

Henipaviruses

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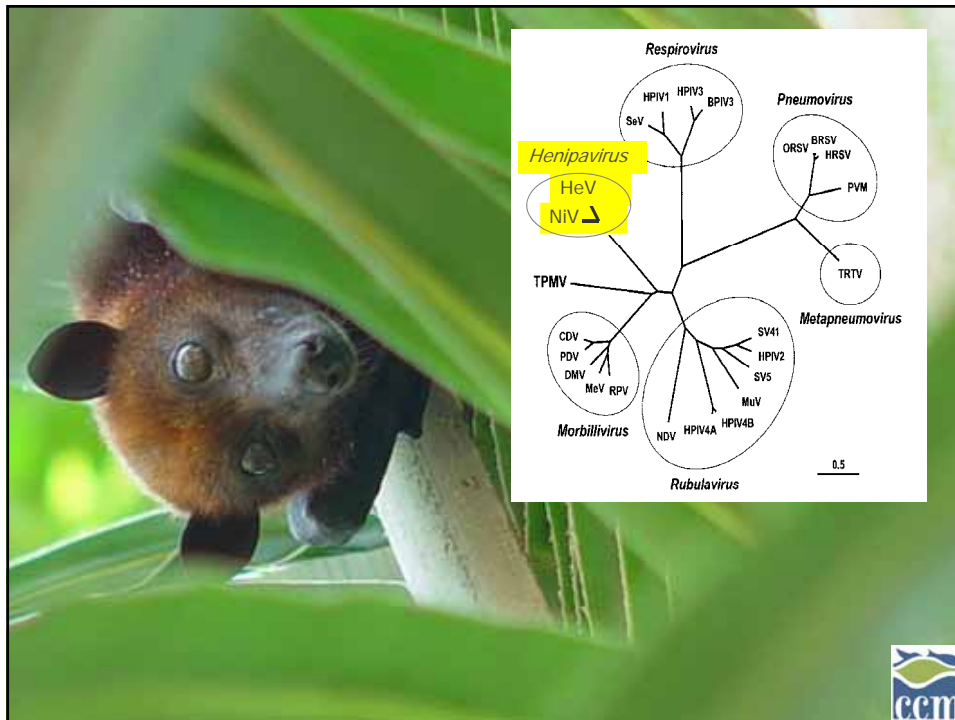
There have been a number of new viruses from fruit bats – including:

- ✓ 1994 – Hendra virus (Australia)
- 1996 – Australian bat lyssavirus (Australia)
- 1997 – Menangle virus (Australia)
- ✓ 1999 – Nipah virus (Malaysia)
- 2000 – Tioman virus (Malaysia)
- 2007 - Melaka virus (Malaysia)



Henipaviruses

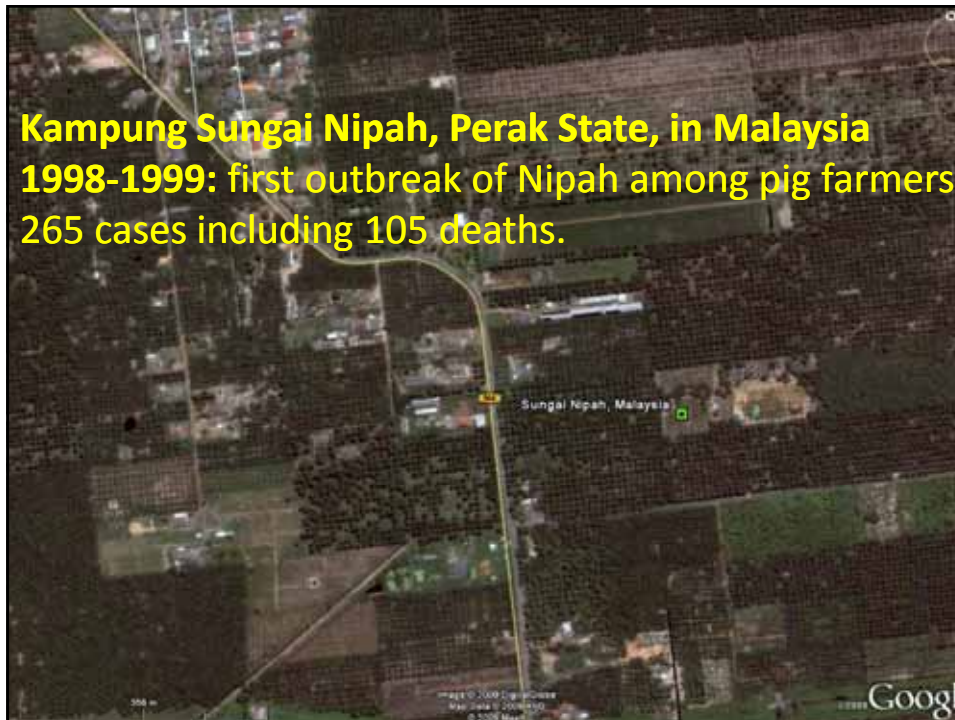
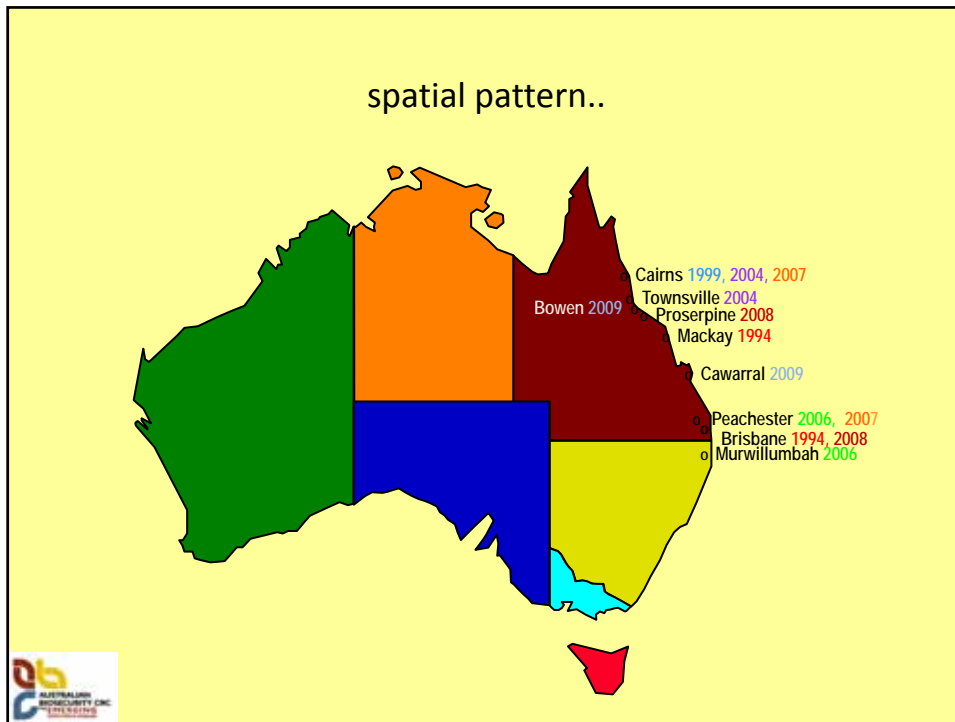
- Henipaviruses represent a novel genus in the Paramyxovirus family;
- Hendra virus first emerged in 1994 in Brisbane, Queensland, as a severe acute respiratory disease of race horses and humans, with a high case fatality rate. Some cases were later shown to be neurological.
- Nipah virus emerged in Malaysia in 1999 as a severe disease of pigs and humans with both respiratory and neurological syndromes, and also with a high fatality rate.
- Since 2001, a number of outbreaks of Nipah virus infection have occurred in Bangladesh and India's West Bengal.
- The natural reservoirs of both viruses are fruit bats (flying foxes) in the family *Pteropidae* and genus *Pteropus*.





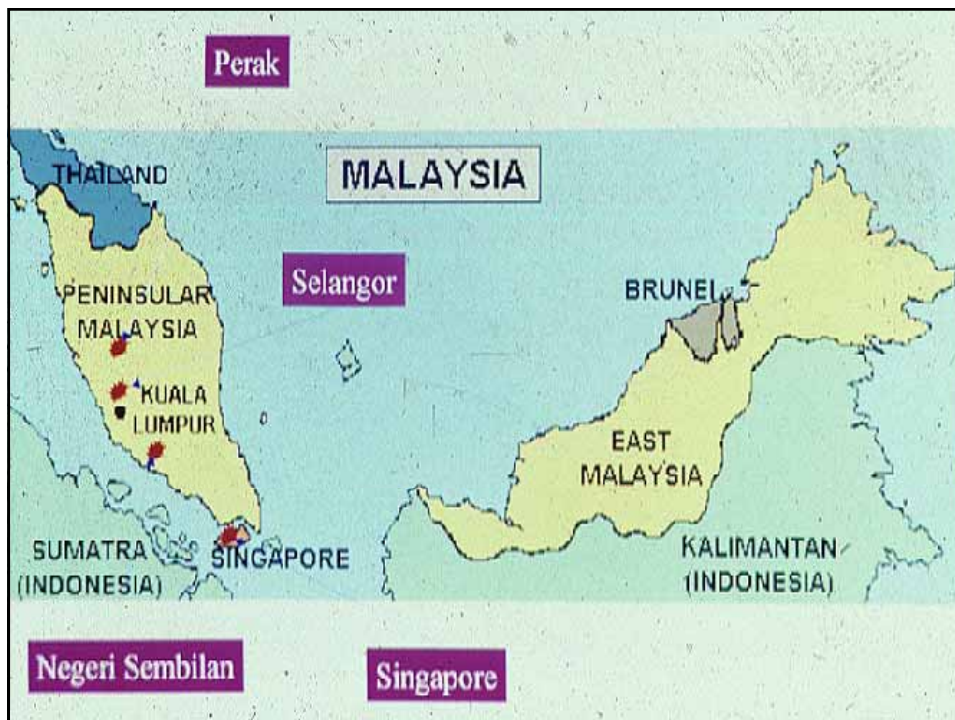
History of Hendra Virus Outbreaks

- **September 1994:** “first” outbreak in 21 horses and 2 human cases with one fatality in **Hendra**, Brisbane, Queensland
- **October 1995:** Retrospective diagnosis of HeV infection in dead two horses in **Mackay**, Queensland with one human fatality from severe encephalitis 13 months after exposure
- **Since 1999**, eleven focal, spatially & temporally unrelated outbreaks: - all confined along the east coast of Australia
 - ten in Queensland
 - one in New South Wales
- **Since Hendra discovery**, five outbreaks involved human cases
 - seven humans affected with four fatalities



History of Nipah Virus Outbreaks

- **1998-1999**: first outbreak of fatal encephalitis among pig farmers in Kampung Sungai Nipah, Perak State, in Peninsular Malaysia with 40% fatality . Initially confused as Japanese encephalitis Malaysia 1999 outbreak cost 625 million USD
- **1999**: small outbreak in Singapore following importation of sick pigs from Malaysia, with one fatal case
- **Since 2001**, 11 outbreaks occurred in India and Bangladesh
 - Nine in Bangladesh (Kushtia, Faridpur, Manikgonj, Meherpur, Naogaon, Rajbari, Tangail and Thakurgaon districts)
 - Two in West Bengal of India (Siliguri and Nadia)
- **Since Nipah discovery**, 477 human cases including 248 deaths



Nipah Virus Outbreaks: Malaysia, Singapore, Bangladesh and India

Dates	Location	No. cases	No. deaths	CFR(%)
Sep1998-Apr 1999	Malaysia; Singapore	265 11	105 1	40 9
Feb 2001	Siliguri, W. Bengal, India	66	45	68
Apr–May 2001	Meherpur, Bangladesh	13	9	69
Jan 2003	Naogaon, Bangladesh	12	8	67
Jan-Apr 2004	Goalando, Bangladesh	29	22	76
	Faridpur, Bangladesh	36	27	75
Jan-Mar 2005	Tangail, Bangladesh	12	11	92
Mar-Apr 2007	Kushtia, Bangladesh	19	5	26
	Nadia, W. Bengal, India	5	5	100
Feb-Mar 2008	Manikganj and Rajbari, Bangladesh	18	8	44

Henipaviruses: natural reservoir

- **Bats of *Pteropodidae* family, *Pteropus* genus.**
- Asymptomatic *Henipavirus* carriers
- Shedding virus in saliva, urine, birthing fluid and products
- Distribution overlaps with Henipavirus outbreak sites
- Evidence of infection in *Pteropus* bats from Australia, Bangladesh, Cambodia, India, Indonesia, Malaysia, Thailand, Timor Leste, Papua New Guinea, Madagascar
- Evidence of infection in *Eidolon helvum* fruit bats from *Pteropodidae* family in Ghana, Africa

Henipavirus Distribution



Hendra virus: transmission

(a) Bats-to-horses transmission

- Ingestion of pasture contaminated birthing products/ aborted fetuses/ urine
- Outbreaks occurred during birthing season of *Pteropus* bats
- Spill over events to horses are rare

(b) Horses-to-horses transmission

- via droplets respiratory particles or via frothy nasal discharges or urine
- more efficient in a stabled situation

(c) Horses-to-human transmission

- horses are the sole identified intermediate host for all human cases
- Close physical contact with ill, dying, dead horses
- exposure to contaminated tissues & body fluids-mucous secretions
- those involved in caring or necropsies of horses (trainer, veterinarians and assistants)

No bats-to-human or human-to-human transmission documented

Nipah virus: transmission

- (a) Ingestion of fruits or fruit products (e.g. raw date palm juice)
 - date palm sap contaminated with urine from infected fruit bats
 - fruit contaminated with saliva from infected fruit bats

- (b) Human-to-human transmission
 - direct contact with ill patients
 - exposure to body fluids (secretions, excretions)
 - one outbreak in hospital setting, Siliguri, India (hospital staffs or visitors)

- (c) Pig-to-human transmission
 - initial outbreaks only (Malaysia & Singapore)
 - direct contact with ill, dying, dead pig
 - exposure to contaminated tissues & body fluids
 - droplets respiratory particles or urinary secretions
 - occasional transmission from other domestic animals (goat, sheep, cow,...)

Nipah in Bangladesh and India

Of particular concern:

- The CFR of Nipah infection in India and Bangladesh is higher than in Malaysia.
 - Good evidence of human-to-human transmission in Bangladesh and India, with at least 8 cycles of transmission reported from Bangladesh, and nosocomial infections in a hospital setting in Siliguri, West Bengal.
 - The mechanism of transmission remains to be determined.
 - No evidence of pigs as intermediate hosts, and little direct evidence of bats in Siliguri or in Bangladesh in 2007 – thus source of virus remains to be determined in many instances.
- *These issues indicate that Nipah virus is a potential pandemic threat.*



Nipah virus: clinical disease in humans

- Incubation period: 4 – 45 days
- Asymptomatic infection reported
- Start with feverish syndrome: Flu-like fever, headaches, myalgia, vomiting, sore throat
- Neurological manifestations and/or Respiratory manifestations (more frequent in later outbreaks)
- Long term sequelae
 - 80% whom survived acute encephalitis made full recovery
 - 20% with residual neurological sequelae after NiV encephalitis : persistent convulsions, behavioural changes
 - Small proportion of cases develops relapse or delayed encephalitis with a 18% mortality rate

Hendra and Nipah: treatment

- No antiviral drug
- No vaccine
- Intensive supportive care is the mainstay
- Therapeutics and vaccine are under development

Henipavirus: prevention and control (1)

1. Control in domestic animals

- Routine cleaning & disinfection of pig farm/horse stable is expected to be effective in preventing infection
- Reducing the risk of bat-to-domestic animal transmission: bat proof buildings, bat exclusion strategy, fruit trees...
- Outbreak suspected:
 - Quarantine animal premises
 - ± euthanasia or culling of infected animal(s)
 - Restrict/ ban animals movements
- Establish active animal health surveillance system for early warning for veterinary and human public health authorities.

Henipavirus: prevention and control (2)

2. Reducing risk of infection in people

- Reduce risk of bats-to-human transmission:
 - Protect collection process of date palm juice (bamboo)
 - Wash & peel fruits thoroughly
- Reduce risk of human-to-human transmission:
 - Avoid or minimize physical contact with ill patient
 - Hand hygiene + use of personal protective equipment (PPE)
- Reduce risk of domestic animal-to-human transmission:
 - Avoid or minimize contact with ill or dead pig, horse
 - Hand hygiene + use of personal protective equipment(PPE)
 - Particularly important in veterinary practices (care, necropsies)



How did these Henipaviruses emerge? Hendra virus

- Hendra virus is believed to have emerged because fruit bats have become much more urbanised as they seek new sources of food (nectar or fruit).
- The natural food sources for these animals have been in forest settings, but these have been destroyed with increasing land clearance for agriculture.
- Although all human infections with Hendra virus have been acquired through intermediate hosts, horses, the potential for this interaction with horses is due largely to the peri-urban/urban locations of fruit bats 'camps'.
- Horses become infected by grazing on pastures contaminated with bat 'spats', urine, and possibly birthing fluids.

How did these Henipaviruses emerge? Nipah virus

- Nipah virus may also have emerged because of fruit bats seeking food in areas where agricultural intensification and changes in land use had made natural sources scarce, but where orchard fruit was readily available, often as shade for piggeries. Thus bats were brought into contact with pigs through bat urine, saliva-contaminated half-eaten fruit, and spats, etc falling into pig pens.
- However, other factors were also essential components in the emergence of Nipah, one of which was the intensification of pig production.

Could we have predicted their emergence?

- For Hendra virus, answer is probably not – there had been no previous indication of diseases associated with fruit bats.
- For Nipah virus – the answer really has to be ‘yes’ - but in hindsight. Pteropid bats were known to occur as overlapping populations from Australia, PNG and Indonesia to South, South-east and East Asia, so this ‘open conduit’ should have raised alarm bells as a possible avenue for virus movement.

Could they have emerged/occurred previously?

- Deforestation activities in many parts of SE Asia will undoubtedly have brought opportunities for bat-human interactions;
- Bats are a popular source of food in many countries in SE Asia and Oceania, and thus this human-bat interface is a possible route of past and continuing emergence.



Lessons/Comments

- Henipaviruses, like Arenaviruses, Hantaviruses, etc, appear to have evolved as genetically diverse but related viruses in a wide variety of related mammalian species – thus related but genetically distinct viruses have been described in Australia, Bangladesh/India (and both in Thailand), and based on serological data, in many other countries in SE Asia and Oceania, SW Indian Ocean (Madagascar), and most recently in Ghana. **So we can confidently predict that similar species might be expected to harbour related viruses, but also other data from West Africa and China strongly suggest that other Megachiropteran and Microchiropteran bat genera may also have related viruses.**
- Human infections with these viruses may present with a disparate clinical picture – ranging from fever with mild respiratory or meningitic symptoms to severe neurological and/or interstitial pneumonia, and with relapse possible after apparent recovery, or a late onset of severe symptoms. **These presenting symptoms may also be common to other unrelated viruses, thus care needs to be taken in initial diagnoses and in handling specimens.**

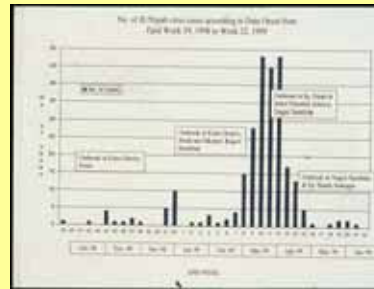
Lessons/Comments

- The ecology of recent outbreaks in Bangladesh and India appears to be different from the original outbreak, and there is no evidence ,or apparent need, for any pig involvement . **Thus, other related viruses in different geographic niches may have different patterns, with or without spillover hosts, and for the former, the spillover hosts may be novel, previously unrecognised hosts. – that is, they may not be pigs or horses**
- Emergence of these viruses appears to be most likely due to human activities, especially deforestation, resulting in the need for these animals to seek food (fruit and nectar) elsewhere – gardens with ornamental shrubs and orchards. **Thus the major ecological factors conducive to emergence are related to human activities causing changes in the environment or in the food chain.**

Lessons/Comments

Sporadic cases and small clusters of encephalitis had been reported in the Perak area for a number of months prior to the outbreak in Malaysia, but they were thought to be due to Japanese encephalitis virus and vaccine was administered. At the same time, pigs were dying. Unfortunately there was little communication between medical and veterinary authorities.

This demonstrates the importance of communication between medical and veterinary health, and of the One Health approach. JE vaccine did not protect people from disease, and pigs do not die from JEV – so with communication, this outbreak could possibly have been averted!



Lessons/Comments

- There was a considerable delay in reporting the first West Bengal Nipah virus outbreak in 2001, despite its importance in demonstrating the occurrence of nosocomial transmission. This serves to remind us that transparency, especially through rapid and shared surveillance, is essential if we are to detect novel emergent agents quickly.

Future.....

- Many questions still remain about the geographic range, pathogenicity, modes of transmission, ecology, drivers of spillover events, etc.
- Also fundamental questions remain about evolution and diversity of viruses throughout the geographic range.
- Improved and extended surveillance of fruit bats and their movements in SW Indian Ocean, Africa, and Oceania is needed to better understand ecology of these viruses, and thus their potential for emergence.
- This requires various partnerships with local communities as well as wildlife experts, ecologists, as well as medical and veterinary specialists.

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