

African horse sickness: A practice update

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ABSTRACT

The aim was to a practice update include historical review, methods of diagnosis, prevention and control of infection by the African Horse Sickness virus. African horse sickness (AHS) is caused by a virus of the family Reoviridae of the genus Orbivirus. Usual hosts are equids: horses, mules, donkeys and zebra and the reservoir host are believed to be zebras and *Culicoides* spp. and unlikely to play a role in transmission. In the majority of cases, the subclinical cardiac form is suddenly followed by marked dyspnoea and other signs typical of the pulmonary form a Nervous form may occur, though it is rare. Diagnosis requires sampling and multidisciplinary auxiliary tools: clinical, serological, pathological (necropsy and sampling, histopathology, ultrastructural), molecular and viral isolation. Prevention measures include quarantine in the movement of equines including zebras, vector control, monitoring and vaccination in enzootic areas, confinement as a containment measure in case of outbreaks with vaccination programs. In conclusion greater control and monitoring of the international spread of equine diseases is an objective, considering the teamwork of horse industries and the equine health regulatory authority.

Keywords: AHSV, equine, reovirus, sickness, Orbivirus.

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INTRODUCTION

African horse sickness (AHS) is caused by a virus of the family Reoviridae of the genus Orbivirus (OIE, 2013). Usual hosts are equids: horses, mules, donkeys and zebra and the reservoir host are believed to be zebras and *Culicoides* spp. and unlikely to play a role in transmission (OIE, 2013). The virus is non-enveloped, approximately 90 nm in diameter and has an icosahedral capsid that is made up of three distinct concentric protein layers (the prototype orbivirus) (Mellor and Mertens, 2008). There are 9 antigenically distinct serotypes of AHS virus (AHSV) identified by virus neutralization, but some cross-reaction has been observed between 1 and 2, 3 and 7, 5 and 8, and 6 and 9, no cross-reactions with other known orbiviruses have been observed (OIE, 2013). The outer capsid layer surrounds the AHSV core particle (~70 nm diameter), which has a surface layer composed of 260 trimers of VP7 attached to the virus subcore. These VP7 trimers form a closed icosahedral lattice, which is made up of five- and six-membered rings that are visible by electron microscopy (Mellor and Mertens, 2008). The five viral proteins present in the AHSV core particle and two of the nonstructural proteins

(NS1 and NS2) that are also synthesized within the cytoplasm of infected cells are relatively more conserved than the outer capsid proteins. NS1 forms long tubules within the infected cell cytoplasm that are characteristic of orbivirus infections. NS2 is a major component of the granular matrices (viral inclusion bodies or VIBs) that represent the major site of viral RNA synthesis and particle assembly during the replication of AHSV and other orbiviruses (Mellor and Mertens, 2008). It is listed as a notifiable viral disease by the World Organization for Animal Health (OIE) because of its severity and the potential risk it poses for rapid global spread⁵. African horse sickness virus (AHSV) is a lethal arbovirus of equids that is transmitted between hosts primarily by biting midges of the genus *Culicoides* (Diptera: Ceratopogonidae) (Carpenter et al., 2017).

HISTORICAL REVIEW

In a historical review, for several centuries, the devastating African horse sickness (AHS) has been a

cruel scourge to horse owners in sub-Saharan Africa (Dennis et al., 2019). Outbreaks in central and east Africa have occasionally extended to Egypt, the Middle East, and southern Arabia. In 1959 to 1961, a major epidemic, caused by AHSV serotype 9, extended from Africa through the Near East and Arabia as far as Pakistan and India, causing the deaths of an estimated 300,000 equids (Mellor and Boorman, 1995). A further epidemic of the same serotype in 1965–1966 centered on northwest Africa (Morocco, Algeria, and Tunisia) but also extended briefly into southern Spain (Mellor and Boorman, 1995). This outbreak in Spain was eliminated by a vigorous vaccination and slaughter campaign. In July 1987, AHS caused by AHSV serotype 4 was reported in central Spain, due to the importation of infected zebra from Namibia (Overview of African Horse Sickness, nd). The outbreaks of African horse sickness (AHS) in Spain, Portugal and Morocco, which persisted for at least 5 years (1987-1991) therefore, seem to have established a new pattern in AHSV survival in an epidemic zone (Mellor and Boorman, 1995). The recent AHS epizootics in Iberia and North Africa seem to have established a new pattern in AHS virus persistence (Mellor, 1994). African horse sickness virus (AHSV) repeatedly caused large epizootics in the Mediterranean region (North Africa and southern Europe in particular) as a result of trade in infected equids (Zientara et al., 2015). Since 2010 the Countries that have reported the disease to the World Organization for animal Health (OIE) were Botswana (last notification in 2010), Eritrea (last notification in 2010), Ghana (last notification in 2010), Lesotho (last notification in 2011), Namibia (last notification in 2011), Somalia (last notification in 2011), Swaziland (last notification in 2011), South Africa (last notification in 2011) and Ethiopia (last notification in 2012, the endemic disease has been declared) (ASH, nd2). OIE list of African Horse Sickness free Members, according to Resolution No. 12 (Adapted Procedure, May 2020): Algeria, Andorra, Argentina, Australia, Austria, Azerbaijan, Belgium, Bolivia, Bosnia and Herzegovina, Brazil, Bulgaria, Canada, Chile, China (Peop. Rep. of), Chinese Taipei, Colombia, Croatia, Cyprus, Czech Rep., Denmark, Ecuador, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, India, Ireland, Italy, Japan, Kazakhstan, Korea (Rep. of), Kuwait, Latvia, Liechtenstein, Lithuania, Luxembourg, Malaysia, Malta, Mexico, Morocco, New Caledonia, New Zealand, North Macedonia, Norway, Oman, Paraguay, Peru, Philippines, Poland, Portugal, Qatar, Romania, Singapore, Slovakia, Spain, Sweden, Switzerland, The Netherlands, Tunisia, Turkey, United Arab Emirates, United Kingdom, United States of America, Uruguay (OIE, 2013). An outbreak of AHS in a disease free region would have catastrophic effects on equine welfare and industry, particularly for international events such as the Olympic Games (Robin et al., 2016). In Portugal in 1999 the cost of eradication was US\$1,955,513 (US\$11±5) Portuguese equine)

(Portas et al., 1999). The recently suspension of AHS free status are Myanmar and Thailand. As African horse sickness (AHS) continues to spread across Thailand, more than 500 horses are now reported dead, up 38 since last week (Lesté-Lasserre, 2020b). It is the first major outbreak of the disease outside Africa in 30 years, and AHS experts are worried that it could spread to neighboring countries in Southeast Asia (Lesté-Lasserre, 2020a). Following an immediate notification received from the OIE Delegate of Thailand on an outbreak of AHS in Pak Chong, Nakhon Ratchasima district, the "AHS free country" status of Thailand, as recognised by the OIE World Assembly of Delegates in terms of Resolution No. 19 in May 2014, is suspended with effect from 27 March 2020 (OIE, 2013). Based on the assessment of Myanmar's dossier to monitor compliance with the OIE *Terrestrial Code* provisions for the maintenance of its AHS free country status, as recognised by the OIE World Assembly of Delegates in terms of Resolution No. 27 in May 2018, this status is suspended with effect from 16 November 2018 (OIE, 2013). This extended persistence may be due to the 'all-year-round' presence in the area of adult *Culicoides imicola*, the major AHSV vector (Mellor and Boorman, 1995). This is probably due to a number of factors including the absence of a long term vertebrate reservoir, the prevalence and seasonal incidence of the vectors and the efficiency of control measures (Mellor, 1994). It has been suggested that recent changes in the global distribution of several vector borne viral diseases may be associated with climate change and the increasing international movement of animals and animal products (Robin et al., 2016). The unexpected emergence of a closely related virus, the bluetongue virus, in northern Europe in 2006 has raised fears about AHSV introduction into Europe, and more specifically into AHSV-free regions that have reported the presence of AHSV vectors, e.g. *Culicoides* midges, North African and European countries should be prepared to face AHSV incursions in the future, especially since two AHSV serotypes (serotypes 2 and 7) have recently spread northwards to western (e.g. Senegal, Nigeria, Gambia) and eastern Africa (Ethiopia), where historically only serotype 9 had been isolated (Zientara et al., 2015). There is mounting evidence that climate-related phenomena, such as El Niño-southern oscillation and global warming, can have an influence on the occurrence and distribution of certain diseases, especially vector-borne diseases such as AHS, study of the climatic patterns for the western region of South Africa, where most epidemics of AHS have occurred, has shown that all but 1 of the 14 epidemics of the disease recorded since 1803 have been in El Niño years (Timoney, 2014). The higher-than-normal temperatures customary of the drought period lead to significant increases in the vector population and favor the transmission of AHS, although not yet conclusively proved, climate phenomena can and will have an

influence on the global distribution and incidence of various vector-borne diseases of equids and other species (Timoney, 2014). Climate change and globalisation have resulted in a myriad of factors that increase the risk of AHS to many parts of the world (Robin et al., 2016).

DIAGNOSIS

Clinical diagnosis: In the majority of cases, the Subclinical cardiac form is suddenly followed by marked dyspnoea and other signs typical of the Pulmonary form a Nervous form may occur, though it is rare (OIE, 2013). Morbidity and mortality vary with the species of animal, previous immunity and the form of the disease of horses are particularly susceptible where mixed and pulmonary forms tend to predominate; mortality rate is usually 50 to 95% of Mules: mortality is about 50%; European and Asian donkeys: mortality is 5 to 10%; African donkeys and zebra: mortality is rare, animals that recover from AHS develop good immunity to the infecting serotype and partial immunity to other serotypes Subclinical form (Horse sickness fever), fever (40 to 40.5°C/104°F to 105°F) (OIE, 2013). *Mild form:* general malaise for 1–2 days, very rarely results in death. *Subacute or cardiac form* Fever (39 to 41°C/102 to 106°F) (OIE, 2013). Swelling of the supraorbital fossa, eyelids, facial tissues, neck, thorax, brisket and shoulders, mortality usually 50% or higher; death usually within 1 week. *Acute respiratory or pulmonary form* fever (40–41°C/104–106°F), dyspnoea, spasmodic coughing, dilated nostrils with frothy fluid oozing out, redness of conjunctivae, nearly always fatal; death from anoxia within 1 week. *Mixed form* (cardiac and pulmonary) Occurs frequently pulmonary signs of a mild nature that do. Incubation period is usually 7 to 14 days, but may be as short as 2 days (OIE, 2013).

Equine Necropsy is an important diagnostic tool for sampling and diagnosis in general at necropsy, pulmonary and subcutaneous oedema, haemorrhages and enlargement of lymph nodes were observed (Scacchia et al., 2015). Key samples to take are: lung, spleen, heart, muscle and lymph nodes and routine samples: brain, liver, kidney, stomach segments, small and large intestine. Macroscopic lesions are characteristic: severe and diffuse pulmonary oedema, gelatinous exudate of the sub-pleural and interlobular connective, and abundant froth within the upper airways was observed; hydrothorax were the main lesions noted in peracute/acute AHS affected horses. Tracheal and sub-pleural haemorrhages were also commonly detected, along with ascites and hyperaemia of gastric mucosa (Scacchia et al., 2015). The sub-acute form was mainly characterized by prominent subcutaneous haemorrhagic-gelatinous oedema. Endocardial and/or epicardial haemorrhages were also founded along to petechiae on the serosal surface of the large intestine.

Typically, a distinct demarcation was noted between affected and unaffected tracts of the intestine. Haemorrhagic gastritis was also commonly recorded. Lymph nodes – with the only exception of the mesenteric ones – appeared enlarged because of oedema and haemorrhages (Scacchia et al., 2015). The differences according to the presentation are: *Respiratory form:* interlobular oedema of the lungs o hydropericardium, pleural effusion o oedema of thoracic lymph nodes o petechial haemorrhages in pericardium o mucosa and serosa of small and large intestines may exhibit hyperaemia and petechial haemorrhages *Cardiac form:* subcutaneous and intramuscular gelatinous oedema o epicardial and endocardia (OIE, 2013). Histopathology is a complementary diagnostic tool. Viral replication was detected in endothelial cells, PIMs, interstitial macrophages and fibroblasts. Alveolar and interstitial oedema and changes in pulmonary microvasculature, consisting mainly of the sequestration of neutrophils and the formation of platelet aggregates and fibrinous microthrombi, were related to endothelial changes and to a high degree of Pulmonary Intravascular Macrophagus activation (Carrasco et al., 1999). Ultrastructural changes in endothelial cells of capillaries in the myocardium, lung, spleen and liver, alterations detected in the endothelial cells of the vessels of infected animals included: the presence of structures associated with viral infection, hypertrophy, degenerative changes, appearance of cytoplasmic projections, changes in permeability, alteration of intercellular junctions, loss of endothelium, subendothelial deposition of cell debris and fibrin, and vascular repair, in association with these changes, oedema, haemorrhages and microthromboses were detected, particularly in the myocardium and lung (Gomez-Villamandos et al., 1999). *Virus isolation:* Unclotted whole blood collected in an appropriate anticoagulant at the early febrile stage and sent at 4°C/39°F to the laboratory spleen, lung and lymph node samples collected from freshly dead animals are placed in appropriate transport media and sent at 4°C/39°F to the laboratory; do not freeze serology preferably paired serum samples should be taken 21-days apart and kept frozen at -20°C/-4°F (OIE, 2013). *Virus isolation:* cell cultures, such as baby hamster kidney-21 (BHK-21), monkey stable (MS) or African green monkey kidney (Vero) or insect cells (KC), intravenously in embryonated eggs intracerebrally in newborn mice (OIE, 2013). *Virus identification* Enzyme-linked immunosorbent assay (ELISA)–rapid detection of AHSV antigen in blood, spleen and supernatant from cell culture (OIE, 2013). *Virus neutralization (VN)* – until recently the ‘gold standard’ for typing as well as identifying virus isolates, but takes 5 days RT-PCR is a highly sensitive technique that allows the detection of a very low number of copies of RNA molecules Real-time PCR – detects all 9 serotypes AHSV typing VN test has been the method of choice for typing as well as the ‘gold’ standard test for identifying AHSV’s isolated from the field using type

specific antiserum, development of a type-specific gel-based RT-PCR and real-time RT-PCR using hybridisation probes for identification and differentiation AHSV genotypes provides a rapid typing method for AHSV in tissue samples and blood (OIE, 2013). There is a good correlation between the results obtained with the type-specific RT-PCR and the VN test, however, the sensitivity of these assays is lower than that obtained with the diagnostic group-specific real-time RT-PCR typing of nine AHSV types has also been performed with probes developed from a set of cloned full length VP2 genes serological diagnosis horses that survive natural infection develop antibodies against the infecting serotype within 8 to 12 days post-infection (OIE, 2013). According to the Seg-10 phylogenetic analysis, AHSV strains are divided in 3 phylogenetic clades, which have been indicated as α , β and γ (Portas et al., 1999). Blocking ELISA (prescribed test in the OIE Terrestrial Manual) Indirect ELISA (prescribed test in the OIE Terrestrial Manual) Complement fixation (prescribed test in the OIE Terrestrial Manual) (OIE, 2013).

Diferencial diagnosis: Anthrax, Equine Infectious Anaemia, Equine viral arteritis, Trypanosomosis, Equine encephalosis, Piroplasmosis, Purpura haemorrhagica, Hendra virus (OIE, 2013).

PREVENTION AND CONTROL

African Horse Sickness in Portugal: a successful eradication programme include: 1) mass vaccination, stamping-out at infected farms and strict control of animal movement were the main methods employed in combatting the spread of AHSV and then achieving eradication in Portugal, 2) confining the AHS epizootic in Portugal to 13 weeks of a single season was a major success of planning and implementation for Emergency and Coordination Team, 3) the coordinated cooperative campaign, involving Government agencies, provincial officers and private practitioners serves as a valuable template for future operations which require a far reaching and rapid response to a potentially highly damaging epizootic (Portas et al., 1999). No efficient treatment available. The OIE recommends the following measures for prevention and control (OIE, 2013):

- Sanitary prophylaxis free areas, regions and countries, identify the virus and serotype.
- Establish strict quarantine zone and movement controls, consider euthanasia of infected and exposed equids.
- Stable all equids in insect-proof housing, at a minimum from dusk to dawn when Culicoides are most active, establish vector control measures: destroy Culicoides breeding areas; use insect repellents, insecticides, and/or larvicides Monitor for fever at least twice daily: place pyrexia equids in insect-free stables or euthanize.
- Consider vaccination o identify vaccinated animals o available vaccines are attenuated produce viraemia, and

may theoretically reassort with the outbreak virus may be teratogenic.

- Affected areas, regions and countries: annual vaccination and vector control. In Spain, we used two types of vaccines for the control and eradication of the diseases a polyvalent live attenuated vaccine and monovalent inactivated vaccines (Sanidad, Spain).

- Medical prophylaxis: At present only the live attenuated AHS vaccines (polyvalent or monovalent) are commercially available Vaccination of non-infected horses: o Polyvalent live attenuated vaccine – commercially available in certain countries o Monovalent live attenuated vaccine – after virus has been typed o Monovalent inactivated vaccine – no longer commercially available o Serotype specific subunit vaccine – currently in development. They have been widely used polyvalent and monovalent vaccines with live attenuated virus. Multipurpose vaccines they are made up of a trivalent (serotypes 1, 3 and 4) and another quadrivalent (serotypes 2, 6, 7 and 8), serotypes 5 and 9 are not included because there is cross protection with the serotypes 8 and 6 respectively. In addition a monovalent vaccine has been developed inactivated (serotype 4) and a vaccine that uses VP2 proteins as immunogen, VP5 and VP7 expressed in the baculovirus system, although the latter has not yet been used in extensive field studies (ASH, nd2).

- Most of the African Horse Sickness outbreaks have been associated with the mobilization and transport of zebras without sanitary controls (includes a strict 40-day quarantine) and control of vectors such as Culicoides.

- In stables or farms the best way to protect animals from African horse sickness is to decrease their exposure to biting midges and other insects (e.g., mosquitoes and biting flies), stabling horses in insect-proof housing, particularly between dusk and dawn when the insects are most active, can help prevent exposure. Insect repellents and insecticides may also be useful. Establish sanitary measures and quarantine for new horses entering the stable and monitor horse's temperature can useful daily.

The 'high-health, high-performance' (HHP) horse concept has been developed by the World Organisation for Animal Health (OIE) together with the Federation Equestre International and the International Federation of Horseracing Authorities (Dominguez et al., 2015).

CONCLUSION

Greater control and monitoring of the international spread of equine diseases is an objective, considering the teamwork of horse industries and the equine health regulatory authority.

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