Neurologic Disease: Current Topics In-Depth (21-Nov-2003)

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1. Introduction

The assessment of the central nervous system (CNS) in horses may seem a difficult task; however, by following a consistent approach and focusing on the neuroanatomic localization, it is not difficult. Subtle neurologic deficits may be hidden by musculoskeletal disease or missed because of lack of knowledge or understanding of these disorders. Accurate evaluation requires a thorough physical and neurological examination as well as knowledge of which musculoskeletal disorders are commonly associated with neurologic disease. Problems such as osteochondrosis of the stifle, hock, and shoulder joints often occur concurrently in horses with neurologic conditions such as cervical vertebral stenotic myelopathy (CVM). Typical histories of horses presented for neurologic examination often include acute onset after a traumatic event or a description of an obscure lameness. Osteochondrosis of the distal tibia or femur and contracted tendons are examples of other conditions that may occur with neurological disorders. Bilateral bog spavin may result from osteochondrosis of the distal tibia or other sites in the tibiotarsal joint. Upward fixation of the patella may be a result from a bony lesion in the stifle joint or may be caused by quadriceps weakness secondary to neurologic disease. This problem is more commonly associated with neurologic disease than many veterinarians realize, and the gait deficits caused by these lamenesses often mimic neurologic disease. It is important to perform a careful musculoskeletal or lameness examination before the neurological examination.

Neurologic Examination - The goals of a neurologic examination are to establish whether a neurologic problem is present and to determine the anatomic localization of the problem. One should try to account for all clinical signs with a single cause or lesion within the CNS; however, if this is not possible, the presence of multifocal disease or multiple diseases should be considered. After anatomic localization, a decision is made about what additional testing is necessary to determine the underlying cause of the clinical signs. Cervical radiography, cerebrospinal fluid (CSF) analysis, and electrodiagnostic testing may be useful in the location and etiology of the lesions. The examination procedure has been previously described [1-3]. The authors follow the format developed by Mayhew, which divides the examination into five categories: head and mental status, gait and posture, neck and forelimbs, trunk and hindlimbs, and tail and anus. The functional divisions of the CNS include the sensory, motor, and integrative systems.

Head posture and coordination are controlled by the cerebellar and vestibular regions of the brain and brainstem in response to sensory input from receptors in the head, limbs, and body. It is helpful to examine head and neck posture with the horse at rest, when eating, and when moving. Careful examination of the vestibular region of the problem is important, because many horses develop a head tilt as a result of head trauma, inner ear infection, or guttural pouch infection. Postural abnormalities of the head and neck may be difficult to distinguish from a head tilt. Horses with torticollis of the head and neck may have a congenital abnormality of the vertebrae or may have injured the muscles of the neck region. Careful examination including palpation should help identify fractures of the cervical vertebrae or painful musculature caused by trauma or an injection reaction. In some horses, radiographs of the cervical vertebrae may be useful to confirm a fracture or osteomyelitis. Blindness may result in an abnormal head or neck posture; thus, sight should be evaluated during the examination. After the horse's alertness, mental attitude, head and neck posture, and coordination have been evaluated, the examiner should closely examine the cranial nerves. Gait deficits are most often observed in horses with brainstem lesions that are in the region from the 7th to 10th cranial nerves. Horses that have damage to the vestibular system will usually compensate for the deficits in a short time period by use of visual and proprioceptive input. Therefore, use of a blindfold should be avoided in horses with suspected vestibular disease. This will hamper the horse's ability to compensate, and the horse may become dangerous. However, blindfolding a horse with a suspected vestibular disease that is no longer showing an obvious head tilt...
may be helpful in localizing the lesion.

**Evaluation of Gait** - Evaluation of a horse's gait can begin with examination of postural reactions in most horses. In newborn foals or very small, young horses and in recumbent horses, evaluation of spinal reflexes may be included. Abnormal postural reactions are sometimes difficult to interpret in horses that are well trained, making it very important to use gait abnormalities to help localize a lesion. Newborn foals often seem weak and ataxic; however, because foals are ambulatory within hours of birth, it is possible to evaluate gait. Gait abnormalities that are commonly observed in horses with neurological disease include ataxia, spasticity, and weakness or paresis. Spasticity and weakness indicate upper motor neuron tract lesions, whereas ataxia is an indication of lesions in the general proprioceptive tracts.

Subtle neurologic gait deficits are best detected by careful evaluation of gait. The examination should be conducted with the horse observed at a walk, and if possible, a trot, both in a straight line and when turning. In some horses, it is helpful to observe the horse negotiate over small obstacles such as a curb, ground poles, or cavelettis. When possible, the examiner should observe the horse turned free and walking up and down an incline. Elevation of the head and walking on a slope may exaggerate a subtle deficit. Spastic horses often appear stiff and short-strided, and their feet may slap the ground when landing.

As previously stated, evaluation of gait should begin with observation of the horse's posture and should continue by carefully observing its first few steps, because subtle deficits are often detected at this time. In other horses, gait deficits may not be obvious until the horse is trotting or cantering or until the horse is ridden. The examiner should note which limbs demonstrate postural and/or gait deficits and must then be able to determine whether the horse has a musculoskeletal problem (painful or mechanical) rather than a neurologic gait deficit.

Important centers for posture and coordination are located in the regions of C6-T2 and L4-S2 in the spinal cord along with centers in the brainstem. Horses that demonstrate a very wide base stance at rest may have a lesion in the cerebellum or vestibular region or may have unconscious proprioceptive abnormalities.

At a walk, the examiner can walk along the side of the horse, first in step with the rear limbs and then in step with the fore limbs. This allows the examiner to more easily determine the stride length and foot placement. A weak limb will often have a low arc and longer stride length. To help exaggerate subtle gait deficits, the horse should be observed walking in circles, walking on a slope, and walking with its head elevated. These procedures help demonstrate persistent irregular movements of the limbs. The gait of horses with a musculoskeletal problem has been described as regularly irregular. On the other hand, a horse with neurologic deficits shows less consistent gait abnormalities, and the gait has been referred to as irregularly irregular. Although it is helpful to have a chance to observe the horse running free in a paddock or round pen and also while being ridden, this is not always possible.

Additional tests that can be helpful during a neurologic examination are blindfolding the horse (described under vestibular syndrome), walking it over a curb or other obstacle, and walking with its head and neck elevated. The strength and ability of the horse to correct body positions can be evaluated by performing a sway test. This test is accomplished by application of lateral pressure at the shoulder, hip, and tail while the horse is standing and walking. Pressure should be applied several times while the horse is walking to catch the limb in various stages of weight bearing. Observing a horse while it is backing is also important. When a normal horse is backing, it should lift each leg and place it in a coordinated and appropriate location. Horses with neurologic abnormalities will often place the limbs in very base, wide positions or lean back and be reluctant or refuse to move.

Ataxia can be observed closely while the horse is being turned in a tight circle. Abnormal wide outward excursions of the rear limb (circumduction) may be identified during this procedure. We also cross the limbs over the opposite thoracic or pelvic limb to determine if the horse recognizes and tolerates these unusual limb positions. After this, we will lift one front limb and force the horse to hop on the opposite front limb in a modified postural reaction.

If a deficit is present after carefully observing the movements of each limb in a variety of exercises as described above, the examiner should assign a grade to the deficit. The system we use is a modification of the grades described by deLahunta and Mayhew and coworkers [1,3-5]. The severity of the deficit is graded between 0 and 5. Grade 0 is assigned when there are no gait deficits. A grade 1 deficit requires careful observation to be certain that the gait abnormality is caused by neurologic dysfunction. Grade 2 deficits are moderate but obvious to most observers as soon as the horse begins to move; however, they are still mild to moderate in severity. Grade 3 deficits are very obvious and are exaggerated during the negotiation of a slope or with head elevation. Grade 4 gait deficits may cause a horse to fall or nearly fall. Animals with these severe deficits often display abnormal positioning when standing in their stall. Grade 5 horses are recumbent.

Weakness is used to describe knuckling, stumbling, or buckling and is sometimes characterized by toe dragging when walking. Weakness may be associated with either an upper motor neuron or lower motor neuron lesion. In the case of a lower motor neuron injury, peripheral nerve injury, or illness, the horse will show muscle atrophy and sensory loss. Ataxia is typified by abnormal foot placement and wide swaying of the foot and limb, especially when turning. The gait abnormalities, along with the findings from other parts of the neurological examination, allow the examiner to determine the neuroanatomic localization.

Horses with an obscure or unusual gait that may have a musculoskeletal disorder should be reexamined after use of regional
anesthetic agents to block selected peripheral nerves or after treatment with intra-articular medications. The use of non-steroidal, anti-inflammatory drugs (NSAIDS) for 3 - 5 days may also alleviate pain and help to distinguish between lameness and a neurological gait deficit. Observing a horse performing modest athletic activities does not eliminate or preclude a diagnosis of neurological disease, because moving fast can often appear easier than moving slow.

**Localizing the Lesion** - If the horse does not exhibit abnormal behavior, seizures, or abnormal mental status and has no cranial nerve deficits, then the lesion is usually caudal to the foramen magnum. Horses with brainstem lesions often show signs of weakness and ataxia similar to horses with a lesion in the cervical spinal cord. If these horses do not have cranial nerve deficits or depression, it is difficult to distinguish them from horses with cervical spinal cord damage. The symptoms of cervical spinal cord disease include gait and proprioceptive deficits in all four limbs with no signs of brain, brainstem, or cranial nerve deficits. Horses with cervical vertebral stenotic myelopathy may have mild pelvic limb deficits with minimal or barely detectable signs in the thoracic limbs.

Horses with signs of neurological gait deficits confined to the pelvic limbs have a neuroanatomic localization that is caudal to the second thoracic spinal cord segment. When examining a horse with a lesion caudal-T2, it is important to be certain that the gait deficits involve only the pelvic limbs. Horses that have lesions in the L4-S1 region may demonstrate gait deficits of the pelvic limbs along with muscle atrophy, which indicates involvement of the gray matter in this region. Lesions caudal-S1 will be associated with abnormal use of the tail and anus.

Horses with peripheral nerve injury, equine motor neuron disease, or polyneuritis equi often appear weak, have muscle atrophy, and, in some cases, may have areas of sensory loss. Horses with primary muscle diseases such as exertional rhabdomyolysis, myotonia, and hyperkalemic periodic paralysis can also appear "stiff" and may sometimes mimic a neurological problem.

**Description of Normal Gaits** - The walk is a natural, four-beat gait in the horse. At this gait, the normal horse has three feet on the ground at all times. Therefore, the walk is a very stable gait. Overtracking and interference may be observed in horses with poor conformation, which is not a result of neurologic disease; however, horses that "overtrack" may be selected for use in dressage. The trot is a two-beat, symmetrical movement in which the diagonal limbs are in contact with the ground at the same time. When the horse is examined moving on hard pavement, the trot is the most helpful gait to distinguish lameness from a neurologic gait deficit.

The pace is a gait that results in significant truncal sway, because the legs on the same side of the body strike the ground simultaneously. Many ataxic horses pace, have an abnormal foot placement when circling, and demonstrate truncal sway. In horses with subtle ataxia, pacing may be observed when horses are walked with the head held in an extended position or on a slope. Horses with profound ataxia often pace when they walk and often demonstrate wide swinging of the outside pelvic limb (circumduction) while turning. These signs are suggestive of general proprioceptive deficits. The gallop is a high-speed, four-beat gait that often seems to be easier to perform than walking in a tight circle or moving at a slow trot. Therefore, some horses with a neurologic gait deficit may perform better at high speed.

Abnormal gaits such as stringhalt, upward fixation of the patella, fibrotic myopathy, and shivers can be observed in horses with neurological disease. When these abnormalities are identified, the horse should be examined carefully to determine the underlying cause. Stringhalt often begins as an abrupt onset of excessive flexion of one or both pelvic limbs. In some horses, the condition may worsen and result in frequent episodes of the foot striking the abdomen. Stringhalt may occur as an outbreak in some areas of the world as a result of exposure to certain toxic plants [6]. The clinical syndrome is similar to the movement of a horse with a tibial neurectomy with unopposed flexion of the hock and extension of the digit. Stringhalt can usually be corrected by performance of a tenectomy of the lateral digital extensor tendon including a portion of the muscle belly. The underlying cause of the disease may be a sensory neuropathy, a myopathy, or a primary spinal cord disease. As has been described, the defect likely affects the neuromuscular spindle as well as the efferent and afferent pathways controlling muscle tone [1].

Fibrotic myopathy is a result of scar tissue formation after injury to the semitendinosus and semimembranosus muscles [7]. The characteristic foot placement coupled with the abrupt rearward movement of the affected limb may be confused as a spastic gait caused by a spinal cord injury or disease. With careful examination, it is not likely that a horse suffering from fibrotic myelopathy will go undiagnosed.

Upward fixation of the patella in horses with neurologic disease may be a result of weakness in the quadriceps muscle group. This weakness is thought to occur because of a lack of use of these muscles or may be caused by abnormal transmission of proprioceptive information to and from the muscles and joint capsule as a result of damage to the spinal cord. If the horse shows signs only in the trunk and pelvic limbs, the neuroanatomic localization of the lesion is between T2 and S2, or it involves the nerves and muscles of the pelvic limbs. However, the examiner needs to realize that horses with cervical spinal cord lesions often demonstrate about one grade worse signs in the pelvic limbs over the thoracic limbs; therefore, a very mild cervical spinal cord or brainstem lesion could show minimal or no thoracic limb signs with grade 1 or very subtle signs in the pelvic limbs.

A sway reaction performed both while the horse is standing and walking is also necessary to assess the pelvic limb strength and proprioceptive functions. The strength may also be evaluated by slow but deliberate and forceful pressure along the back
and sacral muscles. A normal horse should reflexly arch its back upward, whereas a horse with rear limb weakness may be unable to withstand this pressure and may even buckle its rear limbs.

Examination of the tail and anus must be completed as part of the neurologic examination to determine whether damage has occurred to the sacroccygeal nerve and muscle segments. A normal perineal reflex results in contraction of the anus and clamping of the tail in response to light stimulation of the skin in this region.

The evaluation of the major peripheral nerves in the horse is also an important part of the neurologic examination in the horse. Damage to a peripheral nerve can result in both sensory and motor deficits in the area supplied by the nerve, and focal muscle atrophy will follow within a short time (usually 14 - 21 days) after damage to the nerve. A detailed anatomic description of the major peripheral nerves in the horse is published elsewhere [2]. Some classic examples are a dropped elbow joint with radial nerve paralysis, inability to fix the stifle with femoral nerve paralysis, and atrophy of the supraspinatus and infraspinatus muscles ("sweeny") with damage to the suprascapular nerve. These conditions are reminders of what to expect with peripheral nerve injuries [2].

Conclusion - Although it may not be necessary to have every neuron, spinal tract, and muscle working in a horse for it to be athletic, it is very important that the veterinarian be able to distinguish between a musculoskeletal lameness and a neurologic condition that may make a horse unsafe for use and dangerous to itself or the rider. To better assist their client with a diagnosis and treatment plan for her or his horse, it is important for the veterinarian to be able to distinguish between musculoskeletal and neurological conditions and to recognize the conditions that often occur together.

2. Equine Protozoal Myeloencephalitis

Seroprevalence data has been collected from horses in many areas of the United States, and the results demonstrated that, in many areas, 50% of horses have been exposed to Sarcocystis neurona, the primary agent that causes equine protozoal myeloencephalitis (EPM) [8-12]. Little work has been performed regarding the prevalence of antibody to N. caninum/N. hughesi in horses; however, recent work found a seroprevalence of 23.3% in sera examined from two horses in slaughterhouses in the United States and none in horses in slaughterhouses in Argentina or Brazil [10].

Based on a recent national study conducted by the United States Department of Agriculture (USDA), the average incidence of EPM was 14 ± 6 cases/10,000 horses/yr with the lowest incidence in farm/ranch horses (1 ± 1 cases/10,000 horses/yr). The incidence in other horses, in increasing frequency, was pleasure horses (6 ± 5 cases/10,000 horses/yr), breeding horses (17 ± 12 cases/10,000 horses/yr), racing horses (38 ± 16 cases/10,000 horses/yr), and competition/show horses (51 ± 39 cases/10,000 horses/yr).

Early reports suggested that young and old horses had an increased disease risk. Other investigators have corroborated this increased risk in young horses. Historically, EPM has been reported as a sporadic disease; however, clustering of cases may occur when all the risk factors for EPM are present. Important risk factors for development of EPM are opossums seen on the farm, presence of woods on the farm, time of the year, and occurrence of a stressful health event, such as illness or trauma, before development of the clinical signs of EPM [13]. When compared with winter, the risk of EPM increases when ambient temperature increases, with the highest risk of clinical disease in the fall. The National Animal Health Monitoring System (NAHMS) study [13,14] found the same seasonal risk; the NAHMS study also found a decreased risk if a creek or river was present on the farm and if feed was kept protected from wildlife access. Additionally, the NAHMS study found an increased risk if opossums were observed on the premises and an even higher risk if the opossums were seen frequently [14]. Additional risk factors identified in the NAHMS study were an increased risk with increased numbers of horses, purchased versus homegrown grain, use of wood chips or shavings as bedding, presence of rats and mice on the premises, and increased human population density [14]. A decreased risk was seen when there were woods within 5 mi of the premises and where surface water was the primary drinking source [4-6,14]. These findings demonstrate that management may play a role in the development of clinical EPM.

Etiology and Life Cycle - S. neurona, unlike most Sarcocystis spp, may aberrantly infect a large number of intermediate hosts. This wide host range is similar to that of T. gondii, which is phylogenetically close to S. neurona [15,16]. Sarcocysts of S. neurona have not been found in affected horses; thus, the horse is an aberrant, dead-end host [17,18]. Sarcocystis neurona cycles between the opossum and various other intermediate host species that have sarcocysts in their muscles. Intermediate hosts include nine-banded armadillos (Dasypus novemcinctus), striped skunks (Mephitis mephitis), raccoons (Procyon lotor), and sea otters (Enhydra lutris nereis) [19-22]. A study in Missouri and another study in Ohio both suggest that the domestic cat is also a natural intermediate host [23,24]. The life cycle of S. neurona has been completed in a laboratory setting in the striped skunk [21]; however, previous reports of antibodies to S. neurona in striped skunks (22 of 37 skunks) would suggest that they are likely to be a natural intermediate host as well [25]. Muscle from captured wild raccoons and armadillos killed along the road were fed to laboratory-raised opossums. This resulted in the shedding of sporocysts infective for ponies, horses, raccoons, and IFN-γ/KO mice [19,22]. High seroprevalence of S. neurona antibodies in armadillos (100%) tested from three states and raccoons (58.6%) tested from four states further suggests that these species are natural intermediate hosts [22,24]. The variety of species suggests that many
other species may be potential intermediate hosts for this organism. Opossums shed sporocysts in their feces after ingestion of the infected muscle of the intermediate hosts.

The life cycle of *N. caninum* or *N. hughesi* in horses is poorly understood; however, the definitive host of *N. caninum* is likely the dog [26], although it is not known if the dog is the definitive host of *N. hughesi*. Tachyzoites have been found in some horse tissues, including tissue cysts in two of the horses reported to have EPM caused by *Neospora* [27]. One case of neosporosis in a foal was determined to be a congenital infection, which does not occur with infection by *S. neurona* [28].

Several studies have induced experimental infection in horses using *S. neurona* sporocysts. These studies have been conducted in Kentucky, Florida, and Ohio. In all studies, horses that were infected developed mild to moderate neurological deficits, but the investigators were not able to isolate the parasite from the nervous tissue in any of the studies. The most severe signs (mild to moderate) were seen in horses stressed by transport [29-31]. Additionally, in all studies, regardless of the dose of sporocysts administered, some horses demonstrated an improvement in clinical signs using dexamethasone; however, the clinical signs were less severe and seemed to improve over time [29-31].

In severe signs (mild to moderate) were seen in horses stressed by transport [29]. All three studies attempted to mimic stress without treatment [7,27,29-31]. This suggests that horses are capable of clearing large numbers of these organisms and may partially explain the high number of clinically normal horses with parasite-specific antibodies in the (CSF). After orally inoculating horses with 1 x 10^8 *S. neurona* sporocysts, clinical signs of neurologic deficits were readily detectable, but parasites were not found in the CNS at 7 or 14 days post-infection [a]. This is unlike the *S. neurona* infection in the natural intermediate host, the raccoon, where parasites were readily detectable in the CNS at 7 days post-infection [32]. The life cycle of *S. neurona* in the horse remains enigmatic.

The organism seems likely to be transmitted through methods other than direct contact with opossum feces based on the estimated numbers of opossums in North America, the poor survival of opossums, and the limited individual range. Experiments performed by researchers in the 1980s suggested that birds may help disseminate sporocysts [33]. Secondary or vector transmission also was demonstrated by the recovery of sporocysts in the feces of budgerigars, canaries, mice, and chickens fed opossum feces. Recovered sporocysts were then fed to budgerigars to assess viability after transit through the digestive tract of those species [34]. Four of six budgerigars died, suggesting that sporocysts disseminated in this way may be transmitted to intermediate hosts [34]. Control of EPM may be difficult because of the apparent wide range of natural and aberrant intermediate hosts of *S. neurona*.

Insects such as flies and cockroaches may also be transport vectors for *S. neurona*. Earlier work demonstrated that flies may act as transport vectors for *T. gondii* [35,36]. Fatal pulmonary disease developed in psittacine birds that were fed cockroaches after the cockroaches had been fed opossum feces, suggesting that insects may play a role in the transmission of *S. neurona*; however, further investigation is necessary.

The pathogenesis of EPM is poorly understood, but it is assumed that horses ingest *S. neurona* and the course of infection and disease is similar to other species infected with *Sarcocystis* spp. Sporocysts of *S. neurona* are passed in the feces of the opossum and introduced into the feed and water supplies of intermediate hosts [37]. On reaching the gastrointestinal tract, sporocysts excyst release eight sporozoites, which penetrate the gut and enter arterial endothelial cells in various organs [37]. Meronts develop within host cells, resulting in cell rupture and merozoites release into the blood stream. This may be followed by a second round of merogony in vascular endothelial cells throughout the body [37]. In the appropriate intermediate host, a final round of merogony results in the formation of sarcocysts in various muscles [37]. The predator or definitive host subsequently ingests the infected muscle tissue to complete the life cycle [37]. At the present time, sarcocysts of *S. neurona* have not been found in affected horses, indicating that the horse is likely to be an aberrant, dead-end host [37]. Mares suspected to have EPM have produced many normal foals. The earliest EPM case reported occurred in a 2-mo-old foal [38]. Assuming transplacental transmission does not occur, the minimum incubation period may be 8 wk. However, a recent case suggests the incubation period may be much shorter. Serum and CSF collected 4 days after onset of clinical signs were both negative for antibodies to *S. neurona*. Serum and CSF collected 3.5 wk later were both positive. This indicates that the parasite was ingested and then caused the clinical signs in the 10 - 12 days required to produce a detectable antibody response.

*Sarcocystis neurona* has been recovered from CNS lesions in several horses and subsequently, propagated in culture in the laboratory. Cultured merozoites have not induced clinical disease in the horse when administered to horses parenterally or introduced through the epidural space [39,40]. The merozoite stage of *Sarcocystis* spp. is not known to be transmissible to other animals either [40]. However, nude mice have been inoculated intraperitoneally with cultured merozoites and subsequently, developed evidence of *S. neurona*-associated encephalitis [41]. These were immunosuppressed strains of mice, and intraperitoneal injection would not likely be the normal route of infection with *S. neurona* in horses. It seems that at least three species of *Sarcocystis* are excreted in opossum feces; therefore, use of IFN-γ/KO mice that develop encephalitis in response to *S. neurona* infections would help to differentiate the strain of *Sarcocystis* spp. present [40]. The mechanism by which the merozoites enter the CNS of horses is currently unknown. The organism is believed to enter the CNS through infected leukocytes or directly through the cytoplasm of endothelial cells [40].

Diagnosis - Immunoblot analysis of serum and CSF provides antemortem information regarding exposure to *S. neurona* [42]. Other types of immunoassays are confounded by cross-reactivity with *S. fayeri* or other organisms that share antigens with *S.
delayed-type hypersensitivity, which also increases the phagocytic activity of macrophages [63]. The use of

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immunomodulators or other therapies that may have a non-specific enhancement of the immune system may be helpful.

Because of the suspicion that protozoal infections occur more commonly in immunocompromised patients,

avoided [45]. Ancillary treatments may include padded helmets, slings, good supportive care, and a deeply bedded stall.

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sulfoxide [c] at a dose of 1.0 ml/kg (approximately 1 g/kg) in a 10% solution is administered once daily for 3 days in a row,

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of a small persistent focus of infection, or perhaps the re-exposure of the horse to the parasite [62]. Anecdotal estimates of the

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A growing concern, regardless of what medication is used, is the percentage of horses which have a relapse in clinical disease

after cessation of therapy, because some horses will relapse days, weeks, or even months after cessation of therapy. The

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diclazuril for the treatment of EPM was < 5% [61]. Anti-inflammatory medications are recommended when acute onset
results in dramatic and progressive clinical signs [11,58-60]. The use of flunixin meglumine or phenylbutazone may be
helpful. The usual dose of flunixin meglumine is 1.1 mg/kg, q 12 h, parenterally. IV administration of medical grade dimethyl
sulfoxide [c] at a dose of 1.0 ml/kg (approximately 1 g/kg) in a 10% solution is administered once daily for 3 days in a row,
and although not uniformly recommended, some clinicians use dexamethasone parenterally in severely affected horses (0.05
mg/kg, q 24 h) or sometimes empirically at 50 mg, q 24 h. The exacerbation of signs in stressed patients and the reports of
horses with EPM showing a worsening of signs after the use of these medications suggest immunosuppression should be
avoided [45]. Ancillary treatments may include padded helmets, slings, good supportive care, and a deeply bedded stall.
Because of the suspicion that protozoal infections occur more commonly in immunocompromised patients,
immunomodulators or other therapies that may have a non-specific enhancement of the immune system may be helpful. Studies have shown that levamisole is a non-specific immunomodulator that affects T cell-mediated immunity, including delayed-type hypersensitivity, which also increases the phagocytic activity of macrophages [63]. The use of
immunomodulators may have merit, but further investigation is necessary. Although unlikely, it is possible that these drugs may also enhance the immunopathologic effects associated with CNS infection. Prolonged therapy with antifolate medications should be monitored for signs of bone marrow suppression with resultant anemia, thrombocytopenia, or neutropenia [55,56]. The combination of trimethoprim-sulfamethoxazole and pyrimethamine also has an effect on reproductive function in pony stallions [64]. It may induce changes in copulatory form and agility, and it may also alter the pattern and strength of ejaculation [64]. Therefore, caution should be used when treating stallions for a neurologic disease believed to be EPM.

Supplementation with folic acid, folinic acid, and/or brewer's yeast has been recommended for treatment of presumed folic acid deficiency in horses treated with the standard therapy, particularly pregnant mares [56,65]. However, folic acid supplementation has been discouraged by some investigators because of poor absorption and the potential for toxic effects on the bone marrow [11]. Toxicity has been reported in newborn foals born to mares that were treated for EPM. These mares had been treated with anti-folate medications and, concurrently, supplemented with folic acid [66]. Therefore, particularly in pregnant mares, folic acid supplementation should not be used until controlled clinical trials can be performed to corroborate or refute these findings.

Some clinicians recommend the use of additional supplements such as vitamin E (6000 - 8000 IU/day, orally) and thiamine that may facilitate healing of nervous tissue when treating horses with EPM [11,67]. However, clinical trials have not been performed to establish the efficacy of this supplementation.

Prevention - Because of the nature of the horse business, prevention of clinical cases of EPM will be difficult. Another complicating factor is the widespread distribution of the parasite throughout many parts of the United States. Although a vaccine is currently available, it remains unproven. In light of the difficulties experienced in the development of effective vaccines for other protozoan parasites, development of an efficacious vaccine for EPM will most likely be in the distant future [68,69]. Closely monitoring high-risk age groups such as young horses and old horses for evidence of neurologic disease may help detect EPM early. Additionally, EPM may be the cause of the clinical signs that horses present for neurologic disease in the warmer months. Because many major horse competitions take place in the fall of the year, monitoring of horses subsequent to transport and competition may be helpful. Wildlife, such as opossums, and pests, such as mice and rats, should be denied access to feed by using rodent-proof containers and by storage in enclosed facilities. Excluding birds from facilities may help prevent some cases of EPM. Case histories from affected horses indicate that the development of clinical signs often occurs after some other health event. Close monitoring of broodmares close to foaling and horses that develop a major illness or injury is important, because it may aid the early diagnosis of EPM cases.

In addition to designing a prevention plan that minimizes risk factors associated with the definitive host, it is also important to consider the intermediate host's role in EPM. Several species of mammals have been reported to act as natural or laboratory intermediate hosts in the life cycle of S. neurona, and these animals only represent a threat after death. Therefore, veterinarians should encourage horse owners to pick up dead cats, armadillos, skunks, and raccoons on their property and dispose of the carcass. This will prevent opossums from eating the dead animals and excreting more sporocysts. Carcass retrieval should be done carefully with an inverted plastic garbage bag or some other similar tool. Cleaning the horse's stall, barn, and environment may also be helpful. However, a recent report suggests that all common disinfectants used in veterinary hospitals do not kill the parasite. The only effective way to kill the parasite is through the use of heat (> 60°C for 1 min). Therefore, feeding heat-treated feed and steam cleaning the horse's environment may help to reduce some cases of EPM.

3. CVM

CVM is the leading cause of non-infectious spinal cord ataxia in horses throughout the world. This condition has been reported most frequently in Thoroughbreds, but it has also been identified in most breeds of horses. The underlying cause of the clinical signs is stenosis, which can be a result of a congenital malformation/malarticulation or may be a developmental problem that results from either symmetrical or asymmetrical overgrowth of the articular processes of the cervical vertebrae [4,46,70].

CVM is characterized by ataxia and weakness as a result of stenosis or a narrowing of the vertebral canal combined with malformation and/or malarticulation of the cervical vertebrae. In a previous study, we recognized an association between widespread osteochondrosis and spinal canal stenosis, which suggests that CVM may represent a systemic failure in the development or maturation of cartilage and bone [71]. In general, horses presented with CVM are less than 3 yr of age, although the problem can occur at any age. Male horses seem to be more commonly affected with CVM than are female horses. The reason for this prevalence is unclear. It may partly be a result of the fact that ataxia in fillies is more often overlooked than it is in males, and as a result, such fillies are sometimes retired from exercise to the breeding shed. However, this prevalence may also result from the influence of testosterone on the rate of growth or on the development of osteochondrosis, which seems to be an important part of this condition [4,72,73].

CVM is characterized by spinal ataxia and weakness of all four limbs as a result of compression of the cervical vertebral
infection. One or all of these tests may be useful during an outbreak of EHV-1 neurological disease. The virus can be isolated from the finding of xanthochromic cerebrospinal fluid. There are four tests that are commonly used to help diagnose EHV-1 infection.

The criteria, which have been used for the diagnosis of the neurologic form, have been described, but, in general, a prospective diagnosis can be made based on clinical signs, a history of antecedent or concurrent upper respiratory disease, and the finding of xanthochromic cerebrospinal fluid. There are four tests that are commonly used to help diagnose EHV-1 infection. One or all of these tests may be useful during an outbreak of EHV-1 neurological disease. The virus can be isolated in a narrow vertebral canal. The compression of the spinal cord is caused by stenosis of the vertebral canal either within an individual vertebral body or between adjacent vertebrae. The stenosis of the vertebral canal may be identified anywhere from C1 to T1, although it is most often observed in the mid-cervical region. Spinal cord compression may be intermittent or continuous, and depending on the duration and severity of the compression, the signs can be quite variable. Rooney described three forms of cervical vertebral stenotic myelopathy in the horse. These three forms include a flexion-fixation form that is often present at birth, a symmetrical overgrowth of articular processes resulting in compression most often observed during neck flexion, and an overgrowth or proliferation of the articular processes leading to bony compression of the vertebral canal. These descriptions are no longer in use, and Mayhew et al., [4] have best described the condition as stenosis of the vertebral canal that is present at all times. Powers et al., and Rush Moore et al., [73] have since described the forms of the spinal cord compression as either dynamic or static, depending on when the compression is best recognized on myelogram.

Diagnosis of affected horses involves recognition of clinical signs of weakness, ataxia, and spasticity in all four limbs along with stenosis of the vertebral canal. Indication of vertebral canal stenosis may be obtained by examination of radiographs of the cervical vertebral column taken in the standing lateral position [73]. Use of minimal sagittal diameter as well as intra-vertebral and inter-vertebral ratios based on measurements made on the standing lateral radiographs can be useful for veterinarians in the field. The evidence of the exact location of stenosis is obtained by performing a myelogram, which is an essential procedure before surgical correction is undertaken.

CVM is found most often in young, well-fed, growing horses. The onset can be very early in life, although, in most horses, the clinical signs are first recognized between 1 and 2 yr of age. In some horses, a significant arthropathy of the vertebral facet joints may occur. When this is the case of stenosis, many of these horses do not begin to demonstrate clinical signs until later in life, often 5 - 7 yr of age. More recently, we have observed many young horses with compression located in the caudal cervical region that are < 2 yr of age. Characteristic clinical signs are a result of damage to the white matter in the cervical spinal cord. Because the tracts to the pelvic limbs are more superficial, the usual presentation is for weakness, ataxia, and spasticity that is most noted in the pelvic limbs over the thoracic limbs.

Management of affected horses may be medical or surgical [70,71,74,75]. In medical management, the use of anti-inflammatory medications to reduce swelling, edema formation, and, subsequently, reduction of spinal cord compression is involved. Use of non-steroidal medications and dimethyl sulfoxide are most common. Corticosteroids are indicated in horses demonstrating signs of acute spinal cord trauma. Some horses < 1 yr of age have been managed by use of a modification in their diet and exercise programs. Surgical correction is aimed at stopping repetitive trauma to the spinal cord that results from the stenosis, and, thus, it allows the inflammation in and around the spinal cord to resolve. The biggest dilemmas facing the surgeon and the owner are safety concerns involved with the use of the horse after the surgery. Surgical correction has been very helpful with 80% of the horses demonstrating improvement after surgery and a period of rehabilitation.

### 4. EHV-1 Myeloencephalopathy

Herpes viride are divided into three groups, alpha, beta, and gamma, based on host range, reproductive cycles, cytopathology, and genome structures. Equine herpes virus type 4 (EHV-4) is responsible for upper respiratory infection in young horses and, rarely, abortion, whereas EHV-1 infection of pregnant mares can produce syndromes of late gestation abortion, still birth, and weak neonatal foals and can sometimes result in myeloencephalopathy. EHV-1 is associated with the neurologic form of rhinopneumonitis. In a paper by Slater et al., [76]. EHV-1 was shown to be a neurotrophic. Alpha herpes viruses cause neurologic signs in horses as a result of vasculitis, thrombosis, necrosis, and direct damage to neurological tissue. EHV-1 is considered most important to the equine industry because of the economic impact that results from multiple abortions, although outbreaks of equine respiratory disease, usually in young horses, and occasional outbreaks of myeloencephalopathy are also important and can be quite expensive and devastating. The respiratory and abortion outbreaks have resulted in a detailed tracking of this virus worldwide; through this surveillance, variations in the composition of the nucleic acid have been detected. EHV-1, equine herpes virus type 3 (EHV-3) and EHV-4 are typical alpha herpes viruses with a DNA genome, whereas equine herpes virus type 2 (EHV-2) and equine herpes virus type 5 (EHV-5) are gamma herpes viruses. The alpha herpes viruses have a wide host range, short reproductive cycle, and, most importantly, have the capacity to establish latent infections. EHV-1, EHV-3, and EHV-4 (alpha) can be distinguished from EHV-2 and EHV-5 (beta) and from each other by the use of DNA fingerprinting, polymerase chain reaction (PCR) testing, and several immunologic tests [50,77]. These genetic and biologic markers help to track the viruses and explain the changes in virulence of the virus. Additionally, they may partially explain the inability to predict when and why cases of neurological disease occur.

The criteria, which have been used for the diagnosis of the neurologic form, have been described, but, in general, a prospective diagnosis can be made based on clinical signs, a history of antecedent or concurrent upper respiratory disease, and the finding of xanthochromic cerebrospinal fluid. There are four tests that are commonly used to help diagnose EHV-1 infection. One or all of these tests may be useful during an outbreak of EHV-1 neurological disease. The virus can be isolated.
from pharyngeal or nasal secretions. If isolated from these areas only, it strongly suggests that this virus is the cause of the neurological disease.

PCR testing can be used to look for the virus antigen in pharyngeal or nasal secretions. A positive test indicates presence of the virus in these tissues. PCR testing can also be used to look for virus antigens in the blood stream. This test uses white blood cells (WBC) harvested from the buffy coat. The presence of viral antigens indicates that the horse is currently viremic or has recently been viremic. Serology is used to look for the antibody to EHV-1 in the blood. A three to four-fold rise in anti-EHV-1 neutralizing antibody titers between the acute and convalescent indicates recent virus infection. In addition, histologic evaluation of nervous tissue from an affected horse will show the classic vasculitis changes.

The natural spread of this disease is through inhalation and ingestion, primarily by nasal aerosols from infected horses. Infections first occur on the mucosal surface of the respiratory tract, although direct contact with infected aborted fetuses or placental tissues may also serve as a probable source of infection.

Spread of infection may occur in three ways: (1) through direct cell-to-cell contact, (2) hematogenously through infected peripheral blood monocytes, (3) neurally through where the virus is considered to be both neurotrophic and endotheliotrophic and where the virus results in vasculitis. Glycoproteins on the surface of the viral membrane bind to the surface of the host cell and allow fusion of the virus to the host cell to occur. Replication occurs in the nucleus, and protovirions derive their envelope from the inner lamella of the nuclear membrane. Virus particles bud from the cell surface and result in necrosis of the respiratory epithelial cells.

The neural lesions are a result of the vasculitis. There is a cell-associated viremia that, in the presence of high antibody titers, endothelial cells become infected and, in combination with the immunologic reaction on the endothelium (antigen-antibody complexes), leads to vasculitis and thrombosis. The vasculitis and thrombosis results in spinal cord malacia and the onset of clinical signs. Latency seems to occur with this virus, resulting in persistent viral presence in the body with intermittent episodes of reactivation of infection. This is usually after some stressful event such as illness, transportation, or management change.

The first definitive association between EHV-1 and myeloencephalopathy was made after the isolation of the virus from the brain and spinal cord of a horse in Norway in 1966. Since that time, examples of similar cases have been demonstrated to have a worldwide distribution. In most instances, the myeloencephalopathy occurs as an outbreak of cases, although sporadic cases of the disease can also be observed. When the host has contacted the virus, it enters the respiratory epithelium and associated lymphoreticular tissues. After the virus has entered the susceptible host, it will rapidly enter lymphocytes and circulate throughout the body in virus-infected phagocytes. When the virus is within the cell, it seems to be able to circulate without destruction, even in the face of high circulating antibody titers. In this location, the virus can disseminate to other tissues including the CNS [49].

**Immunity** - Cell mediated immunity is reported to be more important than humoral immunity. This is because of the high degree of cell association in infection and the ability to have cell-to-cell infection without release of virions. Antibody concentrations are associated with protection from disease; during an outbreak of respiratory disease, protection is more likely to occur in seronegative mares.

Vascular endothelium is the site of viral replication of EHV-1. The vasculitis caused by EHV-1 may be a result of two mechanisms. The first is caused by direct damage to the endothelial cells lining small blood vessels. The second may be caused by formation of immune complexes of EHV-1 virus and antibody. The finding of endothelial necrosis is not limited to the vessels of the CNS but occurs in many other sites throughout the body. The neurological signs are a result of the vasculitis, hemorrhage, necrosis, and ischemia, which can result from the virus having a profound endothelial tropism. Thus, the deficits will correspond to the site of damage, but, in general, the ischemia and necrosis cause the most severe damage to the grey matter. The propensity of certain viral strains to induce neurological signs does not seem to be the result of those viruses having specific neurotropism, although some recent work using specific pathogen-free ponies resulted in chorioretinopathy and neural lesions. This suggests that neurotropism is present with this disease [50,76,78-80].

**Clinical Signs** - Clinical signs include acute fever, inappetence, and depression combined with serous nasal discharge and cough. Infection is usually confined to the upper respiratory tract, except in cases where secondary bacterial infection occurs. The spread of virus is slower than with influenza, although both viruses are transmitted by aerosolization. Abortion and fatal neonatal disease can occur; abortions may occur at any stage of the gestation but seems to occur most often late in pregnancy. Foals may become infected in utero, are born very weak, and often die.

Neurological signs are often preceded by a fever or upper respiratory disease in the 2 wk before the onset of neurological signs. The clinical signs observed as a result of EHV-1 myelitis can be quite variable and, in my experience, has even included unilateral lameness caused by involvement of the brachial plexus to cerebral signs. In most affected horses, the EHV-1 virus results in symmetrical ataxia and weakness of the pelvic limbs along with urinary incontinence, loss of sensation, and motor deficits around the tail and perineal area of one or more horses on the premises. Affected horses often begin with minor neurologic gait deficits, which sometimes rapidly progress to significant clinical signs.

Management of horses with suspected EHV-1 myeloencephalopathy should be directed toward achieving a safe environment and providing excellent nursing care. The disease may be transmitted from horse to horse, which means that segregation or
isolation of affected horses is important. However, in most instances, the affected horses are not likely to be contagious at the
time of the neurological signs. In addition, the management of a recumbent horse in a small isolation stall that restricts its
ability to hoist itself makes keeping the horse in isolation difficult and often impossible. The level of care necessary is
dependent on the severity of clinical signs. A horse with obvious bladder dysfunction should quickly and as frequently as
possible have aseptic evacuation of the bladder. In both mares and stallions, we have successfully placed an indwelling Foley
catheter that is attached to a simplex or other fluid delivery tube. This is then glued together and sutured to the leg of the
horse to allow continuous drainage at a site low enough on the leg so as to prevent urine scald. In stallions, placement has
been made through a perineal urethrostomy site. Prophylactic antibiotics are essential to combat the problems associated with
the development of cystitis. In addition, one author has observed one Quarter horse stallion, recumbent for an extended period
of time, that developed pressure necrosis of several sites on the body. These sites became infected and led to septicemia and
eventual seeding of the CNS with organisms.

It is our opinion that the use of anti-inflammatory agents such as IV dimethyl sulfoxide (DMSO) at a rate of 0.9 g/kg as a
10% solution is helpful. This means that a 500 kg horse would receive 500 ml of DMSO diluted in 5000 ml of normal saline.
The osmolality of this solution is approximately 1660 mosm. We routinely use this once daily for 3 days; after that, the
solution is administered once every other day for three or four additional treatments or longer if necessary. Furthermore, it is
our opinion that administration of corticosteroids such as dexamethasone (0.05 - 0.1 mg/kg, IV) or prednisone (1 mg/kg/day)
is useful. Larger doses of corticosteroids have sometimes been recommended, but it is important to maintain as short a course
as possible. Careful use of NSAIDS is essential, because many of the horses may be unable to walk to water to drink and
dehydration is a serious complication. The daily water needs for an affected horse should be 60 - 80 ml/kg daily. Along with
the water, it is important to feed a gruel or, if the horse can eat, to provide a highly palatable source of energy and protein
daily. Use of anti-viral agents such as Acyclovir has been attempted in horses, although there are only a few publications
supporting this use in the veterinary literature.

The prognosis is guarded to favorable if one is willing and able to provide long-term management for the horse. Treatment of
not only the neurological disease but also the complications such as cystitis, urine scald, inability to rise, and constipation or
fetal incontinence also sometimes enter the picture and are very important to remember when informing the owner of his or
her long-term commitment. None of the vaccines on the market provide protection against the neurological form of the
disease. Still, the risk of viral shedding may be decreased in herds of vaccinated horses. Therefore, vaccination is important
and recommended, although the ideal frequency is not known.

Management of an outbreak has recently been the focus of many veterinarians in the state of Ohio and elsewhere. Although
EHV-1 is entrenched in most horse populations as a result of life-long latent infection that results in intermittent shedding, it
is unusual for the virus to undergo changes that make in more virulent. However, this potential to increase its virulence and
expand its cellular tropism has been demonstrated [81-93]. This past January, an outbreak of the neurological form of EHV-1
occurred in the state of Ohio. The details of this outbreak are currently under investigation and the subject of other
publications. However, a review of the important management features when faced with such an outbreak are appropriate for
this paper. Important items to remember are that the communicability of an EHV-1 infected horse is greatest during the initial
period of fever and respiratory signs. Nasal shedding may occur for as long as 14 days with clinical respiratory disease being
observed 3 - 6 days after exposure.

The elements that are important to the management of an outbreak are the minimization of exposure to the pathogen by
safeguarding the introduction of horses into a new group, the maintenance of as high a level as possible of innate and
immunologic resistance (healthy, low-stressed, well-vaccinated horses), and the maintenance of horses in small groups of like
horses, being especially careful to segregate affected from nonaffected groups.

Outbreaks of respiratory disease, abortions, or myeloencephalopathy may occur despite the best vaccination schedules. If
faced with an extremely aggressive virus or an excessive quantity of virus or if the currently available vaccines are not fully
protective, then an outbreak may occur despite vaccination. When this happens, all horses in physical contact or sharing the
same facility should be considered as exposed and should be placed under restricted movement; if possible, they should be
placed in an isolation facility. Restricted movement should be for a period of at least 21 days, which is approximately three
times the infective period.

5. WNV Encephalitis

WNV had not been seen in the Western Hemisphere before 1999. This virus is currently recognized to have a geographic
range greater than any other known Arbovirus and can be found throughout Africa, north to central Europe, and eastern Asia
[84]. The virus was first isolated from the blood of a woman in Uganda in 1937 [84]. The earliest reported epidemic of WNV
encephalitis was recognized retrospectively, and it involved more than 500 hospitalized patients in Israel in 1957 [84]. The
largest epidemic of WNV encephalitis on record occurred in South Africa during 1974, and it resulted in thousands of human
infections [85]. More recently, epidemics of WNV encephalitis have occurred in Romania (1996 - 1997), Czechland (1997),
Italy (1998), and Russia (1999). It is now considered a reemerging, mosquito-borne disease in Europe [85]. How or when
WNV was introduced into the United States is unknown. There is speculation that it was introduced through the importation of birds or through, possibly, the transportation of a mosquito into the United States by ship or airplane.

WNV is a member of the Japanese encephalitis virus complex of the genus Flavivirus, family flaviviridae. Some of the common members of this serocomplex include: Japanese encephalitis, Kunjin, Murray Valley encephalitis, St. Louis encephalitis (SLE), and WNV. Until 1999, the only members of the Flavivirus genus detected in North America were Powassan and SLE. The epidemiology of WNV is nearly identical to that of SLE in that both diseases are principally transmitted by a species of Culex mosquitoes and have birds as the reservoir [84]. The differences are that WNV causes disease and mortality in wildlife (birds, particularly crows and blue jays) and domestic animals (particularly horses) [84]. While SLE virus does not cause any remarkable disease in wildlife or domestic animals, both can cause disease in humans.

**Epidemiology in Horses** - Early outbreaks of WNV encephalitis in horses occurred in 1962 in France, 1963 in Egypt, 1996 in Morocco, 1998 in Italy, and 1999 - 2002 in the United States [53,85]. The case fatality rate was 44.7% (42 of 94 horses) in Morocco, 42% (6 of 14 horses) in Italy, 36% in the United States in 1999, and 38% (23 of 60 horses) in the United States in 2000 [53]. The age of the horses ranged from 4 mo to 38 yr with a mean age of 14 yr [53]. There were more males affected (36 of 60 horses) than females, and there did not seem to be a breed predilection, because there were 11 breeds affected [3]. In the United States in 2001, there were 738 equine cases of WNV in 19 states. Mortality data is not yet available. In 2002, 14,717 equine cases of WNV were recognized in 40 states.

**Clinical Signs in Horses** - In U.S. cases, most of the cases were ataxic (85%), almost one-half of the cases were weak (48%), many cases were recumbent or had difficulty rising or both (45%), some cases had muscle fasciculations (40%), less than one-quarter of the cases had fever (23%), and less than one-fifth of the cases had a paralyzed or droopy lip (18%), a twitching face or muzzle (13%), teeth grinding (7%), or blindness (5%) [3]. When profound weakness and tremors are identified in concert with hyperesthesia and ascending paralysis, rabies, botulism and EHV1 myeloencephalopathy should also be considered along with other encephalitides such as western equine encephalitis (WEE), eastern equine encephalitis (EEE), and Venezuelan equine encephalitis (VEE).

**Pathology** - No gross pathologic lesions were detected in the Italian cases. Histologically, all animals exhibited slight to moderate non-suppurative encephalomyelitis, primarily in the spinal cord and lower brainstem, affecting both gray and white matter [86]. The most severe lesions were in the thoracic and lumbar spinal cord [86]. The lesions in U.S. equine cases were similar to those found in the Italian cases, except that the brainstem lesions were more severe in U.S. cases [87]. Unlike encephalitis caused by alpha viruses such as WEE and EEE, there was a lack of significant changes to the cerebral and cerebellar cortices [88].

**Diagnosis** - Several serologic tests have been used to diagnose WNV disease including plaque reduction neutralization (PRN), hemagglutination inhibition (HI), complement fixation (CF), enzyme-linked immunosorbent assay (ELISA), and antigen capture ELISA [84]. Virus isolation may also be attempted from whole blood, serum, CSF, or brain or spinal cord tissues [84]. Other diagnostics include reverse transcription polymerase chain reaction (RT-PCR) of CNS tissues and immunohistochemistry [84]. The plaque reduction neutralization test requires BSL3 laboratory capabilities; therefore, few laboratories are equipped to perform this test. In the acute cases of WNV encephalitis in horses, antigen-capture ELISA has been used to detect WNV-specific immunoglobulin M (IgM) [53]. In experimentally and naturally infected horses, IgM antibodies are detected within 8 - 10 days and persist for < 2 mo [53]. In recent reports, they were also able to isolate WNV from the CNS tissues in some (7 of 10) cases and detect WNV RNA using RT-PCR in all 10 cases where brain tissue was submitted [3]. Veterinarians should consult with their state's Department of Agriculture and Department of Health to determine the requirements for sampling and the place where samples are to be sent.

**Treatment** - Supportive care is the only treatment available. Anti-inflammatory medications such as NSAIDS, steroids, and 10% DMSO may help to alleviate CNS inflammation and pain. Some horses may require IV fluids and possible nutrient support. In some cases where horses are recumbent and unable to rise, slings may be helpful as well [9].

**Prevention** - There are two methods of preventing or controlling WNV infections in horses. Both methods are very important: (1) integrated mosquito control, (2) vaccination. The integrated mosquito control includes the reduction of mosquito breeding sites and the use of larvicides and adulticides. Additionally, horses should be housed indoors during peak periods of mosquito activity (dusk and dawn). Avoid turning on the lights inside the stable during the evening and night. Place incandescent bulbs around the perimeter of the stable to attract mosquitoes away from the horses. Additionally, black lights do not attract mosquitoes. Remove all birds that are in or close to the stable to reduce the potential reservoirs. Eliminate areas of standing water on your property. Shallow standing water, used tires, manure storage pits, and drainage areas with stagnant water are ideal mosquito breeding places. Topical preparations containing mosquito repellents are available for horses. Read the product label before using, and follow all instructions. Use fans on the horses when they are in the stable to help deter mosquitoes. Fog stable premises with a pesticide in the evening to reduce mosquitoes. Read directions carefully before using. Local mosquito control authorities may be able to help in assessing the mosquito breeding risks associated with your clients' specific properties. The second method of controlling WNV infections in horses is through vaccination. A vaccine was developed using killed virus and has been sold under a conditional license since August 2001. As of February 2003, the vaccine has received approval for full license. A recent experimental study involving 30 horses was performed. In the study,
Cranial nerve involvement is primarily reported to affect cranial nerves V, VII, and VIII, but cranial nerves II, III, IV, VI, IX, and abnormal use of forelimbs or hindlimbs [1,12,13,15]. Damage to peripheral motor nerves may result in gait deficits and muscle atrophy in the gluteal region is sometimes present along with mild degrees of ataxia [2,3,5,6,9]. Muscle atrophy associated with cranial nerve involvement may occur in the head region. Damage to peripheral motor nerves may result in gait deficits and muscle atrophy. The area of anesthesia may be surrounded by an area of hyperesthesia [1,2,8].

Diagnosis - The definitive diagnostic test is a post-mortem examination. The peripheral WBC count usually reveals a mature neutrophilia with hyperfibrinogenaemia, mild-to-moderate anemia, and increased total protein, all indications of a chronic inflammatory process [3,5,13,15]. Examination of the CSF may reveal an elevated protein (70 - 300 mg/dl) along with an elevated WBC count. The WBC count indicates a mononuclear inflammatory reaction, although CSF cytology may be normal, particularly in the acute stage of the disease [2,3,5,6,8,11,13]. Radiography may be required to rule out trauma to the tail head or cranial nerve involvement such as a fractured petrous temporal bone [2,8]. Some horses with clinical signs exhibit the presence of circulating P2 myelin antibody in the serum [10,17]. However, the presence of this antibody is only supportive of the diagnosis; the same antibody has been detected in horses with EHV-1 and equine adenovirus infections [1,2,10,13,16,18].

6. Polyneuritis Equi
Polyneuritis equi (PNE) is an uncommon neurologic disease in all equine species. It is characterized by tail and anal sphincter paralysis and is often accompanied by cranial and peripheral nerve damage [90,91]. Previous reports described the disease as neuritis of the cauda equina; however, frequent involvement of the cranial and peripheral nerves led to the term polyneuritis equi. Although the disease has been more readily recognized in Europe, cases have been reported from Great Britain, Canada, and the United States [90,91]. There does not seem to be a breed, sex, or age predilection, but the youngest horse affected was 17 mo of age [92].

The cause of this disease is unknown, although primary immune reaction and viral inflammatory disease have been suggested; however, it is very possible that one may be a consequence of the other [92]. Several infectious agents have been suggested, such as EHV-1, equine adenovirus, Campylobacter spp., and streptococcal bacteria [93,94]. The pathologic lesions resemble those of Guillain-Barre syndrome in humans and, to some extent, appear similar to experimental allergic neuritis (EAN) in rats [10,13]. There is evidence to suggest that the immune system is involved, because horses with PNE have circulating antibodies to the P2 myelin protein that is present in rats with EAN [10,17]. The significance of this is that PNE may be both an inflammatory and immune-mediated disease.

Clinical Signs - The disease will often manifest itself in two forms. The acute signs include hyperesthesia of the perineal or head region or both. In the chronic form, horses show paralysis of the tail, anus, rectum, and bladder. This is often accompanied by fecal and urinary retention, urinary scalding of the hindlimbs, and, in male horses, penile paralysis [1-3,6,8,9,12,13,15].

The hindlimb signs in affected horses are often symmetrical, whereas the head signs are often asymmetrical [6,13,15]. Muscle atrophy in the gluteal region is sometimes present along with mild degrees of ataxia [2,3,5,6,9]. Muscle atrophy associated with cranial nerve involvement may occur in the head region. Damage to peripheral motor nerves may result in gait deficits and abnormal use of forelimbs or hindlimbs [1,12,13,15].

Cranial nerve involvement is primarily reported to affect cranial nerves V, VII, and VIII, but cranial nerves II, III, IV, VI, IX, X, and XII may also be involved [2,4,5,8,13]. Affected horses most often present with a loss of sensation in the perineal region combined with poor tail tone, urine and fecal incontinence, and muscle wasting of the gluteal region. At times, affected horses may have trouble with mastication or swallowing, a head tilt, an ear or lip droop, and ptosis [8,12,13]. There has been one report of a horse with brachial neuritis along with involvement of cranial nerves V, VII, and XII [2]. The horse also exhibited mild ataxia and weakness in all four limbs [2].

Colic caused by fecal retention and impaction is often accompanied by an atonic, distended bladder [1]. An acute or hyperaesthetic form is usually observed first, but this often progresses to the chronic form, which is characterized by hypalgesia or anesthesia and muscle atrophy. The area of anesthesia may be surrounded by an area of hyperesthesia [1,2,8].

Diagnosis - The definitive diagnostic test is a post-mortem examination. The peripheral WBC count usually reveals a mature neutrophilia with hyperfibrinogenaemia, mild-to-moderate anemia, and increased total protein, all indications of a chronic inflammatory process [3,5,13,15]. Examination of the CSF may reveal an elevated protein (70 - 300 mg/dl) along with an elevated WBC count. The WBC count indicates a mononuclear inflammatory reaction, although CSF cytology may be normal, particularly in the acute stage of the disease [2,3,5,6,8,11,13]. Radiography may be required to rule out trauma to the tail head or cranial nerve involvement such as a fractured petrous temporal bone [2,8]. Some horses with clinical signs exhibit the presence of circulating P2 myelin antibody in the serum [10,17]. However, the presence of this antibody is only supportive of the diagnosis; the same antibody has been detected in horses with EHV-1 and equine adenovirus infections [1,2,10,13,16,18].

Classically, the primary pathologic lesions involve the extradural nerve roots, but the intradural nerve roots may also be involved [2,3,5,12,13]. The lesions are granulomatous with various degrees of inflammation and infiltration of lymphocytes, eosinophils, macrophages, giant cells, and plasma cells. This inflammation leads to myelin degeneration, subsequent axonal demyelination, and eventual Wallerian degeneration of the affected nerve fibers. The histologic findings in PNE are consistent with those seen in EAN in rats [10,17].

The hindlimb signs in affected horses are often symmetrical, whereas the head signs are often asymmetrical [6,13,15]. Muscle atrophy in the gluteal region is sometimes present along with mild degrees of ataxia [2,3,5,6,9]. Muscle atrophy associated with cranial nerve involvement may occur in the head region. Damage to peripheral motor nerves may result in gait deficits and abnormal use of forelimbs or hindlimbs [1,12,13,15].

Cranial nerve involvement is primarily reported to affect cranial nerves V, VII, and VIII, but cranial nerves II, III, IV, VI, IX, X, and XII may also be involved [2,4,5,8,13]. Affected horses most often present with a loss of sensation in the perineal region combined with poor tail tone, urine and fecal incontinence, and muscle wasting of the gluteal region. At times, affected horses may have trouble with mastication or swallowing, a head tilt, an ear or lip droop, and ptosis [8,12,13]. There has been one report of a horse with brachial neuritis along with involvement of cranial nerves V, VII, and XII [2]. The horse also exhibited mild ataxia and weakness in all four limbs [2].

Colic caused by fecal retention and impaction is often accompanied by an atonic, distended bladder [1]. An acute or hyperaesthetic form is usually observed first, but this often progresses to the chronic form, which is characterized by hypalgesia or anesthesia and muscle atrophy. The area of anesthesia may be surrounded by an area of hyperesthesia [1,2,8].

Diagnosis - The definitive diagnostic test is a post-mortem examination. The peripheral WBC count usually reveals a mature neutrophilia with hyperfibrinogenaemia, mild-to-moderate anemia, and increased total protein, all indications of a chronic inflammatory process [3,5,13,15]. Examination of the CSF may reveal an elevated protein (70 - 300 mg/dl) along with an elevated WBC count. The WBC count indicates a mononuclear inflammatory reaction, although CSF cytology may be normal, particularly in the acute stage of the disease [2,3,5,6,8,11,13]. Radiography may be required to rule out trauma to the tail head or cranial nerve involvement such as a fractured petrous temporal bone [2,8]. Some horses with clinical signs exhibit the presence of circulating P2 myelin antibody in the serum [10,17]. However, the presence of this antibody is only supportive of the diagnosis; the same antibody has been detected in horses with EHV-1 and equine adenovirus infections [1,2,10,13,16,18].

Classically, the primary pathologic lesions involve the extradural nerve roots, but the intradural nerve roots may also be involved [2,3,5,12,13]. The lesions are granulomatous with various degrees of inflammation and infiltration of lymphocytes, eosinophils, macrophages, giant cells, and plasma cells. This inflammation leads to myelin degeneration, subsequent axonal demyelination, and eventual Wallerian degeneration of the affected nerve fibers. The histologic findings in PNE are consistent with those seen in EAN in rats [10,17].
degeneration, and thickening of the epineurium, endoneurium, and perineurium with proliferation, which causes obliteration of the neural architecture by the fibrous tissue [1,2,9,13]. The most severe lesions are in the cauda equina, but swelling, edema, and hemorrhage of cranial nerves may be seen. The fibrous tissue formation may lead to adhesions between the meninges and the periosteum of the vertebral bodies [13]. There are reports of involvement of the autonomic nervous system, but no changes in clinical signs have been reported [2,4]. The polyneuritis lesions are typical of the Guillain-Barre syndrome in humans, EAN in rats, and coon-hound paralysis in dogs [2,5,11-13]. This may indicate a combination of inflammatory and immune-mediated mechanisms in the pathophysiology of PNE. 

**Treatment** - The primary therapy is palliative. There is no known treatment for the disease. Removing feces from the rectum and evacuating the bladder are usually necessary. If there is cystitis caused by bladder distention, systemic antibiotics may be indicated. Some attempts have been made to treat the inflammation with corticosteroids, but the effects have been short-lived. The prognosis is usually poor, but the progression of the disease is slow. Some animals may be maintained for many months [2,4-6,8,12,13,15].

**Footnotes**

**References**

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