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EPIDEMIOLOGIC STUDIES ON EQUINE MOTOR NEURON DISEASE

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Equine motor neuron disease (EMND) is a newly recognized neurodegenerative disorder of bulbospinal motor neurons in the horse (Cummings et al., 1990). Postmortem studies reveal degeneration and loss of motor neurons in the spinal ventral horns and brain stem motor nuclei. These changes closely resemble those described in humans amyotrophic lateral sclerosis (ALS) (Hirano, 1982). Degenerating neurons are swollen, chromatolytic, and often contain distorted karyolytic nuclei (Cummings et al., 1990; Divers et al., 1992).

Since the initial report of EMND in 1990 (Cummings et al., 1990) the disease has been recognized with increasing frequency over a widening area of North America (Mohammed, et al., 1993). Sightings of EMND have been made recently in England (Hahn and Mahew, 1993) and postmortem studies have documented cases in Belgium (Sustronck et al., 1994), Japan (Kuwamura et al., 1994), and Brazil (Personal communication). As in ALS the etiology of EMND is not known. The objectives of this study were to identify factors associated with the likelihood of EMND and to quantify their effects on the risk of the disease.

MATERIALS AND METHODS

Study population

We conducted an ambidirectional epidemiologic study to identify factors associated with the risk of this disorder. Cases included all horses diagnosed with EMND in North America between January, 1985 and December, 1993.

Case definition

Horses with a tentative clinical diagnosis of EMND based on the signs of weight loss (<200 lb), generalized weakness, muscle atrophy, short strided gait and elevated levels of serum creatine kinase (CK) and/or serum aspartate aminotransferase (AST) were ultimately confirmed by histopathologic examinations. The histopathologic examinations were conducted on the caudal brain stem and spinal cord or on the spinal accessory nerve.

Control definition

Two sets of controls were selected in this study. The first set was used in the evaluation of the role of intrinsic factors on the risk of EMND. The second set was selected to evaluate the association of the antioxidant, Vitamin E, with the risk of the disease. The first set of control horses were chosen from the equine population admitted to the colleges of Veterinary Medicine where cases had been identified between January 1985 and December 1993. Three selection criteria were considered: 1) control horses originated at the the same veterinary teaching hospitals where the cases were diagnosed; 2) controls were identified during the same time period as the cases were diagnosed; 3) the control population was restricted to horses with a histologically confirmed diagnosis of one of the following neurologic conditions: cervical stenotic

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myelopathy (CSM), equine degenerative myeloencephalopathy (EDM) or equine protozoal myeloencephalitis (EPM). Each of the second set of controls for antioxidant levels orignated at the same farm as the case, where they had been for a comparable period of time. The purpose of matching was to control for management and nutritional factors that might influence the association between the level of antioxidants and the risk of EMND. In selecting these controls for antioxidant measurements, we have also applied the first set of controls.

Statistical analysis

Bivariate association between each factor and the likelihood of EMND was evaluated by either chi-square, Fisher's exact, or t-test, depending on the number of observations and the nature of the variable (categorical or continuous). Logistic regression analysis was used to evaluate the association of each of these putative factors while simultaneously controlling for the effect of other factors.

RESULTS

Eighty seven cases of EMND have been identified in North America so far. The distribution of EMND-cases throughout the world is shown in Figure 1. In North America, the disease appears to occur sporadically and the majority of the cases were diagnosed in riding stables, ie, pleasure horses.

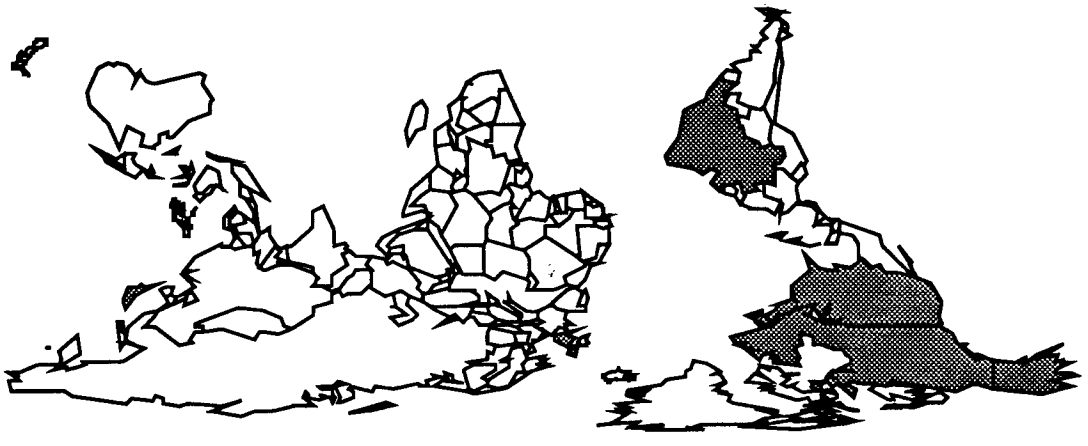

Fig 1. The distribution of EMND cases in the world.

Affected horses were likely to originate from stables where there was very little or no pasture. EMND horses had significantly lower Vitamin E plasma levels in comparison to control horses from the same stables (0.394 μg/ml vs. 1.319 μg/ml). Factors found to be significantly associated with the risk of the disease were breed and age of the horse. Quarterhorses are at a higher risk in comparison to other breeds of horse. The risk of EMND appeared to increase with age, peaked around 16 years of age and then decline (Fig. 2). that are common for quarterhorses.

Fig 2. Association between age and the likelihood of EMND

DISCUSSION

One of the most controversial and difficult aspects of the ambidirectional studies is the choice of the comparison group (controls). We have decided to select two controls for each case in this study. We have imposed three selection criteria for the controls as stated above. The first criterion was intended to have consistency in the physical and histologic examinations so that information bias arising from different diagnostic approaches in the cases and the controls was minimized. The second criterion was meant to attain comparability between cases and controls with respect to past potential for exposure during the period of risk under consideration. As with EMND, these are three neurodegenerative disorders whose diagnosis can only be confirmed by careful neurological exam and postmortem microscopic examination of the spinal cord.

Our studies to date indicate that quarterhorses are at greatest risk to develop EMND. However, studies of equine leukocyte antigens and examination of breeding records have revealed no consanguinity among affected horses, thus this breed association might reflect an environmental or management factors

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