AAEP EQUINE VIRAL HEPATITIS GUIDELINES

In recent years, two viral causes of liver disease have been identified in horses. Equine parvovirus-hepatitis (EqPV-H) causes acute hepatitis, while Equine hepacivirus (EqHV) causes chronic hepatitis.

Equine Parvovirus-Hepatitis (EqPV-H)

Disease Name: Parvoviral hepatitis
The severe form of this condition was formerly known as Theiler's disease, serum hepatitis, or acute hepatic necrosis.

Disease Type
Acute viral hepatitis (liver disease) of horses

Transmission
This virus infects approximately 15% of US horses. Most infections occur through natural routes and are not associated with clinically recognized disease. Two modes of transmission—biologic and nasal—have been identified in horses. Other routes of transmission, such as vertical transmission and insect vectoring, have not been demonstrated.

> **Biologic transmission** occurs when healthy horses become infected through the administration of biologic products containing EqPV-H. To date, EqPV-H has been identified in equine antitoxins and plasma products. The USDA now requires testing of licensed products, which has greatly reduced the risk of transmission. Further information on equine biologic product regulation and safety testing can be found in the AAEP white paper: USDA and CFIA Regulation of Equine Plasma & Serum Products for the Equine Practitioner.
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> **Nasal transmission** occurs when horses with high viral load are in close contact with healthy horses. Horses can shed virus early in infection, before they show clinical signs. Most horses in the chronic or carrier phase of infection do not appear to shed virus. Transmission is suspected to be through direct contact and not respiratory droplets, although this is not proven.

Incubation Period
The time from exposure to detectable virus in the blood can be 1 to 12+ weeks. The time from exposure to clinically detectable hepatitis can be 4 to 12+ weeks.

Clinical Signs

Horses infected with EqPV-H can develop a wide range of clinical signs, varying from inapparent or very mild illness to fulminant liver failure. It is not currently known why some horses do not develop any clinical signs while others are severely affected.

Asymptomatic infection: *Most horses infected with EqPV-H will not have clinical signs of liver disease or illness.* Liver enzyme activities on bloodwork may or may not be transiently elevated but normalize within 1 to 12 weeks with no long-term health effects.

Clinical Hepatitis: *A small percent of horses infected with EqPV-H will develop clinical hepatitis.* Affected horses show signs of liver disease of varying severity (mild to severe), which may include one or more of the following:

- Lethargy
- Anorexia
- Jaundice
- Photosensitization
- Neurologic signs (altered behavior, head pressing, staggering, blindness)
- Elevated liver enzyme activities on bloodwork, especially AST, SDH, GLDH
- Elevated blood ammonia and bile acid concentrations
- Discolored urine
- Colic
- Recumbency
- Death (usually within 72 hours for severe cases)
- *Note: EqPV-H does NOT cause fever*

Carrier Status

Horses infected with EqPV-H typically remain asymptomatically infected for years. These silent carriers have low levels of virus in the blood and appear to be of low or no risk to transmit to other horses naturally. Blood products from these horses remain infectious.

A small number of horses remain carriers with high viral load for months to years. These horses are often co-infected with Equine hepacivirus (see below). Whether these horses are infectious is not known.

Diagnosis

EqPV-H should be considered in horses with signs of liver disease. EqPV-H causes hepatocellular disease and increases in AST, SDH, and GLDH predominate early in disease, while GGT concentrations have a more delayed response. A definitive diagnosis of EqPV-H infection can be achieved using a PCR test on liver biopsies, serum, EDTA plasma, or whole blood. However, **the presence of the virus does not always mean it is actively causing disease**. Therefore, a veterinarian must perform additional tests to rule out other causes. Serial testing showing that

the viral load decreases as the horse improves and *in situ* hybridization (ISH) test of a liver biopsy should be used to support the diagnosis. If the horse has a history of receiving biologic products in the preceding months, the possible adverse event should be reported to the USDA and product manufacturer.

Summary of diagnostics:

- Initial approach:
    - PCR of liver biopsy, serum, EDTA plasma, or whole blood to identify EqPV-H infection. For acute parvovirus with high viral load, all aforementioned samples should be sufficient for diagnosis. Currently, testing is available at the Cornell Animal Health Diagnostic Center.
        - Serum or plasma is preferred for serial monitoring and might be more sensitive than liver for low positive samples. Paired serum or plasma and liver is optimal.
        - Nasal swabs and feces should not be used to diagnose clinical EqPV-H disease.
    - Rule out other causes (history, physical examination, hematology, ultrasound, liver biopsy and culture).
- Confirmation:
    - Preferred: Biopsy with histopathology and *in situ* hybridization (ISH) for EqPV-H to demonstrate the virus is actively causing disease.
    - Alternative: Serial serum biochemistry and EqPV-H PCR to show viral load drops as disease improves.

Treatment

There is no specific treatment for EqPV-H infection. Asymptomatic horses do not require any treatment. Treatment of clinically affected horses relies primarily on supportive care and treatment of liver dysfunction. Referral to an intensive care facility might be required for severely ill horses. Rest from intensive exercise is recommended at least until hepatocellular enzymes (AST, SDH, GLDH) normalize, although the effect of exercise on recovery has not been studied.

Prognosis

The prognosis for horses with no clinical signs (asymptomatic infections) and mild-to-moderate clinical signs (e.g., mild lethargy, inappetence, icterus) is excellent. The prognosis for horses with signs of fulminant liver failure, especially with neurologic signs, is guarded to poor, with a mortality rate of 50–90%.

Prevention

There is no vaccine for EqPV-H. When administering equine biologic products (e.g., stem cells, plasma), it is best to administer autogenous biologics (made from the patient's own blood), or commercial biologics that have tested negative.

The USDA APHIS Center for Veterinary Biologics (USDA APHIS CVB) has taken measures to ensure that all commercially licensed equine plasma or serum biologic products have tested negative for EqPV-H. Whenever possible, it is recommended that veterinarians administer USDA APHIS-licensed products. When unlicensed biologics are used, consider testing the donor and/or product to prevent the spread of EqPV-H. Further information on equine biologic product regulation and safety testing can be found in the AAEP white paper: USDA and CFIA Regulation of Equine Plasma & Serum Products for the Equine Practitioner.

Biosecurity

Not enough is known about EqPV-H transmission to recommend a proven biosecurity protocol. Traditional approaches to limiting spread of disease in outbreaks rely on identifying exposed and infected horses and separating them from healthy horses. However, it can take at least 12 weeks from exposure to having detectable EqPV-H in the blood, and horses show no clinical signs of early infection. Horses appear to start shedding virus before the onset of hepatitis and can likely spread the virus to at least some members of the herd before they are found to be ill. Additionally, they are potentially shedding virus from the nose, mouth, and feces[1] [JT2] for at least another 4 weeks after hepatitis. Horses in the chronic phase of infection appear to have low risk of spreading the virus to others; however, we do not know when horses transition from infectious to a lower-risk phase.

While best practices to prevent the spread of EqPV-H are not currently known, biosecurity efforts should likely focus on the isolation of recently infected horses who may be contagious to others. Along these lines, biosecurity guidelines for management of a horse with parvovirus hepatitis may include:

- Keep the horse isolated for 4-8 weeks past onset of hepatitis (see guidelines linked below)
- Individual turnout with no nose-to-nose contact is acceptable
- Infected horses can be safely housed/turned out with other PCR positive horses

A moderate approach to reduce risk of viral spread assumes the following:

- Transmission is suspected to require direct nose-to-nose contact, or fomite contact (e.g. sharing bits, water troughs, etc.)
- Horses that have had direct contact with the affected horse should not be mixed with horses that have been kept separate. For example, do not mix pasture mates or paddock neighbors into paddocks that were completely separated from the affected horse.
- Separations should be maintained for at least 20 weeks.

For very cautious owners with available resources, an approach to managing an outbreak could include:

- Screen all horses by serum PCR weekly for 16-20 weeks past the last new infection.
- Based on results, divide the horses into two groups by positive or negative PCR status. All positive horses can safely be housed together, and all negative horses should be kept separate with appropriate biosecurity as in the guidelines below.
- Horses that become positive should be moved to the positive group.
- The positive horses should be kept separate from the negative group for at least 16 weeks after they are first found to be positive.

Please note, the author does NOT recommend keeping low positive horses isolated beyond the recommendations above, and these horses should not be limited in movement between premises.

Further information regarding protocols for isolating horses with potentially infectious disease can be found in the AAEP Biosecurity Guidelines.

Risk to Humans and Other Animals

None known

Equine hepacivirus (EqHV)

Disease Name: Hepaciviral hepatitis
Previously known as non-primate hepacivirus (NPHV)

Disease Type
Viral hepatitis (liver disease) of horses

Transmission
This virus infects approximately 40% of US horses. Most infections occur through natural routes and are not associated with clinically recognized disease. Multiple modes of transmission have been identified or suspected in horses:

> **Biologic transmission** occurs when healthy horses become infected through the administration of biologic products containing EqHV. To date, EqHV has been identified in equine plasma products.
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> **Non-biologic horizontal transmission** occurs primarily during spring through fall. Horses do not have to be in direct contact with infected horses to become infected. An insect vector is suspected, but this is an area of open investigation. Foals born to infected mares may also become positive within the first few months of life; the mechanism of this transmission has not been elucidated.

Sexual transmission may occur, although this has not been demonstrated. The closely related virus that infects humans, hepatitis C virus (HCV), can be sexually transmitted. HCV is shed into semen; however, it is unknown if HCV transmission requires blood contact. Sexual transmission of EqHV has not yet been evaluated in horses.

Incubation Period

After biologic transmission, the time from exposure to detectable virus in the blood is 1 to 3 days. The time from exposure to detectable acute hepatitis can be 1 to 14 weeks. The time from infection to development of chronic hepatitis is unknown but is hypothesized to be months to years.

Clinical Signs

Horses infected with EqHV can develop a wide range of clinical signs, varying from inapparent or very mild illness to fulminant liver failure. It is not currently known why some horses do not develop clinical signs while others are severely affected.

Acute infection: *Most horses infected with EqHV will clear the infection within 20 weeks and will not have clinical signs of liver disease or illness.* Liver enzyme activities on bloodwork may or may not be transiently elevated and will normalize within 4 to 16 weeks with no long-term health effects. Clinical signs have not been reported in horses with acute hepaciviral hepatitis.

Chronic hepatitis: *Approximately 20% of horses infected with EqHV will develop persistent infection lasting longer than 6 months. A small percentage of those horses will develop hepatitis over months to years.* Affected horses can have subclinical disease or show signs of liver disease of varying severity (mild to severe), which may include one or more of the following:

- Lethargy
- Anorexia
- Weight loss
- Elevated liver enzyme activities on bloodwork, especially GGT
- Elevated blood ammonia and bile acid concentrations
- Jaundice
- Photosensitization
- Neurologic signs (altered behavior, head pressing, staggering, blindness)
- Discolored urine
- Colic
- Recumbency
- Death
- *Note: EqHV does NOT cause fever*

Carrier Status

Horses can be infected with EqHV for months to years with or without liver disease. These horses are presumed to be infectious.

Diagnosis

EqHV should be considered in horses with signs of liver disease. EqHV causes hepatocellular disease, but biliary remodeling predominates in chronic disease, resulting in mixed elevations of AST, SDH, GLDH, and GGT. A definitive diagnosis of EqHV infection can be achieved using a PCR test on liver biopsies, serum, EDTA plasma, or whole blood. However, **the presence of the virus does not always mean it is actively causing disease**. Therefore, a veterinarian must perform additional tests to rule out other causes. The diagnosis is supported by serial PCR tests demonstrating a reduction in viral load coinciding with clinical improvement in acute cases, or PCR tests that remain elevated for >6 months for chronic cases. Histology of a liver biopsy should also be used to support the diagnosis. If the horse has a history of receiving biologic products in the preceding months, the possible adverse event should be reported to the USDA and product manufacturer.

Summary of diagnostics:

- Initial approach:
    - PCR of liver biopsy, serum, EDTA plasma, or whole blood to identify EqHV infection. Currently, testing is available at the Cornell Animal Health Diagnostic Center.
        - Paired serum or plasma and liver is preferred as results are occasionally discrepant.
    - Rule out other causes (history, physical examination, hematology, ultrasound, liver biopsy and culture).
- Confirmation:
    - Acute: Serial biochemistry and serum PCR to demonstrate a dropping viral load as clinical signs improve.
    - Chronic: Serial biochemistry and serum PCR to demonstrate that viremia and hepatitis persist >6 months.

Treatment

There is no approved treatment for EqHV infection. Asymptomatic horses do not require any treatment. Treatment of clinically affected horses relies primarily on supportive care and treatment of liver dysfunction. The effect of corticosteroids on reducing inflammation is unknown. Corticosteroids might improve disease in the short term but might also increase viral load. They are not recommended in the treatment of the related virus, HCV, in humans.

Whether to continue exercise should be based on clinical signs and informed consent of an adult rider. Asymptomatic horses in good body condition can likely continue to be worked at low to moderate intensity depending on the severity of disease, but this guidance is based solely on expert clinical experience. Serum biochemistry should be routinely monitored, and clients counseled to look for signs of progression and hepatic encephalopathy, which should prompt retirement from work.

Prognosis

The prognosis for horses with no clinical signs (asymptomatic infections) is excellent in the short-term, although the rate of progression is not known. Multiple outcomes have been observed, including progression to liver failure, stable disease for years, clinical recovery with continued infection, and clinical recovery with viral clearance. At this time, it is not possible to predict the progression of individual cases. Notably, despite marked liver enzyme elevations and severe changes on biopsy, some horses show minimal clinical signs for prolonged periods.

The prognosis for horses with signs of fulminant liver failure, especially with neurologic signs, is guarded to poor, with a mortality rate of 50–90%.

Prevention

There is no vaccine for EqHV. When administering equine biologic products (e.g., stem cells, plasma), it is best to administer autogenous biologics (made from the patient's own blood), or biologics that have been tested and confirmed free of the virus. *The USDA APHIS Center for Veterinary Biologics (USDA APHIS CVB) currently does NOT regulate or test for EqHV in equine biologic products.*

Biosecurity

Because of the ubiquitous nature of this virus and the high prevalence in equine populations, preventing infection over the lifetime of a horse is likely impossible without vaccination. Therefore, isolation of infected horses is not currently recommended. Additionally, horses that are infected as adults appear to be at very low risk of developing persistent infection and are therefore at very low risk of serious disease. Preliminary evidence suggests that horses infected as foals are at higher risk of developing persistent infection. Therefore, biosecurity efforts could potentially focus more on preventing exposure to foals.

While not enough is known about transmission of EqHV to recommend a proven biosecurity protocol currently, horses with hepacivirus infection are presumably contagious. Because an insect vector is suspected, if isolation is desired, separation by at least 200 yards from susceptible horses is recommended.

Further information regarding protocols for isolating horses with potentially infectious disease can be found in the AAEP Biosecurity Guidelines.

Risk to Humans and Other Animals
None known

Author: Joy Tomlinson, DVM, PhD, DACVIM
Supported and reviewed by: AAEP Infectious Disease Committee