EQUINE HERPESVIRUS – BEST MANAGEMENT PRACTICE

ABSTRACT

Equine herpesviruses (EHV) are some of the most widespread pathogens in the equine world. EHV1 and EHV4 cause diverse and important disease syndromes. One of these – equine herpes myeloencephalopathy (EHM) – is potentially increasing in frequency and regarded as an emerging disease. The accurate diagnosis and treatment of EHM is a challenge and an evolving area. Practical biosecurity and herd health measures are critical to the prevention of EHV and the critical, but complicated role of vaccination is discussed.

Diagnosis

History and clinical signs are important, but usually insufficient on their own to confirm diagnosis. EHV infections often do not cause clinically apparent respiratory disease, and even then there is little to distinguish EHV respiratory disease from other viral and bacterial pathogens.

A common misconception is monitoring for respiratory clinical signs provides a warning for impending abortion or EHM, most horses that abort or develop neurologic disease after EHV infection do not show signs of respiratory disease first.

When sampling, case selection is critical – all samples for direct demonstration of virus should be collected from early clinical cases (ideally less than five days) whenever possible. The accurate diagnosis and treatment of EHV is a challenge and an evolving area. Practical biosecurity and herd health measures are critical to the prevention of EHV and the critical, but complicated role of vaccination is discussed.

Management

Management of these are beyond the scope of this article and we will focus on the commonest and most important clinical pathologies, EHV1 and EHV4.

Different syndromes

EHV1 is associated with three clinical disease syndromes:


The virulence of individual isolates shows considerable variation. There are neuro-pathogenic and non-neuro-pathogenic strains, however, both can cause BHM and the differentiation is not very useful clinically. EHV4 is principally a cause of respiratory disease, although some highly virulent endotheliotropic, abortogenic strains exist.

Samples

Nasopharyngeal swab

A nasopharyngeal swab is a long, highly absorbent swab (Figure 1) passed into the ventral meatus of the nasal passages to the level of the medial canthus to ensure adequate sampling of the nasopharyngeal mucosa – and placed in a viral transport medium (for example, a white top tube from the Animal Health Trust). The sample should be refrigerated and time minimised before it arrives at the laboratory.

Quantitative polymerase chain reaction (qPCR) detects viral DNA, is sensitive, allows estimation of the amount of virus (“viral load”) in the sample (1) and gives quick results.

Immunofluorescence (IF): detects viral antigen expressed on the surface of infected cells. It is quick, but not as sensitive as qPCR and does not give an estimate of the amount of virus.

Virus isolation (Mayo): detects viral antigen in tissue culture cells inoculated with the supernatant from the sample. This usually takes five to seven days of culture.

Blood

qPCR: to detect virus DNA in buffy coat cells (mainly lymphocytes).

Serology: to detect antibody induced by infection – IgG detectable four to five days after infection, peaking at 20 to 30 days and returning to baseline between 60 to 80 days. It is measured by complement fixation (CF) (6–8: IgM detectable eight to 10 days after infection, peaking at 30 to 40 days and persisting for many months (greater than nine months). It is measured by virus neutralisation (VN) or ELISA (can differentiate between EHV1 and EHV4).

Take a baseline sample and repeat the sample 10 to 14 days later. Significant increase in IgM antibody level is usually taken as threefold to fourfold increase. A high complement fixation titre (IgM) in a single serum sample from a non-vaccinated horse provides good preliminary evidence of infection and is a valuable initial diagnostic test in suspected EHM cases. Note, previous vaccination and maternal antibodies can interfere with serological investigations.

Haematology: non-specific and difficult to interpret. There is initial (first seven to 10 days) transient leucopaenia with lymphopaenia, which is replaced by a leukocytosis with lymphocytosis up to 21 days after infection.

Tissue: (for example, fetal, placental or CNS)

Histopathology: characteristic eosinophilic inclusion bodies or vacuolitis and often thrombosis of CNS blood vessels (1, 7–10).

Immunohistochemistry (IHC): paraffin-embedded, formalin-fixed tissue that demonstrates the viral antigen.

In situ hybridisation (ISH): paraffin-embedded, formalin-fixed tissue that demonstrates viral DNA.

PCR: Fresh, frozen and fixed tissue samples. Frozen sections from aborted fetal and placental tissues.

Cerebrospinal fluid: EHM cases

Cerebrospinal fluid (CSF) may be xanthochromic (yellow discolouration (Figure 2)) or clear. Increased total protein without a concomitant increase in total white cell – plus characteristic clinical signs – are suggestive, but not diagnostic of, BHM. Antibodies to BHM in the CSF may be from leakage from the vasculature, and may not be from local production, so this does not definitively confirm EHM, only EHV exposure.

Treatment

Respiratory disease

Respiratory disease is generally mild and self-limiting, and does not require specific treatment. Rest, dust-free management and biosecurity measures to stop transmission are indicated. Broad-spectrum antibiotics are often administered, but seldom indicated to prevent secondary antimicrobial infections; clindamycin stimulates mucociliary clearance, but is usually not required. Respiratory disease is preventable when stress or mixing has had to take place and there is potential value in immunostimulants, such as paravaccines.

Abortion

There is no evidence treatment of in-contact mares with antibacterial agents (for example, oxytetracycline) prevents abortions. The whole placenta has been passed (this is usually the case), in the rare event this does not occur, treat for retained fetal membranes. Treat with rigorous biosecurity (see further on).

EHM

For BHM, provide adequate bedding to prevent trauma and a quiet environment to prevent excitement. Recumbent horses can be nursed successfully in slings (for example, an Anderson sling, Figure 3).

Indwelling Foley catheter in horses with bladder paralysis, urinary retention and overflow. Apply petroleum jelly around the perineum, along with an extension line to direct urine away and prevent scaling. Maintain sterility, but cystitis is a common complication and antimicrobial therapy is often indicated. If nasal discharge is present, there is nasal incontinence.

Fluids and indwelling feeding tubes.

NSAIDs for example, flunixin meglumine 1.1mg/kg IV, twice a day.

Corticosteroids for example, sodium phospho dexamethasone 0.1mg/kg SC or IM, once a day.

Antibiotics: vitamycin 5–10mg/kg IV, once a day.

Acyclovir: 10mg/kg orally, five times daily. There is poor bioavailability and questionable efficacy with EHV1.

Valaciclovir: 25mg/kg PO twice a day.

1. Immunohistochemistry (IHC)

2. Indwelling Foley catheter in horses with bladder paralysis, urinary retention and overflow. Apply petroleum jelly around the perineum, along with an extension line to direct urine away and prevent scaling.
To limit the spread and severity of disease

Limiting spread to adjacent properties

If a suspect case occurs, the horse should be isolated immediately and appropriate samples taken. Any in-contact sites should be isolated and monitored for disease (take twice-daily temperatures). If the in-contact group is large, and it is practical to do so, it should be subdivided.

In terms of environmental contamination, the virus can survive for limited periods, depending on the surface and prevailing weather conditions. All discharges from affected horses should be removed and the area disinfected with approved disinfectant. Bedding should be burned.

Stop all movements by isolating aborted mares for 28 days and not mixing them with pregnant mares for 56 days. BMV horses should be kept isolated for minimum of 14 days and sometimes up to 28 days to account for the maximum possible duration for viraemia. Testing of viral shedding can be undertaken to shorten the isolation period. Movement of all horses on and off the premises should stop for a period of 28 days.

Limiting spread to adjacent properties

To limit any spreading to adjacent properties, there should be efficient communication between attending vets, premises owners and other parties working with the affected premises, as well as care with personnel and families, where easy and clear biosecurity measures should be implemented.

Vaccination: pros and cons

There are two BMV vaccines licensed in the UK. One is used presently is an inactivated vaccine containing BMV and EHV-4. The other (currently off the market) is also an inactivated vaccine containing BMV and EHV-4 and inactivated influenza virus. Worldwide, there are 10 killed commercial BMV vaccines available (eight in the United States and two in Europe) and two live vaccines (one in the United States and one in Europe). None of these vaccines induce a “perfect” sterile immunity (complete clinical and virological protection) that prevents all disease syndromes and the development of a more effective BMV vaccine is a priority worldwide in BMV research. However, it is important to be clear that vaccination with current vaccines has an important role to play in reducing the risk and impact of clinical disease.

The UK vaccines induce high titres of complement fixing and virus neutralisation antibodies. They reduce the duration and titre of nasal virus shedding of virus, but there are contradictory reports of the ability of killed vaccines to reduce viraemia and hence stop abortion.[7,9] With regards to abortion, the field data is unclear: The introduction of vaccination in the early 1960s coincided with a marked reduction in BMV abortion rates across the world.[8] However, simultaneously vigorous hygiene measures were introduced and the relative impact of both is impossible to assess in light of the lack of randomised, controlled field studies. Current vaccines do not make any claims for efficacy against BMV because the syndrome is difficult to reproduce experimentally and there are no reliable field data on the effect of vaccination of prevention of BMV because the syndrome is uncommon and large-scale outbreaks are infrequently reported in the UK. The reasonable expectation of current vaccines should not be to produce sterile immunity, but rather to reduce the severity of clinical disease (respiratory) and limit virus shedding from infected horses, thus reducing contamination. Vaccines should therefore be used to supplement hygiene control measures, which, as previously discussed, have a central role in reducing exposure to the virus. The use of vaccination in prevention of EHM is even less clear as this is, thankfully, rare and assessing vaccine efficacy is more difficult. Vaccinated horses do get EHM and none of the current UK vaccines are licensed to protect against EHM. The case for vaccination is further complicated by the initial analyses of a large outbreak in 2003 at Ohio State University, which seemed to show an increase risk of EHM in vaccinated horses.[22] This also seemed to support the then theory of immune-mediated pathogenesis for EHM. We now know EHM is caused...
VARIOUS regimes have been described for the treatment of hypothyroidism, however, not all are suitable for horses, as many are not approved for use in horses.

A complete response was seen in 30 cases, including a median overall survival time of 170 days. Four- and a half doses of prednisolone were administered on average. The authors note that the outcome was similar to previous studies using single-agent corticosteroids. However, they conclude that the potential benefit of a multi-agent treatment for the protocol easier for owners.

Doxorubicin. However, they studies using single-agent similar to previously reported doses of doxorubicin were measured and owners completed questionnaires regarding efficacy and side effects. The remission rate was not significantly different between the two groups, although it was higher in the budeso- side group. However, the frequency of adverse events was also similar between the two groups. The authors con- clude that no difference between prednisone and budesonide in remission rate or side effects was found in this study for initial therapy of IBD in dogs.

Side effects of IBD therapy Contextualized treatment is often necessary to control the signs of inflammatory bowel disease (IBD), but side effects can be severe, especially at high doses and with prolonged use. To address this issue, budesonide has been used, which acts locally and has a high first pass metabo- lism in the liver, reducing steroid side effects. Dye et al performed a study involving 40 dogs with newly diagnosed IBD. Dogs were randomised to receive either budesonide or prednisolone for six weeks. IBD activity scores were measured and owners completed questionnaires regarding efficacy and side effects. The remission rate was significantly different between the two groups, although it was higher in the budeso- side group. However, the frequency of adverse events was also similar between the two groups. The authors con- clude that no difference between prednisone and budesonide in remission rate or side effects was found in this study for initial therapy of IBD in dogs.

Feline heart study Hypertrophic cardiomyopathy (HCM) in cats can be a cause of heart failure and arrhythmo- embryol (AFIB). Payne et al performed a retrospective study of 282 cats diagnosed with HCM to assess whether echocardiographic variables had prognostic value. Cats with left ventricular dia- tock wall thickness of 6.5 mm or above were included. It was found that of the 164 cats that died, 107 were consid- ered to be cardiac causes. An increased risk of cardiac death was found in cats with severe congestive heart failure, atrial thromboembolism, extreme left ventricular hypertrophy and left ventricular filling pattern. The authors conclude echocardiographic measurements of left atrial function, extreme left ven- tricular hypertrophy and left ventricular filling pattern are useful prognostic indi- cators in cats with HCM.

Osteoarthriti trial Autologous platelet concen- trate has been proposed as a treatment for osteoarthri- tis (OA) in dogs. Falbe et al performed a randomised controlled trial involving 20 owner-owned dogs. The dogs were divided into two groups: one group was randomised to treatment and control groups, and the other were assessed by owner scoring as well as force platform analysis. Treated dogs were sedated, a blood sample taken, platelets recovered and then injected intra-articularly. Control dogs were sedated and given an intra-articular injection of saline. There were no significant differences in activity scores were measured.

The remission rate was not significantly different between the two groups, although it was higher in the budeso- side group. However, the frequency of adverse events was also similar between the two groups. The authors con- clude that no difference between prednisone and budesonide in remission rate or side effects was found in this study for initial therapy of IBD in dogs.

Side effects of IBD therapy Contextualized treatment is often necessary to control the signs of inflammatory bowel disease (IBD), but side effects can be severe, especially at high doses and with prolonged use. To address this issue, budesonide has been used, which acts locally and has a high first pass metabo- lism in the liver, reducing steroid side effects. Dye et al performed a study involving 40 dogs with newly diagnosed IBD. Dogs were randomised to receive either budesonide or prednisolone for six weeks. IBD activity scores were measured and owners completed questionnaires regarding efficacy and side effects. The remission rate was significantly different between the two groups, although it was higher in the budeso- side group. However, the frequency of adverse events was also similar between the two groups. The authors con- clude that no difference between prednisone and budesonide in remission rate or side effects was found in this study for initial therapy of IBD in dogs.

Hypertrophic cardiomyopathy (HCM) in cats can be a cause of heart failure and arrhythmo- embryol (AFIB). Payne et al performed a retrospective study of 282 cats diagnosed with HCM to assess whether echocardiographic variables had prognostic value. Cats with left ventricular dia- tock wall thickness of 6.5 mm or above were included. It was found that of the 164 cats that died, 107 were consid- ered to be cardiac causes. An increased risk of cardiac death was found in cats with severe congestive heart failure, atrial thromboembolism, extreme left ventricular hypertrophy and left ventricular filling pattern. The authors conclude echocardiographic measurements of left atrial function, extreme left ven- tricular hypertrophy and left ventricular filling pattern are useful prognostic indi- cators in cats with HCM.

Osteoarthriti trial Autologous platelet concen- trate has been proposed as a treatment for osteoarthri- tis (OA) in dogs. Falbe et al performed a randomised controlled trial involving 20 owner-owned dogs. The dogs were divided into two groups: one group was randomised to treatment and control groups, and the other were assessed by owner scoring as well as force platform analysis. Treated dogs were sedated, a blood sample taken, platelets recovered and then injected intra-articularly. Control dogs were sedated and given an intra-articular injection of saline. There were no significant differences in activity scores were measured.

The remission rate was not significantly different between the two groups, although it was higher in the budeso- side group. However, the frequency of adverse events was also similar between the two groups. The authors con- clude that no difference between prednisone and budesonide in remission rate or side effects was found in this study for initial therapy of IBD in dogs.

Hypertrophic cardiomyopathy (HCM) in cats can be a cause of heart failure and arrhythmo- embryol (AFIB). Payne et al performed a retrospective study of 282 cats diagnosed with HCM to assess whether echocardiographic variables had prognostic value. Cats with left ventricular dia- tock wall thickness of 6.5 mm or above were included. It was found that of the 164 cats that died, 107 were consid- ered to be cardiac causes. An increased risk of cardiac death was found in cats with severe congestive heart failure, atrial thromboembolism, extreme left ventricular hypertrophy and left ventricular filling pattern. The authors conclude echocardiographic measurements of left atrial function, extreme left ven- tricular hypertrophy and left ventricular filling pattern are useful prognostic indi- cators in cats with HCM.

Osteoarthriti trial Autologous platelet concen- trate has been proposed as a treatment for osteoarthri- tis (OA) in dogs. Falbe et al performed a randomised controlled trial involving 20 owner-owned dogs. The dogs were divided into two groups: one group was randomised to treatment and control groups, and the other were assessed by owner scoring as well as force platform analysis. Treated dogs were sedated, a blood sample taken, platelets recovered and then injected intra-articularly. Control dogs were sedated and given an intra-articular injection of saline. There were no significant differences in activity scores were measured.

The remission rate was not significantly different between the two groups, although it was higher in the budeso- side group. However, the frequency of adverse events was also similar between the two groups. The authors con- clude that no difference between prednisone and budesonide in remission rate or side effects was found in this study for initial therapy of IBD in dogs.

Feline heart study Hypertrophic cardiomyopathy (HCM) in cats can be a cause of heart failure and arrhythmo- embryol (AFIB). Payne et al performed a retrospective study of 282 cats diagnosed with HCM to assess whether echocardiographic variables had prognostic value. Cats with left ventricular dia- tock wall thickness of 6.5 mm or above were included. It was found that of the 164 cats that died, 107 were consid- ered to be cardiac causes. An increased risk of cardiac death was found in cats with severe congestive heart failure, atrial thromboembolism, extreme left ventricular hypertrophy and left ventricular filling pattern. The authors conclude echocardiographic measurements of left atrial function, extreme left ven- tricular hypertrophy and left ventricular filling pattern are useful prognostic indi- cators in cats with HCM.