Herpesvirus is a particularly well-evolved virus that occurs in many mammals, such as humans, horses, cats, and cows. Each strain tends to be species-specific, meaning that viruses infecting one animal species do not usually infect another species. In the world of microbes, viruses are specialized in their ability to infect and survive within a host. After a virus inserts itself into a host's cells, a concert of adaptive strategies enables the virus to propagate within a herd. Although the host animal might become sick, it rarely dies; that would be counterproductive to viral continuity.

Instead, an infected animal serves as a reservoir for viral infection. Viruses are masters at the game of hide-and-seek. Some, like influenza virus, mutate to elude recognition by a host's immune response. Others, like equine infectious anemia, debilitate a host's immune system so it cannot counteract the virus. Herpesvirus has developed its own adaptation: It maintains itself within its host by evading detection by the host's immune system. And herpesvirus is unique in its ability to persist in the host in a latent form, recurring at intermittent periods that correspond with stress events.

In humans, we are most familiar with herpesvirus in the form of recurrent cold sores. In the horse, equine herpesvirus (EHV) is classified into five different strains: EHV-1, EHV-2, EHV-3, EHV-4, and EHV-5. Of these, EHV-1 and EHV-4 are the strains associated with viral respiratory disease. EHV-1 is the most prevalent concern in horse populations not only because its respiratory disease is more virulent than that caused by EHV-4, but also because it is incriminated in causing viral abortion or neurologic disease (myeloencephalopathy).

**Spread of Infection**

With a cough or a snort, an infected horse can eject aerosolized nasal secretions containing equine herpesvirus as far as 35 feet, readily passing virus from horse to horse.
Latent Infection
What makes herpesvirus peculiarly unique is its ability to persist in a latent state, reappearing at intervals through an animal’s life. Herpesvirus might be present in as many as 50% of adult horses, maintaining its presence in its hiding place within the trigeminal nerve. During the course of the latent infection, the virus resides within the cell’s nucleus, a safe haven from the immune recognition. While virus rests in a dormant state within latently infected cells, it does not turn on its machinery to replicate itself. Instead, it lurks and waits. During this stealth period while it is not expressing antigenic proteins that might alert the host to its presence, it is “silent” to the immune system, effectively escaping detection and destruction by the horse.

Direct nose-to-nose contact passes copious quantities of viral material from one horse to another, as do shared water sources that are contaminated with nasal secretions. Ingested organic material clings to feed, water tanks, stalls, horse trailers, tack, equipment, wheelbarrows, rakes, muck buckets, shoes, and clothing with the potential to move across a farm. Direct contact with an aborted fetus or placental tissue readily spreads infection due to the high concentration of virus within aborted tissues. Of key importance in transmission of this virus is exposure by carrier horses that are incubating disease and not yet showing clinical signs, or from horses that silently shed virus when a latent infection is reactivated by stress or illness.

Invasion of the Host
To understand the dynamics of effective vaccination, it is helpful to understand how herpesvirus infects a horse. Its primary attack assault is the respiratory tract within 24 hours of exposure. Virus entering these tissues attempts to attach to and penetrate epithelial lining cells of the upper respiratory tract. At that site in the respiratory lining, a horse’s immune response has its first opportunity to neutralize the virus. It can do this through protective antibodies that prevent cellular invasion, and by balancing specialized white blood cells contained within the clearance apparatus (mucociliary system) of the respiratory tract. It is here a viral immune system has the best chance of thwarting viral replication, which recognizes specific foreign proteins on herpesvirus particles before they invade the host cells. To mount an effective immune response, it is important for the respiratory lining to remain healthy and in optimal working condition. Poor air quality, dust, allergic and irritant airway disease, and other viruses create conditions that detract mightily from a host’s defensive immune function in the upper airways.

If herpesvirus breaches the defenses of the upper respiratory tract, it then follows two routes: In 48 hours it makes its way to the trigeminal nerve of the face, where it will remain as a latent infection as described previously. The other route is dissemination within 72 hours to the lymphatic and blood circulatory systems. Once virus infects a white blood cell, it is able to circulate through the bloodstream without interference from the host immune system even in the presence of high antibody titers.

Direct contact with aborted fetuses or placental tissue readily spreads infection due to the high concentration of virus within aborted tissues.

Researching herpesvirus immunity is the special focus of Cormac Breathnach, PhD, who earned his doctorate under the mentorship of Allen at the Gluck Center. Breathnach observes, “The virus evades the host antibody system, and this is why we see the abortus storm.” The potential to move across a farm in viral material clings to feed, water tanks, stalls, horses trailers, tack, equipment, wheelbarrows, rakes, muck buckets, shoes, and clothing with the potential to move across a farm. Direct contact with an aborted fetus or placental tissue readily spreads infection due to the high concentration of virus within aborted tissues. Of key importance in transmission of this virus is exposure by carrier horses that are incubating disease and not yet showing clinical signs, or from horses that silently shed virus when a latent infection is reactivated by stress or illness.

The recommended protocol for protecting pregnant mares against viral abortion is to administer herpesvirus vaccine prior to breeding, then at five, seven, and nine months of gestation.
VACCINATIONS

PART 6

Poor nutrition, a heavy parasite load, overcrowding, and rigorous climatic events are just some of the stressors that adversely affect a horse’s immune defenses.

rhinopneumonitis are poor tail tone along with fecal incontinence and urinary leakage due to, what could be, a biventer paralysis. The hind limbs become weak or hind limb coordination falters (ataxia), usually in a symmetric fashion. Many horses with EHV-1 rhinopneumonitis go down and remain recumbent with the effects of the infection lasting for one to three weeks or more. Breathnach notes, “The incidence of EHV-1 neurologic disease in the field is presumably low, even allowing for the fact that many neurologic cases may be mild and self-limiting. Again, however, some strains can apparently induce severe neurologic disease. Some virus-infected circulating lymphocytes. Use of such vaccines could be expected to reduce the number of virus particles and the decrease the risk of spread of virus to vulnerable endothelial cells.”

Of available vaccines worldwide, there are killed or “inactivated” forms and “modified live” (MLV) forms. When given intramuscularly, inactivated vaccines stimulate circulating antibodies in the bloodstream, but are not designed to effectively elicit responses at the level of the respiratory lining or within white blood cells of the cell-mediated arm of immune defense. When given intramuscularly, MLV vaccines stimulate circulating antibodies along with a cell-mediated immune response. EHV-1 gets into the bloodstream and circulates by hiding in lymphocytes and monocytes. It is therefore largely inaccessible to serum antibodies. The virus can then pass directly from infected lymphocytes to vascular endothelial cells lining the blood vessels (endothelium), and the relative inefficacy of all current vaccines for preventing infection by such aggressive strains of EHV-1 is not surprising. It is clear that improved vaccines are desirable. One thing to keep in mind is that even live virus infection of horses results in relatively short-term protective immunity. Typically a young horse that has had limited exposure to the virus can become sick, recover, then be vulnerable to re-infection within six months. With this in mind, it becomes very difficult to design vaccines that elute this protective immune system, at least if we want to keep the virus at bay. Most likely, the best we can hope for in vaccine design is to create one that is as protective as a live virus infection. To do so, we would have to create a vaccine that stimulates the various arms of the immune response that are activated by live virus infection (far more than just serum antibodies). With inactivated vaccines this is virtually impossible. Our best hope remains MLV vaccines, or recombinant subunit vaccines (where a small component of the virus is inserted into a live—but innocuous—carrier virus for vaccination). However, development of such a vaccine for EHV-1 remains years away.

Breathnach speculates on improvements in vaccine availability in the future: "While vaccine with the currently available products is important, it is clear this outdated concern to rest, saying the following: "The only MLV for EHV-1 currently approved for use by the FDA is a vaccine that is prepared from a non-neuropathogenic strain of EHV-1 and has been used for many years without any indication of causing either paralysis, abortion, or even respiratory disease. The concern about the potential for MLV vaccine to cause secondary complications is probably a belief based on the use of a neuropathogenic mutant in the 1970s, which did result in a large number of paralytic cases in vaccines." Some recent research on herpesvirus infection dynamics experiences, the potential of the currently available MLV herpesvirus vaccine to induce secondary complications in neurologic disease is innominately small.”

To Vaccinate, and With What?
The argument over equine herpesvirus vaccination is controversial. Some maintain since at least half of the horse population has already been exposed to equine herpesvirus, then vaccination cannot prevent disease, so why bother? Even with vaccines for EHV-1 that are currently available, there are sound reasons to implement a vaccination protocol. Foremost is to diminish the level of viremia and reduction of shedding of the virus. This is virtually impossible. Our best hope remains MLV vaccines, or recombinant subunit vaccines. When to Vaccinate?

When to Vaccinate?
The recommended protocol for protecting pregnant mares against equine herpesvirus infection involves the use of a non-viable vaccine prior to breeding, then at five, seven, and nine months of gestation. For this protocol, EHV-1 MLV and EHV-4 herpesvirus vaccines labeled specifically for pregnant mares. Currently, these are inactivated vaccine products, given as an intramuscular injection.

Most initial cases of herpesvirus infection occur from weaning age to 12 months, and it is speculated that 80-90% of young horses will have been infected by two years of age. If a young horse encounters herpesvirus for the first time when he’s over a year of age, he is likely to develop a serious bout of infection. In light of these facts, the best immunization strategy is to vaccinate young horses at an age until three to five months of age, a foal is unlikely to respond to vaccination due to maternal antibodies. The presence of herpesvirus bodies of passive transfer that came from a mare’s colostrum, particularly if she was vaccinated prior to foaling.

Allen says that vaccination titers are highest when a foal receives its first immunization at five months of age or older. A series of at least three immunizations should be administered to start a young horse on a herpesvirus vaccine program. For the best protection, all horses (young and old) within a herd should be properly immunized. Many vaccines target both EHV-1 and EHV-4. An adult horse should receive boosters at one to two month intervals. Frequency is dependent on the risk of exposure and the risk of stress-related travel and competition. Owners must be aware of their horse’s immunization according to manufacturer’s labels.

ABOUT THE AUTHOR

Nancy E. Lodwig, DVM, owns Lodwig Equine Clinic in Boulder, Colo., and has a special interest in managing the care of young horses. An enthusiastic endurance rider, Lodwig is a past vestry judge for the American Endurance Ride Conference and a former judge for FEI endurance events. She authored the book The Quality Horse: Horseman’s Guide to Choosing a Healthy Horse and also contributes to Horse and Rider Magazine.

Distance: The Complete Resource for Endurance Horses,

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