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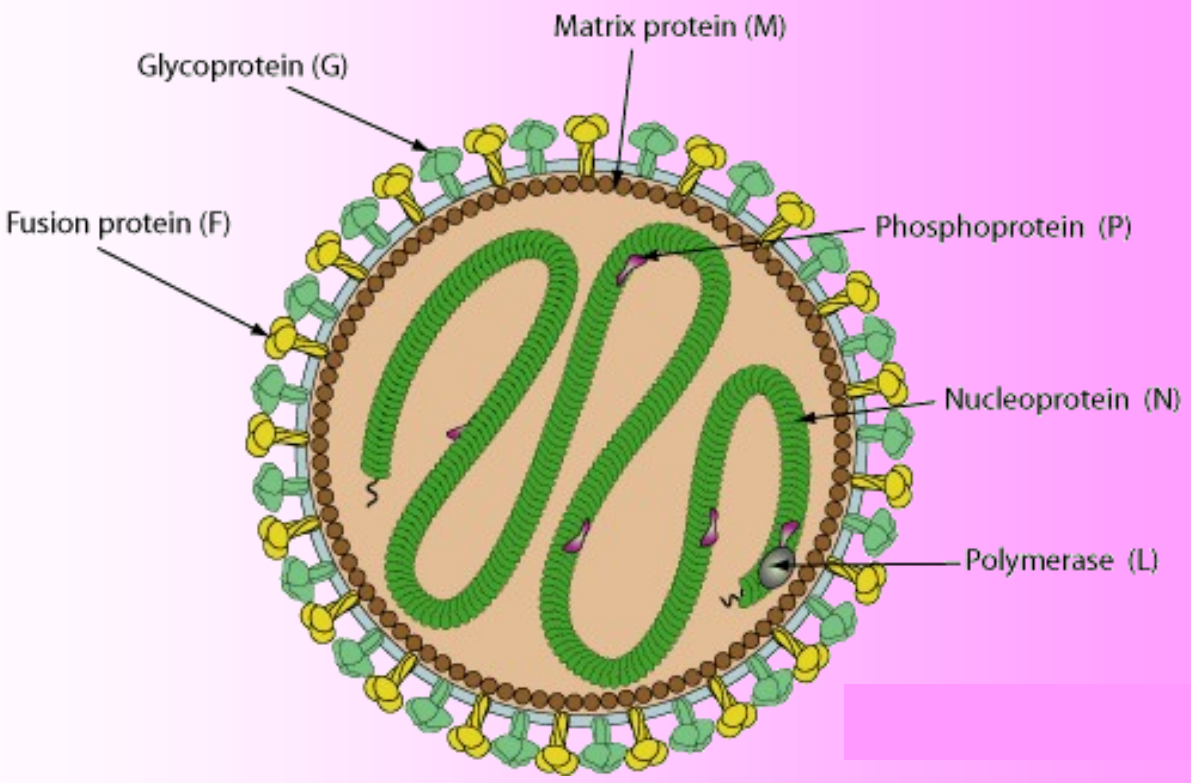

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Nipah Virus (NiV): 21st Century Novel Emerging Zoonotic Virus with Pandemic Potential

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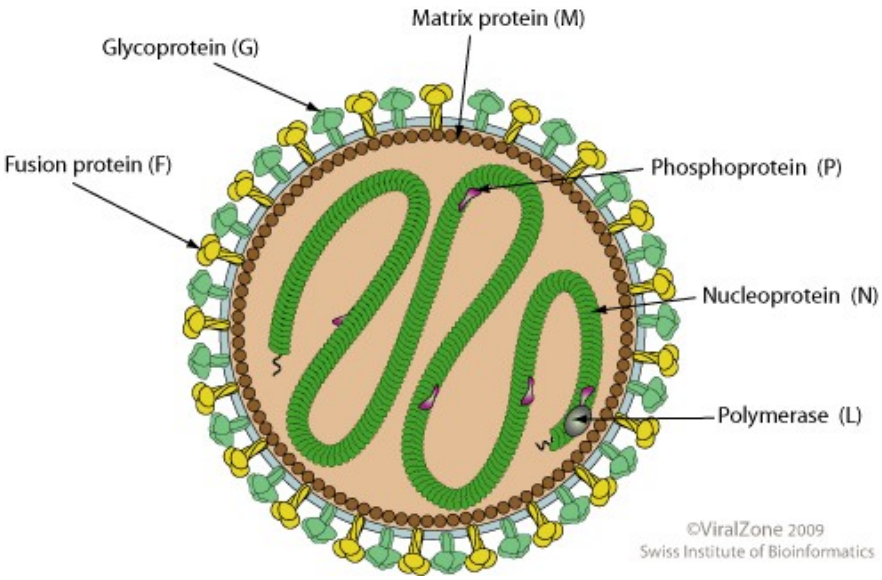
Nipah virus (NiV) is a paramyxovirus (genus Henipavirus) whose wildlife reservoir is bats of the genus Pteropus. The emergence of pandemic potential of NiV is due to the fact that one or more pigs was infected from bats, and the virus then spread efficiently from pig to pig, then from pigs to people. Characteristics of Nipah virus that increase its risk of becoming a global pandemic includes: humans are already susceptible; many strains are capable of limited person-to-person transmission; as an RNA virus, it has an exceptionally high rate of mutation and that if a human-adapted strain were to infect communities, high population densities and global interconnectedness would rapidly spread the NiV.

The disease transmission from pigs acting as an intermediate host during Malaysian and Singapore outbreaks has changed in NiV outbreaks in India and Bangladesh, transmitting the disease directly from bats to human followed by human to human. It is apparent from the presence of the virus and antibodies in the fruit bats of the region and 13 years of continuous NiV outbreaks in humans in Bangladesh that it is the potential threat to the Indian subcontinent. Due to lack of vaccines and effective antivirals, Nipah encephalitis poses a great threat to public health. This paper describes the potential of Nipah virus to cause an expanding pandemic threats, epidemiological patterns observed to date and suggests measures that should be taken for surveillance , provide early warning for veterinary and human public health authorities, prevention and infection control.

Epidemiology

First Nipah virus (NiV) outbreak in India occurred in Siliguri district of West Bengal in 2001, where direct transmission of the NiV virus from bats-to-human and human-to-human was reported in contrast to the role of pigs in the Malaysian NiV outbreak. Nipah virus (NiV) derives its name from Kampung Sungai Nipah; a



village in Malaysia from where it was first reported with acute encephalitis for those workers handling pigs in 1998-99. The mortality rate in the first 265 identified human cases was 40%. The recent epidemic in May 2018 in Kerala for the first time has killed over 17 people in 7 days with high case fatality and highlighted the importance of One Health approach.

The recently emerging zoonotic Nipah virus (NiV) comes under *Henipavirus* in the subfamily *Paramyxovirinae*. NiV is a single-stranded negative-sense RNA virus, pleomorphic ranging from 40 to 600 nm in diameter covered by a lipid bilayer envelope. The virus has three important internal proteins, Nucleocapsid proteins (N), Phosphoproteins (P) and large polymerase proteins (L).

The envelope has two types of spikes called Fusion proteins (F) and receptor-binding Glycoproteins (G). While fusion proteins are responsible for the fusion of the viral membrane with the host cell membrane enabling release of viral contents into the cell, the glycoproteins generally bind to Ephrin B2surface proteins. The Matrix proteins (M) responsible for the structural integrity and the budding of virus particles.

In nature, the virus is maintained in the bats-pigs cycle. Pigs act as intermediate as well as amplifier hosts. In addition to pigs, other animals like cats, dogs, goats, and horses have also been shown to be positive for anti-NiV antibodies, but their role in transmitting infection in humans has not been established.

***Pteropus* bat Natural reservoir: Nipah virus**

Frugivorous (fruit-eating) bats of Pteropus genus are the main natural reservoir hosts of the virus. The bats shed the virus in their secretions and excretions. The humans acquire the infection by coming in contact with bat

Transmission of NiV: Bats to Human via consumption of raw date palm sap.

excreta or saliva or consuming partially eaten or licked fruits by bats. Human to human spread has been recorded on many occasions. Once the virus is transmitted to pigs, they are highly infectious to other pigs and humans. The virus is seldom present in pig's urine. Outbreak investigations identified consumption of raw date palm sap as the primary route of transmission of Nipah virus from Pteropus bats to people (Luby et al., 2013).

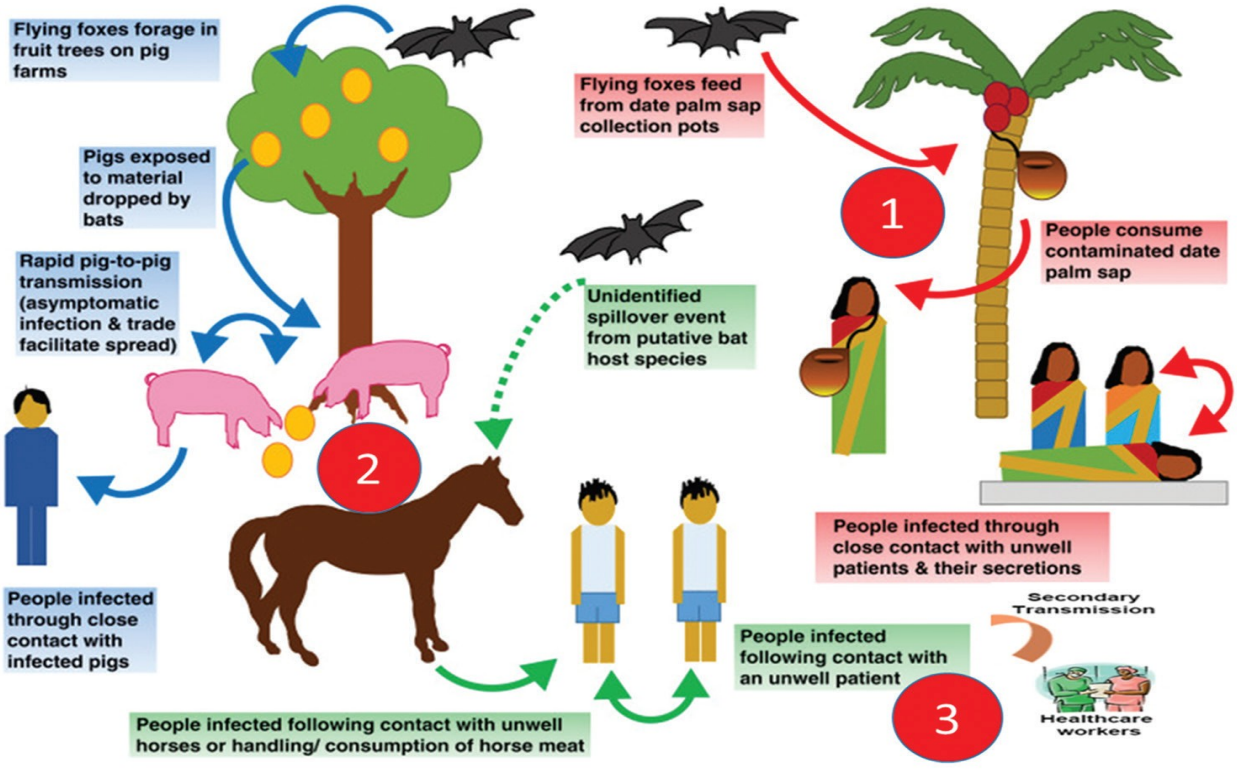
The consumption of date palm sap (which is also known as toddy, kallu, tuak and tuba in other countries) is popular in a number of Southeast Asian countries, including Bangladesh, India, Indonesia. Fruit bats also consume date palm sap and can contaminate it with saliva, urine, and faeces. This is the means by which NiV is thought to be transmitted from infected fruit bats to humans. There is strong evidence that the emergence of bat-related viral infection communicable to humans and animals has been attributed to the loss of natural habitats of bats. As the flying fox habitat is destroyed by human activity, the bats get stressed and hungry, their immune system gets weaker, their virus load goes up, and a lot of virus spills out in their urine and saliva.

Deforestation and urbanization of some areas in Bangladesh have contributed to greater overlap between human and bat habitats. By promoting human–bat interactions, this overlap can increase the risk of "spillover" events, with NiV crossing the species barrier and infecting people

Major Outbreaks

The latest at present century of NiV epidemic reported in May 2018 which involved two northern districts of Kerala State, India resulted in 16 fatal cases. The epicenter of this out-

Year	Place
1998	Kampung Sungai Nipah,Malaysia
2001	Siliguri, West Bengal, India
	Meherpur, Bangladesh
2007	Nadia,West Bengal, India
	Thakurgaon, Bangladesh
2014	Tinalon, Philippines
	Midtungok, Philippines
2018	Kozhikode, Kerala, India
	Malappuram, Kerala, India



Schematic representation of three modes of Nipah virus spread: (1) bat-to-human, (2) animal-to-human, and (3) human-tohuman (including nosocomial).
(Chattu *et al.*, 2018)

break was in Kozhikode district with a few cases recorded in the adjoining Malappuram district. Bats are the main reservoir hosts involved in transmitting NiV in Bangladesh and India, unlike Malaysia and Singapore where the infection was mediated through infected pigs.

Clinical Prognosis

Humans: The incubation period is usually 4 to 14 days long.

- Patients will have a fever, headache, dizziness, and vomiting, abnormal doll's eye reflex, pupillary reflexes, vasomotor changes, myoclonic jerks, seizures which developed into a picture of severe encephalitis.
- Neurological involvement is diverse and multifocal, including aseptic meningitis, diffuse encephalitis, and focal brainstem involvement.
- A unique and interesting feature of NiV infection is the development of relapse and late-onset encephalitis, some of which occurred months or years after the acute illness.

Case fatality rates ranges from 40% to 100%.

In Malaysian outbreak, Ribavirin was given orally or intravenously to patients with NiV encephalitis. The mortality rate was reduced up to 36% when the infected patients were treated with ribavirin

In Singapore outbreak, acyclovir was given to all NiV encephalitis patients and only one death reported due

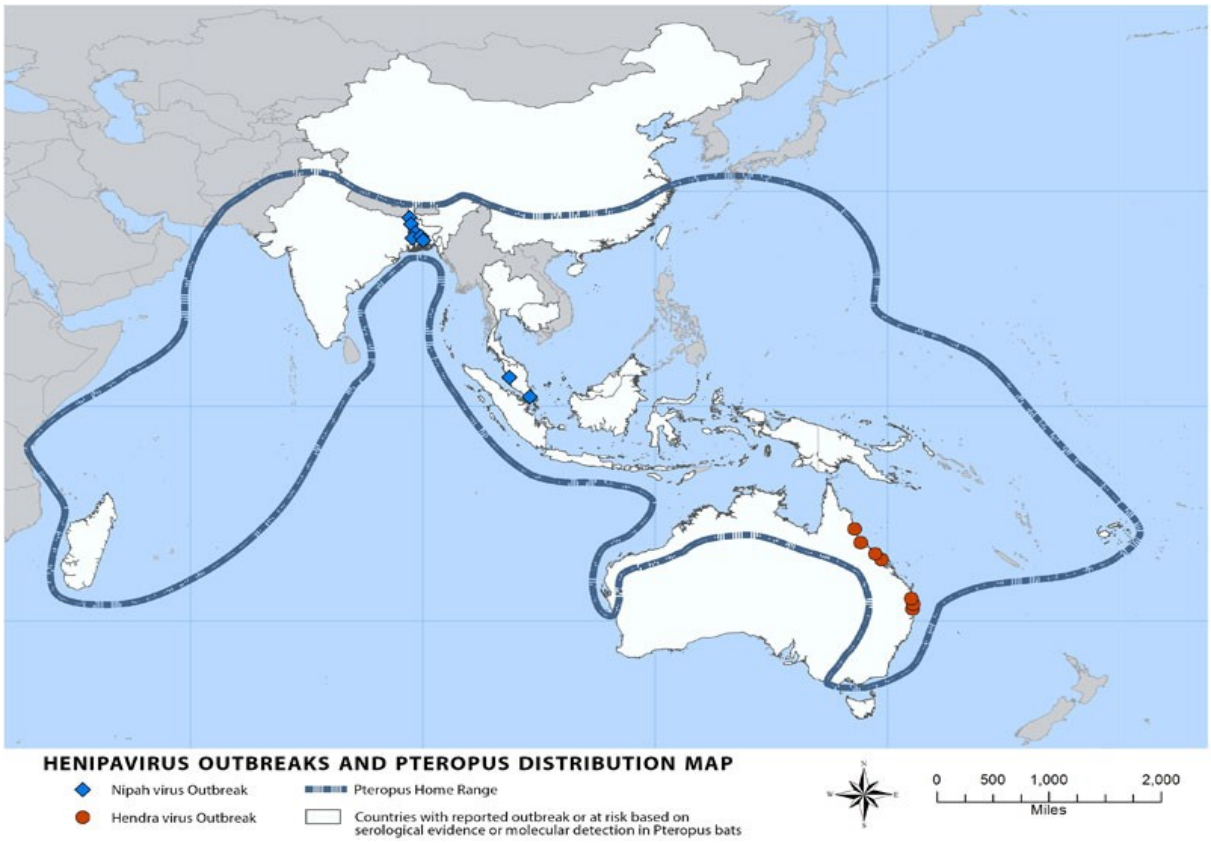
NiV infection, but the role of acyclovir drug is still unclear.

I n a recent in vivo study, Favipiravir viral RNA-dependent RNA polymerase inhibitor (T-705) antiviral showed promising results when tested on NiV infected golden hamsters.

The experimental monoclonal antibody, m102.4, which targets the ephrin-B2 and ephrin-B3 receptor binding domain of the Henipavirus G envelope glycoprotein is a potent cross-reactive neutralizing antibody in vitro.

Pigs:

- Pigs manifest respiratory and neurologic symptoms and present with a typical barking cough which is recognized as a tell-tale sign of NiV infection in pigs.
- Young pigs show epistaxis, dyspnea and characteristics coughing and older animals showed neurological signs such as ataxia, paresis,seizures, and muscle tremors.
- Naturally infected pigs developed tracheitis and bronchointerstitial pneumonia with hyperplasia of the airway epithelium.
- A concurrent disease in pigs was characterized by a febrile respiratory illness, epistaxis,coughing in young and older pigs showed neurological signs.
- Some progress in developing a protective vaccine called ALVAC Canarypox vectored Nipah F and G vaccine was quoted to be a



Map of henipavirus outbreaks and distribution of *Pteropus* bats. Adapted from Nipah virus distribution map, Centers for Disease Control and Prevention (www.cdc.gov/vhf/nipah/outbreaks/distribution-map.html).

promising vaccine for swine with a potential for humans as well.

- Candidate vaccines using a vesicular stomatitis virus vector are the most advanced, having demonstrated protection in hamsters, ferrets, and African green monkeys.

A recombinant subunit vaccine formulation protects against the lethal NiV challenge in cats.

Diagnosis

The virus can be isolated from kidneys, CSF and other body tissues including liver.

ELISA

RT-PCR

Sequence analysis

Immunofluorescent tests

Ferrets have been used as a laboratory model for Nipah virus infection and

Usage of PPE while working

pathogenesis.

Prevention

Biosafety Issues of Nipah Virus: For those who have to work in the field or on farms where Nipah infection is suspected, personal protection, such as masks, goggles, gloves, gowns, and boots, is advocated together with hand-washing and disinfection of equipment.

With its high virulence, animal–to- human, and human- to –human spread, significant morbidity and mortality, resultant fear and panic and tremendous economic losses caused, it fulfills some criteria to be considered a potential agent for bioterrorism and is thus listed as aCategory C agent on a list of Bioterrorism Agents by Centres of Disease Control and any handling has to be done in BSL-4 facilities.

The Historical devastation of zoonotic diseases, the high case fatality rate of human Nipah infection and its recognition as a stage III zoonotic disease suggest that scientists, the public health community and policy-makers should respect the pandemic risk of Nipah virus.

- Mass education at all levels about the NiV, avoidance of contact with bats and pigs and their secretions and excreta and ensuring that these animals do not lick or contaminate foods, drinks, and drinking water supplies.
- People should be advised not to consume any vegetables or fruits partially eaten by bats.
- Drinking of date palm sap contaminated by bats should be discouraged.

Conclusion

NiV Emerged as a zoonotic virus, causing severe morbidity and mortality in both humans and animals and

destroyed the pig-farming industries and it continues to cause human fatalities in recent outbreaks in Kerala also. As the reservoir host, Pteropus bat is widespread, and NiV has been found in bats in various countries,the potential for outbreaks to occur in new regions remains significant. The interest in NiV has remained limited to small research communities and affected countries but its control needs more than research and diagnostics.

REFERENCES

Ang, B.S., Lim, T.C. and Wang, L., 2018. Nipah Virus Infection. Journal of clinical microbiology, pp.JCM-01875

Banerjee, S., Gupta, N., Kodan, P., Mittal, A., Ray, Y., Nischal, N., Soneja, M., Biswas, A. and Wig, N., 2019. Nipah virus disease: A rare and intractable disease. Intractable & Rare Diseases Research, pp.2018-01130.

Chadha, M.S., Comer, J.A., Lowe, L., Rota, P.A., Rollin, P.E., Bellini, W.J., Ksiazek, T.G. and Mishra, A.C., 2006. Nipah virus-associated encephalitis outbreak, Siliguri, India. Emerging infectious diseases, 12(2), p.235.

Chattu, V.K., Kumar, R., Kumary, S., Kajal, F. and David, J.K., 2018. Nipah virus epidemic in southern India and emphasizing "One Health" approach to ensure global health security. Journal of family medicine and primary care, 7(2), p.275.

Drexler, J.F., Corman, V.M., Gloza-Rausch, F., Seebens, A., Annan, A., Ipsen, A., Kruppa, T., Müller, M.A., Kalko, E.K., Adu-Sarkodie, Y. and Oppong, S., 2009. Henipavirus RNA in African bats. PloS one, 4(7), p.e6367.

Joshi, R.M., 2018. Nipah Virus: A Novel Emerging Zoonotic Disease. Clinical Microbiology.

Luby, S.P., 2013. The pandemic potential of Nipah virus. Antiviral research, 100(1), pp.38-43.

Simons, R., Gale, P., Horigan, V., Snary, E. and Breed, A., 2014. Potential for introduction of bat-borne zoonotic viruses into the EU: A review. Viruses, 6(5), pp.2084-2121.