

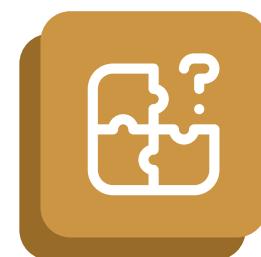
THEILER'S DISEASE

ACUTE HEPATITIS
SERUM-ASSOCIATED HEPATITIS
SERUM SICKNESS

CASSANDRA CELINE J. SEGUMBAN
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VET MED 517: EQUINE MEDICINE



OUTLINE



Basics



Diagnosis



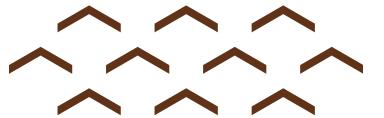
Treatment



Medications



Follow-up

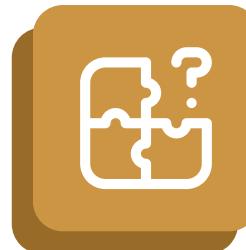




Basics

OVERVIEW THEILER'S DISEASE

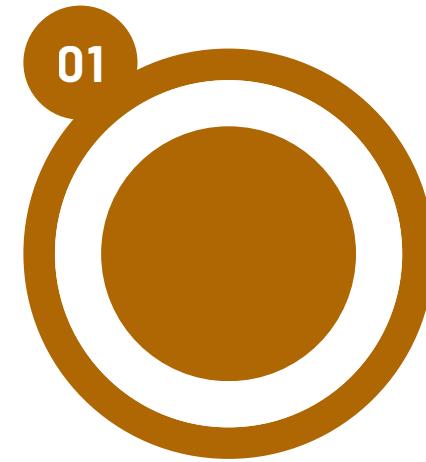
- The clinical disease is characterized by fulminant hepatic failure and encephalopathy in adult horses.
- Has been reported in horses for nearly 100 years, but the exact cause remains unknown.
- It is considered to be one of the most common causes of acute hepatic failure.
- The disease typically occurs in individual horses, but outbreaks of multiple horses have occurred.



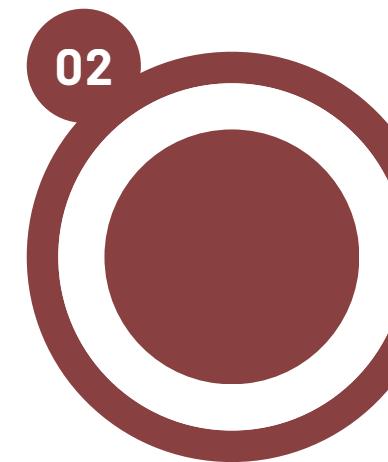
Basics

OVERVIEW

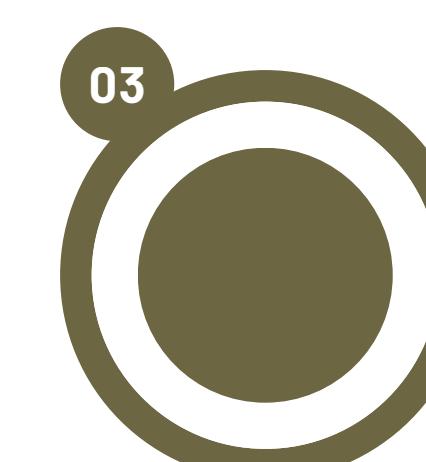
There are 3 separate epidemiologic diseases with identical clinical, clinicopathologic, and pathologic findings.



Acute, often fulminant hepatitis in horses that have **received equine-origin blood products** approximately 4–10 weeks earlier and less severe to subclinical disease in other horses receiving the same product



Acute, sometimes fulminant hepatitis occurring in a horse that was **in contact with a blood product-inoculated Theiler disease horse**, but that did **not itself receive** the equine-origin blood product



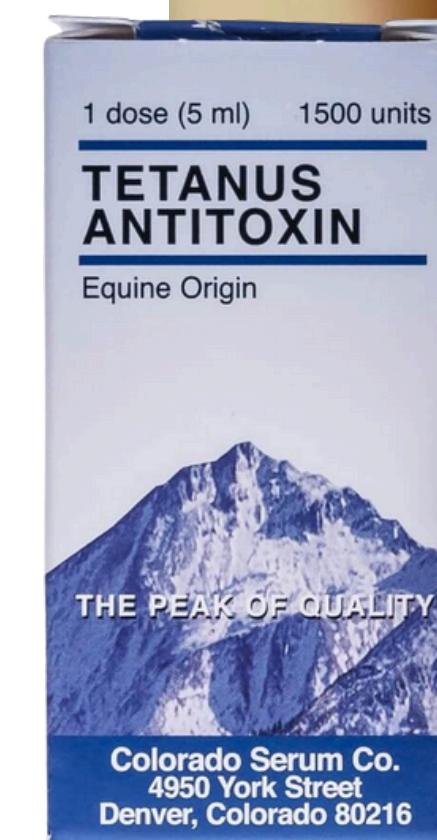
Acute, fulminant hepatitis in horses (often **broodmares** on pasture in the fall) with **no known equine-origin blood product administration**. This last syndrome can occur as **farm outbreaks**.



Basics

SIGNALMENT

- Adult horses, particularly those with a history of receiving **equine-origin serum** (especially **tetanus antitoxin**) or **plasma** approximately 4–10 weeks earlier.
- May also be horses **without a recent history** of equine blood product administration (nonbiologic origin acute hepatitis).





Basics

SIGNS

- Sudden in onset and rapidly progressive, with death occurring 2–6 days later
- Icteric (jaundice) and pass dark urine (bilirubinuria)
- Signs of hepatic encephalopathy (acute blindness and aimless wandering around the stall or paddock)
- Frequent yawning
- Neurologic signs (mild to severe depression or coma, to maniacal behavior or seizures)
- Hemolysis and hemoglobinuria (poor prognostic indicators)
- Photosensitivity and abdominal pain





Basics

CAUSES AND RISK FACTORS

Most commonly associated with **administration of an equine-origin blood product** 4–10 weeks before the onset of signs. Some epidemiologic evidence suggests that some cases **may result from an infectious agent**

Viruses that establish chronic/persistent infection in horses and their possible association with **liver disease**:

- **NPHV** (also called equine hepacivirus [EHCV]),
- **TDAV**/Theiler disease-associated virus
- **EPgV**/Equine pegivirus (Flaviviridae, genus Hepacivirus)
- **EqPV-H**/Equine parvovirus (Parvoviridae, genus unclassified)



Diagnosis

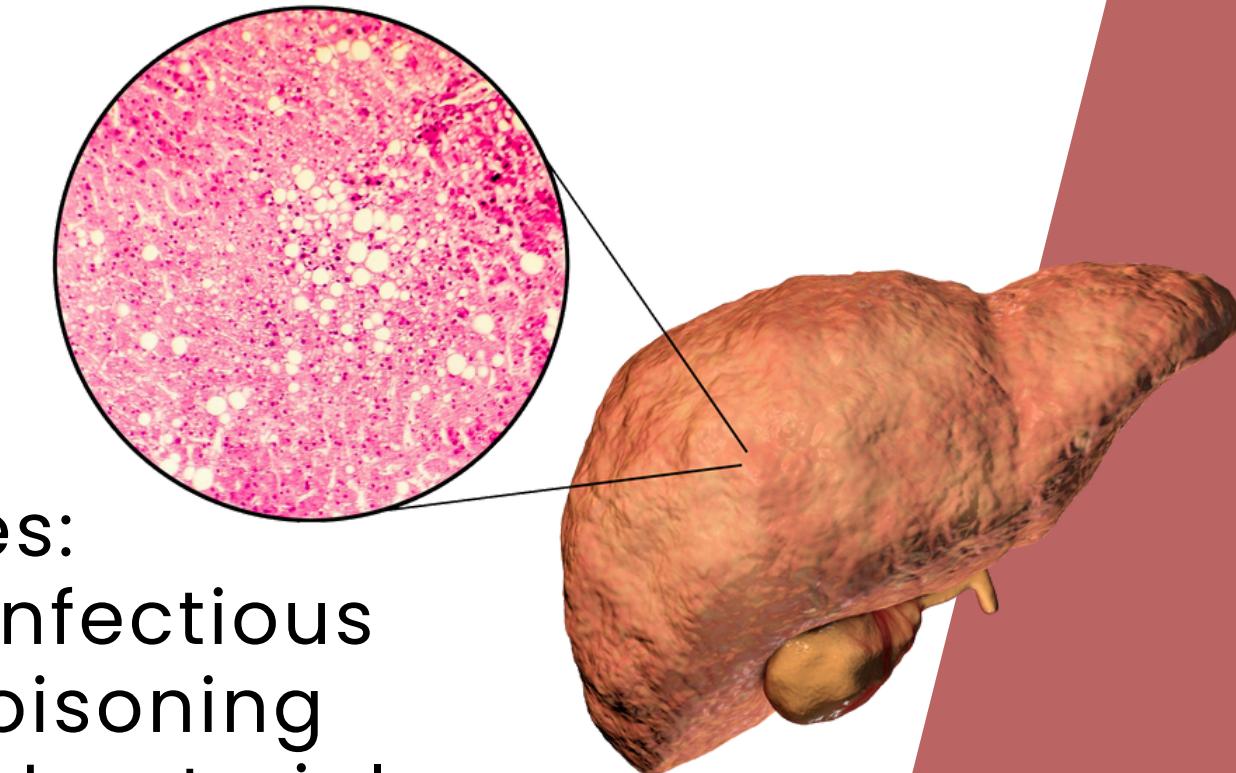
DIFFERENTIAL DIAGNOSIS

Acute onset of icterus in adult horses has multiple causes:

- **Prehepatic**—red maple or wild onion toxicity, equine infectious anemia, and immune-mediated hemolytic anemia poisoning
- **Hepatic**—anorexia, Theiler disease, Clostridium novyi, bacterial cholangiohepatitis, hepatotoxicity
- **Posthepatic**—cholelithiasis and other causes of biliary obstruction

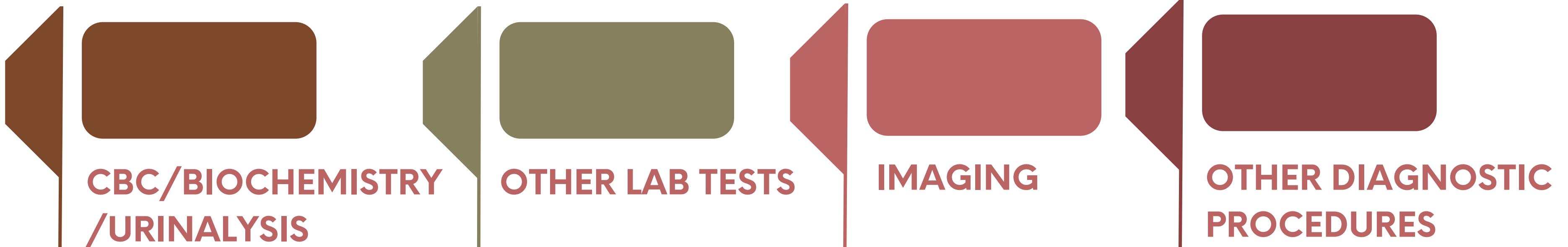
Signs of HE can be very similar to those of several acute neurologic diseases—**rabies, Eastern equine encephalomyelitis, Western equine encephalitis, and acute protozoal myeloencephalitis.**

Hematuria, hemoglobinuria, myoglobinuria, and bilirubinuria may cause pigmenturia





Diagnosis





Diagnosis



CBC/BIOCHEMISTRY /URINALYSIS

- CBC (usually normal, some have thrombocytopenia associated with DIC)
- Biochemistry (acute, severe liver disease)
- Marked increase in aspartate aminotransferase (often nearly 2000 IU/L; >4000 IU/L seems to be associated with a poor prognosis)
- Marked elevations in SDH and GLDH
- Moderate increases in biliary-derived enzymes (GGT usually increased to 100–300 IU/L)
- Both conjugated and unconjugated bilirubin are increased
- Increased anion gap
- Mild hyperglycemia, rarely hypoglycemia
- Urinalysis—bilirubinuria and hemoglobinuria (latter is a poor prognostic indicator)

OTHER LAB TESTS

IMAGING

OTHER DIAGNOSTIC PROCEDURES



Diagnosis



**CBC/BIOCHEMISTRY
/URINALYSIS**

OTHER LAB TESTS

IMAGING

**OTHER DIAGNOSTIC
PROCEDURES**

- Prolongation of prothrombin time and partial thromboplastin time
- Hyperlactatemia
- Hyperammonemia
- Elevated bile acids
- Equine hepatitis virus PCR panel
- Submit serum, fresh or formalin-fixed paraffin-embedded liver, or equine biologic products



Diagnosis



CBC/BIOCHEMISTRY
/URINALYSIS

OTHER LAB TESTS

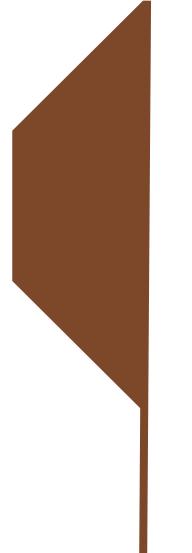
IMAGING

OTHER DIAGNOSTIC
PROCEDURES

- Ultrasonography may suggest the liver is smaller and more hypoechoic than normal.
- May appear otherwise unremarkable.



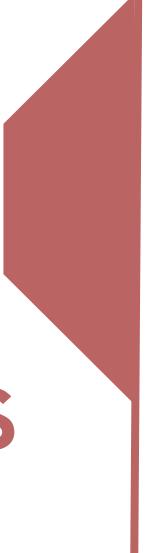
Diagnosis



**CBC/BIOCHEMISTRY
/URINALYSIS**



OTHER LAB TESTS



IMAGING



**OTHER DIAGNOSTIC
PROCEDURES**

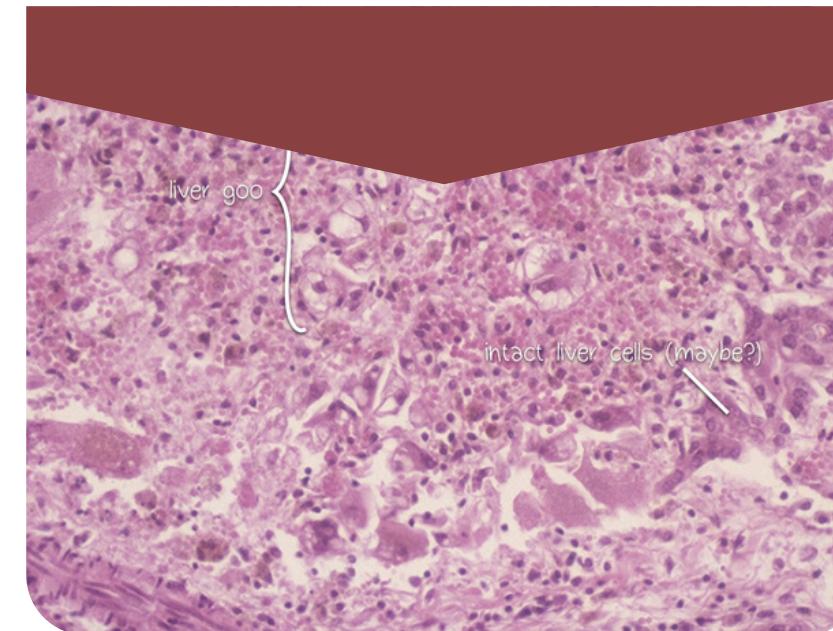
- Liver biopsy is not indicated in horses with “classic” signs of Theiler disease as histologic data will likely not change therapy.



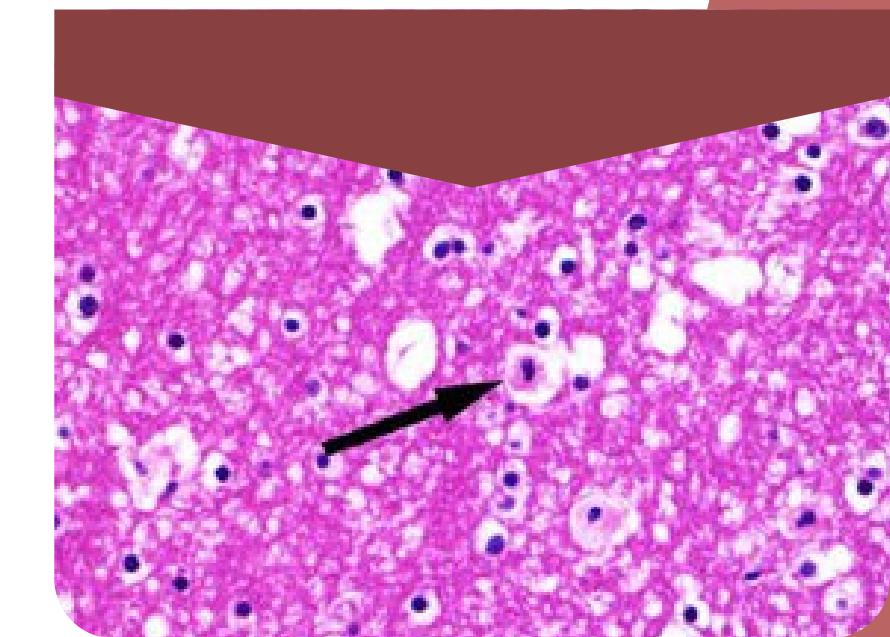
Diagnosis

PATHOLOGIC FINDINGS

- The liver is almost always smaller than normal.
- Histologically, affected livers show severe centrilobular or massive liver necrosis/apoptosis with portal areas less severely affected but with a mononuclear cell infiltration and slight to moderate bile duct proliferation, with or without fibrosis.
- Vasculitis has occasionally been reported.
- Alzheimer type II astrocytes are present in the brain in virtually all of the cases



Massive hepatocellular necrosis with remaining viable hepatocytes

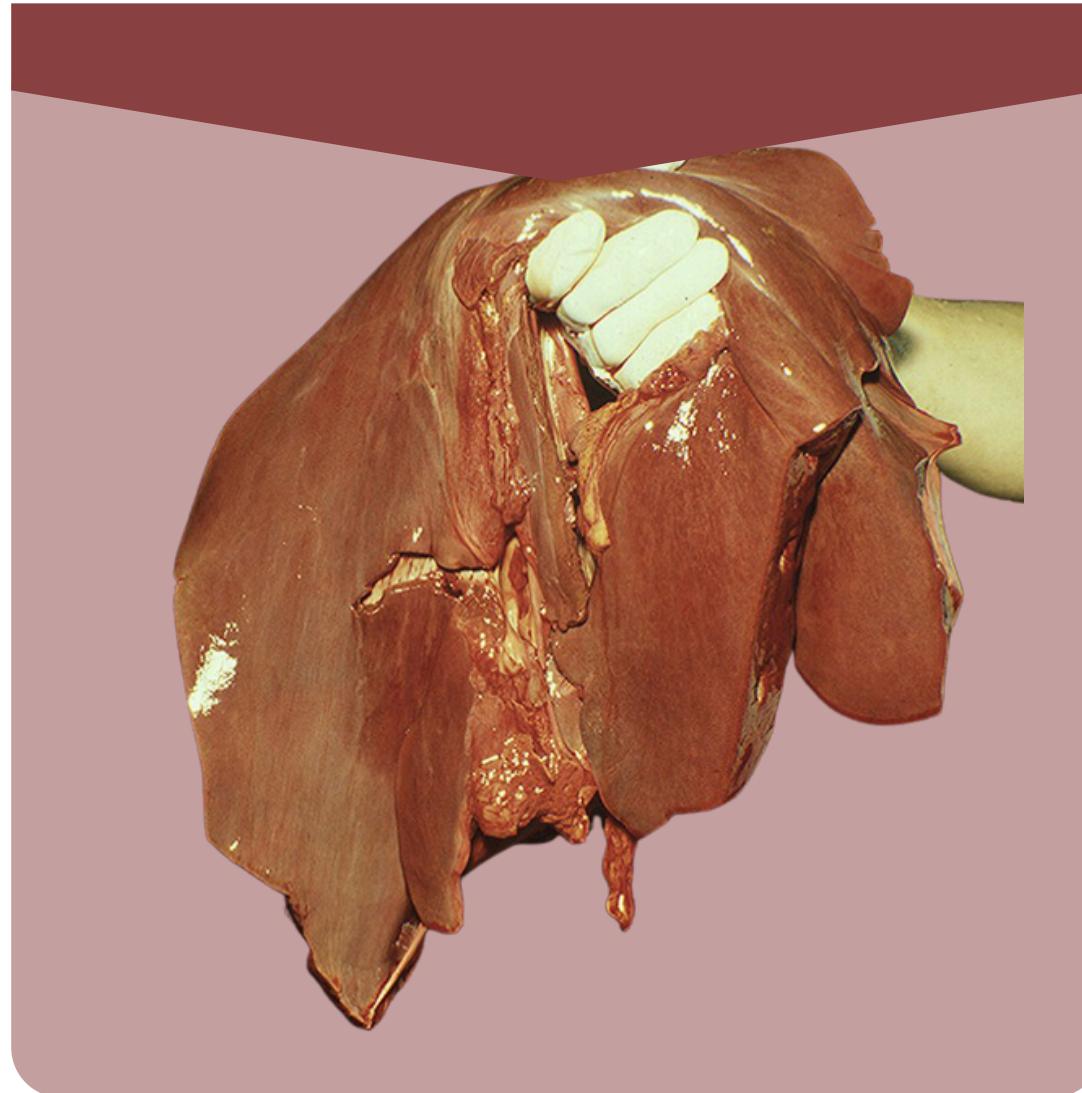


Alzheimer type II astrocytes



Diagnosis

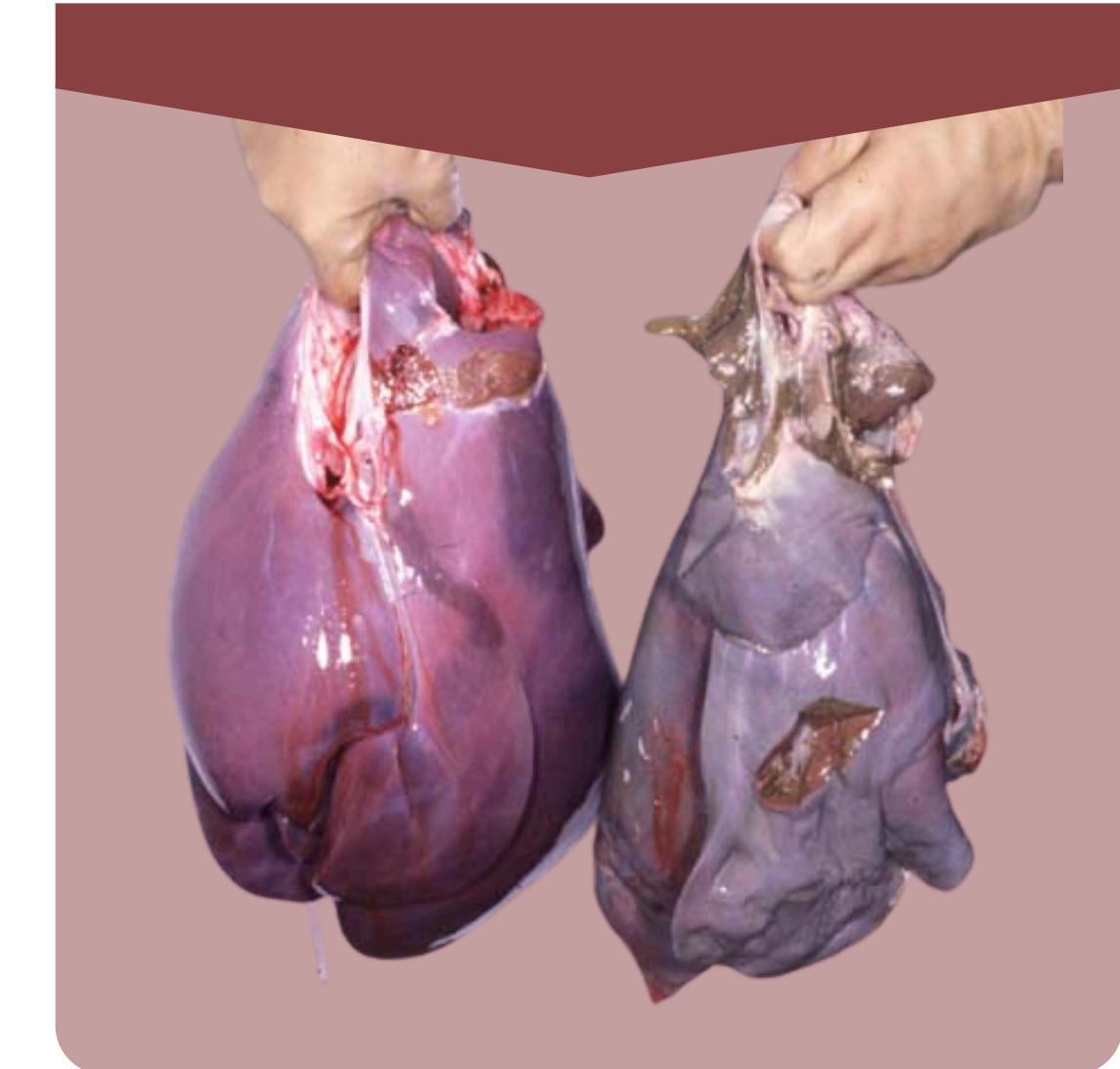
PATHOLOGIC FINDINGS



Normal equine liver



Enlarged, flaccid, and dark reddish-brown to purple, with a soft, easily deformable texture, resembling a "dish rag."



Normal liver (on the left) is firm, smooth, and has a consistent reddish-brown color, while the affected liver (on the right) is pale, mottled, and friable



Treatment

GOALS OF THERAPY

Provide supportive care including IV fluids, nutritional support, and antioxidant, anti-inflammatory, and antibiotic therapies

- Restrict activity, and avoid sunlight
- House the horse in a quiet place, preferably padded to prevent injury



- Fluid therapy
 - Hypertonic saline (7.5%, 4 mL/kg) or balanced isotonic crystalloid fluid
 - Continue at the maintenance rate (not eating and drinking)
 - Multiple B vitamins



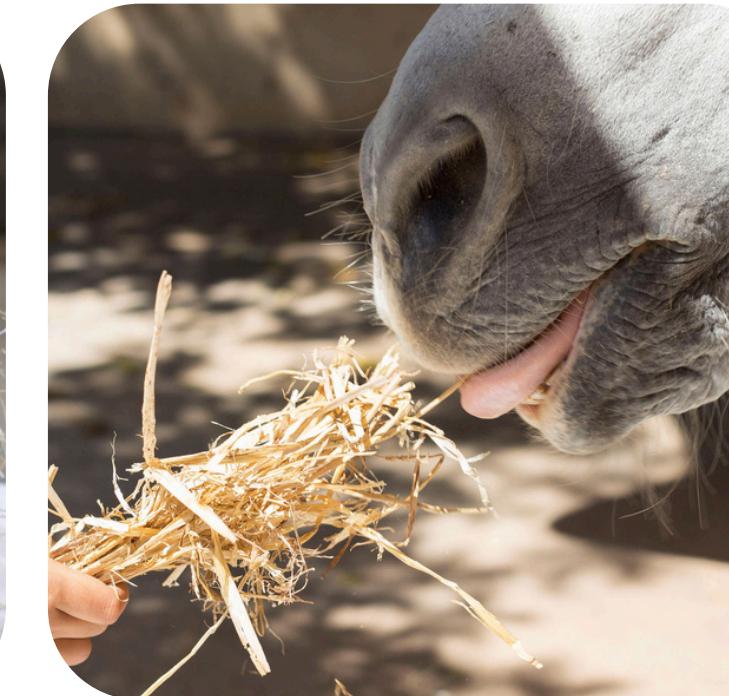


Treatment

GOALS OF THERAPY

Provide supportive care including IV fluids, nutritional support, and antioxidant, anti-inflammatory, and antibiotic therapies

- Nutritional support
 - Highly palatable grass hay (fed 1.5% of body weight per day), along with small amounts of high glycemic feeds at <1.0 g/kg/day should be offered in 4–6 meals per day (sorghum or soaked beet pulp)





Medications

DRUGS OF CHOICE

To decrease GI-derived neurotoxins (predominantly ammonia), decrease cerebral edema, correct glucose, electrolyte, and acid-base abnormalities, and maintain perfusion and oxygenation to the brain and other vital organs.

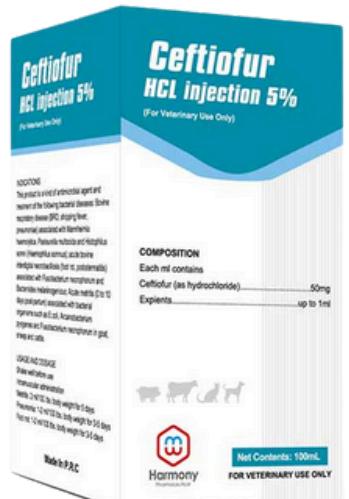
- All sedation should be avoided; however, to prevent injury, **detomidine** (5–10 µg/kg IV) can be used.
- If more long-term sedation is required, **gabapentin** (5–12 mg/kg PO every 12 h) or **pregabalin** (2–4 mg/kg PO every 12 h) could be considered.
- Conversely, in horses with profound coma, **sarmazenil** (0.04 mg/kg IV) or **flumazenil** (0.01–0.02 mg/kg IV) may be useful GABA receptor antagonists





Medications

DRUGS OF CHOICE



- **Metronidazole** (15 mg/kg PO every 12 h), **Neomycin** (10–20 mg/kg PO every 8 h) and/or **lactulose** (0.3–0.5 mL/kg PO or per rectum every 8 h) may help reduce ammonia production and absorption from the GI tract
- Anti-inflammatory treatment—**pentoxifylline** (7.5 mg/kg PO or IV (compounded) every 8–12 h) to reduce systemic inflammation
- Antimicrobial therapy—**bactericidal antibiotic (e.g. ceftiofur)** to prevent bacterial translocation from GI tract to blood
- Antioxidant therapy—**acetylcysteine** by slow IV administration (up to 100 mg/kg) diluted in 5% dextrose. **S-adenosyl methionine** (10–15 mg/kg PO) to provide antioxidant effect



Medications

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

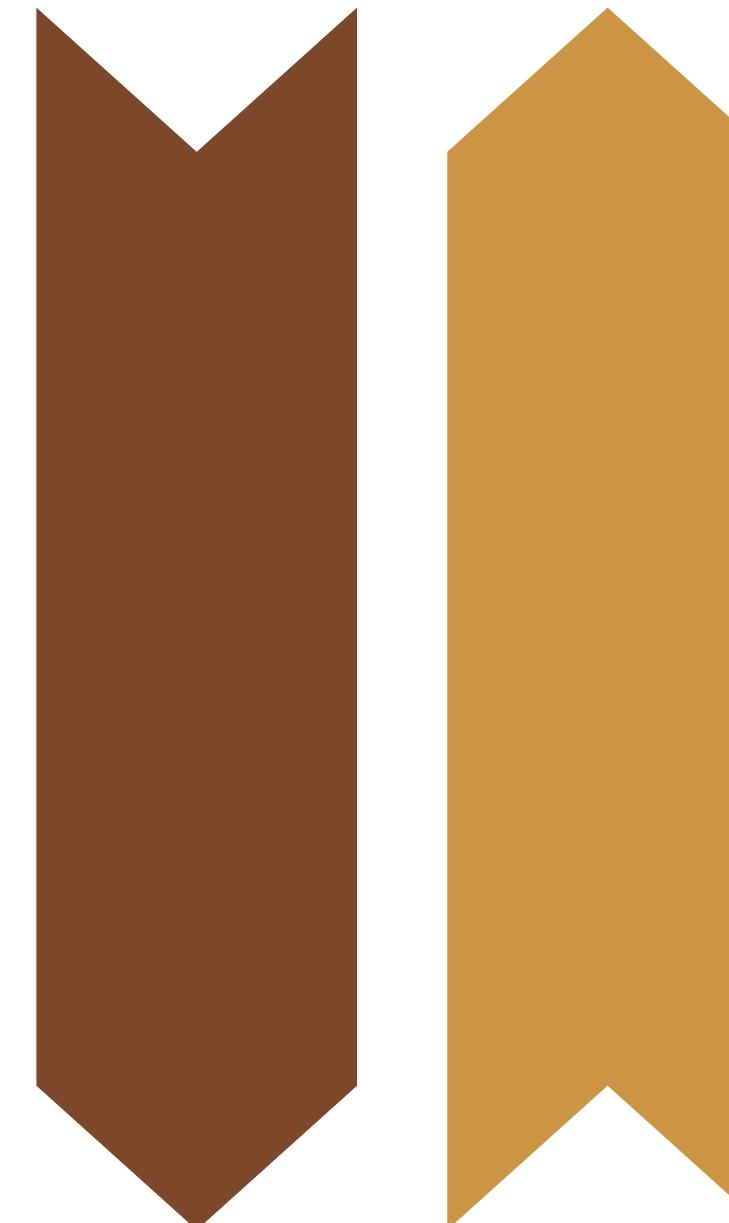
- **Neomycin** should not be given for more than 24–36 h; it may **induce severe diarrhea**
- Avoid **overly sedating horses** with HE, as excessive lowering of the head in the standing horse may **induce cerebral edema**
- Ideally, all oral medications should be **given by dose syringe** rather than nasogastric tube as nasal bleeding resulting from passage of a stomach tube can result in ingestion of considerable amounts of blood protein, which would likely increase blood ammonia production
- Because the **liver metabolizes many drugs**, their duration of action may be **increased in acute hepatic disease**



Follow-up

EXPECTED COURSE & PROGNOSIS

- Severe HE has a poor prognosis
- Those who continue to eat for 3 days and have supportive treatments may fully recover
- Decline in serum SDH and GLDH after 2–3 days of treatment, along with concurrent improvement in clinical signs, suggests a favorable prognosis
- No proven long-term consequences in horses that recover



PATIENT MONITORING

- Monitor liver enzymes and bilirubin every 2–3 days. Maintain adequate serum potassium levels to reduce hyperammonemia.

REFERENCES

01

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A photograph of two horses grazing in a field at sunset. The lighting is warm and golden, casting long shadows. One horse is in the foreground, facing away from the camera, while another is partially visible behind it.

THANK YOU

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