Guidance on clinical care and Infection control Practices
Pathology

- Nipah – necrotising vasculitis with predeliction especially for brain and lung.

- In the current outbreak, myocarditis was also present in 51% of patients.

- Fibrinoid necrosis in kidneys also observed.
Clinical cases

• Clinical presentations – Encephalitis, ARDS or Myocarditis
• One patient had only fever, headache, tiredness, cervical adenopathy
• Myocarditis, Encephalitis. ARDS
• Vasomotor dysautonomia
• Flu like illness
Profile

Complication profile

- Encephalitis + ARDS: 37%
- Encephalitis + ARDS + Myocarditis: 5%
- Encephalitis + Myocarditis: 5%
- ARDS: 27%
- ARDS + Myocarditis: 5%
- Flu-like symptoms: 5%
- 21%
<table>
<thead>
<tr>
<th>S No</th>
<th>Symptom</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fever</td>
<td>100%</td>
</tr>
<tr>
<td>2</td>
<td>Headache</td>
<td>94.73%</td>
</tr>
<tr>
<td>3</td>
<td>Fatiguability</td>
<td>94.73%</td>
</tr>
<tr>
<td>4</td>
<td>Cough</td>
<td>73.68%</td>
</tr>
<tr>
<td>5</td>
<td>Sore throat</td>
<td>52.63%</td>
</tr>
<tr>
<td>6</td>
<td>Vomitting</td>
<td>73.68%</td>
</tr>
<tr>
<td>7</td>
<td>Diarrhoea</td>
<td>10.5%</td>
</tr>
<tr>
<td>8</td>
<td>Breathlessness</td>
<td>78.94%</td>
</tr>
<tr>
<td>9</td>
<td>Alteration of sensorium</td>
<td>84.2%</td>
</tr>
<tr>
<td>10</td>
<td>Seizures</td>
<td>36.84%</td>
</tr>
<tr>
<td>11</td>
<td>Myoclonus</td>
<td>10.5%</td>
</tr>
<tr>
<td>12</td>
<td>Vasomotor dysautonomia</td>
<td>52.63%</td>
</tr>
<tr>
<td>13</td>
<td>Neurologic deficit</td>
<td>26.3%</td>
</tr>
<tr>
<td>14</td>
<td>Bilateral ptosis and ophthalmoplegia</td>
<td>26.3%</td>
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<tr>
<td>15</td>
<td>Neck stiffness</td>
<td>10.5%</td>
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Management

• General measures
• Proper Triaging
• Standards of care of
  Encephalitis
  ARDS
  Myocarditis
Use of Ribavirin

• Dose 2 g stat, 1 g 6 hourly 4 days followed by 500mg 6 hourly for 5 days (based on WHO guideline)
• Started on confirmation of NiV

• Ribavirin has broad activity against RNA and some DNA viruses
• RIBAVIRIN HAS NO ROLE IN PROPHYLAXIS
Nipah virus, a newly identified paramyxovirus caused a severe outbreak of encephalitis in Malaysia with high fatalities. We report an open-label trial of ribavirin in 140 patients, with 54 patients who were managed prior to the availability of ribavirin or refused treatment as control. There were 45 deaths (32%) in the ribavirin arm; 29 deaths (54%) occurred in the control arm. This represents a 36% reduction in mortality ($p = 0.011$). There was no associated serious side effect. This study suggests that ribavirin is able to reduce the mortality of acute Nipah encephalitis.
Combined chloroquine and ribavirin treatment does not prevent death in a hamster model of Nipah and Hendra virus infection

Alexander N. Freiberg,1 Melissa N. Worthy,1 Benhur Lee2,3,4 and Michael R. Holbrook1,5,6†

Hendra virus (HeV) and Nipah virus (NiV) are recently emerged, closely related and highly pathogenic paramyxoviruses that cause severe disease such as encephalitis in animals and humans with fatality rates of up to 75%. Due to their high case fatality rate following human infection and because of the lack of effective vaccines or therapy, they are classified as Biosafety Level 4 pathogens. A recent study reported that chloroquine, an anti-malarial drug, was effective in preventing NiV and HeV infection in cell culture experiments. In the present study, the antiviral efficacy of chloroquine was analysed, individually and in combination with ribavirin, in the treatment of NiV and HeV infection in in vivo experiments, using a golden hamster model. Although the results confirmed the strong antiviral activity of both drugs in inhibiting viral spread in vitro, they did not prove to be protective in the in vivo model. Ribavirin delayed death from viral disease in NiV-infected hamsters by approximately 5 days, but no significant effect in HeV-infected hamsters was observed. Chloroquine did not protect hamsters when administered either individually or in combination with ribavirin, the latter indicating the lack of a favourable drug–drug interaction.
Therapeutic Treatment of Nipah Virus Infection in Nonhuman Primates with a Neutralizing Human Monoclonal Antibody

Thomas W. Geisbert¹,²,*,†, Chad E. Mire¹,²,*, Joan B. Geisbert¹,², Yee-Peng Chan³, Krystle exposure before animals show signs of disease. We assessed the efficacy of a fully human monoclonal antibody, m102.4, at several time points after virus exposure including at the onset of clinical illness in a uniformly lethal nonhuman primate model of NiV disease. Sixteen African green monkeys (AGMs) were challenged intratracheally with a lethal dose of NiV, and 12 animals were infused twice with m102.4 (15 mg/kg) beginning at either 1, 3, or 5 days after virus challenge and again about 2 days later. The presence of viral RNA, infectious virus, and/or NiV-specific immune responses demonstrated that all subjects were infected after challenge. All 12 AGMs that received m102.4 survived infection, whereas the untreated control subjects succumbed to disease between days 8 and 10 after infection. AGMs in the day 5 treatment group exhibited clinical signs of disease, but all animals recovered by day 16. These results represent the successful therapeutic in vivo efficacy by an investigational drug against NiV in a nonhuman primate and highlight the potential impact that a monoclonal antibody can have on a highly pathogenic zoonotic human disease.
Current Primary Challenges, Key Needs, and Knowledge Gaps

Primary challenges

- Patients typically present late in the clinical course of disease, which decreases the likelihood of successful treatment.
- The absence of improved diagnostic assays for timely diagnosis of infection creates an important challenge in providing early treatment and PEP to exposed persons.
- In the NiV-endemic region of Bangladesh, hundreds of patients are admitted to hospitals annually with a diagnosis of encephalitis, but do not have NiV infection. In the absence of confirmatory testing, treating all patients with encephalitis and their contacts for NiV infection would be costly and labor intensive, with relatively little benefit; therefore accurate and rapid diagnosis is critical.
- Studies in animals often evaluate usefulness of therapeutics when delivered prior to disease onset or early during the disease course. Patients with NiV infection often are detected later in the clinical course, which creates challenges for predicting how well an agent will work in the field.
- Nipah virus can infect the central nervous system (CNS), which creates challenges for generating therapeutic agents that cross the blood-brain barrier to inhibit viral replication and prevent severe neurologic disease.
Key needs

- A TPP for NiV therapeutic agents, identifying optimal and desirable characteristics to guide the development of promising treatment approaches in the context of individual and community priorities.
- Safe, easily administered, well-tolerated, and effective therapeutic agents that treat acute NiV infection to improve survival and decrease associated morbidity and long-term disability.
- Safe, easily administered, well-tolerated, and effective therapeutic agents that treat chronic (relapsing) NiV infection to decrease associated long-term disability.
- Safe and effective PEP to prevent infection following exposure to NiV and guidance on PEP use. PEP could be used to prevent illness in healthcare workers, family caregivers, and persons exposed to infected livestock.
- Improved patient care in endemic areas (such as the ability to provide ventilator support for seriously ill patients).
Knowledge gaps

• Ribavirin may be an option, but further research needed to prove its potential effectiveness
• Studies are needed to assess safety, efficacy and tolerability of mAb 102.4 as a therapeutic agent in early clinical disease and as PEP
• Pre clinical and clinical data are needed on safety and efficacy of other novel agents such as GS 4734, fusion inhibitory peptides and others
• Further research needed to broaden the number of novel antiviral agents
Prevention Is Better Than Cure. Especially When Something Has No Cure.

~ The Fresh Quotes ~
INFECTION CONTROL AND PREVENTION
Screening and Triage

Protect healthcare workers (HCWs) from infection

• Recognize and isolate suspected NiV cases to prevent further transmission.

• Alert public health authorities and healthcare workers when an NiV case has occurred in their or an adjoining district.

• Set up isolation and safe referral of suspected cases to Treatment facility

• Manage contact tracing.

• Inform patient and family.
Preparedness- Set up

• A system to manage waste and contaminated materials

• Clear instructions for cleaning and disinfecting surfaces and equipment

• Ensure availability of adequate supplies of personal protective equipment (PPE)

• Set up safe burials practices of deceased patient
Preparedness- Set up

Set up hand hygiene stations (soap and water, alcohol-based hand rub [ABHR]).

Reinforce hand washing with poster in local language

Train all clinical and non clinical staff on infection prevention and control (IPC) measures and screening strategy.
Respiratory hygiene

• Maintain a social distance (at least 1 metre) from others

• Cover nose and mouth during coughing or sneezing with medical mask, cloth mask, tissue, or flexed elbow

• – Followed by hand hygiene after contact with respiratory secretions.
Sample collection

• Sample collection should be done
  • only AFTER ADMISSION
  • in an appropriately secure isolation facility,
  • ensure that the person doing the collection is using adequate PPE

• During sample collection
  • wear complete disposable Personal Protective Equipment
  • Wash hands with soap and water properly
  • then clean hands using 1-2 ml alcohol based hand sanitizer before and after collection of samples.
Collection and transportation of samples

- Sample vials & other accessories
- Suitable sample containers, gel packs & coolant box
- Arrange the sample vials with proper labeling
- Place vials in leak-proof secondary container
- Arrange the packed container in outer shipment container with case report form & labeled address
Transmission based precautions

A. Contact precautions
B. Droplet precautions.
C. Airborne precautions

• Aerosol generating procedures like suction, intubation, resuscitation, nebulization etc
• All patients in ICU, airborne precautions must be adopted.
 IPC ADVISORY

- Wash hands thoroughly with soap and water for 20/30 seconds after contact with a sick patient
- Use appropriate mask and gloves during history taking, physical examination, sample collection and other care-giving to suspected Nipah cases
- Follow Standard precautions for infection control at hospital settings
- Safe waste disposal for potentially infected material including used PPE, linen, clothing of patient
DONNING STEPS

SEQUENCE FOR PUTTING ON PERSONAL PROTECTIVE EQUIPMENT (PPE)

The type of PPE used will vary based on the level of precautions required, such as standard and contact, droplet or airborne infection isolation precautions. The procedure for putting on and removing PPE should be tailored to the specific type of PPE.

1. GOWN
   - Fully cover torso from neck to knees, arms to end of wrists, and wrap around the back
   - Fasten in back of neck and waist

2. MASK OR RESPIRATOR
   - Secure ties or elastic bands at middle of head and neck
   - Fit flexible band to nose bridge
   - Fit snug to face and below chin
   - Fit-check respirator

3. GOGGLES OR FACE SHIELD
   - Place over face and eyes and adjust to fit

4. GLOVES
   - Extend to cover wrist of isolation gown

USE SAFE WORK PRACTICES TO PROTECT YOURSELF AND LIMIT THE SPREAD OF CONTAMINATION

- Keep hands away from face
- Limit surfaces touched
- Change gloves when torn or heavily contaminated
- Perform hand hygiene
**DOFFING PROCEDURE**

**EXAMPLE 1**

There are a variety of ways to safely remove PPE without contaminating your clothing, skin, or mucous membranes with potentially infectious materials. Here is one example. **Remove all PPE before exiting the patient room except a respirator, if worn.** Remove the respirator after leaving the patient room and closing the door. Remove PPE in the following sequence:

1. **GLOVES**
   - Outside of gloves are contaminated!
   - If your hands get contaminated during glove removal, immediately wash your hands or use an alcohol-based hand sanitizer
   - Using a gloved hand, grasp the palm area of the other gloved hand and peel off first glove
   - Hold removed glove in gloved hand
   - Slide fingers of ungloved hand under remaining glove at wrist and peel off second glove over first glove
   - Discard gloves in a waste container

2. **GOGGLES OR FACE SHIELD**
   - Outside of goggles or face shield are contaminated!
   - If your hands get contaminated during goggle or face shield removal, immediately wash your hands or use an alcohol-based hand sanitizer
   - Remove goggles or face shield from the back by lifting head band or ear pieces
   - If the item is reusable, place in designated receptacle for reprocessing. Otherwise, discard in a waste container
3. **GOWN**
- Gown front and sleeves are contaminated!
- If your hands get contaminated during gown removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Unfasten gown ties, taking care that sleeves don’t contact your body when reaching for ties
- Pull gown away from neck and shoulders, touching inside of gown only
- Turn gown inside out
- Fold or roll into a bundle and discard in a waste container

4. **MASK OR RESPIRATOR**
- Front of mask/respirator is contaminated — DO NOT TOUCH!
- If your hands get contaminated during mask/respirator removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Grasp bottom ties or elastics of the mask/respirator, then the ones at the top, and remove without touching the front
- Discard in a waste container

5. **WASH HANDS OR USE AN ALCOHOL-BASED HAND SANITIZER IMMEDIATELY AFTER REMOVING ALL PPE**

**PERFORM HAND HYGIENE BETWEEN STEPS IF HANDS BECOME CONTAMINATED AND IMMEDIATELY AFTER REMOVING ALL PPE**
Doffing (Removal) = Critical Process

Most Provider exposures occur during PPE Removal (doffing)!
TRAINING
Handling corpse
“An ounce of prevention worth a pound of cure”

– Benjamin Franklin