Nipah Virus Infection

World Health Organization
Regional Office for South-East Asia

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Nipah Virus Infection (NiV) is an emerging infectious disease of public health importance in the South-East Asia Region.

The virus

The virus is named after the Malaysian village where it was first discovered.[1] This virus along with Hendra virus comprises a new genus designated Henipavirus in the subfamily *Paramyxovirinae*.[2]

Reservoir of virus

Fruit bats of the genus *Pteropus* have been identified as natural reservoirs of NiV. A seroepidemiologic study in Malaysia implicated four fruit bat species, *Pteropus hypomelanus*, *P. vampyrus*, *Cynopterus brachyotis*, *Eonycteris spelaea,* and an insectivorous bat, *Scotophilus kuhlii*.[3] Nipah virus has been isolated from the brain and spinal fluid of victims in Malaysia.[4] Infective virus has also been isolated from environmental samples of bat urine and partially-eaten fruit in Malaysia.[5]

The species-wise distribution of fruit bats in Asia is presented in Table 1. Given the distribution of the locally abundant fruit bats in South Asia, NiV outbreaks are likely to continue to occur in affected countries. The bats are migratory.[6] This has generated intensive surveillance for evidence of Nipah virus infection in bats in these countries. Evidence of NiV could be demonstrated in P. giganteus in Bangladesh.[7] Nipah virus has been isolated from Lyle's flying fox (*Pteropus lylei*) in Cambodia[8] and viral RNA found in urine and saliva from *P. lylei* and Horsfield's roundleaf bat (*Hipposideros larvatus*) in Thailand.[9] Antibodies to a Nipah-like virus have been found in sera from fruit bats collected in India, Indonesia and Timor-Leste.[10] The status of NiV infection in other countries of the South-East Asia Region is not known.

Antibodies to henipaviruses have also been found in fruit bats in Madagascar (*Pteropus rufus, Eidolon dupreanum*)[11] and Ghana (*Eidolon helvum*)[12] indicating a wide geographic distribution of the viruses. No infection of humans or other species has been observed in Cambodia, Thailand or Africa.

Epidemiology

So far, NiV has infected 477 people and killed 252 since 1998. The distribution of NiV outbreaks in Bangladesh and India during 2001 to 2008 is shown in Figure 1. Outbreaks of Nipah in south Asia have a strong seasonal pattern and a limited geographical range. The morbidity and mortality data of human NiV infection is presented in Table 2. Case fatality rate of NiV ranges from 40-70% although it has been as high as 100% in some outbreaks.

Figure 1: Chronological distribution of outbreak of Nipah virus infection in South Asia, 2001-2008

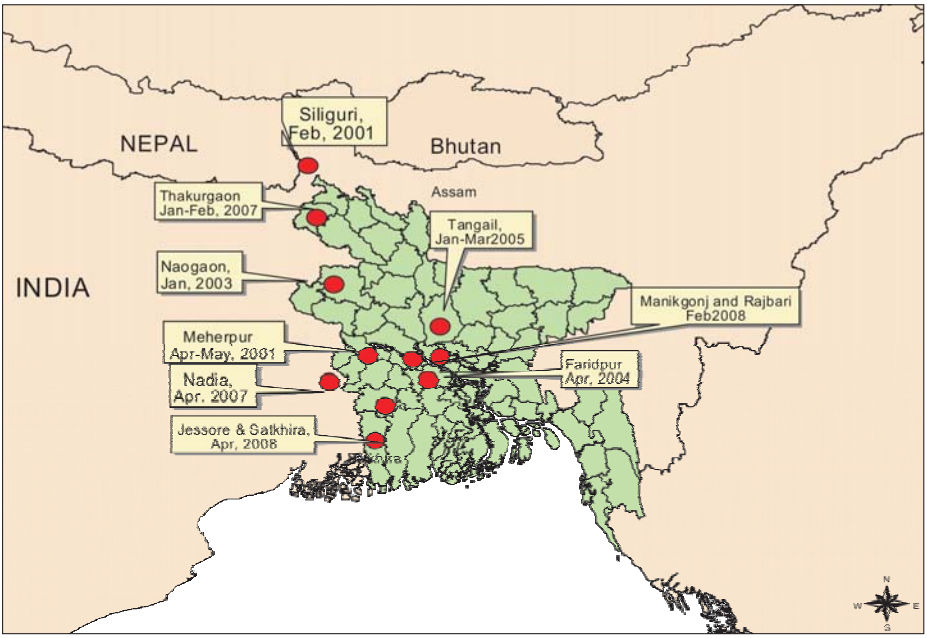

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Table 1: Distribution of bat species previously shown to have Nipah virus (adopted from 2007 International Union for Conservation of Nature and Natural Resources Red List of Threatened Species. www.iucnredlist.org.)

Species	Geographic range
Pteropus	Australia; Cambodia; Indonesia; **Malaysia***; Maldives;
hypomelanus	Myanmar; Papua New Guinea; Philippines; Solomon Islands;
	Thailand; Viet Nam
Pteropus vampyrus	Brunei Darussalam; **Cambodia**; Indonesia; **Malaysia**; Myanmar; Philippines; **Thailand**; Tonga; Vanuatu
Pteropus lylei	**Cambodia***; **Thailand#**; Viet Nam
Pteropus giganteus	**Bangladesh**; China; **India**; Maldives; Nepal; Pakistan; Sri Lanka
Eonycteris spelaea	China; India (Andaman Is., Andhra Pradesh, Assam, Karnataka, Manipur, Meghalaya, Nagaland, Nicobar Is., Sikkim, Tamil Nadu, Uttaranchal); Indonesia; **Malaysia**; Myanmar; Philippines; Thailand
Cynopterus	Cambodia; China; India (Andhra Pradesh, Bihar, Goa, Karnataka, Maharashtra, Nagaland, Tamil Nadu); Indonesia (Sulawesi, Sumatra); Lao People's Democratic Republic; **Malaysia**; Myanmar; Nepal; Philippines; Singapore; Sri Lanka; Thailand; Viet Nam
Scotophilus kuhlii	Bangladesh; India; Indonesia; **Malaysia**; Pakistan; Philippines; Sri Lanka
Hipposideros larvatus	Bangladesh; Cambodia; China; India; Indonesia (Bali, Jawa, Kalimantan, Sumatra); Lao People's Democratic Republic; Malaysia (Peninsular Malaysia, Sabah, Sarawak); Myanmar; **Thailand#**; Viet Nam

Bold, countries where Nipah virus infection in bats was demonstrated by antibody detection method.
*, countries where Nipah virus infection in bats was confirmed by isolation.
#, countries where Nipah virus infection in bats was confirmed by RNA detection.

The presence of Nipah virus antibodies have indicated that dogs, cats, goats and horses were infected, but only if exposed to infected pigs in Malaysia.[13] Their role in transmitting infection to humans was not determined.

Table 2: Morbidity and mortality due to Nipah or Nipah-like virus, Asia-Pacific Region, 1998-2008

Year/Month	Location	No. cases	No. deaths	Case Fatality
Sep 1998 - Apr 99 Mar 1999	Malaysia (Perak, Selangor and Negeri Sembilan states) Singapore	265 11	105 1	40% 9%
Feb 2001	Siliguri (India)	66	45	68%
Apr-May 2001	Meherpur, Bangladesh	13	9	69%
Jan 2003	Naogaon, Bangladesh	12	8	67%
Jan 2004 Apr 2004	Goalando, Bangladesh Faridpur, Bangladesh	29 36	22 27	76% 75%
Jan-Mar 2005	Tangail, Bangladesh	12	11	92%
Jan-Feb 2007 Mar-Apr 2007 April 2007	Thakurgaon, Bangladesh Kushtia, Bangladesh Nadia, India	7 8 5	3 5 5	43% 63% 100%
Feb 2008 Apr 2008	Manikgonj and Rajbari, Shatkira and Jessore	11 2	6 1	55% 50%
Total		**477**	**248**	**52%**

The mode of transmission

Infected bats shed virus in their excretion and secretion such as saliva, urine, semen and excreta but they are symptomless carriers. The NiV is highly contagious among pigs, spread by coughing. Direct contact with infected pigs was identified as the predominant mode of transmission in humans when it was first recognized in a large outbreak in Malaysia in 1999.[14] Ninety percent of the infected people in the 1998-1999 outbreaks were pig farmers or had contact with pigs.

There is strong evidence that 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.[15] Similar fluctuation of virus shedding may be associated with the stressful physiological conditions or seasons. Evidence of seasonal preference of transmission in P. lylei was recently demonstrated in a study in Thailand. The period April-June was the time (highest in May) when viral RNA could be mainly detected in urine which was associated with a fluctuation of population numbers that was observed only in May and correlated with young bats leaving to fly.

There were focal outbreaks of NiV in Bangladesh and India in 2001 during winter. Drinking of fresh date palm sap, possibly contaminated by fruit bats (P. giganteus) during the winter season, may have been responsible for indirect transmission of Nipah virus to humans.[16]

There is circumstantial evidence of human-to-human transmission in India in 2001. During the outbreak in Siliguri, 33 health workers and hospital visitors became ill after exposure to patients hospitalized with Nipah virus illness, suggesting nosocomial infection.[17]

During the Bangladesh outbreak the virus is suggested to have been transmitted either directly or indirectly from infected bats to humans. Strong evidence indicative of human- to-human transmission of NiV was found in Bangladesh in 2004.[18]

Clinical presentation

In animals, typical clinical symptoms are observed in pigs where respiratory symptoms dominate. Nipah virus disease in pigs is also known as porcine respiratory and neurologic syndrome as well as barking pig syndrome based on clinical observation.

Symptoms of NiV infection in humans are similar to that of influenza such as fever and muscle pain. In some cases, inflammation of the brain occurs leading to disorientation or coma. Encephalitis may present as acute or late onset. The latter may be difficult to diagnose since exposure may have taken place several months earlier. Further, those who may have recovered from an acute episode may also have a relapse. Nevertheless, magnetic resonance of the brain is helpful in differentiating

Nipah encephalitis from other encephalitis as well as in defining between acute and late onset or a relapsed form of the disease. The case fatality rate ranges from 9 to 75%.

Incubation period: 4 to 18 days.

Laboratory diagnosis

Procedures for the laboratory diagnosis of NiV include serology, histopathology, PCR and virus isolation. Serum Neutralization Test, ELISA, RT-PCR are used for laboratory confirmation.

Most countries in the South-East Asia Region do not have adequate facilities for diagnosing the virus or on ways of controlling it. Bangladesh, India and Thailand have developed laboratory capacity for diagnostic and research purposes.

Nipah virus is classified internationally as a biosecurity level (BSL) 4 agent. BSL 2 facilities are sufficient if the virus can be first inactivated during specimen collection.[19] There are a few laboratories in which the virus can be studied safely without a risk of it "escaping" and infecting more people.

Prevention and control

There is no effective treatment for Nipah virus disease, but ribavarin may alleviate the symptoms of nausea, vomiting, and convulsions.[20] Treatment is mostly focused on managing fever and the neurological symptoms. Severely ill individuals need to be hospitalized and may require the use of a ventilator.

Human-to-human transmission of NiV has been reported in recent outbreaks demonstrating a risk of transmission of the virus from infected patients to healthcare workers through contact with infected secretions, excretions, blood or tissues. Healthcare workers caring for patients with suspected or confirmed NiV should implement Standard Precautions when caring for patients and handling specimens from them. A WHO Aide–memoire on Standard Precautions in health care is available at: http://www.who.int/csr/resources/publications/standardprecautions/en/index.html

A vaccine is being developed. A recombinant sub-unit vaccine formulation protects against lethal Nipah virus challenge in cats.[21] ALVAC Canarypox vectored Nipah F and G vaccine appears to be a promising vaccine for swine and has potential as a vaccine for humans.[22]

The main strategy is to prevent NiV in humans. Establishing appropriate surveillance systems will be necessary so that NiV outbreaks can be detected quickly and appropriate control measures initiated.

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