

# Hendra Virus Infection

*Equine Morbillivirus Pneumonia,  
Acute Equine Respiratory Syndrome*

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## Importance

Hendra virus infection is an emerging viral disease of horses and humans in Australia. Although this disease is uncommon, cases have been reported periodically since it was first recognized in 1994. Current understanding of its epidemiology is limited; however, horses appear to be incidental hosts infected by contact with flying foxes (fruit bats). Horse-to-horse transmission seems to be rare among animals kept on pastures, but infected horses brought into stables have spread the virus to a few animals in close contact. Infected horses usually experience a brief, severe respiratory or neurological disease with a high case fatality rate. In several incidents, Hendra virus spread from horses to humans during close contact; human infections from other sources, including direct contact with flying foxes, have not been reported. Four of the seven clinical cases in humans were fatal. Disease control currently relies on management strategies that prevent contact between flying foxes and horses, and barrier precautions to prevent transmission from suspect cases to humans or other horses.

## Etiology

Hendra virus (HeV) is a member of the genus *Henipavirus* in the family Paramyxoviridae. This genus includes the closely related Nipah virus.

## Geographic Distribution

Hendra virus infections have been seen only in Australia, where this virus is endemic in flying foxes. Seropositive flying foxes have been found from Darwin in north central Australia to Melbourne in southeastern Australia. Most cases in horses have occurred in Queensland, but one infected horse was reported from New South Wales in 2006. Antibodies to Hendra virus have also been detected in flying foxes in Papua New Guinea. Antibodies to henipaviruses have been found in these animals in Madagascar and Cambodia, but the circulating viruses may be distinct from Hendra or Nipah virus.

## Transmission

Horses and humans seem to be spillover hosts for Hendra virus. Bats of the genus *Pteropus* (fruit bats/ flying foxes) appear to be the reservoir hosts. In flying foxes, Hendra virus has been isolated from blood, fetal tissues and uterine fluids, and unpublished research also reports the virus in urine, feces and saliva. A recent study suggests that Hendra virus is probably transmitted between bats mainly by horizontal rather than vertical transmission. Whether this virus persists in local populations of flying foxes or is transmitted between groups is unknown.

The route of transmission from flying foxes to horses is uncertain, but the virus is thought to be spread by environmental contamination, and ingested or inhaled by the horse. The upper respiratory tract and/or the oropharynx are the most likely sites of entry. The index case is usually a horse kept outside, near flying fox activity. Hendra virus does not appear to be highly contagious among horses, and close contact seems to be necessary for it to spread. Infected horses on pastures have rarely transmitted the virus to their companions. However, transmission appears to occur more readily in closed environments such as stables. In two outbreaks, infected animals that were brought inside have spread the virus to several contacts. In horses, Hendra virus has been isolated from the urine and the oral cavity, and viral nucleic acids have been found by PCR in nasal secretions, blood and a wide variety of tissues. This virus may be present in nasal secretions two days before the onset of clinical signs.

Naturally infected cats have not been detected, but cats can be infected experimentally by intranasal, oral or subcutaneous inoculation. Experimentally infected cats shed Hendra virus in urine, but virus was not detected in nasal secretions, oral secretions or feces. Experimental cat-to-cat or cat-to-horse transmission has been reported among animals in close contact.

Humans have been infected during close contact with sick horses and during necropsies, probably via body fluids or aerosols. No one has apparently been infected by direct or indirect exposure to infected flying foxes, and surveys have found no

evidence of Hendra virus infections among people who care for these animals. Person-to-person transmission has not been seen.

Transmission may be possible on fomites, particularly in closed environments such as stables. Hendra virus has been shown to survive for more than four days in flying fox urine at 22°C (72°F). This virus can also remain viable for a few hours to a few days (generally less than four days) in fruit juice. It does not survive well at higher temperatures, and is inactivated in less than a day in either urine or fruit juice at 37°C (98.6°F).

## Disinfection

Like other paramyxoviruses, Hendra virus is expected to be susceptible to soaps, detergents and many common disinfectants including hypochlorite, iodophors, biguanidines (e.g. chlorhexidine) and quaternary ammonium compounds. This virus is susceptible to desiccation or heat, but resists inactivation by acids or alkalis; it can survive a wide pH range from 4 to 11.

## Infections in Humans

### Incubation Period

In published cases, the initial symptoms developed in 5 to 12 days. One person became ill shortly after contact with infected horses, but recovered before developing recurrent, fatal encephalitis a year later.

### Clinical Signs

Hendra virus infections have been reported in seven people. The syndromes have included influenza-like illness and progressive encephalitis. The two initial cases were characterized by a serious influenza-like disease with fever, myalgia, and respiratory signs. One of the two people died; the other recovered over the next six weeks. In the third case, a mild meningoencephalitic illness was followed by a long asymptomatic period before fatal encephalitis developed a year later. The fourth person reported a self-limited influenza-like illness with a dry cough, sore throat, cervical lymphadenopathy, fatigue, body aches and a fever that lasted for approximately one week.

Detailed reports of the most recent three cases have not been published, but all three people were infected by contact with horses. One of the two cases reported in 2008, as well as a case that occurred in August 2009, were fatal.

### Communicability

Human-to-human or human-to-horse transmission has not been seen; however, Hendra virus infections are still poorly understood. This virus was isolated from the kidneys of one person who died, suggesting that it might be shed in the urine.

## Diagnostic Tests

Hendra virus infections can be diagnosed by virus isolation, the detection of nucleic acids, or serology.

Hendra virus can be isolated in a number of cell lines including Vero, BHK-21, MDCK, RK13, LLC-MK2 and MRC5 cells. It can also be cultured in embryonated chicken eggs, but due to the ease of culture in cells, this system is not generally used. This virus can be identified in cultures by immunostaining, virus neutralization or molecular techniques. Electron or immunoelectron microscopy can also be helpful in identification. Hendra virus is a biosafety level 4 (BSL4) pathogen and culture is conducted under high-security conditions.

Viral antigens can be detected by indirect immunoperoxidase or immunofluorescence assays on formalin-fixed tissues. A reverse-transcription polymerase chain reaction (RT-PCR) test can also be used on tissues. Immunohistochemistry and electron microscopy have been helpful in some cases.

Serological tests used in humans include indirect immunofluorescence, enzyme-linked immunosorbent assays (ELISAs) and serum neutralization.

## Treatment

Hendra virus infections in humans are very rare, and proven drug therapies have not been developed; however, treatment with antiviral drugs, combined with supportive care, has been tried in recent cases.

## Prevention

Human infections have been reported after nursing or examining sick horses, or handling equine tissues at necropsy. Stringent precautions should be taken to prevent contact with blood, tissues and body fluids, particularly respiratory secretions, saliva and urine, whenever Hendra virus is among the differential diagnoses. Personal protective equipment (PPE) recommendations are available from the Queensland Department of Primary Industries and Fisheries (DPIF; see Internet Resources). In general, the minimum recommendations during an investigation of a suspected case include impervious gloves, a particulate (P2 [N95] or higher) respirator, a face shield or safety eyewear to protect the eyes, impervious overalls (or a clothing combination that provides the same protection) and impervious boots. Excellent hygiene should be practiced at all times. If the skin becomes contaminated, it should be washed with soap and water as soon as possible. Cuts or abrasions that have been exposed should be washed with soap and water, then disinfected with an iodine-based antiseptic or ethyl alcohol if it is available. In higher risk situations, precautions and PPE requirements increase. Detailed recommendations for conducting investigations of suspected Hendra virus infections, as well as precautions to be used when the likelihood of Hendra virus is first revealed during an examination of the case, are available from the DPIF.

Because Hendra virus infections can look like other diseases and are often diagnosed retrospectively, good infection control precautions should be used routinely with horses. Veterinarians in endemic areas should keep a dedicated Hendra virus field kit with appropriate PPE, disinfectants, waste disposal bags and other necessary items for use in unexpected cases. All human exposure should be minimized once the case is suspected, and any contamination should be washed off with soap and water. Investigations should be continued only if suitable precautions can be taken and PPE is available.

People who have been exposed should seek medical advice, and the area health department should be contacted to report the case. Prophylactic treatment with antiviral drugs has been tried in some recent cases.

## Morbidity and Mortality

Hendra virus infections have been reported in seven people, all of whom had close contact with infected horses during their illness or at necropsy. Only a percentage of those exposed to infected horses have become ill. Two people, a stablehand and the trainer, were infected during an outbreak in 1994; the stablehand recovered but the trainer died. In a separate episode, a farmer who had close contact with two sick horses (both during their illness and at necropsy) became infected and died of the illness a year later. In 2004, a veterinarian who conducted the necropsy on an infected horse became ill but recovered. Two assistants at the necropsy remained seronegative. The same year, eighteen people were exposed to another infected horse or to its tissues at necropsy, but none seroconverted. No human infections were associated with the horses that died of this disease in 1999, 2006 or 2007, but illness was reported in a veterinarian and an animal nurse during one of the two clusters in 2008. A veterinarian was also infected during an outbreak in 2009. Two of the latter cases were fatal. There has been no evidence of seroconversion in people who are often in close contact with flying foxes.

## Infections in Animals

### Species Affected

Bats of the genus *Pteropus* (fruit bats/ flying foxes) appear to be the reservoir hosts; Hendra virus is found in all four species of Australian flying foxes (*Pteropus alecto*, *P. poliocephalus*, *P. scapulatus* and *Pteropus conspicillatus*). Other species are thought to be spillover hosts. Natural infections have been documented in horses, and experimental infections have been established in cats, horses and guinea pigs. Dogs, mice, rats, rabbits and chickens do not develop clinical signs after inoculation. Of the latter four species, significant seroconversion occurred only in rabbits.

### Incubation Period

In horses, the incubation period is estimated to be five to 16 days. The incubation period in experimentally infected cats is 4 to 8 days.

### Clinical Signs

Two syndromes, one characterized primarily by respiratory disease and the other mainly by neurological signs, have been reported in horses. Because Hendra virus causes vasculitis, other syndromes may be possible. Most known cases have been severe and acute, and progressed rapidly to death within days. Milder cases have also been seen, and a few horses have recovered.

In one group of experimentally infected horses, the initial clinical signs were an elevated temperature and an increased heart rate. Apparent discomfort was another early sign; some animals shifted their weight constantly from leg to leg. High fever, anorexia, depression, sweating and uneasiness have been reported in naturally infected animals.

In horses with respiratory signs, the respiration tends to be rapid, shallow and labored, and the mucus membranes may be congested. Jaundiced mucus membranes, ataxia, mild neurologic signs or subcutaneous edema have also been seen. Just before death, animals often develop a copious nasal discharge, which becomes frothy and may be bloodstained. The clinical course is acute; death usually occurs one to three days after the initial signs. Some convalescent horses may develop neurological signs, but others seem to recover fully.

In other horses, neurological rather than respiratory signs have predominated. Neurological signs that have been reported in Hendra virus-infected horses include an altered gait (e.g. high stepping), a “wobbly gait” that progresses to ataxia, altered consciousness or aimless walking, apparent blindness in one or both eyes, a head tilt, circling, muscle twitches or tremors, facial paralysis, a locked jaw, spasms of the jaw and involuntary chomping.

Other reported clinical signs include colic and straining to defecate. Some horses have had difficulty urinating or dribbled urine in the terminal stages.

In experimentally infected cats, fever and increased respiratory rates were followed by severe illness and death within 24 hours. Experimental infections in guinea pigs resulted in generalized, fatal vascular disease. Flying foxes appear to remain asymptomatic, and all infected animals may not seroconvert.

### Communicability

In flying foxes, Hendra virus has been reported in blood, fetal tissues, uterine fluids, urine, feces and saliva. Unpublished research in experimentally infected flying foxes suggests that these animals shed the virus for approximately one week. Transmission from flying foxes to horses seems to be inefficient and is reported only sporadically.

In horses, Hendra virus occurs in nasal and oral secretions, urine and a wide variety of tissues. Horses are thought to be most contagious after they become symptomatic or during the preceding febrile stage; however, virus has been found in nasal secretions two days before the initial signs. Transmission seems to be uncommon between horses on pastures, but it occurs more readily in closed environments such as stables.

Experimentally infected cats can transmit the infections to horses or cats that are in close contact. No naturally infected cats have been identified.

Humans have been infected, to date, only during close contact with sick horses. Necropsies are a particularly high-risk procedure, but any contact with blood, tissues or secretions (including on fomites) also carries a risk.

## Post Mortem Lesions [Click to view images](#)

**Necropsies have been linked to human cases, and should be performed only if they can be carried out safely, using recommended PPE and other precautions. Routine necropsy precautions may not be sufficient to protect people.**

In horses with the respiratory syndrome, post-mortem lesions have been found mainly in the lower respiratory tract. Common lesions include marked pulmonary edema, dilation of the pulmonary lymphatics, and congestion and ventral consolidation of the lungs. Petechial hemorrhages have been seen on the pleural surfaces, and patchy hemorrhages may be found in the lung parenchyma. The airway often contains white or blood-tinged foam, and edema fluid oozes from cut tissues. Swollen and congested lymph nodes, excess pleural and pericardial fluid, and visceral edema have also been reported. Scattered petechiae and ecchymoses may be found in the stomach, intestines and perirenal tissues. Yellowing of the subcutaneous tissue is common. Endometrial edema and purplish discoloration of the serosa of the uterus was reported in one experimentally infected mare.

In experimentally infected cats, severe pulmonary edema, hydrothorax and edematous bronchial lymph nodes were seen.

## Diagnostic Tests

**Stringent precautions should be used when collecting and shipping any diagnostic samples from live or dead animals. Only those samples that can be collected safely should be taken. A description of the limited necropsy procedure used to collect diagnostic samples, as well as necropsy and sample collection recommendations, can be found on the Queensland DPIF Web site (see Internet Resources).**

Hendra virus infections can be diagnosed by virus isolation, detection of nucleic acids or antigens, or serology.

In live animals, virus isolation can be attempted from the blood, nasal or oral secretions, or urine; however, this virus is more likely to be recovered from the lung, liver, spleen, kidney and superficial lymph nodes of the head after death. It has also been isolated from the brain and other tissues. Hendra virus can be isolated in a number of cell lines, and grows particularly well in Vero and RK13 cells. It can also be cultured in embryonated chicken eggs, but due to the ease of culture in cells, this system is not generally used. This virus can be identified in cultures by immunostaining or virus neutralization. Electron or immunoelectron microscopy can also be helpful. Hendra virus is a biosafety level 4 (BSL4) pathogen and virus isolation is conducted under high-security conditions.

Viral antigens can be detected by immunoperoxidase or immunofluorescence assays on formalin-fixed tissues. Because Hendra virus antigens may be cleared from the lung early in the infection, a variety of tissues should be submitted for immunohistochemistry. In addition to the lung, viral antigens may be found in the mediastinal lymph nodes, spleen, kidney, brain and other tissues. When practical and safe, samples of the uterus, placenta and fetal tissues should also be collected from pregnant animals. RT-PCR, used on either fresh or formalin-fixed tissues, is often used for rapid diagnosis. Samples for PCR can include blood, nasal or oral swabs, urine, or tissue samples collected at necropsy.

Serology can also be helpful, but titers may not be detectable until 10 to 14 days after infection in horses. Low-to-moderate titers can be found in some flying foxes; all infected animals may not seroconvert. The most commonly used serological tests are ELISAs and serum neutralization tests. False positives are common in ELISAs, which are often used for the initial screening of horses. Other serological tests include indirect immunofluorescence and immunoblotting. Cross-reactions can occur between Hendra and Nipah viruses in all serologic assays including virus neutralization; however, reactions to Hendra virus can be identified by comparative neutralization tests. Identification of the specific virus is particularly important in areas where neither virus is known to be endemic.

### **Samples to collect**

In live horses, the most valuable samples are a nasal swab and whole blood in EDTA. The nasal swab should be transported in virus transport medium if possible, but if this cannot be done, it can be tested by PCR. Other samples to collect include oral and urine swabs, and blood collected into a plain tube. Oral or urine swabs are handled similarly to nasal swabs.

In Australia, the minimum recommended post-mortem samples are a nasal swab and oral swab, and blood (if available) collected into EDTA and a plain tube. Limited necropsy with minimal penetration of the carcass can be used to collect fresh and fixed (10% formalin)

samples from the lung, spleen and/or kidney, as well as fresh urine. Superficial lymph nodes of the head, such as the submandibular lymph nodes, can also be collected. A wider range of samples can be taken if the person performing the necropsy is experienced in safe collection procedures for Hendra virus.

## Treatment

Other than supportive therapy, there is no treatment for Hendra virus infections in animals. In some cases, surviving horses have been euthanized due to uncertainties about virus persistence.

## Prevention

In horses, prevention is based on minimizing exposure to flying foxes, their tissues and secretions. All index cases, to date, have occurred in horses stabled in open paddocks. Horse paddocks should not contain food or roosting trees favored by flying foxes. Feed bins and water troughs should not be placed under trees where bats might be found (i.e., feeding and roosting areas). Horses may be stabled full time or moved away from areas of high flying fox activity during high-risk seasons. In the past, the highest risk months were considered to be August to January, which coincide with the period when most species of flying foxes give birth, but cases have also been reported in June and July. Any dead flying foxes should be removed and destroyed by burning or burial; precautions should be taken to prevent human exposure while this is done.

Horses that develop signs consistent with Hendra virus infection should be isolated, and stringent infection control measures should be taken to avoid spreading the virus to other horses or people. People should interact with the horse as little as possible, using PPE to protect the skin, mucous membranes and eyes. Caution should be used to avoid generating aerosols or splashing material, both when examining the horse and during disinfection. Other horses, as well as domesticated animals (particularly cats) should be kept away from the suspect case. If any horses have been exposed, they should be examined daily for signs of disease. Quarantines and rigorous hygiene have been effective in containing past outbreaks. The low rate of horse-to-horse transmission also aids control.

Carcasses should also be isolated until Hendra virus infection can be ruled out. Necropsies should be avoided unless the operator can carry them out safely using recommended guidelines and PPE (see human Prevention section). Government authorities should be consulted for the most appropriate disposal method for carcasses; deep burial has been used in the past.

## Morbidity and Mortality

Hendra virus infections seem to be uncommon in horses. All of the approximately 4000 horses tested in two Australian surveys were seronegative. Clinical cases were

first recognized during outbreaks in Hendra, Australia (Queensland) in 1994. During the following decade, cases or clusters were reported rarely; the virus infected horses once in 1999, and on two occasions in 2004. From 2006 to September 2009, Hendra virus infections appeared more regularly, with two incidents reported each year. The index case usually occurs in a horse kept outside, near flying fox activity. In rare cases, the horse has transmitted the virus to a companion. Outbreaks seem to be more likely when the infected horse is brought into a stable with other susceptible animals. The case fatality rate, as of September 2009, is 75%.

Hendra virus infections in horses appear to be seasonal, but do not occur every year. Most incidents have been seen between August and January, when most flying foxes give birth, but they have also occurred in June and July. Epidemiological factors may influence whether the infection spills over from flying foxes to horses in a given year. A recent study suggests that both nutritional stress and pregnancy/ lactation are independently linked to higher seroprevalence rates in little red flying foxes (*Pteropus scapulatus*). It is possible that seasonality and environmental stresses influence virus transmission among flying foxes, and the virus spills over into horses during epizootics. Whether Hendra virus persists in local populations of flying foxes or is transmitted between groups is unknown.

Naturally occurring infections have not been reported in any species other than horses or flying foxes. In a survey conducted in the Brisbane area, where the initial cases were reported in horses, all of the 500 cats tested were seronegative. Experimental infections in cats and guinea pigs have been fatal.

## Internet Resources

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Centers for Disease Control and Prevention

<http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/nipah.htm>

Queensland Department of Primary Industries and Fisheries.

Hendra virus (includes guidelines for veterinarians handling cases)

[http://www.dpi.qld.gov.au/cps/rde/dpi/hs.xml/27\\_2900\\_ENA\\_HTML.htm](http://www.dpi.qld.gov.au/cps/rde/dpi/hs.xml/27_2900_ENA_HTML.htm)

The Merck Veterinary Manual

<http://www.merckvetmanual.com/mvm/index.jsp>

World Organization for Animal Health (OIE)

<http://www.oie.int>

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

[http://www.oie.int/eng/normes/mmanual/a\\_summry.htm](http://www.oie.int/eng/normes/mmanual/a_summry.htm)

OIE Terrestrial Animal Health Code

[http://www.oie.int/eng/normes/mcode/A\\_summry.htm](http://www.oie.int/eng/normes/mcode/A_summry.htm)

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\*Link defunct as of 2009