



FOCUS ARTICLE: HENDRA VIRUS INFECTION: AN EMERGING DISEASE OF HORSES AND HUMANS

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In September 1994 an emergency response was initiated to investigate an outbreak of acute, fulminant respiratory disease in a group of racehorses in South-Eastern Queensland, Australia. After ruling out African Horse Sickness, virologists from the Australian Animal Health Laboratory identified a new virus, which was initially called equine morbillivirus, but subsequently named Hendra virus after the Brisbane suburb of Hendra where the outbreak occurred. Hendra virus is now classified in the Henipavirus genus in the Family Paramyxoviridae. This first outbreak affected 20 horses, 7 of which died within 12 hours of showing any clinical signs of illness. Unfortunately, the outbreak also affected two people, one of whom, the trainer in charge of the stable, subsequently died. Although it was not known at the time, these people were not the first to be infected by the Hendra virus. In August 1994 a veterinarian in the north Queensland town of Mackay conducted a post-mortem examination of a horse that had died suddenly. The veterinarian's husband, who assisted with the necropsy, developed a fever and other "flu-like" symptoms shortly afterwards and although he recovered from this acute episode, he subsequently died from Hendra virus encephalitis some 14 months after the original infection.

Following the original outbreak in Hendra a large-scale investigation was conducted to identify the source of the virus and any potential reservoir or vector species involved in the epidemiology of the disease with a view to preventing any further outbreaks. Serological studies of a very large number of possible vertebrate host species in and around the racing stables found no evidence of Hendra virus infection in cats, dogs or horses in stables other than the outbreak stable, but antibodies to Hendra virus were found in local fruit bats. Subsequent studies have found that the natural reservoir of Hendra virus is fruit bats of the genus *Pteropus* in the Order Chiroptera. There are four species of these bats distributed around the northern and eastern coast of Australia, and all four species have serological evidence of Hendra virus infection. Hendra virus has been detected in foetal and neonatal lung and from uterine fluid and renal tissue of adult bats. Hendra virus has also been detected in bat urine and faeces. From these data it is proposed that horses become infected from being exposed to virus infected bat faeces, urine or birthing fluids when sheltering or feeding under trees in which bats are roosting. Currently, it is not understood precisely how Hendra virus jumps species from bats to horses. It is also not known how Hendra virus is transmitted from horses to humans, or indeed if infection of horses is necessary for human infection to occur, although all human cases to date have been linked to clinically infected horses. There are many investigators around the world currently studying bat paramyxoviruses, such as Hendra virus and the closely related Nipah virus, in order to improve our knowledge of how these viruses infect humans.

Between the first outbreak in 1994 and 2008 there were a number of individual cases of equine sudden death that were diagnosed, following post-mortem examination and further testing, as Hendra virus deaths. Fortunately, these were all single horse events with no associated human infection. In 2008, however, another multiple horse outbreak was reported, this time in a veterinary hospital in Brisbane. In this outbreak, all horses were in residence at the veterinary hospital at the commencement of the outbreak and affected horses presented with signs of central nervous system disease, rather than the previously reported signs of respiratory



disease. Five horses were affected, out of a population of more than 30 horses. Four of the five horses were so severely ill that they were euthanased for humane reasons. The surviving horse was also euthanased due to public health concerns. In this outbreak a veterinarian and a veterinary nurse became infected, both were admitted to hospital and the veterinarian subsequently died from viral encephalitis. It was likely that both affected people were exposed to the virus prior to the infected horses showing any obvious clinical signs of disease.

The 2008 outbreak in Brisbane highlighted the risks facing veterinarians and veterinary staff due to the lack of knowledge regarding mode(s) of transmission of Hendra virus from bats to horses and from horses to humans and the appropriate preventive methods they need to take. Experimental challenge studies to describe the pathogenesis of Hendra virus infection in horses and the routes of virus excretion were conducted, but unfortunately, before these results could be widely disseminated another veterinarian, in Rockhampton, was exposed to Hendra virus, and subsequently died from viral encephalitis, after performing an endoscopic examination on a clinically normal horse.

To date, of the seven people confirmed to have been infected with Hendra virus, four have died. The case-fatality rate in horses is approximately 80%, and the horses that have survived the acute stage of disease have been euthanased subsequently for public health reasons. Another two incidents of equine Hendra virus infection have been reported in 2009 and 2010. No human cases have been diagnosed in either event, but tests are still ongoing on the people exposed in the most recent episode.

Horse infection studies have been conducted recently at the Australian Animal Health Laboratory high biosecurity facility. Horses were exposed to Hendra virus via the respiratory tract and swab samples collected to determine the route of virus excretion. While no infectious virus was detected in tissue culture assays prior to onset of clinical signs, the nucleic acid of Hendra virus was detected by polymerase chain reaction (PCR) in nasal and oral swabs, as well as in blood and urine prior to the onset of fever. Samples collected from the respiratory tract of the experimentally infected horses were consistently PCR positive following the first febrile episode until they were euthanased on humane grounds. Samples were collected from multiple organ systems during post-mortem examination and infectious virus was isolated from a large number of tissues indicating that during infection the virus spreads widely throughout the horse's body. Importantly, however, there were large amounts of virus detected in the endothelial cells lining the blood vessels of the mucosa of the upper respiratory tract, which may explain how veterinarians performing endoscopy or lavage procedures might become exposed to infectious virus prior to the onset of obvious clinical signs.

No vaccine is currently available to protect either horses or humans against disease caused by Hendra virus. There are several groups working towards a vaccine and hopefully clinical trials will be commenced in the near future, now that funding has been secured from the Queensland state Government and the Australian federal Government.

Hendra virus is an important emerging disease of horses and humans and highlights the disease dangers that arise when humans and their companion animals move into ecological niches previously only occupied by native animals and their attendant viruses. Unfortunately, we know little to nothing about the viruses carried by most wildlife species until there is a spill-over of one of their viruses into humans or our domestic animals and a "new" disease appears, as has occurred several times in recent years.