*Journal of Zoonotic Diseases*
https://jzd.tabrizu.ac.ir/
Published by the University of Tabriz
Online ISSN: 2717-2910

# Hendra virus influences meningoencephalitis-based mortality: A comprehensive review

**Margret Chandira Rajappa*, Nagasubramanian Venkatasubramaniam, Harish Kesavan, Jagadhish Balaji, Mohan Kumar Saravanan, Hari Rajamanikam**

Department of Pharmaceutics, Vinayaka Mission's College of Pharmacy, Vinayaka Mission's Research Foundation, Tamil Nadu, India

**Article type:**
Review article

**Keywords:**
Hendra virus
Paramyxovirus
Meningoencephalitis
Pulmonary

**Article history:**
Received:
July 25, 2024
Revised:
August 5, 2024
Accepted:
August 12, 2024
Available online:
August 31, 2024

**Abstract**

This article looks at the zoonotic paramyxovirus known as Hendra virus (HeV) was initially discovered in Hendra, Queensland, which is located in Australia, in 1994. In the Paramyxoviridae family and Mononegavirales order, HeV is the first member of the recently formed Henipavirus genus. It belongs to a distinct clade together with Nipah virus (NiV) and Cedar virus (CedV). Initially discovered during a severe outbreak affecting horses and humans, HeV has been implicated in numerous equine morbidity cases and occasional human transmission in Australia. This review provides a comprehensive analysis of HeV's clinical features, pathophysiology, transmission pathways, and diagnostic methodologies, emphasizing its substantial effect on animal and human health. Current human treatment strategies for HeV infection are primarily supportive, though emerging antiviral therapies show potential. Furthermore, the creation and application of vaccination for horses represent a crucial advancement in controlling the spread of this deadly virus. This review highlights the necessity for continued surveillance, research, and preventive measures to manage HeV outbreaks and safeguard public health.

## Introduction

In the Brisbane neighborhood of Hendra, Queensland, a zoonotic paramyxovirus known as the Hendra virus (HeV) first appeared, which is in Australia, in 1994 (1). Forming a separate clade alongside Nipah virus (NiV) and Cedar virus (CedV), it was the first characterized member of the novel viral genus Henipavirus under the family Paramyxoviridae and the order Mononegavirales (2,3). In the first outbreak, horses were suffering from a severe form of febrile pulmonary sickness; 14 out of 21 affected horses were put down naturally or put to death. One of the two humans who contracted influenza-like sickness (ILI) after being near the infected horses passed away from severe interstitial pneumonia. HeV's function as the

***Corresponding author:** *mchandira172@gmail.com*
https://doi.org/10.22034/jzd.2024.18394
https://jzd.tabrizu.ac.ir/article_18394/html
Cite this article: Rajappa MC., Venkatasubramaniam N., Kesavan H., Balaji J., Saravanan MK. and Rajamanikam H. Hendra virus influences meningoencephalitis based mortality: A comprehensive review. Journal of Zoonotic Diseases, 2025, 9 (1): 636-650

field event's etiologic agent was confirmed when it was separated from the lung tissue of the afflicted horses and the human kidney in the instance of the deceased.

Both humans and horses can contract acute, frequently deadly infections from HeV. Urine is the main method of viral excretion. The virus's natural hosts are flying foxes, as they are sometimes called pteropid bats. The virus is more frequently detected in *Pteropus alecto* and *P. conspicillatus*. There is seasonal variation in flying fox infection; in certain areas, winter is when virus shedding increases (4). Horses are most likely to contract the disease from flying foxes through direct contact with contaminated urine or contaminated surfaces (5). Horse-to-horse transmission is thought to be ineffective and necessitates intimate contact with contaminated bodily fluids. There are no known occurrences of flying foxes directly transmitting the infection to humans; instead, every human case has been linked to intimate contact with sick horses. Only premises housing sick horses have reported cases involving dogs (6). Even with a successful horse vaccination available, managing interspecies spread requires an understanding of HeV ecology and transmission. HeV is one of five species that make up the genus Henipavirus, which additionally contains NiV, CedV, Ghana virus (GhV), and Mojiang virus (MojV). Australia's flying foxes have been shown to carry both HeV and CedV; of these, only HeV is very dangerous to humans and horses (7).

**Henipavirus**

The Hendra virus is a member of the family Paramyxoviridae and is classified under the genus Henipavirus. The genus Henipavirus, which belongs to the Mononegavirales order of the Paramyxoviridae family, has six known species (8-10), and numerous others still under study (11). Several species of tiny animals, including shrews, microbats of various types, and pteropid fruit bats (flying foxes), naturally harbor henipaviruses (12-14). Henipaviruses are distinguished by their extensive host range and lengthy genomes. It is concerning as they have just come to light as zoonotic infections that can infect humans and domestic animals and result in illness (15,16).

**History and Outbreak of Hendra virus**

Acute pulmonary disease was discovered in September 1994 in 21 horses who were kept in the Queensland, Australia suburb of Hendra, on a ranch. High rectal temperatures, acute pulmonary distress, and influenza-like symptoms, such as nasal discharge, were the hallmarks of horse sickness (17). Within two weeks, 14 of the horses died or were put down due to this illness. A trainer and a stable hand who worked closely with a pregnant mare who had the same virus and died from comparable symptoms. Acute pulmonary illness symptoms appeared two weeks before the major outbreak (18). While the stable hand recovered fully, the trainer succumbed to interstitial pneumonia after six days. Two healthy horses were infected with the virus that was obtained. A stable hand and a trainer who was nearby a pregnant mare who was affected. Following a six to ten-day incubation period, symptoms appeared in both infected horses, including a high temperature and pulmonary sickness. By doing comparative sequence analysis on a portion of the matrix protein gene, the virus in question was shown to belong to the genus Morbillivirus (19). The virus was first discovered to be equine morbillivirus, but it was subsequently dubbed HeV, or the Hendra virus, after the Hendra suburb (20). Based on phylogenetic research and observations of the virus's huge size and shape (21), placed HeV under the newly created Henipavirus, a kind of virus belonging to the Paramyxoviridae family.

Henipavirus is a category of virus pertaining to the Paramyxoviridae family. Numerous further cases of HeV-related sickness in Australian horses have been recorded after the first pandemic in Hendra, with sporadic human transmission (22). The Queensland city of Mackay was the site of 1995 saw

the second fatal HeV case in a person (23). This case was connected to two horses that had passed away in 1994 on the land where the case is being handled from what was originally thought to be snakebite or avocado poisoning but was an HeV infection. In 1999, there was another report of HeV activity in Cairns, Queensland, following the unexpected death of a thoroughbred mare from a pulmonary disease. HeV was isolated from the horse's nasal discharge, which was yellow and foamy, at the time of death. Two times in the year 2004, HeV caused morbidity in horses: one time in Townsville, Queensland, and one time in Cairns, again after there had been no activity for another five years (24). There was only one horse that died in each of the events. The Cairns case's veterinarian had a clinical sickness, but she made a full recovery and was still clinically well at the time her illness report was released. Queensland has been recording HeV-related morbidity every year since 2006, leading to the death of two additional humans and fifteen additional horses, as well as the designation of HeV-related sickness as notifiable in Australia (25).

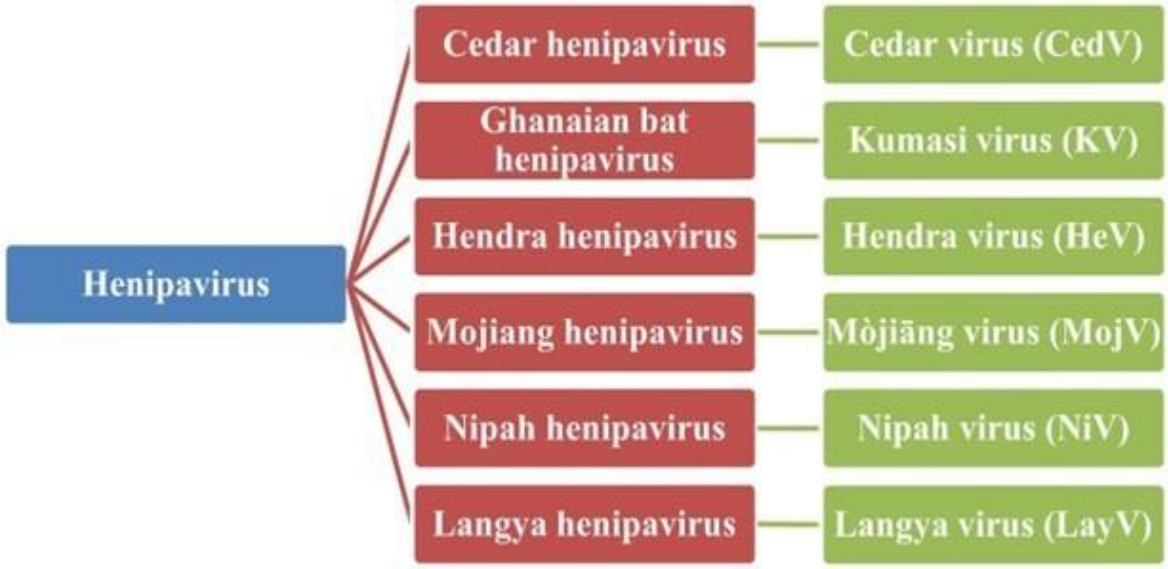


**Fig. 1.** Classification of Henipavirus[17].

**Hepatitis virus infection in humans: clinical characteristics**

Four of the seven people with HeV infections (Table 1) have passed away. This results in an approximate mortality rate of 57%; a more precise death rate may vary in value based on the number of cases. The time frame for incubation was originally believed to be 6–8 days after the first four human cases; however, subsequent instances showed signs of a prolonged incubation time of a maximum of 21 days (26). Human HeV infection results in meningoencephalitis and acute pulmonary sickness, two separate but related symptoms. Cases comprise six patients (C-1 to C-6) who first appeared with pulmonary symptoms and an illness resembling influenza, including fever, myalgia, headaches, lethargy, and pharyngitis. Due to a suspicion of HeV exposure, the seventh patient (C-7) received a post-exposure prophylaxis treatment that included oral hydroxychloroquine and an intravenous ribavirin course lasting five days (26).

**Table 1.** Outbreak of Hendra virus in human

| The exposure date | Age and gender | Occupation | Clinical condition | Exposure | Incubation period | Out come |
|---|---|---|---|---|---|---|
| August 1994 (*C-1) | 35-year-old male | Farmer | Proximity to the blood and pulmonary secretions of sick horses helped with the necropsy of the afflicted horse's Skin on hands and arms that were not intact | Aseptic meningitis (neck stiffness) and influenza-like illness (headache, sleepiness, vomiting) in August 1994, with partial recovery Relapse, September 1995; encephalitis (fever, focal and generalized convulsions, back pain, and irritable mood); right hemiplegia; symptoms of brainstem injury; and unconsciousness | 6–7 days | Day 25 of hospitalization saw a fatal relapse after an initial period of recuperation (around day 39 of recurrent sickness) and died. |
| September 1994 (C-2) | 40-year-old male | Stable-Hand | Close encounter with an infected horse's pulmonary secretions | disease similar to the influenza virus (fever, headaches, pharyngitis, myalgia, drowsiness, and vertigo) | Nearly 8 days | recuperation without a relapse |
| September 1994 (C-3) | 49-year-old male | Horse trainer | Proximity to an infected horse's pulmonary secretions | Skin on hands and arms that is not intact fever, myalgia, fatigue, headaches, dry cough, pharyngitis, nausea, and vomiting) that resembles the flu, as well as dyspnea that results in multiple organ failure (renal and pulmonary), right leg thrombosis, and deadly cardiac arrhythmia. | 7 days | Died on day 13 of illness |
| October 2004 (C-4) | 25-year-old female | Veterinarian | Conducted a necropsy on the afflicted horse | fever, myalgia, sleepiness, pharyngitis, dry cough, and cervical lymphadenopathy are symptoms of an influenza-like disease. | 7 days | recuperation without a relapse |
| July 2008 (C-5) | 33-year-old male | Veterinarian | Intimate contact with a horse that was afflicted pulmonary secretions examined infected horses necropsiously | fever, headache, myalgia, and confusion along with bilateral ptosis, ataxia, fever, seizures, and ensuing encephalitis (fatigue) and eventually leads to unconsciousness | 9–16 days | Died on day 45 of illness |
| July 2008 (C-6) | 21-year-old female | A nurse veterinarian | Proximity to an infected horse's pulmonary secretions | close encounter with an infected horse's pulmonary secretions disease similar to influenza (fever, headache, and myalgia) followed on day 12 by encephalitis (ataxia, bilateral ptosis, and dysarthria). | 9–16 days | Recuperated, no relapse, but ongoing neurological impairments |
| August 2009 (C-7) | 51-year-old male | Veterinarian | Proximity to an infected horse's pulmonary secretions | Encephalitis (drowsiness, ataxia, and seizures) after intravenous ribavirin and hydroxychloroquine prophylaxis for five days post-exposure | 11–21 days | Died on day 19 of illness |

***** 'C' is referred as 'Case'

The patient did not have any pulmonary symptoms or influenza-like disease; nonetheless, shortly after the 5-day regimen concluded, the patient developed encephalitis, which ultimately led to their death. Although the pulmonary disease was probably avoided thanks to this medication, the virus was still able to propagate throughout the body, attack the nervous system, and kill people. Comparable results were observed in HeV-infected African green monkeys given ribavirin therapy (27). Out of the three individuals who made it through, two fully recovered from the influenza-like illness (C-2, C-4) (24,26) without experiencing any neurological symptoms or relapse. Following the first influenza-

like symptoms, after contracting encephalitis, the third survivor (C-6) still experiences certain neurological anomalies related to the illness. Six years after the initial diagnosis, no virus is found in any of these individuals during follow-up visits. The illnesses that killed the other four patients all occurred. After recovering from the original disease (aseptic meningitis and influenza-like symptoms), one of these (C-1) developed encephalitis 13 months later, which proved to be fatal (18). There was no more HeV exposure for this patient. This implies that HeV may normally exist in humans for a long time before reactivating at a later time. Before passing away from a deadly cardiac arrhythmia, C-3 experienced significant pulmonary signs, but no neurological symptoms, as well as multiorgan failure (renal and pulmonary failure). The final patient (C-5) appeared with symptoms similar to influenza but within days developed acute encephalitis. In the end, the encephalitis proved lethal. According to cases that have been documented thus far, HeV infections in people seem to invariably start with a sickness similar to the flu (unless ribavirin and hydroxychloroquine are given). Once the condition advances to a systemic level, individuals may experience acute encephalitis that could be fatal or not, recover with or without an encephalitic relapse, or pass away from multiorgan dysfunction.

**Hendra virus infection in horses**

It is believed that horses contract HeV through intimate contact with the virus in flying fox excretions, though it's unclear exactly how this happens. The virus strikes infrequently, usually affecting just one horse in each group. An estimate of the field incubation period between 4 and 16 days has been made possible by sporadic multi-horse outbreaks when there is evidence of horse-to-horse transmission, most likely due to the contamination of surfaces or equipment by infectious fluids (28). Acute symptoms include fever, dyspnea, sadness, apathy, tachycardia, tachypnea, facial edema, aimless wandering, muscle fasciculation, and ataxia. Approximately 75% of cases end in death within 48 to 72 hours of the sickness starting. In the last phases of ill animals, an abundance of foamy nasal discharge might also indicate significant pulmonary edema (29). Some afflicted horses may turn up dead. Even while a horse's clinical recovery may be complete, no extended investigation was conducted on those that survive the acute illness because it is currently national policy to put convalescent horses to death. This is particularly true in regard to the potential for viral replication to reappear in the central nervous system (28).

**Pathophysiology of Hendra Virus**

**Transmission:** Although horses are the primary host of the Hendra virus (HeV), humans can contract the infection by coming into touch with an infected horse's body fluids or pulmonary secretions. The HeV virus naturally lives in the fruit bats Pteropus, also called flying foxes (30). When horses come into touch Using the urine or saliva of diseased bats, they can get infected with the virus. Zoonotic transmission occurs when humans interact closely with infected horses. No cases of HeV transfer from person to person have been reported (31). The Pteropodidae family of fruit bats, whose range extends beyond the epidemic areas to West Africa, is the reservoir for HeV and related viruses. The Cedar virus, also found in Australia, is not harmful to humans (32-34). Infected bats primarily excrete HeV through urine, which can infect horses (HeV) or pigs (related to Nipah virus or NiV). Bat urine-tainted raw date palm sap has been connected to NiV epidemics in Bangladesh (35–37). Human-to-human transmission of NiV in Bangladesh has happened when people have come into touch with aerosols or pulmonary secretions (38).

**Pulmonary Infection:** The first barrier against HNV is the pulmonary epithelium (39). Early on, HeV is present and affects the epithelial cells of the bronchi and is secreted by the nasopharynx and trachea. Infected individuals may experience severe pulmonary symptoms, such as necrotizing alveolitis, pulmonary edema, and aspiration

pneumonia (40). Hemorrhage, edema, and severe pulmonary disease were the results of the first fatal human HeV infection. Viral antigens are found in type II pneumocytes and the bronchial epithelium. HeV and NiV can potentially spread via aerosols, although Transmission from one person to another person has only been documented for NiV (27,41,42). Acute pulmonary distress syndrome (ARDS) can be brought on by the release of pro-inflammatory cytokines in reaction to an HeV infection. The pulmonary system exhibits different inflammatory responses in different sections. The trachea and bronchi express fewer cytokines than the tiny airways, which produce a large amount of them (43).

**Viremia:** When HeV infection reaches its advanced stages, the virus spreads to the brain, spleen, and kidneys as well as producing vasculitis in small blood vessels. It does this by moving from the pulmonary epithelium to the pulmonary endothelium (40,44). Viremia can cause the failure of multiple organs. HeV can attach itself to CD3+ leukocytes, which could let the virus spread without replicating. HeV can infect NK cells, monocytes, and (45) T lymphocytes in certain animals. ALCAM, which, on endothelial cells in the blood-brain and blood-air barriers, is highly expressed, is liganded by CD6. HeV's predilection for tiny blood arteries in the brain and lungs may be explained by infection of CD6-expressing T cells by the virus (46). HeV can reach the central nervous system (CNS) by the bloodstream or the olfactory nerve, leading to brain inflammation, necrosis, thrombosis, and vasculitis (47).

**Entry into the CNS:** The disruption of the blood-brain barrier (BBB) and the expression of pro-inflammatory cytokines TNF-α and IL-1β are associated with HeV infection of the central nervous system and the onset of neurological symptoms. These factors enhance BBB permeability and cause neuronal damage (48). Although the exact source of these cytokines in the brain is unknown, diseased microglia may be one. According to research on animals, HeV can access the central nervous system (CNS) through the olfactory nerve, infect the olfactory epithelium, and then travel to the brain (49). This route's relevance to human infections is unknown due to differences in olfactory epithelial surface size between species.

**Signs and Symptoms of Hendra Virus Infection**

Indications and manifestations of the Hendra virus can be similar in both people and horses, similar to those of a flu-like illness. Fever, malaise, headache, myalgias, cough, dyspnea, and appetite loss are among the early warning signs and symptoms (50). In certain cases, an infection with the Hendra virus can result in an abrupt

onset of sickness and a swift decline in health, accompanied by severe pulmonary symptoms such as dyspnea and pulmonary failure. Uncommon neurological symptoms include meningitis, or meningeal inflammation, and encephalitis, or inflammation within the brain. The period between infection and the development of symptoms, is known as the nine to sixteen-day incubation period for the Hendra virus (51,52).

**Impact:** Human and equine Hendra virus infections have a significant death rate. Seventy percent of infected humans and eighty percent of horses with Hendra virus die. Until it is determined that there is no risk of further transmission, properties holding confirmed instances of biosecurity Queensland is in charge of ill animals in collaboration with the owner of the animal and the doctor. Rarely, adjacent properties are also affected. There are no limitations on normal horse population mobility during a Hendra virus incident. Properties with verified cases of infectious animals and those near them may have movement restrictions.

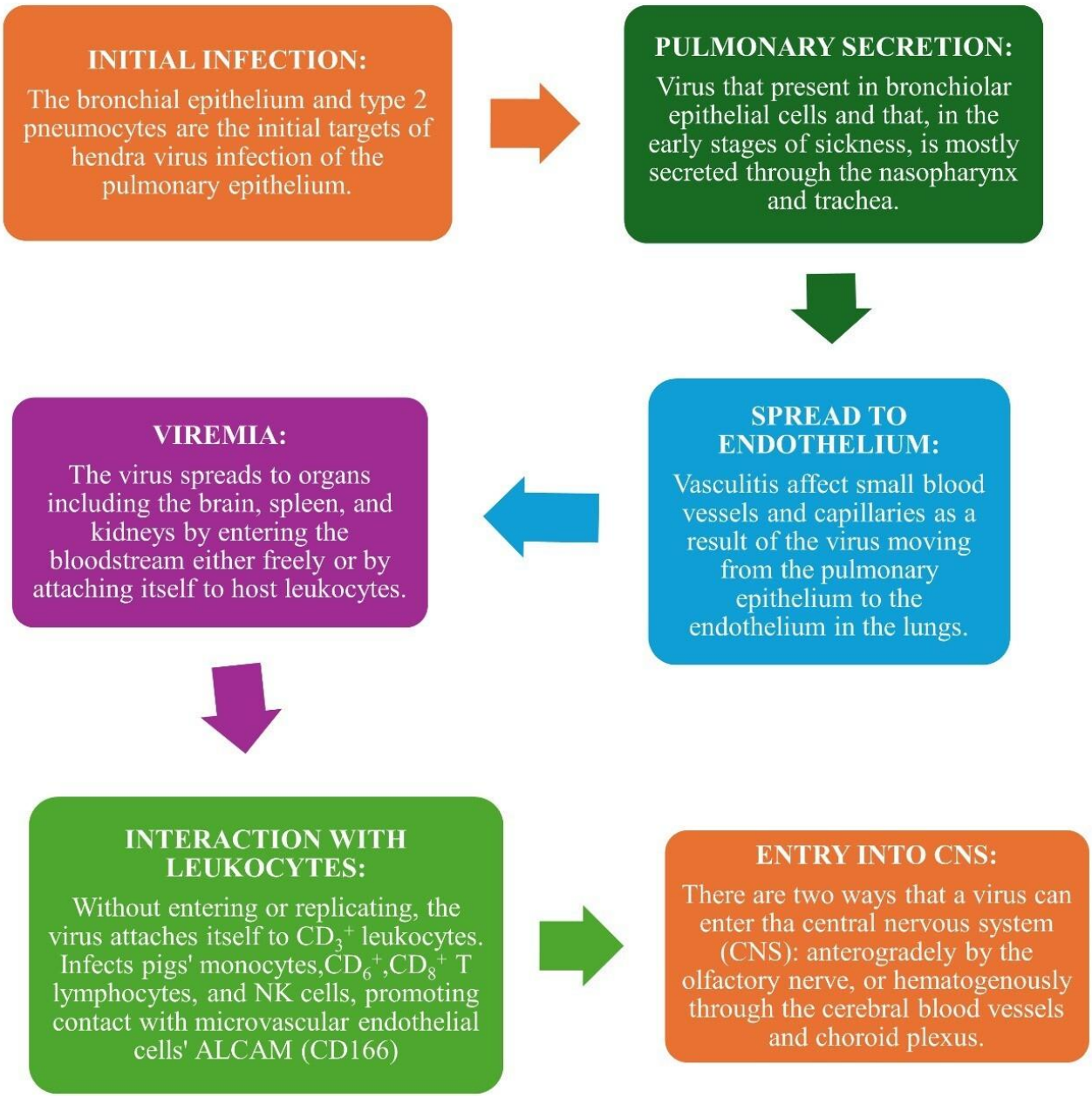


**Fig. 2.** Transmission Path of Hendra Virus (HeV)

**Diagnosis of Hendra virus**

Anyone who has recently had intimate interaction with an ill or deceased horse in the endemic zone who passed away from an infection exhibiting indications of neurological or pulmonary involvement may be suspected of having an HeV infection. This is especially true that if the horse's HeV infection is found. As previously mentioned, the initial indications and manifestations of a HeV infections in humans are non-specific. Therefore, even in circumstances where Suspected HeV infection, laboratory testing procedures are the sole means of confirming a diagnosis of infection. The several laboratory techniques covered include

electron microscopy, serology, IHC, PCR-based tests, virus isolation, and some novel experimental techniques (26,53). Every one of these techniques has particular benefits and is applied in specific scenarios. The only certain technique to determine whether someone has HeV infection is to isolate the virus found in a sample of fluid or tissue (54). HeV (or NiV) can be detected by the development of syncytia and punctate holes in the cell monolayer's surface after clinical samples are injected into Vero or RK13 cells (55). At least 20 nuclei make up each syncytium, and HeV and NiV can be distinguished from one another by observing how the nuclei are arranged within a syncytium. Although HeV has been recovered from a variety of tissues, serological, enzymatic, and genomic techniques are frequently used to aid in viral isolation efforts. Lethal viral infections can be cultured from post-mortem tissue samples, such as those from liver, spleen, and kidney necropsies. HeV can be isolated from serum, urine-tract swabs, or throat swabs in non-fatal instances (56).

Only labs with the highest biosafety classification should culture materials suspected of carrying the virus, since as of now, there isn't any efficient vaccine or therapy for HeV infection, and because the virus kills people and horses at a significant rate. If the serum has undergone prior processing to make the virus inactive, then level-3 or even level-2 facilities in Australia can do serological testing, such as ELISA, in the event of an outbreak. After the virus has been isolated, uninfected animals like golden hamsters can be vaccinated to conduct characterization and confirmation testing (57) as well as by immunohistopathology (58), serology (59), and PCR (60). HeV laboratory work is limited to BSL-4 standards. However, for diagnostic purposes, first attempts may be made at BSL-3 to extract HeV from suspicious clinical samples. Following the observation of cytopathic effects or the identification of HeV using immunological or genetic approaches, Subsequent culture work must only be completed in BSL-4 laboratories (26, 60).

**Testing**

**Immunohistochemistry (IHC) and Electron Microscopy:** Among the easiest and most efficient ways to identify HeV post-mortem is to apply a monoclonal or polyclonal antiserum specific to Hendra on tissue wrapped in formalin to recognize HeV-specific antigen (61). Numerous tissue samples, such as those from the kidney, uterus, placenta, brain, spleen, lung, and fetal matter, can be used for this kind of IHC. Tissue samples shouldn't be limited to the lung because, even though the HeV antigens may be removed from the lung quite quickly after infection, the vascular endothelium is the site of initial infection (62). Electron microscopy may be used to show HeV in viral cultures once the virus has been retrieved post-mortem. Viral cultures can be observed using immuno-electron microscopy techniques either directly after specific labeling or after negative staining at a minimum of 108 units of plaque formation per milliliter (63).

**Serology:** As the HeV "gold standard" reference test, the serum neutralization test is used. The neutralization test stops the virus from producing its typical cytopathogenic effect (CPE) on a monolayer of cells. This is based on the hypothesis that blood from an animal or patient who tests positive for the virus has HeV-specific antibodies. The traditional method includes culturing a Vero-cell monolayer and introducing the virus after incubation of a test serum with HeV. If the serum sample is small, the test serum may be diluted 1:2 or even 1:5 (64). Three days later, the cultures are examined for a CPE. The conventional serum neutralization test has been altered in the last ten years to offer a quick immune plaque assay that allows for the measurement of viral load and makes use of the syncytia that develops in Vero-cell cultures infected with HIV within 24 hours of culture inoculation (65). After any viruses are inactivated with methanol, sera can be tested using this plaque assay, which yields results after just one day of incubation. However, Real-time PCR and ELISA are more frequently utilized in scenarios that call for quick,

urgent detection, like an outbreak. While the most often used test for detecting anti-HeV antibodies is an indirect ELISA, other methods such as Luminex-based assays and antigen-capture ELISA are also being utilized with increasing credibility (53,66).

**Real-time PCR:** In Australia, HeV has been found using a TaqMan PCR-based real-time test (60, 67). RNA is extracted for this test, either manually or with the aid of a commercial kit for extracting viral RNA. cDNA, or complementary DNA, is made based on the viral RNA template and amplified Using probes and primers designed to target the HeV M gene specifically. The sensitivity of this test, which *Smith et al.* (60) found to be 1000 times greater than that of normal PCR, can be increased by employing additional primers that target various regions of the HeV genome (such as the P gene) increased to the point where direct culture is no longer necessary (67). Diagnostic centers around Australia utilize a plethora of different, modified PCR-based tests, some of which are based on the TaqMan or SYBR Green method. One of these modified assays that target the N gene and is based on SYBR-Green chemistry appears to be the most sensitive, with a detection limit of just 200 HeV virions (67).

## Treatment

**For humans:** The treatment is aimed at supportive care measures to improve symptom burden in both pulmonary and neurologic involvement. In addition to getting enough sleep and staying hydrated with oral fluids, supportive measures include using over-the-counter painkillers such as ibuprofen or acetaminophen to treat fever and ease aches and pains in the muscles. Saltwater rinses can help ease sore throats, while saline nasal sprays and humidifiers may aid with nasal congestion. People should seek emergency medical assistance right away if their symptoms intensify and cause serious pulmonary compromise (such as wheezing or shortness of breath), as they may need to be hospitalized for airway management. Based on in vitro (i.e., tests conducted outside of a living organism) trials, treatment with ribavirin, an antiviral medicine, and post-exposure therapy with a Hendra virus-neutralizing antibody are emerging treatments that are effective. To verify their effectiveness in people, more clinical research is necessary. The death rate from Hendra virus infection is substantial despite its rarity. Four (57%) of the Hendra virus's seven potential causes in humans that have been documented have resulted in fatalities. Notably, a vaccination against the Hendra virus can be given to horses to stop re-infection and lessen the chance of human exposure.

## A Hendra virus vaccine for horses

Preventing horses from being exposed to HeV shed by flying foxes is not an easy task. Within peri-urban and rural populations, the contact between bats and horses cannot be removed, and factors impacting interspecies transmission are probably complicated and poorly understood. Therefore, vaccination of horses has been implemented as a more direct method to safeguard their health and lower the possibility of infection in humans. To remove the extremely sick horse from the human supply chain, measures to suppress the transmission of the HeV virus in animals exposed to field viruses are being taken. One of the two necessary envelope glycoproteins needed for the infection of the host cell is the HeV G attachment glycoprotein. In 2005, Bossart and associates revealed that they had created a recombinant soluble HeV G (sG) that caused rabbits to produce antibodies that neutralize the virus (68). The efficacy of a potential vaccination based on the antigen HeV sG was initially evaluated in cats against the Nipah virus (69,70) and then in ferrets against the HeV virus (71). The investigation was applied to horses because of the good outcomes of viral exposure in these species (72). The inactivated subunit vaccination known as sG was specifically reformulated for use in horses utilizing a proprietary adjuvant that was licensed for use in that species. Data acquired following the application of a prime-boost vaccination strategy showed the

formation of neutralizing antibodies in horses who have received vaccinations following exposure to a potentially fatal HeV challenge in BSL4 environments. All of the vaccinated horses were also immune to disease. Except for a brief decrease in the number of copies of the HeV N gene found in the nasal swabs of one horse exposed to the virus six months following booster vaccination, there was no additional evidence of viral replication in animals that had received vaccinations. Nevertheless, no horse tissue contained the viral genome. After a priming series consisting of three injections (day 0, days 21, and 6 months), antibody titer remains at a high level for a whole year, according to more recent serological tests using various vaccination regimens. No HeV replication was found in the tissues, blood, or swabs of horses exposed to the virus 12 months after obtaining a third vaccination (Middleton, unpublished observations). By the end of 2012, veterinarians may administer the horse HeV vaccination (Equivac HeV, Zoetis, Parkville, Vic, Australia). As expected, vaccination rates have been highest in coastal Queensland and northeastern NSW, the areas with the highest perceived risk. However, because HeV infections are irregular, it may take some time to determine how vaccinations affect the frequency of acute HeV infections in horses. Due to a variety of issues, such as varying views regarding which horse groups are most susceptible to the virus and the expensive cost of vaccination, the Australian horse herd will not be completely vaccinated against HeV. Therefore, better infection control practices and continued awareness of the potential for HeV infection will be necessary while managing sick horses, especially in cases where the status of HeV vaccination is unknown. (72)

**Prevention**

Human infection with Hendra has only been associated with infection of an intermediate host, such as a horse, or "middleman" animal. One key strategy to reduce future human infections with Hendra is early diagnosis of illnesses in horses.

Individuals who live in regions where flying foxes or the Hendra virus are present can avoid getting sick by:

- Avoiding sick horses
- Steer clear of horses that might be Hendra virus-infected

When handling an infected horse, it is recommended that individuals wear personal protection equipment such as gloves, boots, masks or respirators, gowns, and protective eyewear.

Australia has approved a commercial vaccine for equines. Other animal species that might be susceptible to contracting Hendra could benefit from this, as well as eventually humans.

**Other vulnerable hosts of animals**

In laboratory settings, a wide range of animals, including cats, ferrets, hamsters, pigs, and guinea pigs, have demonstrated susceptibility to HeV infection. All of them display sickness that is almost the same as what is seen in horses, and hamsters and ferrets in particular are used to evaluate the effectiveness of anti-henipavirus medications and immunizations (73). Dups et al. recent study (74) of acute encephalitis in wild-type laboratory mice has great promise for research on the neurological after-effects of HeV infection, which are unique to the disease in humans and occur when there isn't a serious systemic infection. Although field infections in cats, guinea pigs, or pigs have not yet been documented, ferrets are prohibited as pets in Queensland. On the other hand, a dog taken from an epidemic site in 2011 had positive HeV antibody tests but no clinical signs. Investigating the HeV-related horse mortality in New South Wales in 2013, a similar dog case was found. To evaluate the consequences of HeV infection and the possibility of canines being exposed to the virus in BSL4 confinement settings, where there was a danger of transmission (Middleton, unreported findings). Even in situations where they showed little or no clinical indications, dogs were shown to remain continuously vulnerable to infection under exposure settings; the formation of neutralizing

antibodies was linked to the virus's eradication (75). Replication of the virus in the pharynx resulted in an infectious virus being shed, and this was sufficient to infect unsuspecting ferrets for a brief period of time. Thus far, every instance of HeV infection in humans has been definitively associated, through epidemiology, with intimate contact with an infected horse. How dangerous it is to be around HeV-positive dogs in the field is still unknown.

**Discussion**

Four of the seven people with Hendra virus (HeV) infections have passed away, resulting in an approximate mortality rate of 57%. The incubation period initially believed to be 6–8 days long, has shown signs of extending up to 21 days. Human HeV infection typically results in meningoencephalitis and acute pulmonary sickness. Patients (C-1 to C-6) had fever, myalgia, headaches, lethargy, pharyngitis, and other influenza-like symptoms in addition to pulmonary symptoms. C-7 avoided pulmonary symptoms after receiving post-exposure prophylaxis with oral hydroxychloroquine and intravenous ribavirin, but ultimately suffered from deadly encephalitis. This implies that even while the drug might shield the body against pulmonary illnesses, the virus is still able to propagate and infect the nervous system.

Comparable results were observed in HeV-infected African green monkeys given ribavirin therapy. The third survivor suffered encephalitis and still has some neurological abnormalities, but the other two recuperated from the influenza-like illness without relapsing or exhibiting any neurological signs. No virus was detected in these individuals during follow-up visits six years later. The illnesses of the four patients (C-1, C-3, C-5, C-7) who died varied: one developed fatal encephalitis 13 months after recovery, another died from cardiac arrhythmia and multiorgan failure, and the last two succumbed to acute encephalitis. These cases show that HeV infections in humans typically start with an influenza-like illness and can progress to severe outcomes, including encephalitis and multiorgan failure, with the potential for long-term dormancy and reactivation.

**Conclusion**

Future development of a Hendra virus (HeV) vaccine should leverage insights into the pathological progression of the diseases. HeV infections typically start with influenza-like symptoms and can progress to severe neurological and systemic complications, including encephalitis and multiorgan failure. Researchers should focus on targeting specific disease mechanisms and immune responses to create a vaccine that reduces mortality rates, mitigates severe symptoms, and prevents viral reactivation and long-term complications. A thorough vaccination is necessary despite the fact that existing therapies like ribavirin and hydroxychloroquine may stop pulmonary symptoms not the virus's ability to spread to the brain system. In order to tackle this fatal zoonotic infection and provide improved health outcomes for individuals who are at risk, a vaccination of this kind would be essential.

**Acknowledgments**

Not applicable.

**Ethical approval**

Not applicable.

**Conflicts of Interest**

The author declares no conflict of interest.

**References**

1. Murray K, Selleck P, Hooper P, Hyatt A, Gould A, Gleeson L, et al. A Morbillivirus that Caused Fatal Disease in Horses and Humans. Science. 1995 Apr 7; 268(5207): 94–7. doi:10.1126/science.7701348
2. Chua KB, Goh KJ, Wong KT, Kamarulzaman A, Tan PSK, Ksiazek TG, et al. Fatal encephalitis due to Nipah virus among pig-farmers in Malaysia. Lancet. 1999 Oct 1; 354(9186): 1257–9. doi:10.1016/s0140-6736(99)04299-3
3. Marsh GA, De Jong C, Barr JA, Tachedjian M, Smith C, Middleton D, et al. Cedar Virus: A

Novel Henipavirus Isolated from Australian Bats. PLOS Pathogens. 2012 Aug 2; 8(8): e1002836. doi:10.1371/journal.ppat.1002836
4. Khusro A, Aarti C, Pliego AB, Cipriano-Salazar M. Hendra Virus infection in horses: A review on emerging mystery paramyxovirus. J. Equine Vet. Sci. 2020 Aug 1; 91: 103149. doi:10.1016/j.jevs.2020.103149
5. Halpin K, Rota P. A review of Hendra virus and nipah virus infections in man and other animals. Springer eBooks. 2014 Dec 9; 997–1012. doi:10.1007/978-94-017-9457-2_40
6. Wild TF. Henipaviruses: A new family of emerging Paramyxoviruses. Pathol. Biol. 2009 Mar 1; 57(2): 188–96. doi:10.1016/j.patbio.2008.04.006
7. Wang J, Anderson DE, Halpin K, Hong X, Chen H, Walker S, et al. A new Hendra virus genotype found in Australian flying foxes. Virol J. 2021 Oct 13; 18(1). doi:10.1186/s12985-021-01652-7
8. Yuen KY, Fraser NS, Henning J, Halpin K, Gibson JS, Betzien L, et al. Hendra virus: Epidemiology dynamics in relation to climate change, diagnostic tests and control measures. One Health. 2021 Jun 1; 12:100207. doi:10.1016/j.onehlt.2020.100207
9. Rima B, Balkema-Buschmann A, Dundon WG, Duprex P, Easton A, Fouchier R, et al. ICTV virus taxonomy profile: Paramyxoviridae. J. Gen. Virol. 2019 Dec 1; 100(12):1593–4. doi:10.1099/jgv.0.001328
10. Lee B, Ataman ZA. Modes of paramyxovirus fusion: a Henipavirus perspective. Trends Microbiol. 2011 Aug 1; 19(8): 389–99. doi:10.1016/j.tim.2011.03.005
11. Wu Z, Yang L, Yang F, Ren X, Jiang J, Dong J, et al. Novel Henipa-like virus, Mojiang Paramyxovirus, In Rats, China, 2012. Emerg. Infect. Dis. 2014 Jun 1; 20(6). doi:10.3201/eid2006.131022
12. Li YY, Wang J, Hickey AC, Zhang Y, Li Y, Wu YY, et al. Antibodies to nipah or nipah-like viruses in Bats, China. Emerg. Infect. Dis. 2008 Dec 1; 14(12): 1974–6. doi:10.3201/eid1412.080359
13. Zhang XA, Li H, Jiang FC, Zhu F, Zhang YF, Chen JJ, et al. A zoonotic henipavirus in febrile patients in China. N. Engl. J. Med. 2022 Aug 4; 387(5): 470–2. doi:10.1056/nejmc2202705
14. Zhang XA, Li H, Jiang FC, Zhu F, Zhang YF, Chen JJ, et al. A zoonotic henipavirus in febrile patients in China. N. Engl. J. Med. 2022 Aug 4; 387(5): 470–2. doi:10.1056/nejmc2202705
15. Coste AT, Vandeputte P. Antifungals: from genomics to resistance and the development of novel agents. Caister Academic Press eBooks. 2015. doi:10.21775/9781910190012
16. Drexler JF, Corman VM, Gloza-Rausch F, Seebens A, Annan A, Ipsen A, et al. Henipavirus RNA in African bats. PloS One. 2009 Jul 28; 4(7): e6367. doi:10.1371/journal.pone.0006367
17. Afonso CL, Amarasinghe GK, Bányai K, Bào Y, Basler CF, Bavari S, et al. Taxonomy of the order Mononegavirales: update 2016. Arch Virol. 2016 May 23; 161(8): 2351–60. doi:10.1007/s00705-016-2880-1
18. O'Sullivan J, Allworth A, Paterson D, Snow T, Boots R, Gleeson L, et al. Fatal encephalitis due to novel paramyxovirus transmitted from horses. Lancet. 1997 Jan 1; 349(9045): 93–5. doi.10.1016/s0140-6736(96)06162-4
19. Geisbert TW, Daddario-DiCaprio KM, Hickey AC, Smith MA, Chan YP, Wang LF, et al. Development of an acute and highly pathogenic nonhuman primate model of Nipah virus infection. PloS One. 2010 May 18; 5(5): e10690. doi:10.1371/journal.pone.0010690
20. Field H, Schaaf K, Kung N, Simon C, Waltisbuhl D, Hobert H, et al. Hendra Virus Outbreak with Novel Clinical Features, Australia. Emerg. Infect. Dis. 2010 Feb 1; 16(2): 338–40. doi:10.3201/eid1602.090780
21. Wang LF, Yu M, Hansson E, Pritchard LI, Shiell B, Michalski WP, et al. The Exceptionally Large Genome of Hendra Virus: Support for Creation of a New Genus within the Family Paramyxoviridae. J Virol. 2000 Nov 1; 74(21): 9972–9. doi:10.1128/jvi.74.21.9972-9979.2000
22. Halpin K, Mungall BA. Recent progress in henipavirus research. Comp. Immunol. Microbiol. Infect. Dis. 2007 Sep 1; 30(5–6): 287–307. doi:10.1016/j.cimid.2007.05.008
23. Rogers R, Douglas I, Baldock F, Glaville R, Seppanen K, Gleeson L, et al. Investigation of a second focus of equine morbillivirus infection in coastal Queensland. Aust. Vet. J. 1996 Sep 1; 74(3): 243–4. doi:10.1111/j.1751-0813.1996.tb15413.x

24. Hanna JN, McBride WJ, Brookes DL, Shield J, Taylor CT, Smith IL, et al. Hendra virus infection in a veterinarian. Med J Aust. 2006 Nov 1; 185(10): 562–4. doi:10.5694/j.1326-5377.2006.tb00692.x
25. Field H, Breed A, Shield J, Hedlefs R, Pittard K, Pott B, et al. Epidemiological perspectives on Hendra virus infection in horses and flying foxes. Aust. Vet. J. 2007 Jul 1; 85(7): 268–70. doi:10.1111/j.1751-0813.2007.00170.x
26. Mahalingam S, Herrero LJ, Playford EG, Spann K, Herring B, Rolph MS, et al. Hendra virus: an emerging paramyxovirus in Australia. Lancet Infect. Dis. 2012 Oct 1; 12(10): 799–807. doi:10.1016/s1473-3099(12)70158-5
27. Rockx B, Baas T, Zornetzer GA, Haagmans B, Sheahan T, Frieman M, et al. Early upregulation of acute pulmonary distress Syndrome-Associated cytokines promotes lethal disease in an Aged-Mouse model of severe acute pulmonary syndrome coronavirus infection. J Virol. 2009 Jul 15; 83(14): 7062-74. doi:10.1128/jvi.00127-09
28. Chua KB, Bellini WJ, Rota PA, Harcourt BH, Tamin A, Lam SK, et al. Nipah virus: a recently emergent deadly paramyxovirus. Science. 2000 May 26; 288(5470): 1432–5. doi:10.1126/science.288.5470.1432
29. Field H, Young P, Yob JM, Mills J, Hall L, Mackenzie J. The natural history of Hendra and Nipah viruses. Microbes Infect. 2001 Apr 1; 3(4): 307–14. doi:10.1016/s1286-4579(01)01384-3
30. Taylor J, Thompson K, Annand EJ, Massey P, Bennett J, Eden JS, et al. Novel variant Hendra virus genotype 2 infection in a horse in the greater Newcastle region, New South Wales, Australia. One Health. 2022 Dec 1; 15: 100423. doi:10.1016/j.onehlt.2022.100423
31. Young P. Serologic evidence for the presence in pteropus bats of a paramyxovirus related to equine morbillivirus. Emerg. Infect. Dis. 1996 Sep 1; 2(3): 239–40. doi:10.3201/eid0203.960315
32. Olson JG, Rupprecht C, Rollin PE, An US, Niezgoda M, Clemins T, et al. Antibodies to Nipah-Like Virus in Bats (Pteropus lylei), Cambodia. Emerg. Infect. Dis. 2002 Sep 1; 8(9): 987–8. doi:10.3201/eid0809.010515
33. Hayman DTS, Suu-Ire R, Breed AC, McEachern JA, Wang L, Wood JLN, et al. Evidence of henipavirus infection in West African fruit bats. PloS One. 2008 Jul 23; 3(7): e2739. doi:10.1371/journal.pone.0002739
34. Marsh GA, De Jong C, Barr JA, Tachedjian M, Smith C, Middleton D, et al. Cedar Virus: A Novel Henipavirus Isolated from Australian Bats. PLOS Pathogens. 2012 Aug 2; 8(8): e1002836. doi:10.1371/journal.ppat.1002836
35. Luby SP, Gurley ES, Hossain MJ. Transmission of Human Infection with Nipah Virus. Clin Infect Dis. 2009 Dec 1; 49(11): 1743–8. doi:10.1086/647951
36. Rahman MA, Hossain MJ, Sultana S, Homaira N, Khan SU, Rahman M, et al. Date Palm SAP linked to Nipah virus outbreak in Bangladesh, 2008. Vector Borne Zoonotic Dis. 2012 Jan 1; 12(1): 65–72. doi:10.1089/vbz.2011.0656
37. Gurley ES, Montgomery JM, Hossain MJ, Bell M, Azad AK, Islam MR, et al. Person-to-Person transmission of Nipah virus in a Bangladeshi community. Emerg. Infect. Dis. 2007 Jul 1; 13(7): 1031–7. doi:10.3201/eid1307.061128
38. Chua KB, Lam SK, Goh KJ, Hooi PS, Ksiazek TG, Kamarulzaman A, et al. The Presence of Nipah Virus in Pulmonary Secretions and Urine of Patients during an Outbreak of Nipah Virus Encephalitis in Malaysia. J Infect. 2001 Jan 1; 42(1): 40–3. doi:10.1053/jinf.2000.0782
39. Homaira N, Rahman M, Hossain MJ, Epstein JH, Sultana R, Khan MSU, et al. Nipah virus outbreak with person-to-person transmission in a district of Bangladesh, 2007. Epidemiol Infect. 2010 Apr 12; 138(11): 1630–6. doi:10.1017/s0950268810000695
40. Wong KT, Shieh WJ, Zaki SR, Tan CT. Nipah virus infection, an emerging paramyxoviral zoonosis. Semin Immunopathol. 2002 Nov 1; 24(2): 215–28.doi:10.1007/s00281-002-0106-y
41. Escaffre O, Borisevich V, Carmical JR, Prusak D, Prescott J, Feldmann H, et al. Henipavirus pathogenesis in human pulmonary epithelial cells. J Virol. 2013 Mar 15; 87(6): 3284–94. doi:10.1128/jvi.02576-12
42. Puneet P, Moochhala S, Bhatia M. Chemokines in acute pulmonary distress syndrome. Am. J. Physiol. Lung Cell Mol. Physiol. 2005 Jan 1; 288(1): L3–15. doi:10.1152/ajplung.00405.2003
43. Baskin CR, Bielefeldt-Ohmann H, Tumpey TM, Sabourin PJ, Long JP, García-Sastre A, et al. Early and sustained innate immune response

defines pathology and death in nonhuman primates infected by highly pathogenic influenza virus. Proc. Natl. Acad. Sci. U.S.A. 2009 Mar 3; 106(9): 3455–60. doi:10.1073/pnas.0813234106
44. Selvey LA, Wells RM, McCormack JG, Ansford AJ, Murray K, Rogers RJ, et al. Infection of humans and horses by a newly described morbillivirus. Med J Aust. 1995 Jun 1; 162(12): 642–5. doi:10.5694/j.1326-5377.1995.tb126050.x
45. Mathieu C, Pohl C, Szecsi J, Trajkovic-Bodennec S, Devergnas S, Raoul H, et al. Nipah Virus Uses Leukocytes for Efficient Dissemination within a Host. J Virol. 2011 Aug 1; 85(15): 7863–71. doi:10.1128/jvi.00549-11
46. Stachowiak B, Weingartl HM. Nipah virus infects specific subsets of porcine peripheral blood mononuclear cells. PloS One. 2012 Jan 27; 7(1): e30855. doi:10.1371/journal.pone.0030855
47. Weingartl H, Czub S, Copps J, Berhane Y, Middleton D, Marszal P, et al. Invasion of the central nervous system in a porcine host by Nipah virus. J Virol. 2005 Jun 15; 79(12): 7528–34. doi:10.1128/jvi.79.12.7528-7534.2005
48. Rockx B, Brining D, Kramer J, Callison J, Ebihara H, Mansfield K, et al. Clinical outcome of henipavirus infection in hamsters is determined by the route and dose of infection. J Virol. 2011 Aug 1; 85(15): 7658–71. doi:10.1128/jvi.00473-11
49. Munster VJ, Prescott JB, Bushmaker T, Long D, Rosenke R, Thomas T, et al. Rapid Nipah virus entry into the central nervous system of hamsters via the olfactory route. Scientific Reports. 2012 Oct 15; 2(1). doi:10.1038/srep00736
50. Hendra Virus: what it is, mode of transmission, signs and symptoms, treatment, and more | Osmosis (Internet). Available from: https://www.osmosis.org/answers/hendra-virus. (Accessed 15th May 2024)
51. World Health Organization: WHO. Hendra virus infection (Internet). 2019. Available from: https://www.who.int/health-topics/hendra-virus-disease#tab=tab_1. ((Accessed 27th December 2019)
52. About Hendra Disease (Internet). Hendra Virus Disease. 2024. Available from: https://www.cdc.gov/hendra-virus/about/index.html. (Accessed 19th April 2024)
53. Daniels P, Ksiazek T, Eaton BT. Laboratory diagnosis of Nipahand Hendra virus infections. Microbes Infect. 2001 Apr 1; 3(4): 289–95. doi:10.1016/s1286-4579(01)01382-x
54. Hyatt AD, Zaki SR, Goldsmith CS, Wise TG, Hengstberger SG. Ultrastructure of Hendra virus and Nipah virus within cultured cells and host animals. Microbes Infect. 2001 Apr 1; 3(4): 297–306. doi:10.1016/s1286-4579(01)01383-1
55. Halpin K, Hyatt AD, Fogarty R, Middleton D, Bingham J, Epstein JH, et al. Pteropid Bats are Confirmed as the Reservoir Hosts of Henipaviruses: A Comprehensive Experimental Study of Virus Transmission. Am. J. Trop. Med. Hyg. 2011 Nov 1; 85(5): 946–51. doi:10.4269/ajtmh.2011.10-0567
56. Williamson M, Hooper P, Selleck P, Gleeson L, Daniels P, Westbury H, et al. Transmission studies of Hendra virus (equine morbilli-virus) in fruit bats, horses and cats. Aust. Vet. J. 1998 Dec 1; 76(12): 813–8. doi:10.1111/j.1751-0813.1998.tb12335.x
57. Williamson MM, Hooper PT, Selleck PW, Westbury HA, Slocombe RF. Experimental Hendra Virus Infectionin Pregnant Guinea-pigs and Fruit Bats (Pteropus poliocephalus). J. Comp. Pathol. 2000 Feb 1; 122(2–3): 201–7. doi:10.1053/jcpa.1999.0364
58. Guillaume V, Wong KT, Looi RY, Georges-Courbot MC, Barrot L, Buckland R, et al. Acute Hendra virus infection: Analysis of the pathogenesis and passive antibody protection in the hamster model. Virology. 2009 May 1; 387(2): 459–65. doi:10.1016/j.virol.2009.03.001
59. Bossart KN, Wang LF, Eaton BT, Broder CC. Functional expression and membrane fusion tropism of the envelope glycoproteins of Hendra virus. Virology. 2001 Nov 1; 290(1): 121–35. doi:10.1006/viro.2001.1158
60. Smith IL, Halpin K, Warrilow D, Smith GA. Development of a fluorogenic RT-PCR assay (TaqMan) for the detection of Hendra virus. J. Virol. Methods. 2001 Oct 1; 98(1): 33–40. doi:10.1016/s0166-0934(01)00354-8
61. Black P, Cronin J, Morrissy C, Westbury H. Serological examination for evidence of

infection with Hendra and Nipah viruses in Queensland piggeries. Aust. Vet. J. 2001 Jun 1; 79(6): 424–6. doi:10.1111/j.1751-0813.2001.tb12989.x
62. Hooper P, Zaki S, Daniels P, Middleton D. Comparative pathology of the diseases caused by Hendra and Nipah viruses. Microbes Infect. 2001 Apr 1; 3(4): 315–22. doi:10.1016/s1286-4579(01)01385-5
63. Hyatt AD, Daszak P, Cunningham AA, Field H, Gould AR. Henipaviruses: Gaps in the knowledge of emergence. Ecohealth. 2004 Mar 1; 1(1): 25–38. doi:10.1007/s10393-004-0017-6
64. Halpin K, Young PL, Field HE, Mackenzie JS. Isolation of Hendra virus from pteropid bats: a natural reservoir of Hendra virus. J. Gen. Virol. 2000 Aug 1; 81(8): 1927–32. doi:10.1099/0022-1317-81-8-1927
65. Crameri G, Wang LF, Morrissy C, White J, Eaton BT. A rapid immune plaque assay for the detection of Hendra and Nipah viruses and anti-virus antibodies. J Virol Methods. 2002 Jan 1; 99(1–2): 41–51. doi:10.1016/s0166-0934(01)00377-9
66. Chiang CF, Lo MK, Rota PA, Spiropoulou CF, Rollin PE. Use of monoclonal antibodies against Hendra and Nipah viruses in an antigen capture ELISA. J Virol. 2010 Jun 3; 7(1). doi:10.1186/1743-422x-7-115
67. Feldman KS, Foord A, Heine HG, Smith IL, Boyd V, Marsh GA, et al. Design and evaluation of consensus PCR assays for henipaviruses. J. Virol. Methods. 2009 Oct 1; 161(1): 52–7. doi:10.1016/j.jviromet.2009.05.014
68. Bossart KN, Crameri G, Dimitrov AS, Mungall BA, Feng YR, Patch JR, et al. Receptor binding, fusion inhibition, and induction of Cross-Reactive neutralizing antibodies by a soluble G glycoprotein of hendra virus. J Virol. 2005 Jun 1; 79(11): 6690–702. doi:10.1128/jvi.79.11.6690-6702.2005
69. Mungall BA, Middleton D, Crameri G, Bingham J, Halpin K, Russell G, et al. Feline Model of Acute Nipah Virus Infection and Protection with a Soluble Glycoprotein-Based Subunit Vaccine. J Virol. 2006 Dec 15; 80(24): 12293–302. doi:10.1128/jvi.01619-06
70. McEachern JA, Bingham J, Crameri G, Green DJ, Hancock TJ, Middleton D, et al. A recombinant subunit vaccine formulation protects against lethal Nipah virus challenge in cats. Vaccine. 2008 Jul 1; 26(31): 3842–52. doi:10.1016/j.vaccine.2008.05.016
71. Pallister J, Middleton D, Wang LF, Klein R, Haining J, Robinson R, et al. A recombinant Hendra virus G glycoprotein-based subunit vaccine protects ferrets from lethal Hendra virus challenge. Vaccine. 2011 Aug 1; 29(34): 5623–30. doi:10.1016/j.vaccine.2011.06.015
72. Middleton D, Pallister J, Klein R, Feng YR, Haining J, Arkinstall R, et al. Hendra Virus Vaccine, a one health approach to protecting horse, human, and environmental health. Emerg. Infect. Dis. 2014 Mar 1; 20(3). doi:10.3201/eid2003.131159
73. Li M, Embury-Hyatt C, Weingartl HM. Experimental inoculation study indicates swine as a potential host for Hendra virus. Vet. Res. 2010 Jan 20; 41(3): 33. doi:10.1051/vetres/2010005
74. Dups J, Middleton D, Yamada M, Monaghan P, Long F, Robinson R, et al. A new model for Hendra virus encephalitis in the mouse. PloS One. 2012 Jul 10; 7(7): e40308. doi:10.1371/journal.pone.0040308
75. Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, et al. Global trends in Emerging Infectious Diseases. Nature. 2008 Feb 1; 451(7181): 990–3. doi:10.1038/nature06536