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Nipah Virus



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Overview

- Organism
- History
- Epidemiology
- Transmission
- Disease in Humans
- Disease in Animals
- Prevention and Control





In today's presentation we will cover information regarding the organism that causes Nipah and its epidemiology. We will also talk about the history of the disease, how it is transmitted, and the clinical signs seen in species it affects (including humans). Finally, we will address prevention and control measures for Nipah virus.

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Agent

- Genus *Henipavirus*
 - Newly discovered virus
 - Related to Hendra virus
- Severe, rapidly progressive encephalitis in humans
 - High mortality rate
 - Close contact with infected pigs
- Severe, respiratory disease in pigs

Nipah virus is a newly discovered (1999) Paramyxovirus that has been placed with another recently emergent viral zoonotic disease, Hendra virus, in the new genus Henipavirus. Nipah virus causes severe, rapidly progressive encephalitis in humans and severe respiratory illness in pigs. Some pigs may demonstrate nervous system signs. Nipah virus has a high mortality rate in humans (40%). The transmission of the disease to humans is associated with close contact to infected pigs. In vitro studies of Nipah virus show syncytial cytopathic effects on cell cultures. Currently survival of the virus outside the host is unknown.

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History




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History

- 1998-1999: Peninsular Malaysia
 - Human febrile encephalitis with high mortality
 - Cases similar to Japanese encephalitis
 - Discovered new virus similar to Hendra
- 1999: Singapore
 - Outbreak in abattoir workers
 - Pigs imported from Malaysia



From September 1998–April 1999, human cases of febrile encephalitis with high mortality were reported by the Malaysian Ministry of Health. Initially Japanese encephalitis (JE) was suspected. However serological tests and the epidemiology of the disease indicated it was different from JE. Tissue culture isolation from cases suggested a previously unrecognized paramyxovirus, closely related to Hendra virus. Nipah virus was named after the village (Sungai Nipah) where the first cases were found. (NOTE: Hendra virus is a severe respiratory and encephalitic disease causing virus that affects humans and horses.) In March 1999, a similar type of outbreak occurred in Singapore. The disease affected abattoir workers that had been exposed to pigs imported from Malaysia for slaughter.

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This is a map showing peninsular Malaysia and the close proximity of Singapore, the two locations of Nipah virus outbreaks in 1998 and 1999. Serological surveys (indicated by the boxes and circles) of various animal species were conducted to determine the reservoir and potential spread to humans. [The map is from Emerging Infectious Diseases 2001;7(3):439-41].


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Reservoir

- Flying foxes (fruit bats)
 - Carry the virus
 - Are not affected
 - Virus found in
 - Urine
 - Partially eaten fruit
 - Migratory



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The reservoir for Hendra virus has been found to be flying foxes (fruit bats). Investigations of these species as reservoirs for Nipah virus were conducted due to the similarity of Nipah virus to Hendra virus (which also has fruit bats as reservoirs). Additionally, many species of fruit bats are found in Malaysia. It has been found that several species of fruit bats in Malaysia have neutralizing antibodies to Nipah virus. The highest prevalence was for two species of flying foxes, the island flying-fox (*Pteropus hypomelanus*) and Malayan flying fox (*Pteropus vampyrus*). Additionally, studies indicate Nipah virus can be found in the urine and partially eaten fruit (saliva?) from these species. These animals are able to carry the virus without being affected by it and are common to caves in Malaysia. Several of the same species of fruit bats are also found in Australia, Indonesia, and the Philippines. Since these bats are migratory, increased surveillance for Nipah virus is being conducted in these countries. Investigation of potential secondary hosts (peridomestic species) have also been conducted. Species such as rats, house shrews, dogs and chickens, located on the outbreak farms were tested. No indication of a secondary host has been found. This is a picture of a Malayan flying fox (*Pteropus vampyrus*) (picture is courtesy of Dr. Jasbir Singh, Veterinary Research Institute, Ipah Malaysia).

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Transmission

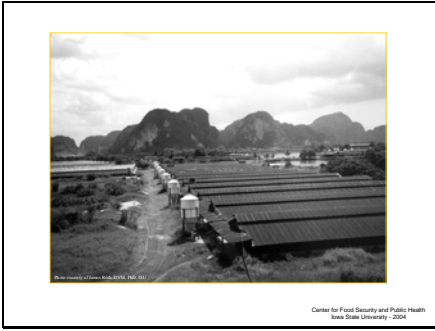
- Pigs
 - Direct contact
 - Contact with body fluids
 - Aerosolization of respiratory or urinary secretions
- No person-to-person transmission
- No bat-to-human transmission

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Currently it is unclear how the virus is transmitted from bats to pigs. However, it is suspected that fruit trees close to pig confinement areas are foraged by the bats and the virus is spread by this close proximity (urine or saliva on partially eaten fruit). The majority of human cases (93%) have been related to close contact with pigs, either from direct contact or contact with body fluids, urine or feces. Aerosolization of urinary or respiratory secretions may be a possible route of transmission and is being investigated. The role that dogs and cats in close contact with infected pigs may also play in the transmission of the disease is being explored. To determine the potential for person-to-person transmission, a survey of persons involved with case-patients was conducted. Family members, physicians, nurses, and pathologists who had direct contact with infected persons had no signs of illness or serological evidence of Nipah virus infection. Additionally, there was no serological evidence of human infection among bat handlers.

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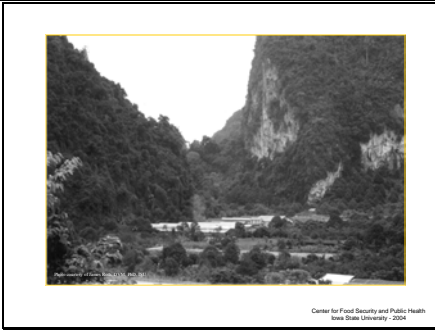
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These are several of the hog confinement barns that were affected during the Malaysia Nipah virus outbreak. The reservoir fruit bats live in these caves and feed on the fruit trees that are in close proximity to the hog confinement barns. Photo is courtesy of James Roth, DVM, PhD – Iowa State University.

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This slide shows additional hog confinement barns in Malaysia. There are many fruit trees and caves close to this location. Photo is courtesy of James Roth, DVM, PhD – Iowa State University.

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Epidemiology

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Epidemiology

- 1998-1999: Malaysia
 - 265 persons hospitalized
 - Many required mechanical ventilation
 - 105 deaths (40%)
 - Mostly adult males - pig farmers
 - 1.1 million pigs culled
 - Pig population prior to outbreak was 2.4 million
 - Great economic loss
 - Surveillance and testing

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The 1998-1999 outbreak of Nipah virus in Malaysia occurred in three clusters. A total of 265 persons were infected and required hospitalization. Many required mechanical ventilation. There were 105 fatalities (40% mortality). Ninety-three percent (93%) of these cases had close contact with infected pigs. Adult males, in particular pig farmers, were the majority affected. The male to female ratio was 4.5:1. Pigs were also affected during this outbreak. Severe respiratory disease was rapidly spread by movement of infected pigs from farm to farm. Some pigs also demonstrated neurological signs. The pig population in Malaysia prior to the outbreak was 2.4 million animals. [The total value of annual national output was estimated at about US\$ 400 million and total export value at US\$100 million.] During the outbreak, over 1.1 million pigs were culled to prevent the further spread of the disease, which resulted in a substantial economic loss for this country (an estimated cost of about US \$97 million) and loss of export trade (estimated cost of about US\$120 million). Additionally, local pork consumption during the outbreak dropped by 80%. Serological surveillance of farms and random testing of pigs at abattoirs is currently being performed.

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Epidemiology

- 1999: Singapore
 - 22 infected persons
 - Mean age 37 years old
 - 10 asymptomatic
 - 12 symptomatic
 - Encephalitis, pneumonia or both
 - 1 death

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Shortly after the 1999 outbreak in Singapore, a serological survey of various risk groups was conducted in Singapore. From the 1,469 persons tested, 22 were found to be infected with Nipah virus. Ten of these individual were asymptomatic. Of the 12 persons (54.6%) demonstrating symptoms, 9 had encephalitis, 2 pneumonia and 1 had both.

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Epidemiology

- 2004: Bangladesh
 - Mid-March
 - Faridpur District of Bangladesh
 - 34 human cases
 - 26 deaths
- No new cases reported since mid-April

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The most recent outbreak of Nipah virus occurred in the Faridpur District of Bangladesh in mid-March 2004. Thirty-four human cases were identified, and 26 people died of the disease. No new cases have been reported since mid-April. Data as of May 26, 2004 from the CDC; http://www.cdc.gov/travel/other/nipah_bangladesh_2004.htm.

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Disease in Humans



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Human Illness

- Incubation period: 3-14 days
 - Fever and headache
 - Encephalitis
 - Dizziness, drowsiness, vomiting
 - Seizures
 - Progresses to coma in 24-48 hours
 - Respiratory difficulty
 - Hypertension, tachycardia

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The incubation period for Nipah virus in humans has been found to be from 3-14 days. The first symptoms are fever and headache. This is then followed by dizziness, drowsiness, disorientation and vomiting. Encephalitis and seizures occur in severe cases. This progresses to coma within 24-48 hours. A few patients had respiratory illness. The mean time from onset of illness to death was found to be 10.3 days. Duration of illness for those that recovered was found to be 14.1 days.

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Human Illness

- Complications
 - Septicemia (24%)
 - GI bleeding (5%)
 - Renal impairment (4%)
- Asymptomatic
 - Relapse or late-onset encephalitis
 - Residual neurological deficits
- Treatment: Supportive, ribavirin

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Complications that were noted during the Malaysian outbreak included septicemia (24%), intestinal bleeding (5%) and renal impairment (4%). Some of the cases were found to be asymptomatic. However, relapses (late-onset encephalitis and residual neurological deficits) were documented. Current treatment involves intensive supportive care. Early treatment with ribavirin may reduce the severity of the disease.

Disease in Animals



Disease in Animals

- Pigs
 - Highly contagious
 - May be asymptomatic
 - Acute fever (> 104°F)
 - Severe respiratory disease
 - Characteristic cough – harsh, “barking”
 - Neurological changes
 - Head pressing, agitation, aggression
 - Low mortality



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Nipah virus in swine is highly contagious and easily spread by transport of pigs from farm-to-farm. The incubation period has been reported as 7-14 days. Many swine affected can be asymptomatic. Those affected develop an acute fever (>104 degree F) and rapid, labored, open-mouth breathing. They will also have an unusual loud and explosive barking cough (called “1 mile cough”). Clinical disease in swine varies according to the age of the pigs. In nursery and grower pigs, acute febrile illness with respiratory signs (rapid, labored breathing, harsh non-productive cough) is most commonly seen. In severe cases, blood-tinged mucous discharge from the nostrils may be seen. In less severe cases, open mouth breathing occurs. Neurological signs are also possible and include trembling, twitching, muscular spasms, rear leg weakness and possible lameness or spastic paresis. In sows and boars, affected animals may be found dead overnight or may demonstrate acute febrile illness with labored breathing (panting), increased salivation and serous, mucopurulent or blood tinged nasal discharge. Neurological signs can also be seen in sows and boars and may include agitation and head pressing, tetanus-like spasms and seizures, nystagmus, and pharyngeal muscle paralysis. Abortions in affected sows have also been reported. In some instances, illness in pigs occurred 1-2 weeks before illness in humans.

Disease in Animals

- Horses
 - 1 death from encephalitis
- Dog
 - Distemper-like signs
 - Fever, respiratory distress
 - Ocular and nasal discharge
- Cat
 - Fever, depression
 - Severe respiratory signs

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Disease in other animal species is poorly documented. However, serological evidence of Nipah virus infection has been reported in bats, 3 horses, dogs and 1 cat. Over 3,000 horses in Malaysia were serologically examined (by serum neutralization test). Two had neutralizing antibodies to Nipah virus. Another with neurological signs showed Nipah virus infection. All three horses were from a single property surrounded by infected pig farms. Nipah virus antibody prevalence in domestic dogs near infected pig farms during the outbreak was reported to be 46%. However, after the outbreak, it dropped to 15% in these areas and 1.6% five km away from the farms. This indicates disease depends on close contact with infected pigs. Clinical signs reported for infected dogs include signs that resemble canine distemper, fever, respiratory distress, conjunctivitis, mucopurulent nasal and conjunctival discharge. There has only been 1 reported field case of a cat infected with Nipah virus. However, experimental study on 2 cats indicate they are affected by Nipah virus. Both cats became febrile and depressed. One demonstrated open-mouthed breathing and was eventually humanely euthanized. On necropsy, hydrothorax, edema of the lungs and severe, diffuse meningitis were found. The second cat recovered 12 days after inoculation.

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Diagnosis

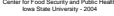


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Diagnosis

- Differentials for swine
 - Classical swine fever, PRRS, pseudorabies, swine enzootic pneumonia, porcine pleuropneumonia
- Diagnostic tests
 - ELISA
 - Immunohistochemistry
 - PCR
 - Virus isolation




Differential diagnosis for suspect swine include classical swine fever, PRRS (porcine reproductive and respiratory syndrome), Aujeszky's disease (pseudorabies), swine enzootic pneumonia (*Mycoplasma hyopneumoniae*) and porcine pleuropneumonia (*Actinobacillus pleuropneumoniae*). Laboratory diagnostic methods for Nipah virus infections include serology, histopathology, immunohistochemistry, electron microscopy, polymerase chain reaction (PCR), and virus isolation. **Remember Nipah virus is a Biolevel 4 agent.** For more detailed information, see <http://www.fao.org/docrep/1005/ac449e/ac449e07.htm>.

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Prevention and Control




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Control and Prevention

- Avoid all contact with potentially infected pigs
- IMMEDIATELY contact state authorities
- Who to call
 - State Veterinarian
 - USDA-APHIS Veterinarian-In-Charge for your state
 - State Public Health Veterinarian




Nipah virus is a very dangerous pathogen. It has been classified as a Biolevel 4 agent. If you suspect a potential Nipah virus outbreak, contact your state veterinarian, USDA-APHIS Veterinarian-In-Charge (AVIC) for your state, or your state public health veterinarian **IMMEDIATELY!** Avoid all contact with potentially infected species (pigs, dogs, cats) until the proper authorities are consulted.

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Nipah as a Biological Weapon

- CDC Category C Bioterrorism Agent
- Emerging pathogen
- Potentially high morbidity and mortality
- Major health impact
- Aerosolization potential
- Economic impact
- Social disruption (fear, panic)



Nipah virus has been listed by the Centers for Disease Control and Prevention as a Category C potential bioterrorist agent. This is described as an emerging pathogen which has a potentially high morbidity and mortality as well as a major health impact. Currently spread of the disease involves close contact with pigs. However, aerosolization may be a possible bioterrorist method of dispersal. Additionally, the potential for this virus to infect a wide range of hosts and produce significant mortality in humans makes this emerging virus one of public health concern. Due to the need to cull infected pigs, attack with this agent could produce a great economic impact in our pork industry. Additionally, during the Nipah outbreak in Malaysia, widespread panic and fear occurred until the outbreak was brought under control.

Additional Resources

- FAO – Food and Agriculture Organization
 - Manual on the diagnosis of Nipah virus infection in animals
 - www.fao.org/DOCREP/005/AC449E/AC449E00.htm
- CDC–Special Pathogens Branch
 - www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/nipah.html
- World Health Organization
 - www.who.int/inf-fs/en/fact262.html
- USDA-APHIS–CEI
 - www.aphis.usda.gov/vs/ceah/cei/nipah.html

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