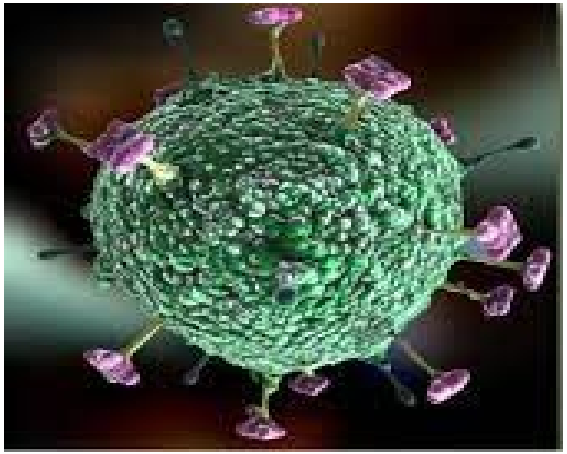
NIPAH VIRUS INFECTION

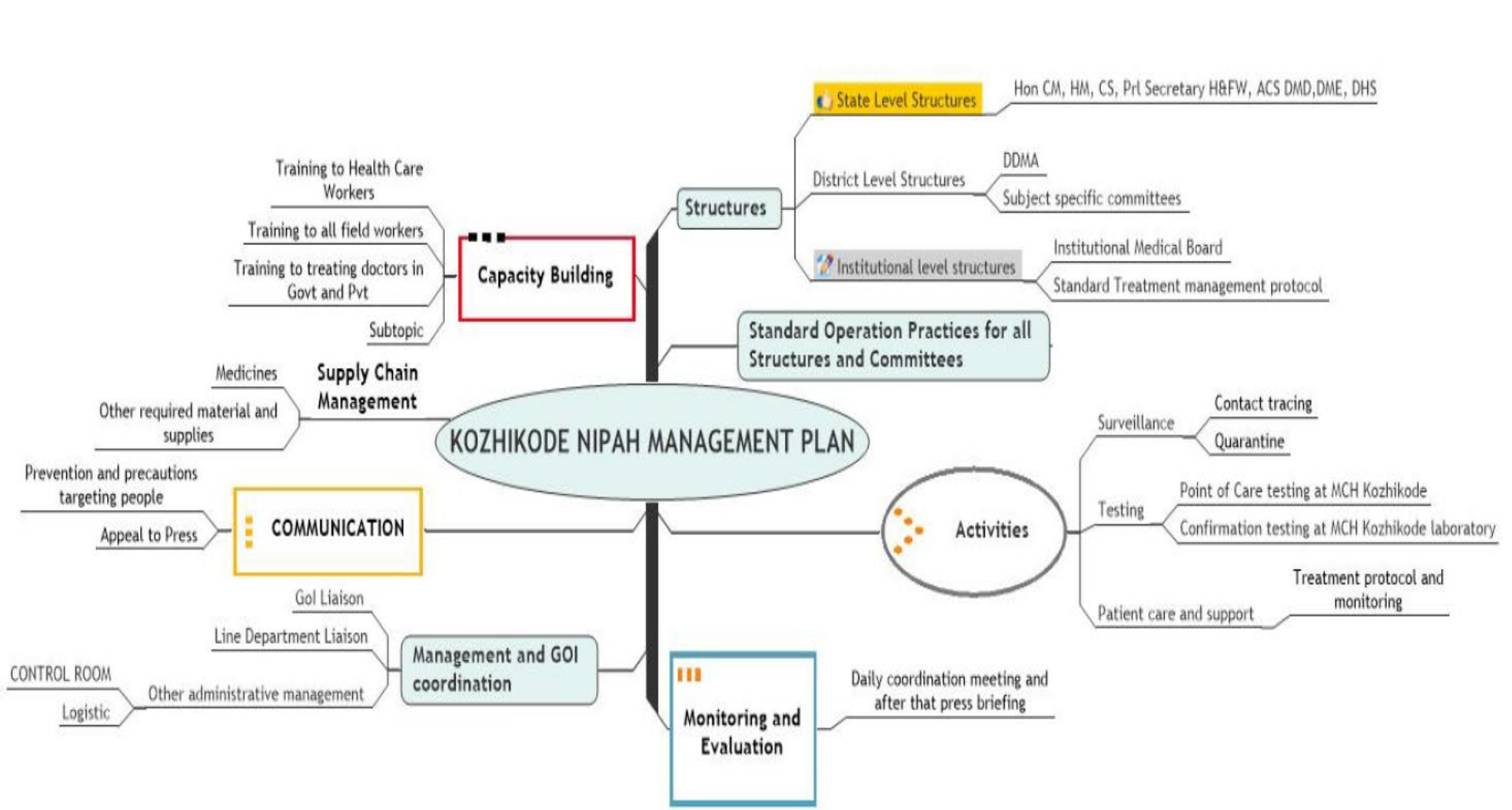
GUIDELINES FOR SURVEILLANCE, DIAGNOSIS,TREATMENT, PREVENTION AND CONTROL



Date – 05/09/2021

Health & Family Welfare Department,
Govt of Kerala.
Thiruvananthapuram, Kerala

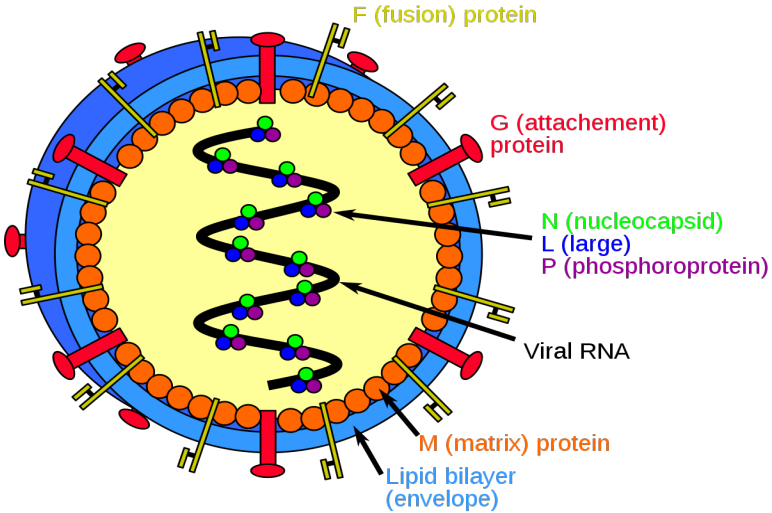
MANAGEMENT PLAN FOR NIPAH OUTBREAK IN KOZHIKODE – 5TH SEPT 2021


KOZHIKODE NIPAH MANAGEMENT PLAN
Capacity Building
Training to Health Care Workers
Training to all field workers
Training to treating doctors in Govt and Pvt
Subtopic
Structures
State Level Structures
Hon CM, HM, CS, Prl Secretary H&FW, ACS DMD,DME, DHS
District Level Structures
DDMA
Subject specific committees
Institutional level structures
Institutional Medical Board
Standard Treatment management protocol
Standard Operation Practices for all Structures and Committees
Supply Chain Management
Medicines
Other required material and supplies
COMMUNICATION
Prevention and precautions targeting people
Appeal to Press
Activities
Surveillance
Contact tracing
Quarantine
Testing
Point of Care testing at MCH Kozhikode
Confirmation testing at MCH Kozhikode laboratory
Patient care and support
Treatment protocol and monitoring
Management and GOI coordination
GoI Liaison
Line Department Liaison
Other administrative management
CONTROL ROOM
Logistic
Monitoring and Evaluation
Daily coordination meeting and after that press briefing

- Nipah Virus (NiV) Infection is recognized as a deadly infection in 1998 came to a better attention in Kerala with the outbreak in 2018 and 2019

NIPAH VIRUS

Nipah Virus (NiV) is a highly pathogenic RNA virus belonging to the Paramyxoviridae family and grouped under the genus Henipavirus.



- Two NiV clades have been proposed so far; B genotype in Bangladesh, and M genotype in Malaysia.
- The complete NiV genome of the Kerala strain had 85.14%–96.15% similarity with M and B NiV genotype.

NATURAL RESERVOIR

- Large fruit bats of Pteropus genus are the natural reservoir of NiV.
- High positivity of NiV was detected in bat throat swabs, and showed persistence of virus for a couple of hours on contaminated fruits, which enhance the chances of human infection.

- Pigs are identified as intermediate hosts.
- NiV positivity was identified in bats from North Eastern Region states and Kerala.

SEASONALITY

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

INCUBATION PERIOD

Incubation period: varies from 4-14 days.

MODE OF TRANSMISSION

- Human infection results from spillover transmission from bats or through human-to-human transmission.
- Direct bat-to-human transmission occur through fruits contaminated by bat's secretions - urine or saliva- or consumption of raw date palm sap [tari] contaminated by bat saliva.

Malaysian outbreak, human infection occurred through contact with respiratory secretions and urine from infected pigs, which got infected after consumption of partially bat eaten fruits dropped.

- In the 2014 Philippines outbreak, infected horses were identified as the intermediate hosts.
- Clustering of symptomatic cases mainly adults among close contacts and households is an important clinical clue to this infection.
- In 2018 Kerala outbreak, all cases except the index case the transmission was from human to human.

DIAGNOSIS AND SURVEILLANCE

- Early identification and diagnosis is of prime importance in NiV infection.
- The case management includes strategic plans to prevent spread through contacts and this requires proper triaging and isolation.

CASE DEFINITIONS

SUSPECT NIPAH CASE

Person from an area/ locality affected by a Nipah virus disease outbreak who has:

- Acute Fever with new onset of altered mental status or seizure and/or
- Acute Fever with severe headache and/or
- Acute Fever with Cough or shortness of breath

PROBABLE NIPAH CASE

Suspect case-patient/s who resided in the same village where suspect/confirmed case of NIPAH were living during the outbreak period and who died before complete diagnostic specimens could be collected

OR

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

CONFIRMED NIPAH CASE

Suspected case who has laboratory confirmation of Nipah virus infection either by:

- Nipah virus RNA identified by PCR from throat swab, urine, serum or cerebrospinal fluid (optional).
- Isolation of Nipah virus from throat swab, urine, serum or cerebrospinal fluid.

DEFINITION OF A CONTACT

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

- Was admitted simultaneously in a hospital ward/ shared room with a suspect/confirmed case of Nipah virus disease

- Has had direct close contact with the suspect/confirmed case of Nipah virus disease during the illness including during transportation.
- Has had direct close contact with the (deceased) suspect/confirmed case of Nipah virus disease at a funeral or during burial preparation rituals

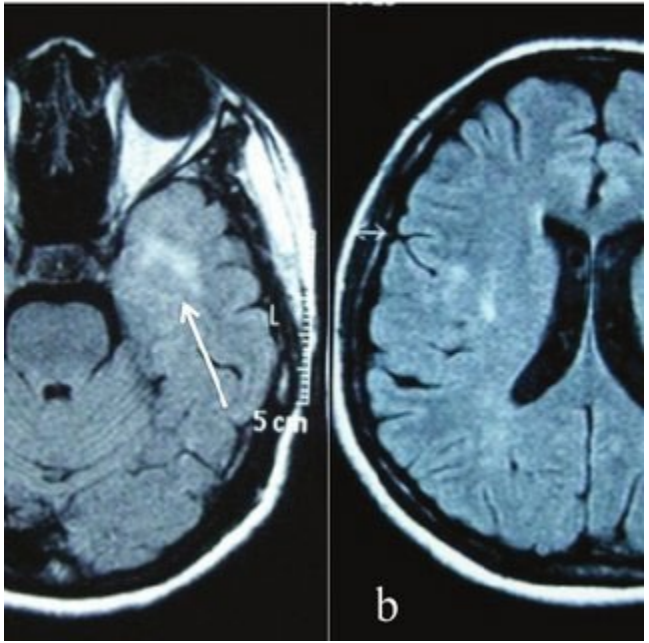
- Has touched the blood or body fluids (saliva, urine, vomitus etc.) of a suspect/confirmed case of Nipah virus disease during their illness
- Has touched the clothes or linens of a suspect/confirmed case of Nipah virus disease

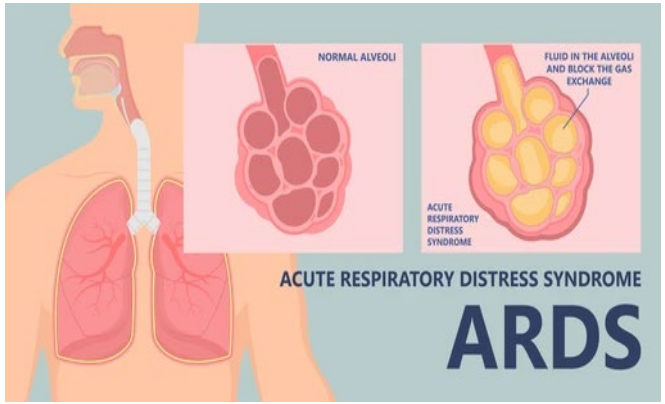
These contacts need to be followed up for appearance of symptoms of NiV for the longest incubation period (21 days). They must be transported to appropriate care facility if they develop symptoms with proper infection control practices.

CLINICAL FEATURES

- Fever, Altered mental status, Severe fatigue, Headache, Respiratory distress, Cough, Vomiting, Muscle pain, Convulsion, Diarrhoea

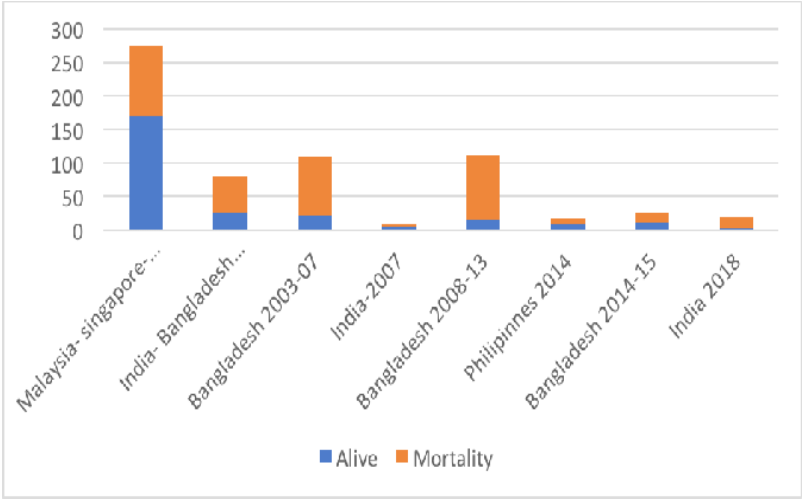
- In infected people, Nipah virus causes severe illness characterized by inflammation of the brain (encephalitis) or respiratory diseases.





- The syndromic presentations are ARDS, Myocarditis and Encephalitis.
- Patients can present with fever alone.
- All patients coming with fever with any other symptom having an epidemiological link and history of contact must be treated as NiV infection and must be tested for the NiV infection.

- In general, the case–fatality rate is estimated at 40–75%; however, this rate can vary by outbreak and can be upto 100%.



LAB DIAGNOSIS

Investigations to be done for confirmation of diagnosis

- Real-Time RT-PCR Viral RNA
- Anti-NiV IgM
- IgG antibodies by enzyme-linked immunosorbent assay

SAMPLE COLLECTION AND TRANSPORT AND TESTING GUIDELINES

- Laboratory confirmation of a suspect and also a symptomatic with definite history of contact case can be made during the acute and convalescent phases of the disease by using a combination of tests.
- The samples have to be sent to designated laboratories identified as per protocols prepared.

- Universal, standard droplet and bio-containment precautions should be followed during contact with excretions, secretions and body fluids of suspected patient for Nipah virus.
- Adequate bio-safety precautions should be adopted during collection/transport/ storage/ processing of suspected sample.

The samples should be collected in all patients (suspect or symptomatic with contact with Nipah) as early as possible with all biosafety precautions and documenting the clinical details on the proforma (provided from the testing laboratory).

- Sample collection should be done only AFTER ADMISSION into an isolation facility, and ensuring that the staff member doing the collection is following proper infection control practices.

- During sample collection wear complete disposable Personal Protective Equipments (N 95 mask, double surgical gloves, gowns, goggles foot cover, etc).
- Wash hands with soap and water at least for 30 seconds and then clean hand using alcohol based hand sanitizer before and after collection of samples.

SAMPLE TRANSPORTATION TO NIV PUNE

- Sample Management team under the Nodal Officer for NIPAH Lab Surveillance processed and triple packed samples labelled as Biological Specimen through Spice Jet Cargo/Indigo Airlines from CIAL
- Cargo booked under the name of official concerned and the required declarations submitted and sent along with the CARGO as per the IATA guidelines

- Clinical details of the patient and SRF Forms sent to ICMR-NIV,BSL4 lab division head by the district Nodal Officer.
- The reports were received at the district after 24-32 hours of sending the samples to PUNE (including the transit time)

THE RECOMMENDED SAMPLES ARE

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

- Samples should be safely packed in triple container packing and should be transported securely under cold chain (2-8°C) to the testing laboratory with prior intimation.
- Sample containing vials, tightly closed, should be kept in good quality zip-lock bags wrapped with sufficient absorbent cotton padding so that inside material should not come out of bag if it leaks.

- The plastic bag should be kept in another Zip-lock bag similarly, which should be sealed with adhesive tape.
- This carrier should be placed in a hard container sealed with impermeable tape or plaster and placed in thermocol box /vaccine carrier containing ice packs.

- The case sheets with complete information should be placed in plastic bag and should be pasted outside the container.
- Samples should be transported at 2-8°C to the have to be sent to designated testing centers as per the testing protocols.

OTHER INVESTIGATIONS

- All treatable cases like bacterial infections, malaria and herpes encephalitis must be included in the differentials depending on the clinical presentation.
- Tests must be ordered appropriately.

SURVEILLANCE

Case identification and Contact tracing:

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

RISK STRATIFICATION OF CONTACTS

RISK CATEGORY	DESCRIPTION
High Risk	1. Any contact with body fluids (blood, urine, salivaetc) of a confirmed case of Nipah 2. Any contact with body fluids of a probable case who died without a lab confirmation of Nipah 3. Spend time in close proximity or in closed spacefor more than or equal to 12 hrs
Low Risk	Any other contact such as touching, contact with clothes or linen or any other item used

FOLLOW UP ACTION

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

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MANAGEMENT OF NIPAH VIRUS INFECTION

- NiV infection is different from other viral infections or pathogens because of its potential of transmission from human to humans with high mortality and no definite treatment or vaccine so far identified.
- So the management essentially involves infection control practices and triaging, isolation and management of patients including intensive supportive care.

TRIAGING OF PATIENTS

All patients having fever must report to Fever triage from where they will be sent to the isolation facility

- Ensure strict adherence to proper Triaging
- Proper infection control practices must be followed up.
- Ensure personal safety. Wear apron and gloves as appropriate.

- General measures – ABCDE approach (Airway, Breathing, Circulation, Disability, Exposure)
- Plan for appropriate care including intensive supportive care

The most important step in patient care is intensive supportive care.

SETTING UP AN ISOLATION FACILITY

Who should be kept in isolation facility/ward/ICU

- History of close contact with confirmed case presenting with fever or any symptoms suggestive of Nipah infection (*vide clinical features)*
- Health care provider who has come in contact with the patient with fever / severe headache / altered sensorium / breathlessness/cough

ISOLATION FACILITY

- Enter all the details of HCWs entering the isolation facility in the Register for ensuring appropriate follow up
- Only HCWs trained in infection control practices should be posted in the isolation facility.
- Monitor staff health, sick people should not be allowed at work.

- They must report immediately through the contact numbers provided if they develop any health related problems during the period and up to another 21 days after the last day of duty
- Patients with high clinical suspicion Encephalitis /ARDS/Myocarditis during an outbreak

- Infection control practices should be strictly adhered and audited
- Proper instructions should be followed while entering the room
- The entry of the health care provider should be through Donning area, and then to the triage or treatment area.
- The exit should be separate for the health care provider and there should be facility for doffing and appropriate facility for hand washing / bathing.

- Patient entry and shifting should be separately marked.
- The deceased should be handled separately as per protocols.
- Single room with attached toilet facility must be provided for each patient.
- Separate equipments (BP apparatus, Stethoscope, Thermometer, Pulse oximeter) for each room and use only disposable consumables to be used.

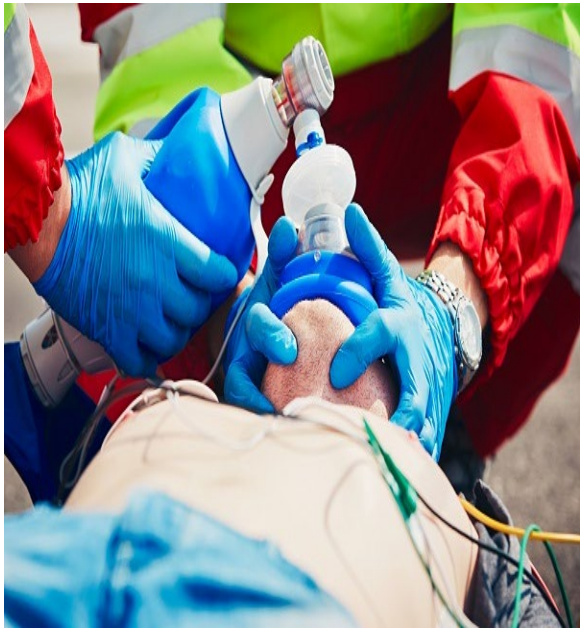
TREATMENT

- Standard care must be provided as in any other infection presenting with Encephalitis, ARDS, and or Myocarditis.
- Care should be individualized according to the clinical presentation and management decisions of the treating clinician.

The basic supportive measures are outlined below:

- Isolation of patient in the isolation facility
- Use of PPEs
- Hand washing with soap & water before and after handling/visiting patients

- Resuscitation (if needed): ABC : Airway, Breathing , Circulation
- Care of unconscious patient: change of posture, care of eye, bladder, bowel and mouth
- O2 inhalation if there is respiratory difficulty



- Nutritional support: oral/NG tube feeding according to the condition of the patient
- Maintain fluid and electrolyte balance (Adults: 5% DNS, Children: 5% DNS, half or quarter strength saline)
- 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
- Maintain intake output chart
- Bronchodilators when needed may be given through spacers

DRUG TREATMENT OPTIONS

- No approved drugs or vaccines are currently available.
- There is an unmet need for newer therapeutic options for NiV infection.
- Currently the available treatment options are very limited.

RIBAVIRIN

- Ribavirin, a nucleoside analogue with broad activity against several RNA and some DNA viruses.
- Used in Malaysian outbreak in an open label trial with 36% reduction in mortality, but further studies in animal models proved ineffective.

- The dose used was 2 g stat, 1 g 6 hourly 4 days followed by 500mg 6 hourlyfor 5 days (based on WHO guideline for other haemorrhagic fevers)on confirmation of NiV infection.
- (Available as 200 mg capsules –Day 1- 10 capsules stat, then 5 capsules of 200 mg 6 hourly for first four days followed by 200 mg capsules 3-2-3-2 for 5th to 10th day – total of 150 capsules).

Adverse effects of Ribavirin

- Rare if used for short term.
- The Major adverse effects on long term treatment are hypersensitivity, hemolytic anemia, significant teratogenic and/or embryocidal effects in animal studies, bone marrow suppression.
- The complete haemogram and LFT need to be monitored.

Monoclonal antibody m102.4

M102.4 recognizes the G envelope protein of NiV and appears to block the receptor binding site on the protein preventing adhesion to the Ephrin B2 protein and thereby inhibiting viral entry into the host cell.

STANDARD CARE FOR ENCEPHALITIS

- Patients with increased intracranial pressure
- Management of fever, pain, control of cough and other strains.

  Manage Fever, pain with paracetamol, avoid NSAIDs
- Prevention of seizures
- Control of systemic hypertension
- Elevate head above the heart (usually 30 degrees)

- Furosemide 0.5 to 1.0 mg/kg IV and / or mannitol 1 g/KgIV over 30-60 minutes, Repeat dosing can be given as needed, generally every eight hours–provided circulatory volume is protected
- IV Sedation and mechanical ventillation

- Seizures

  - ✓ Lorazepam 4 mg IV or
  - ✓ Phenytoin 100mg IV q6-8h or
  - ✓ Fosphenytoin 150PE q8h IV or
  - ✓ Levetiracetam 500mg q8-12h IV

STANDARD CARE FOR MYOCARDITIS

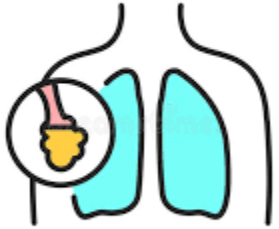
- Supportive therapy for symptoms of acute heart failure with use of diuretics, nitroprusside, ACE inhibitors.
- Inotropes- Dobutamine- 2–5 micrograms/kg/ min, titrated up to 20 micrograms/kg/min- Inotrope and potential vasodilator; lowers blood pressure; give as individual agent as long as systolic blood pressure (SBP) ≥90. Can use with dopamine.

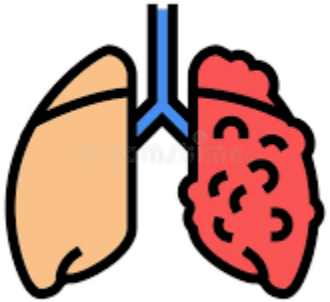
- Dopamine-3–5-micrograms/kg/ min, titrated up to 20micrograms/kg/ min as needed-Inotrope and vasoconstrictor; increases left ventricular end-diastolic pressure and causes tachycardia.
- Can be used with dobutamine.

- Norepinephrine-2 - 50 micrograms/min (0.02 – 2 micrograms/kg/minute) titrate to response-Vasoconstrictor and inotrope; preferred as a single agent over dobutamine if SBP <70.
- Can use combined with dobutamine.

STANDARD OF CARE FOR ARDS

- For mild ARDS, non invasive ventilation stands as the first-line approach.
- Patients who have a diminished level of consciousness, vomiting, upper GI bleed, or other conditions that increase aspiration risk are not candidates for NIPPV.





- Other relative contraindications include hemodynamic instability, agitation, and inability to obtain good mask fit
- Severe ARDS is often associated with refractory hypoxemia, and early identification and treatment of hypoxemia is mandatory.

- For mechanical ventilation specific settings are recommended: limitation of tidal volume (6 ml/kg predicted body weight), adequate high PEEP , a recruitment manoeuvre in special situations, and a 'balanced' respiratory rate (20-30/min)for appropriate baseline minute ventillation.
- Consider the use of incremental FiO2 /PEEP combinations to achieve oxygenation 2 goal (PaO2 55-80 mm Hg or SpO2 88-95 %)

CRITERIA FOR DISCHARGE AND FOLLOW UP

- Tested negative and totally symptom free can be discharged with observation at home for total of 21 days.
- Tested negative and continue to have fever and other symptoms need a repeat testing after two days to exclude NiV infection and there exist a strong history of contact with NiV infected patient/sample must have repeat testing in every two days till patient becomes symptom free.

- No need of repeat testing if tested negative on two occasions found negative and an alternate diagnosis is made.

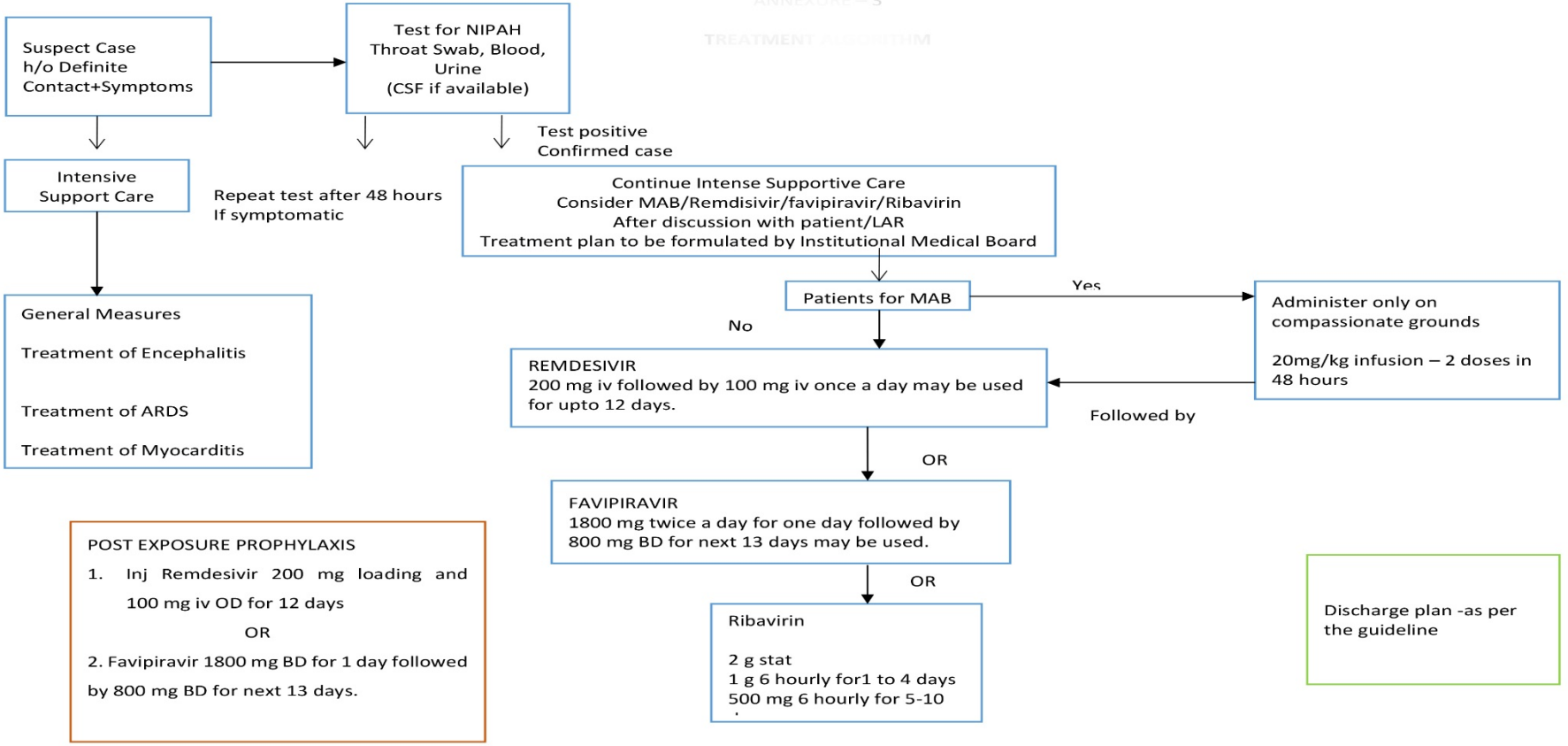
Criteria for discharge of confirmed case

- Clinically stable
- Nipah RT-PCR from all three samples (Throat swab, Urine and blood)reported negative on two occasions at least 5 days apart.
- To be decided by the treating clinician and confirmed by the Medical board

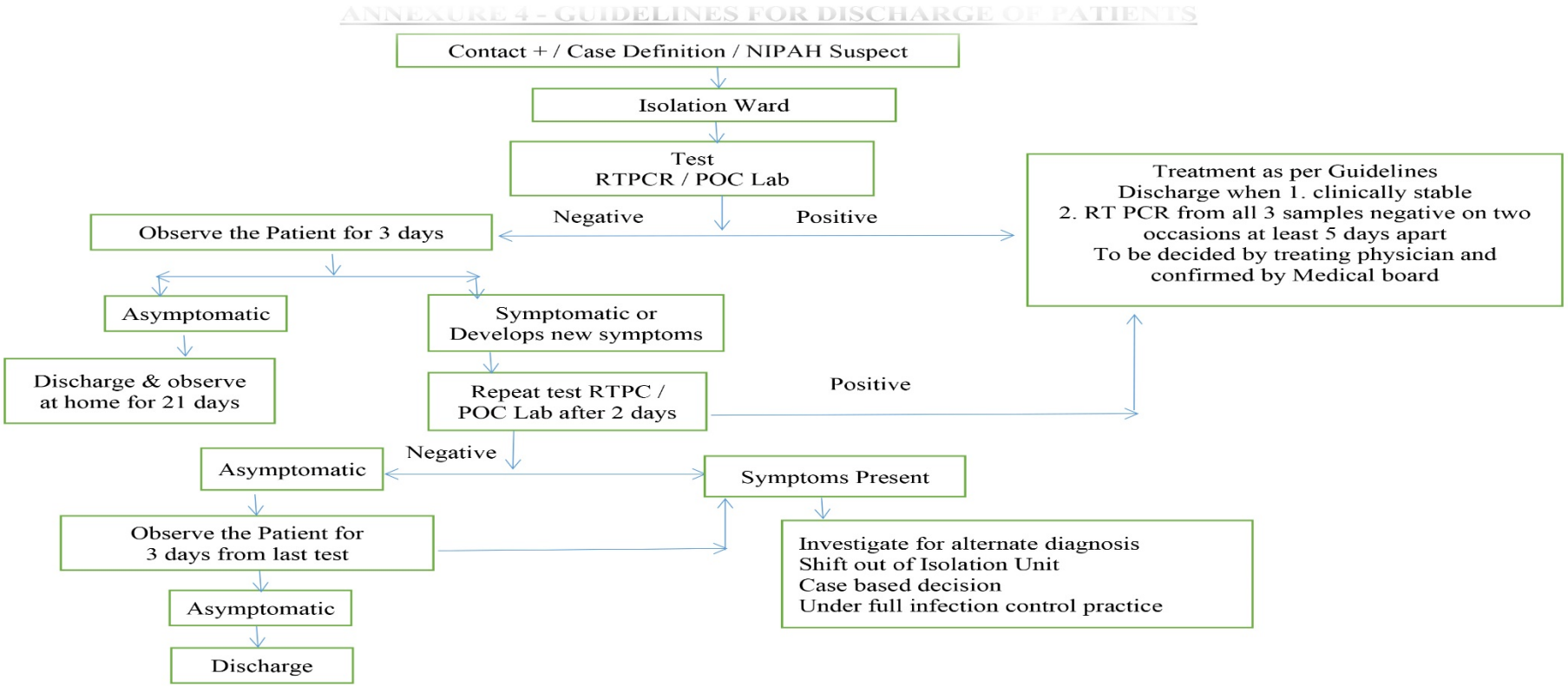
Follow up

- The discharged patient should remain in isolation at their residence for 4 weeks after the discharge.
- Patient is advised follow up on 28days, 56 days and 90 days of discharge
- All patients with confirmed NiV infection should be kept under long term follow up as there were reports of relapse and late onset encephalitis in an earlier series.

TREATMENT ALGORITHM

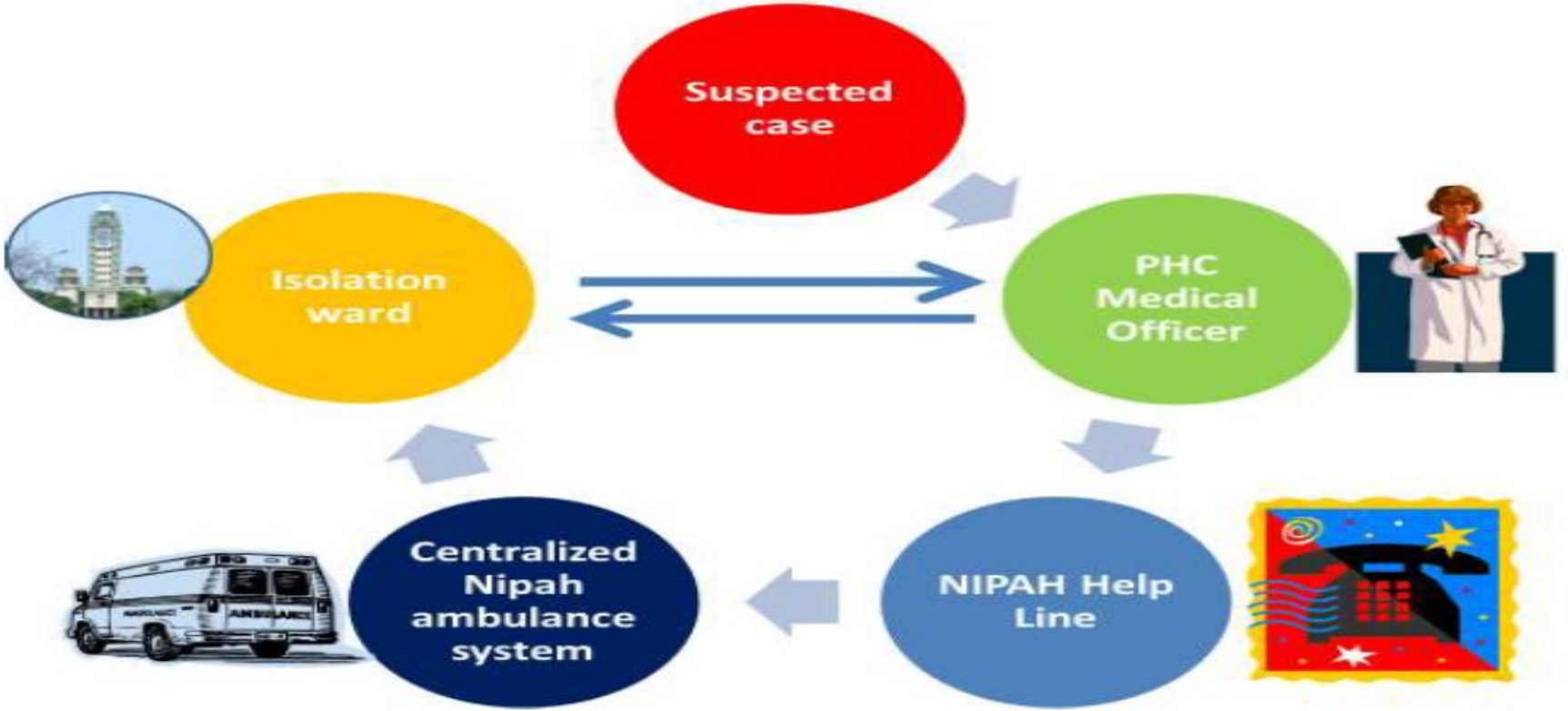


GUIDELINES FOR DISCHARGE OF PATIENTS



NB: Any amendment to this Guidelines be done only with the concurrence of Medical Board

PATIENT TRANSPORTATION



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