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LOSING CONTROL: NUTRITION-RELATED DISEASES OF THE CENTRAL NERVOUS SYSTEM

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Introduction

Neurological diseases can be some of the most devastating and dangerous clinical problems seen in horses. Due to their size, strength, and temperament, neurological horses can become a danger to themselves or to those around them. Several neurological diseases of the horse have nutritional origins. Large, fast-growing young horses which are overfed can sometimes become wobblers. Equine protozoal myelitis is caused by organisms which are transmitted to the horse orally, via grain, hay, pasture, or water. Equine degenerative myelopathy and equine motor neuron disease are both rarer conditions which have been linked to dietary vitamin E deficiencies. Some of these neurological diseases are treatable, but most are preventable with proper, balanced nutrition in appropriate daily amounts.

Equine Cervical Vertebral Malformation

DEFINITION AND HISTORY

Equine cervical vertebral malformation (CVM) is a developmental defect of the cervical vertebrae. As a result of abnormal growth, two adjoining vertebrae articulate abnormally, resulting in compression of the spinal cord as it traverses those two vertebrae. The most commonly affected joint is between the third and fourth cervical vertebrae (designated C3-C4).

These horses are often termed “wobblers” because they wobble or walk as if drunk or uncoordinated. Other synonyms for the condition include true wobblers, wobbles, cervical vertebral instability (CVI), and cervical vertebral stenosis (CVS). Many of these horses may be from families which typically produce large, fast-growing racehorses. These families may have a tendency to produce young horses with other signs characteristic of osteochondrosis (abnormal cartilage maturation into bone) such as a tendency toward rapid growth compared to their cohorts (age-matched pasturemates); osteochondritis dissecans (OCD) of the hock, shoulder, or stifle; and epiphysitis (asymmetry or overactivity in one or more of the growth plates of the long bones such as the distal radius at the level just above the carpus [knee] and the distal cannon bone just above the fetlock).

EPIDEMIOLOGY

Because the disease is one of rapid growth and overdevelopment, it is seen most often in young, growing horses of large breeds. Yearling and two-year-old Thoroughbreds, warmbloods, and Thoroughbred crosses, including appendix Quarter Horses, are most commonly affected. Sucklings, weanlings, and three- and four-year-olds are less commonly affected. Older horses rarely develop CVM because most have achieved their adult height by four to five years old. Typically, affected horses have been overfed, with higher than necessary levels of dietary energy, protein, or both (Reed and Moore, 1993). Unfortunately, this rapid growth is encouraged in younger horses raised for the commercial weanling and yearling markets, where size and premature athletic phenotypes bring higher prices. Dietary imbalances in the calcium to phosphorus ratio (1.5:1.0 recommended) and in trace mineral concentrations (copper and zinc) have also been implicated (Reed and Moore, 1993), but the data documenting their involvement are less clear.

CLINICAL SIGNS

Signs usually begin gradually and insidiously. Early signs may be a mildly stiff neck and mild proprioceptive (limb placing) deficits. Gradually more obvious signs appear as the spinal cord is compressed more severely. The affected horse may wobble more obviously, manifesting increased ataxia (loss of awareness of where its limbs are at rest and in motion), paresis or weakness (dragging toes, decreased range of motion), hypermetria (increased range of motion due to an inability to control movements in a normal range of motion), and spasticity (stiffness of movement, often observed as a decreased flexion of the hock and stifle joints). These signs are usually worse in the hind limbs than in the front limbs, due to the more superficial location and larger size (more susceptible to injury) of the hind limb nerve tracts in the spinal cord.

Neurological signs are graded on a scale of 0 to 4, where 0 is normal and 4 is falling down at normal gaits. A horse scored one grade worse behind than in front usually has a single focal cervical lesion. Horses with the hind limbs graded two or more grades worse behind than in front usually have more than one lesion contributing to the neurological signs. Horses with hind and front limbs graded equally may have a lower cervical lesion (e.g., C6-C7), resulting in some affectation of the lower motor neuron tracts to the forelimbs.

DIAGNOSIS

Definitive diagnosis is made by obtaining cervical radiographs and a myelogram (Rantanen et al., 1981). Simple standing or recumbent cervical radiographs may be sufficient to demonstrate that there is so much narrowing of the spinal canal

that the horse has CVM. If plain films do not definitively demonstrate a lesion, then a myelogram is indicated and is performed under general anesthesia. A radiopaque contrast agent (sometimes incorrectly termed a “dye”) is injected into the foramen magnum, the opening between the base of the skull and the first cervical vertebra. The needle is placed deeply into the space between the overlying membranes (the meninges) and the spinal cord. Subsequent radiographs document any narrowing of the spinal canal by compression of the dye column. Flexion or extension of the neck (stressed views) may be necessary under anesthesia to recreate the position in which the cord may become pinched (as the awake horse normally moves its neck around while eating, drinking, and exercising).

Cerebrospinal fluid (CSF) is obtained before the contrast agent is injected during the myelogram. If the myelogram results are positive for CVM, the CSF may be saved but not analyzed. However, if the myelogram is negative, or if money is no object in diagnosing all possible causes of the horse’s ataxia, then the CSF is analyzed subsequently for evidence of equine protozoal myelitis, equine herpesvirus-1 myelitis, meningitis, and neoplasia.

TREATMENT

Treatment of horses with CVM is controversial. Years ago these horses were all considered unsalvageable and euthanized. Research and clinical experience at some universities since then have resulted in the development of various surgeries for stabilization of the pinched vertebrae and spinal cord (Wagner et al., 1981). The most commonly performed procedure is ventral body fusion, in which a bone plug graft or, more recently, a metal basket is placed into a predrilled hole to prevent flexion of the two vertebrae. Over time the basket fills with new bone growing in from the sides, and the space becomes fused and unable to flex. Dorsal slot laminectomy also has been used to relieve spinal cord pressure in horses with static cervical vertebral stenosis diagnosed by myelogram without requiring flexion or extension to observe the lesion. The equine mortality insurance industry has embraced these surgical procedures and sometimes requires that they be performed on insured horses under threat of policy vitiation.

Observed sequelae include cervical muscle atrophy either due to nerve damage or from disuse due to bone pain subsequent to surgery; fracture of one or both vertebrae; misplacement of the basket implant resulting in failure to stabilize the joint; development of instability in the joint rostral or caudal to the stabilized joint; and the whole litany of possible complications of general anesthesia in any horse, including recovery fractures, pneumonia, diarrhea, and renal disease.

Another controversial method of minimizing neurological signs in these horses is the use of a near starvation diet and stall confinement to reduce growth rate and minimize further development of osteochondrosis (Donawick et al., 1989, 1993). The premise is that by decreasing nutritional impetus for fast growth, the growth

rate can be slowed and the already abnormal vertebrae can be afforded time to remodel until no cervical compression is apparent. This technique has been described twice in unrefereed literature but has not gained wide acceptance due to its possible humane aspects and due to it not having been evaluated in a controlled experimental setting. Young Thoroughbred horses were observed with very early, mild neurological deficits (Donawick et al., 1989, 1993). They then were fed poor quality grass hay, no grain, and no pasture, and they received strict stall rest over several months. The result was that most eventually had minimal neurological deficits, and most went on to perform adequately as racehorses. Their marketability was diminished by severely slowing their growth rate, but their neurological signs were minimized without surgical intervention.

PROGNOSIS

Many horses which survive the immediate postoperative period improve as a result of the ventral fusion surgery. However, few if any are normal afterward; there are nearly always residual neurological deficits. From a liability standpoint, one must question the wisdom of having these horses, previously diagnosed as neurological, ridden and raced in the company of other horses.

PREVENTION

Preventive measures primarily involve careful breeding and feeding programs with slower dietary pushing for fast growth. Breedings observed to produce wobblers in the past should be avoided. Mares which have produced wobblers previously should be monitored carefully for level of milk production, as heavily milking mares may be predisposed to producing faster growing foals. This phenomenon has been most apparent to this observer in Thoroughbred foals raised on nurse mares of draft heritage. Creep feeding must be done judiciously to prevent overfeeding by a greedy suckling or weanling which pushes its pasturemates away from the feeder. Feeding for the commercial market may be necessary but again must be done wisely to prevent creation of a large, well-muscled but ataxic yearling. Allowing individuals to mature at a more natural rate of growth results in adults of similar size; however, some may develop as athletes later if allowed to mature more naturally.

Equine Protozoal Myeloencephalitis

DEFINITION AND HISTORY

Equine protozoal myeloencephalitis (EPM) is a sporadic and sometimes fatal neurological disease of horses (but not donkeys or mules) caused by *Sarcocystis neurona*, a protozoan parasite which invades the central nervous system. EPM is

not contagious because the parasite stages in the infected horse do not produce protozoal stages which are infective to other horses. Synonyms for EPM include equine protozoal myeloencephalopathy, equine protozoal myelitis, equine protozoal encephalitis, EPM, and protozoal.

EPM was first reported as a clinical disease in horses in Kentucky in 1970 (Rooney et al., 1970). In 1974, an unidentified protozoal parasite was first associated with spinal cord disease in horses (Cusick et al., 1974). Initially, the organism was thought to be *Toxoplasma gondii* (Cusick et al., 1974) but was later shown to be a *Sarcocystis* species (Simpson and Mayhew, 1980). *Sarcocystis neurona* was first isolated from infected equine spinal cord and identified as the causative agent of EPM in 1991 (Dubey et al., 1991). In 1996, another protozoal parasite, *Neospora*, was also found to be associated with abnormal clinical signs of spinal cord disease in horses in California (Marsh et al., 1996).

LIFE CYCLE

Although the definitive life cycle is not completely known at this time, *Sarcocystis neurona* is believed to have a classic two-host predator-prey life cycle similar to all other *Sarcocystis* species. The opossum (*Didelphis virginiana*) is the definitive host (Fenger and Granstrom, 1995). Extrapolating from the known life cycle of another intramuscular parasite of opossums, *Sarcocystis falcatula*, it has been proposed that the organism normally lives in the muscles of cowbirds (*Molothrus ater*), pigeons, grackles, some finches, and other birds (the prey). Opossums (the predators) eat these birds. The organism then escapes from the bird muscle and sets up new life cycle stages in the intestine of the opossum. Recent work has shown that *Sarcocystis* spp. organisms (collected from infected bird muscle) can be given to naïve opossums, and *Sarcocystis* oocysts eventually can be collected from those opossums as the life cycle is completed (Cutler et al., 1999). The opossum excretes the parasite in its feces and possibly in its urine. Normally, the parasite is then ingested by another bird (the intermediate host), and the life cycle continues in a circular or cyclical manner.

The North American opossum is a definitive host for at least three species of *Sarcocystis*: *S. neurona* (Dubey et al., 1991), *S. falcatula* (Box et al., 1984), and *S. speeri* (Dubey and Lindsay, 1999). Genetic testing has shown that *S. neurona* and *S. falcatula* are >99.5% identical (Dame et al., 1995; Fenger and Granstrom, 1995). Combined with >99.5% genetic similarity with the parasite isolated from cowbird muscle, these data have been cited previously as evidence that *Sarcocystis neurona* and *Sarcocystis falcatula* are the same organism (Dame et al., 1995; MacKay, 1997). However, more recent work has disproven the identity problems between *S. neurona* and *S. falcatula* (Cutler et al., 1999). *S. falcatula* oocysts from naturally infected cowbirds were fed to naïve opossums. The infective opossum feces were then administered to naïve horses. There were no clinical signs in the horses and no conversion in *S. neurona* antibodies in either serum or

cerebrospinal fluid (Cutler et al., 1999). Subsequent work from the same laboratory has shown differences in DNA markers between *S. neurona* and *S. falcatula* (Tanhauser et al., 1999).

In the most recently published work on the intermediate host of the EPM organism, the common domestic cat (*Felis domesticus*) was shown to be capable of carrying and transmitting *Sarcocystis neurona* (Dubey et al., 2000). These data have led to the suspicion that the cat may be the intermediate host for *S. neurona* (Dubey et al., 2000). At the very least, this experiment will allow investigators to study the disease more easily in the laboratory since they now have a functional intermediate host for experimental reproduction of the disease.

It is suspected but unproven that, after excretion by the opossum, the parasite may be spread further by insects or other animals, including skunks. If a horse comes in contact with infective opossum feces or urine, regardless of how they arrived in its environment, the horse may ingest the parasite and become infected. Once ingested by the horse, the parasite reproduces in the lining of most blood vessels and can spread via blood (parasitemia) throughout the horse's body, including the central nervous system. Usually the parasite does not enter nervous tissue, so most horse infections are inapparent or subclinical. Recent data have shown as many as 50% of clinically normal horses are seropositive for EPM (blood test positive), indicating exposure to the parasite, but only a small fraction of all horses actually develop clinical neurological signs (MacKay, 1997; Saville et al., 1997; Bentz et al., 1997; Blythe et al., 1997).

Because the stages of the parasite in the horse are not capable of sexual reproduction, the horse is a dead-end host and cannot transmit the infection any further. However, if the two horses have been living under the same conditions for several months, the normal horse is subject to the same routes of parasite ingestion which proved infective for the sick horse.

EPIDEMIOLOGY

In recent studies, approximately half of the clinically normal horses tested were EPM seropositive in Pennsylvania (45% positive), Ohio (53% positive), and Oregon (45% positive) (Saville et al., 1997; Bentz et al., 1997; Blythe et al., 1997). Older horses were routinely positive more often than younger horses. These data illustrate that as horses age, they are more likely to have been exposed to the EPM organism at some point in their lifetimes. There were no significant breed or gender effects on seroprevalence. Seroprevalence was lower in areas with low rainfall (Blythe et al., 1997) and longer, colder winters (Saville et al., 1997). These findings imply that the organism cannot survive as easily in very hot and dry climates or in much colder (frequently below freezing) climates.

Except for the rare horse exported from the U.S. that contracts EPM after leaving the country, EPM is restricted to those areas of the world where the opossum may be found naturally. Clinical disease has been reported widely in North America

(Fayer et al., 1990) and parts of Central and South America. Most cases are sporadic and isolated (singular) on a given farm, but widespread farm outbreaks have been reported occasionally in Kentucky, Ohio, Indiana, Michigan, and Florida. In the first report of a large number (n=364) of microscopically confirmed cases of EPM, infection was most common in Thoroughbreds, Standardbreds, and Quarter Horses (Fayer et al., 1990). The ages of affected horses ranged from 2 months to >19 years.

Recent epidemiological investigations have described several risk factors for the development of clinical EPM (Saville et al., 2000a). Horses had increased risk for developing EPM in spring, summer, and fall when compared to winter; when all feed materials (hay and grain) were not secured from wildlife; when hay alone was not secured; when opossums had been observed on the farm; when there was a previous diagnosis of EPM on the farm; when horses were used as racehorses or show horses as compared to breeding or pleasure horses; and when horses had been ill in the 90 days prior to admission for EPM diagnosis. Horses had decreased risk for developing EPM when feed was protected from wildlife (opossums and birds) and when the barn or pasture was close to a creek or river. The proximity of creek or river bottoms probably provides a more attractive habitat for opossums, which then have no need to invade the artificial environment of the barn and its feed sources. The implications from these data are obvious. Whenever possible, horses must be kept in an opossum-free environment and feed materials must be secured.

CLINICAL SIGNS

Clinical signs of disease may not occur for a year or more after ingestion of the organism. Stress (exercise, transport, pregnancy, illness) may precipitate signs in carriers of the organism. Fever has not been reported as a clinical sign. Neurological signs may present rapidly (acutely) or slowly (chronically). Acute onset signs are often severe and debilitating, rendering the horse very ill. Chronic onset of disease means that the signs are usually less severe at onset. A slower, more insidious onset of disease often carries a better prognosis because the signs may be recognized while still mild, and treatment may begin before the horse becomes very ill.

Most horses present with signs of spinal cord abnormalities. These signs include incoordination, stiffness, and weakness. The horse may walk “like it is drunk.” These horses may be confused with true wobblers. Horses with EPM may develop muscle atrophy because of the decreased trophic input from abnormal spinal cord neurons. Especially when muscle atrophy is unilateral, EPM should be suspected because there is rarely a reason for other neurological diseases such as CVM or equine degenerative myelopathy (EDM) to be lateralizing.

Occasionally, horses present with signs of brain disease. Severe intracranial signs include depression, blindness, walking in circles, and an inability to stand.

These horses usually deteriorate quickly and have a poor prognosis. The severity of their signs means that they should be considered dangerous, and clients are encouraged to handle them with caution.

Sometimes signs may be mild and may be confused with lameness (Foreman et al., 1990). With these neurological lamenesses, the source of the lameness cannot be determined through routine diagnostic testing such as nerve blocks, radiographs, and scintigraphs. There may be a history of stifle locking. Some performance horses are reported not to bend as well as previously or to misbehave at odd times (perhaps an early sign of brain disease).

DIAGNOSIS

Diagnosis of EPM may be presumed from the history and neurological signs, especially if lateralizing. EPM testing may be performed on blood samples, but there is a 50% chance that even a normal horse will test positive on an EPM blood test. One EPM scientist has stated that “positive results of a serum immunoblot test have no value in ruling in a diagnosis of EPM” (MacKay, 1997). Practitioners often use serum screening as a method to rule out EPM as a possible diagnosis because EPM is unlikely to be the cause of the neurological signs if the serum is negative for EPM exposure.

The current standard for positive clinical diagnosis of EPM is testing of CSF. This fluid must be obtained in a sterile manner from one of two sites, the atlantooccipital (AO) space directly behind the head or the lumbosacral (LS) space found at the highest point of the horse’s hindquarters. The LS tap is frequently performed on standing horses under tranquilization. The AO space is sometimes sampled under general anesthesia in nervous horses, horses with conformation preventing successful LS taps (preexisting LS subluxations), and horses undergoing anesthesia for another reason, such as elective surgery. Appropriate and adequate restraint followed by meticulous spinal fluid collection are critical to the value of the results because even microscopic amounts of blood introduced into the CSF may cloud the results (Miller et al., 1999). Blood contamination makes interpretation difficult and introduces the likelihood of false positives (Miller et al., 1999).

CSF is tested for EPM in two ways, a Western blot or immunoblot test for EPM antibodies (proteins which fight the EPM organism), and a polymerase chain reaction (PCR) test specific for the DNA or RNA of the EPM organism. There is a high correlation (>90% agreement) between a positive immunoblot spinal fluid test and the presence of the parasite at postmortem (Granstrom and Saville, 1998). There is a similarly high correlation between a negative CSF test and a lack of organism at postmortem. There is a poor correlation between being seropositive and finding the organism or its associated changes at postmortem (MacKay, 1997). The PCR test is less accurate when negative but is quite specific for the presence of the EPM organism when positive. The current interpretation

of these false negative PCR tests is that the organism may be present, causing antibody to be formed (and a positive Western blot result), but the organism is present in the spinal cord, not the CSF, making the CSF PCR-negative. Obtaining and properly testing CSF costs approximately \$250-400 and more if general anesthesia is required.

TREATMENT

The conventional method of treatment for EPM is oral administration of drugs classified as folic acid inhibitors (sulfonamides and pyrimethamine) for a minimum of 90-120 days. These drugs prevent folic acid production within the protozoa, resulting in their death. They usually do not cause folic acid deficiency in the horse because horses absorb considerable dietary folic acid from their intestine as long as they are eating a good quality diet with either grass or green hay. Gastrointestinal absorption of pyrimethamine may be delayed by simultaneous feeding (MacKay et al., 2000), so it is recommended that hay not be fed for 30-120 minutes after drug administration. In many management situations this delay is impractical, and there are no data to prove that simultaneous feeding and drug administration decrease the chances of successful treatment. To further complicate matters, if folic acid is to be supplemented, it should be given separately, several hours apart from drug administration intervals, to prevent drug interference with gastrointestinal absorption of the supplemented folic acid.

Treatment rarely has adverse side effects. Some horses develop soft stools, probably due to the antibacterial effects of the sulfonamide, but this diarrhea is mild and self-limiting. Very rarely, foals born to mares treated during pregnancy may show signs of folic acid deficiency (Toribio et al., 1998). These signs include low red and white blood cell counts leading to weakness and inability to fight off infections, severe renal hypoplasia, and ultimately death in only a few days. Most of these foals were born to mares that received folic acid supplementation while undergoing EPM treatment. Folic acid requirements in mares may be 5-10 times higher in pregnancy than when not pregnant, but investigators have suggested that additional dietary folic acid given with pyrimethamine actually may inhibit absorption of most or all of the dietary folic acid, resulting inadvertently in folic acid deficiency despite folic acid supplementation (Toribio et al., 1998). If there is concern over possible toxicity, weekly blood counts and/or folic acid determinations can be made on blood samples, but these tests cumulatively can become expensive. Horses already eating good quality grass or green hay are thought to consume sufficient dietary folic acid to prevent folic acid deficiency during treatment.

Recent epidemiological research has shown that “the likelihood of clinical improvement after diagnosis of EPM was lower in horses used for breeding and pleasure activities. Treatment for EPM increased the probability that a horse would have clinical improvement. The likelihood of survival among horses with EPM

was lower among horses with more severe clinical signs and higher among horses that improved after EPM was diagnosed” (Saville et al., 2000b). In other words, conventional treatment works, improvement is a good prognosticator, and severity of clinical signs correlates with likelihood of response to treatment.

Most horses are treated for a minimum of 30 days, at which time they are reexamined to determine whether or not they have improved with treatment. If improved, treatment is continued for another 60-90 days in most cases. If unimproved within the first 30 days, it is unlikely that improvement will be seen with further treatment. Ideally, testing of CSF for EPM antibodies should be repeated, and the results should be negative before treatment is discontinued.

Newer drugs are currently being tested, but their efficacy is unproven, their toxicity remains undocumented, they are not yet widely available, and they can be quite expensive. Diclazuril (Clinacox, Pharmacia and Upjohn) is used twice daily for 21-28 days as a grain top-dressing (Granstrom et al., 1997; Cohen, 1998). It has a long half-life (>50 hours) and seems to be similar in treatment efficacy to conventional therapies (about 75% positive results) (Tobin et al., 1997). One disadvantage is that the volume of powder may make the grain unpalatable. Toltrazuril (Baycox, Bayer) is available as a 5% suspension which is administered daily for 28 days. It also has a long half-life (>50 hours) and approximately 75% efficacy compared to conventional therapy (Tobin et al., 1997). Nitazoxanide (NTZ) is available as an oral paste formulation which is administered in an increasing dose over a 28-day period. Initial reports indicate 75% efficacy even in horses which have proven refractory to conventional treatment. Some possible side effects from NTZ include self-limiting febrile episodes early in treatment, worsening of clinical signs about two weeks into treatment, discoloration of urine, lethargy, diarrhea, and increased digital pulses (suspicious of laminitis).

In acute and severe presentations, other supportive treatments may be necessary. Intravenous fluids are important if the horse is not drinking or eating. Analgesics (e.g., phenylbutazone) are given if trauma is suspected. In acute cases with brain signs, rabies cannot be ruled out easily, so gloves are mandatory when handling the horse while awaiting the results of EPM testing. Corticosteroids (prednisone, dexamethasone) are contraindicated since they may actually make the infection worse due to their ability to suppress the immune system.

PROGNOSIS

Fewer than 1% of horses which are seropositive actually develop clinical signs of EPM. Early detection and treatment of EPM increases the chances of complete recovery (Saville et al., 2000a). Approximately 60-70% of treated horses return to their previous athletic function with no further abnormal signs. Approximately 10% of treated horses relapse after treatment is discontinued. At the first sign of a relapse, the horse should be reexamined and treatment should be reinstated. Horses will rarely continue to test positive on CSF. In these horses, treatment may

have to be continued for months or even years. Residual clinical signs after treatment may include varying degrees of ataxia, muscle atrophy, paresis, and focal cranial abnormalities such as facial nerve paralysis or dysphagia (difficulty in swallowing).

Treatment of pregnant mares is sometimes necessary. The real risk of treatment is to the fetus, although some studies have shown this risk to be minimal especially early in pregnancy (Brendemuehl et al., 1998). Supplementation with folic acid during pregnancy may actually increase risk to the fetus (due to impaired gastrointestinal absorption of folic acid after administration of both folic acid inhibitors and folic acid) (Toribio et al., 1998). Supplementation is not necessary if the mare is eating good quality grass or green hay routinely.

PREVENTION

The obvious method of prevention of EPM is to limit horses' exposure to opossums and their feces. Opossums should be kept out of the barn and especially away from sources of hay, feed, and water. It may even be necessary to keep cats or dogs loose in the barn to discourage midnight raids by opossums on the feed. Bagged feed may be safer than bulk feed, especially if the top of the bulk feed bin is open. However, the organism probably survives transport in bagged feed if the feed was contaminated before processing. Any shipment of feed or hay that may be contaminated with animal feces should be rejected. Extruded feeds are likely to be most protective since the heat exposure during the extrusion process seems to kill the parasite before it is ingested by horses.

Preventative treatment of a normal horse which is in the same barn as another horse with a definitive EPM diagnosis is not recommended. It should be remembered that an infected horse cannot infect a normal horse; the parasite must come from the opossum, not from an infected horse. Unnecessary use of the medications to treat EPM may lead eventually to development of parasite drug resistance, making it more difficult to treat all EPM cases.

Recently an EPM vaccine (Fort Dodge Animal Health) has received conditional licensure by the USDA. This restricted category of licensing means that the company has demonstrated product purity and safety; that there is a reasonable expectation of efficacy but it has not yet been demonstrated; that there is a clear need for the product in the community (a "special need" provision); and that individual states still have the right to refuse to allow its use within their borders. Approval is therefore on a state-by-state basis. The license must be renewed annually, and the company must demonstrate efforts to prove efficacy for the conditional license to be renewed. One example of a vaccine which was provisionally licensed in this manner is the rotavirus vaccine from the same manufacturer.

The EPM vaccine consists of inactivated whole *Sarcocystis neurona* merozoites from infected equine spinal cord. The merozoites are chemically inactivated, with

that inactivation tested by three blind passages in tissue culture followed by cell fixation and fluorescent antibody examination to ensure that no living merozoites remain. The vaccine has an adjuvant (MetaStim, Fort Dodge Animal Health) added to help to stimulate immunological response to the merozoites. This adjuvant has been shown to be effective in enhancing the response to an eastern and western equine encephalitis vaccine given to 9-11 month old foals (n=10). The adjuvant's safety was demonstrated in the equine rotavirus vaccine given to pregnant mares (n=235). Vaccine safety has been demonstrated in horses (n=897) in California, Illinois, Indiana, Kansas, Kentucky, Minnesota, and Oklahoma. Only four horses had adverse reactions consisting of localized swelling (n=4), stiffness (n=3), and lethargy (n=1). Vaccination elicited demonstrable serum neutralizing (SN) antibody titer against *S. neurona* merozoites. The question then becomes one of clinical efficacy because it is not agreed upon scientifically that SN antibody is protective against EPM. Use of the vaccine under field conditions followed by demonstration of efficacy in the form of decreased EPM incidence will be required for full licensure by the USDA.

Equine Degenerative Myeloencephalopathy

DEFINITION AND HISTORY

Equine degenerative myeloencephalopathy (EDM) is a progressive, symmetrical disease of neuronal degeneration first described in 1977 (Mayhew et al., 1977). The disease is familial and dietary in origin. Neuraxonal dystrophy (NAD) is a similar but less diffuse disease of Morgan horses (Beech, 1984; Beech and Haskins, 1987) and is included for discussion here because the causes of both diseases are similar, varying primarily in severity. It is thought that certain families of horses may have a predisposition to poor dietary absorption of vitamin E, so that when a diet is lacking in vitamin E, minimal amounts may be absorbed. Vitamin E is critical to normal neuronal health in its role as a scavenger of free radicals produced in most metabolic processes.

EPIDEMIOLOGY

A familial predisposition for EDM has been described in Appaloosas (Blythe et al., 1991), Standardbreds, Arabians, Paso Finos, and Grant's zebras (Mayhew et al., 1987), and for NAD in Morgans (Beech and Haskins, 1987). Affected horses are routinely young, growing horses (sucklings, weanlings, and yearlings), although some aged horses have been described. There is no sex predilection. One report indicated that horses in the northeastern U.S. were more commonly affected with EDM than horses in other regions (Dill et al., 1990).

No specific heritable mode has been described, but it is clear that some families are affected more than others (Mayhew et al., 1987). In one report (Mayhew et

al., 1987), one Standardbred farm had a 40% incidence of EDM in farm-raised yearlings two consecutive years prior to dietary intervention. Eventually, 19 EDM-affected young horses were observed in three crops (1983-1985), with 14 of the 19 sired by one Standardbred stallion. Progeny of that stallion raised on other farms were not affected. After the supplementation of pregnant and nursing mares with daily vitamin E (1500 IU/horse/day), the incidence of EDM in progeny from those same stallions was <5%. Similar responses have been observed in specific families of Morgans, Appaloosas, and Paso Finos (Mayhew et al., 1987).

One report also implicated other risk factors for EDM (Dill et al., 1990), including application of insecticide to affected foals, exposure of foals to wood preservatives, and foals housed primarily on dirt lots when turned outside. Affected foals were born more often to affected mares than to non-affected mares. Foals spending time outside on green pastures had decreased risk for developing EDM, lending further credence to the argument that affected foals have been deprived of sufficient vitamin E found in good-quality green grass and hay.

CLINICAL SIGNS

Onset of clinical signs is usually slow and insidious. Mild symmetrical hind limb ataxia progresses to involve the forelimbs. The initially mild ataxia worsens over time, and paresis, spasticity, and hypometria become evident. In later stages, EDM horses become recumbent and unable to rise without assistance. In terms of neurological signs, these horses may be indistinguishable from horses with CVM, but the size (perhaps smaller) and breed (perhaps Paso Fino, Arabian, and Morgan) may be an indication that CVM is not the most likely cause of the neurological disease. EDM horses are often remarkably weaker (more paretic) than CVM horses.

DIAGNOSIS

Testing for CVM and EPM are negative. EDM is essentially a rule-out diagnosis in that no antemortem test exists. Serum vitamin E concentrations may be measured and if low, are considered evidence for a presumptive diagnosis of EDM. Breed and familial history may also be important in making a diagnosis.

TREATMENT

Vitamin E supplementation has been cited as beneficial in treating EDM, especially if begun while signs are early and mild (Mayhew et al., 1987). Signs may only arrest but not reverse in severity (the affected horse may never be normal). It should be noted that the units "IU" and "mg" are the same for vitamin E but not for other vitamins, so conversion from one to another is not necessary in dosing. Recommended dosages of vitamin E range from 2000-9000 IU orally daily, with 6000-7000 IU/day commonly given to affected animals and 1500-2000 IU/day

commonly used as a preventative. In acute cases, intramuscular injection of 1500-2000 IU in oil every 10 days has also been used (Mayhew et al., 1987). Follow-up measurements of serum vitamin E concentration may be used to assess efficacy of the dose. Supplementation has also been used as a preventative.

PROGNOSIS

EDM is a progressive disease, usually with an unrelenting course resulting in death. Horses affected at younger ages usually progress to recumbency and death, while the sporadic cases of horses affected at older ages often plateau and fail to progress to recumbency. Some of these horses have been used successfully as brood animals, but supplementation of progeny with vitamin E may be warranted.

PREVENTION

Feeding good-quality green grass or hay is the easiest and least expensive way to ensure that horses are ingesting sufficient vitamin E. If pasture is unavailable, or hay or pasture quality is suspect, then dietary vitamin E supplementation may be indicated. Heat-extruded feeds, oats stored for lengthy periods, and sun-bleached hays should be considered suspect with respect to available vitamin E concentrations (Matthews, 1998). Farms with large EDM problems have benefited from farm-wide vitamin E supplementation (Mayhew et al., 1987).

Equine Motor Neuron Disease

DEFINITION AND HISTORY

Equine motor neuron disease (EMND) is a progressive, debilitating, usually fatal neurological disease of horses first described in New England in 1990 (Cummings et al., 1990). An association between vitamin E deficiency and EMND has been described (De La Rúa-Domènech et al., 1997). The dramatic paresis in EMND is due to its affection primarily of lower motor neurons (LMN), those nerves which supply the direct neurological input into all muscles. Without the normal trophic influence of the LMN, the associated muscles atrophy, resulting in the remarkable paresis and weight loss characteristic of this disease. This symmetrical wasting distinguishes the disease from CVM, EPM, and EDM as these diseases frequently occur in horses with good body condition. The disease in horses is similar to one in humans known as amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease. As found in familial ALS, it has recently been shown that EMND horses have abnormally high copper concentrations in their spinal cords (Polack et al., 2000), providing further evidence that oxidative spinal cord injury in EMND may be related to high copper and low vitamin E concentrations.

EPIDEMIOLOGY

EMND is sporadic and rare. Since the original 1990 description of EMND in New York, more than 200 cases have been reported in many states, Canada, Europe, Japan, and Brazil (Divers et al., 1997). Cases are clustered, however, in the northeastern United States and Canada (from Pennsylvania north through Prince Edward Island and west through Ohio). Seldom is more than one horse in a stable affected, although there are rare reports of multiple cases at a single site.

EMND more commonly affects middle-aged adult horses, with a mean age of onset of signs of 9 years (range 2-23 years)(Mohammed et al., 1993). Many breeds have been affected, but Standardbreds are underrepresented. Quarter Horses are overrepresented, perhaps owing to the non-pasture conditions under which they are often housed (Mohammed et al., 1993). Horses with EMND are nearly always housed in boarding stables with minimal or no turnout or turnout only on drylots with no grass (Mohammed et al., 1993; Divers et al., 1994; De La RúaDomènech et al., 1997). Affected horses generally receive large amounts of pelleted or sweet feed, no vitamin E supplements, no pasture, and poor-quality hay (described consistently as light green or brown or even sun-bleached grass hay with no alfalfa).

CLINICAL SIGNS

Horses affected with EMND have dramatic weight loss, muscle atrophy, paresis, recumbency, trembling, and hind limb treading when standing. Some of these signs may be easier initially to attribute to laminitis or colic than to neurological disease. Muscle atrophy is most commonly observed in the quadriceps, triceps, and gluteal areas (Divers et al., 1997). More than half of these horses carry their heads in a lowered posture with obvious neck muscle atrophy. Ataxia is not seen since the upper motor neurons are not affected, thus distinguishing this disease from CVM, EPM, and EDM. Horses may look better when walking than when standing, since the LMN supplying postural muscles are more commonly affected. Despite the weight loss, the affected horse's appetite is normal to ravenous. In approximately 50% of the cases, coprophagia is observed even though these are adult horses (Divers et al., 1997).

DIAGNOSIS

Diagnosis is based on history (no pasture exposure and a poor-quality hay diet), clinical signs, mild to moderate elevated serum muscle enzymes, and measurably low serum or plasma vitamin E concentrations. Electromyography reveals denervation atrophy but is best done in affected horses under general anesthesia because they tread so much when required to stand still (Divers et al., 1997).

Retinal abnormalities also have been described (Riis et al., 1999). Muscle biopsy has a high sensitivity but an unproven specificity for diagnosis of EMND (Divers et al., 1997).

TREATMENT

The only known treatment for EMND is supplementation with vitamin E (5000-7000 IU/horse/day orally). Good quality hay and/or pasture should also be provided whenever possible. If a response to therapy is seen, it takes a minimum of 3-6 weeks for observable improvement in trembling, followed eventually by increased weight and strength (Divers et al., 1997).

PROGNOSIS

The prognosis even with vitamin E supplementation remains guarded for life and poor for return to function (Divers et al., 1997). Most EMND horses are euthanized, but some reach plateaus in clinical signs where they can be comfortable even if they are unable to return to work.

PREVENTION

Proper balanced diet with less confinement and greater exposure to green pasture should be preventative. Daily vitamin E supplementation is recommended whenever diet or management considerations render the diet suspect in vitamin E intake.

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