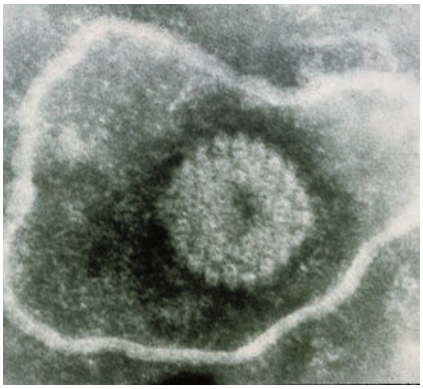
"While computed tomographic (CT) myelography is increasingly available and has been evaluated in alive horses, objective criteria for diagnosing cervical vertebral compressive myelopathy (CVCM) are lacking," explained researchers.

The prospective observational study was designed to establish morphometric dimensions of the cervical vertebral canal and spinal cords from horses with CVCM and compare those to unaffected horses with the use of cone beam CT (CBCT).

A total of four control horses and 10 horses with CVCM were used during the study, and they underwent diagnostic imaging and histopathology. Researchers found that intravertebral sagittal ratios were significantly different between CVCM and control horses.

"Dorsal myelographic column reduction was significantly different between compressed sites and non-compressed sites," researchers concluded. "Full myelographic area, dural area, and spinal cord area were significantly smaller in the CVCM horses and were significantly smaller at compressed sites when compared to non-compressed sites. Reductions of full myelographic area and dural area and ratios of spinal cord area to full myelographic area and dural area were significantly larger at compressed sites when compared to non-compressed sites.

"Limitations of this study include the small number of horses and the age difference between CVCM and control horses. A prospective follow-up study to evaluate cut-offs for full myelographic area, dural area, and spinal cord area for the diagnosis of CVCM and cut-offs for full myelographic area, dural area, full myelographic area reduction, and dural area reduction for the diagnosis of specific compressed sites is needed and should involve a larger number of horses with age-matched control horses. Additionally, including other morphometric and volumetric indices in the analysis could provide more insight into the relationship between vertebral structures and the spinal cord in healthy and diseased cervical vertebral columns."



Equine herpesvirus myeloencephalopathy is another common neurological disease

"UNTIL PROVEN OTHERWISE, PRACTITIONERS ARE URGED TO APPROACH HORSES WITH ACUTE-ONSET NEUROLOGIC DISEASE CAUTIOUSLY AND CONSIDER DIFFERENTIAL DIAGNOSES THAT ARE CONTAGIOUS, LIKE EQUINE HERPESVIRUS-1, OR HAVE PUBLIC HEALTH IMPLICATIONS, SUCH AS RABIES, WEST NILE VIRUS, EASTERN EQUINE ENCEPHALITIS AND MORE."

—AMERICAN ASSOCIATION OF EQUINE PRACTITIONERS

Wobbler syndrome is also sometimes called cervical vertebral stenotic myelopathy (CVSM). In June 2022, the Journal of Veterinary Medical Science published "Investigation of a contributing factor for cervical vertebral stenotic myelopathy using computed tomography for measuring the cervical vertebral volume."

"Thoroughbred horses appear to be particularly predisposed to cervical vertebral stenotic myelopathy (CVSM), also known as wobbler syndrome," researchers explained. "We hypothesized that variations in the cervical vertebral volumes can affect the dynamic instability of the cervical vertebrae."

The observational study used computed tomography (CT) to investigate a total of 21 male Thoroughbred horses. Of those, 17 of them had CVSM and four did not.

"A significant difference in the variation of cervical vertebral volumes among C2 to C4 and C3 to C5 was identified in the CVSM group," researchers concluded. "While no significant differences were found in the variation in cervical vertebral volumes among C4 to C6, C3 demonstrated a significantly smaller cervical vertebral volume than C2 and C4. In the non-CVSM group, no significant differences were found in the variation of cervical vertebral volume among C2 to C4, C3 to C5, and C4 to C6. Our findings suggest that variations in cranial cervical vertebral volume in CVSM male horses can be considered as an important contributing factor in CVSM development.

"Previous studies have shown that male horses are more prevalent of CVSM. The limitation of the present

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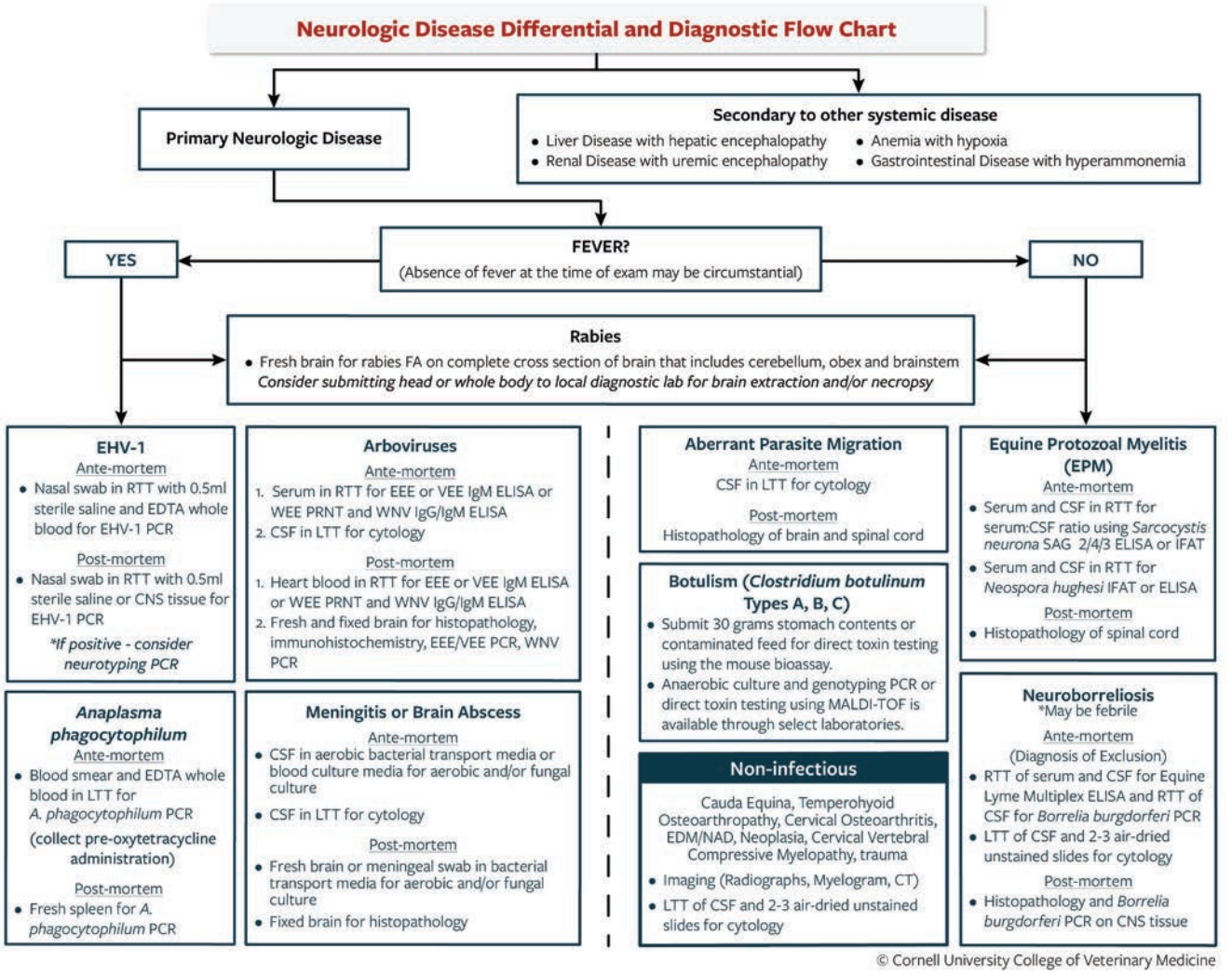


study is that sex differences in the cervical vertebral volume were not discussed because the number of female samples was very small. In the future, we aim to measure the cervical vertebral volume in female horses to perform a comparative study with our present findings."

The battle to better understand neurologic diseases in horses is an ongoing one. At any given time, there are a number of research studies underway. For example, the Grayson-Jockey Club Research Foundation is currently funding the study "Use Of Equine IFNL3 mRNA For Prevention Of EHV-1 And EHM" by Michigan State University.

"Equine herpesvirus 1 (EHV-1) neurological disease (EHM) continues to cause significant disease and extensive economic losses through closure of racetracks and sales barns, delays in training schedules and death of valuable animals," explained researchers. "The substantial impact of EHV-1 on equine health is highlighted by a series of major outbreaks in North America and Europe over the past decade resulting in fatalities and enormous financial costs to the equine industry. Major outbreaks of EHM remain a problem demonstrating the fact that current vaccination strategies have not shown to offer protection from EHM.

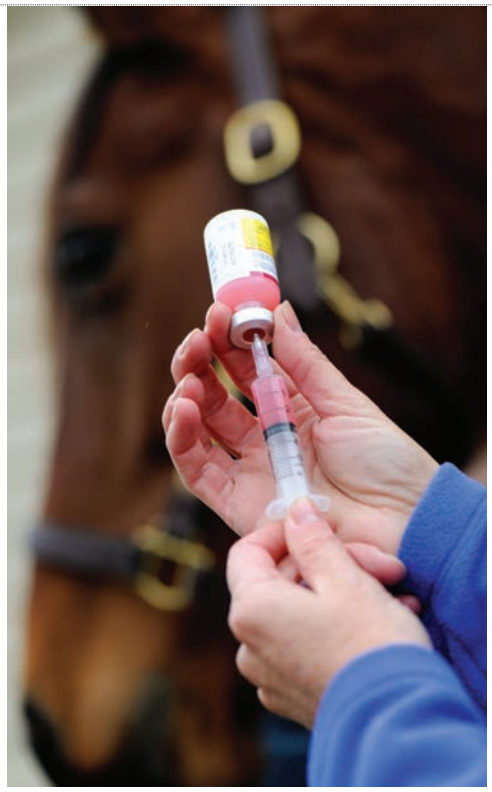
"We propose to address this problem by using novel RNA technologies to deliver a natural protein called interferonlambda 3 (IFNL3) to the horse based on the success of the current COVID-19 vaccines that employ this technology."

When it comes to EPM, the Virginia-Maryland College of Veterinary Medicine is currently recruiting horses for the study "Identifying Molecules to Aid in Developing a Vaccine Against EPM (Equine Protozoal Myeloencephalitis)."

"Our goal in this study is to identify potential immune targets that can protect horses against infection with S. neurona, the primary organism that causes EPM," explained researchers. "Identifying these immune targets is a first step towards developing a vaccine against EPM."

To be eligible for the study, all enrolled horses must be aged 3+ years, sound, neurologically normal, and with a normal gait. They also will need to remain in the area, with no planned rehoming for 1-2 years.

"We will perform neurologic exams on each horse at the screening exam," explained researchers. "If the horse is neurologically normal, the horse will be enrolled and we will collect a blood sample, approximately 10mL, for testing for antibodies to S. neurona. If the horse has been exposed to S. neurona but remains neurologically normal, the horse is assumed to have made a protective immune response against the disease. Based on these antibody results, we will classify the horse in either the resistant or control population.



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◄ **An RNA vaccine to combat EHV-1 and EHM is being researched at Michigan State University through funding provided by the Grayson-Jockey Club Research Foundation**

"We will then collect blood, approximately 40-60mL, for immune cell function tests to see if we can identify molecules that may have the ability to stimulate a protective immune response. For some enrolled horses, blood collections may occur up to four times over a two-year period."

Due to the overlapping symptoms and difficulty in achieving a clear diagnosis, neurologic diseases in horses continue to be important areas of research. BH

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