

On the Origin, Spread and Consequences of Nipah Virus

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Abstract The report of the outbreak of Nipah Virus Disease (NiV), in May, in Kerala, India was a shocking news around the globe. Proportionately, Kerala ships the maximum number of expatriates as professional, skilled and unskilled workers. Hence, the reporting of NiV attracted global attention. It took the life of 17 people within a couple of days including that of a health worker. In this paper we try to present a brief study on the Nipah Virus Disease covering, but is not limited to, the structure of the virus, its nature, seriousness, geography, its life, mode of spread and reproduction etc. We also try to put in the precautions to take on NiV, medical solutions, mathematical models associated with it.

1. Introduction

Most of the Emerging infectious diseases (EID) are caused by pathogens that are already present in the environment unnoticed. They tend to emerge when provided with favorable conditions and infect a new host. On rare instances, some of them evolve into a new variant and cause a new disease. [12]

International trade and commerce, change in human demographics and behavior, [4, 11, 15, 16] lack of public health services and infrastructure, and antibiotic resistance have also contributed significantly in the emergence and re-emergence of infectious diseases.[13]

Several factors contribute to this, including the recent growth and geographic expansion of human populations, the intensification of agriculture, and the disruption of habitats owing to climate change and deforestation. In addition, increased global travel means that there is a greater likelihood that EIDs will rapidly spread.

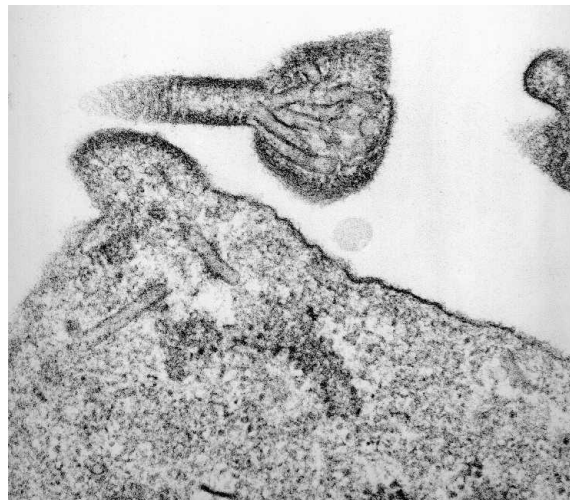


Figure 1: Nipah Virus seen through Electron Microscope (<https://www.csiro.au/>)

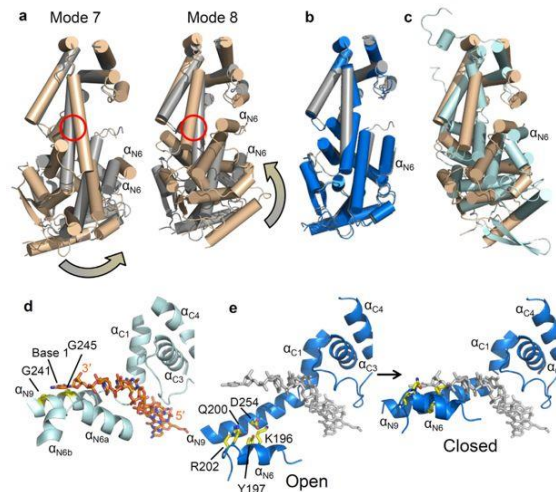


Figure 2: Structure of Nipah virus unassembled nucleoprotein in complex with its viral chaperone [19]

Among the global “hotspots” for EIDs are countries related to the Indo-Gangetic Plain and the Mekong River Basin. Nipah virus (NiV), Crimean-Congo hemorrhagic fever (CCHF), and AI A (H5N1) are examples of diseases that have recently emerged and have affected the World Health Organization (WHO) South-East Asia Region.[2,3,5,6]

2. What is Nipah?

Nipah is a Zoonotic virus similar to Japanese encephalitis. It is More dangerous than Zika but less dangerous than Ebola or influenza. Nipah is probably best compared to the Middle Eastern respiratory syndrome coronavirus—a dangerous zoonotic virus that needs watching but hasn’t taken the steps necessary to become a true pandemic. Nipah henipavirus [Viral abbreviation: Nipah virus (NiV)] is an RNA virus which is one of the five established viral species of genus Henipavirus in the family Paramyxoviridae, order Mononegavirales. It is transmitted to people chiefly from wild and domesticated animals.

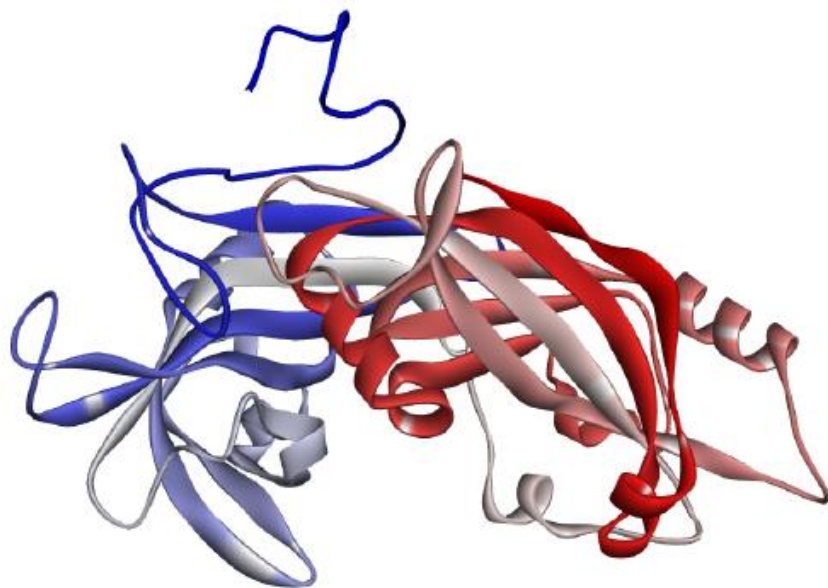


Figure 3: Three dimensional structure of Native Matrix-protein of Nipah Virus [10]

- Birth place: Kampung Sungai Nipah, Malaysia in 1998
- Fruit bats were the hosts. Pigs were infected with Nipah probably after eating the fruits half-eaten by the bats.
- Pigs then infected pig farmers.
- Killed 105 out of 265 human beings,
- More than a million pigs had to be slaughtered.

There is no case in Malaysia and Singapore since 1999. In Bangladesh since 2001, there are almost annual outbreaks blamed on humans and fruit bats consuming the same date palm tree sap. It occurs seasonally in winter months. In West Bengal, India at Siliguri, 50 died in 2001 and later in Nadia, 5 died in 2007.

In May 2018, there are 19 reported cases (18 lab confirmed). Out of 19 reported cases 17 died, from the two affected districts of Kozhikode and Malappuram in Kerala State.
(<http://www.searo.who.int/india/topics/emergencies/ministry-of-health-and-family-welfare-press-release-2june2018.pdf>)

There have been no new infections since 17 May, 2018. It is declared over on June 4, 2018 by the govt. of Kerala. However, on June 4, 2019, a 23 year old student was infected with Nipah virus in the Ernakulam district of Kerala. Nevertheless, the young man was out of danger after proper care.

3. Structure of Virus

Nipah virus is a paramyxovirus and is very closely related to Hendra virus. It was named after one of the Malaysian villages affected, Sungai Nipah, and was isolated by Dr Chua Kaw Bing from the University of Malaya in March 1999. Nipah virus (NiV) is an RNA virus belongs to family Paramyxoviridae and genus Henipavirus with an approximate size of 40-600nm having a pleuromorphic shape with the presence of envelope.

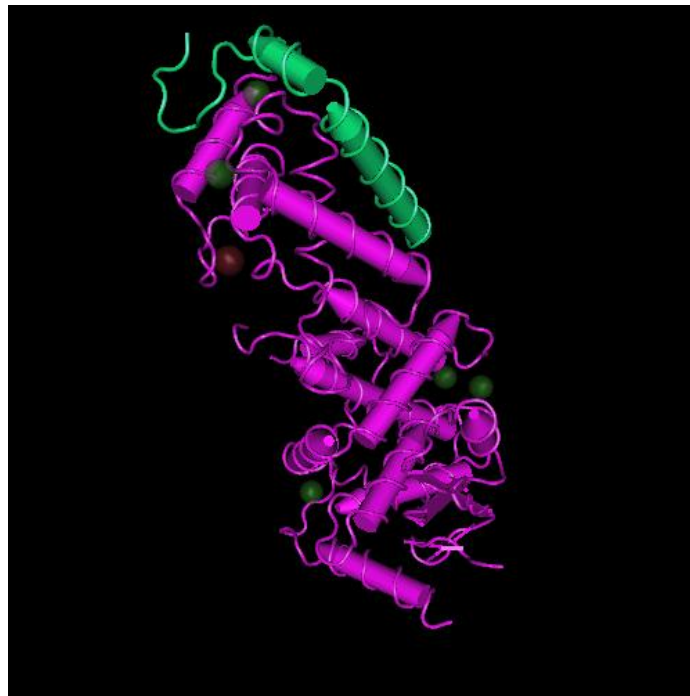


Figure 4: Crystal Structure of The Nipah Virus Rna Free Nucleoprotein-phosphoprotein Complex [19]

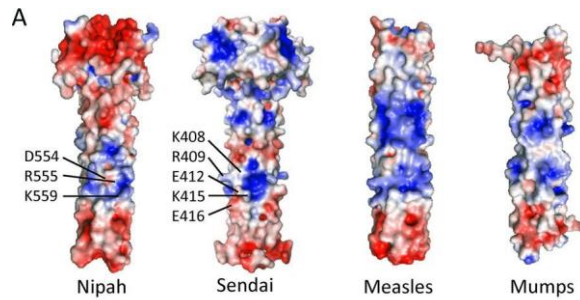


Figure 5: Electrostatic surface potential representations, generated in APBS, of the four paramyxovirus P multimerization domain structures [1]

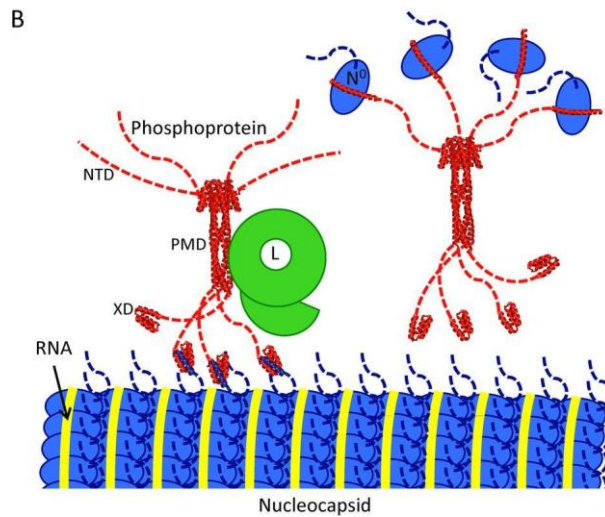


Figure 6: Model of the organization of the Nipah virus replication machinery, roughly to scale, based on dimensions visualized by electron microscopy and X-ray crystallography [1]



Figure 7: Crystal Structures Of Nipah Virus G Attachment Glycoprotein In Complex With Its Receptor Ephrin-b3 [18]

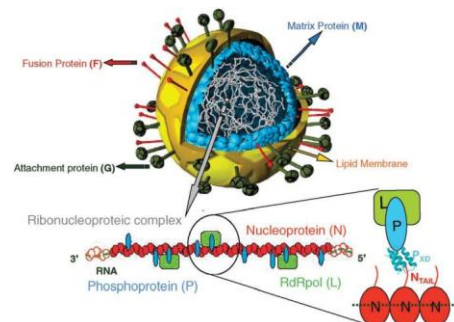


Figure 8: Schematic illustration of a Paramyxovirus particle. The virion is enveloped by a lipid bilayer membrane [7]

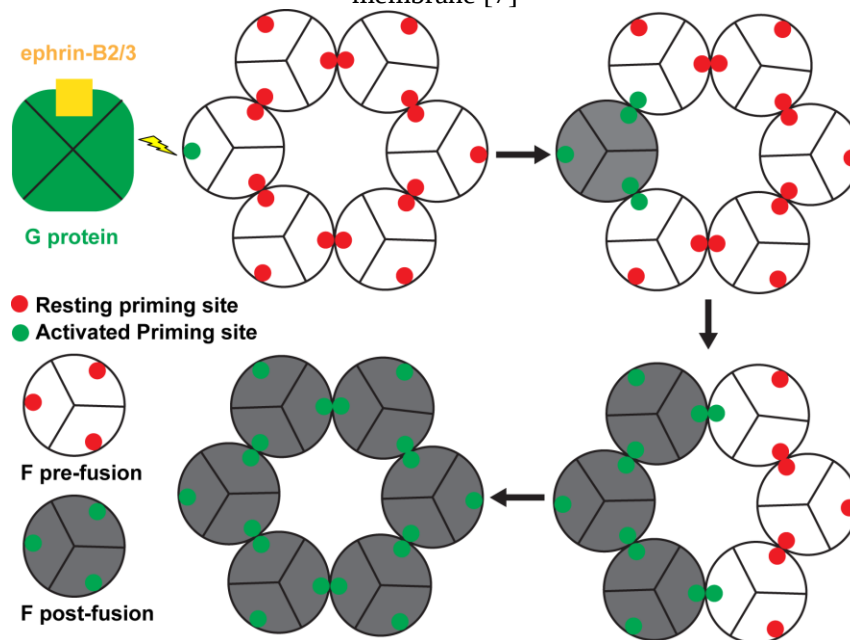


Figure 9: Schematic representation of the proposed NiV-F activation model[17]

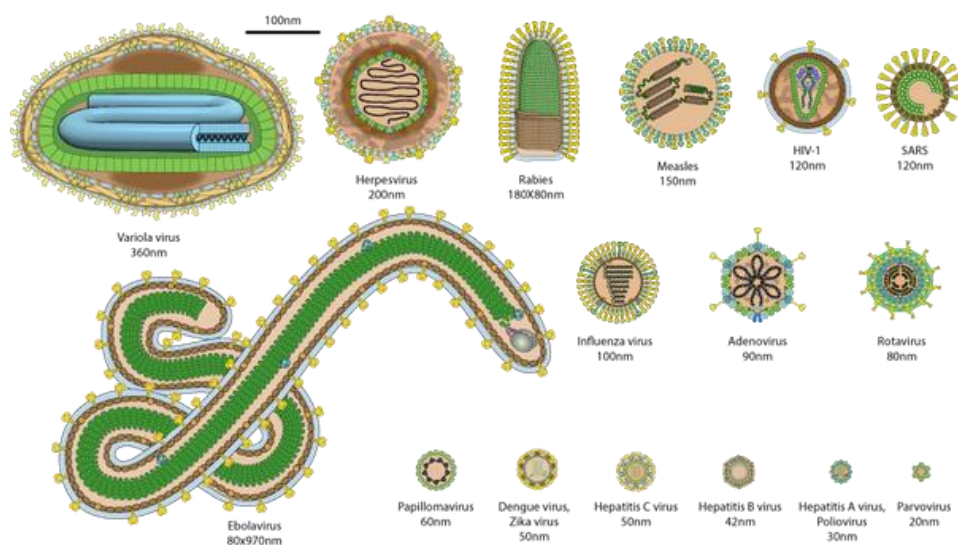


Figure 10: Nipah Cross Section [14]

4. Major Symptoms, Causes and Effects

The virus that causes high fever, headache and coma in extreme cases. Body fluids can cause human-to-human transmission of Nipah, which has a mortality rate of 70 % and has no vaccine.

The characteristic features of victims ranges from asymptomatic to acute respiratory and fatal encephalitis.[9] Nipah kills mostly through brain inflammation, and the symptoms of the original Malaysian outbreak were largely neurological. But the patients in the Bangladeshi and Indian cases seem to have respiratory symptoms as well, and this could make Nipah more transmissible between humans.

The contributory factors that enable the infectious agents to evolve into new ecological niches, to reach and adapt to new hosts, and to spread more easily among the new hosts include urbanization and destruction of natural habitats, leading to close contact of humans with animals, climate change and changing ecosystems, changes in population of reservoir hosts or intermediate insect vectors, and microbial genetic mutation.

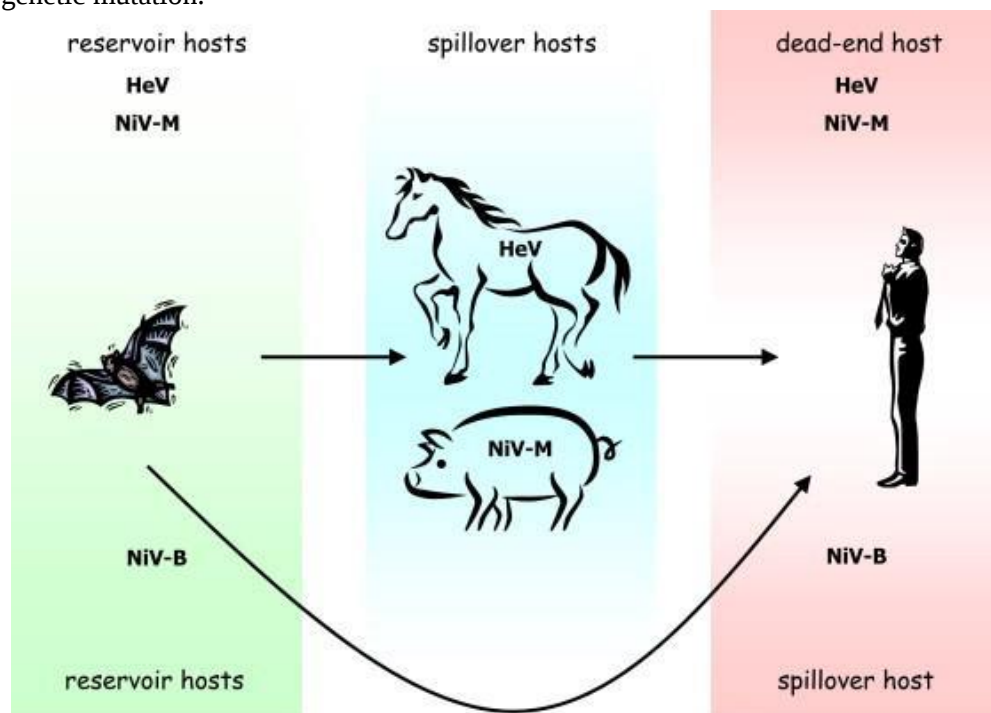


Figure 11: Ways of Spreading of Nipah Virus(<http://wiki.ggc.edu/wiki/Henipavirus>)

The natural host of the virus is believed to be fruit bats of the Pteropodidae family, Pteropus genus. Drinking tari (fermented date palm sap) is a potential pathway of NiV transmission which is the most common reason in Bangladesh. [8]

Those who survive acute encephalitis make a full recovery, but around 20% are left with residual neurological consequences such as persistent convulsions and personality changes.

5. Medical Solutions

The only treatment for human is intensive care to the infected individuals.[9] Isolation is so far the best medicine.

6. How deadly is it?

Valachekutti Moosa (62) of Changaroth village, Kozhikode district, and his sons Mohamed Saliah, 28, and Mohammed Sadiq, 26, and his brother's 50 year old wife Mariumma. The fiancée of Moosa's eldest son Saliah is also in hospital with similar symptoms.

A nurse, Lini, who treated them at a government hospital also succumbed to the viral disease. 17 out of the reported 19 cases could not survive.

7. Its life, mode of spread and reproduction

Nipah mutates fast and has pandemic potential if a strain emerges that can easily jump between humans. Most of the Malaysian patients seemed to have caught the disease from other people, several of those infected in India merely shared a hospital ward with members of the family that first contracted the disease.

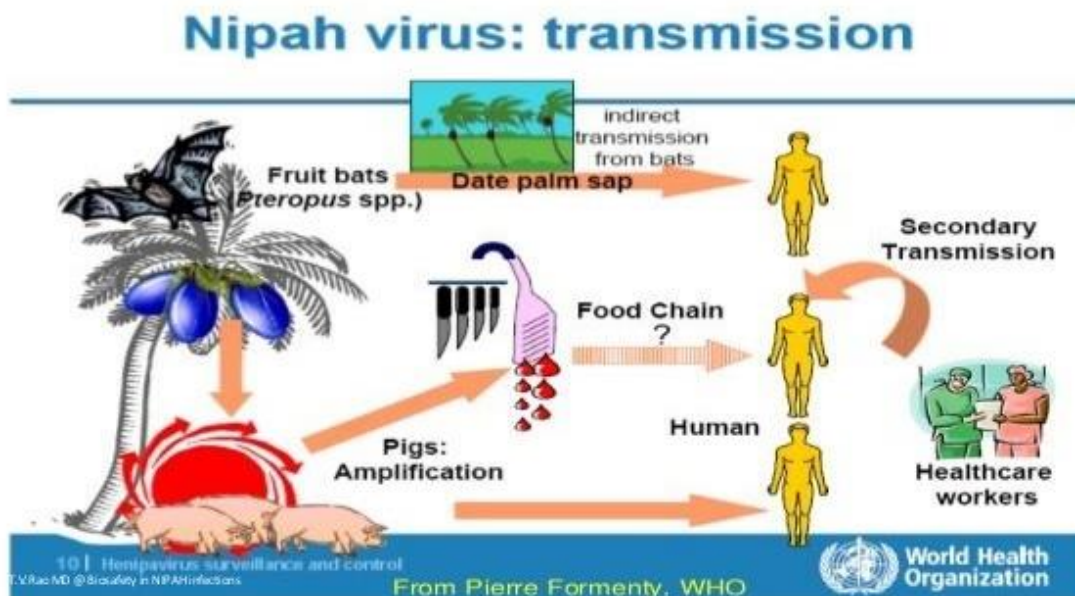
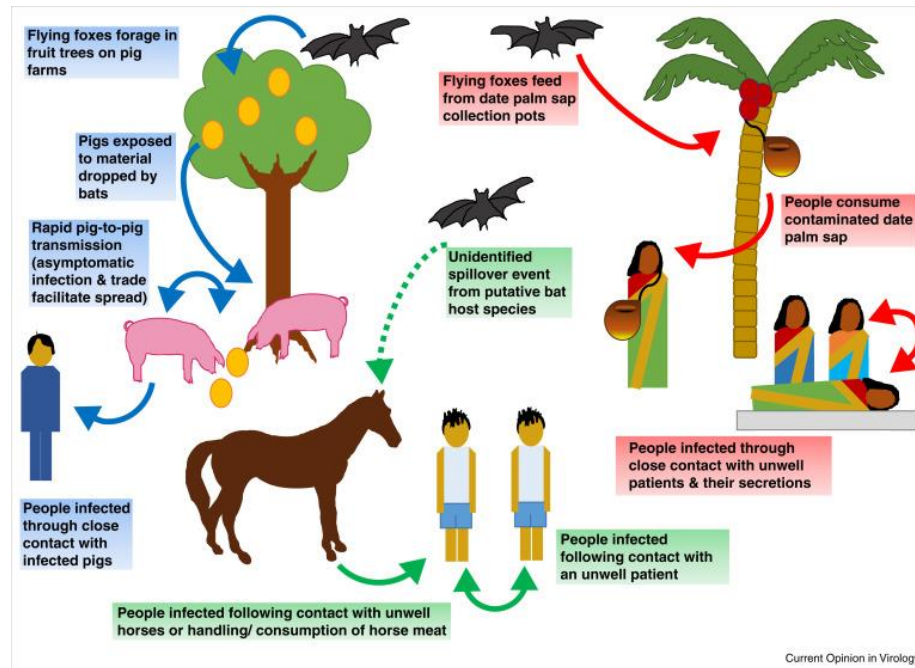


Figure 12: Difference in transmission between Malaysia and Bangladesh-India (WHO)

Strong evidence indicative of human-to-human transmission of NiV was found in Siliguri (India) in 2001 and in Bangladesh in 2004.

Outbreaks of Nipah in South-East Asia have a strong seasonal pattern and a limited geographical range. The geographical distribution of NiV outbreaks is shown in Figure 15. All the outbreaks occurred during winter and spring (December-May). This could be associated with several factors like the breeding season of the bats, increased shedding of virus by the bats and the date palm sap harvesting season.



The primary route of exposure was through direct exposure to infected horses, contact with contaminated body fluids during slaughtering of sick horses, and/or consumption of undercooked meat from infected horses. However, for at least 5 cases in Bangladesh, clinical and epidemiologic evidence suggest direct human-to-human virus transmission. [4]

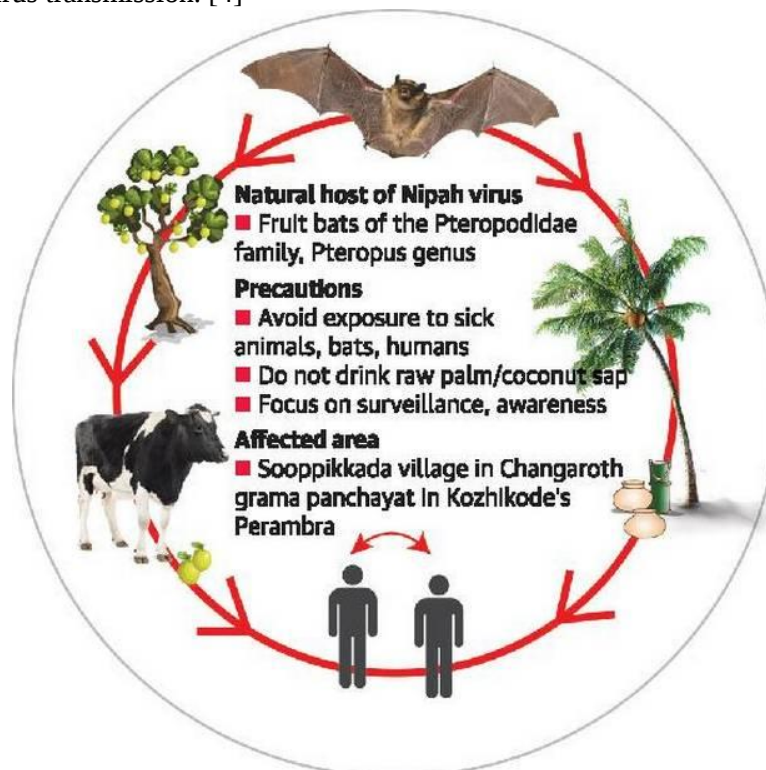


Figure 14: Nipah Virus Cycle (<https://www.thehindu.com/>)

8. Precautions

An anthropological study says drinking raw date or palm sap in the morning is an old practice in Bangladesh, especially in rural areas, where there is a general lack of hygiene.[4] Avoiding eating half-eaten fruits, consuming the date palm tree sap in the habitats of fruit bats, sharing of food and water etc. are major precautionary measures. People around the affected persons should compulsorily wear masks.

9. Methods to prevent

As poor sanitation, lack of cleanliness, climatic changes due to deforestation and lack of rainfall, lack of fresh water, water contamination with human and animal waste etc. are the major causes of out-break and spread, geographical isolation is the best strategy to prevent. By monitoring the spread of infectious disease helps in early warning to the population and hence have both economic and health benefits. Awareness programs could help the population to follow a healthy lifestyle and hence lower the risk of diseases [9]

From the Bangladesh experience, it is noted that it is 100 percent preventable if we can prevent people from drinking raw date sap. But once infected, we don't have a cure. It usually takes 7-8 days on average between exposure and signs of symptoms -- fever, altered mental status, and seizure. Up to 21 days are required to come out of danger.

Increasingly, non-laboratory animals, such as bats, chickens and ferrets, are being used for the study of host–pathogen relationships and immune responses to EIDs. This new approach, based on the One Health concept, together with the adoption of new genomic information and genome-editing technologies, will allow the identification of strategies to prevent and minimise the impact of EIDs and enhance our preparedness for potential pandemics.

10. Geographical areas of the spread of the virus

A total of 35 outbreaks of NiV encephalitis were reported in Bangladesh and India during 2001–2015. Mostly it is in Bangladesh.



Figure 15: Route of NIPAH

In India, as there are a good amount of migrant laborers from West Bengal, more care must be taken. In the initial days of outbreak, people came in contact with the affected persons traveled to Kolkata, Mangaluru and Kottayam. There were some suspicious cases reported from these regions as well. The districts of Gorakhpur and Maharajganj, of UP are highly susceptible to Nipah.

11. Morbidity and mortality due to Nipah or Nipah-like virus encephalitis

Time	Location	Cases	Deaths	Case Fatality Rate(%)
1998-1999	MAL, SNG	276	106	38
Jan-Feb 2001	Siliguri (IND)	66	45	68
Apr-May 2001	Meherpur (BGL)	13	9	69
(Jan) 2003	Naogaon (BGL)	12	8	67
Jan 2004	Rajbari (BGL)	31	23	74
(Apr) 2004	Faridpur (BGL)	36	27	75
Jan-Mar 2005	Tangail (BGL)	12	11	92
Jan-Feb 2007	Thakurgaon (BGL)	7	3	43
(Mar) 2007	Kushtia, Pabna, Natore (BGL)	8	5	63
(Apr) 2007	Naogaon (BGL)	3	1	33
(Apr) 2007	Nadia (IND)	5	5	100
(Feb) 2008	Manikgonj (BGL)	4	4	100
(Apr) 2008	Rajbari and Faridpur (BGL)	7	5	71
(Apr) 2009	Gaibandha, Rangpur and Nilphamari (BGL)	3	0	0
(Apr) 2009	Rajbari (BGL)	1	1	100
Feb-Mar 2010	Faridpur, Rajbari, Gopalganj, Madaripur (BGL)	16	14	88
Jan-Feb 2011	Lalmohirhat, Dinajpur, Comilla, Nilphamari and Rangpur (BGL)	44	40	91
(Feb) 2012	Joypurhat, Rajshahi, Natore, Rajbari and Gopalganj (BGL)	12	10	83
Jan-April 2013	Bhaluka in Mymensingh (BGL)	24	21	88
March 3–May 24, 2014	Sultan Kudarat, Mindanao (PHL)	17	9	53
March 3–May 24, 2014	(BGL)	18	9	50
(Feb) 2015	(BGL)	9	6	67
(May) 2018	Kozhikode, Malappuram (IND)	19	17	89
(June) 2019	Ernakulam (IND)	1	0	0

Updated version of the table from <http://www.searo.who.int/>

12. Speed of the spread and reproduction

Several of the dead seem to have contracted Nipah in hospital. It is not clear why the virus is widespread in some districts, and why it strikes new places, but the date tree is very common in those areas in Bangladesh. Tracking the history of Nipah [virus] in Bangladesh, it is found that it is highly communicable and can be passed on with minimal human contact. Many victims were infected and they died after not taking precautions in taking care of patients. Infection can be prevented by washing hands

with soap and not sharing the same food and caregivers should wearing masks. There should be a strong campaign not to drink raw date/palm sap from the habitats of fruit bats.

13. Some popular information

It is a major public health threat. Scientists are studying bat ecology and the bat immune system to determine how viruses, such as Nipah, maintain themselves in bats and how the viruses 'spill over' into other animals and humans. It has huge socioeconomic impact in the developing countries due to mass exodus and social alienation.

In the recent outbreak in Kerala, the Government Taluk Hospital in Perambra looked like a ghost house and all the streets leading to the hospital empty. Even patients at the blood transfusion unit and operation theatres have left the hospital. Kerala tourism industry was heavily affected during the vacation season.

Governments should immediately come with advisories to the General Public and Health Care Personnel. Guidelines for sample collection for Nipah Virus, Hospital infection control and Laboratory Biosafety should be adhered to.

14. Conclusion

Every new virus brings huge chaos in various fabrics of the society. Positively, it helps human beings, organizations, nations to come together. Nipah virus unattended may cause serious damage to the society in family environment, health, economy and reputation. More preventive measures are always better than treatment procedures.

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