Slide 1

Nipah Virus

Barking Pig Syndrome,
Porcine Respiratory and
Encephalitis Syndrome,
Porcine Respiratory and
Neurologic Syndrome

Slide 2

Overview

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

In today's presentation we will cover information regarding the organism that causes Nipah virus infection 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 infection, as well as actions to take if an infection with Nipah virus is suspected.

Slide 3

Agent

- Genus *Henipavirus*
  - Virus discovered, 1999
  - 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 was discovered in 1999. It is a paramyxovirus in the genus *Henipavirus;* Hendra virus is also within this genus. Different variants of Nipah virus were involved in outbreaks in Malaysia, Bangladesh, and India, and t least two major strains of Nipah virus were isolated from pigs in Malaysia. Nipah virus causes severe, rapidly progressive encephalitis in humans, and severe respiratory illness in pigs. Some pigs may also demonstrate nervous system signs. Nipah virus infection has a high mortality rate in humans. Transmission of the disease to humans is associated with close contact with infected pigs. Nipah virus survives in the environment for long periods in favorable conditions; it survives for days in fruit bat urine and contaminated fruit juice.

Slide 4

History

Slide 5

History
- 1998-1999: Peninsular Malaysia
  - Human febrile encephalitis, high mortality
  - New virus discovered
- 1999: Singapore
  - Outbreak in abattoir workers
  - Pigs imported from Malaysia
- Since 2001 – Bangladesh, India

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From September 1998 to 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 disease epidemiology suggested a different disease. Tissue culture isolation from cases identified an unrecognized paramyxovirus closely related to Hendra virus. Nipah virus was named after the village (Sungai Nipah) where the first cases were reported. (NOTE: Hendra virus is a severe respiratory and encephalitic disease causing virus that affects humans and horses.) In March 1999, a similar outbreak occurred in Singapore. The disease affected abattoir workers that had been exposed to pigs imported from Malaysia for slaughter. Since 2001, human outbreaks and clusters of cases have been reported periodically in Bangladesh and a neighboring region of northern India.

Slide 6

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This is a map showing peninsular Malaysia and its close proximity to Singapore; these are the two locations of the 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 host as well as the potential spread to humans.

[The map is from Emerging Infectious Diseases 2001;7(3):439-41].

Slide 7

Transmission

Slide 8

Reservoir
- Flying foxes (fruit bats)
  - Carry the virus
  - Are not affected
- Virus found in
  - Urine
  - Partially eaten fruit (saliva?)
- No known secondary host

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The primary reservoir for Nipah virus are flying foxes (also known as fruit bats) of the genus *Pteropus*. Transmission of Nipah virus from bats to swine has not been shown conclusively; however, there are various biologically plausible means for infected secretions of primary hosts to enter pigs, including direct contact with infected secretions contaminated fruit or dead bats. Scavenging animals may also play a role in the transport of virus into proximity of pigs. Flying foxes are able to carry the virus without being affected by it. Investigation of potential secondary hosts (peridomestic species) have also been conducted. Rats, house shrews, dogs, and chickens have been tested, but 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).]

Slide 9

Transmission

- Pigs in Malaysia
  - Direct contact
  - Contact with body fluids
  - Aerosolization of respiratory or urinary secretions
  - Vertical transmission across the placenta?
  - Semen and iatrogenic spread?

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It is unclear how the virus was transmitted from bats to pigs in Malaysia. However, it is suspected that fruit trees close to pig confinement areas are foraged by the bats and the virus is spread by urine or saliva-contaminated partially-eaten fruit on which the pigs feed. 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 of dogs and cats (in close contact with infected pigs) in the transmission of the disease is also being explored. Anecdotal evidence suggests that vertical transmission may occur across the placenta. Transmission in semen and iatrogenic spread on re-used needles have also been suggested.

Slide 10

Transmission

- Person-to-person
  - Not reported in Malaysia
  - Likely in Bangladesh and India
    - Nosocomial infections
- Bat-to-person
  - Not reported in Malaysia
  - Common in Bangladesh and India
    - Contaminated fruit, unpasteurized date palm juice

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To determine the potential for person-to-person transmission in Malaysia, 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, although children who ate contaminated fruit did become sick in Bangladesh. Ingestion of virus in contaminated, unpasteurized date palm juice may have been the source of an outbreak in Bangladesh in 2005. Since 2001, human outbreaks and clusters of cases have been reported periodically in Bangladesh and a neighboring region of northern India. In some of these outbreaks, Nipah virus seems to have been transmitted directly from bats to humans, with person-to-person transmission the most significant means of spread. Humans can shed Nipah virus in upper respiratory secretions and urine. Nipah virus may be transmitted on fomites. Nipah virus survives in the environment for long periods in favorable conditions; it survives for days in fruit bat urine and contaminated fruit juice.

Slide 11

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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 courtesy of James Roth, DVM, PhD – Iowa State University)

Slide 12

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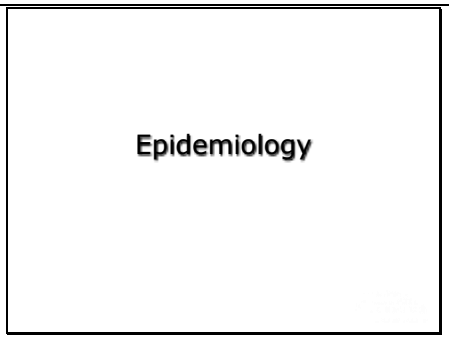
This slide shows additional hog confinement barns in Malaysia. There are many fruit trees and caves close to this location.

(Photo courtesy of James Roth, DVM, PhD – Iowa State University)

Slide 13



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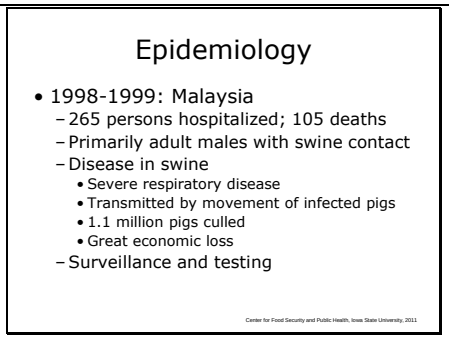
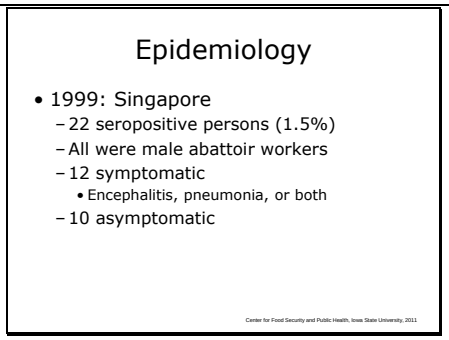


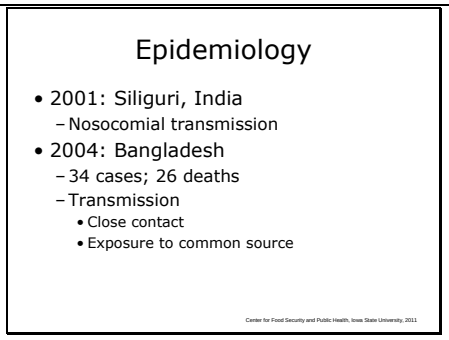
The 1998-1999 outbreak of Nipah virus in Malaysia occurred in three clusters. A total of 265 persons were infected and required hospitalization. There were 105 fatalities (40% mortality). Ninety-three percent (93%) of these cases had close contact with infected pigs. Adult males, pig farmers in particular, were the majority affected. 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 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.

Slide 15



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 individuals were asymptomatic. Of the 12 persons (54.6%) demonstrating symptoms, 9 had encephalitis, 2 pneumonia, and 1 had both.

Slide 16



An outbreak in Siliguri, India in 2001 was linked to nosocomial transmission in hospitals and ended after effective barrier nursing precautions were put in place. A 2004 outbreak of Nipah virus occurred in the Faridpur District of Bangladesh in mid-March 2004. Thirty-four human cases were identified, and 26 people (76%) died of the disease. Transmission of the disease may have occurred through close contact with infected patients or exposure to a common source (www.cdc.gov/eid).

Slide 17

Epidemiology

- 2005: Bangladesh
  - 44 cases; 12 deaths
  - Contaminated palm fruit juice
- 2007: Bangladesh
  - 7 cases; 3 deaths
  - Person-to-person transmission

In 2005, an outbreak began in the Tangail District on Bangladesh when 13 people lost consciousness after drinking palm fruit juice. The fruit may have either been contaminated with fruit bat droppings or saliva as the fruit may have been partially eaten by the bats. Blood samples from the suspected cases were sent to the CDC to confirm Nipah virus infection, and one was a confirmed positive. There were a total of 44 cases and 12 deaths from Nipah virus as of February, 2005 (http://www.promedmail.org).

In February 2007 an outbreak of Nipah virus encephalitis occurred in Thakurgaon District of northwest Bangladesh. Seven people were infected, three of whom died. Although the source of infection for the index case was not identified, 50% of *Pteropus* bats sampled from near the outbreak area 1 month after the outbreak had antibodies to Nipah virus confirming the presence of the virus in the area. The outbreak was spread by person-to-person transmission.

Slide 18

Disease in Humans

Slide 19

Human Illness

- Incubation period: 4 to 20 days
  - Fever and headache
  - Encephalitis
    - Dizziness, drowsiness, vomiting
    - Seizures
    - Progresses to coma in 24-48 hours
  - Respiratory difficulty
  - Relapsing neurologic symptoms

The incubation period in humans is usually four to 20 days; however, incubation periods as short as two days or as long as a month have been reported. Some people may remain asymptomatic during the initial infection, but develop serious neurological disease up to four years later. The first symptoms are generally fever, headache, and myalgia followed by dizziness, drowsiness, disorientation, and vomiting. Encephalitis and seizures occur in severe cases which progress to coma within 24-48 hours. Some patients have respiratory illness.

Slide 20

Human Illness

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

Septicemia, bleeding from the gastrointestinal tract, renal impairment, and other complications can occur in severely ill patients. In the Malaysia outbreak, the mean time from onset of illness to death was 10.3 days. Duration of illness for those that recovered was 14.1 days. Cases that progress to encephalitis are often fatal. Surviving patients may have mild to severe residual neurological deficits, or remain in a vegetative state. Patients who recover from neurologic disease may relapse with encephalitis several months to several years later. Encephalitis can also occur as long as four years or more after an asymptomatic or non-encephalitic infection. In the Malaysian outbreak, the subclinical infection rate was estimated to be 8 to 15%. The case fatality rate in the various outbreaks has varied from 33% to approximately 75%; the overall case fatality rate for all outbreaks in Bangladesh between 2001 and February 2005 was 64%. Current treatment involves intensive supportive care. Early treatment with ribavirin may reduce the severity of the disease.

Slide 21

Disease in Animals

Slide 22

Disease in Animals

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

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Nipah virus in swine is highly contagious and easily spreads by transport of pigs from farm-to-farm. The incubation period has been reported to be 7 to 14 days (as short as 4 days). Many affected swine can be asymptomatic. Those affected develop an acute fever (>104 degree˚F) and rapid, labored, open-mouth breathing. They also have an unusual loud and explosive barking cough (called the "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 are 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 in sows appear to be more common than in younger animals, 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. The morbidity rate is estimated to approach 100% but the mortality rate is low (1 to 5%), except in piglets (40%). In some instances, illness in pigs occurred 1-2 weeks before illness in humans, making pigs good sentinels for human disease.

Slide 23

Disease in Animals

- Dog
  - Distemper-like signs
  - Fever, respiratory distress
  - Ocular and nasal discharge
- Cat
  - Fever, depression
  - Severe respiratory signs
- Horses
  - Encephalitis

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Disease in other animal species is poorly documented; however, serological evidence of Nipah virus infection has been reported in bats, dogs, horses, and cats. Clinical signs reported for infected dogs include signs that resemble canine distemper: fever, respiratory distress, conjunctivitis, and mucopurulent nasal and conjunctival discharge. There has only been 1 reported field case of a cat infected with Nipah virus; however, an experimental study on 2 cats indicated they are affected by Nipah virus. Both cats became febrile, depressed, and exhibited respiratory distress. 3,000 horses in Malaysia were serologically examined (by the serum neutralization test); two had neutralizing antibodies to Nipah virus and one showed neurological signs. All three horses were from a single property surrounded by infected pig farms.

Slide 24

Sampling

- Before collecting or sending any samples, the proper authorities should be contacted
- Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease

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Before collecting or sending any samples from animals with a suspected foreign animal disease, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease.

Slide 25

Diagnosis

Slide 26

Diagnosis

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

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Differential diagnoses for Nipah virus in 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 include serology, histopathology, immunohistochemistry, electron microscopy, polymerase chain reaction (PCR), and virus isolation.

Slide 27

Prevention and Control

Slide 28

Recommended Actions

- IMMEDIATELY notify authorities
- Federal
  - Area Veterinarian in Charge (AVIC)
    http://www.aphis.usda.gov/animal_health/area_offices/
- State
  - State veterinarian
    http://www.usaha.org/StateAnimalHealthOfficials.pdf
- Quarantine

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Nipah virus is a very dangerous pathogen. It has been classified as a Biosafety level 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. Because Nipah virus can be transmitted from person-to-person, barrier nursing should be used when caring for infected patients. Patients should be isolated, and personal protective equipment, such as protective clothing, gloves, and masks should be used.

Slide 29

Prevention and Control

- Keep fruit bats away from pigs
- Do not drink unpasteurized fruit juices
- Wash, peel, and/or cook all fruit thoroughly before eating

Preventing infections in pigs can decrease the risk of infection for humans. In endemic areas, pigs and fruit bats should be avoided whenever possible. Fruit tree plantations should be removed from areas where pigs are kept. Wire screens can help prevent contact with bats when pigs are raised in open-sided pig sheds. Run-off from the roof should be prevented from entering pig pens. Transmission on fomites is also possible; re-used vaccination needles may have contributed to the spread of the virus in Malaysia. During an outbreak, equipment and other fomites should be cleaned and disinfected. In addition, dogs and cats should be prevented from contacting infected pigs or roaming between farms. Unpasteurized juices should not be drunk, and fruit should be washed thoroughly, peeled, or cooked. Good personal hygiene, including hand washing, also reduces the risk of infection.

(Photos of flying fox and partially eaten fruit taken from the Department of Sustainability and Environment, Victoria, Australia at www.dse.vic.gov.au)

Slide 30

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 - an emerging pathogen which has potentially high morbidity and mortality rates 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 have a great economic impact on our pork industry. Additionally, during the Nipah virus outbreak in Malaysia, widespread panic and fear occurred until the outbreak was brought under control.

Slide 31

Additional Resources

- World Organization for Animal Health (OIE)
  - www.oie.int
- U.S. Department of Agriculture (USDA)
  - www.aphis.usda.gov
- Center for Food Security and Public Health
  - www.cfsph.iastate.edu
- USAHA Foreign Animal Diseases ("The Gray Book")
  - www.usaha.org/pubs/fad.pdf

Slide 32

Acknowledgments

Development of this presentation was funded by grants from the Centers for Disease Control and Prevention, the Iowa Homeland Security and Emergency Management Division, and the Iowa Department of Agriculture and Land Stewardship to the Center for Food Security and Public Health at Iowa State University.

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