**Equine herpesvirus-1: Dealing practically but effectively with an ever present threat**

**Alpha herpesviruses and equine disease**

Alpha herpesviruses are ubiquitous pathogens affecting many mammals, including equids [equine herpesvirus (EHV)-1, EHV-3 and EHV-4]. Infections with EHV-1 and EHV-4 are among the most common causes of equine respiratory disease worldwide and estimates of prevalence show that most mature horses are infected with EHV-1, EHV-4 or both during their lifetimes [1].

The establishment of lifelong latency in a large proportion of infected animals ensures the survival of herpes viruses in horse populations and is of major importance for EHV-1 and its ability to cause several clinical syndromes (clinical features of note outlined in Table 1).

Initial EHV-1 infection occurs through the respiratory route by either inhalation of aerosolised infectious virus or close contact with an infectious individual or fomites. The virus replicates in the respiratory mucosa and spreads quickly to adjacent tissues establishing a cell-associated viremia between 4 and 10 days after infection. During this phase the virus is transported to sites of secondary infection, particularly the vascular endothelium of the central nervous system and/or endometrium, where the infection may trigger neurological signs and/or abortion/neonatal foal death. All 3 disease syndromes are widely recognised after EHV-1 infection, and chorioretinitis has also been recently described [2]. Although EHV-4 infection is widely recognised as a cause of respiratory disease and occasionally as a cause of individual abortions, it has not been shown so far to be a direct cause of neurological disease.

**Managing EHV-1 disease outbreaks**

When dealing with EHV-1 disease outbreaks, creating adequate segregation between groups of animals and allowing time for monitoring are key factors for successfully countering the spread of infection and limiting the occurrence of disease. Improvements in molecular diagnostic testing techniques have also greatly helped in the rapid confirmation of diagnoses, prompt identification of infectious individuals within affected populations and informing of the most effective biosecurity measures, before safe resumption of normal activities.

To this end, the Horserace Betting Levy Board (HBLB) Codes of Practice for breeders provide a now long-established standard for the management and control of several infectious diseases that affect horses and particularly those that have a major impact on breeding, including EHV-1. The recommendations are designed for breeding farms in particular and since they were first published for the 1978 breeding season, the HBLB Codes have provided an authoritative reference for breeders and their veterinary surgeons and have played an important role in decreasing equine infectious disease frequency.

In this edition of *Ev* Schuman and colleagues [2015] illustrate 2 presentations of EHV-1 abortion outbreaks on separate Thoroughbred breeding farms in South Africa, although in both outbreaks described, recrudescence of EHV-1 from the latent state seems to have been the most likely trigger [3].

Latent infections are undoubtedly the cornerstone of EHV-1’s success, as latently infected individuals are highly prevalent within the equine population [4–6] and cannot be readily identified by any currently available laboratory test. Consequently, viral replication may be initiated spontaneously by exposure of latently infected horses to stressors, with the extent and type of necessary initiating stress undoubtedly varying between individual animals. Unlike equine influenza and even strangles caused by infection with Streptococcus equi, EHV-1 is not an infection that can be practically eradicated from equine populations. Therefore, for the foreseeable future the pragmatic paradigm must remain to confirm and manage EHV-1 related disease outbreaks as and when they occur as absolute prevention is realistically unfeasible.

As reported by Schuman et al. [3], even if adequate quarantine protocols exist for new entries to a resident population, risks remain relatively high when introducing mares in late gestation because of the risks from reactivation of latent EHV-1 even in an otherwise healthy animal. In mares in late pregnancy, transport, relocation, social group change and other forms of stress may increase the risk of latently infected horses starting nasal shedding of EHV-1 as well as the virus crossing the placenta in the pregnant uterus, resulting in fetal infection and abortion [5]. As recommended in the HBLB Codes of Practice and by Schuman et al. [3] pregnant mares with similar foaling dates should be maintained in small groups from as early in their pregnancies as possible without transportation and re-mixing until they have successfully foaled. Pregnant mares, that arrive following transportation and social disruption, such as those bought from sales or attending veterinary clinics, should always be considered as being ‘high risk’ for EHV abortion and should be managed accordingly with particular due diligence to the potential risk they pose.

Aborted fetuses, placental membranes and/or dead newborn foals should be immediately but hygienically removed from the ground and placed in a double wrapped strong leak-proof bag or container and sent as soon as is practical to a suitably experienced laboratory for detailed investigation of the cause of abortion and, in particular, to determine whether EHV infection was involved. If EHV is confirmed, procedures outlined in the HBLB Codes of Practice should then continue to be implemented.

**Stages of an EHV-1 disease outbreak investigation and control strategy**

Although there are no legal requirements for official notification of EHV-1 related disease in the UK, confirmation and containment of outbreaks is required in order to avoid spread of infection and to minimise the potential for significant impact to the equine industry from more widespread outbreaks. In particular, large and widely disseminated outbreaks of EHV-1 neurological disease that have occurred in the USA [7–9] should reinforce warnings to the UK Thoroughbred industry to remain vigilant of the threats from EHV-1 related diseases.

In broad terms there may be considered to be 6 fundamental stages in an EHV-1 disease outbreak investigation and control strategy (Table 2).

In recent years, EHV-1 neurological disease outbreaks have not only been more prevalent in equine populations, not only in the UK but also in the USA, and therefore experience gained through management of these outbreaks has led to establishment of protocols to control the spread of disease and minimise industry losses. The HBLB Codes of Practice are designed for breeding establishments and there is a need for advice applicable to horses in training yards, livery yards and other management systems where there are nonpregnant animals with frequent horse mixing and movements (for racing, competition etc.). To that end the Equine Infectious Disease Service at the Animal Health Trust (funded by the HBLB, Racehorse Owners Association via the race entry levy and the Thoroughbred Breeders Association) has proposed 3 possible tiers of approach as to how EHV-1 neurological outbreaks can be practically managed.

**Three tiers of approach (Gold, Silver and Bronze) for managing EHV-1 neurological disease outbreaks**

The strategy for dealing with an EHV-1 neurological disease outbreak is an important decision that should look to take into account the type of premises and number of animals involved and the availability of personnel and space to facilitate effective segregation and management, including taking and testing of samples for laboratory testing. A very important issue is also the cost and time involved in implementing the strategy, particularly those that can accrue from conducting laboratory testing for providing both evidence of freedom from infection and confidence to be able to return safely to normal activity.
Three tiers of approach have been proposed and variously utilised in dealing with recent significant outbreaks of EHV-1 neurological disease in the UK. These are here referred to as Gold, Silver and Bronze tiers (Table 3) and while they are all based on the same set of principles of Segregation of the population, Collection and Testing of samples, and Observation of clinical disease, there are clear differences between them in terms of the strength of evidence accrued, the time required and the costs incurred. Segregation into smaller discrete groups is common to all 3 approaches and is believed to be key to a successful strategy through minimising the spread of disease through the population and allowing clearance and release of quarantine measures as soon as possible.

The Gold tier option provides insight into both the extent of recent infectious spread (based on complement fixation test serology [10]) and current infectiousness (based on agent detection tests [11]) in each segregated group while allowing risk management to then be optimised specifically to each group. This option also facilitates prompt removal to an isolation area of infectious horses from segregated groups, so reducing likelihood of ongoing infectious transmission within the group and overall morbidity. The Silver tier option incurs lower costs than the Gold option as whole blood samples are not screened for viraemia by virus isolation (quantitative polymerase chain reaction is not optimised for this purpose), but it only provides an insight into the extent of actively shedding and exposed horses without detecting potentially infectious vireamic animals. The Bronze tier option provides a retrospective insight into the extent of infectious spread but relies on observation of neurological signs and/or abortions/neonatal foal deaths to trigger further investigations, thereby potentially missing subclinical infectious spread, which is a recognised phenomenon in propagating EHV-1 outbreaks. This option may be the cheapest of the three with respect to laboratory costs but the lack of initial information about the infectious status in all segregated groups might ultimately lengthen the time for effecting overall control of the outbreak and depending on how many segregated groups are further investigated, may ultimately not significantly reduce laboratory costs.

**Conclusions**

Effective EHV-1 outbreak control requires rapid confirmation of EHV-1 infection as the cause of disease, prompt restrictions placed and maintained on movements of horses on and off affected premises,
TABLE 3: Three tiers of approach for managing outbreaks of equine herpesvirus (EHV-1) neurological disease

<table>
<thead>
<tr>
<th>Action</th>
<th>Gold tier</th>
<th>Silver tier</th>
<th>Bronze tier</th>
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<tbody>
<tr>
<td>Segregate</td>
<td>Yes – the smaller the groups the better to minimise the impact of ongoing disease and possibly reduce later laboratory test costs</td>
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<tr>
<td>Collect samples</td>
<td>Collect full set from all animals – NP swab in VTM, serum (5–10 ml) and heparinised whole blood (30 ml)</td>
<td>Collect partial set from all animals – NP swab in VTM and serum (5–10 ml)</td>
<td>Collect partial set from all animals – NP swab in VTM and serum (5–10 ml)</td>
</tr>
<tr>
<td>Test samples</td>
<td>Test full set from all animals – NP swab by qPCR, serum by CFT and heparinised blood by virus isolation</td>
<td>Test partial set from all animals – NP swab by qPCR and serum by CFT</td>
<td>Don’t test but freeze the partial set from all animals for possible testing later</td>
</tr>
<tr>
<td>Observe for clinical disease</td>
<td>Observe all groups for 3–4 weeks:</td>
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<tr>
<td>(neurological disease and/or abortion – noting that pregnant mares should only be considered clear once they have a foaled successfully and have a healthy foal at foot)</td>
<td>If no clinical disease is observed in a group: collect NP swabs and sera (pair with already tested sample in CFT) and test – consider EHV-1 free if all results are negative</td>
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<tr>
<td></td>
<td>If clinical disease is observed in a group: immediately collect and test a full set of samples from all horses in the affected group. Remove positives to an isolation area. Repeat after 2–3 weeks and only consider EHV-1 free when all results are negative</td>
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CFT, complement fixation test; NP, nasopharyngeal; qPCR, quantitative polymerase chain reaction; VTM, virus transport medium.

Segregation of the affected population into small groups and use of laboratory tests to provide confidence in freedom from infection when dealing with neurological EHV-1 infection. In addition, the experience of Schulman et al. [3] indicates that additional benefit may arise in breeding farms from avoiding addition of late pregnant mare groups, instituting subdivisions of the population as soon as possible after abortion occurs, minimising separation-associated stress by maintaining group mates in ‘sight and sound’ of aborting mares and use of responsive vaccination in all pregnant mares at risk of aborting [3].

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References