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Compendium

African Horse Sickness

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Abstract: *African horse sickness (AHS) is a reportable, noncontagious, arthropod-borne viral disease that results in severe cardiovascular and pulmonary illness in horses. AHS is caused by the orbivirus African horse sickness virus (AHSV), which is transmitted primarily by* Culicoides imicola *in Africa; potential vectors outside of Africa include* Culicoides variipennis *and biting flies in the genera* Stomoxys *and* Tabanus*. Infection with AHSV has a high mortality rate. Quick and accurate diagnosis can help prevent the spread of AHS. AHS has not been reported in the Western Hemisphere but could have devastating consequences if introduced into the United States. This article reviews the clinical signs, pathologic changes, diagnostic challenges, and treatment options associated with AHS.*

African horse sickness (AHS)—also known as *perdesiekte*, *pestis equorum*, and *la peste equina*—is a highly fatal, arthropod-borne viral disease of solipeds and, occasionally, dogs and camels.[1] AHS is noncontagious: direct contact between horses does not transmit the disease. AHS is caused by African horse sickness virus (AHSV). Although AHS has not been reported in the Western Hemisphere, all equine practitioners should become familiar with the disease because the risk of its introduction is increasing as horses are shipped between countries for breeding and sporting events; quarantine of horses entering the United States minimizes this risk. Introduction of virus-laden vector species via airplane or ship is another potential source of infection with AHSV.

AHSV belongs to the genus *Orbivirus* in the family Reoviridae. Reoviruses are icosahedral, 60 to 80 nm in diameter, and nonenveloped and have a segmented, double-stranded RNA genome.[2] Nine antigenically distinct serotypes of AHSV are designated 1 through 9.[3,4] Other important orbiviruses include the bluetongue virus and epizootic hemorrhagic disease virus of ruminants.

AHS is endemic in the central tropical region of Africa. AHS has also been reported in southern Africa and, occasionally, across the Sahara Desert into northern Africa.[5] Disease outbreaks have been reported in several non-African countries. A major outbreak of AHSV-9 was reported in 1959, spreading from northern Africa to Saudi Arabia, Syria, Jordan, Iraq, Iran, Turkey, Cyprus, Afghanistan, Pakistan, and India.[5] Additional outbreaks were reported in Spain (multiple outbreaks of AHSV-4 infection from 1987 through 1990[6–8]) and Portugal (an outbreak of AHSV-4 infection in 1989[8,9]). AHS is a reportable disease in the United States. If the presence of AHS were suspected in the United States, notification of state or federal authorities would be imperative. If AHSV entered the United States, it could have a devastating economic effect.[10]

Zebras are the natural reservoir hosts of AHSV and are generally not clinically affected, but can be viremic for up to 28 days. Although horses, mules, and donkeys are not natural reservoir hosts, they can develop a viremia sufficient enough to infect *Culicoides* sp. The virus is transmitted via biting arthropods. Vectors of AHSV include *Culicoides imicola* and *Culicoides bolitinos*.[6,11,12] Other biting insects, such as mosquitoes, are thought to have a minor role in disease transmission. *C. imicola* is the most important vector of AHSV in the field and is commonly found throughout Africa, Southeast Asia, and southern Europe (i.e., Italy, Spain, Portugal).[6,13] The presence of *C. imicola* in these regions is important for transmitting AHSV during disease outbreaks. In Europe, *C. imicola* has not been identified in non–Mediterranean basin countries,[14] although it has been predicted that a rise in global temperature will extend the distribution of *C. imicola*.[13] *C. imicola* is not present in the United States; however, potential vectors such as *Culicoides variipennis* exist in the Western Hemisphere.[6]

After an arthropod carrying AHSV bites an animal, the virus replicates in the regional lymph node. After amplification in the lymph node, the virus disseminates throughout the body via the blood, resulting in primary viremia.[2,11] Once in the circulation, the virus enters endothelial and mononuclear cells within multiple targets, including the lungs, spleen, and lymphoid tissue. Replication of AHSV within these targets results in secondary viremia.[11] Viral replication results in endothelial cell damage and macrophage activation. Cytokine (i.e., interleukin-1, tumor necrosis factor α) production is initiated, resulting in increased vascular permeability and leakage of fluid into the subcutis and lungs. Variable tropisms of AHSV for pulmonary and cardiac endothelial cells account for the various clinical forms of AHS.[6,12]

Key Points

- AHS is considered one of the most lethal diseases of horses. Although AHS is exotic to the United States, it is imperative that equine practitioners be aware of this disease and its potential effect on the equine industry.
- Appropriate state or federal authorities should be contacted if the presence of AHS is suspected.

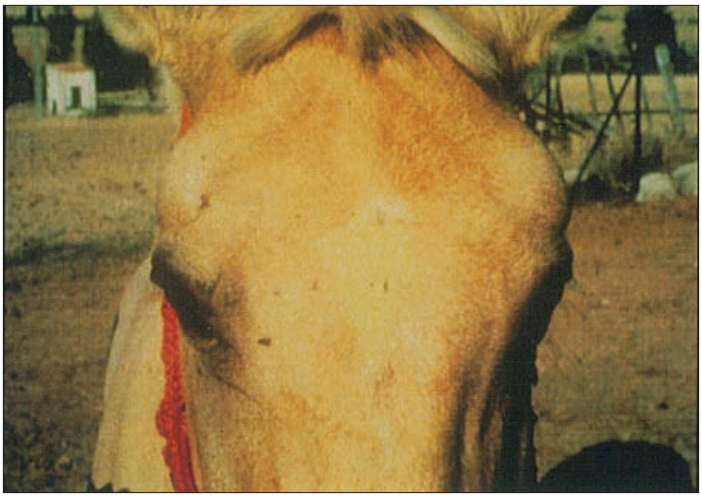

Figure 1. A horse with supraorbital edema. *(From United States Animal Health Association.* Foreign Animal Diseases. *1998; with permission)*

Diagnostic Criteria

Historical Information

- **Breed predispositions:** All breeds of horses are susceptible to AHSV infection. Other solipeds, including mules and donkeys, are also susceptible, but with reduced disease severity. Southern African donkeys and zebras rarely exhibit clinical signs of infection.[11,12] Zebras are considered to be the reservoir for AHSV.
- **Age and gender predispositions:** There is no age or gender predisposition.
- **Other considerations:** A history of travel to or from countries with AHSV or exposure to animals from countries known to have AHSV should raise suspicion for AHS. Additional risk factors include close proximity to airports or seaports and the presence of appropriate vectors within the region.

Physical Examination Findings

Four forms of AHS have been described: the pulmonary (peracute) form, the cardiac (subacute edematous) form, the mixed (acute) form, and horse sickness fever. In the early stages of all forms of AHS, a field diagnosis is virtually impossible because fever is typically the only abnormality. However, as clinical disease progresses and characteristic signs begin to appear,[7,11,12,15,16] AHS should be included in the differential diagnosis. Major clinical signs for each form follow.

The pulmonary (peracute) form

- Acute fever of 40°C to 42°C (104°F to 107.6°F)[17]
- Respiratory distress
- Abnormal posture (widely spread forelegs and an extended neck)
- Tachypnea
- Forced expiration
- Coughing
- Frothy nasal exudate
- Death within minutes to hours

The cardiac (subacute edematous) form

- Fever of 39°C to 41°C (102.2°F to 105.8°F; lasting 3 to 6 days)[17]
- Edema of the supraorbital fossae **(FIGURE 1)**, eyelids, cheeks, lips, tongue, laryngeal region, neck, shoulders, and chest
- Severe depression
- Colic
- Death within 4 to 8 days

The mixed (acute) form

- A combination of clinical signs from the pulmonary and cardiac forms
- Death within 3 to 6 days

Horse sickness fever

- Fever of up to 40°C (104°F; lasting 3 to 5 days)[17]
- Anorexia
- Depression
- Congested mucous membranes
- Tachycardia

Laboratory Findings

All forms of AHS may produce the following abnormalities on a complete blood count: leukopenia characterized by neutropenia with a left shift, thrombocytopenia, and hemoconcentration. Serum chemistry abnormalities are nonspecific indicators of this illness in horses; however, these abnormalities may include increased levels of creatine kinase, lactate dehydrogenase, alkaline phosphatase, creatinine, and/or bilirubin.

Other Significant Diagnostic Findings

- Thoracic radiography may reveal pulmonary edema.
- Thoracic ultrasonography may reveal pleural and/or pericardial effusion.

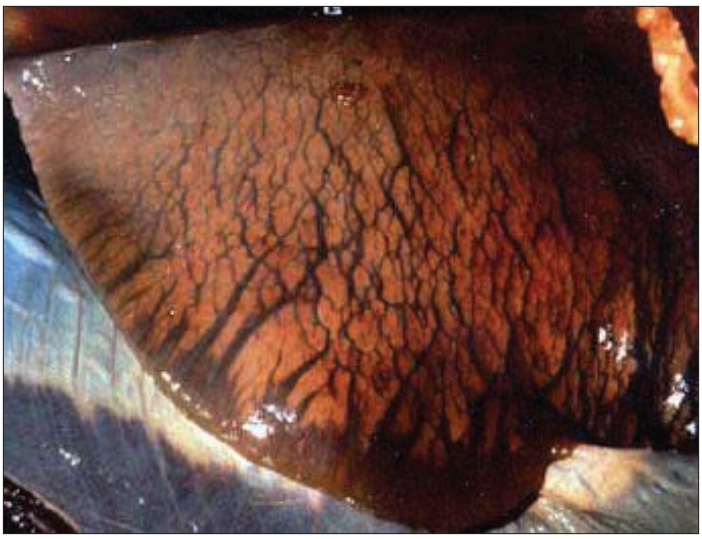

Figure 2. A horse's thoracic cavity showing marked pleural effusion and pulmonary edema as well as distended interlobular septa. *(From United States Animal Health Association.* Foreign Animal Diseases. *7th ed. 2008; with permission)*

Box 1. Primary Differential Diagnosis for African Horse Sickness[a]

Pulmonary form
- Equine viral arteritis
- Equine influenza
- Bacterial pneumonia
- Anthrax
- Hendra virus infection[b]

Cardiac form
- Purpura hemorrhagica
- Congestive heart failure
- Equine infectious anemia
- Equine granulocytic ehrlichiosis
- Equine piroplasmosis

Mixed form
- All diagnostic differentials for the cardiac and pulmonary forms

Horse sickness fever
- An extensive list of diagnostic differentials because the main clinical finding is fever

Major features of common diagnostic differentials

Congestive heart failure
- Heart murmur and/or venous distention is present.
- Fever may be present, depending on the etiology.

Equine infectious anemia (equine infectious anemia virus)
- A complete blood count reveals anemia.
- Affected animals are jaundiced in acute stages and emaciated in chronic stages.
- Gross necropsy findings include hepatomegaly and splenomegaly.

Equine viral arteritis (equine viral arteritis virus)
- The clinical presentation includes ventral edema and dependent edema of the distal limbs.
- Gross necropsy findings include widespread hemorrhage, pulmonary edema, pleural effusion, and peritoneal effusion.

Purpura hemorrhagica
- Anemia, neutrophilia, thrombocytopenia, hyperfibrinogenemia, and hyperglobulinemia are identified.
- Ecchymotic and petechial hemorrhages are found throughout the body.

Equine piroplasmosis (infection with Babesia caballi *or* Babesia equi*)*
- The clinical presentation includes jaundice, congested mucous membranes, colic, and ventral edema.
- Blood smear examination reveals an intraerythrocytic protozoan during the acute phase of disease.

[a]Differentials vary depending on the clinical signs.

[b]Disease that is currently exotic to the United States.

Differential Diagnosis

BOX 1 outlines the differential diagnosis for AHS.

Necropsy Findings

At necropsy, each form of AHS can have specific gross findings that vary in severity (minimal to marked)[1,7,11,12,15] and result from (1) an increase in permeability of blood vessel walls and (2) disturbances in the circulation. No pathognomonic lesions are associated with AHS. The pulmonary form of AHS is characterized by marked pulmonary edema and pleural effusion (**FIGURE 2**). In most acute cases, large amounts of frothy fluid are present within the nostrils, trachea, and pulmonary airways. The lungs feel heavy but have not collapsed and are reddened due to expansion of the interlobular septa. Several liters of a clear yellow-tinged fluid are found within the thorax. Other, less common gross lesions include subcapsular splenic hemorrhages, pericardial petechiae, vascular engorgement or petechiae of the small and large intestinal serosa, vascular engorgement of the gastric fundus, vascular engorgement of the renal cortex, and edema surrounding the trachea and aorta. Thoracic and abdominal lymph nodes are commonly enlarged and edematous.

Necropsy findings associated with the cardiac form of AHS include expansion of the subcutaneous and intermuscular fascia of the head, neck, and shoulders by a yellow, gelatinous material (edema). The pectoral area, ventral abdomen, and gluteal area are less commonly affected. There are petechial and ecchymotic hemorrhages of the epicardium as well as pericardial effusion. Pleural effusion is rarely observed. Similar to the pulmonary form, there is hyperemia or petechiation of the small and large intestinal serosa and/or hyperemia of the gastric fundus. In addition, submucosal edema may be prominent in the cecum, large colon, and rectum.

In the mixed form of AHS, gross lesions associated with the pulmonary and cardiac forms can be present.

Gross lesions are not commonly associated with horse sickness fever because affected patients are rarely evaluated by necropsy.

Ancillary Diagnostics

Histopathology

Histopathologic changes, although not specific for AHS, occur due to (1) an increase in permeability of blood vessel walls and (2) disruption of the circulation.[1] Examination of the lungs reveals

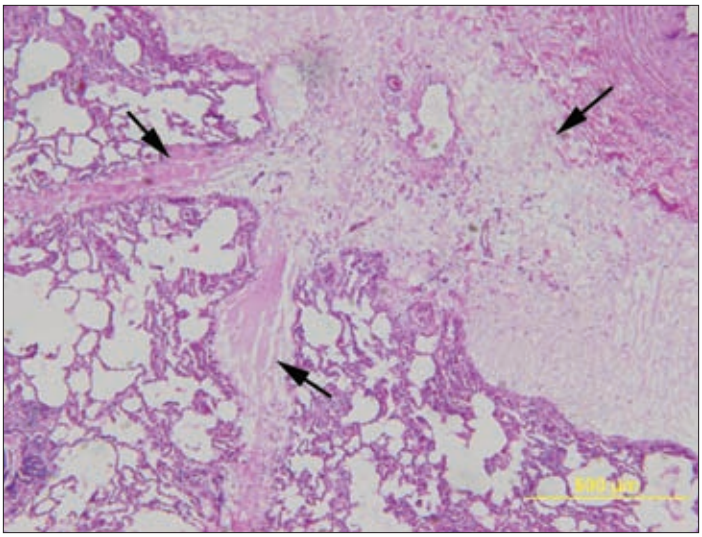

Figure 3. Photomicrograph of an equine lung showing expansion of the interlobular septa and perivascular adventitia due to edema (*arrows;* hematoxylin–eosin; original magnification ×40).

an alveolar exudate composed of proteinaceous fluid, fibrin, and mixed inflammatory cells (macrophages and lymphocytes). In addition, there is interstitial, subpleural, and perivascular edema (**FIGURE 3**). Histopathologic changes within the heart include epicardial and endocardial hemorrhage, multifocal myocardial necrosis (secondary to hypoxic injury), and hemorrhage surrounding the aorta and pulmonary vessels. The lymph nodes and gastrointestinal tract are often edematous.

Virology

Quick and accurate diagnosis of AHSV infection is imperative for preventing the spread of disease. Viral antigen or nucleic acid can be identified in whole blood or tissue samples using ELISA or reverse transcription polymerase chain reaction testing, respectively.[2,16] Virus can be isolated from the spleen, lungs, or lymph nodes using cell culture media. After isolation, serotyping of AHSV is determined by virus neutralization.[2] Virus isolation is performed at Plum Island Animal Disease Center in Orient Point, New York.

Treatment Recommendations

No specific antiviral treatment is available for AHS. Supportive care, including stall rest and diuresis to control pulmonary edema, may improve the outcome in some cases; however, treatment does not usually alter the clinical progression of any form of AHS.[12,15,18]

Prognosis

The morbidity and mortality associated with AHS vary by species and the immune status of the infected animal.[11,15] Horses are the most susceptible species, with mortality rates ranging from 50% to 95%, depending on the clinical form of disease. In horses, the pulmonary form is invariably fatal, the mixed form is associated with a mortality rate of >80%, the cardiac form is associated with a mortality rate of 50% to 70%, and horse sickness fever rarely results in death. In other equid species (donkeys and mules), mortality rates are generally lower. In mules, the mortality rate is approximately 50%. In European and Asian donkeys, the mortality rate is 5% to 10%.[15] African donkeys and zebras rarely die of this disease.

Prevention and Control

In areas where AHS is nonenzootic, such as the United States, the goals are to prevent the introduction of AHS and to eradicate it if it becomes introduced. Current US import restrictions require a 60-day quarantine of horses imported from a country affected by AHS.[15] Importation of infected insects could also result in an outbreak of AHS.

During an outbreak of AHS, the primary control strategy should involve quarantine and animal transport restrictions, vector control, alterations in animal husbandry, slaughter of viremic animals, and vaccination.[11,15,19] Quarantine and animal transport restrictions can prevent infected animals from being moved to unaffected regions, helping to prevent the initiation of new foci of disease outbreaks. If possible, animals should be kept in insect-proof stables. At a minimum, animals should be permitted outdoors only when insects are less active during the daytime. *C. imicola*, the principal vector of AHSV, is most active in the evening; therefore, keeping susceptible animals indoors at this time can lower the incidence of insect bites.[20]

Vector control can be implemented by destroying breeding sites, administering adulticides such as ivermectin, and applying repellents to susceptible animals. Diethyltoluamide (DEET) is reported to be effective against *C. imicola*.[11,19]

Vaccination against AHSV has been used in multiple outbreaks of AHS.[8] Currently, only attenuated live vaccines (monovalent and polyvalent) are manufactured. An inactivated, monovalent, serotype-4 vaccine was commercially produced but is no longer available.[8] There are a number of concerns regarding the use of these vaccines in epidemic situations. Concerns range from teratogenic effects in pregnant mares to reverting of the attenuated stain to a virulent form.[11]

Conclusion

AHS is considered one of the most lethal diseases of horses. Although AHS is exotic to the United States, it is imperative that equine practitioners be aware of this disease and its potential effect on the equine industry. Appropriate state or federal authorities should be contacted if the presence of AHS is suspected. If AHS were introduced into the United States, an epidemic would be likely, and early, accurate diagnosis and notification would be important for limiting the spread of disease.

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