Controlling Equine Herpesvirus-1 Infections
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Introduction
Equine herpesvirus-1 (EHV-1) is an extremely successful pathogen: it is ubiquitously distributed; maintains a stable and continuously-renewable reservoir of infection in apparently healthy horses; has evaded veterinary science’s best attempts to control them; and clinical disease, especially neurological disease, continues to be a major problem for the breeding, racing and recreational horse industries of the United States, Europe and Australia (i).

Epidemiology
EHV-1 epidemiology has four key features; (i) early and widespread infection of young horses; (ii) a widespread carrier (latent) state in adult horses; (iii) transmission from latently infected adults to new generations of young stock and (iv) widespread ‘silent’ adult-adult, adult-foal and foal-foal endemic infection cycles of transmission. The almost universal reservoir of latently-infected adult horses is responsible for infection of new horses early in life, generally as foals (2,3) producing a continuous cycle of endemic infection. Although environmental transmission is important during outbreaks, it is unimportant virus maintenance in the horse population since environmental virus survival is short (≤7 days in field conditions).

Transmission of infection
All clinical cases are contagious: respiratory and neurological cases via the respiratory route and aborting mares via placental fluids, fetal membranes and the aborted foal. Clinical cases should be isolated for 28 days: transmission risk is highest in first 7-10 days after infection and is unlikely after 28 days. Silent transmission occurs following acquisition of new infection and reactivation of latent infection. The actual frequency of reactivation is unknown but probably occurs very frequently, becoming detectable following a variety of stressful events including transport, housing and weaning as well as following corticosteroid treatment (with 10x therapeutic doses).

Pathogenesis
Although viral genotype influences clinical outcome, not all horses manifest the same clinical signs of disease: viral load, age, previous EHV-1 exposure, immunity and hormonal status all modulate the severity of clinical signs. There are several virus genetic subgroups, which partially correlate with pathogenicity. Dimorphism in the DNA polymerase gene (ORF30) correlates with neuropathogenic phenotype thus allowing identification of horses carrying neurological viruses and hence ‘test and segregate’ strategies in the field (4,5).

EHV-1 has a wide cellular tropism and following infection of respiratory epithelium, sequentially infects vascular endothelial cells and circulating leukocytes establishing a cell-associated viraemia. Viraemia delivers virus to the uterus and CNS where endothelial cell infection causes ischaemia, abortion and neurological disease. Within the uterus, endothelial cell infection triggers clotting and complete or partial failure of blood supply to cotyledons. Infectious virus may spread across the damaged endometrial/fetal interface causing abortion of a virus-positive foal. However, virus-negative abortions occur where extensive thromboischaemia causes severe placental necrosis and rapid expulsion of the fetus. Almost all field abortions occur in the last 4 months of pregnancy: the factors that render the late pregnant uterus susceptible to infection are not clear, although hormonal up-regulation of adhesion factors has been proposed. Similar events occur in the CNS and direct infection of neurones appears to be a rare event: clinical disease is due primarily to ischaemic injury following endothelial cell infection.

Immunity
The immune response to EHV-1 has been investigated intensively, with the aim of identifying correlates of protective immunity (6,7). Humoral immune responses (CF and VN antibody), directed mainly against viral surface glycoproteins, are efficiently generated after infection. Mucosal (IgA) antibody is also generated (8). Not surprisingly humoral immune responses are not protective, although may shorten the duration of virus shedding. In contrast, virus-specific T cell responses do appear to be protective, specifically the frequency of EHV-specific CD8+ T cell correlates directly with protection against viraemia and abortion (9). A key question for vaccine design has been which of the 76 virus genes encode proteins that act as CTL targets. Recent evidence suggests that the immediate-early gene (ORF 64) is a major CTL target although this is influenced by the MHC/ELA haplotype of the horse and different virus epitopes may be important in different MHC/ELA backgrounds (10).

Control programmes
EHV-1 is controlled by management and hygiene measures supplemented by vaccination. Disease control...
Programmes have three aims: prevention of disease entry onto premises; limiting the extent of spread and severity of clinical disease once EHV-1 enters the premises or appears in the herd; and limiting the spread of disease to adjacent premises during an outbreak. In the United Kingdom, these measures are formalised into a voluntary code of practice (www.hblb.org.uk) that has greatly assisted in disease control. Latent infections greatly complicate control measures and accurate identification of latently-infected horses has the potential to assist management decisions. Recent evidence suggests that treatment of clinical cases, including neurological disease, with acyclovir is unlikely to be clinically effective since the dosage regimes used fail to produce therapeutic concentrations \(^{(11)}\). Both killed and live-attenuated vaccines are commercially available although it is not clear that either vaccine type protects against viraemia and hence, presumably, abortion and neurological disease. The killed vaccines, marketed for protection against abortion, contain small quantities of viral antigen whereas the live-attenuated vaccines marketed for respiratory disease protection contain higher antigen concentrations. Vaccine research is aimed at producing live vaccines (either recombinant vaccines containing humoral and CTL target epitopes or modified live virus) delivered intranasally to achieve the immunological goal of a primed mucosal and systemic immune responses.

**References**