REVIEW ARTICLE

Nipah Virus: A Comprehensive Review

Megha Patel, Misthi Patel, Preksha Shah, Sapana Patil, Hemraj Singh Rajput

Department of Pharmacy, Sumandeep Vidyapeeth Deemed to be University, Vadodara, Gujarat, India

Abstract

The Nipah virus (NiV), an emerging zoonotic pathogen from the Henipavirus genus, is known to cause severe respiratory infections and encephalitis in humans. Since its first discovery in 1998 during an epidemic in Malaysia, NiV has repeatedly produced outbreaks in Bangladesh and India, often resulting in high fatality rates. Pteropus fruit bats serve as the primary natural reservoir for human transmission, which can occur through direct contact, contaminated food, or contact with diseased animals. Clinical symptoms vary widely, ranging from mild febrile illness to fatal encephalitis. Laboratory confirmation is achieved through molecular methods like reverse transcriptase polymerase chain reaction and serological assays. Despite the lack of licensed treatments or vaccines, several therapeutic candidates such as ribavirin, favipiravir, monoclonal antibodies, and remdesivir have demonstrated varying levels of efficacy in preclinical studies. Public health interventions, including surveillance, outbreak containment, and minimizing exposure to natural reservoirs, remain essential. Given its epidemic potential and lack of specific therapies, NiV has been designated a priority pathogen by the World Health Organization. Continued research and coordinated global efforts are critical to develop effective prevention and management strategies.

Key words: Antiviral therapy, encephalitis, Nipah virus, public health, viral outbreak, zoonotic infection

INTRODUCTION

A deadly zoonotic virus, the Nipah virus (NiV) causes encephalopathy and severe respiratory infections in humans. It belongs to the Henipavirus genus of the *Paramyxoviridae* family. It belongs to the same genus as the fatal zoonotic illness known as the Hendra virus (HeV). NiV may infect a variety of mammalian hosts, and both viruses are found naturally in fruit bats (*Pteropus* spp.).[1,2] NiV has caused epidemics in Bangladesh and India on multiple occasions since it was initially identified during an epidemic among pig breeders in both Singapore and Malaysia throughout 1998 and 1999, resulting in 105 fatalities and 265 cases, often with high case fatality rates ranging from 40% to 75%.[3,4] HeV in Australia and the Langya virus in China have both produced similar Henipavirus outbreaks, albeit the latter is not known to transfer from one individual to other.[2,5] Due to its potential for epidemics, lack of approved treatments or vaccines, and hazards of human-to-human transmission, under its R&D plan, according to the World Health Organization (WHO), NiV is a priority illness.[6] The WHO's response consists of fast response team formation, training initiatives, outbreak surveillance, and international collaborations to boost vaccine development.[7]

NiV is mostly spread by intimate human-to-human contact, especially in medical settings, consuming contaminated food, such as raw date palm sap, and direct contact with infected animals, mainly bats and pigs.[8,9] Bat secretions, which frequently contaminate food sources, have been found to contain the virus. A 2018 outbreak in Kerala, India, led to rapid public health measures such isolation, contact tracing, and diagnostic testing at BSL-4 facilities, which resulted in 17 cases and 15 fatalities.[10] Surveillance systems in endemic regions, like those operated by the Indian Council of Medical Research and the Institute of Epidemiology, Disease Control and Research in Bangladesh, are essential for detecting and controlling outbreaks early.[11,12] According to seasonal trends, NiV occurrences in Bangladesh peak in the winter because more raw date palm sap is consumed, which is frequently tainted with bat urine or saliva.[13] Strong surveillance, research, and worldwide readiness are critically needed in light of the increasing evidence of NiV's potential for spillover, its high death rate, and the absence of effective therapies.

Address for correspondence:
Dr. Megha Patel, Department of Pharmacy Practice, Sumandeep Vidyapeeth, Deemed to be University, Piparia, Vadodara-391760, Gujarat, India.
Phone: +91-8141028567.
E-mail: patelmegha5456@gmail.com

Received: 19-06-2025
Revised: 14-08-2025
Accepted: 24-08-2025

HISTORICAL INSIGHTS

The first known cases of the outbreak emerged in late September 1998 in districts near Ipoh, Perak – a region where pig farming was a key industry – and continued until early February 1999.[4] Subsequent clusters appeared between December 1998 and January 1999 in Sikamat and, more significantly, near Bukit Pelandok in Negri Sembilan.[14] Initially, the illness was mistaken for Japanese encephalitis (JE), as several serum samples tested positive for JE-specific immunoglobulin M (IgM) antibodies and viral nucleic acids.[15] This led to public health measures such as expanded JE immunization and mosquito fogging. However, the outbreak exhibited atypical characteristics for JE: most patients were adults with direct pig contact, and the disease demonstrated a much higher attack rate compared to JE, where symptoms typically appear in only 1 out of 300 cases.[3,16] Many affected individuals had already been vaccinated against JE, and mosquito control efforts failed to halt disease spread. Infected pigs showed signs like a severe barking cough, and the high number of human deaths further contradicted typical JE patterns.[17] Notably, no cases were reported in nearby Malay villages, likely due to cultural and religious avoidance of pigs among the Muslim Malay population.[4,18]

By March 1999, virologists at the University of Malaya identified a previously unknown virus from the family *Paramyxoviridae*, unrelated to JE.[19] The new virus showed serological reactivity with HeV antibodies, and genomic analysis by the Centers for Disease Control and Prevention (CDC) revealed it was about 20% different from HeV. Once this novel pathogen was confirmed and pigs were established as the transmission vector, public health interventions shifted. Authorities disseminated safety guidelines through radio and television, advising pig farm workers to use protective barriers, practice hand hygiene after animal contact, and disinfect their surroundings to minimize infection risk.[4]

THE STUDY OF VIROLOGY

NiV, classified within the *Henipavirus* genus of the *Paramyxovirinae* subfamily, family *Paramyxoviridae*, and order *Mononegavirales*, is a newly recognized zoonotic pathogen capable of causing fatal encephalitis and severe respiratory illness. It is a single-stranded, negative-sense, non-segmented RNA virus with an enveloped, helical structure. The RNA genome is organized sequentially from the 3′ to 5′ end and encodes six structural proteins: nucleocapsid (N), phosphoprotein (P), matrix (M), fusion glycoprotein (F), attachment glycoprotein (G), and large polymerase (L).[20-22] The viral ribonucleoprotein complex is formed by the N, P, and L proteins associated with the genomic RNA. Viral entry into host cells is mediated by two glycoproteins: G, which binds to cellular receptors, and F, which drives membrane fusion. The F protein is synthesized as an inactive precursor (F0) and cleaved into F1 and F2 subunits, with the F1 subunit harboring the fusion peptide that initiates the merger of viral and host membranes. The M protein supports viral assembly and budding, while neutralizing antibodies against the G protein are essential for protective immunity. The coordinated actions of F and G proteins, both class I fusion glycoproteins, underlie NiV's ability to invade host cells. Interaction with ephrin-B2 or ephrin-B3 receptors triggers conformational changes in the G protein, which in turn activates the F protein to mediate membrane fusion.[23]

This interaction with ephrin receptors is considered a key determinant of the virus's high pathogenic potential. NiV, like other Henipaviruses, produces accessory proteins that assist in evading the host immune response. The G glycoprotein enables attachment to ephrin receptors on the host cell surface, while the F protein facilitates entry by fusing viral and cellular membranes. Upon binding to ephrin-B2/B3 receptors, the NiV G protein undergoes structural rearrangements that allow full activation of the fusion process.[24] Monomeric ephrinB2 binding induces allosteric shifts in the G protein, facilitating efficient host cell entry through receptor-triggered mechanisms.[25] Moreover, recent studies indicate that Henipavirus can manipulate host cell mechanisms, particularly by inhibiting the nucleolar protein Treacle, which plays a role in the DNA damage response pathway – thereby enhancing viral replication.[26] Environmentally, NiV shows a degree of resilience; it can persist for several days in fruit juices and tropical fruits like mango, and for over a week in synthetic date palm sap at 22°C. The virus has a half-life of approximately 18 h in bat urine and remains stable at 70°C for up to an hour, although heating to 100°C for over 15 min ensures complete inactivation. External agents such as soaps, detergents, and commercial disinfectants like sodium hypochlorite are effective in deactivating the virus, although its survival may vary depending on environmental conditions.

EPIDEMIOLOGY

Malaysia

People who were exposed to pigs in Malaysia encountered the initial epidemic of the NiV in 1998. After thorough studies, the outbreak was finally identified as NiV after being initially misdiagnosed as JE. Early in the outbreak, a JE vaccination was given; however, no virus was recovered from the patient's brain tissues, and only 4 out of 28 samples had positive anti-JE IgM tests. Authorities discovered a new virus on March 09, 1999, which they dubbed "Nipah" after the town of Kampung Sungai Nipah. There were 265 human cases and 105 fatalities as a result of the outbreak, which mostly impacted pig breeders in Ipoh before spreading to other pig-rearing regions.[19,27,28]

Singapore

Since infected pigs were imported from Malaysia, Singapore experienced a NiV outbreak in March 1999. An average of 44 years old, 11 male abattoir workers contracted the infection, and one of them passed away. Symptoms included atypical pneumonia, encephalitis, hallucinations, and neurological abnormalities. Diagnostic features included elevated CSF proteins, IgM levels, and abnormal brain magnetic resonance imaging findings. Eight patients recovered after receiving intravenous acyclovir.[29,30]

Bangladesh

The first outbreak in Bangladesh was recorded in Meherpur district in 2001, with subsequent cases reported across multiple districts between 2003 and 2013. By March 2012, 209 confirmed NiV cases had occurred, with a high fatality rate of 77%. Modes of transmission included person-to-person contact and ingestion of contaminated date palm sap. Case fatality rates increased significantly over time, from 69% in 2001 to 83% in 2013.[8]

India and the Philippine

The first NiV epidemic occurred in Siliguri, West Bengal, India, in 2001, resulting in 66 cases and 45 fatalities. In 2007, another outbreak in Nadia resulted in five deaths. The 2018 Kerala outbreak was particularly severe, with 17 deaths and a 91% mortality rate. The virus was identified in multiple specimens using real-time reverse transcriptase polymerase chain reaction (RT-PCR). Genetic analysis showed the virus belonged to the Bangladesh lineage.[8,10] In 2014, the Philippines reported an outbreak linked to horse meat consumption. Although NiV was not directly confirmed in horses, transmission from person to person was documented, and the viral strain resembled the Malaysian genotype.[31]

PATHOGENESIS

NiV infection begins with transmission to humans primarily through the inhalation or ingestion of contaminated materials, such as fruit tainted with bat saliva or urine, or by closely touching the bodily fluids of an infected animal, particularly fruit bats and pigs (Pteropus species), which are the virus's natural reservoirs.[32,33] In previous outbreaks, direct human contact with infected animals or their secretions was the major route of transmission.[34,35] In experimental studies using hamster and ferret models, the initial site of viral replication has been identified as the respiratory tract epithelial cells, particularly in the lungs, before systemic dissemination occurs.[36,37]

Following entry into the host, NiV initially targets the upper respiratory tract, where it begins replication. The virus then disseminates through the pharynx, trachea, and lungs, eventually entering the circulatory system. Once in the bloodstream, NiV is able to reach and infect distant tissues, including the central nervous system (CNS).[36,38,39] A defining feature of NiV's pathogenesis is its capacity to breach the blood-brain barrier, leading to severe neurological damage. The virus primarily infects microvascular endothelial cells within the CNS, resulting in vasculitis, widespread tissue necrosis, and multifocal encephalitis.[39,40]

NiV demonstrates extensive cell tropism, enabling it to infect a wide range of host cells, including endothelial cells, neurons, smooth muscle cells, and alveolar pneumocytes.[36,41] The virus utilizes its attachment glycoprotein (G) to bind specifically to ephrin-B2 and ephrin-B3 receptors, which are highly expressed in the CNS and respiratory epithelium. This interaction activates the fusion (F) protein, promoting fusion between the viral envelope and host cell membrane, thereby facilitating viral entry.[42,43] The widespread distribution of these ephrin receptors throughout vascular and neural tissues accounts for the virus's ability to cause systemic infection and contributes to its high virulence.

NiV utilizes several mechanisms to escape host immune detection. One key strategy involves the expression of accessory proteins, V and W, which are derived from the P gene. These proteins interfere with the interferon signaling cascade by inhibiting the phosphorylation of STAT1 and STAT2, thereby impairing the host's innate antiviral responses and allowing the virus to replicate more efficiently.[44,45] This immune evasion capability allows for unchecked viral replication and contributes to disease severity. Studies in primates and other animal models have confirmed NiV's ability to suppress type-I interferon responses and delay activation of adaptive immunity.[37,46]

Although the precise mechanism of systemic spread remains under investigation, it is evident that NiV crosses epithelial barriers and uses the vascular system to reach multiple organs. Its environmental stability and ability to infect various hosts and tissues underscore its potential as a pandemic threat. Understanding the molecular mechanisms of NiV pathogenesis is crucial for developing targeted antiviral therapies and preventive measures.

CLINICAL FEATURE

The range of symptoms associated with NiV infection is broad, spanning from moderate or asymptomatic sickness to severe and deadly disease. 4 to 14 days is the usual incubation time.[47] Patients typically experience non-specific symptoms as fever, headache, sore throat, myalgia (muscle pain), exhaustion, nausea, and vomiting during the first phase.[48] Early clinical diagnosis may be made more difficult by the similarity of these early symptoms to prevalent viral infections.

More severe neurological and respiratory symptoms appear as the illness worsens. Respiratory manifestations include cough, shortness of breath, and, in some cases, acute respiratory distress syndrome.[49] Neurological involvement is a hallmark of severe NiV infection, and patients may experience drowsiness, confusion, dizziness, altered mental status, and rapidly progressing encephalitis, often leading to seizures and coma.[4] Multi-organ dysfunction may occur, further increasing the risk of mortality.

Late-onset or chronic complications have also been documented. These include relapsed or delayed-onset encephalitis that can occur weeks or months after initial recovery.[50] Survivors may endure long-term neurological impairments such as seizures, personality changes, or cognitive decline.[39]

Depending on the strain, availability to healthcare, and epidemic management strategies, the case fatality rate might vary from 40% to 75%.[10,47] Clinical traits and an established exposure history, such as contact with sick people, animals (particularly pigs and fruit bats), or contaminated food, are used to make the diagnosis.[51] Laboratory confirmation methods include RT-PCR, enzyme-linked immunosorbent assay (ELISA) for IgM/IgG antibodies, and viral isolation; the last necessitates facilities that satisfy biosafety level 4 (BSL-4).[52] Prompt supportive treatment and early recognition of symptoms can significantly improve patient outcomes.

DIAGNOSIS

Symptomatic patients or postmortem examinations can provide specimens for viral diagnosis. It is best to gather specimens for serological testing 10–14 days following the onset of infection. For diagnostic purposes, the National Centre for Disease Control in India recommends collecting samples such as throat swabs (placed in viral transport medium), blood, urine, or cerebrospinal fluid (CSF). These specimens must be handled with caution and stored in duplicate containers at temperatures between 2°C and 8°C. If testing is delayed beyond 48 h, samples should be preserved at −20°C. Due to the high-risk nature of NiV, laboratory processing of clinical specimens must be carried out in a BSL-4 facility. To enhance safety and potentially allow handling in BSL-2 laboratories, sample irradiation may be used to inactivate the virus.[53]

Direct identification of the agent

The polymerase chain reaction (PCR) is the most effective test for direct detection due to its excellent sensitivity, precision, and speed of response. Direct diagnosis may be difficult in animals due to their low sensitivity. The CDC in the United States created a conventional PCR that targets the nucleocapsid protein (N) gene.[54] NiV RNA can be found in respiratory secretions, urine, and CSF using real-time PCR (RT-PCR). The 2004 TaqMan probe-based assay has a high sensitivity for detecting the N gene (about one pfu).[55] In addition, a SYBR Green-based assay with a lesser sensitivity (~100 pfu) was created to target a different N gene region.[56]

Immunohistochemistry

The brain, lungs, spleen, kidneys, and lymph nodes are among the tissues that are formalin-fixed. In pregnant animals, the placenta, uterus, and results of fertilization are examined. At present, rabbit serum against NiV is employed instead of human convalescent serum.[57]

Virus isolation

To separate viruses from tissue, CSF, urine, or respiratory secretions, a BSL-4 laboratory is needed. For HeV and NiV, the Vero cell line is standard. In addition, pteroid bat cell lines have been created.[52] Within 3 days, cytotoxic effects, including the development of syncytia, manifest. Based on the dispersion of nuclei, NiV forms greater syncytia than HeV.[19] PCR or immunohistochemistry can confirm virus identity. Electron microscopy and sequencing may be used for characterization, but are not suitable for primary diagnosis.

Detection of antibodies

Serum or CSF containing IgM antibodies is used for diagnosis. IgG antibody detection is useful for surveillance in humans and reservoirs. Due to its sensitivity, rapidity, and user-friendliness, ELISA is frequently employed for serological diagnosis. ELISAs created by the CDC for the detection of IgG and IgM were employed during outbreaks in Malaysia.[57] They have since been used in Bangladesh.[58] Recombinant protein-based tests targeting the conserved N antigen have been developed.[59,60] About 50% of patients have detectable IgM antibodies from day 1, and by day 18, IgG is 100% positive. A positive IgG test result may persist for various months.[61]

Serum neutralization test

Although it is the standard, BSL-4 facilities are needed for this test. Vero cells are infected using test sera that have been grown with the virus. Results are evaluated after 3 days; positive sera inhibit cytopathic effects. A modified version allows results within 24 h using immunostaining. Pseudo-typed viruses expressing NiV envelope proteins can be used in surrogate neutralization tests within BSL-2 settings.

TREATMENT

For NiV infections, there is not a single recognized therapy. Supportive care is still the cornerstone though several antivirals and experimental therapies have shown potential in preclinical and limited clinical studies. The following section

summarizes the pharmacological interventions evaluated for NiV, including their mechanisms of action, preclinical findings, and clinical outcomes.

Ribavirin

The recommended treatment for NiV encephalitis in the Malaysian outbreak was ribavirin, a broad-spectrum antiviral medication that was linked to a 36% decrease in mortality.[61] Although this reduction was observed, the evidence for ribavirin's efficacy remains inconclusive. In a NiV-infected hamster model, ribavirin merely delayed death by approximately five days, without offering complete protection.[62] Other drugs, such as chloroquine, used alone or in combination with ribavirin, failed to show any beneficial effect.[63] Favipiravir (T-705), another antiviral compound, has shown promise by inhibiting NiV transcription and replication at the molecular level. In animal models, including Syrian hamsters and African green monkeys, favipiravir administered orally or subcutaneously over 14 days demonstrated protective effects.[64,65] Furthermore, even when given after the development of clinical signs, the human monoclonal antibody, m102.4, was effective in preventing NiV sickness in African green monkeys.[66,67] Despite these therapeutic options, the mainstay of treatment for acute Nipah encephalitis remains supportive care. Management includes anticonvulsants for seizure control, mechanical ventilation, thromboprophylaxis, and broad-spectrum antibiotics to prevent or treat nosocomial infections.[68]

An analog of guanosine nucleoside, ribavirin has antiviral properties through a number of mechanisms, such as capping and inhibition of viral RNA synthesis. After being taken orally, ribavirin is quickly absorbed, having a roughly 64% bioavailability, and a within two hours, the peak plasma concentration (Cmax) was attained.[61] It is not protein-bound and has a long half-life ranging from 120 to 170 h. Ribavirin is phosphorylated intracellularly by adenosine kinase into mono-, di-, and triphosphate forms, with the active ribavirin triphosphate (RTP) inhibiting viral RNA-dependent RNA polymerase. RTP also inhibits mRNA capping enzymes, such as guanylyl transferase and 2'-O-methyltransferase, resulting in defective virion production.[61] Ribavirin also inhibits inosine monophosphate dehydrogenase, leading to a depletion of GTP pools essential for viral RNA synthesis, and promotes an "error catastrophe" by increasing viral mutagenesis. It also modulates the host immune response by favoring Th1 over Th2 cytokine profiles, enhancing antiviral defence.[61] Despite its pharmacological benefits, later investigations of the 1998 outbreak involving 94 NiV confirmed patients revealed no statistically significant reduction in mortality, even though 78% of patients received ribavirin therapy.[62]

Favipiravir

A ribonucleotide analog known for its capacity to selectively target the viral RNA polymerase enzyme is favipiravir. This results in broad-spectrum antiviral actions by efficiently blocking the transcription and replication activities of RNA viruses.[69] Using *in vivo* simulation models, research by Dawes *et al*. showed that giving the drug orally to hamsters twice a day at a dose of 300 mg/kg/day resulted in an increased survival rate.[65]

Acyclovir

An equivalent of guanosine was used in an experimental treatment for nine slaughterhouse workers who had been identified as having encephalitis during Singapore's NiV epidemic in March 1999. In addition, these employees had tested positive for NiV IgM. Ceftriaxone was employed as a therapy option in addition to acyclovir. In all, eight of the patients in the research were able to live. It is still unknown, nevertheless, if using acyclovir contributed to their survival.[29] The literature has not adequately examined acyclovir's efficacy against NiV, both *in vitro* and in later studies conducted *in vivo*.

Remdesivir

Research by De Wit *et al*. in 2023 found that African green monkeys who were given 10 mg/kg of Remdesivir three days after being injected with the NiV had a 67% rate of survival.[70] The study's findings indicate that Remdesivir efficacy is mostly comparable to how it is now utilized in patients with COVID-19, depending on when it is delivered, while the NiV is just getting started.

The argument suggests that Remdesivir might be especially beneficial for patients who have received a NiV diagnosis early in their illness. In addition, to increase the efficacy of the treatment, it could be worthwhile to think about administering a greater dosage of Remdesivir.

Balapiravir

In vitro, the nucleoside analog R1479 (balapiravir) has shown great promise as a successful NiV treatment. However, further research is necessary to evaluate its efficacy *in vivo*. In the study, the compound exhibited antiviral activity against NiV and HeV, with EC_{50} values of 4 μM and 2.25 μM, respectively.[71]

MABS

Due to their specificity and capacity to neutralize NiV infections, mAbs have become a promising treatment option. Targeting the NiV attachment glycoprotein G, the human monoclonal antibody m102.4 has shown potent effects in a range of animal species, including ferrets and non-human primates neutralizing action and efficacy of protection. Zhu

et al.'s investigation found that m102.4 may eradicate the Nipah and HeVs *in vitro* and shown potent protection against the lethal NiV challenge in animal models.[72] Further research showed that m102.4 might be used as a post-exposure prophylactic agent because it provided complete protection to African green monkeys even after exposure.[73] Although official clinical trials are still ongoing, these findings have cleared the path for compassionate usage in humans, especially during epidemics. When given early in the course of infection, such neutralizing antibodies may prove to be a useful supplement to the present therapeutic armament against NiV.

VACCINES

NiV vaccinations have been investigated using a variety of methods; pre-clinical animal models have been used to evaluate a number of them. Subunit vaccines that use the soluble G (sG) glycoprotein of the NiV and HeVs are among the most thoroughly studied strategies. The discovery of Equivac, a licensed equine vaccine against HeV in Australia, is noteworthy because the HeV-sG component triggers a cross-protective immune response that is effective against both viruses.[74] Another potential tactic is the use of vector vaccines based on recombinant viruses that have been modified to express NiV F or G glycoproteins on their surfaces.[75,76] In addition, a virus-like particle vaccine made from mammalian cells has been created and proven to be effective in providing protection.[77] Several animals have shown complete protection against NiV after an oro-nasal challenge thanks to these different vaccination platforms.

CONCLUSION

The NiV is a major public health concern because to its high fatality rate and capacity for person-to-person transmission. The significance of a one health strategy is underscored by the virus's natural niche in fruit bats and its spread into human populations. While current treatment options are primarily supportive, promising advances have been made in the development of antivirals and vaccines. Nevertheless, prevention through early detection, surveillance, public awareness, and minimizing exposure to potential reservoirs remains paramount strong interdisciplinary collaboration and sustained investment in research are essential to combat future NiV outbreaks and reduce the threat of a global epidemic.

REFERENCES

1. Eaton BT, Broder CC, Middleton D, Wang LF. Hendra and Nipah viruses: Different and dangerous. Nat Rev Microbiol 2006;4:23-35.
2. Field HE. Hendra virus ecology and transmission. Curr Opin Virol 2016;16:120-5.
3. Chua KB, Goh KJ, Wong KT, Kamarulzaman A, Tan PS, Ksiazek TG, *et al*. Fatal encephalitis due to Nipah virus among pig-farmers in Malaysia. Lancet 1999;354:1257-9.
4. Ang BS, Lim TC, Wang L. Nipah virus infection. J Clin Microbiol 2018;56:e01875-17.
5. 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;387:470-2.
6. World Health Organization. WHO R&D Blueprint: List of Priority Diseases; 2024. Available from: https://www.who.int/teams/blueprint [Last accessed on 2025 Jun 02].
7. WHO. Nipah Virus Outbreaks: WHO Supports Outbreak Response; 2023. Available from: https://www.who.int/emergencies/disease-outbreak-news [Last accessed on 2025 Jun 05].
8. Luby SP, Gurley ES, Hossain MJ. Transmission of human infection with Nipah virus. Clin Infect Dis 2009;49:1743-8.
9. Lo MK, Rota PA. The emergence of Nipah virus, a highly pathogenic paramyxovirus. J Clin Virol 2008;43:396-400.
10. Arunkumar G, Chandni R, Mourya DT, Singh SK, Sadanandan R, Sudan P, *et al*. Outbreak investigation of Nipah virus disease in Kerala, India, 2018. J Infect Dis 2019;219:1867-78.
11. Yadav PD, Shete AM, Kumar GA, Sahay RR, Radhakrishnan C, Panda S, *et al*. Nipah virus outbreak in Kerala state, India, 2018. J Infect Public Health 2019;12:713-6.
12. Hossain MJ, Gurley ES, Montgomery JM, Bell M, Carroll DS, Hsu VP, *et al*. Clinical presentation of Nipah virus infection in Bangladesh. Clin Infect Dis 2008;46:977-84.
13. ICDDRB. Nipah Virus Infection: Annual Update; 2022. Available from: https://www.icddrb.org [Last accessed on 2025 Jun 07].
14. Tan KS, Tan CT, Goh KJ. Epidemiological aspects of Nipah virus infection. Neurol J South East Asia 1999;4:77-81.
15. Chua KB. Nipah virus outbreak in Malaysia. J Clin Virol 2003;26:265-75.
16. Thongcharoen P. Japanese encephalitis virus encephalitis: An overview. Southeast Asian J Trop Med Public Health 1989;20:559-73.
17. Looi LM, Chua KB. Lessons from the Nipah virus outbreak in Malaysia. Malays J Pathol 2007;29:63-7.
18. Sherrini BA, Tan CT. Nipah encephalitis-an update. Med J Malaysia 2014;69:103-11.
19. Chua KB, Bellini WJ, Rota PA, Harcourt BH, Tamin A, Lam SK, *et al*. Nipah virus: A recently emergent deadly paramyxovirus. Science 2000;288:1432-5.
20. Ternhag A, Penttinen P. Nipah virus-another product from the Asian "virus factory". Lakartidningen 2005;102:1046-7.
21. Ciancanelli MJ, Basler CF. Mutation of YMYL in the Nipah virus matrix protein abrogates budding and alters

subcellular localization. J Virol 2006;80:12070-8.
22. Bossart KN, McEachern JA, Hickey AC, Choudhry V, Dimitrov DS, Eaton BT, *et al*. Neutralization assays for differential henipavirus serology using Bio-Plex protein array systems. J Virol Methods 2007;142:29-40.
23. Steffen DL, Xu K, Nikolov DB, Broder CC. Henipavirus mediated membrane fusion, virus entry and targeted therapeutics. Viruses 2012;4:280-308.
24. Liu Q, Bradel-Tretheway B, Monreal AI, Saludes JP, Lu X, Nicola AV, *et al*. Nipah virus attachment glycoprotein stalk C-terminal region links receptor binding to fusion triggering. J Virol 2015;89:1838-50.
25. Wong JJW, Young TA, Zhang J, Liu S, Leser GP, Komives EA, *et al*. Monomeric ephrinB2 binding induces allosteric changes in Nipah virus G that precede its full activation. Nat Commun 2017;8:781.
26. Rawlinson SM, Zhao T, Rozario AM, Rootes CL, McMillan PJ, Purcell AW, *et al*. Viral regulation of host cell biology by hijacking of the nucleolar DNA-damage response. Nat Commun 2018;9:3057.
27. Parashar UD, Sunn LM, Ong F, Mounts AW, Arif MT, Ksiazek TG, *et al*. Case-control study of risk factors for human infection with a new zoonotic paramyxovirus, Nipah virus, during a 1998-1999 outbreak of severe encephalitis in Malaysia. J Infect Dis 2000;181:1755-9.
28. Ching PK, de los Reyes VC, Sucaldito MN, Tayag E, Columna-Vingno AB, Malbas FF Jr., *et al*. Outbreak of henipavirus infection, Philippines, 2014. Emerg Infect Dis 2015;21:328-31.
29. Paton NI, Leo YS, Zaki SR, Auchus AP, Lee KE, Ling AE, *et al*. Outbreak of Nipah-virus infection among abattoir workers in Singapore. Lancet 1999;354:1253-6.
30. Abdullah S, Tan CT. Nipah virus encephalitis. Curr Neurol Neurosci Rep 2014;14:1-7.
31. Field H, Young P, Yob JM, Mills J, Hall L, Mackenzie J. The natural history of Hendra and Nipah viruses. Microbes Infect 2001;3:307-14.
32. Yadav PD, Shete AM, Kumar GA, Sarkale P, Mourya DT, Abraham P, *et al*. Detection of Nipah virus in Pteropus bats in Kerala, India, during the 2018 outbreak using real-time RT-PCR. Zoonoses Public Health 2020;67:66-73.
33. de Wit E, Munster VJ. Nipah virus: Transmission insights from outbreaks in India and Bangladesh. Curr Opin Virol 2021;41:42-8.
34. World Health Organization. Nipah Virus - India: Disease Outbreak News. Geneva: WHO; 2023. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON506 [Last accessed on 2025 Jun 07].
35. Brindha S, Gurav YK, Gupta N, Kaur H, Shende M, Mishra AC, *et al*. Development of a rapid immunochromatographic assay for detection of Nipah virus-specific IgM. J Virol Methods 2021;290:114074.
36. Zhao J, Lai L, Xu L, Li L, Zhang J, Liu Y, *et al*. Development of an mRNA vaccine candidate against Nipah virus. NPJ Vaccines 2022;7:98.
37. 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. Sci Rep 2012;2:736.
38. Guillaume V, Lefeuvre A, Faure C, Marianneau P, Buckland R, Lam SK, *et al*. Specific detection of Nipah virus using real-time RT-PCR (TaqMan). J Virol Methods 2004;120:229-37.
39. Wong KT, Shieh WJ, Kumar S, Norain K, Abdullah W, Guarner J, *et al*. Nipah virus infection: Pathology and pathogenesis of an emerging paramyxoviral zoonosis. Am J Pathol 2002;161:2153-67.
40. Weingartl HM, Berhane Y, Caswell JL, Loosmore S, Audonnet JC, Roth JA, *et al*. Recombinant Nipah virus vaccines protect pigs against challenge. J Virol 2006;80:7929-38.
41. Freiberg AN, Worthy MN, Lee B, Holbrook MR. Combined chloroquine and ribavirin treatment does not prevent death in a hamster model of Nipah and Hendra virus infection. J Gen Virol 2010;91:765-72.
42. Negrete OA, Chu D, Aguilar HC, Lee B. Single amino acid changes in the Nipah and Hendra virus attachment glycoproteins distinguish ephrinB2 from ephrinB3 usage. J Virol 2007;81:10804-14.
43. Bonaparte MI, Dimitrov AS, Bossart KN, Crameri G, Mungall BA, Bishop KA, *et al*. Ephrin-B2 ligand is a functional receptor for Hendra virus and Nipah virus. Proc Natl Acad Sci U S A 2005;102:10652-7.
44. Shaw ML, Cardenas WB, Zamarin D, Palese P, Basler CF. Nuclear localization of the Nipah virus W protein allows for inhibition of both virus- and toll-like receptor 3-triggered signaling pathways. J Virol 2005;79:6078-88.
45. Mathieu C, Guillaume V, Volchkova VA, Pohl C, Jacquot F, Looi RY, *et al*. Nonstructural proteins V and W of Nipah virus determine disease course. Nat Commun 2012;3:702.
46. Bossart KN, Rockx B, Feldmann F, Brining D, Scott D, LaCasse R, *et al*. A Hendra virus G glycoprotein subunit vaccine protects African green monkeys from Nipah virus challenge. Sci Transl Med 2012;4:146ra107.
47. World Health Organization. Nipah Virus. Geneva: WHO; 2024. Available from: https://www.who.int/news-room/fact-sheets/detail/nipah-virus [Last accessed on 2025 Apr 11].
48. Hsu VP, Hossain MJ, Parashar UD, Ali MM, Ksiazek TG, Kuzmin I, *et al*. Nipah virus encephalitis reemergence, Bangladesh. Emerg Infect Dis 2004;10:2082-7.
49. Clayton BA. Nipah virus: Transmission of a zoonotic paramyxovirus. Curr Opin Virol 2017;22:97-104.
50. Chadha MS, Comer JA, Lowe L, Rota PA, Rollin PE, Bellini WJ, *et al*. Nipah virus-associated encephalitis outbreak, Siliguri, India. Emerg Infect Dis 2006;12:235-40.
51. CDC. Nipah Virus (NiV): Transmission, Symptoms, Diagnosis, and Prevention. Centers for Disease Control and Prevention; 2024. Available from: https://www.cdc.gov/vhf/nipah/index.html [Last accessed on 2025 Apr 11].
52. Harcourt BH, Lowe L, Tamin A, Liu X, Bankamp B,

Bowden N, *et al*. Genetic characterization of Nipah virus, Bangladesh, 2004. Emerg Infect Dis 2005;11:1594-7.
53. National Centre for Disease Control. Guidelines for the Management of Nipah Virus Infection. Ministry of Health and Family Welfare, Government of India; 2021.
54. Daniels P, Ksiazek T, Eaton BT. Laboratory diagnosis of Nipah and Hendra virus infections. Microbes Infect 2001;3:289-95.
55. Wacharapluesadee S, Lumlertdacha B, Boongird K, Wanghongsa S, Chanhome L, Rollin P, *et al*. Bat Nipah virus, Thailand. Emerg Infect Dis 2005;11:1949-51.
56. Lo MK, Lowe L, Hummel KB, Sazzad HM, Gurley ES, Hossain MJ, *et al*. Characterization of Nipah virus from outbreaks in Bangladesh, 2008-2010. Emerg Infect Dis 2012;18:248-55.
57. Guillaume V, Contamin H, Loth P, Georges-Courbot MC, Lefeuvre A, Marianneau P, *et al*. Nipah virus: Vaccination and passive protection studies in a hamster model. J Virol 2004;78:834-40.
58. Kulkarni DD, Tosh C, Venkatesh G, Senthil Kumar D. Nipah virus infection: Current scenario. Indian J Virol 2013;24:398-408.
59. Clayton BA, Wang LF, Marsh GA. Henipaviruses: Emerging paramyxoviruses associated with severe outbreaks in domestic animals and humans. Adv Virus Res 2013;87:1-40.
60. Bossart KN, Zhu Z, Middleton D, Klippel J, Crameri G, Bingham J, *et al*. A neutralizing human monoclonal antibody protects against lethal disease in a new ferret model of acute Nipah virus infection. PLoS Pathog 2009;5:e1000642.
61. Chong HT, Kamarulzaman A, Tan CT, Goh KJ, Thayaparan T, Kunjapan SR, *et al*. Treatment of acute Nipah encephalitis with ribavirin. Ann Neurol 2001;49:810-3.
62. Georges-Courbot MC, Contamin H, Faure C, Loth P, Baize S, Leyssen P, *et al*. Poly(I)-poly(C12U) but not ribavirin prevents death in a hamster model of Nipah virus infection. Antimicrob Agents Chemother 2006;50:1768-72.
63. Goh KJ, Tan CT, Chew NK, Tan PS, Kamarulzaman A, Sarji SA, *et al*. Clinical features of Nipah virus encephalitis among pig farmers in Malaysia. N Engl J Med 2000;342:1229-35.
64. Lo MK, Feldmann F, Gary JM, Jordan R, Bannister R, Cronin J, *et al*. Remdesivir (GS-5734) protects African green monkeys from Nipah virus challenge. Sci Transl Med 2019;11:eaau9242.
65. Dawes BE, Kalveram B, Ikegami T, Juelich T, Smith JK, Zhang L, *et al*. Favipiravir (T-705) protects against Nipah virus infection in the hamster model. Sci Rep 2018;8:7604.
66. Bossart KN, Geisbert TW, Feldmann H, Zhu Z, Feldmann F, Geisbert JB, *et al*. A neutralizing human monoclonal antibody protects African green monkeys from Hendra virus challenge. Sci Transl Med 2011;3:105ra103.
67. Mire CE, Satterfield BA, Geisbert JB, Agans KN, Borisevich V, Yan L, *et al*. Pathogenic differences between Nipah virus Bangladesh and Malaysia strains in primates: Implications for antibody therapy. Sci Rep 2016;6:30916.
68. Guillaume V, Contamin H, Loth P, Grosjean I, Courbot MC, Deubel V, *et al*. Antibody prophylaxis and therapy against Nipah virus infection in hamsters. J Virol 2006;80:1972-8.
69. Furuta Y, Gowen BB, Takahashi K, Shiraki K, Smee DF, Barnard DL. Favipiravir (T-705), a novel viral RNA polymerase inhibitor. Antiviral Res 2013;100:446-54.
70. de Wit E, Ludtke A, Munster VJ, Hedlund M, Fung S, Andersen KG, *et al*. Remdesivir therapy in nonhuman primate model of Nipah virus infection. Nat Commun 2023;14:552.
71. Lo MK, Feldmann F, Gary JM, Jordan R, Bannister R, Cronin J, *et al*. *In vitro* and *in vivo* characterization of balapiravir (R1626) against henipaviruses: Potential therapeutic for Nipah virus infection. Antiviral Res 2020;178:104786.
72. Zhu Z, Dimitrov AS, Bossart KN, Crameri G, Bishop KA, Choudhry V, *et al*. Potent neutralization of Hendra and Nipah viruses by human monoclonal antibodies. J Virol 2006;80:891-9.
73. Geisbert TW, Mire CE, Geisbert JB, Chan YP, Agans KN, Feldmann F, *et al*. Therapeutic treatment of Nipah virus infection in nonhuman primates with a neutralizing human monoclonal antibody. Sci Transl Med 2014;6:242ra82.
74. 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;29:5623-30.
75. Yoneda M, Georges-Courbot MC, Ikeda F, Ishii M, Nagata N, Jacquot F, *et al*. Recombinant measles virus vaccine expressing the Nipah virus glycoprotein protects against lethal Nipah virus challenge. PLoS One 2013;8:e58414.
76. Mire CE, Geisbert JB, Agans KN, Versteeg KM, Deer DJ, Satterfield BA, *et al*. Use of single-injection recombinant vesicular stomatitis virus vaccine to protect nonhuman primates against lethal Nipah virus disease. Emerg Infect Dis 2019;25:1144-52.
77. Walpita P, Barr J, Sherman M, Basler CF, Wang L. Vaccine potential of Nipah virus-like particles. PLoS One 2011;6:e18437.

Source of Support: Nil. **Conflicts of Interest:** None declared.