

## Equine Herpesvirus 1 & 4 Related Diseases

### Definition

Equine herpesviruses are very common DNA viruses in horse populations worldwide. The two most significant are EHV-1, which causes respiratory disease, abortion, and neurologic disease; and EHV-4, which primarily causes respiratory disease and only occasionally can cause abortion or neurologic disease.

Equine herpes viral respiratory disease is usually caused by EHV-4 and is most commonly seen in weaned foals and yearlings, often in autumn and winter. Older horses are more likely than younger ones to transmit the virus without showing signs of infection. Although EHV-1 is the principal cause of outbreaks of viral abortion, some strains of EHV-4 have been associated with sporadic cases of the disease.

EHV-1 myeloencephalopathy (EHM) results from damage to the vasculature in the CNS. Certain strains of the virus are endotheliotropic; therefore, this results in vasculitis, thrombosis, and areas of infarction that lead later to foci of malacia in neurologic tissue. Herpesvirus myeloencephalopathy cases occur singly or as outbreaks affecting 20-50% of the at-risk population. Occurrences may or may not be preceded by a febrile episode or signs of respiratory disease. Strains that contain aspartate (D) at amino acid position 752 in the DNA polymerase have been more strongly associated with EHM outbreaks than strains containing asparagine (N) at this position. However, neuropathogenicity is likely multifactorial and both variants can cause EHM. [See ACVIM Consensus Statement.](#)

### Clinical Signs

#### Fever

Fever is often biphasic and can be transient. The initial febrile phase (peaking day 1-2) precedes infection of the upper respiratory tract. The second febrile phase (6-7 days) often precedes a systemic viremia. Fever may go undetected and may be the only clinical sign noted in an infected horse. Temperature monitoring twice a day is recommended.

#### Respiratory disease

- Fever (A horse whose body temperature is >101.5 °F (38.6 °C) or 1.5 °F greater than the horse's normal body temperature is considered febrile.)
- Coughing
- Nasal discharge
- Variable enlargement of the mandibular and/or retropharyngeal lymph nodes
- Lethargy, anorexia
- Conjunctivitis
- Ocular disease including uveitis and keratitis
- Neonatal foals infected in utero are usually sick from birth and exhibit any combination or all of the following:
  - Fever
  - Lethargy
  - Weakness
  - Jaundice

- Respiratory distress/stridor/pneumonia
- CNS signs (occasionally)
- Death commonly occurs within 3 days.
- Older foals: nasal discharge is the most common sign of disease.

### Abortion

Most often, no warning signs of impending abortion in the mare. Typically occurs in late pregnancy (7+ months); very occasionally as early as 4 months.

### Neurologic disease:

- Incoordination of the hind (and occasionally fore) limbs
- Ataxia or wobbly gait
- Urine retention/dribbling
- Bladder atony
- Recumbency with inability to rise
- Neurologic signs are often preceded by fever and/or respiratory signs

### **Incubation Period**

After exposure by any route, incubation period may be as short as 24 hours but is typically 4-6 days, or longer.

*Note: EHV-1 abortion can occur from two weeks to several months following exposure to the virus with mares showing no clinical signs.*

### **Risk Factors**

- Evidence of transmission of EHV-1 virus
- Strain of EHV-1 virus detected
- Number of horses potentially exposed (Areas of high commingling of horses such as racetracks, hospitals, show grounds, etc.)
- Immune status of exposed horses, i.e. hospital or geriatric, horse rescue (Stress or immunosuppression: transport, hospitalization, training, showing, weaning, high doses of steroids)
- Testing results of exposed and clinically affected horses
- Movement of horses once released from restrictions/isolation
- A recent case control study of the 2011 multistate EHM outbreak found the following risk factors for EHM compared to EHV-1 cases that did not develop neurologic disease:
  - Exposure to a greater number of biosecurity risks at the event
  - Female sex
  - Increasing number of classes competed in
  - EHV-1 vaccination in the 5 weeks before the event
- Because mules and donkeys can be silent shedders of EHV-1, comingling during an outbreak could pose increased risk of transmission and disease to horses

### **Transmission**

Respiratory transmission (most common route of exposure)

Inhalation of droplets from coughing and snorting. (Note: EHV is not believed to spread by this route as efficiently as equine influenza virus.)

Direct contact with virus containing respiratory tract secretions, especially mucus.

Mares which have aborted, or whose foals have died, can transmit infection via the respiratory route.

Shedding by the respiratory route typically lasts for 7-10 days, but can be much longer. Therefore, based on a thorough risk analysis of the particular outbreak or case, a period of 14 to 28 days after resolution of clinical signs may be necessary before release from movement restrictions/isolation. EHV-1 testing of horses considered exposed or infected provides increased confidence in the release of restrictions/isolation period prior to 28 days.

#### Direct transmission

Aborted fetuses, fetal membranes and/or fluids are significant sources of the virus.

Infected foals are highly contagious and can transmit infection to other horses via the respiratory route through shedding virus into the environment.

#### Indirect transmission

Virus can be viable for several weeks in the environment once it has been shed by the horse.

Virus contaminated fomites are a significant factor in EHV spread.

### **Diagnostic Sampling, Testing and Handling**

#### **EHV 1 and 4**

<b>Sample</b>	<b>Test</b>	<b>Shipping</b>	<b>Handling</b>
Nasal or nasopharyngeal Swab  and  EDTA or citrated blood  Both blood and N/NP swab should be tested together	EHV 1 or 4 qPCR; Viral Isolation	PCR testing send swab in plain red top tube; for viral isolation place swab in viral transport media or red top tube with a few drops of sterile saline	Chilled overnight

Sera	EHV 1 and 4 Serum neutralization (SN)	Leak proof container	Chilled overnight
Sera	ELISA* Differentiation of EHV 1 from 4	Leak proof container	Chilled overnight

\* detects antibodies directed against viral glycoprotein gG (Svanovir™)

Virus isolation is considered the gold standard laboratory diagnostic test. It is highly specific and unequivocally confirms the presence of infectious virus. Although virus isolation should be attempted during outbreaks, it is time-consuming and can lack sensitivity. Quantitative PCR (qPCR) is more sensitive and rapid, and has become the test of choice for rapid detection during outbreaks.

Serology - Serological diagnosis using the viral neutralization test (synonym: serum neutralization [SN] test) cannot distinguish between EHV-1 and EHV-4 infection. Nevertheless, in combination with specific clinical signs, a four-fold or greater rise in antibody titer between acute and convalescent samples collected 14-21 days apart is confirmatory of a recent infection. When a single virus neutralization titer is very high (typically 1024 to 2048 or greater) this is likely to be the result of recent infection rather than vaccination.

A commercial ELISA test kit, suitable for use in practice, is available for detection and differentiation of EHV-1 and EHV-4 specific antibodies directed against viral glycoprotein gG ([Svanovir™](#)).

Contact your diagnostic laboratory for specific instructions regarding sample procurement and further information regarding sampling. Many diagnostic laboratories sell viral transport media and other products. Other sources are available from veterinary distributors.

#### [Nasal Swab/Transport Media Resource Option](#)

(Note: This is just one resource and is not specifically a recommended or endorsed supplier or product of the AAEP.)

#### **Nasopharyngeal or Nasal Swab Collection procedure for EHV 1/4 and related diseases**

##### Supplies Needed

- Dacron Swabs with plastic sticks 5-7 inches (Softens supplied with bacterial transport medias)
- Plain red top tube (blood tube) or viral transport media
- Few milliliters sterile saline
- Clean exam gloves
- Disinfectant material or wipe

## Procedure

1. Horse should be restrained. Pass the swab(s) along the left/ right ventral meatus being careful to avoid the false nostril, until you are in the horse's nasal passage. Rotate the swab to increase the collection of respiratory secretions for 5-10 seconds. Two swabs can be done at the same time if more than one sample is needed by the laboratory. Some labs request one sample for qPCR and one for viral isolation. Swabs that contain large amounts of environmental dirt after collection (from horses being kept on a dry lot or in a dusty environment) should be discarded and a new swab collected, since dirt often inhibits PCR analysis. Alternatively, clean the nostril to be collected with a disposable cloth prior to swab collection.
2. Place swab(s) into plain red top tube and, if available, add 1-2 drops of sterile saline for qPCR/viral isolation. **DO NOT PLACE qPCR/VIRAL ISOLATION SAMPLES IN BACTERIAL TRANSPORT MEDIA.**
3. If sampling more than one horse, fresh gloves should be used for each animal.
4. The outside of tubes should be wiped down with a disinfectant wipe to prevent contamination of other samples or gloves of handlers.
5. Consider all waste materials to be infectious including gloves and swabs, etc.
6. Any restraining equipment such as twitches, nose chains, etc. must be disinfected between use.
7. Keep tubes refrigerated and ship on ice overnight to a diagnostic laboratory of your choice.

## **Post-mortem**

**EHM:** Fatal outcome in horses infected with EHV-1 are most often associated with the neurologic form of the disease, EHM. Definitive diagnosis of EHM in an individual horse is only possible after histological and immunohistochemical examination of CNS tissues in many cases.

Examination of fresh CNS tissue by qPCR can also be attempted. This requires dissection of the entire spinal cord, followed by both gross and extensive histological examination of each part of the spinal cord.

This procedure is both time- and labor-intensive, and is typically only practical at a properly equipped necropsy laboratory, typically at a state diagnostic laboratory, or at a school of veterinary medicine.

In the USA, the necropsy facility should be accredited by the [American Association of Veterinary Diagnosticians](#). A full list of accredited laboratories is maintained on their website.

The complete carcass should be presented for post-mortem examination as soon as possible after death.

**EHV abortion:** When EHV results in abortion the fetus is usually expelled while still in the placenta and within the amnionic membrane. Almost all abortions occur in the last 4

months of pregnancy. Both the placental and fetal tissues should be submitted for necropsy and specific testing to detect EHV. Biosecurity precautions are indicated when handling the placenta and fetus as both can contain high levels of infective virus. Detailed instructions for veterinarians on how to collect and submit aborted equine fetal and other diagnostic samples from the mare are available at the [Animal Health Diagnostic Center at Cornell University](#).

### **Shedding Time of Virus Following Resolution of Clinical Signs**

Possibly up to a week, but may be longer in exceptional cases.

Recovered horses typically develop latent infections and are capable of shedding virus following reactivation (with or without signs of clinical disease) particularly under conditions of stress, for the remainder of their lives.

Horses with residual stable neurological signs are not considered when determining the countdown to release from isolation.

### **Environmental Persistence**

Environmental transmission plays a minor role in the maintenance of virus in the horse population since environmental persistence of EHV-1 is short, estimated to be no more than 35 days under ideal conditions and probably less than 7 days in most practical field situations.

### **Specific Control Measures**

#### Biosecurity

Please view and follow the [AAEP Biosecurity Guidelines](#).

Clinically normal horses housed within the primary perimeter may be permitted segregated exercise periods outside the perimeter. Precautions should be taken, and may include:

- Exercise scheduled *after* general population's exercise period to avoid potential virus transfer to unaffected horses/barns by exercise riders.
- Access to starting gate or similar equipment denied.
- Restricted use of ponies/outriders' horses – horses housed within the primary perimeter may only be escorted by horses housed within the same facility.
- Direct horse-to-horse contact is to be avoided.
- Prompt post-contact use of alcohol hand sanitizer by individuals having contact with horses during exercise. Clothing can also be a source of transmission.

#### Vaccination

EHV-1 vaccines have been shown to reduce nasal shedding and in some cases, reduce viremia. These products may therefore have some theoretical value against EHM (by reducing viremia), and certainly against spread of the virus by reducing viral shedding in the environment. However, there is not a licensed EHV product with a label claim for prevention or control of EHM.

Booster vaccination of healthy animals in both primary and secondary contagion control perimeters may have some value.

Vaccination in these circumstances is controversial, as some authorities speculate that immunity to EHV-1 may play a role in the development of EHM. While this remains unproven, it remains a possibility. The use of vaccination is therefore a risk-based decision.

If animals are unvaccinated prior to an outbreak there is unlikely to be time to administer an effective vaccination series during the risk period based on currently available EHV-1 vaccines. Do not vaccinate clinically ill animals. Please see [AAEP Vaccination Guidelines](#).

#### Release of Animals from Isolation

Maintain isolation procedures for 14-28 days after last clinical signs are detected, basing the release date on risk analysis.

1. No horse had a fever (temperature taken at least one time every 24-hour period and without any treatment of non-steroidal anti-inflammatory drug)
2. No horse had an abortion
3. No new cases of neurologic disease (Note: Neurological clinical signs are considered to be resolved when they stabilize, i.e. residual neurological signs are not considered in determining a day 0 for countdown of release of restrictions/isolation.)
4. All exposed horses have been tested and have given a negative result based on testing nasal swabs for EHV-1 by qPCR. EHV-1 testing of horses considered exposed or infected would allow for increased confidence in the release of restrictions/isolation prior the 28-day time period. There should be compliance with requirements by state animal health officials for duration of quarantine and testing.

#### **Biosecurity Issues for Receiving Animals**

Horses having been housed within primary perimeter:  
Isolate from general population for 28 days

Horses having been housed within secondary biosecurity perimeter:  
After having determined its level of risk-aversion, the recipient facility may consider the following:

1. Vaccination requirements for entrance into facility
2. Health certificate specifications
3. Test findings (a negative qPCR result on a nasal swab)

Update vaccination for animals at recipient facility before arrival of potentially infected/exposed animal.

#### **Zoonotic Potential**

None known

References:

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