# Equine Herpes Virus Myeloencephalopathy: A Potentially Emerging Disease

## Introduction

Concern has been voiced within the U.S. horse industry that the neurologic (also known as myeloencephalopathic or paralytic) form of equine herpes virus type-1 (EHV-1) may be increasing in prevalence and/or morbidity and mortality. This concern is based on an increased number of neurologic cases reported in recent years, as well as the occurrence of several high profile outbreaks of neurologic EHV-1 affecting several sectors of the U.S. equine industry. These outbreaks are the first reported EHV-1 outbreaks at large facilities or events involving neurologic cases that resulted in euthanasia. At least part of the increased interest and concern are related to these highly publicized events. It is possible that reporting has increased, as opposed to an actual increase in number and severity of cases; more data is needed to determine the actual situation.

## Profile of Disease Emergence

The question of whether neurologic EHV-1 is emerging can be evaluated using standard definitions of disease emergence. A disease is considered to be "emerging" when it meets at least one of three general criteria. The first is when a disease is identified for the first time. Recent examples of this would be SARS or Ebola. Another criterion is when a disease evolves and changes in virulence, host capable of being infected or other pathogen behavior. The monkey pox outbreak in prairie dogs in 2003 in the United States would be an example of this type of disease emergence, as a new species was infected. The third criterion is a change in disease geographic range or incidence within a range. The appearance of West Nile virus in the United States in 1999 is a good example of emergence in a new geographic location, as is the previously mentioned monkey pox example. The current EHV-1 outbreaks are of concern because they likely fit the criteria of a disease that is evolving and changing in virulence and behavior. It is possible that the disease has not changed in incidence or character, and that testing and/or reporting has been increasing awareness, or that the animals affected are higher profile, causing more interest. However, it is not possible at this time to make this distinction.

All types of disease emergence are driven by a variety of emergence factors. The factors can be environmental, agent- or host-specific, related to use of the animal, industry standards or any other factor that can affect the health of an animal or place selective pressure on an infectious agent. Typically, multiple factors come together to create a situation where a disease can evolve, newly emerge or spread to new environments. In the case of neurologic EHV-1 in the United States, the disease appears to be increasing in incidence, mortality and morbidity. While there has not been much field research on neurologic EHV-1, mainly due to the sporadic nature of outbreaks, the available data support the theory of disease emergence and are cause for concern. Some research has been done that suggests that a mutation in the virus is playing a role in these changes in the disease behavior, which could indicate evolution of the viral agent.

***Source:*** *USDA:APHIS:Veterinary Services: Centers for Epidemiology and Animal Health, Center for Emerging Issues*

## Background of EHV-1

Equine herpes virus type 1 (EHV-1) is primarily a respiratory pathogen associated with a variety of clinical manifestations in horses. In addition to being a significant cause of respiratory illness and abortion in horses, EHV-1 is responsible for paralytic neurological disease. EHV-1 is enzootic throughout the world and almost all horses older than 2 years of age have been exposed. Following initial exposure, EHV-1 has the ability to develop into an inapparent, latent infection. It is this ability to reside as a silent and persistent infection in horses which provides a reservoir of virus for continual transmission. The incubation period of EHV-1 is 1-10 days; typically signs are seen within 1-3 days. Viral shedding occurs for 7-10 days, but can occur up to 28 days from the onset of signs. The neurologic signs include ataxia, urinary bladder atony and reduced tail tone. In severe cases, horses will be unable to stand; these cases have a very poor prognosis. Foals are rarely affected with the neurologic form of EHV-1, and no sex predilection is seen. Treatment is supportive and tailored to the specific case. Antivirals such as acyclovir, valacyclovir, famiciclovir and penciclovir have been used, but efficacy of these drugs has yet to be determined in equids.

***Sources:****USDA-APHIS 2005 United States Animal Health Report, pp. 78-79, http://www.aphis.usda.gov/publications/animal_health/2005animal_health.shtm; Equine Infectious Diseases, Sellon & Long; Chapter 13; Josh Slater; pp.150-152; Equine Herpesvirus Type 1 Virulence and Vaccine Efficacy, Osterrieder, Zweig Memorial Fund for Equine Research, Cornell; EHV-1 Outbreaks, Lenz, TR, www.xcodesign/aaep/displyArticles.cfm?ID=222;*

## History of Recent Neurologic EHV-1 Outbreaks in the United States

Prior to 2003, the U.S. reports of neurologic EHV-1 outbreaks in the United States were sporadic, with typically none to few outbreaks identified annually. Table 1. shows outbreaks that were reported as neurologic outbreaks of equine herpes virus; many of these cases may not have been typed for the neuropathogenic mutation, and there was not a standard method of defining a case across the time period. In 2005, seven outbreaks of neurologic EHV-1 were reported in 5 different states. In 2006, the number of reported outbreaks grew to 11, and involved 8 states. The outbreaks have been primarily concentrated in the eastern United States, with a few midwestern and western states experiencing outbreaks. The last outbreak of 2006 involved a group of 15 horses shipped from Germany that were subsequently shipped to 8 states. Five of the horses went to Florida; this resulted in 13 horses identified as infected, with neurologic signs in seven cases and 6 associated deaths. Ten Florida premises were quarantined. One horse was shipped to California from the original group from Germany and died shortly after arrival due to the neurologic form of EHV-1. The exposed horses were identified, and the horses that were shipped to the remaining 6 states were quarantined and monitored for EHV-1 signs; none were found.

Outbreaks of neurologic EHV-1continue to be identified in early 2007.

**Table 1. Reported Neurologic EHV-1 Outbreaks in the United States Annually from 2001-2006**

| State | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 |
|---|---|---|---|---|---|---|
| CO | | | | | | 1 |
| FL | | | | | | 1 |
| GA | | | | | | 1 |
| KY | | | 1 | | 3 | |
| MD | | | | 1 | 1 | 4 |
| MI | | | | 1 | | 1 |
| NH | | | 1 | | | |
| NJ | | | | | | 1 |
| NY | | | | | 1 | |
| OH | | | 1 | | | |
| OR | | | 1 | | | |
| PA | | | 1 | | 1 | 1 |
| VA | | 1 | | | | |
| WI | | | | | | 1 |
| WY | 1 | | | | | |
| Totals | 1 | 1 | 4 | 2 | 6 | 11 |

***Sources:*** *2006 NIAA Proceedings, Emerging Diseases, "Neurological Equine Herpes Update", Promed, The Horse, Pittsburgh Post Gazette, Kentucky Dept. Of Agriculture, 2005 U.S. Animal Health Report, WJZ-TV Baltimore, U.S. States News, Newark Star Ledger*

The clustering of outbreaks in certain regions of the country could be related to where high-level performance horses are located or where they tend to travel, but other ecological factors could also play a role in outbreaks; this aspect of the disease is not well understood at this time. The number of reported outbreaks in the United States has increased, and the numbers infected in an outbreak appear to be much higher than what was seen previous to 2001. Data from 6 U.S. neurologic EHV-1 outbreaks (2001-2005) involving 403 at-risk
horses were combined and analyzed; a mean attack rate of 33%, and a mean case fatality rate of 40% were found *(2006 NIAA Proceedings)*.

Nationally, reports of neurologic EHV-1 have increased in recent years; this may be attributable to a strain of EHV-1 with a mutation that encodes for a particularly robust replicase enzyme. The result of this mutation is that the virus can reproduce rapidly with a predilection for nervous tissue, therefore the viremia occurs earlier, it reaches a higher peak, and it lasts longer. Beginning with the Ohio outbreak during January 2003, the progression of the disease in a population as well as in individual cases has been seen to be much more rapid than in the past. Response to currently available vaccines for EHV-1 does not appear to be strong enough to protect all immunized animals against the disease induced by the mutated strain of EHV-1. In some outbreaks, such as the Ohio outbreak of 2003, well-vaccinated populations of horses have experienced severe disease outbreaks and some animals have died. However, serious outbreaks have occurred in equine populations where no EHV-1 vaccines are used, such as in the Netherlands. It is still unknown what factors are involved in the emergence and/or maintenance of the viral mutants. It is also unclear at this time what role the poor immunogenic response to the mutated strain is playing in the outbreaks that have occurred in recent years.

Variations in EHV-1 reporting requirements and case definitions make it difficult to accurately identify the true number of cases. Creating a standard case definition for both the first case on a premises, as well as for subsequent cases, would alleviate some of the discrepancies seen in reporting and facilitate better understanding of the epidemiology of the disease.

***Sources:*** *Florida Department of Agriculture and Consumer Services, http://www.doacs.state.fl.us/ai/ehv1/daily_status_table_and_definitions.shtml, Equine herpesvirus-associated myeloencephalopathy; Aspects of epidemiology and pathogenesis, Goehring, L.S., Univeritiet Utrecht, 2005; Gluck Equine Research Center, University of Kentucky, http://www.ca.uky.edu/gluck/; 2006 NIAA Proceedings, Emerging Diseases, "Neurological Equine Herpes Update," Harrison, LR; Promed; The Horse; Pittsburgh Post Gazette, Kentucky Dept. Of Agriculture; 2005 U.S. Animal Health Report, http://www.aphis.usda.gov/publications/animal_health/2005animal_health.shtml; WJZ-TV Baltimore; U.S. States News, Newark Star Ledger*

## International EHV-1 Situation

The United States is not the only region or country that has recognized the issue regarding neurologic EHV-1 cases; other countries have also seen an increase in the number and virulence of reported neurologic EHV-1

outbreaks. In 2005, significant outbreaks occurred in Canada, Ireland, South Africa and Switzerland as well as the United Kingdom and the United States. Studies conducted by the Gluck Equine Research Center in Kentucky indicate that in both the United States and the United Kingdom, the number of paralytic outbreaks of EHV-1 has increased dramatically since 2001. Greater than 85% of the outbreaks identified over a 30 year period have been caused by the mutated strain of EHV-1 as compared to the wild-type or "original" strain of EHV-1.

### Horse Industry in the United States

Estimates on the value and numbers of equids of the U.S. horse industry vary widely. The Census of Agriculture estimates that there were 3.6 million horses and ponies in the United States in 2002 residing on operations fitting the definition of a "farm." Although this source of equine population data only estimates a segment of the industry, one can compare across states for relative size of their equine population. Texas, California, Oklahoma, Kentucky, Missouri and Ohio were the 5 states with the largest equine populations based on the Census of Agriculture. The overall value of the horse industry in the United States is in the billions of dollars. The most valuable subgroups of the horse industry are racing, competition and recreation.

In the United States, the recent outbreaks of the neurologic form of EHV-1 appear to be affecting race horses and other types of competition horses. The response to these outbreaks has been to identify potentially exposed animals and quarantine them. Since these sectors of the horse industry require horse movement in order to function, the EHV-1 outbreaks have had a major impact on these segments of the industry.

***Sources:*** *American Horse Council Foundation, USDA-NASS Census of Agriculture*

**Table 2. EHV-1 Paralytic Outbreaks: United States and United Kingdom caused by wild-type and mutant virus strains**

| 5-year interval | No. outbreaks | No. outbreaks caused by wild-type | No. outbreaks caused by mutant |
|---|---|---|---|
| 1970-1975 | 1 | 0 | 1 |
| 1976-1980 | 3 | 0 | 3 |
| 1981-1985 | 4 | 2 | 2 |
| 1986-1990 | 6 | 1 | 5 |
| 1991-1995 | 5 | 1 | 4 |
| 1996-2000 | 6 | 2 | 4 |
| 2001-2005 | 32 | 2 | 30 |

***Source:*** *2006 NIAA Proceedings, Emerging Diseases, "Neurological Equine Herpes Update," Harrison, LR*

### International Horse Trade in the United States

The United States imported 25,000 to 30,000 live horses per year from 2003 through 2006 (statistics for 2006 are not yet complete). The vast majority (60-70%) of these live horse imports originated from Canada. Import requirements for horses from Canada are a health certificate and negative Coggins or ELISA test for equine infectious anemia (EIA) within 180 days preceding exportation to the United States.

The Netherlands, Mexico and Germany are the next top exporters to the United States. Horses from these countries are required to be detained at the United States port of entry while tests for dourine, glanders, equine piroplasmosis, and EIA are conducted. Test results from NVSL are generally available three days after the date of arrival of the horses.

The index case for the recent outbreak affecting Florida originated from a shipment of 15 horses from Germany.

***Sources:*** *World Trade Atlas, APHIS Veterinary Services National Center for Import-Export*

### Discussion

Equine herpes virus-1 neuropathogenic form is not a "new" disease, but the evidence currently supports the observation that paralytic EHV-1 is emerging as a more virulent strain that has a higher incidence, morbidity and mortality. In the past, outbreaks of neurologic EHV-1 were sporadic and typically involved one or a few cases within a herd or on a premises. The recent outbreaks in the U.S. and Europe have involved large numbers of infected animals with many of these showing neurologic signs. In the EHV-1 outbreak in Ohio during 2003, more than 30% of the 138 horses on the premises developed neurologic disease (*http://www.the horse.com, article #4104 and #4272*). This disease behavior is different than what was seen prior to 2001 in U.S. outbreaks.

The factors involved in this emergence are not clearly identified, but several factors have been suggested. Animal movement appears to be associated with several of the recent outbreaks. Movement could result in introduction of the virus to a new population; it is also possible that transport stress plays a role in allowing the disease to express itself or re-emerge from the latent stage. The role of vaccination is controversial; based on available information from recent outbreaks the disease has occurred in well vaccinated animals. What the attack rate would have been had the population been unvaccinated is unknown. The disease has occurred in equine populations where no vaccination occurred. There is much yet to learn about the ecology of the disease. It is likely that other factors may be playing a role. Potential temporal associations also exist; most

outbreaks have been seen in the fall and early spring, yet there is likely more horse movement nationally in the summer.

The interest level in this disease remains high. The economic impact is substantial; not only are the horses that die from the disease lost, but there are many costs associated with treatment, quarantines, cancelled events, and the inability of horses to compete in events.

Horse practitioners and horse owners should continue to quarantine suspect and diagnosed cases. Using strict biosecurity measures in day-to-day procedures, even when disease is not suspected, is a key strategy in preventing the introduction and spread of infectious diseases. APHIS Veterinary Services has developed a brochure titled *Biosecurity – The Key to Keeping Your Horses Healthy*, which can be found at http://www.aphis.usda.gov/lpa/pubs/HorseBioSecurity_final.pdf Another resource available to equine veterinarians who are members of the American Association of Equine Practitioners (AAEP) is *Equine Infectious Disease Outbreak: AAEP Control Guidelines*. The AAEP guidelines provide guidance for veterinarians who encounter contagious infectious disease in horses, and covers topics such as pre-outbreak considerations, considerations when equine infectious disease is suspected, and sign-based flowcharts and guidelines for response-plan recommendations.

## Conclusions

It appears that neurologic EHV-1 is emerging as a more virulent strain of the disease than seen previously in the United States. Many data gaps exist, and more investigations need to be done to better understand the situation and to identify factors playing a role in possible emergence. Identifying such factors will also assist with control of future outbreaks. The general ecology of this disease is not fully understood; additional research is needed. A standard case definition and standardized reporting requirements for the neurologic form of EHV-1 would be good starting points for further study, with subsequent studies comparing cases to controls to determine risk factors for the disease.

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