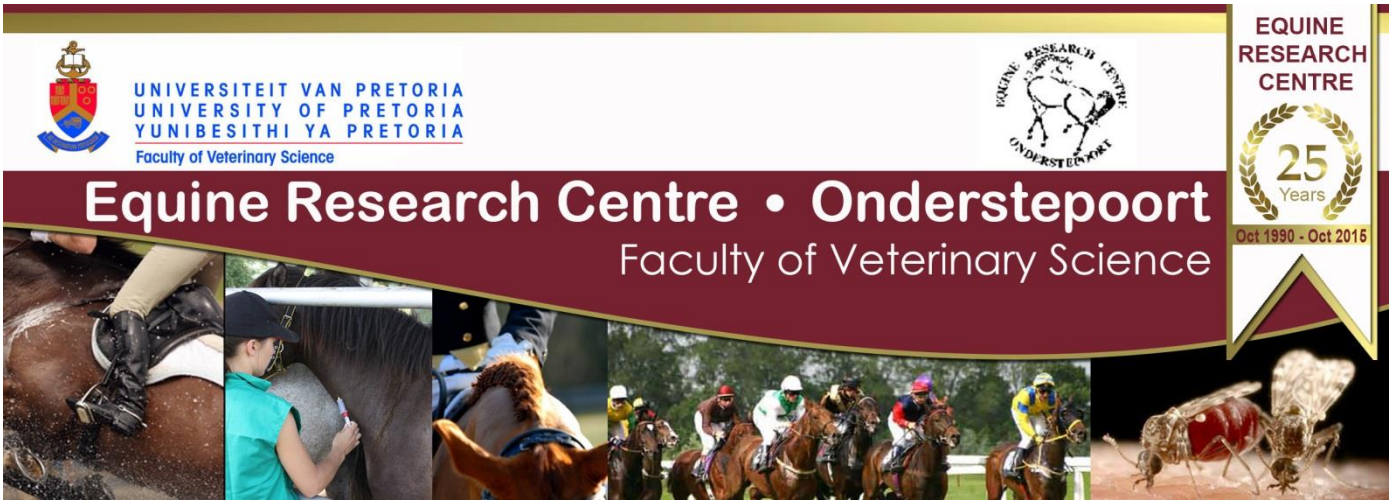

EQUINE RESEARCH … what you need to know

Brought to you by the Equine Research Centre, University of Pretoria

Still wondering why the AHS Vaccination Period has been restricted to 1 June to 31 October in the AHS Controlled Area, and why this period is highly recommended for the rest of the country? This scientific paper will tell you why.

AFRICAN HORSE SICKNESS CAUSED BY GENOME REASSORTMENT AND REVERSION TO VIRULENCE OF LIVE, ATTENUATED VACCINE VIRUSES, SOUTH AFRICA, 2004-2014

African horse sickness (AHS) is a haemorrhagic viral fever of horses. It is a severe, often fatal disease of equids that is caused by AHS virus (AHSV), and is transmitted to horses by biting midges (Culicoides). It is the only equine disease for which the World Organisation for Animal Health (OIE) observes official recognition status, such that OIE member countries are required to have legally enforceable AHS control measures in place and are required to immediately notify OIE of any change to their country's AHS status.

The Western Cape Province of South Africa has historically been free from AHS, and for this reason a legislatively defined AHS controlled area (CA) was created in 1997 to facilitate export of horses from South Africa. Within this area is an AHS free zone, surrounded by an AHS surveillance zone, which in turn is surrounded by an AHS protection zone. Movement of equids into and between these zones is strictly controlled. Vaccination with the polyvalent (many types included) AHSV live, attenuated vaccine (LAV), the only registered vaccine in South Africa, in the surveillance zone and free zone is prohibited, and may only be done with written permission from the state veterinary services. Since March 2015 vaccination in the AHS CA is only allowed during the period of low vector activity (1 June to 31 October).

One of the concerns related to live virus vaccines is the possibility of reversion to virulence by mutation. Furthermore, it is believed that polyvalent virus vaccines present a greater potential for reassortment due to the co-administration of different strains which are then co-multiplying in the host and creating a pool of genomic segments with the potential to reassort with one another to create new genetic combinations with different pathogenicity, transmissibility or how the host organisms deal with the virus.

Since the creation of the AHS CA in 1997, a total of six outbreaks of AHS have been reported to OIE in this area, in 1999, 2004, 2006, 2011, 2013 and 2014, and now more recently in 2016. Before the 2014 outbreak, these outbreaks were assumed to be caused by illegal movement of infected animals into the CA, although the source was established for only two of these outbreaks: a type 7 virus for the 1999 outbreak in the surveillance zone and a type 5 virus for the 2006 outbreak in the protection zone. Because the source of the viruses responsible for the other outbreaks was never established, the goal of this study was to further investigate the AHSV type 1 (AHSV-1) outbreaks in the controlled area by:

- Whole-genome sequencing of viruses from individual outbreaks (2004, 2011 and 2014);
- Comparison of these sequences with those of the polyvalent AHSV-LAV and AHSV reference strains;
- correlation of epidemiologic and clinical findings with molecular findings; and
- confirmation of the source of the virus strains responsible for the 2004, 2011 and 2014 outbreaks of AHS in the controlled area.

Results and Discussion

Whole-genome sequences were compared from 55 field, LAV, and laboratory strains of AHSV. The field viruses were obtained from horses during outbreaks of AHS of varying clinical severity (case fatality rates [CFRs] ranging from 4.5% to 78.3%) in the AHS Controlled Area of South Africa during 2004, 2011 and 2014. Phylogenetic analyses confirmed that genetically distinct viruses were responsible for each outbreak and that these were closely related to viruses contained in the trivalent AHSV-LAV (combination 1) used in South Africa. There were other findings linking the viruses to the trivalent vaccine preparation.

The results of our study further confirm that changes in multiple viral proteins can affect the virulence of AHSV, in that reversion (to the virulent parental type) and novel changes were present in field-isolated viruses at multiple sites that differentiates the attenuated AHSV-1-LAV strain from its virulent parent strain. Given the genetic diversity of field strains of AHSV, our analyses overwhelmingly support the premise the potential reversion-to-virulence mutants and reassortants detected arose from viruses within the polyvalent AHSV-LAV formulation, and predominantly from AHSV-1-LAV. Although these mutants and reassortants most likely arose within vaccinated horses, the reason for the predominance of AHSV-1-LAV components in the emergent outbreak viruses is unknown.

Although the CFRs in 2004 Stellenbosch and 2011 Mamre outbreaks were very high (78.3% and 76.2% respectively), the CFR for the 2014 outbreak in Porterville (14.6%) and Robertson (4.5%) was considerably lower. The 2011 Mamre and 2004 Stellenbosch outbreaks were associated with the lowest vaccination rates among AHSV-infected horses. It is unclear if the differences in the CFRs are a consequence of lower virulence among the outbreak viruses or the result of existing vaccine-induced immunity in the exposed horses. What should also be noted is that changes in case definition only came into effect in 2008 (after the 2004 Stellenbosch outbreak) and probably resulted in an underestimation of subclinical AHSV infections during that outbreak. While only clinically affected, deceased horses were classified as having confirmed cases in the 2004 Stellenbosch outbreak, major advances in AHS diagnostic testing (e.g. rRT-PCR-based methods) have occurred during the past 10 years that likely substantially increased the detection of subclinical infections by the time of the 2014 outbreaks, which likely account for the lower CFR percentage.

The results of this study highlights the importance of genetic characterisation of circulating strains of AHS epidemiologic investigations of AHS outbreaks. Although the prevailing opinion is that illegal movement of viraemic equids into the AHS Controlled Area is the highest risk for the repeated occurrences of AHS in the controlled area, this is clearly not the only cause, or even the most likely source of AHSV to cause and outbreak in the controlled area. Data from this study confirms that use of polyvalent AHSV-LAV can result in emergence and spread of virulent viruses to adjacent susceptible horses, presumably by Culicoides midge vectors that are already resident within the AHS Controlled Area. Collectively, these findings have major implications for strategies to control AHS, both in AHS-endemic regions and during future incursions into currently AHS free areas.

It should be noted, however, that AHSV-LAV confers critical and effective protection for susceptible horses in AHS-endemic areas and, although potentially safer recombinant AHSV vaccines have proven effective in laboratory studies, these are not yet available commercially and they are yet to be evaluated in the field. Until alternative vaccines are commercially available, control of AHS in endemic area therefore remains reliant on the use of AHSV-LAV coupled with the adoption of strategies to minimise the likelihood of AHSV-LAV transmission by the Culicoides vector.

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