

Recent advances in the development of a Hendra virus horse vaccine

By Dr Peter Reid



Professor Chris Broder, USU, Bethesda, Maryland USA with Dr Reid

There are currently no registered human or veterinary therapies or vaccines for the treatment or prevention of HeV or NiV infection. The International Henipavirus Workshop held in Queensland in October 2009 was co-sponsored by the World Health Organisation (WHO) and the Food and Agriculture Organisation of the United Nations.

Major clinical recommendations made to WHO as a result of that Workshop were that "Vaccination for horses should be prioritised for Hendra control" and "Further clinical studies were needed to evaluate the safety and effectiveness of therapies for treatment and post exposure prophylaxis".

Because of the lethality and broad tropism of the viruses, particularly the affinity for the central nervous system, the window of opportunity for successful treatment after exposure or infection is currently unknown and is likely to be very narrow. In the unfortunate circumstance that a person does become exposed or infected then we need to know the best treatment options available, based on the latest cutting-edge research.

HeV horse vaccine development

The possibility of preventing HeV infection in horses by effective immunisation will be a far better option than trying to treat human infection from horse-to-human transmission. Two potential vaccine candidates have been identified with the soluble G glycoprotein (sG), which contains no RNA genetic material, and was identified in 2006 as a potent immunogen in vaccine



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trials using cats as the experimental model (Mungall et al 2006). In mid-2010, approval of \$600,000 was received from the Queensland and Australian Governments for the conduct of HeV horse vaccine trials at the Australian Animal Health Laboratory (AAHL) under the leadership of Dr Deborah Middleton. After rigorous safety testing and a concerted

collaborative effort between Professor Christopher Broder from the Uniformed Services University of the Health Sciences, Bethesda, Maryland, USA, a USA pharmaceutical company and AAHL, an adjuvanted HeV soluble G (HeV sG) vaccine was eventually made available to AAHL's scientific team and the first phase of the horse vaccination trials commenced in mid-October 2010. This was a monumental event in the fight against HeV which first emerged 16 years previously.

A primary vaccine dose followed by a booster after 3 weeks resulted in increasing titres of serum neutralising anti-Hendra antibodies. These vaccinated animals were fully protected and survived a lethal oronasal live virus challenge 3 weeks later. In subsequent testing there was no evidence of viral replication in any of the tissues examined in the vaccinated animals. (D Middleton pers. comm.) The control (unvaccinated) animal developed fulminating lethal disease identical to that seen in a previous 2008 live virus challenge study (Middleton 2008).

The other vaccine candidate, the ALVAC canarypox vectored recombinant subunit coding for Hendra G and Hendra F glycoproteins has also been identified as a potential vaccine candidate against HeV based on the effectiveness of this platform of delivery in immunisation trials against NiV using pigs (Weingartl et al 2006).

Canarypox virus (ALVAC) vaccine vectors induce antibody and cytotoxic T-cell responses and were used in Australia in 2007 as the vaccine viral vector for the highly successful control and eradication of equine influenza virus in Australia.

Significant steps are being made towards making HeV horse vaccine a commercial reality but full funding and evaluation of vaccine candidates for efficacy, safety, immunogenicity, duration of immunity and subsequent field trial testing is crucial. The Queensland Horse Council www.qldhorsecouncil.com has established a special Hendra Virus Horse Vaccine Development Fund where all donations are forwarded to AAHL for this purpose.

Conclusion

Practitioners should remain focused on the risks that Hendra virus represents to personal safety and should never be lulled into a false sense of security even if an outbreak does not occur for several months. Based on the known pathogenesis and lethality of the virus, there is likely to be only a narrow window of opportunity for prophylaxis after exposure or treatment after confirmed infection; and the effectiveness of current modalities is still uncertain.

For this reason, prevention is better than cure, and a safe, effective horse vaccine will provide additional protection in addition to the adoption of good personal biosecurity practices.



Hendra Virus sG horse vaccination trials commence in October 2010 at the Australian Animal Health Laboratory- a monumental event.