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Abstracts
Equine motor neuron disease (EMND) is associated with and likely caused by prolonged vitamin E deficiency. Horses without access to at least seasonal pasture and fed forages and concentrates with low concentrations of vitamin E are at risk of developing EMND. At risk horses should be orally supplemented with additional vitamin E.

1. Introduction
Equine motor neuron disease (EMND) is a neurodegenerative disorder of the somatic lower motor neurons of horses. The disease was first described in 11 horses in 1990 [1]. Since that first report, a goal of our laboratory has been to find the cause of EMND so that it can be prevented. The purpose of this paper is to briefly review the epidemiologic, pathological, clinical, and laboratory findings of EMND in addition to the recent experimental reproduction of the disease. A review of this data provides strong support for a causative factor, and guidelines are provided for prevention of the disease.

2. Clinical Findings
Horses with acquired EMND are 2 yr of age or older [2,3]. There is generally an acute onset of trembling, almost constant shifting of weight in the rear legs when standing, and excessive recumbency. Muscle wasting is noticeable, and in retrospect, owners remarked that weight loss was apparent before the trembling [2]. Funduscopic examination reveals brown streaking discoloration in nearly 40% of cases, although visual impairment is rarely reported [4]. The tail head is often carried in an elevated position, whereas the head and neck are in abnormally low positions [2]. In a smaller percentage of cases, trembling and constant shifting of weight may either not occur or not be observed, and the predominant clinical sign may be muscle wasting. Although the clinical signs are characteristic for EMND, other neuromuscular disorders, especially chronic myopathies, may look clinically similar. A biopsy of the sacrocaudalis dorsalis medialis (tail head) muscle or spinal accessory nerve can be useful in confirming the diagnosis (sensitivity > 90%) [5,6]. Approximately 40% of horses with EMND continue to deteriorate and are euthanized within 4 wk of onset of signs; approximately 40% have marked improvement in clinical signs within 4 - 6 wk after either relocation to another stable or administration of antioxidants, and approximately 20% remain permanently and noticeably atrophied.

3. Laboratory Findings
The only consistently abnormal laboratory finding on routine complete blood count (CBC) and serum chemistry is a mild to moderate elevation in muscle enzymes (creatine kinase and aspartate aminotransferase) [2]. Plasma vitamin E values are consistently low (< 1 g/ml), selenium is normal, vitamin A is slightly low to normal, and serum ferritin is frequently high in horses with EMND [7]. In the spinal cord of EMND horses, copper is increased compared with controls [8], and vitamin E has always been low. Hepatic concentrations of copper are normal, iron is frequently elevated, vitamin A is usually normal, and vitamin E is consistently low. Glucose absorption tests performed on EMND cases have revealed reduction in glucose levels in several cases [2]. Xylose absorption may also be slightly abnormal but not to the same degree as glucose. Red blood cell superoxide dismutase (SOD1) activity was found to be lower in a group of EMND cases than in a control group, but there was no excessive polymorphism in the SOD1 gene between the two groups [9].
4. Pathology
The pathology is generally limited to the lower motor neuron system [1,10]. Loss of approximately 30% of motor neurons must occur before clinical signs are obvious [11]. Muscles with a predominance of type I fibers are more severely atrophied than are those with mostly type II fibers [1,12]. Lipofuscin deposition is always observed in the endothelial capillaries in the spinal cord and the retinal epithelium [4,13]. Abnormal lipopigment deposition is occasionally found in the liver and gut (brown bowel disorder).

5. Epidemiology
Horses with EMND have almost always been housed at the same location for at least 18 mo [3,14,15]. There is no sex predilection; Quarter horses and Thoroughbreds are over-represented in the patient population [14]. There is minimal or no pasture for the great majority of cases [16]. The few horses having both EMND and normal pasture had infiltrative bowel disease (malabsorption) [2]. Almost all EMND cases were fed a grass hay (no alfalfa) [16]. Mineral supplements, especially selenium, were more common in the EMND horses than the off-farm control horses [16]. There was often more than one case on a property over a 2-yr period [17]. For example, one property, a police cavalry in the middle of a city with a population of 18 million, had more than 80 cases since 1991. The disease is more prevalent in the Northeastern United States, but it has been reported in most states and many countries of the world [17-22].

6. Experimental Reproduction
Four horses fed a low vitamin E, high copper, and high iron diet (all other National Research Council [NRC] nutrient recommendations were normal) developed EMND 22 mo or more after the diet was started. Another horse had moderately severe microscopic lesions of EMND without having obvious clinical signs of EMND. Three additional horses fed a low vitamin E but normal copper and iron diet also developed EMND beginning at 18 mo. The control horses that were kept on the same farm and fed the same concentrate (normal copper and iron) and hay, but had access to pasture, did not develop EMND.

7. Discussion
EMND is a devastating disease resulting in either death of the affected horse or chronic debilitation. Some horses have dramatic improvements in clinical signs but undoubtedly have permanent loss of some motor neurons [2]. It seems plausible that when horses are clinically affected with EMND, there are both dead motor neurons and alive but dysfunctional motor neurons. If there are significant numbers of dysfunctional (vs. dead) motor neurons, clinical improvement can be marked. We are not able to determine clinical outcome in subacute EMND, because it is not possible to distinguish between dead and dysfunctional motor neurons. In more chronic cases, the tail head is elevated because of atrophy and contracture of the sacrocaudalis medialis dorsalis muscle [5,12]. The recently completed experimental studies help confirm that there could be a low percentage of horses with subclinical EMND in stables with previously confirmed cases and/or sufficient risk factors. These horses would have lost less than 30% of motor neurons, but they might be at an increased risk of injury during exercise because of some permanent weakness.

Laboratory and pathologic findings are supportive of an oxidative disorder affecting ventral horn motor neurons, especially those supplying muscles with highly oxidative type I fibers. The lipopigment deposition in the retinal pigment epithelium is a result of light generated oxidative damage [4]. We do not know the reason for abnormal glucose absorption tests in many horses with EMND. Although microscopic changes were not observed in the bowel of most horses, it seems plausible that the antioxidant deficiency that occurs in EMND horses might also affect the intestinal epithelial mitochondria. The sporadic finding of marked lipofuscin in the liver and bowel of some horses with EMND would support the hypothesis that organs, other than those in the central nervous system (CNS), may sometimes have oxidative damage caused by the prolonged vitamin E deficiency. The abnormality in glucose absorption was not found consistently enough, and there was loss of body fat in most cases, which suggest that malabsorption was the cause of the antioxidant deficiency in the great majority of cases. In a few cases, inflammatory and infiltrative bowel disease was likely responsible for causing EMND from decreased enteric absorption of antioxidants [2]. The epidemiologic, laboratory and pathologic, and experimental studies strongly support vitamin E deficiency as the primary risk factor for EMND. The time required for development of clinical signs in the experimental horses was similar to the epidemiologic finding that affected horses had been on the property for at least 18 mo [3,14,15]. Tissue stores of vitamin E are likely abundant in most horses such that several months of vitamin E deficiency is required for marked oxidative damage to incur. We are not certain why some horses develop EMND while others fed the identical feeds do not; it might be individual susceptibility to a disturbed antioxidant/pro-oxidant balance. We were also unable to determine the role of copper and iron as pro-oxidants in EMND, because both experimental groups (high copper and iron with low vitamin E, and normal copper and iron with low vitamin E) developed clinical disease at a similar rate and time. This does not rule out copper and/or iron as causative factors, because even normal NRC amounts of these and other pro-oxidants might be excessive when there is a severe depletion of antioxidants such as vitamin E.

In both naturally occurring cases of EMND and experimental cases, vitamin E deficiency has been the only consistent
nutrient abnormality. Green forages are the major source of vitamin E, and, until recently, most grain concentrates had less vitamin E than the NRC recommendations for horses (50 IU/kg) [23]. Recently, concentrates with increased amounts of vitamin E and/or more vitamin E supplements have become available. Increased owner awareness of the possibility of vitamin E deficiency and increased use of vitamin E supplements may be partially responsible for what we believe to be a decline in EMND cases since 1997.

EMND is not the only neurological disease of the horse believed to be associated with vitamin E deficiency. In young equines, vitamin E deficiency, along with a familial component, are thought to be responsible for equine degenerative myeloencephalopathy (EDM) [13]. Although EMND and EDM are distinctly different disorders, both clinically and pathologically, we have examined three yearlings with clinical signs and pathology of EDM that also had lesions without clinical signs of EMND. It may be that vitamin E has a protective effect against oxidative damage in the spinal cord of horses with the neuroanatomical site differing based on age.

8. Summary
Epidemiological, pathological, laboratory, and experimental studies all support the hypothesis that EMND occurs after prolonged vitamin E deficiency. All horses, young and old, without access to green forage high in vitamin E for prolonged periods, should be supplemented with vitamin E. Two 10,000 SU vitamin E/day doses are commonly used, but smaller amounts would probably suffice in preventing EMND.

References


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