



National Guideline for Management, Prevention and Control of Nipah Virus Infection including Encephalitis





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Institute of Epidemiology, Disease Control and Research (IEDCR)
Directorate General of Health Services
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Government of the People's Republic of Bangladesh

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National Guideline for Management, Prevention and Control of Nipah Virus Infection including Encephalitis

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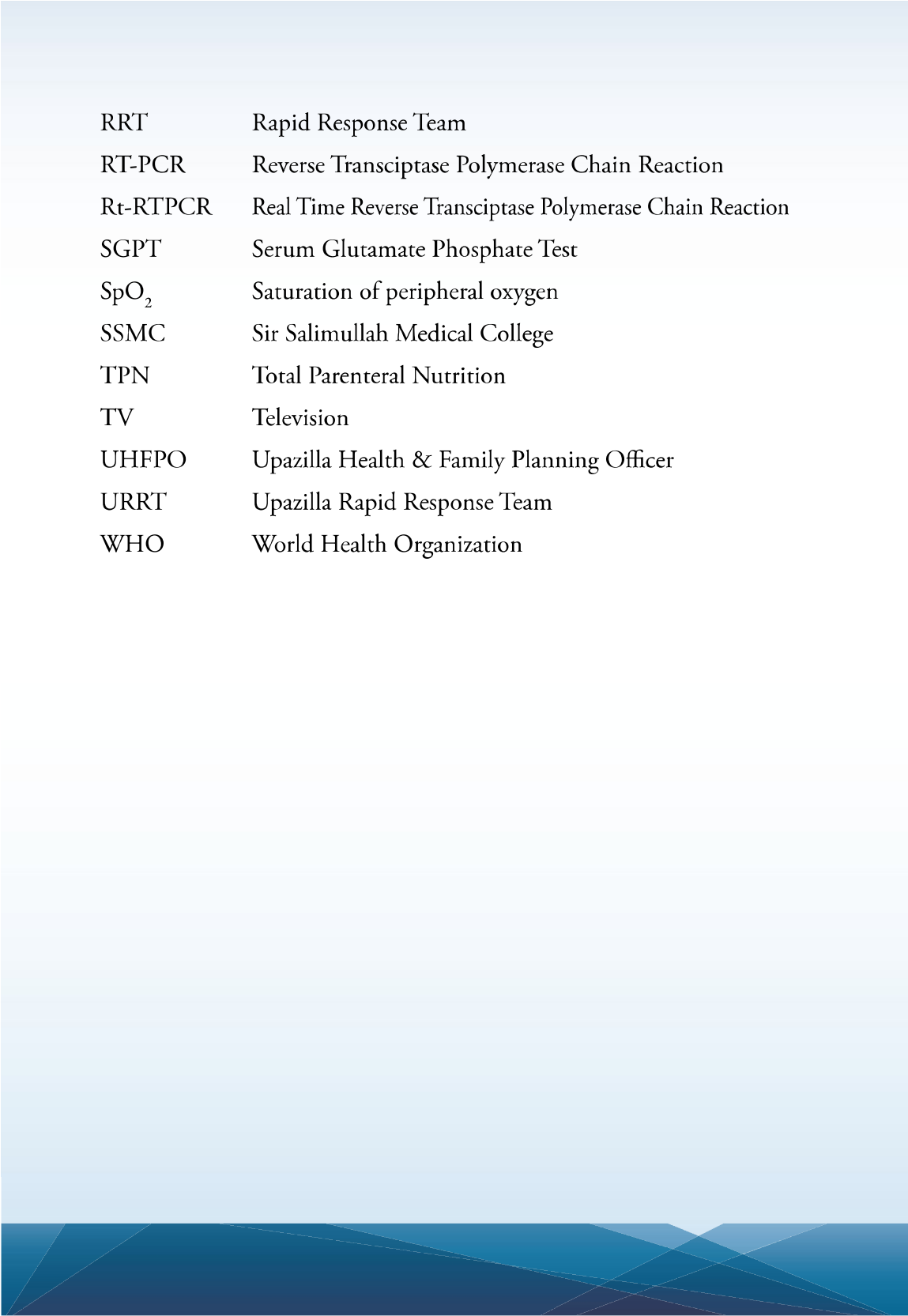
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2nd edition: November 2016

LIST OF ABBREVIATIONS AND ACRONYMS

ACT	Artemisinin-based combination therapy
Ag	Argentum (Silver)
AHC	Anterior hippocampus
BD	Bis die (twice a day)
BP	Blood Pressure
BSMMU	Bangabandhu Sheikh Mujib Medical University
CBC	Complete Blood Count
CDC	Center for Disease Control & Prevention, USA
CNS	Central Nervous System
CRP	C-reactive protein
CS	Civil Surgeon
CSF	Cerebrospinal fluid
DGHS	Directorate General of Health Services
DMC	Dhaka Medical College
DK	Don't know
DNA	Deoxyribonucleic Acid
DNS	Dextrose in Normal Saline
DRRT	District Rapid Response Team
EEG	Electro Encephalogram
ELISA	Enzyme Linked Immunosorbent Assay
FLAIR	Fluid Attenuated Inversion Recovery Image
FRA	Field Research Assistant
GCS	Glasgow Coma Scale

HDU	High Dependency Unit
HEO	Health Education Officer
HME	Heat and Moist Exchange
HSV	Herpes Simplex Virus
icddr,b	International Center for Diarrheal Disease Research, Bangladesh
ICP	Intra Cranial Pressure
ICU	Intensive Care Unit
IEDCR	Institute of Epidemiology, Disease Control & Research
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IV	Intra venous
JBE	Japanese B Encephalitis
JE	Japanese Encephalitis
LAMA	Left against medical advice
MP	Malarial Parasite
MRI	Magnetic Resonance Imaging
NG	Naso gastric
NIBP	Non invasive Blood Pressure
O ₂	Oxygen
PBS	Phosphate buffered saline
PCR	Polymerase Chain Reaction
PIDVS	Program for Infectious Diseases & Vaccine Science
PLED	Periodic lateralized epileptiform discharges
PPE	Personal Protective Equipment
RDT	Rapid Diagnostic Test
RNA	Ribonucleic acid



RRT	Rapid Response Team
RT-PCR	Reverse Transcriptase Polymerase Chain Reaction
Rt-RTPCR	Real Time Reverse Transcriptase Polymerase Chain Reaction
SGPT	Serum Glutamate Phosphate Test
SpO ₂	Saturation of peripheral oxygen
SSMC	Sir Salimullah Medical College
TPN	Total Parenteral Nutrition
TV	Television
UHFPO	Upazilla Health & Family Planning Officer
URRT	Upazilla Rapid Response Team
WHO	World Health Organization



PREFACE

SECOND EDITION

Nipah virus (NiV) infection is an emerging zoonosis that causes severe disease in humans with high case fatality (70-100%). The natural hosts of the virus are fruit bats of the Pteropodidae family, *Pteropus* genus. NiV was first identified during an outbreak of disease that took place in Kampung Sungai Nipah, Malaysia in 1998. Pigs were the intermediate hosts. However, in subsequent NiV outbreaks, there were no intermediate hosts.

NiV has been identified in Bangladesh in 2001, where humans became infected with NiV as a result of consuming date palm sap that had been contaminated by infected fruit bats. Human to human transmission has also been documented, in Bangladesh and India.

Since the deadly pathogen appeared in Bangladesh 15 years ago, 298 cases and 209 deaths have been reported. The findings from identified cases in Bangladesh also provide us important information that the infection is caused by the consumption of the raw sap of a date palm tree which has been contaminated with urine or saliva from infected fruit bats. When the sap is consumed, the virus infects the human body. Once infected, the patient can spread the virus to other people through physical contact. Winter (December to early February) is the traditional date palm sap collecting season in Bangladesh and the raw sap is a popular drink in rural areas. The outbreak coincides with this season, appearing between December and May.

Leading clinicians in the discipline of internal medicine, chest medicine, paediatrics, neuro-medicine, critical care; leading epidemiologists, public health specialists, laboratory scientists developed the initial guideline in 2011, which helped clinicians and public health specialists in the country in detection, case management and prevention of Nipah virus infection including encephalitis.

The 2nd edition of guidelines on clinical management of Nipah Encephalitis has updated with new information. I am confident that these will guide the clinicians for early diagnosis and appropriate management of the patients with Nipah and any other encephalitis and would help in reducing the case fatality and spread of Nipah infection in the country. These are only broad guidelines; the consulting physician should consider the condition of the patient in totality and decide the course of treatment accordingly to save the life. This will also help in infection control to prevent spread of the disease.

Professor (Dr.) Meerjady Sabrina Flora, PhD
Director, IEDCR

PREFACE

FIRST EDITION

In the last decade, in several districts of north-western and central part of Bangladesh, Nipah infection has become a public health emergency. High case fatality rate and person-to-person transmission has made Nipah a highly dangerous pathogen. The public health alertness about Nipah is not only applicable for Bangladesh, but it has become a worldwide public health concern.

Winter is the usual Nipah 'season' in Bangladesh. The health professionals of Bangladesh are on constant surveillance for Nipah. We are well prepared for response to any outbreak of Nipah.

Leading clinicians in the discipline of internal medicine, chest medicine, paediatrics, neuro-medicine, critical care; leading epidemiologists, public health specialists, laboratory scientists worked to draft this guideline which will be used for detection, case management and prevention of Nipah infection including encephalitis. This draft was also discussed in a regional meeting of WHO at Bangkok in June 2011. After making the final draft it was uploaded in the website of IEDCR for further suggestion for improvement. Following a rigorous process of discussion, taking all the suggestions and advice we have finalised this guideline. This guideline will be updated regularly to accommodate real time experience and latest scientific findings.

The persons involved in preparing the guideline deserve special mention for our gratitude. And of course, we cannot end here without acknowledging WHO Bangladesh Country Office for their valuable support in making and printing this guideline.

We wish every Nipah patient will be cared with fullest attention as the guideline underscored, and gets a newer life on earth. That is the ultimate objective of the guideline.

15 December 2011
Dhaka, Bangladesh

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Introduction

Human Nipah virus (NiV) infection, an emerging zoonotic disease, was first recognized in a large outbreak of 276 reported cases in Malaysia and Singapore from September 1998 through May 1999[1-4]. Almost all patients had contact with sick pigs and presented primarily with encephalitis; 39% died. Large fruit bats of *Pteropus* genus are the natural reservoir of NiV [6-8]. Presumably, pig became infected after consumption of partially bat eaten fruits that dropped in pigsty [1, 5]. In 1994, Hendra virus similar to Nipah was detected among horses in Australia. So Nipah and Hendra virus together constitute the genus Henipah virus [5]. In India, during 2001 and 2007 two outbreaks in human were reported from West Bengal, neighboring Bangladesh. Large fruit bats of *Pteropus* genus are the natural reservoir of NiV [6-8].

In Bangladesh, NiV was first identified as the cause of an outbreak of encephalitis in 2001 [9]. Since then, 11 Nipah outbreaks have been identified in Bangladesh, involving 31 districts, all occurring between December and May [10, 11]; Till September, 2016, a total of 298 human cases of Nipah infection in Bangladesh were recognized; 209 (70%) died, indicating a very high mortality [10].

Respiratory involvement including pneumonia has been found to be considerably more among patients in Bangladesh than Malaysia [18, 19]. This may be due to genetic diversity of the viral strains. The prominent respiratory involvement probably is responsible for human to human transmission [19, 20].

It is important to develop guidelines for surveillance, diagnosis, case management, prevention and control of Nipah virus encephalitis so that human cases can be detected promptly and further human-to-human transmission can be prevented.

Table 1: Yearly distribution of Nipah cases in Bangladesh from 2001-2015*

Year	Total number of NiV cases in a year	Total number of NiV deaths in a year	% deaths from NiV in a year
2001	13	9	69
2002	0	0	0
2003	12	8	67
2004	67	50	75
2005	13	11	85
2006	0	0	0
2007	18	9	50
2008	11	9	82
2009	4	0	0
2010	18	16	89
2011	42	36	86
2012	18	13	72
2013	26	22	85
2014	38	15	39
2015	18	11	61
Grand Total	298	209	70

***No laboratory confirmed Nipah case identified in 2016.**

Since April 2001 upto September 2016, a total of 298 lab confirmed human cases of Nipah infection, which included 209 (70%) death were identified in Bangladesh. During 2016 upto September no lab confirmed Nipah case has been identified. Highest number of cases (67) identified during 2004 with a mortality rate of 75%.

Transmission

Outbreak investigations in Bangladesh have identified two routes of transmission of Nipah virus from its natural reservoir to human: drinking of raw date palm sap (*khejurer rosh*) contaminated with NiV and close physical contact with Nipah infected patients [9,11-17]. The outbreaks were reported during date palm sap harvesting season of Bangladesh between December to May [13]. *Pteropid* fruit bats drink the sap and, occasionally, spoil the contents of the sap collection pot with urine or feces [21, 22] . Therefore, human might be infected by drinking NiV contaminated raw date palm sap [13]. The person-to-person transmission may occur from close physical contact, specially by contact with body fluids [12]. Infected bat often bite fruits and few partially-eaten fruits are left by the bats. When man or animals consumes those partially eaten fruits, may transmit NiV to man or other animals. From the pig, virus may be transmitted to human when comes in close contact [3].

Fruit bats of the genus *Pteropus* have been identified as natural reservoirs of NiV. Given the distribution of the locally abundant fruit bats in South Asia, NiV outbreaks are likely to continue to occur in affected countries. The bats are migratory and they migrate within the Asia-Pacific Region [23]. A telemetry study tracked the movements of three pteropid species (*P. alecto*, *P. vampyrus* and *P. neohibernicus*) which all were found to cover large distances between countries [24]. These are NiV and hendravirus carrying species. This has generated intensive surveillance for evidence of Nipah virus infection in bats in these countries. Evidence of NiV could be demonstrated in *P. giganteus* in Bangladesh [25].

Infected bats shed the virus in their excretion and secretions such as saliva, urine, semen and excreta, but they are symptomless carriers [6]. The NiV is highly contagious amongst pigs, spread by droplet infection. Pigs acquire NiV and act as an intermediate and possibly amplifying host after contact with infected bats or their secretions. Direct human contact with infected pigs were identified as the predominant mode of transmission in humans when it was first recognized in a large outbreak

in Malaysia in 1999 [14]. Ninety-three percent of the infected people in the 1998-1999 outbreaks were pig farmers or had contact with pigs [3]. The presence of NiV in respiratory secretions and urine of patients were demonstrated and this posed a danger for nosocomial transmission [15].

There were focal outbreaks of NiV in Bangladesh and India in 2001 during the winter. Drinking of fresh date palm sap, possibly contaminated by fruit bats (*P. giganteus*) during the winter season, may have been responsible for indirect transmission of Nipah virus to humans [26].

Date palm sap is consumed as a drink in Asia. A V-shaped cut is made on the head of the stem of the date palm tree and a container collects the sap. The sap can then either be consumed in the raw form as a sweet drink, fermented to form an alcohol beverage or boiled to form date palm molasses. The consumption of date palm sap (which is also known as toddy, kallu, tuak and tuba in other countries) is popular in a number of South East Asian countries including Bangladesh, India, Indonesia and Thailand as well as countries such as Malaysia and the Philippines. Fruit bats also consume date palm sap and can contaminate it with saliva, urine and faeces. This is the means by which NiV is thought to be transmitted from infected fruit bats to humans [27]. Subsequent person-to-person transmission occurs from close physical contact, especially contact with body fluid.

There is circumstantial evidence of human-to-human transmission in India in 2001. During the outbreak in Siliguri, 33 health workers and hospital visitors became ill after exposure to patients hospitalized with Nipah virus illness, suggesting nosocomial infection [28].

During the Bangladesh outbreak the virus is suggested to have been transmitted either directly or indirectly from infected bats to humans. Strong evidence indicative of human-to-human transmission of NiV was found in Bangladesh in 2004 and onwards [12, 14, 17, 20]. More than one third of Nipah cases are due to human to human transmission.

Agent

NiV is a highly pathogenic paramyxovirus belonging to genus Henipavirus [2]. It is an enveloped RNA virus [29].

The nucleotide sequences of NiV strains isolated from pigs and persons in Malaysia were remarkably similar and suggest that the entire outbreak was caused by 1 or 2 closely related strains. Indeed, all human cases of NiV infection in Malaysia and Singapore could have originated from a single or perhaps 2 introduction of NiV from its bat reservoir into pigs [30].

In Bangladesh, by contrast, recurrent Nipah outbreaks have been recognized since 2001 and the strains of Nipah isolates show substantial heterogeneity in their nucleotide sequences. This heterogeneity suggests repeated introductions of Nipah virus from its host reservoir into the human population in Bangladesh [20, 9].

Nipah cases tend to occur in a cluster or as an outbreak, although 18% cases in Bangladesh were isolated. There is strong evidence that the emergence of bat-related viral infection communicable to humans and animals has been attributed to loss of natural habitat of bats. It has been speculated that migratory fruit bats were forced away from their natural habitats in 1998 because of forest fires prevalent at that time in the region and attracted by the fruit trees in pig farms [3]. As the flying fox habitat is destroyed by human activity the bats become stressed, their immune system weakens, their viral load increases and more virus is shed in the urine and saliva [31]. Similar fluctuations of virus shedding may be associated with stressful physiological conditions or seasons. Habitat destruction also physically brings bats into closer contact with humans.

Seasonality was strongly implicated in NiV outbreaks in Bangladesh and India. All of the outbreaks occurred during the months of winter to spring (December-May). This could be associated with several factors like the breeding season of the bats, increased shedding of virus by the bats and the date palm sap harvesting season.

Incubation Period

The median incubation period of the secondary cases who had a single exposure to Nipah case was nine days (range 6–11 days) but exposure to onset of illness varies from 6-16 days [18, 13, 22]. The median incubation period following single intake of raw date palm sap to onset of illness is 7 days (range: 2-12 days) in Bangladesh.

Pathogenesis

Figure 1: Pathogenesis of Nipah virus infection

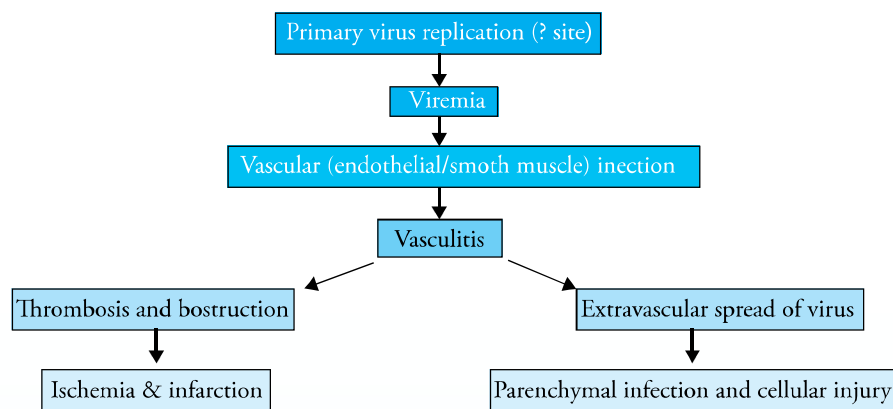


Fig: Pathogenesis of Nipah virus infection

Reproduced from: Nipah Virus Infection Pathology and Pathogenesis of an Emerging Paramyxoviral Zoonosis

Kum Thong Wong, Wun-Ju Shieh, Shalini Kumar, Karim Norain, Wahidah Abdullah, Jeannette Guarner, Cvnthia S.Goldsmith, Kaw Bing Chua, Sai Kit Lam, Chong Tin Tan, Khean Jin Goh, Heng Thay Chong, Rani Jusoh, Pierre E. Rollin, Thomas G. Ksiazek, Sherif R. Zaki, and the Nipah Virus Pthology Working Group; *American Journal of Pathology*, Vol. 161, No. 6, December 2002

All pathologic findings of NiV infection in human that have been identified so far are based on Malaysian studies. The pathologic findings in the brain of Nipah encephalitis cases showed evidence of necrotizing vasculitis. There was widespread central nervous system (CNS) involvement due to severe vasculitis of mainly small blood vessels, which resulted in endothelial damage [32]. Eosinophilic cytoplasmic and nuclear viral inclusions were detected in many neurons adjacent to vasculitic vessels, a finding which is present in infections caused by other paramyxoviruses. The main pathology appeared to be widespread ischemia and infarction caused by vasculitis-induced thrombosis, although direct neuronal invasion may also play a major role in the pathogenesis of the encephalitis.

Alveolar hemorrhage, pulmonary edema and aspiration pneumonia were often encountered in the lungs [32]. These may lead to pneumonia and acute respiratory distress syndrome (ARDS) ultimately.

Nipah virus is classified internationally as a biosecurity level (BSL) 4 agent. NiV has a number of important attributes that makes it a potential to be agents of bioterrorism [33].

Surveillance

Beginning in 2006, The Institute of Epidemiology, Disease Control and Research (IEDCR) in collaboration with icddr,b established Nipah surveillance in 10 District level Government hospitals of the country where Nipah outbreaks had been identified. Presently surveillance system is functioning in four hospitals. Establishing appropriate surveillance systems are necessary to detect NiV outbreaks quickly and appropriate control measures can be initiated.

Objectives

- To ensure management of Nipah infection including encephalitis at health care settings as well as in the community
- To set up isolation and high dependency units/ICUs at health care facilities in Nipah endemic areas
- To raise awareness of health care professionals about personal protection and infection control
- To prevent transmission by interrupting person-to-person transmission of Nipah infection
- To provide a standard case definition for surveillance and outbreak investigation of Nipah virus encephalitis
- To provide standard guidance for outbreak investigation of Nipah virus encephalitis based on past experiences
- To strengthen the capacity of emergency response to outbreaks
- To share lessons learnt from previous Nipah virus encephalitis outbreaks

Case Management of Nipah Encephalitis

Case Definition of Nipah Encephalitis

Suspected case

A person fulfilling both of the following criteria is defined as a suspected case:

1. Features of acute encephalitis as demonstrated by
 - a. Acute onset of fever AND
 - b. Evidence of acute brain dysfunction as manifested by
 - i. Altered mental status OR
 - ii. New onset of seizure OR
 - iii. Any other neurological deficit
2. Epidemiological linkage
 - a. Drinking raw date palm sap OR
 - b. Occurring during Nipah season OR
 - c. Patient from Nipah endemic area

Probable case

A person with features of acute encephalitis

- during a Nipah outbreak in the area OR
- with history of contact with confirmed Nipah patient

In both suspected and probable cases, the patient might present with respiratory features with or without encephalitis. The respiratory features are

- Illness < 7 days duration AND
- Acute onset of fever AND
- Severe shortness of breath, cough AND
- Chest radiograph showing diffuse infiltrates

Confirmed case

A suspected or probable case with laboratory confirmation of Nipah virus infection either by:

- IgM antibody against Nipah virus by ELISA in serum or cerebrospinal fluid
- Nipah virus RNA identified by PCR from respiratory secretions, urine, or cerebrospinal fluid

Definition of Cluster

Two or more suspect cases living within a 30 minute walk of each other who develop symptoms within 21 days of each other.

Clinical Features

Symptoms

The following symptoms were observed (in order of frequency in Bangladeshi cases)

1. Fever
2. Altered mental status
3. Severe weakness
4. Headache
5. Respiratory distress
6. Cough
7. Vomiting
8. Muscle pain
9. Convulsion
10. Diarrhoea

General Signs

- Reduced GCS score
- Raised temperature
- Increased respiratory rate (Adult: $\geq 25/\text{min}$; children of ≥ 12 months: $\geq 40/\text{min}$)
- Increased heart rate (Adult: $\geq 100/\text{min}$; children of ≥ 12 months: $\geq 140/\text{min}$)
- Crepitations in lung
- Hypertension/Hypotension

Neurological signs

- i. Oculoparesis
- ii. Pupillary abnormality
- iii. Facial weakness
- iv. Bulbar weakness
- v. Limb weakness
- vi. Reduced deep tendon reflexes
- vii. Plantar-absent/extensor

Differential Diagnosis

1. Other viral encephalitides e.g. Herpes simplex encephalitis, Japanese B Encephalitis (JBE)
2. Bacterial meningitis
3. Cerebral Malaria

Table 2: Differential Diagnosis of Nipah Virus, Japanese Encephalitis and Herpes Simplex Encephalitis

Characteristics	Nipah virus	Japanese encephalitis	Herpes Simplex encephalitis
Agent	Nipah virus (Paramyxovirus family)	JBE virus (RNA, Flavivirus)	HSV
Incubation Period	Median 10days (range: 2-21 days)	1-6 days, max. 14 days	2-12 days, mean 4 days
Transmission	Drinking raw date palm sap, human-to-human, (close physical contact with Nipah case), animal (pig) to man	Culex mosquito (v e c t o r) , human-to-human not reported	H u m a n - h u m a n , respiratory, droplet
Site of involvement	Cortico-subcortical areas of cerebrum /cerebellum, brain stem	Thalamus, cortex, cerebellum, AHC	Fronto-temporal area
Clinical feature	Fever, headache, altered sensorium but specially associated with segmental myoclonus & respiratory involvement	Fever, headache, altered sensorium (100%) followed by convulsions and meningeal sign, a b n o r m a l movements	Same as JE but typically associated with a constellation of frontotemporal features with aphasia or mutism, personality change, and focal or generalized seizures
Serology / PCR	IgM /IgG (ELISA), PCR	Ag /Ab in blood /CSF	CSF PCR for HSV DNA is diagnostic
CSF	Pleocytosis (10-60 cells /mm ³), ↑ Protein (30-60 mg/L), Normal glucose	P l e o c y t o s i s (10-980×10 ⁶ /L) , ↑ Protein (900mg/L), Normal glucose	Lymphocytic pleiocytosis (typically 10–200 cells/ mm ³), normal glucose, and increased protein (0.6 to 6 g/l). Red blood cells and xanthochromia may be present

Investigations

General

- CBC with CRP- Leucopenia and lymphocytosis, thrombocytopenia
- Blood film for Malarial Parasite (MP) or RDT for P. Falciparum malaria
- Chest X-ray: Diffuse infiltrates, consolidation
- Blood glucose
- Serum bilirubin and SGPT
- S. creatinine
- S. electrolytes
- S. amylase and lipase
- CSF study- mild pleocytosis. Normal or slightly raised protein and normal sugar level; mainly done for exclusion of other causes
- MRI of brain- diffuse, confluent high signal lesions involving mainly the cortical grey matter and to a lesser extent sub-cortical and deep white matter on T2W and FLAIR sequences
- Electroencephalogram: The electroencephalogram (EEG) shows continuous diffuse slow waves with or without periodic bitemporal independent sharp wave discharges. It is important especially to differentiate from HSV encephalitis [periodic lateralized epileptiform discharges (PLED) mainly from temporal lobe]

Specific

- Enzyme-linked immunoassay
The diagnosis of Nipah virus infection can be established by enzyme-linked immunosorbent assay (ELISA). Nipah IgM capture ELISA and an indirect IgG ELISA have high specificity for the diagnosis. Rapid immune plaque assays have been developed to quantify Hendra and NiV and detect neutralizing antibodies to both viruses. Specimens include CSF and serum.
- Polymerase chain reaction (PCR)
RT PCRs can be used for detection of viral sequences in CSF, throat swab or urine specimens.

Indication of specific testing for Nipah

Since treatment does not depend totally on confirmation of the cases, testing can be requested to IEDCR selectively only in clusters and highly suspected cases in Nipha season and in Nipah endemic areas.

Treatment

Supportive/General Management

- a. Isolation (preferably in a separate unit)
- b. Barrier nursing e.g. personal protection using masks, gloves, gowns, shoe covers
- c. Hand washing with soap & water before and after handling/visiting patients
- d. Resuscitation (if needed): ABC (Annex 2):
 - Airway
 - Breathing
 - Circulation

- e. Care of unconscious patient: posture change, care of eye, bladder, bowel and mouth
- f. O₂ inhalation if there is respiratory difficulty
- g. Nutritional support: oral/NG tube feeding according to the condition of the patient
- h. Maintain fluid and electrolyte balance (Adults: 5% DNS, Children: 5% DNS, half or quarter strength saline)
- i. Fluid restriction: 30% restriction particularly in children. 2/3 of the daily maintenance can be given in children if the child is not in shock
- j. Maintain intake output chart
- k. Bronchodilators may be given through large spacers

Symptomatic Treatment

- a. Treatment of fever:

Paracetamol -15mg/kg/dose or 500 mg for adult if temperature $\geq 101.3^{\circ}\text{F}$ ($\geq 38.5^{\circ}\text{C}$). (Not more than 4 times in 24 hours)

- b. Treatment of convulsion:

- i. If patient present with convulsion:
 - Adult: IV Diazepam 10mg stat
 - Children: per rectal diazepam: 0.5mg/ kg (maximum 10mg) as stat dose
 - It can be repeated once again after 10 min
- ii. If seizure persists despite above measures, treat as status epilepticus (Annex 3)
- iii. If presents with history of convulsion(s): Give maintenance treatment with phenobarbiton (Adult: 60 mg BD; Children: 5 mg/ kg/ day BD)

- c. Treatment of raised intracranial pressure (i.e., bradycardia, hypertension, papilloedema and deterioration of consciousness)
 - i. Elevation of head to 30° with straight head
 - ii. Mannitol
 - Adult: 200ml IV running stat and 8 hourly until features of raised ICP resolved or not beyond eight doses of mannitol.
 - Children: 2.5 – 5 ml/kg over 20 minutes as bolus dose stat and 6 hourly, not beyond eight doses of mannitol
- d. Treatment of hypoglycemia (<40 mg/dl or <2.2 mmol/L)
 - Adult: 25% glucose-40 ml IV
 - Children: 10% glucose 5 ml/kg bolus and can be repeated if necessary
- e. Treatment of Shock:
 - i. 0.9% Normal Saline
 - Adult: 1 litre in 1st hour
 - Children: 20ml/kg over 20 mins
 - ii. Dopamine (when needed):
 - Adult: 05-20 microgram/kg/min)
 - Children: 5-10 microgram/ kg/ min

Other treatment

The following may be given if indicated.

- i. Antibiotic e.g. IV ceftriaxon (Children: 100mg/ kg once daily, Adult: 2gm BD for 10 days in suspected case of bacterial meningitis)
- ii. IV Acyclovir 10mg/ kg 8 hourly as infusion over 20 min for 10 days
- iii. Broad spectrum antibiotics + Metronidazole/Clindamycin (for aspiration pneumonia/secondary bacterial infection)
- iv. Anti-malarials according to national guideline (Annex 4)

Criteria for transferring patient to ICU

- a) Signs of impending respiratory failure
 - Respiratory rate:
Adult: > 30/min
Children: $\geq$ 70/min
 - O₂ saturation < 90%
 - Central cyanosis

despite breathing in Oxygen 5 litres/min through mask.

In children, severe chest indrawing - is also important.

- b) Uncontrolled seizures
- c) GCS $\leq$ 8
- d) Hemodynamic instability (i.e., bradycardia, hypotension and capillary refilling time > 3 seconds)
- e) Multi organ failure

Criteria for referral to higher centre

1. Deteriorating level of consciousness
2. Uncontrolled convulsion
3. Worsening respiratory distress
4. Uncontrolled haemodynamic instability

Care during transportation of the patient

- 1) Maintaining patent airway
 - lateral position
 - airway suction if required
- 2) Oxygenation
- 3) Monitoring during transport
- 4) Personal protection for the person related to transport

Requirements for an isolation room

- Standard should be equivalent to High Dependency Unit (HDU)
- Exhaust fan should be switched on
- Separate Pulse oxymeter, Non invasive BP, stethoscope, BP machine, Thermometer, Torch light

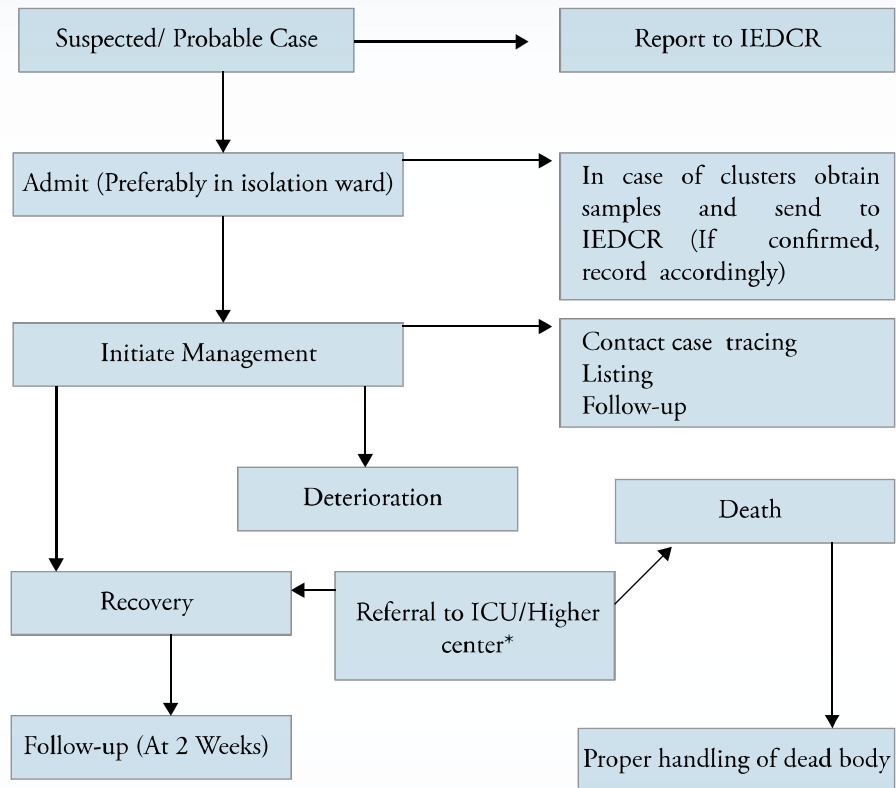
- Supply of adequate
 - disposable gloves,
 - gown (either disposable/autoclavable),
 - surgical mask/N95 mask,
 - hand washing facilities,
 - chlorhexidine hand washing solution/ alcohol 60%
- One Mechanical Ventilator for each four bedded HDU
 - HME filter
 - close circuit suction apparatus

Monitoring and follow up of surviving Nipah cases (two weeks from discharge)

1. Higher psychic functions – intact/ impaired
2. Orientation (time, place, person) fully oriented/impaired
3. Speech– intact/ impaired
4. Swallowing— intact/ impaired
5. Seizures- controlled/uncontrolled
6. Motor activities- upper limbs- power, coordination
7. Lower limbs- power, coordination, gait
8. Daily activities (feeding, dressing, washing, bathing) - fully independent, partially dependent, fully dependent

(Ref: Extended Disability Scoring system. WHO Bulletin. 88[8]: 2010. 561-640; WHODAS 2.0)

Patient Management Flow Chart



* Referral doesn't always ensure better outcome, rather it may increase the risk of person to person transmission while transporting. So managing the patient in the health care facility, where the patient got admitted, is preferable as long as possible.

Prevention and Control of Nipah Encephalitis

Goal

To prevent transmission of the virus from:

- Bat to human
- Human to Human
 - Patient to health care workers
 - Patient to other care givers/ close contact
 - Patient to patient with other disease(s)

So, strategies for prevention of Nipah virus transmission are:

- Awareness program
- Early case detection through different surveillance systems
- Case management
- Infection control measures:
 - Household
 - Community
 - Hospital

Data from outbreak investigations suggest that there are different risk factors for transmission of Nipah virus in Bangladesh, which are:

1. Ingestion of-
 - Raw date palm sap contaminated by NiV
2. Person to person transmission of Nipah virus
 - a. From patient to care giver or contact
 - b. From patient to health care worker
 - c. Through objects used by patient
 - d. During handling deceased

Prevention and control of Nipah transmission depends upon controlling these risk factors. The following approaches should be implemented to prevent and control Nipah transmission in Bangladesh:

Risk factor 1: Ingestion of raw date palm sap

Approach: Provide message before and during Nipah season (December to March) of each year

- At national level:
 - Mass media campaign involving Health Education Bureau of DGHS, development partners, NGO partners and other relevant agencies through documentary film, TV spot, radio message, advertisement, leaflet, poster etc.
- At District and Upazilla level: Civil Surgeon and UHFPO will be responsible for dissemination of following key message (see Box 1) through-
 - Person to person or court yard/group meeting at the community level (such as local bazaar, school ground, mosque, public gatherings) by health workers (health assistants). Present Nipah prevention message using multimedia projectors at community level in collaboration with District Information Office using the short documentary prepared at national level.

Box 1: Key Message for prevention of Nipah transmission through ingestion of raw date palm sap

- Don't drink raw date palm sap: some bats carry Nipah virus and could contaminate raw sap during collection process at night. Human can get infected by consuming the raw date palm sap
- Consuming boiled sap or molasses is safe

Risk Factor 2: Person to person transmission of Nipah virus from patient to care giver/contact, patient to health care worker, touching objects used by patients or during handling deceased

a. Prevention of transmission

Approach: Provide message as soon as a cluster or an outbreak has been identified in any area

– At national level:

- Mass media campaign involving Health Education Bureau of DGHS, development partners, NGO partners and other relevant agencies through documentary film, TV spot, radio message, advertisement, leaflet, poster etc.

– At district and upazilla level:

- i) As soon as a cluster identified in any area, Civil Surgeon and UHFPO of the respective area will take steps to disseminate the following message (Box 2) to the family members and neighbors of the cluster
- ii) As soon as an outbreak has been identified in any area, Civil Surgeon and UHFPO of respective area will take steps to disseminate the following message (see Box 2) to the family and community members of outbreak area/village/Union/Upazilla through-
 - Inter personal communication by court yard/group meeting at the community level (such as local bazaar, school ground, mosque, public gatherings) by health workers and NGOs, volunteers and others
 - Present Nipah prevention message using projectors at community level in collaboration with District Information Office using the short documentary prepared at national level

Box 2: Key Message for prevention of Nipah transmission from person-to-person

- Wash hands thoroughly with soap and water after coming in contact with patient
- Sleep in separate bed
- Maintain >1 full-stretched arm distance (1 metre or 3 feet) from patient
- Keep personal items of patient separately
- Wash used items of patient with soap and water, separately

b. *Prevention of transmission from Nipah patient to health care worker at the hospital*

Approach 1: Provide message to health care workers at District level and Upazilla level health care facilities before and during Nipah season (December to March) (see Box 3)

- At Nipah surveillance hospitals and in districts with report of Nipah outbreaks: Dissemination of prevention message through meetings, posters and leaflets before and during Nipah season (December to March) should be organized by hospital authorities and from National level
- At districts and upazillas where no Nipah outbreak has been reported before: As soon as a cluster or outbreak has been identified in any area, Civil Surgeon and UHFPO of respective area will take steps to disseminate the following message (see Box 3) through meetings, posters and leaflets to the health care workers of the hospitals in that Upazilla/District (including Upazilla Health Complex, District Hospital, Infectious Disease Hospital, Medical College Hospital or other specialized hospital)

Box 3: Key Message for prevention of Nipah transmission at hospital setting

- Admit all cases with fever and unconsciousness/ convulsion/ difficulty in breathing to the isolation ward/ facility in the hospital
- Use mask and gloves during history-taking, physical examination, sample collection and other care-giving to suspected Nipah cases
- Avoid unnecessary contact with suspected Nipah cases
- Follow standard precautions* for infection prevention at hospital setting
- Immediately report admission of a suspected Nipah case to IEDCR and relevant authority.

* Standard precaution: Personal protection by practicing standard precaution:

- Hand hygiene: Hand washing /alcohol based hand rub
- Use personal protective equipment (PPE)
- Safe handling of patient, equipment and linen

Box 4: Precaution for isolation ward/ facility

- Segregate Nipah patients from other patients in the isolation ward/ facility
- Restrict the number of service providers in the isolation ward
- Maintain at least 1 meter (3 feet: one fully stretched arm's length) distance between two beds for Nipah patients

Also to follow

- ◆ Barrier nursing (PPE use, Isolation)
- ◆ Environmental cleaning and decontamination
- ◆ Safe waste disposal

Approach 2: Provide instruction to follow infection control practices during provision of care for potential infectious patients at regular basis, especially during a Nipah outbreak

- Identify Nipah patients (suspected/ probable/ confirmed) for isolation (see Box 4)
- Health care provider should use the personal protective equipments (PPE) strictly while providing care to possible Nipah/encephalitis patients (Box 5)
- Disposable items used for suspected/probable Nipah patients in the hospital should be disposed following standard waste disposal protocol (see Box 6)
- Reusable items used for suspected/probable Nipah patients in the hospital should be clamed or decontaminated following standard protocol (see Box 6)

Box 5: Personal protection during care for Nipah patient

Use personal protection equipments

- During history- taking, physical examination, wear surgical mask, surgical gloves (examine, specimen collection) and gown
- During specimen collection and other invasive procedures (such as nasopharyngeal suction, endotracheal intubation) wear N95 mask, surgical gloves and gown

Maintain Hand Hygiene

- Wash hands in with soap and water at least for 20 seconds, or
- Clean hand using 1-2 ml alcohol based hand sanitizer (chlorhexidine or 70% alcohol hand sanitizers) after providing any care to patient

Use disposable items

- Use disposable items while providing NG tube, oxygen mask, and endotracheal tube, Or
- If disposable items are not available, reuse after sterilization by autoclave or 2% glutaraldehyde

c. During handling deceased at family/community level

Secretion and excretion from a deceased person are considered to be equally infectious like that of a living infected person. Adequate precautionary measures have to be taken during handling such dead body during transportation, washing and burial or cremation.

Box 6: Waste disposal

- Keep disposable and non-disposable PPEs and items in separate containers/ biohazard bags
- Keep sharp wastes in separate designated rigid container (box, bottle etc.)
- Decontaminate wastes by autoclaving/chemicals [Sodium hypochlorite (Clotech)]
- Clean and disinfect patient's room (detergent and Clotech) at least once daily, specially frequently touched surfaces (e.g. doors, windows, table top, etc)

Decontamination of reusable items

- Soak reusable items in 0.05%-0.5% bleach solution or in soap/detergent water for 10-30 min
- Autoclave for reuse

Approach: Precautions should be followed while handling corpse of suspected Nipah patient

- Health care worker/mortuary staff should wear PPEs (disposable surgical mask, gloves and gown) while handling corpse of Nipah case
- Hand wash with soap and water (or hand sanitizer), should be done immediately after handling the corpse
- Used PPE should be disposed using standard protocol for infectious waste disposal (see Box 6)
- During transportation, deceased persons should be carried in an air sealed bag; if not possible, by covering with clothes
- Health care worker will provide message to family members/community people of deceased person (dead by Nipah infection) to follow precaution during transportation and handling of the deceased from hospital to community (Box 7)

Box 7: Key Message for prevention of Nipah transmission from deceased body to person

Precaution to be followed by family members/community members

- During transportation of dead body from hospital to home, avoid close contact with deceased's face, especially respiratory secretion
- Avoid close contact with deceased's face, especially respiratory secretion during grieving situation
- Cover face of yourself with a piece of cloth or gamcha during washing/ritual bath of deceased body
- Wash hands with soap, if possible take bath with soap immediately after performing ritual bath of the dead body

Handling reusable items of deceased

- Wash reusable items (cloths, utensils, etc.) with soap/detergent and
- Dry mattress, quilt/comforter, pillow, etc. in sunlight for several consecutive days

নিপাহ রোগ বিষয়ে স্বাস্থ্য বার্তা

নিপাহ একটি ভাইরাসজনিত রোগ, যা বাদুড় থেকে মানুষে সংক্রমিত হয়। এ রোগের প্রধান লক্ষণগুলো হচ্ছে- জ্বরসহ মাথাব্যথা, খিঁচুনি, প্রলাপ বকা, অজ্ঞান হওয়াসহ কোন কোন ক্ষেত্রে শ্বাসকষ্ট।

**নিপাহ রোগ প্রতিরোধে সর্বসাধারণকে নিম্নোবর্ণিত
নিয়মাবলী অনুসরণের পরামর্শ দেয়া হচ্ছে-**

- ❖ খেজুরের কাঁচা রস খাবেন না
- ❖ কোন ধরনের আংশিক খাওয়া ফল খাবেন না
- ❖ ফলমূল পরিস্কার পানি দিয়ে ভালো মতো ধুয়ে খাবেন
- ❖ রোগীকে যত দ্রুত সম্ভব নিকটস্থ সরকারি হাসপাতালে প্রেরণ করুন
- ❖ আক্রান্ত রোগীর সংস্পর্শে আসার পর সাবান ও পানি দিয়ে হাত ধুয়ে ফেলুন।

**নিপাহ উপদ্রুত অঞ্চলের সরকারি হাসপাতালে
বিশেষজ্ঞ দল সার্বক্ষণিকভাবে কাজ করছে।**



স্বাস্থ্য শিক্ষা বুরো, স্বাস্থ্য অধিদপ্তর
স্বাস্থ্য ও পরিবার কল্যাণ মন্ত্রণালয়

Epidemiological Surveillance System

A systematic surveillance system is a necessary method to identify clusters of meningo-encephalitis cases resulting early detection of Nipah outbreaks.

Objectives of surveillance

- Identify clusters of acute meningo-encephalitis cases
- Investigate clusters of cases for quick detection of Nipah outbreak
- Inform policy makers for appropriate public health intervention for prevention and control of Nipah virus encephalitis

Setting up a surveillance system for Nipah virus encephalitis

The main goal of setting up surveillance is to determine the disease prevalence, risk of virus infections and transmission in human and animal populations as well as the source and reservoir hosts of Nipah virus [35]. Surveillance of NiV in different host species (humans, domestic animals, reservoir hosts) needs to be performed.

Screening of patients who have meningitis, encephalitis or unusual neurological diseases should be done by ELISA and/or RT-PCR. This is mandatory, particularly in cases of meningitis/ encephalitis with atypical or interstitial pneumonia. This should also be applied whenever there are outbreaks of unexplained neurological/pulmonary illness in humans or animals, such as horses and pigs. Such laboratory testing for Nipah virus should be done with no delay, or not waiting for negative results of Japanese encephalitis or enterovirus tests. High risk group surveillance should be conducted in individuals who reside in the vicinity of animal reservoirs such as bats. During an outbreak, surveillance should involve patient's families, transport drivers and attendants, abattoir workers, health-care providers who had contact with patients, veterinary officers (public and private), field workers, laboratory staff, and spot testing of sick people in nearby villages to affected areas [35].

The surveillance for detection of Nipah virus outbreaks including other potential outbreaks:

There could be multiple approaches for surveillance systems for detection of Nipah virus outbreaks including other pathogens.

Hospital based active surveillance in ‘Nipah belt’ areas

Surveillance in tertiary and district hospitals where Nipah cases are more likely to come from ‘Nipah belt’ areas is necessary to identify Nipah cases. Physicians in selected hospitals are trained to know about case selection, cluster identification and reporting. One to two surveillance physicians should work in each hospital depending on hospital beds. The surveillance physicians undertake the following:

- Check cases of acute meningo-encephalitis daily in adult medicine and paediatrics units (Annex 5).
- Make line list of all the cases of acute meningo-encephalitis in line list form (Annex 6)
- Identify a cluster of cases (Annex 7)
- Report cluster of cases to hospital supervisor and surveillance coordinator of assigned hospital.

Hospital based passive surveillance

- Periodic training to Civil Surgeon/UHFPO/physicians/health care workers at sub-district/district level in ‘Nipah belt’ areas for updating outbreak recognition, outbreak response, preliminary data collection and reporting.
- Reinforcing the surveillance on case identification and reporting at the sub-district and district level in Nipah season (December-March) in ‘Nipah belt’ areas where cases are repeatedly identified.
- Reporting the cluster of unusual illness including meningo-encephalitis to the authority assigned for outbreak investigation.

Standard case definition

The clinical case definitions for Nipah are highly context dependent. The particular symptoms of Nipah are non-specific, but in the context of an outbreak they efficiently identify persons at risk for Nipah infection.

Suspect Nipah patient

Person from a community affected by an outbreak who has:

- 1) fever with new onset of altered mental status or seizure and/or
- 2) fever with headache and/or
- 3) cough with shortness of breath.

Probable Nipah patient

Suspect case-patients who resided in the same village where confirmed case-patients were living during the outbreak period and who died before complete diagnostic specimens could be collected.

Confirmed Nipah Patient

Person who has laboratory confirmation of Nipah virus infection either by:

- 1) IgM antibody against Nipah virus identified in serum or cerebrospinal fluid.
- 2) Nipah virus RNA identified by PCR from respiratory secretions, urine, or cerebrospinal fluid.
- 3) Isolation of Nipah virus from respiratory secretions, urine or cerebrospinal fluid.

Reporting of suspected cases

Patient with Nipah infection may attend at OPD/ IPD of UHC or district general hospital or in the medical college hospital. The attending doctor will examine the patient and if the doctor finds that the patient's signs and symptoms have similarity to Nipah encephalitis s/he will treat the case as suspected Nipah encephalitis. As soon as the patient would be managed as Nipah encephalitis, the hospital authority must inform IEDCR (instantly by telephone/ mobile/ e-mail and later by official letter) without any delay.

Outbreak investigation

Since Nipah virus encephalitis is a major zoonosis and outbreaks may be associated with multiple factors such as animal reservoirs, socio-cultural practices, food habits and possible human-to-human transmission, a multidisciplinary team is needed and preparation should be done for pre-outbreak, outbreak and post-outbreak phases. The outbreak investigation should lead to formulation of an appropriate public health intervention considering the locality specific situation.

Pre-outbreak phase

Preparedness in terms of technical, logistic and management of Nipah outbreak is essential in endemic countries. Event-based surveillance provides a clue to possible outbreaks of acute public health events. In addition to hospital based active and passive surveillance, the following non-traditional sources of information will be valuable during the pre-outbreak phase:

Media monitoring: This is an important source of information for detection of unusual health events and outbreak detection, including Nipah virus. A core group of RRT evaluates media news and decides on unusual events. The RRT checks the unusual events on health and communicates with local health authorities at the place of the unusual event for confirmation and to get an update report.

Telephone hot line: These are in 24-hour use by responsible authorities at the central or peripheral level to receive news of unusual acute health events, outbreaks or epidemic situations. The CSs at district and UHFPOs at sub-district levels are instructed to send immediate reports by telephone for any of these unusual events for immediate planning and response.

Intensification of surveillance during Nipah season

Surveillance is enhanced or intensified during Nipah season from January through March, when most Nipah outbreaks have been identified. This will increase the possibility of identification of Nipah virus infection and to understand the characteristics of the virus. Blood, cerebrospinal fluid and throat swabs are collected from suspected patients and sent for laboratory investigation.

Formation of multi-sectoral team: Multi-sectoral team working at national for the monitoring, evaluation and response to unusual acute public health events and outbreak response, including Nipah outbreaks. The team should have a holistic, multidisciplinary approach consisting of public health personnel, epidemiologists, veterinarians, anthropologists, social scientists, clinicians and laboratory personnel who would bring relevant expertise in outbreak response.

National Rapid Response Team (NRRT): The NRRT is stationed at IEDCR headed by Director. The team members consist of epidemiologist, clinicians, lab scientists, social scientists, communication experts. Animal science experts, toxicologists, clinicians, local health care providers often join NRRT from other government departments, Medical Colleges, ICDDR, Universities, DRRT and URRT.

District Rapid Response Team (DRRT): The DRRT is headed by CS and consists of clinical and laboratory expertise, health educators, and other experts in public health.

Upazilla Rapid Response Team (URRT): It is headed by UHFPO and consists of clinical and laboratory expertise, health educators, and other experts in public health.

Key steps for Nipah outbreak investigation

The outbreak investigation depends on the status of the outbreak including the number of cases, spread of disease, case fatality and local circumstances such as panic and rumor in the community.

- **Confirmation of outbreak:** The combined team initially visit health care centres and the community:
 - To understand the current situation of outbreak
 - To take initial line listing of cases
 - To understand clinical presentation
 - To identify additional cases in health care centres and communities
- **Develop a case definition and update the list of cases:** The team should define suspected, probable and confirmed cases. The team will identify cases in hospital and community thorough:
 - Daily visits to the health care centre
 - Review of media records and collect copies
 - Interview the physician and other health care providers about patient illness, clinical course, treatment, epidemiological/exposure information.
 - Visit outbreak community
 - Identify contacts of the cases and follow up 3 weeks after last contact with the cases during acute illness or death
 - Meeting with community people and community leaders
 - Monitor health care workers who provided services to Nipah patients
 - Risk communication
- **Clinical and Epidemiological investigation:** The team will explore possible risk factors of the illness, evaluate the outbreak in relation to 'time, place and person', formulate a hypothesis and consider immediate control measures. The team will undertake the following:

Clinical examination:

- Review hospital documents for clinical findings, laboratory investigation and treatment.
- Collect clinical information from survived patients
- Collect information from laboratory investigations done
- Collect blood, CSF and throat swab samples at the time of recruitment, and follow up serum samples 2 week after onset of illness.

Risk assessment:

The experienced and trained Field Research Assistant (FRA) will take the exposure history of cases and controls. Three neighborhood controls for each case will be taken to identify risk factors of illness. The exposure history mainly includes animal exposure, environmental exposure and contact with a case patient. The exposure history from cases and controls is considered from one month before onset of illness of the case.

Close contact study:

The close contact is defined as the patient or the person who came in contact with a Nipah case (confirmed and probable cases) AND stayed in the room or veranda or vehicle for at least 15 minutes. The FRA conducts the following:

- Make a line list of close contacts of cases
- Fill close contact questionnaire until at least 3 weeks after last contact with the patient during acute stage of illness or death
- Collection of 5 ml blood samples

Health care worker study:

There is evidence of nosocomial transmission in Bangladesh, India and Malaysia. It is important to investigate the health care workers who provided service to Nipah patients to understand the exposure for Nipah transmission (Annex 8):

- Make a list of health care workers who provided care to Nipah patients
- Take consent from health care workers (Annex 9)

- Fill a structured 'Health care workers exposure questionnaire' (Annex 10) until at least 3 weeks after providing last services to Nipah patients during acute illness
- Collect 5 ml of blood

Anthropological study:

Anthropologists or other social scientists with extensive community based experience should join the broader multidisciplinary Nipah outbreak investigation team. The activities of an anthropological team in the investigation are as follows:

- Explore detailed exposure histories of the cases with a time line of events, perception of the case and the community regarding Nipah outbreak, and their practices to prevent the transmission of disease.
- Assist in framing questions for the case-control questionnaire within the context of the activities, understanding, and language of local residents, and identify appropriate proxy respondents for deceased case-patients
- The anthropologists also spend a considerable time with affected communities to understand their concerns and discuss these concerns with the broader investigation team.
- The anthropologists often assist Health Education Officer (HEO) to develop communication messages combining both local explanatory models and biomedical models using the local terms and languages, and deliver the message in such a way so that it is meaningful to the community.

Sample collection, storage and transportation of specimens for laboratory diagnosis

- Specimen:
 - o Blood: 5 ml blood
 - Acute
 - Convalescent: Two week after onset of illness
 - o CSF: 3 ml extra CSF
 - o Throat swab
 - o Urine

Zoonotic and environmental investigations during Nipah outbreaks

Zoonotic and environmental investigation during a Nipah virus outbreak primarily aims to determine the primary reservoir, likely source of the virus, route of transmission, and the extent of the spread of the virus in animals.

To understand the reservoir and primary source of the virus the team may take samples from Pteropus bats near to the outbreak site. The samples may include oropharyngeal swabs, and serum samples to detect the virus and antibodies to identify recent and prior infections.

Sampling to understand the route of transmission depends on the nature of an outbreak. For example, in Bangladesh, bat-contaminated date palm sap may contain NiV; therefore the team may also collect sap from the trees linked with the outbreak(s). It is possible that the virus may spill over from reservoir bats to other domestic and peri-domestic animals. Therefore, the team may investigate cattle, goat, pigs, dogs, cats, and other suspected animals in an outbreak site.

Sample collection, sample shipment and laboratory testing:

- Serum, throat swabs and urine swabs should be collected in a cryovial and stored in liquid nitrogen tank or dry ice or -20°C freezer in the field.
- The cryovials containing samples can be shipped in liquid nitrogen tank or dry ice or cold box in the national centre for storage in -70°C freezer

Serological assays to identify recent or old Nipah infection in reservoirs and other susceptible animals are also useful in interpreting the outbreak condition. These tests include virus neutralisation test and ELISA to detect IgM and IgG antibody against Nipah. To reduce risk exposure of the laboratory personnel, it is recommended to treat the animal serum samples with gamma-irradiation or diluted 1/5 in PBS containing 0.5% Tween 20 and 0.5% Triton-X100 and heat-inactivated at 56°C for 30 minutes; rtRT-PCR of animal samples is recommended.

After the Nipah outbreak investigation

- Develop outbreak report

A written report should be submitted immediately at the end of the investigation to the concerned authority. The investigation should contain the following:

- ◆ Method of investigation
- ◆ Socio-demographic characteristic of cases (geography, age, sex, occupation)
- ◆ Distribution of cases by the date of onset of illness
- ◆ Clinical presentation of cases and outcome of illness
- ◆ Risk factors for illness
- ◆ Pathway of transmission
- ◆ Prevention and control measure
- ◆ Recommendations

Intersectoral coordination and One Health approach

Nipah virus encephalitis is a zoonotic disease that is transmitted from bats, affects domestic animals, primarily pigs. Intersectoral coordination is very important in the control and prevention of Nipah virus outbreaks as the disease is related to wildlife, agriculture farming and socio-behavioural practices at the community level. The involvement of livestock, agriculture, environment ministries and local administration is crucial for decision-making and the implementation of appropriate public health interventions. Coordinated epidemiological and field investigations and cross-checking of samples at both human and animal laboratories may be considered. Journalists, electronic media personnel, social activists, community leaders and non-government organizations all play an active role in early case reporting, social mobilization and raising public awareness, which is essential in rapid control of any outbreak. Discussion with media people in pre-outbreak time will help to develop a common understanding and a constructive role for media during outbreaks. One Health approach should be followed within every sector involved with Nipah prevention, control and management.

District and sub-district level administration should be involved in discussions on Nipah virus. Such discussions should occur not only during outbreaks, but also prior to the season to highlight the possibility of an outbreak. Possible prevention measures can be discussed at routine intersectoral monthly meetings. These would be crucial for better coordination and cooperation at the community level. Local community leaders such as Councillors of the local Union Parishad, village heads, religious leaders, school teachers, doctors, pharmacists and primary health care providers all can act on their own capacity and it is therefore important that they are kept up to date with planned awareness building process.

Lesson learnt from Nipah outbreak in Bangladesh

1. Nipah virus infection has a high mortality rate of up to 80% in settings without ICU support, which can be reduced to 40% when appropriate ICU services can be administered in a timely fashion. However, the fatality rate is still very high and so prevention rather than cure is more appropriate and more cost-effective also.
2. The key to controlling the outbreak and reducing mortalities is early detection of the outbreak and installing preventive measures as soon as possible.
3. Proper and prompt field investigations with risk assessments were found to be very useful in early detection of the outbreaks. Facility based infection control measures were employed including standard case management and increasing levels of intersectoral coordination raised community awareness.
4. It has been found that preventive measures work very well not only for outbreak control. They are successful also when routinely used prior to the proven Nipah season.
5. The principles of outbreak detection, response and control used in Nipah outbreaks could be successfully used in similar settings in case of other outbreaks with known or unknown agents.

6. Intersectoral coordination and One Health approach in dealing with any disease outbreaks or public health events of concern, as shown in Nipah outbreaks, can play a major role for the rapid control of outbreaks or unwanted impacts including preventing morbidities and mortalities.
7. The media can play a very positive and proactive role in outbreak control when they are kept well informed and trusted as partners.

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Annex 1A: Glasgow Coma Scale (Adults)

(Source: www.who.int)

TABLE 38-2

Glasgow Coma Scale

BEHAVIOR	RESPONSE	SCORE
Eye opening response	Spontaneously	4
	To speech	3
	To pain	2
	No response	1
Best verbal response	Oriented ot time, place and person	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No response	1
Best motor response	Obeys commands	6
	Moves to localized pain	5
	Flexion withdrawal from pain	4
	Abnormal flexion (decorticate)	3
	Abnormal extension (decerebrate)	2
	No response	1
Total score:	<i>Best response</i>	15
	<i>Comatose client</i>	8 or less
	<i>Totally unresponsive</i>	3

Annex 1B : Modified Glasgow Coma Scale for Infants and Children

Area Assessed	Infants	Children	Score*	
Eye opening	Open spontaneously	Open spontaneously	4	
	Open in response to verbal stimuli	Open in response to verbal stimuli	3	
	Open in response to pain only	Open in response to pain only	2	
	No response	No response	1	
Verbal response	Coos and babbles	Oriented, appropriate	5	
	Irritable cries	Confused	4	
	Cries in response to pain	Inappropriate words	3	
	Moans in response to pain	Incomprehensible words or nonspecific sounds	2	
	No response	No response	1	
Motor response**	Moves spontaneously and purposefully	Obeys commands	6	
	Withdraws to touch	Localizes painful stimulus	5	
	Withdraws in response to pain	Withdraws in response to pain	4	
	Responds to pain with decorticate posturing (abnormal flexion)	Responds to pain with flexion	3	
	Responds to pain with decerebrate posturing (abnormal extension)	Responds to pain with extension	2	
	No response	No response	1	

Interpretation:

- A score of 12 suggests a severe head injury.
- A score of 8 suggests need for intubation and ventilation.
- A score of 6 suggests need for intracranial pressure monitoring

**If the patient is intubated, unconscious, or preverbal, the most important part of this scale is motor response. This section should be carefully evaluated.

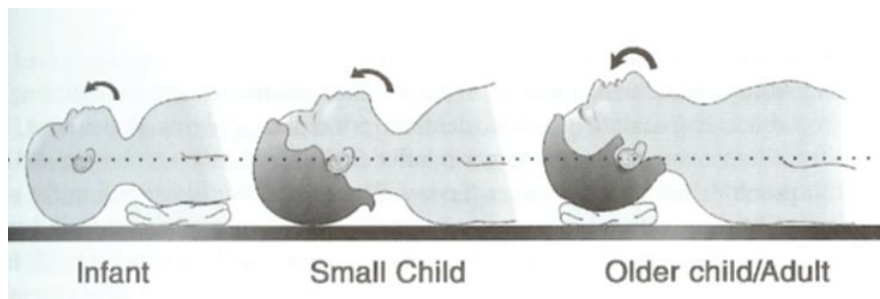
(<http://www.northeastcenter.com/modified-glasgow-coma-scale-for-infants-and-children.htm>)

Annex 2: Resuscitation Through ABC Management

To stabilize patient for maintaining vital functions

A-Airway (oral cavity, nostrils):

- i) Opening up the airway by Head Tilt-Chin Lift maneuver (by Head and neck slightly extended & line from chin to jaw angle perpendicular to floor) or by putting airway tube



- ii) Clearing up the airway of secretions, vomitus by suction with sucker machine (closed circuit) or by manual rubber sucker
- iii) Put the patient in the recovery position

Recovery position



The mouth is downward so that fluid can drain from the patient's airway; the chin is well up to keep the epiglottis opened. Arms and legs are locked as to stabilize the position of the patient

- iv) Endotracheal intubation may be necessary

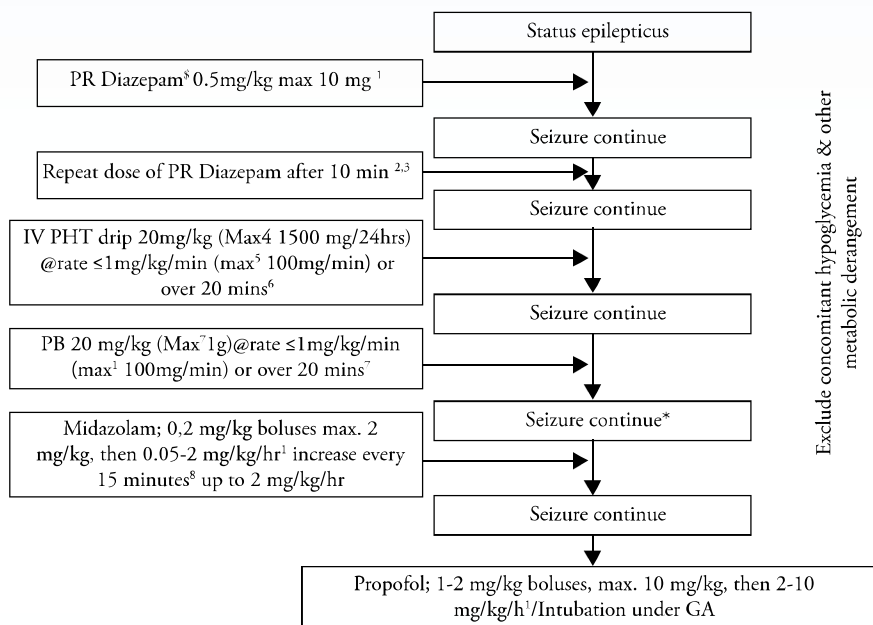
B-Breathing:

- i) Assess breathing
 - a. signs of respiratory distress (Adult: > 25/min, Children: $\geq$ 40/min)
 - b. oxygen saturation (SpO_2 <90% at room air)
 - c. flaring alae nasi
 - d. clinical examination of the chest (symmetry, expansibility, intercostals & subcostal recession)
- ii) If the patient has dyspnoea or cyanosis, give oxygen through face mask (>5L/min) or nasal catheter (1-2 L/min)
- iii) If impending respiratory failure, provide assisted ventilation by bag and mask ventilation or intubation and mechanical ventilation

C-Circulation:

- I. Assess circulation – pulse rate, blood pressure, capillary refill time, cardiovascular examination
- II. Secure an IV line and infuse crystalloid fluid if required
- III. If patient is in shock (low systolic blood pressure and capillary refill time >3 seconds) then s/he will be managed with-
 - a. IV Normal saline (20 ml/kg) bolus rapidly, then reassess and if no improvement, repeat
 - b. Injection Dopamine (0.5-20 microgram/kg/min)-if necessary

Annex 3: Treatment Algorithm for the Management of Status Epilepticus



* Give IV glucose, Sodium bicarb, anti-edema measures (e.g. corticosteroid & mannitol) ^{1,2,9}

20 mg of phenytoin is equivalent to 30 mg of fosphenytoin

Annex 4: Treatment of Cerebral Malaria

Hospital treatment:

- IV Artesunate/IM Artemether will be preferred antimalarials for SM when available
- IV Quinine drip/IM Quinine will be alternative parenteral antimalarials if IV Artesunate/IM Artemether is not available
- Loading dose of Quinine should be given

Parenteral treatment is either:

- Intravenous artesunate (2.4mg/kg stat followed by 1.2mg/kg daily until the patient can tolerate oral medication (or)
- Intramuscular artemether (3.2 mg/kg stat followed by 1.6mg/kg daily until the patient can tolerate oral medication (or)
- Quinine dihydrochloride 20mg salt/kg stat followed by 10mg/kg/8hourly. This may be given by slow intravenous infusion, no faster than 50mg/kg/hour, or by intramuscular injection to the anterior thigh diluted 1:1 in sterile water for injection (the first 20mg/kg dose is splitted; 10mg/kg to each thigh)

Tab ACT/Tab Quinine can be used alternatively once the patient can tolerate oral medication. Tab ACT should be used in full dose (6 dose: e.g., 24 tab for adult). Tab Quinine should be continued as 10 mg/kg/dose 8 hourly to complete a total duration of 7 days (IV+oral)

Artemesinin derivatives	Quinine:
Artesunate: 2.4 mg/kg IV on admission (o hours) followed by 2.4 mg/kg at 12 hours and 24 hours. Then once a day. If the patient is able to swallow, then follow-on oral medication can be given.	Loading dose: Quinine dihydrochloride 20 mg salt/kg of body weight (loading dose) by infusion over 4 hours in 5% dextrose saline (5-10 ml/kg of body weight depending on the patients overall fluid balance).

Artemesinin derivatives	Quinine:
Artemether: 3.2 mg/kg IM on admission followed by 1.6 mg/kg per day until the patient is able to swallow, then follow-up oral medication can be given.	Maintenance dose of Quinine : Eight to twelve hours after the start of the loading dose, give a maintenance dose of quinine 10mg salt/kg of body weight in dextrose saline diluted as above over 4 hours. This maintenance dose should be repeated every 8 hours and upto 6 doses (including loading dose). Thereafter the quinine dose will be reduced to 15-20 mg salt/kg body weight until the patient can take oral medication (e.g. 08hrs, 16hrs, 24hrs).
Artesunate is dispensed as a powder of artesunic acid. This is dissolved in sodium bi-carbonate (5%) to form sodium artesunate. The solution is then diluted in approximately 5 ml of 5% dextrose and given IV. The solution should be prepared freshly for administration and should not be stored.	In children it is infused over a period of 2 hours and repeated every 8 hours (calculated from beginning of the previous infusion) for 6 dose. Then reduction of the dose like adult patient until the patient can tolerate oral medication.
Artemether ampoules of injectable solution of IM containing 80 mg of Artemether in 1 ml for adults or 40 mg of Artemether in 1 ml for paediatrics use	

Source: The Diagnosis and Management of Severe Malaria: Learners guide 2010, Malaria and Parasitic Disease Control Unit, Directorate General of Health Services, Mohakhali, Dhaka 1212, Bangladesh

ANNEX 5: Suspected Acute Meningo-Encephalitis Cases

1. Acute meningo-encephalitis syndrome case definition
 - History of fever or documented fever (axillary temperature $>38.5^{\circ}\text{C}$ [101.3°F]) with any of the following brain pathology:
 - o Altered mental status or
 - o New onset seizures (excluding simple febrile seizure*)
 - o New neurological deficit either diffuse or localized** to the brain
 - OR
 - * Pulmonary presentation
 - i. Illness < 7 days duration AND
 - ii. Fever (axillary temperature $>38.5^{\circ}\text{C}$) AND
 - iii. Severe shortness of breath (i.e. dyspnoea prevents patient from walking unassisted for 10 steps) AND
 - iv. Chest radiograph consistent with diffuse acute respiratory distress syndrome.
 - * Child 6 months to 6 years old whose only finding is fever and single generalized seizure lasting <15 minutes with recovery of consciousness within 60 minutes
 - ** Localized neurological deficit: aphasia, hemiparesis, cranial nerve deficits, movement disorders such as myoclonus/tremors, dysphagia, unilateral sensory or motor dysfunction, partial/focal seizures.

ANNEX 6: Line Listing of all the Cases of Acute Meningo-Encephalitis

Date			
Hospital ID			
Hospital S. No.			
Name			
Occupation			
Caretaker (Relation with pt)			
Age (mo/ yr)			
Sex			
Village/ward			
Location			
District			
Encephalitis +/-			
Pulmonary illness +/-			
Date of illness onset			
Date of admission			
Date of outcome			
Outcome (LAMA, Absconded, Referred, Death)			
Date of Blood collection (Serum1)			
Date of CSF collection			
Date of Throat swab collection			
Date of Urine collection			
Date of Blood collection (Serum2)			
Comments			

ANNEX 7: Cluster Definition and Identification

- Cluster definition: A cluster is defined as two or more patients meeting the case definition who are within 21 days of each other and who live within 30 minutes walking distance of each other or have had contact with one another patient with similar illness.
- Cluster identification
 - a. With each new case that is added to the list the surveillance physician will check the address of the line listed cases in previous three weeks. If they are from the same village or ward, they will probably fit the cluster definition.
 - b. The surveillance physician will also ask the case whether anyone they know has had a recent onset of similar illness in their family, relatives, village or ward who were either hospitalized or did not visit hospital. If the answer is yes, they will be likely form a cluster.
 - c. If they are from the same sub-district but different wards or villages the latest line listed case can be asked about the distance of address of the previous case. Be sure to keep other information from the line listing confidential. If they are within 2 km or 30 minutes walking distance with other they likely form a cluster.

ANNEX 8: Guidelines for Health Care Workers: Nipah Contact Study

Site selection

We are planning to collect Health Care Worker data from the health care centres where the HCWs were almost certain that they provided care to Nipah patients.

Time period

We are fixing the time period from the day of 1st admission of known Nipah case to the last date of discharge/death of Nipah cases in the particular hospital.

Case list in respective hospitals

The respondents will be provided a list of patients considered as “Nipah encephalitis patients” for the purposes of this questionnaire. This option would help ensure consistency between respondents

Health care workers selection

- The healthcare workers who provided any of the following service for Nipah encephalitis patients during the time period as mentioned above

	Activities	Put tick (√) mark
1	Physical examination	
2	Drawing blood	
3	Lumbar puncture	
4	Placing an NG tube	
5	Catheterization	
6	Placing Oxygen tube/mask	
7	Oropharyngeal suction	
8	Changing bed pans	
9	Recording temperature	
10	Washing soiled linens	
11	Other: (Specify) _____	

ANNEX 9: Health Care Worker Encephalitis Transmission Study Consent Form

ID no.: _____ Hospital/Clinic: _____
Name: _____ Age in yrs: _____ Date: ____/____/____

As you may know, a number of individuals living in _____ have recently been afflicted with Nipah encephalitis, many of whom have died. We are conducting an investigation to determine how this disease is spread.

There is evidence of Nipah infection in health care workers in India and Bangladesh from previous outbreaks. As part of this investigation, we are studying the risk to health care workers who have provided care for these patients. We are seeking people who have provided care to the Nipah patients who were admitted in your hospital or service centre. If you agree to participate you will be asked to answer questions on a questionnaire and provide 5 ml blood sample for serological testing. It will take approximately 10 to 15 minutes. The questionnaire will ask about general health, activities related to your job and the services you provided for Nipah encephalitis for patient care.

If you wish to know the results of the testing, that information will be available by calling (Telephone no.) _____

Participation is voluntary and your samples will not be tested for HIV or any genetic tests.

This investigation has important implications for other health care workers as well as the general public and your participation is greatly appreciated.

I agree to participate in the study:

Signature: _____ Date: ____/____/____

Name: _____

Signature of the investigator: _____ Date: ____/____/____

ANNEX 10: Questionnaire on Contact with Encephalitis Patients: Health Care Worker Study

ID No. _____ Interviewer: _____

Date of Interview: ____/____/____

dd/mm/yyyy

Personal information:

1. What is your name? _____
2. What is your age? _____ years
3. Sex: 1. Male 2. Female

Work related questions:

4. What type of ward did you work on from/...../....
(dd/mm/yyyy) to/...../..... (dd/mm/yyyy)? (give tick in all
appropriate boxes):

Working place	Put tick (✓) mark
a. ICU	☐
b. Isolation unit	☐
c. Pediatric unit	☐
d. Female Internal Medicine unit	☐
e. Male Internal Medicine unit	☐
f. Emergency unit	☐
g. Psychiatric unit	☐
h. Pathological unit	☐
i. X-ray/CT scan/MRI/Ultrasonography	☐
j. Other (<i>specify</i>): _____	☐

5. What is your occupation? (Put tick in appropriate box):

	Occupation	Put tick (✓) mark
1	Doctor	☐
2	Nurse	☐
3	Ayah	☐
4	Ward boy	☐
5	Cleaner	☐
6	Phlebotomist/ Lab Technician	☐
7	Kitchen worker/food server	☐
8	X-ray/CT scan/MRI/Ultrasonography	☐
9	Others (Specify) _____	☐

6. Did you provide services to any Nipah encephalitis patients from from .../.../.... (dd/mm/yyyy) to -----/-----/-----/ (dd/mm/yyyy)?

1. Yes 2. No 9. DK

☐

7. If Yes, how many total days would you estimate that you provided direct care of Nipah encephalitis patients from between/...../.... (dd/mm/yyyy) and/.../.... (dd/mm/yyyy)?

8. When (date) did you first provide care (exposure) to a Nipah encephalitis patient from ?
-----/-----/-----/

9. How many Nipah encephalitis patients from did you provide care between/...../.... (dd/mm/yyyy) and/...../..... (dd/mm/yyyy)?

1. Only one patient 2. 2-5 patients 3. More than 5 patients

☐

10. What types of patient care activities did you provide to Nipah encephalitis patients from during/...../.... (dd/mm/yyyy) and/...../..... (dd/mm/yyyy)?

	Activity	Put tick (✓) mark
1	Physical examination	☐
2	Drawing blood	☐
3	Lumbar puncture	☐
4	Placing an NG tube	☐
5	Catheterization	☐
6	Placing Oxygen tube/mask	☐
7	Oropharyngeal suction	☐
8	Providing medications	☐
9	Recording temperature	☐
10	Administering injection (IM)	☐
11	Administering IV saline/injection	☐
12	Changing bed pans	☐
13	Washing soiled linens	☐
14	Other: (Specify)_____	☐

11. In working with a Nipah encephalitis patient from _____
 did you ever receive a needle stick injury from a needle which was
 in contact with the patient's blood? ☐
1. Yes 2. No

12. In working with a Nipah encephalitis patient from _____
 _____ were you ever splashed in the eye, nose or mouth
 with the following body fluids from the patient?

	Body fluid	Put tick (✓) mark
1	Cough/sputum	☐
2	Sneeze	☐
3	Spit	☐
4	Vomitus	☐
5	Saliva	☐
6	Stool	☐
7	Urine	☐
8	Blood	☐
9	CSF	☐

13. In working with an Nipah encephalitis patient from _____ did you ever have direct skin contact with respiratory secretions, stool, urine, or blood from the patient?

	Body fluid	Put tick (✓) mark
1	Cough/sputum	☐
2	Sneeze	☐
3	Spit	☐
4	Vomitus	☐
5	Saliva	☐
6	Stool	☐
7	Urine	☐
8	Blood	☐
9	CSF	☐
10	Sweat	☐
11	Tear	☐

14. What type of protection have you worn most of the time when performing patient care activities involving contact with body fluids of encephalitis patients from _____?

	Activity	Put tick (✓) mark
1	No protection	☐
2	Gown only	☐
3	gloves only	☐
4	gloves and surgical mask	☐
5	surgical mask alone	☐
6	gloves, mask and gown	☐
7	gloves, mask, gown and eye protection	☐
8	other (specify): _____	☐

Recent illness:

15. Have you had any illness since ____/____/____dd/mm/yyyy

1. Yes 2. No

if yes,

☐

15.1 What was the date of your first symptoms? ____/____/____dd/mm/yyyy

15.2 Which of the following symptoms did you have:

(circle one answer for each symptom)

	Symptom	Put tick (✓) mark
1	Fever	☐
2	Sore throat	☐
3	Cough	☐
4	Head ache	☐
5	Generalized body ache	☐
6	Nausea/vomiting	☐
7	Altered mental status	☐
8	Lethargy	☐
9	Convulsion	☐
10	Other: (please describe): _____	☐

15.3 Did you see a physician for treatment of your illness?

1. Yes 2. No ☐

16. Have you missed work since January 1, 2011 for any medical reason?

1. Yes 2. No ☐

if yes:

16.1 What was the reason? _____

17. Serum sample collection

1. Yes 2. No ☐

if yes, Date of sample collection: ____/____/____ dd/mm/yyyy

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(not according to warrant of precedence)

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LIST of GLOSSARY

<i>Gamcha</i>	A thin, coarse, traditional cotton towel that is usually used to dry the body after bathing or wiping sweat
<i>Khejurer rosh</i>	Date palm sap
Malaysia, peninsular	Also known as West Malaysia (formerly Malaya), is the part of Malaysia which lies on the Malay Peninsula
N95	Particulate respirator/mask
Nipah	A village in Malaysia
Nosocomial	Hospital acquired
One Health	One Health is a concept that seeks to address emerging health challenges by promoting increased communications and collaborations between human, animal, and environmental health specialists
Outbreak	An occurrence of disease or health event greater than would otherwise be expected at a particular time and place
Surveillance	Systematic ongoing collection, collation and analysis of data for public health purposes and the timely dissemination of public health information for assessment and public health response as necessary
Telemetry	Technology that allows remote measurement and reporting of information
Zoonotic	Any infectious disease that can be transmitted (in some instances, by a vector) from non-human animals, both wild and domestic, to humans or from humans to non-human animals (the latter is sometimes called reverse zoonosis or anthroponosis)



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