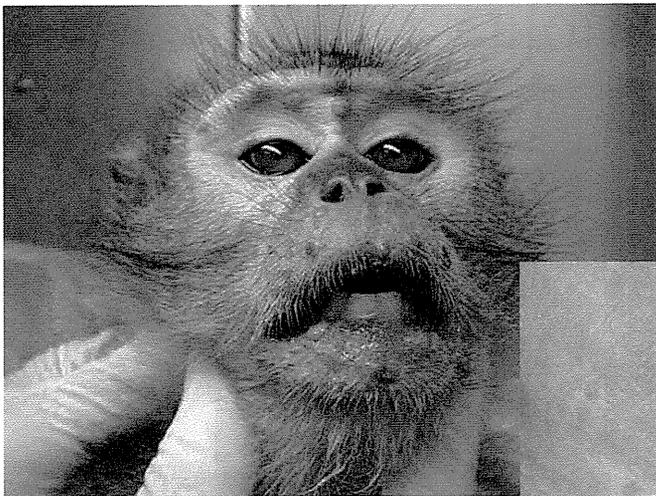


Monkeypox in human

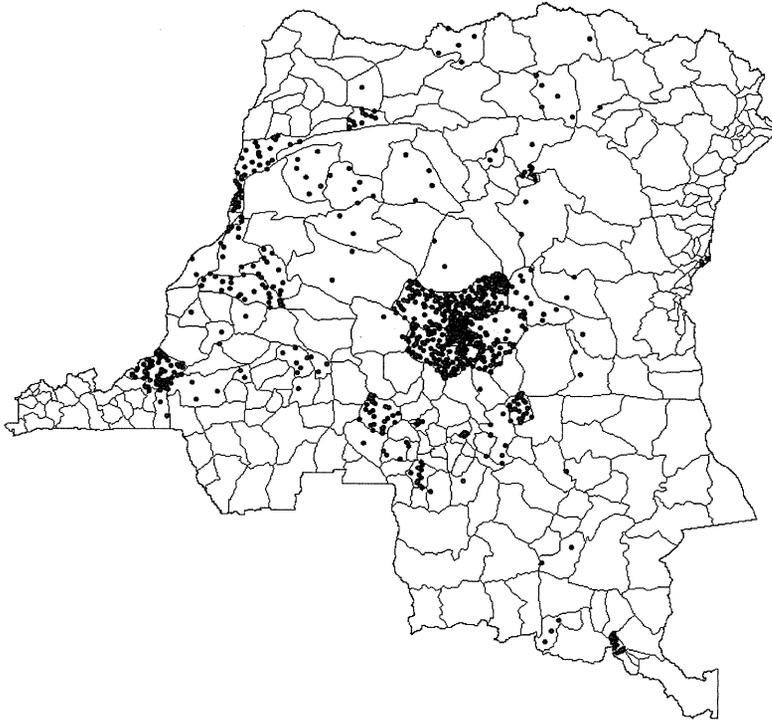


with the permission of Prof Muyembe-Tamfum, Director of the National Institute for Biomedical Research-INRB- DR Congo

Monkeypox



**DISTRIBUTION OF SUSPECTED CASES OF HUMAN
MONKEYPOX IN DRC (1998-Jan2006).**



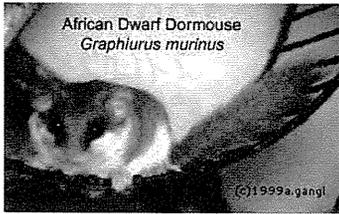
**Outbreak of Human Monkeypox
in the USA in 2003**

Route of monkeypox virus-introduction to the USA (2003)



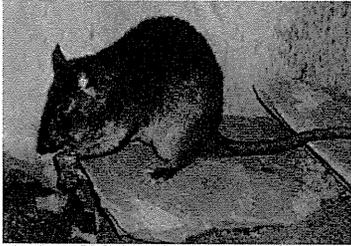
Patients with monkeypox virus infection

- As of 1 July 2003, 81 patients with human monkeypox have been reported. 32 of the 81 were virologically diagnosed as having human monkeypox.
- Wisconsin (39), Indiana (22), Illinois (16), Missouri (2), Kansas (1), Ohio (1)
- One child showed symptoms of encephalitis.
- No human-to-human transmission has been documented.

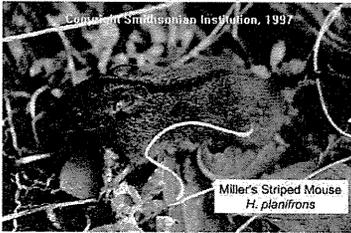


courtesy rodentfancy.org

Gambian giant-pouched rat (*C. gambianus*)



courtesy Utah Hogle Zoo

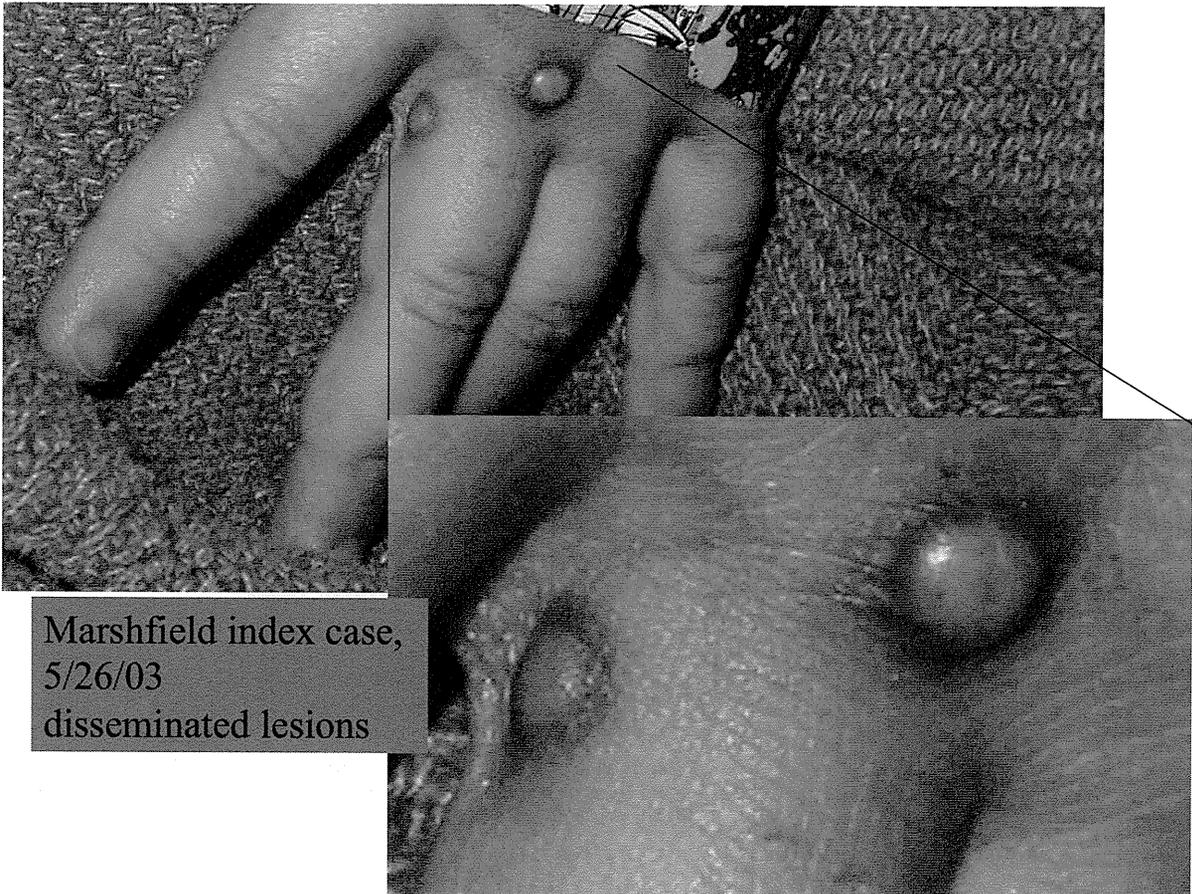


courtesy www.mnh.si.edu
photographer: Mike Carleton



Human

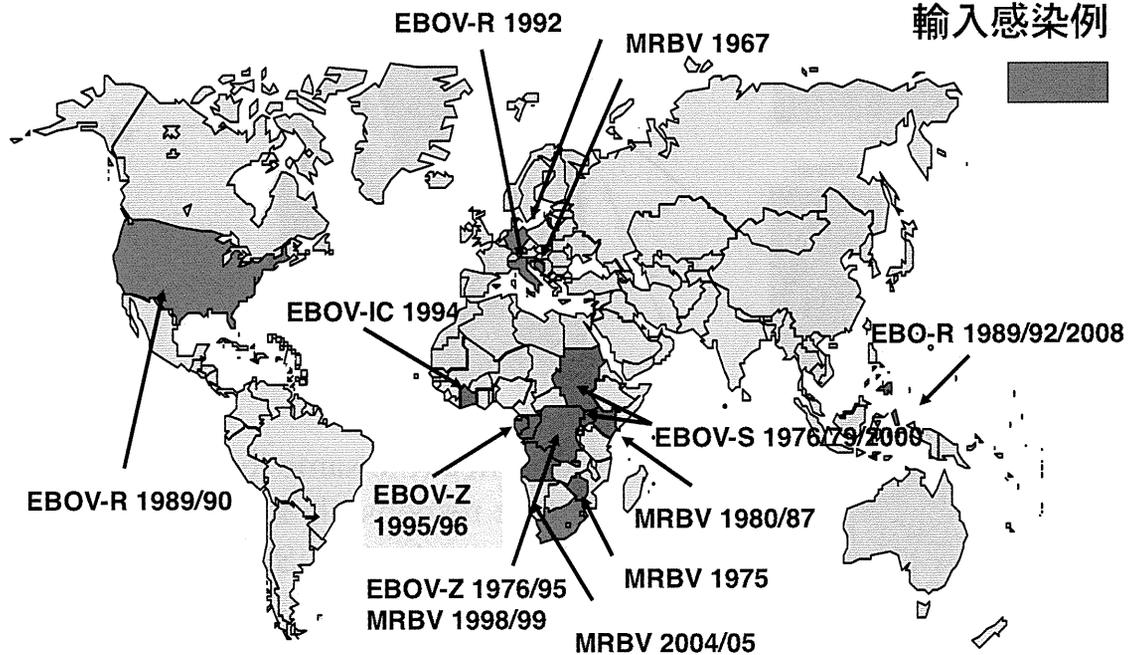
18 dormice (the same lot of dormice responsible for human monkeypox in the USA) have also been imported from Ghana through Texas to Japan.



Marshfield index case,
5/26/03
disseminated lesions

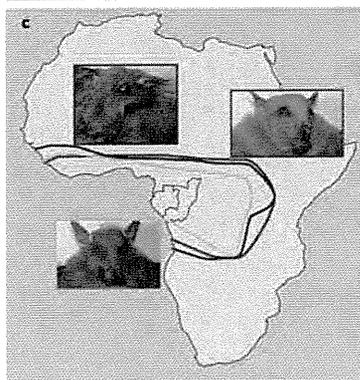
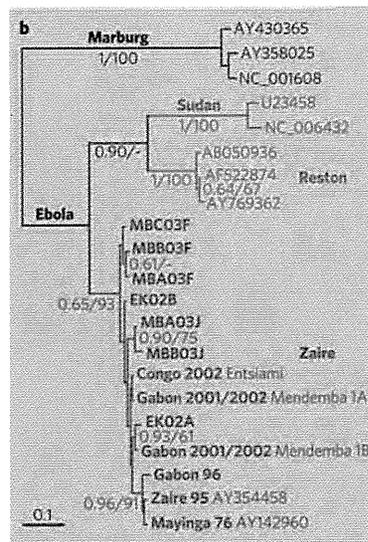
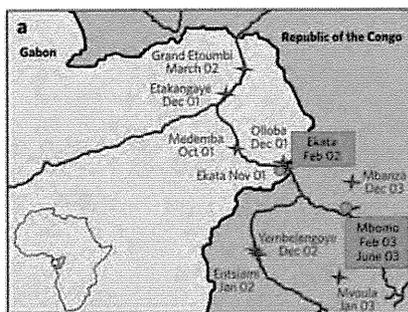
Ebola outbreak in Kikwit, DRC, 1995

フィロウイルス
輸入感染例



エボラウイルスの宿主はオオコウモリ

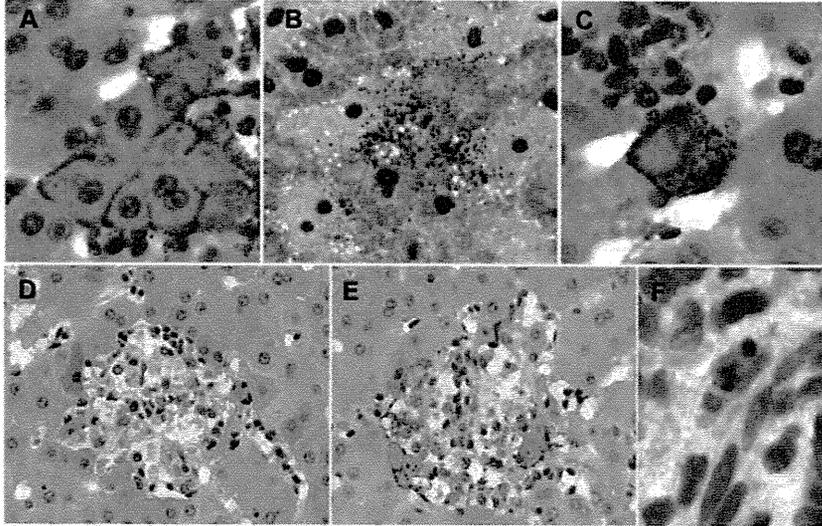
-EBOV genome was amplified from tissue samples of fruit bats



Geographic distribution (inside coloured lines) of the fruit bats *Hypsignathus monstrosus* (blue), *Epomops franqueti* (red) and *Myonycteris torquata* (yellow)

Ref: Nature 438, 575-576 (2005)

オオコウモリからマールブルグウイルスが分離される -Isolation of Genetically Diverse Marburg Viruses from Egyptian Fruit Bats-



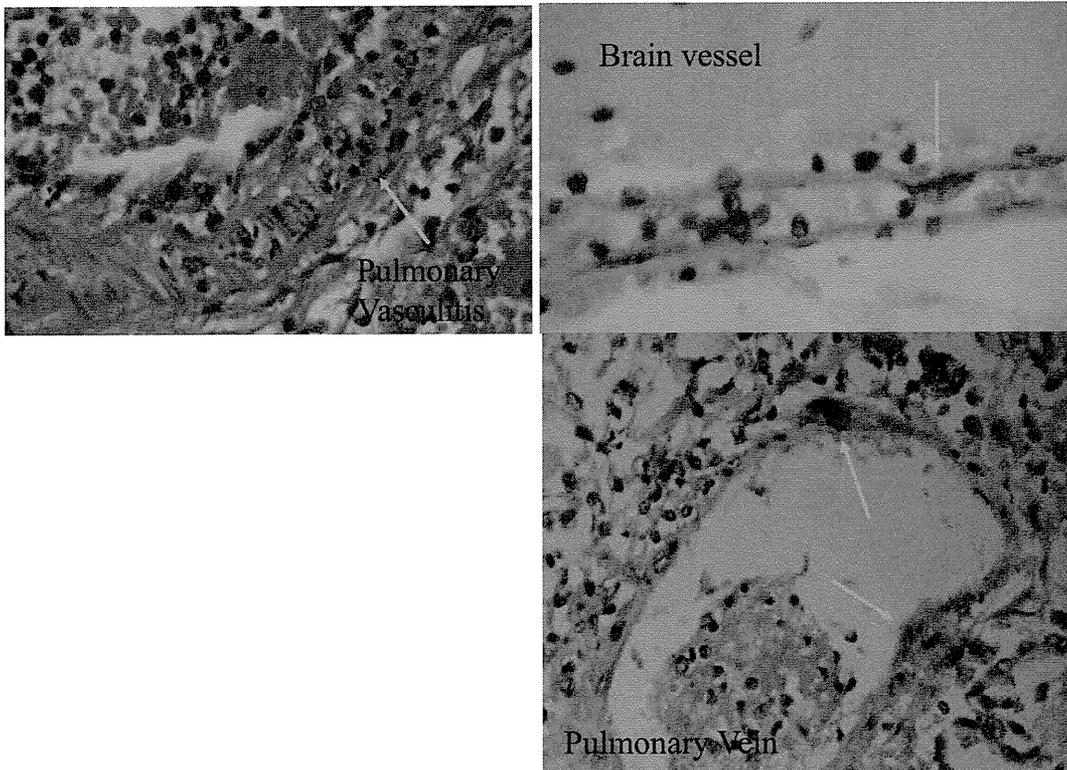
In the liver, viral antigens were distributed in and around hepatocytes in a dense (A) or loose (B) perimembranous pattern. Rarely, entire hepatocytes were involved (C). These infected foci were characteristically sparse and were often associated with small collections of mononuclear inflammatory cells and hepatocyte necrosis (D and E), although infected cells could also be identified without conspicuous inflammatory infiltrates. Only rare viral antigens were seen in a few mononuclear cells of the spleen of 1 bat (F). Immunoalkaline phosphatase with naphthol fast-red and hematoxylin counterstain (A–C, E, F), and hematoxylin and eosin (D); original magnifications $\times 100$ (A, B, D, E) and $\times 258$ (C, F).

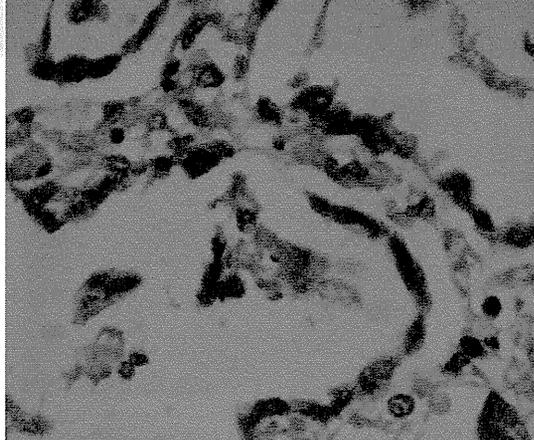
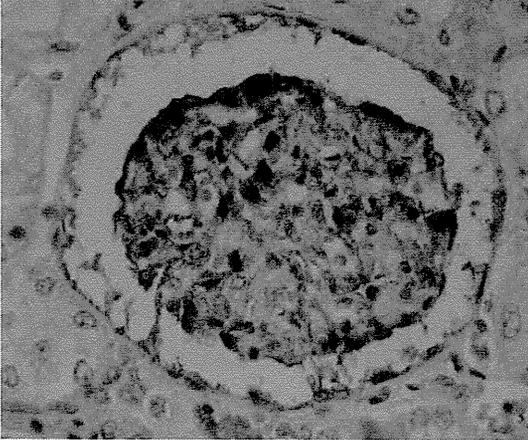
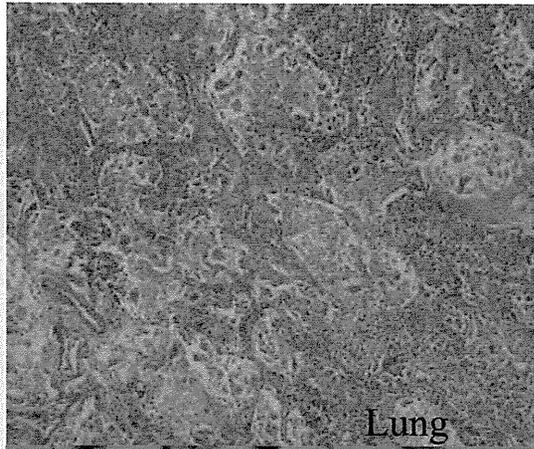
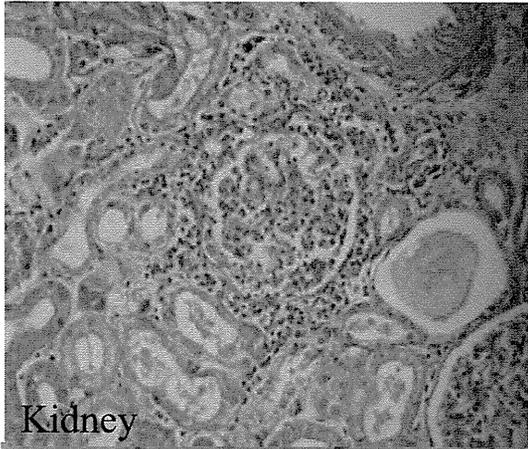
Hendra virus infections

Human Hendra Virus Infection

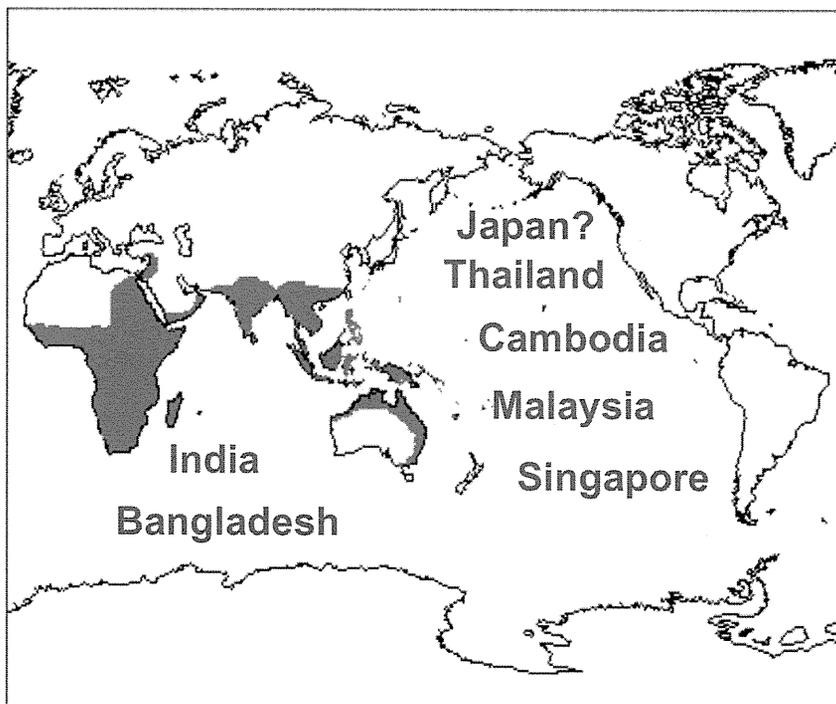
- **Four human cases so far, two fatalities**
- **Case 1**
 - **49-year-old male, horse trainer**
 - **Severe, acute pulmonary symptoms requiring ventilation; no apparent clinical encephalitis**
 - **Died after 1 week of admission**
- **Case 2**
 - **35 year old male farmer**
 - **12 day history of aseptic meningitis, headache, drowsiness, vomiting; recovered**
 - **13 months later died after admission for fever, seizures, reduced consciousness**

Case 2: Acute Hendra Infection with encephalitis





Distribution of Fruit Bats in Asia

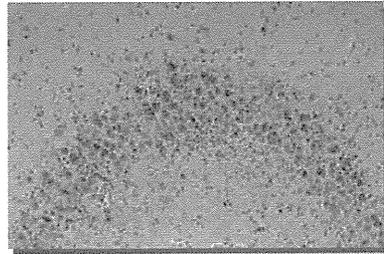


Encephalitis caused by Hendra virus



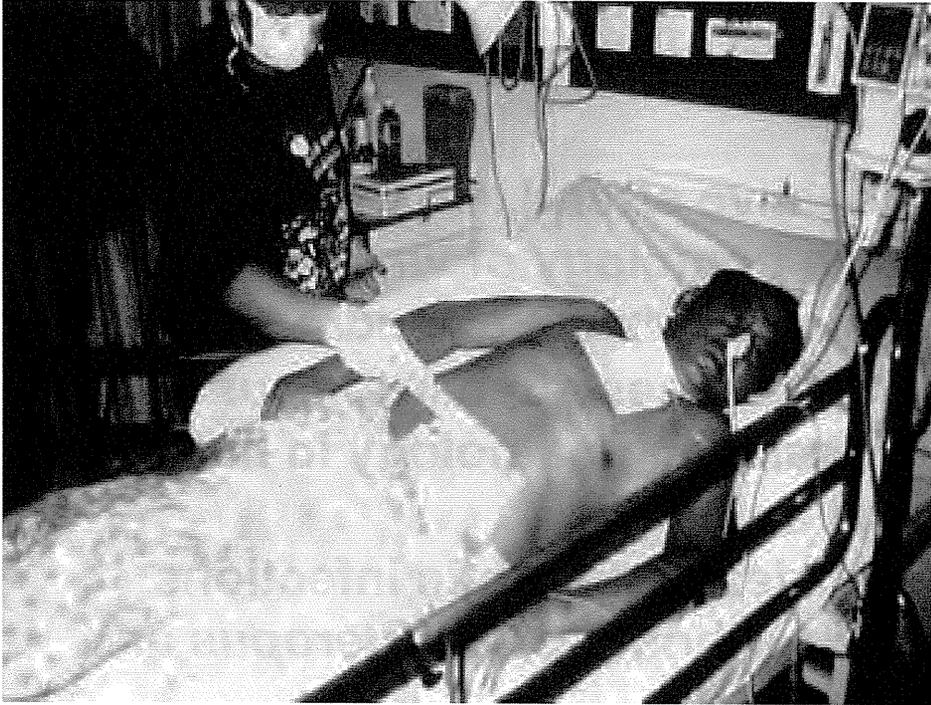
Family Paramyxoviridae
Genus Morbirvirus

Reservoir: Fruits bat (J
Gen Virol. 81:1927-32,
2000)

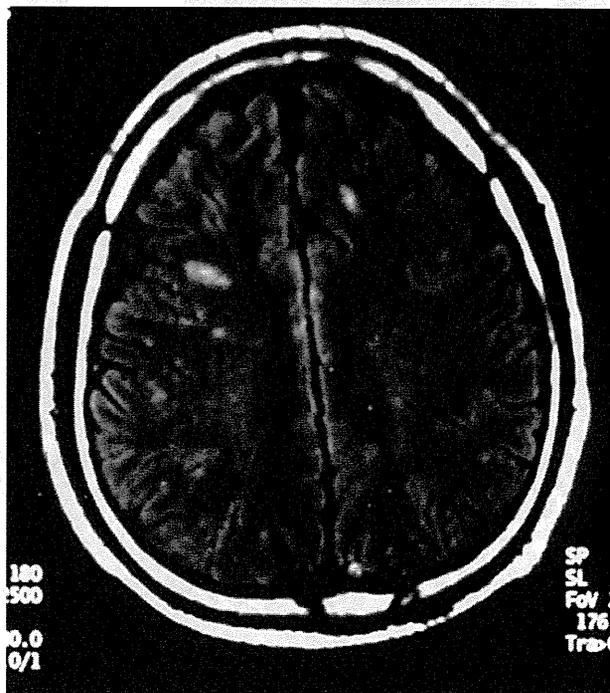


Nipah encephalitis

Malaysia
Singapore
Bangladesh
India



Acute Nipah Encephalitis



Brain MRI
Courtesy of Prof C T Tan

Nipah Virus

- **Negative strand, RNA virus**
- **High homology of viral genome and amino acids with Hendra virus**
- **Both viruses appear to cause similar disease and pathology in humans and animals**
- **Accidental zoonotic infections**
- **Animal host : Bats (*Pteropus* and other sp.)**



Courtesy: Dr KB Chua

Nipah Virus Outbreaks

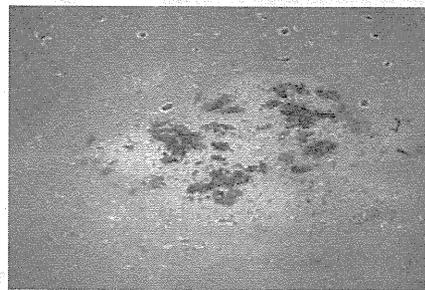
- 1998 - 1999
 - Malaysia, Singapore
 - > 350 cases; mortality 30-40%
- 2001, 2003, 2004, 2008
 - Bangladesh
 - > 60 cases; > 70% mortality
- 2001, 2007 (?)
 - India
 - > 60 cases; ~ 70% mortality

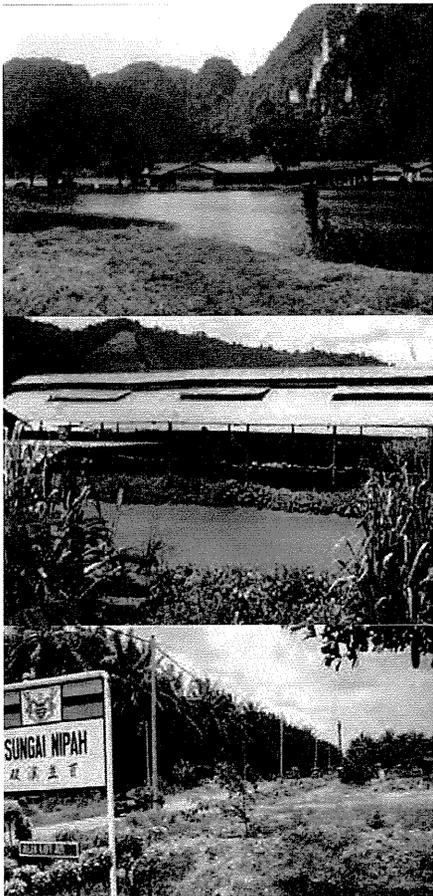
Refs:

1. Chadha, et al. Nipah Virus-associated Encephalitis Outbreak, Siliguri, India Emerg Inf Dis 2006; 12: 235-40
2. Harit, et al. Nipah/Hendra virus outbreak in Siliguri, West Bengal, India in 2001. Indian J Med Res 2006; 123: 553-60
3. Hsu, et al. Nipah Virus Encephalitis Reemergence, Bangladesh. Emerg Inf Dis 2004; 10: 2082-2087
4. Anonymous. ICDDR, B Health Sci Bull 2004; 2: 5-9

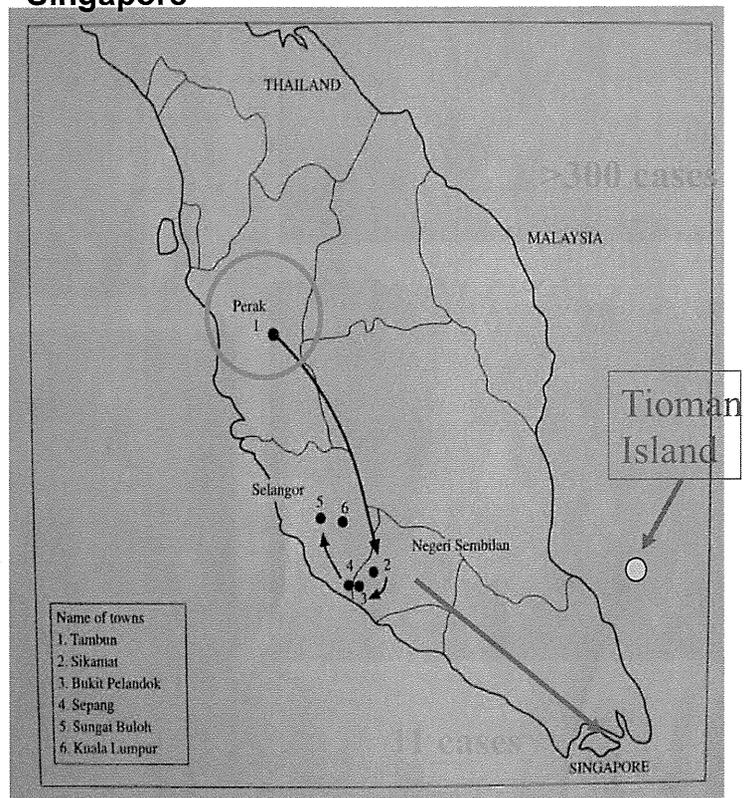


Nipah virus, Malaysia, 1999





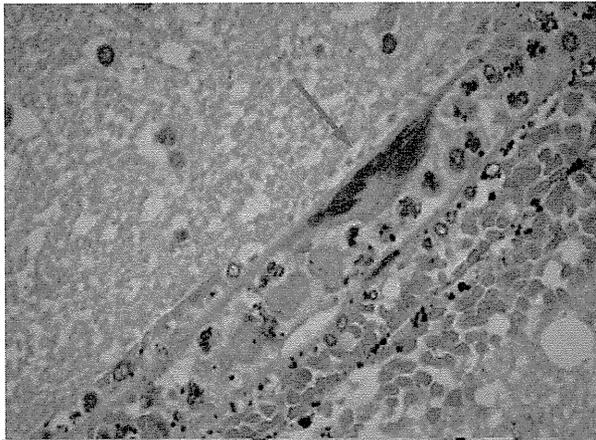
Nipah Virus Outbreaks in Malaysia and Singapore



Nipah Virus Infection: Clinical Manifestations

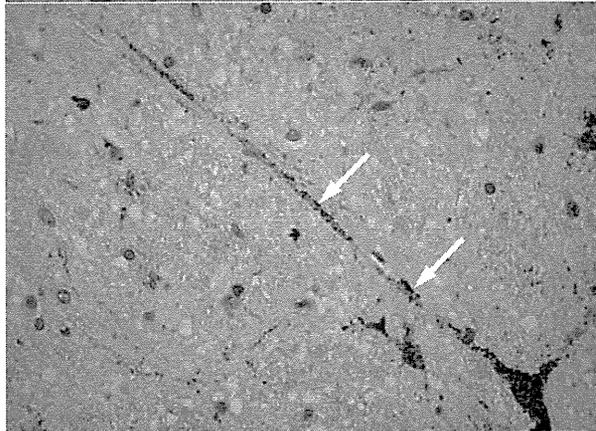
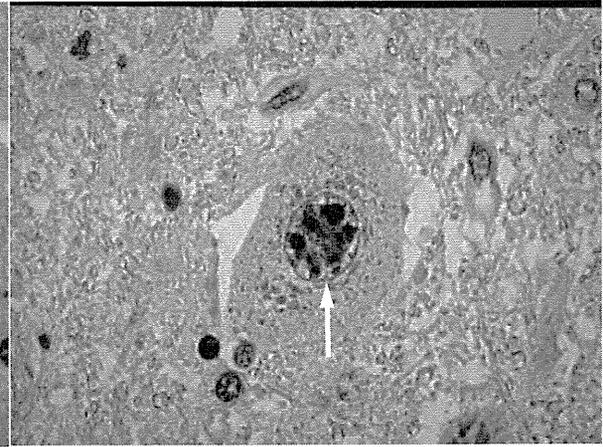
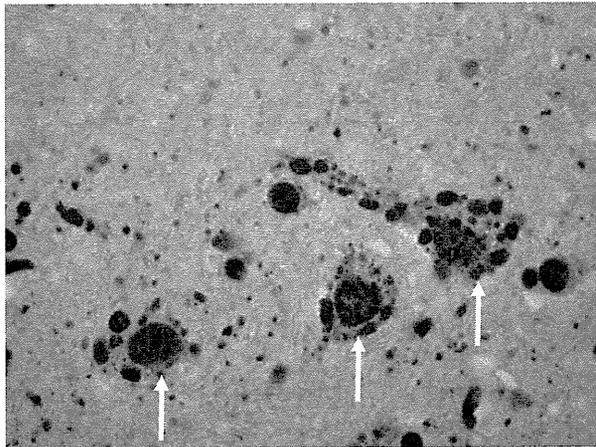
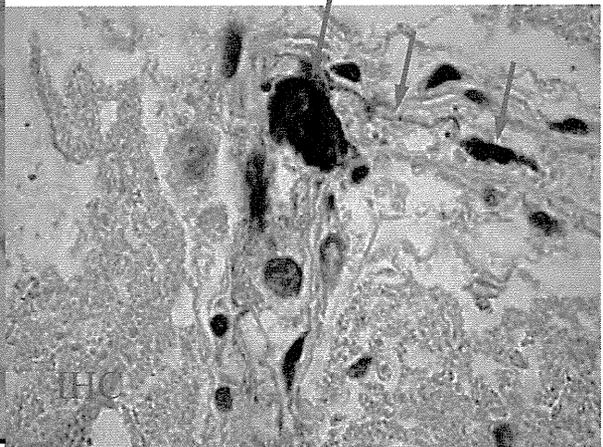
| | |
|-------------------------|-----|
| • Symptoms | % |
| • Fever | 100 |
| • Drowsiness | 88 |
| • Headache | 82 |
| • Confusion | 76 |
| • Cough | 28 |
| • Signs | |
| • Altered consciousness | 89 |
| • Segmental myoclonus | 50 |
| • Areflexia | 50 |
| • Seizure | 40 |
| • Cranial nerve palsy | 29 |

Acute Nipah infection is a multi-organ, systemic infection, affecting the CNS (most involved), lung, kidney, spleen, heart, lymph node etc.

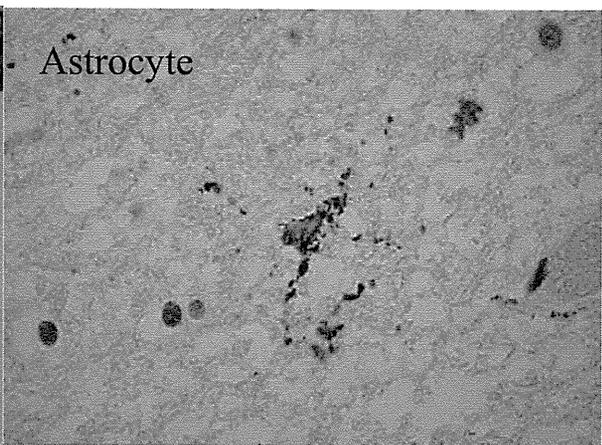
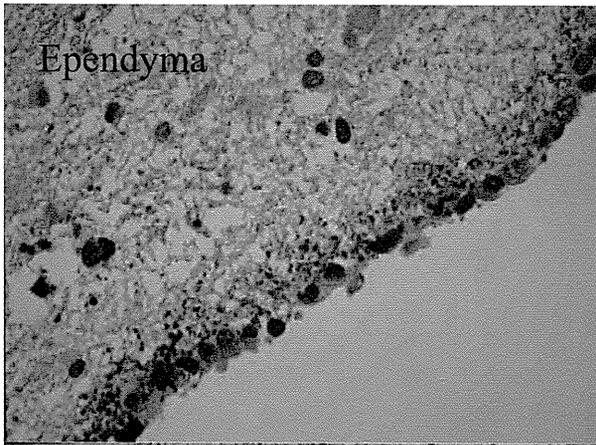


Endothelial infection by Nipah virus

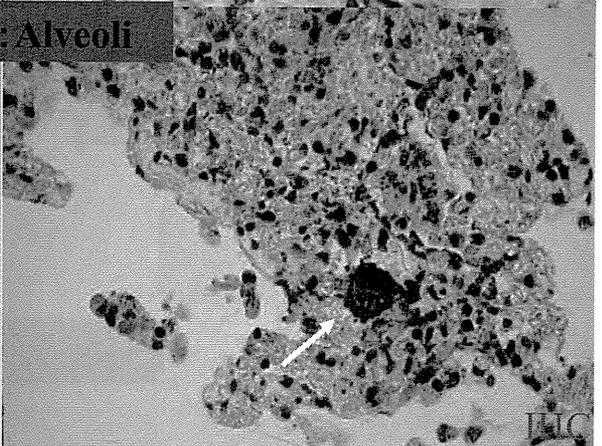
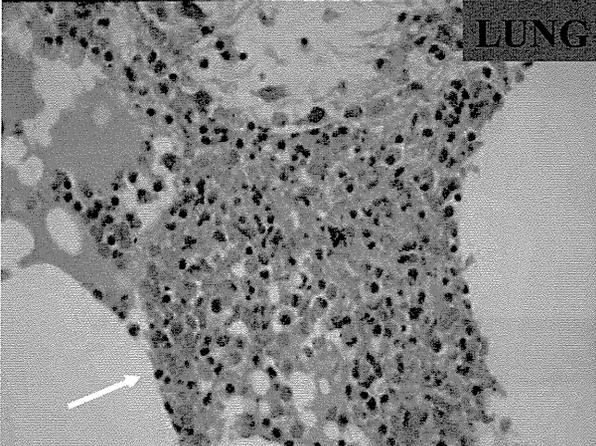
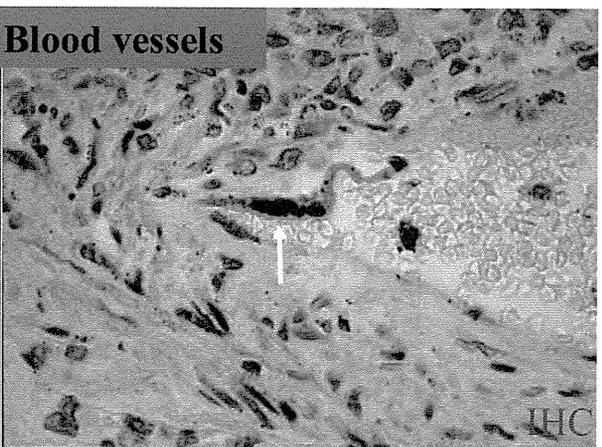
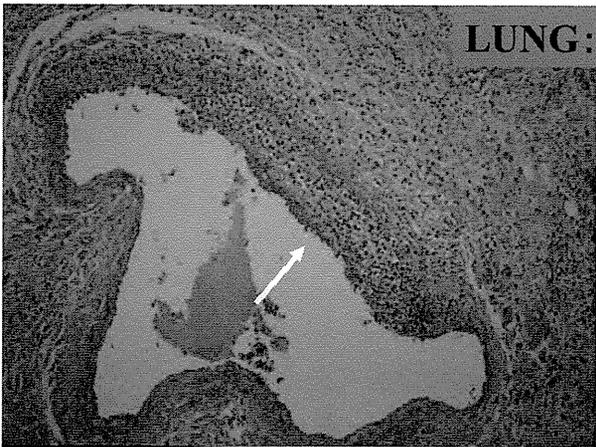
- Multinucleated syncytia or giant cell arising from endothelium
- Viral antigens in endothelium

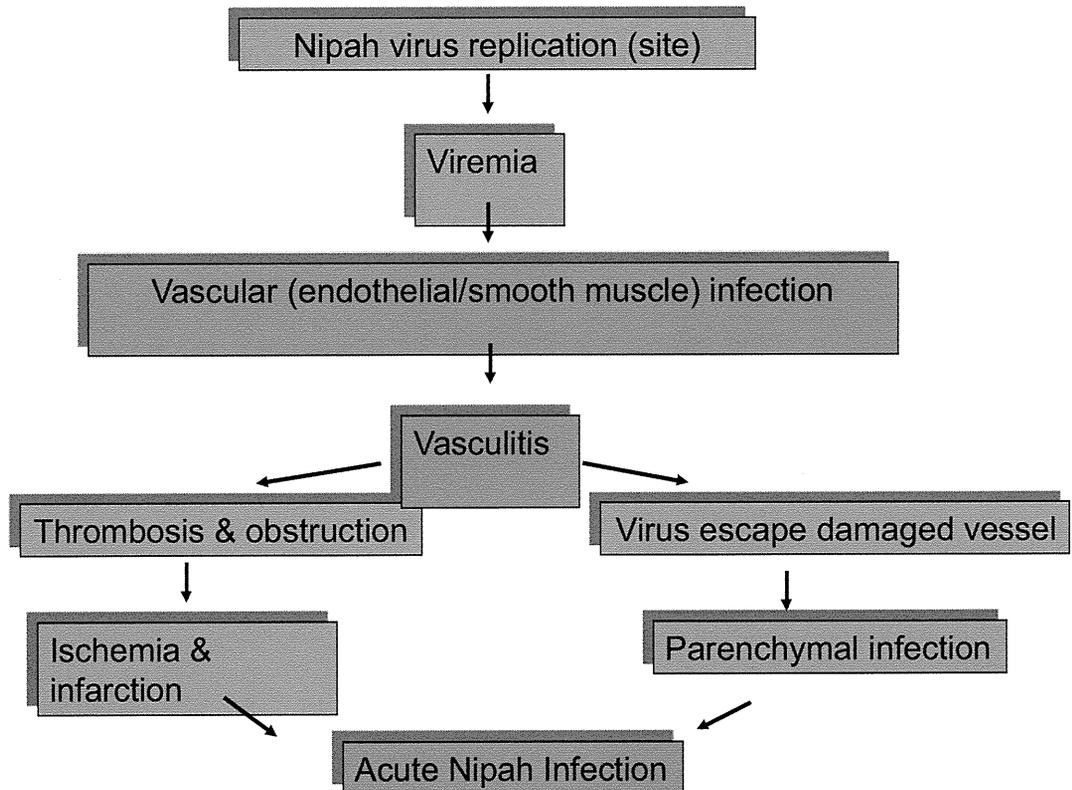
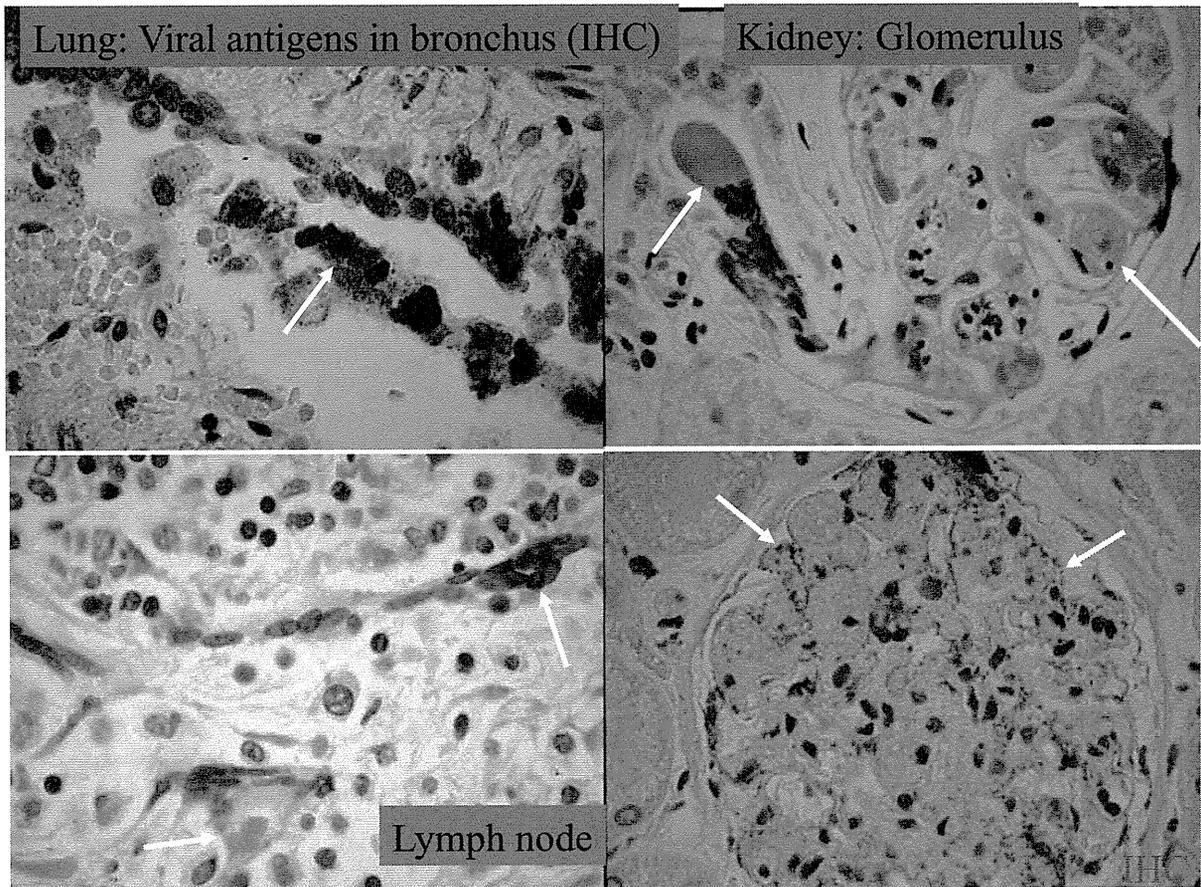


Viral antigens in neuronal cytoplasm, nuclei and processes

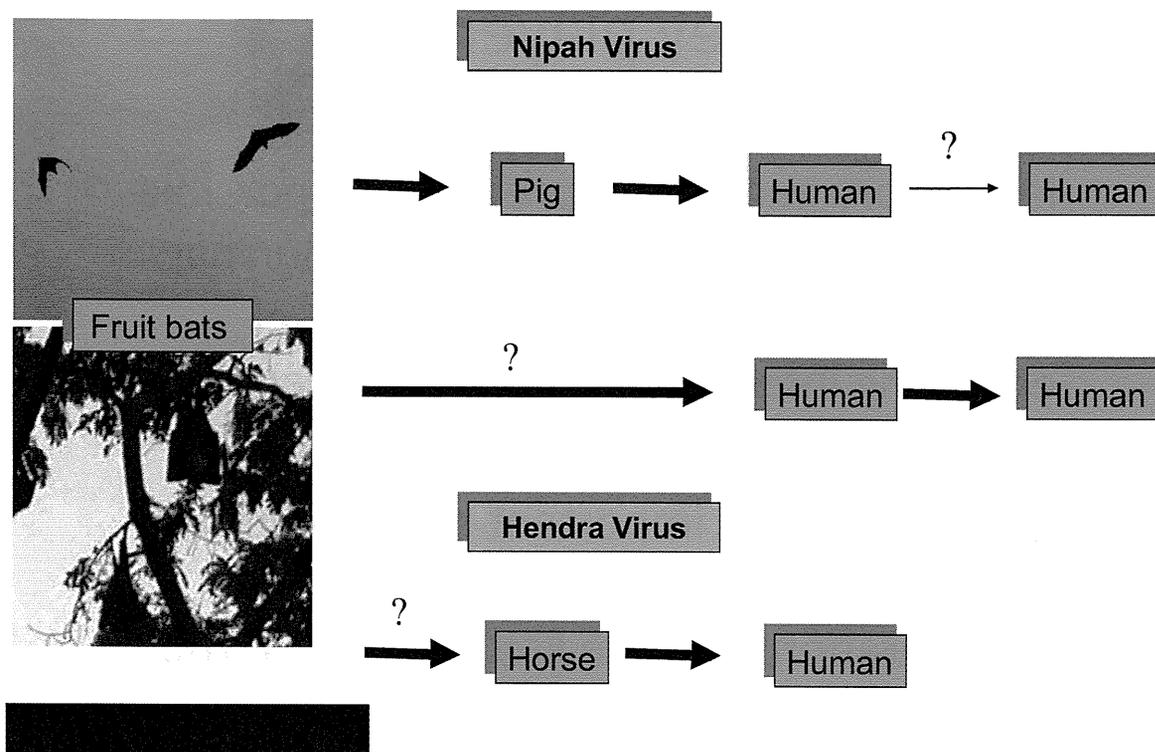


Infection of glial cells was rare





Probable Modes of Henipavirus Transmission



Evidence for Human to Human Transmission

- A nurse who had taken care of Nipah patients, seroconverted but remained asymptomatic; Brain MRI showed a few small discrete lesions
✓ (Tan KS et al, Neurol J South East Asia 2000; 5: 69-73)
- Virus could be isolated from patients' respiratory secretions and urine
✓ (Chua et al, J Infect 2001; 42: 40-2)
- Relatives in close contact with patients developed infection; no health care worker involved
✓ (Hsu et al, Emerg Infect Dis 2004; 20: 2082-7)
- Health care workers caring for patients developed infection (> 40 people)
✓ (Harit et al, Indian J Med Res 2006; 123: 553-60)

Future challenges

-key player-

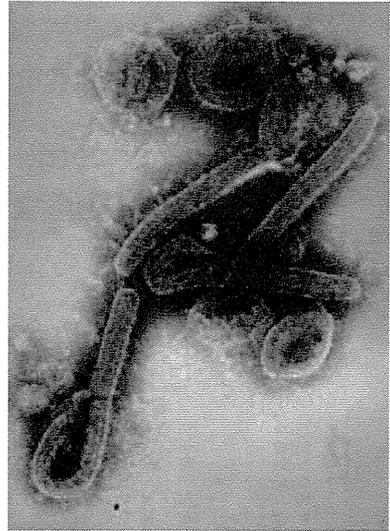
- Need to operate the facility as BSL-4 laboratory in order to prepare the possible outbreak of highly pathogenic hemorrhagic fever virus infections and other novel emerging infections not only in Japan, but also in the other part of the world.
 - Need to play an important role to combat the highly pathogenic infections in collaboration with the key partners in the world.
-

International framework for improvement of global diagnostic capacity

- Global health security action group-laboratory network: G7 + Mexico
- Emerging dangerous pathogens laboratory network: WHO and key institutes
 - AFRO
 - SEARO

family *filoviridae*

- genus ebolavirus
 - Zaire ebolavirus
 - Sudan ebolavirus
 - Cote d'Ivoire ebolavirus
 - Bundibugyo ebolavirus
 - Reston ebolavirus
- genus marburgvirus
 - Lake Victoria marburgvirus



Filovirus TaqMan PCR