

PATHOLOGY & DIAGNOSIS OF NIPAH VIRUS ENCEPHALITIS



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NIPAH VIRUS ENCEPHALITIS

INTRODUCTION

- RNA virus :family *Paramyxoviridae* ,genus *Henipavirus*
- Occurred only in *South East Asia*
- Fruit bats of genus *Pteropus*-reservoir host of virus
- Important *emergent zoonotic* disease with CFR->60%
- Ist report-Unusual *encephalitis* in pig farm workers in *Malaysian state of Perak* in 1998

- 1999-identified as *Paramyxovirus* & related to Hendravirus (Chua et al. ,2000)
- Infection occur by spill over of virus from bats to domestic animals (Choo ,2001)
- Human being- neurological signs predominate
- Pigs- respiratory sign but many infection in pig-asymptomatic
- Dog & cat -infection pantropic with high case fatality rate (Choo et al.,2001)

ETIOLOGY

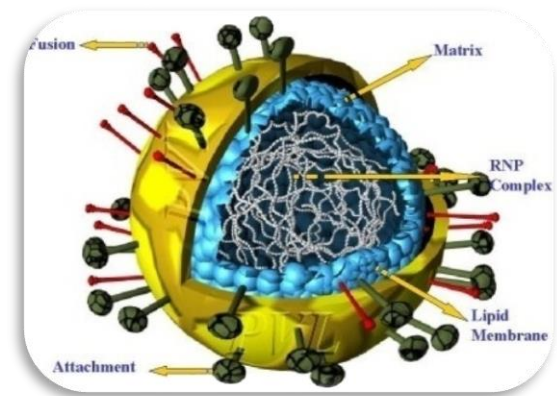
Nipah virus -

🦠 **Enveloped RNA** virus

Order - Mononegavirales

Family - *Paramyxoviridae*

Genus - *Henipa virus*



🦠 Name '**Nipah**', after the village where the first viral isolate was obtained (Sungai nipah)

HISTORY

■ 1998-1999, Malaysia

➤ Encephalitis in humans

★ More than 250 cases

★ More than 100 deaths

★ Respiratory and neurologic syndrome in swine

■ Virus isolated in March 1999

■ 1.1 million pigs culled (out of 2.4 million total)

■ No new cases in Malaysia since 1999

Cont...

- ⊕ 1999: Singapore
 - ⊕ Outbreak in abattoir workers
 - ⊕ Pigs imported from Malaysia



(Nor 2001)

- ⊕ 2001,2007- **India**
- ⊕ 2001-2012- 10 outbreaks in Bangladesh
- ⊕ Bangladesh -**consuming date palm sap** that had been contaminated by **infected fruit bats**

Project on 'Development of diagnostic and zoo epidemiology of Nipahvirus infection in India'

- **HSADL, Bhopal**

Objective of the project

- To develop the diagnostic tests for detection of NiV infection.
- To evaluate the status of the infection in pigs, *Pteroid* bats, other domesticated animals and human beings in India.
- To enhance the understanding of zoo-epidemiology of NiV infection

Epidemiology

Hosts

- Primary reservoir -fruit bats of the genus *Pteropus*
- Domestic swine - amplifying host
- Infections reported in dogs, cats, horses

TRANSMISSION



Source of infection

- **Urine and uterine fluids of wild pteropid bats**

Experimentally isolated from urine, kidney and uterus of infected bats

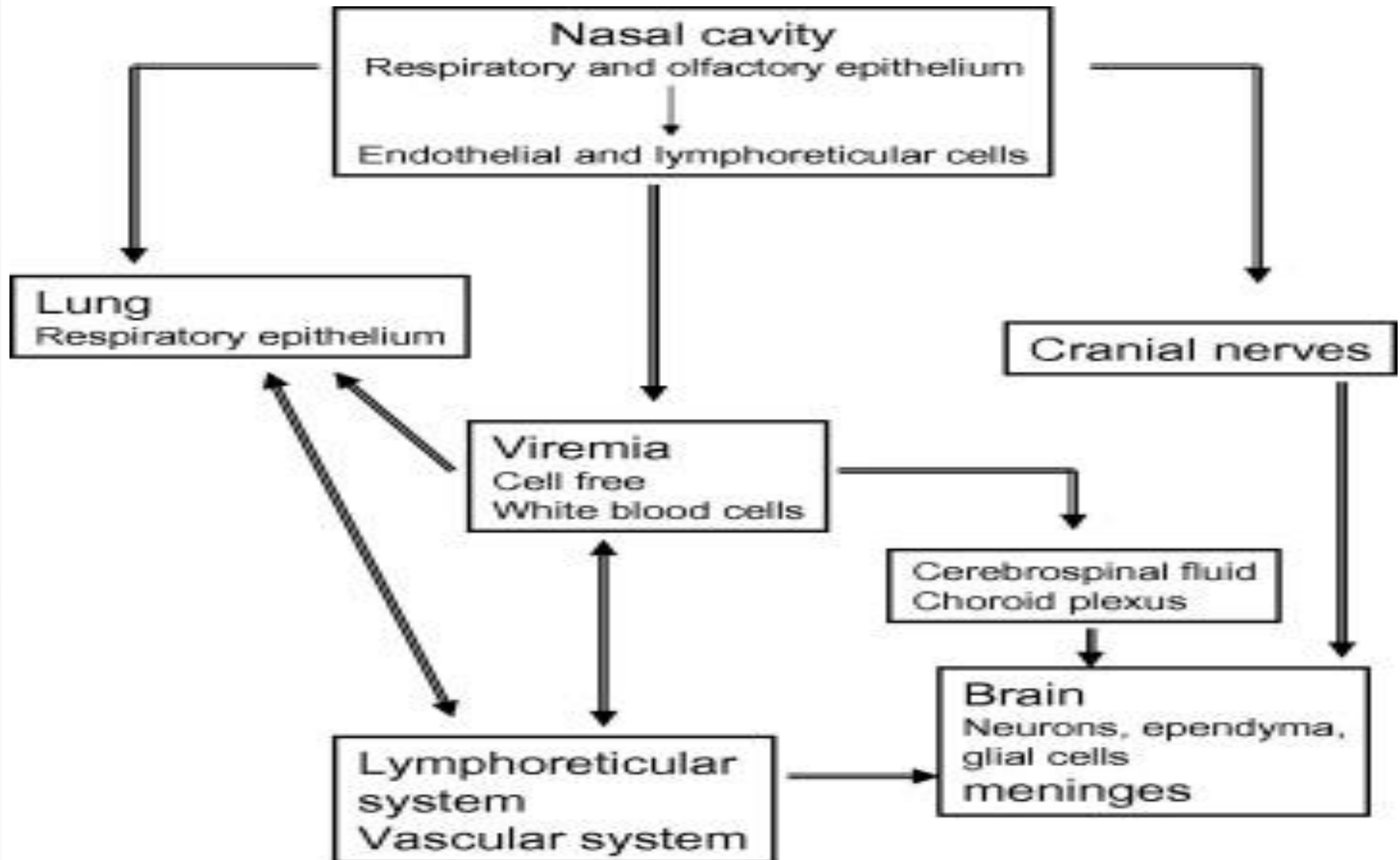
- **Fruit contaminated with bat saliva or urine**

- **Contaminated drinking water and access to aborted bat foetuses or other fluids/tissues of parturition**

- **Increasing overlap between bat habitats and piggeries**

- **Respiratory secretions and saliva ,urine of infected swine**

PATHOGENESIS



SYMPTOMS

- **Suckling pigs and piglets (< 1 month old)**
coughing, open-mouth breathing, abnormal posturing
convulsions
Mortality in piglets can be high (40%)
- **Young swine (1 to 6 months old)**
Respiratory signs
Loud nonproductive cough ("barking pig syndrome" and "one-mile cough")

(Bunning *et al.*, 2000; Daniel *et al.*, 2001)
- **Adult-** Respiratory signs ,nervous signs & abortion
Some of affected pigs may be asymptomatic

HUMANS

- @ Fever, Migraine, Vomiting, Emphysema, Myalgia
- @ Encephalitis (may relapse after recovery)
- @ Meningitis
- @ Disorientation
- @ Neurologic deficits (may persist after recovery)
- @ Coma
- @ Death

- Case-fatality rate: 40-60%

LESIONS

- No pathognomonic pathology in RT-co infections common

(Goh *et al.*, 2000; Harcourt *et al.*, 2000)

- Lungs and/or central nervous system

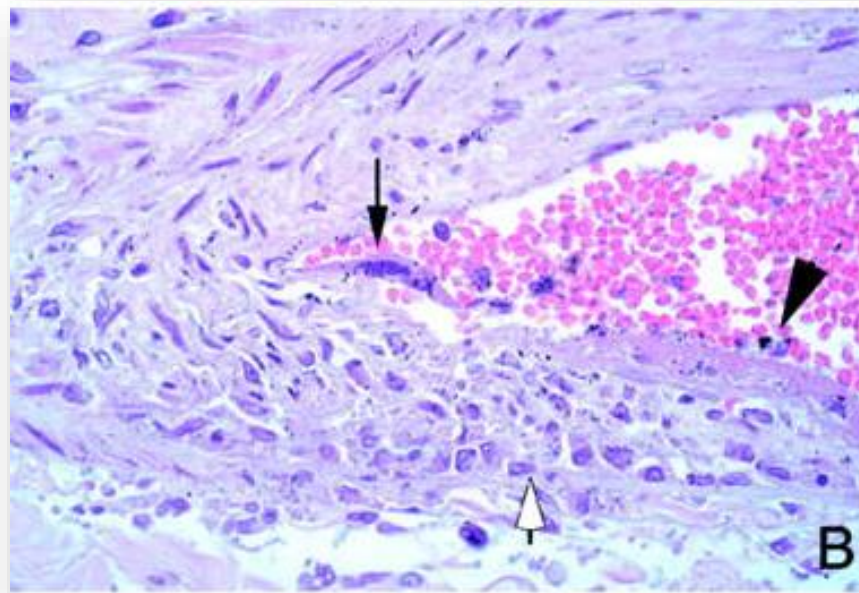
CNS : Meningeal oedema with congestion of the cerebral blood vessels

- Lung lesions -mild to severe pulmonary consolidation with petechial or ecchymotic haemorrhages and distended interlobular septa
- Trachea and bronchi -frothy exudate which varies in appearance from clear to blood-tinged

(Daniel *et al.*, 2001)

MICROSCOPIC LESIONS

- ✗ **Pneumonia** with involvement of alveolar, bronchiolar, bronchial & tracheal epithelium
- ✗ **Syncytial cell**-respiratory epithelium, endothelium
- ✗ Antigen are readily detected by IHC in syncytia & epithelium of respiratory tract
- ✗ **Mononuclear vasculitis** with **fibrinoid necrosis** is often observed associated with **thrombosis**



MICROSCOPIC LESIONS

- ✗ **Alveolar macrophages**-prominent, infiltration of **neutrophil**
- ✗ Small no of pig -CNS manifestations
non suppurative meningitis
- ✗ Principal histologic changes in the brain, if present, are **perivascular cuffing and gliosis**
- Virus demonstrated in meninges

(Harcourt et al., 2000)

DIFFERENTIAL DIAGNOSIS

- Any respiratory or neurological conditions of swine in an area known to have pteropid bats, should consider Nipah as a rule out
- Also among swine;
 - deaths of suckling pigs and piglets
 - sudden death in boars ,sows
 - abortions and other reproductive dysfunction
- Respiratory diseases with harsh, non-productive coughing
- Cases with encephalitic manifestations of trembling, muscular incoordination and myoclonus leading to lateral recumbency

DIAGNOSIS

SEROLOGICAL TEST

ELISA-safe & quick

SNT - accepted reference serological test



IMMUNOHISTOCHEMISTRY (lung, kidney, spleen, heart)

- Initial test, formalin fixed tissue
- Viral antigen can be detected in **endothelium, cellular debris in lumen of URT** (Hooper et al., 2001)
- Also in porcine **meninges, lung, trachea, kidney**
- Pregnant animal - **uterus, placenta, foetal tissue** (Daniel et al., 2001)
- Not having perfect sensitivity & specificity

VIRUS ISOLATION (kidney, liver, spleen, tonsil, cerebrospinal fluid)

- ✗ Virus grow well in green monkey kidney (Vero) and rabbit kidney (RK-13) cell. CPE with in 2-3 days
- ✗ Large syncytia formation ,nuclei in periphery

(Daniel *et al.*, 2000)

Confirmation of isolate by

Immunofluorescence

Immunoperoxidase staining

Definitive diagnosis -VNT

- ✗ Plaque reduction
- ✗ Microtitre neutralisation
- ✗ Immune plaque assay

ELECTON MICROSCOPY- culture or in lesions

- Paramyxo viridae

- Nucleocapsid & membranes of virus (Hooper *et al.*, 2000)

PCR-diagnostic tool (Choo *et al.*, 2001)

- ◆ SNT, ELISA, RT-PCR

are used for laboratory confirmation

- ◆ Nipah virus is classified internationally as a biosecurity level (BSL) 4 agent

CONTROL

- Management of pig farm -important
- Countries with pteropid bats acting as reservoir ,pig farms should be devoid of fruit trees & other vegetation that attracts bats
- Strict biosecurity to preclude introduction of infected animals
- If introduction necessary-strict quarantine



Thank you . . .