Neurology Asia 2009; 14 : 73 – 76

Nipah virus and bats

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Abstract

Since the initial outbreak in Malaysia, small outbreaks of Nipah encephalitis have been reported almost annually in Bangladesh. Epidemiological studies have shown that the virus could be transmitted from bat to human and from human to human. Wildlife studies have also shown that the virus was widely distributed in at least 10 genera and 23 species of bats in a large part of Asia and Africa – a region that stretches from Australia and southern China, and from Indonesia to as far west as Ghana, a region with a total population of more than 1.4 billion people. As bats are long distant flying, gregarious animals living in large colonies which could exchange novel viruses from one species to another, it is not unexpected that the seroprevalence of Henipavirus among bat colonies are relatively high. The widespread distribution of both the Henipavirus and its hosts also means that the virus will remain an important cause of zoonotic disease.

INTRODUCTION

In late September 1998, outbreak of acute febrile encephalitis associated with high mortality was reported in Kinta, a district in Perak, Malaysia, among the pig-farming community. This was subsequently followed by another outbreak in 3 districts in Negeri Sembilan, namely Sikamat, Sungai Nipah and Bukit Pelanduk, from December 1998 through February 1999.[1-3] The later outbreak was associated with the movement of pigs from Kinta district and between farms.[4] In March 1999, a similar illness was reported among 11 abattoir workers in Singapore, with 1 fatality. The pigs were imported from the outbreak region in Malaysia. This led to the discovery of Nipah virus in March 1999, a highly virulent virus of the *Paramyxoviridae* family, as the aetiological agent of this fatal outbreak.[4]

Nipah virus is a single stranded RNA virus, belonging to the family *Paramyxoviridae*, in the subfamily *Paramyxovirinae*, in the genus *Henipavirus* that it shares with Hendra virus. The genome of Nipah virus contains 6 genes (N-P-M-F-G-L) flanked by a leader sequence at the 3' end and a trailer sequence at the 5" end. The Malaysian genome of Nipah virus comprises 18 246 nucleotides, compared to a slightly longer Bangladesh strain of 18 252 nucleotides, which indicates its high mutation rate. It has the ability to infect across many mammalian species (dogs, cats, ferrets, pigs, horses).

In the laboratory, the virus caused rapid syncytial formation on Vero cell culture and reacted strongly with antibodies to Hendra virus. This prompted the search for the virus among fruit bats, the natural host and vector of Hendra virus.[5] Surveillance of wildlife species during the outbreak using a novel collection method isolated the virus from the urine and saliva of fruit bats of the pteropus family, namely *Pteropus hypomelanus*.[6] Two years later, recurrent outbreaks of encephalitis in north eastern India[7] and Bangladesh[8] were proven to be due to Nipah virus. Since then, there has been almost annual recurrence of small outbreaks of Nipah infection in the region.[8, 9]

BATS AND NIPAH VIRUS

When Hendra virus was first discovered in 1994 after causing an outbreak of horse and human disease in Queensland, Australia, extensive sero-epidemiological testing in a large number of human contacts, more than 2000 horses and more than 5000 samples from 46 other animals did not identify the source of the virus.[10] As the matrix gene of the virus in the Brisbane outbreak was identical to that in Mackay, the vector was thought to be flying foxes or birds, and since the virus was mammalian virus, flying foxes were thought to be the most likely candidate. Subsequent serological survey of 4 species of bats (*Pteropus conspicillatus, P. alecto, P. scapulatus, P. poliocephalus*) along the eastern coast of Queensland from Cairns to Brisbane were shown to seropositive.[11] It has since been found that Hendra virus is widely distributed among

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most if not all of the species of pteropid bats in Australia, with serologic evidence of infection in an average 42% of wild-caught bats; though the actual proportion varies with species and age of the bats. Studies in Papua New Guinea further identified 6 more species of bats which were seropositive – *Dobsonia moluccense* and *P. neohibernicus* from Madang on the north coast, and *D. andersoni, P. capistratus, P. hypomelanus, P. admiralitatum*) in Port Moresby and New Britain.[12]

When the Nipah outbreak occurred in Malaysia in 1998 - 1999, bats were the suspected vector and host of the newly discovered virus because of the similarity between the two viruses. Within the same year, both fruit bats – *Cynopterus brachyotis, Eonycteris spelaea*, including two species of flying foxes, *P. hypomelanus, P. vampyrus*; as well as insectivorous bat (*Scotophilus kuhlii*) were found to be seropositive on the west coast of Peninsular Malaysia, near the epicentre of the outbreak.[13] *P. hypomelanus* on the east coast of Peninsular Malaysia were shown to secrete the virus by 2001.[6] Subsequent studies showed that the virus was widespread in both geographical distribution and the species of bats affected. Altogether, 23 species of bats from 10 genera (see table 1) were found to have evidence of contact with the virus, not just in Australia, Papua New Guinea and Malaysia, but also in Bangladesh[8], Cambodia[14], Thailand[15], Indonesia[16], Madagascar[17], India[18], China[19] and Ghana.[20] This showed that the henipavirus is found widely across the region from East and Southeast Asia to West Africa (figure 1), an area with a

Table 1: Nipah virus and fruit bats

Location	Bat species	Evidence of infection
East coast, Australia[11]	*Pteropus conspicillatus, P. alecto, P. scapulatus, P. poliocephalus*	Serology
Papua New Guinea[12]	*Dobsonia moluccense*, *P. neohibernicus*, *D. andersoni, P. capistratus, P. hypomelanus, P. admiralitatum*	Serology
West coast, Peninsular Malaysia[13]	*Cynopterus brachyotis, Eonycteris spelaea, P. hypomelanus, P. vampyrus*, *Scotophilus kuhlii*	Serology (ELISA) and serum neutralizing test
Tioman Island, East coast, Peninsular Malaysia[6]	*Pteropus hypomelanus*	Virus culture, gene sequencing
Bangladesh[8]	*P. giganteus*	Serology
Thailand[15]	*Pteropus hypomelanus, P. lylei, P. vampyrus, Hipposideros larvatus*	Serology (ELISA) and RT-PCR
Cambodia[14]	*Pteropus lylei*	Serology (ELISA), seroneutralizing test and PCR
Sumatra, Java, Indonesia[16]	*Pteropus vampyrus*	Serology (ELISA), virus neutralizing test
Yunan and Hainan Island, China[19]	*Myotis* sp., *Rousettus leschenaultia,*	Serology (ELISA), serum neutralizing, PCR
India[18]	*Pteropus giganteus*	Serology (ELISA) and serum neutralizing test
Ghana[20]	*Eidolon helvum, Epomophorus gambianus, Hypsingathus monstrosus*	Serology (Luminex multiplexed binding assay)
Madagascar[17]	*Eidolon dupreanum, Pteropus rufus*	Serology (ELISA), serum neutralization test,

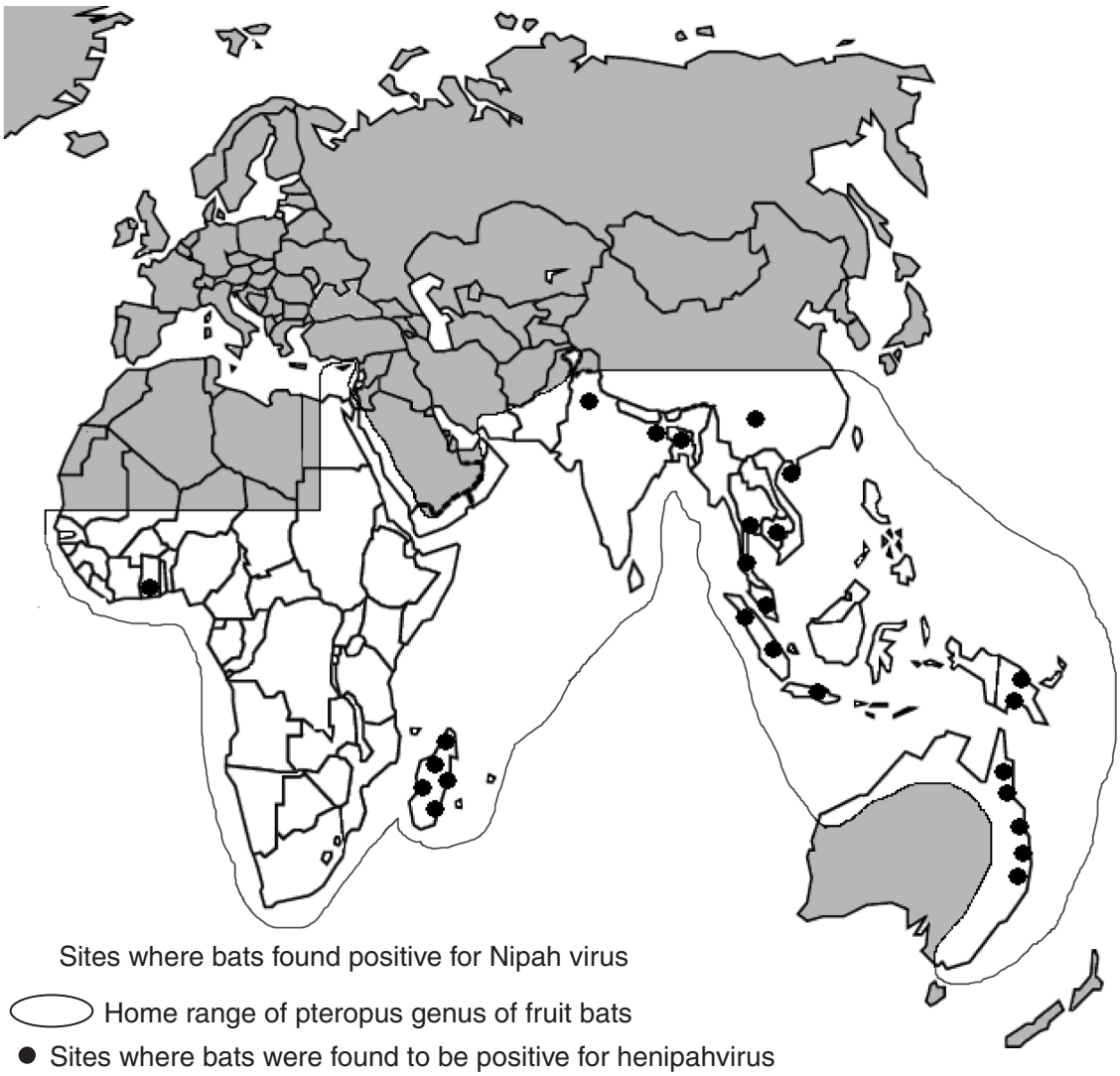

Figure 1: Distribution of bats and Nipah virus
(Adapted from WHO website: http://www.who.int/csr/disease/nipah/en/index.html)

total population in excess of 1.4 billion people, or roughly a quarter of the world population.

Bats are one of the most abundant and widely distributed mammals. They are highly gregarious, with some species of bats aggregate with a density of more than 3,000 bats/m^2, in population of up to several million individual animals. Bats are also long distance flyers, with some species travelling up to 640 km during seasonal migration. Migratory bats have been shown to exchange novel viruses with non-migratory ones.[21] This probably explains the relatively high prevalence of positive Henipavirus serology among colonies of bats. With the widespread distribution of both the virus and its vectors, and the ease of bat-to-human and human-to-human transmission, the Henipavirus will remain an important cause of zoonotic disease.

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