Journal of Veterinary Science & Animal Husbandry

Open Access

Austin Publishing Group

Review Article

Review on African Horse Sickness

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Received: March 25, 2023
Accepted: May 06, 2023
Published: May 13, 2023

Summary

African Horse Sickness (AHS) is a disease that commonly affects equines. The disease is known to be spread by insect vectors (insect-borne) caused by African Horse Sickness Virus (AHSV) in the family *Reoviridae* genus *Orbivirus.* The genome of an AHSV comprises 10 segments of linear dsRNA, encoding seven structural (four major and three minor) and five non-structural proteins. The most common hosts of the diseases are horses, mules, donkeys, and zebras where zebras are natural reservoir host and play vital role in the persistence of the virus. There are four known clinical forms of African horse sickness: pulmonary, cardiac, mixed, and horse sickness fever (mild) forms. The clinical signs and lesions aligned with previous epidemiological information might be enough for clinical diagnoses of African horse sickness virus. But, the clinical signs and lesions showed for AHS can be confused with other disease, Equine Encephalosis Virus (EEV) as both viruses are similar, have a similar geographical distribution, host range and the same vector species. Thus diagnosis of AHSV can be confirmed from whole blood collected in anticoagulant in the febrile stage of infection and other tissues using RT-PCR, cell culture and sandwich ELISA. There is no an exact and specific treatment for animals suffering from AHS. Secondary infections must be treated during the recovery period with antibiotic. The disease is non-contagious and can only be spread through the bites of infected vector species of Culicoides. Control may therefore be effective by: animal movement restrictions, Slaughter of viraemic animals, Husbandry modification, Vector control and Vaccination.

Keywords: African Horse Sickness (AHS); African Horse Sickness Virus (AHSV); Equines

Introduction

African Horse Sickness (AHS) is a disease that commonly affects equines which is highly infectious, not directly contagious and known to be spread by insect vectors (insect-borne) caused by African Horse Sickness Virus (AHSV) in the family *Reoviridae* genus *Orbivirus* [1]. The virus is non-enveloped, segmented and a double-stranded RNA virus that has nine serotypes [2]. Because of its severity and fast global spread, the disease is registered by the World Organization for Animal Health [1].

The virus' virion is structurally complex and highly organized [3]. The genome of an AHSV comprises 10 segments of linear dsRNA, encoding seven structural (four major and three minor) and five non-structural proteins [4]. The complete virion particles have consecutive layers of proteins structured into two capsids. The first one is an outer capsid that has two proteins (VP2 and VP5) and the second is an inner capsid or ''core" that is composed of two major proteins, VP7 and VP3, as well as the transcription complex of three proteins, VP1, VP4 and VP6. [5]. The two of the major structural proteins, VP5 and VP2, make up the outer capsid layer, while the other two major structural proteins VP3 and VP7, and the three minor structural proteins, VP1, VP4 and VP6, and make up the AHSV core particle [5].

There are four known clinical forms of African horse sickness: pulmonary, cardiac, mixed, and horse sickness fever (mild) forms [6]. Horses are the most susceptible host with close to 90% followed by mules (50%) and donkeys (10%). African horse sickness is first occurred in 1327 in the Yemen [7]. The most common hosts of the disease are horses, mules, donkeys, and zebras where zebras are natural reservoir host and play vital role in the persistence of the virus [8].

The pathogenesis of the virus start at an entry and After entry, the first multiplication of the virus take place in the regional lymph nodes followed by dissemination through the body via the blood (primary viraemia) and succeeding infection of the

Citation: Emiyu K. Review on African Horse Sickness. Austin J Vet Sci & Anim Husb. 2023; 10(3): 1123.

target organs and cells, specifically the lungs, spleen and other lymphoid tissues, and certain endothelial cells [5]. This was causes fever, subcutaneous oedema, mainly on the head, neck, chest and supraorbital fossae, congested conjunctivae, petechial hemorrhages might be seen in the eyes that is finally results death [5].

Nowadays AHSV is endemic in tropical and sub-tropical areas of Africa, south of the Sahara, from Senegal in the west to Ethiopia plus Somalia in the east and spreading as far south as northern South Africa [9]. The virus may also be endemic outside Africa, in Yemen in the Arabian Peninsula and generally aligned with the epidemiology of insect vectors [9].

Clinical signs and lesions in suggestion with previous epidemiological information might be sufficient for clinical diagnoses of African horse sickness virus [10]. However, the clinical signs and lesions indicated for AHS can be confused with other disease that is a closely related Orbivirus, Equine Encephalosis virus (EEV). For instance the diseases caused by these two viruses are similar and have a similar geographical distribution, host range and the same vector species of Culicoides epidemiologically [11]. This is due to the absence of pathognomic signs in AHSV [11]. As a result both can occur concurrently in the same locations and even in the same animal and therefore diagnosis of AHSV can be confirmed from whole blood collected in anticoagulant in the febrile stage of infection and other tissues using RT-PCR, cell culture and sandwich ELISA is vital [12].

There is no specific treatment for animals suffering AHS [13]. The Secondary infections and other complicating must be treated in the recovery period. Control might be therefore: Animal movement restrictions, Slaughter of viraemic animals, Husbandry modification, Vector control and Vaccination are crucial [13].

History

African horse sickness virus was first identified in South Africa. The outbreak of the disease occurred in the Cape region in 1719 which over 1,700 animals died. However, the virus was circulating in the wildlife population of the area before this [14]. The pathology was first described in Africa following the introduction of European horses during the exploration of central and eastern Africa [15].

Etiology

African horse sickness is caused by African Horse Sickness Virus (AHSV), a member of the genus Orbivirus in the family Reoviridae. The virus has nine serotypes and some serotypes are cross-protective (e.g., serotypes 6 and 9), while others are not [9].

Host range

The principal hosts for AHSV are: Horses, Donkeys, Mules and Zebras. The virus is also known to affect dogs. Among equids, the most serious infections occur in horses and mules, which are thought to be accidental hosts. Zebras, which are often asymptomatic and believed to be the natural reservoir hosts in most regions of Africa [16].

Pathogenesis

Once an animal is bitten by Culicoides midges, AHSV initially replicates in the regional lymph nodes and subsequently spreads via the bloodstream. This result in an intense viraemia, with virus particles tightly bound to erythrocytes [17]. In the blood, secondary replication takes place in endothelial and mononuclear cells and enters target organs (lung, heart, spleen and lymphoid tissue) [18]. The replication of the virus in the target organs results in a second viraemia phase, that damage to endothelial cells and macrophage activation, which is responsible for the release of inflammatory cytokines for instance interleukin-1 and tumour necrosis factor alpha [18].

The oedema and effusion are typical forms of AHS [18]. This is result of increased vascular permeability caused by direct viral injury to endothelial cells and indirect effects mediated by inflammatory cells [17]. The variable AHSV tropism for cardiac or pulmonary endothelial cells can account for the various clinical forms of the disease [17].

Clinical signs

Four different forms of African horse sickness exist: the peracute (pulmonary) form, the sub-acute edematous (cardiac) form, the acute (mixed) form, and horse sickness fever (mild) [19]. Sudden death can also happen without previous signs and symptomatic infections are seen most often in horses and mules, with the pulmonary and mixed forms usually predominating in susceptible populations of horses. The mildest form, horse sickness fever, tends to develop in resistant species for instance donkeys and zebras [19].

Pathology

Macro-Lesions

The most visible lesions in the pulmonary form are: interlobular oedema of the lungs and hydrothorax. The sub-pleural and interlobular tissues are infiltrated with a yellowish gelatinous exudate and the entire bronchial tree may be filled with surfactant, stabilized froth [20]. Ascites can occur in abdominal and thoracic cavities and the mucosa of the stomach may be hyperaemic and edematous [20].

The lesions are gelatinous exudate in the subcutaneous, subfascial, intramuscular tissues and lymph nodes. Hydropericardium is seen and hemorrhages are found on the epicardial and/or endocardia surfaces. Petechial hemorrhages and/or cyanosis may also occur on the serosa surfaces of the caecum and colon [20]. Ascites occur in the pulmonary however oedema of the lungs is either slight or absent. The lesions are common to both the pulmonary and cardiac forms in the mixed form of AHS.

Microlesions

The histo-pathological alterations are a result of increased permeability of the capillary walls and injury in circulation. The lungs reveal serous infiltration of the interlobular tissues with distension of the alveoli and capillary congestion [21]. The central veins of the liver are swollen and interstitial tissue holds erythrocytes and blood pigments. Cellular infiltration can be seen in the cortex of the kidneys. Congestion may be seen in the spleen, intestinal and gastric mucosae, as well as cloudy swelling in the myocardial and skeletal muscles [21].

Vectors, Transmission and Climate

Africa horse Sickness virus has been transmitted between its natural hosts by biting arthropods, species of *Culicoides*. The disease is able to replicate in a species of *Culicoides* subsequent to ingestion by a factor of up to 10,000-folds and that transmission was also possible after 7 to 10 days incubation at 26°C [18].

Culicoides Imicola: In Africa, the major vector of AHSV is *C. imicola* and it is an Afro-Asiatic species that is common all over Africa and south east of Asia. However, it is currently known to be widespread across Portugal, Spain, Italy, large areas of mainland Greece, many Mediterranean islands [18].

Estimate of AHS Risk by Showing the Distribution of the Major Vector: The presence populations of midge clearly confer a risk of AHS [18]. The Normalized Vegetation Index (NDVI) is the most important which affords a measure of photosynthetic activity. This is therefore allied with soil moisture, and Land Surface Temperature (LST). Normalized vegetation index is important because *C. imicola* breeds in damp or wet soil and potentially correlates with the presence of breeding sites. The predictive models of C. imicola abundance and distribution were altitude, NDVI, middle infra-red reflectance, LST and air temperature [18].

Other Culicoides Vectors of AHSV: The distant past 1975 it was shown that C. sonorensis is the North American vector of BTV and an efficient vector of AHSV. This suggests that must viraemic equids gain entry to those parts of North America where C. sonorensis occurs and transmission of the virus would be possible. In the Old World, C. imicola has been considered to be the only field vector of AHSV [22]. But, now a second African species, C. bolitinos, is a potential field vector of this virus. During the 1987–1990 outbreaks of AHS in Spain and Portugal, C. imicola is expected major field vector of AHSV. However, amazingly isolations were also made from mixed pools of Culicoides comprising almost entirely of C. obsoletus and C. pulicaris but excluding C. imicola suggesting that one or both of these species might also be involved in the transmission AHSV in Europe. As a result, as BTV and AHSV use the same species of Culicoides as vectors it is possible that in areas where C. obsoletus and C. pulicaris are abundant future invasions of the equid virus could also extend well beyond the distribution of C. imicola [22].

Moreover, replication of AHSV does not appear to occur below 15°C and the temperatures below this level the apparent infection rate rapidly falls to zero9 [10]. However, when midges are sustained for extended periods at these cooler temperatures and latent virus that has apparently persisted at very low levels in some individuals begins replication and rapidly reaches sufficiently high titers for transmission to occur [10].

Temperature and AHSV Infection of Vector Culicoides: Temperature is the most important factor for AHSV infection rates of vector Culicoides and rates of virogenesis. As temperature rises infection rates also tend to increase, virogenesis is faster and transmission can occur sooner [10]. However, midge survival rates decrease contrariwise; as temperature is reduced the reverse is true for each of these variables. The probability of transmission is therefore a function of the interaction of these two opposing sets of trends [10].

Diagnosis

The Clinical signs and lesions aligned with previous epidemiological information might be enough for clinical diagnoses. However most of the clinical signs and macroscopic lesions are not pathognomic [11]. So this must be confirmed by isolation and identification of the virus from whole blood collected in anticoagulant (preferably EDTA) during the febrile stage of infection [11]. The whole blood should be washed and lysed immediately after collection to remove the anticoagulant and any antibody that might be present in the serum component. Usually susceptible horses die following an acute infection. In this situation the virus must identify from tissues such as spleen, lung, lymph nodes and salivary glands from recently died equines. The diagnosis of AHS include: Virus isolation, Antigen identification, Antibody identification and real time RT-PCR [16].

Virus Isolation

The isolation of AHSV is the intracerebral inoculation of 2 to 4 day old suckling mice [16]. Once again the virus will adapt and grow in embryonated hens' eggs subsequent intravenous inoculation [16]. In addition AHSV can also be propagated in insect cell cultures like mosquito (Aedes albopictus) C6/36 cells and Culicoides (KC) cells. But, they do not show Cytopathic Effects (CPE). So such cell assay systems are commonly used only as a sensitive intermediary to amplify virus as an introduction to virus isolation in mammalian cells. In general numerous mammalian derived cell lines like Baby Hamster Kidney (BHK), African green monkey (Vero) and Monkey kidney (MS) cells are used for AHSV isolation and show CPE within seven days [11].

Antigen Identification

The sandwich ELISA and RT-PCR are extremely useful for the rapid identification of AHSV antigen from whole blood, tissues and virus cultures [23]. Furthermore, isolated viruses can be identified by complement fixation and direct and indirect fluorescence [24].

Antibody Identification

The specific antibody against AHSV can be detected using diagnostic assays that are directed toward the VP7, An indirect ELISA based on the detection of antibody against segment 10 (NS3) has also been designated for AHSV serotype and can be used to distinguish between naturally infected animals and those vaccinated with purified, inactivated vaccine [24]. In endemic areas where multiple AHSV serotypes are probably to be present, it is critical that paired sera collected at a minimum of two week intervals be examined to confirm a diagnosis [25].

Differential Diagnosis

The differential diagnosis of AHS includes equine infectious anaemia, equine arteritis, infection with equine encephalosis virus (another orbivirus), equine pneumonia caused by Hendra virus infection, anaplasmosis, babesiosis or theileriosis, anthrax, and purpura hemorrhagic [26]. The clinical signs and lesions reported for AHS can be confused with those caused by a closely related Orbivirus, Equine Encephalosis Virus (EEV). Several features of the epidemiology of the diseases caused by these two viruses are similar. They have a similar geographical distribution, host range and vector species of Culicoides [27]. As a result both can occur concurrently in the same locations and in the same animal. Clinical symptoms, post-mortem examination,

epidemiological factors (seasonal abundance of competent vectors) and laboratory diagnosis all together will provide a rapid and efficient differential diagnosis for conformation of AHS [23].

Prevention and Control

There is no specific treatment for animals suffering from AHS (28). Complicating and secondary infections must be treated during the recovery period with antibiotic. The disease is non-contagious and can only be spread through the bites of infected

vector species of Culicoides. Control may therefore be effective by: animal movement restrictions, Slaughter of viraemic animals, Husbandry modification, Vector control and Vaccination [29].

Husbandry Modification

This method is planned to reduce vector access to susceptible animals as most vector species of Culicoides including C. imicola are exophilic [30]. So stabling susceptible equids during times of maximum vector activity (i.e. the crepuscular periods and during the night) will reduce biting rates and hence the chance of infection [30]. Furthermore, if obvious gateways of access to such housing such as windows and doors are screened with material of fine mesh (e.g. sand-fly netting) or with coarser material impregnated with insecticide (e.g. a synthetic pyrethroid) this will further reduce biting rates [27].

Vector Control

It is hardly probable to entirely eliminate populations of vector Culicoides [28]. The main objective is to reduce the number of potentially infecting bites of susceptible animals receive, to levels where maintenance of an epidemic becomes unsustainable and Vector control can be undertaken in a number of ways but it is important to remember that a combination of approaches is probable to yield the best results [27].

Changing Habitat: This control method is based on the abolishing the breeding sites of vector species of Culicoides as the vector commonly breeds in organically enriched moist but not waterlogged soils [30]. Such areas may be bare and/or covered with short grass and need to persist moist for enough time to complete the developmental part of the vector's life cycle. Thus, slow draining or clay soils are better for C. imicola than free draining; nutrient-poor, sandy soils [30].

Adulticiding: The targeted application of insecticides (e.g. the synthetic pyrethroids) in and around stables, and directly to equids can be effective against Culicoides species. Application of systemic drugs like Ivermectin may also be effective at killing biting Culicoides [31]. In addition an insecticidal food additives like tetrachlorvinphos, is the drugs which are eliminated in the faeces. So they deposit on breeding sites that are toxic to the immature stages of Culicoides [31].

Larviciding: A larvicide like 5% temephos granulated with gypsum reduces the population of vectors when applied on breeding sites because it riches in organic matter which makes them mainly suitable in Culicoides control [31].

Repellents: There are several applicant and well-known repellents that have been tested on Culicoides [32]. But, none are completely effective and the limiting effect [32]. The Di-Ethyl toluamide (DEET) is the only commercially available repellent that has been shown to have a significant deterrent effect against Culicoides for periods of up to four hours Since C. imicola attacks highest during the first four hours of the night. When applied nightly DEET may have a significant but temporary effect in reducing the biting rate of this species [32].

Vaccination

Attenuated Vaccines

Polyvalent, attenuated vaccines are commercially available and gave solid immunity but rarely resulted in serious side effects mostly after primary vaccination [4]. These problems were reduced by more attenuation of the vaccine virus strains through passage in cell culture. This cell culture adapted viruses till it forms the basis of the currently available OPB vaccine [4].

The OPB, AHS vaccines currently used in southern Africa and supplied in two polyvalent vials having AHSV types 1, 3 and 4, and 2, 6, 7 and 8, respectively. AHSV-5 is currently not included because of reports of severe reactions and deaths in some vaccinated animals. AHSV-9 is also not included because type 6 is strongly cross protective [4].

Inactivated Vaccines

Inactivated vaccines have the advantage that they do not contain a live and potentially dangerous agent. But, they may be expensive to produce as well as multiple inoculations may be essential to provoke and maintain high levels of protective immunity [4].

Conclusion

African horse sickness is one of the most lethal of equid diseases. The distribution of the disease is mainly aligned with the seasonal incidence of insect vectors and Climate-change. The interrelated BTV, which is transmitted by the same vector species of Culicoides has already now numerous of these locations and is causing unprecedented outbreaks of disease in ruminants. This powerfully suggests that at some stage in the future AHSV could do the same. Now, Culicoides vector control measures are poorly developed. The only vaccines available are live attenuated preparations that are not registered for use. So an urgent need to enhance our predictive ability, inactivated vaccines, improve vector control measures, develop efficient and inherently safe are the most powerful.

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