



EQUINE PARVOVIRUS-HEPATITIS VIRUS (EqPV-H)

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Definition	<p>Equine serum hepatitis, formerly referred to as Theiler's Disease, is caused by infection with equine parvovirus-hepatitis virus (EqPV-H). EqPV-H is a hepatotropic single-stranded DNA virus capable of causing hepatitis in infected horses. Two distinct etiologies of EqPV-H infection are recognized: biologic transmission and non-biologic transmission. Asymptomatic infection is common, and only a small percentage of infected horses will develop clinical signs of liver disease.</p> <p><i>Note: EqPV-H is a recently discovered virus and the focus of rapidly evolving research. This document reflects knowledge at the time of writing, and practitioners are encouraged to seek out further consultation for questions regarding clinical cases of EqPV-H.</i></p>
Prevalence	<p>Surveillance studies suggest the prevalence of EqPV-H infection in equine populations varies from 3-17%, most of which are asymptomatic. Although seroprevalence up to 54% has been reported on farms with clinical cases of serum hepatitis, it is estimated that only 2% of horses infected with EqPV-H develop clinical disease.</p>
Transmission	<p>Two modes of transmission are recognized in horses:</p> <p><u>Biologic transmission</u> occurs through the administration of biologic products containing EqPV-H. To date, EqPV-H has been identified in tetanus antitoxin (TAT), botulinum antitoxin, <i>Streptococcus equi</i> antiserum, pregnant mare's serum, allogenic stem cell preparations and equine plasma products. Cases generally present 4-13 weeks after receiving equine biologic products.</p> <p><u>Non-biologic transmission</u> occurs sporadically in horses with no history of receiving biologic products. Herd outbreaks are possible, and while the mechanism for this type of infection has not yet been elucidated, seasonal incidence in late summer to early fall (when insects are active) suggests an insect-borne mode of transmission. This is an area of ongoing research.</p>



Incubation Period

Clinical signs of liver disease occur 4-13 weeks after administration of an EqPV-H infected biologic. The incubation period for non-biologic transmission cases is unknown, but is likely also approximately 4-13 weeks.

Risk Factors

- Administration of allogeneic biologic products that have not been tested for EqPV-H by PCR
- Sharing of needles across multiple horses
- Introduction into herds with confirmed cases of serum hepatitis, especially during late summer to early fall months

Clinical Signs

Horses infected with EqPV-H may develop a wide range of clinical signs, varying from asymptomatic to mild illness to fulminant liver failure. The factors that determine host response to infection have not yet been elucidated.

Asymptomatic infection: **Most horses infected with EqPV-H remain asymptomatic.** Some may develop evidence of subclinical hepatitis characterized by transiently elevated serum liver enzyme activities that return to normal concentrations within 1-4 weeks without any clinical signs or long-term health effects.

Clinical hepatitis: It is estimated that **approximately 2% of infected horses will develop clinical liver disease, ranging from mild illness to acute fulminant liver failure.** Clinical signs in affected horses may include one or more of the following:

- Lethargy
- Anorexia
- Jaundice
- Neurological signs associated with hyperammonemic encephalopathy (altered mentation, maniacal behavior, head pressing, blindness, staggering)
- Discolored urine (secondary to hemolysis and/or bilirubinuria)
- Colic
- Recumbency
- Death usually within 72 hours

Horses with clinical hepatitis will have serum biochemical profiles that reflect acute liver dysfunction and sometimes failure. Specific abnormalities may include:

- Elevated serum liver enzyme activities (GGT, AST, SDH, GLDH) (*Elevated GGT is the most commonly observed abnormality*)
- Abnormal liver function assays (bile acids)



Diagnostic Sampling, Testing, and Handling

- Elevated blood ammonia
- Hyperbilirubinemia (both direct and indirect)
- BUN may be elevated or decreased
- Blood glucose may be decreased

EqPV-H should be suspected in horses with signs of illness and/or liver disease and a history of receiving biologic products in the preceding months. **A definitive diagnosis of EqPV-H is achieved using PCR, and current recommendations are to submit fresh liver, fixed liver and serum for concurrent testing.** EqPV-H PCR testing is currently performed at the Animal Health Diagnostic Center (AHDC) at Cornell University. Fresh tissue and blood samples should be shipped chilled in insulated containers for overnight delivery. Specific instructions for sample collection, handling, and submission are available on the [AHDC website](#).

Blood:

- Serum (removed from clot) is the preferred blood sample, but EDTA whole blood or EDTA plasma may also be used.
- Samples from EqPV-H viremic horses will be PCR positive.

Liver tissue (biopsy):

- Liver tissue from EqPV-H infected horses will be PCR positive
- Acceptable samples include fresh, frozen, or formalin-fixed liver
- Histopathologic findings include varying degrees of centrilobular hepatitis and hepatocellular necrosis. Lymphocytic/plasmacytic infiltration of the periportal area is common with a fewer number of neutrophils. Remaining hepatocytes may be vacuolated.
- Histology results are useful for identifying additional causes of liver disease that may be contributing to clinical signs, such as chronic pyrrolizidine alkaloid toxicosis, hepatic fibrosis, etc.

Note: Liver mass may be severely reduced in fulminant hepatitis cases and ultrasound guidance is recommended to determine if a biopsy is possible

Post-Mortem Findings

Hepatic lesions in EqPV-H infected horses will vary depending on severity of disease. Asymptomatic or subclinically affected horses may have grossly normal livers with histologic findings of mild centrilobular to midzonal hepatocellular necrosis and mild lymphocytic/plasmacytic periportal infiltration. Livers from horses with fulminant hepatitis are often discolored and markedly reduced in size, with a flaccid texture and 'dish-rag' appearance. Histologic findings in severely affected horses include widespread, severe, centrilobular to mid-zonal hepatocellular necrosis with hemorrhage and lymphocytic/plasmacytic periportal infiltration.



Additional Hepatotropic Viruses	The recently discovered hepatotropic virus, equine hepacivirus (EqHV), can also infect horses and cause transient mild elevations in liver enzyme activities, however, clinical illness has not been reported as a result of EqHV infection. Equine pegivirus (EPgV) and Theiler's Disease Associated Virus (TDAV) are also hepatotropic viruses known to infect horses, but neither are associated with known clinical disease. Donkeys have been shown to be infected with EqPV-H and EqHV but disease manifestations and clinical course are unknown.
Treatment	There is no specific treatment for EqPV-H infection. Asymptomatic horses do not require any treatment, although serial monitoring of serum biochemistry may be helpful for monitoring elevations in liver enzyme activities. Treatment of clinically affected horses relies primarily on supportive care and treatment of liver dysfunction. Referral to an intensive care facility may be required for severely ill horses.
Virus Shedding	Viremia detectable by PCR generally occurs 1-4 weeks after exposure, and viral loads may continue to increase for an additional 2-4 weeks before decreasing. In experimental infection, virus has been found in nasal secretions and feces. It is important to note that experimental infection is achieved using very high viral challenge doses, and it is not currently known whether nasal and fecal shedding occurs under natural infection conditions. Some horses will continue to have persistent low-level viremia detectable by PCR, but it is unclear whether this low-level viremia is associated with chronic viral shedding.
Carrier Status	Horses clinically or subclinically infected with EqPV-H can remain asymptotically infected for long periods of time. This chronic low-level viremia (as determined by quantitative PCR) has not been associated with clinical signs of chronic liver disease. The percentage of horses that become chronic carriers is unknown, however, carrier horses may serve as reservoirs for infection to others. The mechanism and likelihood of transmission from a chronic carrier to a healthy horse is unknown at this time.
Prognosis	The prognosis for asymptomatic infections is excellent. Cases of subclinical hepatitis (no clinical signs, transient elevations in liver enzyme activities) generally return to normal within 1-4 weeks with no long-term health effects. Prognosis for horses with acute fulminant hepatitis is guarded to poor with a mortality rate of 50-90%.
Environmental Persistence	Unknown



Prevention	<ul style="list-style-type: none"> ▪ There is no vaccine for EqPV-H. ▪ At this time, the only means of preventing EqPV-H in horses is to administer autogenous biologics and/or USDA licensed biologics that have been PCR tested and confirmed free of the virus. ▪ Any biologic donor horses should be routinely tested for EqPV-H and other potential blood borne pathogens. The optimal frequency of donor testing is not currently known.
Testing of Biologic Products	<p>USDA APHIS regulates veterinary biologics (vaccines, bacterins, antisera, diagnostic kits, and other products of biological origin) to ensure that commercial veterinary biologics are safe and effective. Recently, the USDA APHIS Center for Veterinary Biologics (USDA CVB) has taken measures to ensure that all commercially licensed equine plasma or serum biologic products are tested and negative for EqPV-H. Whenever possible, it is recommended that veterinarians administer USDA APHIS licensed and tested biologic products to prevent the spread of EqPV-H.</p> <p><i>NOTE: Practitioners should be advised that not all commercial plasma and serum products are licensed or actively regulated. Plasma and serum products licensed by USDA APHIS will bear a U.S. Veterinary Biologicals Establishment License Number (VLN) or U.S. Veterinary Biological Product Permit Number (VPN) as well as the Product Code Number (PCN).</i></p> <p>Additional Resources from USDA APHIS: Licensed veterinary biologic products Common questions about veterinary biologics</p>
Biosecurity	<p>Horses with fulminant hepatitis may be shedding virus and should be isolated from other horses. Visit AAEP Biosecurity Guidelines for isolation of infected horses.</p>
Zoonotic Potential	<p>None known</p>
Additional Resources	<ol style="list-style-type: none"> 1. New Parvovirus Associated with Serum Hepatitis in Horses After Inoculation of Common Biological Products. Divers TJ, et al. <i>Emerg Infect Dis</i> 2018;24 (2) 303-310. 2. What Do We Know About Hepatitis Viruses in Horses? Tomlinson JE, Van de Walle GR, Divers TJ. <i>Vet Clin North Am Equine Pract</i> 2019;35(2) 351-362.

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