



सत्यमेव जयते
Ministry of Health & Family Welfare
Government of India



A Comprehensive Learning Guide

Nipah Virus



**NATIONAL CENTRE FOR DISEASE CONTROL
DIRECTORATE GENERAL OF HEALTH SERVICES**
Ministry of Health & Family Welfare, Government of India



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National Centre for Disease Control
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Government of India

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DIRECTOR GENERAL OF HEALTH SERVICES



भारत सरकार
स्वास्थ्य एवं परिवार कल्याण मंत्रालय
स्वास्थ्य सेवा महानिदेशालय

Government of India
Ministry of Health & Family Welfare
Directorate General of Health Services



Message

Zoonotic diseases pose a significant and ongoing threat to biodiversity, human and public health and economic stability. Given India's diverse ecosystem, high population density and increasing human-animal action, the country remains particularly susceptible to zoonotic outbreaks. Past occurrences of plague, Nipah virus, avian influenza, leptospirosis, and Kyasanur Forest Disease emphasizes a critical need for robust surveillance, early detection, and a coordinated, intersectoral response.

Recognizing the importance of addressing zoonotic diseases as a public health priority, the Centre for One Health, under the National Centre for Disease Control (NCDC), is committed for strengthening surveillance, prevention, and response mechanisms through an integrated One Health approach. As part of this effort, the Centre for One Health has developed comprehensive learning guides on Priority Zoonotic Diseases. These modules provide scientifically validated, evidence-based guidance on the epidemiology, diagnosis, treatment, and prevention of key zoonotic diseases.

Strengthening disease surveillance, ensuring early diagnosis, and implementing timely interventions through a coordinated and multi-sectoral approach are critical to mitigating the risks associated with zoonotic diseases.

I am pleased to release these learning guides as a significant step in our ongoing efforts to combat zoonotic diseases. I urge all healthcare professionals, veterinary experts, and community leaders to actively utilize these resources to enhance their clinical index of suspicion for zoonosis and eventually contribute towards strengthening our health care system for responding timely and more efficiently to future outbreaks.

(Atul Goel)



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MESSAGE

It is my pleasure to know that the Centre for One Health at NCDC has prepared **Comprehensive Learning Guides** on 10 priority zoonotic diseases, which is now being shared with all concerned.

These resources become relevant in considering; India has encountered multiple zoonotic disease outbreaks in recent years, highlighting their persistent and evolving threat to public health. The re-emergence of **Nipah virus** in Kerala, **Kyasanur Forest Disease (KFD)** in Karnataka, and **avian influenza** across several states underscores the complex interconnections between human, animal, and environmental health. The rising cases of **leptospirosis** and **scrub typhus**, driven by climatic changes and ecological disruptions, further illustrate the unpredictable nature of zoonotic spillovers. With the additional challenges posed by **emerging coronaviruses** and **antimicrobial resistance (AMR)**, there is an urgent need for a **cohesive, evidence-based approach** to mitigate these risks effectively.

In recognition of this pressing need, the **National Centre for Disease Control (NCDC)** has intensified its efforts to fortify **zoonotic disease surveillance, outbreak preparedness, and intersectoral coordination**. As part of this initiative, the **Centre for One Health, NCDC**, has meticulously curated **Comprehensive Learning Guides** on priority zoonotic diseases. These guides, underpinned by the latest scientific insights and global best practices, serve as indispensable resources for **healthcare professionals, veterinarians, and epidemiologists**, equipping them with the knowledge to anticipate, detect, and mitigate zoonotic threats with precision.

To effectively curtail the impact of zoonotic diseases, a **harmonized One Health approach** is paramount—one that transcends disciplinary boundaries and fosters synergies across the human, animal, and environmental health sectors. I urge all stakeholders to **leverage these scholarly resources, enhance disease intelligence networks, and champion research-driven interventions**. By embracing a proactive and interdisciplinary ethos, we can **bolster pandemic preparedness, fortify national health security, and avert future spillover events**.

I sincerely **appreciate** my colleagues at the Centre for One Health, NCDC for their dedication to strengthening zoonotic disease control. Their efforts in enhancing surveillance, preparedness, and public health response are crucial in preventing and managing emerging health threats.

I am glad to see their commitment translating into evidence-based interventions and capacity-building initiatives that enhance zoonotic disease surveillance, outbreak preparedness, and overall health system resilience.

Through continuous innovation, collaboration, and unwavering dedication, we can fortify our health systems and safeguard our nation against zoonotic threats.

Wishing you all happy learning and skill enhancement wherever possible.

रंजन दास 19/3/25
Prof. (Dr.) Ranjan Das



Antibiotic resistance Containment Stewardship: Our Role, Our Responsibility
Judicious Use of Antibiotic: Key to Contain Antibiotic Resistance





भारत सरकार

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Message

Zoonotic diseases of public health importance continue to pose significant challenges to public health. These diseases, often driven by intricate human-animal-environment interactions, present substantial health risks, particularly to vulnerable populations, and demand a coordinated and robust response from the health sector.

In recognition of the pivotal role healthcare providers play in addressing these challenges, the **Centre for One Health** has developed a **Comprehensive Learning Guide for Priority Zoonotic Diseases**. This guide is designed to build capacity across the health sector, equipping professionals with the essential knowledge and skills needed to identify, manage, and prevent these diseases effectively. By enhancing surveillance systems, fostering rapid and accurate diagnostics, and implementing targeted prevention and control measures, healthcare providers can play a transformative role in mitigating the impact of zoonotic diseases.

The guide emphasizes the importance of building a resilient health workforce capable of responding to outbreaks, engaging communities, and collaborating across disciplines. Through these efforts, we aim to reduce the burden of zoonotic diseases, improve health outcomes, and contribute to the creation of a safer and healthier future.

I encourage all healthcare professionals to utilize this guide as a resource for improving their understanding and response to zoonotic diseases. Together, let us strengthen our health systems and work towards a future free from the threats posed by zoonotic diseases.

Dr. Simmi Tiwari
Joint Director and Head
Centre for One Health



Antibiotic Resistance Containment Stewardship: Our Role, Our Responsibility
Judicious Use of Antibiotic: Key to Contain Antibiotic Resistance



Acknowledgement

The **Comprehensive Learning Guide** for Nipah virus has been developed to address the significant public health challenges posed by zoonotic diseases, which have serious health, economic, and social implications, particularly for vulnerable populations. The priority zoonotic diseases necessitate robust surveillance, timely diagnosis, and effective prevention and control measures. This guide aims to strengthen the capacity of healthcare professionals by equipping them with the requisite knowledge and skills to mitigate these public health threats and improve health outcomes.

We acknowledge with deep appreciation the valuable contributions of the **subject matter experts** from leading medical institutions and research organizations, whose guidance and technical expertise has been critical in shaping this **Comprehensive Learning Guide**.

The Centre for One Health, NCDC, expresses its sincere gratitude to Ms. Punya Salila Srivastava, Secretary, Health and Family Welfare, Government of India; Ms. L.S. Changsan, Additional Secretary, Ministry of Health and Family Welfare, Government of India; Prof. (Dr.) Atul Goel, Director General of Health Services (DGHS), Government of India; Ms. Latha Ganapathy, Joint Secretary, Department of Health & Family Welfare, Government of India for their leadership, guidance, and support.

Lastly, we acknowledge the USAID-funded RISE project team, implemented by Jhpiego, for their technical support in drafting and finalizing this guide. Their collaboration has been pivotal in ensuring the quality and relevance of this resource.

Dr. Simmi Tiwari
Joint Director and Head
Centre for One Health
National Centre for Disease Control
Directorate General of Health Services
Ministry of Health & Family Welfare
Government of India

Preface

Nipah virus (NiV) is a zoonotic disease originating from fruit bats in Southeast Asia, causing severe respiratory and neurological issues in humans and animals. Main outbreaks occur in Bangladesh, India, and Malaysia. Human symptoms include fever, coughing, seizures, and coma, often leading to high mortality rates.

Preventive measures involve biosecurity in animal farms and protective gear. Diagnostic methods like ELISA and PCR are also available. Treatment lacks specific antivirals or vaccines; supportive care is primary.

Climate change and increased human-bat contact raise zoonotic disease outbreaks, making surveillance crucial. Risk factors include contact with infected animals and consuming contaminated food. Prevention involves hygiene, personal protection, and avoiding raw food. Culling infected livestock, especially pigs, has been effective.

Nipah virus poses a significant threat with high mortality. Active surveillance, control measures, and research for diagnostics and treatments are essential. Regulations are crucial in affected areas, emphasizing prevention in both human and animal contexts.

This module aims to equip learners with the knowledge and tools necessary to educate and train individuals involved in various aspects of Nipah Virus Disease management. It provides a comprehensive overview of the disease, covering its epidemiology, clinical presentation, laboratory diagnosis, treatment options, and preventive measures.

The module is structured in a user-friendly manner, allowing learners to effectively communicate complex scientific concepts to their audience. It contains detailed explanations to enhance understanding and engagement. The content is supported by the latest scientific research and public health guidelines, ensuring the information presented is accurate and up to date.

It is our sincere hope that this module will serve as a valuable resource for learners and educators, enabling them to grasp essential knowledge and skills. By equipping professionals and individuals at risk with the necessary information, we can enhance our collective ability to detect, prevent, and respond to Nipah Virus outbreaks, thereby safeguarding public health.

We would like to express our gratitude to all the experts, researchers, and contributors who have provided their invaluable insights and expertise in developing this module. Their dedication and commitment to public health have been instrumental in creating a comprehensive resource that will contribute to the effective management of Nipah Virus.

We hope you find this module informative, engaging, and ultimately, empowering. Together, let us work towards building a safer and healthier future by combating Nipah Virus through knowledge and preparedness.

Abbreviations

ABI 7500 FAST	Applied Biosystems 7500 Fast Real-Time PCR System
ALT	Alanine Aminotransferase
ANTI F MAB	Anti-Fusion Protein Monoclonal Antibody
ANTI G MAB	Anti-Glycoprotein Monoclonal Antibody
ARDS	Acute Respiratory Distress Syndrome
AST	Aspartate Aminotransferase
BBB	Blood-Brain Barrier
BD	Twice Daily (Bis in Die)
BHQI	Black Hole Quencher I
BPS	Blood Pressure Systolic
BSL	Biosafety Level
CD	Cluster of Differentiation
CFR	Case Fatality Rate
CNS	Central Nervous System
CPE	Cytopathic Effect
CRP	C-Reactive Protein
CSU	Central Surveillance Unit
DCGI	Drug Controller General of India
ELISA	Enzyme-Linked Immunosorbent Assay
ESR	Erythrocyte Sedimentation Rate
ET	Endotracheal
FAM	Fluorescein Amidite
HSV	Herpes Simplex Virus
ICU	Intensive Care Unit
IDSP	Integrated Disease Surveillance Programme
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IV	Intravenous
JE	Japanese Encephalitis
LAR	Local Adverse Reaction
MAB	Monoclonal Antibody
mFIT	Micro-fusion inhibition assay
mRNA	Messenger RNA
NCDC	National Centre for Disease Control
NIAID	National Institute of Allergy and Infectious Diseases
NCT	National Clinical Trial
NG	Nasogastric
NIH	National Institutes of Health
NIV	National Institute of Virology
NiV	Nipah Virus
NVBN593R	Nipah Virus Bangladesh Nucleoprotein Reverse Primer 593R
NVBNF2B	Nipah Virus Bangladesh Nucleoprotein Forward Primer 2B
OD	Once Daily

PEP	Post-Exposure Prophylaxis
PPE	Personal Protective Equipment
PRES	Porcine Respiratory and Encephalitic Syndrome
RNA	Ribonucleic Acid
RT PCR	Reverse Transcriptase Polymerase Chain Reaction
SOP	Standard Operating Procedure
SYBR qRT-PCR	SYBR Green Quantitative Real-Time Polymerase Chain Reaction
TNF	Tumor Necrosis Factor
US	United States
UV	Ultraviolet
WBC	White Blood Cell
WHO	World Health Organization
WOAH	World Organization for Animal Health (formerly OIE)

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Introduction to Learning Guide for Nipah Virus

Historically, zoonotic diseases have had a significant impact on human evolution, particularly on cultures and societies that domesticated and raised animals for food and clothing. Zoonoses pose a frequent and feared risk to humanity, transcending natural boundaries and occurring worldwide. Their profound effect on the global economy and health is well recognized, ranging from the international movement of animals and the importation of diseases to bans on animal product imports and restrictions on other international trade practices. Thus, zoonoses are no longer confined to national borders, and global surveillance is necessary for effective control.

Controlling zoonoses remains a priority for international agencies, addressing the specific health and economic challenges of each region. Despite being poorly documented, zoonotic diseases pose a significant public health problem in India. They equally impact animal, human, and environmental sectors, causing substantial damage to the nation's economy. To protect all sectors, it is essential for India to rapidly identify, diagnose, and manage these diseases. The One Health approach plays a crucial role in this endeavor, as we have learned valuable lessons from the COVID-19 pandemic regarding the need for strong surveillance and diagnostic preparedness to handle future pandemic situations.

To provide comprehensive training, the Center for One Health, NCDC has developed Learning Resource Guide. This guide serve as both trainers' guides and self-directed learning resources. The training focuses on zoonoses and zoonotic diseases of public health importance in India (ZPHI) and emphasizes the One Health approach to responding to zoonotic diseases. By the end of the training, participants should have a solid understanding of the core principles of Nipah Virus, its outbreak potential, health emergencies, risk communication, diagnostic procedures, laboratory safety, surveillance, data reporting, and their applications.

To provide comprehensive training, the Center for One Health, NCDC has developed Learning Resource Guide. This guide serve as both trainers' guides and self-directed learning resources. The training focuses on zoonoses and zoonotic diseases of public health importance in India (ZPHI) and emphasizes the One Health approach to responding to zoonotic diseases. By the end of the training, participants should have a solid understanding of the core principles of Nipah Virus, its outbreak potential, health emergencies, risk communication, diagnostic procedures, laboratory safety, surveillance, data reporting, and their applications.

The guide caters to various audiences, including medical professionals including doctors, veterinarians, paramedical staff and laboratory personnel who are expected to acquire knowledge and competencies beyond their regular field of work.

The guide consists of a Facilitators' Guide (FG). The FG provides instructional processes and supports educators in facilitating and assessing learning. Each module follows a standardized structure, including a session outline, detailed session plans, slide decks, and a wide range of references and resources for further reading. These resources offer comprehensive information on the respective topics.

The guide aims to provide a comprehensive education for medical professionals including doctors, veterinarians, paramedical staff and laboratory personnel. It helps them understand, identify, and differentiate between zoonotic diseases and equips them with the necessary knowledge and orientation for diagnostics procedures and surveillance systems.

COURSE DESCRIPTION

Course Design

This comprehensive Nipah virus guide tailored for medical professionals including doctors, veterinarians, paramedical staff and laboratory personnel. The course is designed to enhance their understanding and expertise in dealing with Nipah cases, spanning various aspects of prevention, diagnosis, and treatment. The training approach emphasizes practical application, aiming to equip participants with hands-on skills and competencies that can be directly applied in their professional roles.

Evaluation Approach

The evaluation approach for the Nipah preparedness and response guide includes a comprehensive pre-training and post-training quiz questionnaire designed to assess participants' knowledge and learning progression. The questionnaire utilizes multiple-choice questions (MCQs) to gauge participants' understanding of Nipah related concepts before and after the training. This approach allows for a clear measurement of knowledge enhancement and provides valuable insights into the effectiveness of the training program.

- ***Pre-Training Quiz:***

Before the training begins, participants will undergo a pre-training questionnaire. This questionnaire serves as a baseline assessment of participant's existing knowledge and awareness of Nipah Virus. The pre-training quiz will consist of MCQs that cover various aspects of Nipah Virus, including its etiology, modes of transmission, clinical manifestations, preventive measures, and response strategies. The purpose of the pre-training quiz is to establish a starting point and identify areas where participants may require more focused training.

- ***Post-Training Quiz:***

Upon completion of the Nipah Virus preparedness and response training guide, participants will be given a post-training quiz questionnaire. This questionnaire will contain a similar set of MCQs as the pre-training quiz, covering the same topics related to Nipah Virus. The aim of the post-training quiz is to evaluate participant's knowledge advancement and to measure the effectiveness of the training in enhancing their understanding of Nipah Virus

COURSE SYLLABUS

Course Goals

- Foster in depth knowledge of Nipah virus, its diagnosis, management, and prevention.
- Emphasize the importance of the One Health approach in addressing zoonotic diseases.
- Develop the learner's competency in risk communication, laboratory safety, and surveillance strategies.

Participant's Learning Objectives

By the course's conclusion, participants will be able to:

- Know about Nipah Virus disease
- Apply diagnostic and treatment protocols for Nipah Virus management.
- Know about the preventive strategies and outbreak management tactics.

Participant Selection Criteria

Participants for this Nipah Virus response and preparedness training should be professionals from various fields involved in emergency response and public health:

- Emergency Responders: Including public health experts, medical personnel, and first responders, forest officials and personnel from animal husbandry department
- Laboratory and Biosafety Staff: Those experienced in handling biohazards.
- Government and Decision-Makers: Officials with authority in emergency coordination including those of animal husbandry departments and forest officials
- Community Leaders and Experts: Community influencers, researchers, and mental health specialists.

Using the Resource Guide

All training activities in this course will be conducted in an interactive, participatory manner using the training guide appropriately as suggested in the course outline in the facilitators' guide. To accomplish this, the trainer will have to change roles throughout the course. For example, the trainer is a facilitator when conducting small group discussions and finally, when objectively assessing performance, the trainer serves as an evaluator.

Composition of participants

The training is intended for 15-20 participants hailing from various state and healthcare fraternities. There can be a single facilitator as an expert of the disease.

COURSE SCHEDULE

Morning Session

Introduce and welcome participants

- Discuss participant expectations and prior knowledge
- Outline the objectives of the course and learning outcomes

Review the course schedule and its components

- Provide an overview of the training guide materials
- Conduct a pre-course knowledge assessment to gauge participants' baseline understanding
- Distribute course materials, including handouts and resources

Interactive presentations

- Take Sessions 1-4 and discuss in detail about basics of Nipah Virus, its epidemiology, bioweapon potential, clinical disease and its significant features in humans and animals.
- Interactive discussion and Q&A session after the lecture

Afternoon Session

Interactive presentations

- Take Sessions 5-10 and discuss in detail about frequently asked questions, diagnosis of Nipah Virus, its treatment, prevention & control, outbreak management and surveillance.

Debriefing and group discussions on simulation outcomes

- Interactive discussion and Q&A session after the lecture

Review, Assessment, and Closing

- Comprehensive review of key concepts covered during the training
- Interactive quiz to reinforce learning
- Final assessment to measure participants' understanding of course material
- Reflection session: Participants share insights and takeaways from the course
- Closing remarks, thanking participants for their engagement

COURSE OUTLINE

The course outline presented here follows a model structure for the training curriculum. It delineates the enabling objectives necessary to achieve the participant learning goals outlined in the course syllabus. The outline offers recommendations for suitable learning activities and essential resources and materials for each enabling objective. Depending on specific participant requirements, the trainer has the option to introduce supplementary practice activities, devise case studies, role-play scenarios, or tailor learning situations accordingly.

The course outline comprises four columns:

Duration: This column specifies the estimated time allocated for each learning activity. This allocation ensures an equitable distribution of time across the diverse training components.

Learning Objectives: This column lays out the enabling objectives and their alignment with corresponding learning activities. The objectives are sequenced to provide guidance on the training structure. The interplay of objectives and activities—ranging from icebreakers and interactive group tasks to practical exercises and breaks—constitutes the overall training progression.

Pre-requisite Knowledge/Skill: This column addresses the foundational knowledge or skills that participants should possess prior to the session. It underscores the importance of existing competencies for effective engagement in the training.

Competencies to be Achieved: The fourth column enumerates the competencies participants are expected to acquire by the conclusion of the session. It underscores the practical outcomes that participants will attain through engagement in the training.

AGENDA

S. No	Topic	Duration
1.	Welcome & Introduction of the training agenda and setting ground rules	15 mins
2.	Ice breaker: Talk about yourself. - Contribution to the management & control of zoonoses - Expectations from the training	30 mins
3.	Training objectives	15 mins
4.	Pre-Test Quiz	15 mins
5.	Session 1: Introduction to Nipah Virus Disease	15 mins
6.	Session 2: Epidemiology	30 mins
7.	Session 3: Etiology, Transmission & Emergence	20 mins
8.	Session 4: Laboratory Diagnosis	20 mins
9.	Session 5: Case Definition & Treatment and Prevention	15 mins
10.	Session 6: Nipah Virus Disease in Animals	20 mins
11.	Session 7: Outbreak Management	20 mins
12.	Session 8: Surveillance & Risk Communication	20 mins
13.	Post - Test Quiz	15 mins
14.	Q/A session, review, and discussion	15 mins
15.	Group activity: Understanding priorities, concerns and challenges of state on zoonoses	15 mins
16.	Closing remarks	05 mins

Session-1

Introduction

Course No. 001	Session 1: Introduction to Nipah Virus Disease
Duration	15 minutes
Learning Objective	• Know the historical timeline of Nipah virus outbreaks • Seasonality of the Nipah Virus
Pre-requisite knowledge/skill	• Basic knowledge of emerging viral zoonoses and their public health impact. • Familiarity with outbreak timelines and epidemiological trends of infectious diseases. • Awareness of seasonal patterns and environmental factors influencing disease occurrence.
Competencies to be achieved	• Learners would gain knowledge of the basic characteristics and features of Nipah Virus • Learners would understand the historical context and significant milestones in the study and understanding of Nipah Virus • Learners would be able to describe the key aspects of Nipah Virus Disease

INTRODUCTION

Human Nipah virus (NiV) infection is a newly emerging disease transmitted from animals to humans. The first identified outbreak occurred between **1998-1999** in **Malaysia and Singapore**, where the virus caused **276 cases** and more than **100 deaths**, leading to significant damage to the swine industry. The virus, named after the Malaysian village **Sungai Nipah**, spread to Singapore in **March 1999** through infected pigs, resulting in **11 cases** and **1 death** among abattoir workers.

Since its discovery, Nipah virus has caused multiple outbreaks, notably in **Bangladesh** between **2001 and 2007**, and **India (West Bengal)** in **2001 and 2007**, where evidence of human-to-human transmission emerged. More recently, localized outbreaks have occurred in **Kerala, India**, in **2018, 2019, 2021, and 2023**, with the most recent outbreak involving **6 cases** and **2 deaths**. Additionally, **Bangladesh** has continued to experience seasonal outbreaks, particularly linked to fruit bat exposure during the **date palm sap** harvesting season.

Fruit bats are considered the natural reservoir of NiV, spreading the virus through secretions and excretions. The consumption of contaminated fruits and date palm sap has been identified as a key transmission route to humans.

This section provides an overview of **Nipah Virus (NiV) outbreaks** between 1998 and 2021. Nipah is an emerging **zoonotic disease** of public health importance in Southeast Asia and the Western Pacific. The first major outbreak occurred in **Malaysia and Singapore** from 1998-1999, resulting in over 100 deaths, with control measures including the culling of pigs. From 1998 to 2021, **674 human cases** have been reported across Malaysia, Singapore, Bangladesh, India, and the Philippines, with approximately **400 deaths**. The map illustrates the geographical distribution of cases, with **India** and **Bangladesh** being significantly affected. The fatality rate varies by region, with **Malaysia** at 68%, **Bangladesh** at 79%, and the **Philippines** at 9%.

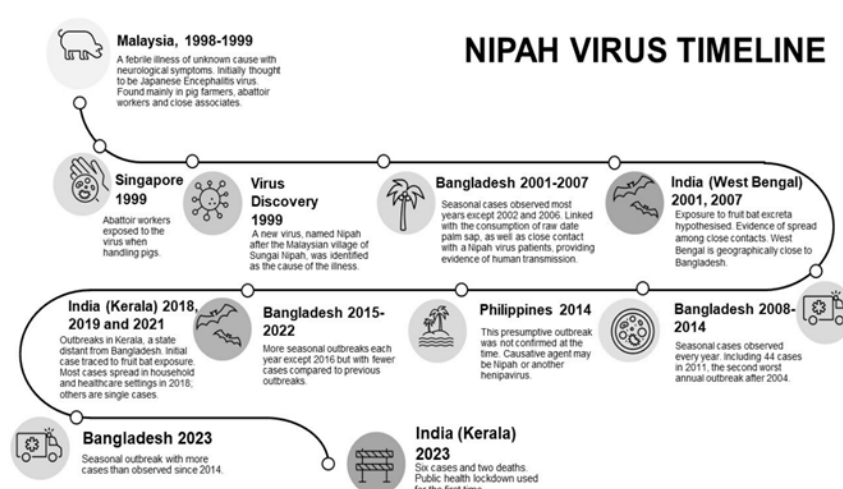


Fig 1: Timeline of Nipah virus outbreaks

(Image source: Johnson, T., Jamrozik, E., Hurst, T., Cheah, P., & Parker, M. (2023). Ethical issues in Nipah virus control and research: addressing a neglected disease. *Journal of Medical Ethics*, 50, jme-2023. <https://doi.org/10.1136/jme-2023-109469>)

An overview of the seasonal patterns, and the risk factors associated with Nipah Virus (NiV) outbreaks, particularly in Southeast Asia and India has also been discussed in the document. NiV outbreaks in Southeast Asia typically follow a seasonal pattern, occurring during the winter and spring months from December to May. NiV has been identified by the World Health Organization (WHO) as a high-priority pathogen and classified as a risk group 4 pathogen due to its potential for bioterrorism. The case fatality rate (CFR) for NiV ranges from 40% to 75%, highlighting its high mortality rate.

There have been significant NiV outbreaks in India, with West Bengal and Kerala being the most affected regions. For instance, the 2001 outbreak in West Bengal resulted in 66 cases with a CFR of 68%, while the 2018 outbreak in Kerala had 19 cases with a CFR of 89.4%. More recently, the 2023 outbreak in Kerala has reported 6 cases with a CFR of 33.33%. Despite the ongoing outbreaks, there is no specific treatment or vaccine available for NiV in either humans or animals, underscoring the importance of preventive measures and surveillance.

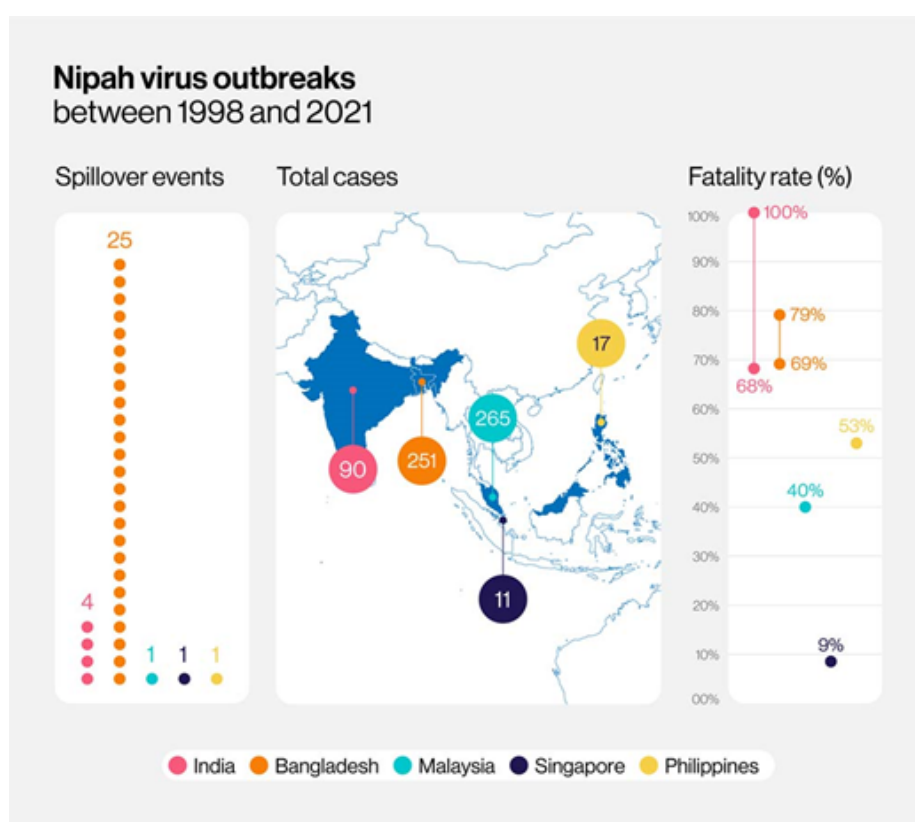


Fig 2: Nipah virus outbreaks between 1998 and 2021

(Image source: <https://www.gavi.org/vaccineswork/seven-things-you-need-know-about-nipah-virus>)

Table 1: Nipah Virus outbreaks in India

Duration	Cases	Deaths	CFR (%)	Remarks
Jan-Feb 2001	66	45	68	Investigations revealed possible epidemiological linkages in 43 cases, person-to-person transmission in Siliguri, West Bengal
Jan-Apr 2007	5	5	100	Nadia District, West Bengal
Apr-May 2018	19	17	89.4	Kerala (Kozhikode and Malappuram)
2019	1	0	0	Kerala (Ernakulum)
2021	1	1	100	Kerala (Kozhikode)
2023* Current Outbreak	6	2	33.33	Kerala (Kozhikode)

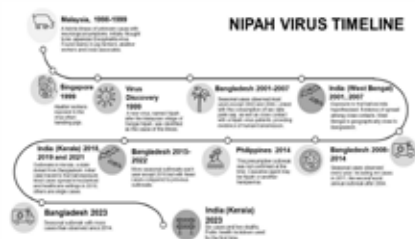
(Source: National Centre for Disease Control (NCDC). (2023). CD Alert: Nipah Virus Disease. Retrieved from <https://ncdc.mohfw.gov.in/wp-content/uploads/2024/04/CD-Alert-Nipah-Virus-Disease.pdf>)

Seasonality was strongly implicated in NiV outbreaks in Bangladesh and India. All the outbreaks occurred during the months of December to May.

Incubation period: varies from 4-14 days.

Historical timeline of Nipah virus

- **1998-1999:** Nipah virus (NiV) first identified in a large outbreak in **Malaysia and Singapore**, resulting in **276 cases** and **over 100 deaths**. The outbreak also caused severe economic damage to the local swine industry.
- The virus is named after **Sungai Nipah**, a village in Malaysia.
- **March 1999:** NiV spread to **Singapore** via imported live pigs, causing **11 cases** and 1 death.
- **March 18, 1999:** Dr. **Chua Kaw Bing** of the University of Malaya identified the virus.



Source: Johnson, T., Jaramilla, E., Hunt, T., Choudhury, P., & Parker, M. (2023). Ethical issues in Nipah virus control and research: addressing a neglected disease. *Journal of Medical Ethics*, 37, June 2023. <https://doi.org/10.1136/jme-2023-102646>

- **Fruit bats known to be natural reservoir of the virus infecting pigs through their secretions and excretions**
- **Bats known to secrete virus by shedding onto date palm, and other fruits, hence most common source of transmission to humans**

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NIPAH VIRUS

Nipah Virus (Niv) Outbreaks

- Nipah virus disease is an emerging **zoonotic disease** of public health importance in the South East Asian and Western Pacific regions
- An outbreak in Malaysia during 1998-1999 with reported cases in Singapore with more than 100 deaths reported were brought under control after culling pigs
- From 1998 to 2021, approximately 674 human cases of Nipah viral disease have been reported in Malaysia, Singapore, Bangladesh, and India with approximately 400 deaths



Image source: <https://www.govt.org/vaccinework/seven-things-you-need-know-about-nipah-virus>

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NIPAH VIRUS

Nipah Virus outbreaks in India

- Outbreaks in South-East Asia have a seasonal pattern with occurrence during winter and spring (**December-May**).
- NiV has been identified as a **high-priority pathogen** by WHO and considered as **risk group 4** pathogen of potential bioterrorism
- The case fatality rate is estimated at **40% to 75%**.

There is no specific treatment or vaccine available for either humans or animals.

Duration	Cases	Deaths	CFR (%)	Remarks
Jan-Feb 2001	66	45	68	Investigations revealed possible epidemiological linkages in 43 cases, person-to-person transmission in Siliguri, West Bengal
Jan-Apr 2007	5	5	100	Nadia District, West Bengal
Apr-May 2018	19	17	89.4	Kerala (Kozhikode and Malappuram)
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2023* Current Outbreak	6	2	33.33	Kerala (Kozhikode)

Source: National Centre for Disease Control (NCDC), (2023). CD Alert: Nipah Virus Disease. Retrieved from <https://rick-mohfw.gov.in/wp-content/uploads/2024/04/CD-Alert-Nipah-Virus-Disease.pdf>

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NIPAH VIRUS

Notes

Session-2

Epidemiology

Course No. 002	Session 2: Epidemiology of Nipah
Duration	20 minutes
Learning Objective	• Understand epidemic potential of Nipah Virus • Describe seasonality and case fatality rate of Nipah Virus • Understand geographical distribution of Nipah Virus in India • Get brief overview of global distribution and prevalence of Nipah Virus
Pre-requisite knowledge/skill	• Basic understanding of viral zoonotic diseases and their epidemic potential. • Familiarity with epidemiological indicators such as case fatality rate and seasonal trends. • Awareness of regional and global distribution patterns of emerging infectious diseases.
Competencies to be achieved	• Understand the seasonality, geographic distribution and the case fatality rate • Understand the distribution and prevalence of Nipah.

EPIDEMIOLOGY

This section outlines the epidemiology of **Nipah Virus (NiV)**, focusing on both global and Indian contexts. Since **1999**, sporadic outbreaks of NiV have been reported in **Malaysia, Singapore, Bangladesh, India, and the Philippines**. From **2001 to 2021**, outbreaks occurred almost annually in **Bangladesh**, particularly in the northern and central districts, except for the years **2002, 2006, 2016, and 2021**. In **India**, significant outbreaks were reported in **West Bengal** in **2001** and **2007**, with more recent outbreaks in **Kerala** in **2018, 2019, and 2021**. Additionally, the **Philippines** experienced an outbreak in Mindanao in 2014.

In **India**, the first NiV outbreak was reported in **Siliguri, West Bengal, in 2001**, followed by another outbreak in **Nadia district, West Bengal, in 2007**. More recent outbreaks occurred in **Kerala**, with cases reported in **Kozhikode district in 2018** and **Kochi district in 2019**. **Pteropus spp. fruit bats** were identified as the probable source of the **2018 outbreak** in Kerala, reinforcing the role of these bats as natural reservoirs for NiV. There was a recent outbreak in Kerala which reported a total of 6 confirmed cases out of which 2 died.

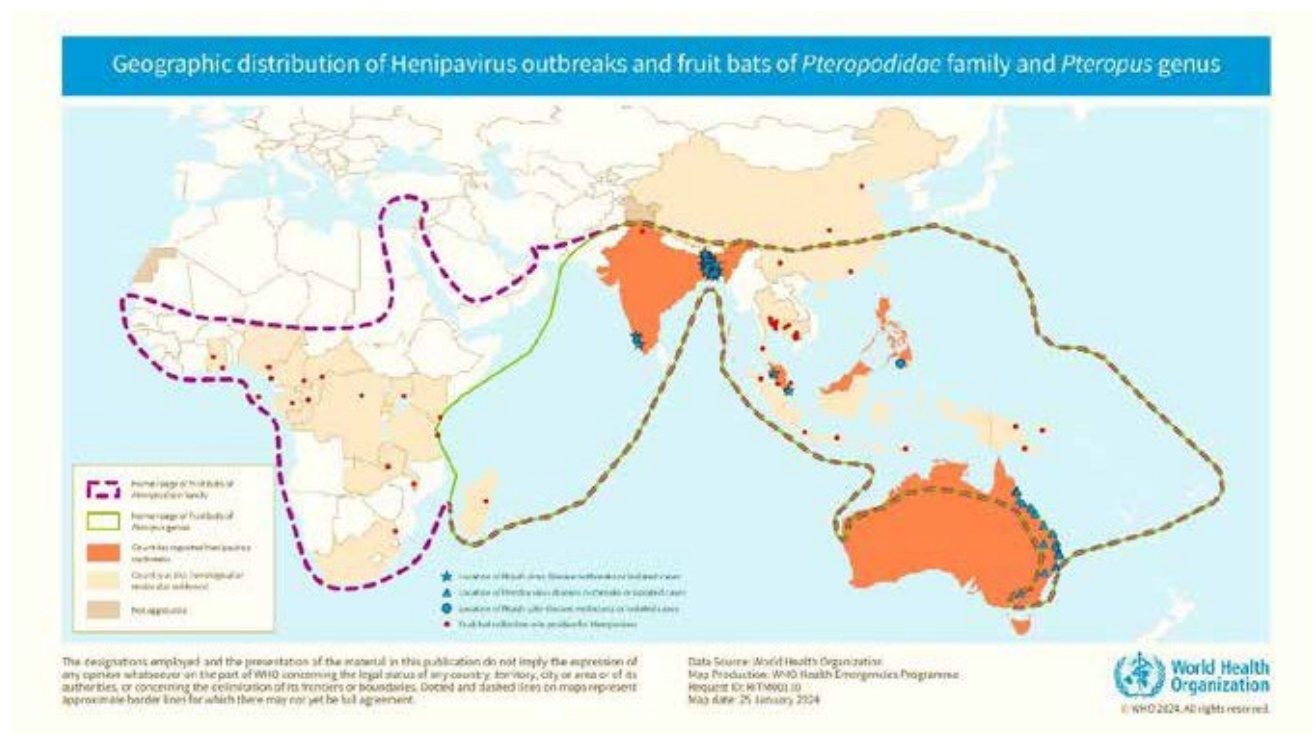


Fig 3: Geographic distribution of Henipavirus outbreaks (WHO)

This image illustrates the **geographic distribution of Henipavirus outbreaks** and the **home range of fruit bats** from the **Pteropodidae family**, which are known to be natural reservoirs for Henipaviruses, including Nipah and Hendra viruses. **Outbreak locations** are marked by **blue stars**, indicating regions that have experienced Henipavirus outbreaks between **1981 and 2008**, such as parts of **India, Bangladesh, Southeast Asia, Australia**, and **Africa**. **Fruit bat collection sites** that have tested positive for Henipaviruses are represented by **red dots**, overlapping with these outbreak zones. The map highlights the **home range of the Pteropus genus of fruit bats**, outlined by a **green line**, covering areas in **South Asia, Southeast Asia, and Northern Australia**, which closely align with known outbreak regions. Additionally, the **home range of the Pteropodidae family** is outlined with a **purple dashed line**, spanning across **Africa, South Asia, Southeast Asia, and Australia**, suggesting a broader potential risk for Henipavirus transmission in these areas. The map underscores the strong link between the distribution of fruit bats and the occurrence of Henipavirus outbreaks, highlighting the significance of these animals in the virus's transmission cycle.

Epidemiology of NiV

Global

- Sporadic outbreaks of human NIV infection have occurred in Malaysia, Singapore, Philippines, India and Bangladesh since 1999
- Since 2001 to 2021, Nipah virus disease have been reported :
 - In Bangladesh (in Northern and Central districts, every year except for 2002, 2006, 2016 and 2021)
 - In India (West Bengal in 2001 and 2007; and Kerala in 2018, 2019 and 2021)
 - In the Philippines (Mindanao in 2014)

India

- In India, the first Nipah virus disease outbreak was reported in Siliguri town in 2001,
 - A second outbreak in Nadia district in 2007, both in West Bengal state.
- In 2018, an outbreak was reported in Kozhikode district, Kerala
- In 2019, another outbreak in Kochi district, Kerala.
- Bats from the *Pteropus* spp. were the probable source of the 2018 outbreak in Kerala state.
- 2023 Kerala Outbreak : 6 confirmed case, including 2 dead

Source: NCDC Manual on Zoonotic Diseases of Public Health Importance

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NIPAH VIRUS



Source: https://cdn.who.int/media/images/default-source/health-topics/nipah-virus/geographical-distribution-nipah-2008.png?sfvrsn=h32e0557_4

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NIPAH VIRUS

Notes

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Session-3

Etiology, Transmission & Progress

Course No. 003	Session 3: Etiology, Transmission & Emergence of Nipah Virus
Duration	40 minutes
Learning Objective	• Identification and characterization of NIPAH virus • Understand the host and environmental characteristics • Understanding mode of transmission • Know the various case definitions of Nipah • Understand the pathogenesis and disease progression
Pre-requisite knowledge/skill	• Basic knowledge of virology, including virus identification and host-pathogen interactions. • Familiarity with transmission routes and environmental factors influencing zoonotic infections. • Understanding of clinical case definitions and the progression of viral diseases.
Competencies to be achieved	• Understand the epidemiological triad of the NIPAH virus • Understanding transmission dynamics and disease progression

NiV STRUCTURE

The **Nipah Virus (NiV)** is a highly pathogenic virus that belongs to the **Henipavirus genus** within the **Paramyxoviridae family**. It is a **non-segmented, single-stranded RNA virus** with a **negative-sense genome**. The virus is **pleomorphic**, meaning it can take on different shapes, typically ranging in size from **40 to 600 nm**. The NiV genome encodes for six structural proteins, including **nucleocapsid protein (N)**, **phosphoprotein (P)**, **matrix protein (M)**, **fusion protein (F)**, **glycoprotein (G)**, and **polymerase protein (L)**. These proteins play critical roles in the virus's ability to replicate and infect host cells. The **F protein** is responsible for fusion with host cell membranes, while the **G protein** facilitates viral entry by binding to specific receptors on the host cell surface. The virus's ability to spread rapidly and infect multiple species makes it a significant public health threat. NiV is classified as a **biosafety level 4 pathogen** due to its high fatality rate and potential use as a bioterrorism agent. There are currently no vaccines or specific antiviral treatments available, making it a priority pathogen for global health security.

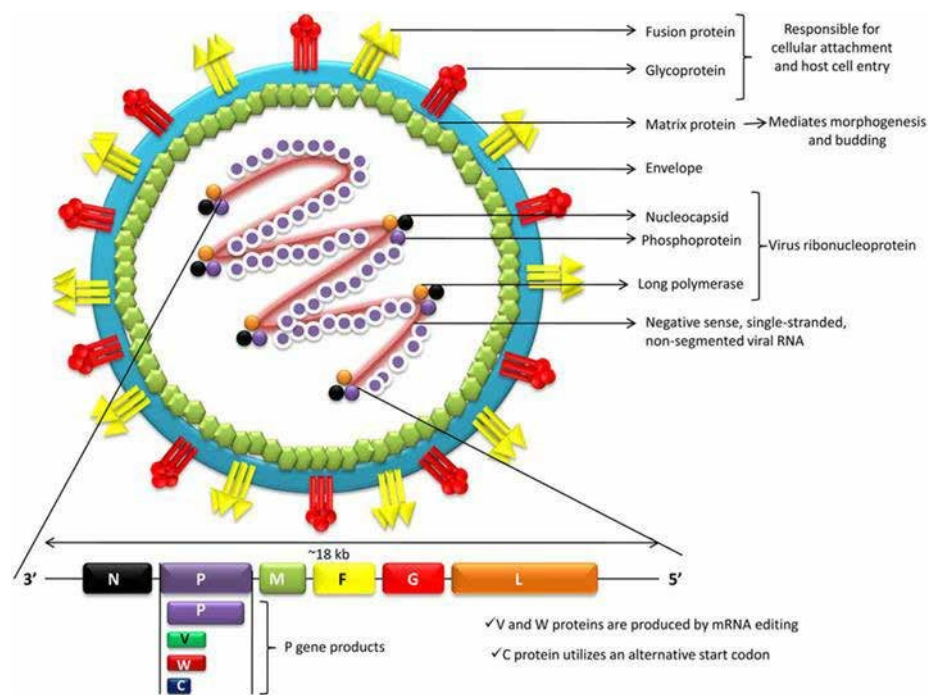


Fig 4: Illustration of NiV Genome

(Image source: https://www.researchgate.net/figure/Structure-of-Nipah-virus_fig1_332558975)

HOST

The **natural reservoir** for Nipah virus is the **Pteropid fruit bat**, commonly referred to as the **flying fox**. These bats are widespread across **South and Southeast Asia**, as well as parts of **Africa and Australia**, and they carry the virus asymptomatically. Other animals, particularly **pigs**, serve as **amplifier hosts**, meaning they can become infected and then transmit the virus.

to humans. Human-to-human transmission has also been documented, especially in healthcare settings, where contact with infected bodily fluids can lead to the spread of the virus. **Serologic evidence** has shown that other animals such as **horses, dogs, goats, and cattle** may also be susceptible to infection, though their role in transmission is not fully understood. Human infections usually occur when people come into contact with contaminated materials, such as food or liquids that have been exposed to bat secretions, or through direct contact with infected pigs. In past outbreaks, those who were in close contact with pigs or consumed food contaminated with bat saliva or urine were at a heightened risk of infection. In some cases, the virus has been transmitted from human to human, particularly among caregivers and healthcare workers who had close contact with infected patients.

ENVIRONMENTAL FACTORS

The **environmental context** of Nipah virus transmission is a critical factor in understanding the conditions that allow for spillover events from animal to human hosts. The virus thrives in environments where humans, animals, and bats have close interactions.

Deforestation and **urban expansion** have disrupted bat habitats, forcing bats into closer proximity to human populations, which increases the risk of zoonotic transmission. For example, bats often feed on fruits, and if these fruits are consumed by humans or domestic animals, the virus can be transmitted. Similarly, the **harvesting of date palm sap**, which is consumed in many regions of South and Southeast Asia, presents a significant risk when bats contaminate the sap with their saliva or urine. The close interaction between wildlife, livestock, and humans in these regions provides an ideal environment for the virus to spread. **Agricultural practices**, such as keeping pigs near orchards or fruit trees, further increase the risk, as pigs can serve as intermediate hosts, amplifying the virus before it jumps to humans. In addition, poor **infection control practices** in healthcare settings have led to the spread of the virus between humans during outbreaks. Environmental conditions, combined with the practices of **bush meat consumption**, wildlife trade, and **improper waste management**, exacerbate the chances of Nipah virus emergence and spread.

TRANSMISSION OF NIV DISEASE

Nipah Virus (NiV) is primarily transmitted through a variety of routes involving bats, animals, and humans. **Fruit bats** are the natural reservoirs of NiV, and they spread the virus when they feed on fruit trees. **Animal-to-animal transmission** occurs when other animals, particularly pigs, consume fruits contaminated with bat saliva or come into contact with infected bats' urine or saliva. **Animal-to-human transmission** often happens through contact with infected animals or by consuming contaminated foods such as date palm sap. Finally, **human-to-human transmission** occurs through contact with an infected person's body fluids, such as saliva, urine, or respiratory secretions. Caregivers and family members are at high risk of contracting the virus through these means.

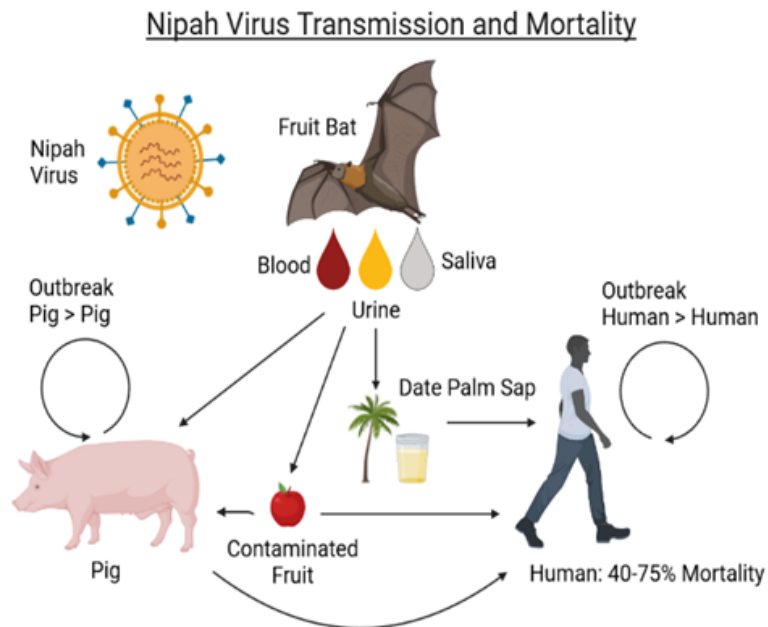


Fig 5: Nipah Virus transmission and Mortality

(Image source: <https://www.jenner.ac.uk/research/emerging-pathogens/nipah>)

CASE DEFINITIONS

In the case of NiV infection, early detection and diagnosis is of paramount importance. Case management includes strategic plans to prevent the spread of contacts, and this requires appropriate triage and isolation. This is where it becomes very important to understand the definition of cases and contacts.

Suspect Nipah Case- Any person residing in a community of a confirmed Nipah virus (NiV) disease outbreak and has:

- Fever with new onset of altered mental status or seizure AND/OR
- Fever with headache AND/OR
- Fever with Cough or shortness of breath AND/OR
- Direct contact with a confirmed case

Probable Nipah Case- Suspect case- Any suspected person who resided in the same village/ house where suspect/confirmed case of NIPAH were living during the outbreak period or such a patient who died before complete diagnostic specimens could be collected.

OR

Who came in direct contact with confirmed case-patients in a hospital setting during the outbreak period and/or who died before completing diagnostic specimens could be collected.

Confirmed Nipah Case- Suspected case that has laboratory confirmation of Nipah virus infection either by:

- Nipah virus RNA identified by PCR from respiratory secretions, urine, or cerebrospinal fluid.
- Isolation of Nipah virus from respiratory secretions, urine or cerebrospinal fluid and blood

DEFINITION OF A CONTACT

A close contact is defined as a patient or a person who came in contact with a Nipah case (confirmed or probable cases) in at least one of the following ways:

- Was admitted simultaneously in a hospital ward/ shared room with a suspect/confirmed case of Nipah
- Has had direct close physical contact with the suspect/confirmed case of Nipah during the illness including during transportation.
- Has had direct close contact with the (deceased) suspect/confirmed case of Nipah at a funeral or during burial preparation rituals
- Has touched the blood and body fluids (saliva, urine, vomitus, etc) of a suspect/ confirmed case of Nipah during their illness
- Has touched the clothes or linens of a suspect/ confirmed case of Nipah

These contacts need to be followed up for appearance of symptoms of NiV for the longest incubation period (21 days).

INCUBATION PERIOD

The incubation period varies from 6-21 days for acute presentation, however, for 90% of the episodes, the incubation period will be less than 2 weeks. According to WHO, incubation period as long as 45 days has been reported.

PATHOGENESIS

In the early stages of human disease, NiV can be detected in bronchial epithelial cells. Viral antigens can be detected in experimental animal models in bronchi and alveoli; the primary targets are bronchial epithelium and type II pneumocytes. Inflammatory cytokines are induced due to infection of the airway epithelium; This recruits immune system cells, ultimately leading to the development of an acute respiratory distress syndrome (ARDS)-like illness. Significant inflammatory mediators, namely interleukin (IL)-1a, IL-6, IL-8; Granulocyte colony stimulating factor (G-CSF), C-X-C motif chemokine 10 (CXCL10), etc. are induced when the (smaller) airway epithelium becomes infected. In later stages of the disease, the virus is transmitted from the epithelium of the airways to the endothelial cells of the lungs. The virus can then enter the bloodstream, followed by dissemination, either free or in host leukocyte-bound form. In addition

to the lungs, the spleen and kidneys as well as the brain can also act as target organs that lead to multiple organ failure. Fatal infection develops in hamsters upon passive transfer of NiV-loaded leukocytes.

In pigs, there is productive infection of monocytes, natural killer (NK) cells along with CD6-CD8 T lymphocytes.

Two pathways are clearly involved in the process of viral entry into the central nervous system (CNS), namely the hematogenous pathway (through the choroid plexus or blood vessels of the cerebrum) and/or the anterograde pathway via the olfactory nerves. The blood-brain barrier (BBB) becomes disrupted and IL-1 β is expressed along with tumor necrosis factor (TNF) due to infection of the CNS by the virus, ultimately leading to the development of neurological symptoms. Inclusion bodies may be present in humans with CNS infection. Necrosis and plaque can occur in both gray and white matter. Remarkably, in several experimental animal models, the virus can enter the CNS directly via the olfactory nerve. In such animal models, the olfactory epithelium of the turbinates is infected by NiV. The viral infection then spreads through the perforated plate into the olfactory bulb. Ultimately, the virus is spread throughout the ventral cortex along with the olfactory tubercle.

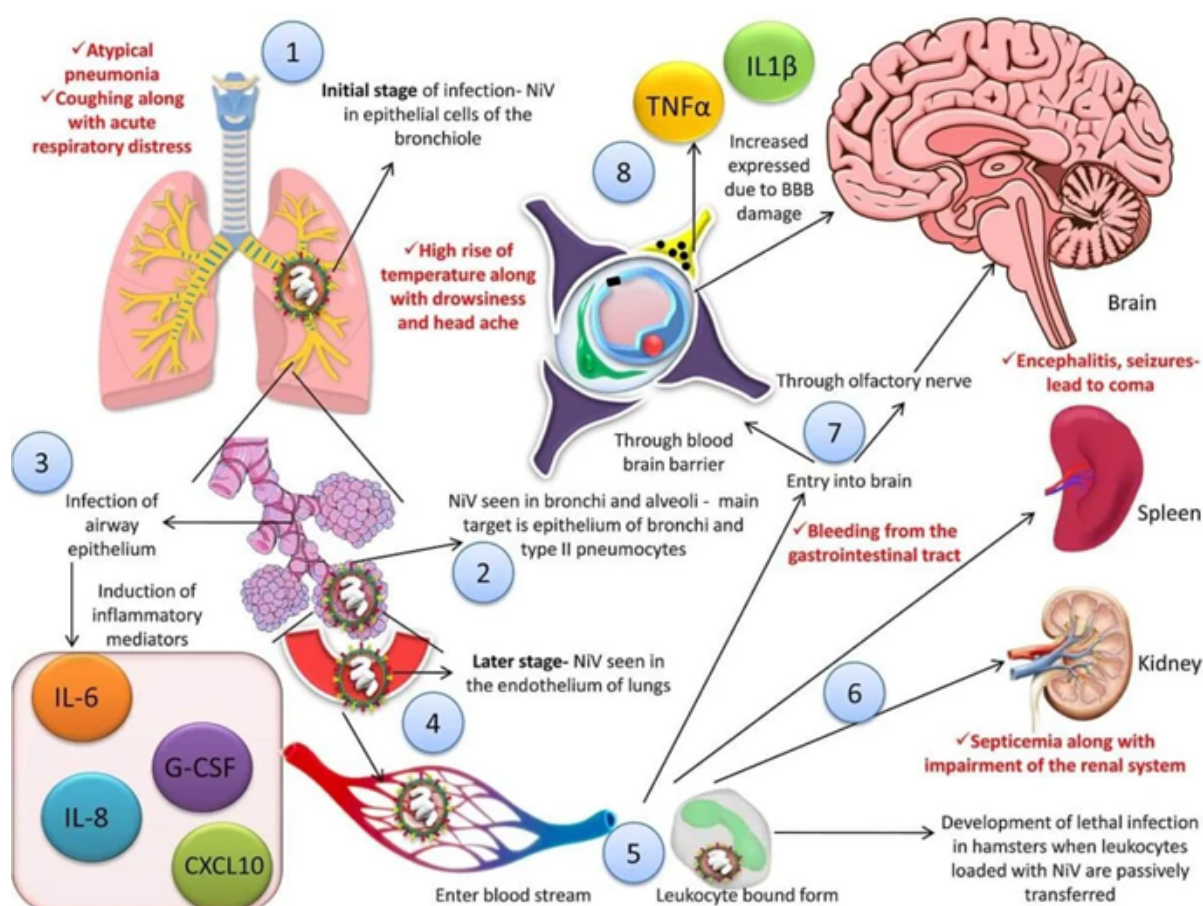


Fig 6: Pathogenesis of Nipah virus

(Image source: Raj Kumar Singh et al. 2019. <https://microbenotes.com/nipah-virus-niv/>)

NiV DISEASE OVERVIEW

Nipah virus disease presents with a range of symptoms, including fever, **altered mental status**, **severe weakness**, **headache**, **respiratory distress**, **cough**, **vomiting**, and **muscle pain**. The incubation period varies between **6 to 21 days**, after which symptoms manifest. NiV is diagnosed using techniques such as **RT-PCR**, **ELISA**, and **virus isolation**. Currently, there is **no specific treatment** for Nipah virus infection, and management is limited to supportive care aimed at relieving symptoms.

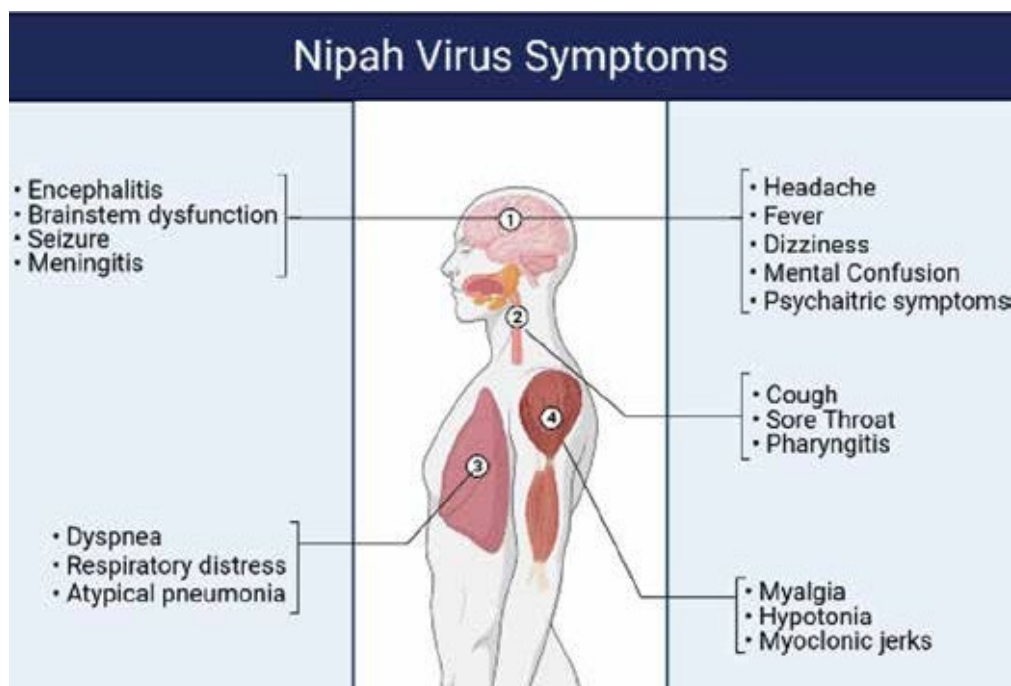


Fig 7: Symptoms of Nipah virus infection

(Image source: J Pure Appl Microbiol. 2022;16(1):26-34 | Article Number: 7346 <https://doi.org/10.22207/JPAM.16.1.72>)

CLINICAL MANIFESTATIONS

Infection with Nipah virus can result in mild to severe illness, with severe cases leading to **encephalitis** (swelling of the brain), which can be fatal. Symptoms typically appear **4 to 14 days** after exposure to the virus, and death may occur in **40-75%** of cases. Long-term complications in survivors can include **persistent convulsions** and **personality changes**. In some instances, Nipah virus can remain dormant, with symptoms only appearing months or even years after the initial exposure, a phenomenon known as **latent infection**.

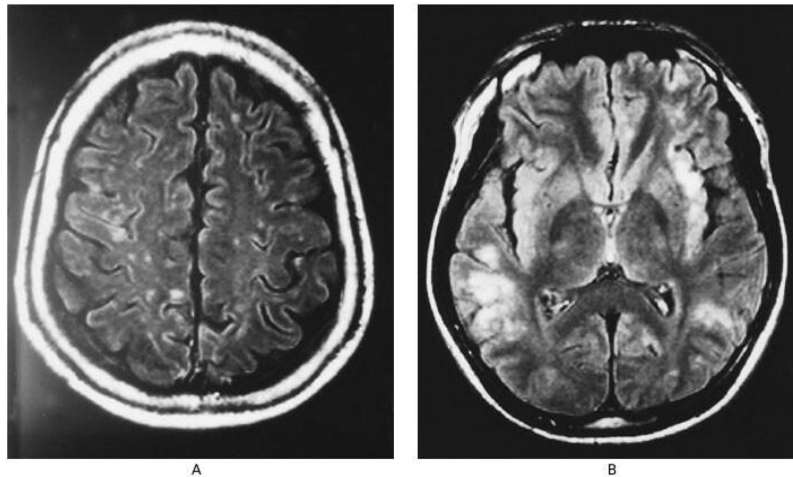


Fig 8: Axial MRI Findings in Patients with Acute (Panel A) and Relapsed (Panel B) Nipah Virus Encephalitis with Use of Fluid-Attenuated Inversion Recovery. **In Panel A**, an image of the brain of a patient with acute Nipah virus encephalitis shows multiple discrete hyperintense lesions in the white and gray matter. **In Panel B**, an image of the brain of a patient with relapsed Nipah virus encephalitis shows confluent lesions involving primarily the cortical gray matter.

(Image source: *N Engl J Med* 2000;342:1229-1235 DOI: 10.1056/NEJM200004273421701. <https://www.nejm.org/doi/full/10.1056/NEJM200004273421701>)

Primary and Severe Symptoms

Nipah virus infection is characterized by primary symptoms such as **fever, headache, vomiting, and dizziness**. More severe symptoms may include **segmental myoclonus, hypertension, hypotonia, and pulmonary syndrome**, which manifests as respiratory distress and **abnormal chest X-ray findings**. Neurological complications can include **confusion, motor deficits, seizures**, and, in severe cases, **coma or brain swelling (encephalitis)**.

PEOPLE AT RISK

Certain groups of people are at higher risk of contracting Nipah virus, particularly those who handle infected animals or consume contaminated foods. These include individuals working in **piggeries, stables, and abattoirs**. People who consume **raw date palm sap** contaminated by infected bats are also at risk. The World Health Organization (WHO) has identified Nipah virus as a **high-priority pathogen** due to its zoonotic potential, broad geographical distribution of host reservoirs, and the absence of specific treatments or vaccines.

DIFFERENTIAL DIAGNOSIS

Nipah virus (NiV) infection presents a unique challenge in clinical diagnosis because its symptoms overlap significantly with several other febrile illnesses, particularly in the early stages of infection. One of the most common difficulties is distinguishing NiV from viral pneumonia or encephalitis caused by other pathogens. Conditions like Japanese encephalitis (JE), cerebral malaria, herpes encephalitis, dengue encephalitis, and bacterial meningitis can mimic the early symptoms of NiV, such as fever, headache, altered mental status, and respiratory distress.

Among the common viral causes of pneumonia, Adenovirus and Influenza must also be considered, as they share a similar respiratory presentation to NiV. Since Japanese encephalitis is also transmitted via swine in certain cases, it is critical to rule this out due to the potential for zoonotic transmission overlap. The diagnostic challenge is heightened in regions where multiple zoonotic diseases are endemic, necessitating a detailed clinical history, environmental exposure assessment, and laboratory investigations.

When dealing with suspected cases of NiV, it is essential for healthcare providers to carefully consider and exclude these other potential differential diagnoses to avoid misdiagnosis, as each condition may require different management protocols. Accurate diagnosis ensures that the most effective treatment is initiated promptly and that public health interventions, such as isolation and contact tracing, are appropriately directed.

Table 2: Detailed Differentiating Features of Common Differential Diagnoses

Disease	Key Clinical Features	Key Distinguishing Features	Laboratory Tests and Expected Results	Epidemiological Clue
Nipah Virus	Fever, headache, respiratory distress, altered mental state, seizures	May progress to encephalitis or respiratory failure	RT-PCR, serology (IgM/ IgG): Positive for Nipah virus; CSF analysis: lymphocytic pleocytosis; Elevated ALT/ AST, creatinine	Exposure to bats, pigs, or close contact with infected individuals
Japanese Encephalitis (JE)	Fever, headache, neck stiffness, altered mental state	Fever usually precedes neurological symptoms	CSF analysis: lymphocytic pleocytosis, increased protein; Elevated liver enzymes (ALT/ AST) if hepatic involvement	Exposure to mosquito bites in endemic areas
Cerebral Malaria	Fever, headache, altered mental state, seizures	Neurological symptoms often more severe, may include coma	Blood smear: presence of malarial parasites; Elevated liver enzymes (ALT/ AST), bilirubin	Travel history to malaria-endemic areas
Herpes Encephalitis	Fever, headache, altered mental state, seizures	Focal neurological deficits may be present	CSF analysis: elevated protein, lymphocytic pleocytosis; PCR for HSV; Mild elevation in ALT/ AST	No specific epidemiological clue

Disease	Key Clinical Features	Key Distinguishing Features	Laboratory Tests and Expected Results	Epidemiological Clue
Dengue Encephalitis	Fever, headache, rash, joint pain, bleeding manifestations	Less severe neurological involvement than JE	NS1 antigen test, serology: Positive for dengue; Elevated ALT/AST, increased haematocrit	Exposure to Aedes mosquito bites in endemic areas
Bacterial Meningitis	Fever, headache, neck stiffness, altered mental state	Rapid onset of severe symptoms, may include rash or petechiae	CSF analysis: increased WBCs, increased protein, positive culture; Elevated CRP, ESR, WBC count in blood and CSF	Contact with infected individuals, exposure to contaminated water sources
Leptospirosis	Fever, headache, muscle aches, jaundice, renal failure	Gradual onset of symptoms, may include pulmonary involvement	Urine culture, serology: Positive for Leptospira; PCR for Leptospira; Elevated creatinine, bilirubin	Exposure to contaminated water or soil, contact with infected animals
Scrub Typhus	Fever, headache, rash, eschar (black scab)	Rash may be maculopapular or haemorrhagic	Weil-Felix test, serology: positive for Orientia tsutsugamushi; Elevated CRP, ESR, mild ALT/AST elevation	Exposure to mite bites in endemic areas
Measles	Fever, cough, coryza, conjunctivitis, rash	Characteristic maculopapular rash	Serology: positive for measles; Elevated WBCs, mild ALT/AST elevation	Exposure to measles virus
Rabies	Fever, headache, anxiety, agitation, hydrophobia, aerophobia	Progressive neurological symptoms, may include paralysis	Negri bodies in brain tissue, direct fluorescent antibody test; Elevated WBC count, mild ALT/AST elevation	History of animal bite

Key Highlights:

- **Nipah Virus:** Positive **RT-PCR** and **serology** for Nipah virus; **elevated ALT/AST** and **creatinine**.
- **Japanese Encephalitis (JE):** CSF analysis shows **lymphocytic pleocytosis** with **elevated protein**; **liver enzymes (ALT/AST)** may be mildly elevated.
- **Cerebral Malaria:** Blood smear shows **malaria parasites**; **elevated liver enzymes (ALT/AST)** and **bilirubin** due to hepatic involvement.
- **Herpes Encephalitis:** CSF analysis shows **elevated protein** and **lymphocytic pleocytosis** with **PCR for HSV**; mild **ALT/AST** elevation.
- **Dengue Encephalitis:** **NS1 antigen test** and **serology** confirm dengue; **elevated ALT/AST** and **increased haematocrit**.
- **Bacterial Meningitis:** CSF analysis with increased WBCs and protein, **positive culture**; **CRP** and **ESR** are elevated.
- **Leptospirosis:** **Urine culture** and **serology** positive for *Leptospira*; **elevated creatinine** and **bilirubin**.
- **Scrub Typhus:** Positive **Weil-Felix test** and **serology** for *Orientia tsutsugamushi*; **elevated CRP, ESR**, and **mild ALT/AST** elevation.
- **Measles:** **Serology** confirms measles; **elevated WBCs** and **mild ALT/AST** elevation.
- **Rabies:** **Negri bodies** in brain tissue; **direct fluorescent antibody test**; **elevated WBC count** and **mild ALT/AST** elevation.

NiV Structure - Agent

- Nipah virus (NiV) is a non-segmented single-stranded negative polarity **RNA virus**
- Belongs to the Family **Paramyxoviridae** and genus **Henipavirus**
- It is related to Hendra virus that infects horses.
- Nipah virus is an enveloped virus measuring **40 to 600 nm** in size and **pleomorphic in shape**
- The genome consists of **six genes**, translating into nucleocapsid (N), phosphoprotein (P), matrix protein (M), fusion protein (F), glycoprotein (G) and polymerase (L) proteins
- F and G proteins are responsible for **adhesion and penetration** of virus to host cell
- Phosphoprotein (P) gene also codes for the synthesis of non-structural proteins C, V, and W

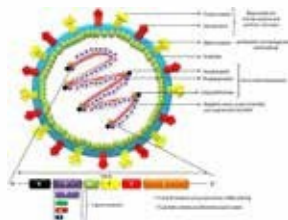


Illustration of Nipah virus genome

Image source: <https://www.researchgate.net/publication/figure/fig/312558975>

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NIPAH VIRUS

Host and Environment Characteristics

Host:

- Natural reservoir:** Pteropid fruit bats (flying foxes).
- Affected hosts:** Pigs, humans, horses, and potentially dogs. Serologic evidence in other farm animals (cattle, goats, etc.).
- Human infection is rare, likely due to infrequent virus shedding by bats.

Environment:

- Spillover events:** Occur when bats contaminate food sources like fruit or sap. Infected pigs or horses act as intermediate hosts.
- Human-to-human transmission:** Documented, particularly in hospital settings.
- Environmental factors:** Proximity of pig farms to fruit-bearing trees, bat-infected sap collection, and contact with contaminated animals facilitate transmission.

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NIPAH VIRUS

Factors affecting emergence of NiV Infection

- Intensive livestock farming
- Deforestation
- Urbanization emanating from deforestation
- Spillover of pathogen from animal reservoirs to human
- Wild animal trade
- Bush meat consumption

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NIPAH VIRUS

NiV disease outbreaks in humans



In the first known NiV outbreak, people were infected through close contact with infected pigs.



In Malaysian outbreak, human-to-human transmission resulted from direct contact with respiratory secretions from severely ill patients.



In the 2014 Philippines outbreak, infected horses were identified as the intermediate hosts.



In 2018 Kerala outbreak, all cases except the index case the transmission was from human-to-human contacts

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NIPAH VIRUS

Notes

- **Bats:** Fruit bats are the natural reservoirs of NIV
- **Bats to Animals:** Bats harboring NIV opportunistically forage in trees producing ripe fruit. Consumption of these contaminated foods by animals can lead to infection in animals.
- **Animals to Animals:** Transmission of NIV infection between pigs as well as domesticated animals through contaminated urine or saliva of infected bats.
- **Animal to Human:** Humans coming into contact with infected animals or bats. Consumption of contaminated date palm sap
- **Human to Human:** Family members or care-givers coming in contact with infected humans through nasal discharge, body fluids (saliva & urine), fomites such as clothing, shoes, etc., and utensils

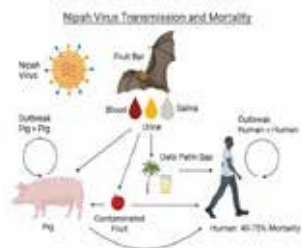


Image source: <http://www.jesmar.ac.uk/research/emerging-pathogens/wipe>

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NIPAH VIRUS

The diagram is divided into three vertical sections, each with a circular icon at the top and a list of criteria below. The first section, 'Suspected case', has a light green circle with a dark green bottom half. The second, 'Probable case', has a light green circle with a dark green bottom half. The third, 'Confirmed case', has a light green circle with a dark green bottom half.

Suspected case	Probable case	Confirmed case
• A person residing in a community with a confirmed Nipah virus outbreak and presenting with: • Fever with new onset of altered mental status or seizure	• Any suspected person: • who resided in the same village/ward, where suspect/confirmed case of Nipah were living during the outbreak period and who died before complete diagnostic specimens could be collected	• A presumptive case with: • Nipah virus RNA identified by PCR from respiratory secretions, urine, or cerebrospinal fluid
• AND/OR • Fever with headache	• who came in direct contact with confirmed patient(s) in a hospital setting during the outbreak period and/or who died before complete diagnostic specimens could	• Isolation of Nipah virus from respiratory secretions, urine or cerebrospinal fluid
• AND/OR • Direct contact with a confirmed case		

Source: Our Definitions of ADHD Were Wrong - Ministry of Health and Family Welfare (2013)

Center for Oral Health, WDC, Atlanta, Ga.

NIPAH VIRUS

A close contact is defined as a patient or a person who came in contact with a Nipah case (confirmed or probable cases) in at least one of the following ways.

- | | | | |
|---|---|---|---|
| 1. Was admitted simultaneously in a hospital ward/ shared room with a suspect/confirmed case of Nipah virus disease | 1. Has had direct close contact with the (deceased) suspect/confirmed case of Nipah virus disease at a funeral or during burial preparation rituals | 1. Has touched the blood or body fluids (saliva, urine, vomitus etc.) of a suspect/confirmed case of Nipah virus disease during their illness | 1. Has touched the clothes or linens of a suspect/confirmed case of Nipah virus disease |
|---|---|---|---|

These contacts need to be followed up for appearance of symptoms of NiV for the longest incubation period (21 days), or preferably double incubation period, of 42 days.

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NIPAH VIRUS

The diagram illustrates the pathogenesis of Hepatocellular Carcinoma (HCC). It shows the progression from initial liver damage (e.g., cirrhosis) through various stages of cellular transformation, including dysplasia and carcinoma in situ, leading to the development of HCC. Key factors like chronic inflammation, oxidative stress, and genetic mutations are highlighted as contributing to the disease process.

Image source: Raj Kumar Singh et al. 2019. <https://microbenotes.com/nipah-virus-nih/>

Center for New Media, MIT: 2007.

NIPAH VIRUS

[illegible]

NiV disease overview

- Symptoms**- Common symptoms include fever, altered mental status, Severe weakness, headache, respiratory distress, cough, vomiting, muscle pain, convulsions, and diarrhea.
- Small percentage of infected individuals remain asymptomatic.
- Early stage- most experience prodromal symptoms such as fever, headache, and myalgia
- Severe cases- may progress to encephalitis and respiratory distress.
- Encephalitis can recur months to years after recovery from the initial infection.
- Incubation period**- varies from 6-21 days.
- Diagnosis**- RT-PCR, ELISA, virus isolation
- Transmission**- direct contact with infected bats, infected pigs or animals, or from other Nipah virus infected people.
- Treatment**- Currently, no effective treatment exists, only supportive care.



[Image source: J Pure Appl Microbiol. 2022;16(1):26-34 | Article Number: 7346 <https://doi.org/10.22020/JPM.16.1.72>

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NIPAH VIRUS

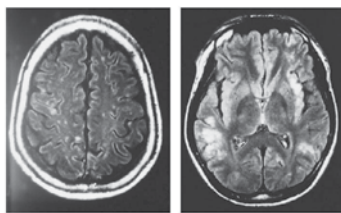
NiV Disease in Human-Clinical Manifestation

Infection with NiV can cause mild to severe disease, including swelling of the brain (encephalitis) and potential death.

Symptoms typically appear in 4-14 days following exposure to the virus.

Death may occur in 40-75% of cases. Long-term side effects in survivors of NiV infection include persistent convulsions and personality changes.

Dormant or latent infections- Refer to a type of infection where symptoms may only manifest much later after initial exposure, sometimes even months or years later.



[Image source: N Engl J Med 2006;352:1229-1235 DOI: 10.1056/NEJM000047542701 <https://www.nejm.org/doi/full/10.1056/NEJM000047542701>

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NIPAH VIRUS

Symptoms of Nipah virus infection



Source - MoHFW Nipah pamphlet

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NIPAH VIRUS

NiV Disease in Human- Clinical Manifestation

Primary clinical signs	Fever	Headache	Vomiting	Dizziness
Characteristics symptoms	Segmental myoclonus	Hypertension and tachycardia	Hypotonia and areflexia	Abdominal pupillary reflexes
Severe symptoms	Pulmonary syndrome		Neurological signs	
	1. Cough 2. Diffuse alveolar shadowing and acute respiratory distress syndrome 3. Hypoxemia 4. Abnormal X ray chest findings		1. Confusion 2. Motor deficits and reduced level of consciousness 3. Seizure 4. Abnormal MRI finding 5. Coma 6. Brain swelling (encephalitis)	

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NIPAH VIRUS

Notes

Potential threat

NiV has been identified as a high-priority pathogen by WHO due to:

-  Broad geographical distribution of the host reservoir
-  Potential for zoonotic and human transmission
-  Absence of specific treatment or available vaccines

Centre for Disease Control, CDC, Atlanta

NIPAH VIRUS

People at Risk

Handling or coming in contact with infected animals such as pigs, horses, raw meat etc.



Piggyeries



Stables



Abattoir workers

Drinking raw date palm sap (contaminated by an infected bat)

(Source: Prof. Dinesh Behera, ICIDC, Bhubaneswar)

NIPAH VIRUS

Differential Diagnosis

Distinguishing NiV from various other febrile illnesses during its early stages can be challenging. Among the most common causes of viral pneumonia are Adenovirus, Influenza, and viral encephalitis, such as Japanese encephalitis, which is also spread by swine and must be ruled out when dealing with suspected NiV cases, it is crucial to carefully consider and exclude these potential differential diagnoses

Japanese encephalitis (JE)	Cerebral malaria	Herpes encephalitis	Dengue encephalitis	Bacterial Meningitis
Leptospirosis	Scrub typhus	Measles	Rabies	

Courtesy: Prof. David, ICMR, New Delhi

NIPAH VIRUS

Disease	Key Clinical Features	Key Distinguishing Features	Laboratory Tests and Expected Results	Epidemiological Cue
Nipah Virus	Fever, headache, respiratory distress, altered mental state. <i>spontaneous</i>	May progress to encephalitis or respiratory failure	RT-PCR, serology (IgM/IgG): Positive for Nipah virus; CSF analysis: lymphocytic pleocytosis; Elevated ALT/AST, creatinine	Exposure to bats, pigs, or close contact with infected individuals
Javanese Encephalitis (JE)	Fever, headache, neck stiffness, altered mental state	Fever usually precedes neurological symptoms	CSF analysis: lymphocytic pleocytosis, increased protein; Elevated liver enzymes (ALT/AST) if hepatic involvement	Exposure to mosquito bites in endemic areas
Cerebral Malaria	Fever, headache, altered mental state, seizures	Neurological symptoms often more severe, may include coma	Blood smear: presence of malarial parasites; Elevated liver enzymes (ALT/AST), bilirubin	Travel history to malaria-endemic areas
Herpes Encephalitis	Fever, headache, altered mental state, seizures	Focal neurological deficits may be present	CSF analysis: elevated protein, lymphocytic pleocytosis; PCR for HSV; Mild elevation in ALT/AST	No specific epidemiological clue
Dengue Encephalitis	Fever, headache, rash, joint pain, bleeding manifestations	Less severe neurological involvement than JE	NS1 antigen test, serology: Positive for dengue; Elevated ALT/AST, increased hematocrit	Exposure to Aedes mosquito bites in endemic areas

[illegible]

Differential Diagnosis for Nipah Virus continued.....

Bacterial Meningitis	Fever, headache, neck stiffness, altered mental state	Rapid onset of severe symptoms, may include rash or petechiae	CSF analysis: increased WBCs, increased protein, positive culture; Elevated CRP, ESR, WBC count in blood and CSF	Contact with infected individuals, exposure to contaminated water sources
Leptospirosis	Fever, headache, muscle aches, jaundice, renal failure	Gradual onset of symptoms, may include pulmonary involvement	Urine culture, serology: Positive for Leptospira; PCR for Leptospira; Elevated creatinine, bilirubin	Exposure to contaminated water or soil, contact with infected animals
Scrub Typhus	Fever, headache, rash, eschar (black scab)	Rash may be maculopapular or hemorrhagic	Weil-Felix test, serology: positive for Orientia tsutsugamushi; Elevated CRP, ESR, mild ALT/AST elevation	Exposure to mite bites in endemic areas
Measles	Fever, cough, coryza, conjunctivitis, rash	Characteristic maculopapular rash	Serology: positive for measles; Elevated WBCs, mild ALT/AST elevation	Exposure to measles virus
Rabies	Fever, headache, anxiety, agitation, hydrophobia, aerophobia	Progressive neurological symptoms, may include paralysis	Negri bodies in brain tissue, direct fluorescent antibody test: Elevated WBC count, mild ALT/AST elevation	History of animal bite

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NIPAH VIRUS

Notes

Session-4

Laboratory Diagnosis

Course No. 004	Session 4: Laboratory Diagnosis
Duration	20 minutes
Learning Objective	• Understand the various laboratory investigations recommended for the NIPAH virus
Pre-requisite knowledge/skill	• Basic understanding of molecular and serological diagnostic techniques. • Familiarity with biosafety protocols and specimen handling in high-risk pathogen testing. • Awareness of the role of reference laboratories and confirmatory testing for emerging viral infections.
Competencies to be achieved	• Comprehension of the various diagnostic tests employed to detect and validate the presence of nipah virus • Understand the various samples to be collected and adherence to safety protocols during its collection and transport

SAMPLES FOR DIAGNOSIS

The various types of clinical samples required for the laboratory diagnosis of **Nipah Virus (NiV)** infection, based on the patient's clinical presentation and the day of illness are as follows:

1. **Swabs (Nasal and oropharyngeal):** These are essential for collecting respiratory tract samples where initial viral replication may occur. These samples are crucial for early detection of the virus in the respiratory system.
2. **Blood/Serum:** Blood samples are used to detect viremia, especially during the acute phase of the infection, and help monitor the body's immune response to the virus.
3. **Urine Sample:** Urine can contain viral particles, and its collection can offer insights into systemic infection, particularly in the later stages of the disease.
4. **CSF (Cerebrospinal Fluid):** If neurological symptoms such as encephalitis develop, CSF is collected to detect the virus in the central nervous system, indicating the virus has crossed the blood-brain barrier.
5. **Tissue Samples:** Postmortem tissue samples from organs such as the brain, kidney, and spleen are collected with extreme caution due to the high viral load they may contain. These samples require processing under **BSL-4 containment** to prevent viral transmission to laboratory personnel.

Each of these samples plays a critical role in diagnosing and managing Nipah virus infection. All sample collections must follow stringent biosafety and infection control protocols to ensure safe handling and transport.

PRECAUTIONS AND TRANSPORT

When handling samples for Nipah Virus (NiV) diagnosis, strict precautions are necessary to prevent infection and ensure safe sample collection and transport. **Standard, contact, and droplet precautions** must be employed to protect healthcare workers during the collection process. This involves using personal protective equipment (PPE) to minimize the risk of viral exposure.

Once samples are collected, they must be **transported following internationally recognized protocols**, ensuring that samples are handled safely. This step is crucial to prevent contamination during transit, and it should only occur after prior consultation with the designated reference laboratory.

Given the high contagion of NiV and the absence of specific treatment, it is recommended that only **essential samples** necessary for clinical management be collected to reduce unnecessary risks. Additionally, for any biochemical or pathological testing, **closed automated systems** should be used to ensure proper containment and safe disposal of biohazardous waste.

INVESTIGATIONS FOR NIPAH VIRUS DISEASE

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.

Table 3: Clinical investigations

Routine hematological tests	Thrombocytopenia Leucopenia Raised liver enzymes. Hyponatremia
Cerebrospinal fluid analysis	Lymphocytic pleocytosis Raised proteins Normal glucose levels
Imaging	2-7mm multifocal discrete lesions in the subcortical and deep white matter
NiV specific tests	ELISA for detection of antibodies Polymerase Chain Reaction Virus isolation

Nipah virus infection can be diagnosed with clinical history during the acute and convalescent phase of the disease.

Laboratory confirmation involves two key diagnostic methods:

- **Serology:** Involves the detection of IgM antibodies against NiV in serum or cerebrospinal fluid (CSF), indicating an immune response to the infection.
- **Molecular testing:** The identification of NiV RNA via RT-PCR from respiratory secretions, urine, or CSF is crucial during the acute phase of the infection for early detection.

Isolation of the virus from respiratory secretions, urine, or cerebrospinal fluid requires stringent **biosafety measures** and must be carried out only in a **BSL-4 laboratory** to ensure safe handling of the highly contagious pathogen. These precautions are vital in preventing the spread of NiV during laboratory testing.

The diagnosis of Nipah virus (NiV) infection can be confirmed using a combination of laboratory tests. During the acute phase of the disease, RT-PCR can detect viral RNA in respiratory secretions, urine, or cerebrospinal fluid. Later, during the convalescent phase (10-14 days), serological tests such as ELISA can detect IgM and IgG antibodies against NiV. While virus isolation from respiratory secretions, urine, or cerebrospinal fluid is possible, it requires a BSL-4 laboratory due to the high risk of infection.

Samples for diagnosis

Swabs: Nasal and oropharyngeal.

Blood/Serum

Urine sample

CSF

Tissue samples (brain, kidney, spleen) – *Postmortem samples require BSL-4 containment due to high viral load.*

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NIPAH VIRUS

Investigations for Nipah virus disease

• Routine haematological tests	• Thrombocytopenia • Leucopenia • Raised liver enzymes • Hyponatremia
• Cerebrospinal fluid analysis	• Lymphocytic pleocytosis • Raised proteins • Normal glucose levels
• Imaging	• 2-7mm multifocal discrete lesions in the subcortical and deep white matter
• NiV specific tests	• ELISA for detection of antibodies • Polymerase Chain Reaction • Virus isolation

Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6409114/pdf/0008-1168.pdf>

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NIPAH VIRUS

Laboratory Diagnosis of Nipah Virus Disease – Specific Tests

Laboratory diagnosis of a patient with a clinical history of NiV can be made during the acute and convalescent phases of the disease by using a combination of tests.

Laboratory confirmation of NiV infection includes:

• **Serology:**

• Detection of IgM antibody against NiV in serum or CSF,

• **Molecular:**

• NiV RNA identification by RT-PCR from respiratory secretions, urine or cerebrospinal fluid

Acute phase:
Detection of NiV
RNA via RT-PCR.

Later phase (10-14
days): Detection via
serological
methods (ELISA).

[CD-Avert-Nipah-Virus-Disease.pdf \(moHFW.gov.in\)](#)

Isolation of virus from respiratory secretions, urine or cerebrospinal fluid or other tissue specimens
(Only to be carried out in a BSL 4 laboratory)

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NIPAH VIRUS

Precautions and Transport

Use **standard, contact, and droplet precautions** when collecting samples.

Transport samples following international protocols, only after prior consultation with reference laboratories.

Due to **high contagion** and no treatment for NiV, only essential samples for clinical management should be collected.

For other tests (e.g., biochemistry/pathology), ensure containment and use **closed automated systems** for processing.

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NIPAH VIRUS

Notes

Laboratories available for diagnostic facilities



National Institute of
Virology , Pune
(IgM ELISA, RT-PCR and
virus isolation)



National Centre for
Disease Control, Delhi
(RT PCR)

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NIPAH VIRUS

Notes

Session-5

Case Study, Treatment & Prevention

Course No. 005	Session 5: Case Study, Treatment & Prevention
Duration	20 minutes
Learning Objectives	• Describe a sample case of NIPAH VIRUS • Understand treatment options • Describe preventive measures
Pre-requisite knowledge/skill	• Basic understanding of clinical case management and supportive care for viral infections. • Familiarity with infection prevention and control measures for high-risk pathogens. • Awareness of preventive strategies for zoonotic diseases.
Competencies to be achieved	• Comprehension of the case study and general understanding of handling of NIPAH VIRUS cases • Explanation of strategies for treatment and prevention of NIPAH VIRUS

CASE STUDY

A 45-year-old male presented with a history of fever, headache, and altered sensorium for the past 3 days. He had no history of cough, dyspnea, or gastrointestinal symptoms. The patient was a farmer and had a history of contact with pigs and bats.

- On examination, the patient was febrile and disoriented. There were no signs of meningeal irritation or focal neurological deficits.
- Investigations revealed leukocytosis and thrombocytopenia.
- The liver function tests were abnormal, and there was evidence of acute kidney injury.
- The chest X-ray was normal.
- The cerebrospinal fluid (CSF) analysis showed lymphocytic pleocytosis, elevated protein, and normal glucose levels.
- The CSF was negative for bacterial and fungal cultures.

The patient was diagnosed with Nipah virus infection based on the clinical presentation and history of contact with pigs and bats.

The patient was started on supportive care, including mechanical ventilation, and antiviral therapy with ribavirin. Despite aggressive management, the patient's condition deteriorated, and he succumbed to the illness on the 5th day of hospitalization.

Patient Profile	
Patient's age	45 years old
Gender	Male
Medical conditions	Fever, headache, and altered sensorium for the past 3 days.
Previous treatments	None reported
Medical Examination	On examination, the patient was febrile and disoriented. There were no signs of meningeal irritation or focal neurological deficits. Investigations revealed leukocytosis and thrombocytopenia. Liver function tests were abnormal Evidence of acute kidney injury. Chest X-ray was normal. The cerebrospinal fluid (CSF) analysis showed lymphocytic pleocytosis, elevated protein, and normal glucose levels. The CSF was negative for bacterial and fungal cultures.
History	The patient was a farmer and had a history of contact with pigs and bats.

TREATMENT

Currently, there is no specific treatment or vaccine available for Nipah virus infection in humans or animals. Intensive supportive care and symptom management are the primary approaches for treating the infection in humans.

Monoclonal antibody therapies, such as m102.4, are under development and have been used on a compassionate basis after completing phase 1 clinical trials. The antiviral drug remdesivir has shown effectiveness in non-human primates when used as post-exposure prophylaxis and may complement immunotherapeutic treatments.

Although no established treatment exists for Nipah virus disease, observational data suggests Ribavirin may reduce mortality in patients with encephalitis caused by the virus. However, there is no evidence supporting its use as a preventive or prophylactic drug.

The treatment algorithm for Nipah virus (NiV) infection presented in this slide provides a structured approach for managing suspected and confirmed cases.

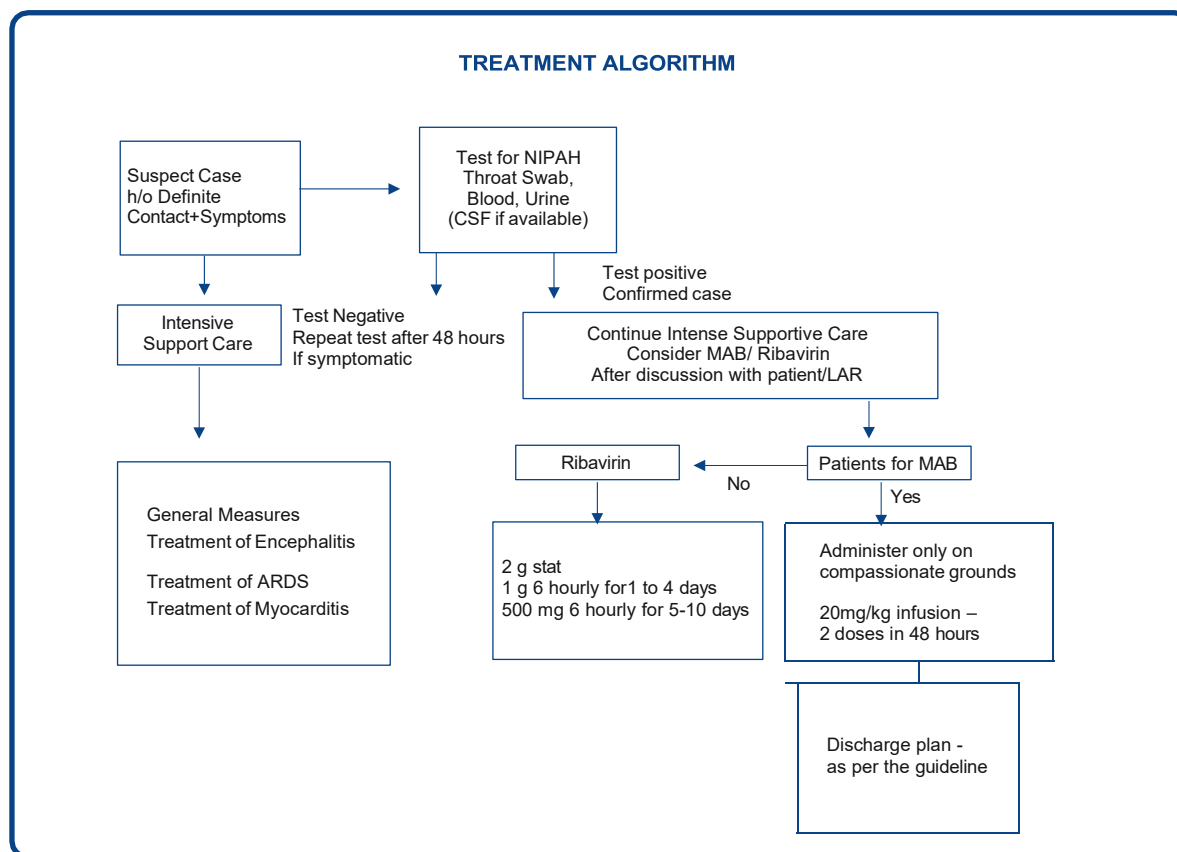


Fig 9: Treatment algorithm

(Image source: <https://dhs.kerala.gov.in/wp-content/uploads/2021/09/Nipah-Guidelines-9-04-21-2-1.pdf>)

- 1. Initial Assessment:** It begins with a suspected case, where the patient shows symptoms and has a history of contact with a confirmed or probable case. The first step is to perform tests for Nipah virus, including throat swab, blood, urine, and possibly cerebrospinal fluid (CSF), if available.
- 2. Test Results:**
 - If the test is **negative**, the patient should continue receiving intensive supportive care, and the test should be repeated after 48 hours if symptoms persist.
 - If the test is **positive**, the case is confirmed, and intensive supportive care should continue. Depending on the patient's condition, treatments such as Monoclonal Antibody (MAB) therapy or Ribavirin may be considered.
- 3. Treatment Decisions:**
 - **Ribavirin:** If the decision is to administer Ribavirin, the dosing starts with a high dose (2 grams stat) followed by smaller doses (1 gram every 6 hours for 1 to 4 days, then 500 mg every 6 hours for 5 to 10 days).

- **Monoclonal Antibody (MAB) Therapy:** This is only administered on compassionate grounds, with a dosing of 20 mg/kg infusion over two doses in 48 hours.
4. **Discharge and Monitoring:** Once treatment is complete, a discharge plan is followed as per the established guidelines, ensuring the patient's recovery and preventing further transmission.

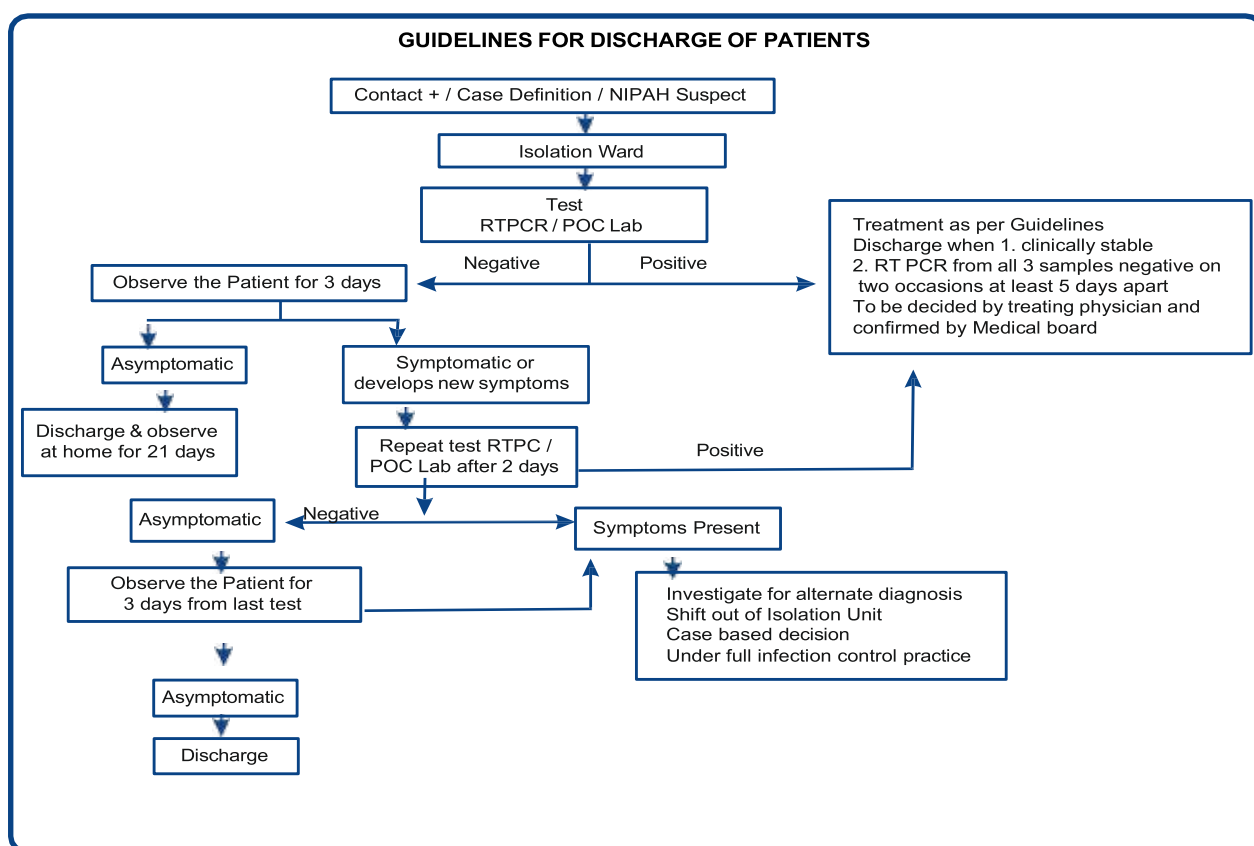


Fig 10: Guidelines for discharge of patients

(Image source: <https://dhs.kerala.gov.in/wp-content/uploads/2021/09/Nipah-Guidelines-9-04-21-2-1.pdf>)

The management of Nipah virus patient involves several critical steps:

1. **Symptomatic and supportive treatment:** This is essential and should begin immediately in all clinically suspected cases of NiV infection.
2. **Maintain airway, breathing, and circulation:** Ensuring these fundamental aspects of care is crucial for stabilizing patients.
3. **Patient advice:** Patients are advised to take proper rest and consume plenty of fluids to maintain electrolyte balance as part of supportive care and treatment.
4. **Infection control and isolation:** Patients with NiV infection should be isolated, following strict infection control practices to prevent further transmission.
5. **Barrier nursing:** Protective measures such as wearing masks, gloves, gowns, and shoe covers, along with thorough hand hygiene, are essential for anyone handling or visiting infected patients.

The recommended dosages of Ribavirin for the treatment of Nipah virus infection, divided into specific protocols for adults, children, and parenteral administration.

- **For Adults:** The treatment begins with a loading dose of 2000 mg (10 tablets of 200 mg), followed by a regimen of 1000 mg every 6 hours for the first 4 days (equivalent to 5 tablets each time, 4 times daily). From Day 5 to Day 10, the dosage is reduced to 500 mg every 6 hours (3 tablets followed by 2 tablets with a 6-hour gap). This adds up to approximately 150 capsules for a 10-day treatment course.
- **For Children:** The loading dose is calculated based on weight, with 30 mg/kg administered initially. From Day 1 to Day 4, 3 mg/kg is given every 6 hours, and from Day 5 to Day 10, the dosage is reduced to 7.5 mg/kg every 6 hours.
- **Parenteral Dose:** For patients requiring IV administration, a loading dose of 30 mg/kg is given, followed by 15 mg/kg every 6 hours for 4 days, then 7.5 mg/kg every 8 hours for 6 days. Ribavirin is diluted in 150 ml of normal saline and infused slowly.

Newer Experimental Drugs

Favipravir has recently been shown to be effective against Nipah viral infections in animal model. Immunomodulating drugs have not been found to be beneficial in treatment of ARDS or sepsis associated multi organ failure.

High dose corticosteroids in particular have no evidence of benefit and there is potential for harm.

Post Exposure Prophylaxis

- There is no evidence to support the role of ribavirin as post-exposure prophylactic treatment for Nipah fever.

Human monoclonal antibody:

- Human Monoclonal antibodies targeting the viral glycoproteins (anti-G MAb or anti-F Mab). However, its use in emergency setting is subject to DCGI approvals.

Prevention of Nipah

In areas where there have been outbreaks of Nipah virus (NiV) (Bangladesh, Malaysia, India and Singapore), people should:

- Wash hands regularly with soap and water
- Avoid contact with sick bats or pigs
- Avoid where bats are known to be present could be bat-contaminated, e.g. B. raw date palm juice, raw fruits or fruits found on the ground.
- Avoid contact with the blood or body fluids of people known to be infected with NiV

Because NiV can be transmitted from person to person, standard infection control practices and appropriate protective techniques are important to prevent hospital-acquired infections (hospital-acquired transmission) in settings where a patient has confirmed or suspected NiV infection. Other geographic locations may be at risk for future NiV outbreaks, such as B. Regions inhabited by flying foxes (bat genus *Pteropus*). These bats are currently found in Cambodia, Indonesia, Madagascar, the Philippines and Thailand. People living in or visiting these areas should take the same precautions as those living in areas that have had outbreaks and encourage vulnerable communities to continue to educate themselves about NiV to prevent future outbreaks. Broader prevention efforts include:

Increased surveillance of animals and humans in areas where NiV is known.

- Increased research on fruit bat ecology to understand where they live and how they transmit the virus to other animals and humans.
- Evaluate novel technologies or methods to minimize the spread of the virus within bat populations.
- Improve tools for early detection of the virus in communities and livestock.
- Reinforce health facility protocols on standard infection control practices to prevent human-to-human transmission Awareness of the signs, symptoms and risk of NiV among higher-risk populations due to:
 - Geographical location
 - Contact with fruit bats or fruit bat-contaminated objects
 - Contact with pigs or animals that may come into contact with fruit bats
- Working in a healthcare facility or caring for people infected with NiV
- Increased surveillance of animals and humans in areas where NiV is known.
- Increased research on fruit bat ecology to understand where they live and how they transmit the virus to other animals and humans.
- Evaluate new technologies or methods to minimize the spread of the virus within bat populations.
- Improving tools for early detection of the virus in communities and livestock.
- Reinforce healthcare facility protocols on standard infection control practices to prevent human-to-human transmission. Awareness of the signs, symptoms and risk of NiV in higher-risk populations due to:
 - Geographical location
 - Contact with fruit bats or fruit bat-contaminated objects
 - Contact with pigs or animals that may come into contact with fruit bats, work in a healthcare facility, or have NiV care for infected people

Controlling Nipah Virus in Pigs

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.

Reducing the Risk of Infection in People

In the absence of a vaccine, the only way to reduce or prevent infection in people is by raising awareness of the risk factors and educating people about the measures they can take to reduce exposure to the Nipah virus.

Public Health Educational Messages should focus on

Reducing the risk of bat-to-human transmission-

Efforts to prevent transmission should first focus on decreasing bat access to date palm sap and other fresh food products. Keeping bats away from sap collection sites with protective coverings (such as bamboo sap skirts) may be helpful. Freshly collected date palm juice should be boiled, and fruits should be thoroughly washed and peeled before consumption. Fruits with sign of bat bites should be discarded.

Reducing the risk of animal-to-human transmission-

Gloves and other protective clothing should be worn while handling sick animals or their tissues, and during slaughtering and culling procedures. As much as possible, people should avoid being in contact with infected pigs. In endemic areas, when establishing new pig farms, considerations should be given to presence of fruit bats in the area and in general, pig feed and pig shed should be protected against bats when feasible.

Reducing the risk of human-to-human transmission-

Close unprotected physical contact with Nipah virus-infected people should be avoided. Regular hand washing should be carried out after caring for or visiting sick people.

Controlling infection in health-care settings-

Health-care workers caring for patients with suspected or confirmed infection, or handling specimens from them, should always implement standard infection control precautions.

As human-to-human transmission has been reported, in health-care settings, contact and droplet precautions should be used in addition to standard precautions. Airborne precautions may be required in certain circumstances.

Samples taken from people and animals with suspected Nipah virus infection should be handled by trained staff working in suitably equipped laboratories.

Vaccines

Currently, there is no licensed vaccine or treatment for Nipah virus infection. However, the US National Institute of Allergy and Infectious Diseases (NIAID) has launched a Phase I clinical trial to evaluate a messenger RNA (mRNA) vaccine developed to prevent infection with Nipah virus.

The experimental vaccine, mRNA-1215, is manufactured by Moderna and was developed in collaboration with NIAID's Vaccine Research Center. It is based on the same platform as Moderna's COVID-19 vaccine. NIAID is sponsoring the Phase 1 study (NCT05398796), which is being conducted at the NIH Clinical Center in Bethesda, Maryland.

No approved vaccine or treatment currently exists for Nipah virus infection. However, a phase I clinical trial is underway for an experimental mRNA vaccine, mRNA-1215, developed by Moderna in collaboration with the US National Institute of Allergy and Infectious Diseases (NIAID). This vaccine aims to prevent Nipah virus infection and is based on the same platform as Moderna's COVID-19 vaccine. Sponsored by NIAID, the Phase 1 trial (NCT05398796) is conducted at the NIH Clinical Center in Bethesda, Maryland.

Case Scenario

Patient Profile	
Patient's age	45 years old
Gender	Male
History	The patient was a farmer and had a history of contact with pigs and bats.
Medical conditions	Fever, headache, and altered sensorium for the past 3 days.
Previous treatments	None reported
Medical Examination	- On examination, the patient was febrile and disoriented. - There were no signs of meningeal irritation or focal neurological deficits. - Investigations revealed leukocytosis and thrombocytopenia. - Liver function tests were abnormal. - Evidence of acute kidney injury. - Chest X-ray was normal. - The cerebrospinal fluid (CSF) analysis showed lymphocytic pleocytosis, elevated protein, and normal glucose levels. - The CSF was negative for bacterial and fungal cultures.

The patient was diagnosed with Nipah virus infection based on the clinical presentation and history of contact with pigs and bats.

The patient was started on supportive care, including mechanical ventilation, and antiviral therapy with ribavirin. Despite aggressive management, the patient's condition deteriorated, and he succumbed to the illness on the 5th day of hospitalization.



Typical Symptoms

- Fever & Headache
- Cough, Vomiting
- Drowsiness, Disorientation
- Sore throat, Confusion
- Seizures & Coma
- Brain swelling (encephalitis)
- Difficulty breathing

Laboratory tests

- Molecular: RT-PCR from the throat and nasal swabs, CSF, urine, and blood
- Serological: Antibodies detected by ELISA
- Hematological: Leukopenia, Thrombocytopenia
- Biochemical: Elevated AST and ALT levels

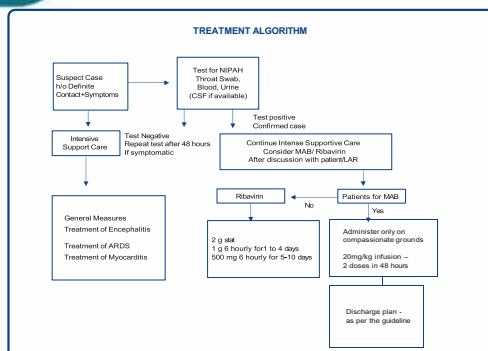


Treatment

- No specific treatment or vaccine is available either for humans or animals.
- Ribavirin is advised to all confirmed cases of Nipah virus infection to reduce the mortality
- Acyclovir, chloroquine, and ephrin-B2 are under review as potential therapeutic options.
- Favipiravir, licensed for influenza treatment in Japan, has shown effectiveness in hamsters.
- Human monoclonal antibody has been useful in ferrets and non-human primates.
- Discharged patients should have a negative RT-PCR test on a throat swab.
- Discharged patients remain in isolation for 21 days after confirmation of the infection.



No specific treatment or vaccine available either for humans or animals



<https://dhs.bhrcs.gov.in/wp-content/uploads/2021/09/Nipah-Guidelines-9-04-21-2-1.pdf>

Notes

General management

• Symptomatic and supportive treatment should be started immediately in all clinically suspected cases

- Maintain airway, breathing and circulation

Institute barrier nursing, e.g., personal protection using masks, gloves, gowns, shoe covers and hand-washing with soap and water before and after handling/visiting patients.

Patients with NiV infection should be isolated with infection control practices in place.

Patient is advised to take proper rest and plenty of fluids to maintain the electrolyte balance as a supportive care and treatment

Dosage of Ribavirin

For Adults	For Children	Parenteral dose of Ribavirin
• 2000 mg loading (10 tabs of 200 mg) • Day 1-4- 1000 mg 6 hrly (5 tabs of 200 mg each 4 times daily for 4 days = 80 tablets) • Day 5-10- 500 mg 6 hrly (200 mg each tablet 3 tab - 3 tab, 2 tab 2 tab at 6hrs gap daily for 6 more days = 60 tablets)	• Load 30mg/kg • Thereafter, for Day 1- 4 to give 3 mg/kg 6 hrly • Day 5- Day 10 to give 7.5 mg/kg 6 hrly.	• IV Ribavirin loading dose of 30 mg/ kg • Then 15 mg / kg every six hourly for 4 days • Then 7.5 mg / kg every eight hourly for 6 days. • Ribavirin should be diluted in 150 ml of 0.9% Normal Saline and infused slowly.

On an average each patient (adult) would require 150 capsules for a 10 days course.

Serious Reactions can include:

- ☐ 1.Hemolytic anemia, Aplastic anemia
- ☐ 1.Neutropenia, Thrombocytopenia
- ☐ 1.Teratogenicity, Embryocide, Autoimmune disorders
- ☐ 1.Arrhythmias, myocardial Infarction
- ☐ 1.Severe depression, Suicidal ideation,
- ☐ 1.Pulmonary toxicity, Pancreatitis,
- ☐ 1.Diabetes, Colitis
- ☐ 1.Retinal hemorrhage, Retinal thrombosis
- ☐ 1.Hypothyroidism, Hyperthyroidism

Common Reactions can include:

- ☐ Dizziness, Diarrhea, Impaired concentration
- ☐ Fatigue, Headache, Fever, Rigors
- ☐ Vomiting, Anorexia, Depression, Pruritis
- ☐ Cough, Rash, or Thrombocytopenia.
- ☐ Myalgias, Arthralgias, Anxiety, Irritability
- ☐ Insomnia, Alopecia, Neutropenia, Nausea,

Newer experimental drugs

- Favipravar has recently been shown to be effective against Nipah viral infections in animal model.
- Immunomodulating drugs have not been found to be beneficial in treatment of ARDS or sepsis associated multi organ failure.
- High dose corticosteroids in particular have no evidence of benefit and there is potential for harm.

Post Exposure Prophylaxis:

- There is no evidence to support the role of ribavirin as post-exposure prophylactic treatment for Nipah fever.

- **Human monoclonal antibody:**

- Human Monoclonal antibodies targeting the viral glycoproteins(anti-G MAb or anti-F Mab). **However, its use in emergency setting is subject to DCGI approvals**

Notes



Journal of China Medical University 2012; 47(1): 24-27

NIPAH VIRUS

- The case fatality rates of Nipah virus infection can range between 40% and 100%.
- Poor prognostic factors include old age and severe brain-stem involvement.
- Prognosis and case fatality rates can also vary depending on the strain of the virus.
- The Malaysian variant of the Nipah virus has shown lower case fatality rates compared to other strains.

Center for Data Needs, INC; Atlanta, GA

NIPAH VIRUS

Consume only washed/peeled fruits	Drink Chlorinated and boiled water	Wear protective clothing while handling or cleaning animals & sheds	Always wash hands with soap and water	Protect animal feed against bats and other animals
Follow the advice of local authorities	Ensure personal protection while contacting infected individuals	Protect sap, juice collection sites & wells from bats	Avoid eating contaminated & half eaten fruits fallen from trees	Avoid drinking date palm juice and toddy like liquids kept in open pots
	Avoid exposure to bats and visiting areas like abandoned wells, houses, caves and mines	Avoid contact with NiV infected person	Avoid exposure to sick or dead animal	

Gender and Age Needs, 2010: 44, 49, 50

NIPAH VIDEO

- Regions with flying foxes (bat genus *Pteropus*) may be at risk for NIV outbreaks, and similar precautions should be taken in those areas.
- Increase **surveillance** of animals and people in NIV-affected areas.
- Conduct research on the ecology of fruit bats to understand their habitats and transmission of the virus.
- Develop technologies and methods to control the spread of the virus within bat populations.
- Improve **early detection** tools for NiV in communities and livestock.

Raise awareness about the signs, symptoms, and risks of NiV among high-risk populations based on geographic location, contact with fruit bats or contaminated items, contact with pigs, and healthcare or caregiving roles for infected individuals.

Center for New Media, MIT: 2007.

NIPAH WIDING

[illegible]

Session-6

Nipah Virus Disease in Animals

Course No. 006	Session 6: Nipah Virus Disease in Animals
Duration	20 minutes
Learning Objectives	• Overview of the Nipah virus disease in animals • Understand the transmission dynamics, presentation in different species • Know about the recommended prevention and control measures for Animal Husbandry
Pre-requisite knowledge/skill	• Basic knowledge of zoonotic diseases and animal health management. • Familiarity with species-specific clinical signs and transmission pathways in domestic and wild animals. • Awareness of biosecurity, surveillance, and control measures in animal husbandry practices.
Competencies to be achieved	• Comprehensive understanding of the Nipah virus disease • Capability to distinguish NIPAH VIRUS from other similar clinical diseases through a thorough differential diagnosis

This section provides an overview of Nipah Virus (NiV) disease in animals, particularly focusing on the following key points:

1. **Reservoir:** The primary reservoir of the Nipah virus is large fruit bats of the *Pteropus* genus. These bats are not known to become ill from the infection but are responsible for the spread of the virus to other animals.
2. **Agent:** Nipah virus is a highly pathogenic paramyxovirus with a single-stranded RNA genome. It belongs to the genus **Henipavirus** and the family **Paramyxoviridae**.
3. **Transmission:** NiV infection in pigs occurs through transmission from the reservoir bat species. Once the virus enters an intensive swine husbandry setting, the infection can spread rapidly among animals within the premises. The diagram illustrates the transmission pathways from bats to pigs, humans, and other animals.
4. **Symptoms:** Pigs infected with Nipah virus commonly develop a febrile respiratory disease characterized by severe coughing. This condition is colloquially known as "barking pig syndrome" or "one-mile cough" due to the intensity of the symptoms.
5. **Treatment:** Currently, there is no effective treatment for Nipah virus infection in animals.
6. **Mortality:** While the overall mortality rate in pigs is generally low, it is higher in piglets, making them more vulnerable to the disease.

Nipah Virus Encephalitis is a **WOAH-listed reportable disease** and is one of the **notifiable diseases in India**.

TRANSMISSION

Nipah Virus (NiV) emerged at the end of the 20th century as a cause of outbreaks involving both respiratory and neurological diseases, affecting a variety of animal species as well as humans. Animals such as pigs, dogs, cats, and horses can contract NiV. In pigs, the infection often manifests with fever and respiratory involvement, sometimes accompanied by neurological symptoms, though many infections remain subclinical. One distinctive sign seen in infected pigs is an unusually loud, barking cough.

The virus is primarily transmitted among animals through contact or ingestion of materials contaminated with the urine, feces, or saliva of infected fruit bats (flying foxes), which are the natural carriers. Transmission between pigs can occur through direct contact or aerosols. Other animal species may become infected through contact with sick pigs or contaminated objects, further highlighting the zoonotic and transmissible nature of NiV across various species.

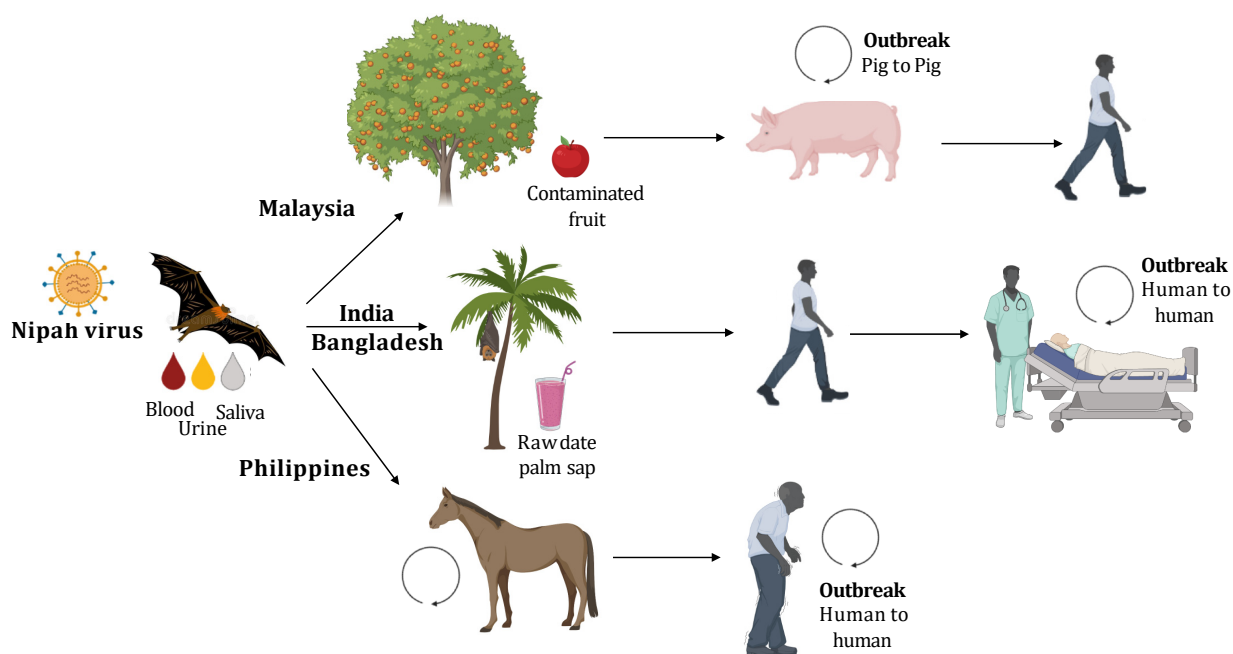


Fig 11: Different Nipah virus (NiV) transmission routes.

(Image Source: www.mdpi.com/2076-0817/11/12/1419)

NiV DISEASE IN DIFFERENT SPECIES

Nipah virus (NiV) in animals primarily affects pigs, where it manifests as respiratory and neurological disease, known as Porcine Respiratory and Encephalitic Syndrome (PRES) or "barking pig syndrome" (BPS). It is highly contagious among pigs, with clinical signs varying based on age and the individual animal's immune response. Mortality from the disease tends to be low, except in piglets, where the risk of death is higher. However, morbidity rates are significant across all age groups. The most common pathological findings in pigs affected by NiV include lung and central nervous system lesions.

Dogs infected with NiV display symptoms similar to distemper, with a high mortality rate. In cats, NiV outbreaks have been observed, particularly during the Malaysian outbreaks, with some infected cats succumbing to the disease. Interestingly, fruit bats, which are natural reservoirs of NiV, do not show significant signs of illness despite harboring the virus. These findings highlight the zoonotic and multi-species impact of NiV, which underscores the importance of controlling the virus in animals to prevent spillover to humans.

PREVENTION AND CONTROL FOR ANIMAL HUSBANDRY

Effective prevention and control measures in animal husbandry are crucial in managing Nipah virus outbreaks. The first step involves the immediate quarantine of the affected premises and culling of infected animals to prevent further spread. Following the culling, proper disposal methods, such as incineration, must be employed to handle contaminated carcasses safely. Another essential measure includes controlling bat access to pig farms, as bats are known to be natural reservoirs of the virus. Finally, a complete ban on the movement of animals from infected farms to other areas must be enforced to reduce the risk of spreading the infection to new locations. These steps are vital for limiting the transmission of the virus within and beyond the farm.

Notes

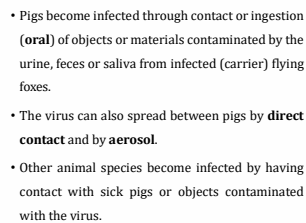
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Nipah Virus Encephalitis is a WOAAH-listed reportable disease and is one of the notifiable disease in India

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NIPAH VIRUS

Notes



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Fruit bats show no serious signs of infection

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NIPAH VIRUS

Session-7

Outbreak Management

Course No. 007	Session 7: Outbreak Management
Duration	30 minutes
Learning Objectives	• Describe outbreak management and case classification • Understand outbreak situation in India • Understanding public health scenario • Describe outbreak response and preparedness • Describe collaboration between healthcare providers and public health authorities
Pre-requisite knowledge/skill	• Basic understanding of outbreak investigation, case classification, and emergency preparedness. • Familiarity with public health infrastructure and past outbreak scenarios in India.
Competencies to be achieved	• Understanding potential sources of outbreak • Describing reported Nipah virus outbreaks in India • Understanding roles of departments in combatting outbreaks • Explain measures to improve outbreak response and preparedness • Competency in effectively managing outbreaks of Nipah virus

Outbreak investigations of Nipah Virus disease are critical endeavors aimed at understanding the dynamics of the virus's transmission and implementing effective control measures. Typically initiated in regions where Nipah outbreaks occur, these investigations involve a multidisciplinary approach, combining epidemiological, clinical, and laboratory analyses. The process includes identifying and confirming cases, tracing contacts, and studying the patterns of transmission. Researchers collect biological samples for laboratory testing, helping in the confirmation of Nipah cases. Additionally, environmental assessments are conducted to identify potential sources and modes of transmission, often focusing on areas with a high prevalence of fruit bats, the natural reservoir of the virus. Timely and thorough outbreak investigations play a pivotal role in implementing targeted interventions, such as quarantine measures, culling of infected animals, and public health education, ultimately contributing to the containment and prevention of further Nipah virus spread.

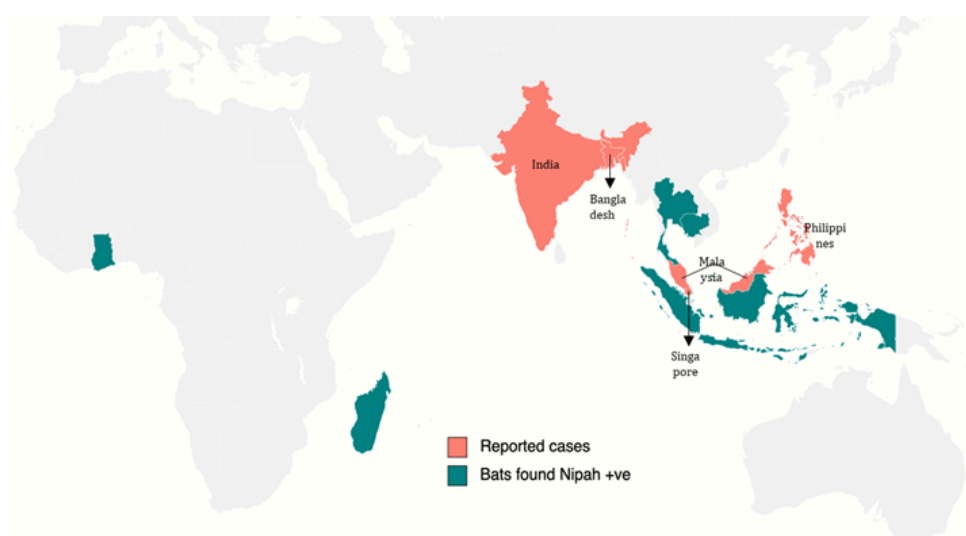


Fig 12: Distribution of nipah virus affected countries and potential countries under threat of future nipah virus outbreak

(Image source: <https://jhpn.biomedcentral.com/articles/10.1186/s41043-024-00666-5>)

HOSPITAL-BASED INTERVENTION TO CONTROL OUTBREAKS

Several outbreak investigations indicated that caregivers of Nipah patients and medical staff in hospitals can become infected through physical contact, e.g. while caring for or examining patients without precautions such as the use of gloves and masks. This human-to-human transmission can occur through Nipah-contaminated respiratory secretions entering the airway of an uninfected individual. Several pilot intervention studies have been conducted to improve hygiene behaviors of health workers and nurses in hospitals in Bangladesh and prevent such transmission through improved hand hygiene or use of gloves and masks and establishment

of isolation corners in three tertiary hospitals in three districts (personal communication to Shahana Parveen?). Although these studies suggest that hygienic behaviors with focused attention can reduce the risk of Nipah transmission in hospitals, cultural norms for caring for family members that require close physical contact as well as hand hygiene remain challenging in resource-constrained hospitals.

STEPS IN OUTBREAK INVESTIGATION

The steps involved in an outbreak investigation are summarized as follows:

1. Determine the existence of an outbreak:

- Assess whether a clustering of cases, a disease-prone cluster, or a single case of a disease of international concern has emerged.
- Review past incidence rates, changes in surveillance systems, and population changes.

2. Confirm the diagnosis:

- Clinically describe the cases and collect appropriate biological samples.
- Ensure samples are sent under appropriate conditions to a referral laboratory for diagnosis.

3. Define a case:

- Formulate a case definition that aligns with the generic case definitions provided in the guidelines.

4. Search for cases:

- Search within time and space limits based on the case definition.
- Compile and update a line listing of cases for monitoring.

5. Generate hypotheses using descriptive findings:

- Describe the outbreak over time using an epidemic curve.
- Calculate incidence based on population groups (age, gender, etc.).
- Conduct interviews to generate hypotheses and identify the common point of infection.

The key elements for Nipah should focus on the following areas:

1. Case Identification and Reporting:

- Immediate identification of suspected Nipah Virus cases based on clinical symptoms (fever, altered mental status, respiratory issues) and epidemiological links to affected areas or known cases.
- Confirmation through laboratory testing such as RT-PCR of throat swab, urine, or blood samples.
- Ensure reporting to local health authorities and isolation of suspected cases immediately upon suspicion.

2. Contact Tracing:

- Detailed contact tracing of individuals who had close contact with confirmed or probable cases, focusing on those with high-risk exposure (direct contact with body fluids or prolonged proximity).

- Monitor these contacts for 21 days for symptoms and manage them with home quarantine or hospital isolation as needed.
- 3. Surveillance and Risk Categorization:**
 - Categorize contacts into high-risk and low-risk based on their exposure and provide tailored follow-up actions, including regular health checks and symptom monitoring.
 - Surveillance should be maintained in both healthcare and community settings to capture any new cases or clusters.
 - 4. Laboratory Investigations:**
 - Conduct laboratory confirmation for suspected cases, with samples transported to designated laboratories (NIV Pune or other reference labs).
 - Ensure biosafety protocols for sample collection, transportation, and testing to minimize risk of laboratory transmission.
 - 5. Quarantine and Isolation Measures:**
 - Immediate isolation of confirmed cases in designated healthcare facilities, with strict infection control protocols in place.
 - Isolation protocols must include well-demarcated isolation wards, use of PPE, and proper donning/doffing procedures for healthcare staff.
 - 6. Community and Healthcare Education:**
 - Raise awareness among healthcare workers and the community about the transmission dynamics of Nipah virus and preventive measures.
 - Ensure healthcare workers are trained in infection control practices and are aware of protocols for managing suspected cases.

CASE DEFINITIONS TO BE USED FOR NIPAH OUTBREAK

Suspect Nipah Case:

- A person from an affected community exhibiting:
 - ◊ Fever with new onset of altered mental status or seizure.
 - ◊ Fever with headache and/or cough or shortness of breath.

Probable Nipah Case:

- A suspect case who lived in the same area as a confirmed Nipah case and died before diagnostic specimens could be collected.
- A suspect case who had direct contact with a confirmed case in a hospital setting during the outbreak period and died without complete diagnostic testing.

Confirmed Nipah Case:

- A suspected case with laboratory confirmation through:
 - Nipah virus RNA identified via PCR from respiratory secretions, urine, or cerebrospinal fluid (CSF).
 - Isolation of Nipah virus from respiratory secretions, urine, or CSF.

WHY TO INVESTIGATE AN OUTBREAK?

Investigating an outbreak is crucial for several reasons. Firstly, it helps in understanding the epidemiology of the disease, including how the virus is transmitted, its incubation period, and the population at risk. This information is essential for developing effective prevention and control strategies. Secondly, outbreak investigations aid in the early detection and confirmation of cases, allowing for prompt medical intervention and treatment. Identifying and isolating confirmed cases also helps prevent further transmission within the community. Thirdly, investigating the outbreak enables the identification of potential sources of the virus, such as infected animals or contaminated food, facilitating targeted interventions to mitigate the spread. Moreover, understanding the patterns of transmission informs public health measures, including quarantine, contact tracing, and vaccination strategies if available. Overall, investigating a Nipah Virus outbreak is instrumental in safeguarding public health, preventing further cases, and implementing timely and appropriate control measures.

WHO TO PREPARE FOR OUTBREAK INVESTIGATION

Establish a Rapid Response Team:

Assemble a multidisciplinary team comprising epidemiologists, clinicians, laboratory experts, and communication specialists.

Develop Standard Operating Procedures (SOPs):

Create comprehensive SOPs for case identification, confirmation, and data collection to ensure consistency and accuracy throughout the investigation.

Enhance Surveillance Systems:

Strengthen existing surveillance systems to promptly identify and report suspected cases, enabling a swift response.

Training and Capacity Building:

Train healthcare workers and field staff on outbreak investigation protocols, sample collection, and safety measures.

Secure Laboratory Capacity:

Ensure that laboratories are equipped with necessary diagnostic tools and have the capacity to handle a surge in samples.

Stockpile Necessary Supplies:

Stockpile medical and protective equipment, testing kits, and other supplies required for field investigations.

Establish Communication Protocols:

Develop clear communication channels within the response team, with healthcare facilities, and with the public to disseminate accurate information promptly.

Community Engagement and Education:

Prepare educational materials for the public, emphasizing preventive measures, symptoms, and the importance of reporting suspected cases.

Coordination with Local Authorities:

Collaborate with local health departments, government agencies, and international organizations to ensure a coordinated and effective response.

Logistical Planning:

Plan logistics for field investigations, including transportation, accommodation, and security measures for the response team.

Risk Assessment:

Conduct a risk assessment to identify potential hotspots, vulnerable populations, and factors contributing to the outbreak.

Legal and Ethical Considerations:

Understand and adhere to legal and ethical guidelines regarding patient privacy, data confidentiality, and informed consent during the investigation.

Simulation Exercises:

Conduct simulation exercises to test the preparedness of the response team and identify areas for improvement.

Continuous Monitoring and Evaluation:

Implement a system for continuous monitoring and evaluation of the outbreak investigation process to make real-time adjustments as needed.

In regions where Nipah virus (NiV) outbreaks have occurred, adopting preventive measures becomes paramount to mitigate the risk of infection. People should prioritize regular handwashing with soap and water to maintain proper hygiene standards. Avoiding contact with sick bats or pigs is crucial, as these animals can serve as potential carriers of the virus. Additionally, individuals should steer clear of areas where bats are known to roost to minimize the risk of exposure. Dietary precautions are also advised, urging people to refrain from consuming products that could be contaminated by bats, such as raw date palm sap, raw fruit, or fruit found on the ground. Equally important is the avoidance of contact with the blood or body fluids of individuals known to be infected with NiV, as these fluids can serve as sources of transmission. Adhering to these guidelines plays a pivotal role in preventing the further spread of Nipah virus and safeguarding community health.

- NIV outbreaks have so far been reported in Malaysia, Bangladesh, India, and Philippines.
- However, Several surveillance studies have provided evidence of antibody presence in various countries, including Cambodia, Thailand, Madagascar, and Ghana.



Image source: <https://phn.biomedcentral.com/articles/10.1186/s41043-024-00666-5>

Center for Data Mining, MIT, Boston

NIPAH VIRUS

A map of Southeast Asia with a red box highlighting the location of Malaysia. The text "MALAYSIA" is written inside the red box, with "with Penang Island" written below it.

September 1998

- The first outbreak of a novel virus, Nipah, occurred among farmers in Malaysia's pig farming industry near Ipoh, Perak,
- Bat bitten fruits contaminated with NiV-M were consumed by pigs and workers handling the pigs were infected with NiV

December 1998

- The second outbreak occurred in the state of Negri Sembilan
- During this period, a similar and third outbreak was reported in the nearby areas of Bukit Pelandok

In the beginning, the causative agent for the outbreaks was mistaken to be Japanese encephalitis virus and preventive measure were taken accordingly.

By March 1999, Nipah was confirmed as the cause, transmitted from infected pigs to humans.

Transmission was contained by May 1999, with total of 105 deaths occurred from 265 cases with 39.6% mortality.

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NIPAH VIRUS

- In late September 1998, virus began from Malaysia, spreading quickly from the Kinta Valley in Perak to areas in Negri Sembilan, resulting in 11 cases and 1 death in Singapore.
- Singapore took immediate preventive measures, suspending live pig imports from affected farms, increasing fogging and larvicides, and ordering checkups for abattoir workers and pig traders.



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NIPAH VIRUS

Bangladesh

Population: 150 million
 Area: 147,570 km²
 Capital: Dhaka
 Language: Bengali

- The first outbreak was recorded in the district of Meherpur, Bangladesh in April 2001 with 13 confirmed cases.
- Bat saliva- and excreta-contaminated palm sap consumption led to NiV-B infection in humans and was spread further via nosocomial mode.
- Down the line, many districts faced NiV outbreak from April 2001 to February 2015 with few districts also faced recurrent outbreaks.
- About 261 confirmed cases with 199 deaths were reported with a mortality rate of 76.2% up till 2015.

Center for One Health, INC, 2019

NIPAH VIRUS

[illegible]

NIPAH VIRUS

- Center for One Health, INC; AAU/WHO

NIPAH VIRUS

Center for One Health, INC; Atlanta

NIPAH VIRUS

2019

- 2023

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NIPAH VIRUS

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Clinical picture of 10 cases of the outbreak in Kerala of which six were positive for Nipah infection and four cases were probable Nipah cases including the index case who was admitted and treated in Govt Medical college Calicut.

Clinical features	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
Age (years)	26	49	43	23	48	27	19	32	75	28
Sex (M/F)	M	M	F	F	M	M	F	F	F	M
Residence period (days)	154	154	12	4	7	7	11	9	6	7
Fever	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Severe illness	No	No	No	No	No	No	No	No	No	No
Myalgia	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Headache	Yes	No	No	Yes	No	No	Yes	No	No	Yes
Vomiting	Yes	No	No	Yes	No	No	Yes	No	No	No
Altered consciousness	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes
Seizures	Yes	No	No	No	No	No	Yes	No	Yes	No
Central nervous system	No	No	No	No	No	No	No	No	No	Probable
Respiratory	No	No	No	No	No	No	No	No	No	No
Diarrhoea	Yes	Yes	No	No	No	No	Yes	No	No	No
Cough	No	Yes	No	Yes	No	No	Yes	No	No	No
Rhinorrhoea	No	No	No	No	No	No	No	No	No	No
Lower respiratory	Yes	No	No	No	No	No	No	Yes	No	Yes
Chest X-ray	-	No	Fluffy	ADH	Not taken	Normal	RT-PCR	Not taken	Not taken	No
Tracheal	Increased	No	Increased	Increased	Increased	No	No	Increased	Increased	No
Tracheobronchitis	Yes	Yes	No	No	No	No	No	No	No	No
Hyperpnea	No	No	No	No	No	No	No	No	No	No
Respiratory distress	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes
Antibiotic resistance	No	No	No	No	No	No	No	No	No	No

<https://jcp.org/2016/04/16/case-series-on-the-recent-nipah-epidemic-in-kerala>

Centre for One Health, NCDC, MoHFW

NIPAH VIRUS

Outbreak Investigation

Components of an outbreak investigation (General)

- | | |
|---|--|
| Determine the existence of an outbreak. | <ol style="list-style-type: none"> 1. Determine whether there is a clustering of case, a cluster of cases of a prone disease or a single case of disease of international importance. 2. Review incidence in the past. 3. Check for recent changes in the surveillance system. 4. Check for recent changes in the population size. |
| Confirm the diagnosis. | <ol style="list-style-type: none"> 1. Make clinical description. 2. Collect appropriate biological samples for diagnosis. 3. Send the biological samples in appropriate condition to referral laboratory. |
| Define a case | <ol style="list-style-type: none"> 1. Formulate case definition using the generic case definition (as per the guidelines). |
| Search for cases | <ol style="list-style-type: none"> 1. Search for cases within the time and space limits of the case definition. 2. Compile and update a line listing of cases. |
| Generate hypothesis using descriptive findings. | <ol style="list-style-type: none"> 1. Describe the outbreak over time using an epidemic curve. 2. Calculate population-based incidence of age and gender groups. 3. Conduct hypothesis generating interviews to understand the common point of infection. |

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NIPAH VIRUS

Outbreak Investigation- for Nipah

1. Case Identification and Reporting

- Immediate identification of suspected Nipah Virus cases based on clinical symptoms (fever, altered mental status, respiratory issues) and epidemiological links to affected areas or known cases.
- Confirmation through laboratory testing such as RT-PCR of throat swab, urine, or blood samples.
- Ensure reporting to local health authorities and isolation of suspected cases immediately upon suspicion.

2. Contact Tracing

- Detailed contact tracing of individuals who had close contact with confirmed or probable cases, focusing on those with high-risk exposure (direct contact with body fluids or prolonged proximity).
- Monitor these contacts for 21 days for symptoms and manage them with home quarantine or hospital isolation as needed.

3. Surveillance and Risk Categorization

- Categorize contacts into high-risk and low-risk based on their exposure and provide tailored follow-up actions, including regular health checks and symptom monitoring.
- Surveillance should be maintained in both healthcare and community settings to capture any new cases or clusters.

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NIPAH VIRUS

4. Laboratory Investigations

- Conduct laboratory confirmation for suspected cases, with samples transported to designated laboratories (NIV Pune or other reference labs).
- Ensure biosafety protocols for sample collection, transportation, and testing to minimize risk of laboratory transmission.

5. Quarantine and Isolation Measures

- Immediate isolation of confirmed cases in designated healthcare facilities, with strict infection control protocols in place.
- Isolation protocols must include well-demarcated isolation wards, use of PPE, and proper donning/doffing procedures for healthcare staff.

6. Community and Healthcare Education

- Raise awareness among healthcare workers and the community about the transmission dynamics of Nipah virus and preventive measures.
- Ensure healthcare workers are trained in infection control practices and are aware of protocols for managing suspected cases.

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NIPAH VIRUS

[illegible]

Control measures for outbreak area

In areas where Nipah virus (NiV) outbreaks have occurred, people should –

- Practice handwashing regularly with soap and water
- Avoid contact with sick bats or pigs
- Avoid areas where bats are known to roost
- Avoid eating or drinking products that could be contaminated by bats, such as raw date palm sap, raw fruit, or fruit that is found on the ground
- Avoid contact with the blood or body fluids of any person known to be infected with NiV

Session-8

Surveillance and Risk Communication

Course No. 008	Session 8: Surveillance & Risk Communication
Duration	20 minutes
Learning Objectives	• Understand surveillance of NIPAH VIRUS • Describe risk communication and public awareness
Pre-requisite knowledge/skill	• Basic knowledge of infectious disease surveillance systems and reporting mechanisms. • Familiarity with principles of risk communication and community engagement. • Awareness of strategies for public education and behavior change during health emergencies.
Competencies to be achieved	• Comprehension of the various methods employed for surveillance and monitoring of NIPAH VIRUS cases. • Description of strategies for risk communication and raising public awareness about NIPAH VIRUS • Understanding the importance of collaboration between healthcare providers and public health authorities in addressing NIPAH VIRUS cases

Surveillance of Nipah Virus is a critical component in managing and preventing outbreaks. It involves systematic monitoring of communities and healthcare facilities to detect and track the occurrence of Nipah cases. Surveillance efforts include the timely identification and reporting of suspected cases, allowing for prompt investigation and intervention. Diagnostic testing, often involving laboratory confirmation of cases, ensures accuracy in identifying Nipah infections. Additionally, surveillance extends to monitoring potential sources of the virus, such as bats and other animals, as well as assessing environmental factors that may contribute to its transmission.

An effective surveillance system provides essential data for understanding the epidemiology of Nipah Virus, enabling public health authorities to implement targeted control measures, such as quarantine, contact tracing, and public awareness campaigns. Continuous vigilance through surveillance is indispensable in preventing and managing Nipah Virus outbreaks.

CASE IDENTIFICATION AND CONTACT TRACING

These contacts must be followed for the appearance of symptoms of NiV during the longest incubation period (21 days). They must be transported to an appropriate care facility if they develop symptoms with proper infection control practices.

RISK STRATIFICATION OF CONTACTS

RISK CATEGORY	DESCRIPTION
High risk	- Any contact with body fluids (blood, urine, saliva etc) of a confirmed case of Nipah - Any contact with body fluids of a probable case who died without a lab confirmation of Nipah - Spend time in proximity or in closed space form or ethanol equal to 12 hrs.?
Low risk	Any other contact such as touching, contact with clothes or linen or any other item used

FOLLOW-UP ACTION

RISK CATEGORY	Follow-up Action
High risk	- Asymptomatic- Home quarantine with active follow up for fever, by health workers using telephone, twice a day for 21 days. - Symptomatic (fever)- Immediate admission in designated isolation ward with ICU facility
Low risk	Asymptomatic-Home quarantine and follow up for fever by telephone. Symptomatic (fever)- Immediate admission in designated isolation facility

WHEN TO INVESTIGATE ON NIPAH OUTBREAK?

Investigating a Nipah outbreak is crucial as soon as there is suspicion or confirmation of cases. Early detection and response are vital to understanding the dynamics of the outbreak, implementing effective control measures, and preventing further transmission.

Suspected Cases Arise:

Initiate an investigation when individuals exhibit symptoms consistent with Nipah Virus Disease, such as fever, encephalitis, or acute respiratory distress syndrome.

Confirmed Cases are Identified:

Upon confirmation of nipah cases through laboratory testing, immediate investigation is necessary to understand the source, mode of transmission, and potential contacts.

Investigation should commence when?

Cluster of Cases Occurs:

Investigate promptly when a cluster of Nipah cases is identified, indicating potential localized transmission and the need for targeted interventions.

Unexplained Deaths:

Investigate if there are unexplained deaths in the community, especially if there is a history of exposure to potential sources of the virus.

Epidemiological Link to Animals:

Investigate when there is an epidemiological link between human cases and animals, particularly bats or pigs, which are known reservoirs for the virus.

Unusual Clinical Presentation:

Investigate cases with an unusual clinical presentation or severity that raises concerns about the potential involvement of Nipah virus.

High-Risk Areas:

High-risk areas, such as those with a history of previous outbreaks or where there is evidence of the presence of potential reservoirs, warrant immediate investigation.

Timely initiation of an outbreak investigation is essential for implementing control measures, protecting public health, and preventing further spread of the Nipah virus.

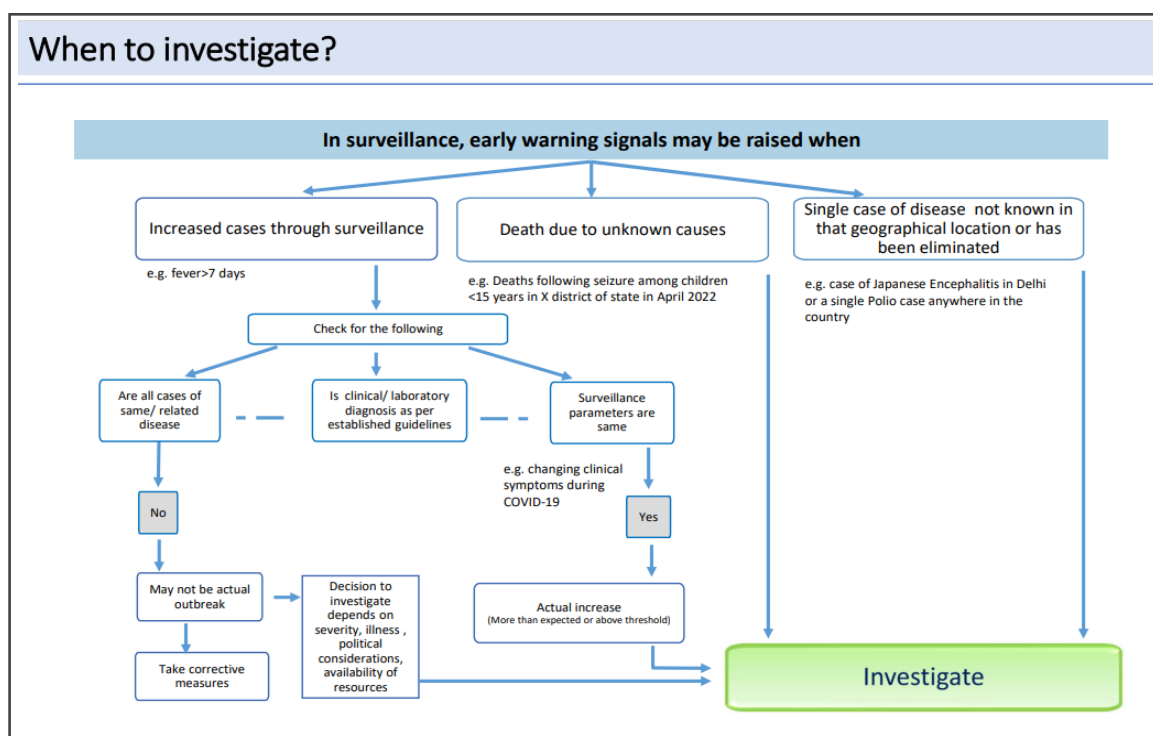
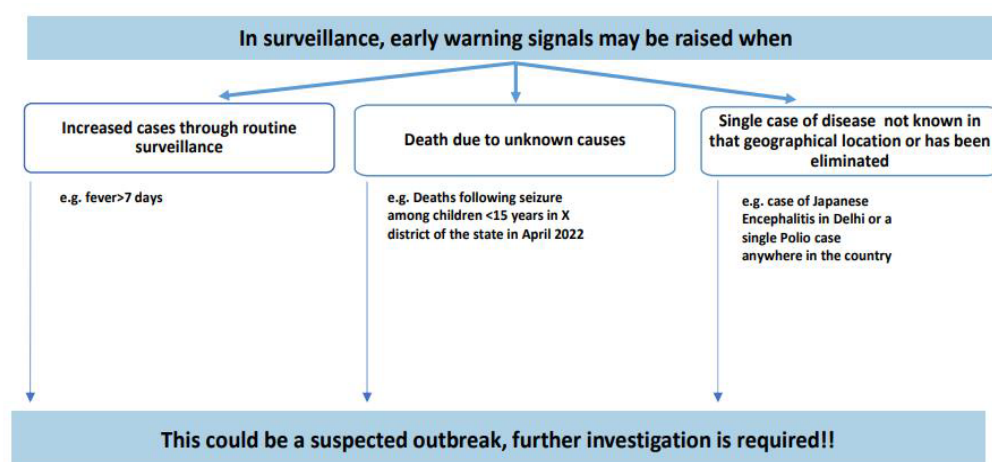


Fig 13: When to investigate an Outbreak



In addition to above mentioned, shifting in the age distribution of cases, high vector density, and natural disasters could also be early warning signs

Any Reporting unit can submit an early warning signal of an impending outbreak in their area to the District Surveillance Unit, irrespective of the fact that the signal may or may not be a confirmed outbreak

Fig 14: Early warning signs of an outbreak

COMMUNICATION AND PUBLIC AWARENESS

Communication and public awareness are integral components of managing a Nipah virus outbreak. Establishing clear and transparent communication channels is essential to disseminate accurate information, address public concerns, and promote preventive measures. Here's how communication and public awareness can be effectively managed:

Clear Messaging:

Develop clear and concise messages about the Nipah virus, its symptoms, modes of transmission, and preventive measures.

Local Language and Culture:

Tailor communication to the local language and cultural context to ensure that information is easily understood and accepted by the affected community.

Engage Community Leaders:

Involve community leaders, religious figures, and local influencers to convey messages, build trust, and encourage compliance with preventive measures.

Public Service Announcements:

Develop and broadcast public service announcements highlighting key information about Nipah virus prevention, symptoms, and the importance of seeking medical attention.

Education Materials:

Distribute educational materials, such as pamphlets and posters, in healthcare facilities, community centers, and public spaces to reinforce key messages.

Hotlines and Helplines:

Establish hotlines or helplines to provide a direct channel for the public to seek information, report symptoms, and receive guidance during the outbreak.

Address Misinformation:

Monitor and address misinformation promptly to prevent the spread of rumors and false information that may contribute to fear and panic.

Use of Multiple Channels:

Utilize various communication channels, including radio, television, social media, and community meetings, to reach a broad audience and maximize the impact of awareness campaigns.

Interactive Workshops and Training:

Conduct interactive workshops and training sessions to empower communities with the knowledge and skills to protect themselves from Nipah virus.

Regular Updates:

Provide regular updates on the status of the outbreak, control measures implemented, and any changes in guidelines to keep the public informed.

Community Engagement:

Engage with the community through town hall meetings, focus group discussions, and feedback sessions to understand their concerns and tailor communication accordingly.

Effective communication and public awareness play a pivotal role in fostering community cooperation, encouraging adherence to preventive measures, and ultimately containing the spread of the Nipah virus during an outbreak.

HOW TO PREVENT INFECTION FROM NIPAH VIRUS

Support Animal Health Surveillance:

Support efforts to monitor and control Nipah virus in animals through health surveillance and quarantine measures.

Seek Prompt Medical Attention:

If experiencing symptoms such as fever, headache, and respiratory issues, seek prompt medical attention and inform healthcare providers about any potential exposure to the virus.

Preventing infection from Nipah virus involves adopting various measures to minimize exposure. Here are some preventive steps:

Practice Good Hand Hygiene:

Wash hands regularly with soap and water, especially after being in public places or in contact with animals.

Avoid Contact with Sick Animals:

Avoid contact with sick bats, pigs, or other animals that may be carriers of the virus.

Avoid Close Contact with Infected Individuals:

Steer clear of close contact with individuals known to be infected with Nipah virus, especially with their blood or body fluids.

Practice Safe Burial Procedures:

Follow safe burial practices to minimize the risk of virus transmission during funeral ceremonies.

Educate Yourself and Others:

Stay informed about Nipah virus, its symptoms, and preventive measures. Share this knowledge with others to enhance community awareness.

Avoid Consuming Raw Date Palm Sap:

Refrain from consuming raw date palm sap or any raw fruits that could be contaminated by bat saliva or urine.

Use Personal Protective Equipment (PPE):

If working with animals or in areas at risk, use appropriate PPE such as gloves and masks to minimize the risk of exposure.

Implement Quarantine Measures:

If an outbreak is suspected, adhere to quarantine measures to prevent the spread of the virus within the community.

Avoid Consuming Contaminated Food or Water:

Be cautious about consuming food or water that may have been contaminated by bat saliva, urine, or other animal secretions.

Promote Community Engagement:

Engage with the community to build awareness, address concerns, and encourage the adoption of preventive measures.

It's important to note that, as of latest update in January 2022, there is no specific vaccine or antiviral treatment for Nipah virus. Therefore, preventive measures focus on reducing the risk of exposure and transmission. Stay updated with local health authorities for any new guidelines or developments related to Nipah virus prevention.

Surveillance

- Surveillance is the ongoing systematic collection, collation, analysis, and interpretation of data; and the dissemination of information to those who need to know in order that action may be taken.
- One of the major aspects of surveillance is generation of early warning signals
- Early warning signals could be used to anticipate a critical transition before it is reached.



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NiV Disease Surveillance

Surveillance tools for NiV should include

- Surveillance programmes for humans and animals in endemic and bordering non-endemic areas can be used to monitor the spread of disease.
- Reliable laboratory assays for early detection of disease in communities and livestock.
- One Health approach to understand the fruit bat ecology, NiV disease seasonality and the transmission risk of other intermediate hosts.
- Understanding the wildlife reservoir, to manage the risk of reintroduction into animal or human populations
- Improvement of diagnostic algorithms building on clinical experiences;
- Validation of procedures to inactivate infectivity of clinical samples;



Image source: <http://www.informaworld.com/doi/10.1080/10447310600580000>

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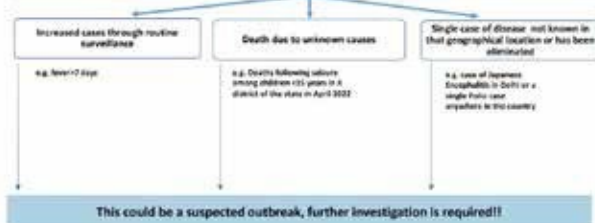
When to investigate?



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In surveillance, early warning signals may be raised when



In addition to above mentioned, shifting in the age distribution of cases, high vector density, and natural disasters could also be early warning signs

Any Reporting unit can submit an early warning signal of an impending outbreak in their area to the District Surveillance Unit, irrespective of the fact that the signal may or may not be a confirmed outbreak

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Notes

ANNEXURES

Annexure 1-Sampling, Storage and Transportation of samples for diagnosis

Sample collection

The samples should be collected as early as possible (preferably within 4 days) with all biosafety precautions and accompanied with detailed history of patients on the proforma which can be obtained from the testing laboratory.

To ensure safety, sample collection should be conducted exclusively after the patient's admission to a properly secured isolation facility. It is crucial to guarantee that the staff member performing the collection is equipped with appropriate personal protective equipment (PPE). During sample collection wear complete disposable Personal Protective Equipment's (N95 mask, double surgical gloves, gowns, goggles foot cover, etc). Wash hands with soap and water at least for 30 seconds and then clean hand using 1-2 ml alcohol-based hand sanitizer before and after collection of samples. Exercise special carefulness while taking off PPE components after doing a sample collection/nursing procedure.

The recommended samples are:

- Throat swab in viral transport medium
- Urine 5ml in universal sterile container
- Blood in red vacutainer (5ml)
- CSF(1-2ml) in sterile container

Samples should be collected as soon as possible (preferably within 4 days), all biosafety precautions should be observed, and a detailed patient history should be attached to the form available from the testing laboratory.

Specimen collection should be done post-collection in a well-protected isolation facility, ensuring that the person performing the collection is wearing appropriate PPE for her.

Wear fully disposable personal protective equipment (N95 mask, double surgical gloves, gown, goggles, foot covers, etc.) during sample collection. Wash hands with soap and water for at least 30 seconds and clean with 1-2 mL of alcohol-based hand sanitizer before and after sample collection.

The recommended pattern is:

- Pharyngeal swabs as viral delivery vehicles
- 5 ml of urine in a sterile universal container

- Blood Red Vacuum Cleaner (5ml)
- Sake (1-2ml) in a sterile container

Transportation and Storage of samples

Samples should be safely packed in triple container packing and should be transported securely under cold chain (2-8°C) to the testing laboratory with prior intimation.

Samples in vials should be securely sealed and placed within high-quality zip-lock bags. To prevent leakage, the bags should be wrapped with an ample amount of absorbent cotton padding. Furthermore, the plastic bag containing the samples should be enclosed in another zip-lock bag and securely sealed with adhesive tape. This double-layered carrier should then be positioned inside a rigid container, sealed with impermeable tape or plaster, and placed within a thermocol box or vaccine carrier containing ice packs. Additionally, the case sheets containing comprehensive information should be enclosed in a plastic bag and affixed to the outside of the container. Samples should be transported at 2-8°C to the designated lab within 24 hours.

Samples must be securely packed in triple container packages and transported with advance notice to the laboratory safely via the cold chain (2-8°C).

Vials containing sealed specimens are placed in high-quality zip-lock bags wrapped with sufficient absorbent batting to prevent the inner material from leaking out of the bag. Plastic bags should likewise be stored inside another zip-lock bag that is sealed with tape. This carrier should be placed in a rigid container sealed with impermeable tape or plaster and placed in a thermal box/vaccine pack with ice packs. Full Information Drop sheets should be placed in a plastic bag and taped to the outside of the container.

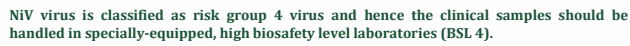
Samples should be transported to a designated laboratory within 24 hours at 2-8°C.

Safety considerations

1. Wash hands thoroughly with soap and water for 20 seconds after contact with sick patients.
2. Appropriate masks and gloves should be worn during history taking, physical examinations, specimen collection, and other procedures managing suspected cases of Nipah.
3. Follow standard nosocomial infection control precautions.
 - Hand hygiene
 - Use PPE, especially when removing PPE components.
 - Use disposable equipment (NG tubes, ET tubes, oxygen masks) when handling patients.
 - Safely dispose of potentially infectious items such as his used PPE, linen, and patient clothing
4. All suspected cases should be admitted to a designated hospital isolation ward/facility prior to sample collection. If Nipah is suspected, bystanders should not enter the station. Access to isolation areas for hospital staff should be kept to a minimum and mandatory purpose restriction protocols should be followed.

5. Isolate all suspected Nipah cases from all patients in the isolation ward/facility.
6. Avoid unnecessary contact with questionable nipa falls or use barrier grooming. Keep beds at least 2 meters apart
7. Spills of bodily fluids in operating rooms/wards should be handled according to the Department of Health's infection control guidelines.
8. Immediately report approval of suspected cases of Nipah to State Surveillance and CSU (IDSP) in prescribed daily reporting format
9. The funeral director must wear PPE while handling the corpse. A sealed bag provided for this purpose should be used to transport the remains.

- **The following samples are collected**
 - Throat swab to be collected in viral transport medium
 - Urine approx 10 ml in universal sterile container
 - Blood in plain vial (at least 5ml)
 - CSF (at least 1 ml) in a sterile container

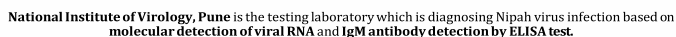


NIPAH VIRUS

Samples should be safely packed in triple container packing and should be transported under cold chain (2-8°C) to the testing laboratory with prior intimation.

NIPAH VIRUS

- NIV blood sample [Serum or plasma or blood in EDTA]
- Collect in screw cap or plastic vials, with proper label.
- Keep in good quality plastic bags
- Sealed by hand or tied with rubber bands to avoid leakages
- Place in another plastic container which should be sealed with adhesive tape.
- Use third plastic bag sealed with rubber bands
- Place in a thermocol or vaccine carrier containing ice
- The case sheets with complete information should be placed in a plastic bag or envelop
- Paste on the outside of the thermocol or vaccine container.
- Decontaminate the outer surface of the container with
 - bleach or 1% hypochlorite solution or 5% lysol



NIPAH VIRUS

- 1 Samples must be transported at 2-8°C
- 2 Samples should be stored at 2-8°C if they arrive at the laboratory within 48 hours
- 3 If shipping time is expected more than 48 hours, the samples should be sent using dry ice
- 4 Sample must be stored at -70°C if storage is required for longer periods

NIPAH VIRUS

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The packaging consists of three layers as follows –

Secondary receptacle: A second durable, watertight, leak-proof receptacle to enclose and protect the primary receptacle(s). Several wrapped primary receptacles may be placed in one secondary receptacle. Sufficient additional absorbent material must be used to cushion multiple primary receptacles.

Diagram illustrating the components of a product packaging assembly:

- Sealed, bagged primary microcapsule
- Absorbent material
- Sealed, bagged secondary microcapsule
- Outer packaging
- 1% Specification Mark

Image Source: Monkeypox Preparedness and response, OpenWIKOry

NIPAH VIRUS

Foot cover N-95 respirator Face Shield

Gloves Gown

Image Source: PPE, Microbeonline.com



NIPAH VIRUS

Steps	Supplies
Safety precautions	Appropriate PPE, waste disposal and disinfectants
Sample collection	Swabs, transport medium, suitable collection tools and containers
Sample labelling	Marker pens or barcodes
Triple layer packaging	Absorbent material, plastic bag, sturdy outer container, racks, cooler box, thermometer, etc.
Transportation	Regular schedule and method to move the samples to the laboratory, personnel trained in sample handling
Biosafety facility	BSL 3 or 4

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Annexure 2- Diagnostic Procedures

NiV is a BSL-4 agent. Persons collecting samples should wear personal protective equipment, including respirators. A diagnostic test that does not amplify the virus and minimizes specimen handling is preferred. Laboratory diagnosis in patients with a history of NiV can be performed using a combination of tests during the acute and convalescent stages of illness.

Virus isolation should be performed in an area with a suspected new outbreak for definitive diagnosis. Vero cells are preferred, but NiV can also be isolated in RK-13, BHK, and porcine spleen cells. Formation of large syncytia is usually observed within 23 days. However, an isolation attempt should only be failed after several passages of at least five days.

Reverse transcriptase polymerase chain reaction (RT-PCR) tests are faster, more sensitive, and safer than virus isolation. A series of highly sensitive quantitative RT-PCR (qRT-PCR) tests have been developed. As described by Mazzola and colleagues, these include RT-PCR (P,N genes), qRT-PCR (N gene, P gene, M gene), SYBR qRT-PCR (N gene), duplex nested RT-PCR (N gene), nested RT-PCR (P gene or L gene), multiplex bead-based qRT-PCR (N and P genes, NiV and Hendra virus) and multiplex array map qRT-PCR (N gene).

In addition, qRT-PCR primers and probes for the N gene of two different NiV strains, mNiV and bNiV, have been developed. High-throughput sequencing for a panel of viruses including NiV has recently been described. Oropharyngeal or nasal swabs RT-PCR is preferred.

Virus is detectable before the onset of clinical symptoms and three weeks after infection. Detection of viral antigens in fixed tissues by immunohistochemistry is also rapid and accurate. An antigen-capture enzyme-linked immunosorbent assay (ELISA) has been described for NiV and Hendra virus.

Real Time PCR Protocol

Real-time RT-PCR will be performed with the Superscript III Platinum One-Step Quantitative RT-PCR System Kit (Invitrogen, USA). For the real-time RT-PCR reaction, a volume of 25 µl was utilized and tested in duplicate. The forward primer NVBNF2B (5-CTGGTCTCTGCAGTTATCACCATCGA-3) and the reverse primer NVBN593R (5-ACGTACTTAGCCCATCTTCTAGTTTCA-3) were employed. Additionally, the primer NVBN542P (5-CAGCTCCCGACACTGCCGAGGAT-3) was also utilized in the reaction, as a probe, labeled with a fluorescent reporter dye, 6-carboxyfluorescein (FAM), and a non-fluorescent quencher, black hole 1 (BHQ1), at the 5' end and at the 3' end. The reaction, respectively contained 1 x 2 x SS buffer, 0.4 U RNase inhibitor (Applied Biosystems, Foster City, CA), 0.9 µM forward and reverse primers, 0.4 µM probe, 0.05 U/µl ROX and 0.1 U/ul SS III /Taq mix. The assay was performed on an ABI 7500 FAST (Applied Biosystems, Foster City, CA). The temperature cycling conditions were: (a) 1 cycle of 48 °C for 30 min and 95 °C for 10 min and (b) 45 cycles of 95 °C for 15 s and 60 °C for 1 minute.

Serological Methods

Virus neutralization is the OIE reference standard. A high throughput micro fusion inhibition assay (mFIT) that can identify and quantify neutralizing antibodies against NiV has recently been described. However, ELISA is the most used serological test for NiV. Testing is rapid and the use of recombinant proteins makes it feasible to perform in BSL-2 facilities is safe. As described by Mazzola and colleagues, ELISAs have been developed that target NiV IgG and IgM and the viral proteins G, N, M, and P. A multiplex bead-based antibody capture ELISA targeting the G-glycoprotein of both NiV and Hendra viruses has been described. A positive ELISA result should be confirmed by virus neutralization in a BSL-4 facility. The protocols for inactivating NiV in serum have been outlined, aiming to ensure safe handling within a BSL-2 facility. The recommended approach involves covering samples with aluminum foil and subjecting them to 30 minutes of UV irradiation, followed by heating at 56 °C for an additional 30 minutes.

Virus Culture

Virus isolation (virus culture) is performed in a Biosafety Level 4 (BSL-4) laboratory. Nipah virus (NiV) can be isolated from swabs (nasal or oropharyngeal), serum, urine, brain, lungs, kidney, and spleen samples, which should be transported at 4°C within 48 hours or frozen if stored for over 48 hours. The commonly used cell lines include Vero cells from African green monkey kidney and RK-13 cells from rabbit kidney, with Pteroid bat cell lines also developed. Infected monolayers are incubated at 37°C and examined for syncytia formation after 24–48 hours. NiV-induced syncytia appear as large multinucleated cells containing viral antigen, with nuclei initially aggregating in the center and later dispersing to the periphery in mature syncytia. Cytopathic effects (CPE) typically develop within three days, and if absent, two additional passages are recommended to confirm negative results. Virus identification from culture is performed using PCR or immunohistochemistry.

The diagram illustrates the steps of an ELISA assay:

- SAMPLE** (red liquid) is added to a **SERUM** vial.
- SERUM** is added to an **ELISA PLATE**.
- ELISA REAGENTS** (blue and yellow liquids) are added to the plate.
- The plate is placed in an **ELISA READER**.
- The reader displays the **READING OF OD VALUES** on its screen.

- Recombinant N protein based-ELISA - to screen the serum samples of pigs, developed at the High Security Animal Disease Laboratory (HSADL), Bhopal.**

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NIPAH VIRUS

Performed in BSL-4 laboratory.

Cytopathic effect (CPE) usually develops within 3 days.

Nipah virus-induced syncytia are large multinucleated cells containing viral antigen.

In absence of CPE, two 5-day additional passages are recommended to confirm negative results.

Identification of virus from cell culture is done by PCR or Immunohistochemistry

Contact for Data Needs: JCTPC, 880070

NIPAH VIRUS

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NOTE TO FACILITATORS

This guide has been meticulously designed to enhance the understanding and expertise doctors, veterinarians, paramedical staff, and laboratory personnel in dealing with Nipah cases. Your role is crucial in ensuring the success of this training, so please follow these instructions carefully:

Familiarize Yourself with the Content:

Thoroughly review all the materials provided in the Nipah training guide. This includes presentations, handouts, case studies and assessment tools.

Tailor the Training to Your Audience:

Understand the professional backgrounds of your participants (doctors, veterinarians, paramedics, and lab personnel). Tailor your examples and discussions to make the training relevant to their specific roles.

Set Clear Objectives:

Begin each session by clearly stating the objectives participants are expected to achieve by the end. This will give them a sense of direction and purpose throughout the training.

Create an Interactive Learning Environment:

Encourage active participation and open discussions. Use real-world scenarios to prompt critical thinking and problem-solving.

Use Multimodal Techniques:

Utilize a mix of teaching methods, such as presentations, group discussions and case-based learning. This will cater to different learning styles and keep participants engaged.

Encourage Questions:

Welcome questions and create a safe environment for participants to seek clarifications. This fosters deeper understanding and engagement.

Provide Regular Feedback:

Throughout the training, provide constructive feedback on participants' performance. This will help them identify areas for improvement and enhance their skills.

Summarize and Review:

At the end of each module, summarize key points and takeaways. Conduct a brief review to reinforce learning before moving on to the next topic.

Assessment and Certification:

Develop an assessment mechanism, such as quizzes, practical assessments, or case presentations. Issue certificates of completion to participants who meet the training requirements.

Adapt to Participants' Pace:

Gauge the participants' pace of learning. Adjust the training speed, accordingly, ensuring that everyone can follow and grasp the content.

Facilitate Networking:

Create opportunities for participants to interact and network with each other. This can lead to valuable knowledge exchange and collaboration.

Remember, your role as a trainer or facilitator is to guide participants through this comprehensive Nipah training with expertise, enthusiasm, and a dedication to enhancing their professional skills. Your efforts will contribute to building a more capable and knowledgeable medical workforce prepared to handle Nipah cases effectively.

Course Outline

It is imperative to underscore that the course outline harmonizes with the course schedule. Consequently, any modifications or adaptations made to the course schedule should be duly reflected in this course outline. This synergy between the schedule and the outline ensures consistency and alignment between training plans and their actual implementation.

NOTE: Make copies of the schedule, one for each participant and include in the training material bag.

Time	Topics/Activities	Training/Learning Methods	Resources/Materials
20 min	Welcome participants Facilitate introductions of participants Explore participants' expectations for the course	Open course with a word of welcome by organizers, lead trainers, etc. Facilitate the introductions of all participants and trainers. Explore participants' expectations for the course. Allow participants to freely explore their expectations. In the next session on review of the course objectives, address which expectations can be met, and which cannot be met.	Prepare welcome sign, Name badges
20 min	Review course objectives and schedule. Review components of the training guide	Review the course goals and objectives; the course design and expected outcomes; Review the course schedule, including starting and ending times and times for breaks and lunch; Review the materials to be used in the course and ensure that participants understand the use of course materials.	Copies of course schedule, one for each participant from Facilitators' Guide (FG). Full set of the training guide: Facilitators' Guide (FG) Questionnaire
20 min	Assess participants' pre-course knowledge	Distribute the Pre-course Knowledge Assessment sheet to each participant. Ask them to answer each question. Allow 15 minutes for assessment. Immediately review the correct responses—Have participants grade the papers while the trainer reviews the correct answers with them and collect the papers after reviewing all the answers.	Pre-Training Quiz Sheet for each participant
4-5 hours	Presentation/ Discussion	Use the PowerPoint slides to present information	Power Point slides on the sessions planned as per agenda
20 min	Assess participants' post training knowledge	Distribute the Post Training Knowledge Assessment sheet to each participant. Ask them to answer each question. Allow 15 minutes for the Post Training Knowledge Assessment.	Copies of Post Training Knowledge Assessment Sheets (one for each participant)
15 min	Course Evaluation	Ask questions of the participants and engage them in the presentation of the information.	
15 min	Closing	Closing remarks by training organizers. Distribute certificates to participants.	Certificate for each participant

PRE/POST TRAINING QUIZ

Trainee Name:

Date:

Designation:

Test taken before the training (yes/no):

Test taken after the training (yes/no):

Instructions for the trainee:

- The test quiz carries 22 questions
- Attempt all the questions.
- Put a tick mark on the correct option or fill the blanks with True/ False
- Please check whether all questions are answered before submitting

1. How is Nipah virus primarily transmitted to humans?

- a. Mosquito bites
- b. Inhalation of contaminated air
- c. Direct contact with infected animals
- d. Consumption of contaminated water

2. What is the primary host of the Nipah virus?

- a. Pigs
- b. Dogs
- c. Fruit bats
- d. Cattle

3. What are common symptoms of Nipah Virus Disease?

- a. Joint pain and muscle aches
- b. Visual disturbances
- c. Fever, headache, and encephalitis
- d. Gastrointestinal bleeding

4. Which regions are more prone to Nipah Virus outbreaks?

- a. North America
- b. Southeast Asia, including Bangladesh and India
- c. South America
- d. Europe and Australia

- 5. How can Nipah Virus Disease be prevented?**
 - a. Vaccination
 - b. Avoiding contact with infected animals
 - c. Wearing long sleeves and pants
 - d. Consuming raw meat from reliable sources
- 6. What role do fruit bats play in the epidemiology of Nipah Virus Disease?**
 - a. They are the primary reservoir of the virus
 - b. They transmit the virus through bites
 - c. They amplify the virus in pigs
 - d. They are not associated with the disease
- 7. What preventive measures are crucial to reduce the risk of Nipah Virus transmission in endemic areas?**
 - a. Proper hand hygiene
 - b. Use of mosquito nets
 - c. Vaccination of livestock
 - d. All the above
- 8. Who is at an increased risk of Nipah Virus infection due to their involvement in the cultivation of fruits like date palms?**
 - a. Health care workers
 - b. Urban residents
 - c. Agricultural communities
 - d. Students
- 9. According to the suspect case definition of Nipah Virus, an individual from an affected area is considered a potential case if presenting with which of the following symptoms?**
 - a. Acute fever with joint pain
 - b. Acute fever with severe headache
 - c. Chronic fever with fatigue
 - d. Acute fever with abdominal pain
- 10. In the context of Nipah Virus surveillance, what defines a Probable Nipah Case?**
 - a. Suspect case-patient with recent international travel history
 - b. Suspect case-patient with acute fever and joint pain
 - c. Suspect case-patient residing in the same village/house as a confirmed case during the outbreak or coming in direct contact with a confirmed case in a hospital setting and dying with suggestive symptoms
 - d. Suspect case-patient with chronic fever and fatigue

11. How would you define a Suspected Nipah Case based on the provided criteria?

- a. Individuals with chronic illnesses living in the same area as confirmed cases
- b. Patients with recent international travel history during the outbreak
- c. Individuals residing in the same villages/houses as suspected or confirmed Nipah cases during the outbreak period or having direct contact with a confirmed patient in a hospital, and who died with suggestive symptoms before a full diagnostic sample was collected
- d. Patients with mild respiratory symptoms and no known exposure to Nipah cases

12. How is a Confirmed Nipah Case determined based on laboratory confirmation?

- a. Presence of clinical symptoms consistent with Nipah Virus Disease
- b. Detection of Nipah virus RNA by PCR from blood samples
- c. Isolation of Nipah virus from feces or saliva
- d. Identification of Nipah virus RNA by PCR from respiratory secretions, urine, or cerebrospinal fluid, or isolation of the virus from these samples

13. How is a close contact defined in the context of Nipah Virus Disease?

- a. Anyone living in the same village as a Nipah case
- b. Individuals who have a history of international travel during the outbreak period
- c. Patients or individuals who have been in contact with a Nipah case (confirmed or probable) through admission to the same ward/common room, direct close contact during transport, contact during funeral ceremonies, exposure to bodily fluids, or touching clothing/linen of a suspected/confirmed case
- d. Individuals with mild respiratory symptoms and no known exposure to Nipah cases

14. What is the median incubation period for secondary cases that had a single exposure to a Nipah case?

- a. 5 days (range 3-9 days)
- b. 9 days (range 6-11 days)
- c. 12 days (range 8-16 days)
- d. 7 days (range 2-12 days)

15. In patients with fever and encephalitis and/or ARDS, which of the following diseases should be considered as differentials along with Nipah infection?

- a. Influenza
- b. Yellow fever
- c. Japanese encephalitis (JE)
- d. Typhoid fever

16. What is the status of treatment recommendations for Nipah virus disease?

- a. Ribavirin is widely recommended as a prophylactic agent.
- b. There is no established treatment for Nipah virus disease.
- c. Supportive care and symptomatic treatment are the main methods of treating human infections.
- d. Antiviral drugs are the primary mode of treatment for Nipah virus disease.

17. What is the recommended dosing regimen of ribavirin for adults with Nipah virus disease?

- a. 1000 mg loading dose on Day 1, followed by 500 mg every 12 hours for 10 days
- b. 2000 mg loading dose on Day 1, followed by 1000 mg every 6 hours for 4 days and 500 mg every 6 hours for the next 6 days
- c. 1500 mg loading dose on Day 1, followed by 750 mg every 8 hours for 7 days
- d. 2500 mg loading dose on Day 1, followed by 1250 mg every 4 hours for 5 days

18. What is the recommended dosing regimen of ribavirin for children with Nipah virus disease?

- a. Loading dose of 10 mg/kg, followed by 5 mg/kg every 12 hours for 10 days
- b. Loading dose of 30 mg/kg, followed by 3 mg/kg every 6 hours for 4 days and 7.5 mg/kg every 6 hours for the next 6 days
- c. Loading dose of 20 mg/kg, followed by 10 mg/kg every 8 hours for 7 days
- d. Loading dose of 40 mg/kg, followed by 20 mg/kg every 4 hours for 5 days

19. What is the recommended parenteral dosing regimen of ribavirin for Nipah virus disease?

- a. IV loading dose of 20 mg/kg, followed by 10 mg/kg every 12 hours for 10 days
- b. IV loading dose of 30 mg/kg, followed by 15 mg/kg every 6 hours for 4 days and 7.5 mg/kg every 8 hours for the next 6 days, diluted in 150 ml of 0.9% Normal Saline and infused slowly
- c. IV loading dose of 25 mg/kg, followed by 12.5 mg/kg every 8 hours for 7 days
- d. IV loading dose of 40 mg/kg, followed by 20 mg/kg every 4 hours for 5 days, diluted in 100 ml of 0.9% Normal Saline and infused rapidly.

20. What preventive measures are recommended for people in areas with outbreaks of Nipah virus (NiV)?

- a. Consuming raw date palm juice and fruits found on the ground
- b. Regularly washing hands with water only
- c. Avoiding contact with sick bats or pigs
- d. Encouraging contact with the blood or body fluids of people known to be infected with NiV

21.What measures are recommended for controlling Nipah virus in pigs during an outbreak?

- a. Promoting unrestricted movement of animals from infected farms to other areas
- b. Delaying the quarantine of animal premises during a suspected outbreak
- c. Culling infected animals with no supervision of burial or incineration of carcasses
- d. Establishing an animal health/wildlife surveillance system using a One Health approach for early detection of Nipah cases

22.How can the risk of Nipah virus infection in people be reduced in the absence of a vaccine?

- a. Relying on vaccination as the primary preventive measure
- b. Implementing quarantine measures for infected individuals
- c. Educating people about the risk factors and measures to reduce exposure to the virus
- d. Ignoring public awareness campaigns and educational initiatives

ANSWER KEY

1. **How is Nipah virus primarily transmitted to humans?**
 - a. Mosquito bites
 - b. Inhalation of contaminated air
 - c. Direct contact with infected animals**
 - d. Consumption of contaminated water

2. **What is the primary host of the Nipah virus?**
 - a. Pigs
 - b. Dogs
 - c. Fruit bats**
 - d. Cattle

3. **What are common symptoms of Nipah Virus Disease?**
 - a. Joint pain and muscle aches
 - b. Visual disturbances
 - c. Fever, headache, and encephalitis**
 - d. Gastrointestinal bleeding

4. **Which regions are more prone to Nipah Virus outbreaks?**
 - a. North America
 - b. Southeast Asia, including Bangladesh and India**
 - c. South America
 - d. Europe and Australia

5. **How can Nipah Virus Disease be prevented?**
 - a. Vaccination
 - b. Avoiding contact with infected animals**
 - c. Wearing long sleeves and pants
 - d. Consuming raw meat from reliable sources

6. **What role do fruit bats play in the epidemiology of Nipah Virus Disease?**
 - a. They are the primary reservoir of the virus**
 - b. They transmit the virus through bites
 - c. They amplify the virus in pigs
 - d. They are not associated with the disease

7. **What preventive measures are crucial to reduce the risk of Nipah Virus transmission in endemic areas?**
- Proper hand hygiene
 - Use of mosquito nets
 - Vaccination of livestock
 - All the above**
8. **Who is at an increased risk of Nipah Virus infection due to their involvement in the cultivation of fruits like date palms?**
- Health care workers
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9. **According to the suspect case definition of Nipah Virus, an individual from an affected area is considered a potential case if presenting with which of the following symptoms?**
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Developed by
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