

# **Research Update: Hendra Virus**

## Overview

Hendra virus was first isolated in 1994 from an outbreak of disease in a racing stable located in the northern Brisbane suburb of Hendra less than 10km from the city centre. The outbreak resulted in death of a horse trainer and 13 horses and left a stable hand seriously ill. A further seven horses with evidence of exposure to the virus were humanely destroyed to avoid possible further spread of the disease. Subsequent incidents from the north of Queensland in Cairns to the New South Wales border at Murwillimbah have led to the deaths of a further three people and 22 horses. Despite these periodic and ongoing incidents, Hendra remains one of the world's rarest diseases.

Scientific evidence suggests that Hendra virus is carried by flying foxes. Under unknown but rare circumstances, the virus spills over from these bats to susceptible horses, killing over 70% of the horses it infects. Under even rarer circumstances, the virus spreads to humans who have had very close contact with Hendra infected horses. While there is strong evidence to support this mode of transmission (bat-to-horse-to-human) there is no evidence of bat-to-human, human-to-human, or human-to-horse transmission of the virus.

Hendra is a notifiable disease and suspected infections must be reported to the Emergency Animal Disease Hotline on: 1800 675 888. Signs to suggest horses may be infected with Hendra virus include acute onset, increased body temperature, increased heart rate, and rapid progression to death associated with either respiratory or neurological signs. See Guidelines for veterinarians handling potential Hendra Virus infection in horses. Download available on: http://www.dpi.qld.gov.au/cps/rde/dpi/hs.xs I/4790 13371 ENA HTML.htm

Since Hendra virus was first isolated, significant progress has been made in understanding the virus, where it originates in nature, and how to detect infection and past exposure. Shortly after the September 1994 outbreak, researchers isolated and characterised the virus, developed laboratory tests to detect infection in both humans and animals, and identified the likely source of the virus. Processes have been put in place to reduce the likelihood of outbreaks based on the knowledge obtained from these studies.

While there have been significant gains in knowledge about Hendra, much remains to be learnt. Ongoing studies address the nature of the infection in bats including how and where infection occurs, how Hendra persists in bat populations, and how the virus is transmitted to horses and subsequently to humans. As new technologies are developed, better laboratory tests will be designed to detect and monitor past and current infections. And future research will be directed towards developing better outbreak prevention and control, and potential vaccines and treatments.

# Hendra virus incidents

Since 1994, there have been 13 identified incidents of Hendra virus infection in horses. In each of these incidents the first confirmed cases (known as the index cases) were housed in paddocks or yards, not stalls or stables. Seven incidents were single horse events, with infection identified in the index case alone. Two incidents involved the infection of one or more companion horses after close contact with the index case. The remaining four incidents involved both horses and humans. After close contact with infected horses, three people developed an influenza-like illness and recovered. Another four people died from influenza-like illnesses and encephalitis (inflammation of the brain).

The incubation period (time from exposure to the appearance of the first clinical signs of infection) of Hendra virus in horses is five to 16 days. Fatally infected horses died on average two days after the first sign of infection. While approximately 25% of horses are thought to survive acute infection, the current national policy requires these horses to be euthanased. The incubation period in humans is believed to be five to 14 days. As four of the seven people infected have died, the current human case fatality rate is more than 50%.

# Incident 1:

Mackay, August 1994. Not recognised until the death of the farmer who had assisted his veterinarian wife with an autopsy of two horses that died of unknown causes. The farmer appeared full recovered after hospitalisation but relapsed and died 13 months later. Retrospective testing showed the horses were infected with Hendra.

# Incident 4:

Redlands, June 2008.

A veterinarian and veterinary nurse at the Redlands Veterinary Clinic were infected after close direct contact with infected horses. The veterinarian tested positive for Hendra virus and died in August after spending several weeks in intensive care. The veterinary nurse also spent several weeks in intensive care but was later discharged.

#### Incident 3:

Gordonvale, October 2004. A veterinarian tested positive for Hendra virus after performing a post mortem on a horse that died suddenly. While no samples were available from the horse for testing, the clinical and post mortem signs were consistent with Hendra virus infection.

#### Incident 2:

Hendra, September 1994. Resulted in the death of a horse trainer, 13 of his horses, and caused severe febrile illness in a stable-hand. The trainer had very close physical contact sick horses, as did the stable hand.

# Incident 5:

Cawarral, August 2009. A Queensland veterinarian died in September after being exposed to Hendra. Infection has been confirmed in two horses that died recently and another had to be destroyed after returning a positive test. The incident was discovered after a property manager and a local veterinarian alerted Biosecurity Queensland with the death of a horse suffering from respiratory distress.

Figure 1: Details of all Hendra virus incidents associated with human cases.

Date	Location	Deceased or euthanised horses	Positive human cases	Human deaths
August 1994	Mackay, Queensland	2	1	1
September 1994	Hendra, Queensland	20	2	1
January 1999	Trinity Beach, Queensland	1		
October 2004	Gordonvale, Queensland	1	1	
December 2004	Townsville, Queensland	1		
June 2006	Peachester, Queensland	1		
October 2006	Murwillumbah, New South Wales	1		
June 2007	Peachester, Queensland	1		
July 2007	Clifton Beach, Queensland	1		
July 2008	Redlands, Queensland	8	2	1
July 2008	Proserpine, Queensland	4		
August 2009	Cawarral, Queensland	3	1	1
September 2009	Bowen, Queensland	1		
Total		45	7	4

# Table 1. Summary of Hendra virus incidents

The likely route of transmission of Hendra virus from bats-to-horses has yet to be identified but does not appear to involve other domestic animals or wildlife. Horse-to-horse transmission of the virus is plausible, as a proportion of incidents involved infection of both the index case and companion horses. In these incidents, transmission of the virus appears to have been more efficient in horses housed in stables or stalls. The possibility, however, that companion horses were infected as a result of separate bat-to-horse transmissions cannot be ruled out.

Transmission of the Hendra virus from horses-to-humans is rare. The greatest risk of human infection appears to be through the direct physical contact with the body fluids of ill, dying or dead horses. As evidence suggests that horses have a potential to excrete virus through nasal secretions up to two days before showing signs of infection, contact with apparently healthy horses early in the early stages of disease may also pose a real but lesser risk of infection.

# Identification of Hendra virus

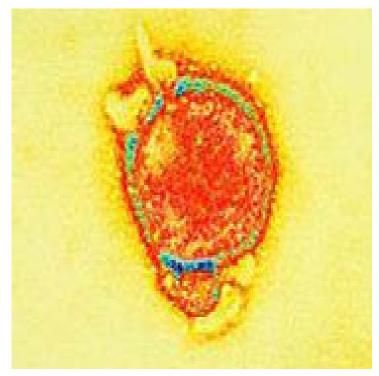
After the outbreak at the Hendra stables in Brisbane in September 1994, quarantine and movement restrictions were immediately put into place and the horse racing industry in southeast Queensland was temporarily shut down. The epidemiological investigations that followed focussed initially on possible toxic agents and known viruses that produce similar symptoms in horses. These tests were negative, so samples taken from sick and dying horses were then analysed for infection by an unknown virus.

For more details about PC4 laboratories (also known as BSL4) see http://www3.niaid.nih.gov/topics/Bio defenseRelated/Biodefense/Public Media/labtour/

For more details about the PC4 laboratory at CSIRO AAHL where the Hendra virus is handled see: http://www.csiro.au/resources/psd6

As the suspected virus had caused a human death, the virus was cultured in a Physical Containment Level 4 (PC4) laboratory. PC4 laboratories provide the highest level of biological containment, These enclosed facilities are designed for the safe handling of highly infectious biological agents and materials. Within weeks of the outbreak, the virus was isolated from cell culture. Identical viruses were also isolated from the cell cultures of samples taken from the first human case and horses experimentally infected with the virus.

The virus was characterised using a number of laboratory procedures following its isolation. Visualisation of the virus in affected horse and human tissues by electron microscopy confirmed that virus was the causative agent of the outbreak. The virus was shown to infect a wide range of cells, but predominantly the endothelial cells which form the thin, inside layer of blood vessels. Combined with genome sequencing data, this work led to the reclassification of the virus as a member of the Paramyxoviridae - a diverse family of large RNA viruses including mumps and measles viruses. The provisional name for the virus, equine morbillivirus, was subsequently discarded and the virus was renamed Hendra after the Brisbane suburb where the horses were stabled in the September 1994 outbreak. Rapid molecular tests to detect the virus were developed using the sequence data.



Artificially coloured Hendra virus electron micrograph Courtesy AAHL Biosecurity Microscopy Facility.

Further molecular analysis showed this virus was sufficiently different from existing paramyxoviruses to warrant the creation of a new genus within the family. This new genus, the Henipaviruses, now includes Hendra virus and Nipah virus which both have genomes up to 15% larger than other paramyxoviruses. In addition to a number of unique molecular characteristics, these viruses are distinguished from other members of the Paramyxoviridae family by their ability to infect a broad range of species and fatally infect both animals and humans.

Nipah virus emerged in pigs and humans in Malaysia. Since then over 470 known human infections and over 240 deaths have been linked to outbreaks of Nipah in Malaysia, Singapore, Bangladesh and India. Pteropid bats are thought to be the natural reservoirs of the virus. There have been no reported outbreaks in Australia.

For more details about Nipah see: www.who.int/mediacentre/factsheets/fs

Serological studies confirmed that horses and humans affected in the outbreaks had been exposed to Hendra virus. Serum antibodies are formed in response to viral infection. By immunoelectronmicroscopy, Hendra virus was shown to be neutralised with antibodies from the blood of symptomatic horses and humans, confirming these animals had been exposed to the virus. Serum neutralisation tests showed the growth of the virus in cell culture could be halted by these antibodies.

## **Reservoir hosts**

After isolating Hendra and developing a number of specific diagnostic tests for the virus, extensive investigations looked for the source of the virus in nature. Early research focussed on animals present in the locations of index cases found no evidence of Hendra virus infection. The search was then broadened to include sick or injured wildlife in temporary captivity. A total of 168 animals (from more than 16 species of rodents, marsupials, birds, amphibians, and insects) returned negative antibody tests. Retrospective investigations of diagnostic laboratory records and stored specimens from horses failed to identify any sign of previous infection.

Pteropus bats, also known as flying foxes or fruit bats, are mammals and members of the Pteropididae bat family. They have the largest body of all bats. Four species of these mammals are native to mainland Australia; the little red flying fox (Pteropus scapulatus), black flying fox (Pteropus alecto), grey-headed flying fox (Pteropus poliocephalus) and spectacled flying fox (Pteropus conspicullatus).

For further information about flying foxes see: http://www.dse.vic.gov.au/dse/nrenpa.nsf/FID/-BAA86C6B029BC723CA256BF2001E4069?O A multidisciplinary task group reviewed the available laboratory and epidemiological data for clues to which animal or animals may harbour the virus in nature. Flying foxes were targeted for further investigation because they fulfilled the criteria of the possible viral reservoir host. They were present in both of the locations of the incidents at Hendra and Mackay, were capable of moving between and/or had overlapping populations spanning these two locations, and could plausibly have had indirect contact with horses at both locations. By early 1996, sampling of sick or injured flying foxes in temporary captivity showed that several

species of Australian flying foxes had antibodies to Hendra virus. Broader serological surveillance revealed antibodies to the virus in all four mainland pteropid species – the black, grey headed, little red and spectacled flying foxes. The theory that the risk of bat-to-human transmission of the virus is low was supported when wildlife carers in close and regular contact with sick and injured bats showed no evidence of Hendra virus infection.

Further sampling throughout eastern Queensland involving over 5000 sera samples collected from 46 species (including 34 species of wildlife) found no evidence of antibodies in species other than the horses and humans involved in incidents and flying foxes. No domestic animals tested have shown any signs of Hendra virus infection.



Sampling bat saliva, Photo: Dr. Andrew Breed

Ongoing research supports the theory that flying foxes are the natural reservoir of the virus. In September 1996, live Hendra virus was isolated from a grey-headed flying fox euthanised after becoming tangled and injured in a wire fence. This bat had recently aborted twin foetuses and virus was also isolated from a pooled sample of tissue collected from the foetuses. A third viral isolate was obtained from the lung of a foetus collected from a black flying-fox which had been euthanised for spinal injuries. It has been detected periodically in urine samples collected under flying fox roosts. Surveys of 1043 flying foxes in Queensland between 1996 and 1998 showed evidence of exposure to Hendra virus in 47% of the bats sampled. Similar frequencies have since been observed in samples taken from flying foxes across mainland Australia. Antibodies have also been detected in archived blood samples taken from flying foxes in the 1980s.

The high frequency of Hendra antibodies observed in flying foxes suggests transmission of the virus between these bats is efficient. Flying fox camps often consist of thousands of bats roosting together in the canopy of trees. In these dense roosts, bats excrete urine and faeces throughout the day and a fine mist of urine is commonly observed. Under these conditions, and given their regular grooming activities, transmission from one bat to another in the roost is highly plausible.

It is less clear if Hendra virus is maintained within flying fox colonies as an acute or ongoing infection. Computer modelling of flying fox populations suggests that Hendra virus does not persist as a constant endemic infection in discrete populations of bats, but persists throughout the range of flying foxes in a pulsing pattern. In this pattern of infection, a nomadic individual or small group of bats from an infected colony may make contact with a colony of flying foxes susceptible to infection either because they have not yet been exposed to the virus or

their immunity has waned. These nomadic bats then introduce (or reintroduce) the virus to bats within the susceptible colony, resulting in an increase (or pulse) of infection followed by a period of waning immunity.

Little red flying foxes may play a key role in this pattern of pulsing endemicity of Hendra infection, making them a possible key reservoir of the virus. A rapid decline in immunity to Hendra virus was observed between seasons during a study sampling flying foxes over two years from 2004. Periods of waning immunity may correspond to times when these bats are susceptible to infection. This is in contrast to two other Australian flying fox species. Both the grey-headed and spectacled flying foxes appear to develop long lived immunity to the virus.

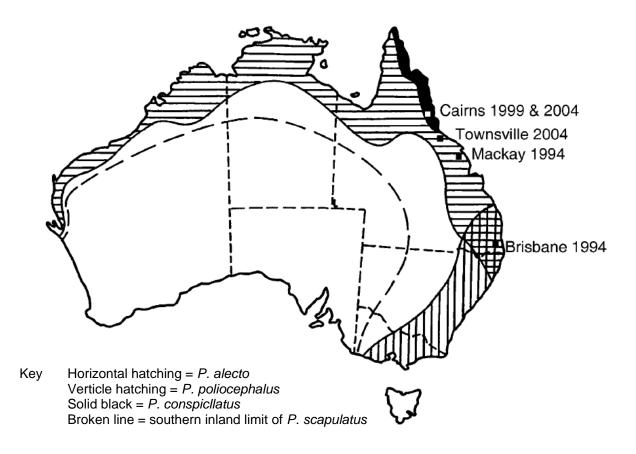


Figure 2. Distribution of flying foxes on mainland Australia and location of Hendra virus spillover events to horses.

Adapted from Hall and Richards, 2000 by Field et al 2007. Used with permission.

The exact mechanics of Hendra virus transmission from flying foxes to horses is not known as no virus has been isolated from flying foxes during incidents. However transmission of the virus to horses is thought to be through the ingestion of grass or partially eaten fruit contaminated with bat urine, saliva or other bodily fluids. The timing of Hendra virus infection in horses may then be linked to the pattern of pulsing endemicity in flying foxes. A period of the peak virus excretion may follow the introduction of infection to a susceptible bat colony. This period is likely to correspond increased risk of exposure and infection of susceptible horses in the vicinity.

Contact with Hendra infected bat birthing products may also be a significant route of infection for horses, suggested by the coincident timing of a number of Hendra virus incidents with the birthing seasons of Australian flying foxes and the isolation of the virus from the uterine fluid and aborted foetuses of grey headed flying foxes.

All reproducing female little red flying foxes, including near-term pregnant and lactating females, are thought to be susceptible to Hendra infection. A three year study of little red flying foxes, found that reproduction and nutritional stress were important drivers of Hendra virus infection, plausibly associated with immune system compromise during these periods. Infection risk in flying foxes is also high at times of nutritional stress. Food availability is disturbed and nutritional stress caused in flying fox populations through habitat loss and alteration, roost disturbance, urbanisation and being hunted. These times may therefore also represent an increased risk of transmission of Hendra virus from bats-to-horses.

Diversity and distribution of flying foxes in Australia are two other factors which may contribute to transmission of the virus from bats-to-horses. The large numbers of little red flying fox populations in Australia have an extensive distribution that overlaps geographically with all known Hendra incident locations. While this supports the theory that these bats may be the key reservoir host for Hendra, all known incidents of Hendra virus infection have been limited to north eastern Australia. And while it is possible that wherever flying foxes and horses are found in close proximity there may be a risk of bat-to-horse transmission, the geographical range of flying foxes with proximity to horses is much broader than north eastern Australia. This suggests that Hendra virus infection in flying foxes, and/or the risk of spill over to horses, may be related to the type or mix of flying foxes in this region. It may not be coincidental that North eastern Australia has the greatest diversity of flying fox species, the spectacled flying fox is found only in this region, and the eastern distribution of the black flying fox does not extend past northern New South Wales.

Further investigation of both the dynamics of Hendra virus infection in flying foxes and the mode of transmission to horses is clearly required to determine which factors play a role in flying fox infection, and the timing and location of virus spill over from bats-to-horses. An understanding of these factors is likely to improve management strategies which seek to minimise the opportunity for contact between bats and horses and reduce transmission of the virus.

## Improved laboratory tests for Hendra virus

There has been significant advances in test development and the application of these tests to human and animal surveillance since the first serological and molecular tests were developed to detect Hendra virus, A program of basic Hendra virus research and development has increased Australia's capacity to rapidly and accurately diagnose this disease. International capacity to detect Hendra virus has also been improved by sharing methods and reagents developed in Australia with laboratories in America, Malaysia and beyond.

The original molecular test developed for Hendra virus detection used a particular combination of polymerase chain reaction (PCR) techniques, reverse transcription and nested PCR. New tests still use reverse transcription but the innovation of real time PCR makes the test much faster, requiring significantly less viral material. Further refinements allow these tests to distinguish Hendra virus from Nipah virus which is important for disease control and prevention.

A number of Hendra virus isolates have been fully sequenced. Prior to 2006, the gene sequence of these viral isolates were virtually identical, irrespective of the species from which they were recovered, the location of the incident, or the time of recovery. In more recent incidents, genetic differences have been detected between the isolates and those sequenced previously. While it is possible the virus may be changing, it is more likely that flying foxes have carried this virus for a long time and over the years variants have evolved. As more isolates

are identified and sequenced, the likelihood of detecting these variants increases, hence the observed differences. These genetic variations could explain the range of clinical symptoms observed in infected horses across the 11 incidents. However, recent experimental studies suggest these variations are more likely due to differences in the route of Hendra infection or the system that is first compromised in an infected horse.

Molecular tests for Hendra are fast, accurate and sensitive, but they are only effective in detecting virus when it is present at the time of testing. As viruses usually disappear in infected individuals a few days after infection, PCR tests are ineffective in the longer term. Antibodies, however, are detectable long after infection, so serological assays are effective in detecting viral exposure over long periods.

While the serum neutralisation test remains the gold standard for detection of an antibody response to Hendra virus infection, other serological tests have been developed that do not use live Hendra virus either directly in the assay or in the preparation of the assay reagents. Enzyme linked immunosorbent assays (ELISAs) developed shortly after the serological studies of the September 1994 outbreak have been particularly useful for serological surveillance. Early in the development of these ELISAs, non-containment laboratories performed the assays using virus that had been cultured and irradiated for safe use. However, preparation of the viral reagents for

The enzyme linked immunosorbent assay or ELISA measures antibody concentrations in serum samples by immobilising a known amount of inactivated virus (antigen) onto the bottom of a well in an ELISA plate. This viral antigen is then used to capture and quantify specific antibodies present in the samples.

For a more detailed description of ELISA tests see: http://en.wikipedia.org/wiki/ELISA

use in the ELISA still required cell culture-based growth of the virus in a PC4 laboratory. A number of recombinant Hendra virus antigens have subsequently been developed for use in these tests. Production of antigen using these methods provides test reagents that are robust, specific, and affordable. Importantly, they can be also be produced and used in non-PC4 environments.

More recently, another serological assay using bead-based flow cytometry has been developed to detect and differentiate antibodies against Hendra virus and Nipah virus in a single test. Also using recombinant antigens, this test represents a significant advance in serological capability in Australia.

Despite significant advances in laboratory testing for Hendra virus, viral isolation in cell culture remains an important diagnostic tool, especially in a new case or outbreak when isolation of the virus is sought for absolute confirmation of the disease. Despite advances in technology that allow for Hendra tests to be developed and performed independent of PC4 facilities, the virus remains classified as a PC4 pathogen because of its high case fatality rate in humans and lack of effective vaccine or therapy.

#### **Disease Control & Animal Management**

Control of Hendra virus infection has focussed on strategies for managing infected horses. When Hendra virus infection has been confirmed, the premises involved are quarantined and the disease investigated. Measures are put into place to care for the animals on the premises, to reduce the risk of transmission to people and other horses, to disinfect the environment, and safely dispose of infected horses that die or are euthanised.

Other management strategies are used to reduce the opportunity for contact between bats and horses, to monitor horses and other species for evidence of infection, and improve biosecurity in areas at risk of infection.

Significant effort has also been made to improve awareness of Hendra virus, particularly for veterinarians, horse handlers and wildlife carers.

Studies suggest that at least 290 plant species worldwide rely on large populations of flying foxes for propagation. The indiscriminate or targeted killing of flying foxes is not considered as an effective Hendra virus management strategy. As these bats are nomadic, culling may create a niche that other bats fill, possibly increasing rather than decreasing the number of flying foxes in the target area. Culling could also contribute to altering the ecology of the region as flying foxes play a key role in the pollination and seed dispersal for a large number of plants. And while flying foxes remain relatively conspicuous in some areas, many of their current populations are in rapid decline and require protection.

## **Experimental models**

The key to understanding Hendra viruses may lie in studying suitable animal models of the disease. Early experimental infections of horses and bats conducted with virus isolated from the September 1994 outbreak confirmed that this virus was the agent responsible for the outbreak. Further experimental infections have also been undertaken to study replication of the virus, antibody development, virus shedding, transmission, and pathogenesis.

Flying foxes infected with Hendra virus show no clinical signs and appear to be unaffected by the virus. It has been suggested that the immune system of bats is special, and allows them to sustain viral infections in the absence of overt disease. This has yet to be established.

Work is ongoing to learn more about bats' immune systems.

Hendra virus has an affinity for endothelial cells and infection in horses

causes inflammation of the blood vessels (vasculitis) throughout the body. The spectrum of respiratory and neurological clinical signs observed in various infected horses is thought to be a consequence of this vasculitis in different body systems. So the organ or system where the greatest vascular damage lead to the first clinical signs linked to these observed in this horse. The detection of viral genetic material in the blood, nasal secretions and a wide range of body tissues of infected horses indicates that by the time a horse shows clinical signs of infection the virus is widespread throughout the body. Most virus is shed from these horses when they are sickest, suggesting that this is the time when transmission is most likely. However, studies have also shown that a horse can potentially excrete the virus through nasal/naso-pharyngeal secretions at least two days prior to the appearance of clinical signs.

Experimentally infected flying foxes develop a viraemia (where the virus enters into the blood stream) then excrete the virus in their urine, faeces and saliva for approximately one week. But unlike horses, there is no indication of illness in these bats.

Experimental infections have also been performed to preclude certain animals as carriers of the disease. Mice, rats, rabbits, chickens, and dogs do not develop disease following inoculation with the virus. In contrast, cats and guinea pigs are highly susceptible. The cat has been the preferred choice for experimental studies of Hendra virus infection. Experimentally infected cats develop symptoms of Hendra virus that closely resemble the lethal respiratory disease in humans and horses and they are easier to manage under PC4 conditions than large domestic animals such as horses. However ferrets are now becoming the preferred animal model because of their ease of handing. While the susceptibility of cats to experimental infection raises the possibility

that cats may play a role in the transmission of this virus to horses, no evidence of natural infection has ever been found in cats.

Horses, bats and cats have also been used to examine possible routes of virus transmission between susceptible animals. In these laboratory studies, the virus shows low levels of transmissibility under most circumstances. Attempts to recreate transmission have been largely unsuccessful in cats-to-cats, cats-to-horses, bats-to-bats, bats-to-horses, horses-to-horses and horses-to-cats.

Further studies have shown that the virus does not survive for extended periods after excretion from infected animals. There has been very little virus detected in urine collected from the floor of horse stalls containing horses with high levels of virus in their bladder urine, and research into persistence of the virus under various environmental conditions suggests the virus is highly sensitive to temperature and dessication. These results suggest that natural transmission is likely to require close contact with an infected animal or exposure to contaminated material shortly after excretion.

#### Vaccines and Therapy

There are currently no vaccines or drugs for preventing or treating Hendra virus infection. Development of these agents has been hampered by a lack of knowledge about the initial sites and duration of virus replication following infection and issues associated with funding vaccine development for a rare disease. However, a number of vaccines and drugs are in the pipeline and it is likely that animal models will be particularly useful in both the development and testing of these new therapeutic agents.

The proteins involved in Hendra virus infection have also been studied in detail as these proteins may provide clues to blocking infection. Viral proteins, which have been crystallised and their structures and genomic sequences determined, could possibly be used to reduce infection by preventing viral entry into cells. Because both attachment to cells and fusion are critical steps for infection, therapeutic agents that block either process could be used as antiviral drugs. To date, the most extensively characterised novel therapeutic agents for Hendra target the host cell protein that binds the virus, ephrin B2.

Advances have also been made in the development of possible Hendra virus vaccines. While inactivated viruses have been used as the basis for a number of other commonly used vaccines, it is unlikely that this type of vaccine will ever be developed for Hendra because of the risk, albeit remote, of infection. However, vaccine trials have been initiated that use recombinant viral antigens. These antigens represent only a small fraction of the virus, but may be sufficient to stimulate an immune response and protect against infection with the live virus. If successful, this vaccine could be administered without any risk of infection.

## Conclusions

Despite the recent emergence of Hendra virus and the difficulties associated with researching a virus carried by flying foxes, there have been significant advances in understanding this virus and the disease it causes. The virus has been fully characterised and monitoring sequence changes in isolates is ongoing. The species that are susceptible to infection have been determined and how the virus infects the cells of these species (and the symptoms it causes) has been well documented. The viral reservoir in nature has been identified and measures have been taken of the prevalence of flying foxes exposed to this virus. A suite of laboratory tests have been

developed for detection of the virus during incidents and for surveillance, and these tests can now be performed in a number of national and international laboratories. And the analysis of experimental infections continues, yielding new data to be used to improve management of the disease and to develop novel vaccines and therapies.

Hendra virus research, however, is challenging and complicated and much remains to be learnt. Research continues into understanding the behaviour of the virus in flying foxes in the wild and what factors cause the virus to spill over from these bats to horses and subsequently to humans. Significant questions remain concerning how and when the virus is transmitted and whether any domestic animals or wildlife other than flying foxes are involved in the disease cycle. Research that addresses these questions will lead to a better understanding of how to predict and prevent incidents and how best to manage them when, and if, they occur. Ultimately it is hoped that future research will lead to the development of a vaccine to prevent the disease, and/or a treatment that will stop the disease in infected individuals.

# Resources

General articles:

Further information about Hendra virus can be found at the following websites:

Hendra Virus Feature Article - CSIRO Australian Animal Health Laboratory (AAHL)

http://www.csiro.au/science/Hendra-Virus.html Hendra Virus Overview – Queensland Primary Industries and Fisheries (QPIF) http://www.dpi.qld.gov.au/cps/rde/dpi/hs.xsl/4790 11127 ENA HTML.htm Hendra Virus Disease and Nipah Virus Encephalitis Fact Sheet- Centres for Disease Control and Prevention (CDC) http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/nipah.htm Information for the community, veterinarians and horse owners: Hendra Virus. Important Community Information- Queensland Health http://www.dpi.qld.gov.au/documents/Biosecurity\_GeneralAnimalHealthPestsAndDiseases/HendraVirusCommu nity.pdf Guidelines for Veterinarians Handling Potential Hendra Virus Infection in Horses - QPIF http://www.dpi.qld.gov.au/cps/rde/dpi/hs.xsl/4790\_13371\_ENA\_HTML.htm Hendra Virus. Important Information for Horse Owners - QPIF http://www.dpi.gld.gov.au/documents/Biosecurity\_GeneralAnimalHealthPestsAndDiseases/Hendra-virus-horseowner-guidelines.pdf Hendra Virus Infection – Queensland Health http://access.health.qld.gov.au/hid/InfectionsandParasites/ViralInfections/hendraVirusInfection fs.asp Hendra Research: Research into Hendra Virus. The Story So Far - QPIF http://www.dpi.qld.gov.au/cps/rde/dpi/hs.xsl/4790\_11599\_ENA\_HTML.htm Hendra Virus. The Initial Research - QPIF http://www.dpi.gld.gov.au/cps/rde/dpi/hs.xsl/4790 11112 ENA HTML.htm

Flying Foxes Information: Consortium for Conservation Medicine The *Henipavirus Ecology Collaborative Research Group* http://www.henipavirus.org/ Bat Care Brisbane http://www.bats.org.au/ Flying Foxes - Victorian Department of Sustainability & Environment http://www.dse.vic.gov.au/DSE/nrenpa.nsf/LinkView/C330BE1115AF2EAACA256BF2001CF9DB16C869C35C A02BB14A256DEA00247222 The Action Plan for Australian Bats – Australian Government Department of the Environment, Water, Heritage and the Arts http://www.environment.gov.au/biodiversity/threatened/publications/action/bats/index.html Australian Bats – Australian Museum

http://australianmuseum.net.au/Australian-bats

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