

EHM in New Zealand – What Next?

Introduction:

The existence of Equine Herpes Virus -1 (EHV-1) viruses with different pathogenic potential has been described by several authors (Gardiner et al., 2012; Patel et al., 1982; Tearle et al., 2003), although the virus, host, and environmental factors that influence the various clinical outcomes of EHV-1 infection are poorly understood. Many infections with EHV-1 occur asymptotically, others are accompanied by respiratory disease of various severity (Dunowska et al., 2002a,b; Gilkerson et al., 1999). However, EHV-1 infection can also result in comparatively more serious clinical outcomes such as abortion (Barbic et al., 2012; Carrigan et al., 1991; Hong et al., 1993), neonatal death (Frymus et al., 1986) and neurological disease (Friday et al., 2000; Henninger et al., 2007). The latter is often referred to as equine herpesvirus myeloencephalopathy (EHM). Prior to 2014 the position in New Zealand was that the emerging mutant strain of Equine Herpes Virus -1 (EHV-1) responsible for EHM was considered to be exotic to New Zealandⁱ. EHM had been reported in most countries in the world and little was known as to why the syndrome had not emerged in the New Zealand horse population despite it being reported as a syndrome present in equine populations internationally for well over 50 years (Saxegaard,1966).

By 2008, the apparent increase in the incidence of EHM, especially in North America, had resulted in the EHV-1 Consensus statement becoming published in Journal of Veterinary Internal Medicine in 2009ⁱⁱ as a means to provide the veterinary community with up to date information on the pathophysiology, diagnosis and treatment of this clinically important animal disease.

A disease is considered to be considered to be “emerging” when it satisfies at least one of three criteria:

1. The disease is identified for the first time in a region or a country;
2. A disease changes in severity, type of animal that can be infected, or other changes in pathogen behaviour; or
3. There is a change in geographic range of a disease or in its incidence within a range.ⁱⁱⁱ

EHM likely meets two or three of the criteria of an emerging disease in New Zealand though it is possible that the disease has previously occurred here and failed to be reported. Although this outbreak of Equine Herpes Myeloencephalopathy (EHM) is over the question remains about what is the likely future pattern of this disease going to be and what is the best strategy to position the equine industry for the future. I will describe three current areas of NZEHA involvement with the hope that it will increase our knowledge on the EHV-1 situation in New Zealand and better position our industry to manage future outbreaks.

1. Research Project:

Recently, an amino acid substitution from asparagine (N) to aspartic acid (D) at amino acid position 752 of the viral DNA polymerase, encoded by open reading frame (ORF)30, has been associated with increased neurovirulence (Goodman et al., 2007; Nugent et al., 2006). However, it should be noted that not all infections with D₇₅₂ viruses lead to development of EHM, and not all EHM cases are caused by D₇₅₂ viruses.

As part of a study performed at the virology laboratory at Massey University trigeminal ganglia (TG), retropharyngeal lymph nodes (RPLN) and blood samples were collected from 52 equine heads from a single day's production in a South Island based slaughter facility in February 2012. This sample group was drawn from predominantly South Island derived horses and those of the standardbred breed. The tissue samples were processed as described previously (Allen, 2006), with some modifications. Provisional results of this study included detection of EHV-1 DNA in 16 out of 52 (26.9%) RPLN and in one of the TG tested (unpublished confidential data, pers comm Dunowska). The samples are currently being re-tested using a more sensitive reaction mix, and the final results of this testing will be available once completed.

The preliminary results of the Massey University study are comparable with the results of similar studies performed overseas, which all demonstrated that a considerable proportion of horses tested were latently infected with EHV-1. For example, in a Great Britain based study, latent EHV-1 was detected in 50% of 40 horses at slaughter, often concurrently with EHV-4 (Edington et al., 1994). Pusterla *et al* (2010b) detected latent EHV-1 in 26/147 (17.7%) horses, 2/4 (50%) mules and 2/2 (100%) donkeys at routine post-mortem examination at the University of California, Davis. In another study, latent EHV-1 was detected in 25.7% of 70 TB racehorses from four Californian racing tracks (Pusterla et al., 2012). Finally, Allen *et al.* (2008) detected latent EHV-1 in 54% of 132 TB broodmares submitted for necropsy to the University of Kentucky. It remains to be established whether discrepancies between the numbers reported in those studies reflect true differences between the sampled populations or simply the differences in the study design or testing methods used. In general, the percentage of latently infected horses was higher in studies that employed the pre-PCR enrichment for EHV-1 sequences using sequence-capture, magnetic bead method (Allen, 2006; Allen et al., 2008) than PCR without such enrichment (Pusterla et al., 2012). The study performed at the Massey University used a modified sequence-capture, magnetic bead method. The modifications to the Allen protocol included scaling down the starting DNA from 2400 µg to 240 or 100 µg starting DNA for RLN and TC, respectively. Thus, it is possible that the prevalence of latent EHV-1 infection in New Zealand is lower than that in the UK, but this is currently unknown. The purpose of the current proposal is to extend the data obtained from the initial New Zealand-based survey by testing further samples from the broader population of New Zealand horses. This will both increase the confidence around the baseline prevalence estimate and increase the external validity of the work, which would better enable extrapolation of the study results to horses that were not sampled.

Research Goals:

- To estimate the prevalence of latent EHV-1 infections in the New Zealand horse population.
- To estimate the proportion of latently infected horses that are carrying the D752 genotype.
- To provide initial data on the distribution characteristics (breed, geographical etc) of the D752 genotype of EHV-1 within New Zealand

- To take an initial look at risk factors associated with the expression of Equine myeloencephalopathy in New Zealand.

Industry benefit:

In North America and Europe, the D₇₅₂ genotype appears to be associated with the neurological form of the disease, although there are likely other virus- and host-related factors that influence the outcome of EHV-1 infection (Pronost et al., 2010).

This project seeks to advance epidemiological understanding of the disease in the New Zealand equine population. This will be beneficial because currently very little is known about the occurrence and distribution of the D₇₅₂ genotype in this country. If the genotype is frequently detected in this study, it would suggest that the D₇₅₂ genotype may not be a primary driver for the expression of neurological EHV-1 disease here and therefore large outbreaks of disease more likely to occur infrequently. Conversely, if the D₇₅₂ genotype is rarely detected, the current outbreak may represent the start of a more frequent trend, as has been seen in the USA. Furthermore, with just one reported outbreak in NZ, conducting a case-control study to investigate risk factors is not yet a possibility. By collecting epidemiological data from the horses sampled in this study it would be possible to have a preliminary, descriptive look at potential risk factors for being latently infected with (and hence previously exposed to) the D₇₅₂ genotype. The risk factors for which information is available include: age, breed, recent travel history and vaccination status. This information would be of value in the event of another outbreak of neurological disease.

2. Determine an optimal strategy for control of future outbreaks of EHM in New Zealand

The prevalence of outbreaks of EHM internationally is relatively low however some authors have observed that EHM is occurring more commonly in their populations than in the past. (Centre for Equine Health Davis). In recent years, equine events and shows, private veterinary clinics and University teaching hospitals have been shut down to limit the spread of EHM. There are no indications that New Zealand is going to be flooded with outbreaks of EHM however it is likely that future outbreaks will occur and it is very important that they are notified, investigated and that quarantine and movement restrictions are implemented early.

Around the world many countries instituted regulatory conditions on the organism to expedite and underpin early notification and implementation of disease control.

In NZ the question arises, can early notification of disease and implementation of controls be achieved longterm given that EHV-1 is not unwanted, notifiable nor categorised as a pest under existing legislation? Do we have the optimal mechanisms for managing an outbreak, especially those occurring at venues where there is regular mixing of large numbers of horses.

The Australian situation and approach for surveillance and control of EHV-1

The Australian equine population has many similar characteristics to the New Zealand equine pool. We have similar horse populations in terms of history, composition and use. We import from similar countries, have similar biosecurity controls and approaches and trade extensively with each other. The abortigenic and neurological strains of EHV-1 are on

the Australian Government Department of Agriculture, Fisheries and Forestry (DAFF's) list of nationally notifiable diseases. EHV-1 abortions are generally sporadic, but outbreaks do occur. DAFF notes that EHV-1 neurological disease is an emerging disease of increasing prevalence overseas, and new cases have been diagnosed in recent years in Australia. (Australia, 2012) It includes EHV-1 in its list of Endemic Diseases of National Concern

The following is copied from the most recent Australian Annual Animal Surveillance Report - 2012

During 2012, no cases of EHV-1 abortion or neurological disease were reported in the Northern Territory, South Australia, Tasmania or Victoria. New South Wales -Abortion due to EHV-1 occurred on five thoroughbred studs in the Hunter Valley in 2012; EHV-1 was confirmed by positive PCR tests on foetal tissues. On three studs, only a single mare aborted; one stud had four mares abort, and another stud had five. Queensland -Three cases of EHV-1 associated with abortion or weak foals occurred in Queensland in 2012. The virus was detected by PCR examination of tissues from aborted foetuses or moribund newborn foals. Western Australia - In 2012, there was one case of equine abortion that may have been caused by EHV-1. The mare was found to have a very low antibody titre to EHV-1, and sampling was not repeated.

We can conclude that EHM has remained relatively rare in Australia to date.

What is the best mechanism for facilitating early diagnosis, prevention of further spread and management of clinical cases of EHM infection in New Zealand?

- The Biosecurity Act 1993 and its regulations represent the only legislative tool available within New Zealand under which animal disease management measures can be enforced.
- Part V of the Biosecurity Act provides for the continuous monitoring of New Zealand's status in regards pests and unwanted organisms.
- Part IV of the Biosecurity Act provides for continuous monitoring of New Zealand's status in regards pests and unwanted organisms and institution of exigency arrangements. There is no current pest management strategy nor pest management agency for the management of EHV-1.
- EHV-1 is currently not designated as a pest, a notifiable organism or an unwanted organism in New Zealand, under section 2 of the Biosecurity Act 1993 (the Act) and, as such, EHV-1 is not subject to any official controls in New Zealand.
- Declaring EHV-1 to be an unwanted organism in New Zealand would have implications that will require attention, given that this organism is known to be relatively widespread in New Zealand. Section 2 of the Act defines an unwanted organism very broadly as follows: "unwanted organism means any organism that a chief technical officer believes is capable or potentially capable of causing unwanted harm to any natural and physical resources or human health"
- The Chief Technical Officer (CTO) for the Ministry for Primary Industries (MPI) would need to make a case for declaring EHV-1 to be an unwanted organism. The reason for determining an organism to be unwanted is so that powers under the Act can be exercised against those organisms as, and when, necessary.
- In the case of EHV-1 there are a number of constraints (mainly that the virus has a latent state) that make eradication impossible, and containment difficult. This difficulty could possibly be managed if the goal is altered so that notification and containment of the neurogenic disease entity as a result of EHV-1 rather than control of the EHV-1 organism as the objective. (This could be facilitated by the use

of section 53 Subsections 2 and 3 where there is the ability for the CTO through notice in the Gazette to permit owners with horses to carry out acts prohibited by section 53 if some ambiguity remained. Such a notice might allow owners/persons in charge of horses to move horses provided they have been free of any signs of EHV-1 neurogenic disease for at least 21 days.)

- Practical diagnostic tools are available to determine if an animal showing clinical signs of the neurogenic form of disease is infected with EHV-1 and infective to others. It is these animals that should be isolated to prevent further spread and propagation of disease.
- It is clear that Equine herpes myeloencephalopathy syndrome is capable of causing unwanted harm to any natural and physical resource could meet the test required by the CTO to declare the entity unwanted. It is also noted in "MPI Policy on Unwanted Organisms" that "There is no obligation on any agency to take action against an unwanted organism simply because it has that status, except that inspectors under the Biosecurity Act, before giving biosecurity clearance to any goods or organisms, must be satisfied that the goods or organisms show no signs of harbouring unwanted organisms."
- Notwithstanding the above MPI are reluctant to confer an unwanted status on the EHM disease entity and suggest that if we wish to control it beyond voluntary means that we consider creating a pest management pathway for equine diseases. NZEHA is still working through the logistics and implications of this approach.

It is clear that neurological disease associated with EHV-1 is rare in Australia and should this pattern be repeated in New Zealand then the costs associated with the development of a Pest pathway Strategy would outweigh those gained from the control of a very low prevalence of disease. Should the prevalence of the neurological form increase then this is MPI's notification and control mechanism of choice.

(With regard to export; horses that are to be exported from New Zealand to certain countries must meet the export requirements, most of which require premises freedom from signs of EHV-1 disease (abortigenic or paralytic) for a minimum period. Although MPI are comfortable with the current verification processes in place to ensure the credibility of our export process, making such a disease notifiable/unwanted removes any criticism that could be leveled at the voluntary nature of such information sharing. Disease declarations underpinned with an imperative to report supported by statute is the approach that New Zealand industries support for countries seeking to comply with our import health standards.)

The gain from utilising either provision of the Biosecurity Act is that it optimizes surveillance for outbreaks of myeloencephalopathy due to EHV-1 and offers a more robust mechanism to limit the size of outbreaks

The equine industry could in the future argue more vehemently for unwanted organism status to be conferred or submit a proposal for implementing a national pest pathway strategy if it was agreed this was an appropriate course of action. At this point in time this would seem inappropriate until the pattern of disease is known.

The equine industry is working in partnership with MPI to look at best biosecurity practice as the most cost effective and practical way to mitigate the impacts of disease attributable to EHV. We do recognize however that there are some disincentives to individuals to report

this disease.

Should the industry experience a significant outbreak associated with a large equine facility or event in the future it is likely that the industry might also look with more energy to redress this balance by way of rules.

The Status Quo of equine industry and veterinary voluntary cooperation is retained in the mean time:

The current situation remains. Horse owners should contact their veterinarian if they are concerned about an animal under their care. Veterinarians are still required to contact MPI if they encounter suspect cases of EHM. Early voluntary implementation of strict biosecurity and quarantine measures are key to preventing spread of this disease. All horses introduced onto a property should be quarantined for at least 21 days. Horse owners should seek veterinary advice immediately if any horse shows signs of neurologic disease.

If a suspect case of EHV-1 is seen then separate sick horses from healthy horses. Stop movements of horses off premises where there are sick horses. Do not bring pregnant mares onto premises where active EHV-1 is circulating.

It is extremely important that people in contact with horses on an affected property use proper biosecurity measures (MPI 2014)iv

3. Resources for horse owners and event organisers

A voluntary code for the control of endemic diseases including EHV1 and strangles was circulated to horse organisations in 2012. It can be used by equine organisations, or modified as required to enable event organisers seeking to manage the risk that owners with unwell horses might consider competing in contact and potentially infected horses at events and so spread disease. A modified draft code is appended to this paper.

Horse owners or persons associated with the equine industry need information to assist them prevent and manage spread of equine disease, both those present in NZ and in the event of an exotic disease outbreak so a range of documents have been drafted and are located across various NZEHA member organisation websites.

Take Home messages

Notify equine neurological symptoms characteristic of EHM to 0800 809 966 immediately and recommend to the owner that they immediately implement movement control and biosecurity measures for in contact horses. By notifying cases then we also facilitate the opportunity to undertake case control studies which will be essential if we are ever able to understand the complex epidemiological factors that contribute to the expression of EHM.

Only research and time will answer whether EHM will be an emerging disease of significance to the New Zealand equine population

Appendix

NEW ZEALAND CODE FOR THE CONTROL OF EQUINE CONTAGIOUS DISEASES.

(Modified to be specific to EQUINE HERPES VIRUS)

The New Zealand Equine Health Association (NZEHA Inc) endorses that each of its member bodies adopts codes as a way to handle equine disease outbreaks. At the last meeting of the NZEHA the committee moved that each of the member organisations would be approached to endorse codes for the control of equine contagious diseases.

New Zealand is relatively free of many of the world's worse infectious diseases but do face ongoing outbreaks of disease which can be contained if those in charge of horses followed good containment measures. For Equine Herpes Virus, we would recommend you take the following steps immediately:

- Isolate the horse and any horses that have had nose-to-nose contact with the suspect horse away from other horses on the property.
- If possible create three groups
 - Infected horses
 - Horses that have had close contact with the infected horses
 - Clean horses
- Call your veterinary surgeon to make a diagnosis. This will generally require sampling and the submission of the samples for laboratory testing.
- Discuss with your veterinary surgeon isolation and handling procedures, and implement these as quickly as possible. Immediate introduction of strict hygiene between the groups will reduce the risk of spread and the time taken to control the outbreak.
- Separate the groups by at least 35 metres.
- As few people as possible should handle affected horses with application of strict hygiene standards.
- If possible separate staff for the separate groups.
- Attend unaffected horses first if separate people are not available.
- Protective clothing, ideally disposable, should be available.
- Ensure separate water troughs, grooming, cleaning and feeding equipment.
- Careful disposal of bedding, uneaten food and water and in the case of abortions fetuses and foetal membranes.
- Do not allow any horses onto or off the property at this time.
- Discourage visitors to the property and confine pets such as cats and dogs.
- Contact the owners of the affected horses and owners of other horses on the property.
- Notify any neighbouring properties with horses that you have a suspected case of Equine Herpes Virus associated disease, (rhinopneumonitis, abortion or neurological

disease) and recommend that they check their horses.

- In the case of Herpes virus, infected animals should be kept for at least 4 weeks but there remains the potential for ongoing latent infection hence quarantine measures must be judiciously applied when new horses arrive on any property. Owners or persons in charge should share information of the disease status of their property and horses coming in or leaving their care to enable appropriate and timely disease control measures.

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Voluntary code courtesy of Dr John O'Flaherty.

ⁱ Email to NZEHA from MPI (IRA team) 26 May 2011

ⁱⁱ J vet Intern med 2009; 23:450-461

ⁱⁱⁱ <http://www.oie.int/for-the-media/editorials/detail/article/emerging-and-re-emerging-zoonoses/>

^{iv} <http://www.mpi.govt.nz/Portals/0/Documents/biosecurity/pests-and-diseases/Ehv1-response/technical-q-and-a-for-neurological-ehv-11-feb-2014.pdf>