Equine Herpesvirus (EHV-1 & EHV-4) Disease Guidelines

Summary
Equine alphaherpesviruses (formerly 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 rarely causes abortion or neurologic disease. Fatal neonatal disease infrequently occurs as a result of in utero infection. Asymptomatic infection is common and facilitates transmission within groups of horses.

Equine herpes viral respiratory disease (rhinopneumonitis) can be caused by EHV-1 or -4 and is most commonly seen in weaned foals and yearlings, often in autumn and winter. Older horses are more likely 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.

EHV-1 myeloencephalopathy (EHM) occurs when cell-associated viremia leads to vasculitis, thrombosis, and focal infarction within CNS vasculature, ultimately resulting in focal spinal cord malacia and neurologic disease. Herpesvirus myeloencephalopathy cases can occur sporadically in individuals or as outbreaks affecting multiple horses. Occurrences of EHM may or may not be preceded by a febrile episode or signs of vasculitis or respiratory disease. Retrospective analysis of multiple EHM outbreaks have clearly demonstrated that all EHV-1 strains ('neuropathic' G2254/D752, A2254/N752 and C2254/H752) are capable of causing outbreaks of EHM.

Additional detailed information regarding EHV-1 is available open-access in the 2024 EHV-1 ACVIM Consensus Statement.

Clinical Signs

Fever:

Fever is often biphasic and can be transient. The initial febrile phase (peaking at 1–2 days following exposure) precedes upper respiratory tract signs. The second febrile phase (6–7 days) often precedes systemic viremia. Fever may go undetected or may be the only clinical sign noted in an infected horse. To minimize the potential of missing a fever, temperature monitoring twice daily is recommended in at-risk horses.

Respiratory disease:

- Fever (body temperature >101.5 F/38.6 C)
- Coughing
- Nasal discharge (most common sign in older foals)

- Variable enlargement of the submandibular and/or retropharyngeal lymph nodes
- Lethargy and/or anorexia
- Conjunctivitis, ocular disease including uveitis and keratitis
- Lower limb swelling

Abortion:
EHV-1 abortion can occur from two weeks to several months following exposure to the virus without mares showing clinical signs of illness nor warning signs of impending abortion. This typically occurs in late pregnancy (7+ months), although rare cases as early as 4 months are possible.

Neurologic disease:
- Neurologic signs are often (but not always) preceded by fever and/or respiratory signs
- Incoordination of the hind (and occasionally fore) limbs
- Ataxia
- Urine retention/dribbling, bladder atony
- Recumbency with inability to rise
- Rarely, cranial nerve deficits, seizures, and/or brainstem signs
- Be aware that many cases of EHM do not fit the 'classic' description of hindlimb ataxia and urinary incontinence

Neonatal disease:
Foals infected in utero are usually sick at birth and exhibit any combination or all of the following:
- Fever
- Lethargy
- Weakness
- Jaundice
- Respiratory distress/stridor/pneumonia
- Severe leukopenia
- CNS signs (occasionally)
- Death (usually within 3 days)

Transmission
<u>Respiratory transmission (most common route of exposure)</u>
- Inhalation of droplets from coughing and snorting. (Note: EHV is not believed to be spread by this route as efficiently as equine influenza virus.)
- Direct contact with 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, a period of 14–28 days after resolution of clinical signs in all exposed horses may be necessary before release of horses from movement restrictions/isolation.

Direct transmission

- Aborted fetuses, fetal membranes and fetal fluids are significant sources of the virus. This material should be put in doubled plastic bags immediately to avoid contamination of other areas on the farm and disposed of using appropriate biosecurity measures.
- Any horses in the paddock or pasture where an abortion occurs should be removed from the area and kept isolated from unexposed horses.
- 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.
- Fomites contaminated with nasal secretions of infected horses can transmit EHV virus. Fomites may include clothing and footwear of personnel, shared grooming equipment or tack, water/feed sources, and surfaces such as stalls, wash racks and tie points.

Incubation Period

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

Risk Factors for Development of EHV Infection

- Movement of horses during confirmed or potential outbreak situations, especially prior to placement or release of quarantine restrictions.
- Commingling with mules and donkeys, which can serve as silent shedders of EHV-1.

Risk factors for the development of EHM are less clearly defined. The following factors have been found to be associated with EHM in one or more reported outbreak:

- Exposure to biosecurity risks at equine events
- Female sex
- Increasing age
- Prior EHV-1 vaccination

Selection of Horses to Sample for Diagnostic Testing

Horses showing clinical signs consistent with EHV infection, particularly when febrile or showing neurologic signs, should be tested. During outbreak situations when multiple horses are febrile, if initial testing for EHV is negative and other likely causes of the clinical signs are not identified, resampling in 24–72 hours is recommended. Horses with known exposure to EHV may need to be sampled in order to comply with quarantine release protocols depending on the venue and requirements by State Animal Health Officials.

Note: Surveillance screening via testing of asymptomatic horses is not recommended.

Note: In acute EHV-1 infection, fever can precede both nasal shedding and viremia. Therefore, it is recommended that febrile horses with suspected exposure to EHV-1 positive horses (or any horse identified with a fever during an outbreak situation) found to be negative on initial PCR testing of blood and/or nasal swab be retested via PCR on blood and nasal swab 24–72 hrs. after initial testing. Horses should remain quarantined until results of the second tests are available.

Diagnostic Sampling, Testing and Handling

EHV-1 and -4			
Sample	**Test**	**Shipping**	**Handling**
Nasal(N) or nasopharyngeal (NP) swab (collected with Dacron swab) and EDTA or citrated blood **Both blood and N/NP swab should be tested together**	EHV 1 or 4 qPCR; Viral Isolation	For PCR testing, send swab in plain red top tube with a few drops of sterile saline; for viral isolation, place swab in viral transport media or red top tube with a few drops of sterile saline	Chilled, ship overnight
Paired Sera	EHV 1 and 4 Serum neutralization (SN)	Leak-proof container	Chilled, ship overnight
Paired Sera	ELISA* Differentiation of EHV 1 from 4	Leak-proof container	Chilled, ship overnight

* Detects antibodies directed against viral glycoprotein gG (Svanovir™)

Virus isolation: Virus isolation (VI) 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.

PCR: Quantitative PCR (qPCR) is more sensitive and more rapid than virus isolation and is the test of choice for rapid detection during outbreaks. Initial testing for EHV should be performed with PCR assays that detect and quantify the glycoprotein B (gB) gene. Assays used to further characterize EHV-1 strains based on point mutations in the DNA polymerase gene (ORF30: A2254G, N752D) are not appropriate as screening tests, as some EHV-1 strains lack either genotype.

Serology: Serological diagnosis using the viral neutralization test (requires paired serology with no vaccination against EHV between sampling times) (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.

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.

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.

Nasopharyngeal or Nasal Swab Collection Procedure for EHV 1/4 and Related Diseases

Supplies Needed

- Dacron swabs with plastic sticks 5–7 inches (often supplied with bacterial transport medias)
- Plain red top tube (blood tube) or viral transport media
- Few drops of sterile saline
- Clean exam gloves
- Disinfectant material or wipe

Procedure

1. The 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 virus isolation. Swabs that contain large amounts of dirt that may be present in the nasal passage 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 a 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, change gloves between each horse.

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, nasal cleaning cloth, discarded swabs, etc.
6. Any restraining equipment such as twitches, nose chains, etc. must be disinfected after each use.
7. Keep tubes with swabs refrigerated and ship on ice/cooler packs overnight to a diagnostic laboratory of your choice.

Postmortem Findings

EHM:
Fatal outcomes in horses infected with EHV-1 are most often associated with the neurologic form of the disease, EHV-1 myeloencephalopathy (EHM). Definitive diagnosis of EHM in an individual horse is only possible after histological and immunohistochemical examination of CNS tissues in many cases. *Note: All cases of undiagnosed neurologic disease should be handled as potential zoonotic risks, particularly horses with unknown or inadequate rabies vaccination history.*

- If nasal swabs and whole blood have not already been collected for testing on suspect EHM cases, they should be collected prior to euthanasia in an effort to facilitate diagnostic testing while the necropsy results are pending.
- 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 Laboratory Diagnosticians. A full list of accredited laboratories is maintained on their website.
- The complete carcass should be presented for postmortem examination as soon as possible after death. It is important that a complete history be provided when submitting the horse for necropsy, including the suspicion of EHM as a cause of neurologic disease. A request for expedited processing should be made if the horse is part of a potential outbreak situation.
- The State Animal Health Official should be alerted to any horses euthanized or dead from suspected EHM and where the carcass was taken for necropsy. In some states, a permit may be needed to transport the carcass.

EHV abortion:
When EHV results in abortion, the fetus is usually expelled while still in the placenta and within the amniotic membrane. 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. It is important to remove all mares from the area where the abortion occurred as soon as possible. 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.

Neonatal disease:
Foals are generally sick at birth and most die of progressive respiratory failure within 1–3 days. Gross necropsy reveals consolidated lungs, reddened intestinal mucosa, and an orange hue to the liver and viscera. Lung tissues are positive for EHV via PCR and/or viral isolation, and histopathologic examination reveals severe necrotizing bronchopneumonia with intralesional Cowdry type A inclusions.

Shedding of Virus Following Resolution of Clinical Signs
Typically, 7–10 days 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 stressful conditions, for the remainder of their lives.

Horses with EHM may have residual neurological deficits for weeks to months following cessation of viral shedding and are not considered a risk when determining the countdown to release from isolation.

Environmental Persistence
Environmental persistence of EHV-1 is estimated to be no more than 35 days under ideal conditions and probably less than 7 days in most practical field situations. While direct contact with infected animals and exposure to aerosols, infected respiratory secretions, placenta and uterine fluids, and fetal tissue from aborted fetuses remain the most common and direct pathways for EHV transmission, indirect pathways through environmental and fomite contamination may play a more important role in viral transmission than previously thought, particularly in outbreak situations.

Specific Control Measures
EHV and/or EHM is reportable to the State Animal Health Official (SAHO) in many states. The veterinarian should know their responsibility for reporting of suspect or confirmed cases in the state in which the horse(s) has been sampled. In many states, the SAHO will place a hold order or official quarantine on the premises where affected horses are located and may also place requirements for testing and biosecurity protocols. Information regarding the role of the State Animal Health Official in EHV response is found in the USAHA Equine Herpesvirus Myeloencephalopathy Incident Guidelines for State Animal Health Officials.

Biosecurity

Veterinarians should immediately report any neurologic horse positive for EHV-1 to their local SAHO. Premises found to have positive cases will undergo quarantine under the guidance of state and local animal health officials.

Biosecurity for non-neurologic EHV infection (may or may not be reportable, depending on state) is focused on reducing viral transmission both on and off the affected premises. Further detailed recommendations regarding how to effectively isolate EHV suspect cases can be found in the AAEP Biosecurity Guidelines.

Vaccination

For EHM: There are no licensed vaccine products with label claims for prevention or control of EHM. Some EHV-1 vaccines reduce nasal shedding of EHV and reduce viremia. These products therefore have some theoretical value against EHM (by reducing viremia), and certainly against spread of the virus by reducing viral shedding in the environment.

Controlled, peer-reviewed research to determine whether vaccinating horses during an outbreak of EHM reduces transmission does not currently exist.

For Respiratory disease: There are labeled vaccines for protection against respiratory disease caused by EHV-1 or EHV-4. Details are available in the AAEP Vaccination Guidelines.

For Abortion: Vaccines are available for and specifically labeled for protection against abortion caused by EHV-1. Details are available in the AAEP Vaccination Guidelines.

Release of EHM Cases from Isolation

Horses with confirmed EHM should be isolated immediately, and the premises quarantined (under the guidance of SAHOs) for a minimum of 28 days. During this period, all horses are monitored at least twice daily for fever or other signs of EHV or EHM. Identification of any of the following will trigger a re-start of the 28-day quarantine period:

1. Fever (temperature taken at least twice every 24-hour period and without any treatment of non-steroidal anti-inflammatory drug)
2. Abortion
3. 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. In some cases, state animal health officials may allow horses to be released from quarantine/isolation prior to 28 days from the last detected fever. EHV-1 testing (by qPCR)

of horses considered exposed or infected would allow for increased confidence in the release of restrictions/isolation prior to the 28-day time period. All quarantine decisions should be in compliance with requirements by state animal health officials for the duration of quarantine and testing.

Biosecurity for Receiving Animals from Quarantined Sites

Horses transported to new facilities after release from EHM quarantine should be isolated from the general population for 28 days with twice daily temperature recordings. Any signs of fever or illness should prompt immediate testing for EHV.

Additionally, the recipient facility may want to consider requiring the updating of vaccinations for horses at the facility before the arrival of any potentially infected/exposed animal.

Zoonotic Potential

None known.

Additional Reading

ACVIM Equine Herpesvirus-1 Consensus Statement (updated 2024)

Equine Herpesvirus Myeloencephalopathy Incident Guidelines for State Animal Health Officials

Reviewed and approved by: AAEP Infectious Disease Committee