



Equine Research Centre • Onderstepoort

Faculty of Veterinary Science

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EQUINE RESEARCH ... what you need to know

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

OUT WITH AFRICAN HORSE SICKNESS SEASON, IN WITH HERPES SEASON

As the foaling season approaches, breeders will be anxiously hoping for few or no equine herpes virus (EHV) related abortions. As with humans, most horses are latent carriers of EHV, which can then manifest itself when the carrier is under stress. As Prof James Gilkerson says, "You got horses, you got herpes".

EHV is the number one threat to any horse breeding operation and has put more commercial horse breeding organisations out of business worldwide than any other disease.

The disease may manifest itself in respiratory disease (EHV-4), or, more worryingly, with EHV-1, respiratory disease, nervous symptoms and abortion. Management of this disease is critical to prevent it spreading. For instance, if a mare aborts, and other mares in the group have access to the aborted foetus material, the disease will spread to these mares. Rule of thumb is that you must treat each abortion as though it is herpes unless proven otherwise and separate the mares immediately. It is also very important to note that pregnant mares that may have been exposed to the virus must not be moved to where they could spread the disease to other breeding mares.



While vaccinations do not guarantee that EHV will not result in abortions, it does reduce impact, and it makes sense for commercial breeders to vaccinate their breeding mares.

The Equine Research Centre (ERC) has, over a number of years, developed standard operating procedures for breeders to deal with these situations. For more information please feel free to contact Prof Alan Guthrie (Alan.Guthrie@up.ac.za) or Prof Martin Schulman (Martin.Schulman@up.ac.za). In the event of an abortion, the first person you should call is your local veterinarian to make arrangements for samples to be submitted for testing.

At the end of this newsletter are summaries of two interesting research publications on the subject of EHV.



THE EQUINE HEALTH FUND TAKES OVER THE REINS FROM RACING SOUTH AFRICA

South Africa has come out of the period of isolation post-apartheid to participate in the globalization of trade, and using the innovative approach inherent in our cultural diversity has rapidly begun participating in more high-technology, biotech development industries to address public and veterinary health challenges facing Africa as a region.

The Equine Sports of racing, endurance, and other equestrian sports have demonstrated exceptional competitiveness internationally. However, in recent years these sports industries have reduced in size due to economic conditions, difficulty accessing global markets, and in part due to infectious diseases hampering conditions for export and trade. The infectious diseases of African Horse Sickness, Herpes, Influenza have also been recognized as a major threat to the economic viability of the industry, as major outbreaks have the potential to cripple the industry with movement controls, cancelled events and export bans.

The Horse Racing Industry has for the past 17 years used funding options available to support the activities of the Equine Research Centre, Faculty of Veterinary Science, University of Pretoria. With relatively modest investments key successes have been achieved. The major industry role players have in the last XX years contributed their funding through the Racing South Africa (Pty) Ltd Company, to support equine research and the export of horses. The key organizations which have traditionally supported the development include:

1. Thoroughbred Breeders Association
2. Phumelela (Pty) Ltd
3. Gold Circle
4. Racing Association
5. Thoroughbred Racing Trust

Key to the success of the private funding support for surveillance, research development and vaccine development is an understanding of the environment in which the funding is utilized. Key role players include (1) Department of Agriculture Forestry and Fisheries (2) University of Pretoria (3) Private sector biotechnology companies (4) Department of Science and Technology for funding opportunities (5) and Department of Trade and Industry.

From the 1 August, 2014 this mechanism of joint funding has come to an end, with agreement of the existing partners to continue the monitoring, evaluation, and research and development activities through the Wits Health Consortium (Pty) Ltd, Equine Health Fund.

The Equine Health Fund seeks to secure long-term funding commitments from industry role players and individual donors, not limited to the racing industry as has been the case up until now, to stabilize and grow the output and impact of the biomedical research initiatives. The vision of the Equine Health Fund is to set funding goals; independently evaluate the research strategy, projects and proposals presented by the researchers; AND implement the grants management of funding received from multiple sources to ensure compliance and performance



management of recipients. This approach places the funding agency into the driving seat, assisting to rationalize the proposals, adjudicate the methodological approach, and monitor performance of the grant recipients.

In the first 1-3 years the following key objectives have been set.

1. To address key infectious diseases with a major public health impact on the performance of horses, and growth of the industry.
2. To address key equine reproductive health questions which have an impact on the performance of the horse breeding industry.
3. To support the research in performance enhancing drugs, and exercise physiology.
4. To develop a framework of post-graduate training and research activity in horses to continue the capacity development of veterinary and laboratory personnel to secure the future of the industry.

Wits Health Consortium (Pty) Ltd is a wholly owned subsidiary of the University of Witwatersrand, established in 2001 to manage research funding in the Faculty of Health Sciences of the University. Prof Ian Sanne has initiated the EHF under Wits Health Consortium due to the deep experience of the organization in grants management for major international agencies such as National Institute for Health, USAID, EU, Bill and Melinda Gates Foundation.

SA'S EXPORT HOPES

Extracted from Sporting Post article

Following on from the recent Wits Health Consortium press release and report on the April Export Workshop, we caught up with Professor Ian Sanne to find out more about the recent changes on our AHS research and export status landscape. At the invitation of various role players Professor Sanne has taken on the role of coordinating the scientific response to African horse sickness and other diseases affecting horses.



Professor Sanne is probably best known in the racing community as the son of Oldlands Stud's Barbara Sanne. He also breeds Thoroughbreds in his own right and his wife is a competitive dressage rider. However, to the rest of the world he is a respected authority in his chosen field of medical research - HIV, TB and infectious diseases. Sanne is a trained specialist physician and infectious disease sub-specialist at the University of the Witwatersrand (Wits). He holds an MBBch (Wits), FCP SA (Wits), DTM&H (Wits), FRCP(Ion). In 2008, Ian was appointed an Associate Professor in the Faculty of Health Sciences of Wits University. He is the founder and director of the Clinical HIV Research Unit at Wits and he is also a founder and CEO of Right To Care, an internationally recognised and well supported NGO focused on HIV/AIDS and TB prevention and treatment in support of the Department of Health National Strategic Plan. He has an impressive body of research to his credit and critically is also well versed in regulatory work as well as the ins and outs of the registration of new drugs and vaccines.



Somewhat more pertinently for our readers, Professor Sanne has expanded his interests into the field of African horse sickness and as of 1 August 2014, has initiated the Equine Health Fund as a mechanism to access donor funding for research and surveillance of horse diseases including African horse sickness. What this means in practice, is that Sanne will take over the role of managing and distributing the funding for AHS and export research previously managed by Racing South Africa.

Professor Sanne told the *Sporting Post*, “When I came to the field of AHS, I felt that there was significant discord within the industry around the direction that should be taken. Much of the dissatisfaction that was voiced was related to the investment made to date, which stands at a little in excess of 20 million Rand in the Equine Research Centre (ERC). My response to that would be that if I tried to match the successes that the ERC has had in my own field of speciality, I’d have had to spend 20 million US dollars.”

“It is important to recognise that the ERC have in fact been successful in a number of core areas.

- They have set up a dedicated Pretoria University recognised research unit and maintained it for a number of years now. The unit trains a lot of competent post-graduate students interested in horse diseases who currently populate the University of Pretoria, Onderstepoort, and the private sector. This function in particular is key to maintaining a response to equine diseases in SA.
- The ERC has developed modern diagnostic tests using the PCR methodology. There are other registered testing methods, but the ability to make an accurate diagnosis of AHS based on Virus measured in blood is a huge step forward. The PCR test also allows for much faster diagnosis (4 hours) than the currently accepted method, which can take 3 to 4 weeks. It is the first step in moving on to serotype specific testing (so that we can identify which of the 9 serotypes we’re dealing with), and in collaboration with Wits and UP researchers, the ERC is moving on to being able to differentiate between a genuine infection and a vaccine virus (i.e. whether a horse is infected with AHS or simply showing a positive from being vaccinated). That in itself is a huge achievement.
- The ERC has been able to sustain – albeit inconsistently – census data for horses in the Western Cape and surveillance data for African horse sickness outbreaks. There was an unfortunate 1 year gap where the surveillance was not performed due to stop-start funding and even more unfortunately, that happened the year before the EU audit visit in 2013. Going forward, it is critical the surveillance in the WC is strengthened, both in terms of documenting the situation in the WC and the disease incidence throughout South Africa, as well as for our attempt to get back to having the WC as an AHS free area.
- The ERC has an AHS vaccine in development based on the ALVAC vaccine, the same vaccine construct successfully being used in HIV vaccine. This is still in early phase research and will require funding to get to future phase 3 trial. Interestingly, there are 2 other vaccines in developmental stages – one in the private sector in South Africa in a company Deltamune and another in the UK at The Pirbright Institute, which might offer viable alternatives.



“HIV has spent upwards of 400-500 million US dollars to achieve the results that the ERC has managed with 3 million Rand, so it is clear that the investments made to date have been extremely successful and it is my intention to lobby for an increase in investment in order to continue the ERC’s activities.”

Sanne proposes exploring additional funding options (such as the competitive riding community) as well as government funding and the fact that South Africa aims to bid for hosting the 2024 Olympic Games may prove pivotal.

Workshop

The April Export Workshop, hosted by Wits Health Consortium in collaboration with Racing South Africa was a productive one. It was staged as a collaborative effort with input from international experts in the fields of veterinary medicine and export, as well as a number of local authorities and interest groups. Perhaps most significantly, the Department of Agriculture, Forestry and Fisheries (DAFF) was also in attendance. Agreements with South Africa’s desired trading partners will need to be made at government to government level and therefore the support and involvement of DAFF is critical and enormously appreciated.

There is significant interest within the South African equine industries in re-instating trade directly to the EU and other AHS-Free countries - with manageable quarantine requirements - to allow SA horses to compete fairly on the world stage and eventually (if feasible) to allow SA to host major international equine competitions. A number of approaches were discussed and although there are significant hurdles to overcome, what has emerged is a clear strategy with the primary goal of re-instating the safe export of horses from South Africa to AHS Free countries.

The strategy aims to provide a staged plan for achieving these outcomes in an open and transparent manner and in a way that is sustainable and will suffer from minimal disruptions to trade in the future.

The strategy includes the following 6 options:-

- Export from low-risk Infected Zone (ie the existing Kenilworth quarantine facility)
- Export to/via Mauritius
- Export to/via USA
- Export from re-instated (Western Cape) Free Zone
- Export from additional/alternative Free Zone (Northern Cape is being considered)
- Export from current Infected Zone (Johannesburg)

There are a number of advantages and disadvantages to each. For the time being and until the current ban is lifted, our best viable export option is via Mauritius, so efforts will be made to optimise and protect this option. The route through Mauritius is however long, taking up to 6 months and Mauritius is not



recognised by the OIE as officially free of AHS. (The OIE have included AHS on the list of diseases for OIE official recognition of status. This means countries cannot declare freedom unless they have gone through the OIE process and a list of countries that have official free status is published by the OIE.) The Strategy Meeting recommended the use of the Western Cape route as a low-risk AHS zone to protect Mauritius from the risk of importing a horse infected with AHS.

Energy is also being focussed on optimising the Kenilworth quarantine station to convert it into a full lock down facility. The Strategy Meeting concluded that for South Africa to have consistent export of horses the approach in the Western Cape needs to be changed to one of "Low-risk Infected zone", with exportation from a lock-down quarantine facility. This will facilitate the export of horses from the Cape ahead of the lifting of the two-year ban period that accompanies any outbreak of the disease in the surveillance zone.

Additional research, surveillance and the hoped for additional scientific breakthroughs will support the export of horses throughout the year despite incidents of African horse sickness in the surveillance zone. The improved infrastructure at Kenilworth Quarantine Station, with full vector protection will facilitate trade negotiations with partner countries.

SOME OF THE ERC'S OUTPUTS

Following on what Prof Ian Sanne has to say about the achievements of the Equine Research Centre, headed by Prof Alan Guthrie, it is interesting to note that this Centre is highly respected worldwide.



Prof Jim MacLachlan is an academic veterinary pathologist who studies various aspects of viral diseases in livestock, with emphasis on pandemic, trans-boundary diseases such as bluetongue that adversely affect international trade and commerce. He has worked on various projects with Prof Guthrie and his team for the past 16 years. He speaks highly of the ERC team.

Prof MacLachlan says that very few research establishments are capable of achieving the multiple ambitious projects that ERC has so successfully mastered. In addition to the projects mentioned by Sanne in the Sporting Post article, other projects that ERC has accomplished are the development of successful programmes to :

1. Investigate the epidemiology of African horse sickness in South Africa, an activity that has become increasingly necessary and complex. The ERC programme is now the internationally respected laboratory that is monitoring the occurrence of this OIE reportable trans-boundary disease in South Africa. The ERC laboratory has a substantial archive of recent as well as historic field strains of the virus for genetic analyses. The ERC Team is also evaluating the immune response of horses to the virus and the data has been used to create a novel recombinant vaccine and new-generation



diagnostic technologies such as RT-qPCR. Ongoing molecular epidemiological investigations unquestionably will better characterize how African horse sickness is maintained and spread, and this type of information is absolutely prerequisite to any effort to challenge current regulatory barriers to the movement of horses into and from South Africa.

2. Confirm by genetic analysis the parentage of every Thoroughbred foal born in South Africa each year, an activity that also provides the capacity to serologically monitor the annual foal cohort for the occurrence of various diseases. Prof MacLachlan knows of no other program anywhere in the world that compares with the one created in South Africa – it is a priceless and unique resource, but one that requires an enormous ongoing logistical effort to sustain.
3. Better characterise the molecular epidemiology and improve methods for the diagnosis and control of diseases such as biliary (piroplasmiasis), which has resulted in a substantial improvement in the status of SA horses in relation to these regulatory diseases and the ERC's work is held in the highest esteem by the relevant researchers in the United States and is considered state of the art.
4. Undertake the most sophisticated and ambitious trial ever conducted anywhere in the world to evaluate the effect of prophylactic use of furosemide on exercise-induced pulmonary haemorrhage in racing horses. This is a highly contentious topic of great contemporary relevance to the horse industry in the United States (and elsewhere).
5. Undertake novel and highly relevant epidemiological studies of several infectious agents that are important to different components in the SA horse industry, including (but not limited to) West Nile virus and equine encephalosis. These investigations not only provide critical information to the entire South African horse industry, they also assure global trading partners that credible disease surveillance is being done in the country.
6. Work with the competent Veterinary Authority of SA to initiate successful efforts to eradicate introduced (i.e. exotic) reportable infectious diseases of horses. Especially notable in this regard were the efforts to contain and then eliminate equine influenza, equine viral arteritis, and contagious equine metritis. Prof MacLachlan re-emphasized that these remarkable accomplishments reflect very favourably on South Africa.

SUMMARISED PUBLICATIONS

Epidemiology and reproductive outcomes of EHV-1 abortions in unvaccinated Thoroughbred mares in South Africa

Equine herpesvirus 1 (EHV-1) is the most important viral cause of equine abortion, both because it is relatively common and because of its potential for *epizootic** spread, particularly within naïve populations.



Under natural conditions, EHV-1 abortion rarely occurs before 4 months of gestation: 95% of diagnosed EHV-1 abortions occur in the last third of pregnancy and 75-80% between 8 and 10 months of gestation. The reported incubation time varies between 9 and 121 days and abortion typically occurs without any warning signs. Previous reports have indicated that mares who have only foaled once, and Lipizzaner mares are at higher risk.

Following abortion, EHV-1 is cleared from the genital tract and future breeding capacity is not impaired unless the reproductive tract was damaged.

In this study, we retrospectively analysed the relationships between epidemiological factors and reproductive outcomes following EHV-1 abortion epizootics on 2 separate Thoroughbred farms in South Africa. The aim was to improve the understanding of infectious abortion epizootics in horses in order to enhance future prevention and management strategies.

The following table summarises the comparisons between the 2 epizootics.

FARM 1	FARM 2
Recorded abortions in the period 10 May to 22 September 2007.	Experienced abortion epizootic between 20 June and 24 July 2009
30 pregnant broodmares	316 pregnant broodmares
9 abortions (30%)	43 abortions (13.6%)
9 (100%) of abortions were EHV-1 related	18 (42%) of abortions were EHV-1 related.
1 st abortion – 10 May (Day 0) Samples submitted for diagnosis	1 st abortion – 20 June (Day 0), 12 days after introduction of newly acquired mares.
2 nd abortion – Day 39	3 abortions – 22 June (Day 2) – in same paddock as first. Foetuses and membranes retrieved intact and samples submitted to ERC.
Confirmation of EHV-1 status of first abortion – Day 40	Results of PCR test available on Day 3 (within 24 hrs of second group of abortions.)
Last Abortion – Day 135	Last Abortion – Day 34

The rapid diagnosis in the instance of Farm 2 enabled the farm's management to immediately institute EHV-1 outbreak-control measures aimed at isolating the focus of infection, interrupting virus transmission and reducing the susceptibility of high-risk late gestation mares. This response was based on a number of key decisions. The first was to vaccinate all pregnant broodmares and to re-vaccinate at 2 month intervals until foaling. In addition, the mares were subdivided, within each paddock, into groups of 4-6 using electrical tape barriers and maintaining a distance of at least 20m between each enclosed area, while ensuring that the groups still had visual and auditory contact until the mares either foaled or aborted. This manner of separation aimed to balance the risks of virus transmission between mares, particularly at the



time of foaling or abortion, against additional separation stress that could otherwise conceivably cause the virus to re-appear or lead to abortion for other reasons. After abortion, in-contact mares were relocated to another electrically fenced enclosure at least 20m away, precluding direct contact with fetal fluids. The aborted fetus and membranes were immediately sealed in plastic drums and removed for diagnostic sampling and disposal. An EHV-1-appropriate biosecurity protocol was applied concurrently. The fetus and associated membranes were examined by the farm's veterinarian and tissue samples obtained during a standardised autopsy protocol and submitted for laboratory diagnosis.

Conclusions

The following preventative and response measures appeared to help :

1. subdivide into the smallest practicable groups early in gestation;
2. avoid additions to late pregnant mare groups and maintain newly acquired late pregnant mares as separate groups until after foaling;
3. investigate all abortions and prioritise EHV-1 diagnosis;
4. rapidly implement EHV-1-appropriate biosecurity measures until a diagnosis is obtained (availability of a rapid diagnostic test facilitates compliance with these measures);
5. submit appropriate samples for diagnostics (including fetal tissues and membrane samples);
6. if the first abortion occurs in a large group of mares, subdivide as soon as possible to reduce the number of mares exposed to transmission by any subsequent abortions;
7. minimise separation associated stress by maintaining group mates within 'sight and sound' of aborting mares and
8. institute preventative vaccination in all at-risk mares.

**Epizootic = Epidemic among animals of a single kind within a particular region.*

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A predictive model for reproductive performance following abortion in Thoroughbred mares

Pregnancy losses include early embryonic death (EED) and later abortion. Abortions, particularly Equid herpesvirus (EHV-1) abortion epizootics, cause severe economic and production losses. The long term effects of EHV-1 and other abortions on subsequent reproductive performance in broodmare populations,



however, remain undefined. This study described the relationships of EED and abortion with the following reproductive outcomes in Thoroughbred systems :

- breeding efficiency
- month of last breeding
- subsequent pregnancy and live foal rates.

A study in broodmare populations following EHV-1 epizootics on two South African farms was used to develop predictive models of the relative influences and interactions of reproductive performance. These were the summarised findings :

- EED predicted all the reproductive outcomes;
- Abortion predicted increased effort and month of breeding to establish pregnancy, but not becoming pregnant or foaling;
- Increasing age predicted decreased reproductive efficiency, and pregnancy and foaling probabilities;
- Mare reproductive status (barren, maiden or foaling) predicted breeding efficiency and the last month of breeding, but not establishing pregnancy;
- The last month of breeding predicted efficiency, pregnancy and foaling.
- Interestingly, breeding in the first month of the season was associated with an improved probability of pregnancy among barren mares.

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