



Prodigy[®] vaccine with Havlogen[®]*

The Disease – Equine Herpesvirus

- EHV-1 and EHV-4 are transmitted by aerosol or by direct contact with secretions
- EHV-4 causes primarily **respiratory** disease
 - ~ 80 – 85% of EHV respiratory disease caused by EHV-4 ... more common in younger horses
- EHV-1 is the more virulent equine herpesvirus and is capable of producing **abortion, respiratory disease, stillbirths, perinatal foal death and neurologic disease** in infected animals
- EHV-1 replicates in the respiratory epithelium
 - ~ Localizes in respiratory tract lymph nodes within 2 – 3 days of infection
- EHV-1 is shed in nasal secretions (viral shedding) in large quantities during the first infection and quickly becomes intracellular ...persisting in white blood cells for days or even weeks
- EHV-1 initially enters the body through the respiratory mucosa and invades the respiratory tract
 - ~ EHV-1 may also infect endothelial cells of the fetus and/or the endometrium and placenta in pregnant mares, and of small blood vessels in the nose, lungs, brain and spinal cord, as well as circulating leukocytes, which carry the virus to other parts of the body where it can cause abortion or neurologic disease
- EHV-1 induces lifelong latent infection in the majority of exposed horses
 - ~ Establishes latency in cytotoxic T lymphocytes, local lymph nodes and trigeminal ganglion
 - ~ Recrudescence of EHV-1 may cause clinical signs of respiratory disease, abortion and cell-associated (CTL) viremia and nasal shedding

The Goal – Management & Prevention

- Reduce nasal discharge and viral shedding between horses
- Reduce dissemination of virus within the infected horse
 - ~ Neutralize free virus (VN antibody titers) at mucosal surface and free virus circulating in the blood
 - ~ Stimulate production/activation of cytotoxic lymphocytes (CTL) in order to lyse virus infected cells in the upper respiratory tract (URT) and in lymphocytes
 - ~ IFN γ production is used as a marker of T cell activity
- EHV vaccines are currently labeled as an aid in the prevention of abortion or respiratory disease associated with EHV infection
 - ~ No EHV vaccine is labeled for prevention of neurologic disease

Prodigy® – Proven Results

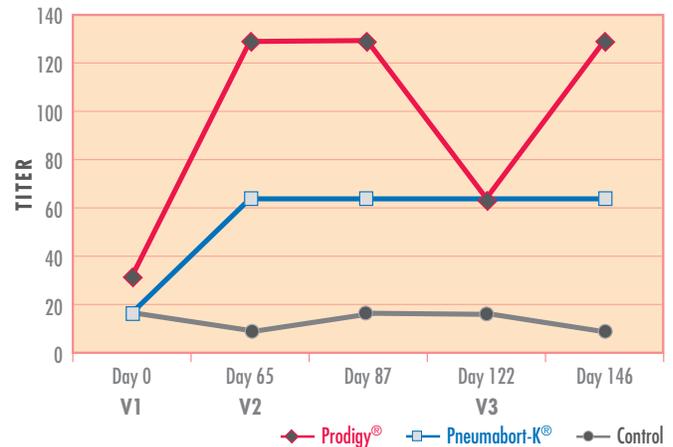
- In a severe EHV-1 challenge study, Prodigy-vaccinated mares demonstrated a **96.1% reduction in virus shedding** from nasal exudates¹

Virus Isolated from Nasal Swabs Following Intranasal Challenge With EHV-1 Virus



- In an independent research study, Prodigy produced a **statistically significant EHV-1 antibody response** (VN antibody titers)²

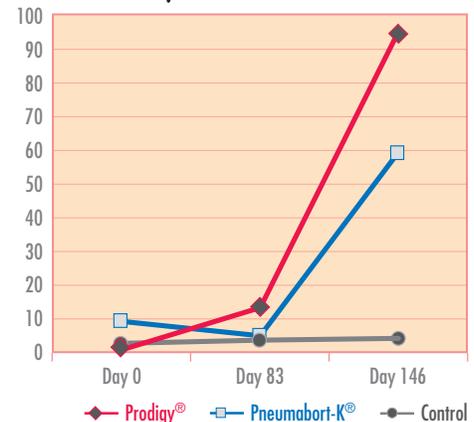
EHV Virus Neutralization Median Titers



- In an independent research study, Prodigy produced a **statistically significant IFN-γ response**²

~ Cytokine, ie: IFN-γ response, can be a useful surrogate for quantifying cytotoxic lymphocyte responses³, shown to be a measure of cell-mediated protective immunity (CMI) to EHV-1 infection⁴

IFN-γ Stimulation Index



Conclusion

Prodigy® reduces nasal discharge and virus shedding, produces a superior VN antibody response and stimulates a cell-mediated immune (CMI) response, suggesting that it generates a comprehensive immune response for protection from EHV-1 infection.

¹ Intervet Research Data

² Holmes MA, Townsend HGG, Sussey S, Breathnach C, Barnett C, Holland RE, Lunn DP: Immune responses to commercial equine vaccines. AAEP Proceedings, Vol. 49, 2003.

³ Murali-Krishna K, Altman JD, Suresh M, et al. In vivo dynamics of anti-viral DC8 T cell responses to different epitopes. Adv Exp Med Biol 1998; 452: 123-142.

⁴ O'Neil T, Kydd JH, Allen GP, et al. Determination of equid herpesvirus 1 specific, CD8+ cytotoxic T lymphocyte precursor frequencies in ponies. Vet Immunol Immunopathol 1999; 70:43-54.

* Adjuvant - Intervet's proprietary technology.