

## Popular Article

## Nipah Virus: Another Threat from the World of Zoonotic Disease

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### Introduction

Nipah viral disease is a zoonotic infection caused by Nipah virus (NiV), a paramyxovirus belonging to the genus Henipavirus of the family Paramyxoviridae. It is a biosafety level-4 pathogen, which is transmitted by specific types of fruit bats, mainly *Pteropus* spp. which are natural reservoir host. Nipah virus (NiV) emerged in the last decade of the twentieth century. They were the cause of a number of outbreaks of respiratory and neurological disease infecting pigs. The disease was reported for the first time from the Kampung Sungai Nipah village of Malaysia in 1998. Nipah virus has caused fewer than 700 diagnosed human cases in the 20 years since its discovery, and, so far, outbreaks have been contained within a few chains of transmission. However, Nipah virus is among the most lethal viruses currently known.

### Epidemiology

Over the past 20 years, our understanding of the epidemiology of Nipah virus has grown substantially, thanks to increased capacity and efforts to identify and study human Nipah virus infections. The development of diagnostics tests after the outbreak in Malaysia offered a significant leap in our capability to identify cases. In 2001, just 1 year after the development of these tests, 2 outbreaks of Nipah virus occurred in India and Bangladesh, almost simultaneously.

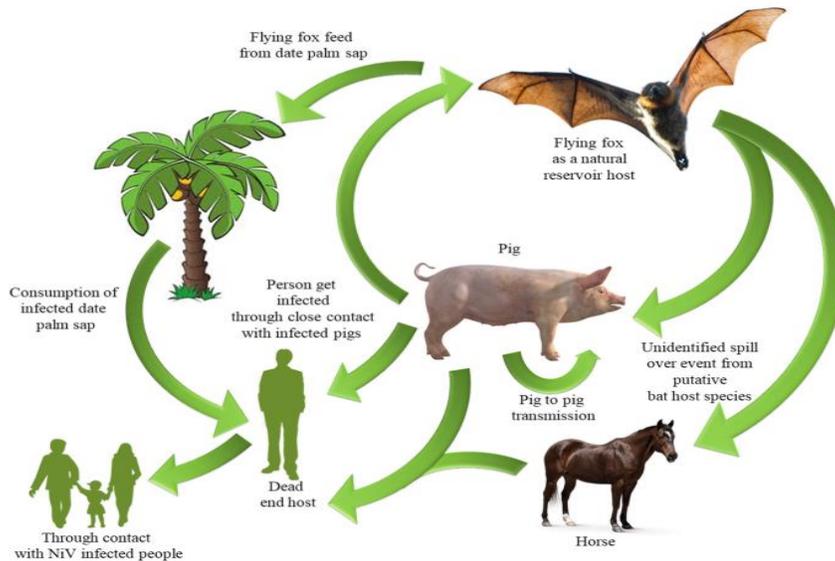
Since 2015, the World Health Organization has listed Nipah virus as one of the most dangerous emerging viruses, due in large part to its capacity to transmit from person to person. Although only ~10% of Nipah patients transmit the virus to others, transmission is highly heterogeneous and super-spreaders have infected dozens of people. Close caregivers, typically family members but also some times healthcare workers, are at highest risk for infection, which most likely occurs through contact with infectious respiratory secretions from the patient. Prevention of human-to-human transmission through quick diagnosis and infection prevention measures are among the best prevention strategies currently available.

## **Pathogenesis**

- Nipah virus mainly causes encephalitis in infected individuals; a subset of patients also suffers from virus-induced respiratory disease. The incubation time for Nipah virus disease in Malaysia was estimated to be 10 days; time from onset of symptoms to death in fatal cases was approximately 16 days.
- During the Nipah virus outbreak in Malaysia and Singapore patients generally presented with fever and altered mental status or decreased consciousness.
- Neurological signs of disease progressed over time and resulted in coma, and ultimately death in severe cases. Mechanical ventilation was required in most of the severe cases.
- Magnetic resonance imaging during the acute as well as during later phases of illness revealed focal lesions disseminated throughout the brain, mainly in the subcortical and deep white matter of the cerebral hemispheres.
- Nipah virus was isolated from throat swabs, nose swabs, urine, tracheal secretions, and CSF collected from patients in Malaysia. From day 7 after onset of symptoms onwards, infectious virus could no longer be detected in swabs or urine. There was no correlation between shedding of virus and disease outcome; however, the presence of Nipah virus in CSF was correlated with a poor prognosis.

## **Transmission**

- During the first recognized outbreak in Malaysia, which also affected Singapore, most human infections resulted from direct contact with sick pigs or their contaminated tissues. Transmission is thought to have occurred via unprotected exposure to secretions from the pigs, or unprotected contact with the tissue of a sick animal.
- In subsequent outbreaks in Bangladesh and India, consumption of fruits or fruit products (such as raw date palm juice) contaminated with urine or saliva from infected fruit bats was the most likely source of infection.
- Human-to-human transmission of Nipah virus has also been reported among family and care givers of infected patients.
- During the later outbreaks in Bangladesh and India, Nipah virus spread directly from human-to-human through close contact with people's secretions and excretions. In Siliguri, India in 2001, transmission of the virus was also reported within a health-care setting, where 75% of cases occurred among hospital staff or visitors. From 2001 to 2008, around half of reported cases in Bangladesh were due to human-to-human transmission through providing care to infected patients.



### Transmission Cycle of Nipah Virus

### Clinical Signs and Symptoms

- Human infections range from asymptomatic infection to acute respiratory infection (mild, severe), and fatal encephalitis.
- Infected people initially develop symptoms including fever, headaches, myalgia (muscle pain), vomiting and sore throat. This can be followed by dizziness, drowsiness, altered consciousness, and neurological signs that indicate acute encephalitis. Some people can also experience atypical pneumonia and severe respiratory problems, including acute respiratory distress. Encephalitis and seizures occur in severe cases, progressing to coma within 24 to 48 hours.
- The incubation period (interval from infection to the onset of symptoms) is believed to range from 4 to 14 days. However, an incubation period as long as 45 days has been reported.
- Most people who survive acute encephalitis make a full recovery, but long-term neurologic conditions have been reported in survivors. Approximately 20% of patients are left with residual neurological consequences such as seizure disorder and personality changes. A small number of people who recover subsequently relapse or develop delayed onset encephalitis.
- The case fatality rate is estimated at 40% to 75%. This rate can vary by outbreak depending on local capabilities for epidemiological surveillance and clinical management.

### Diagnosis

- Initial signs and symptoms of Nipah virus infection are nonspecific, and the diagnosis is often not suspected at the time of presentation. This can hinder accurate diagnosis and creates challenges in outbreak detection, effective and timely infection control measures, and outbreak response activities.
- In addition, the quality, quantity, type, timing of clinical sample collection and the time needed to transfer samples to the laboratory can affect the accuracy of laboratory results.

- Nipah virus infection can be diagnosed with clinical history during the acute and convalescent phase of the disease. The main tests used are real time polymerase chain reaction (RT-PCR) from bodily fluids and antibody detection via enzyme-linked immunosorbent assay (ELISA).
- Other tests used include polymerase chain reaction (PCR) assay, and virus isolation by cell culture.

## **Treatment**

### **Vaccines and Antivirals**

Increasing concerns about Nipah virus have spurred investment in vaccines. Several vaccine candidates, which have been efficacious in animals' models, have been selected by the Coalition of Epidemic Preparedness Innovation (CEPI) to progress through phase I and II clinical trials.

Many antivirals have been tested in the quest for Nipah virus therapeutics, but only 2 have shown good therapeutic efficacy in non-human primates: the monoclonal antibody m102.4 and the nucleotide prodrug remdesivir. Efficacy data for m102.4 are most promising, with protection from both lethal Nipah virus strains Malaysia and Bangladesh when administered at 5 (Malaysia strain) or 3 days (Bangladesh strain) after challenge.

### **Prevention**

- Controlling Nipah virus in pigs
  - Based on the experience gained during the outbreak of Nipah involving pig farms in 1999, routine and thorough cleaning and disinfection of pig farms with appropriate detergents may be effective in preventing infection.
  - If an outbreak is suspected, the animal premises should be quarantined immediately. Culling of infected animals with close supervision of burial or incineration of carcasses may be necessary to reduce the risk of transmission to people.
  - Restricting or banning the movement of animals from infected farms to other areas can reduce the spread of the disease.
  - As Nipah virus outbreaks have involved pigs and/or fruit bats, establishing an animal health/wildlife surveillance system, using a One Health approach, to detect Nipah cases is essential in providing early warning for veterinary and human public health authorities.

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