Equine herpesvirus (EHV) infection has been a recognized disease of horses for decades, one that continues to reassert its clinical importance. Most recently, this has been in the form of the sometimes fatal equine herpesvirus myeloencephalopathy (EHM) syndrome. Two related but antigenically distinct viral causative agents [equine herpesvirus type 1 (EHV-1) and type 4 (EHV-4)] are involved in four different EHV syndromes: EHM, respiratory disease, abortion, and neonatal foal death. EHV-4 is predominantly associated with the commonplace but low-mortality respiratory syndrome, equine rhinopneumonitis. In contrast, EHV-1 has the ability to clinically impact three systems: the reproductive and central nervous systems, and less often, the respiratory tract, and can cause viremia in neonatal foals which survive in utero infection.

Occasional but persistent outbreaks of the more serious and potentially devastating EHV-1 neurologic syndrome (EHM) have been described (Figure 1). An example is the 2011 outbreak of 26 confirmed primary EHM cases originating at the National Cutting Horse Association Western National Championship in Ogden, Utah. Recurring reports of similar outbreaks have resulted in a perceived increase in the incidence of EHM in North America and concern that EHM may be an emerging disease threat. As a result of these events, an EHV-1 consensus statement has been proposed, well-designed EHV-1-specific biosecurity protocols have been published, and AAEP vaccination guidelines for EHV have been developed.

The route of infection for all EHV syndromes caused by either EHV-1 or -4 is the epithelium of the upper respiratory tract. EHV respiratory infection is the precursor of the non-respiratory syndromes, including EHM, although clinical signs of respiratory infection may be lacking. The other proposed EHM etiology is recrudescence of latent EHV infection, which exists on a lifetime basis in most horses exposed to the virus. Latency and reactivation are key features of EHV-1 infection, “an evolutionary survival strategy” in the words of one expert. EHV-1 has been found to latently persist in T-lymphocytes and in neurons of the trigeminal ganglia. Latently infected horses are subclinical and have virologically negative nasal secretions until EHV-1 reactivation. Reactivation occurs under conditions of stress. Physical exertion, travel, environmental extremes, and
overcrowding are thought to be potential triggers of reactivation. When this occurs, clinically normal but latently infected horses can shed EHV, silently transmitting the virus to other horses. Thus, a likely scenario in an EHM outbreak is the arrival of a latently infected horse at an equine event, recrudescence of EHV-1 latency due to the stress of transport and physical performance, shedding of virus to susceptible contact horses, and a clinical outbreak of neurologic disease. In the individual horse, amplification of latent EHV-1 leading to viremia and endogenous dissemination of virus to the uterus or CNS has also been described. EHV is highly contagious. When an EHM outbreak occurs, primary transmission (to other horses in the group), secondary transmission (to other groups on the premises), and tertiary transmission (to other premises) have been verified. The effect of this dissemination is to multiply the economic and epidemiologic impact far beyond the index case, leading to large-scale outbreaks. This report describes an appropriate biosecurity response to outbreaks of clinical EHM as well as recommended preventive measures at the resident farm, in transit, and at performance events.

Biosecurity recommendations to help prevent or control an EHM outbreak

Risk Factors
An understanding of the risk factors for EHM is the foundation of an effective mitigation strategy. The following factors can predispose horses to EHM:

1. Comingling of susceptible horses with those that are actively shedding EHV-1, such as during a multi-horse clinical outbreak.
2. Seasonal prevalence in the autumn, winter and spring.
3. Older horses (e.g., in a large North American EHM outbreak, age >5 years was associated with clinical disease).
4. Rectal temperature >103.5° F, indicating active infection coinciding with peak levels of viral shedding.
5. Introduction of new horses into the resident population.
6. Lower prevalence in ponies and smaller breeds.
7. Environmental stressors (suspected stressors include transportation, weather, physical exertion), which contributes to recrudescence of latent EHV-1 infection.
8. Recent occurrence of EHV-1 respiratory disease or abortions, which may seed the premises with neurovirulent EHV-1 that can subsequently cause EHM.

The role of vaccination
The role of vaccination status in EHM risk is unknown. The latency status of these animals is unaffected by vaccination. Horses vaccinated for EHV at frequent intervals with either killed-virus (KV) or modified-live virus (MLV) vaccines have gone on to develop EHM. On the other hand, recent vaccination can help reduce EHV shedding (both amount and duration of virus shedding) from the nasopharynx and duration of viremia. Thus, vaccination will not prevent EHM, but it may minimize the extent of EHV infection in the individual horse and the likelihood of transmission to susceptible horses. Regular vaccination in general is considered a standard component of EHV-1 control in horses. The incidence of EHV abortions has declined dramatically in areas such as central Kentucky since the beginning of widespread vaccination in the 1970s. When vaccination coverage is high, as the epidemiology of abortigenic EHV-1 disease in Kentucky illustrates, the ensuing herd-immunity effect can reduce exposure risk. No commercial vaccine is approved for prevention of EHM.

Horse owners and veterinarians often ask if vaccination is useful during an active outbreak. The following guidelines apply:

- Vaccination is recommended for any non-exposed, healthy horse if there is an outbreak on the premises or imminent risk of exposure. For example, in a scenario where a horse is returning from an equine event where there was an EHV outbreak, all clinically normal, non-febrile horses that remained on the home premises are legitimate candidates for vaccination. A booster vaccination can lead to a rapid
anamnestic response in previously vaccinated horses, potentially reducing the spread of virus to other horses.

- If an outbreak occurred within the resident population, vaccination is advisable for any clinically normal horse that had no contact with sick horses, particularly if they did not share the same air space.
- Vaccination of clinically sick horses infected with EHV-1 or -4 is likely of no value.
- Vaccination of normal horses that have been in contact with sick horses or that have shared the same air space is of dubious value and not well studied; helping prevent post-vaccination disease in such situations should not be expected.

The role of immunomodulators

The role of immunomodulators in prevention of EHM is unknown. Several immunomodulators (also known as immunostimulants) are approved for use in horses as an aid in reducing the effect of viral respiratory disease. Immunomodulators are parenteral agents that contain inactivated viral or bacterial antigens that induce a rapid, non-specific immune response. Activation of macrophages and expression of cytokines such as interferon occur within hours after the immunomodulator is administered and can last for several days. If natural exposure to EHV occurs during that period, the activated, non-specific immune system can help provide immediate immune recognition and cellular-immune protection until the adaptive, antibody-specific immune response is mobilized in 7 to 14 days.

For helping prevent respiratory disease associated with EHV-1, immunomodulators are best given in advance of anticipated exposure or stress-inducing situations such as travel to a performance event or exposure to new horses. A potential application of immunomodulators is to treat clinically normal resident horses prior to the return of traveling horses that may have been exposed to EHV. A controlled study evaluated the efficacy of inactivated Parapox ovis virus

Figure 1 – Two clinical presentations of equine herpesvirus myeloencephalopathy (EHM) are shown: A, Front-leg ataxia and gait impairment, and B, lateral recumbency. In cases where the horse fails to show neurologic improvement after 2 or 3 days or where recumbency occurs, prognosis for full recovery is poor, and euthanasia is often required. (Photos courtesy of the U.S. Department of Agriculture.)
(iPPOV) in 4-10 month old horses subjected to weaning, transport and crowding with yearlings from different sources. These horses were exposed to clinical respiratory disease during natural exposure to EHV-1 and EHV-4. The iPPOV-treated horses (n=26) had significantly (p<0.05) lower clinical respiratory disease scores and significantly lower incidence and duration of purulent nasal discharge (p<0.01) compared to controls (n=27).

**Biosecurity guidelines for disease prevention**

To prevent recrudescence of latent EHV-1, husbandry practices designed to avoid physiologic stress should be practiced. These include providing good nutrition and parasite control, preserving intra-herd social hierarchies, and maintaining a well ventilated environment that avoids temperature extremes.

Wherever possible, resident horse populations should be divided into small, closed groups to minimize epidemiological risk. Broodmares should be segregated from other horses on the premises, and if possible sub-divided into small groups of 5 or less.

Regular vaccination of all horses will help maintain herd immunity and help minimize EHV shedding and intra-herd transmission of the virus. Especially in older horses, EHV-associated fever tends to be transient and can go unnoticed. Obtaining a daily rectal temperature reading will enable prompt identification of febrile horses, early diagnosis of infection, and rapid intervention. Investigators have found that the risk of EHM is 20-fold greater (p=0.01) when an EHV-1 infected horse is febrile.

Horses arriving on the premises for whatever reason should be quarantined in a separate barn (optimally with its own airspace) or paddock that is at least 30 feet removed from all other horses. There is no consensus on the quarantine period for newly arriving, clinically normal horses. However, a 3-week interval likely will exceed the period in which EHV remains viable in the environment and is 3 times the usual duration of viremia and viral shedding in infected horses. EHV-1 shedding typically lasts 7 to 9 days. However, longer periods of shedding lasting ≥21 days have been reported, particularly in young, immunologically naïve horses and in clinical cases of EHM.

A higher level of vigilance would be to screen incoming horses for EHV-1 shedding by obtaining nasal or nasopharyngeal swabs and submitting the sample for PCR analysis. This added precaution may be appropriate for intensively managed farms or locations where elite horses are in residence. Hand sanitizers, foot baths, and barrier precautions help provide an added measure of infectious disease control. Young horses are more susceptible to EHV respiratory disease, and older horses to non-respiratory EVH-1 syndromes, including EHM. However, the same disease control measures apply to all horses regardless of age.

**Biosecurity in response to an outbreak**

It is important to have in place a simple, written action plan or protocol that spells out procedures and individual responsibilities in case of an EHV outbreak. Too often, when a clinical EHV case occurs, next steps are ill defined and a ‘what do we do now’ mentality exists. In the absence of specific control measures, a coughing or febrile horse could remain in a barn or paddock for several days, directly or indirectly exposing most or all of the horses on the premises. A disease-prevention protocol should be designed expressly to help prevent that from happening. In other words, business as usual, where horses commingle and personnel come and go at will, should not prevail during an EHV outbreak.

The American Association of Equine Practitioners has published EHV-specific and general infectious-disease biosecurity guidelines. Additionally, the University of California-Davis has published detailed guidance online (http://www.vetmed.ucdavis.edu) for managing an EHV outbreak. The following comments are a simplified overview that is consistent with these existing recommendations. Treatment is not discussed here since it does not directly affect biosecurity.

Infection control in response to an active EHV-1 outbreak can be broken down into the four basic components: monitoring, diagnosis, containment, and environmental management. The overarching goal of this response strategy is rapid execution to limit the number of horses that are affected.

- **Monitoring** – Daily monitoring for clinical signs and fever will enable prompt diagnosis,
i.e., within 24 hours of clinical onset. Twice daily temperature monitoring will detect early-stage fever. The goal of monitoring is to identify the index horse or horses in case of an outbreak, then monitor the disease status of horses in contact with or close proximity to the index horse.

• **Diagnosis** – Nasopharyngeal or nasal swabs (rayon tip swabs) are the usual EHV diagnostic sample. Venous blood obtained during viremia, ideally in the febrile stage, is suitable as an additional sample. Nasopharyngeal swabs from a subclinical, suspect horse, or nasopharyngeal swabs or blood samples obtained promptly after onset of clinical signs should be submitted to a diagnostic laboratory for PCR analysis. The California Animal Health and Food Safety Laboratory at the University of California-Davis, the Gluck Equine Research Center in Lexington, Kentucky, and other veterinary diagnostic laboratories provide real-time PCR testing for EHV.

• **Containment** – Isolation of clinically sick horses is critical to limiting an EHV outbreak, whether respiratory or non-respiratory syndromes are involved. The isolation facility should be a separate barn with its own airspace. Ideally, personnel who handle sick horses should be different from those who manage the rest of the herd. Use of barrier clothing, disinfectant foot baths, and hand sanitizer should be scrupulously enforced. A secondary quarantine of the farm, meaning no equine traffic on or off the premises, will limit EHV spread beyond the site of the original outbreak. Duration of the quarantine should be at least 21 days after clinical diagnosis of the last horse to become sick. A convalescent horse should not be released from quarantine until at least one, and optimally two, EHV-negative nasopharyngeal swabs are obtained. Release from quarantine after 14 days in the case of horses with negative PCR tests for 2 to 4 consecutive days has been proposed. Booster vaccination of clinically normal, a febrile horses that have not had contact with sick horses may help provide an immunological barrier between infected and non-infected horses.

• **Environmental management** – Creation of sanitary zones in the areas where sick horses are held and after the quarantine is lifted will preempt viral transmission via fomites and external contamination by the recovering horse. After removal of bedding, chemical disinfectants are effective in killing EHV in stalls and elsewhere in the hospital environment. Equipment in contact with the sick horse should likewise be disinfected or discarded. Because survival of EHV in the environment is brief, 21 days is considered to be a safe interval before repopulating the area previously occupied by EHV-infected horses.

**Biosecurity for traveling horses**

If possible, traveling horses should be maintained at the resident farm in a separate location with their own air space. Transient horses should be handled last, after the on-farm resident horses, for routine husbandry procedures as well as for treatment. Traveling horses should be vaccinated for EHV, preferably 3 to 4 weeks before leaving the home premises.

Maintaining biosecurity during transit is especially challenging if a commercial hauler is used. Biosecurity precautions practiced by commercial haulers vary considerably and bear close scrutiny to ensure that a traveling horse receives the best possible treatment during transport. During shipment, horses should be allowed to lower their heads periodically for purposes of respiratory drainage. After arrival, obtaining a rectal temperature daily or twice-daily will enable early diagnosis of infection. Daily temperatures should be obtained for up to 2 weeks after returning to the home farm.

**Biosecurity at an off-site event**

A show or other performance event is an ultra-high risk setting for EHV because it combines multiple risk factors – intermingling of horses of unknown immune and infection status, marginal barrier protection, and the stress of transportation and physical exertion. A key biosecurity precaution at a performance event is to control access to clinically healthy horses by other horses and humans. An inoffensive way to restrict human access is to put a drape, perhaps with the stable’s name, over the front of the horse’s stall or barn breezeway. Handlers should use hand sanitizer at every access. Visitors should be instructed to not touch or feed the horse, and tack or equipment should not be shared.
Prior to stabling a horse at a public event, old bedding should be stripped out and stalls should be cleaned with a detergent and sanitized with disinfectant. When the horse is outside the stall, physical separation between it and other horses should be maintained, and horses should not be allowed to touch noses with each other.

**Clinical relevance and conclusion**

Latent EHV-1 infection in a high percentage of horses ensures that a permanent natural reservoir of this pathogen exists and that exposure is inevitable. When active EHV-1 infection occurs or latent infection recrudesces, EHM neurologic disease can develop in a small percentage of horses, more commonly in adults 5 years of age and older. The clinical effects of EHM can be devastating and sometimes fatal, and the potential for transmission of neurovirulent EHV-1 to other horses can be high. The risk of EHM is greatest during equine performance events, a setting where several risk factors converge. These include commingling of horses of variable immune and infection status, stress of transportation and physical exertion, and limited barrier protection and infection control policies. When EHM occurs under these circumstances, the risk of a multi-case outbreak can be high.

Equine practitioners should be prepared to provide their clients with basic guidance on how to help prevent and respond to an EHV-1 outbreak. An effective response strategy consists of close monitoring for clinical disease, confirmatory diagnosis of sick or recovered horses, containment of sick horses, and environmental management to limit EHV-1 transmission. The role of vaccination in EHV control is to help limit the extent and duration of viral shedding and to create a herd-immunity effect that can help minimize the risk of exposure and infection.

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References


